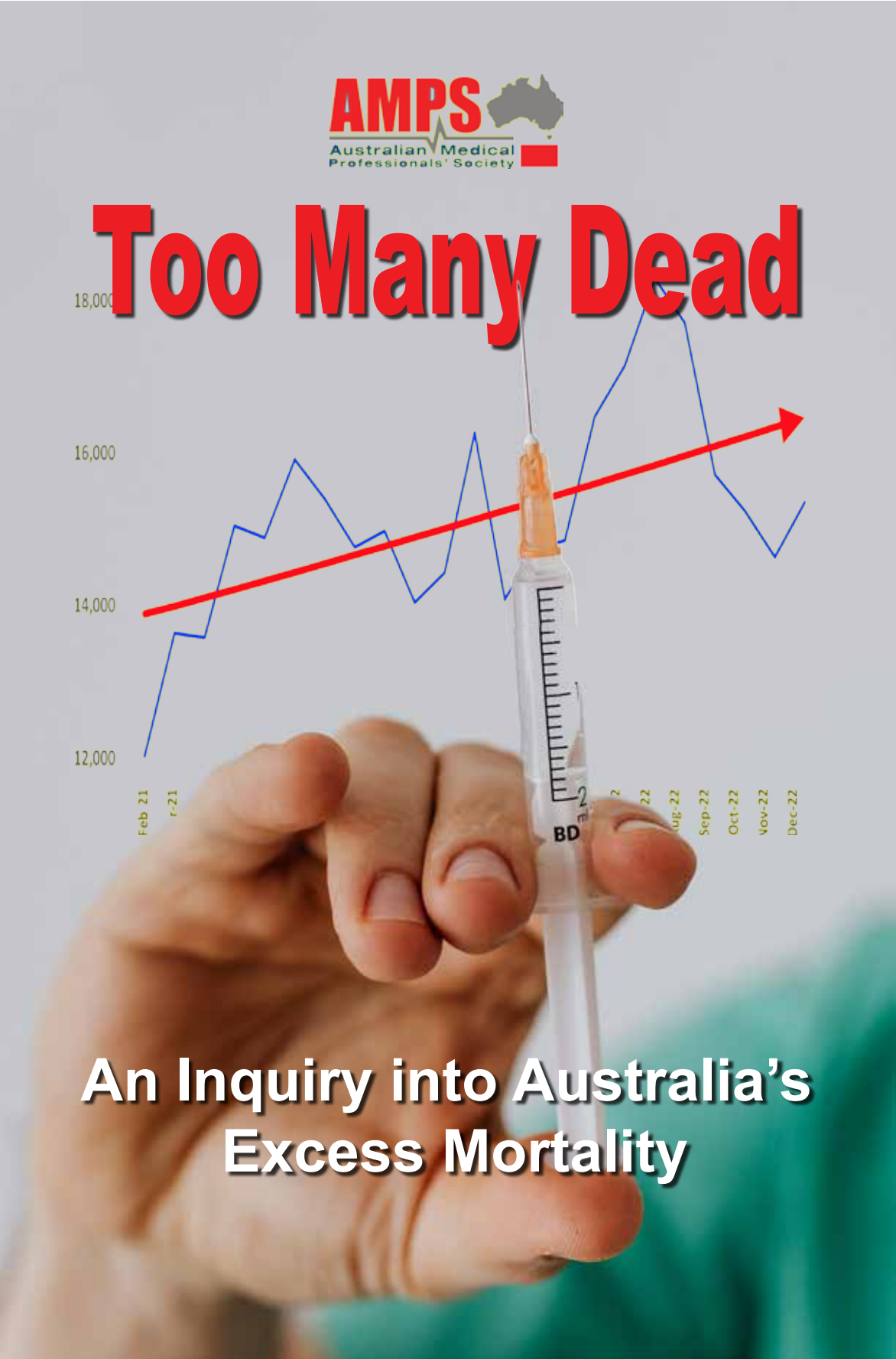
AMPS
Australian Medical Professionals' Society

Too Many Dead



An Inquiry into Australia's Excess Mortality

Ethical doctors and scientists investigate what is killing so many Australians

Australians are dying at disturbing rates, beginning in 2021. Political and medical authorities continue to ignore this. The Australian Senate voted against holding an inquiry into this excess mortality, but independent, committed Australian medical people have conducted an investigation. This book shows that even the inadequate pharmacovigilance systems of global regulators reveal alarming numbers of adverse events, disability and death.

Australia is in the midst of a health crisis, and this analysis indicates it is iatrogenic. Too many people are dead and harmed. Australians deserve accountability, transparency and justice.

ISBN 978-0-646-88551-3

Too Many Dead

This book is dedicated to all Australians
who have been harmed by the government's
public health response to COVID-19.

Too Many Dead – An Inquiry into Australia's Excess Mortality

E: hotline@amps.asn.au
T: 61 7 3497 5048

Red Union publishing
41 Campbell Street
Bowen Hills
QLD 4006
Australia

First edition 2023
Canberra, Australia
ISBN 978-0-646-88551-3
Cover photograph: Karolina Grabowska

National Library of Australia http://nla.gov.au.obj-135682653
Cover design: Gary Delahunty
Typeset: Gary Delahunty

Contents

Introductory remarks

Something different is killing Australian people in a most unusual way, and in large numbers. This unsettling fact has been evident to the Australian Medical Professionals Society and the time has come to confront it. Authorities in medicine, and the mainstream media as well, seem to be unwilling to address the matter in detail and with clarity. Given the inherent priory, this is simply disgraceful. There is no possible excuse for it. Medical paternalism, which has been enabled by drastic public health policies, needs to be rebalanced with respect for the patient. Australia's current excess death rate should be common knowledge and under careful examination. If the health authorities are not driving this, the Prime Minister should be. And if neither house of Parliament will inquire in the public interest, we will.

In all societies, human beings die at certain rates, which become known, expected, modelled and understood in detail. Illness, accident, murder and suicide are all components of a nation's usual rates of death. These figures are compiled, including deaths from all causes, to form all-cause mortality rates. They are surprisingly predictable. It is only if something goes radically wrong in a country, perhaps a war, or an extreme natural or economic disaster, that this can be sufficient to drive up the number of deaths to a clear excess, by comparison to a statistical average, by a range of

possible methodologies. In Australia, we contend that this statistical excess has been clear and present for 30 consecutive months.

To put it simply, Australian deaths have risen dramatically and are staying far above the expected monthly and annual numbers: many more people are dying than should be and it is time to find out why. This book is the result of a collaboration begun by some committed Australian doctors and scientists. It was a gathering of people of good standing and high qualifications, with opinions developed after considerable study, and all of them well used to the peer-review process. The result in these proceedings is a total of eighteen published papers.

This introduction might well have started off from a position of curiosity, adopted before the publishing of the conference proceedings took place. It is customary for seminar proceedings to begin by adopting a naïve position and then paper by paper being led to a conclusion to the question the conference was posing. In this case, however, a problem arose to make that approach difficult – the studies kept coming in, over a six-month period, from independent researchers, not bound by the system, and, as it turned out, people every bit as concerned as we are. The evidence began mounting, and the conclusion the writers all point to became ever clearer. The reader can now easily ascertain just how persuasive that evidence is.

It should be said that the health authorities were formally invited to attend the conference, to produce and to bring a study of their own. Strangely, no reply was received from them.

If this makes our health authorities seem less than apt on this topic of dying Australians, they are not alone. Too many people in political power have the same standpoint. AMPS has only taken this action after the Australian Federal Senate voted down a motion to hold a hearing into the excess death our country is experiencing. As an association of concerned health practitioners, we considered it our duty to advance knowledge and agitate for the genuine attention of those who serve at the pleasure of the public, both elected and non-elected. Why so many people are dying unexpectedly is the kind of thing that medical systems on every level should routinely be tracking closely and communicating to politicians; if they fail in this duty then politicians and public servants alike should be holding them accountable. Certainly, none should be found helping to smother real inquiry.

On the other hand, it is quite possible that the problem and its solution are as obvious to many of them, just as it is to us. Party politics will have its way with the elected, in just the same way that the unelected medical bureaucracy will seek domination on behalf of the system and at the expense

of the rank-and-file medical practitioners who wish to uphold their oaths of service and to stand strong in their ethics. Hence, in order to approach the truth, we have had to make a detour around the existing system and provide independent publishing.

What was the government definition of COVID public health success? Is there a public health measurement more indicative of success or failure than all-cause mortality? If it is claimed that many Australian lives were saved, a claim that can only be based on assumption-rich modelling, how is that compatible with rising excess death rates, per week and month, evident from the first half of 2021, well before COVID-19 disease could be construed to be making a serious contribution? Even if we accept, as former Prime Minister Scott Morrison claimed during his ill-fated 2022 election campaign (based very heavily on modelling assumptions), that early pandemic policies had saved 30,000 Australian lives, why is this not evident in the bottom line of all-cause mortality? Were these poor souls saved only to be lost again, alongside many others, to produce the observed excess death? And if so, what factors were and are in play?

We do not agree that COVID-19 itself, or its sequel, so-called Long COVID, is the true driving force of excess mortality. Several of the papers we present demonstrate this elegantly, in particular with Queensland data, with excess death evidenced eight months prior to any sizable burden of SARS-CoV-2 in that locked-down state. Hence, the trend is initiated in the absence of the infection, but squarely in the midst of policies like lockdowns and the vaccine rollout. These easily verifiable facts should have triggered critical evaluation of such policies by public servants, according to the Precautionary Principle. To continue to assert that SARS-CoV-2 is the only explanation needed may constitute wilful blindness; it causes failure to evaluate the possibility that the cure was, in fact, worse than the disease (at last by the time it reached Australian shores).

Much more needs to be said about the role of COVID-19 in the excess death, but we note a paradox that is as yet unexplained by the sanctioned experts. Why did the official death rates attributable to COVID-19 disease only become notable after the vast majority of Australians had received allegedly 'safe and effective' vaccines for the infection?

Furthermore, why did the much milder Omicron variant take such a toll on a heavily vaccinated population, if indeed the much-repeated therapeutic claim of protection from severe illness and death was in effect? The Cambridge Dictionary defines 'failure' as the fact of someone or something not succeeding. Thus, given the basic issue of excess all-cause mortality, how can mass vaccination and other related policies continue to escape critical review?

There is continued appeal to COVID-19 itself as all the explanation necessary for the phenomenology of excess mortality. This is seen in Australia and consistently around the heavily vaccinated parts of the developed world. In September 2023, we were informed of the planned non-royal commission into Australia's pandemic management, with extremely limited investigative scope and presided over by only the most committed government apologists. Is this likely to further the science? Is it likely to give any answers beyond the engrained position?

It is noteworthy that until the implementation of the coercive mandatory lockdowns and vaccination-only strategy, there was no pandemic of death. Yet we now find ourselves in just that, with consecutive increases in excess mortality not seen since wartime. In continued secrecy, our authorities implemented authoritarian pandemic policies, which we and others have noted were in complete contradiction of their own pandemic preparedness plans. Has this behaviour, in one way or another, cost a great many lives? The consequences of the failures are difficult to ignore.

In Australia, we have a serious problem. Government excesses of power created through emergency legislation have been allowed to violate our liberties. They were justified by largely unscientific and readily refutable claims. Fear was wrongly employed by political leaders, using secret health advice to control the public. Health laws gave chief health officers unprecedented powers to do almost anything they thought was reasonable during a pandemic – which can be declared on opinion, and not on evidence, without having to justify their decision.

When has there been a society that prospers because people have been cancelled or removed from their vital work because they dared to disagree with some regime's unquestionable truth? Do our modern medical authoritarians want to be looked back on with the same disdain with which we judge historical despots?

There are doctors and scientists across the country – and the world – trying to raise safety signals, seeking answers to questions, writing letters, seeking data transparency for analysis, and sending reports as they fight to fulfil their medical codes and oaths. We are unable to produce the scale bar to measure their make-up or the sum of their efforts, since many work alone and communicate their findings directly. However, we have no doubt that there are vast numbers of Australians who believe in the power of truth, honour and integrity and are willing to pay the price to stand behind them. We need real debate, open scientific discourse, acknowledgement of injuries, and unhindered access to unredacted data. The doctor-patient relationship should never have third parties such as government and bureaucracy interfering.

In this book, we present the work of a tiny fraction of those willing to sacrifice careers and livelihoods to seek the truth from evidence-based science, adhering to time-honoured medico-scientific principles. The reader needs to bear in mind during the course reading that the doctors whose work is featured here have had to face summary suspension and loss of their jobs merely for daring to speak the facts – not the opinions, but the facts – about the conduct of the people in the medical hierarchy. They dared to question the protocol, on scientific grounds, and have paid a huge price, that of their livelihood and their capacity to serve. It is a great shame that more people in the mainstream media have not had the same level of courage and commitment to human welfare.

Trust in public health, according to the Organization for Economic Cooperation and Development, requires that government actions be open to public scrutiny and that public institutions involve themselves by 'proactively releasing timely information,… enhancing transparent and coherent public communications… and engaging with the public.'

Fundamental principles of public health, political due diligence, institutional regulation and legal recourse have all been ignored or subsumed by a single focus of achieving consensus to maximize compliance. It has been compliance-based on false and misleading information where those who have power appear to have declined to do the most basic levels of review by failing to read even their own reports.

Winston Churchill said, 'Courage is what it takes to stand up and speak; courage is also what it takes to sit down and listen.' We believe that authorities in health departments and the medical system as we know it are not going to enjoy the contents of this book. In any segment of bureaucracy, it can no doubt be tempting to think that the data, analysis and opinion possessed and expressed within one's department are superior to that from all other available sources. However, the people in the unelected, executive arm of government now need to let themselves be informed as a result of this small but representative sample of science. It is being delivered to them from truly independent and unconstrained researchers drawing from official data, and who are free to follow those data where they lead. Our public servants need to pay attention, because the system they are presiding over appears to be doing a great deal of damage. Australians are observing the continuing silence of our political leaders and medical authorities as they permit it to continue.

Part 1

This is real, and it's happening

A lot of people are dying and we need to know why.

Death does not fall onto human beings by accident from a neighbouring star. There are always causes. These are categorized in great detail and the numbers are kept. Somehow, in Australia in early 2021, events came together to raise the numbers of dying in a way that can only be called alarming. The facts in this book from various highly-qualified writers point this out in a way that can no longer be ignored. It is past time to review and reflect on the potential harms of this nation's pandemic policy response. The people running the Australian health system cannot explain why the excess-death figure has risen so far above historical averages, and they appear to be making no efforts to change this, or even to discuss it. In early 2021 there was virtually no COVID-19 in the Australian community, whilst coincidentally the excess mortality rates began their notable rise. The observed trend can be linked to the introductory phase of highly novel pharmaceuticals, combined with some of the world's harshest pandemic policy responses. Here is what one of our authors, Australian Dr Astrid Lefringhausen, has to say:

> The public message heard everywhere was 'the vaccines are safe and effective,' although by then almost all that was said about them early on had already started to be proved wrong. The vaccines were supposed

> to stay at the injection site, be taken up by the lymphatic system, and be quickly degraded afterwards. As it turned out, none of this was correct…. Everybody was expected to trust the vaccine to deliver health and protection, although this was physically improbable, if not impossible…. Despite all promises, the COVID-19 vaccines were not safe.

Other countries find themselves in the same conditions. The American author Ed Dowd identified early trends in the deaths of healthy young people. His book is titled Cause Unknown: the epidemic of sudden deaths in 2021 and 2022.

Dowd contends that all-cause mortality data are showing truly disturbing trends in excess deaths, disproportionately experienced by healthy working-age Australians. Similar trends are being witnessed in other countries such as the United States where, he says, 'Millennials have experienced the equivalent of a Vietnam war, with more than 60,000 excess deaths' in a mere 12 months. Dowd discovered report after report from American life insurance companies that confirmed an extraordinary 40% increase in deaths among working-age people, and most of the deaths could not be attributed to COVID.

For example, OneAmerica CEO Scott Davison made comments to a commerce meeting picked up by the media: 'We are seeing, right now, the highest death rates we have seen in the history of this business – not just at OneAmerica. The data is consistent across every player in that business.' As has been shown in Australia, the majority of these deaths were not attributed to COVID. Similar findings can be seen in Australia through various data sources. Dowd again: 'Ignoring these deaths is the greatest disrespect we could ever show' to these people and their grieving families.

Cause unknown — the epidemic of sudden deaths[1]

by Ed Dowd

Almost all regulatory agencies, chief medical officers and politicians presented the COVID-19 vaccines as 100% effective against getting and spreading the virus. Mass vaccination of the population was the only solution presented for people to go back to normal life. The safe and effective claims have been proved false. According to government reports such claims were never justifiable as there was never any conclusive evidence these novel therapeutics could stop infection, stop disease and most important from a public policy point of view, stop transmission. As it became obvious that the vaccines did not and could not prevent infection with or transmission of COVID-19, the public discourse changed. The vaccines were then said to be effective at 'preventing serious hospitalisation and death.' This is a claim that to this day has never been proved, a claim that looks to be more marketing than science.

Interestingly on September 1, 2021, the CDC quietly changed the definition of vaccine. Rather than a vaccine being an inoculant that 'produces immunity to a specific disease,' the definition became 'a preparation that is used to stimulate the body's immune response against disease.' The definition change would make these COVID products more therapeutics than vaccines.

1 This article is based on Ed Dowd's recent book, *Cause Unknown: The Epidemic of Sudden Deaths in 2021 & 2022*; it was reviewed and approved by him. The data analysis can be found at www.phinance-technologies.com in the section listed as the Excess Mortality Project.

The data that are slowly being revealed and analysed appear to confirm that being employed in 2021-22 was actually detrimental to health. All the public policy measures introduced during the pandemic to apparently keep us safe have resulted in what seems to be an iatrogenic pandemic of excess death. The rate change in deaths was particularly striking as it coincided with the corporate mandates – it simply was not statistically possible that suicides, overdoses and deaths from delayed treatment of rapid-onset fatal cancers all spiked after the introduction of mandates.

The following quarterly excess death rate analysis for Australia has been undertaken using as sources the Australia Bureau of Statistics, the Department of Health and Aged Care, Our World in Data and the UN.[2] The data are based upon weekly deaths data from the Australian Bureau of Statistics spanning 2015 to 2022. The data are only available for certain selected age groups.

Quarterly excess mortality analysis

We obtain quarterly excess deaths estimates by aggregating in quarters data that are based on our weekly analysis of excess deaths.

In order to estimate weekly excess mortality we perform a two-step approach to estimate the baseline deaths. The first step is by estimating the trend in death rates using annual data as described in our methodology papers, while using method 2C.[3]

The second step is to estimate weekly excess deaths by comparing deaths or death rates in a given week with the average death rate, which is computed using the average weekly frequency of deaths over a period of N-years (typically 5 to 10 years depending on the data availability). By using both methods in conjunction we obtain a trend-adjusted and week-of-year adjusted estimate for excess mortality.

A quarterly analysis of excess deaths allows us to then use different metrics to estimate seasonally adjusted patterns in excess mortality. For example, we can compare excess mortality in Q1 of 2022 *versus* Q1 of 2021 to observe the effect of the vaccination policy on excess mortality.

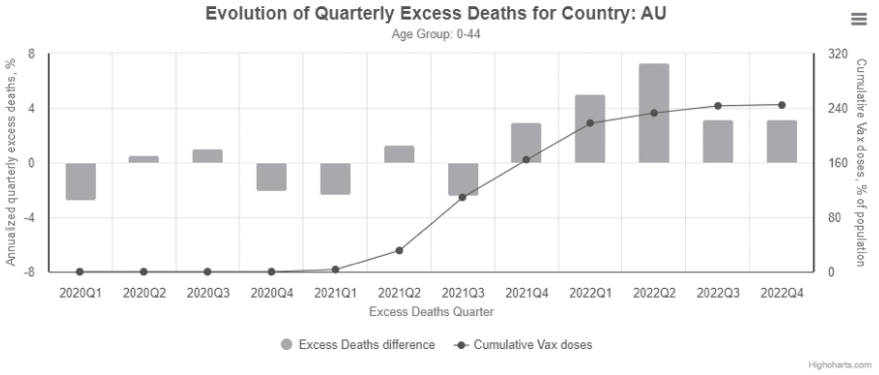
Quarterly evolution in excess mortality *vs* vax.

The following chart shows the quarterly (annualised) excess mortality from 2020 to 2022, for different age groups. The COVID-19 vaccinations data (right hand scale) refers to the total accumulated doses at the end of each quarter, as a percentage of the respective age group population.

2 The charts in this article are derived from the Australian Bureau of Statistics and can be found at https://phinancetechnologies.com/HumanityProjects/Quarterly%20Excess%20Death%20Rate%20Analysis%20-%20AU.htm

3 https://phinancetechnologies.com/HumanityProjects/Resources.htm

Quarterly excess mortality, from 2020 to 2022.

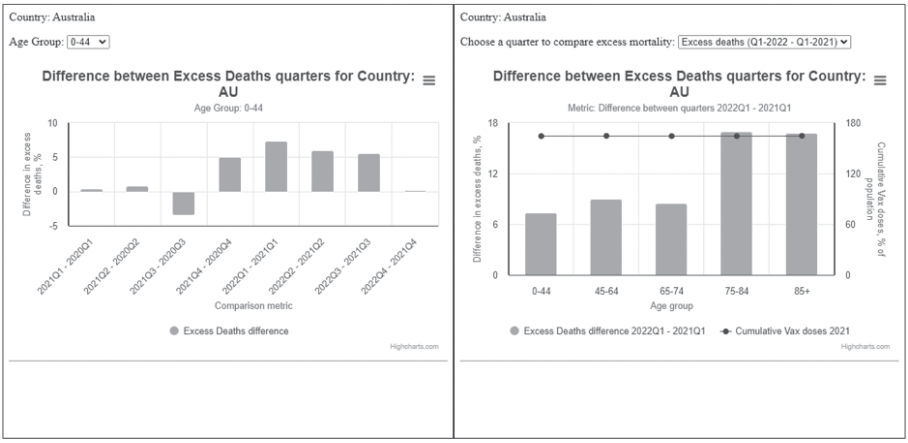


Excess Mortality - Comparative Metrics

Quarterly comparative metrics for excess death rates

The chart below shows the evolution of the quarter-to-quarter change in excess mortality from 2020, 2021 and 2022. The user can select the desired age group. What one would have been expected to observe is that as the pandemic evolved, changes in excess deaths should turn negative as a result of the rise in natural immunity and or vaccination.

The chart below shows the quarter-to-quarter change in excess mortality for all age groups, for a specific period. The individual COVID-19 vaccination doses as a percentage of the age group population are also shown. The user can specify the period.

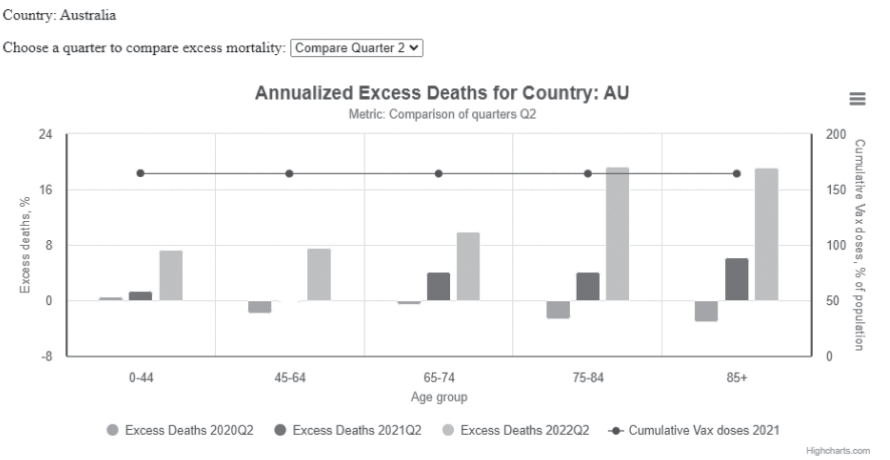


Quarter Comparison of Excess Mortality, by age group

The following chart allows the user to perform quarter-to-quarter comparisons in excess mortality during 2020, 2021 and 2022, for the different age groups.

This chart is particularly interesting to investigate excess mortality in seasonally equivalent periods in different years. The vaccine penetration rate for the end of 2021 is also shown.

Quarter comparison of excess mortality for different age groups.



According to Australian data excess all-cause mortality for working age Australians began to surge in 2022 following vaccine mandates when mutating strains were already becoming less virulent. Knowing the virus affected mostly older, vulnerable people with pre-existing comorbidities, how can public health officials explain these statistically significant increases in deaths among working age Australians? And why does it appear no one is interested in finding out?

We live in a world where regulatory institutions are captured by financial and political interests, either unwilling or unable to get to the truth of the issues they set out to investigate and regulate on behalf of the society. Without unbiased and comprehensive research, there is a risk of misguided policy decisions at best, and at worst, negligence and malpractice. Never has this been more apparent than during the COVID-19 pandemic.

In this context, we need independent agents to act as gatekeepers of the public interest. We intend to be such agents, and to provide high-quality research to other individuals and institutions who seek similar outcomes.

Our data analysis confirms that healthy young people have been dying and becoming disabled with alarming frequency. The rate of these incidents is new

and unusual, and not sufficiently explained by government officials. Glaringly public health questions are not being asked or answered by those in power. At this point it appears the response to this pandemic of excess death by authorities has moved beyond something we could write off as incompetence. They are allowing (and even forcing) mass use of products they know are harmful. It does look like powerful people in public health and pharma are in full cover-up mode. At this point, the negligence could be considered criminal.

Edward Dowd is currently a founding partner with Phinance Technologies, a global macro alternative investment firm. He has worked in the financial industry for most of his career, spanning both credit markets and equity markets. Some of the firms he worked for include HSBC, Donaldson Lufkin & Jenrette, Independence Investments, and most notably at Blackrock as a portfolio manager where he managed a $14 billion growth equity portfolio for ten years. After BlackRock, he founded OceanSquare Asset Management with two former BlackRock colleagues.

His new book is *Cause Unknown: The Epidemic of Sudden Deaths in 2021 & 2022.*

Vaccination meets genetic modification – what could possibly go wrong?

by Conny Turni and Astrid Lefringhausen[1]

Since the vaccines predominantly used in Australia are to this day the mRNA vaccines by Moderna and Pfizer-BioNTech, they are also the topic of this essay.

The review is written from an Australian perspective and at the time of writing the COVID-19 vaccines were still heavily promoted in Australia. The government at that point was pushing a fourth injection and injections for small children and pregnant women in particular, in spite of the fact that the Therapeutic Goods Administration (TGA), the Australian equivalent of the FDA in the US, stated at the same time on their website that they had no full data package from any vaccine producer and large-scale trials were still progressing.

However, the public message heard everywhere was 'the vaccines are safe and effective,' although by then almost all that was said about the vaccines early on had already started to be proved wrong. The vaccines were supposed to stay at the injection site, be taken up by the lymphatic system and be quickly degraded afterwards. As it turned out, none of this was correct. The naming itself was already misleading as the injections cannot be correctly called vaccines – a vaccine until 2020 was always the injected substance causing the immune reaction that ultimately led to immunity. That substance, the antigen, usually

1 This article is based on a review paper by Conny Turni and Astrid Lefringhausen from September 2022 1, the first publication in Australia looking critically at the COVID-19 vaccines and comparing public statements with scientific facts. It, in turn, is based on roughly 1100 case studies and scientific publications from around the globe looking specifically at side effects of the COVID-19 vaccines.

was either the pathogen or a part of it (with some exceptions like the Tetanus vaccine being a toxoid), and was always an extracellular, separate entity and given in precise and well-defined concentrations.

The COVID-19 injections are working more like synthetic viruses and should better be called transient genetic pro-vaccines. They contain genetic information that is protected by a fatty envelope, and enters into an unknown number of cells of the injected person. depending on the integrity of the vial content, dilution method, injection technique and physiological status of the vaccinee. The genetic information forces the host cells to produce the viral spike protein that is afterwards presented on the cell surface and serves as a vaccine by eliciting an attack by the immune system on the spike protein producing cells, essentially an autoimmune reaction.

The lipid nanoparticles (LNP) making up the envelope are a mix of cholesterol and two synthetic lipids: ALC-0315 and ALC-0159. Echelon, the manufacturer of these nanoparticles, specifies that they are 'for research only and not for human use). ALC-0315 is an ionizable cationic amino lipid that has been used in combination with other lipids in the formation of lipid nanoparticles,[2] while ALC-0159 is a polyethylene glycol (PEG) lipid conjugate, by its nature a non-ionic surfactant. LNPs are able to cross all biological barriers as a result of their size and reactivity – examples are the blood brain and the blood-placenta barrier. The Japanese government demanded a biodistribution study from Pfizer that showed the LNPs accumulating rapidly in liver, ovaries and adrenal glands, but also in smaller amounts in the brain and other organs. A similar study was submitted to the TGA in January 2021 and was released in response to a freedom of information request later that year as part of a Non Clinical Evaluation report (FOI 2389 document 6 (tga.gov.au)). Table 1 is an excerpt from that report and shows accumulation of LNPs in various organs including blood and plasma within minutes to hours. Pfizer summarize their results on page 4 of their report and also point out the scope of the evaluation done. They tested the vaccine in mice, rats and rhesus macaques and found that BNT162b2, their mRNA COVID-19 vaccine, induced humoral and cellular immune responses in monkeys and mice.

'However, antibodies and T cells in monkeys declined quickly after 5 weeks after the second dose, raising long term immunity concerns.' The vaccine dose given to monkeys was 100 ug, more than three times the dose given to humans, and since 'rhesus macaques do not show clinical signs and generally develop only mild lung pathology from SARS-CoV-2 infection' it might not have been the best study object. Even more worryingly, 'there were no studies on protection of older animals from SARS-CoV-2 infection or duration of protection after immunization. The animal studies were of short term; long term immunity

Table 1 from Non Clinical Evaluation Report BNT162b2 (mRNA) COVID-19 vaccine, page 45: Mean concentration of radioactivity (sexes combined) in tissue and blood following a single IM dose of 50ug mRNA/rat

Sample	Total Lipid Concentration (µg lipid equiv/g (or mL))						
	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h
Adipose tissue	0.057	0.100	0.126	0.128	0.093	0.084	0.181
Adrenal glands	0.27	1.48	2.72	2.89	6.80	13.77	18.21
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687
Bone marrow (femur)	0.48	0.96	1.24	1.24	1.84	2.49	3.77
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112
Heart	0.28	1.03	1.40	0.99	0.79	0.45	0.55
Injection site	128.3	393.8	311.2	338.0	212.8	194.9	164.9
Kidneys	0.39	1.16	2.05	0.92	0.59	0.43	0.42
Large intestine	0.013	0.048	0.09	0.29	0.65	1.10	1.34
Liver	0.74	4.62	10.97	16.55	26.54	19.24	24.29
Lung	0.49	1.21	1.83	1.50	1.15	1.04	1.09
Lymph node (mandibular)	0.064	0.189	0.290	0.408	0.534	0.554	0.727
Lymph node (mesenteric)	0.050	0.146	0.530	0.489	0.689	0.985	1.366
Muscle	0.021	0.061	0.084	0.103	0.096	0.095	0.192
Ovaries (females)	0.104	1.34	1.64	2.34	3.09	5.24	12.26
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264
Skin	0.013	0.208	0.159	0.145	0.119	0.157	0.253
Small intestine	0.030	0.221	0.476	0.879	1.279	1.302	1.472
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112
Spleen	0.33	2.47	7.73	10.30	22.09	20.08	23.35
Stomach	0.017	0.065	0.115	0.144	0.268	0.152	0.215
Testes (males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.000
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.456
Whole blood	1.97	4.37	5.40	3.05	1.31	0.91	0.42
Plasma	3.96	8.13	8.90	6.50	2.36	1.78	0.81
Blood:plasma ratio	0.815	0.515	0.550	0.510	0.555	0.530	0.540

was not assessed. The sponsor indicated that long term immunity would be addressed by human data.'

Since the official clinical trial had been finished and invalidated by vaccination of the placebo group in late 2020, this means the TGA was informed in January 2021 that the Australian population would be one of the groups used for testing long term immunity of these new injections. It also clearly shows that there was no information on duration of protection, protection for the elderly or long-term side effects, which sounds neither safe nor effective. Even the transient nature of the pro-vaccine turned out to be only partially true, as the mRNA was nucleoside-modified to reduce potential innate immune recognition, rendering it vastly more stable than normal cellular mRNA which has a half-life of minutes only.

The vaccine mRNA could be found in the bodies of vaccinated people 60 days after injection,[3,4] which makes it impossible to predict how much spike

protein each vaccinated person will produce and for how long. Unfortunately, the spike protein is toxic to human cells and is responsible for most of the severe side effects of the respiratory infection in humans. Its S1 subunit is found to circulate within the blood shortly after vaccination and can induce clotting by binding fibrinogen and ACE2 on platelets,[5] while the S2 subunit has been shown to interact in silico with BRCA-1 and 2 as well as P53,[6] all of which are connected to cancer. P53 is a gene coding for a protein that controls cell division and apoptosis and is known as a general tumor suppressor. BRCA-1 and 2 gene products are involved in repair of damaged DNA and are connected to breast and ovarian cancer in women and prostate cancer in men. Other possible ways in which the mRNA vaccines can interfere with cellular DNA repair mechanisms are downregulation by spike of housekeeping genes like RNA polymerase I and its promoters; and miRNA dysregulation. MiR-148 is one such microRNA which is excreted in exosomes by transfected cells following spike protein production and has been shown to downregulate homologous G1 phase recombination as well as hyperactivate human microglia, damaging the central nervous system (CNS) in the process.[7]

A further serious concern was brought up very recently by Kevin McKernan and his team, who found up to 30% plasmid DNA contamination in the mRNA vaccines when they sequenced them. Most concerning are simian virus promoters (SV40) in the bivalent vaccines which have been suspected of causing cancers in humans. Additionally, the presence of bacterial plasmid vectors in the mRNA-LNP complexes must be seen as a warning sign that high levels of contaminating endotoxins – parts of bacterial membranes that strongly stimulate the human immune system up to anaphylactic reactions – might be present in the vaccines. A study by Doshi et al. from August 2021[8] concluded that the Pfizer vaccine was associated with a 36% higher risk of serious adverse events (SAE) *versus* the placebo. For Moderna it was 6% higher risk of SAE *versus* placebo. Another study by Shimabukuro[9] followed pregnant participants in the v-safe pregnancy registry and found that only 21% of women enrolled completed their pregnancy.

Regarding the proclaimed effectivity of the mRNA vaccines, it is highly likely to be inferior to natural infection which produces much broader and more robust protection by the fact alone that the person is exposed to the entire virus with all its proteins – spike, envelope, membrane and nucleocapsid proteins – *versus* only the spike protein. Studies showed that only natural infection upregulated genes associated with type I interferon production, cytotoxicity and increased circulating plasmablasts, while the mRNA injections seem to suppress interferon responses. Studies from Sweden, California, Finland and Israel showed that the rate of re-infection after recovery from COVID-19 was lower than in the vaccinated, and that vaccinated health care workers in

hospitals around the world were infected post-vaccination at high rates. Since Omicron entered the world in late 2021, it was increasingly vaccinated people who were infected and severely affected by COVID. One of the few states that published COVID-19 cases, hospitalizations and deaths by vaccination status until late 2022 was NSW.

Figure 1 shows the data obtained in the two weeks leading up to December 31st 2022 and the worsening effects of the booster injections. For those Australians whose COVID-19 infection turned serious, the recommendation was only to contact a health care provider when experiencing difficulty breathing, loss of speech or mobility, confusion or chest pain. The recommended treatments

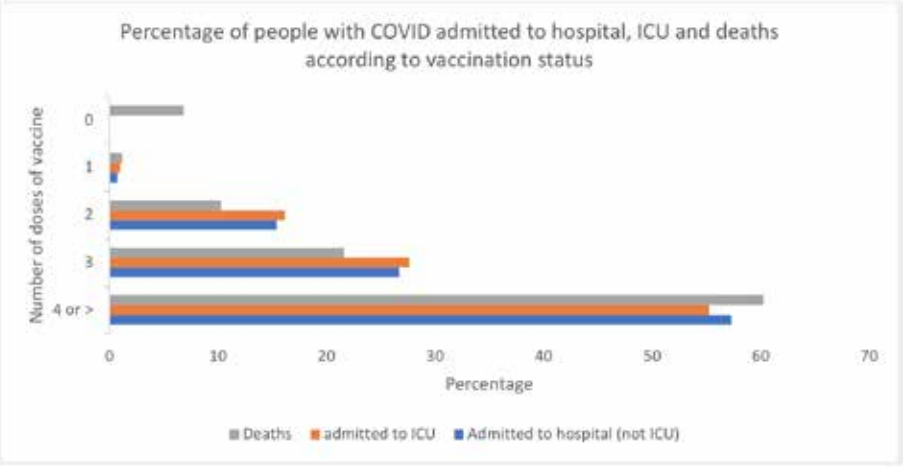


Figure 1 People with a COVID-19 diagnosis in the previous 14 days who were admitted to hospital, to ICU or reported as having died in the two weeks ending December 31st 2022. Numbers represented as percentage of the total numbers admitted to hospital, to ICU and of deaths of patients whose vaccination status was known. Of the patients with known vaccination status, a total of 1415 were admitted to hospital; 105 went to ICU and 88 died. (https://www.health.nsw.gov.au/Infectious/covid-19/Documents/weekly-covid-overview-20221231.pdf)

were the provisionally-approved and expensive new drugs like Molnupiravir and Paxlovid. Disregarded were drugs that had been used successfully for years in respiratory disease treatments. Most COVID-19 deaths were due to secondary pneumonia, and while it was standard-of-care to give antibiotics to patients in respiratory distress as a result of influenza and secondary bacterial infection before 2020, this practice was all but stopped during the COVID-19 pandemic, with disastrous consequences. Everybody was expected to trust the vaccines to deliver health and protection although this was physically improbable, if not impossible. The mucosal immune system is the largest component of the entire immune system, having evolved to provide protection at the main sites of infectious threat: the mucosae. As SARS-CoV-2 initially

infects the upper respiratory tract, its first interactions with the immune system must occur predominantly at the respiratory mucosal surfaces, during both inductive and effector phases of the response,[10] and it is at this stage that it can

Table 2: All symptoms reported from 1016 case studies and publications regarding serious adverse events following the mRNA vaccines by either Pfizer or Moderna.

* signifies a side effect with several subtypes that were individually reported but are combined in this table

System organ class	Side Effect induced by at least one of the two mRNA vaccines
Auditory and balance disorders	Acute vertigo, Tinnitus
Autoimmune disease	Autoimmune hepatitis, Graves' disease, Limbic encephalitis, MS, Myasthenia gravis, Psoriasis, Severe autoimmune hemolytic anemia, Systemic lupus erythematosus, Vogt-Koyanagi-Harada Syndrome
Cardiac disorders	Arrhythmia, Cardiac tamponade, Cardiomyopathy, Endocarditis, Kounis hypersensitivity-associated acute myocardial infarction, Myocardial infarction, Myocarditis*, Myocarditis-induced sudden death, Myopericarditis, Pericarditis, Takotsubo cardiomyopathy, Transient cardiac injury
Death	Sudden death, Multiple organ failure, Cardiac arrests etc.
Dermal disorders	Chilblains, delayed adverse skin reactions*, Dermal hypersensitivity (COVID arm), Exacerbated Hailey-Hailey, Petechiae and peeling of fingers, Purpuric rash*, Reactivation of Bacille Calmette-Guerin scar, Sweet's syndrome
Endocrine disorders	Menstrual disorders, Heavy menstrual bleeding
Gastrointestinal	Appendicitis, Gastroparesis, Oral aphthous ulcers
Immune and Lymphatic disorders	Allergy to PEG-ASNase, Anaphylaxis*, Arthritis, Immune-mediated disease outbreaks, Lymphadenopathies*, Multisystemic inflammatory syndrome, Rapid Progression of Angioimmunoblastic T Cell Lymphoma, Seronegative polyarthritis, Thymic hyperplasia
Infections	COVID-19, Herpes Simplex, Herpes Zoster (Shingles), Hepatitic C reactivation, Non-disseminated Herpes Zoster
Liver and gallbladder	Acute liver injury, ANCA glomerulonephritis
Musculoskeletal disorders	Fasciitis, Myositis, Polymyalgia rheumatica, Rhabdomyolysis, Synovitis
Neurological disorders	Acute inflammatory neuropathies, Abducens nerve palsy, Adrenomyeloneuropathy, Bell's palsy, Cerebral haemorrhage*, Cerebral venous sinus thrombosis, CNS demyelination, CNS inflammation, Encephalomyelitis*, Encephalopathy (acute), Guillain-Barré syndrome, Miller-Fisher syndrome, Myelitis*, Optic neuritis, Parsonage-Turner syndrome, Stroke, Status epilepticus, seizures*
Olfactory disorders	Phantosmia
Optical disorders	Acute corneal endothelial graft rejection, Central serous chorioretinopathy, Retinal necrosis due to varicella zoster reactivation, Transient visual field loss, Tolosa-Hunt syndrome, Uveitis, Panuveitis
Pancreatic disorders	Pancreas allograft rejection, Pancreatitis
Pregnancy outcomes	Miscarriage (Pfizer's own data)
Psychiatric disorders	Depression
Pulmonary disorders	Squamous cell carcinoma of the lung
Renal and urinary disorders	Crescentic Pauci-Immune glomerulonephritis, Genital necrosis with cutaneous thrombosis, IgA nephropathy, Acute renal failure, Macroscopic hematuria, Minimal change disease and acute kidney injury
Respiratory and thoracic disorders	Asthma exacerbation, Pulmonary embolism, Vaccine-induced interstitial lung disease
Vascular disorders	Giant cell arteritis, Haemolysis, Haemorrhage*, Microscopic polyangiitis, Thrombocytopenia*, Thromboembolic events*, Thrombotic events*, Vasculitis*

be neutralized by mucosal immunity, predominantly mediated by T lymphocytes and mucosal antibodies of the type IgA. The serological IgG antibodies produced by vaccination play only a minor role in combatting respiratory viral infections; only after the virus has replicated for days on the mucosal membranes can it enter the blood and encounter the vaccine-induced antibodies.

When looking at the DAEN database maintained by the TGA, it was impossible to ignore the spike in reported adverse events starting in 2021 when compared to the previous 20 years. Large insurance companies in the US and Germany noted that all-cause death rates went up by 40% in ages 18-64 years, which could not be attributed to COVID-19 alone. Table 2 above is a concentrated version of the SAE table in the root paper 'COVID-19 vaccines – an Australian review', and summarizes 1016 case reports and studies published until July 2022.[11] COVID-19 vaccines cause without a doubt more side effects than any other vaccine, likely because both components, mRNA and LNP as well as the product – the spike protein – are highly inflammatory, reactive molecules that interfere with type I interferon signalling and dysregulate protein synthesis, thus affecting both formation and apoptosis of immune cells.

The spike protein has been found to be freely circulating after the immune attacks on presenting cells begin, and can in this form attach to any ACE2-expressing cells, which unfortunately are in almost every organ system. It causes an atypical signal cascade in the cells by binding to ACE2, which usually acts as a type I integral membrane protein that when bound gets activated and cleaves antiotensin II to angiotensin, thus regulating blood pressure. In SARS-CoV-1 infection, binding of the spike protein (which is 76-78% identical to that of SARS-CoV-2) to ACE2 triggered the casein kinase II-dependent activation of activator protein-1 transcription factor and subsequent gene transcriptional events which induced the production of usually not-transcribed mRNA.[12] Spike protein can also induce syncytia formation in lung tissue, a cell fusion that ultimately leads to cell death but can during viral infection allow the virus to spread without breaking out of the human cell and exposing itself to the immune system.

Aside from the proved serious adverse events listed in Table 2, other possible side effects can be seen but are so far not connected to the injections and possibly never will be conclusively proved to be caused by them, because of the extreme variety in amount and quality of the vaccines as well as differences in the physiology and pathology of the vaccine recipients. A study by Lyons-Weiler[13] showed that more than one third of SARS-CoV-2 proteins show problematic homology to human key proteins, which could lead to the development of autoimmune disease. Two autoimmune diseases that are already being seen but played down as extremely rare are immune thrombocytopenia and Guillain-Barré Syndrome; there are discussions about the officially rare post-vaccine myocarditis being an

autoimmune reaction as well. The spike protein has been implicated in causing or exacerbating neurodegenerative diseases like Dementia, Alzheimer's and Parkinson's disease by being amyloidogenic – aggregation prone – and initiating protein aggregation through interaction with heparin-binding amyloid proteins. [14] Antibody dependent enhancement (ADE) is a very real concern and could explain the increasing morbidity of vaccinated *versus* unvaccinated people when infected with SARS-CoV-2. Because of the very high rate of spike protein mutation, almost every vaccine will force the body to produce an extinct spike protein from day one of deployment. If this leads to non-neutralizing antibodies, these can be used by the new, mutated virus during an infection to more easily invade immune cells and multiply using the cells' resources.

Despite all promises, even for the elderly the COVID-19 vaccines were not safe. A recent study by Wilson Sy[15] looking at Simpson's Paradox in the correlations between excess mortality and COVID-19 injections found 'Earlier epidemiological evidence that COVID injections reduce illness and death is now methodologically invalidated, and the claim that the injections are beneficial for the vulnerable is refuted. The injections explain the mystery of significant numbers of non-COVID excess deaths. The Australian pandemic is shown to be iatrogenic in nature, particularly for the elderly, who have suffered disproportionate harm. Deliberately ignoring this clear evidence is tantamount to iatrogenic geronticide.'

References

[1] Turni, C., Lefringhausen, A. (2022) COVID-19 vaccines – An Australian Review. Journal of Clinical & Experimental Immunology. 7(3):491-508.

[2] Saadati, F., Cammarone, S., Ciufolini, M.A. (2022) A Route to Lipid ALC-0315: a Key Component of a COVID-19 mRNA Vaccine. Chemistry. 28(48):e202200906. doi: 10.1002/chem.202200906.

[3] Röltgen, K., Nielsen, S.C.A., Silva, O., Younes, S.F. et al. (2022). Immune imprinting, breadth of variant recognition, and germinal center response in human SARS-CoV-2 infection and vaccination. Cell. 185, 1025 – 1040. DOI: https://doi.org/10.1016/j.cell.2022.01.018

[4] Fertig, T.E., Chitoiu, L., Marta, D.S., Ionescu, V.-S., Cismasiu, V.B., Radu, E., Angheluta, G., Dobre, M., Serbanescu, A., Hinescu, M.E., et al. (2022) Vaccine mRNA Can Be Detected in Blood at 15 Days Post-Vaccination. Biomedicines. 10, 1538. https://doi.org/10.3390/biomedicines10071538

[5] Zhang, S., Liu, Y., Wang, X., Yang, L., Li, H., Wang, Y., ... &Hu, L. (2020). SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. Journal of Hematology & Oncology. 13(1), 1-22.

[6] Singh, N., Singh, A. B. (2020). S2 subunit of SARS-nCoV-2 interacts with tumor suppressor protein p53 and BRCA: an in silico study. Translational Oncology. 13(10), 100814.

[7] Mishra R and Banerjea AC (2021) SARS-CoV-2 Spike Targets USP33-IRF9 Axis via Exosomal miR-148a to Activate Human Microglia. Frontiers in Immunology. 12:656700. doi: 10.3389/fimmu.2021. 656700

[8] Doshi, P. (2020) COVID-19: Do many people have pre-existing immunity? 17 September 2020 BMJ. 2020; 370 doi: https://doi.org/10.1136/bmj.m3563

[9] Shimabukuro, T. T., Kim, S. Y., Myers, T. R., Moro, P. L., Oduyebo, T., Panagiotakopoulos, L., Meaney-Delman, D. M. (2021) Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons. New England Journal of Medicine. 384:2273-2282 DOI: 10.1056/NEJMoa2104983

[10] Russell, M.W., Moldoveanu, Z., Ogra, P.L., Mestecky, J. (2020) Mucosal Immunity in COVID-19: A Neglected but Critical Aspect of SARS-CoV-2 Infection. Frontiers in Immunology. 11, 611337. doi: 10.3389/fimmu.2020.611337.

[11] Seneff, S., Nigh, G., Kyriakopoulos, A. M., McCullough, P. A. (2022). Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs. Food and Chemical Toxicology, 164, 113008.

[12] Suzuki, Y.J., Gychka, S.G. (2021) SARS-CoV-2 Spike Protein Elicits Cell Signaling in Human Host Cells: Implications for Possible Consequences of COVID-19 Vaccines. Vaccines (Basel). 9(1):36. doi: 10.3390/vaccines9010036. PMID: 33440640; PMCID: PMC7827936.

[13] Lyons-Weiler, J. (2020) Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity. Journal of Translational Autoimmunity, 3, 100051.

[14] Idrees, D., Kumar, V. (2021) SARS-CoV-2 spike protein interactions with amyloidogenic proteins: Potential clues to neurodegeneration. Biochemical and Biophysical Research Communications, 554, 94-98.

[15] Sy, Wilson. (2023) Simpson's Paradox in the correlations between excess mortality and COVID-19 injections: a case study of iatrogenic pandemic for elderly Australians. https://www.researchgate.net/publication/371342838_Simpson's_Paradox_in_the_correlations_between_excess_mortality_and_COVID-19_injections_a_case_study_of_iatrogenic_pandemic_for_elderly_Australians

Dr Astrid Lefringhausen was born in Duesseldorf, Germany and first studied molecular biology and immunology. She worked in parallel as a nurse in radiology, teaching medicinal microbiology to nurse students at the German Red Cross, and also in the biotechnology research facility of Bayer. She gained a PhD in virology in 1996 and in the same year began working for the biotech industry, first in sales, and later as export manager and technical trainer. From 1999 to 2006 she worked internationally across Asia, Eastern Europe, Africa and South America as staff and customer trainer in molecular biology, installing and training in the use of cell-sorting equipment, assisting in stem cell treatments in paediatric departments worldwide. She moved to Australia in 2006 and since 2015 has worked in the diagnostics industry across Australia and New Zealand in the area of cell chemistry, immunohaematology, immunology and molecular biology.

Part 2

Poorly tested – they should have known

Our next authors point toward the importance of the precautionary principle in the presentation of pharmacological products to the general populace. To begin taking a deeper look at this, we need to observe the novel delivery system – this is the first time mRNA vaccines have ever been approved for use with humans. They operate by providing a synthetic code. The m-Ψ-RNA delivery system does not provide a natural form of mRNA to encode the spike protein, but a modified mRNA code manipulated to remain in the human body for longer without rapidly degrading (through substitution of pseudouridine, designated Ψ, for the naturally occurring nucleotide base, uridine). There are potential harms associated with the lipid nanoparticle delivery system. Long-term consequences remain entirely unknown. Potentially dangerous experimental, novel gene-based products were never tested for efficacy in stopping transmission and spread of COVID-19, nor in the opinion of the Australian Medical Professionals Society, adequately tested for genotoxicity, carcinogenicity, immunotoxicity and reproductive toxicity. Such a reduction in evidentiary standard is not justifiable.

In July, 2021, Australians were being mandated through coercive techniques to be vaccinated with poorly-tested provisionally-approved gene-based vaccines that our health bureaucrats and politicians repeatedly told us had

been proved safe and effective. The Therapeutic Goods Administration (TGA) was amending the Therapeutic Goods Regulation Act to further reduce the safety and efficacy requirements for any medicine that is for the treatment or prevention of COVID.

According to court-ordered released documents, the Emergency Use Authorisation (EUA) of the Pfizer-BioNTech COVID-19 Vaccine-BNT 162b2 was granted on the efficacy data of only 170 patients. The TGA should have been concerned that major disqualifying protocol deviations were identified in the 170 patients upon whom the EUA was granted. These protocol deviations raise serious concerns about the legitimacy of the clinical trial and the scientific norms and ethical principles upon which good medical practice is founded. Pfizer gained provisional approval for their COVID-19 injection following a mere two-month trial, claiming 95 per cent efficacy for the prevention of coronavirus disease. However, there have been important concerns expressed with regard to statistical power as well as the protocol deviations apparent in these data. Despite the pressure exerted by international medicine regulators marching in lockstep and ignoring these concerns, the TGA should have been concerned to probe the legitimacy of the clinical trial.

An analysis by Fraiman et al. titled 'Serious Adverse Events of Special Interest Following mRNA COVID-19 Vaccination in Randomized Trials in Adults' goes on in this section to review the randomized trial data from Pfizer and Moderna. It finds a risk of serious adverse events stands at approximately one in 800 vaccine recipients. This 'number needed to harm' is a much higher figure than the most generous estimate of vaccination benefits, or 'number needed to vaccinate'. Did regulators consider such a high harm potential against any perceived potential benefits? Regardless, we are aware that many have drawn the attention of health officials to the enormous value of this paper.

It is often stated by those incredulous of our doubts that the trial samples for novel vaccines were very large. However, when one halves the sample sizes to account for the fact that only half were exposed to investigational mRNA vaccines, the sample sizes become less impressive. Safety for mRNA vaccine platforms was reported as of November 14th 2020 for Pfizer-BioNTech Comirnaty and November 25th for Moderna's SpikeVax. By combining the two studies and utilising data submitted to the FDA as of December 2020, the authors conducted a unique analysis comparing adverse event profiles in 33,986 mRNA vaccine recipients, compared to 33,951 placebo recipients. Importantly, even though the duration of the studies up until that date was still short, this is vastly preferable to the less

mature safety datasets used for the inaugural publications for the Pfizer and Moderna offerings. Although many have tried to refute this paper and its alarming message, none have refuted its methodology, including the Health Department and related entities like The Australian Technical Advisory Group on Immunisation (ATAGI); we believe they cannot possibly be unaware of it.

Now we come to consider the way vaccines are manufactured. This is an integral part of the regulatory process to ensure safety and efficacy. An analysis of the Pfizer clinical trial identified that nearly all of the vaccine doses administered during the trial originated from what is known as Process One clinical batches. A second method of manufacture, using E.coli, rapidly replicates the DNA from which RNA can be drawn quickly and mass-produced. It was decided this was necessary, to meet the demands of large-scale global production; it came to be known as Process Two.[1] The differences between the two are profound, and involve the second process having lowered mRNA integrity. This poses an inestimable risk to population health and the human genome from the possible contamination with plasmid DNA and endotoxins. Let this be clear. The regulators approved the Pfizer vaccine endorsing a process carrying monstrous risk, based on Process One; only 250 people were then tested with the vaccine using Process Two, and an EUA was granted for mass global injection. To restate it: the regulators approved the Pfizer gene-based vaccine utilising a manufacturing process that was then not used for the mass global production of the Pfizer product. It needs to be understood that the Process Two manufacturing protocol, which was tested on a mere 250 people, carries risk nothing short of catastrophic. The magnitude of this error must not be underestimated. Its implications are frightening because of the risk posed by the presence of plasmid DNA and endotoxins. The word endotoxin is never heard in non-scientific discussion, but it is at the peak of the most toxic products on the planet. This is discussed by our authors in this part.

Pfizer gained provisional approval for their COVID-19 injection following a mere two-month trial, claiming 95% efficacy for the prevention of coronavirus disease. At the same time, Pfizer set out to have a 75-year embargo on release of information about not only their clinical trial data but also about the contents of their products. On these extremely narrow trial data, we were told two 'safe and effective' injections would stop the virus and society would return to normal. Soon it was three injections. Then it became four. Now it is more. Records of The Australian Advisory Committee on Vaccines tell us that pregnant women were not included in

1 Prof Josh Guetzkow, in the *BMJ*, May 13th, 2023.

this or any other studies, and that there were no data on mRNA distribution and degradation, and also on the toxicity of lipid nanoparticles. This reduces the safe-and-effective governmental mantra to nothing more than propaganda, repeated claims that the Pfizer products were 'not expected' to pose a risk. Hopeful expectations are not conclusive data and are not the usual considerations upon which the precautionary principle rests.

Not only did manufacturers have six years to provide the government with safety and efficacy data on these provisionally-approved injections. They also no longer have to demonstrate the medicines could provide a greater benefit than other available ones, or that the medicine is likely to provide a major therapeutic advance.

> COVID-19 mRNA vaccine products have a novel delivery system, being the first mRNA vaccines approved for use in humans, as well as the first approved coronavirus vaccines in humans. The speed at which they were designed, developed, approved and administered is also unprecedented in pharmaceutical history and defies traditional timelines for testing of biological products for use in humans.
>
> – Halma, et al.

And:

> These results raise concerns that mRNA vaccines are associated with more harm than initially estimated at the time of emergency authorization. In addition, our analysis identified a 36% higher risk of serious adverse events in vaccinated participants in the Pfizer trial.
>
> – Fraiman, et al.

The novelty of mRNA viral vaccines and potential harms: a scoping review

by Matthew T.J. Halma,
Jessica Rose and Theresa Lawrie

Abstract: Pharmacovigilance databases are showing evidence of injury in the context of the modified COVID-19 mRNA products. According to recent publications, adverse event reports linked to the mRNA COVID-19 injections largely point to the spike protein as an aetiological agent of adverse events, but we propose that the platform itself may be culpable. To assess the safety of current and future mRNA vaccines, further analysis is needed on the risks due to the platform itself, and not specifically the expressed antigen. If harm can be exclusively and conclusively attributed to the spike protein, then it is possible that future mRNA vaccines expressing other antigens will be safe. If harms are attributable to the platform itself, then regardless of the toxicity, or lack thereof, of the antigen to be expressed, the platform may be inherently unsafe, pending modification. In this work, we examine previous studies of RNA-based delivery by a lipid nanoparticle (LNP) and break down the possible aetiological elements of harm.

1. Introduction

Pharmaceutical drug and medical device approvals are predicated on the completion of a structured approval process through various regulatory agencies. Historically, the approval process has contributed to patient safety by subjecting all new approvals to a rigorous safety assessment. However, there

are many examples of over-turnings of approvals of pharmaceuticals post facto, because of the emergence of oversights of particular safety factors that occurred during the approval process.[1] These failures of regulatory bodies to sufficiently assess safety during the approval process are costly in terms of health and economic harms.[2] To put this issue into perspective, of 309 novel cardiovascular, orthopaedic, and neurologic devices approved in the EU between 2005 and 2010, 73 (24%) were subjected to either a safety alert or product recall,[3] consistent with reported rates for other medical devices.[4] Importantly, as the complexity of novel products increases, approval success rates decrease;[5] for example, new drug approvals are marred by low phase III trial success rates (~10%).[6]

Given the low success rates of novel and unprecedented drugs,[6,7,8] and the potential risks to the population, it is important to adopt the precautionary principle[9] when approving any pharmacological products, especially those given to large populations. COVID-19 mRNA vaccine products have a novel delivery system, being the first mRNA vaccines approved for use in humans, as well as the first approved coronavirus vaccines in humans. The speed at which they were designed, developed, approved, and administered is also unprecedented in pharmaceutical history,[10] and defies traditional timelines for testing of biological products for use in humans.

With the approval of the mRNA platform by health regulators across the globe, the industry is poised to develop new vaccines using mRNA, as it is a versatile platform that only requires the genetic sequence of the target antigen. The administration of billions of doses has resulted in great industry enthusiasm for the platform, and other mRNA products are being developed using the same core technology.[11,12]

To assess the novelty of COVID-19 mRNA products, we look at the history of mRNA vaccines, which begins with experiments on *in-vitro*-transcribed RNA, that is, delivering RNA to a cell for expression of a protein of interest. [13] Synthetic RNA technology has a wide variety of applications, from the delivery of small interfering RNAs (siRNAs) to reduce gene expression, or messenger RNAs (mRNAs) to encode for a protein of therapeutic value, or to encode for an antigen to stimulate an immune response, as in the strategy of mRNA vaccination (Supplementary Table SI).[1v4]

Early attempts to express proteins from injected mRNA faced several challenges.[35,36] First, bare RNA produces an inflammatory response, limiting the expression potential of the RNA, as it is broken down.[37] Secondly, it is difficult for the bare RNA to enter through a cell membrane.[38] These issues were addressed through the processes of pseudouridylation[39] and encapsulation of mRNA in a lipid nanoparticle (LNP), respectively.[40] The

former discovery decreased the lability of RNA, enabling it to remain in the body for longer periods of time.[41] The latter discovery not only shielded the RNA from the host's immune response, as well as from RNAses, but it also enabled efficient uptake by cells,[40,42] where it could be efficiently translated by host ribosomes. Pseudouridine was later replaced by Nl-methyl-pseudouridine,[43] owing to its greater translation fidelity, higher expression, and better evasion of the host immune response.[44]

LNP development was improved through two innovations, PEGylation,[45] and the use of cationic lipids.[46] (Figure 1) LNP surface modifications by polyethylene glycol (PEG) enable lipid nanoparticles to survive for longer lengths of time,[47] so that their package contents can be delivered to cells to provoke an immune response when the antigen is expressed.[48] Another important development for LNPs is the use of cationic lipids, enabling efficient self-assembly and encapsulation of the mRNA.[49] Cationic lipids can additionally be modified to deliver drugs to certain cell types, an important consideration when delivering mRNA.[50,51] Conventional liposome by lipid nanoparticles were the Pfizer-BioNTech BNT162b2 vaccine and the Moderna mRNA-1273 vaccines.[40]

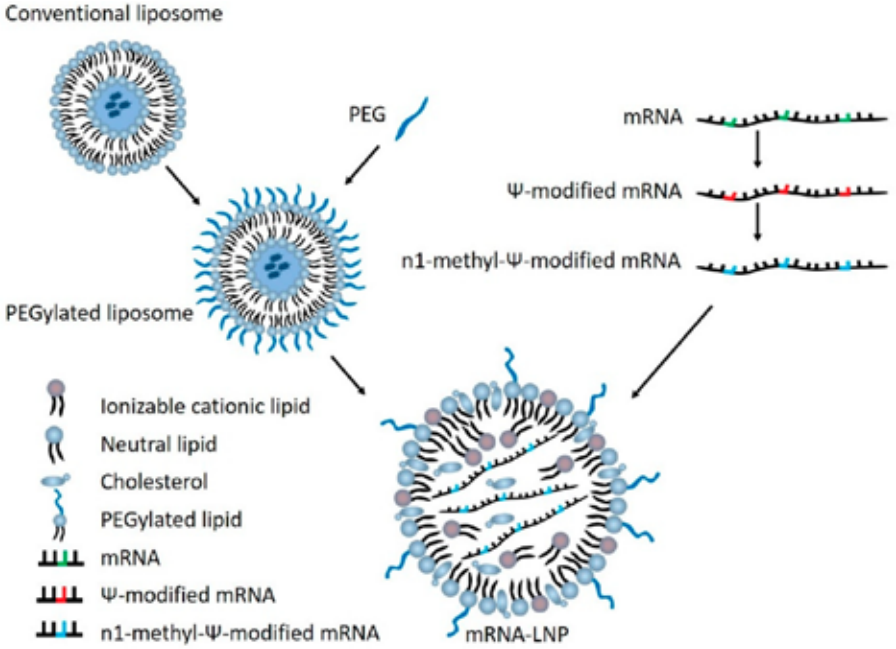


Figure 1. Overview of mRNA–LNP vaccine components.

Several of the assumptions have been either challenged or overturned by experimental[53] and clinical evidence.[54] Quoted theoretical safety advantages were the ease of production without contamination (mRNA vaccines do not require the use of live viruses),[55] and lower (in theory non-existent) risks of infection or host genome integration.[55,56] Beforehand, concerns existed over the induction of type I interferon responses by mRNA vaccines,[57,58] which are associated with inflammation and autoimmunity.[59,60]

For example, the dual assumptions that LNPs remain at the injection site, and that the mRNA degrades quickly, have been demonstrated to be false; biodistribution and bioaccumulation data indicate that LNPs can enter the bloodstream,[53] and studies have shown the durability of both mRNA and spike protein *in vivo* two months after injection.[61] Another study found circulating spike protein four months post-injection.[62] Given the novelty of mRNA vaccines, and the increasing evidence of harm from clinical reports,[54] epidemiology,[63] and laboratory science,[64] there are open safety concerns to be addressed by future research.

This review summarises known mechanisms of harm to mRNA vaccine recipients, where we examine historical data on mRNA vaccines to determine whether safety signals were apparent during production or testing. Prior to the trials on COVID-19 vaccines involving tens of thousands of people, public data exist on only 285 patients administered various mRNA vaccines, with the earliest trials finishing in 2018 and exhibiting high rates (>10%) of severe adverse events (Supplementary Table SI). The novelty of mRNA-LNP products must be stressed in guiding their safety assessment, as current approvals still leave many questions unanswered, and serious risks cannot be definitively ruled out based on current evidence.

In this review, we summarise what is known about the distinct components of mRNA vaccines, by reviewing the literature on past therapeutics. Additionally, we review the known safety effects of mRNA vaccines prior to COVID-19, as well as other coronavirus vaccines, which, while using a non-mRNA platform, inform us of safety risks when vaccinating against coronaviruses.

2. mRNA vaccine elements and potential for harm

2.1 Harms due to lipid nanoparticle (LNP)

Lipid nanoparticles have been used in the delivery of drugs for decades, beginning with the 1990 EU approval of the drug AmBisome (LNP-encapsulated amphotericin B) for fungal infections.[52] In the US environment, the first LNP-administered drugs were Doxil (LNP-encapsulated doxorubicin)

for Kaposi's sarcoma and Abelcet (LNP-encapsulated amphotericin B) for aspergillosis.[52]

The simplest form of LNP is a liposome, which is produced endogenously.[65] This consists merely of a lipid bilayer that separates the contents from the outside environment.[66] While simple liposomes are detected and destroyed by the body's immune system,[67,68] the addition of polyethylene glycol (PEG) enables the liposome to evade the host's immune response and last longer in the body to deliver the encapsulated product.[69] While PEG is often inert in the body, the injection of PEG does elicit anti-IgM antibodies, and subsequent injections containing PEG are cleared faster as a result of this immune response.[70] Additionally, a small proportion of the population has an allergy to PEG, and injection can trigger anaphylaxis, as did happen for several people receiving COVID-19 vaccines.[71,72,73,74]

The safety of 1,2-Distearoyl-Sn-Glycero-3-Phosphocholine (DSPC), a component of the LNP used in both the Pfizer and Moderna COVID-19 vaccines, has been studied.[75] Studies in mice ruled that it was likely not toxic to humans, as no clinical manifestations were present.[75] LNPs have been claimed as safe for the delivery of therapeutic agents, according to a review.[76] However, pro-inflammatory concerns remain over LNPs, even in isolation.[77,78]

2.2 Harms due to exogenous RNA

Foreign RNA triggers an inflammatory response, as toll-like receptors (TLR)[79] and retinoic acid-inducible gene I (RIG-I)[80] are activated. Extracellular RNA exists as a pro-coagulant,[81] and increases the permeability of the endothelial cells in brain microvasculature.[82] The initial reason for modification of the RNA by pseudouridylation was to bypass activation of TLR.[83] As pseudouridylated RNA was translated at lower fidelity than RNA,[84] the nucleosides were modified to Nl-methyl-pseudouridine, which brought translation fidelity to near that of RNA.[85]

The properties of both YRNA and Nl-mYRNA have been studied in some depth, though questions still remain. For example, through some application of the central dogma of molecular biology, it is assumed that RNA vaccines cannot be incorporated into the genome. This statement is not supported by experiments,[86] and is, in fact, contradicted by experiments showing reverse transcription of the Pfizer BioNTech COVID-19 mRNA vaccine into a human liver-cell line.[64]

YRNA exists in nature and comprises between 0.2% and 0.6% of uridine content in human cell lines, and has biologically significant differences from RNA.[87] While Nl-mYRNA exists in nature, found within archaea,[88] studies

on its properties go back only as recently as 2015.[44] Additionally, important biological differences exist between unmodified and modified RNA.

2.3. Harms due to *in-vitro*-transcribed (IVT) RNA

The next step in complexity is moving onto RNA therapeutics that are actively transcribed by host ribosomes. These applications typically replace a damaged protein of interest by supplying it exogenously.[89] Using an LNP-mRNA platform here is better than supplying the protein itself, as a protein expressed from IVT RNA is more likely to have the correct post-transcriptional modifications (and subsequent conformation) for its target cell type than an exogenously supplied protein.[90] For these applications, it is typically necessary for the drug to be administered repetitively over long time-periods.[90,91] With repetitive dosing, safety is very important, as even a low per-dose AE rate can compound over the many doses of the treatment.

Most studies of this therapeutic modality so far focus on drug efficacy, and limited safety data exist. In a 2021 review of non-immunologic application of mRNA, all studies using LNP-mRNA as protein replacement therapy demonstrated liver toxicity or lacked safety data.[90] Several studies also demonstrate the development of anti-drug antibodies (ADAs),[92,93,94] which can deactivate the drug and prevent treatment.[95,96,97,98] Immunemediated toxicity is also a cause for concern.[99,100]

Another concern is the potential development of cross-reactivity to endogenous proteins, which can occur if the endogenous protein possesses similar structural motifs to the protein expressed from the administered mRNA.[101] Thromboembolic events have been observed in ADA reactions.[96] Typically, ADA reactions are decreased in cases where the encoded protein is a 'self' protein, as opposed to an exogenous protein.[102]

Recent work demonstrated a class switch towards an IgG4 antibody response, observed after three doses of Pfizer BNT162b2 (COVID-19 vaccine) and not adenoviral vector COVID-19 vaccines,[103] and this raises concerns over possible immune tolerance, which is linked to an IgG4-dominated response.[104,105]

2.4 Harms of RNA vaccination

In addition to the other harms present in IVT RNAs, RNA vaccines also have the safety challenges of expressing an exogenous protein for the express purpose of generating an immune response and immune memory.[106] Of the RNA therapeutic systems introduced so far in this review, the mRNA vaccines are the most complex drug-like therapeutic biologic.

Limited safety data exist on RNA vaccines against infection[16-23] (Supplementary Table SI). Prior to the trials for COVID-19 vaccines, there were data on 285 patients, with the earliest trials on a non-HIV vaccine only completed in 2018. The serious adverse event (SAE) rate of these exploratory trials was 14 zb 2% (grade 3 or above). As a comparison, a post-marketing surveillance study of influenza vaccines in the UK found an SAE rate of 0.16%,[107] almost 100 times less than the SAE rate for mRNA vaccines.

Given their novelty, mRNA vaccines have limited long-term safety data. While the type of vaccination (that is, attenuated live virus, inactivated virus, mRNA) should not have a significant effect on the IgG antibodies produced, an important consideration must be mentioned: mRNA vaccines encode for a single antigen in most cases, which better enables immune escape rather than a broader antibody response including other proteins. Recent evidence revealed a subclass switch from IgGl to IgG4 in the context of the Comirnaty mRNA product, which may have consequences with regard to cancer,[108] pregnancy,[109] and IgG4-related diseases.[103,110] COVID-19 mRNA vaccines are commonly used in Europe and North America; these encode specifically and exclusively for the spike (S) protein.[111,112] Since the introduction of vaccines, mutations have occurred, lessening the neutralizing capacity of these vaccines.[113,114]

2.5 Harms of coronavirus vaccination

In addition to the considerations on the novelty of mRNA vaccines, the C19 mRNA vaccines are also unprecedented in terms of another quality, namely, they are the first coronavirus vaccines approved in humans. Following the 2002-2003 outbreak of SARS- CoV[115] and the 2012 outbreak of MERS-CoV,[116] vaccines against coronaviruses infecting humans gained more attention, and were subsequently tested on animal models as well as on human subjects.[117]

A SARS-CoV candidate vaccine given to ferrets elicited enhanced hepatitis. [118] Animal trials on four SARS vaccine candidates in ferrets demonstrated an initial protective period against infection, followed by hypersensitivity to rechallenge with SARS-CoV. The ferrets developed histopathological changes in the lungs induced from virus challenge after all four vaccine candidates, suggesting immune-mediated damage.[119] However, a study of MERS-CoV vaccines on mice and rhesus macaques[120] demonstrated protection without visible histopathology.

Mice given an inactivated virus later developed a pro-inflammatory pulmonary response upon challenge.[121] Anti-spike IgG antibodies are produced by all mRNA COVID- 19 vaccines,[122] and at significantly lower levels by other

COVID-19 vaccines.[123] Anti-spike IgG antibodies are demonstrated to cause severe acute lung injury in rhesus macaques on re-exposure to the virus, suggesting a negative effect of a narrow immune response.[124]

Immune-mediated danger from vaccines has been widely acknowledged to be an extant issue in the development of coronavirus vaccines,[125-131] and is supported by current evidence.[132] During the rapid development of COVID-19 vaccines, it was an issue of concern that sufficient long-term monitoring for antibody-dependent enhancement (ADE) be established.[133,134] Unfortunately, as of the time of writing, there are no data available on the long-term effects of COVID-19 vaccines, including effects resulting from rechallenge with the virus.

Veterinary vaccines for other coronaviruses are available, and are summarised in a recent review.[135] Evidence of immune-dependent enhancement was present for cell culture experiments on vaccination against feline coronaviruses.[136,137,138] ADE is also a concern for avian infectious bronchitis virus (IBV), a coronavirus.[139,140] In IBV, suboptimal vaccination alters the evolutionary dynamics of the viruses and can contribute to the production of escape mutants.[141,142,143] Finding broadly neutralizing IBV vaccines remains a substantial challenge for the poultry industry.[144-148]

Early canine coronavirus vaccines were withdrawn because of neurological symptoms,[149,150] though current vaccines do not carry the same safety issues.[151,152] Bovine coronavirus vaccinations often fail to provide immunity against subsequent reinfections.[153,154,155] Immunizations against transmissible gastroenteritis virus (TGEV) in swine have historically had issues in inducing immune protection,[156,157] but are widely used now. Too-frequent exposure to vaccine antigens can lower the immune response against TGEV.[158] Another swine coronavirus vaccine, porcine epidemic diarrhoea virus (PEDV), is widely used.[159] Extant safety concerns for the PEDV vaccine are minor, and mostly deal with lack of efficacy; these are summarised in a review.[159]

There were several human trials of coronavirus vaccines prior to the approval of COVID-19 vaccines (Table 1). In addition to the endemic corona viruses that infect humans, several epidemic strains of coronaviruses have occurred in the past two decades, namely, the coronaviruses associated with severe acute respiratory syndrome (SARS-CoV) in 2003[115] and Middle East respiratory syndrome (MERS-CoV) in 2012.[160] These outbreaks impelled the production of coronavirus vaccine candidates, summarised in a recent review[117] (Table 1). In total, before the development of the COVID-19 vaccines, data existed on a total of 179 human participants given a SARS or MERS vaccine candidate, of whom 7 (4 zb 2%) experienced a serious adverse event (Table 1). A human trial of 63 adults for a MERS vaccine candidate showed no severe adverse events, but infections in 36% of participants.[161,162]

Table 1. Summary of human trials of non-COVID-19 coronavirus vaccines. Adapted from.[117]

Platform	Vaccine	Group	Status	Severe Adverse Events	NCT ID	Study
SARS Vaccine Clinical Trials						
Inactivated virus	Inactivated SARS-CoV vaccine (ISCV)	Sinovac	Phase I, completed	[0/24, 0%]	No NCT ID	[163]
DNA vaccine	VRC-SRSDNA015-00-VP	NIAID	Phase I, completed	[0/9, 0%]	NCT00099463	[164]
MERS Vaccine Clinical Trials						
DNA vaccine	GLS-5300 (INO-4700)	GeneOne Life Science/Inovio Pharmaceuticals/International Vaccine Institute	Phase I, completed	[0/75, 0%] Infections in 36% of participants	NCT02670187	[162]
DNA vaccine	GLS-5300 (INO-4700)	GeneOne Life Science/Inovio Pharmaceuticals/International Vaccine Institute	Phase I/IIa, completed	No results available	NCT03721718	
Viral vector vaccine	MVA-MERS-S	CTC North GmbH & Co. KG	Phase I, completed	[0/23, 0%]	NCT03615911	[165]
Viral vector vaccine	MVA-MERS-S_DF1	CTC North GmbH & Co. KG	Phase Ib, not yet recruiting	No data	NCT04119440	[166]
Viral vector vaccine	ChAdOx1 MERS	University of Oxford	Phase I, recruiting	[1/24, 4%]	NCT03399578	[167]
Viral vector vaccine	ChAdOx1 MERS	King Abdullah International Medical Research Center/University of Oxford	Phase I, recruiting	[6/24, 25%]	NCT04170829	[168]
Viral vector vaccine	BVRS-GamVac-Combi	Gamaleya Research Institute of Epidemiology and Microbiology/Acellena Contract Drug Research and Development	Phase I/II, recruiting	No data	NCT04128059	
Viral vector vaccine	BVRS-GamVac	Gamaleya Research Institute of Epidemiology and Microbiology	Phase I/II, recruiting	No data	NCT04130594	

Studies of corona virus vaccines have a limited number of human participants and still represent a novel technique, though the recent implementation of large-scale vaccination programs for COVID-19 increases the data available to assess the safety of human coronavirus vaccines.

2.6 Harms of RNA vaccination with SARS-CoV-2 spike (S) antigen

There is reason to believe that vaccines encoding the spike (S) protein of SARS-CoV- 2 have additional mechanisms of harm, owing to the biological impacts of S protein specifically. There is some research in the literature,[169-172] and it is beyond the scope of this review to cover it in substantial depth. However, the addition of spike protein adds another factor in assessing the

complexity of RNA vaccines. The complexity and the uncertainties about possible harms are non-trivial and cannot be dismissed based on current data. This section briefly covers some of the hypothesised mechanisms of harm from spike-protein-encoding mRNA vaccines and the evidence for each from a clinical-epidemiological outlook, as well as any mechanistic data from laboratory work.

Several observations have been made that contradict fundamental claims of RNA vaccine safety. For example, it was assumed that the RNA was relatively labile and transient in the cell. However, several studies identified spike protein and vaccine mRNA months post-injection.[61,62] Spike protein has been shown in laboratory settings to cause inflammation[173,174] and vascular damage,[175] and to act as a seed for amyloid formation.[176]

3. Discussion

There is limited information to make a safety assessment of mRNA vaccines. In the category of mRNA vaccines, there are patient data for 385 patients. For mRNA vaccines against an infection, there are data for 285 patients. The rate of serious adverse events was 64 out of 385 for the broad category of RNA vaccines (including cancer vaccines), or 17%; restricting the definition to vaccines against infection, the rate of SAEs is 41/285 or 14%. While high levels can be expected for trials of a novel technology where dosage levels must be determined (many of these trials are phase I),[177] these findings showcase the relative immaturity of mRNA vaccination as a strategy. Given the low efficacy and short duration of protection of SARS-CoV-2 mRNA products,[178,179] and the low risk of many populations from COVID-19 complications,[180] it may be advisable to suspend mRNA vaccines in certain risk cohorts.

The key to the reactivity of mRNA vaccines is the fact that they express a foreign antigen, for which the antigen-presenting cells are marked for destruction. While the lipid nanoparticle exhibits an acute inflammatory response by itself,[77,78,181] the trials using LNPs, so far, have not found a large safety signal when using LNPs to deliver small molecules, non-expressing RNAs, or RNAs for endogenous proteins.[77,78,181] In addition to there being harms attributable to the general immune response from an LNP-RNA delivery system, there are also some harms specific to the spike protein. Several of these mechanisms are supported by laboratory experiments and clinical findings, but need more investigation. Medicine is replete with cases for which safety was assumed without adequate evidence at the time, which later regrettably led to loss of health and life. mRNA vaccines are demonstrating great unintended harms, and these harms demand further investigation into the mechanisms, which is important for identifying treatment modalities.

Novel biomedical technologies can bring relief for a wide variety of conditions and diseases. However, their use must take into consideration their possible harms. Here, we argue that the mRNA technology is novel enough that safety concerns in current and future products cannot be definitively ruled out, and further research must be performed to ensure their safety for current and future users.

Other vaccine platforms have longer-term data on their mechanisms, and these have fewer unknown long-term effects. Considering the lack of data on the platform itself, we recommend a robust, independent, and wide-ranging safety audit of mRNA-LNP formulations, and we call on regulators to hold manufacturers to high safety standards, especially for products used prophylactically in the general population.

Supplementary Materials: The following supporting information can be downloaded at: https:/ /www.mdpi.com/article/10.3390/j6020017/si. Table SI: Safety profile of previous LNP-mRNA products.

Author Contributions: Conceptualization, M.T.J.H.; writing—original draft preparation, M.T.J.H.; research, M.T.J.H., J.R. and T.L.; writing—review and editing, M.T.J.H., J.R. and T.L.; supervision, M.T.J.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: We thank Cristof Plothe for his comments.

Conflicts of Interest: M.T.J.H and T.L. are members of The World Council for Health, a non-profit organisation for holistic health promotion.

4. References

[1] Nagaich, U.; Sadhna, D. Drug Recall: An Incubus for Pharmaceutical Companies and Most Serious Drug Recall of History. *Int. J. Pharm. Investig.* 2015, 5,13-19. [CrossRef] [PubMed]Wang, B.; Gagne, J.J.; Choudhry, N.K. The Epidemiology of Drug Recalls in the United States. *Arch. Intern. Med.* 2012, *172,* 1109-1110. [CrossRef] [PubMed]

[2] Hwang, T.J.; Sokolov, E.; Franklin, J.M.; Kesselheim, A.S. Comparison of Rates of Safety Issues and Reporting of Trial Outcomes for Medical Devices Approved in the European Union and United States: Cohort Study. *BMJ* 2016, 353, i3323. [CrossRef] [PubMed]

[3] Vajapey, S.P.; Li, M. Medical Device Recalls in Orthopedics: Recent Trends and Areas for Improvement. *J. Arthroplast.* 2020, 35, 2259-2266. [CrossRef]

[4] Young, R.; Bekele, T.; Gunn, A.; Chapman, N.; Chowdhary, V.; Corrigan, K.; Dahora, L.; Martinez, S.; Permar, S.; Persson, J.; et al. Developing New Health Technologies for Neglected Diseases: A Pipeline Portfolio Review and Cost Model. *Gates Open Res.* 2020, 2, 23. [CrossRef]

[5] Dowden, H.; Munro, J. Trends in Clinical Success Rates and Therapeutic Focus. *Nat. Rev. Drug Discov.* 2019, *18,* 495-496. [CrossRef]

[6] Wong, C.H.; Siah, K.W.; Lo, A.W. Estimation of Clinical Trial Success Rates and Related Parameters. *Biostatistics* 2019, *20,* 273-286. [CrossRef]

[7] Dahlin, E.; Nelson, G.M.; Haynes, M.; Sargeant, F. Success Rates for Product Development Strategies in New Drug Development. *J. Clin. Pharm. Ther.* 2016, *41,*198-202. [CrossRef]

[8] Hayes, A.W. The Precautionary Principle. *Arh. Hig. Rada Toksikol.* 2005, 56,161-166.

[9] Ball, P. The Lightning-Fast Quest for COVID Vaccines—And What It Means for Other Diseases. *Nature* 2020,*589,*16-18. [CrossRef]

[10] Le, T.; Sun, C.; Chang, J.; Zhang, G.; Yin, X. MRNA Vaccine Development for Emerging Animal and Zoonotic Diseases. *Viruses* 2022,*14,*401. [CrossRef] [PubMed]

[11] Ladak, R.J.; He, A.J.; Huang, Y.-H.; Ding, Y. The Current Landscape of MRNA Vaccines Against Viruses and Cancer-A Mini Review. *Front. Immunol* 2022,*13,* 885371. [CrossRef] [PubMed]

[12] Dolgin, E. The Tangled History of MRNA Vaccines. *Nature* **2021,** *597,* 318-324. [CrossRef] [PubMed]

[13] Mu, X.; Hur, S. Immunogenicity of In Vitro-Transcribed RNA. *Ace. Chem. Res.* **2021,** *54,* 4012-4023. [CrossRef]

[14] Guo, S.; Li, H.; Ma, M.; Fu, J.; Dong, Y.; Guo, P. Size, Shape, and Sequence-Dependent Immunogenicity of RNA Nanoparticles. *Mol. Ther. Nucleic Acids* **2017,** *9,* 399-408. [CrossRef]

[15] Wadhwa, A.; Aljabbari, A.; Lokras, A.; Foged, C.; Thakur, A. Opportunities and Challenges in the Delivery of MRNA-Based Vaccines. *Pharmaceutics* 2020,*12,*102. [CrossRef]

[16] Pandey, M.; Ojha, D.; Bansal, S.; Rode, A.B.; Chawla, G. From Bench Side to Clinic: Potential and Challenges of RNA Vaccines and Therapeutics in Infectious Diseases. *Mol. Asp. Med.* **2021,** *81,*101003. [CrossRef]

[17] Anderson, B.R.; Muramatsu, H.; Nallagatla, S.R.; Bevilacqua, PC.; Sansing, L.H.; Weissman, D.; Kariko, K. Incorporation of Pseudouridine into MRNA Enhances Translation by Diminishing PKR Activation. *Nucleic Acids Res.* **2010,** *38,* 5884-5892. [CrossRef]

[18] Hou, X.; Zaks, T.; Langer, R.; Dong, Y. Lipid Nanoparticles for MRNA Delivery. *Nat. Rev. Mater.* **2021,** *6,*1078-1094. [CrossRef]

[19] Morais, P.; Adachi, H.; Yu, Y.-T. The Critical Contribution of Pseudouridine to MRNA COVID-19 Vaccines. *Front. Cell Dev. Biol.* 2021, *9,* 789427. [CrossRef]

[20] Strachan, J.B.; Dyett, B.P.; Nasa, Z.; Valery, C.; Conn, C.E. Toxicity and Cellular Uptake of Lipid Nanoparticles of Different Structure and Composition. *J. Colloid Interface Sci.* 2020, *576,* 241-251. [CrossRef] [PubMed]

[21] Nance, K.D.; Meier, J.L. Modifications in an Emergency: The Role of Nl-Methylpseudouridine in COVID-19 Vaccines. *ACS Cent. Sci.* **2021,** 7, 748-756. [CrossRef] [PubMed]

[22] Andries, O.; Me Cafferty, S.; De Smedt, S.C.; Weiss, R.; Sanders, N.N.; Kitada, T. N(l)-Methylpseudouridine-Incorporated MRNA Outperforms Pseudouridine-Incorporated MRNA by Providing Enhanced Protein Expression and Reduced Immunogenicity in Mammalian Cell Lines and Mice. *J. Control. Release* **2015,** *217,* 337-344. [CrossRef] [PubMed]

[23] Suk, J.S.; Xu, Q.; Kim, N.; Hanes, J.; Ensign, L.M. PEGylation as a Strategy for Improving Nanoparticle-Based Drug and Gene Delivery. *Adv. Drug Deliv. Rev.* **2016,** *99,* 28-51. [CrossRef] [PubMed]

[24] Kulkarni, J.A.; Darjuan, M.M.; Mercer, J.E.; Chen, S.; van der Meel, R.; Thewalt, J.L.; Tam, Y.Y.C.; Cullis, PR. On the Formation and Morphology of Lipid Nanoparticles Containing Ionizable Cationic Lipids and SiRNA. *ACS Nano* **2018,***12,*4787-4795. [CrossRef] [PubMed]

[25] Yuan, H.; Chen, C.-Y.; Chai, G.; Du, Y.-Z.; Hu, F.-Q. Improved Transport and Absorption through Gastrointestinal Tract by PEGylated Solid Lipid Nanoparticles. *Mol. Pharm.* **2013,***10,*1865-1873. [CrossRef] [PubMed]

[26] Teijaro, J.R.; Farber, D.L. COVID-19 Vaccines: Modes of Immune Activation and Future Challenges. *Nat. Rev. Immunol.* **2021,** *21,* 195-197. [CrossRef]

[27] Brader, M.L.; Williams, S.J.; Banks, J.M.; Hui, W.H.; Zhou, Z.H.; Jin, L. Encapsulation State of Messenger RNA inside Lipid Nanoparticles. *Biophys. J.* **2021,***120,* 2766-2770. [CrossRef]

[28] Kim, M.; Jeong, M.; Hur, S.; Cho, Y.; Park, J.; Jung, H.; Seo, Y.; Woo, H.A.; Nam, K.T.; Lee, K.; et al. Engineered Ionizable Lipid Nanoparticles for Targeted Delivery of RNA Therapeutics into Different Types of Cells in the Liver. *Sci. Adv.* **2021,** 7, eabf4398. [CrossRef]

[29] Han, X.; Zhang, H.; Butowska, K.; Swingle, K.L.; Alameh, M.-G.; Weissman, D.; Mitchell, M.J. An Ionizable Lipid Toolbox for RNA Delivery. *Nat. Commun.* **2021,***12,* 7233. [CrossRef]

[30] Akinc, A.; Maier, M.A.; Manoharan, M.; Fitzgerald, K.; Jayaraman, M.; Barros, S.; Ansell, S.; Du, X.; Hope, M.J.; Madden, T.D.; et al. The Onpattro Story and the Clinical Translation of Nanomedicines Containing Nucleic Acid-Based Drugs. *Nat. Nanotechnol.* **2019,** *14,*1084-1087. [CrossRef] [PubMed]

[31] Ogata, A.F.; Cheng, C.-A.; Desjardins, M.; Senussi, Y.; Sherman, A.C.; Powell, M.; Novack, L.; Von, S.; Li, X.; Baden, L.R.; et al. Circulating Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccine Antigen Detected in the Plasma of MRNA-1273 Vaccine Recipients. *Clin. Infect. Dis.* 2022, 74, 715-718. [CrossRef]

[32] Deb, A.; Abdelmalek, J.; Iwuji, K.; Nugent, K. Acute Myocardial Injury Following COVID-19 Vaccination: A Case Report and Review of Current Evidence from Vaccine Adverse Events Reporting System Database. *J. Prim. Care Community Health* **2021,** *12,* 21501327211029230. [CrossRef]

[33] Pardi, N.; Hogan, M.J.; Porter, F.W.; Weissman, D. MRNA Vaccines—A New Era in Vaccinology. *Nat. Rev. Drug Discov.* **2018,***17,* 261-279. [CrossRef]

[34] Park, J.W.; Lagniton, P.N.P.; Liu, Y.; Xu, R.-H. MRNA Vaccines for COVID-19: What, Why and How. *Int. J. Biol. Sci.* **2021,***17,* 1446-1460. [CrossRef] [PubMed]

[35] Pepini, T.; Pulichino, A.-M.; Carsillo, T.; Carlson, A.L.; Sari-Sarraf, F.; Ramsauer, K.; Debasitis, J.C.; Maruggi, G.; Often, G.R.; Geall, A.J.; et al. Induction of an IFN-Mediated Antiviral Response by a Self-Amplifying RNA Vaccine: Implications for Vaccine Design. *J. Immunol.* **2017,***198,* 4012-4024. [CrossRef] [PubMed]

[36] Edwards, D.K.; Jasny, E.; Yoon, EL; Horscroft, N.; Schanen, B.; Geter, T.; Fotin-Mleczek, M.; Petsch, B.; Wittman, V. Adjuvant Effects of a Sequence-Engineered MRNA Vaccine: Translational Profiling Demonstrates Similar Human and Murine Innate Response. *J. Transl. Med.* **2017,***15,*1. [CrossRef]

[37] Theofilopoulos, A.N.; Baccala, R.; Beutler, B.; Kono, D.H. Type I Interferons *(oc/* (3) in Immunity and Autoimmunity. *Annu. Rev. Immunol.* **2005,** 23, 307-335. [CrossRef]

[38] Nestle, F.O.; Conrad, C.; Tun-Kyi, A.; Homey, B.; Gombert, M.; Boyman, O.; Burg, G.; Liu, Y.-J.; Gilliet, M. Plasmacytoid Predendritic Cells Initiate Psoriasis through Interferon-a Production. *J. Exp. Med.* **2005,** *202,*135-143. [CrossRef]

[39] Roltgen, K.; Nielsen, S.C.A.; Silva, O.; Younes, S.F.; Zaslavsky, M.; Costales, C.; Yang, F.; Wirz, O.F.; Solis, D.; Hoh, R.A.; et al. Immune Imprinting, Breadth of Variant Recognition, and Germinal Center Response in Human SARS-CoV-2 Infection and Vaccination. *Cell* 2022,*185,*1025-1040.el4. [CrossRef]

[40] Bansal, S.; Perincheri, S.; Fleming, T.; Poulson, C.; Tiffany, B.; Bremner, R.M.; Mohanakumar, T. Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer-BioNTech) Vaccination Prior to Development of Antibodies: A Novel Mechanism for Immune Activation by MRNA Vaccines. *J. Immunol.* **2021,** *207,* 2405-2410. [CrossRef] [PubMed]

[41] Welsh, K.J.; Baumblatt, J.; Chege, W.; Goud, R.; Nair, N. Thrombocytopenia Including Immune Thrombocytopenia after Receipt of MRNA COVID-19 Vaccines Reported to the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* **2021,** *39,3329-3332.* [CrossRef] [PubMed]

[42] Alden, M.; Olofsson Falla, F.; Yang, D.; Barghouth, M.; Luan, C.; Rasmussen, M.; De Marinis, Y. Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 MRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line. *Curr. Issues Mol. Biol.* 2022, *44,* 1115-1126. [CrossRef] [PubMed]

[43] Tenchov, R.; Bird, R.; Curtze, A.E.; Zhou, Q. Lipid Nanoparticles-From Liposomes to MRNA Vaccine Delivery, a Landscape of Research Diversity and Advancement. *ACS Nano* **2021,***15,*16982-17015. [CrossRef]

[44] Nsairat, H.; Khater, D.; Sayed, U.; Odeh, F.; Al Bawab, A.; Alshaer, W. Liposomes: Structure, Composition, Types, and Clinical Applications. *Heliyon* 2022, *8,* e09394. [CrossRef] [PubMed]

[45] Harashima, H.; Hiraiwa, T.; Ochi, Y.; Kiwada, H. Size Dependent Liposome Degradation in Blood: In Vivo/In Vitro Correlation by Kinetic Modeling. *J. Drug Target.* **1995,** *3,* 253-261. [CrossRef]

[46] Vemuri, S.; Rhodes, C.T. Preparation and Characterization of Liposomes as Therapeutic Delivery Systems: A Review. *Pharm. Acta Helv.* **1995,** *70,* 95-111. [CrossRef]

[47] Hattori, Y. Delivery of Plasmid DNA into Tumors by Intravenous Injection of PEGylated Cationic Lipoplexes into Tumor-Bearing Mice. *Pharmacol. Pharm.* **2016,** 7, 272-282. [CrossRef]

[48] Wang, X.; Ishida, T.; Kiwada, H. Anti-PEG IgM Elicited by Injection of Liposomes Is Involved in the Enhanced Blood Clearance of a Subsequent Dose of PEGylated Liposomes. *J. Control. Release* **2007,***119,* 236-244. [CrossRef]

[49] Kuehn, B.M. Rare PEG Allergy Triggered Postvaccination Anaphylaxis. *JAMA* **2021,** *325,*1931. [CrossRef]

[50] Cox, F.; Khalib, K.; Conlon, N. PEG That Reaction: A Case Series of Allergy to Polyethylene Glycol. *J. Clin. Pharmacol.* **2021,** *61,* 832-835. [CrossRef] [PubMed]

[51] Sellaturay, P; Nasser, S.; Ewan, P. Polyethylene Glycol-Induced Systemic Allergic Reactions (Anaphylaxis). *J. Allergy Clin. Immunol. Pract.* **2021,** *9,* 670-675. [CrossRef] [PubMed]

[52] Castells, M.C.; Phillips, E.J. Maintaining Safety with SARS-CoV-2 Vaccines. *N. Engl. J. Med.* 2020, *384,* 643-649. [CrossRef] [PubMed]

[53] Ohgoda, O.; Robinson, I. Toxicological Evaluation of DSPC (1,2-Distearoyl-Sn-Glycero- 3-Phosphocholine). *Fundam. Toxicol. Sci.* 2020, 7, 55-76. [CrossRef]

[54] Doktorovova, S.; Kovacevic, A.B.; Garcia, M.L.; Souto, E.B. Preclinical Safety of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers: Current Evidence from in Vitro and in Vivo Evaluation. *Eur. J. Pharm. Biopharm.* **2016,***108,* 235-252. [CrossRef]

[55] Moghimi, S.M.; Simberg, D. Pro-Inflammatory Concerns with Lipid Nanoparticles. *Mol. Ther.* ***2022****, 30,* 2109-2110. [CrossRef]

[56] Ndeupen, S.; Qin, Z.; Jacobsen, S.; Bouteau, A.; Estanbouli, H.; Igyarto, B.Z. The MRNA-LNP Platform's Lipid Nanoparticle Component Used in Preclinical Vaccine Studies Is Highly Inflammatory. *iScience* **2021,** 24,103479. [CrossRef]

[57] Kawasaki, T.; Kawai, T. Toll-Like Receptor Signaling Pathways. *Front. Immunol.* 2014, *5,*461. [CrossRef]

[58] Wienert, B.; Shin, J.; Zelin, E.; Pestal, K.; Corn, J.E. In Vitro-Transcribed Guide RNAs Trigger an Innate Immune Response via the RIG-I Pathway. *PEoS Biol.* **2018,***16,* e2005840. [CrossRef]

[59] Kannemeier, C.; Shibamiya, A.; Nakazawa, F.; Trusheim, H.; Ruppert, C.; Markart, P; Song, Y.; Tzima, E.; Kennerknecht, E.; Niepmann, M.; et al. Extracellular RNA Constitutes a Natural Procoagulant Cofactor in Blood Coagulation. *Proc. Natl. Acad. Sci. USA* **2007,***104,* 6388-6393. [CrossRef]

[60] Fischer, S.; Gerriets, T.; Wessels, C.; Walberer, M.; Kostin, S.; Stolz, E.; Zheleva, K.; Hocke, A.; Hippenstiel, S.; Preissner, K.T. Extracellular RNA Mediates Endothelial-Cell Permeability via Vascular Endothelial Growth Factor. *Blood* **2007,***110,* 2457-2465. [CrossRef] [PubMed]

[61] Kariko, K.; Buckstein, M.; Ni, H.; Weissman, D. Suppression of RNA Recognition by Toll-like Receptors: The Impact of Nucleoside Modification and the Evolutionary Origin of RNA. *Immunity* **2005,** 23,165-175. [CrossRef] [PubMed]

[62] Eyler, D.E.; Franco, M.K.; Batool, Z.; Wu, M.Z.; Dubuke, M.L.; Dobosz-Bartoszek, M.; Jones, J.D.; Polikanov, Y.S.; Roy, B.; Koutmou, K.S. Pseudouridinylation of MRNA Coding Sequences Alters Translation. *Proc. Natl. Acad. Sci. USA* **2019,** *116,* 23068-23074. [CrossRef] [PubMed]

[63] Kim, K.Q.; Burgute, B.D.; Tzeng, S.-C.; Jing, C.; Jungers, C.; Zhang, J.; Yan, L.L.; Vierstra, R.D.; F>j'uranovic, S.; Evans, B.S.; et al. Nl-Methylpseudouridine Found within COVID-19 MRNA Vaccines Produces Faithful Protein Products. *Cell Rep.* 2022,*40,*111300. [CrossRef]

[64] Domazet-Loso, T. MRNA Vaccines: Why Is the Biology of Retroposition Ignored? *Genes* 2022,*13,* 719. [CrossRef]

[65] Borchardt, E.K.; Martinez, N.M.; Gilbert, W.V. Regulation and Function of RNA Pseudouridylation in Human Cells. *Annu. Rev. Genet.* 2020, *54,* 309-336. [CrossRef]

[66] Pang, H.; Ihara, M.; Kuchino, Y.; Nishimura, S.; Gupta, R.; Woese, C.R.; McCloskey, J.A. Structure of a Modified Nucleoside in Archaebacterial TRNA Which Replaces Ribosylthymine. 1-Methylpseudouridine. /. *Biol. Chem.* **1982,** 257, 3589-3592. [CrossRef]

[67] Kwon, H.; Kim, M.; Seo, Y.; Moon, Y.S.; Fee, H.J.; Fee, K.; Fee, H. Emergence of Synthetic MRNA: In Vitro Synthesis of MRNA and Its Applications in Regenerative Medicine. *Biomaterials* **2018,***156,*172-193. [CrossRef]

[68] Vlatkovic, I. Non-Immunotherapy Application of FNP-MRNA: Maximizing Efficacy and Safety. *Biomedicines* **2021,** 9, 530. [CrossRef]

[69] Kowalski, PS.; Rudra, A.; Miao, L.; Anderson, D.G. Delivering the Messenger: Advances in Technologies for Therapeutic MRNA Delivery. *Mol. Ther.* **2019,** 27, 710-728. [CrossRef]

[70] Zhu, X.; Yin, F.; Theisen, M.; Zhuo, J.; Siddiqui, S.; Fevy, B.; Presnyak, V.; Frassetto, A.; Milton, J.; Salerno, T.; et al. Systemic MRNA Therapy for the Treatment of Fabry Disease: Preclinical Studies in Wild-Type Mice, Fabry Mouse Model, and Wild-Type Non-Human Primates. *Am. J. Hum. Genet.* **2019,***104,* 625-637. [CrossRef] [PubMed]

[71] An, D.; Schneller, J.L.; Frassetto, A.; Liang, S.; Zhu, X.; Park, J.-S.; Theisen, M.; Hong, S.-J.; Zhou, J.; Rajendran, R.; et al. Systemic Messenger RNA Therapy as a Treatment for Methylmalonic Acidemia. *Cell Rep.* 2018, 24, 2520. [CrossRef] [PubMed]

[72] Jiang, L.; Berraondo, P; Jerico, D.; Guey, L.T.; Sampedro, A.; Frassetto, A.; Benenato, K.E.; Burke, K.; Santamaria, E.; Alegre, M.; et al. Systemic Messenger RNA as an Etiological Treatment for Acute Intermittent Porphyria. *Nat. Med.* **2018,** 24, 1899-1909. [CrossRef]

[73] Bartelds, G.M.; Krieckaert, C.L.M.; Nurmohamed, M.T.; van Schouwenburg, P.A.; Lems, W.F.; Twisk, J.W.R.; Dijkmans, B.A.C.; Aarden, L.; Wolbink, G.J. Development of Antidrug Antibodies against Adalimumab and Association with Disease Activity and Treatment Failure during Long-Term Follow-Up. *JAMA* **2011,** *305,*1460-1468. [CrossRef] [PubMed]

[74] Moots, R.J.; Xavier, R.M.; Mok, C.C.; Rahman, M.U.; Tsai, W.-C.; Al-Maini, M.H.; Pavelka, K.; Mahgoub, E.; Kotak, S.; Korth-Bradley, J.; et al. The Impact of Anti-Drug Antibodies on Drug Concentrations and Clinical Outcomes in Rheumatoid Arthritis Patients Treated with Adalimumab, Etanercept, or Infliximab: Results from a Multinational, Real-World Clinical Practice, Non-Interventional Study. *PLoS ONE* **2017,***12,* e0175207. [CrossRef]

[75] Pratt, K.P Anti-Drug Antibodies: Emerging Approaches to Predict, Reduce or Reverse Biotherapeutic Immunogenicity. *Antibodies* 2018, 7,19. [CrossRef] [PubMed]

[76] Krishna, M.; Nadler, S.G. Immunogenicity to Biotherapeutics—The Role of Anti-Drug Immune Complexes. *Front. Immunol.* **2016,** 7, 21. [CrossRef]

[77] Clarke, J.B. Mechanisms of Adverse Drug Reactions to Biologies. In *Handbook of Experimental Pharmacology;* Springer: Berlin/Heidelberg, Germany, 2010; pp. 453-474. [CrossRef]

[78] Pichler, W.J. Adverse Side-Effects to Biological Agents. *Allergy* **2006,** *61,* 912-920. [CrossRef]

[79] Sathish, J.G.; Sethu, S.; Bielsky, M.-C.; de Haan, L.; French, N.S.; Govindappa, K.; Green, J.; Griffiths, C.E.M.; Holgate, S.; Jones, D.; et al. Challenges and Approaches for the Development of Safer Immunomodulatory Biologies. *Nat. Rev. Drug Discov.* **2013,***12,* 306-324. [CrossRef]

[80] Banugaria, S.G.; Prater, S.N.; Ng, Y.-K.; Kobori, J.A.; Finkel, R.S.; Ladda, R.L.; Chen, Y.-T.; Rosenberg, A.S.; Kishnani, PS. The Impact of Antibodies on Clinical Outcomes in Diseases Treated with Therapeutic Protein: Lessons Learned from Infantile Pompe Disease. *Genet. Med.* **2011,***13,* 729-736. [CrossRef]

[81] Irrgang, R; Gerling, J.; Kocher, K.; Lapuente, D.; Steininger, R; Habenicht, K.; Wytopil, M.; Beileke, S.; Schafer, S.; Zhong, J.; et al. Class Switch towards Non-Inflammatory, Spike-Specific IgG4 Antibodies after Repeated SARS-CoV-2 MRNA Vaccination. *Sci. Immunol.* 2022, *8,* eade2798. [CrossRef] [PubMed]

[82] Vidarsson, G.; Dekkers, G.; Rispens, T. IgG Subclasses and Allotypes: From Structure to Effector Functions. *Front. Immunol.* **2014,** *5,* 520. [CrossRef] [PubMed]

[83] Bianchini, R.; Roth-Walter, F.; Ohradanova-Repic, A.; Flicker, S.; Hufnagl, K.; Fischer, M.B.; Stockinger, H.; Jensen-Jarolim, E. IgG4 Drives M2a Macrophages to a Regulatory M2b-like Phenotype: Potential Implication in Immune Tolerance. *Allergy* **2019,** 74, 483-494. [CrossRef] [PubMed]

[84] Chaudhary, N.; Weissman, D.; Whitehead, K.A. MRNA Vaccines for Infectious Diseases: Principles, Delivery and Clinical Translation. *Nat. Rev. Drug Discov.* **2021,** *20,* 817-838. [CrossRef]

[85] Suhr, O.B.; Coelho, T.; Buades, J.; Pouget, J.; Conceicao, I.; Berk, J.; Schmidt, H.; Waddington-Cruz, M.; Campistol, J.M.; Bettencourt, B.R.; et al. Efficacy and Safety of Patisiran for Familial Amyloidotic Polyneuropathy: A Phase II Multi-Dose Study. *Orphanet J. Rare Dis.* **2015,***10,*109. [CrossRef]

[86] Balwani, M.; Sardh, E.; Ventura, P.; Peiro, P.A.; Rees, D.C.; Stolzel, U.; Bissell, D.M.; Bonkovsky, H.L.; Windyga, J.; Anderson, K.E.; et al. Phase 3 Trial of RNAi Therapeutic Givosiran for Acute Intermittent Porphyria. *N. Engl. J. Med.* 2020, *382,* 2289-2301. [CrossRef]

[87] Alberer, M.; Gnad-Vogt, U.; Hong, H.S.; Mehr, K.T.; Backert, L.; Finak, G.; Gottardo, R.; Bica, M.A.; Garofano, A.; Koch, S.D.; et al. Safety and Immunogenicity of a MRNA Rabies Vaccine in Healthy Adults: An Open-Label, Non-Randomised, Prospective, First-in-Human Phase 1 Clinical Trial. *Lancet* **2017,** *390,*1511-1520. [CrossRef]

[88] Aldrich, C.; Leroux-Roels, I.; Huang, K.B.; Bica, M.A.; Loeliger, E.; Schoenborn-Kellenberger, O.; Walz, L.; Leroux-Roels, G.; von Sonnenburg, F.; Oostvogels, L. Proof-of-Concept of a Low-Dose Unmodified MRNA-Based Rabies Vaccine Formulated with Lipid Nanoparticles in Human Volunteers: A Phase 1 Trial. *Vaccine* **2021,** *39,*1310-1318. [CrossRef]

[89] Feldman, R.A.; Fuhr, R.; Smolenov, I.; Ribeiro, A.M.; Panther, L.; Watson, M.; Senn, J.J.; Smith, M.; Almarsson, 6.; Pujar, H.S.; et al. MRNA Vaccines against H10N8 and H7N9 Influenza Viruses of Pandemic Potential Are Immunogenic and Well Tolerated in Healthy Adults in Phase 1 Randomized Clinical Trials. *Vaccine* **2019,** *37,* 3326-3334. [CrossRef]

[90] Bahl, K.; Senn, J.J.; Yuzhakov, O.; Bulychev, A.; Brito, L.A.; Hassett, K.J.; Laska, M.E.; Smith, M.; Almarsson, O.; Thompson, J.; et al. Preclinical and Clinical Demonstration of Immunogenicity by MRNA Vaccines against H10N8 and H7N9 Influenza Viruses. *Mol. Ther.* **2017,** *25*,1316-1327. [CrossRef]

[91] Jacobson, J.M.; Routy, J.-P; Welles, S.; DeBenedette, M.; Tcherepanova, I.; Angel, J.B.; Asmuth, D.M.; Stein, D.K.; Baril, J.-G.; McKellar, M.; et al. Dendritic Cell Immunotherapy for HIV-1 Infection Using Autologous HIV-1 RNA: A Randomized, Double- Blind, Placebo-Controlled Clinical Trial. *J. Acquir. Immune Defic. Syndr.* **2016,** 72, 31-38. [CrossRef] [PubMed]

[92] de Jong, W.; Aerts, J.; Allard, S.; Brander, C.; Buyze, J.; Florence, E.; van Gorp, E.; Vanham, G.; Leal, L.; Mothe, B.; et al. IHIVARNA Phase Ha, a Randomized, Placebo-Controlled, Double-Blinded Trial to Evaluate the Safety and Immunogenicity of IHIVARNA-01 in Chronically HIV-Infected Patients under Stable Combined Antiretroviral Therapy. *Trials* **2019,** *20,* 361. [CrossRef] [PubMed]

[93] Leal, L.; Guardo, A.C.; Moron-Lopez, S.; Salgado, M.; Mothe, B.; Heirman, C.; Pannus, P; Vanham, G.; van den Ham, H.J.; Gruters, R.; et al. Phase I Clinical Trial of an Intranodally Administered MRNA-Based Therapeutic Vaccine against HIV-1 Infection. *AIDS* **2018,** *32,* 2533-2545. [CrossRef] [PubMed]

[94] Gandhi, R.T.; Kwon, D.S.; Macklin, E.A.; Shopis, J.R.; McLean, A.P; McBrine, N.; Flynn, T.; Peter, L.; Sbrolla, A.; Kaufmann, D.E.; et al. Immunization of HIV-1-Infected Persons With Autologous Dendritic Cells Transfected With MRNA Encoding HIV-1 Gag and Nef: Results of a Randomized, Placebo-Controlled Clinical Trial. *JAIDS J. Acquir. Immune Defic. Syndr.* **2016,** *71,* 246-253. [CrossRef]

[95] Sahin, U.; Oehm, P; Derhovanessian, E.; Jabulowsky, R.A.; Vormehr, M.; Gold, M.; Maurus, D.; Schwarck-Kokarakis, D.; Kuhn, A.N.; Omokoko, T.; et al. An RNA Vaccine Drives Immunity in Check-point-Inhibitor-Treated Melanoma. *Nature* 2020, *585,* 107-112. [CrossRef]

[96] Papachristofilou, A.; Hipp, M.M.; Klinkhardt, U.; Frith, M.; Sebastian, M.; Weiss, C.; Pless, M.; Cathomas, R.; Hilbe, W.; Pall, G.; et al. Phase lb Evaluation of a Self-Adjuvanted Protamine Formulated MRNA-Based Active Cancer Immunother- apy, BI1361849 (CV9202), Combined with Local Radiation Treatment in Patients with Stage IV Non-Small Cell Lung Cancer. *J. Immunother. Cancer* **2019,** 7, 38. [CrossRef]

[97] Eigentler, T.; Bauernfeind, F.G.; Becker, J.C.; Brossart, P; Fluck, M.; Heinzerling, L.; Krauss, J.; Mohr, P; Ochsenreither, S.; Schreiber, J.S.; et al. A Phase I Dose-Escalation and Expansion Study of Intratumoral CV8102 as Single-Agent or in Combination with Anti-PD-1 Antibodies in Patients with Advanced Solid Tumors. *JCO* 2020, *38,* 3096. [CrossRef]

[98] Doener, F.; Hong, H.S.; Meyer, I.; Tadjalli-Mehr, K.; Daehling, A.; Heidenreich, R.; Koch, S.D.; Fotin-Mleczek, M.; Gnad-Vogt, U. RNA-Based Adjuvant CV8102 Enhances the Immunogenicity of a Licensed Rabies Vaccine in a First-in-Human Trial. *Vaccine* **2019,** *37,*1819-1826. [CrossRef]

[99] Translate Bio Announces Results from Second Interim Data Analysis from Ongoing Phase 1/2 Clinical Trial of MRT5005 in Patients with Cystic Fibrosis (CF). Available online: https:// www.biospace.com/article/translate-bio-announces-results-from- second-inter-im-data-analysis-from-ongoing-phase-1-2-clinical-trial-of-mrt5005-in-patients-with-cystic-fibrosis-cf- / (accessed on 13 October 2022).

[100] Burris, H.A.; Patel, M.R.; Cho, D.C.; Clarke, J.M.; Gutierrez, M.; Zaks, T.Z.; Frederick, J.; Hopson, K.; Mody, K.; Binanti-Berube, A.; et al. A Phase I Multicenter Study to Assess the Safety, Tolerability, and Immunogenicity of MRNA- 4157 Alone in Patients with Resected Solid Tumors and in Combination with Pembrolizumab in Patients with Unresectable Solid Tumors. *JCO* **2019,** 37, 2523. [CrossRef]

[101] Costello, C.L.; Gregory, T.K.; Ali, S.A.; Berdeja, J.G.; Patel, K.K.; Shah, N.D.; Ostertag, E.; Martin, C.; Ghoddusi, M.; Shedlock, D.J.; et al. Phase 2 Study of the Response and Safety of P-Bcma-101 CAR-T Cells in Patients with Relapsed/Refractory (r/r) Multiple Myeloma (MM) (PRIME). *Blood* **2019,***134,* 3184. [CrossRef]

[102] Gregory, T.; Cohen, A.D.; Costello, C.L.; Ali, S.A.; Berdeja, J.G.; Ostertag, E.M.; Martin, C.; Shedlock, D.J.; Resler, M.L.; Spear, M.A.; et al. Efficacy and Safety of P-Bcma-101 CAR-T Cells in Patients with Relapsed/Refractory (r/r) Multiple Myeloma (MM). *Blood* **2018,***132,*1012. [CrossRef]

[103] Anttila, V.; Saraste, A.; Knuuti, J.; Jaakkola, P; Hedman, M.; Svedlund, S.; Lagerstrom-Fermer, M.; Kjaer, M.; Jeppsson, A.; Gan, L.-M. Synthetic MRNA Encoding VEGF-A in Patients Undergoing Coronary Artery Bypass Grafting: Design of a Phase 2a Clinical Trial. *Mol. Ther. Methods Clin. Dev.* 2020,*18,*464-472. [CrossRef] [PubMed]

[104] Late-Breaking Science Abstracts and Featured Science Abstracts From the American Heart Association's Scientific Sessions 2021 and Late-Breaking Abstracts in Resuscitation Science From the Resuscitation Science Symposium 2021. *Circulation* 2021,*144,* e564-e593. [CrossRef]

[105] Gan, L.-M.; Lagerstrom-Fermer, M.; Carlsson, L.G.; Arfvidsson, C.; Egnell, A.-C.; Rudvik, A.; Kjaer, M.; Collen, A.; Thompson, J.D.; Joyal, J.; et al. Intradermal Delivery of Modified MRNA Encoding VEGF-A in Patients with Type 2 Diabetes. *Nat. Commun.* 2019, *10,* 871. [CrossRef]

[106] de Lusignan, S.; Damaso, S.; Ferreira, F.; Byford, R.; McGee, C.; Pathirannehelage, S.; Shende, V.; Yonova, I.; Schmidt, A.; Schuind, A.; et al. Brand-Specific Enhanced Safety Surveillance of GSK's Fluarix Tetra Seasonal Influenza Vaccine in England: 2017/2018 Season. *Hum. Vaccines Immunother.* 2020,*16,*1762-1771. [CrossRef]

[107] Crescioli, S.; Correa, I.; Karagiannis, R; Davies, A.M.; Sutton, B.J.; Nestle, F.O.; Karagiannis, S.N. IgG4 Characteristics and Functions in Cancer Immunity. *Curr. Allergy Asthma Rep.* 2016,*16, 7.* [CrossRef]

[108] Schlaudecker, E.P; McNeal, M.M.; Dodd, C.N.; Ranz, J.B.; Steinhoff, M.C. Pregnancy Modifies the Antibody Response to Trivalent Influenza Immunization. *J. Infect. Dis.* 2012, *206,*1670-1673. [CrossRef]

[109] Zhang, X.; Lu, H.; Peng, L.; Zhou, J.; Wang, M.; Li, J.; Liu, Z.; Zhang, W.; Zhao, Y.; Zeng, X.; et al. The Role of PD-1 /PD-Ls in the Pathogenesis of IgG4-Related Disease. *Rheumatology* 2022, *61,* 815-825. [CrossRef]

[110] Pfizer-BioNTech COVID-19 Vaccine, COMIRNATY®(Tozinameran). Available online: https://www.who.int/publications/m/ item/comirnaty-covid-19-mrna-vaccine (accessed on 30 December 2022).

[111] Moderna MRNA-1273, COVID-19 Vaccine. Available online: https://www.who.int/publications/m/item/moderna-covid-19 -vaccine-(mrna-1273) (accessed on 30 December 2022).

[112] Chakraborty, C.; Bhattacharya, M.; Sharma, A.R. Present Variants of Concern and Variants of Interest of Severe Acute Respiratory Syndrome Coronavirus 2: Their Significant Mutations in S-Glycoprotein, Infectivity, Re-Infectivity, Immune Escape and Vaccines Activity. *Rev. Med. Virol.* 2022, 32, e2270. [CrossRef]

[113] Chakraborty, C.; Sharma, A.R.; Bhattacharya, M.; Lee, S.-S. A Detailed Overview of Immune Escape, Antibody Escape, Partial Vaccine Escape of SARS-CoV-2 and Their Emerging Variants With Escape Mutations. *Front. Immunol.* 2022,*13,* 801522. [CrossRef]

[114] Zhong, N.; Zheng, B.; Li, Y.; Poon, L.; Xie, Z.; Chan, K.; Li, P; Tan, S.; Chang, Q.; Xie, J.; et al. Epidemiology and Cause of Severe Acute Respiratory Syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. *Lancet* 2003, *362,*1353-1358. [CrossRef] [PubMed]

[115] Gastanaduy, P.A. Update: Severe Respiratory Illness Associated with Middle East Respiratory Syndrome Coronavirus (MERS-CoV)—Worldwide, 2012-2013. *MMWR Morb. Mortal. Wkly. Rep.* 2013, 62,480-483.

[116] Li, Y.-D.; Chi, W.-Y.; Su, J.-H.; Ferrall, L.; Hung, C.-F.; Wu, T.-C. Coronavirus Vaccine Development: From SARS and MERS to COVID-19. *J. Biomed. Sci.* 2020, 27,104. [CrossRef] [PubMed]

[117] Weingartl, H.; Czub, M.; Czub, S.; Neufeld, J.; Marszal, R; Gren, J.; Smith, G.; Jones, S.; Proulx, R.; Deschambault, Y.; et al. Immunization with Modified Vaccinia Virus Ankara-Based Recombinant Vaccine against Severe Acute Respiratory Syndrome Is Associated with Enhanced Hepatitis in Ferrets. *J. Virol.* 2004, *78,*12672-12676. [CrossRef] [PubMed]

[118] Tseng, C.-T.; Sbrana, E.; Iwata-Yoshikawa, N.; Newman, PC.; Garron, T.; Atmar, R.L.; Peters, C.J.; Couch, R.B. Immunization with SARS Coronavirus Vaccines Leads to Pulmonary Immunopathology on Challenge with the SARS Virus. *PLoS ONE* 2012, 7, e35421. [CrossRef]

[119] van Doremalen, N.; Haddock, E.; Feldmann, F.; Meade-White, K.; Bushmaker, T.; Fischer, R.J.; Okumura, A.; Hanley, P.W.; Saturday, G.; Edwards, N.J.; et al. A Single Dose of ChAdOxl MERS Provides Broad Protective Immunity against a Variety of MERS-CoV Strains. *bioRxiv* 2020, preprint.

[120] Bolles, M.; Deming, D.; Long, K.; Agnihothram, S.; Whitmore, A.; Ferris, M.; Funkhouser, W.; Gralinski, L.; Totura, A.; Heise, M.; et al. A Double-Inactivated Severe Acute Respiratory Syndrome Coronavirus Vaccine Provides Incomplete Protection in Mice and Induces Increased Eosinophilic Proinflammatory Pulmonary Response upon Challenge. *J. Virol.* 2011,*85,*12201-12215. [CrossRef]

[121] Bliden, K.P.; Liu, T.; Sreedhar, D.; Kost, J.; Hsiung, J.; Zhao, S.; Shan, D.; Usman, A.; Walia, N.; Cho, A.; et al. Evolution of Anti-SARS-CoV-2 IgG Antibody and IgG Avidity Post Pfizer and Moderna MRNA Vaccinations. *medRxiv* 2021. [CrossRef]

[122] Macdonald, P.J.; Schaub, J.M.; Ruan, Q.; Williams, C.L.; Prostko, J.C.; Tetin, S.Y. Affinity of Anti-Spike Antibodies to Three Major SARS-CoV-2 Variants in Recipients of Three Major Vaccines. *Commun. Med.* 2022, 2,109. [CrossRef]

[123] Liu, L.; Wei, Q.; Lin, Q.; Fang, J.; Wang, H.; Kwok, H.; Tang, H.; Nishiura, K.; Peng, J.; Tan, Z.; et al. Anti-Spike IgG Causes Severe Acute Lung Injury by Skewing Macrophage Responses during Acute SARS-CoV Infection. *JCI Insight* 2019, 4, 123158. [CrossRef]

[124] Lee, W.S.; Wheatley, A.K.; Kent, S.J.; DeKosky, B.J. Antibody-Dependent Enhancement and SARS-CoV-2 Vaccines and Therapies. *Nat. Microbiol.* 2020, 5,1185-1191. [CrossRef] [PubMed]

[125] Wen, J.; Cheng, Y.; Ling, R.; Dai, Y.; Huang, B.; Huang, W.; Zhang, S.; Jiang, Y. Antibody-Dependent Enhancement of Coronavirus. *Int. J. Infect. Dis.* 2020,*100,*483-489. [CrossRef] [PubMed]

[126] Xu, L.; Ma, Z.; Li, Y.; Pang, Z.; Xiao, S. Antibody Dependent Enhancement: Unavoidable Problems in Vaccine Development. *Adv. Immunol.* 2021,*151,* 99-133. [CrossRef] [PubMed]

[127] Sanchez-Zuno, G.A.; Matuz-Flores, M.G.; Gonzalez-Estevez, G.; Nicoletti, F.; Turrubiates-Hernandez, F.J.; Mangano, K.; Munoz- Valle, J.F. A Review: Antibody-Dependent Enhancement in COVID-19: The Not so Friendly Side of Antibodies. *Int. J. Im- munopathol. Pharm.* 2021, *35,* 20587384211050200. [CrossRef] [PubMed]

[128] Thomas, S.; Smatti, M.K.; Ouhtit, A.; Cyprian, F.S.; Almaslamani, M.A.; Thani, A.A.; Yassine, H.M. Antibody-Dependent Enhancement (ADE) and the Role of Complement System in Disease Pathogenesis. *Mol. Immunol.* 2022,*152,* 172-182. [CrossRef] [PubMed]

[129] Ricke, D.O. Two Different Antibody-Dependent Enhancement (ADE) Risks for SARS-CoV-2 Antibodies. *Front. Immunol.* **2021,** *12,* 640093. [CrossRef]

[130] Wan, Y.; Shang, J.; Sun, S.; Tai, W.; Chen, J.; Geng, Q.; He, L.; Chen, Y.; Wu, J.; Shi, Z.; et al. Molecular Mechanism for Antibody-Dependent Enhancement of Coronavirus Entry. *J. Virol.* 2020, *94,* e02015-e02019. [CrossRef]

[131] Shimizu, J.; Sasaki, T.; Koketsu, R.; Morita, R.; Yoshimura, Y.; Murakami, A.; Saito, Y.; Kusunoki, T.; Samune, Y.; Nakayama, E.E.; et al. Reevaluation of Antibody-Dependent Enhancement of Infection in Anti-SARS-CoV-2 Therapeutic Antibodies and MRNA-Vaccine Antisera Using FcR- and ACE2-Positive Cells. *Sci. Rep.* 2022,*12,*15612. [CrossRef]

[132] Lurie, N.; Saville, M.; Hatchett, R.; Halton, J. Developing Covid-19 Vaccines at Pandemic Speed. *N. Engl. J. Med.* 2020, *382,* 1969-1973. [CrossRef]

[133] London, A.J.; Kimmelman, J. Against Pandemic Research Exceptionalism. *Science* 2020, *368,*476-477. [CrossRef]

[134] Tizard, I.R. Vaccination against Coronaviruses in Domestic Animals. *Vaccine* 2020, *38,* 5123-5130. [CrossRef] [PubMed]

[135] Olsen, C.W.; Corapi, W.V.; Ngichabe, C.K.; Baines, J.D.; Scott, F.W. Monoclonal Antibodies to the Spike Protein of Feline Infectious Peritonitis Virus Mediate Antibody-Dependent Enhancement of Infection of Feline Macrophages. *J. Virol.* **1992,** *66,* 956-965. [CrossRef] [PubMed]

[136] Hohdatsu, T.; Yamada, M.; Tominaga, R.; Makino, K.; Kida, K.; Koyama, H. Antibody-Dependent Enhancement of Feline Infectious Peritonitis Virus Infection in Feline Alveolar Macrophages and Human Monocyte Cell Line U937 by Serum of Cats Experimentally or Naturally Infected with Feline Coronavirus. *J. Vet. Med. Sci.* **1998,** *60,*49-55. [CrossRef] [PubMed]

[137] Takano, T.; Nakaguchi, M.; Doki, T.; Hohdatsu, T. Antibody-Dependent Enhancement of Serotype II Feline Enteric Coronavirus Infection in Primary Feline Monocytes. *Arch. Virol.* 2017,*162,* 3339-3345. [CrossRef]

[138] Hamilton, Z.; Simpson, B.; Donald Reynolds, D.V.M. *Antibody Dependent Enhancement of Infectious Bronchitis Virus in Poultry;* UCARE Research Products: Minneapolis, MN, USA, 2022.

[139] Toro, H.; Pennington, D.; Gallardo, R.A.; van Santen, V.L.; van Ginkel, F.W.; Zhang, J.; Joiner, K.S. Infectious Bronchitis Virus Subpopulations in Vaccinated Chickens after Challenge. *Avian Dis.* 2012, *56,* 501-508. [CrossRef]

[140] Brandao, P.E.; Berg, M.; Silva, S.O.S.; Taniwaki, S.A. Emergence of Avian Coronavirus Escape Mutants Under Suboptimal Antibody Titers. *J. Mol. Evol.* 2022, *90,*176-181. [CrossRef]

[141] Bande, F.; Arshad, S.S.; Bejo, M.H.; Moeini, H.; Omar, A.R. Progress and Challenges toward the Development of Vaccines against Avian Infectious Bronchitis. *J. Immunol. Res.* **2015,** *2015,*424860. [CrossRef]

[142] Eldemery, F.; Li, Y.; Yu, Q.; van Santen, V.L.; Toro, H. Infectious Bronchitis Virus S2 of 4/91 Expressed from Recombinant Virus Does Not Protect Against Ark-Type Challenge. *Avian Dis.* **2017,** *61,* 397-401. [CrossRef]

[143] Ravikumar, R.; Chan, J.; Prabakaran, M. Vaccines against Major Poultry Viral Diseases: Strategies to Improve the Breadth and Protective Efficacy. *Viruses* 2022,*14,*1195. [CrossRef]

[144] Shao, G.; Chen, T.; Feng, K.; Zhao, Q.; Zhang, X.; Li, H.; Lin, W.; Xie, Q. Efficacy of Commercial Polyvalent Avian Infectious Bronchitis Vaccines against Chinese QX-like and TW-like Strain via Different Vaccination Strategies. *Poult. Sci.* 2020,*99,*4786-4794. [CrossRef]

[145] Sjaak de Wit, J.J.; Cook, J.K.A.; van der Heijden, H.M.J.F. Infectious Bronchitis Virus Variants: A Review of the History, Current Situation and Control Measures. *Avian Pathol.* 2011, *40,* 223-235. [CrossRef] [PubMed]

[146] Cavanagh, D. Severe Acute Respiratory Syndrome Vaccine Development: Experiences of Vaccination against Avian Infectious Bronchitis Coronavirus. *Avian Pathol.* **2003,** 32, 567-582. [CrossRef] [PubMed]

[147] Legnardi, M.; Tucciarone, C.M.; Franzo, G.; Cecchinato, M. Infectious Bronchitis Virus Evolution, Diagnosis and Control. *Vet. Sci.* 2020, 7, E79. [CrossRef] [PubMed]

[148] Wilson, R.B.; Holladay, J.A.; Cave, J.S. A Neurologic Syndrome Associated with Use of a Canine Coronavirus-Parvovirus Vaccine in Dogs. *Compend. Contin. Educ. Pract. Vet.* **1986,** *8,*117-118,120-122,124.

[149] Martin, M. Canine Coronavirus Enteritis and a Recent Outbreak Following Modified Live Virus Vaccination. *Compend. Contin. Educ. Pract. Vet.* **1985,** 7,1012-1017.

[150] Pratelli, A.; Tinelli, A.; Decaro, N.; Martella, V.; Camera, M.; Tempesta, M.; Martini, M.; Carmichael, L.E.; Buonavoglia, C. Safety and Efficacy of a Modified-Live Canine Coronavirus Vaccine in Dogs. *Vet. Microbiol.* **2004,** *99,* 43-49. [CrossRef]

[151] Pratelli, A. High-cell-passage Canine Coronavirus Vaccine Providing Sterilising Immunity. *J. Small Anim. Pract.* **2007,** *48,*574-578. [CrossRef]

[152] Cho, K.-O.; Hasoksuz, M.; Nielsen, PR.; Chang, K.-O.; Lathrop, S.; Saif, L.J. Cross-Protection Studies between Respiratory and Calf Diarrhea and Winter Dysentery Coronavirus Strains in Calves and RT-PCR and Nested PCR for Their Detection. *Arch. Virol.* **2001,***146,* 2401-2419. [CrossRef]

[153] Heckert, R.A.; Saif, L.J.; Hoblet, K.H.; Agnes, A.G. A Longitudinal Study of Bovine Coronavirus Enteric and Respiratory Infections in Dairy Calves in Two Herds in Ohio. *Vet. Microbiol.* **1990,** 22,187-201. [CrossRef]

[154] Fulton, R.W.; d'Offay, J.M.; Landis, C.; Miles, D.G.; Smith, R.A.; Saliki, J.T.; Ridpath, J.F.; Confer, A.W.; Neill, J.D.; Eberle, R.; et al. Detection and Characterization of Viruses as Field and Vaccine Strains in Feedlot Cattle with Bovine Respiratory Disease. *Vaccine* **2016,** *34,* 3478-3492. [CrossRef]

[155] Hu, S.; Bruszewski, J.; Smalling, R.; Browne, J.K. Studies of TGEV Spike Protein Gpl95 Expressed in E. Coli and by a TGE-Vaccinia Virus Recombinant. *Adv. Exp. Med. Biol.* **1985,***185,* 63-82. [CrossRef] [PubMed]

[156] Gomez, N.; Wigdorovitz, A.; Castanon, S.; Gil, F.; Orda, R.; Borca, M.V.; Escribano, J.M. Oral Immunogenicity of the Plant Derived Spike Protein from Swine-Transmissible Gastroenteritis Coronavirus. *Arch. Virol.* 2000,*145,*1725-1732. [CrossRef] [PubMed]

[157] Lamphear, B.J.; Streatfield, S.J.; Jilka, J.M.; Brooks, C.A.; Barker, D.K.; Turner, D.D.; Delaney, D.E.; Garcia, M.; Wiggins, B.; Woodard, S.L.; et al. Delivery of Subunit Vaccines in Maize Seed. *J. Control. Release* 2002, *85,*169-180. [CrossRef] [PubMed]

[158] Gerdts, V.; Zakhartchouk, A. Vaccines for Porcine Epidemic Diarrhea Virus and Other Swine Coronaviruses. *Vet. Microbiol.* **2017,** *206,*45-51. [CrossRef]

[159] Al-Abdallat, M.M.; Payne, D.C.; Alqasrawi, S.; Rha, B.; Tohme, R.A.; Abedi, G.R.; Al Nsour, M.; Iblan, I.; Jarour, N.; Farag, N.H.; et al. Hospital-Associated Outbreak of Middle East Respiratory Syndrome Coronavirus: A Serologic, Epidemiologic, and Clinical Description. *Clin. Infect. Dis.* **2014,** *59,*1225-1233. [CrossRef]

[160] Yoon, I.-K.; Kim, J.H. First Clinical Trial of a MERS Coronavirus DNA Vaccine. *Lancet Infect. Dis.* **2019,***19,* 924-925. [CrossRef]

[161] Modjarrad, K.; Roberts, C.C.; Mills, K.T.; Castellano, A.R.; Paolino, K.; Muthumani, K.; Reuschel, E.L.; Robb, M.L.; Racine, T.; Oh, M.; et al. Safety and Immunogenicity of an Anti-Middle East Respiratory Syndrome Coronavirus DNA Vaccine: A Phase 1, Open-Label, Single-Arm, Dose-Escalation Trial. *Lancet Infect. Dis.* **2019,***19,*1013-1022. [CrossRef]

[162] Lin, J.-T.; Zhang, J.-S.; Su, N.; Xu, J.-G.; Wang, N.; Chen, J.-T.; Chen, X.; Liu, Y.-X.; Gao, H.; Jia, Y.-R; et al. Safety and Immunogenicity from a Phase **I** Trial of Inactivated Severe Acute Respiratory Syndrome Coronavirus Vaccine. *Antivir. Ther.* **2007,** *12,*1107-1113. [CrossRef]

[163] Martin, J.E.; Louder, M.K.; Holman, L.A.; Gordon, I.J.; Enama, M.E.; Larkin, B.D.; Andrews, C.A.; Vogel, L.; Koup, R.A.; Roederer, M.; et al. A SARS DNA Vaccine Induces Neutralizing Antibody and Cellular Immune Responses in Healthy Adults in a Phase I Clinical Trial. *Vaccine* 2008, 26, 6338-6343. [CrossRef]

[164] Koch, T.; Dahlke, C.; Fathi, A.; Kupke, A.; Krahling, V.; Okba, N.M.A.; Halwe, S.; Rohde, C.; Eickmann, M.; Volz, A.; et al. Safety and Immunogenicity of a Modified Vaccinia Virus Ankara Vector Vaccine Candidate for Middle East Respiratory Syndrome: An Open-Label, Phase 1 Trial. *Lancet Infect. Dis.* 2020, *20,* 827-838. [CrossRef]

[165] Fathi, A.; Dahlke, C.; Krahling, V.; Kupke, A.; Okba, N.M.A.; Raadsen, M.P; Heidepriem, J.; Muller, M.A.; Paris, G.; Lassen, S.; et al. Increased Neutralization and IgG Epitope Identification after MVA-MERS-S Booster Vaccination against Middle East Respiratory Syndrome. *Nat. Commun.* 2022,*13,*4182. [CrossRef] [PubMed]

[166] Folegatti, P.M.; Bittaye, M.; Flaxman, A.; Lopez, F.R.; Bellamy, D.; Kupke, A.; Mair, C.; Makinson, R.; Sheridan, J.; Rohde, C.; et al. Safety and Immunogenicity of a Candidate Middle East Respiratory Syndrome Coronavirus Viral-Vectored Vaccine: A Dose- Escalation, Open-Label, Non-Randomised, Uncontrolled, Phase 1 Trial. *Lancet Infect. Dis.* 2020, *20,* 816-826. [CrossRef] [PubMed]

[167] Bosaeed, M.; Balkhy, H.H.; Almaziad, S.; Aljami, H.A.; Alhatmi, H.; Alanazi, H.; Alahmadi, M.; Jawhary, A.; Alenazi, M.W.; Almasoud, A.; et al. Safety and Immunogenicity of ChAdOxl MERS Vaccine Candidate in Healthy Middle Eastern Adults (MERS002): An Open-Label, Non-Randomised, Dose-Escalation, Phase lb Trial. *Lancet Microbe* 2022, *3,* ell-e20. [CrossRef] [PubMed]

[168] Buzhdygan, T.P.; DeOre, B.J.; Baldwin-Leclair, A.; Bullock, T.A.; McGary, H.M.; Khan, J.A.; Razmpour, R.; Hale, J.F.; Galie, P.A.; Potula, R.; et al. The SARS-CoV-2 Spike Protein Alters Barrier Function in 2D Static and 3D Microfluidic in-Vitro Models of the Human Blood-Brain Barrier. *Neurobiol. Dis.* 2020,*146,*105131. [CrossRef]

[169] Forsyth, C.B.; Zhang, L.; Bhushan, A.; Swanson, B.; Zhang, L.; Mamede, J.I.; Voigt, R.M.; Shaikh, M.; Engen, PA.; Keshavarzian, A. The SARS-CoV-2 SI Spike Protein Promotes MAPK and NF-KB Activation in Human Lung Cells and Inflammatory Cytokine Production in Human Lung and Intestinal Epithelial Cells. *Microorganisms* 2022,*10,*1996. [CrossRef]

[170] Bhargavan, B.; Kanmogne, G.D. SARS-CoV-2 Spike Proteins and Cell-Cell Communication Inhibits TFPI and Induces Thrombogenic Factors in Human Lung Microvascular Endothelial Cells and Neutrophils: Implications for COVID-19 Coagulopathy Pathogenesis. *Int. J. Mol. Sci.* 2022, 23,10436. [CrossRef]

[171] Choi, J.-Y.; Park, J.H.; Jo, C.; Kim, K.-C.; Koh, Y.H. SARS-CoV-2 Spike SI Subunit Protein-Mediated Increase of Beta-Secretase 1 (BACE1) Impairs Human Brain Vessel Cells. *Biochem. Biophys. Res. Commun.* 2022, *626,* 66-71. [CrossRef]

[172] Hsu, A.C.-Y.; Wang, G.; Reid, A.T.; Veerati, PC.; Pathinayake, PS.; Daly, K.; Mayall, J.R.; Hansbro, P.M.; Horvat, J.C.; Wang, F.; et al. SARS-CoV-2 Spike Protein Promotes Hyper-Inflammatory Response That Can Be Ameliorated by Spike-Antagonistic Peptide and FDA-Approved ER Stress and MAP Kinase Inhibitors in Vitro. *Biorxiv* 2020. [CrossRef]

[173] Khan, S.; Shafiei, M.S.; Longoria, C.; Schoggins, J.W.; Savani, R.C.; Zaki, H. SARS-CoV-2 Spike Protein Induces Inflammation via TLR2-Dependent Activation of the NF-KB Pathway. *eLife* **2021,***10,* e68563. [CrossRef]

[174] Lei, Y.; Zhang, J.; Schiavon, C.R.; He, M.; Chen, L.; Shen, H.; Zhang, Y.; Yin, Q.; Cho, Y.; Andrade, L.; et al. SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2. *Circ. Res.* **2021,***128,*1323-1326. [CrossRef] [PubMed]

[175] Nystrom, S.; Hammarstrom, P. Amyloidogenesis of SARS-CoV-2 Spike Protein. *J. Am. Chem. Soc.* ***2022,144,*** 8945-8950. [CrossRef] [PubMed]

[176] Muglia, J.J.; DiGiovanna, J.J. Phase 1 Clinical Trials. *J. Cutan. Med. Surg.* **1998,** 2, 236-241. [CrossRef] [PubMed]

[177] Meyer-Arndt, L.; Schwarz, T.; Loyal, L.; Henze, L.; Kruse, B.; Dingeldey, M.; Giircan, K.; Uyar-Aydin, Z.; Muller, M.A.; Drosten, C.; et al. Cutting Edge: Serum but Not Mucosal Antibody Responses Are Associated with Pre-Existing SARS-CoV-2 Spike Cross-Reactive CD4+ T Cells Following BNT162b2 Vaccination in the Elderly. *J. Immunol.* 2022, *208,*1001-1005. [CrossRef] [PubMed]

[178] Chau, N.V.V.; Ngoc, N.M.; Nguyet, L.A.; Quang, V.M.; Ny, N.T.H.; Khoa, D.B.; Phong, N.T.; Toan, L.M.; Hong, N.T.T.; Tuyen, N.T.K.; et al. Transmission of SARS-CoV-2 Delta Variant among Vaccinated Healthcare Workers, Vietnam. 2021; *preprint.* [CrossRef]

[179] Pezzullo, A.M.; Axfors, C.; Contopoulos-Ioannidis, D.G.; Apostolatos, A.; Ioannidis, J.P.A. Age-Stratified Infection Fatality Rate of COVID-19 in the Non-Elderly Population. *Environ. Res.* 2023, *216,*114655. [CrossRef]

[180] Kedmi, R.; Ben-Arie, N.; Peer, D. The Systemic Toxicity of Positively Charged Lipid Nanoparticles and the Role of Toll-like Receptor 4 in Immune Activation. *Biomaterials* 2010, *31,* 6867-6875. [CrossRef]

Matthew Halma's research career began in studying the structural dynamics underlying programmed ribosome frameshifting (PRF). PRF is a ubiquitous phenomenon across all kingdoms of life, and attracts attention for its role in the regulation of viral gene expression. Since then, he has been pursuing a doctoral degree at Vrije Universiteit Amsterdam, studying the applications of single molecule tools to molecular motors involved in DNA replication and repair.

The role and dangers of endotoxin in mRNA injections

by Geoff N. Pain
PhD, BSc Hons

Abstract

Traditional concepts in toxicology have to be abandoned when considering the deaths and injuries caused by the COVID-19 injections. All known A-Z documented adverse events, from abortion, anaphylaxis, blindness, and heart injury to tinnitus and zoster can be anticipated via known biological pathways and mechanisms. All mRNA vaccine technology using plasmid growth inside live bacteria is inherently unsafe because the manufacturing techniques cannot remove the supertoxic fragments of the germ cell walls from the liquids ending up in all vials and the arms of a largely compliant public.

1. Essential background and central thesis

This paper examines the potential role of contaminant endotoxin in the mRNA vaccines promoted for the prevention of COVID-19 in Australia. The basis of both batch contamination and batch variation will be set forth, in the light of the E. coli-based manufacturing process known as 'Process 2', together with a pathophysiological examination of endotoxin. It is the author's view that much of the burden of severe adverse events, including deaths as covered by other authors in this volume, may be attributable to contaminant endotoxin; it is necessary to discuss the putative role of

endotoxin in specific pathologies, recognised as complications of vaccine administration.

All of the immunisations marketed in Australia claimed to generate antibodies to SARS-CoV-2, either by injecting synthetic spike protein or a length of synthetic mRNA or DNA designed to take over the cellular machinery of the recipients and to turn them into spike protein factories. This would result in the detection and targeting of these cells expressing foreign antigen, such that the body would react by destroying the cells transfected in this way. This strategy was doomed to fail because it could not generate mucosal antibodies in sufficient quantity or killer capacity to stop viral replication on infection through the eyes, nose or mouth. As the public at large now largely knows, the vaccines have not prevented infection, viral replication or transmission by exhalation.

The central thesis here is that endotoxinaemia explains the unprecedented magnitude of off-target effects, especially those noted in the early phase after administration. Delayed effects and effects of repeat exposure are also possible in the unique toxicology of endotoxin; among other considerations, ways in which contaminant endotoxin may synergise with other elements of the exposure, such as spike protein, are discussed.

Unfortunately, as of the time of writing, clear quantification of endotoxin concentration in vials has not been provided, either by national regulatory authorities, university laboratories or open-source investigations. As this is crucial to the central thesis, an analysis of the measurement of endotoxin, including those methods most likely to prove useful, as well as those most likely to obfuscate and mask the issue, are presented, with a clear and urgent call for the public disclosure of accurate levels in batches.

1.1 What are Process 1 and Process 2?

For both the Pfizer and Moderna mRNA products, two distinct manufacturing processes have been utilised, the first in the early clinical trial phase (Process 1) and the second in the penultimate phase of the clinical study (Process 2), into the worldwide rollout, until now. It is essential to understand the distinctions, in order to understand the differential endotoxin levels likely to be affecting Process 2 batches.

1.1.1 Process 1: reverse transcription PCR

Process 1 employed reverse transcription PCR (polymerase chain reaction) in order to manufacture the mRNA strand encoding spike protein. This offered high sample purity, but little scalability beyond the trial. Pfizer and Moderna trial subjects were therefore exposed to far lower endotoxin because

their vaccines, made by Process 1, were manufactured without the necessity of bacterial exposure.

The RT-PCR-generated mRNA immunisations were encapsulated using the same lipid nanoparticles as the later material injected in the mass rollout, so it is reasonable to surmise that observed differences likely relate to the drug substance manufacture.

A very limited number of Process 1 vaccines have reported endotoxin levels of about 0.5 EU/mL. This relatively low value, which is still capable of causing such problems as anaphylaxis, is likely because the drug substance (mRNA) was made by RT-PCR of synthetic mRNA, designed to code for spike protein. So any endotoxin in Process 1 vaccines used in the trial arose from contamination of materials used in manufacture of drug product, which is the suspension of mRNA in lipid nanoparticles placed in the vials. Sugar is a major component and could be a source of endotoxin.

1.1.2 Process 2: plasmid DNA

The endotoxin in mRNA-based immunisations arises from fragments of the E. coli bacteria being used in production of the plasmid complementary DNA, which is in turn used to produce the mRNA prodrug, and combined with buffer and lipid nanoparticles to form the drug product. The crude filtration processes used in production cannot prevent endotoxin, and especially its concerning Lipid A component, which breaks off easily and is far more toxic than the larger chunks of bacterial wall.

Endotoxin in mRNA vaccines can float freely outside the LNP as well as adhering to the surface or trapped inside. As such, it remains to be seen how much endotoxin is bound to mRNA or contaminant DNA or bioburden.

Approximately 252 trial subjects are thought to have been treated with Pfizer Process 2 immunisations supplied in the tail end of the clinical trial: no human trial results specifically pertaining to this population have been published. Furthermore, Pfizer has stated it has no intention of publishing clinical evaluation results of its tiny 'comparability trial' of Process 2 *versus* Process 1. In the ongoing Phase 3 clinical study C4591001 through the cut-off date of March 13th 2021, there was one anaphylaxis case deemed to be related to the product. I suspect this person received a Process 2 vaccine dose.

Endotoxin in Pfizer Process 2 vaccines is commonly quantified in EU/mL (endotoxin units / per millilitre). However, as experts in the field point out, this is somewhat vague; it is perhaps the case that 1 EU/ml equates to 200 picograms per mL. The European Union allows 12.5 EU/mL, while the FDA allows 5 EU/mL for intramuscular vaccines and immunisations; much lower

limits apply for the eye or spinal injections. No endotoxin levels of Pfizer Process 2 vaccines used in mass rollout have been published. The TGA simply states 'Pass' on its Batch Release page, with minimal detail.

The advent of Process 2 vaccines appears to have greatly expanded the number of anaphylaxis victims, especially starting from the unblinded phases of the main trial. For one example, during the unblinded phase, a 17-year-old female subject, who had received two placebo doses and then a dose of Process 2 vaccine, suffered anaphylaxis six minutes after injection on December 14th 2020. She rescued herself with a shot of adrenalin. She withdrew from the study on January 27th 2021.

Subsequently, a Vaccine Adverse Event Reporting System (VAERS) notification from January 7th 2021 states that a 53-year-old woman suffered anaphylaxis after being injected with her first dose of Process 2 Lot EE8403. By July 2021, Pfizer was more candid and expansive on the anaphylaxis casualties, including nine deaths in the post-marketing injection campaign. It will be seen that the differential rate of incident anaphylaxis in recipients of mRNA vaccine doses manufactured under Process 2 is strong circumstantial evidence that clinically notable endotoxin contamination is taking place.

1.2 What is the evidence for batch variation and batch contamination?

There is now abundant evidence for batch variation, including differential rates of adverse events, raising basic concerns around Good Manufacturing Practice (GMP).

From disclosed ingredients of the various vaccine platforms, we essentially know what is in the vials. A number of the ingredients are clearly toxic. In particular, there is no disclosed evidence for the use of graphene or its derivatives.

1.3 Laboratory methods and the urgent need for quantification

I can find no evidence that the TGA tests for the supertoxin lipid A. The Laboratory Branch of the TGA use the horseshoe blood extract, limulus amebocyte lysate assay (LAL assay), suitable for large fragments only. This test is impaired by the presence of cationic lipids and mRNA – as present in the vaccines – so that the actual concentration of endotoxin is likely to be higher than indicated by the laboratory test. There are more sophisticated tests (based on mass spectrometry after separation and volatile derivative formation) that are not used by regulatory authorities like the TGA, but which arguably should be. Endotoxin is so poisonous that electronic sensors have been made that can detect femtogram levels, that is, a billionth of a millionth of a gram.

1.4 Other essential background

1.4.1 General considerations regarding endotoxin toxicity

This paper concentrates on what may be the most lethal component in the mRNA vaccines, namely endotoxin, also known as lipopolysaccharide (LPS), and especially the fraction called lipid A, with discussion of plausible mechanistic arguments which may link endotoxin to the plethora of adverse manifestations following COVID-19 vaccinations.

The website of the Therapeutic Goods Administration (TGA) in Australia contains some interesting information tucked away in odd places: a slide from a presentation about endotoxin and how it is measured in their laboratory[2] is provided in Figure 1. Endotoxin is a term often used interchangeably with LPS, although it can more broadly refer to any toxic substance released when a bacterial cell disintegrates. LPS is the primary endotoxin in gram-negative bacteria, including E. coli, and is a large molecule found in their outer membranes. LPS plays a crucial role in the structural integrity of the bacterial cell wall and serves as a protective layer against host immune. Free LPS is usually found in micelles and can aggregate *in vivo*.

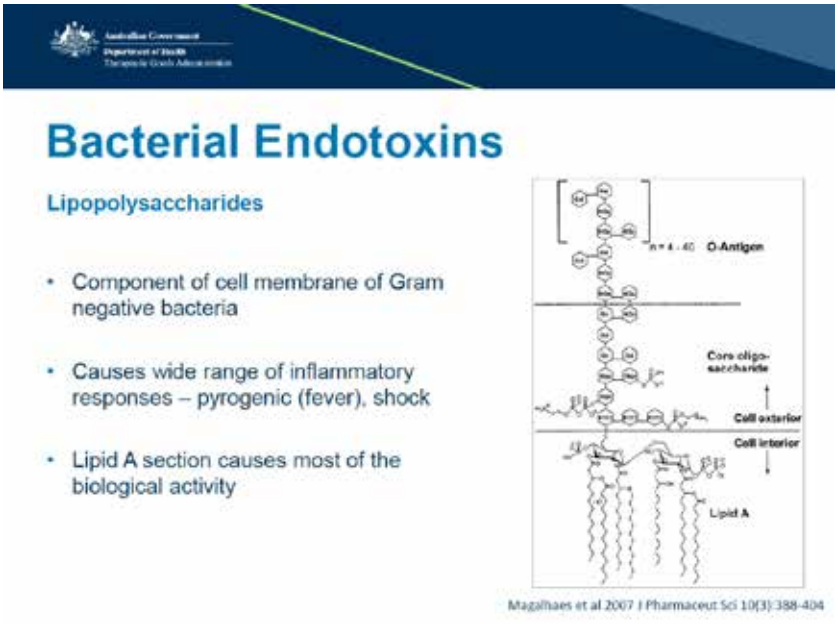


Figure 1

The 16th-century physician Paracelsus famously stated, *sola dosis facit venenumhi*: "All things are poison, and nothing is without poison; the dosage alone makes it so a thing is not a poison."[1] In the case of LPS, however, the demonstrable toxicity of very low-dose exposures challenges this notion. The fact that LPS at very low exposures can have disproportionate biological effects, via multiple amplification mechanisms, has made endotoxin contamination of therapeutic biologics a perennial concern of the pharmaceutical industry and its state regulators, and it is the subject of numerous standards within Good Manufacturing Practice.

1.4.2 Widespread biodistribution

It is the author's belief that BioNTech-Pfizer, and the complicit marketers of their COVID-19 vaccine, including government departments around the globe, were entirely incorrect when they repeatedly said that the LNPs and the mRNA inside or outside them would simply enter muscle cells in the arm, take them over, and force them to become factories for synthetic spike generation and resultant anti-spike antibodies. It is necessary to point out the widespread biodistribution of LNPs to understand how contaminant endotoxin may also be disseminated widely in the body after injection.

In a lecture given by one of the BioNTech founders, it is clear that the actual target of the injection contents is the draining lymph nodes and the wider lymphatic system, including the spleen. Once the mass vaccine program began, others associated with Pfizer vaccine design were also quite straight about the intended action of the vaccine on the lymphatic system.

In an interview of September 2021, Professor Drew Weissman, said:

> LNPs encapsulate the mRNA, protecting it from extracellular degradation, and facilitate endosomal release of the mRNA into the cytoplasm. When the LNP-Ψ-mRNA is injected into the muscle, every cell takes it up, but for muscle cells that is very inefficient, you can barely measure the protein that they make. The LNPs are 80nm in size, which is about the size of a virus. What happens is that the LNPs travel through the lymphatic drainage to lymph nodes, and in the lymph nodes, DCs (Dendritic Cells) take them up. There is also an infiltrate of lymphoid cells into the muscle that picks up the particles. Once the vaccine gets to a lymph node, the DC translates the mRNA and presents it to B and T cells to activate them, and that is how the immune response is started.

From the Pfizer Clinical Trial, it was known that lymphadenopthy was a small-scale problem caused by their Process 1 product, but there was an explosion of cases when they moved to Process 2, resulting from the endotoxin

from the E. coli bacteria used in production. As expected, lymphadenopathy is usually detected on the side of the body that received the dose.

These observations serve to corroborate specific documentary evidence obtained from the TGA by way of a FOIA request, namely the Pfizer Comirnaty Non-Clinical Evaluation Report, which showed widespread biodistribution of 80nm LNPs. These documents have been discussed around the world, popularising the concept of dissemination of LNPs and their payload well beyond the intramuscular injection site, as was popularly understood to the be site of action, and well beyond the lymphatic drainage system, as elaborated by Prof Weissman. In fact, the LNPs go to numerous organs and carry not only mRNA, but contaminants including endotoxin. This is extremely important to the present discussion of potential endotoxin-related toxicities.

Quoting from a Trial document, obtained from the UK government, 'Lymphadenopathy is identified as an adverse reaction for BNT162b2 vaccine.'

I became aware of the big lymphadenopathy problem in Australia when I inspected the Database of Adverse Event Notifications. By 23 August 2021 there were already 1,126 cases. Worldwide Pfizer reported the following case numbers to April 2022: lymphadenopathy 73,287 (5.44 % of all adverse reaction reports); lymph node pain 8,395; vaccination site lymphadenopathy 4,540; lymphadenitis 2,115; lymphoedema 75; lymphopenia 274.

2. The centrality of cytokinopathy in endotoxin toxicity

In 1985, Prof. Peter Hotez, while he worked at New York's Rockefeller University, was part of a team able to kill 'endotoxin-resistant' mice with molecules secreted by endotoxin-altered macrophages. Among the symptoms the doomed animals suffered were anorexia and cachexia (muscle wasting). During subsequent years these experiments laid a foundation for understanding cachectin (murine Tumour Necrosis Factor, TNF) and the way in which cytokines triggered by an exposure such as endotoxin can trigger an exaggerated systemic inflammatory response. This is classically called a positive feedback loop. During the pandemic, thanks to media reporting, cytokines and the notion of a 'cytokine storm' have quite likely been assimilated into the public lexicon.

The scientific reality is that even tiny amounts of endotoxin defeat the Paracelsus doctrine because interleukin 6 (IL-6) and IL-1β (called the apex cytokine) and other pro-inflammatory stimuli are amplified by positive feedback loops.

2.1 How does endotoxin produce tissue damage via cytokinopathy the human body?

Cytokine Storm is not a newly-described concept: as will be seen, endotoxin in Pfizer and Moderna immunisations may create the perfect cytokine storm. Figure 2 provides a partial overview of the damage that endotoxin can do (Fajgenbaum), illustrating how cytokine storm can essentially damage every type of tissue in the human body. Note that effects on the reproductive system are absent in this diagram.

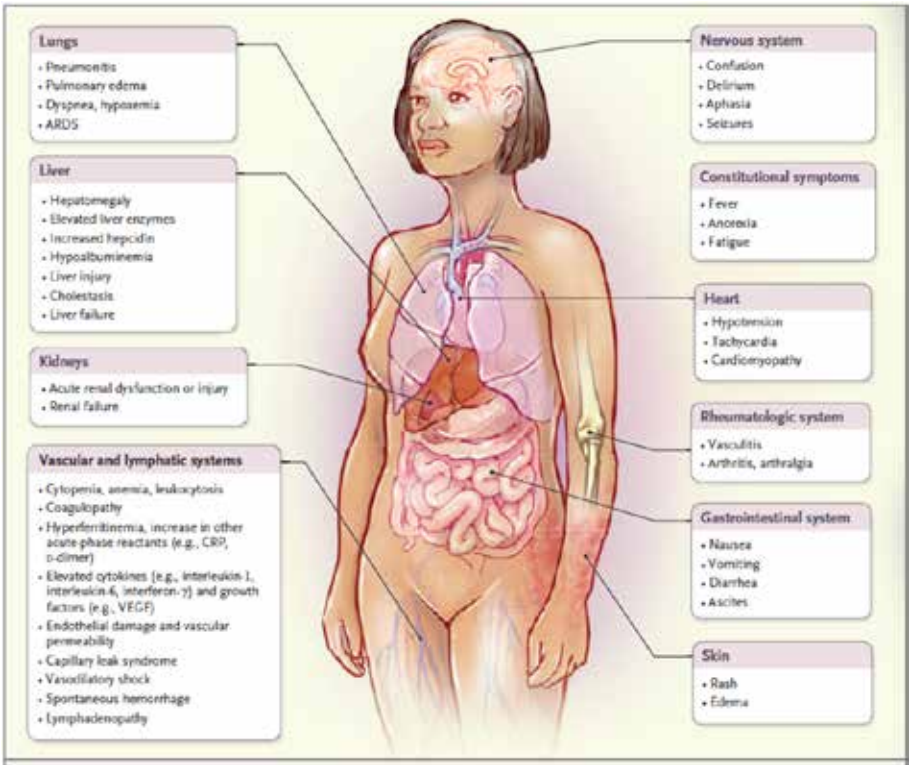


Figure 1. Clinical Presentation of Cytokine Storm.
A wide range of clinical and laboratory abnormalities can be observed in cytokine storm. However, all cases involve elevated circulating cytokine levels, acute systemic inflammatory symptoms, and secondary organ dysfunction (often renal, hepatic, or pulmonary). ARDS denotes acute respiratory distress syndrome, CRP C-reactive protein, and VEGF vascular endothelial growth factor.

Figure 2

Our innate immune system defends against invading pathogens by recognizing conserved Pathogen–Associated Molecular Patterns (PAMPs). Recognition of PAMPs relies on Pathogen Recognition Receptors (PRRs), expressed on the cell surface or in intracellular compartments. Important immune cells include macrophages and monocytes.

There is nothing simple in biological systems and this is best explained with a

diagram: unfortunately a number of acronyms are commonly used, so the text has been modified from Mohammad and Thiemermann.[2]

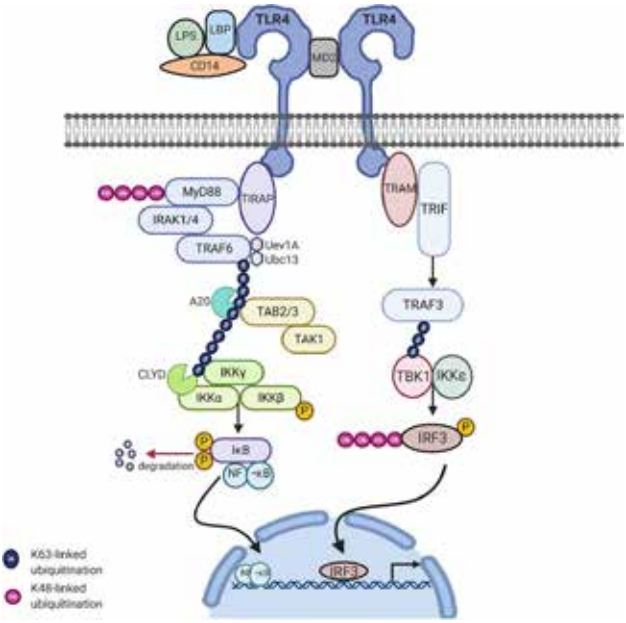


Figure 3

In Figure 3, LPS is bound in blood to lipopolysaccharide binding protein (LPB) and this coordinates to glycerophosphatidylinositol-anchored protein (also called CD14). LBP binds LPS micelles via the N-terminal basic patch and forms transient ternary complexes with secreted (sCD14) or membrane-bound GPI-anchored CD14 (mCD14) on the C terminus. Following the generation of CD14/LBP/LPS micelles, CD14 dissociates from LBP and receives monomeric LPS.

Toll-like receptor 4 (TLR4, a PRR) signalling occurs via the myeloid differentiation primary response protein 88 (MyD88)-dependent and MyD88-independent pathway to activate nuclear factor kappa beta (NF-κB)-related target genes. TLR4 forms a complex with MD-2, a secreted glycoprotein with an LPS-binding pocket.

The MyD88-dependent pathway involves the activation of MyD88 which recruits interleukin IL-1 receptor-associated kinase-4 (IRAK-4). IRAK-4 phosphorylates IRAK-1 and allows tumour necrosis factor receptor associated factor 6 (TRAF6) to associate with IRAK1. IRAK1-TRAF6 then activates TAK1, TAB1, and TAB2. The TRAF6, TAK1, TAB1, and TAB2 form a larger complex with ubiquitin-conjugating enzyme E32 variant 1 isoform A (Ubc13) and Uev1A which activates TAK1. The polyubiquitin chain is then

removed by A20 and conserved cylindromatosis (CYLD). Activated TAK1 phosphorylates the IKK complex (IKKα, IKKβ and IKKγ), ultimately resulting in the translocation of NF-κB into the nucleus, resulting in the transcription of pro-inflammatory cytokines.

The MyD88-independent pathway involves TIR-domain-containing adapter-inducing interferon-β (TRIF) leading to the activation of TNF receptor-associated factor 3 (TRAF3) and the translocation of interferon regulatory factor 3 (IRF3) to the nucleus leading to IFNB gene transcription.

2.2 Endotoxin tolerance *versus* pro-inflammatory priming

Gay men are more at risk of E. coli induced endotoxaemia. A study comparing two samples of differing plasma LPS levels from each person found HIV-negative men with subclinical endotoxemia had altered CD4-CD8 T cell ratio and plasma cytokine levels. Subclinical levels of plasma endotoxin *in vivo* alter T cell proliferative capacity, monocyte cytokine release and HLA-DR expression, and furthermore induce TLR cross-tolerance by decreased phosphorylation of mitogen-activated protein kinase (MAPK) pathway components. Monocytes from high pre-existing endotoxin samples did not significantly increase cytokine production after endotoxin stimulation, whereas monocytes from the matching low endotoxin samples increased cytokine production (except for IL-8) 8 to 150-fold. Thus, evidence of endotoxin tolerance is worthy of discussion.

Repeated exposure to endotoxin leads to chronic non-resolving inflammation but a study of multiple vaccine doses found counter-intuitive results.[6] According to dogma, a second high dose of endotoxin was thought to be characterized by less robust induction of pro-inflammatory cytokines and increased production of anti-inflammatory cytokines – known as endotoxin tolerance. However, retreatment with a very low dose of endotoxin, in contrast, has an opposite effect, potentiating or priming the pro-inflammatory response to subsequent endotoxin challenge, referred to as the Shwartzman-like reaction. The Shwartzman, or Sanarelli-Shwartzman effect, after injections, can perhaps be explained by endotoxin located in at least two compartments, one being free-floating and immediately available and the other being slow-release attached to LNPs, mRNA, DNA and or bioburden.

Mice pre-treated with super-low-dose endotoxin (LPS) exhibit increased mortality in response to challenge with a higher dose. The scheme by Morris et al. in Figure 4 demonstrates the complexity of endotoxin poisoning.

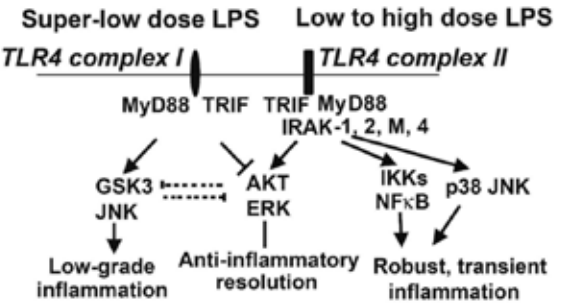


Figure 4

LPS = Endotoxin; TLR4 = Toll-Like Receptor; MyD88 = Myeloid Differentiation primary response 88 protein; TRIF = Toll/IL-1R domain-containing adaptor protein inducing Interferon-β; IRAK = Interleukin-Receptor-Associated Kinase; GSK3 = Glycogen Synthase Kinase 3; JNK = c-Jun N-terminal Kinase; AKT = Protein kinase B (PKB); ERK = Extracellular signal-Regulated Kinase; IKK = IκB Kinase; NFκB Nuclear Factor κ of activated B cells.

Shwartzman found that intradermal injection of a priming dose of sterile culture filtrates from gram-negative strains from bacteria (such as E. coli used to make the COVID-19 mRNA immunisations) into normal rabbits, followed in 24 hours by a second intravenous challenge (the provocative dose) from the same culture filtrate, resulted in dermal necrosis at the first injection. Note that 22% of the rabbits failed to respond at all, likely as a result of 'endotoxin tolerance' which in humans typically lasts no more than 21 days. Subsequently it has been shown that the cytokines generated by endotoxin septic shock, including TNF, IL-1, IL-12, IL-15 and or IFN-γ, can substitute for endotoxin.

In 1952 it was found that rabbits pre-treated with cortisone suffered multiple organ damage, particularly in the kidneys after they were given a single intravenous injection of gram-negative bacterial endotoxin. This was accompanied by heavy fibrin deposition. In 2006 it was shown that multiple organ damage due to the endotoxin Shwartzman effect involves disseminated intravascular coagulation (DIC) resulting in thrombosis in the lung and liver.

Endotoxin in Pfizer and Moderna injections creates the perfect cytokine storm.

The list of adverse events after Pfizer injection amazed people around the world when a US court ordered release of the company reports that they wanted hidden for 75 years. One of the most widely read Pfizer documents is about 170 pages long, running to thousands of separate medical descriptions; it can be downloaded from the TGA Freedom Of Information Log website. The UK government famously issued a contract for Artificial Intelligence to deal with the flood of reports to its Yellow Card reporting system. The US government also had to issue a contract for its VAERS system.

I have shown that endotoxin can account for all adverse events reported in minutes to days after the injection and beyond. The synthetic spike protein manufactured by the mRNA injections taking over healthy cells is of course toxic. In fact, the spike protein works in synergy with endotoxin by binding to it and helping to disrupt large endotoxin micelles into the more toxic lipid A.

While there is no doubt the synthetic SARS-CoV-2 spike protein transcribed from synthetic mRNA in COVID-19 vaccines causes immense long-term damage to a generation, it cannot be responsible for the adverse and sometimes fatal reactions experienced in minutes to days after the vaccines.

A most elegant proof of this was published by a team in Italy in early 2022 who obtained samples of viral spike from commercial labs and tested them for inflammatory action on human macrophages (MΦ). They concluded that a number of earlier studies were negated, or at least possibly confounded, by failure to take into account endotoxin contamination.

Natural virus spike evades the immune system with a coating of glycans as determined by crystallography, enzyme digestion and mass spectrometry. The synthetic spike from the mRNA injections does not have this glycam coating, and this makes it highly inflammatory.

3. Has endotoxinaemia been overlooked as a major driver of vaccine adverse events?

3.1 Plausible roles for endotoxinaemia in lethal events

3.1.1 Plausible mechanistic links to the known risk of anaphylaxis

As mentioned above, a VAERS report from January 7th 2021 states that a 53-year-old woman suffered anaphylaxis after being injected with her first dose of Process 2 Lot EE8403. By July 2021, Pfizer was more candid and expansive on the anaphylaxis casualties, including nine deaths in the post-marketing injection campaign.

Pfizer said 'The most frequently reported relevant PTs (preferred terms) (≥2%), from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy were: Anaphylactic reaction (435), Dyspnoea (356), Rash (190), Pruritus (175), Erythema (159), Urticaria (133), Cough (115), Respiratory distress, Throat tightness (97 each), Swollen tongue (93), Anaphylactic shock (80), Hypotension (72), Chest discomfort (71), Swelling face (70), Pharyngeal swelling (68), and Lip swelling (64).'

Despite this clear danger signal Pfizer reported:

> 'Conclusion: Evaluation of BC cases Level 1–4 did not reveal any significant new safety information. Anaphylaxis is appropriately described in the product labeling as are non-anaphylactic hypersensitivity events. Surveillance will continue.'

Pfizer post-marketing data showed to April 2022 the following numbers of victims known to them to have suffered:

> Anaphylactic reaction 7,214
> Anaphylactic shock 1,184
> Anaphylactoid reaction 197
> Anaphylactoid shock 8
> Anaphylactoid syndrome of pregnancy 1

Pfizer took keen interest in more lethal lot numbers.

Lot ER7449, used in Sunshine Hospital, Victoria, Australia, in early 2021, caused >3% anaphylaxis. The TGA let Lot ER7449 be used without endotoxin testing.

Other lots are listed, including EP9605, ER2659, ER9480, and EY2173, as leading causes of anaphylaxis, injury and death.

A prospective study at Mass General Brigham Hospital in the US followed employees who received their first dose of an mRNA COVID-19 vaccine between December 16th 2020 and February 18th 2021. Follow-up was limited to three days. 25 929 people (40%) received the Pfizer-BioNTech vaccine and 38 971 (60%) received the Moderna vaccine. Interestingly, 19% of staff did not complete any of the survey methods used. Acute allergic reaction symptoms ensued, including itching, rash, hives, swelling, and or respiratory symptoms. Note that this does not match Pfizer Preferred Terms.

Anaphylaxis was confirmed in 16 employees, 7 from Pfizer and 9 from Moderna. 94% of the anaphylaxis victims were female. The mean time to anaphylaxis onset was 17 minutes (and the range was 1 minute to 120 minutes).

3.1.2 Plausible links to the known risk of myocarditis

Can endotoxin contamination be considered a novel mechanism of vaccine-induced cardiac damage, independent of the mRNA or LNP constituents of the COVID-19 vaccines? Alternatively, may LPS prime for later cardiotoxicity or vaccine-associated myopericarditis (VAM)?

The classic profile of those affected by VAM, from its recognition in April 2021, includes younger males, often after their second dose. Having said that,

myocarditis and pericarditis can also occur in males and females of all ages, and can follow booster doses. The time interval from the last dose can be days to weeks.

VAM appears to involve a CD4-predominant lymphocytic infiltrate of the myocardium, rather than an eosinophilic or other form of infiltrate, compatible with a hypersensitivity myocarditis. Current thinking is that VAM may be an autoimmune phenomenon. Baumeier et al. (2022) examined vaccine-derived spike protein in cardiac biopsies and postulated that the inflammation was a reaction to that foreign antigen. Barmada and colleagues (2023) used unbiased immune sampling techniques in a case-control study of VAM sufferers, *versus* vaccinees without VAM. These investigators showed a pattern, on peripheral blood markers, of cytokinopathy including IL-1 and IL-15, with aberrant cytotoxic lymphocytes. Although cardiac tissue was not examined, the absence on peripheral blood samples of cardiac autoantigens or clonal expansion of B and T lymphocytes led these authors to conclude that immune and pro-inflammatory mechanisms other than classical autoimmunity were engaged.

More recently a research article titled 'Sex-specific differences in myocardial injury incidence after COVID-19 mRNA-1273 booster vaccination' published in the *European Journal of Heart Failure* in 2023 (Beurgin et al.) was a prospective study of 777 healthcare workers receiving boosters. Elevated day-3 troponin was detected in 40 cases, but after adjudication, 22 were felt to have no explanation for myocardial injury other than the Moderna vaccine exposure. Interestingly, women were overrepresented in this sample. It is important to delineate this condition, in which cardiac myonecrosis is detected by an ultrasensitive blood test. This finding represents cardiotoxicity with more study required to determine long-term implications; it should not be ignored and should be taken very seriously, but also should not be over-interpreted so as to say 1 in 35 booster recipients suffer myopericarditis. This is because not all of the criteria necessary for a diagnosis of myocarditis were examined and fulfilled.

Heart damage following vaccine dosing may also happen rapidly, in a hyperacute timeframe, which may not be compatible with sufficient transcription of spike protein from mRNA to produce direct cardiotoxicity, and is certainly earlier than would be expected for the generation of antibodies to spike protein. In one case, just one day following Bivalent Pfizer BNT162b2 (wild and BA.4-5) injection, a man was rushed to hospital with dyspnoea, a heartbeat of 207, and blood pressure of 74 mmHg. This was his fifth. The diagnosis was myocarditis with ventricular tachycardia.

On the other hand, deleterious cardiac effects can occur via direct endotoxin damage and via cytokine injury. Endotoxin damage to the heart and its blood

supply system cells from inflammatory interleukins is well known. A prospective multinational study, limited by small sample size, showed that measured blood endotoxin level >50 picogram/ml is a significant risk predictor of cardiovascular disease. Experimental demonstration of heart damage by endotoxin induction of IL-1β in mice confirmed amplification by positive feedback loop of the IL-1β. Importantly, the latter induces expression of miR-155.

Upregulation of miR-155, which is detected in both SARS-CoV-2 infected people and those exposed to endotoxin, is a predictor of myocardial damage and inflammation, independent of COVID-19. During myocardial infarction, miR-155 is sharply upregulated in macrophages in the heart muscle and released into the extracellular milieu within exosomes. These exosomes are delivered to fibroblasts, and miR-155 downregulates proteins in the fibroblasts that protect from inflammation and promote fibroblast proliferation. The resulting impairment predisposes to cardiac rupture in infarction. The most plausible explanation for why death from myocarditis is more prevalent in younger people may be that older people have less muscle mass, which can be measured by the Sarcopenia Index, and therefore generate less miR-155.

Analysed airway biopsy samples showed young people have much higher miR-155 than the elderly, dramatically increasing risk of myocarditis.

Endotoxin induces the calcium-independent NO synthase known as inducible nitric oxide synthase (iNOS). Tachycardia with associated fever, hypotension and lymphopenia is the expected outcome from injection of endotoxin, as has been demonstrated in numerous carefully-managed clinical experiments where human response is known to differ from that of mice.

Pfizer tells us that during their trial,'one (0.3%) participant in the Original-BA.1 30/30μg group reported a life-threatening (Grade 4) adverse event of atrial fibrillation on day 1 of study vaccination'. Once Pfizer changed product to the Process 2 injection, they reported 3,285 cases of atrial fibrillation plus 22,873 cases of tachycardia to April 15th 2022.

Pfizer uses numerous medical terms to dilute the high numbers of hearts damaged by their COVID-19 products.

3.1.3 Plausible links to life-threatening organ dysfunction

Kidney and liver disease can be caused by endotoxin. It is known that Pfizer reported excessive numbers of kidney injuries to April 2022, with the warning signal of the thousands of cases spread over a plethora of specialist medical terms. Endotoxin produces immediate damage to mesangial cells (MC) which maintain the architecture and cellular communication and indirectly join in the glomerular filtration rate for the correct functioning of the glomerulus of our kidneys.

In 1952 it was found that rabbits pretreated with cortisone suffered multiple organ damage, particularly in the kidneys after they were given a single intravenous injection of gram-negative bacterial endotoxin. In 1968, Starzl demonstrated destruction of human kidneys from suspected endotoxin priming, reported in three transplant patients. Researchers used immortalized commercially available mouse kidney cells to show that some particular inflammatory cytokines, including the Apex Cytokine IL-1β and Interleukin 36β (IL-36β), were upregulated in response to LPS exposure. This leads to NLRP3 inflammasome formation and the activation of the IL-17/IL-23 axis in kidney tissue, which in turn induces an increase in the inflammatory and fibrotic factors in tubular epithelial cells that allow the formation of tubulointerstitial lesions (normally associated with chronic kidney disease). A strong effect was found with a concentration of 100 picogram/ml.

Pfizer also knew from its clinical trial and first 90 days of mass vaccination that severe and fatal liver failure was a clear signal of systemic assault by its product with 70 cases and five deaths. The median onset of the liver damage was just three days. It is the author's opinion that many cases of vaccine-induced liver failure are likely hidden under 'sepsis' and 'multi-organ failure' and few autopsies appear to have been conducted. Pfizer uses 122 different, often vague, descriptors of liver damage under the heading 'hepatobiliary disorders' apparently to hide tens of thousands of victims.

MiR-155 upregulation by endotoxin may be a causative factor in rapid liver failure or dysfunction after Pfizer immunisations. In 2007, endotoxin was shown to cause fatal liver damage in E-miR-155 transgenic mice and their wild-type littermates. Death was hastened by administration of D-galactosamine; rats given galactosamine showed elevated activities of serum alkaline phosphatase (ALP), alanine aminotransferase (ALT), levels of triglycerides, total cholesterol, lipid-peroxidation and reduction in the levels of serum total proteins, albumin and cellular glutathione S-transferase (GSH). Galactosamine increased the nuclear translocation of NFκB and elevated iNOS protein expression, tumour necrosis factor (TNF-α), interferon (IFN-γ), inflammatory interleukins IL-1β, IL-6, IL-12, IL-18 and decreased anti-inflammatory IL-10 mRNA expressions. The mechanism of endotoxin-galactosamine liver toxicity involves attack of the Kupffer cells by endotoxin attachment to Toll-like receptor 4 (TLR4).

It is known that TNF-α enhances the liver toxicity of miR-155, which is thought to directly target transcript coding for several proteins – Fas-Associated Death Domain protein (FADD), IκB kinase ε (IKKε), and the receptor (TNFR superfamily)-interacting serine-threonine kinase 1 (Ripk1). Eμ-miR-155 transgenic mice produced higher levels of TNF-α when exposed to endotoxin, promoting the positive feedback loop.

Do the mRNA vaccines upregulate galactosamine in humans, thereby increasing the lethality of the endotoxin miR-155 pathway? Do the vaccines alter the uridine pathways in humans? Are there racial differences in liver damage by the vaccines that might relate to galactose pathways? Will women suffer more liver damage and fatality than men related to galactosamine involvement in follicle-stimulating hormone and luteinizing hormone? It is hoped that answers to these questions will unfold in the near future.

3.2 Plausible roles for endotoxinaemia relating to non-lethal events

3.2.1 Lymphadenopathy

Did BioNTech-Pfizer and complicit marketers of their COVID-19 injection, including government departments around the globe, lie to the public when they said that the lipid nanoparticles and the mRNA floating inside or outside them would simply enter muscle cells in the arm, take them over and force them to become factories for synthetic spike generation and resultant anti-spike antibodies? A lecture given by one of the BioNTech founders makes it clear that the actual target of the vaccine contents is the draining lymph nodes and the wider lymphatic system, including the spleen.

Once the mass injections began, others associated with the Pfizer vaccine design were quite straight with the intended action on the lymphatic system.

In an interview of September 2021, Professor Drew Weissman, said:

> LNPs encapsulate the mRNA, protecting it from extracellular degradation, and facilitate endosomal release of the mRNA into the cytoplasm. When the LNP-Ψ-mRNA is injected into the muscle, every cell takes it up, but for muscle cells that is very inefficient, you can barely measure the protein that they make. The LNPs are 80nm in size, which is about the size of a virus. What happens is that the LNPs travel through the lymphatic drainage to lymph nodes, and in the lymph nodes, DCs (Dendritic Cells) take them up. There is also an infiltrate of lymphoid cells into the muscle that picks up the particles. Once the vaccine gets to a lymph node, the DC translates the mRNA and presents it to B and T cells to activate them, and that is how the immune response is started.

From the Pfizer Clinical Trial, it was known that lymphadenopthy was a small-scale problem caused by their mRNA vaccines made with Process 1, but there was an explosion of cases when they moved to Process 2 because of the endotoxin from the E.coli bacteria used in production. As expected, the lymphadenopathy is usually detected on the side of the body that received the injection.

A trial document obtained from the UK government said, 'Lymphadenopathy is identified as an adverse reaction for BNT162b2 vaccine.' During the blinded placebo-controlled follow-up period, 9 and 2 participants in the BNT162b2 and placebo groups reported AEs of lymphadenopathy, respectively. That is about 0.041 % of the roughly 22,000 who received the Process 1 injection.

The numbers increased in a follow-up study to one month after the second dose of Process 1 vaccine.

By the trial interim cut-off date of 14 November 2020, Pfizer reported the following data to regulatory authorities in Japan:

> 'In the Phase II/III part of foreign Study C4591001, serious adverse events occurred in 126 of 21,621 subjects (0.6%) in the Comirnaty group and 111 of 21,631 subjects (0.5%) in the placebo group.'

The incidence of lymphadenopathy was 0.3% (70 of 21,621 subjects) in the Comirnaty group and 0.0% (7 of 21,631 subjects) in the placebo group. Among these events, those in 50 subjects in the Comirnaty group and four subjects in the placebo group were considered related to the study vaccine. Lymphadenopathy mostly occurred in the arm or neck. Many of the events occurred within two to four days after study vaccination, but those in 12 subjects in the Comirnaty group and three subjects in the placebo group occurred ≥8 days after vaccination (98 days at the latest). One subject in the Comirnaty group experienced lymphadenopathy within 30 minutes of vaccination. The event in one subject in the Comirnaty group was serious and considered related to the study vaccine, with the outcome of 'not recovered' (data cutoff date: November 14, 2020).

The lymphadenopathy problem in Australia is large, as shown by the Database of Adverse Event Notifications. By 23 August 2021 there were 1,126 cases. Worldwide, Pfizer reported the following case numbers to April 2022: lymphadenopathy, 73,287 (5.44 % of all adverse reaction reports); lymph-node pain, 8,395; vaccination-site lymphadenopathy, 4,540; lymphadenitis, 2,115; lymphoedema, 75; lymphopenia, 274.

Also related are cases of lymphadenopathy that can arise as a result of: Epstein-Barr virus infection reactivation, 115; Epstein-Barr virus infection, 109; Epstein-Barr virus antibody positive, 26.

In a huge Israeli study with the vaccinated and control groups each including a mean of 884,828 persons, lymphadenopathy (Risk Ratio, 2.43; 95% CI, 2.05 to 2.78; Risk Difference, 78.4 events per 100,000 persons; 95% CI, 64.1 to 89.3) stood out as one of many harms of the Pfizer injection.

Case reports include lymphadenopathy imaged in the right breast of a woman just

one day after her Pfizer COVID-19 injection. Another Pfizer injection case of lymphadenopathy was reported detected at three days in a 72-year-old woman. Lymphadenopathy was detected during mammograms and the incidence increased with subsequent injections. As stated earlier, lymphadenopathy is recognized as one of many IgG4 diseases caused by multiple injections. Buried in an EMA document, we see 14% of people reporting adverse reaction to Pfizer boosters suffered lymphadenopathy.

Endotoxemia researchers in Scotland found that the Odds Ratios (OR [95% CI]) for the occurrence of splenomegaly and cervical lymphadenopathy were 1•19 [1•01–1•4] and 1•16 [1•02–1•35] respectively for every 10 picogram/mL increase in plasma endotoxin concentration.

Reviews of the explosion of lymphadenopathy have found incidences of cancer reactivation and metastasis and called for extra care in imaging interpretation, to distinguish reactive lymph nodes from metastatic lymph node enlargement, especially in patients with underlying malignancy.

Pfizer boosters were associated with rapid progression of angioimmunoblastic T-cell lymphoma in a detailed case report.

4. Other mechanistic insights

4.1 Immune tolerance and endotoxinaemia

Multiple vaccine doses have been shown to induce immune tolerance to SARS-CoV-2 Spike Protein COVID-19 by IgG4 switching. WHO is officially worried about IgG4 class switching weakening the human immune system.[4]

IgG4-related disease (IgG4-RD) was formerly known as IgG4-related systemic disease. It is a chronic inflammatory condition characterized by tissue infiltration with lymphocytes and IgG4-secreting plasma cells and, various degrees of fibrosis resulting in tissue scarring. IgG4 diseases include lymphadenopathy, atopic dermatitis, autoimmune pancreatitis, bronchial asthma, Riedel thyroiditis, interstitial pneumonitis, interstitial nephritis, prostatitis, retroperitoneal fibrosis, inflammatory aortic aneurysm and many clotting diseases or other blood disorders.

Gram-negative endotoxin is clearly implicated in IgG4 disease. Galectin-3 is an antigen associated with IgG4 disease that drives expansion of circulating plasmablasts and CD4+ cytotoxic T cells in patients and is a marker of severe COVID-19. Galectin enhances the endotoxin inflammatory response. Galectin was shown to allow low endotoxin (LPS) concentrations (1 μg/mL without serum, 1 ng/mL with serum) to upregulate CD11b expression and reactive oxygen species (ROS) generation on human neutrophils *in vitro* and drastically

enhanced the binding efficiency of LPS to the neutrophil surface.[5]

During his lecture and in private discussion afterwards at the AMPS event held in Melbourne on May 31st 2023, Emeritus Professor Robert Clancy mentioned the dangers of IgG4 disease and melanoma, and other cancer susceptibility. Other research groups have found that IgG4 suppresses our capacity to fight off cancers and actually accelerates breast and colorectal cancers and carcinogen-induced skin papilloma.

4.2 Carcinogenesis and endotoxinaemia

Case reports point to both sudden onset of cancer and rapid deterioration of patients with dormant cancer after mRNA immunisation. Pfizer used 468 different descriptors under the heading 'Neoplasms benign, malignant and unspecified (including cysts and polyps)'; these included 35 different types of lymphoma and 14 different terms for leukaemia. Unfortunately, the term 'turbocancer' appears to have been injected into the public lexicon, subsequent to the vaccine roll-out, to convey the rapidity of cancer progression being observed. This notion gained strength when Prof Angus Dalgleish, a prominent UK oncologist and cancer biologist who incidentally worked alongside Dr Fauci in the USA in the 1970s, spoke out in late 2022. He raised the alarm about a prominent pattern seen his practice, of reactivations of previously controlled cancer after mRNA boosters.

Cancer can be caused by a plethora of environmental exposures, including some drugs, sometimes in combination with genetic vulnerabilities, according to the 'multi-hit hypothesis'. It is difficult to imagine a more disturbing scenario than a worldwide program of vaccination enhancing carcinogenesis. However, plausible mechanisms exist, in particular the ability of spike protein, which once trafficked into the nucleus is able to modulate P-53 (suppression) and BRCA (activation) in a deleterious way, shown in a cell culture experiment; this finding has thus far not been replicated *in vivo* but is concerning nonetheless, since any medical student would be able to confirm that P-53 and BRCA are respectively among the most well-known and important tumour suppressor genes and oncogenes. As previously noted, miR-155, which is upregulated by endotoxin, is also capable of promoting and exacerbating cancer. To illustrate, genetically-modified mice that over-express miR-155 are bred for the study of blood cancers.

In the author's opinion, in the light of effects on mIR-155, we may expect to see a surge in diffuse large B-cell lymphomas, Hodgkin's lymphoma and subsets of Burkitt lymphomas (latency type III Epstein–Barr virus-positive Burkitt lymphomas) resulting from the COVID-19 mRNA vaccines.

Over-expression of miR-155 in humans has also been demonstrated in solid tumours such as breast, lung, and colon cancer. In lung cancers in particular, over-expression of miR-155 is an indicator of a bad prognosis. Contaminant endotoxin in mRNA vaccines alters the microRNA suite and should be considered as a contributor to reactivation of dormant cancer, as well as the induction of so-called turbocancers.

Thousands of cancer victims were used in experiments for Pfizer vaccines in Australia as a special subgroup of the AusVaxSafety 3-day surveys. In the case of solid cancers, they suffered much more than the general population. Children as young as 12 were used. About 1 in 40 victims reported having to visit the emergency department of a hospital or a doctor within three days of the injection. Blood cancer sufferers were treated as a separate group in the experiments and suffered horrendous side effects. Pfizer used a number of subjects with pre-existing leukaemia in its trials and reported 14 extra cases in those who received the BNT162b2 vaccine injection *versus* an extra 11 in the placebo group.

4.3 Reproductive health

4.3.1 Women suffer disproportionately from COVID-19 vaccinations; effects on fertility

In a report from Pfizer, 68.5 % of the 1,348,079 Adverse Reaction cases to April 15th 2022 were for females. In Australia the AusVaxSafety short-term survey, which ceased on February 8th 2023, did not supply data differentiated by sex; however, 57% of respondents across all age groups were women.

The number of pregnant women reporting that they had to visit a hospital emergency department or a doctor within three days of their vaccine dose increased to 1 in 50 after the second dose and a similar number for subsequent immunisations. The number of pregnant women reporting gastrointestinal symptoms, (nausea, vomiting, diarrhoea, abdominal pain) after the second injection was 14%, higher than the 11% for the general population.

The range of effects which form pharmacovigilance signals in women overlap with endotoxin effects in women and include irregular menstrual cycles, thrombosis, endometriosis, pregnancy loss, preeclampsia (which is the major cause of maternal and prenatal death), autoimmune disease and developmental damage to surviving children. In particular, LPS is implicated in the pathophysiology of endometriosis, in which LPS is found in menstrual blood.

Endotoxin and nickel both do their damage through attachment to toll-like receptor 4 and it is very provocative that 93% of VAERS reports after Pfizer immunisations from people known to have nickel allergy were women.

There are numerous online reports and studies that have shown that live births have fallen since the COVID-19 pandemic. While some may invoke chronological links to lockdowns and economic uncertainty, leading to fewer marriages and conceptions, there is circumstantial evidence that mass vaccination has contributed to reduction in live births. Pfizer reported 338 different types of 'Reproductive system and breast disorders' and this helps to dilute the warning signals. Thousands of women have reported disrupted menstrual cycles and even postmenopausal bleeding. Pfizer reported a case of postmenopausal haemorrhage within seven days of vaccine administration during the clinical trial.

Official data from authorities in The Netherlands showed a very clear warning signal was available by December 1st 2021. Postmenopausal women have an increased sepsis endotoxin mortality rate compared to pre-menopausal women. Postmenopausal women and women with induced menopause resulting from surgical removal of the ovaries have reduced levels of B cells and anti-inflammatory cytokines, IL-4, and IFN-γ, while NK cell activity and levels of pro-inflammatory cytokines such as TNF-α, IL-1β, IL2, and IL-6 are increased.

Direct effects of endotoxin on the uterus have been studied. Contrary to the previous discussion of a protective role of oestrogen in blood, hitting uterine macrophages with bacterial endotoxin induces production of biologically active proinflammatory IL-1β. Cytokine storm as a potential consequence of endotoxin-contaminated immunisation is by now well understood.

Shedding of the uterine lining during menstruation is primed by reduction in progesterone expression. The RelA(p65) subunit of NF-κB and the progesterone receptor interact with each other, exhibiting mutual repression. Activation of NF-κB by TNF-α also results in repression of the progesterone receptor (PR), while PR is able to repress TNF-α-induced NF-κB activity. Decidual casts may occur when the cessation of progesterone levels results in loss of support for the decidualized endometrial lining. Definitive proof that endotoxin reduces progesterone was performed by measuring the association between systemic levels of lipopolysaccharide-binding protein (LBP), a marker of endotoxin exposure, and levels of inflammation in the ovary (follicular fluid IL-6), plus steroid hormone production in 45 women undergoing IVF treatment.

Endotoxin is known to hit this system so hard that it leads to the permanent reduction of the primordial follicle pool, commonly known as the egg reserve. Estradiol attenuates endotoxin poisoning in human peripheral blood monocytes and macrophages. High doses of estradiol enhance endotoxin-induced IL-1β expression in an oestrogen receptor-dependent manner. Increased cycle length and increased menstrual flow may also be expected through effects on hypothalamus pituitary gland ovaries axis (HPO), follicle stimulating hormone

(FSH), luteinizing hormone, oestrogen and progesterone balance (repeated vaccine dosing).

Numerous animals have been used to demonstrate these effects. Looking at *in vivo* study of the effects of injected endotoxin in mice, infused intra-peritoneally with 100 μg of ultrapure endotoxin (LPS) from E. coli serotype O111:B4 (invivogen), effects are dramatic and dose-dependent. Endotoxin results in atretic ovarian follicles, that is, follicles that will be resorbed after being prevented from maturing. In this work, the attack of the endotoxin on the toll-like receptor 4 (TLR4) was proved by using knockout mice. Similar *in vitro* effects of endotoxin on cows and rats have been reported. Both mother and foetus are threatened by endotoxin circulating in their systems as shown in the scheme in Figure 5.[12]

The focus now shifts to the way endotoxin and LPS attack the human female reproductive system and the developing placenta and embryo. There are acknowledged underreported US VAERS data to August 22nd 2022. In an

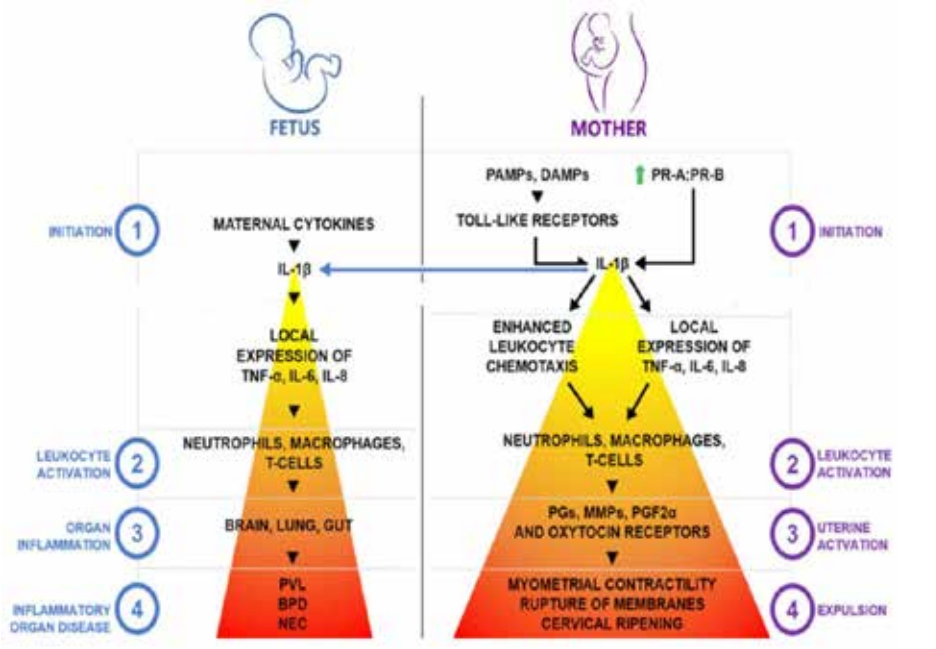


Figure 5

This scheme demonstrates that Interleukin 1-beta, IL-1β is the 'apex cytokine' in the inflammatory cascade of preterm birth and foetal inflammatory injury. As discussed earlier this cytokine is known to self-amplify, defying Paracelsus dogma. PR-A/PR-B = P4 Receptors A and B; PGs = Prostaglandins; MMPs = Matrix MetalloProteinases; PGF2α = Prostaglandin F2α; PLV = Periventricular Leukomalacia; BPD = BronchoPulmonary Dysplasia; NEC = Necrotizing EnteroColitis. Increasing colour intensity represents increasing inflammatory response.

excellent interactive guide to the effect on pregnancies of the Janssen, Moderna and Pfizer COVID-19 injections, Openvaet[1] found 15 maternal deaths and 908 foetal deaths after Pfizer by extracting symptoms in the text of VAERS reports. Also, 27.5% of the reported missed pregnancies happened within one week of the injection.[13] To April 15th 2022, Pfizer reported that 1.3% of all adverse-event cases after their injections were from 17,156 pregnant or breastfeeding women. Pfizer spread these adverse events under 179 different descriptors under two main headings: 'Injury, Poisoning and Procedural Complications' and 'Pregnancy, Puerperium and Perinatal conditions'.

Endotoxin exposure to women and their developing foetuses may result in chorioamnionitis with fever, leukocytosis, tachycardia, uterine tenderness and preterm rupture of membranes. First trimester disruption of placenta formation can be caused by LPS and involves MAPK signalling pathway phosphorylation and resultant increase in IL-8 and IL-6. Endotoxin damages spiral artery remodelling, correlated with monocyte chemokine-1 (MCP-1), and down-regulates markers related to extravillous trophoblast invasion in placentas according to the following scheme.[14]

MyD88 = Myeloid differentiation 88, IRAK = Interleukin Receptor 5Associated Kinase, TLR4 = Toll-Like Receptor 4, ERK = Extracellular

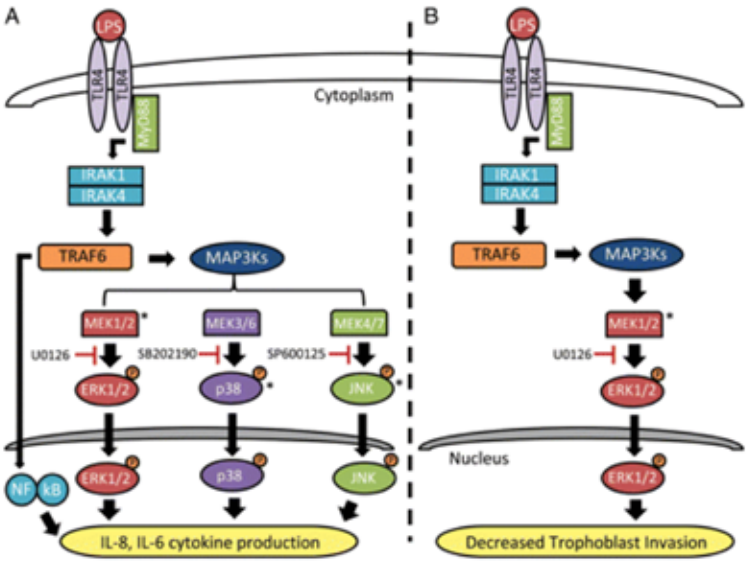


Figure 6

1 https://www.openvaet.org

signal-Regulated Kinase, TRAF6 = TNF Receptor Associated Factor 6, MAP3Ks = Mitogen-Activated Protein Kinase 3, MEK = MAPK Extracellular signal-regulated Kinase, p38 = p38 Mitogen-Activated Protein Kinase, JNK = c-Jun N-terminal Kinase. Note that TLR4 is a target for COVID-19, endotoxin and nickel, all of which elevate IL-8.

Mouse models show what injected endotoxin does at a dose of 10 μg/kg Gestational Day (GD) 13, and 40 μg/kg LPS daily until GD16. Endotoxin substantially elevated the percentage of CD86 +, TNF-α+, IL-1β+ and iNOS+ dMφ (M1 subtype) but diminished the percentage of CD206 +, CD 163+, IL-10+ and Arg-1+ dMφ (M2 subtype) in pregnant mice. Endotoxin damages spiral artery remodelling, correlated with monocyte chemokine-1 (MCP-1), and down-regulates markers related to extravillous trophoblast invasion in placentas. Decidual macrophages (dMφ) are the second most abundant immune cells in pregnancy and are adversely affected by endotoxin, resulting in miscarriage and foetal growth restriction.

Women suffering preeclampsia, the major cause of maternal and perinatal death, experience hypertension, proteinuria, headache, vomiting, and kidney and liver dysfunction. They have increased numbers of circulating leukocytes, neutrophils, and serum levels of TNF-α, interleukin-6 (IL-6), and C-reactive protein (CRP). This is found in endotoxin poisoning. Women with preeclampsia have lower levels of anti-inflammatory interleukin 10 (IL10).

Human placentas from women with and without preeclampsia have been compared. They showed that reduced α7 nicotinic acetylcholine receptor (α7nAChR) is involved in the endotoxin response of exaggerated inflammation. The level of choline acetyltransferase (CHAT) was reduced in women with preeclampsia and endotoxin-treated mice.

Endotoxin is routinely used to induce preterm birth, and sheep are a favoured test animal where the endotoxin can be administered via various routes, including injection into the uterus or amniotic fluid. Preterm birth is a major cause of perinatal death and long-term morbidity.

Pfizer has an ongoing teratology study to see what effects their COVID-19 immunisations have on surviving foetuses of mothers who are injected before or during pregnancy. Intergenerational infertility is a major concern. Teratogenic damage by endotoxin to ovaries is well known. Pregnant rats hit with intraperitoneal endotoxin injections produced intrauterine growth restriction and substantially lower levels of serum anti-Müllerian hormone in offspring. To April 2022, Pfizer reported 376 different types of 'Congenital, familial and genetic disorders'. A case of a woman injected with Pfizer who chose to terminate her pregnancy at 25 weeks' gestation because heart damage

was detected in her developing child is seen in VAERS.

It will take perhaps 20 years to learn the full extent of what will happen in the second-generation descendants of these injections.

4.3.2 Endotoxin reduces male fertility

Male infertility has attracted less attention. So far I have found two cases of hypogonadism listed as adverse events during the Pfizer injection trial.

Pfizer reported numerous cases (numbers in parentheses) of testicular adverse events in a document obtained by FOI demand to the Therapeutic Goods Administration in Australia. These included testicular pain (385), swelling (90), infertility (60), orchitis (52), haematospermia (43), orchitis noninfective (20), disorder (22), testis discomfort (16), torsion (10), oedema (4), cyst (3), infarction (3), abscess, haemorrhage, injury, neoplasm, retraction (two cases each), atrophy, hypertrophy, mass, microlithiasis, necrosis, oligoasthenoteratozoospermia, orchidectomy, spermatozoa abnormal (4), sperm count decreased (9), sperm analysis abnormal, spermatic cord haemorrhage, semen discolouration (1 case each).

GELDING (Gut Endotoxin Leading to a Decline In Gonadal) function is an appropriate term used for endotoxin reduction of testosterone production by testes, both by direct inhibition of Leydig cell steroidogenic pathways and indirectly by reducing pituitary luteinizing hormone drive, leading to a decline in sperm production.

A formal prospective study of 37 sperm donors found vaccine-induced damage three months after the Pfizer dose. A fever of 39°–40°C, as routinely observed in Pfizer trials and mass rollout, causes reduced total sperm count, motility rapidly progressive: grade a and slowly progressive grade b, and vitality for 79 days for a volunteer semen donor. A fever of 38°-39°C is sufficient to produce reduced sperm head size. Complete absence of sperm, azoospermia, can result from fever. Data from the AusVaxSafety survey show that adolescents report more fever than the older vaccine recipients.

Endotoxin in mRNA injections likely attacks male fertility by creating cytokine storm in the human testis and epididymis, reducing messenger RNA and Type 1 parathyroid hormone receptor (PTH1R) expression. Oxidative stress has been identified as a factor in low sperm count. Pro-inflammatory mediators in inflammatory reactions can induce a respiratory burst resulting in oxidative stress. The reactive oxygen species (ROS) formed can lead to leukocytospermia. Elevated nitric oxide levels associated with leukocytes can damage sperm.

Pfizer reported prostatitis (99), prostatic specific antigen increased (63), prostate cancer (35), benign prostatic hyperplasia (26), prostatomegaly (18), prostatic disorder (13), prostatic pain (8) and 17 other prostate disorders. Pfizer also reported balanoposthitis (22), genital tract inflammation (19), ejaculation disorder (18), ejaculation failure (18), oedema genital (18), organic erectile dysfunction (17), priapism (17), spontaneous penile erection (15), genital blister (16), genital erythema (16), genital paraesthesia (16), penile oedema (13), varicocele (13), genital lesion (11), penile haemorrhage (11), genital hypoaesthesia (10), penile erythema (10), penile vein thrombosis (10), scrotal erythema (10), Peyronie's disease (9), genital discharge (8), painful erection (8), penile blister (7), penile rash (7), scrotal oedema (7), penile size reduced (6), painful ejaculation (5), penile discharge (5), penile discomfort (5), epididymal cyst (4), penile exfoliation (4), penile haematoma (4), scrotal discomfort (4), (2). Oedema, varicocele and testicular torsion listed above can cause destruction of sperm via antisperm antibody (ASA) attack, which is permanent. Pfizer reported the instances of blood testosterone abnormal, blood testosterone decreased, (15), and blood testosterone increased (8).

4.3.3 Lactation issues

There have been shocking accounts of Pfizer injection damage to breastfeeding mothers and their babies in VAERS reports. There have been mothers drying up or noting their blue or green milk, or haemorrhaging while collecting, having decided to pump and dump, rather than risk the child. At least that allows mothers to take painkillers for their own symptoms. One study found that 1 in 60 women suffered green breast milk after their mRNA vaccine injection. Another study found 1 in 88 breastfeeding women suffered discoloured milk. Haeme-based enzymes can cause this effect. Haeme peroxidases lactoperoxidase (LPO) and myeloperoxidase (MPO) are present in human milk, with LPO dominating a few days after beginning lactation.

4.4 Endotoxin readily enters the brain

It has been demonstrated that NADPH oxidase (NOX) and iNOS act in synergy to destroy brain cells. Endotoxin iNOS damages oligodendrocyte (OL) progenitor cells (OPCs) causing periventricular leukomalacia (PVL), the most common form of brain damage in premature infants via microglia. Endotoxin injection of mice sees elevation of iNOS with associated memory loss and amyloidosis linking it with Alzheimer's disease.

Endotoxin creates quinolinic acid, in a series of steps from tryptophan, which acts as a neurotoxin, gliotoxin, proinflammatory mediator, pro-oxidant molecule, and can alter the integrity and cohesion of the blood–brain barrier. Quinolinic acid is linked to Alzheimer's disease, HIV-associated

neurocognitive disorders, Parkinson's disease, motor neurone diseases, Huntington's disease, multiple sclerosis and major psychiatric disorders. Further aspects of brain damage are discussed under the heading of autoimmune diseases caused by endotoxin.

The most common symptom after the injection is headache and this is easily understood because human volunteers have literally had their heads examined with magnetic resonance imaging, showing their brain temperature increases very quickly,[8] creating fatigue, headache, with muscle pain, fever and chills.

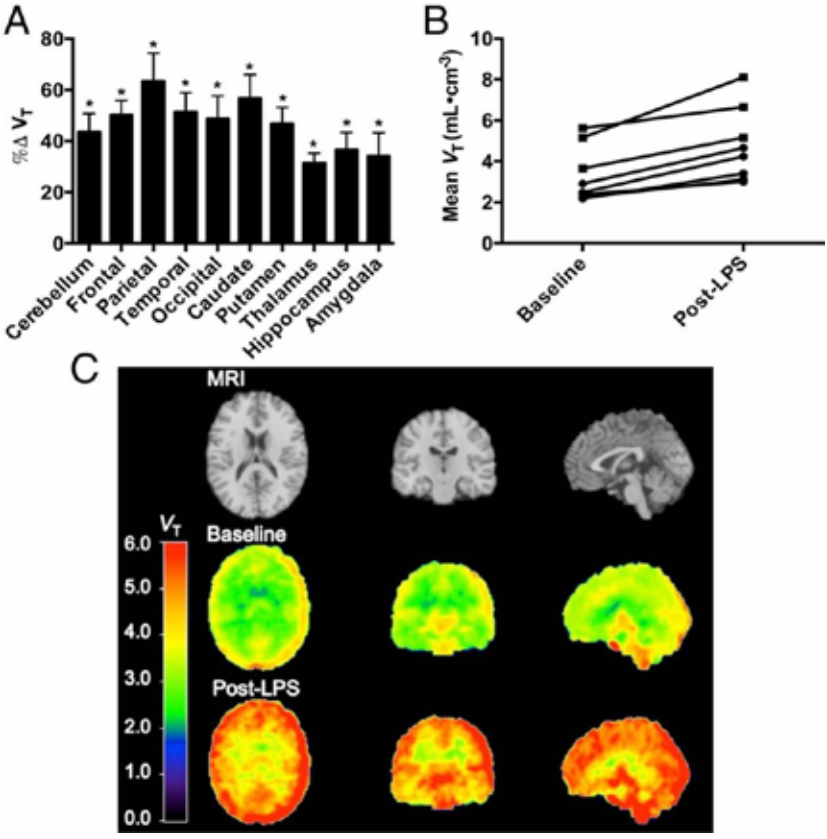


Figure 7
Female volunteers with or without fibromyalgia suffered increased brain temperature when injected with 300 to 400 picograms/kg of endotoxin.

Other effects of endotoxin on the brain include narcolepsy, also known as jypersomnia, with a well-defined mechanism shown in the figure.[9] Narcolepsy is often accompanied by increased feelings of anxiety and fear, and this has been produced experimentally with endotoxin in animals. Further study is

needed in relation to other brain dysfunctions, including multiple sclerosis.

Pfizer reported the following case numbers after their injections: tremor 10,748; resting tremor 21; balance disorder 4,497; movement disorder 2,736; gait inability 1,678; bradykinesia 197; Parkinson's disease 105; Parkinsonism 44; Parkinsonian gait 6; Parkinsonian rest tremor 4; cogwheel rigidity 4; Parkinsonian crisis 1; vascular Parkinsonism 1.

Insulin resistance is a pathological hallmark in the brain of Parkinson's disease sufferers. Pfizer has thousands of cases of diabetes listed in its adverse-event reports, spread under 35 different headings. When endotoxin was injected into the right striatum of male wistar rats, it predictably impaired motor performance of the animals, and increased the levels of α-synuclein and toll-like receptor 4 (TLR4). Endotoxin also reduced mRNA levels of IRS1 and IRS2 and enhanced GSK3β mRNA and protein, indicating the development of insulin resistance.

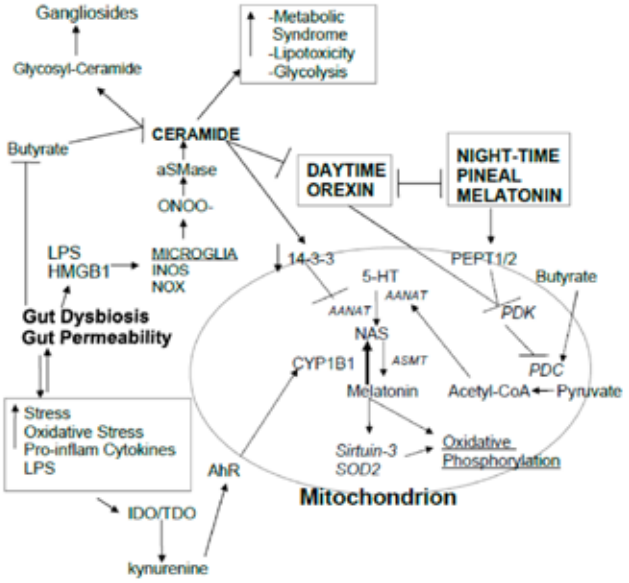


Figure 8

Facial and peripheral paralysis were recognized early as neurological adverse reactions after Pfizer injection trials. Endotoxins from gram-negative E. coli bacteria, as used in Pfizer injection production, cause paralysis via molecular mimicry between bacterial glycoconjugates and peripheral nerve gangliosides.

Guillain-Barré syndrome (GBS), possibly arising from a similar assault on the brain to narcolepsy, has been associated with gram-negative bacterial infection with campylobacter jejuni and mycoplasma pneumoniae. The endotoxin does

the damage and focus has been on the polysaccharide with explanations at molecular mimicry level. Those from campylobacter jejuni are associated with Guillain-Barré Syndrome patients' gangliosides. Influenza vaccine dose endotoxin levels have been correlated with GBS cases reported to VAERS.

Bell's palsy after nasal influenza treatment led to cancellation of the product which used escherichia coli endotoxin as adjuvant.

Microglia are usually in a resting state (M2), but in Parkinson's disease can enter M1 state because of the presence of α-synuclein aggregates. The M1 microglia release pro-inflammatory factors, including TNFα, interleukin (IL)-1β and IL-6, which can cause motor neurones to die. This is due to the known epigenetic effects of endotoxin.

Dying cells can release factors to increase the activation of M1 microglia, leading to a positive feedback loop which causes continually increasing cell death.

α-Synuclein aggregation leads to dopaminergic neuronal cell death through disruption of mitochondrial function.

The substantia nigra has a high density of endotoxin-targeted microglia and is particularly sensitive to a challenge with endotoxin. Figure 9 is adapted from an article discussing long COVID;[10] it can also be used to appreciate how endotoxin will cause a wide range of problems from altered taste to heart palpitations.

Altered taste was reported to VAERS, especially in people who have nickel allergy, after mRNA injections. This might be related to the fact that nickel also uses the TLR4 pathway in its toxic mechanism.

When endotoxin enters the central nervous system, it damages finely-tuned feedback loops that are involved in the sympathetic nerve pathways. This explains the frequent reports of diarrhoea and vomiting after the injection.

The large scale AusVaxSafety survey of millions of injected Australians found 1 in 9 people reported gastrointestinal symptoms, including diarrhoea, vomiting, nausea and abdominal pain after the second dose. This was considerably more than reports after their first dose. This indicates their bodies were made allergic to components.

To April 2022, Pfizer reported 798 different 'Nervous system disorders' as well as numerous serious effects under 'General disorders and administration site conditions'.

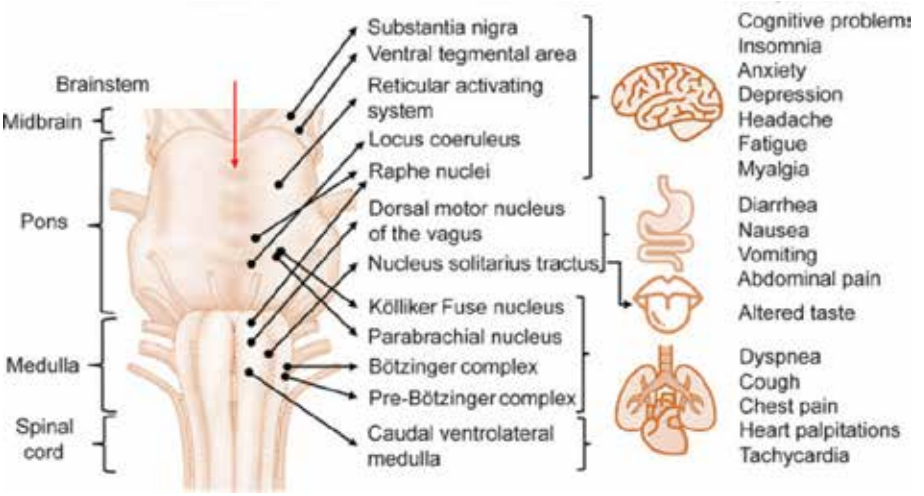


Figure 9

4.4.1 Blindness

Pfizer vaccine products cause 400+ different named eye disorders, according to their own documents.

When lambs are injected with endotoxin the increase in temperature of their corneas can be measured with great accuracy as a non-invasive method of systemic inflammation monitoring. There are probably multiple mechanisms behind the numerous causes of unilateral or bilateral blindness after mRNA injection. A study that famously attracted the attention of Elon Musk found higher risk of all forms of retinal vascular occlusion in two years after vaccination, with an overall hazard ratio of 2.19 (95% confidence interval 2.00–2.39).

The Moderna and Pfizer vaccines were especially bad, compared to other vaccines. A total of 289 cases of vaccine-associated uveitis were reported between 1984 and 2014. Pfizer caused 327 cases of uveitis to April 15th 2022.

Eye damage has been reported after mRNA COVID-19 injections, traced to myeloperoxidase (MPO) anti-neutrophil cytoplasmic antibodies (ANCA). Cytokine storm leads to increased expression of MPO.

VAERS records a 93-year-old woman in France made blind by her Pfizer vaccine injection within 48 hours. She lost consciousness and died. The lot number was EJ6788.

4.4.3 Tinnitus

A survey in Ohio USA in 2022 found 0.038% of all mRNA injection

recipients suffered tinnitus after their first injection and 0.031% after their second, making a combined incidence of 0.069% or 690 per million. Numerous cases of tinnitus were reported during the Pfizer Clinical Trials, and these should have been communicated according to informed consent.

Pfizer decided tinnitus was among numerous 'Signals determined not to be risks' and The European Medicines Agency appears to have shared this view, stating: 'Hearing loss and Tinnitus: In the 3rd MSSR AR (covering 1 February until 28 February 2021), based on a cumulative review of the cases reporting Hearing loss and/or Tinnitus it was concluded that a causal association with Comirnaty exposure was not suggested and the signal was closed.'

To April 15th 2022, Pfizer reported 14,233 cases of tinnitus, representing 1.06% of all people reporting adverse events after their injection. Pfizer also reported huge numbers for 76 other 'Ear and labyrinth disorders'. People often suffer multiple symptoms. A case report of a previously healthy Hong Kong man shows that two days after his first Pfizer injection he was devastated with fever, pain and vesicles in his right ear and canal, together with vertigo, tinnitus and loss of hearing. He also suffered facial palsy, tongue numbness and dysgeusia.

Specialists in the field have traced tinnitus to disruption of the nitric oxide cycle,[11] a known effect of endotoxin.

4.5 Autoimmunity

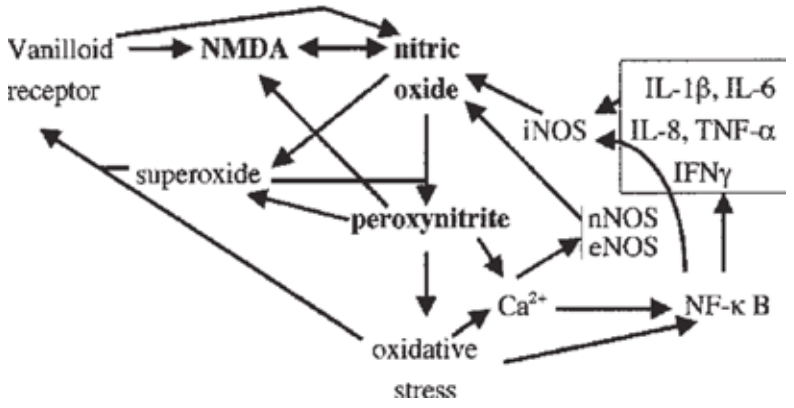


Figure 10

Note the familiar cytokine storm that is indicated on the right-hand side of their figure, where acronyms are as follows: eNOS Endothelial Nitric Oxide Synthase; IFN Interferon; IL Interleukin; iNOS Inducible Nitric Oxide Synthase; NF Nuclear Factor; NMDA N-Methyl-D-Aspartate; nNOS Neural Nitric Oxide Synthase; TNF Tumour Necrosis Factor.

Pfizer listed over 100 different kinds of autoimmune disease as adverse events. Note that these include medical specialist diagnoses using specific disease names, which helps to dilute the clear warning signal. Pfizer appears to show no interest in consolidating this list of suffering.

Monokine Induced by IFN-γ, (MIG, the G is for Gamma) and its receptor are known to cause autoimmunity via a positive feedback loop involving recruitment of Th1 lymphocytes which in turn stimulates MIG secretion from thyrocytes and numerous other types of cells, creating an amplification of the autoimmune process that destroys the organ.

E. coli endotoxin is a stimulator of MIG autoimmune response superior to that derived from other types of bacteria.

There are numerous published reports of thyroid damage by COVID-19 and the injections. One of these showed that the Pfizer injection causes damage to the thyroid gland within two days. Endotoxin as a cause of thyroid diseases via disruption of the kynurenine pathways has been reviewed.

Autoimmune diseases are caused by development of antiphospholid antibodies. Endotoxin lipid A, as found in Pfizer injections, has been shown in rabbits to induce antiphospholid antibodies, specifically systemic lupus erythematosus (SLE) type-aCL (β2GPI-dependent) and lupus anticoagulant.

We can learn from the effects of mass flu treatment. Repeated influenza vaccines increase risk of autoimmune systemic lupus erythematosus (SLE), multiple sclerosis and Guillain-Barré syndrome.

To April 15th 2022, Pfizer reported 1,461 cases of Guillain-Barré syndrome (GBS). Myelin-associated glycoprotein (MAG) antibodies attack the system. It is known that broadly reactive influenza antibodies also bind other proteins including insulin, endotoxin (lipoolysaccharide, LPS), and double-stranded DNA (dsDNA), demonstrating a propensity for autoreactivity.

A key paper by Toshio Hirano covers his work in the identification and isolation of interleukin 6 (IL-6) and its role in autoimmune diseases, including arthritis. [15] Th17 helper cells, an arm of the CD4+ T cell effector response, secrete several proinflammatory cytokines, such as IL-17, and induce various chronic inflammatory conditions, including autoimmune diseases. IL-6–mediated signalling via STAT3 increases the number of Th17 cells by enhancing RORγ expression. Hirano demonstrated this IL-6 catalytic positive feedback loop to non-immune cells in autoimmune disease involving NFκB and STAT3 (JAK–Signal transducer and activator of transcription 3).

In the case of IL-1β, which catalyses expression of itself by initiating a positive

feedback loop, direct attack on multiple organs including the heart is observed.

4.6 The case of shingles

In August 2021, Queensland Health decided to tell us all about shingles with pictures. They used the occasion to promote Zostavax® vaccine which 'is available on prescription to people aged 50 to 69 years and from 80 years, but it must be paid for by the patient.' This followed a surge in shingles cases after COVID-19 injection. They said:

> If you've had chickenpox in the past you can develop shingles. This is because the inactive chickenpox virus stays in your nerve cells near your spine. When shingles develops it's because the virus has become active again. Usually, a person will only get shingles once in their lives, but it can sometimes occur again if you have a weakened immune system.

In 2021 a paper (censored by an editor after two reviewers gave it favourable reviews) by Kevin McKernan et al. asserted that the reactivation of dormant viruses, including shingles, by the mRNA injections is a worrying warning signal, and pointed to possible mRNA mechanisms. Several other papers appeared linking increased numbers of case reports of shingles to Pfizer products.

By July 27th 2021, the European EudraVigilance database had reported 4,103 cases of shingles after receiving Pfizer Tozinameran, accounting for 1.3% of total reported events after the injection, a much higher incidence than reported after AstraZeneca, Janssen or Moderna. By January 2023 the European EudraVigilance database had recorded 15,887 cases of shingles after BNT162b2, accounting for 1.5% of total reported events.

Damage to the eyes is among the serious consequences of vaccine-induced shingles. A report from Japan in August 2022 found synthetic spike in the gaping shingles wounds of one victim.

In the phase-I/II trial with BNT162b1 in 2020, a dose-dependent decrease in lymphocytes in the first days following injection was reported. This is before the change of buffer from phosphate to tromethamine.

Two main signalling pathways have been implicated in shingles reactivation:

1] PhosphatidylInositol-3 Kinase (PI3K)-Akt pathway

2] The MAPK pathway.

Depletion of nerve growth factor (NGF) receptor TrkA can lead to the reactivation of shingles in some *in vitro* experiments. Searching the literature for information on mechanisms of shingles is made a little more difficult by the large volume of research into the related herpesvirus, Kaposi's-sarcoma-associ-

ated herpes virus (KHSV) that causes cancer. This virus can also exhibit latency.

It is interesting that this virus encodes a microRNA known as miR-K12-11 that functions as an orthologue of cellular miR-155, providing a replicative advantage to the KHSV through the down regulation of the expression of genes with known roles in cell growth and apoptosis. Endotoxin is clearly linked to shingles.

In 2014 sepsis patients, that is, those who had no exposure to COVID-19, carried much higher measurable loads of herpes, Epstein-Barr and cytomegalovirus, indicating the inflammatory cytokine storm caused by endotoxin weakened their immune suppression of the dormant viruses.

4.7 Epigenetics of endotoxin

The epigenetic effects of endotoxin are widespread, altering expression of hundreds of proteins in the human body. The complexity involves transformation of mast cells into numerous types of immune response cells triggered in response to threats. These cells secrete toxins that are responsible for the cytokine storm which can result in fatal sepsis.

5. There are questions

Apart from endotoxin, are there other molecules from the E. coli floating around in variable amounts in the mRNA injection vials? (An example I have raised is asparaginase.) Another worthy question: can Pfizer synthetic mRNA fragments enter human DNA?

Did the change of buffer from phosphate to tromethamine affect the relative toxicity? It is possible that the focus on apparent differences in lots, especially those used in Denmark, provides clues. However, there is a fundamental problem of not having complete inventory for the number of doses actually used. I have found that all lots which some people suspected were placebo-produced symptom sets consistent with endotoxin poisoning.

There is an obvious need for more independent laboratory study.

6. Root cause analysis and remedy: some conclusions

The COVID-19 vaccine initiative appears to be suffering from a superficial treatment of the contamination hypothesis and the biohazard which is endotoxin. Had there not been evidence of an unparalleled burden of harms – attributable to COVID-19 vaccines, whatever their apologists in industry and conflicted approving-regulators may say to distract from the obvious and appalling signals – and had there not been evidence of contamination and substandard

manufacturing standards as evidenced by batch variability, then there may be less impetus to press on for clarity and scientific transparency with regard to endotoxin contamination of mRNA vaccines.

But the fact is, there is now abundant evidence for batch variation, including differential rates of adverse events, raising basic concerns around Good Manufacturing Practice (GMP). With a now worldwide focus on the implications of Process 2 in unravelling this conundrum, we expect and demand resolution on the endotoxin issue, by accurate measurement, both within the Health Department and in independent laboratory settings.

As stated in the introductory section, the Laboratory Branch of the TGA use the LAL assay (the horseshoe blood extract, limulus amebocyte lysate assay), which is suitable for large fragments only and which is impaired in the presence of cationic lipids and mRNA. Combined, there is an obvious potential for underestimation and masking of the actual concentrations of endotoxin in vials.

The remedy urgently required is to use more sophisticated tests based on mass spectrometry after separation and volatile derivative formation. Unless the intention is that of a cover-up, there is simply no argument against a repeat phase of testing. Remember, endotoxin is so poisonous that electronic sensors have been made that can detect femtogram levels, that is, a billionth of a millionth of a gram. As stated earlier, I can also find no evidence that the TGA tests for the supertoxin lipid A, and this must be remedied immediately.

We must remember there is a new context, in the form of the Commonwealth's stated intention to develop an onshore manufacturing capacity for new mRNA vaccines, with partners such as Moderna. The sheer madness of failing to review these issues fully and transparently in the interests of the people cannot be overstated, and to proceed without the reckoning specified clearly here would constitute reckless indifference.

7. References

[1] https://en.wikipedia.org/wiki/Paracelsus

[2] Therapeutics Goods Administration Australia.

[3] Mohammad S and Thiemermann C. 2020. Role of Metabolic Endotoxemia in Systemic Inflammation and Potential Interventions. https://www.frontiersin.org/articles/10.3389/fimmu.2020.594150/full

[4] WHO. 18 May 2023. Statement on the antigen composition of COVID-19 vaccines. https://www.who.int/news/item/18-05-2023-statement-on-the-antigen-composition-of-covid-19-vaccines

[5] Lopes Fermino M, et al. LPS-Induced Galectin-3 Oligomerization Results in Enhancement of Neutrophil Activation. 2011. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0026004

[6] Morris MC, et al. 2015. Innate immune programing by endotoxin and its pathological consequences. https://www.frontiersin.org/articles/10.3389/fimmu.2014.00680/full

[7] Fajgenbaum DC and June CH. 2020. Cytokine Storm. https://www.nejm.org/doi/full/10.1056/NEJMra2026131

[8] Sandiego CM, et al. 2015. Imaging robust microglial activation after lipopolysaccharide administration in humans with PET. https://www.pnas.org/doi/10.1073/pnas.1511003112

[9] Anderson G, et al. 2019. Multiple Sclerosis: Melatonin, Orexin, and Ceramide Interact with Platelet Activation Coagulation Factors and Gut-Microbiome-Derived Butyrate in the Circadian Dysregulation of Mitochondria in Glia and Immune Cells. https://www.mdpi.com/1422-0067/20/21/5500

[10] Shin Jie Yong. 2021. Persistent Brainstem Dysfunction in Long-COVID: A Hypothesis. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7874499/

[11] Pall ML and Bedient SA. 2007. The NO/ONOO- cycle as the etiological mechanism of tinnitus. International Tinnitus Journal. 13(2):99-104.

[12] Coler BS, et al. 2021. Landscape of Preterm Birth Therapeutics and a Path Forward. https://www.mdpi.com/2077-0383/10/13/2912

[13] OpenVaet. VAERS Domestic Data - Analyzing COVID Vaccine impact on pregnancies, as per USA's adverse effects watch Study version 1.1, last VAERS report on 2022-08-26 https://openvaet.org/studies/vaers_fertility?currentLanguage=en

[14] Anton L, et al. Lipopolysaccharide induces cytokine production and decreases extravillous trophoblast invasion through a mitogen-activated protein kinase-mediated pathway: possible mechanisms of first trimester placental dysfunction. 2012. https://academic.oup.com/humrep/article/27/1/61/714411

[15] Hirano T. 2010. Interleukin 6 in autoimmune and inflammatory diseases: a personal memoir. https://www.jstage.jst.go.jp/article/pvaccine dose/immunisation/injection/86/7/86_7_717/_article

[16] Ju Y, et al. 2022. Anti-PEG Antibodies Boosted in Humans by SARS-CoV-2 Lipid Nanoparticle mRNA Vaccine. ACS Nano, 16:11769-11780.

Dr Geoff Pain is a scientific consultant. In his undergraduate years he studied biochemistry, chemistry, physics, pure and applied mathematics and information science.

With a PhD in Chemistry from Monash University he worked at universities in Bristol, Cambridge and Adelaide, then returned to Monash. He was recruited by Telecom Australia (now Telstra) for a special project in optoelectronic semiconductor crystal growth. At Telecom he completed a Graduate Diploma in Business Management majoring in Strategy and Innovation. This included qualification in the Law of Negligence. He was then offered a fellowship at UWA to work on plasma deposition of materials in the Electronic Engineering Department. NEC Japan invited him to the Microwave and Satellite Communications Systems division in Yokahama for a three-year appointment. He ran a market research business investigating environmental pollution and toxicology projects for government and community groups. Widely published, he has been granted patents.

Geoff Pain's Substack is:
https://geoffpain.substack.com

Sequencing of bivalent Moderna and Pfizer mRNA vaccines reveals nanogram to microgram quantities of expression vector dsDNA per dose

by Kevin McKernan, Yvonne Helbert, Liam T. Kane, Stephen McLaughlin

Introduction

Scientist Kevin McKernan has had an illustrious career in molecular biology and biotechnology, including managing Research & Development for the Human Genome Project. His story of incidentally discovering contamination of a serious nature in vials of bivalent COVID-19 vaccine has become very well known worldwide and has begun to prompt laboratory work to confirm the findings and broaden analysis. Although, as McKernan et al. point out, the initial and subsequent laboratory steps recorded here are not without limitation, including the fact that some expired vials were studied. However, McKernan correctly called for attempts in independent laboratories to reproduce or falsify his work. As of this writing, Professor Phillip Buckhaults, a molecular biologist with expertise in cancer biology from the University of South Carolina, has indeed reproduced the finding of plasmid contamination and testified in a Senate hearing in September, 2023. This underscores the importance of the McKernan contribution.

To give a wider-angle view on the issue of manufacturing contamination, with potential relevance to excess mortality, some additional context and chronology will help.

A peer-reviewed article in *Vaccines*, prepared in 2020 and published on January 23rd 2021, just as provisional approvals for the first mRNA therapeutics were being granted by the Therapeutic Goods Administration in Australia, also sheds light. This paper, entitled 'Development of mRNA Vaccines: Scientific and Regulatory Issues', is the first to our knowledge to highlight in print the different manufacturing to be employed for the public rollout of mRNA vaccines, namely Process 2. As opposed to Process 1, which is fundamentally cleaner and utilizes a reverse transcription polymerase chain reaction (PCR) in small volumes, Process 2 employs E. coli in giant (~300L) vats. Knowing the process in detail, these sapient authors mentioned the possibility of DNA plasmid contamination in mRNA vaccines, which Dr McKernan would in time demonstrate empirically.

Making matters a little more colourful and fuelling concerns about manufacturing quality, the European Medicines Agency suffered a cyberattack, inconveniently exposing 40 megabytes of emails and other notable files on the dark web. The *BMJ* and other academics worldwide investigated, and reported their findings on March 10th 2021, in an article, 'The EMA COVID-19 data leak, and what it tells us about the mRNA instability'. There were indeed many concerns expressed by EMA scientists, including 'truncated and modified mRNA species in the finished product', as determined by their laboratory evaluation. Since the batches were derivative of Process 2, the disclosure of mRNA instability was an early event, also nominating imperfections in manufacturing.

For some, recognition of safety signals in the rollout of mRNA, including the recognized risk of anaphylaxis and an early appreciation of a diverse burden of complications and fatalities not previously encountered, led them to look at manufacturing processes, batch variation and contamination as a root cause. This could be said to be the starting point of another of our authors in this volume, Dr Jessica Rose, who notes contamination subsequent to Process 2.

Contamination with plasmid DNA has been predictable from knowledge of the manufacturing process. It has not been disclosed by

manufacturers or by authorizing regulatory bodies; it may ultimately be a source of morbidity and mortality in recipients of mRNA vaccinations. The possibility of genomic integration of plasmid DNA encoding for spike proteins into human recipients is here discussed, as it has also been discussed by Prof Buckhaults.

The demonstration of plasmid DNA contamination almost certainly guarantees an amount of bacterial product contamination, since both derive from the fact of E. coli use in manufacture. This has been foundational for the investigations of another of our contributors, Dr Geoff Pain, who elaborates the case for endotoxin contamination in mRNA vaccine vials. In that author's view, this possibility has not been falsified by government laboratories, based especially on an unhelpfully high laboratory cut-off value, arbitrarily defined to denote vial contamination, in addition to other potential methodological flaws. He also takes care to point out how exceedingly small amounts of endotoxin contamination, disseminated along with mRNA and plasmid DNA in lipid nanoparticles, could contribute to disease manifestation. These issues are worthy of scrutiny together, in the context of the so-far silent crisis of excess mortality.

Regardless, it shows that much more care needed to be taken by our relevant authorities, in the public interest; it is inconceivable that our TGA Laboratory Division could derogate its responsibility to know about undisclosed DNA species in vials nominated for Australian use. It is important for this study to be included in the present publication, despite its heavy scientific content, intended as it is for the eyes of elected and non-elected public servants. Of course, it is possible that these findings could also occupy an important place in the outworking of various legal and political processes in Australia. We also point out that advance notice of Dr McKernan's work was sent on July 4th 2023 to two branches of the Health Department, the TGA and the Office of Gene Technology Regulator.

The Australian Medical Professionals Society recognizes that this seminal work employs the most technical language of all the papers in this volume. However, for the reasons elaborated above and because of the likely historical value of this contribution, we have elected to present it here, asking the indulgence of the non-scientific among our readership.

Abstract

Several methods were deployed to assess the nucleic acid composition of four expired vials of the Moderna and Pfizer bivalent mRNA vaccines. Two vials from each vendor were evaluated with Illumina sequencing, qPCR, RT-qPCR, Qubit™ 3 fluorometry and Agilent Tape Station™ electrophoresis. Multiple assays confirm DNA contamination that exceeds the European Medicines Agency (EMA) 330ng/mg requirement and the FDAs 10ng/dose requirements.

These data may have a bearing on the surveillance of vaccine mRNA in breast milk or plasma as RT-qPCR assays targeting the vaccine mRNA cannot discern DNA from RNA without RNase or DNase nuclease treatments. Studies evaluating the reverse transcriptase activity of LINE-1 and vaccine mRNA will need to account for the high levels of DNA contamination in the vaccines. The exact ratio of linear fragmented DNA *versus* intact circular plasmid DNA is still being investigated. Quantitative PCR assays used to track the DNA contamination are described.

Introduction

Several studies have made note of prolonged presence of vaccine mRNA in breast milk and plasma (Bansal et al. 2021; Hanna et al. 2022; Castruita et al. 2023). This could be the result of the stability of N1-methylpseudouridine (m1Ψ) in the mRNA of the vaccine. Nance et al. depict a vaccine mRNA synthesis method that utilizes a dsDNA plasmid that is first amplified in E.coli prior to an *in-vitro* T7 polymerase synthesis of vaccine mRNA (Nance and Meier 2021).

Failure to remove this DNA could result in the injection of spike-encoded nucleic acids more stable than the modified RNA. The EMA has stated limits at 330ng/mg of DNA to RNA (Josephson 2020-11-19). The FDA has issued guidance for under 10ng/dose in vaccines (Sheng-Fowler et al. 2009).

Residual injected DNA can result in type I interferon responses and can increase the potential for DNA integration(Ulrich-Lewis et al. 2022).

Results

To assess the nucleic acid composition of the vaccines, vaccine DNA was deeply sequenced using two different methods. The first method used a commercially available New England Biolabs RNA-seq method that favoured the sequencing of the RNA but still presented over 500X coverage for the unanticipated DNA vectors (Figure 1 and 2). The RNA-seq

assemblies had truncated poly A tracts compared to the constructs described by Nance et al.

The second method eliminated the RNA with RNase A treatment and sequenced only the DNA using a Watchmaker Genomics fragment library kit. The DNA focused assemblies delivered vector assemblies with more intact poly A tracts (Figure 3).

These assemblies were utilized to design multiplex qPCR and RT-qPCR assays that target the spike sequence present in both the vaccine mRNA and the DNA vector while also targeting the origin of replication sequence present only in the DNA vector (Figure 3). The assembly of Pfizer vial 1 contains a 72bp insertion not present in the assembly of Pfizer vial 2. This indel is known for its enhancement to the SV40 promoter and its nuclear localization signal (Dean et al. 1999) (Moreau et al. 1981)

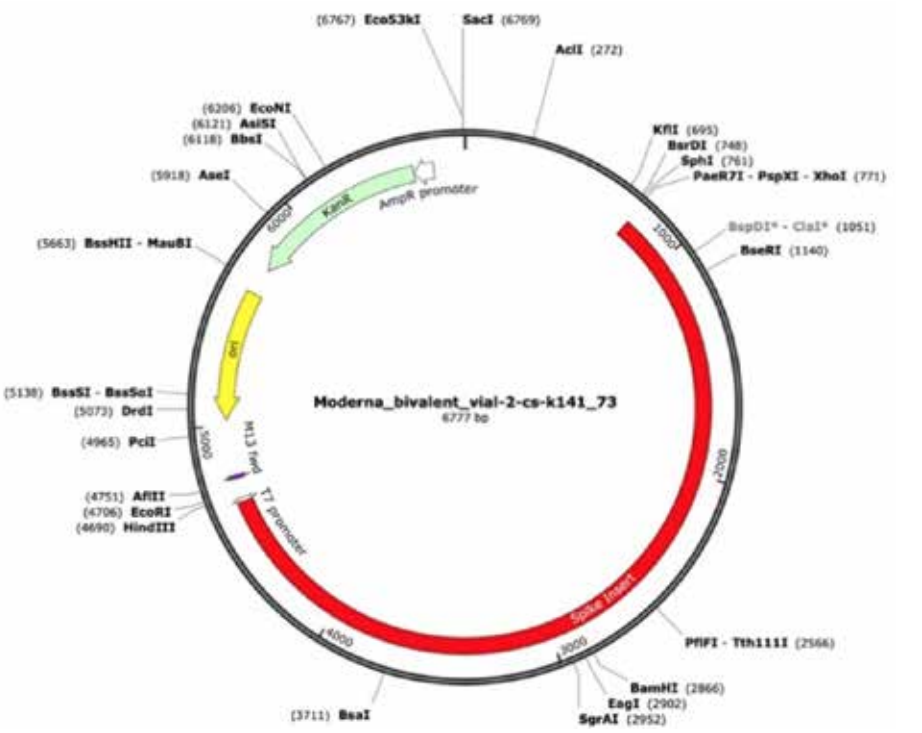


Figure 1

A Moderna vector assembly of an RNA-seq library with a spike insert (red), Kanamycin resistance gene (green) driven by an AmpR promoter and a high copy bacterial origin of replication (yellow).

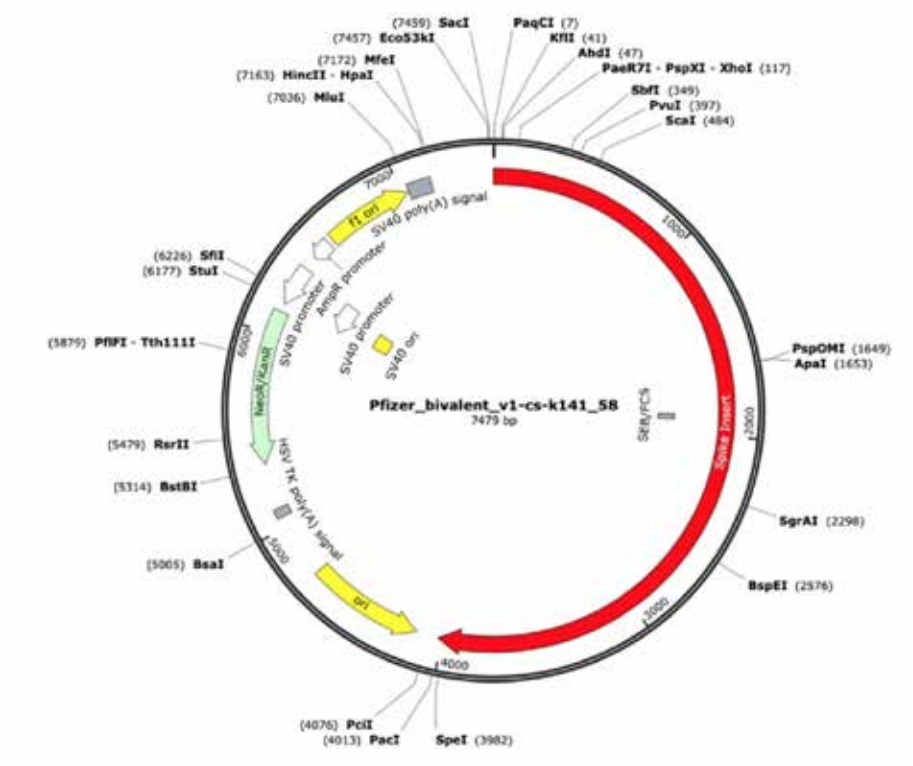


Figure 2

Pfizer bivalent vaccine assembly of the RNA-seq library. Annotated with SEB/FCS, spike insert (red), bacterial origin of replication (yellow), Neo/Kan resistance gene(green), F1 origin (yellow) and an SV40 promoter (yellow and white).

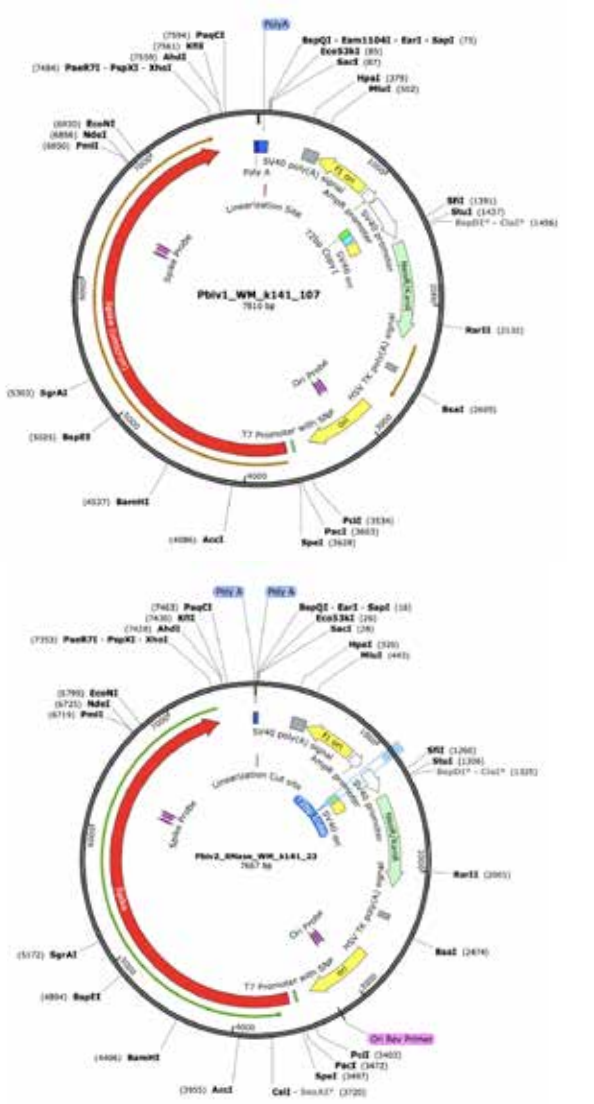


Figure 3

RNase treated vaccines were shotgun sequenced with Illumina (RNase-Seq not RNA-seq). Pfizer vectors from vial 1 (left) and vial 2 (right) contain a 72bp difference in the SV40 promoter (green and light blue annotation). qPCR assays are depicted in pink as spike probe and ori probe. The RNase sequencing provided better resolution over the Eam1104i linearization site and the poly adenylation sequence. The vectors differ in the length of the polyA tail (likely sequencing artifact) and the 72bp indel.

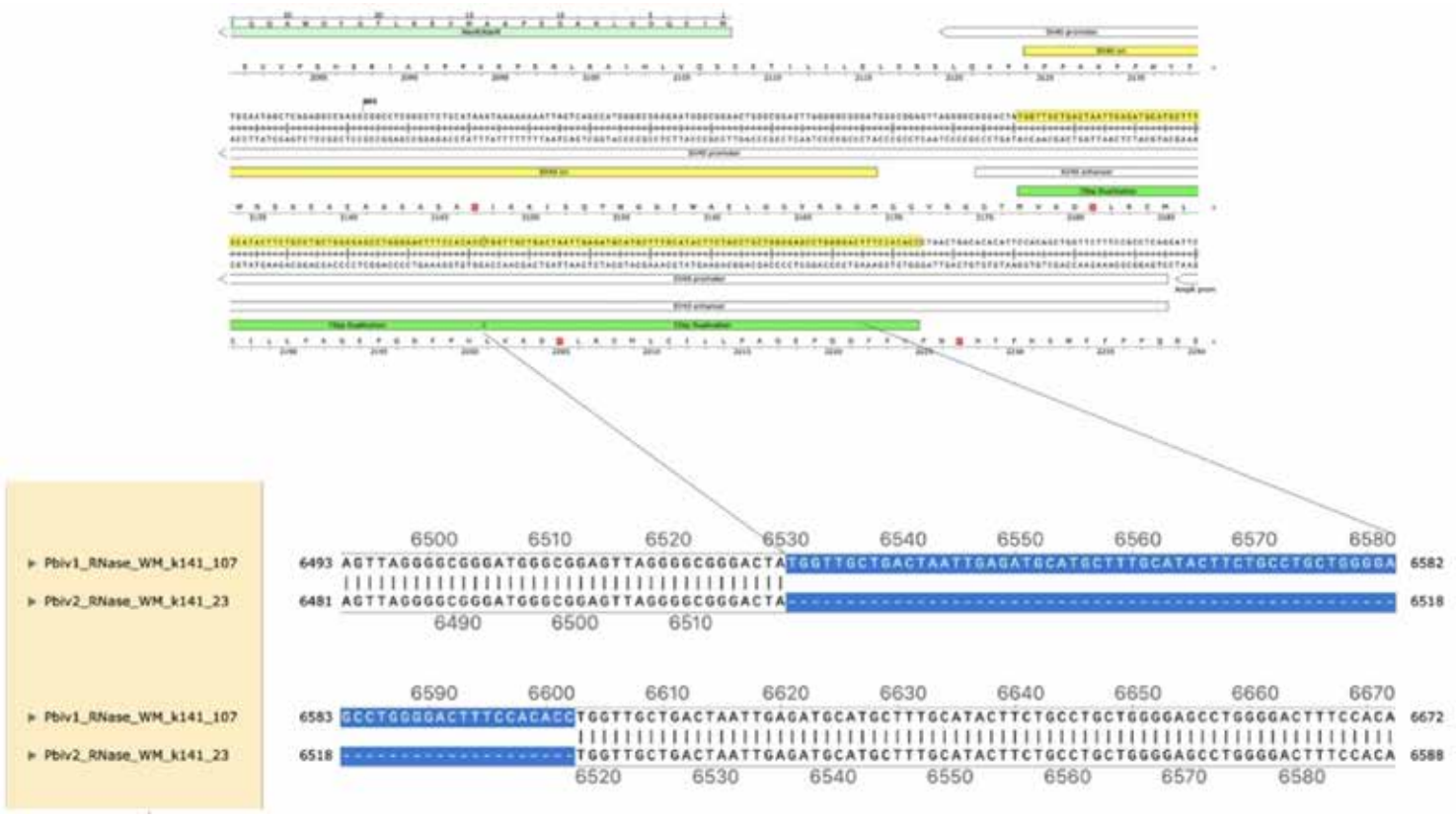

Pbiv1_RNase_WM_k141_107
Pbiv2_RNase_WM_k141_23
6500 6510 6520 6530 6540 6550 6560 6570 6580
6493 AGTTAGGGGCGGGATGGGCGGAGTTAGGGGCGGGACTATGGTTGCTGACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGA 6582
6481 AGTTAGGGGCGGGATGGGCGGAGTTAGGGGCGGGACTA 6518
6490 6500 6510
6590 6600 6610 6620 6630 6640 6650 6660 6670
6583 GCCTGGGGACTTTCCACACGTGGTTGCTGACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCTGGGGACTTTCCACA 6672
6518 TGGTTGCTGACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCTGGGGACTTTCCACA 6588
6520 6530 6540 6550 6560 6570 6580

Figure 4

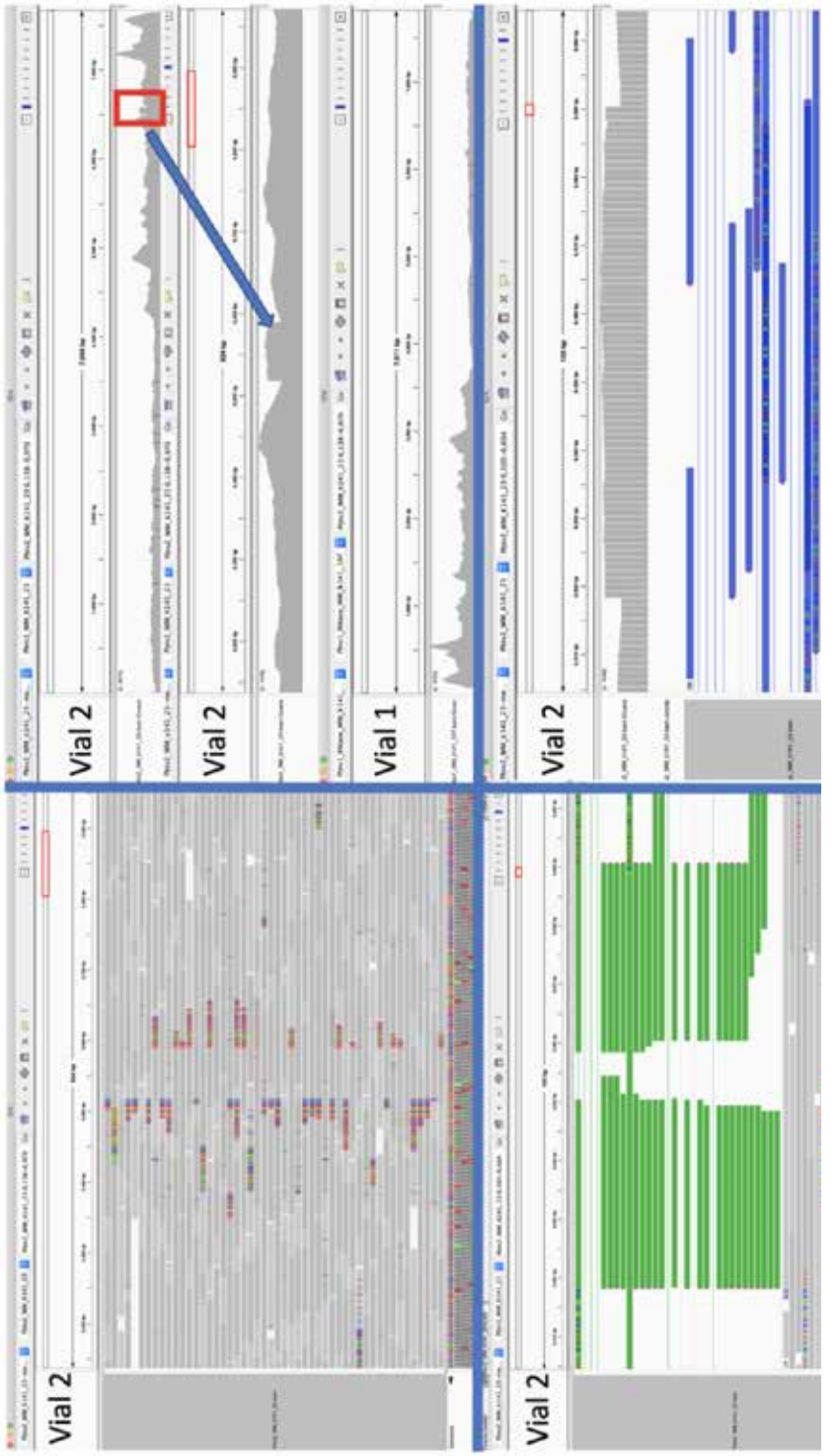


Figure 5A

Local alignment of Pfizer vial 1 to Pfizer vial 2 vectors highlights the 72bp tandem duplication in blue.

Close inspection of the Integrative Genome Viewer (IGV) demonstrates the appearance of a 72bp insertion that is heteroplasmic in Pfizer vial 2. The upper left IGV view is a zoomed-out view where the coloured marks depict the indel. The lower left IGV view shows inverted paired reads as the 72bp insertion is a tandem repeat and paired reads shorter than 72bp can be mapped two different ways. Upper Right IGV view demonstrates a read coverage pile-up or 'plateau'. This occurs when the reference has one copy of the 72bp repeat and the sample has two copies. Note – in the upper right IGV depiction, the sequence in Vial 1 is in the opposite orientation in IGV as Vial 2. Lower right IGV view is a zoomed view of the upper right IGV screen.

Since the two Pfizer vials share the same lot number, finding a heterozygous copy number change between the two vials is unexpected. It was hypothesized that the appearance of a heteroplasmic copy number change is instead the result of the megahit assembler collapsing what is actually two copies of the 72bp sequence into a single copy as a result of the insert sizes in the sequencing libraries being too short (105bp). It is noteworthy that the longer paired-end reads in the library resolve the 72bp tandem repeat.

When references have a single copy of the 72bp repeat and the sample has two copies of the repeat, reads should pile up to twice the coverage over the single copy 72bp loci as seen in Figure 5A. To test this hypothesis, we added a second 72bp sequence to the shorter plasmid assembly and observed that the reads map without artifact and no evidence of heteroplasmy (Figure 5B).

IGV view of the read coverage over Pbiv2_k141_23 shows a discrete 72bp plateau in coverage (red rectangle). Editing the Pbiv2_k141_23 reference to include two copies of the 72bp sequence, and remapping the sequence data to this corrected sequence shows that the coverage over both vectors is more normal with no coverage plateau in Pfizer vial 2.

These data conclude that all Pfizer vectors contain a homoplastic 2 copy 72bp SV40 Enhancer associated with more robust expression and nuclear localization. The initial heteroplastic indel was an artifact of the Megahit assembler and short insert libraries.

To estimate the size of the DNA, the purified vaccines were evaluated on an Agilent Tape Station™ using DNA (genomic DNA screen tapes) and RNA based (high sensitivity RNA tapes) electrophoresis tapes.

Agilent Tape Station™ electrophoresis reveal 7.5 - 11.3 ng/µl of dsDNA compared to the 23.7 -55.9ng/µl of mRNA detected in each 300µl sample.

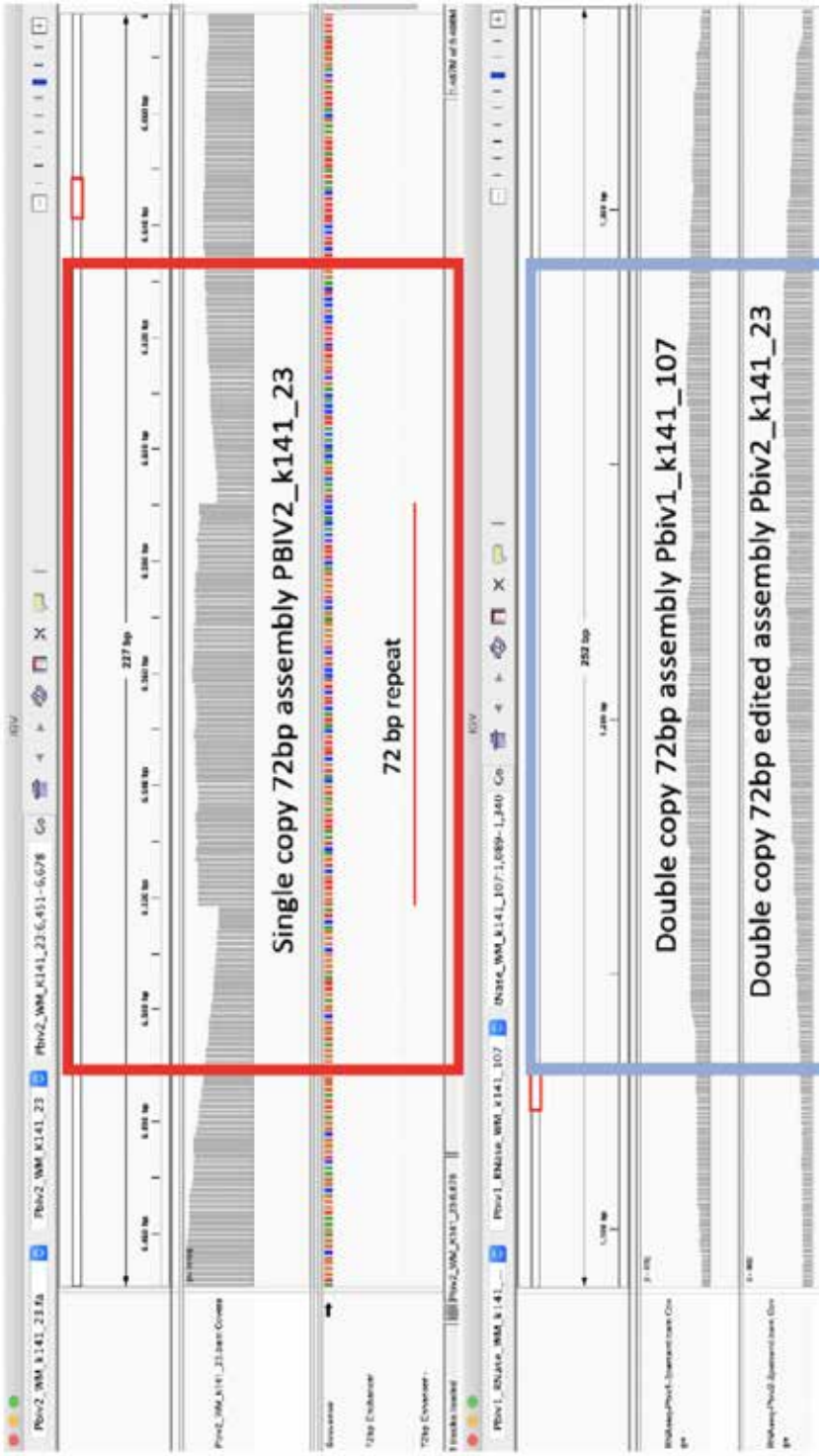

Single copy 72bp assembly PBIV2_k141_23
72 bp repeat
Double copy 72bp assembly Pbiv1_k141_107
Double copy 72bp edited assembly Pbiv2_k141_23

Figure 5B

Qubit™ 3 fluorometry estimated 1-2.8ng/µl of DNA and 21.8ng - 52.8ng/µl of RNA. There is higher fragmentation seen in the DNA electrophoresis. The total RNA levels are less than the expected 30ug (100ng/µl) and 100ug (200ng/µl) doses, suggesting a loss of yield in DNA and RNA isolation, manufacturing variance or RNA decay with expired lots.

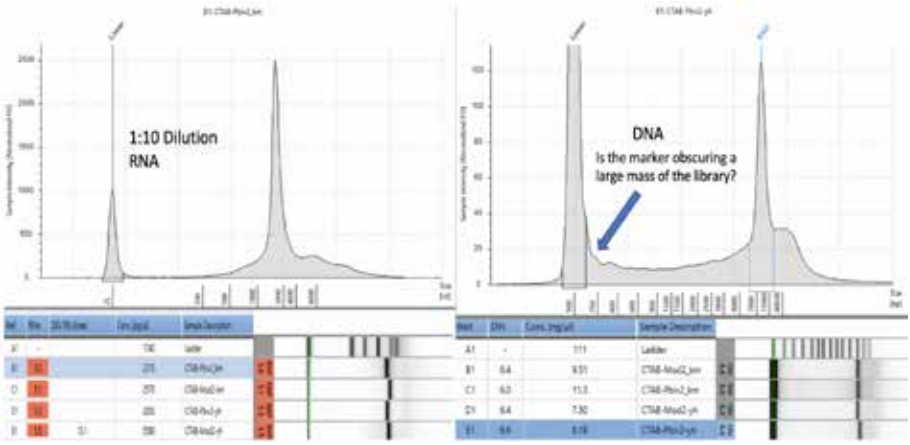


Figure 6

Agilent Tape Station™ electrophoresis demonstrates 23.7ng/µl – 55.9ng/µl of RNA (left). 7.5ng-11.3ng/µl are observed on DNA based Tape Station™. While the DNA electropherogram shows a peak suggestive of a full-length plasmid, this sample is known to have high amounts of N1-methylpseudouridine RNA present. DNA hybrids with N1-methylpseudouridine mRNA may provide enough intercalating dye cross talk to produce a peak. The sizing of the peak on the RNA tape on the left is shorter than expected. This may be the results of N1 methylpseudouridine changing the secondary structure or the mass to charge ratio of the DNA.

Quantitative PCR assays were designed using IDTs Primer Quest software targeting a region in the spike protein that was identical between Moderna and Pfizer spike sequences and a shared sequence in the vectors' origin of replication. This allowed the qPCR and RT-qPCR assessment of the vaccines. qPCR only amplifies DNA while RT-qPCR amplifies both DNA and RNA. Gradient qPCR was utilized to explore conditions where both targets would perform under the same cycling conditions for both RT-qPCR and PCR (gradient PCR data not shown).

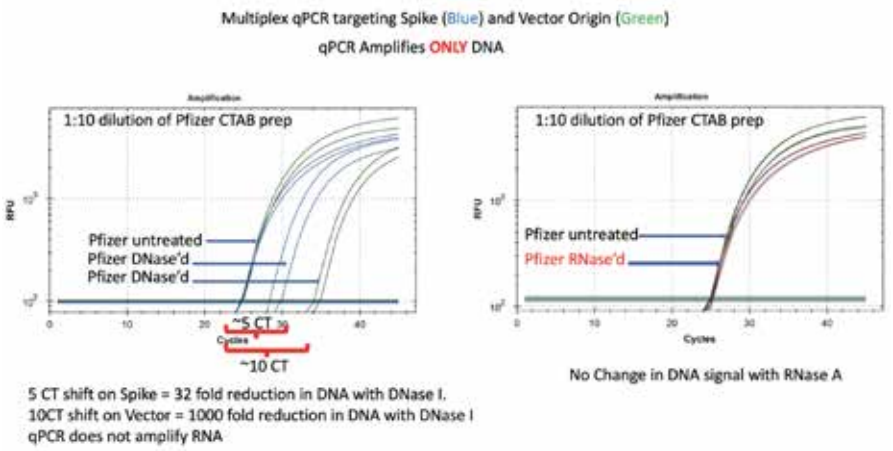


Figure 7

qPCR of Pfizer's bivalent vaccine with and without DNase I (left) and RNase A (right). Untreated mRNA demonstrates equal CTs for Spike and Vector assays as expected. Vector is more DNase I sensitive than the spike suggesting the modRNA may inhibit nuclease activity of DNase I against complementary DNA targets. RNase A treatment does not alter the qPCR signal.

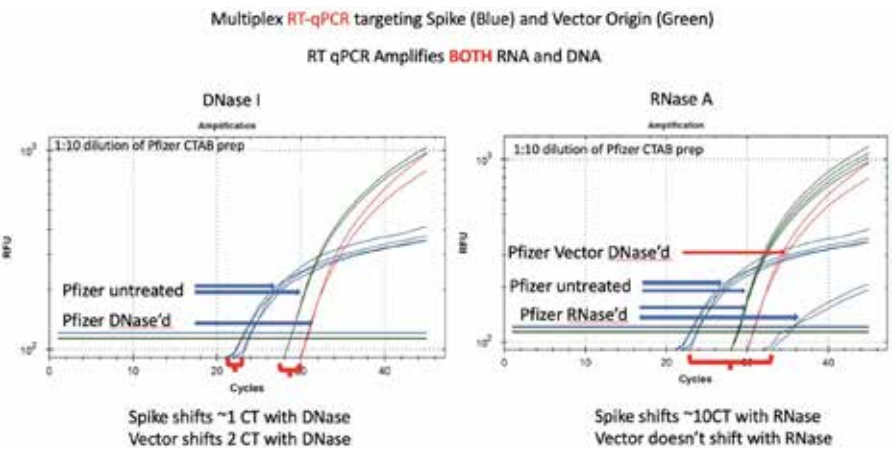


Figure 8

RT-qPCR amplifies both DNA and RNA. The untreated samples show a large CT offset with Pfizer Spike and Vector assays (left blue *versus* green). This is anticipated as the T7 polymerization should create more mRNA over spike than over the vector. Small 1-2 CT shifts are seen with DNase I treatment. This is expected if the DNA is less than equal concentration of nucleic acid in RT-PCR. RNase treatment (right) shows a 10 CT offset but does not alter the DNA vector CT.

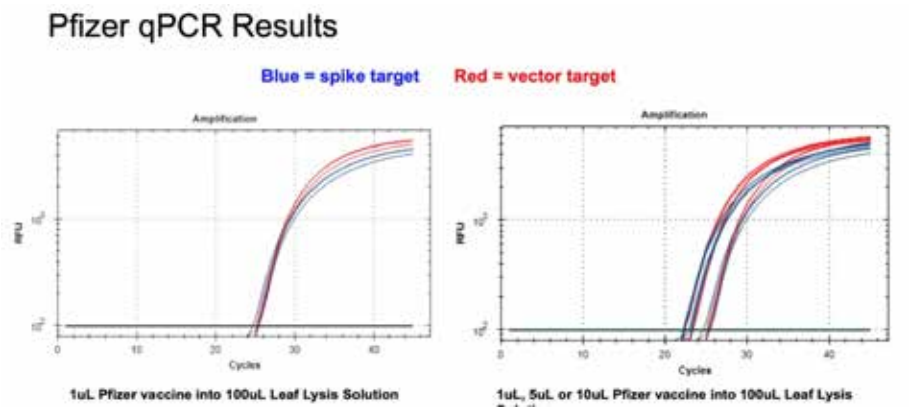


Figure 9

1µl of the Pfizer bivalent vaccine placed in 100µl leaf lysis buffer for an 8-minute boil step delivers a CT of 24 for both Vector and Spike targets in qPCR (left). Assay is responsive to 1,5,10µl of input (right).

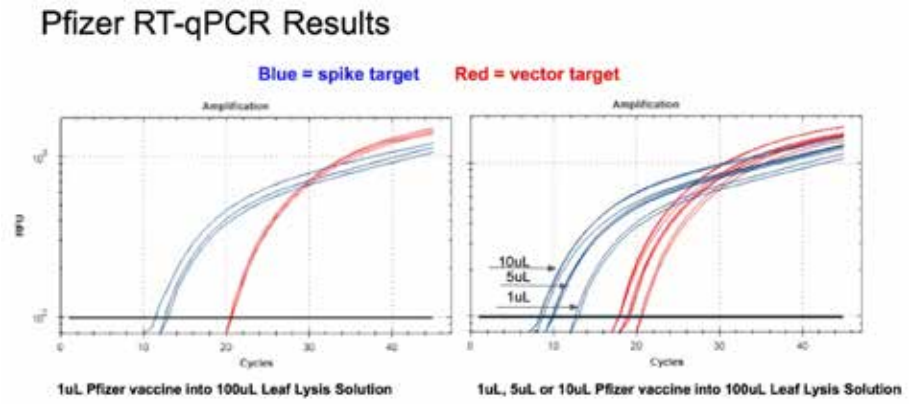


Figure 10

1µl of the Pfizer bivalent vaccine placed in 100µl leaf lysis buffer for an 8-minute boil step delivers a CT of 20 and 12 for both Vector and Spike targets in RT-qPCR (left). Assay is responsive to 1,5,10µl of input (right).

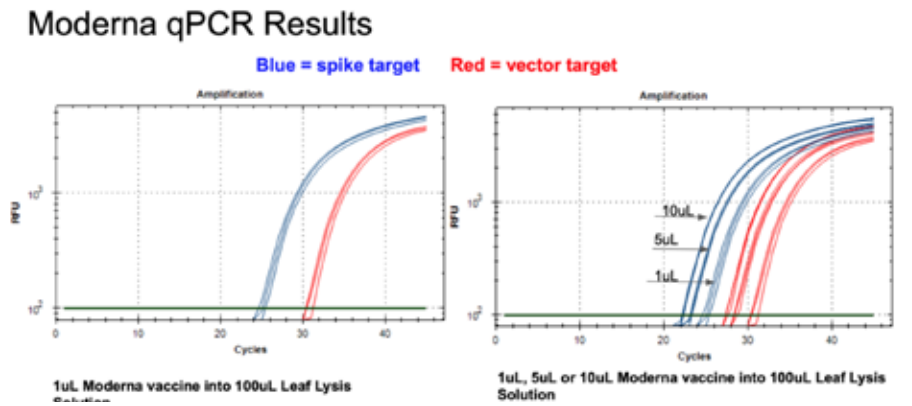


Figure 11

1µl of the Moderna bivalent vaccine exhibits different CTs values for the spike and the vector targets (left) with qPCR. This needs to be explored further as the assays provide equal CT scores on Pfizer's vaccines and the sequence of the amplicon is identical between the two vector origins. There are two mismatches in the spike amplicons between Moderna and Pfizer but none of the mismatches are under a primer or probe. The assay is responsive to 1,5,10µl of direct boil mRNA (right).

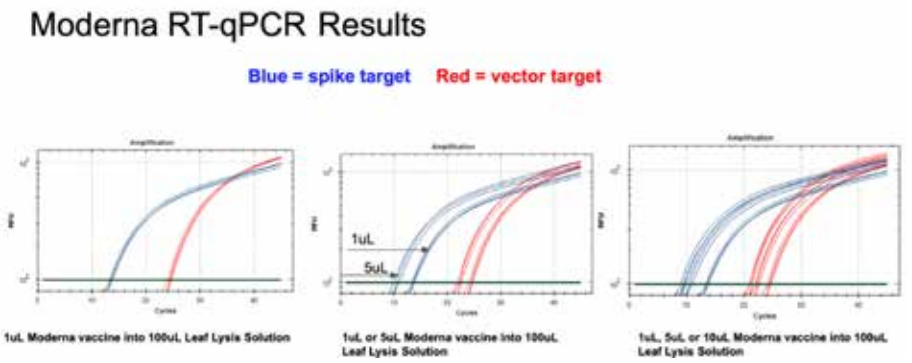


Figure 12

1µl of the Moderna bivalent vaccine exhibits different CTs values for the spike and the vector targets (left) with RT-qPCR. The large 10 CT shift between Spike and Vector needs to take into consideration that qPCR control shows a 5 CT offset. The boil preps can tolerate 1-10µl of vaccine (middle and right).

Table 1

	Qubit DNA ng/µl	Qubit RNA ng/µl
Pbiv1	2.81	30.0
Pbiv2	1.47	52.8
Mod1	2.67	21.8
Mod2	1.04	49.0

Qubit™ 3 Fluorometry estimates 1.04-2.8 ng/µl of dsDNA in the vaccines and 21.8ng-52.8ng/µl of RNA.

Synthetic templates were synthesized with IDT to build RT-qPCR standard curves to benchmark CTs to the mass of DNA in the reaction. This method uses ideal templates and fails to quantitate DNA molecules smaller than the amplicon size. As expected, this method delivers lower DNA concentration estimates than Qubit™ 3 fluorometry or Agilent Tape Station™. It also represents an ideal environment which does not capture the inhibition or primer depletion that can occur when large quantities of mRNA with identical sequence to the DNA target are co-present in a qPCR assay.

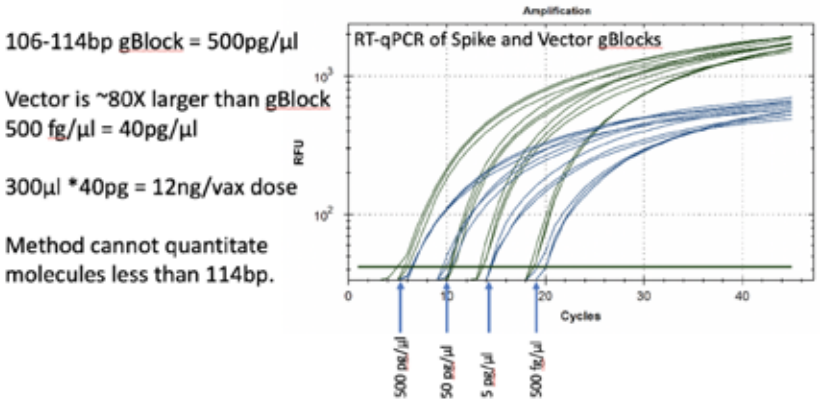


Figure 13

Two gBlocks were synthesized at IDT for Spike and Ori positive control templates used in a RT-qPCR assay. 10-fold serial dilutions were run in triplicate to correlate CT scores with picograms of DNA. The threshold is lowered from 10^2 for review of the background. CT of ~20 = 500fg/RT-qPCR reaction. Since 100bp targets only represent 1/80th of the vector DNA present as a potential contaminant, 500 fg/µl manifests in 40pg/µl of vector DNA. Any DNA that is DNase I-treated and is smaller than the amplicon size cannot

amplify or be quantitated with this method. This method will under-quantitate DNase I-treated samples compared to Qubit™ 3 or Agilent Tape Station™.

This work was further validated by testing eight unopened Pfizer monovalent vaccines with both qPCR and RT-qPCR.

Pfizer Bivalent

Moderna Bivalent

Pfizer Monovalent

Figure 14

Moderna and Pfizer Bivalent vaccines (top). 8 Monovalent Pfizer mRNA vaccines. These were unopened but past expiration (bottom).

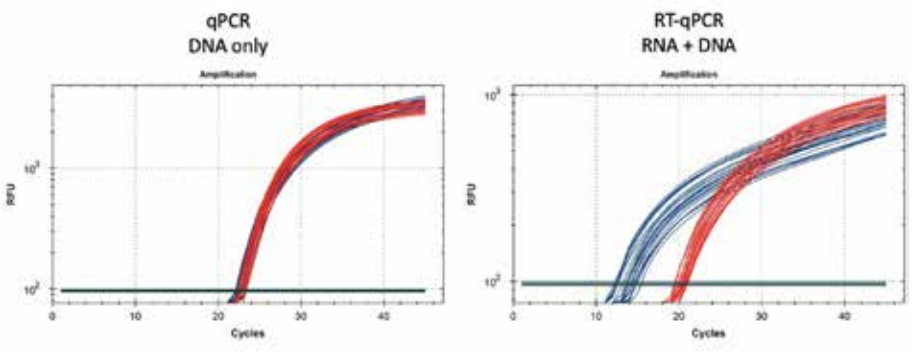


Figure 15

1µl of vaccine boiled in 100µl of leaf lysis buffer was subjected to qPCR (left) and RT-qPCR (right) for Vector (red) and Spike (blue). Eight samples were tested in triplicate.

Table 2.

CT values for Spike and Vector during qPCR (DNA only). Standard deviation for the triplicate measurements run horizontally in black font. Standard deviation for vial to vial run vertically in red. Delta CT or (Vector CT minus Spike CT) represents the ratio of Spike to Vector DNA and should = 1.

qPCR-Spike	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	23.12	22.98	22.58	22.33	22.36	22.68	22.20	22.06	0.401
Replicate 2	23.16	22.90	22.70	22.36	22.20	22.16	22.29	22.22	0.373
Replicate 3	23.22	22.84	22.59	22.29	22.44	22.26	22.29	22.11	0.368
STDEV	0.05	0.07	0.07	0.03	0.12	0.09	0.05	0.08	

qPCR: (Vector-Spike)	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	0.20	0.08	0.27	(0.00)	0.18	0.18	0.19	0.24	0.090
Replicate 2	0.16	0.22	0.29	0.11	0.18	0.12	0.03	0.13	0.078
Replicate 3	0.14	0.21	0.29	0.17	0.31	0.19	0.20	0.13	0.069
STDEV	0.03	0.11	0.05	0.09	0.08	0.04	0.08	0.06	

qPCR-Vector	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	23.33	23.06	22.85	22.32	22.54	22.26	22.30	22.30	0.411
Replicate 2	23.32	23.12	23.00	22.47	22.36	22.28	22.32	22.35	0.419
Replicate 3	23.36	23.15	22.79	22.45	22.75	22.46	22.49	22.23	0.383
STDEV	0.02	0.04	0.11	0.08	0.19	0.11	0.11	0.06	

RATIO RNA/DNA	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	1	1	1	1	1	1	1	1	0.000
Replicate 2	1	1	1	1	1	1	1	1	0.000
Replicate 3	1	1	1	1	1	1	1	1	0.000
STDEV	0.0	0.1	0.0	0.1	0.1	0.0	0.1	0.1	

Table 3

CT values for Spike and Vector during RT-qPCR (RNA+DNA). Ratio of RNA:DNA ranges from 43:1 To 161:1. EMA allowable limit is 3030:1. This is 18-70 times over the EMA limit.

RT-Spike	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	14.05	14.77	13.18	13.77	13.79	12.52	12.62	13.53	0.748
Replicate 2	14.29	14.74	14.38	14.82	13.78	13.82	12.57	12.38	0.825
Replicate 3	14.48	14.91	15.43	13.84	13.74	13.55	12.36	12.19	1.141
STDEV	0.22	0.09	1.12	0.59	0.02	0.69	0.14	0.72	

RT: (Vector-Spike)	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	6.74	5.93	7.20	6.40	6.51	7.31	7.33	5.97	0.570
Replicate 2	6.33	6.06	5.92	5.67	6.34	6.13	6.92	7.06	0.478
Replicate 3	6.33	6.07	5.43	6.39	6.13	6.38	7.09	7.18	0.562
STDEV	0.24	0.07	0.91	0.42	0.19	0.62	0.21	0.67	

RT-Vector	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	20.80	20.71	20.39	20.16	20.30	19.83	19.95	19.50	0.439
Replicate 2	20.62	20.80	20.30	20.49	20.12	19.96	19.49	19.45	0.469
Replicate 3	20.81	20.94	20.86	20.23	19.88	19.93	19.45	19.37	0.636
STDEV	0.11	0.14	0.30	0.17	0.21	0.07	0.28	0.07	

RATIO RNA/DNA	Vial 1	Vial 2	Vial 3	Vial 4	Vial 5	Vial 6	Vial 7	Vial 8	STDEV
Replicate 1	107	81	147	84	91	159	161	83	41.54
Replicate 2	80	67	61	51	81	70	121	134	29.25
Replicate 3	80	67	43	84	70	83	136	145	34.79
STDEV	15.5	3.3	35.8	19.2	10.4	47.9	20.3	44.6	

Discussion

Multiple methods highlight high levels of DNA contamination in both the monovalent and bivalent vaccines. While the Qubit™ 3 and Agilent Tape Station™ differ on their absolute quantification, both methods demonstrate it is orders of magnitude higher than the EMA's limit of 330ng DNA/ 1mg RNA. qPCR and RT-qPCR confirms the relative RNA to DNA ratio. An 11-12 CT offset should be seen between Spike and Vector RT-qPCR signals to represent a 1:3030 contamination limit (2^11.6 = 3100). Instead, we observe much smaller CT offsets (5-7 CTs) when looking at qPCR and RT-qPCR data with these vaccines. It should be noted that Qubit™ 3 and Agilent methods stain all DNA in solution while qPCR measures only amplifiable molecules without DNase I cut sites between the primers. The further apart the spacing of the qPCR primers, the fewer Qubit™ 3 and Agilent detectable molecules will amplify. The primers used in this study are 106bp and 114bp apart, thus any molecules that are DNase I cut below this length will be undercounted with the qPCR methods relative to more general dsDNA measurements from Qubit™ 3 or Agilent Tape Station™.

This also implies that qPCR standard curves using 100% intact synthetic DNA standards will amplify more efficiently and thus undercount the total digested DNA contamination. For example, standard curves with 106-114bp synthetic templates provide CTs under 20 in the picogram range (not low nanogram range) suggesting large portions of the library are smaller than the minimum amplifiable size. Pure standards also do not contain high concentrations of modified mRNA with identical sequence which could serve as a competitive primer sink or inhibitor to qPCR methods.

Alternatively, the Qubit™ 3 and the Agilent Tape Station™ could be inflating the DNA quantification as a result of intercalating dye cross-talk with N1-methylpseudouridine RNA. For this reason, we believe the ratio we observed when these molecules are more scrupulously interrogated with polymerases specific for each template type in qPCR and RT-qPCR is a more relevant metric. The EMA metric is also stated as such a ratio.

This also brings into focus the question of whether these EMA limits took into consideration the nature of the DNA contaminants. Replication competent DNA should arguably have a more stringent limit. DNA with mammalian promoters or antibiotic resistance genes may also be of more concern than just random background E.coli genomic DNA from a plasmid preparation (Sheng-Fowler et al. 2009). Background E.coli DNA was measured with qPCR and had CT over 35.

There has been a healthy debate about the capacity for SARs-CoV-2 to

integrate into the human genome (Zhang et al. 2021). This work has inspired questions regarding the capacity for the mRNA vaccines also to genome-integrate. Such an event would require LINE-1 driven reverse transcription of the mRNA into DNA as described by Alden et al. (Alden et al. 2022). dsDNA contamination of sequence encoding the spike protein would not require LINE-1 for Reverse Transcription and the presence of an SV40 nuclear localization signal in Pfizer's vaccine vector would further increase the odds of integration. This work does not present evidence of genome integration but does underscore that LINE-1 activity is not required given the dsDNA levels in these vaccines. The nuclear localization of these vectors should also be verified.

Prior sequencing of the monovalent vaccines from Jeong et al. only published the consensus sequence (Dae-Eun Jeong 2021). The raw reads for this project are not available and should be scrutinized for the presence of vector sequence.

Given these vaccines exceed the EMA limits (330ng/mg DNA/RNA) with the Qubit™ 3 and Agilent data and these data also exceed the FDA limit (10ng/dose) with the more conservative qPCR standard curves, we should revisit the lipopolysaccharide (LPS) levels. Plasmid contamination from E.coli preps are often co-contaminated with LPS. Endotoxins contamination can lead to anaphylaxis upon injection (Zheng et al. 2021).

A limitation of this study is the unknown provenance of the vaccine vials under study. These vials were sent to us anonymously in the mail without cold packs. RNA is known to degrade faster than DNA and it is possible poor storage could result in faster degradation of RNA than DNA. RNA as a molecule is very stable but in the presence of metals and heat or background ubiquitous RNases, it can degrade very quickly. All of the vaccines in this study are past the expiration date listed on the vial, suggesting more work is required to understand the DNA to RNA ratios in fresh lots. The publication of these qPCR primers may assist in surveying additional lots with more controlled supply chains. Studies evaluating vaccine longevity in breast milk or plasma may benefit from vector DNA surveillance as this sequence is unique to the vaccine and may persist longer than mRNA.

While the sequencing delivered full coverage of the plasmid backbones, it is customary to assemble plasmids from DNase I fragmented libraries. These methods have not discerned the ratio of linear *versus* circular DNA in the vials. While plasmid DNA is more competent and stable, linear DNA may have higher genome integration risks.

The intercalating dyes used in the Qubit™ 3 and Agilent systems are known to

have low fluorescent cross talk with DNA and RNA but it is unknown to what degree N1-methylpseudouridine alters the specificity of these intercalating dyes. As a result, we have relied on the CT offsets between RT-qPCR and qPCR with the vector and spike sequence as the best relative assessment of the EMA ratio-metric regulation. These qPCR and RT-qPCR reagents may be useful in tracking these contaminants in vaccines, blood banks or patient tissues in the future.

Author contributions

KJM- constructed the sequencing libraries, designed the qPCR assays, ran Qubit™ 3s and Agilent Tape Station™ and performed the analysis, drafted the manuscript.

YH-Optimized DNA isolations, Tape Station™ and qPCR results.

SM, LTK- assisted in demultiplexing and trimming the reads and assembly troubleshooting

Conflicts of interest- Authors of this paper are employees of Medicinal Genomics which manufactures some of the qPCR and DNA isolation kits used in this study.

Acknowledgements.

We would like to thank Lei Zhang for organizing the sequencing outsourcing. We would also like to thank Jessica Rose, Sabine Hazan, Jikkyleaks, Pathogenetics, Steve Massey, Valentine Bruttel, Lynn Fynn, Sasha Letypova, David Wiseman and Pharmacoconuts for helpful comments on this topic.

Methods

Purifying the mRNA from the LNPs

LiDs/SPRI purification

100µl of each vial was sampled (1/3rd to 1/5th of a dose)

- 5µl of 2% LiDs was added to 100µl of Vaccine to dissolve LNPs
- 100µl of 100% Isopropanol
- 233µl of Ampure (Beckman Genomics)
- 25µl of 25mM MgCl2 (New England Biolabs)

Samples were tip mixed 10X and incubated for 5 minutes for magnetic bead binding. Magnetic Beads were separated on a 96-well magnet plate for 10 minutes and washed twice with 200µl of 80% EtOH. The beads were left to air dry for 3 minutes and eluted in 100µl of ddH20. 2µl of eluted sample was run on an Agilent Tape Station™.

CTAB/Chloroform/SPRI purification of Vaccines

Some variability in qPCR performance was noted with our LiDs/SPRI purification method of the vaccines. This left some samples opaque and may represent residual LNPs in the purification. A CTAB/Chloroform/SPRI isolation was optimized to address this and used for further qPCR and Agilent electrophoresis. Briefly, 300µl of Vaccine was added to 500µl of CTAB (MGC solution A in SenSATIVAx MIP purification kit. #420004). The sample was then vortexed and heated for 5 minutes at 37°C. 800µl of chloroform was added, vortexed and spun at 19,000 rpms for 3 minutes. The top 250µl of aqueous phase was collected and added to 250µl of solution B and 1ml of magnetic binding buffer. Samples were vortexed and incubated for 5 minutes and magnetically separated. The supernatant was removed and the beads washed with 70% Ethanol two times. Samples were finally eluted in 300µl of MGC elution buffer.

Simple boil preparation for evaluating vaccine qPCR.

This boil prep process simply takes 1-10µl of the vaccine and dilutes it into a PCR-compatible leaf lysis buffer and heats it (Medicinal Genomics part number 420208).

- 65°C for 6 minutes
- 95°C for 2 minutes

Library construction for sequencing

50µl of each 100µl sample was converted into RNA-Seq libraries for Illumina sequencing using the NEB NEBNext UltraII Directional RNA library Kit for Illumina (NEB#E7760S).

To enrich for longer insert libraries, the fragmentation time was reduced from 15 minutes to 10 minutes and the First strand synthesis time was extended at 42°C to 50 minutes per the long insert recommendations in the protocol.

No Ribo depletion or PolyA enrichment was performed as to provide the most unbiased assessment of all fragments in the library. The library was amplified for 16 cycles according to the manufacturer's protocol. A directional library construction method was used to evaluate the single stranded nature of the mRNA. This is an important quality metric in the EMA and TGA disclosure documents as dsRNA (>0.5%) can induce an innate immune response. dsRNA content is often estimated using an ELISA. Directional DNA sequencing offers a more comprehensive method for its estimation and was previously measured and 99.99% in Jeong et al. It is unclear how this may vary lot to lot or within the new manufacturing process for the newer bivalent vaccines.

RNase A treatment of the Vaccines

RNase A cleaves both uracils and cytosines. N1-methylpseudouridine is known to be RNAse-*L* resistant but RNase A will cleave cytosines which still exist in the mRNAs. This leaves predominantly DNA for sequencing. Vaccine mRNA that was previously sequenced was treated at 37°C for 30 minutes with 10µl of 20 Units/µl Monarch RNase A from NEB. The RNase reaction was purified using 1.5X of SenSATIVAx (Medicinal Genomics #420001). Samples were eluted in 20µl ddH20 after DNA purification. 15µl was used for DNA sequencing.

DNase treatment of the vaccines

50µl of CTAB purified vaccine was treated at 37°C for 30 minutes with 2µl DNase I and 6µl of DNase I buffer (Grim reefer MGC#420143). 2.5µl of LiDs Lysis buffer was added to stop the DNase reaction. Reactions were purified using 60µl 100% Isopropanol, 140µl Ampure, 15µl MgCl2. Magnetic beads were tip-mixed 10 times, left for 5 minutes to incubate, magnetically separated and then washed twice with 80% EtOH.

Whole genome shotgun of RNase'd Vaccines.

15µl of the DNA was converted into sequence-ready libraries using Watchmakers Genomics WGS library construction kit. This kit further fragments the DNA to smaller sizes, making fragment length in the vaccines difficult to predict.

Qubit™ 3 fluorometry

Qubit™ 3 fluorometry was performed using Biotum AccuBlue RNA Broad Range kit (#31073) and Biotum AccuGreen High Sensitivity dsDNA Quantitation Kit (#31066) according to the manufacturer's instructions.

E.coli qPCR

Medicinal Genomics PathoSEEK™ E.coli Detection assay (#420102) was utilized according to the manufacturer's instructions.

qPCR and RT-qPCR spike assay

- MedGen-Moderna_Pfizer_Janssen_Vax-Spike_Forward
- >AGATGGCCTACCGGTTCA
- MedGen-Moderna_Pfizer_Janssen_Vax-Spike_Reverse
- >TCAGGCTGTCCTGGATCTT
- MedGen-Moderna_Pfizer_Janssen_Vax-Spike_Probe
- >/56-FAM/CGAGAACCA/ZEN/GAAGCTGATCGCCAA/3IABkFQ/

qPCR and RT-qPCR vector origin assay

- MedGen_Vax-vector_Ori_Forward
- >CTACATACCTCGCTCTGCTAATC
- MedGen_Vax-vector_Ori_Reverse
- GCGCCTTATCCGGTAACTATC
- MedGen_Vax-vector_Ori_Probe
- /5HEX/AAGACACGA/ZEN/CTTATCGCCACTGGC/3IABkFQ/

Elute primer to 100uM according to IDT instructions.

Make 50X primer-probe mix.

1. 25µl 100uM Forward Primer
2. 25µl 100uM Reverse Primer
3. 12.5µl 100uM Probe
4. 37.5µl nuclease free ddH20.

Use 15µl of this mixture in the qPCR master mix setup seen below. (0.5µl primer/probe per reaction)

Use 10µl of this mixture in the RT-qPCR master mix setup seen below.

Medicinal Genomics Master Mix kits were used

1. https://store.medicinalgenomics.com/qPCR-Master-Kit-v3-200-rxns
2. https://store.medicinalgenomics.com/pathoseek-rt-qpcr-master-kit

Reaction setup for 30 reactions of qPCR

- 114µl Enzyme Mix (green tube)
- 24µl Reaction Buffer (blue tube)
- 246µl nuclease free ddH20
- 15µl of Primer-Probe set Spike
- 15µl of Primer-Probe set Ori

Use 13.8µl of above MasterMix and 5µl of purified sample (1µl Vax DNA/RNA + 4µl ddH20 if CT <15)

Reaction setup for 34 reactions of RT-qPCR

- 200µl Enzyme mix
- 96µl nuclease free ddH20
- 20µl RNase Inhibitor (purple tube)
- 4µl DTT (green tube)

- 10µl Primer-Probe set Spike
- 10µl Primer-Probe set Ori

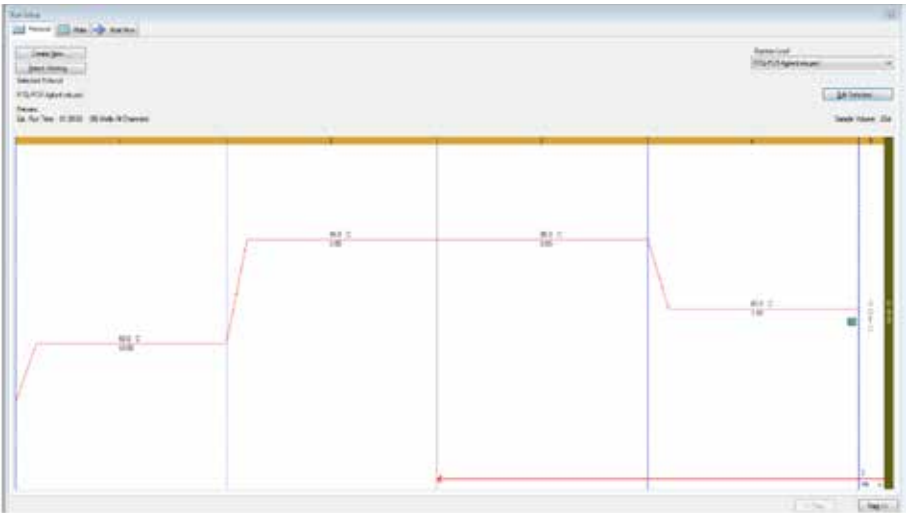
10µl of MasterMix and 1µl of Vax DNA/RNA

A Medicinal Genomics MIP DNA Purification Kit was used.

Cycling conditions

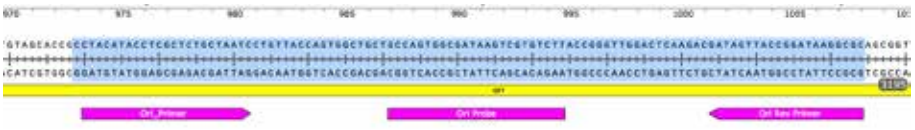
These conditions work for both qPCR and RT-qPCR. Note: The 50°C RT step can be skipped with qPCR. The MGC qPCR MasterMix kits used have a hot start enzyme which are unaffected by this 50°C step. For the sake of controlling RNA to DNA comparisons, we have put qPCR and RT-qPCR assays on the same plate and run the below program with the RT step included for all samples.

Cycling Conditions used for qPCR and RT-qPCR



Sequences of amplicons for gBlock Positive Controls. Ori = 106bp, Spike = 114bp.

Ori target



Spike target

References

Alden M, Olofsson Falla F, Yang D, Barghouth M, Luan C, Rasmussen M, De Marinis Y. 2022. Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line. *Curr Issues Mol Biol* 44: 1115-1126.

Bansal S, Perincheri S, Fleming T, Poulson C, Tiffany B, Bremner RM, Mohanakumar T. 2021. Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer-BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mRNA Vaccines. *J Immunol* 207: 2405-2410.

Castruita JAS, Schneider UV, Mollerup S, Leineweber TD, Weis N, Bukh J, Pedersen MS, Westh H. 2023. SARS-CoV-2 spike mRNA vaccine sequences circulate in blood up to 28 days after COVID-19 vaccination. *APMIS* 131: 128-132.

Dae-Eun Jeong MM, Karen Artiles, Orkan Ilbay, Andrew Fire*, Kari Nadeau, Helen Park, Brooke Betts, Scott Boyd, Ramona Hoh, and Massa Shoura*. 2021. Assemblies of putative SARS-CoV2-spike-encoding mRNA sequences for vaccines BNT-162b2 and mRNA-1273. *GitHub*.

Dean DA, Dean BS, Muller S, Smith LC. 1999. Sequence requirements for plasmid nuclear import. *Exp Cell Res* 253: 713-722.

Hanna N, Heffes-Doon A, Lin X, Manzano De Mejia C, Botros B, Gurzenda E, Nayak A. 2022. Detection of Messenger RNA COVID-19 Vaccines in Human Breast Milk. *JAMA Pediatr* 176: 1268-1270.

Josephson F. 2020-11-19. Rapporteur's Rolling Review assessment report. *Committee for Medicinal Products for Human Use* EMEA/H/C/005735/RR.

Moreau P, Hen R, Wasylyk B, Everett R, Gaub MP, Chambon P. 1981. The SV40 72 base repair repeat has a striking effect on gene expression both in SV40 and other chimeric recombinants. *Nucleic acids research* **9**: 6047-6068.

Nance KD, Meier JL. 2021. Modifications in an Emergency: The Role of N1-Methylpseudouridine in COVID-19 Vaccines. *ACS Cent Sci* **7**: 748-756.

Sheng-Fowler L, Lewis AM, Jr., Peden K. 2009. Issues associated with residual cell-substrate DNA in viral vaccines. *Biologicals* **37**: 190-195.

Ulrich-Lewis JT, Draves KE, Roe K, O'Connor MA, Clark EA, Fuller DH. 2022. STING Is Required in Conventional Dendritic Cells for DNA Vaccine Induction of Type I T Helper Cell- Dependent Antibody Responses. *Front Immunol* 13: 861710.

Zhang L, Richards A, Barrasa MI, Hughes SH, Young RA, Jaenisch R. 2021. Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues. *Proceedings of the National Academy of Sciences of the United States of America* 118.

Zheng Q, Wang T, Zhu X, Tian X, Zhong C, Chang G, Ran G, Xie Y, Zhao B, Zhu L et al. 2021. Low endotoxin E. coli strain-derived plasmids reduce rAAV vector-mediated immune responses both in vitro and in vivo. *Mol Ther Methods Clin Dev* 22: 293-303.

Kevin McKernan is the CSO and Founder of Medicinal Genomics. He managed the Research & Development for the Human Genome Project at Whitehead Institute-MIT, resulting in several patents for nucleic acid purification. He holds a Bachelor of Science in Biology from Emory University with a focus on cloning and expressing Norepinephrine Transporters. Previously, Kevin was the CSO of Courtagen Life Sciences, Inc., and was Vice President and Director of R&D of Life Technologies where he managed the development of the Life Technologies next-generation SOLiD sequencing technology. Integral to the SOLiD R&D process, he oversaw more than 100 research collaborations exploring new biological frontiers with next-generation sequencing. Kevin initiated an R&D project to investigate chemFET semiconductor-based DNA sequencing. His collaborations resulted in hundreds of publications and seven journal covers from *Science Translational Medicine* to *Nature*.

Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults[1]

by Joseph Fraiman, Juan Erviti, Mark Jones, Patrick Whelan, Sander Greenland, Robert M. Kaplan, Peter Doshi

Abstract

Introduction: In 2020, before the COVID-19 vaccine rollout, the Brighton Collaboration created a priority list, endorsed by the World Health Organization, of potential adverse events relevant to COVID-19 vaccines. We adapted the Brighton Collaboration list to evaluate serious adverse events of special interest observed in mRNA COVID-19 vaccine trials.

Method: This is secondary analysis of serious adverse events reported in the placebo-controlled, phase III randomized clinical trials of Pfizer and Moderna mRNA COVID-19 vaccines in adults (NCT04368728 and NCT04470427), focusing analysis on Brighton Collaboration adverse events of special interest.

Results: Pfizer and Moderna mRNA COVID-19 vaccines were associated with an excess risk of serious adverse events of special interest of 10.1 and 15.1 per 10,000 vaccinated over placebo baselines of 17.6 and 42.2 (95% CI −0.4 to 20.6 and −3.6 to 33.8), respectively. Combined, the mRNA vaccines were associated with an excess risk of serious adverse events of special interest of 12.5 per 10,000 vaccinated (95% CI 2.1 to 22.9); risk ratio 1.43 (95% CI 1.07

1 This study first appeared in *Vaccine*, Volume 40, Issue 40, September 22, 2022, pages 5798-5805 and is under a Creative Commons licence. It is republished here with permission from Elsevier, and is available from PubMed Central.

to 1.92). The Pfizer trial exhibited a 36% higher risk of serious adverse events in the vaccine group; risk difference 18.0 per 10,000 vaccinated (95% CI 1.2 to 34.9); risk ratio 1.36 (95% CI 1.02 to 1.83). The Moderna trial exhibited a 6% higher risk of serious adverse events in the vaccine group: risk difference 7.1 per 10,000 (95% CI –23.2 to 37.4); risk ratio 1.06 (95% CI 0.84 to 1.33). Combined, there was a 16% higher risk of serious adverse events in mRNA vaccine recipients: risk difference 13.2 (95% CI –3.2 to 29.6); risk ratio 1.16 (95% CI 0.97 to 1.39).

Discussion: The excess risk of serious adverse events found in our study points to the need for formal harm-benefit analyses, particularly those that are stratified according to risk of serious COVID-19 outcomes. These analyses will require public release of participant-level datasets.

1. Introduction

In March 2020, the Brighton Collaboration and the Coalition for Epidemic Preparedness Innovations partnership, Safety Platform for Emergency vACcines (SPEAC), created and subsequently updated a 'priority list of potential adverse events of special interest relevant to COVID-19 vaccine trials.'[1] The list comprises adverse events of special interest (AESIs) based on the specific vaccine platform, adverse events associated with prior vaccines in general, theoretical associations based on animal models, and COVID-19 specific immunopathogenesis. The Brighton Collaboration is a global authority on the topic of vaccine safety and in May 2020, the World Health Organization's Global Advisory Committee on Vaccine Safety endorsed and recommended the reporting of AESIs based on this priority list. To our knowledge, however, the list has not been applied to serious adverse events in randomized trial data.

We sought to investigate the association between FDA-authorized mRNA COVID-19 vaccines and serious adverse events identified by the Brighton Collaboration, using data from the phase III randomized, placebo-controlled clinical trials on which authorization was based. We consider these trial data against findings from post-authorization observational safety data. Our study was not designed to evaluate the overall harm-benefit of vaccination programs so far. To put our safety results in context, we conducted a simple comparison of harms with benefits to illustrate the need for formal harm-benefit analyses of the vaccines that are stratified according to risk of serious COVID-19 outcomes. Our analysis is restricted to the randomized trial data, and does not consider data on post-authorization vaccination program effects. It does however show the need for public release of participant-level trial datasets.

2. Methods

Pfizer and Moderna each submitted the results of one phase III randomized trial in support of the FDA's emergency use authorization of their vaccines in adults. Two reviewers (PD and RK) searched journal publications and trial data on the FDA's and Health Canada's websites to locate serious adverse event results tables for these trials. The Pfizer and Moderna trials are expected to follow participants for two years. Within weeks of the emergency authorization, however, the sponsors began a process of unblinding all participants who elected to be unblinded. In addition, those who received placebo were offered the vaccine. These self-selection processes may have introduced nonrandom differences between vaccinated and unvaccinated participants, thus rendering the post-authorization data less reliable. Consequently, to preserve randomization, we used the interim datasets that were the basis for emergency authorization in December 2020, approximately four months after trials commenced.

The definition of a serious adverse event (SAE) was provided in each trial's study protocol and included in the supplemental material of the trial's publication.[2,3,4] Pfizer and Moderna used nearly identical definitions, consistent with regulatory expectations. An SAE was defined as an adverse event that results in any of the following conditions: death; life-threatening at the time of the event; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability or incapacity; a congenital anomaly or birth defect; medically important event, based on medical judgement.

In addition to journal publications, we searched the websites of the FDA (for advisory committee meeting materials) and Health Canada (for sections of the dossier submitted by sponsors to the regulator).[5] For the FDA website, we considered presentations by both the FDA and the sponsors.[6] Within each of these sources, we searched for SAE results tables that presented information by specific SAE type; we chose the most recent SAE table corresponding to the FDA's requirement for a safety median follow-up time of at least two months after dose 2.

For each trial, we prepared blinded SAE tables (containing SAE types without results data). Using these blinded SAE tables, two clinician reviewers (JF and JE) independently judged whether each SAE type was an AESI. SAE types that matched an AESI term verbatim, or were an alternative diagnostic name for an AESI term, were included as an AESI. For all other SAE types, the reviewers independently judged whether that SAE type was likely to have been caused by a vaccine-induced AESI, based on a judgement considering the disease course, causative mechanism, and likelihood of the AESI to cause the SAE type. Disagreements were resolved through consensus; if consensus could not be reached, a third clinician reviewer (PW) was used to create a majority opinion.

For each included SAE, we recorded the corresponding Brighton Collaboration AESI category and organ system. When multiple AESIs could potentially cause the same SAE, the reviewers selected the AESI that they judged to be the most likely cause based on classical clinical presentation of the AESI.

We used an AESI list derived from the work of Brighton Collaboration's Safety Platform for Emergency vACcines (SPEAC) Project. This project created an AESI list which categorizes AESIs into three categories: those included because they are seen with COVID-19, those with a proved or theoretical association with vaccines in general, and those with proved or theoretical associations with specific vaccine platforms. The first version was produced in March 2020 based on experience from China. Following the second update (May 2020), the WHO Global Advisory Committee on Vaccine Safety (GACVS) adopted the list, and Brighton commenced a systematic review process 'to ensure an ongoing understanding of the full spectrum of COVID-19 disease and modification of the AESI list accordingly.'[7] This resulted in three additional AESIs being added to the list in December 2020. The subsequent (and most recent fourth) update did not result in any additional AESIs being added to the list.[1]

We matched SAEs recorded in the trial against an expanded list of AESIs created by combining Brighton's SPEAC COVID-19 AESI list with a list of 29 clinical diagnoses Brighton identified as 'known to have been reported but not in sufficient numbers to merit inclusion on the AESI list.'[7] Sensitivity analysis was used to determine whether use of the original *versus* expanded list altered our results.

Risk ratios and risk differences between vaccine and placebo groups were calculated for the incidence of AESIs and SAEs. We excluded SAEs that were known efficacy outcomes (that is, COVID-19), consistent with the approach Pfizer (but not Moderna) used in recording SAE data. The Pfizer study trial protocol states that COVID-19 illnesses and their sequelae consistent with the clinical endpoint definition were not to be reported as adverse events, 'even though the event may meet the definition of an SAE.'[8] For unspecified reasons, Moderna included efficacy outcomes in their SAE tables, effectively reporting an all-cause SAE result. Because we did not have access to individual participant data, to account for the occasional multiple SAEs within single participants, we reduced the effective sample size by multiplying standard errors in the combined SAE analyses by the square root of the ratio of the number of SAEs to the number of patients with an SAE. This adjustment increased standard errors by 10% (Pfizer) and 18% (Moderna), thus expanding the interval estimates. We estimated combined risk ratios and risk differences for the two mRNA vaccines by averaging over the risks using logistic regression models which included indicators for trial and treatment group.

We used a simple harm-benefit framework to place our results in context,

comparing risks of excess serious AESIs against reductions in COVID-19 hospitalization.

3. Results

Serious adverse event tables were located for each of the vaccine trials submitted for EUA in adults (age 16 + for Pfizer, 18 + for Moderna) in the United States: Pfizer-BioNTech COVID-19 vaccine BNT162b2 (NCT04368728) [2,9,10] and Moderna COVID-19 vaccine mRNA-1273 (NCT04470427). [3,11,12] (Table 1).

Table 1. Data sources for phase III trials.
Note: Bold font indicates dataset chosen for analysis;
EUA = Emergency Use Authorization.

Trial	Data cutoff date	Journal articles	FDA sources	Health Canada sources
Pfizer trial in ages 16 and above (NCT04368728)[2]	14 Nov 2020 (supported Dec 2020 EUA)	Aggregate data only	**Table 23 in sponsor briefing document**	**Table 55 in sponsor document C4591001 Final Analysis Interim Report Body**
Moderna trial in ages 18 and above (NCT04470427)[3]	25 Nov 2020 (supported Dec 2020 EUA)	Table S11 in publication	Table 27 in sponsor briefing document	**Table 14.3.1.13.3 in sponsor document mRNA-1273-P301 Unblinded Safety Tables Batch 1 (DS2)**

3.1. Reporting windows and serious adverse events

Moderna reported SAEs from dose 1 whereas Pfizer limited reporting from dose 1 to one month after dose 2. Both studies reported all data at the time of data cutoff (November 14th 2020 for Pfizer, November 25th 2020 for Moderna). 17 SAEs that were efficacy endpoints were removed from the Moderna trial (16 'COVID-19' SAEs and 1 'COVID-19 pneumonia' SAE). One such efficacy endpoint meeting the definition of a SAE was removed from the Pfizer trial ('SARS-CoV-2 test positive' SAE).

The Pfizer trial exhibited a 36% higher risk of serious adverse events in vaccinated participants in comparison to placebo recipients: 67.5 per 10,000 *versus* 49.5 per 10,000; risk difference 18.0 per 10,000 vaccinated participants (95% compatibility[1] interval 1.2 to 34.9); risk ratio 1.36 (95% CI 1.02 to 1.83). The Moderna trial exhibited a 6% higher risk of SAEs in vaccinated

2 *Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals* Link https://classic.clinicaltrials.gov/ct2/show/NCT04368728

3 *A Study to Evaluate Efficacy, Safety, and Immunogenicity of mRNA-1273 Vaccine in Adults Aged 18 Years and Older to Prevent COVID-19.* Link https://classic.clinicaltrials.gov/ct2/show/NCT04470427

people compared to those receiving placebo: 136 per 10,000 *versus* 129 per 10,000; risk difference 7.1 per 10,000 (95% CI –23.2 to 37.4); risk ratio 1.06 (95% CI 0.84 to 1.33). Combined, there was a 16% higher risk of SAEs in mRNA vaccine recipients than placebo recipients: 98 per 10,000 *versus* 85 per 10,000; risk difference 13.2 (95% CI -3.2 to 29.6); risk ratio 1.16 (95% CI 0.97 to 1.39). (Table 2).

Table 2. Serious adverse events.

	Total events (events per 10,000 participants)[a]		Risk difference per 10,000 participants (95 % CI)[e]	Risk ratio (95 % CI)[e]
Trial	**Vaccine**	**Placebo**		
Serious adverse events				
Pfizer[b]	52 (27.7)	33 (17.6)	10.1 (-0.4 to 20.6)	1.57 (0.98 to 2.54)
Moderna[c,d]	87 (57.3)	64 (42.2)	15.1 (-3.6 to 33.8)	1.36 (0.93 to 1.99)
Combined[f]	139 (40.9)	97 (28.6)	12.5 (2.1 to 22.9)	1.43 (1.07 to 1.92)
Serious adverse events of special interest				
Pfizer	52 (27.7)	33 (17.6)	10.1 (-0.4 to 20.6)	1.57 (0.98 to 2.54)
Moderna	87 (57.3)	64 (42.2)	15.1 (-3.6 to 33.8)	1.36 (0.93 to 1.99)
Combined[f]	139 (40.9)	97 (28.6)	12.5 (2.1 to 22.9)	1.43 (1.07 to 1.92)

a. Denominators for Pfizer were 18,801 in the vaccine group and 18,785 in the placebo group, and for Moderna were 15,185 in the vaccine group and 15,166 in the placebo group.

b. Pfizer excluded efficacy outcomes from its SAE table (COVID-19 illnesses and their sequelae meeting the definition of an SAE). However, at least one SAE appears to have been inadvertently included, which we removed from our calculations ('SARS-CoV-2 test positive': 0 vaccine group; 1 placebo group).

c. Moderna included efficacy outcomes in its SAE table (COVID-19 illnesses and their sequelae meeting the definition of an SAE). We removed efficacy SAEs outcomes that could be identified: 'COVID-19' and 'COVID-19 pneumonia.' Lacking access to participant level data, SAEs that were sequelae of serious COVID-19 could not be identified and therefore remain included in this analysis.

d. All SAEs for Moderna was calculated using the 'Number of serious AEs' row in Moderna's submission to FDA.[11]

e. Standard errors used to estimate 95% CIs were inflated by the factor √[#SAE]/[#patients with SAE] to account for multiple SAE within patients.

f. The combined risk differences and risk ratios were computed from the fitted logistic regression models and so may not exactly equal comparisons computed from the first two columns.

3.2. Serious adverse events of special interest

Regarding whether each SAE type was included on the SPEAC-derived AESI list, agreement between the two independent clinician reviewers was 86% (281/325); 40 of the 44 disagreements were resolved through consensus, and only four disagreements necessitated a third clinician reviewer. Supplemental Table 1 includes a full list of included and excluded SAEs across both trials.

In the Pfizer trial, 52 serious AESI (27.7 per 10,000) were reported in the vaccine group and 33 (17.6 per 10,000) in the placebo group. This difference corresponds to a 57% higher risk of serious AESI (RR 1.57 95% CI 0.98 to 2.54) and a risk difference of 10.1 serious AESI per 10,000 vaccinated participants (95% CI −0.4 to 20.6). In the Moderna trial, 87 serious AESI (57.3 per 10,000) were reported in the vaccine group and 64 (42.2 per 10,000) in the placebo group. This difference corresponds to a 36% higher risk of serious AESI (RR 1.36 95% CI 0.93 to 1.99) and a risk difference of 15.1 serious AESI per 10,000 vaccinated participants (95% CI −3.6 to 33.8). Combining the trials, there was a 43% higher risk of serious AESI (RR 1.43; 95% CI 1.07 to 1.92) and a risk difference of 12.5 serious AESI per 10,000 vaccinated participants (95% CI 2.1 to 22.9). (Table 2).

Of the 236 serious AESIs occurring across the Pfizer and Moderna trials, 97% (230/236) were adverse event types included as AESIs because they are seen with COVID-19. In both Pfizer and Moderna trials, the largest excess risk occurred amongst the Brighton category of coagulation disorders. Cardiac disorders have been of central concern for mRNA vaccines; in the Pfizer trial more cardiovascular AESIs occurred in the vaccine group than in the placebo group, but in the Moderna trial the groups differed by only 1 case. (Table 3, Table 4).

3.3. Sensitivity analysis

As a sensitivity analysis, we restricted the serious AESI analysis to those AESIs listed in SPEAC's COVID-19 AESI list (that is, separating out Brighton's list of 29 clinical diagnoses 'known to have been reported but not in sufficient numbers to merit inclusion on the AESI list.') This reduced the total number of AESIs across the two trials by 48 (35 vaccine group, 13 placebo group). There was still a higher risk of serious AESI when limited to the SPEAC COVID-19 AESI list, but the magnitude of the excess (in both relative and absolute terms) was smaller than when using the larger AESI list. (Supplemental Table 2).

Table 3. Serious AESIs, Pfizer trial.

Brighton category	Vaccine	Placebo	Vaccine events per 10,000	Placebo events per 10,000	Difference in events per 10,000	Risk ratio
Association with immunization in general						
Anaphylaxis	1	1	0.5	0.5	0.0	1.00
Association with specific vaccine platform(s)						
Encephalitis/encephalomyelitis	0	2	0.0	1.1	−1.1	0.00
Seen with COVID-19						
Acute kidney injury	2	0	1.1	0.0	1.1	N/A
Acute liver injury	0	1	0.0	0.5	−0.5	0.00
Acute respiratory distress syndrome	2	1	1.1	0.5	0.5	2.00
Coagulation disorder	16	10	8.5	5.3	3.2	1.60
Myocarditis/pericarditis	2	1	1.1	0.5	0.5	2.00
Other forms of acute cardiac injury	16	12	8.5	6.4	2.1	1.33
Subtotal	39	28	20.7	14.9	5.8	1.39
Brighton list of 29 clinical diagnoses seen with COVID-19						
Abscess	4	1	2.1	0.5	1.6	4.00
Cholecystitis	4	2	2.1	1.1	1.1	2.00
Colitis/Enteritis	1	1	0.5	0.5	0.0	1.00
Diarrhoea	1	0	0.5	0.0	0.5	N/A
Hyperglycaemia	1	1	0.5	0.5	0.0	1.00
Pancreatitis	1	0	0.5	0.0	0.5	N/A
Psychosis	1	0	0.5	0.0	0.5	N/A
Subtotal	13	5	6.9	2.7	4.3	2.60
Total	**52**	**33**	**27.7**	**17.6**	**10.1**	**1.57**

3.4. Harm-benefit considerations

In the Moderna trial, the excess risk of serious AESIs (15.1 per 10,000 participants) was higher than the risk reduction for COVID-19 hospitalization relative to the placebo group (6.4 per 10,000 participants).[3] In the Pfizer trial, the excess risk of serious AESIs (10.1 per 10,000) was higher than the risk reduction for COVID-19 hospitalization relative to the placebo group (2.3 per 10,000 participants).

4. Comparison with FDA reviews

In their review of SAEs supporting the authorization of the Pfizer and Moderna vaccines, the FDA concluded that SAEs were, for Pfizer, 'balanced between treatment groups,'[15] and for Moderna, were 'without meaningful imbalances between study arms.'[16] In contrast to the FDA analysis, we found an excess risk of SAEs in the Pfizer trial. Our analysis of Moderna was compatible with FDA's analysis, finding no meaningful SAE imbalance between groups.

The difference in findings for the Pfizer trial, between our SAE analysis and the FDA's, may in part be explained by the fact that the FDA analysed the total number of participants experiencing any SAE, whereas our analysis was based on the total number of SAE events. Given that approximately twice as many persons in the vaccine group than in the placebo group experienced multiple SAEs (there were 24 more events than participants in the vaccine group, compared to 13 in the placebo group), FDA's analysis of only the incidence of participants experiencing any SAE would not reflect the observed excess of multiple SAEs in the vaccine group.

Table 4. Serious AESIs, Moderna trial.

Brighton category	**Vaccine**	**Placebo**	**Vaccine events per 10,000**	**Placebo events per 10,000**	**Difference in events per 10,000**	**Risk ratio**
Association with specific vaccine platform(s)						
Bell's Palsy	1	0	0.7	0.0	0.7	N/A
Encephalitis/ encephalomyelitis	1	0	0.7	0.0	0.7	N/A
Seen with COVID-19						
Acute kidney injury	1	3	0.7	2.0	−1.3	0.33
Acute liver injury	1	0	0.7	0.0	0.7	N/A
Acute respiratory distress syndrome	7	4	4.6	2.6	2.0	1.75
Angioedema	0	2	0.0	1.3	−1.3	0.00
Coagulation disorder	20	13	13.2	8.6	4.6	1.54
Generalized Convulsions	2	0	1.3	0.0	1.3	N/A
Myelitis	0	1	0.0	0.7	−0.7	0.00
Myocarditis/ pericarditis	4	5	2.6	3.3	−0.7	0.80

Other forms of acute cardiac injury	26	26	17.1	17.1	0.0	1.00
Other rash	1	1	0.7	0.7	0.0	1.00
Rhabdomyolysis	0	1	0.0	0.7	−0.7	0.00
Single Organ Cutaneous Vasculitis	1	0	0.7	0.0	0.7	N/A
Subtotal	65	56	42.8	36.9	5.9	1.16
Brighton list of 29 clinical diagnoses seen with COVID-19						
Abscess	1	0	0.7	0.0	0.7	N/A
Arthritis	3	1	2.0	0.7	1.3	3.00
Cholecystitis	4	0	2.6	0.0	2.6	N/A
Colitis/Enteritis	6	3	4.0	2.0	2.0	2.00
Diarrhoea	2	1	1.3	0.7	0.7	2.00
Hyperglycaemia	1	0	0.7	0.0	0.7	N/A
Hyponatremia	1	1	0.7	0.7	0.0	1.00
Pancreatitis	2	0	1.3	0.0	1.3	N/A
Pneumothorax	0	1	0.0	0.7	−0.7	0.00
Psychosis	1	1	0.7	0.7	0.0	1.00
Thyroiditis	1	0	0.7	0.0	0.7	N/A
Subtotal	22	8	14.5	5.3	9.2	2.75
Total	**87**	**64**	**57.3**	**42.2**	**15.1**	**1.36**

A more important factor, however, may be that FDA's review of non-fatal SAEs used a different analysis population with different follow-up windows. The FDA reported 126 of 21,621 (0.6%) of vaccinated participants experienced at least one SAE at data cutoff compared to 111 of 21,631 (0.5%) of placebo participants. In contrast, our analysis found 127 SAEs among 18,801 vaccine recipients *versus* 93 SAEs among 18,785 placebo recipients.[15] While summary results for the population we analysed was provided in a table, FDA did not report an analysis of them. The substantially larger denominators in FDA's analysis (5,666 more participants) reflect the fact that their analysis included all people receiving at least one dose (minus 196 HIV-positive participants), irrespective of the duration of post-injection follow-up time. In contrast, our analysis was based on the study population with median follow-up ≥ two months after dose 2 (minus 120 HIV-positive participants), of whom 98.1% had received both doses.[2,17] The FDA's analysis of SAEs thus included thousands of additional participants with very little follow-up, of whom the large majority had only received one dose.

4.1 Comparison with post-authorization studies

Although the randomized trials offer high-level evidence for evaluating causal effects, the sparsity of their data necessitates that harm-benefit analyses also consider observational studies. Since their emergency authorization in December 2020, hundreds of millions of doses of Pfizer and Moderna COVID-19 vaccines have been administered and post-authorization observational data offer a complementary opportunity to study AESIs. Post-authorization observational safety studies include cohort studies (which make use of medical claims or electronic health records) and disproportionality analyses (which use spontaneous adverse event reporting systems). In July 2021, the FDA reported detecting four potential adverse events of interest: pulmonary embolism, acute myocardial infarction, immune thrombocytopenia, and disseminated intravascular coagulation following Pfizer's vaccine based on medical claims data in older Americans.[18] Three of these four serious adverse event types would be categorized as coagulation disorders, which is the Brighton AESI category that exhibited the largest excess risk in the vaccine group in both the Pfizer and Moderna trials. FDA stated it would further investigate the findings but at the time of our writing has not issued an update. Similarly, spontaneous-reporting systems have registered serious adverse reactions including anaphylaxis (all COVID-19 vaccines), thrombocytopenia syndrome among premenopausal females (Janssen vaccine), and myocarditis and pericarditis among younger males (Pfizer and Moderna vaccines).[19,20]

Using data from three postmarketing safety databases for vaccines (VAERS, EudraVigilance, and VigiBase), disproportionality studies have reported excess risks for many of the same SAE types as in the present study.[21,22,23] For example, a study using VAERS and EudraVigilance comparing the disproportionality of adverse event reports between the influenza vaccine *versus* the mRNA COVID-19 vaccines reported excess risks for the following Brighton AESIs: cardiovascular events, coagulation events, haemorrhages, gastrointestinal events, and thromboses.[22] While CDC published a protocol[24] in early 2021 for using proportional reporting ratios for signal detection in the VAERS database, results from the study have not yet been reported.[25] Among self-controlled case series, one reported a rate ratio of 1.38 (95% CI 1.12–1.71) for haemorrhagic stroke following Pfizer vaccine,[26] another reported 0.97 (95% CI 0.81–1.15),[27] while a cohort study[28] reported 0.84 (95% CI 0.54–1.27).

5. Discussion

Using a prespecified list of AESI identified by the Brighton Collaboration, higher risk of serious AESI was observed in the mRNA COVID-19 vaccine group relative to placebo in both the Pfizer and Moderna adult phase III trials, with 10.1 (Pfizer) and 15.1 (Moderna) additional events for every 10,000 people vaccinated. Combined, there was a risk difference of 12.5 serious AESIs per 10,000 people vaccinated (95% CI 2.1 to 22.9). These results raise concerns that mRNA vaccines are associated with more harm than initially estimated at the time of emergency authorization. In addition, our analysis identified a 36% higher risk of serious adverse events in vaccinated participants in the Pfizer trial: 18.0 additional SAEs per 10,000 vaccinated (95% CI 1.2 to 34.9). Consistent with the FDA evaluation, our analysis found no clear difference in SAEs between groups in the Moderna trial.

Results between the Pfizer and Moderna trials were similar for the AESI analysis but exhibited substantial variation in the SAE analysis. Caution is needed in interpreting this variation as it may be substantially explained by differences in SAE recording practices in the trials rather than differences in actual vaccine harm profiles. For reasons that are not documented in the trial protocol, Moderna included efficacy outcomes in its SAE tabulations, while Pfizer excluded them. As a result, Moderna's SAE table did not present a traditional SAE analysis but rather an all-cause SAE analysis. The FDA analysis of the Moderna trial presented an all-cause SAE analysis, which estimates total vaccine effects on SAEs, including effects transmitted via effects on COVID-19. It did not however present a traditional SAE analysis with efficacy endpoints removed, which attempts to estimate only the direct effects on SAEs. While our analysis attempted to perform a traditional SAE analysis by excluding efficacy SAEs (serious COVID-19 and its sequelae), our effort was hindered because we did not have access to patient level data. Easily recognizable efficacy SAEs ('COVID-19', 'COVID-19 pneumonia', and 'SARS-CoV-2 test positive') could be removed, but many participants who experienced a COVID-19 SAE likely experienced multiple other SAEs (for example, pneumonia, hypoxia, and thrombotic events) which could not be identified and therefore remain included in our analysis. Of 17 total efficacy SAEs (16 'COVID-19' and 1 'COVID-19 pneumonia') removed from our analysis of the Moderna trial, 16 were in the placebo arm. As a consequence, the background SAE risk (risk in absence of COVID-19) would be overestimated by the Moderna placebo group, resulting in underestimation of the actual risk of SAEs and AESIs attributable to the vaccine in the Moderna comparisons as well as in the combined analysis. Access to patient-level data would allow adjustments for this problem.

Rational policy formation should consider potential harms alongside potential

benefits.[29] To illustrate this need in the present context, we conducted a simple harm-benefit comparison using the trial data comparing excess risk of serious AESI against reductions in COVID-19 hospitalization. We found excess risk of serious AESIs to exceed the reduction in COVID-19 hospitalizations in both Pfizer and Moderna trials.

This analysis has the limitations inherent in most harm-benefit comparisons. First, benefits and harms are rarely exact equivalents, and there can be great variability in the degree of severity within both benefit and harm endpoints. For example, intubation and short hospital stay are not equivalent but both are counted in 'hospitalization'; similarly, serious diarrhoea and serious stroke are not equivalent but both are counted in 'SAE'. Second, individuals value different endpoints differently. Third, without individual participant data, we could only compare the number of persons hospitalized for COVID-19 against the number of serious AESI events, not the number of participants experiencing any serious AESI. Some people experienced multiple SAEs whereas hospitalized COVID-19 participants were likely only hospitalized once, biasing the analysis towards exhibiting net harm. To gauge the extent of this bias, we considered that there were 20% (Pfizer) and 34% (Moderna) more SAEs than participants experiencing any SAE. As a rough sensitivity calculation, if we divide the Pfizer excess serious AESI risk of 10.1 by 1.20 it becomes 8.4 compared to a COVID-19 hospitalization risk reduction of 2.3; if we divide the Moderna excess serious AESI risk of 15.1 by 1.34 it becomes 11.3 compared to a COVID-19 hospitalization risk reduction of 6.4.

Harm-benefit ratios will be different for populations at different risk for serious COVID-19 and observation periods that differ from those studied in the trials. Presumably, larger reductions in COVID-19 hospitalizations would have been recorded if trial follow-up were longer, if more SARS-CoV-2 were circulating, or if participants had been at higher risk of serious COVID-19 outcomes, shifting harm-benefit ratios toward benefit. Conversely, harm-benefit ratios would presumably shift towards harm for those with lower risk of serious COVID-19 outcomes – such as those with natural immunity, younger age or no comorbidities. Similarly, waning vaccine effectiveness, decreased viral virulence, and increasing degree of immune escape from vaccines might further shift the harm-benefit ratio toward harm. Large, randomized trials in contemporary populations could robustly answer these questions. Absent definitive trials, however, synthesis of multiple lines of evidence will be essential.[30,48,49]

Adverse events detected in the post-marketing period have led to the withdrawal of several vaccines. An example is intussusception following one brand of rotavirus vaccine: around 1 million children were vaccinated before identification of intussusception, which occurred in around 1 per 10,000 vaccinees.[31] Despite

the unprecedented scale of COVID-19 vaccine administration, the AESI types identified in our study may still be challenging to detect with observational methods. Most observational analyses are based on comparing the risks of adverse events 'observed' against a background (or 'expected') risk, which inevitably display great variation, by database, age group, and sex.[32] If the actual risk ratio for the effect was 1.4 (the risk ratio of the combined AESI analysis), it could be quite difficult to unambiguously replicate it with observational data given concerns about systematic as well as random errors. [33,34,35]

In addition, disproportionality analyses following COVID-19 vaccination also have limitations, particularly with respect to the type of adverse events seen in our study. The majority of SAEs that contributed to our results are relatively common events, such as ischaemic stroke, acute coronary syndrome, and brain haemorrhage. This complicates signal detection because clinical suspicion of an adverse vaccine reaction following an event commonly seen in clinical practice will be lower than for SAEs like myocarditis.[50] For this reason, clinical suspicion leading to the filing of an individual case safety report may be far less common in the post-authorization setting than in the trials. At the same time, heightened awareness about COVID-19 vaccine SAEs can result in under- and over-reporting. Public health messages assuring vaccine safety may lower clinical suspicion of potential causal relationships, whereas messages about potential harms can conversely stimulate reports that otherwise might not have been made. These factors can lead to bias in both directions, further complicating interpretation. In contrast to these problems, in the randomized trials used in this analysis, all SAEs were to be recorded, irrespective of clinical judgement regarding potential causality.

Although our analysis is secondary, reanalyses of clinical trial data have led to the detection of adverse events well after the market entry of major drugs such as rofecoxib and rosiglitazone.[36,37] Our analysis has an advantage over postmarketing observational studies in that the data are from blinded, placebo-controlled randomized trials vetted by the FDA, which were matched against a list of adverse events created before the availability of the clinical-trial results and designed for use in COVID-19 vaccine trials.

Our study has several important limitations. First, Pfizer's trial did not report SAEs occurring past one month after dose 2. This reporting threshold may have led to an undercounting of serious AESIs in the Pfizer trial. Second, for both studies, the limited follow-up time prevented an analysis of harm-benefit over a longer period. Third, all SAEs in our analysis met the regulatory definition of a serious adverse event, but many adverse-event types which patients may themselves judge as serious may not meet this regulatory threshold. Fourth, there are decisions about which SAEs to include or exclude as AESIs require subjective, clinical judgements in the absence of detailed clinical information

about the actual SAEs. We encourage third party replication of our study, with access to complete SAE case narratives, to determine the degree to which these decisions affected our findings. For additional sensitivity analyses, such replication studies could also make use of other AESI lists, such as those prepared by FDA,[38,39,40,41] CDC,[24] Pfizer,[42] or a *de novo* AESI list derived from a list of COVID-19 complications understood to be induced via SARS-CoV-2's spike protein.[43,44]

A fifth important limitation is our lack of access to individual participant data, which forced us to use a conservative adjustment to the standard errors. The 95% CIs[13,14] calculated are therefore only approximate because we do not know which patients had multiple events. Finally, as described above, in the Moderna analysis, the SAEs that were sequelae of serious COVID-19 could not be identified and therefore remain included in our calculations. Because the vaccines prevent SAEs from COVID-19 while adding SAE risks of their own, this inclusion makes it impossible to separately estimate SAEs due to the vaccine from SAEs due to COVID-19 in the available Moderna data, as must be done to extrapolate harm-benefit to other populations. These study limitations all stem from the fact that the raw data from COVID-19 vaccine clinical trials are not publicly available.[45,46]

We emphasize that our investigation is preliminary, to point to the need for more involved analysis. The risks of serious AESIs in the trials represent only group averages. SAEs are unlikely to be distributed equally across the demographic subgroups enrolled in the trial, and the risks may be substantially less in some groups compared to others. Thus, knowing the actual demographics of those who experienced an increase in serious AESI in the vaccine group is necessary for a proper harm-benefit analysis. In addition, clinical studies are needed to see if particular SAEs can be linked to particular vaccine ingredients as opposed to unavoidable consequences of exposure to spike protein, as future vaccines could then be modified accordingly or sensitivities could be tested for in advance. In parallel, a systematic review and meta-analysis using individual participant data should be undertaken to address questions of harm-benefit in various demographic subgroups, particularly in those at low risk of serious complications from COVID-19. Finally, there is a pressing need for comparison of SAEs and harm-benefit for different vaccine types; some initial work has already begun in this direction.[47]

Full transparency of the COVID-19 vaccine clinical trial data is needed to properly evaluate these questions. Unfortunately, as we approach two years after release of COVID-19 vaccines, participant level data remain inaccessible.[45,46]

Author contributions

All authors had full access to all of the data in the study (available at https://doi.org/10.5281/zenodo.6564402), and take responsibility for the integrity of the data and the accuracy of the data analysis.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank Jean Rees for help identifying sources of data.

Funding

This study had no funding support.

Ethical review statement

This research was confirmed to be Not Human Subjects Research (NHSR) by University of Maryland, Baltimore (HP-00102561).

Conflicts of interest

JF, JE, MJ, SG, PW, RK: none to declare. PD has received travel funds from the European Respiratory Society (2012) and Uppsala Monitoring Center (2018); grants from the FDA (through University of Maryland M-CERSI; 2020), Laura and John Arnold Foundation (2017-22), American Association of Colleges of Pharmacy (2015), Patient-Centered Outcomes Research Institute (2014-16), Cochrane Methods Innovations Fund (2016-18), and UK National Institute for Health Research (2011-14); was an unpaid IMEDS steering committee member at the Reagan-Udall Foundation for the FDA (2016-2020) and is an editor at *The BMJ*. The views expressed here are those of the authors and do not necessarily reflect those of their employers.

Appendix A. Supplementary data

The following are the Supplementary data to this article:

Supplementary data 1.

Download Word document (16KB) Link https://ars.els-cdn.com/content/image/1-s2.0-S0264410X22010283-mmc1.docx

Data availability

All of the data in the study are available at https://doi.org/10.5281/zenodo.6564402

References

[1] Law B, Pim C. SO2-D2.1.3 Priority List of COVID-19 Adverse events of special interest [Internet]. 2021 Oct [cited 2022 Feb 17]. Available from: https://brightoncollaboration.us/wp-content/uploads/2021/11/SO2_D2.1.3_COVID-19_AESI-update_V1.0_Part-2_09Nov2021.pdf.

[2] F.P. Polack, S.J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine N Engl J Med, 383 (27) (2020), pp. 2603-2615

[3] L.R. Baden, H.M. El Sahly, B. Essink, K. Kotff, S. Frey, R. Novak, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine N Engl J Med, 384 (5) (2021), pp. 403-416

[4] J. Sadoff, G. Gray, A.n. Vandebosch, V. Cárdenas, G. Shukarev, B. Grinszte jn, et al. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19 N Engl J Med, 384 (23) (2021), pp. 2187-2201

[5] Health Canada. Search for clinical information on drugs and medical devices [Internet]. 2019 [cited 2021 Nov 9]. Available from: https://clinical-information.canada.ca/.

[6] Food and Drug Administration. Meeting Materials, Vaccines and Related Biological Products Advisory Committee [Internet]. U.S. Food and Drug Administration. 2022 [cited 2022 Feb 18]. Available from: https://www.fda.gov/advisory-committees/vaccines-and-related-biological-products-advisory-committee/meeting-materials-vaccines-and-related-biological-products-advisory-committee.

[7] Law B. SO2-D2.1.2 Priority List of COVID-19 Adverse events Google Scholar of special interest: Quarterly update December 2020 [Internet]. 2020 Dec [cited 2020 Dec 20]. Available from: https://brightoncollaboration.us/wp-content/uploads/2021/01/SO2_D2.1.2_V1.2_COVID-19_AESI-update-23Dec2020-review_final.pdf.

[8] Pfizer. PF-07302048 (BNT162 RNA-Based COVID-19 Vaccines) Protocol C4591001 [Internet]. 2020 [cited 2022 Jul 17]. Available from: https://cdn.pfizer.com/pfizercom/2020-11/C4591001_Clinical_Protocol_Nov2020.pdf.

[9] Pfizer-BioNTech. PFIZER-BIONTECH COVID-19 VACCINE (BNT162, PF-07302048) VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE BRIEFING DOCUMENT. [cited 2021 Dec 20]; Available from: https://www.fda.gov/media/144246/download#page=87.

[10] Pfizer. Final Analysis Interim Report: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals (Protocol C4591001) [Internet]. [cited 2022 May 3]. Available from: https://clinical-information.canada.ca/ci-rc/item/244906; https://clinical-information.canada.ca/ci-rc-vu.pdf?file=m5/c45/c4591001-fa-interim-report-body_Unblinded_Redacted.pdf&id=244906.

[11] Moderna. Sponsor briefing document [Internet]. 2020 Dec [cited 2022 Feb 21]. Available from: https://www.fda.gov/media/144452/download.

[12] Moderna. Unblinded Safety Tables Batch 1 (DS2) [Internet]. [cited 2022 May 3]. Available from: https://clinical-information.canada.ca/ci-rc/item/244946; https://clinical-information.canada.ca/ci-rc-vu.pdf?file=m5/5.3.5.1/m5351-mrna-1273-p301-p-unblinded-safety-tables-batch-1.pdf&id=244946.

[13] V. Amrhein, S. Greenland, B. McShane Scientists rise up against statistical significance Nature, 567 (7748) (2019), pp. 305-307, 10.1038/d41586-019-00857-9

[14] Rafi Z, Greenland S. Semantic and cognitive tools to aid statistical science: replace confidence and significance by compatibility and surprise. BMC Med Res Methodol [Internet]. 2020 Sep 30;20(1):244. Available from: http://dx.doi.org/10.1186/s12874-020-01105-9.

[15] Food and Drug Administration. Emergency Use Authorization for Pfizer-BioNTech COVID-19 Vaccine Review Memo [Internet]. 2020 Dec [cited 2022 Feb 21]. Available from: https://www.fda.gov/media/144416/download.

[16] Food and Drug Administration. Moderna COVID-19 Vaccine EUA FDA review memorandum [Internet]. 2020 Dec [cited 2022 Feb 21]. Available from: https://www.fda.gov/media/144673/download.

[17] Food and Drug Administration. Pfizer-BioNTech COVID-19 vaccine EUA review memorandum [Internet]. 2020 Dec [cited 2022 Mar 30]. Available from: https://www.fda.gov/media/144416/download.

[18] Food and Drug Administration. Initial Results of Near Real-Time Safety Monitoring COVID-19 Vaccines [Internet]. 2021 [cited 2022 Mar 30]. Available from: https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/initial-results-near-real-time-safety-monitoring-covid-19-vaccines-persons-aged-65-years-and-older.

[19] Centers for Disease Control and Prevention. Selected adverse events reported after COVID-19 vaccination [Internet]. 2021 [cited 2021 May 28]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

[20] Krug A, Stevenson J, Høeg TB. BNT162b2 Vaccine-Associated Myo/Pericarditis in Adolescents: A Stratified Risk-Benefit Analysis. Eur J Clin Invest [Internet]. 2022 May;52(5):e13759. Available from: http://dx.doi.org/10.1111/eci.13759.

[21] S. Dutta, R. Kaur, J. Charan, P. Bhardwaj, S.R. Ambwani, S. Babu, et al. Analysis of Neurological Adverse Events Reported in VigiBase From COVID-19 Vaccines
Cureus, 14 (1) (2022), p. e21376, 10.7759/cureus.21376

[22] Montano D. Frequency and Associations of Adverse Reactions of COVID-19 Vaccines Reported to Pharmacovigilance Systems in the European Union and the United States. Front Public Health [Internet]. 2021;9:756633. Available from: http://dx.doi.org/10.3389/fpubh.2021.756633.

[23] Jeet Kaur R, Dutta S, Charan J, Bhardwaj P, Tandon A, Yadav D, et al. Cardiovascular Adverse Events Reported from COVID-19 Vaccines: A Study Based on WHO Database. Int J Gen Med [Internet]. 2021 Jul 27;14:3909–27. Available from: http://dx.doi.org/10.2147/IJGM.S324349.

[24] Centers for Disease Control and Prevention. Vaccine Adverse Event Reporting System (VAERS) Standard Operating Procedures for COVID-19 (as of 29 January 2021) [Internet]. 2021 Jan [cited 2022 Mar 30]. Available from: https://www.cdc.gov/vaccinesafety/pdf/VAERS-v2-SOP.pdf.

[25] Centers for Disease Control and Prevention. Vaccine safety publications [Internet]. 2022 [cited 2022 Mar 31]. Available from: https://www.cdc.gov/vaccinesafety/research/publications/index.html.

[26] di, S. Razvi, et al. Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection Nat Med, 27 (12) (2021), pp. 2144-2153, 10.1038/s41591-021-01556-7

[27] M.J. Jabagi, J. Botton, M. Bertrand, A. Weill, P. Farrington, M. Zureik, et al. Myocardial Infarction, Stroke, and Pulmonary Embolism After BNT162b2 mRNA COVID-19 Vaccine in People Aged 75 Years or Older
JAMA, 327 (1) (2022), pp. 80-82, 10.1001/jama.2021.21699

[28] N. Barda, N. Dagan, Y. Ben-Shlomo, E. Kepten, J. Waxman, R. Ohana, et al. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting N Engl J Med, 385 (12) (2021), pp. 1078-1090, 10.1056/NEJMoa2110475

[29] Mörl F, Günther M, Rockenfeller R. Is the Harm-to-Benefit Ratio a Key Criterion in Vaccine Approval? Frontiers in Medicine [Internet]. 2022;9. Available from: https://www.frontiersin.org/articles/10.3389/fmed.2022.879120.

[30] Greenhalgh T, Fisman D, Cane DJ, Oliver M, Macintyre CR. Adapt or die: how the pandemic made the shift from EBM to EBM+ more urgent. BMJ Evid Based Med [Internet]. 2022 Jul 19;bmjebm – 2022–111952. Available from: https://ebm.bmj.com/lookup/doi/10.1136/bmjebm-2022-111952.

[31] L.M. Hampton, R. Aggarwal, S.J.W. Evans, B. Law General determination of causation between Covid-19 vaccines and possible adverse events Vaccine, 39 (10) (2021), pp. 1478-1480, 10.1016/j.vaccine.2021.01.057

[32] Li X, Ostropolets A, Makadia R, Shoaibi A, Rao G, Sena AG, et al. Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study. BMJ [Internet]. 2021 Jun 14 [cited 2022 Mar 28];373. Available from: https://www.bmj.com/content/373/bmj.n1435.

[33] Lash TL, Fox MP, Fink AK. Applying Quantitative Bias Analysis to Epidemiologic Data [Internet]. Springer New York; 2009. 192 p. Available from: https://play.google.com/store/books/details?id=a32fDAEACAAJ.

[34] MacLehose RF, Ahern TP, Lash TL, Poole C, Greenland S. The Importance of Making Assumptions in Bias Analysis. Epidemiology [Internet]. 2021 Sep 1;32(5):617–24. Available from: http://dx.doi.org/10.1097/EDE.0000000000001381.

[35] Greenland S. Invited Commentary: Dealing With the Inevitable Deficiencies of Bias Analysis-and All Analyses. Am J Epidemiol. 2021 Aug 1;190(8):1617–21. Available from: http://doi.org/10.1093/aje/kwab069.

[36] H.M. Krumholz, J.S. Ross, A.H. Presler, D.S. Egilman What have we learnt from Vioxx? BMJ, 334 (7585) (2007), pp. 120-123, 10.1136/bmj.39024.487720.68

[37] S.E. Nissen, K. Wolski Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes N Engl J Med, 356 (24) (2007), pp. 2457-2471, 10.1056/NEJMoa072761

[38] Anderson S. CBER Plans for Monitoring COVID-19 Vaccine Safety and Effectiveness [Internet]. VRBPAC Meeting; 2020 Oct 22 [cited 2022 Jul 19]. Available from: https://www.fda.gov/media/143557/download#page=17.

[39] Anderson S. An Update of FDA Monitoring COVID-19 Vaccine Safety and Effectiveness [Internet]. VRBPAC Meeting; 2021 Feb 26 [cited 2022 Jul 19]. Available from: https://www.fda.gov/media/146268/download#page=8.

[40] Anderson S. FDA Updates of COVID-19 Vaccine Safety Activities [Internet]. VRBPAC Meeting; 2021 Jun 10 [cited 2022 Jul 19]. Available from: https://www.fda.gov/media/150051/download#page=9.

[41] Food and Drug Administration. Background Rates of Adverse Events of Special Interest for COVID-19 Vaccine Safety Monitoring [Internet]. 2021 Jan [cited 2021 Jul 19]. Available from: https://bestinitiative.org/wp-content/uploads/2022/01/C19-Vax-Safety-AESI-Bkgd-Rate-Protocol-FINAL-2020.pdf#page=12.

[42] Pfizer. 5.3.6 Cumulative analysis of post-authorization adverse event reports of PF-07302048 (BNT162b2) received through 28-Feb-2021 [Internet]. 2021 Apr [cited 2022 Jul 19]. Available from: https://phmpt.org/wp-content/uploads/2022/04/reissue_5.3.6-postmarketing-experience.pdf#page=30.

[43] A. Gupta, M.V. Madhavan, K. Sehgal, N. Nair, S. Mahajan, T.S. Sehrawat et al. Extrapulmonary manifestations of COVID-19 Nat Med, 26 (7) (2020), pp. 1017-1032, 10.1038/s41591-020-0968-3

[44] Y. Lei, J. Zhang, C.R. Schiavon, M. He, L. Chen, H. Shen, et al. SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2 Circ Res, 128 (9) (2021), pp. 1323-1326, 10.1161/CIRCRESAHA.121.318902

[45] Tanveer S, Rowhani-Farid A, Hong K, Jefferson T, Doshi P. Transparency of COVID-19 vaccine trials: decisions without data. BMJ Evid Based Med [Internet]. 2021 Aug 9; Available from: http://dx.doi.org/10.1136/bmjebm-2021-111735.

[46] Doshi P, Godlee F, Abbasi K. Covid-19 vaccines and treatments: we must have raw data, now. BMJ [Internet]. 2022 Jan 19;376:o102. Available from: http://dx.doi.org/10.1136/bmj.o102.

[47] Benn CS, Schaltz-Buchholzer F, Nielsen S, Netea MG, Aaby P. Randomised Clinical Trials of COVID-19 Vaccines: Do Adenovirus-Vector Vaccines Have Beneficial Non-Specific Effects? [Internet]. 2022 [cited 2022 May 9]. Available from: https://papers.ssrn.com/abstract=4072489.

[48] M.H. Murad, S. Saadi Evidence-based medicine has already adapted and is very much alive BMJ Evidence-based Medicine (2022), 10.1136/bmjebm-2022-112046 https://ebm.bmj.com/content/early/2022/07/19/bmjebm-2022-112046, Accessed 22nd Aug 2022

[49] A Munro The Pandemic Evidence Failure https://alasdairmunro.substack.com/p/the-pandemic-evidence-failure (2022), Accessed 22nd Aug 2022

[50] S Mansanguan, P Charunwatthana, W Piyaphanee, W Dechkhajor n, A Poolcharoen, C Mansanguan Cardiovascular Manifestation of the BNT162b2 mRNA COVID-19 Vaccine in Adolescents Trop. Med. Infect. Dis., 7 (8) (2022), p. 196, 10.3390/tropicalmed7080196

Dr Joseph Fraiman is an Emergency Medicine physician currently working in New Orleans, Louisiana, and the surrounding rural region. Dr Fraiman served as the medical manager of Louisiana's Urban Search and Rescue Disaster Task Force 1. As an independent clinical scientist, he researches harm-benefit analysis of clinical interventions. His publications regarding the COVID-19 mRNA vaccines include a re-analysis of serious harm from the original clinical trials, and on the FDA's safety surveillance system.

Part 3

Lack of evidence leads to policy failures

When data do not support the government's narrative, the apparent correct response that regulators expect from practitioners is to stay silent while authorities go on to withhold further investigations. This was demonstrated particularly by NSW Health early in 2023 in their Respiratory Surveillance Report from December, 2022: 'Vaccination status of cases admitted to hospital, admitted to ICU, and those who die will no longer be reported.'

What has unfolded over the last few years is what Stanford Professor Jay Bhattacharya called 'the greatest public health mistake in human history.' The officially sanctioned medical misinformation that has characterized the COVID pandemic is unparalleled. For a disease with a highly stratified median infection fatality rate of .05% in 2020, similar to the seasonal flu, and with healthy children having a statistically 0% risk, governments locked down this country (and much of the world), casting about 150 million people into poverty.

Acting on flawed modelling, governments force-quarantined, separated families, let people die alone, impaired child development, closed businesses, amassed generational debt, and made livelihood conditional upon submitting to participation in what former Health Minister Greg Hunt called 'the world's largest clinical trial'. At the same time they were indemnifying manufacturers in secret contracts, reducing legislative safety and efficacy requirements, silencing

doctors and banning early treatments that showed considerable promise. All of this was supported by the Australian Health Practitioner Regulation Agency and the national boards' silencing of health professionals, for our alleged safety.

The pandemic preparedness plans released in 2019 specifically presented the importance of engagement between front-line health professionals and policymakers. Instead, our health professionals were censored, suppressed, and threatened with reprisals if they failed to provide health advice consistent with governmental public health messaging. These threats were not empty. In a time when the need was – and is – obviously there for more medical professionals, qualified and experienced practitioners were summarily suspended and neatly removed from the system. The question of the accuracy of the medical advice they were sacked over never arose. Speak out? – goodbye.

> It is time for an honest conversation about the risk and benefit of these novel products. The reality is that the evidence does not support the notion that these injections saved millions of lives, and the harms and deaths caused by the vaccines cannot be ignored.
>
> – Dr Clare Craig

The fact is that there has been no honesty about risks and benefits because conversation has not been permitted. Dr Malhotra in this part also has a substantial reputation for his interest in rebalancing the role of nutrition and lifestyle education as opposed to pharmacological interventions. Could this be because he has actually done the work and found the benefit? There has been very little room for this in modern Australian orthodox medicine, either.

> Several new pharmaceutical agents have been administered to billions of people worldwide, including the young and healthy at little risk from the virus. Considerable leeway has been afforded in terms of the preclinical and clinical testing of these agents, despite an entirely novel mechanism of action and concerning biodistribution characteristics…. It cannot be said that the consent to receive these agents was fully informed as is required ethically and legally.
>
> Authorities and sections of the medical profession have supported unethical, coercive and misinformed policies such as vaccine mandates and vaccine passports, undermining the principles of ethical, evidence-based medical practice and informed consent. These regrettable actions are a symptom of 'the medical information mess': the tip of a morality iceberg where prescribed medications are estimated to be the third most common cause of death globally after heart disease and cancer….. COVID vaccine administration must stop until all the raw data have been subjected to fully independent scrutiny.
>
> – Dr Aseem Malhotra

The failings of COVID-19 policy

by Clare Craig

The global response to COVID-19 has been fraught with controversy and subject to extensive debate. As we navigate these unprecedented times, it becomes essential to critically assess the decisions made, the validity of the assumptions they were based on and the consequences to the public and to ethical norms.

It is important to start with the profound undermining of foundational medical ethics and human rights. Measures designed to curb the virus's spread have transgressed upon individual autonomy, informed consent, and the principle of direct patient benefit. The most important breaches were the creation of an environment of fear for psychological manipulation and coercion for medical interventions.

Several unevidenced and misguided assumptions about COVID substantially influenced policy decisions. These flawed assumptions, paraded as 'The Science', were seldom contested because of the silencing of critics. To truly gauge the effect of COVID policies, we must examine, as best we can, what would have happened in the absence of these policies. Consequently, this paper delves into several misguided assumptions that shaped our response to the pandemic and shows how they were invalid.

The evidence is examined, first regarding lockdowns and masks and then the pharmaceutical interventions. In particular, I examine the widespread assumption of close-contact droplet transmission of the virus. Evidence indicates there is aerosol transmission over longer distances, which challenges the efficacy of measures designed to restrict close-contact spread. Misguided beliefs about the ubiquity of asymptomatic spread and the entire population being susceptible further complicate the picture and have bolstered the belief that lockdowns would work.

The decisions taken regarding treatments for COVID were irrational and unevidenced and this is briefly discussed, followed by a debunking of the claims made about 'vaccination'. This is a global review and includes evidence from more than one country, but Australia is a particular focus as it can act as a control group, showing what effects can and cannot be attributed to COVID.

This is an evidence-based analysis which I believe to be true, but I do not claim omniscience. No one can. The only way we can learn as humans and as a society is by listening to every voice and dispassionately testing the arguments. Successful silencing of minority voices has slowed the learning about COVID, with disastrous results.

Breaching ethical principles, social norms, and rights

Decisions made in the name of COVID prevention have drastically undermined medical ethics, principles and human rights, once deemed foundational and paramount. Disregarding them in a crisis undermines their status as principles and rights. Acknowledgement and rectification of such breaches are necessary to prevent recurrence.

Medical ethics

Adults should protect children, not *vice versa*. The Convention of the Rights of the Child dictates special safeguards and legal protection for children on account of their physical and mental immaturity. All signatories have an obligation to uphold this. International law precludes giving experimental drugs to those without capacity to consent unless there will be a direct benefit. Proposing children receive COVID 'vaccines', despite being statistically at zero risk from the disease and while the products were still in phase three trials in order to shield adults, contravenes this stipulation.

Many faced coercion to take COVID 'vaccines' through psychological manipulation and under threat to their livelihood or mobility. Bodily autonomy, ensuring individuals have control over their body and their medical decisions, has been threatened. The Universal Declaration on Bioethics and Human Rights affirms that 'the interests and welfare of the individual should have

priority over the sole interest of science or society' (Article 3). The requirement for full informed consent before administering any medical intervention, as laid out in international law and guidance from medical regulators, was also breached.

Finally, a core medical ethical principle is to first do no harm. This principle was inverted and used to justify interventions rather than to ensure caution before doing anything at all.

Societal norms

Aside from breaches of ethical norms, the response to COVID has also violated cultural practices and societal values. Unethical policies included enforced social isolation, the denial of access to dying relatives or support for birthing mothers – a particular affront to our social nature and need for loved ones during vulnerable times. Even in 2023, many care home residents returning from hospital visits face 10-day solitary confinements without visitor rights. It is crucial to recognize these actions as fundamentally immoral. In addition, they were also unsupported by evidence.

Rights

The encroachment on fundamental rights, such as the right to work, freedom of movement, and freedom of speech, has eroded trust in institutions and threatened democracy. Democratic societies uphold free speech as a fundamental right and silencing individuals breaches not only their rights but the rights of the listener. It also acts as an important means of error correction. Dissenting voices have been silenced by a variety of means on social media, in the scientific literature and even by pre-print servers. As a result important, inconvenient truths have not been heard, exposing catastrophic errors in COVID policy.

Exaggeration of the threat

The term 'pandemic' was loosely defined by the WHO until 2009, previously implying the emergence of a novel virus against which the population had no immunity, causing widespread epidemics with substantial death and illness. However, in 2009, prior to the announcement of the swine flu pandemic, WHO removed the phrase 'enormous numbers of deaths and illness' from their website, effectively broadening the definition to include any novel virus. This shift could technically categorize seasonal influenza as a pandemic, as it mutates annually, presenting as a new variant.

The updated definition does not align with the catastrophic implications of societal disruption and extensive loss of life associated with pandemic plans

established after 2009. These plans were 'substantially higher than even the most severe winter epidemics' with mortality 'increased in younger age groups.' They assumed a substantially higher death toll, 4 to 30 times that of a seasonal influenza season, and heavily affecting younger demographics. Despite these grim expectations, pandemic plans acknowledged the limited effectiveness of attempts to control the spread of airborne respiratory viruses.

The unethical use of fear

Despite early recognition that the SARS-CoV-2 virus posed no greater risk than influenza to the large majority of the population, fear levels among the general public were ramped up to disproportionate levels.[9] The collateral damage of this fear inflation to both physical and mental health has been considerable. The deployment of behavioural science strategies (commonly referred to as 'nudges') contributed notably to the increase in fear levels of the general population. Plans to increase levels of fear appear to have been carried out without any consideration as to how to limit or turn off their effects. Objectivity can be lost when people are fearful and there seemed to be a positive feedback loop whereby those responsible for the fear generation were also affected by it, justifying their belief in the need for more fear propaganda.

Surveys from November 2020 revealed that the average person believed the mean age of death from COVID was 65. However, the actual mean age of a COVID death was 80, and the median age was 82, exceeding the average age of death in pre-COVID years. Dr Colin Foad led a UK study surveying attitudes to COVID and found, 'people judged the threat of COVID-19 via the magnitude of the policy response.' It is worth noting that the perceived risk was grossly inflated because of government messaging emphasising the COVID threat. Mortality rates by age calculated by Cambridge University's biostatistics department (see Figure 1) indicate a stark contrast with public perception.

The risk presented in the table below when extrapolated to the whole population would work out at a 1% mortality risk from COVID, which is now known to be far too high. These risks therefore represent what the claimed threat was in March 2020, and not the actual threat. The Omicron variant presented a lower death risk for both 'vaccinated' and 'unvaccinated' populations evident from its first wave in South Africa, despite having low 'vaccination' rates. The first wave of Omicron resulted in lower death rates than typical for winter in Europe and USA.

Testing

Test results exist on a spectrum, from strong to weak, but were presented

	Chance of dying if you catch COVID (add a zero to account for the fact most did not catch any one variant)	Same order of risk as	Number of sequential heads tossed in a row in a coin toss
Under 5 year olds	1 in 270,000	Dying this year from a fire	18
5 to 14 yr olds	1 in 77,000	Dying from a general anaesthetic	16
15 to 24 yr olds	1 in 29,000	A clover is three times more likely to have four leaves and an oyster to have a pearl.	15
25 to 44 yr olds	1 in 4,000	Four times less likely than the chance of finding a double yolk when you crack open an egg.	12
45 to 64 yt olds	1 in 560 to 1 in 280 (at peak deaths)	Picking two aces in a row from a pack. During peak death, it was as likely as drawing four cards in a row from a pack and them all being Kings, Queens or Jacks.	9
65 to 74 yr olds	1 in 120 to 1 in 43 (at peak deaths)	In summer, you would have been more likely to win after placing money on the horse with the worst odds in the grand national than to die if you caught covid. However, in December 2021 it was more likely but still only as likely as placing your money on zero in roulette and winning.	7
75 yr olds and over	1 in 29 to 1 in 5 (at peak deaths)	In summer the risk was of flipping a coin 5 times and it coming up heads every time. At peak deaths four in five survive.	5

Figure 1: Age dependent risks of death based on pre-omicron variants and an overall 1% mortality risk (which is now known to have been too high).

as binary. Determining the cut-off for a positive result involves a trade-off: identifying all possible cases can mistakenly include healthy persons, while focusing on definite cases risks overlooking weak genuine cases. The strategy adopted for COVID aimed to identify every possible case, resulting in

high-volume, high-speed testing with potentially significant implications on quality as PCR testing is a risky undertaking at scale. The difficulties with interpreting test results can be countered using clinical judgement based on symptoms, and on careful labelling such as in defining suspected cases differently to definite cases, or using secondary confirmation of weak positive results. This was not done.

For a test result to be positive in any meaningful sense of the word there must be a clinical implication – for example, the cause of a symptomatic patient's illness or an asymptomatic person's infectious risk. The quantity of virus detected is crucial for meaningful results. Testing protocols, however, did not reflect this. Bystander virus alone in contaminated air that we all breathe was sufficient to declare a result positive. A positive test result based on official criteria could have somewhere between 29 and 58,000 times less viral material present than the lowest level ever identified in an infectious person.

Christian Drosten and co-authors' paper sets out the protocol for the COVID PCR test. He had a prominent role in Germany as a high-profile scientist advising their government on COVID measures. Drosten himself sets out the flaws in using PCR testing for respiratory viruses when commenting in an interview on MERS testing: 'The method is so sensitive that it can detect a single genetic molecule of this virus. For example, if such a pathogen scurries across the nasal mucosa of a nurse for a day without her becoming ill or noticing anything else, then she is suddenly a MERS case.'

His description explains how evidence of the presence of tiny amounts of virus alone in test result samples should not be used as indicative of disease especially with no regard to symptoms of disease and without quantifying it to understand the risk of infectiousness.

In summary, it is clear an approach that maximises positive results has been a consistent policy. Identifying all possible positive results may be an appropriate strategy at the beginning of an epidemic but leads to overdiagnosis longer term.

Death diagnosis

Death certification is not an exact science but an art, subject to physicians' judgement based on available evidence. The process is intended to offer closure for relatives and data for public health research, not to chart the course of an epidemic. Thus, the same death can receive different classifications depending on the certifying physician's perspective.

Policy seemed to maximise COVID death numbers. One study found the presence or absence of symptoms to be insufficient in accurately determining

COVID as the cause of death. Yet, the WHO suggested a plausibility check on those certificates where COVID was reported but not selected as the underlying cause, potentially inflating COVID death numbers. Audits worldwide have illustrated overdiagnosis of COVID death. In California, two counties saw a reduction in COVID deaths after reviews of between 22 and 25%. In Massachusetts, using a federal definition of COVID death led to reclassification of a third of previous COVID deaths. Similarly, in Sweden, only one in six deaths were definitively due to COVID. The USA witnessed an algorithmic error that removed over 77,000 deaths from the COVID tally, reducing child COVID deaths by 24%, after those numbers were used to promote child 'vaccination'. Consequently, COVID death data are not as reliable as might be assumed.

It is important to recognise that a positive test for the presence of virus is more likely in those dying of other causes. Nearly half the deceased in a Spanish study tested positive for a respiratory virus post-mortem, despite only 7% receiving a viral infection diagnosis before death. The presence of a positive test result was enough to result in a death being registered by government as a COVID death. Any doctor who then came to certify that death would have to find evidence that COVID was not a contributory cause to confidently assert that the government had wrongly labelled the death.

Furthermore, a large proportion of COVID deaths occurred in people already close to death. Any assessment of years of life lost and the overall outcome needs to account for this. Neil Ferguson said of the proportion who died from COVID many would have died soon anyway: '(It) might be as much as half or two thirds of the deaths we see, because these are people at the end of their lives or [who] have underlying conditions.' Indeed, the NHS noted that 95% of COVID-related deaths occurred in people with pre-existing conditions. Age was a major determinant in COVID mortality, with most deaths occurring among the elderly. Furthermore, a substantial portion of COVID deaths occurred from infections in hospitals and care homes. Including these deaths in risk calculations for the healthy elderly community can be misleading. For instance, a sample of 30,000 patients who contracted COVID following a lengthy hospital stay before spring 2021 saw a mortality rate exceeding one in four.

The failures of non-pharmaceutical interventions

Lockdowns and masking were both mandated as interventions to slow the spread of the virus. Both failed because the belief that they would work was founded on false assumptions. In the case of lockdown, the false assumptions were that transmission occurred only with close contact, that asymptomatic transmission was a significant driver of spread, and that everyone was

susceptible. With regard to masking, the belief was that stopping droplets would hamper transmission. The reasons why those beliefs were unfounded are set out here.

Close contact transmission

Talking, laughing and breathing result in the emission of droplets and aerosols. Droplets are the larger parts of mouth and nose spray that fall directly to the ground. Smaller parts of the spray remain suspended in the air and are called aerosols. It was broadly assumed that COVID transmission occurred through close contact via droplets. However, this assumption is rooted in myth, not evidence. Because droplets fall to the ground, following the course of a ballistic trajectory, it is almost impossible for them to make contact with the small exposed mucosal surfaces of the eyes, nose and mouth, even at close distances. One analysis of the literature on close contact transmission in March 2020 concluded it could '….find no direct evidence for large droplets as the route of transmission of any disease.'

Actual evidence demonstrates there was aerosol transmission including over long distances. While close contact spread does occur (largely via aerosols), it is not the exclusive method. Belief in close contact droplet transmission originated in 1910 from a US public health doctor with a phobia of germs, Dr Charles Chapin, who adamantly opposed the idea of airborne transmission (excluding in tuberculosis).

With COVID, tracing transmission chains was often impossible, suggesting potential long-distance transmission. It is agreed that spread through close contact would be slow (reaching a peak after 14 weeks),' yet COVID and influenza spread rapidly throughout the country within a few weeks, implying airborne transmission was the driver. Aerosol physicists who suggested SARS-CoV-2 could spread in aerosols were censored. Professor of Primary Care at Oxford University Trish Greenhalgh said aerosol scientists were 'systematically excluded from key decision-making networks and committees.'

Evidence for aerosol transmission of viruses is well-established and is also available for SARS-CoV-2. While aerosols have not been definitively proved to carry SARS-CoV-2 in the outside air, neither has this been ruled out. One study, across four laboratories, demonstrated that intact whole virus capable of causing infection in cells remained at similar levels for the duration of a 16-hour experiment in aerosols in the air. A different type of coronavirus, causing infection in pigs at a farm, was shown to spread through the air over 10 miles away and still be capable of causing infection. In cattle, foot and mouth disease was shown to spread 190 miles over the sea and 37 miles over land from France to the Isle of Wight in 1981. Sand from the Saharan desert, which is certainly larger and heavier than the aerosols, nevertheless can be blown from Africa, turning the

UK sky red and covering cars in a film of dust. In 2018, biologists sampled air one to two miles above sea level in the mountains of Spain. They demonstrated that billions of viruses (and bacteria) could be collected each day. Separately, viruses collected from the air above the sea, travelling miles in the wind, have been shown still to be capable of causing infections.

Further evidence of long-distance spread includes a Cambridge University study which demonstrated that the full range of genetic variation of the virus seen in the general community was present in the viruses sampled from the care home population. Also, when the Delta wave arrived in Australia the index source was believed to be a man who had returned from Sri Lanka and was kept in isolation. Despite his being in isolation there were 44 genetically-related cases that emerged in the community over the course of two weeks.

Infected people produce thousands of particles per breath, each potentially harbouring single-digit numbers of the virus. For other viruses a single virus has been shown to be enough to cause infection and other studies have shown only single digit numbers which could be found in a single aerosol. The actual dose required will be dependent on the level of immune protection of the person being infected. According to the UK government, *sampling of environments where people have influenza or Monkeypox show far more viral RNA than for SARS-CoV-2, yet the outbreak data indicate that both are much less transmissible. This suggests that a lower viral dose is needed to initiate a SARS-CoV-2 infection than for these other diseases.*

The prevalent belief that expelled droplets rapidly fall to the ground within a short distance is a myth, as nearly all matter invisible to the human eye rapidly evaporates and can remain airborne almost indefinitely, under the influence of air currents. Aerosol transmission could explain certain enigmatic COVID outbreaks including an outbreak in December 2021 on the Belgian Antarctic base despite extensive isolation prior to arrival; an outbreak of a thousand cases diagnosed within two days of each other in a garment factory in Sri Lanka, without an identified super-spreader, at a time when there was minimal community COVID, and an outbreak on an Argentinian fishing vessel after a full five weeks at sea, despite everyone testing negative before setting sail. Instead of acknowledging that this was due to long distance transmission, asymptomatic spread was blamed. However, there is negligible evidence to support this (see below).

As 2020 progressed, evidence for aerosol transmission mounted. Outbreaks occurred in restaurants, fitness classes and in a room after the index case had left. Large outbreaks occurred in hospitals despite precautions against droplet transmission. People in quarantine hotels caught a virus with the same genetic fingerprint as people down the corridor whom they had never met. Animal

studies demonstrated that sharing air through ducts between the cages was sufficient to spread infection. One paper presenting such evidence was described as misinformation by the WHO. Despite these findings, it took until December 2021 for the WHO to include 'airborne' in their guidance. Aerosol spread means the virus was virtually omnipresent, making exposure virtually inevitable by the end of each wave.

Because spread occurred at long distances through the air, a person who was sick (and therefore producing plentiful virus) could be an infectious source to others even if they were isolated indoors. There was evidence from 2004 that the original SARS spread in the air currents between apartment blocks. Lockdown could only ever reduce close contact spread, and not long-distance aerosol spread. If close contact spread had been the driver of each wave, lockdowns could have slowed the spread. A group at Johns Hopkins University carried out a meta-analysis of all papers reporting on the effect of lockdown. They concluded that the benefits of lockdown were 'little to none' and that 'lockdowns should be rejected out of hand as a pandemic policy instrument.'

Asymptomatic transmission

With sick people already being isolated, lockdown policy would only reduce contacts between asymptomatic people. The idea that asymptomatic spread occurs also originated with Dr Charles Chapin in 1910. It allowed him to neatly explain why his close contact spread hypothesis could not explain many instances of infections where there was no contact with a source. He used this idea to explain 'the rapidity with which epidemic influenza spreads, its sudden contemporaneous appearance at many distant points, and the difficulty of tracing the route of infection.' The evidence he quoted to support this conjecture was based on the culture of a bacterium which is now known not to be the cause of influenza. From the 1980s, PCR testing became increasingly available and enabled the detection of insignificant quantities of microorganism in the airway which rejuvenated the hypothesis of asymptomatic spread in the absence of evidence of actual spread.

In February 2020, Chinese scientists first classified 'asymptomatic' COVID cases as patients not sick enough to have had investigations that can only be carried out in hospital. However, the WHO's Dr Maria Van Kerkhove noted in March 2020, *Most of the people who were thought to be asymptomatic aren't truly asymptomatic. When we went back and interviewed them, most of them said, actually I didn't feel well but I didn't think it was an important thing to mention. I had a low-grade temperature, or aches, but I didn't think that counted.* There is evidence to support pre-symptomatic transmission as opposed to never symptomatic. One estimate put their contribution to the trajectory of

an outbreak at 6.4% of total spread.

The idea that large numbers of perfectly healthy people could spread disease was based only on the fact that perfectly healthy people can test positive and the fact that people can become infected with no evidence of contact with a known source. The huge variation in the proportion of asymptomatic 'cases', ranging from 4% to 76%, is largely due to erroneous test results and testing volume rather than its being a feature of the disease like a cough, which would have a constant percentage.

Most positive cases in various studies eventually developed symptoms.[9] Antibody testing also indicated that the number of people developing antibodies matched the number of symptomatic positives, suggesting that asymptomatic positives resulted from oversensitive testing.

By the end of 2020, concrete evidence of spread from never-symptomatic people was limited to a handful of instances of only minimal symptoms. Later studies did not conclusively demonstrate transmission from the asymptomatic, despite extensive genetic testing.[10] Thus, despite what the public have been told, the evidence that people who never develop symptoms have spread disease is practically non-existent.

Who was susceptible?

The COVID models were based on unjustified assumptions and were

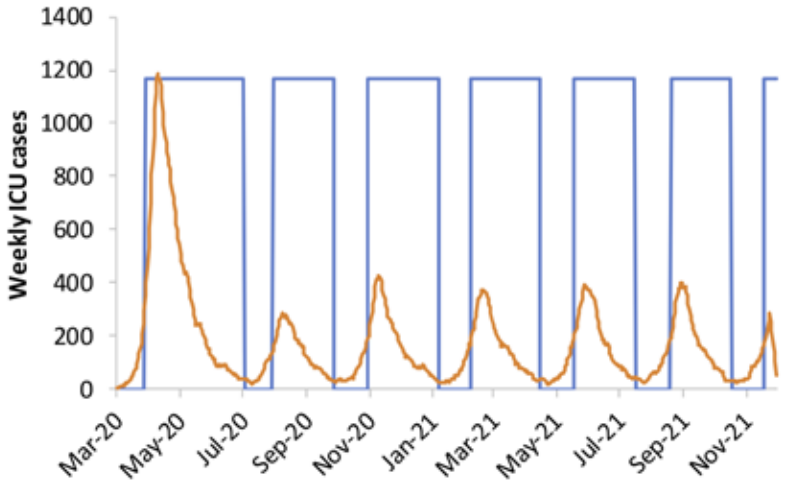


Figure 2: Imperial model assumption was that every release of restrictions would lead to a rebound and short release periods would need to be followed by repeated restrictions calibrated to intensive care bed occupancy.

presented as being far more accurate than they were. One core assumption was that everyone was susceptible. Without intervention there would be an unstoppable tsunami of infection that would spread through the whole population. This did not occur in any country with any wave.

An early COVID outbreak occurred on the Diamond Princess cruise ship in February 2020, where 7.7% of the mostly elderly passengers and crew had a symptomatic infection. Only 8-15% of contacts of both pre-Omicron and Omicron variant cases were susceptible to the virus, as seen in household transmission rates. The percentage of household contacts who were infected was slightly higher at the beginning of a wave and decreased at the end, leading to claims of markedly increased transmissibility of each new variant.

In exceptional distinct superspreader outbreaks, a higher proportion would be susceptible because of the large doses of virus involved – for instance, half the sailors on the *Charles de Gaulle* ship. Occasional superspreaders can emit extraordinary amounts of virus. For example, 90% of virus emission in one study of 37 infected people came from just two people.

Every COVID wave globally has peaked independent of any changes in human behaviour. The cause of such epidemic rises, as seen with influenza, is thought to be due to conditions ripe for a surge, similar to tomato blight, termed the 'seasonal trigger' by Dr Edgar Hope-Simpson in 1981. The specific factors explaining this trigger are still unknown and likely numerous. Such triggers can happen up to four times a year (see figure 3). He did point out, however, that even in experiments where temperature and humidity were controlled for, it was still easier to infect animals with influenza in the winter.

In Spring 2020, there were large geographical regions, including Southeast Asia, Oceania, Eastern Europe, and the central USA, where no seasonal trigger occurred. There was no country or region within these large geographical areas that acted as an exception to the rule. The reasons are unclear but could involve existing levels of immunity as well as some unknown environmental factors. All these areas have since experienced COVID waves, also with no exception. Even attempts at very harsh lockdowns in China, risking starving people and killing pets, did not prevent the Omicron surge.

Masking

The recommendation for mask-wearing was primarily predicated on the belief that COVID spread via droplets at close range, which would hypothetically be reduced with a cover. However, this would not substantially affect aerosol transmission.

The existing body of evidence, including randomised controlled trials, and

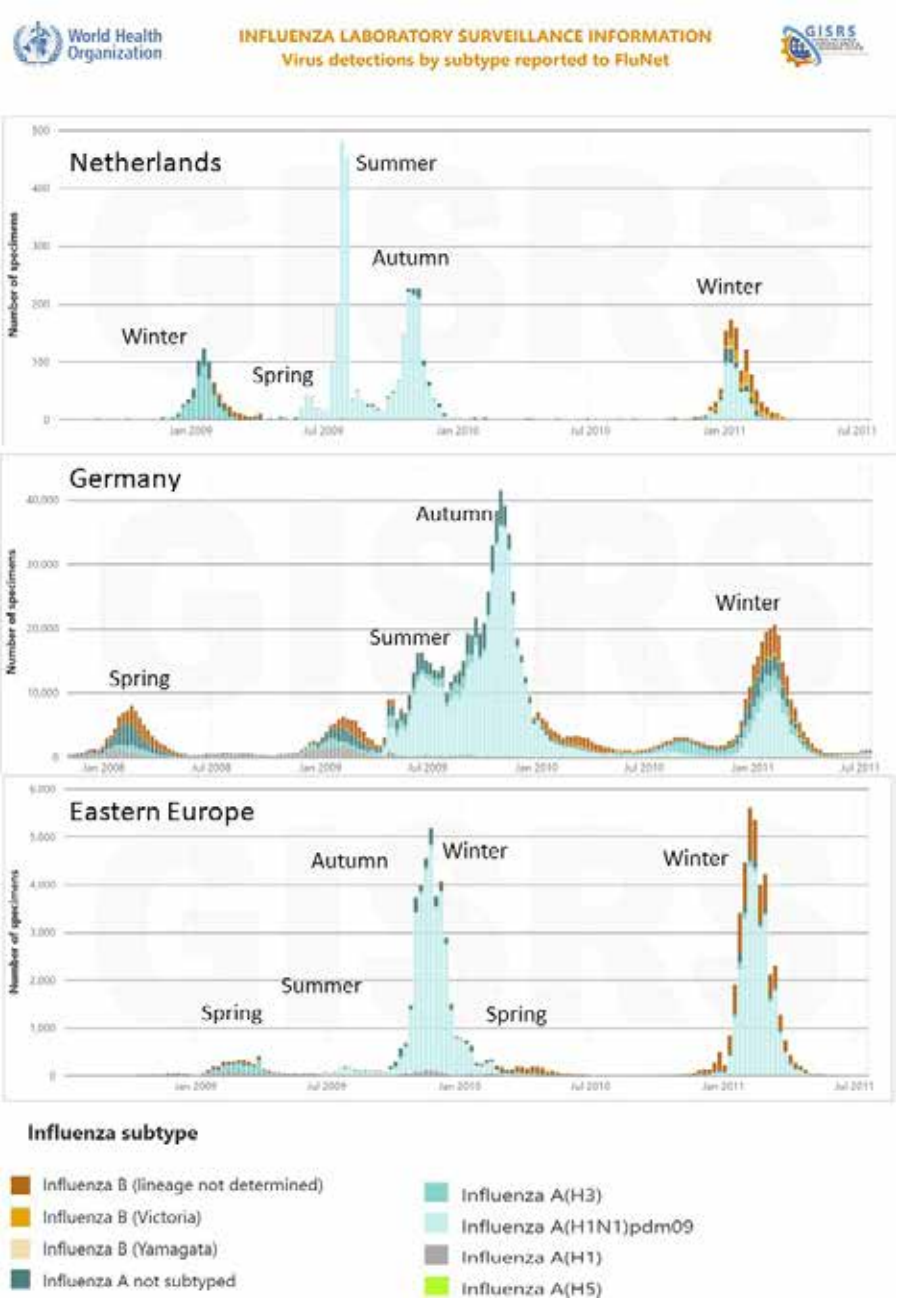


Figure 3: Increased testing in 2009 and 2010 revealed up to one wave in each season in Netherlands and Germany and Eastern Europe.

comprehensive evidence reviews,, suggests that community-wide mask use does not substantially reduce respiratory virus spread. Even surgical masks do not prevent infectious contamination.[7]

Prior to mid-2020, public health authorities largely agreed that community mask usage was unnecessary, with some warning of increased risk.[7] A global shift from recommending against masking to mandating it was not driven by any new evidence and came without an accompanying assessment of its effects. This happened despite the World Health Organisation's document in December 2020 stating limited and inconsistent evidence for mask efficacy in the community.

Studies promoting mask effectiveness have often used biased modelling or selective observational research. Even mask mandates in hospitals did not significantly alter COVID transmission rates. A recent Cochrane review echoed previous findings, stating community mask usage 'probably makes little or no difference to the outcome of laboratory-confirmed influenza SARS-CoV-2 compared to not wearing masks.'

The use of face masks, especially in community settings, is linked to a variety of physical, social, and psychological harms. Recent studies suggest long-term clinical consequences of masking, particularly for vulnerable groups.

Overall, mask use can impede the human connection, which is vital to the healing process, particularly those confused, frightened, or suicidal. Although guidelines on mask-wearing exemptions exist, discrimination has occurred, making it hard for those vulnerable to mask harms to be able to avoid them.

Specific adverse effects of masks in healthcare settings include impaired communication, as they muffle speech and hide non-verbal cues, particularly affecting the hearing-impaired and elderly, resulting in sub-optimal care to patients. Additionally, masks can increase fall risk in the elderly by obstructing the lower peripheral visual field and fogging glasses.

Masks increase the work of breathing and can be associated with an increase in pulse and respiratory rate, with raised CO_2 levels and headaches. They can also raise the risk of acquiring respiratory diseases, potentially increasing susceptibility to bacterial infection after as little as four hours of wearing a mask. Moreover, the risks from inhaling micro-plastics and exposure to textile contaminants are yet to be fully understood.[7]

Masks may also re-traumatise those with a history of abuse as a result of the sensation of material covering the face and mouth; also, the sight of

masked people can trigger disturbing memories. Furthermore, masks can intensify emotional difficulties for people with mental health issues such as panic disorders, autism, obsessive-compulsive disorder, and severe health anxieties.

But more than any of that they have upset child development. Children learn how to interact by watching faces and responding to them, yet masks were mandatory in some nursery settings where staff cared for babies. A team of scientists at Brown University showed that children who were at least 15 months old by March 2020 had normal development. However, children who were born after them had significantly lower verbal, non-verbal, and overall cognitive scores, suggesting a policy effect on child development.

In the words of Dr Tom Jefferson (the lead author of the Cochrane Review): 'We failed to follow an evidence-based approach during the pandemic. We are now left with the human, social and economic aftermath of evidence-free policies.'

The failures of pharmaceutical and hospital interventions

When a patient is sick and especially when in danger of dying the threshold for taking a risk on a treatment should be low. However, when giving a healthy population a vaccine that threshold must be much higher. This principle was inverted with potentially helpful medicines banned under the guise of poorly-evidenced safety concerns, while at the same time safety concerns about the 'vaccines' were ignored even as they were injected into ever-younger arms. For example, an over 80-year-old had a mortality rate of 5%, and for someone with severe disease it would be higher; add in co-morbidities and the risk could be doubled. In such circumstances, there should be no hesitation in prescribing a drug with an established safety record that might reduce mortality.

There are three ways in which pharmaceutical interventions failed. First, protocol-driven medicine led to changes to normal prescribing practice, and these were harmful. Secondly, there was a failure to provide early treatments to the vulnerable and finally there were the failures of the 'vaccine' program.

Changes to the practice of medicine

It is imperative that doctors have the freedom to do what they believe is best for the patient in front of them. Medicine has for several decades been increasingly controlled through creating protocol-driven guidelines which restrict what doctors can offer to patients. Although doctors have the ability to deviate from guidelines, they must be able to provide evidence to defend their decision to do so and it is far easier for them to simply follow the

guidelines. The guidelines often do not have named authors and are not open to debate or discussion. The consequence is medicine being practised by nameless bureaucrats, or politicians including those with no medical qualifications, who have had no contact with the individual patient.

Trust in medicine requires that people know doctors have at heart the best interests of the individual patient in front of them and are free to make those decisions using their professional and ethical judgement and without entertaining thoughts of the so-called 'greater good.'

Antibiotics

New healthcare protocols in Spring 2020 resulted in important alterations to the standard treatment approach for pneumonia. Previously, antibiotics were administered to patients presenting with pneumonia regardless of the exact cause. These could combat possible secondary or incipient bacterial infections and may have direct anti-inflammatory effects, too.[7] COVID protocols resulted in patients being told to self-care unless they needed urgent hospital admission and a positive test often precluded the use of antibiotics, except in vulnerable individuals. Effectively, standard treatment was withdrawn.

Ventilators

A belief had been established that having the patient breathe through an enclosed system was keeping the staff safe by reducing aerosols. In early June 2020, a WHO report said that of those COVID patients treated in critical care, 88% were placed on mechanical ventilation. Ventilator use was a key part of the initial response to severe COVID cases, despite subsequent data revealing an alarmingly high death rate of 80% among ventilated patients, double that of other conditions causing respiratory distress. This led some physicians to ask whether the aggressive use of ventilators was causing more harm than good,[7] prompting a move towards alternative strategies such as patient positioning and high-flow oxygen therapy. It is unclear how many lives were lost from overly aggressive use of ventilators early on.

Morphine and Midazolam

The use of end-of-life medications, such as morphine and midazolam, has also drawn attention and criticism. Both these drugs reduce the respiratory drive. During an acute respiratory infection, that respiratory drive can be lifesaving, even if it is distressing to the patient and those around. These drugs do not reduce the time to death in palliative care situations, but their effects in acute respiratory tract infections have not been looked at separately. Protocols recommended giving these drugs to those with moderate to severe breathlessness, regardless of concerns about respiratory depression. It is

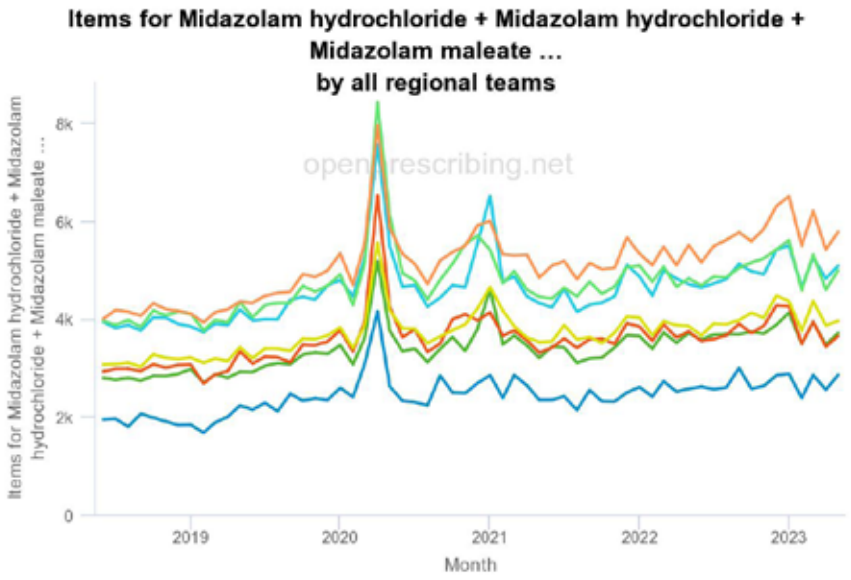


Figure 4: Prescriptions given for Midazolam by region. The blue line at the bottom is London.

speculated that fear-induced messaging during the pandemic, giving a false impression of the chance of survival in the elderly, might have led to a low threshold for placing patients on end-of-life care, potentially hastening their demise.

The counter argument is that these drugs were prescribed at higher levels because of increasing demand for end-of-life care, because of COVID. However, a notable increase in midazolam prescriptions was observed during the first COVID wave in London, but not during the second, despite a larger wave. The reason for this disparity is unclear and calls for a closer examination of drug prescription practices.

Finally, the potential misuse of midazolam and the outcome on patients who might have had reversible causes of deterioration warrant urgent investigation. Given the discrepancies in prescription practices and the serious accusations from multiple relatives and whistleblowers, there is a need to rationally ascertain the facts and see if lessons need to be learnt.

Treatment for COVID

Medical treatments for COVID had to strike a balance between the potential benefits and known or potential risks. However, the approach was skewed, disregarding the body of knowledge on treating acute respiratory tract infections and similar coronavirus infections, like SARS1. Instead of adapting

standard viral pneumonia treatments, protocols were put in place excluding usual therapies and demanding proof of benefits in randomised clinical trials. While this standard ensures safety and efficacy, it disregards the urgency of emergencies, leading to a delayed response to emerging evidence.

COVID involves an initial viraemic phase and a later inflammatory phase, necessitating different treatment strategies at each stage. However, the official response fixated on finding a magic bullet to cure all stages of the illness. This approach overlooked the complexity of the disease and the demonstrated efficacy of multi-drug therapies, including antivirals and vitamins.[7] With a disproportionate emphasis on treating advanced, hospitalised cases, the importance of early intervention was underestimated, causing the adopted strategy to fall short of its aims. The later acceptance of corticosteroids for treating the inflammatory stage marked a shift in understanding but underscored the shortcomings of an oversimplified approach.

Hydroxychloroquine

Hydroxychloroquine is a well-established safe drug used as an antimalarial and to treat autoimmune conditions. It was proposed for early-stage treatment of COVID, particularly in combination with azithromycin and zinc. However, its use became heavily politicised, and despite many empirical reports of its success, the drug's utility was denied in many Western countries. A notable controversy involved a *Lancet* paper claiming that hydroxychloroquine increased mortality, which was later retracted for data fabrication. Yet, the policy shifts it triggered were not reversed. The trial often cited as evidence that 'hydroxychloroquine doesn't work' was actually flawed, administering highly toxic doses that no successful practitioners were advocating, initiating treatment well beyond the viraemic stage, and disregarding previous empirical reports of effective combinations.[11]

Remdesivir

Remdesivir, an antiviral drug, also garnered attention. Most countries added it to national guidance for hospital treatment, starting with the USA on the same day that trial results were published showing no effect on hospitalisations or deaths and despite antiviral drugs having limited ability to alter the inflammatory stage of the disease.[7] Furthermore, a WHO study concluded that remdesivir had little to no effect on 28-day mortality or hospital-stay duration, raising questions about its efficacy. One paper showed a benefit by changing the outcome to length of stay, ignoring readmission rate and ignoring biases with older, sicker and more ventilated patients in the placebo group. The *BMJ* commented that 'the early adoption of remdesivir was a triumph of hope, and probably marketing, over data.' Medical regulators reported serious side

effects. In rats and monkeys given remdesivir 'severe renal toxicity occurred after short treatment durations,' according to the Australian regulator. Because of this concern and the evidence from animal studies the EU proposed several safety trials. A total of only163 patients were given Remdesivir in this safety evaluation before it was terminated because of lack of enrolment.

Ivermectin

Ivermectin has been safely used, even in pregnant women, for the prevention and treatment of various parasitic diseases. Its potential for use in COVID was discovered because of its known anti-viral properties and proved effectiveness against SARS-CoV-2 *in vitro*. Advocates emphasised its efficacy in all stages of COVID, especially when used in combination therapies.[1] Studies that swung these reviews against Ivermectin had authors who all had conflicts of interests, did not give the drug until very late in the illness, underdosed, and one trial even changed the point at which outcomes were measured from 14 days to 28 days after symptom onset, at which point people were all either dead or well, regardless of which treatment they had had. However, despite robust empirical evidence and meta-analyses, the WHO and other health institutions have resisted accepting Ivermectin as a viable treatment. The WHO's own meta-analysis reported a 75% reduction in mortality risk and yet they failed to recommend the use of a very safe drug that has been on the WHO Essential Medicines list for decades. Its proved prophylactic efficacy could potentially challenge the 'vaccine' market and policy.

Paxlovid

Paxlovid, a Pfizer treatment, was approved in December 2021 for use in high-risk groups. Pfizer claimed rebound symptoms occurred at the same rate as in placebo. However, a fifth of treated people experienced rebound symptoms in the real world. The proposed solution was to study Paxlovid itself for effectiveness in treating rebound infections, rather than declaring it a failed drug that gives a high risk of an extended illness.

Vitamin D

Vitamin D, known to improve immunity and suppress inflammatory cytokine response, has been associated with a reduced risk of acute respiratory infection. This is important for COVID, as low vitamin D levels predispose people to an increased risk of respiratory infections and pneumonia. Numerous studies indicate a correlation between low vitamin D levels and more severe COVID symptoms, increased hospital stays, and higher rates of death. In order to fairly test whether Vitamin D treatment has a benefit it is imperative that a sufficient dose is given early in the course of the illness when an enhanced immune

response has an opportunity to protect against viral attack. Despite some claims attributing these observations to coincidental correlations, it is essential to administer high-dose vitamin D early in the course of the illness. High-dose oral vitamin D has been associated with significantly lower mortality rates. The consensus among many experts is that for optimal immunity and severe COVID prevention, a vitamin D level of 100-150 nmol/l is necessary.

Treatment strategies for COVID, consequently, were often contentious. Many argue that maintaining previous treatment protocols with or without more efficient and earlier administration of multi-drug therapies in the vulnerable could have potentially reduced hospitalisations and deaths, suggesting that the rigidity of health protocols may have hindered a more effective response to the pandemic.

The effect of 'vaccines'

Overview of the evidence prior to rollout

It is worth remembering how cautious people were about any novel products that might claim to prevent COVID. In February 2020, England's Chief Medical Officer said: *The rate limiting steps are late clinical trials for safety and efficacy, and then manufacturing. For a disease with a low (for the sake of argument 1%) mortality a vaccine has to be very safe so the safety studies can't be shortcut. So important for the long run.* He was right.

Globally, medical regulators decided that these novel products should be classified as vaccines. This was a critical decision for three reasons. First, the word vaccine is heavily loaded. The public perception of a vaccine is that it will stop infection and will be entirely safe. Secondly, anyone who might have a concern will be smeared as an anti-vaxxer which is a heavily emotionally-laden term that causes people to close their ears to the arguments. Thirdly, despite the reputation for complete safety, the regulatory pathway for a product described as a vaccine is not as demanding. The belief that vaccines were safe had led to a circular belief that vaccines required fewer safety checks than other novel therapies.

All medicines cause side effects and so there is a balance to be struck between risk and benefit. It is imperative that the cure is not worse than the disease but for COVID 'vaccines' the risks have been played down and the benefits have been exaggerated. The benefits are also highly age-dependent because of the big difference in risk from COVID to older people. No account has been made of this in the decisions taken around 'vaccination'.

Regulatory failure

The belief that vaccines were safe had led to a circular belief that vaccines required fewer safety checks than other novel therapies. Novel vaccines take a

decade or more to go through safety checks. Influenza vaccines do not because a well-established technique using eggs to grow influenza virus was used. These novel drugs were treated like influenza vaccines for regulatory purposes despite their being a totally novel delivery platform. Drug withdrawals are not unusual, but it can take a decade or more on average before harmful drugs are withdrawn from the market by regulators.

Regulators permitted pharmaceutical companies to bypass essential tests for gene and cancer toxicity, and even studies showing the production and longevity of spike protein in the body. Pfizer said these studies were 'not considered necessary.' This was in some contrast to what their trial information sheet said: *Due to the urgent need for a vaccine against Covid-19, with agreement from the MHRA, some of the tests usually required for a newly manufactured vaccine have been modified, in order to make the vaccine available more quickly for assessment.* Post-emergency approvals, these tests were not demanded either. No human studies were conducted to investigate the fate of synthetic modified RNA, leaving continuing uncertainties about its degradation timeline in the body. Regulators also allowed termination of the placebo arm of the study after about three months, although it was known from the Pandemrix vaccine experience that diagnosis of harmful effects such as narcolepsy could take an average of eight months.

Additionally, the lipid nanoparticles used for delivery of modified synthetic mRNA are known to have toxicity. This mechanism of delivery was shelved in 2016 for gene therapy to treat inherited genetic conditions because of the multiple doses needed. The viral vector used for delivering the AstraZeneca DNA message had been reported in 2007 to cause platelet activation, which can lead to blood clots. Nevertheless, regulatory bodies failed to act on these critical issues. The regulators also did not ensure timely investigations into deaths, patient complaints, or proper manufacturing processes.

'Vaccine' Design Choices

In the 'vaccine' design, manufacturers chose to use the entire Wuhan spike sequence rather than its parts, or peptides, known to be safer for vaccine design. This choice was problematic as the spike protein is the most toxic part of the virus, causing damage to lungs and vessel walls, and promoting clot formation. Part of the sequence also closely resembles a bacterial sequence that can bind directly to a certain type of white blood cells, triggering lethal cytokine storms. This part of the sequence was heavily mutated in the Omicron variant, making it less lethal. However, even the most recent injections contained the original Chinese spike sequence with this dangerous sequence.

AstraZeneca did not modify the sequence. From November 2020 it was clear

that parts of AZ spike could be shed outside of cells.[7] Some manufacturers modified the spike so that it could not bind to the receptor and enter a cell. This might have reduced some harm from receptor binding but not from the action of spike within cells. The spike was delivered into cells, so spike was produced *inside* the cells in the first place.

The Pfizer and Moderna clinical trial data reveal a higher rate of serious adverse reactions from the treatment group compared to any reduction in serious events from COVID. Overall 1 in 800 'vaccine' recipients had a serious adverse event following vaccination in the trials. However, the claim of over 90% efficacy was highlighted, shaping the decisions on approvals, despite a very large number of injections needed to prevent a single COVID death (see below).

Unjustified broadening of 'vaccine' approval

Initially, the focus was on protecting the old and vulnerable, who accounted for 98% of COVID deaths. Despite this, regulators went on to approve these novel products for younger and younger patients and even pregnant women. Approvals for children were granted on the basis of raised antibodies, without supporting evidence of the effect on COVID itself and despite there being no antibody level which ensures protection from COVID. The government wording says the product aims 'to generate neutralising antibodies, which *may* contribute to protection against COVID-19' (emphasis added). This is not based on any scientific evidence, merely hope. Such regulatory failure in allowing the 'vaccines'

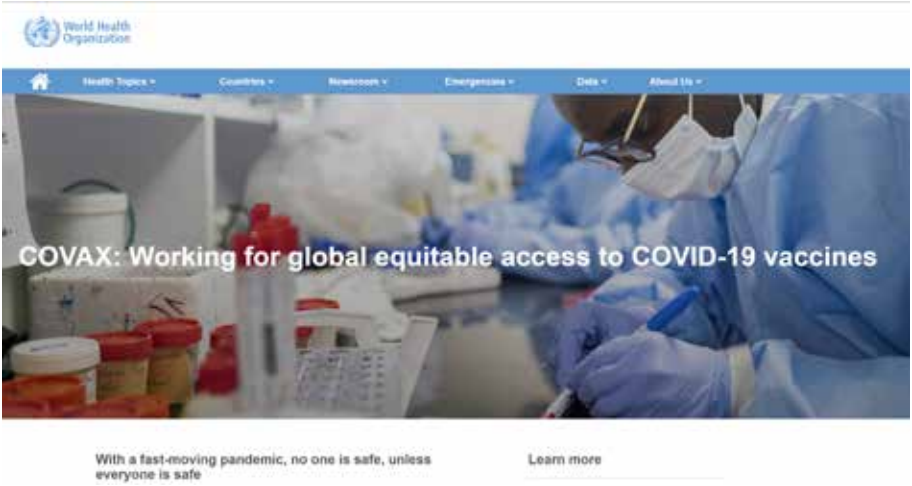


Figure 5: WHO campaign from August 2020: 'no-one is safe, unless everyone is safe.'

to be given to anyone, and not promptly withdrawing them once evidence of clinically relevant issues emerged, constitutes a major failing.

Overview of evidence post rollout

After rollout it was possible, with difficulty, to measure the true extent of adverse reactions from the 'vaccines'. It became evident that there were potential risks associated with different batches and there was a detrimental effect of the rollout on hospital resources and the workforce. However, the WHO started a campaign in August 2020, pushing the mantra that 'no-one is safe until everyone is safe.'

This idea penetrated the consciousness of key decision-makers and the injections started to be aimed at healthy and ever younger arms. The decision to do this came long after it was clear these products were not safe.

The adverse reaction alarm system started to blare red from the beginning of the rollout. It was claimed this was due to increased awareness of the system. Over the same time period, reports for other drugs did not rise. The US VAERS reporting system has been forced to release its data which show signals of harm for 770 conditions. Two thirds of these showed a stronger safety signal than for myocarditis and pericarditis, which were acknowledged as a genuine adverse event in mid-2021. Because the mechanism of harm is likely to be a combination of effects on the immune and clotting systems, manifesting in autoimmune attack and small vessel damage, it is not surprising that almost every organ system can be affected. Small vessel damage was not rare with a tripling in the first three months in the risk of occlusion of the small vessels of the eye, where such damage is easily measured.

'Vaccine' harm icebergs

It is a general rule of thumb that the first indications of a drug safety problem will underestimate the size of the problem. This is due to poor measuring of the extent of illness. The opposite is true for infectious disease epidemics. The early indicators will always overestimate the risk of death per infection because of underestimating how many were infected in the first place.

Side effects from COVID 'vaccines' can be visualized as icebergs, with only the tip visible above water, and an unknown amount hidden beneath the surface. Within the first year of the 'vaccine' rollout, the tips of three such 'icebergs' have been recognized – the risks of myocarditis, the risk of unusual brain clots and the risk of Guillain-Barré syndrome. However, the full extent of the harm hidden below the surface is yet to be measured.

The situation is even more challenging with the rise in a condition that is already common, such as strokes or heart attacks. The additional diagnoses can be lost

in the background noise. To identify such a problem, one needs to focus on younger age groups where the underlying risk is much lower. Such work has barely begun.

Heart disease

There were claims that the myocarditis issue was limited to mRNA 'vaccines' and to young men but neither of these claims has been sustainable over time.[1] Attempts to measure the extent of heart damage in working aged people showed 3% had evidence of dying heart cells after a dose, while in young males up to 29% had cardiac symptoms. Heart cells which have died are replaced with scar tissue. The heart requires smooth electrical conduction and even a tiny amount of scarring will increase the risk of a potentially fatal cardiac rhythm disorder. It has also been hypothesised that the underlying pathology may not be inflammation but abnormal protein deposition causing a condition called amyloidosis.

Added to this issue there is the evidence of the notable rise in cardiac arrests that followed the 'vaccine' rollout. A proportion of these could have been due to such scarring and electrical conduction problems. However, there remains a question about whether there is also inflammation caused by 'vaccination' which increases the risk of cardiac vessel narrowing (atherosclerosis) that leads to the most common cause of a heart attack, a myocardial infarction. 'Vaccinated' people had a rise in cardiovascular risk factors that would predict a significantly increased risk of heart disease (from 11% to 25% risk of a heart

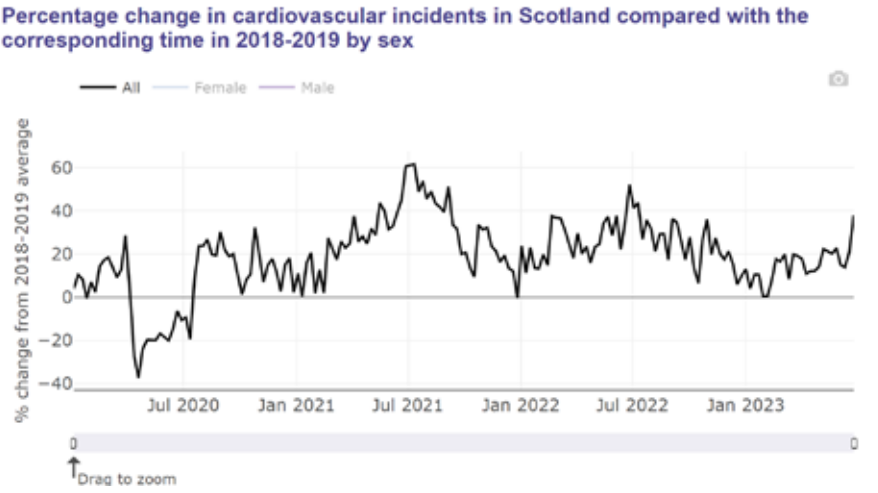


Figure 6: Public Health Scotland Data showing ambulance calls for cardiovascular issues.

attack in five years). An Israeli paper showed a 25% increase in acute coronary syndrome and cardiac arrest calls in 16-39 year olds in Israel associated with the first and second doses of 'vaccine' but not with COVID infection. The Scottish data also show a clear rise in cardiac problems in the young.

There has been a notable rise in deaths since the 'vaccine' rollout. These deaths have predominantly been attributed to cardiac causes, particularly ischaemic heart disease and heart failure (see below). One post mortem demonstrated death due to continuing 'vaccine' injury in the vessels of the heart a full four months after the last dose.

Blood

The first admission of any 'vaccine' injury was the occurrence of potentially fatal rare brain clots. These were caused by 'vaccine'-induced antibodies against platelet factor 4 which results in the activation of clotting. The brain clots were attributed to AstraZeneca which is based on DNA rather than synthetic mRNA.

Subsequently, many clinicians raised concerns about what they were seeing in their practice. In particular, post operative clotting disorders, odd clotting conditions like portal vein thrombosis and clotting of the artery of the gut, both of which are normally incredibly rare, seemed to become more common after 'vaccine' rollout, including in those given mRNA products. Because these are so rare it should be possible to measure any increase but such studies have not yet been published.

Regulators have since acknowledged a risk of abnormal menstruation. An FDA paper showed an increased risk of pulmonary embolism but this finding was denied because of how the data were analysed. Other conditions show a markedly low incidence immediately after 'vaccination' because 'the healthy vaccinee effect' means that people self-select when to be 'vaccinated' such that new diagnoses are rare afterwards. That means the baseline for comparison should be the lower rate seen for other conditions after 'vaccination', not the overall higher rates seen in the whole population. However, the regulators invariably choose a higher threshold and then claim there is no signal present.

Neurological and autoimmune

The third iceberg is the least well defined. Although the government recognised 'vaccination' caused Guillain Barré syndrome in 2021, they continued to advise that those affected should receive further doses.

Many patients complained of new conditions. These included tremors, postural orthostatic tachycardia syndrome, (POTS, a disabling condition

where standing or sitting up leads to a racing heartbeat as blood flow to the heart and brain fails to be maintained), and various autoimmune conditions.

The medical establishment dismissed all these issues as coincidental. People do develop new onset symptoms and conditions randomly and the assumption was that the attribution of these problems to the 'vaccine' was just a case of unfortunate timing and ignorant attribution on the part of those suffering.

However, an important study spanning six neurological departments in the USA demonstrated that these patients have an underlying mechanisms for their neurological symptoms. The study only described the presentation of 23 patients, 92% female, all of whom developed symptoms within days of 'vaccination' (half within minutes or hours of their dose). Those with prior conditions or risk factors for neurological problems or other causes for small nerve damage were excluded. None had had symptomatic COVID. They all had abnormal sensations (especially burning) in face or limbs and 60% had blood pressure drops on standing, heat intolerance and palpitations. Half of those tested had damage to the autonomic nervous system preventing normal sweating or leading to POTS.

These doctors thoroughly investigated these patients and found skin biopsies demonstrated nerve abnormalities. When there has been an immune reaction, where antibodies have bound a target leading to the triggering of immune cascades, a marker is left behind at the site called 'C4d.' This marker was identified at a higher rate in the blood vessel walls of the patients than was the case with controls. Some of those with normal skin biopsies had demonstrable abnormalities of the nerves elsewhere, such as those that control blood pressure and heart rates. Two out of the five tested showed protein within the cerebrospinal fluid in keeping with raised antibody levels and indicating inflammation.

These doctors successfully treated their patients with corticosteroids or immunoglobulins which indicates an underlying autoimmune pathology. (An immune modulation model of disease has also been described for other injuries including myocarditis, Guillain Barré Syndrome and the clotting disorder Thrombotic Thrombocytopenic Purpura).

There may yet be further studies that attempt to measure the extent of the injuries, but they will be faced with a problem. Patients with symptoms that do not neatly fit into categories that doctors commonly see, such as new-onset tremor, sensory changes or palpitations, are often categorised as having psychosomatic problems or anxiety. For those with palpitations there may even be some truth in that as anxiety is a natural consequence of experiencing a racing heartbeat. This misclassification of 'vaccine' injury means that those

Figure 7: Cases of myocarditis and pericarditis compared to overall emergency visits in 40 hospitals in USA over time.

trying to quantify the extent of these icebergs may never be able to see into the depths to get a clear measure.

The known adverse effects of these novel COVID 'vaccines', like myocarditis,

brain clots, and Guillain-Barré syndrome, as well as the rise in common conditions post-'vaccination', deserve serious attention. We must improve monitoring and understanding of these risks, without discounting patient experiences as mere coincidences.

How many people were affected?

It has been difficult to measure the adverse reactions from the 'vaccines' for three separate reasons: some were uncommon, some emerged a time after the injection, and also, the risk appears to be batch-dependent.

Rare side effects such as brain clots and myocarditis are easier to be sure about because they occur shortly after injection and the effect on the total numbers of those rare conditions is large. Demonstrating a raised incidence for a common condition can only occur if there is a marked outcome causing a large number of additional cases.

There is an added complication that certain batches of 'vaccine' have had a much higher adverse reaction and death rate than others. A Danish study showed the rates of reports per dose fell into three categories with high, medium or low adverse events. One batch of Pfizer-BioNTech resulted in the hospitalisation of 120 children in Vietnam.

MHRA, the Medicines and Healthcare products Regulatory Agency, said they

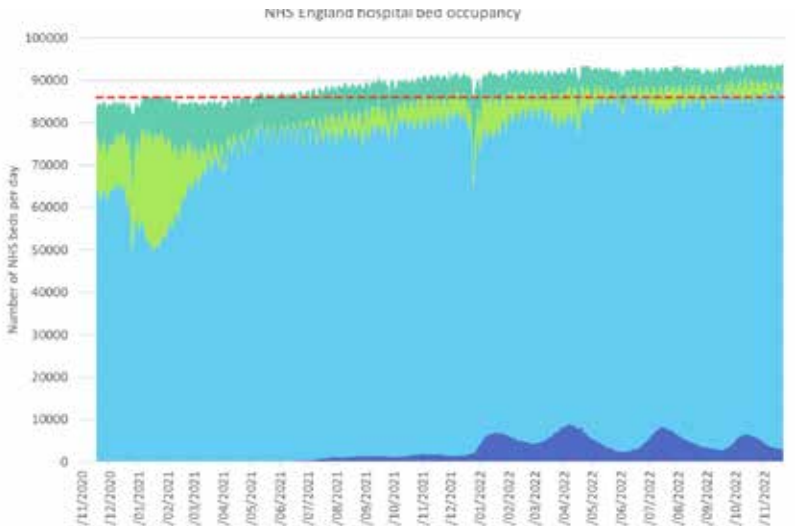


Figure 8: NHS England hospital bed occupancy by diagnosis (Pale blue = non-covid, lime green = COVID, dark green = available beds and dark blue = incidental COVID diagnosis). Dotted red line shows total NHS bed capacity in England in January 2021.

would do a prospective survey of adverse events but have never published their results. A German survey of 500,000 people found events that led to hospitalisation, life-changing disability or death occurred in 1 in 142 people, for AstraZeneca and 1 in 500 for Pfizer-BioNTech. Those will include a small number of genuine coincidences. Reports filed by German doctors put the figure for serious reactions at 1 in 3,300 by September 2022.

The 'vaccine' rollout coincided with a rise in pressures on hospital resources. Whereas with COVID there was never pressure on the number of empty hospital beds, once the 'vaccine' rolled out there were increasing numbers of inpatients, exceeding the expanded total capacity from January 2021.

At the same time as there were reports of an accident and emergency crisis in the UK, hospitals were overwhelmed in the USA. COVID had never overwhelmed total hospital bed capacity anywhere. In late 2021, the 'vaccinated' were attending the emergency department five times more frequently than the

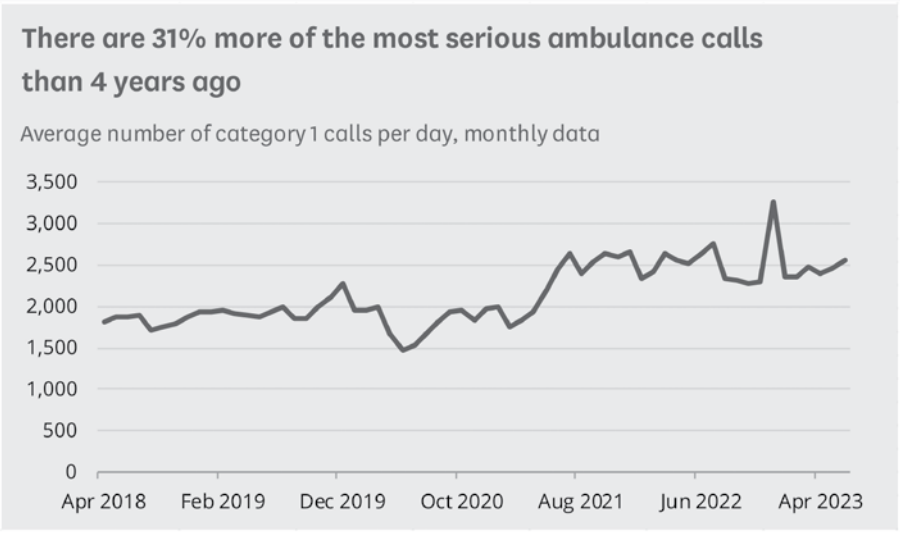


Figure 9: Category 1 ambulance calls (for life threatening conditions) over time in England.

'unvaccinated'. All ambulance calls in England for life-threatening conditions increased by 25 percent, an extra 500 calls every day from June 2021. It is worth reiterating the point evidenced above that there was an increase in cardiac emergencies in this period that correlated with 'vaccination'.

It was claimed this was all due to the Delta wave or long COVID effects. But not everywhere had COVID before Omicron; there is a control group. Australia had had minimal COVID prior to the rollout of the 'vaccines' and had

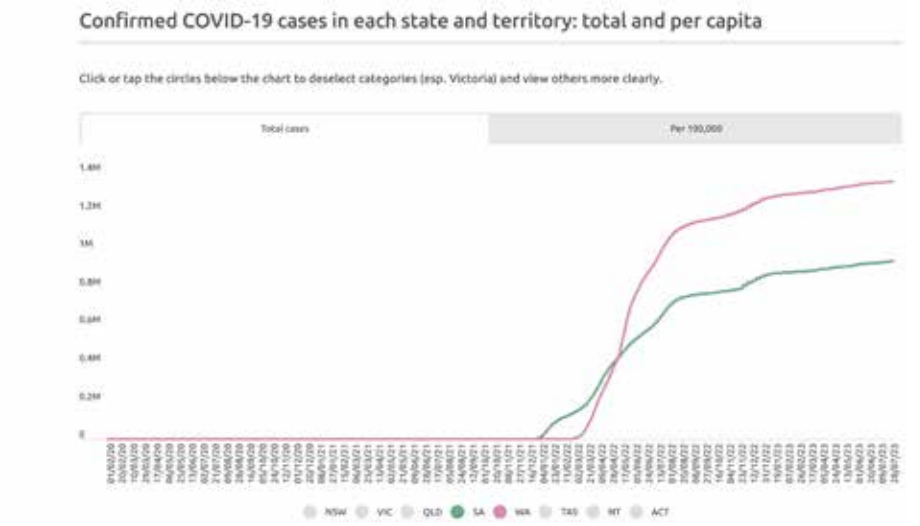


Figure 10: Total cumulative COVID cases diagnosed in Southern and Western Australia

opposite seasons. Yet, its hospitals were also overwhelmed. Queensland doctors called the problem a 'ticking time bomb' in April 2021 and described a 'flood of patients.' By May 2021, there was an ambulance crisis even though there were fewer than 100 COVID patients in all hospitals in Australia. By October, despite its being springtime in Australia, headlines reported on ambulances unable to drop off patients in hospitals that were at full capacity. In Oct 2021, Mark McGowan, Premier of Western Australia, said he could not explain the overwhelmed hospitals: 'Our hospitals are under enormous pressure. This has been something no one has ever seen before. Why it is, is hard to know.' In April 2022, Yvette D'ath, Queensland Health Minister, said she could not explain the rise in the most urgent ambulance calls ('code ones'): 'I don't think anyone can explain why we saw a 40% jump in code ones... We just had a lot of heart attacks and chest pains and trouble breathing, respiratory issues. Sometimes you can't explain why those things happen but unfortunately they do.'

Western Australia and South Australia had almost no COVID before Omicron. Up to mid-December 2021, Western and Southern Australia had had around 1000 cases each. The graph shows total cumulative cases by state.

Despite having fewer than 1000 COVID cases prior to December 2021, South Australia saw 25,800 extra ambulance calls (mostly cardiac) in the year from July 2020 to June 2021 compared to previous years. There was a year-on-year increase from 2018 to 2019 and 2019 to 2020 but the rise in 2021 was about double the increase seen in the preceding two years. There was a clear rise in attendances for particular conditions which correlated with the 'vaccine' rollout.

A Freedom of Information request showed that South Australia normally sees around 1,300 cardiac presentations per month for 15-44 year olds. This rose sharply in August 2021 with 'vaccine' rollout, peaking at 2,172 in December, before COVID hit. This was not due to COVID – the whole state had seen only 1000 COVID cases by 15th December.

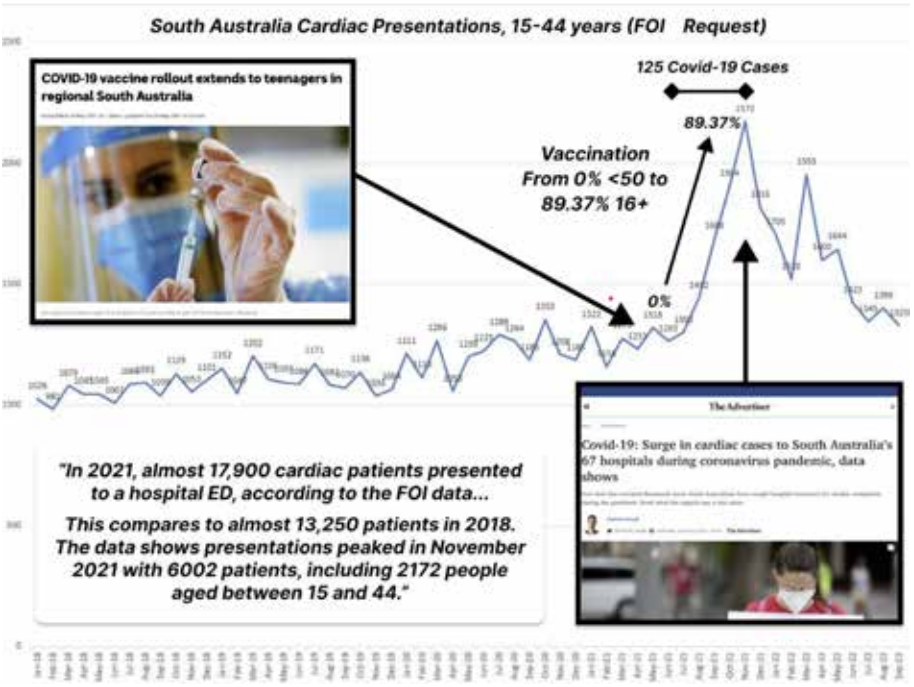


Figure 11: South Australian emergency cardiac presentations in 15-44 year olds in top graph.

A similar control group is Singapore which also had minimal COVID prior to Omicron but saw an excess of cardiovascular deaths from 2021, although data have been annualised.

In England, each COVID wave saw a rise in cardiac or respiratory arrest calls but there was an additional rise seen from the 'vaccine' rollout, which led to numbers far higher than in previous years. Heart attacks can be caused by direct damage to the electrical circuitry of the heart, for instance, from inflammation or scarring because of myocarditis, or else can be due to slow narrowing of the vessel walls supplying the heart muscle because of inflammation. In either case, a time lag should be expected after an event that contributes to the cause.

As well as sickness needing immediate care, there was a notable rise in people who were not working because of long-term sickness which was not seen in 2020 but began in English Spring 2021 when the 'vaccine' was rolled out to the

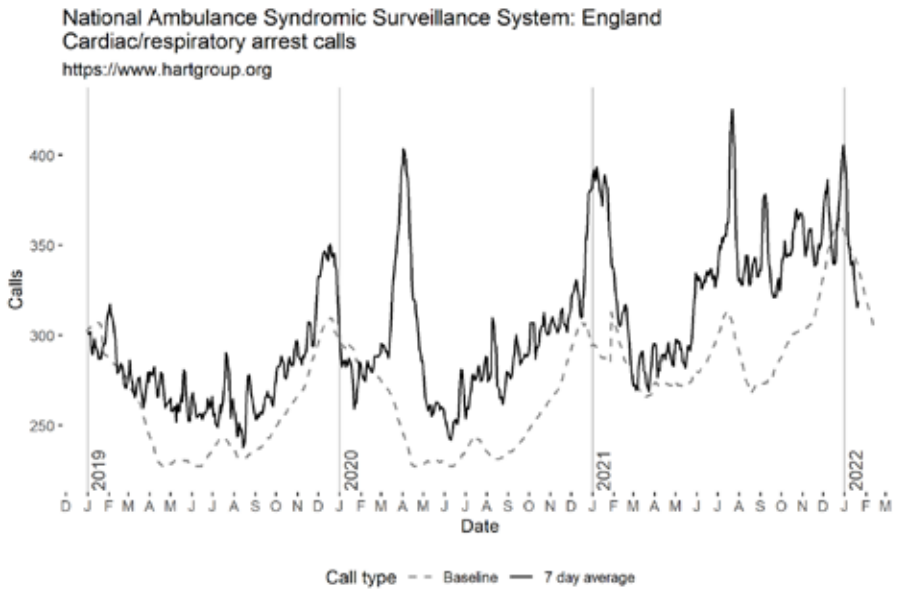
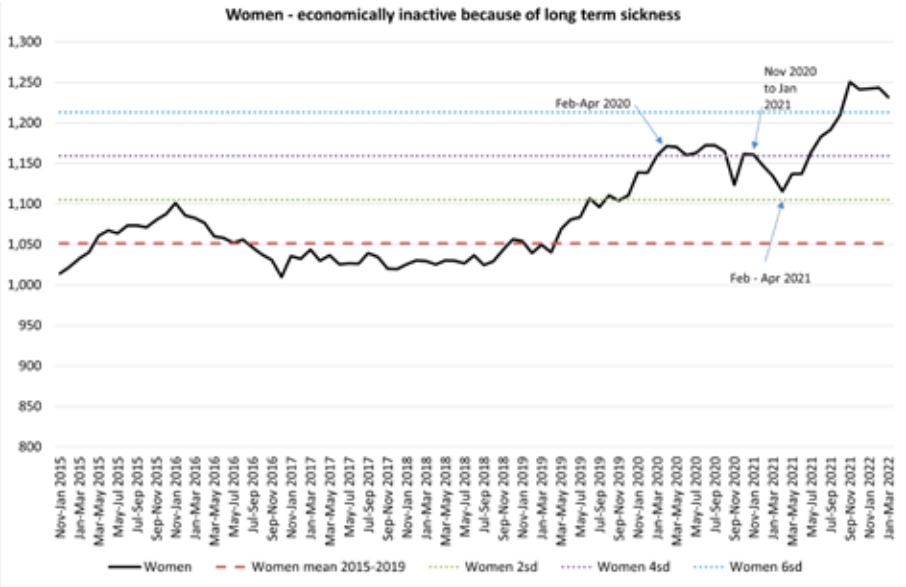


Figure 12: UKHSA data for ambulance calls in England for cardiac or respiratory arrests.



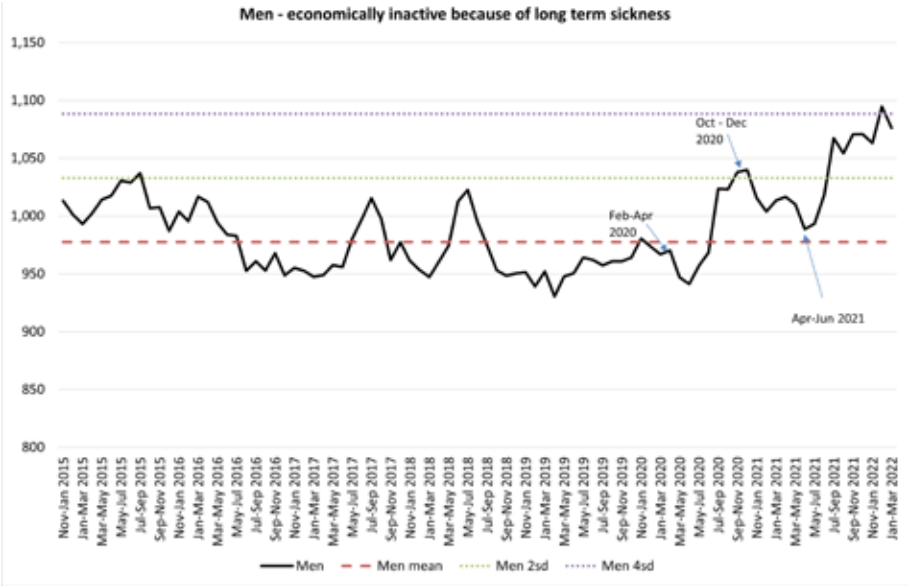


Figure 13a and 13b: The rate of economically inactive working-aged people due to long-term sickness in England, with females in the bottom graph and males in the top graph.

working aged population. In May 2022 the Governor of the Bank of England

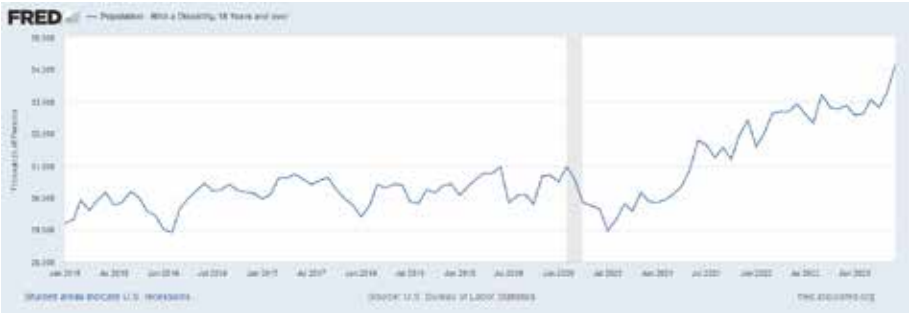


Figure 14: USA data showing rise in people over 16 years of age with a disability.

said there were 320,000 more people not working because they were sick. At the time it was estimated from self-reporting that only 80,000 had ever had symptoms of long COVID.

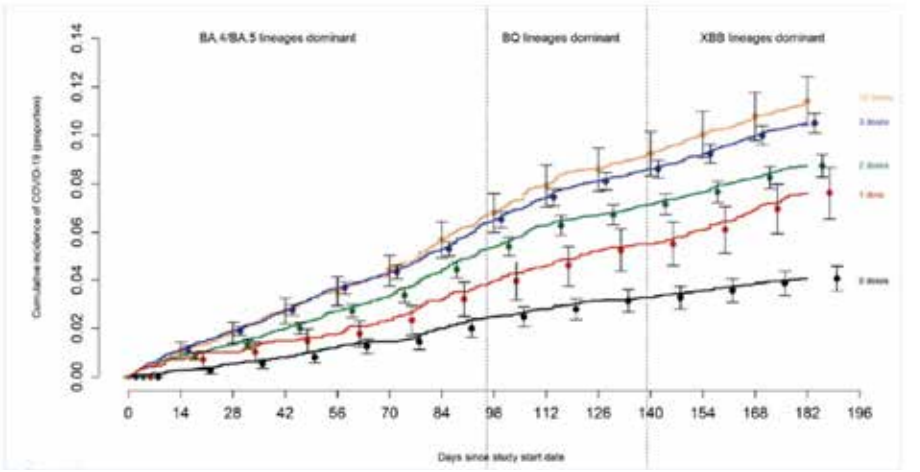


Figure 15: COVID case rates over time by number of doses given.

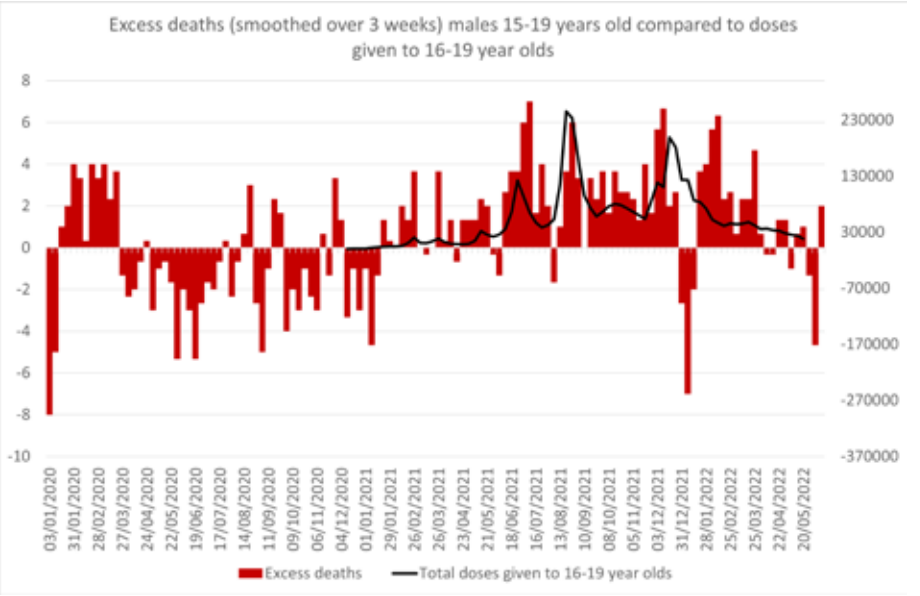


Figure 16: Excess mortality in England and Wales and 'vaccine' doses given in males 15-19.

The rise was also evident in the USA disability data.

As if that were not bad enough, we now have evidence that the more doses given the higher the COVID rates. Repeated injections have been shown to switch the immune response into the same mode used to prevent an immune response to food such that the spike protein is ignored entirely, increasing the risk of infection.

The adverse reaction alarm system has been blaring since early 2021, with reports of serious reactions, hospitalizations, and deaths from COVID 'vaccines.' The rollout of the 'vaccines' has coincided with a rise in hospitalizations and ambulance calls for heart attacks and other serious conditions across the world. The rise in long-term sickness and disability with the exact same timing is also concerning. It is clear that these novel products are not without risks, and more research is needed to fully understand the scope of those risks.

Overview of evidence around deaths

Of the death reported as potentially due to 'vaccination' in VAERS in 2021, there were 60% more males. This suggests these were not random but caused by spike-induced pathology that also caused more males to die of COVID.

If there was a small risk of increased death due to the 'vaccine' in the period shortly after 'vaccination' then this would be hard to detect in age groups where there were high numbers of background deaths. However, in younger age groups, where there are fewer deaths normally, a signal might be noted, and this is what we did actually see for 15-19 year old males. In females there

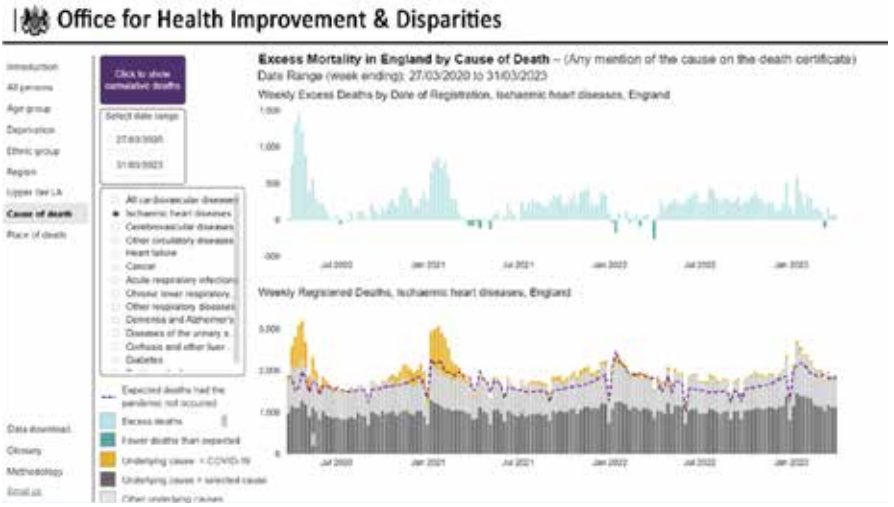


Figure 17: UKHSA data showing deaths mentioning ischaemic heart disease; turquoise bars show total excess deaths, and pale grey bars above the purple dotted line indicate non-COVID excess deaths.

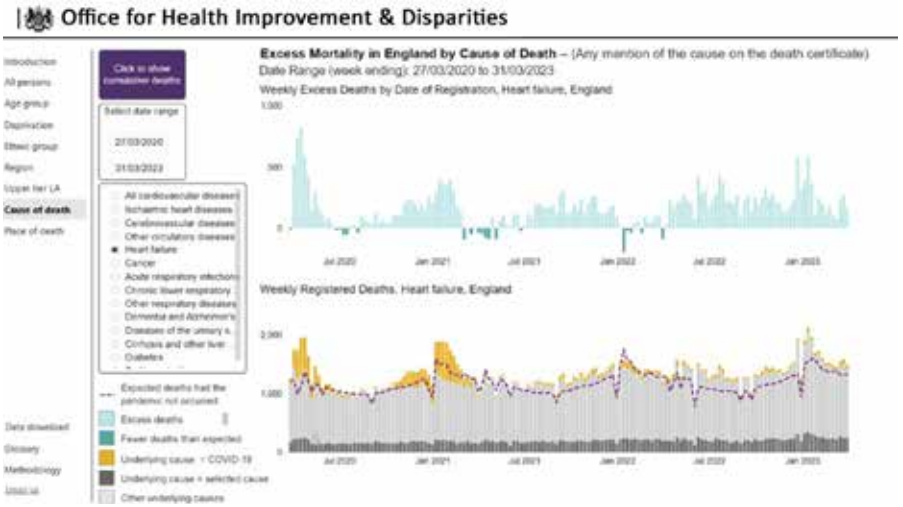


Figure 18: UKHSA data showing deaths mentioning heart failure.

was no signal.

England saw a stepwise rise in cardiac deaths after the 'vaccine' rollout,

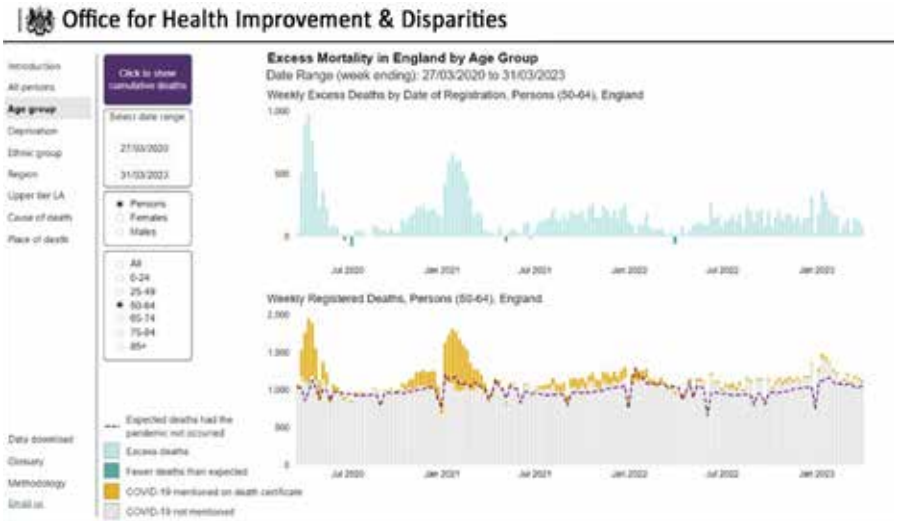


Figure 19: UKHSA excess deaths for 50-64-year-olds.

separate from COVID. This included deaths attributed to ischaemic heart disease. Expected levels are harder to predict in the first months of the year where there is wide annual variation and a mild winter season for viral deaths and low numbers of remaining frail elderly meant the step-wise increase was

not evident for a short period. Heart failure deaths show a similar pattern.

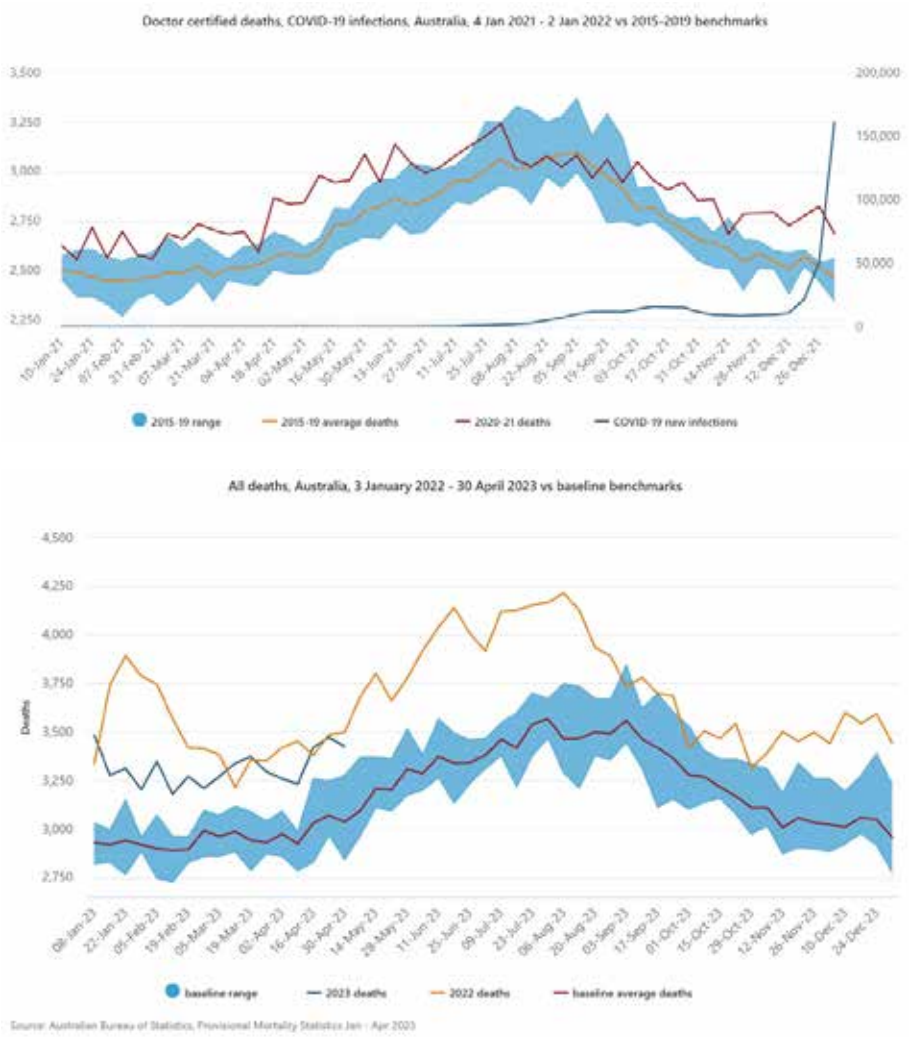


Figure 20a and 20b: Australian total deaths in red plotted against average and range from previous years in 2021 (top graph) and 2022 and 2023 (bottom graph).

A quiet winter for deaths in the elderly (which account for most deaths every year) in 2021-22 hides the high numbers of deaths in the young and cardiac deaths. Here are deaths in the 50-64 year old age group:

Australia also saw a rise in deaths before any significant COVID and it has

just grown worse since. Note the government chose to plot COVID infections rather than COVID deaths on this chart. Apart from a quiet winter season in 2021, there was an excess mortality (red line) above the 2015-2019 baseline

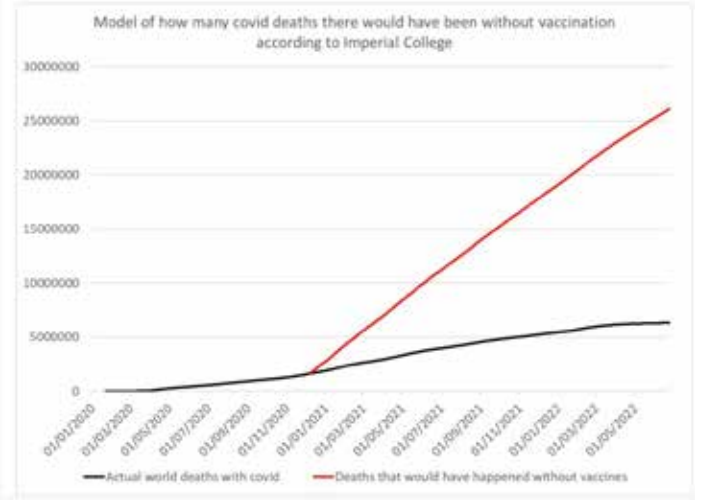


Figure 21: Cumulative global covid attributed deaths (in black) compared to modelled estimate of what would have happened without 'vaccines.'

(orange line) which was more marked from February 2021. Note the marked increase in the 'normal' baseline in the more recent graph.

Finally there have been several studies demonstrating a correlation between

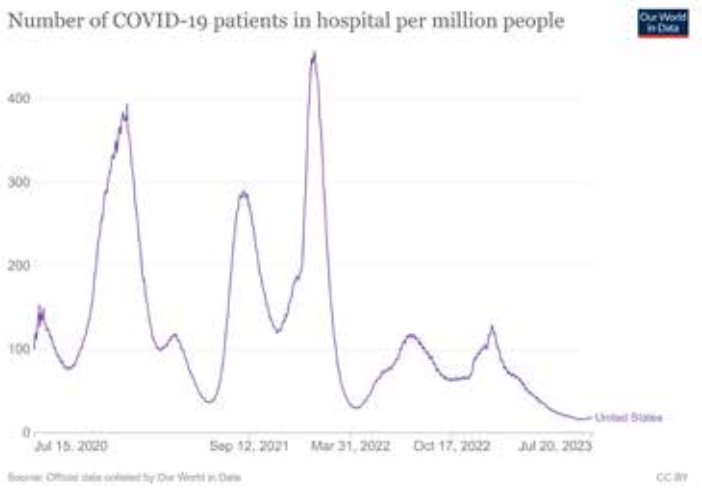


Figure 22: United states COVID hospitalisations per million.

'vaccination' rates and COVID mortality in 2022 comparing geographical regions. This is particularly damning given the marked socioeconomic differences between the 'vaccinated' and 'unvaccinated' populations which meant their pre-'vaccination' mortality rate was higher.

Some people have accepted that there were harms from these novel products but then justify it in their minds saying they saved millions of lives. The evidence does not support that position. The claims are based on fantasy modelling which supposes there would have been a huge increase in COVID deaths in the absence of injections. In reality, the global cumulative deaths (shown in the graph below) increased at a steady trajectory until Omicron arrived. The less deadly Omicron caused the rate of accumulation of death

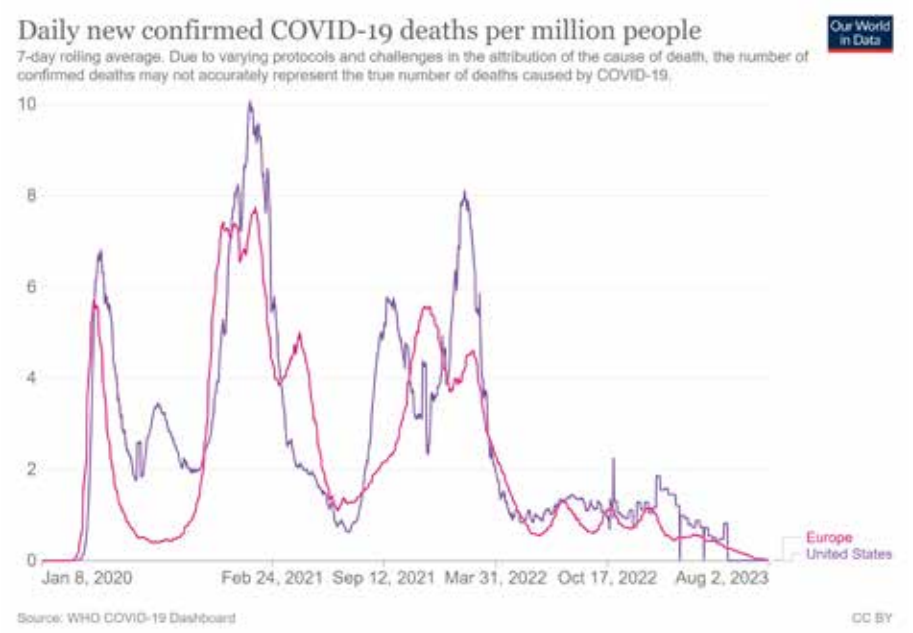


Figure 23: United states and European COVID deaths per million.

to slow in a way that 'vaccines' had failed to.

It is true that the deaths per case fell with Delta, but we have no influenza data to compare that to. All we know is that for influenza each wave has a similar number of hospitalisations and deaths. Here is what happened to USA hospitalisations despite 'vaccination'. Omicron had an effect where 'vaccination' had not.

Here are COVID deaths per million in USA and Europe as a whole. Again,

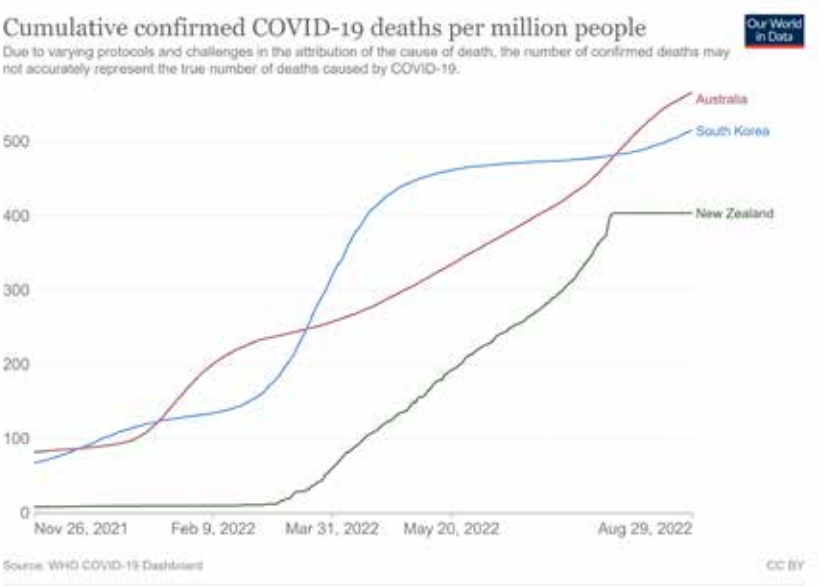


Figure 24: Cumulative COVID deaths per million.

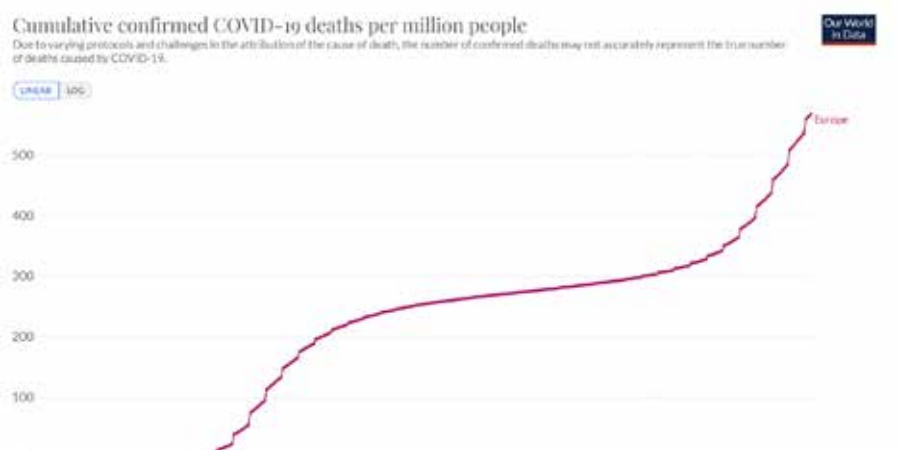


Figure 25: Cumulative COVID-attributed deaths in Europe in the first and autumn wave.

it was Omicron that reduced mortality from early 2022.

We can further show this by looking at mortality in the first wave in places that did not have significant COVID before Omicron. These places reached 500-600 deaths per million by November, 2022.

That was the same order as Europe saw in the first wave despite extensive 'vaccination' and a less lethal variant.

What did the trials show? AZ issued a press release claiming 100% efficacy against hospitalisation and death after only two severe COVID hospitalisations and one death in the placebo arm. This claim was repeated widely and was believed but it is clearly not adequate evidence.

Pfizer-BioNTech reported in their six-month follow-up paper that the number of deaths from any cause was higher in the group given a 'vaccine', which had 15 deaths, compared to 14 in the placebo group.[·] Of these deaths there was only one

Reported Cause of Death[a]	BNT162b2 (N=21,926) n	Placebo (N=21,921) n
Deaths	15	14
Acute respiratory failure	0	1
Aortic rupture	0	1
Arteriosclerosis	2	0
Biliary cancer metastatic	0	1
COVID-19	0	2
COVID-19 pneumonia	1	0
Cardiac arrest	4	1

Figure 26: Pfizer-BioNTech trial results.

COVID pneumonia death which occurred in the 'vaccine' group. Two deaths in the placebo arm were attributed to COVID in the absence of pneumonia. At best, therefore, injection of nearly 22,000 people prevented one death over the course of several months. The trial was global and ran from July to November 2020 including places in the Southern Hemisphere, Brazil, Argentina and South Africa which had notable COVID at the time, and also including the Autumn waves in the Northern Hemisphere. Consequently, the real-world ability of injection to prevent COVID deaths can be seen for the very low effect it could have.

Of note, there were four cases of cardiac arrest in the group that received the Pfizer-BioNTech 'vaccine', compared to one in the placebo group. These are low numbers and it is hard to interpret how much of a safety signal they represent, which in itself illustrates the inadequacy even of a trial including 44,000 people at proving the safety of a product. In addition, Pfizer-BioNTech gave a submission to the FDA based on the same period of follow-up, but after more time had elapsed for them to collect more comprehensive data. In this submission they said there had been 21 deaths in the 'vaccinated' group compared to 17 in the placebo group. The whole purpose of placebo-controlled trials is to allow this type of direct comparison to be made. There is a concerning sign here that the 'vaccines' not only failed to prevent death but may have introduced an increased risk of death from other causes.

The data suggest that there may be a small risk of increased death immediately

after 'vaccination' evident from the data in younger males. The increase in deaths in the months after injection including the increases in cardiac and respiratory arrest, as well as the rise in excess mortality in countries with minimal COVID prior to the 'vaccine' rollout, cannot be dismissed as mere coincidences. It is time for an honest conversation about the risks and benefits of these novel products. The reality is that the evidence does not support the notion that these injections saved millions of lives, and the harms and deaths caused by the 'vaccines' cannot be ignored.

Conclusion

The global response to COVID caused more harm than good. As we grapple with the aftermath of certain policy decisions, it becomes clear that, in the most generous light, these were based on flawed assumptions. The best we can hope for is that lessons are learnt for the future. Foundational medical ethics including individual autonomy and human rights must be safeguarded even in the face of a crisis. An open and vigorous debate that allows for the inclusion of multiple perspectives is crucial in all circumstances and dissenting views must not be silenced. Interventions must never be forced on populations and attempts at persuasion need a sound evidence base regardless of the level of fear. Harms have been caused in terms of the economy, the effects on children and young people on physical and mental health; there has been loss of trust in doctors, scientists and government. The abandonment of ethical principles and rights has been immense and should not be excused as justified.

Dr Clare Craig BM BCh FRCPath is a qualified pathologist, who worked in the NHS and reached consultant level in 2009. She specialized in cancer diagnostics including diagnostic testing for cancer within mass screening programs. She was the day-to-day pathology lead for the cancer arm of the 100,000 Genomes Project. She was clinical lead for the data team and led on research and development projects at Genomics England, writing national guidance and helping build bespoke software. Dr Craig advocates evidence-based policy around COVID issues, and the importance of upholding basic medical ethical principles including informed consent and bodily autonomy. She is Co-chair of the Health Advisory and Recovery Team, a voluntary body of professionals educating the public on COVID issues. Her first book is *Expired – COVID, the untold story*.

Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine Part 1*

by Aseem Malhotra

Background: In response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), several new pharmaceutical agents have been administered to billions of people worldwide, including the young and healthy at little risk from the virus. Considerable leeway has been afforded in terms of the pre-clinical and clinical testing of these agents, despite an entirely novel mechanism of action and concerning biodistribution characteristics.

Aim: To gain a better understanding of the true benefits and potential harms of the messenger ribonucleic acid (mRNA) coronavirus disease (COVID) vaccines.

Methods: A narrative review of the evidence from randomised trials and real-world data of the COVID mRNA products with special emphasis on Pfizer-BioNTech vaccine.

Results: In the non-elderly population the 'number needed to treat' to prevent a single death runs into the thousands. Re-analysis of randomised controlled trials using the messenger ribonucleic acid (mRNA) technology suggests a greater risk of serious adverse events from the vaccines than being hospitalised from COVID-19. Pharmacovigilance systems and

*First Published: *Journal of Insulin Resistance* ISSN: (Online) 2519-7533, (Print) 2412-2785

real-world safety data, coupled with plausible mechanisms of harm, are deeply concerning, especially in relation to cardiovascular safety. Mirroring a potential signal from the Pfizer Phase 3 trial, a significant rise in cardiac arrest calls to ambulances in England was seen in 2021, with similar data emerging from Israel in the 16–39-year-old age group.

Conclusion: It cannot be said that the consent to receive these agents was fully informed, as is required ethically and legally. A pause and reappraisal of global vaccination policies for COVID-19 is long overdue.

Vaccines save lives

The development of safe and highly effective vaccines during the latter half of the 20th century has been one of medicine's greatest achievements. The prominent scars on my left arm are a constant reminder of the success of our ability to curb some of the deadliest diseases such as smallpox, tuberculosis (TB), measles, mumps and rubella to name but a few. Collectively, traditional vaccines are estimated to save approximately 4–5 million lives per year.[1] The greatest success of vaccination was the global eradication of smallpox, which had a 30% mortality rate.[2]

In other words, almost one in three people who contracted it died. The development of a safe and effective vaccine after much trial and error resulted in 95 out of 100 people being protected from symptomatic infection from smallpox with immunity lasting five years, which by the 1970s resulted in complete eradication of the virus. Similarly, one dose of the measles vaccine is said to be '95% effective'. What is meant by this? What most people would assume is that 95 out of 100 who take the inoculation are protected from symptomatic infection and transmission, and they also have long-lasting immunity. Similarly, if exposed to chickenpox, only five out of 100 vaccinated children will catch it.

Vaccines are also some of the safest interventions in the world when compared to most drugs used in chronic disease management, as indeed we should expect, given that they are being administered to prevent something in healthy people, not treat an illness. It was consequently welcome news that in the summer of 2020, several drug companies including both Pfizer and Moderna announced the results of their two-month randomised controlled trial in which they had developed a vaccine with more than '95% effectiveness' at preventing infection from what at the time was the predominantly circulating strain of the coronavirus disease 2019 (COVID-19).

A doctor's experience

Volunteering in a vaccine centre, I was one of the first to receive two doses of Pfizer's messenger ribonucleic acid (mRNA) vaccine, at the end of January 2021. Although I knew my individual risk was small from COVID-19 at age 43 with optimal metabolic health, the main reason I took the injection was to prevent transmission of the virus to my vulnerable patients. During early 2021, I was both surprised and concerned by a number of my vaccine-hesitant patients and people in my social network who were asking me to comment on what I regarded at the time as merely 'anti-vax' propaganda.

I was asked to appear on Good Morning Britain after a previously vaccine-hesitant film director Gurinder Chadha, Order of the British Empire (OBE), who was also interviewed, explained that I convinced her to take the injection.

But a very unexpected and extremely harrowing personal tragedy was to happen a few months later that would be the start of my own journey into what would ultimately prove to be a revelatory and eye-opening experience so profound that after six months of critically appraising the data myself, speaking to eminent scientists involved in COVID-19 research, vaccine safety and development, and two investigative medical journalists, I have slowly and reluctantly concluded that contrary to my own initial dogmatic beliefs, Pfizer's mRNA vaccine is far from being as safe and effective as we first thought. This critical appraisal is based upon the analytical framework for practising and teaching evidence-based medicine, specifically utilising individual clinical expertise and or experience with use of the best available evidence and taking into consideration patient preferences and values.

A case study

Case studies are a useful way of conveying complex clinical information and can elicit useful data that would be lost or not be made apparent in the summary results of a clinical trial.

On 26 July 2021, my father, Dr Kailash Chand OBE, former deputy chair of the British Medical Association (BMA) and its honorary vice president (who had also taken both doses of the Pfizer mRNA vaccine six months earlier), suffered a cardiac arrest at home after experiencing chest pain. A subsequent inquiry revealed that a notable ambulance delay likely contributed to his death.[3] But his post-mortem findings are what I found particularly shocking and inexplicable. Two of his three major arteries had severe blockages: 90% blockage in his left anterior descending artery and a

75% blockage in his right coronary. Given that he was an extremely fit and active 73-year-old man, having walked an average of 10–15,000 steps/day during the whole of lockdown, this was a shock to everyone who knew him, but most of all to me. I knew his medical history and lifestyle habits in great detail. My father, who had been a keen sportsman all his life, was fitter than the overwhelming majority of men his age. Since the previous heart scans (a few years earlier, which had revealed no significant problems with perfect blood flow throughout his arteries and only mild furring), he had quit sugar, lost belly fat, reduced the dose of his blood pressure pills, started regular meditation, reversed his prediabetes and even greatly dropped his blood triglycerides, substantially improving his cholesterol profile.

I could not explain his post-mortem findings, especially as there was no evidence of an actual heart attack but with severe blockages. This was precisely my own special area of research. That is, how to delay progression of heart disease and even potentially reverse it. In fact, in my own clinic, I successfully prescribe a lifestyle protocol to my patients on the best available evidence on how to achieve this. I've even co-authored a high-impact peer-reviewed paper with two internationally reputed cardiologists (both editors of medical journals) on shifting the paradigm on how to most effectively prevent heart disease through lifestyle changes.[4] We emphasised the fact that coronary artery disease is a chronic inflammatory condition that is exacerbated by insulin resistance. Then, in November 2021, I was made aware of a peer-reviewed abstract published in *Circulation*, with concerning findings. In over 500 middle-aged patients under regular follow-up, using a predictive score model based on inflammatory markers that are strongly correlated with risk of heart attack, the mRNA vaccine was associated with substantially increasing the risk of a coronary event within five years from 11% pre-mRNA vaccine to 25% 2–10 weeks post mRNA vaccine. An early and relevant criticism of the validity of the findings was that there was no control group, but nevertheless, even if partially correct, that would mean that there would be a large acceleration in progression of coronary artery disease, and more importantly heart attack risk, within months of taking the injection.[5] I wondered whether my father's Pfizer vaccination, which he received six months earlier, could have contributed to his unexplained premature death and so I began to critically appraise the data.

Questioning the data

I recalled a cardiologist colleague of mine informing me, to my astonishment at the time, that he had made a decision not to take the vaccine for a number of reasons, including his personal low background COVID-19 risk (see Table 1)[6] and concerns regarding unknown short-and longer-term harms. One thing that alarmed him about Pfizer's pivotal mRNA trial published in *The New England*

Journal of Medicine was the data in the supplementary appendix, specifically that there were four cardiac arrests in those who took the vaccine *versus* only one in the placebo group.[7] These figures were small in absolute terms and did not reach statistical significance in the trial, suggesting that it may just be coincidence, but without further studies it was not possible to rule out this being a genuinely causal relationship (especially without access to the raw data), in which case it could have the effect of causing a surge in cardiac arrests once the vaccine was rolled out to tens of millions of people across the globe.

Table 1: Infection fatality rate of ancestral variants of COVID-19 pre-vaccination by age. Source: Adapted from Axfors C, Ioannidis JPA. Infection fatality rate of COVID-19 in community-dwelling elderly populations. Eur J Epidemiol. In press 2022;37(3):235–249. *https://doi.org/10.1007/s10654-022-00853-w* IFR = infection fatality rate.

Age	Median IFR %	Median IFR (absolute)	Survival rate estimate (%)
0–19	0.0027	1 in 37 037	99.9973
20–29	0.0140	1 in 7143	99.9860
30–39	0.0310	1 in 3225	99.9690
40–49	0.0820	1 in 1220	99.9180
50–59	0.2700	1 in 370	99.7300
60–69	0.5900	1 in 169	99.4100
> 70 community	2.4000	1 in 42	97.6000
> 70 overall	5.5000	1 in 18	94.5000

Table 2: Deaths prevented, and number needed to vaccinate to prevent a death based on death rates and case fatality rates from UKHSA data for England during Delta wave. Source: Adapted from HART. How many injections to prevent one covid death? [homepage on the Internet]. No date. Available from: *https://www.hartgroup.org/number-needed-to-vaccinate/* UKHSA, United Kingdom Health Security Agency.

Age	Deaths prevented (in England) based on differences in death rates per 100 000	Number needed to vaccinate per death prevented based on differences in death rates per 100 000
< 18	-0.1	Negative
18–29	70	93 000
30–39	240	27 000
40–49	640	10 000
50–59	2740	2600
60–69	4580	1300
70–79	9100	520
80+	11 900	230
Total	**29 270**	-

In terms of efficacy, headlines around the world made very bold claims of 95% effectiveness, the interchangeable use of 'efficacy' and 'effectiveness' glossing over the big difference between controlled trial and real-world conditions.[8] It

would be understandable for the lay public and doctors to interpret this that if 100 people are vaccinated then 95% of people would be protected from getting the infection. Even the Centers for Disease Control (CDC) director Rochelle Walensky recently admitted in an interview that it was initial news from CNN that made her optimistic that the vaccine would significantly stop transmission and infection, but this was later to be proved far from true for the COVID-19 vaccines.[9] The original trial revealed that a person was 95% 'less likely' to catch the autumn 2020 variant of COVID-19. This is known in medical-speak as relative risk reduction, but to know the true value of any treatment one needs to understand for that person, by how much their individual risk is reduced by the intervention – that is, the absolute individual risk reduction.

Importantly, it turns out the trial results suggest that the vaccine was only preventing a person from having a symptomatic positive test, and the absolute risk reduction for this was 0.84% (0.88% reduced to 0.04%). In other words, if 10,000 people had been vaccinated and 10,000 had not, for every 10,000 people vaccinated in trial 4 would have tested positive with symptoms compared to 88 who were unvaccinated. Even in the unvaccinated group, 9,912 of the 10,000 (over 99%) would not have tested positive during the trial period. Another way of expressing this is that it would be necessary to vaccinate 119 people to prevent one such symptomatic positive test (assumed to be indicative of an infection, which, in itself, is potentially misleading but beyond the scope of this article).[10]

This absolute risk reduction figure (0.84%) is extremely important for doctors and patients to know, but how many of them were told this when they received the injection? Transparent communication of risk and benefit of any intervention is a core principle of ethical evidence-based medical practice and informed consent.[11]

The Academy of Medical Royal Colleges made this clear in a paper published in the *BMJ* in 2015.[12] A co-author at the time was also the then chair of the General Medical Council. In fact, in a 2009 World Health Organization (WHO) bulletin Gerd Gigerenzer, the director of the Max Planck Institute, stated, 'It's an ethical imperative that every doctor and patient understand the difference between relative and absolute risks to protect patients against unnecessary anxiety and manipulation'.[13]

Contrary to popular belief, what the trial did not show was any statistically significant reduction in serious illness or COVID-19 mortality from the vaccine over the 6-month period of the trial, but the actual numbers of deaths (attributed to COVID-19) are still important to note. There were only two deaths from COVID-19 in the placebo group and one death from COVID-19

in the vaccine group. Looking at all-cause mortality over a longer period, there were actually slightly more deaths[14] in the vaccine group (19 deaths) than in the placebo group (17 deaths). Also of note was the extremely low rate of COVID-19 illness classed as severe in the placebo group (nine severe cases out of 21,686 subjects, 0.04%), reflecting a very low risk of severe illness even in regions chosen for the trial because of perceived high prevalence of infection.

Finally, the trials in children did not even show a reduction in symptomatic infections but instead used the surrogate measure of antibody levels in the blood to define efficacy, even though the relationship between Wuhan-spike vaccine-induced antibody levels and protection from infection is tenuous, at best. The Food and Drug Administration's (FDA's) own website states that:

> [R]esults from currently authorised SARS-COV-2 antibody tests should not be used to evaluate a person's level of immunity or protection from COVID-19 at any time, and especially after the person received a COVID-19 vaccination.[15]

Now that we know what the published trial did and did not show in terms of the vaccine efficacy, we can attempt to extrapolate what the effect of the vaccine would be in reducing mortality or any other adverse outcome from the virus. If there is a 1 in 119 chance the vaccine protects against getting symptomatic infection from ancestral variants, then to find the protection against death, this figure (n = 119) must be multiplied by the number of infections that lead to a single death for each age group. This would give (for up to two months after the inoculation) the absolute risk reduction (for death) from the vaccine. For example, if my risk at age 44 from dying from Delta (should I get infected with it) is 1 in 3,000, then the absolute risk reduction from the vaccine protecting me from death is 1 over 3,000 multiplied by 119, that is, 1 per 357,000.

Of course, even for those people who do become infected the vaccination may provide some protection against death. From observational data it is possible to calculate the number who would need to be vaccinated to prevent a COVID-19 death. For example, comparing the population death rates[16] during the Delta wave gives 230 for people over 80 needing to be vaccinated to prevent a single death in that period with that number rising to 520 for people in their 70s and 10,000 for people in their 40s (see Table 2 and Figure 1[17]). However, these figures will be distorted by inaccuracies in the measure of the size of the unvaccinated population. As also pointed out in a recent editorial by John Ioannidis in *BMJ Evidence-Based Medicine* the inferred efficacy of the vaccine from non-randomised studies may be 'spurious', with bias being generated by 'pre-existing immunity, vaccination misclassification, exposure differences, testing, disease risk factor confounding, hospital admission decision, treatment use differences and death attribution'.[18]

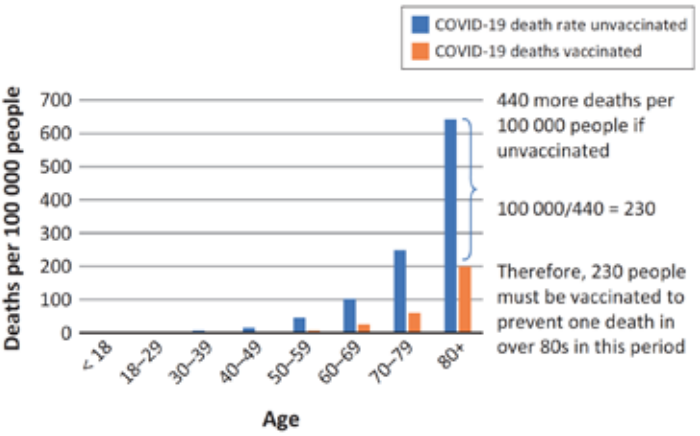


Figure 1: Calculation of number needed to be vaccinated from COVID-19 death rates in vaccinated and unvaccinated from UKHSA data for England during the Delta wave. The difference between the deaths that occurred in the vaccinated and that would have occurred if they had the same rate as the unvaccinated was used to calculate the number of people who would need to be vaccinated to prevent a single death.

Source: Fraiman J, Erviti J, Jones M, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. *Vaccine.* 2022 Aug 30:S0264-410X(22)01028-3. *https://doi.org/10.1016/j.vaccine.2022.08.036* Note: Difference between proportion of unvaccinated and vaccinated population dying with COVID-19 from 27 Aug to 16 Dec 2021. UKHSA, United Kingdom Health Security Agency.

These numbers are for the whole population of England and do not necessarily apply to the healthy; more than 95% of deaths were in people with pre-existing conditions.[19] It is also important to note that the vaccinated and unvaccinated populations are different in other ways, which could bias the death data. For example, the unvaccinated are more likely to be from a lower socioeconomic demographic, which puts them at a greater risk of severe illness or death should they be infected.

Professor Carl Heneghan, the director of the Centre of Evidence Based Medicine in Oxford, has explained his own clinical experience of healthy user bias. Some of his own patients who ended up in intensive care unit (ICU) with COVID-19 (classified as unvaccinated) did not take the vaccine because they were already suffering from terminal illness.

Given these limitations, the above figures are likely an overestimate of the individual benefit of vaccination; the open and frank discussion of such uncertainties is an essential component of shared decision-making.

What should be part of the shared decision-making informed consent discussion when any member of the public is considering taking the injection

is something along these lines: Depending on your age, several hundreds or thousands of people like you would need to be injected in order to prevent one person from dying from the Delta variant of COVID-19 over a period of around three months. For the over 80s, this figure is at least 230, but it rises the younger you are, reaching at least 2,600 for people in their 50s, 10,000 for those in their 40s, and 93,000 for those between 18 and 29 years. For Omicron, which has been shown to be 30% to 50% less lethal, it means that many more people would need to be vaccinated to prevent one death. How long any protection actually lasts is unknown; boosters are currently being recommended after as short a period as four months in some countries.

But how many people have had a conversation that even approaches an explanation similar to that? This is before we get into the known, unknown and as yet to be fully-quantified harms.

Although many have proposed that Omicron is intrinsically less lethal (supported by observed molecular differences between Omicron and the Wuhan-type virus) immunity built up by prior exposure protecting against severe illness is likely to be relevant to some extent as well. The critical point to note is that, whether it is a viral or immune-related phenomenon, the milder nature of Omicron is evident in the unvaccinated and therefore the reduction in mortality should not be attributed to vaccines.

What are the harms?

Concerns have already been raised about the under-reporting of adverse events in the clinical trials for the COVID-19 vaccines. Investigative medical reporter Dr Maryanne Demasi analysed the various ways that the pivotal mRNA trials failed to account for serious harms.[20] Not only were trial participants limited to the type of adverse event they could report on their digital apps, but some participants who were hospitalised after inoculation were withdrawn from the trial and not reported in the final results. After two months into the pivotal trials, the FDA allowed vaccine companies to offer the vaccine to subjects in the placebo group, essentially torpedoing any chance of properly recording adverse events from that point on, forcing a reliance on pharmacovigilance data.

Such data have shown that one of the most common mRNA COVID-19 vaccine-induced harms is myocarditis. A study across several Nordic countries showed an increased risk from mRNA vaccination over background, especially in young males.[21] Authorities have repeatedly maintained that myocarditis is more common after COVID-19 infection than after vaccination.[22] However, trial data demonstrating that vaccination reduces the risk of myocarditis in subsequent infection are elusive, and in fact the risks may be additive. Incidence

of myocarditis rocketed from the northern Spring 2021 when vaccines were rolled out to the younger cohorts. It had remained within normal levels for the full year prior, despite COVID-19.[23] The most up-to-date evidence, a paper from Israel[24] found that the infection itself, prior to roll-out of the vaccine, conferred no increase in the risks of either myocarditis or pericarditis from COVID-19, strongly suggesting that the increases observed in earlier studies were because of the mRNA vaccines, with or without COVID-19 infections as an additional risk in the vaccinated.[24]

Indeed, this reflects my own clinical experience of advising and managing several patients in the community who presented with a clear suggestion from their history of myocarditis post mRNA vaccination but who were not necessarily unwell enough to require hospital admission. A very fit woman in her 50s developed fatigue and shortness of breath on exertion a few weeks after her second Pfizer injection. An echocardiogram revealed severe impairment of her left ventricular function. Another woman in her 30s experienced similar symptoms with distressing palpitations within a few days of her second injection; mild left ventricular impairment was also present on echo and a subsequent cardiac MRI scan revealed several areas of late gadolinium enhancement, a feature seen on the scan, which is consistent with damaged heart tissue, and given that heart cells cannot be replaced this is likely to have a long-term effect.

Although vaccine-induced myocarditis is not often fatal in young adults, MRI scans reveal that, of the ones admitted to hospital, approximately 80% have some degree of myocardial damage.[25,26] It is like suffering a small heart attack and sustaining some – likely permanent – heart muscle injury. It is uncertain how this will play out in the longer-term, including if, and to what degree, it will increase the risk of poor quality of life or potentially more serious heart rhythm disturbances in the future.

A number of reports have produced concerning rates of myocarditis, depending on age, ranging from 1 in 6,000 in Israel[27] to 1 in 2,700 in a Hong Kong study in male children and adolescents aged 12–17 years.[28] Most of the epidemiology studies that have been carried out have measured myocarditis cases that have been diagnosed in a hospital setting, and do not claim to be a comprehensive measure of more mild cases (from which long-term harm cannot be ruled out). In addition, under-reporting of adverse events is the scourge of pharmacovigilance data.[29]

The United Kingdom relies on the Medicines and Health Regulatory Agency's (MHRA's) 'Yellow Card' reporting system,[30] which is far from adequate to cope with a rapid roll-out of a brand-new product. It only detected the clotting problems that resulted in the withdrawal of the AstraZeneca product in April

2021 for younger people after 9.7 million doses had been given in the United Kingdom;[31] in contrast, Denmark detected the problem after only 150,000 doses had been administered.[32]

In the United Kingdom, since the vaccine roll-out there have been almost 500,000 adverse event reports recorded (via the Yellow Card system) in association with the mRNA COVID-19 vaccinations involving over 150,000 people. In terms of the number of reports per person (that is, having received at least one dose), the MHRA figures show around 1 in 120 suffering a likely adverse event that is beyond mild.[30] However, the MHRA are unclear about the rate and furthermore do not separate out the serious adverse events. Nevertheless, this level of reporting is unprecedented in the modern medical era and equals the total number of reports received in the first 40 years of the Yellow Card reporting system (for all medicines – not just vaccines) up to 2020.[33] In comparison, for the measles, mumps and rubella (MMR) vaccine, the number of reports per person vaccinated was around 1 in 4,000, more than thirty times less frequent than the 1 in 120 Yellow Card reports for COVID-19 vaccine recipients.[34] Norway does separate out the reported serious adverse reactions and has shown a rate of approximately 1 in 1,000 after two doses of BioNTech-Pfizer mRNA product that result in hospitalisation or are life changing.[35]

Another, and more useful, source of information (because of the level of detail for each report made available to the public) is the United States (US) Vaccine Adverse Effect Reporting System (VAERS). As with the UK's system, the level of reports – including serious ones – associated with COVID-19 vaccines is completely unprecedented. For example, over 24,000 deaths have now been recorded in VAERS as of March 2nd 2022; 29% of these occurred within 48 hours of injection, and half within two weeks. The average reporting rate prior to 2020 was fewer than 300 deaths per annum. One explanation often given for this is that the COVID-19 vaccine roll-out is unprecedented in scope; however, this is not valid, since (for the last decade at any rate) the United States has administered 150 million to 200 million vaccinations annually. Another criticism of VAERS is that 'anyone can make an entry', yet, in fact, an analysis of a sample of 250 early deaths suggested that the vast majority are hospital or physician entries,[36] and knowingly filing a false VAERS report is a violation of Federal law punishable by fine and imprisonment.[37]

Given that VAERS was set up to generate early signals of potential harm for new vaccines, and was instrumental in doing so for several products, it seems perverse only now to criticise it as unreliable when there seem to have been no changes in the way it operates.

It has been estimated serious adverse effects that are officially reported are

actually a gross underestimate, and this should be borne in mind when the above comments in relation to VAERS reports are considered. For example, a paper by David Kessler (a former FDA Commissioner) cites data suggesting that as few as 1% of serious adverse events are reported to the FDA.[38] Similarly in relation to the Yellow Card scheme in the United Kingdom, it has been estimated that only 10% of serious adverse effects are reported.[39,40] A recent pre-print publication co-authored by some of the most trusted medical scientists in the world in relation to data transparency adds validity to pharmacovigilance data. Accessing data from the FDA and Health Canada websites and combining results from journal articles that published the Pfizer and Moderna trials, the authors concluded that the absolute risk of a serious adverse event from the mRNA vaccines (a rate of one in 800) substantially exceeded the risk of COVID-19 hospitalisation in randomised controlled trials.[17]

What VAERS and other reporting systems (including the yet to be accessed and independently evaluated raw data from randomised controlled trials) will miss are potential medium-to longer-term harms that neither patients nor doctors will automatically attribute to the drug. For example, if the mRNA vaccine increases the risk of a coronary event within a few months (in what was a likely contributory factor in my father's sudden cardiac death), then this would increase event rates well beyond the first few weeks of the injection yet linking it back to the vaccine, and thus reporting it is highly unlikely to occur later on.

It is instructive to note that according to ambulance service data, in 2021 (the year of the vaccine roll-out), there were approximately an extra 20,000 (~20% increase) out-of-hospital cardiac arrest calls compared to 2019, and approximately 14,000 more than in 2020. Data obtained under Freedom of Information laws from one of the largest ambulance trusts in England suggest that there was no increase from November 2020 to March 2021, and thereafter the rise has been seen disproportionately in the young.[41] This is a huge signal that surely needs investigating with some urgency.[42]

Similarly, a recent paper in *Nature* revealed a 25% increase in both acute coronary syndrome and cardiac arrest calls in the 16 to 39-year-old age groups significantly associated with administration with the first and second doses of the mRNA vaccines but no association with COVID-19 infection.[43] The authors state:

> [T]he findings raise concerns regarding vaccine-induced undetected severe cardiovascular side effects and underscore the already established causal relationship between vaccines and myocarditis, a frequent cause of unexpected cardiac arrest in young individuals. (p. 1)

The disturbing findings in this paper have resulted in calls for a retraction. In the past, scientists with a different view of how data should be analysed

would have published a paper with differing assumptions and interpretation for debate. Now they try to censor discussion.

Many other concerns have been raised about potential harms from the vaccines in the mid-to long-term. Although some of these concerns remain hypothetical, it may be a grave mistake to focus only on what can be measured and not on the wider picture, especially for the young.

What could be the mechanism of harm?

For conventional vaccines, an inert part of the bacteria or virus is used to 'educate' the immune system. The immune stimulus is limited, localised and short-lived. For the COVID-19 vaccines, spike protein has been shown to be produced continuously (and in unpredictable amounts) for at least four months after vaccination[44] and is distributed throughout the body after intramuscular injection.[45] For the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines, the spike protein was chosen, possibly because it enables cell entry. However, this protein is not inert, but rather it is the source of much of the pathology associated with severe COVID-19, including endothelial damage,[46] clotting abnormalities[47] and lung damage. It is instructive to note that prior to roll-out of the mRNA products, the WHO endorsed a priority list of potential serious adverse events of special interest that may occur as a direct result of COVID-19 vaccines. The list was based upon the specific vaccine platform, adverse events associated with prior vaccines in general, theoretical associations based upon animal models and COVID-19-specific immunopathogenesis[40] (see Figure 2).

Is the vaccine doing more harm than good?

The most objective determinant of whether the benefits of the vaccines outweigh the harms is by analysing its effects on 'all-cause mortality'. This gets round the thorny issue as to what should be classified as a COVID-19 death, and also takes full account of any negative effects of the vaccine. It would be surprising – to say the least – if during an apparently deadly pandemic, an effective vaccine could not clearly and unequivocally be shown to reduce all-cause mortality.

Pfizer's pivotal mRNA trial in adults did not show any statistically significant reduction in all-cause mortality, and in absolute terms there were actually slightly more deaths in the treatment arm *versus* in the placebo.

Work by Fenton et al. showed an unusual spike in mortality in each age group of the unvaccinated population, which coincides with the vaccine roll-out for each age group.[48] The rapid shrinking in the size of this population means a small-time lag could theoretically produce this effect artifactually. Alternative

Included SAE types (matching AESI list): Abdominal pain, Abdominal pain upper, Abscess, Abscess intestinal, Acute coronary syndrome, Acute kidney injury, Acute left ventricular failure, Acute myocardial infarction, Acute respiratory failure, Anaemia, Anaphylactic reaction, Anaphylactic shock, Angina pectoris, Angina unstable, Angioedema, Aortic aneurysm, Aortic valve incompetence, Arrhythmia supraventricular, Arteriospasm coronary, Arthritis, Atrial fibrillation, Atrial flutter, Axillary vein thrombosis, Basal ganglia haemorrhage, Bile duct stone, Blood loss anaemia, Bradycardia, Brain abscess, Cardiac failure, Cardiac failure acute, Cardiac failure congestive, Cardiac stress test abnormal, Cardio-respiratory arrest, Cerebral infarction, Cerebrovascular accident, Chest pain, Cholecystitis, Cholecystitis acute, Cholelithiasis, Colitis, Coronary artery disease, Coronary artery dissection, Coronary artery occlusion, Coronary artery thrombosis, Deep vein thrombosis, Dermatitis bullous, Diabetic ketoacidosis, Diarrhoea, Diplegia, Dyspnoea, Embolic stroke, Empyema, Facial paralysis, Fluid retention, Gastroenteritis, Gastrointestinal haemorrhage, Haematoma, Haemorrhagic stroke, Hemiplegic migraine, Hepatic enzyme increased, Hyperglycaemia, Hyponatraemia, Hypoxia, Ischaemic stroke, Laryngeal oedema, Multiple sclerosis, Myocardial infarction, Non-cardiac chest pain, Oedema peripheral, Pancreatitis, Pancreatitis acute, Pericarditis, Peripheral artery aneurysm, Peritoneal abscess, Pleuritic pain, Pneumothorax, Post procedural haematoma, Post procedural haemorrhage, Postoperative abscess, Procedural haemorrhage, Psychotic disorder, Pulmonary embolism, Rash, Rash vesicular, Respiratory failure, Retinal artery occlusion, Rhabdomyolysis, Rheumatoid arthritis, Schizoaffective disorder, Seizure, Subarachnoid haemorrhage, Subcapsular renal haematoma, Subdural haematoma, Tachyarrhythmia, Tachycardia, Thrombocytopenia, Thyroid disorder, Toxic encephalopathy, Transaminases increased, Transient ischaemic attack, Traumatic intracranial haemorrhage, Type 2 diabetes mellitus, Uremic encephalopathy, Uterine haemorrhage, Vascular stent occlusion, Ventricular arrhythmia

Figure 2: The World Health Organization endorsed a list of adverse events of special interest associated with COVID-19 vaccinations.

Source: Fraiman J, Erviti J, Jones M, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. *Vaccine*. 2022 Aug 30:S0264-410X(22)01028-3. https://doi.org/10.1016/j.vaccine.2022.08.036.
SAE, serious adverse events; AESI, adverse events of special interest.

explanations must include the (more likely) possibility that a rise in mortality after vaccination was misattributed to the unvaccinated population: in other words, those counted as 'unvaccinated deaths' would in fact be those who had died within 14 days of being vaccinated (a freedom of information [FOI] request has now confirmed that authorities in Sweden were indeed categorising deaths within 14 days of dosing as unvaccinated, creating a misleading picture of efficacy *versus* death).

One has to raise the possibility that the excess cardiac arrests and continuing pressures on hospitals in 2021-2022 from non-COVID-19 admissions may all be signalling a non-COVID-19 health crisis exacerbated by interventions, which would of course also include lockdowns and or vaccines.

Given these observations, and reappraisal of the randomised controlled trial data of mRNA products, it seems difficult to argue that the vaccine roll-out has been net beneficial in all age groups. While a case can be made that the

vaccines may have saved some lives in the elderly or otherwise vulnerable groups, that case seems tenuous at best in other sections of the population, and when the possible short-, medium- and unknown longer-term harms are considered (especially for multiple injections, robust safety data for which simply do not exist), the roll-out into the entire population seems, at best, a reckless gamble. It is important to acknowledge that the risks of adverse events from the vaccine remain constant, whereas the benefits reduce over time, as new variants are (1) less virulent and (2) not targeted by an outdated product. Having appraised the data, it remains a real possibility that my father's sudden cardiac death was related to the vaccine. A pause and reappraisal of vaccination Policies for COVID-19 is long overdue.

References

[1] World Health Organization. Immunization [homepage on the Internet]. No date [cited 2022 Mar]. Available from: *https://www.who.int/news-room/facts-in-pictures/detail/immunization*

[2] World Health Organization. Smallpox [homepage on the Internet]. No date [cited 2022 Mar]. Available from: *https://www.who.int/health-topics/smallpox# tab=tab_1*

[3] Gallagher P. The death of Dr Kailash Chand: How a lethal mix of NHS privatisation and lack of resources led to tragedy [homepage on the Internet]. iNews. 2021 [cited 2022 Jun 5]. Available from: *https://inews.co.uk/news/health/the-death-of-dr-kailash-chand-how-a-lethal-mix-of-nhs-privatisation-and-lack-of-resources-led-to-tragedy-1303449*

[4] Malhotra A, Redberg RF, Meier P. Saturated fat does not clog the arteries: Coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions. Br J Sports Med. 2017;51(15):1111–1112. *https://doi.org/10.1136/bjsports-2016-097285*

[5] Gundry SR. Abstract 10712: Observational findings of PULS cardiac test findings for inflammatory markers in patients receiving mRNA vaccines. Circulation. 2021;144(Suppl_1):A10712. *https://doi.org/10.1161/circ.144.suppl_1.10712*

[6] Axfors C, Ioannidis JPA. Infection fatality rate of COVID-19 in community-dwelling elderly populations. Eur J Epidemiol. In press 2022;37(3):235-249. *https://doi. org/10.1007/s10654-022-00853-w*

[7] Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383(27):2603–2615. *https://doi.org/ 10.1056/NEJMoa2034577*

[8] Burches E, Burches M. Efficacy, effectiveness and efficiency in the health care: The need for an agreement to clarify its meaning. Int Arch Public Health Community Med. 2020;4:35. *https://doi.org/10.23937/2643-4512/1710035*

[9] Smith P. CDC Director Rochelle Walensky: Too little caution and too much optimism [homepage on the Internet]. YouTube; 2022 [cited 2022 Jun 5]. Available from: *https://www.youtube.com/watch?v=8D-PS4nBFXBo*

[10] Walker G. Review COVID analysis 2020 [homepage on the Internet]. TheNNT [updated 2022 May 26]. [cited 2022 Jun 5]. Available from: *https://www.thennt.com/review-covid-analysis-2020/*

[11] Ignorance is not bliss: Why we need more empowered patients. Pharm J [serial online]. 2018 [cited 2022 Jun 5]. Available from: *https://pharmaceutical-journal.com/article/opinion/ignorance-is-not-bliss-why-we-need-more-empowered-patients*

[12] Malhotra A, Maughan D, Ansell J, et al. Choosing Wisely in the UK: The Academy of Medical Royal Colleges' initiative to reduce the harms of too much medicine. BMJ. 2015;350:h2308. *https://doi.org/10.1136/bmj.h2308*

[13] Gigerenzer G. Making sense of health statistics. Bull World Health Organ. 2009;87(8):567. *https://doi.org/10.2471/BLT.09.069872*

[14] Wollersheim S, Schwartz A. BLA Clinical Review Memorandum* [homepage on the Internet]. 2021 [cited 2022 Feb]. Available from: *https://www.fda.gov/ media/152256/download*

[15] US Food & Drug Administration. Antibody testing Is not currently recommended to assess immunity after COVID-19 vaccination: FDA Safety Communication [homepage on the Internet]. 2021 [cited 2022 Jul 15]. Available from: *https://www.fda.gov/medical-devices/safety-communications/antibody-testing-not-currently-recommended-assess-immunity-after-covid-19-vaccination-fda-safety*

[16] UK Health Security Agency. National flu and COVID-19 surveillance reports: 2021 to 2022 season [homepage on the Internet]. GOV. UK; 2021 [cited 2022 Jun 5]. Available from: *https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports-2021-to-2022-season*

[17] Fraiman J, Erviti J, Jones M, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. Vaccine. 2022 Aug 30:S0264-410X(22)01028-3.

[18] Ioannidis JPA. Factors influencing estimated effectiveness of COVID-19 vaccines in non-randomised studies. BMJ Evid Based Med. 2022;1. *https://doi. org/10.1136/bmjebm-2021-111901*

[19] Statistics. Statistics » COVID-19 daily deaths [homepage on the Internet]. [cited 2022 Jun 5]. Available from: *https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-daily-deaths/*

[20] Demasi M. Are adverse events in Covid-19 vaccine trials under-reported? [homepage on the Internet]. Investigative Journalism. Nov 2021 [cited 2022 Jun 5]. Available from: *https://maryannedemasi.com/publications/f/are-adverse- events-in-covid-19-vaccine-trials-under-reported*

[21] Karlstad Ø, Hovi P, Husby A, et al. SARS-CoV-2 vaccination and myocarditis in a nordic cohort study of 23 million residents. JAMA Cardiol. 2022;7(6):600–612. *https://doi.org/10.1001/jamacardio.2022.0583*

[22] Patone M, Mei XW, Handunnetthi L, et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nat Med 2022;28:410–422. *https://doi.org/10.1038/s41591-021- 01630-0*

[23] Diaz GA, Parsons GT, Gering SK, Meier AR, Hutchinson IV, Robicsek A. Myocarditis and pericarditis after vaccination for COVID-19. JAMA. 2021;326(12):1210–1212. *https://doi.org/10.1001/jama.2021.13443*

[24] Tuvali O, Tshori S, Derazne E, et al. The incidence of myocarditis and pericarditis in post COVID-19 unvaccinated patients-a large population-based study. J Clin Med Res. 2022;11(8):2219. *https://doi.org/10.3390/jcm11082219*

[25] Fronza M, Thavendiranathan P, Chan V, et al. Myocardial injury pattern at MRI in COVID-19 vaccine-associated myocarditis. Radiology. 2022;304(3):553–562. *https://doi.org/10.1148/radiol.212559*

[26] Hadley SM, Prakash A, Baker AL, et al. Follow-up cardiac magnetic resonance in children with vaccine-associated myocarditis. Eur J Pediatr. 2022;181(7): 2879–2883. *https://doi.org/10.1007/s00431-022-04482-z*

[27] Vogel G, Couzin-Frankel J. Israel reports link between rare cases of heart inflammation and COVID-19 vaccination in young men. Science [serial online]. 2021 [cited 2022 Jan];10. Available from: *https://covidcalltohumanity.org/wp-content/uploads/2021/06/Science_Israel-reports-link-between-rare-cases-of-heart-inflammation-and-COVID-19-vaccination-in-young-men.pdf*

[28] Chua GT, Kwan MYW, Chui CSL, et al. Epidemiology of acute myocarditis/ pericarditis in Hong Kong adolescents following comirnaty vaccination. Clin Infect Dis. 2021; ciab989. *https://doi.org/10.1093/cid/ciab989*

[29] Gahr M, Eller J, Connemann BJ, Schönfeldt-Lecuona C. Underreporting of adverse drug reactions: Results from a survey among physicians. Eur Psychiatry. 2017;41:S369. *https://doi.org/10.1016/j.eurpsy.2017.02.377*

[30] Coronavirus vaccine – Weekly summary of Yellow Card reporting [homepage on the Internet]. GOV.UK. [cited 2022 Jun 5]. Available from: *https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting*

[31] Yellow Card reports compared for Oxford/AstraZeneca and PfizerBioNTech products [homepage on the Internet]. 2022 [cited 2022 Jun 5]. Available from: *https://www.bmj.com/content/372/bmj.n699/rr-12*

[32] BBC News. AstraZeneca vaccine: Denmark stops rollout completely. BBC [serial online]. 2021 [cited 2022 Jun 5]; Available from: *https://www.bbc.co.uk/news/ world-europe-56744474*

[33] Medicines and Healthcare products Regulatory Agency. Medicines and medical device regulation: What you need to know [homepage on the Internet]. 2008 [cited 2022 Apr]. Available from: *https://www.adam-aspire.co.uk/wp-content/uploads/2011/02/mhra-medicines-and-medical-devices-regulation.pdf*

[34] Medicines and Healthcare products Regulatory Agency. All spontaneous suspected UK Adverse Drug Reaction (ADR) reports associated with the MMR vaccine in 2020 [homepage on the Internet]. 2021 [cited 2022 Apr]. Available from: *https://assets.publishing.service.gov.uk/government/uploads/system/ uploads/attachment_data/file/1041736/FOI_21-877-4.pdf*

[35] Norwegian Medicines Agency. Reported suspected adverse reactions to COVID19 vaccines as of 04.01.2022 [homepage on the Internet]. 2022 [cited 2022 May]. Available from: *https://legemiddelverket.no/Documents/English/ Covid-19/20220107%20Reported%20suspected%20adverse%20reactions%20 coronavirus%20vaccines%20-%20updated%20 20220113.pdf*

[36] McLachlan S, Dube K, Osman M, Chiketero PP. Analysis of COVID-19 vaccine death reports from the Vaccine Adverse Events Reporting System (VAERS) Database Interim: Results and analysis. ResearchGate. In press 2022. *https://doi. org/10.13140/RG.2.2.26987.26402*

[37] VAERS. Report an adverse event [homepage on the Internet]. [cited 2022 Jun 5]. Available from: *https://vaers.hhs.gov/reportevent.html*

[38] Kessler DA. Introducing MEDWatch. A new approach to reporting medication and device adverse effects and product problems. JAMA. 1993;269(21):2765–2768. *https://doi.org/10.1001/jama.1993.03500210065033*

[39] Rawlins MD. Pharmacovigilance: Paradise lost, regained or postponed? The William Withering Lecture 1994. J R Coll Physicians Lond. 1995;29(1):41–49.

[40] Yellow Card: Please help to reverse the decline in reporting of suspected adverse drug reactions [homepage on the Internet]. GOV. UK; 2019 [cited 2022 Jun 5]. Available from: *https://www.gov.uk/drug-safety-update/yellow-card-please-help-to-reverse-the-decline-in-reporting-of-suspected-adverse-drug-reactions*

[41] Patients with heart conditions/strokes from 2017-present day [homepage on the Internet]. WhatDoTheyKnow; 2022 [cited 2022 Jun 7]. Available from: *https://www.whatdotheyknow.com/request/patients_with_heart_conditionsst*

[42] HART. An epidemic of cardiac arrests [homepage on the Internet]. HART. HART Group; 2022 [cited 2022 Jun 5]. Available from: *https://www.hartgroup.org/an-epidemic-of-cardiac-arrests/*

[43] Sun CLF, Jaffe E, Levi R. Increased emergency cardiovascular events among under-40 population in Israel during vaccine rollout and third COVID-19 wave. Sci Rep. 2022;12(1):6978. *https://doi.org/10.1038/s41598-022-10928-z*

[44] Bansal S, Perincheri S, Fleming T, et al. Cutting edge: Circulating exosomes with covid spike protein are induced by BNT162b2 (Pfizer-BioNTech) vaccination prior to development of antibodies: A novel mechanism for immune activation by mRNA vaccines. J Immunol. 2021;207(10):2405–2410. *https://doi.org/10.4049/ jimmunol.2100637*

[45] Seneff S, Nigh G, Kyriakopoulos AM, McCullough PA. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs. Food Chem Toxicol. 2022;164:113008. *https://doi.org/10.1016/j. fct.2022.113008*

[46] Lei Y, Zhang J, Schiavon CR, et al. SARS-CoV-2 spike protein impairs endothelial function via downregulation of ACE 2. Circ Res. 2021;128(9):1323–1326. *https:// doi.org/10.1161/ CIRCRESAHA.121.318902*

[47] Ryu JK, Sozmen EG, Dixit K, et al. SARS-CoV-2 spike protein induces abnormal inflammatory blood clots neutralized by fibrin immunotherapy. bioRxiv. In press 2021. *https://doi.org/10.1101/2021.10.12.464152*

[48] Niel M, Smalley J, Fenton NE, Craig CEH. Latest statistics on England mortality data suggest systematic mis-categorisation of vaccine status and uncertain effectiveness of Covid-19 vaccination. ResearchGate. In press 2022. *https://doi. org/10.13140/RG.2.2.14176.20483*

Special notes

Acknowledgements: The author thanks Dr Clare Craig for edits and data analysis, and Alex Starling for comments and suggestions. The author is also grateful for the assistance of a scientist who wishes to remain anonymous on account of career pressure.

Competing interests: The author declares that he has no financial or personal relationships that may have inappropriately influenced him in writing this article.

Author's contribution: Aseem Malhotra is the sole author of this article.

Ethical considerations: This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability: Data sharing is not applicable to this article, as no new data were created or analysed in this study.

Disclaimer: The views and opinions expressed in this article are those of the author and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine Part 2*

by Aseem Malhotra

A pandemic of misinformation

What has become clear with regard to the coronavirus disease 2019 (COVID-19) vaccines is that we have a pandemic of misinformed doctors and a misinformed and unwittingly harmed public. Coercively mandating these COVID-19 injections (most certainly not an evidence-based policy) has been a particularly egregious mis-step, especially in the light of clear indicators suggesting that the use of these pharmaceutical interventions – especially in younger age groups – should have been suspended. Such policies continue to undermine the principles of ethical evidence-based medical practice and informed consent, to the detriment of optimising patient outcomes.

In his 2017 paper, 'How to survive the medical misinformation mess', Professor John Ioannidis and colleagues highlight that:

> [M]ost clinical trial results may be misleading or not useful for patients. Most guidelines (which many clinicians rely on to guide treatment decisions) do not fully acknowledge the poor quality of data on which they are based. Most medical stories in mass media do not meet criteria for accuracy, and many stories exaggerate benefit and minimise the harms.[1] (p. 1)

A senior doctor in regular contact with the United Kingdom's (UKs) Chief Medical Officer Professor Chris Whitty recently expressed concerns to me that he felt most of his colleagues in leadership positions influencing health policy may not be critically appraising the evidence and instead are relying on media stories on COVID-19 and the vaccine. This is consistent with the admission of Rochelle Walensky, the former chair of the Centers of Disease Control (CDC), whose optimism about the efficacy of Pfizer's COVID-19 vaccine came from reading a CNN news story, which was an almost verbatim reproduction of Pfizer's own press release.[2]

Has the UK's Chief Medical Officer Professor Chris Whitty critically appraised the evidence? Recently, he publicly shared a letter[3] outlining the importance of healthcare staff to become vaccinated against COVID-19, which was neither comprehensive nor consistent with the totality of the evidence: 'The COVID-19 vaccines are safe and effective'. It would have been more accurate to state that 'the vaccine is not completely safe and not anywhere close to being as effective as we'd hoped for. Not even in the same ball park when compared to the efficacy and safety of traditional vaccines'.

Professor Chris Whitty stated:

> Our professional responsibility is to get the COVID vaccines as recommended to protect our patients.[3]

He should have said as far as Omicron is concerned, that the vaccine offers little to no protection against infection. Data on the Delta variant also revealed that once infected there is no significant difference in transmission rates between the vaccinated and unvaccinated patients.

Professor Whitty's statements are especially surprising given that the CEO of Pfizer has stated that in relation to Omicron, 'We know that the two doses of a vaccine offer very limited protection, if any'.[5]

Could it be that Professor Whitty is also a victim of the medical misinformation mess?

There are four key drivers and seven sins that are at the root of the medical misinformation mess:

- Drivers:
    - Much published medical research is not reliable or is of uncertain reliability, offers no benefit to patients or is not useful for decision-makers;
    - Most healthcare professionals are not aware of this problem;

    - Even if they are aware of this problem, most healthcare professionals lack the skills necessary to evaluate the reliability and usefulness of medical evidence; and
    - Patients and families frequently lack relevant, accurate medical evidence and skilled guidance at the time of medical decision-making.[1]
- Sins:
    - Biased funding of research (research that is funded because it is likely to be profitable, not beneficial for patients)
    - Biased reporting in medical journals
    - Biased reporting in the media
    - Biased patient pamphlets
    - Commercial conflicts of interest
    - Defensive medicine
    - An inability of doctors to understand and communicate health statistics.[6]

Ioannidis and colleagues say:

> 'Ignorance of this problem, even at the highest levels of academic and clinical leadership, is profound'[1]

Compounded over several decades, these upstream and downstream risk factors for misinformation have had a devastating effect in the healthcare environment we find ourselves in today. Over-prescription of drugs is considered such a public health threat that two leading medical journals in the past 10 years (the *BMJ* and *JAMA Internal Medicine*) have launched campaigns to reduce the harms of too much medical intervention. According to the cofounder of the Cochrane Collaboration, Peter Gøtzsche, prescribed medications are the third most common cause of death globally after heart disease and cancer.[7] This is not surprising when one understands that most published research is misleading specifically where benefits from drug trials are exaggerated, and harms played down (Box 1[8]).

If a doctor is making clinical decisions on biased information, it will lead (at best) to suboptimal outcomes and (more concerningly) harm to patients.

Shortcomings of the medical profession

According to Professor Carl Heneghan, an urgent care General Practitioner and the director of the University of Oxford's Centre of Evidence-Based Medicine: 'with every intervention you do as a doctor you must ask yourself two questions: how much difference does it make? How do I know this?'[9]

Building on the Academy of Medical Royal College's Choosing Wisely campaign,[10] it is instructive to note that the General Medical Council in 2020 issued guidance on the duty of doctors to engage in shared decision-making with patients, underpinned by informed consent.[11]

1.	Trials are conducted of a study drug against a treatment known to be inferior
2.	Use multiple endpoints in the trial and select for publication those that give favourable results
3.	Do multicentre trials and select for publication results from centres that are favourable
4.	Conduct subgroup analyses and select for publication those that are favourable
5.	Present results that exaggerate the benefit – for example, use of relative risks as opposed to absolute risks
6.	Conduct trials on subjects that are unrepresentative of the patient population
7.	Conflate primary and secondary endpoints in the published report
8.	Conceal unblinded patients and include them in efficacy analyses for publication
9.	Exclude placebo responders in the wash-out phase of the trial
10.	Delay publication of negative trial results until positive trial results are published
11.	Conceal negative trial results whilst publishing only positive trial results
12.	Conceal serious adverse events
13.	Fail to distinguish clinical from statistical significance

BOX 1: Major limitations in the interpretation, external validity and usefulness of drug industry-sponsored clinical trials.
Source: Adapted from Jureidini J, McHenry L. The illusion of evidence-based medicine. Adelaide: Wakefield Press; 2020

There are six components essential to informed decision-making:

(1) description of the nature of the decision; (2) discussion of alternatives; (3) discussion of risks and benefits (in absolute terms); (4) discussion of related uncertainties; (5) assessment of the patient's understanding; and (6) elicitation of the patient's preference.

If the administration of the vaccine did not adhere to these principles (which is likely widespread, consistent with historical evidence,[12]) then it is also a substantial breach of General Medical Council duties of a doctor to 'give patients the information they want or need in a way that they can understand'.[13]

It is instructive to note that the greater the financial interests in a given field, the less likely the research findings are to be true.[14] As has been already demonstrated in Part 1[15] of this article, mandating a novel emergency-use authorisation vaccine to non-vulnerable people has little to no effect on preventing infection and serious illness, therefore does not have any scientific validity, and therefore breaches the principles of informed consent. It does, however, dramatically increase the profits of the manufacturer. By expanding the uptake of the mRNA vaccine to the majority of the population who are very low-risk of serious complications from COVID-19 but are more likely to suffer serious and or life-threatening adverse events such as myocarditis or sudden cardiac death, Pfizer has generated tens of billions of dollars in revenues to date, making it one of the most lucrative products in history. If policymakers had focused more on protecting the vulnerable – and doctors had been given the opportunity to practise shared decision-making with patients using transparent communication of risk and benefit – patient outcomes would likely have been greatly improved,[16] but the drug companies' profits would likely have been a tiny fraction of what they actually generated. As former editor of the *New England Journal of Medicine* Dr Marcia Angell has previously pointed out, 'the real battle in healthcare is one of truth *versus* money'.[17]

Institutional corruption and erosion of public trust

Institutional corruption is defined as an institution's deviation from a baseline of integrity.[18] There is a long-documented history (both through studies and lawsuits) of the strategies in which drug companies hide, ignore or misrepresent evidence about new drugs. Distortion of medical literature and misrepresentation of data by companies keen to expand the marketplace for their product may result in overprescribing with predictable consequences of millions of patients suffering from avoidable adverse reactions.

Prior to 2020 there already existed gross shortcomings in the medical–industrial complex – there has been too much pharmaceutical industry influence on clinical decision- making. This has not gone unnoticed, resulting in a growing crisis of trust in medical research; a report by the Academy of Medical Sciences in 2017 revealed that 82% of GPs and 63% of the public did not believe the results of pharmaceutical industry-sponsored research

to be unbiased.[19] Similarly, only 37% of the public trust medical research compared to 65% who trust the experience of their friends and family.[20]

This growing lack of trust – most recently exacerbated by coercion, vaccine passports and little mainstream media coverage of an unprecedented scale of reported vaccine harms in the population – has been most recently exemplified by eight million people in the UK refusing to take the COVID-19 booster. In addition, all the attention on COVID-19 (which poses almost zero risk to children in its current Omicron form) diverts attention away from, and even worse raises the suspicion about, more efficacious and safe interventions such as the measles, mumps, rubella (MMR) vaccine. Indeed, in the UK MMR vaccination rates have hit their lowest for 10 years.

Failure of regulation and research misconduct

Authorities want the public to 'trust the science', but vaccine manufacturers have successfully negotiated deals with several major governments globally that indemnify them against any financial liability in the event of vaccine-related harm. Interestingly, India, the world's largest democracy, refused to grant Pfizer indemnity from harms for its vaccine. An Indian government source told Reuters:

> [T]he whole problem with Pfizer is the indemnity bond. Why should we sign it? If something happens, a patient dies, we will not be able to question them [Pfizer]. If somebody challenges in a court of law, the central government will be responsible for everything, not the company.[21]

Pfizer walked away from the Indian market rather than undertake a local safety and immunogenicity study.[22]

It is important to first understand that drug companies have a fiduciary obligation to deliver profits to their shareholders, not any legal responsibility to provide patients with the best treatment. At a talk at the Centre of Evidence-Based Medicine in Oxford in 2014, Peter Wilmshurst said the real scandal is that many of those with a responsibility to patients and scientific integrity (doctors, academic institutions and medical journals) often collude with industry for financial gain.[23] It is this very industry that has been found guilty of the most egregious corporate crimes: between 2003 and 2016 the top 11 pharmaceutical companies paid $28.8 billion in fines just within the United States (US),[24] much of it for criminal activity such as the illegal marketing of drugs, manipulation of results and hiding data on harms. As pointed out in the *BMJ*, since then no systemic changes have been made to mitigate these harms.[9]

In an international survey of respondents from higher education institutions, 14% admitted to knowing a colleague who fabricated, falsified and modified data, and 34% of scientists report questionable research practices that

Academic institutions bear responsibility for the pressure to publish for career advancement that can result in research misconduct.

A record of prominent publication is likely to attract future funding, which institutions demand, and good publicity, which institutions desire.

Other pressures for misconduct come from the association of academic institution with industry, such as when investigators or their institutions hold patents or shares, or they receive payments from industry, so that there is financial pressure to publish research that will be profitable for the company and to suppress 'negative' findings.

Some publications are simply organised criminal activities, which may be at the behest of sponsors, when prominent academics are paid large sums of money to publish false data by industry, or a sponsor may be one of the victims, when payments for conducting research are made to 'investigators', who simply fabricate data.

Medical journals have financial pressures to publish positive findings of research on drugs and medical devices, because their manufacturers buy reprints of the papers for distribution to doctors and they pay for advertisements linked to articles favourable to their product.

Academic institutions and journals depend on the public belief in the integrity of science, so they are unwilling to admit the seriousness and frequency of research misconduct.

To protect their reputations academic institutions conceal research misconduct, destroy evidence and silence whistle-blowers.

Journals are reluctant to admit that they published flawed research, so they commonly refuse to publish failures to replicate.

Fear of a libel action contributes to the failure to expose research misconduct.

Investigation of research misconduct may be difficult because there may be international collaboration between investigators, many of whom do not see the full data, and the resulting publications may be in journals that are published in countries where none of the investigators work.

The bodies that investigate research misconduct in the UK (such as the GMC and UKRIO) are hampered by a desire to play down the problem, by lack of proper forensic skills when investigating, by inconsistent interpretation of rules and by inadequate powers to compel the cooperation of academic institutions and journals.

Because lenient sanctions are imposed, institutions believe that the misconduct is not very serious, and potential research fraudsters are not deterred.

Box 2: Written evidence from Dr Peter Wilmshurst to UK Parliamentary Science and Technology Research Integrity Committee (June 2018).

Source: Wilmshurst P. Written evidence [homepage on the Internet]. 2017 [cited 2022 Jun 5]. Available from: *http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology-committee/research-integrity/ written/68813.html*

GMC, General Medical Council; UKRIO, United Kingdom Research Integrity Office.

included selective reporting of clinical outcomes in published research, and concealing conflicts of interest.[25] An egregious documented case of research misconduct involved a prominent Dutch physician whose work influenced the European Society of Cardiology guidelines on the use of beta blocker drugs in non-cardiac surgery. He was dismissed from Erasmus University for 'violations in academic integrity', including using 'fictitious data' in research. It's estimated that these guidelines increased patient mortality by 27% resulting in 800,000 excess deaths across Europe over an 8-year period.[26]

In evidence submitted to the UK parliamentary science and technology review into research integrity committee in 2017 (Chaired by Sir Norman Lamb), Dr Peter Wilmshurst lists a number of risk factors that drive research misconduct in British institutions (see Box 227). His solution, which I agree with, would be to ensure that serious forms of research misconduct are made into criminal offences with meaningful sanctions and that allegations of such activity should be investigated by an independent body with legal powers.[27]

One researcher at a prestigious UK institution contacted me to inform me that in his cardiology department a group of academics were deliberately suppressing research revealing that the mRNA vaccine was shown to significantly increase coronary risk when determined by cardiac imaging as compared to the unvaccinated. The chair of the group expressed concerns that publishing the data may result in loss of funding from the pharmaceutical industry.[28] After I had alluded to this on *GB News*, the whistle-blower informed me that non-disclosure agreement letters were sent to all members of the team involved in this particular area of research.

Evidence-based medicine and COVID-19 vaccine roll-out

Neither the drug regulators nor the vaccine manufacturers have yet to share all the raw data from the pivotal trials for the COVID-19 vaccines.[29] The raw data from clinical trials comprise thousands of pages that have yet to be released for independent scrutiny. This is important because historically when independent researchers have on occasion gained access to these data then it can completely overturn the conclusions of the published trials. A case in point is Tamiflu.[30] Getting access to clinical case reports for Tamiflu ultimately revealed that the drug was no more effective than paracetamol for influenza and also came with small but significant harms. The UK government had spent half a billion dollars stockpiling a drug that in effect proved to be useless despite claims by the manufacturers (Roche, Basil, Switzerland) that it

shortened the duration and severity of the illness. The independent researchers who were able to analyse the data concluded that all industry-sponsored research should be considered marketing until proved otherwise.

It is against this backdrop that transparency advocates sued the Food and Drug Administration (FDA) to gain access to the data upon which the Pfizer (BNT162b2) vaccine was granted emergency use authorisation.[31] The FDA wanted a US Federal court judge to allow the agency 55 years to release these data.[32] Why would the FDA – 'which is responsible for the oversight of more than $2.7 trillion in consumption of food, medical products, and tobacco'[33] – do this? Secrecy should never surround any public health intervention. The lawyer acting on behalf of the plaintiff Aaron Siri reported that:

> [T]he government also sought to delay full release of the data it relied upon to license this product until almost every American alive today is dead. That form of governance is destructive to liberty and antithetical to the openness required in a democratic society.[31]

Instead, the judge ordered the FDA to release the data over a period of eight months after all commercially sensitive information has been redacted.

A major risk factor for failure to protect the public from such harms is lack of independence of the regulator. The FDA's Center for Drug Evaluation Research (CDER) receives 65% of its funding from the pharmaceutical industry (mainly in the form of user fees).[34] For example, as part of the approval process for its COVID-19 vaccine, Pfizer made a wire transfer to the FDA of $2,875,842 in May 2021[35] under the Prescription Drug User Fee Act of 1992.[36] Full FDA approval for Pfizer's COVID-19 injection duly followed in August 2021[37] despite recent evidence emerging that the original RCT data suggested a greater risk of serious adverse events from the vaccine than from hospitalisation because of COVID-19.

Separate analyses have revealed the overwhelming majority of new drugs that have been approved by the FDA in the past few decades have later been shown to be just copies of old ones, which is not surprising when one understands that drug companies spend 19 times more on marketing than they do on researching new molecular entities, which all contributes to considerable waste.

Between 2000 and 2008, of the 667 drugs approved by the FDA, only 11% were found to be truly innovative. In the US it is estimated that 30% to 50% of healthcare activity brings no benefit to patients. Extraordinarily, a survey of FDA scientists revealed 70% of them did not feel the FDA had the resources

to perform effectively in its mission in 'protecting public health … and helping the public get accurate science-based information to use medicines and foods to improve their health'.[38]

An analysis of every new drug product approved in France between 2002 and 2011 revealed only 8% offered some advantages and double that number – at 15.6% – were found to be more harmful than beneficial with the majority of other new drugs being essentially copies of old ones contributing to a colossal waste of public money.[18] Similar conclusions have been drawn in Canada and Holland. In my opinion the evidence is overwhelming that the overall net effect of the pharmaceutical industry in the last few decades on society and population health has been a hugely negative one.

COVID-19 vaccination in lower risk people

Irrespective of the merits of inoculating higher risk groups where a small but significant benefit may exist against the original Wuhan strain, vaccinating lower risk children in the name of preventing asymptomatic transmission has no strong scientific validity and therefore exposes them to possible harm.

In the UK the Office for National Statistics has revealed an as-yet unexplained significant increase in deaths over the 5-year average in 15 to 19-year-old children since May 2021. Given what we now know of potential harms especially in relation to myocarditis, myocardial infarction and sudden cardiac death (even in 16 to 39-year-olds), has the COVID-19 vaccine been excluded as a possible cause?[39]

In September 2021, the Joint Committee on Vaccination and Immunisation (JCVI) made a controversial recommendation that the Pfizer-BioNTech vaccine is marginally beneficial for 12 to 15-year-old children.[40] The Medicines and Healthcare products Regulatory Agency (MHRA, the UK's equivalent of the FDA) had previously stated that:

> [T]hey have carefully reviewed clinical trial data for Pfizer-BioNtech vaccine in over 2000 children aged 12–15 years of age and have concluded that the benefits of this vaccine outweigh any risk and that it is effective and acceptably safe in this age group … No new side effects were identified and the safety data in children was comparable to that seen in young adults. As in the young adult age group, the majority of adverse events were mild to moderate, relating to reactogenicity (e.g. sore arm and tiredness).[41]

Is this in keeping with the totality of the evidence?

Award-winning investigative science journalist Dr Maryanne Demasi published the harrowing story of one of those trial participants, 12-year-old Maddie De Garay. After experiencing severe abdominal pain followed by seizures she was admitted to hospital and is now left permanently disabled, wheelchair-bound and fed through a nasogastric tube. In Pfizer's trial they reported her adverse effect as mild: stomach upset.[42]

It is important to emphasise that the risk of death from COVID-19 in a 12 to 15-year-old is close to zero at 1 in 76,000. In keeping with the principles of ethical evidence-based medical practice through shared decision-making, parents need to be told that there are no high-quality data regarding children to the effect that the vaccine will prevent infection, transmission, serious illness or death, but it may come with serious side effects of myocarditis – particularly in young males where it occurs in up to 1 in 2,700[43] – and serious disability as a general principle of transparent communication of risk and informed consent. Without understanding the numbers involved the public is vulnerable to their hopes and anxieties being exploited by political and commercial interests.

Could financial interests be biasing the recommendations?

On its website the MHRA declares that most of its funding comes from the pharmaceutical industry and £3 million (UK pounds) from the Bill and Melinda Gates Foundation (BMGF). Are policymakers and the public aware that the foundation's corporate stock endowment is heavily invested in food (including McDonald's and Coca-Cola) and pharmaceutical companies, directly and indirectly? As pointed out in a 2009 *Lancet* paper, the funders' priorities are often driven by personal interests, not the health priority interests of the recipient country.[44] 'The BMGF's portfolio of pharmaceutical companies calls for attention given Mr Gates' personal belief in the role of patents as motors for innovation in medicines and medical technology'.[45]

Obesity researcher Dr Zoe Harcombe has also investigated the financial ties that could potentially be biasing the view of the joint committee for vaccines and immunisation and discovered that the subcommittee members work for organisations that receive in total $1bn from the BMGF.[46] It is also worth noting that Professor Wei Shen Lim, chairman of the JCVI vaccine subcommittee, has direct responsibility for material levels of funding received by his department from Pfizer.[47] This is not in any way suggesting that the JCVI have acted in an improper way, but when confidence in an organisation such as the JCVI is imperative it is essential that there should be no perceptions of conflicts of interest. The systems of selection of panellists, the scrutiny of evidence and the methodology and openness of their recommendations need to be beyond reproach.

The most proximate cause of detrimental health outcomes: corporate power and the commercial determinants of health

The commercial determinants of health are best defined by 'strategies and approaches adopted by the private sector to promote products and choices that are detrimental to health'.[48] Corporations exert their power by a combination of factors including intellectual exploitation. This includes the ability to define the dominant narrative: set the rules and procedures by which society is governed; determine the rights, living and working conditions of ordinary people; and take ownership of knowledge and ideas[49] (see Figure 145). It appears that in the case of the mRNA vaccine, Pfizer has at least to some degree taken advantage of this corporate framework strategy by shaping the knowledge environment (Pfizer was responsible for the design and conduct of the trial, data collection, data analysis, data interpretation and the writing of the manuscript), the political environment (lobbying), preference shaping (corporate foundations and philanthropy, spokespersons and key opinion leaders, capture of the media), the legal environment (limit

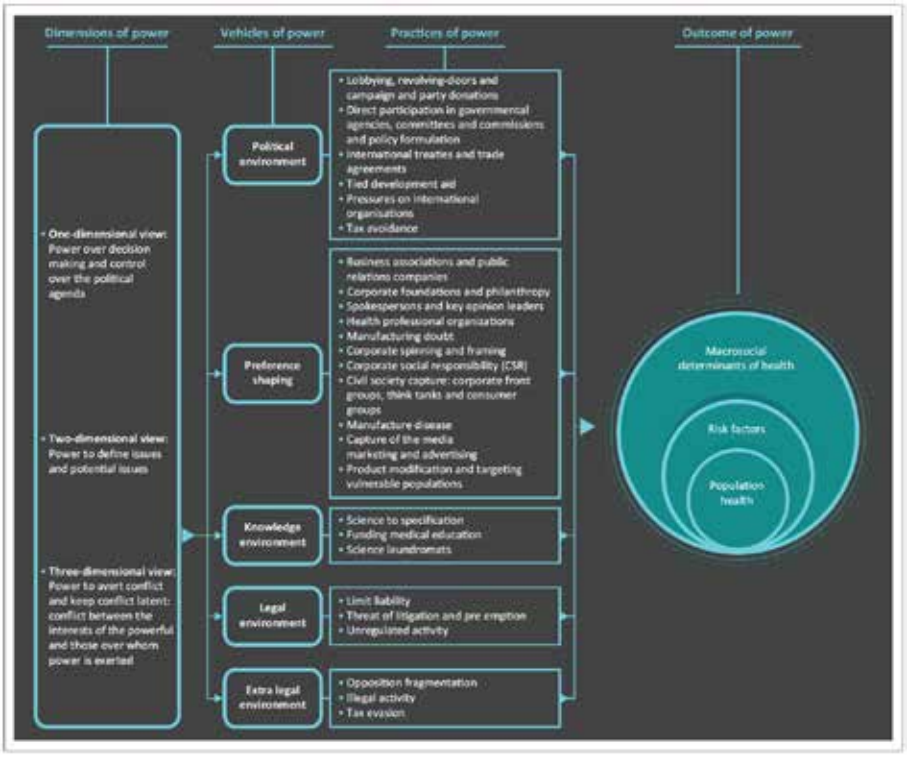


Figure 1: Diagram of dimensions, vehicles, practices and outcomes of power.

Source: Madureira Lima J, Galea S. Corporate practices and health: A framework and mechanisms. Global Health. 2018;14(1):21

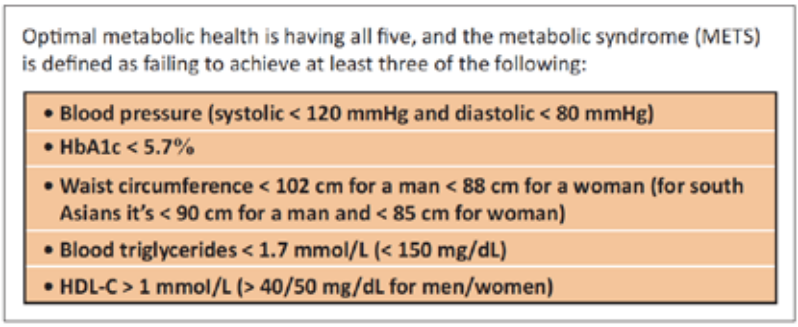


Figure 2: Markers of metabolic health.

Source: Araujo J, Cai J, Stevens J. Prevalence of optimal metabolic health in American adults: National Health and Nutrition Examination Survey 2009–2016. Metab Syndr Relat Disord. 2019;17(1):46–52. https://doi.org/10.1089/met.2018.0105

HDL-C, high density lipoprotein cholesterol.

liability) and the extra-legal environment (opposition fragmentation by de-platforming critics of the current dominant narrative that the vaccine is safe and effective).[45] Consequently, it has made tens of billions of dollars in revenue from a product that in comparison with time-tested traditional vaccines and most other drugs has extremely poor efficacy and unprecedented reports of serious harms.

Biased reporting in the media and censorship of legitimate scientific debate

Corporations are able to shape preferences and frame the dominant narratives on the determinants of health, through unchecked invisible power. One pathway is through the ownership of mass media. The global media market is dominated by seven corporations and chains that own 80% of the newspapers in the US.[50] The grants paid to global media companies by the BMGF are notable – for example, The Guardian Media Group has been in receipt of over $12m in grants from the BMGF over the last 12 years. Control over advertising in print and broadcast media also has an influence over editorial decisions. Most health journalists (including a number I have spoken to) are generally unaware that the information they obtain for stories has been deliberately shaped by the private interests of manufacturers and 'research' universities.

The BBC, though seemingly not directly influenced by industry interests, has traditionally been seen by some as the UK's most trusted media source. Its coverage of issues surrounding COVID-19 has in my view (possibly through additional government pressure) been extremely poor and – specifically on issues surrounding the vaccine – grossly negligent. During a recent report on tennis player Novak Djokovic explaining his decision

not to take the vaccine until he has more information on its benefits and harms, a reporter asked the question 'how much more information does he need?' The reporter failed to mention the fact that Djokovic has had COVID-19 and that evidence suggests that natural immunity offers substantial protection against reinfection and severe disease, and that systemic side effects are almost threefold more likely in those with natural immunity who subsequently get vaccinated. Furthermore, the BBC falsely framed a guest of popular podcast host Joe Rogan, Dr Robert Malone, as a 'known anti-vaxxer, who is against vaccinating kids', failing to mention that Dr Malone is a co-inventor of the very technology that led to the vaccine, has spent 20 years in vaccine development at US government level and was one of the first to actually receive the Moderna injections twice. The BBC also strangely failed to cover perhaps one of the most important stories of the pandemic published in one of the most respected and influential medical journals in the world: An investigation by the *BMJ* revealed evidence of poor practices at a contract research company involved in Pfizer's pivotal COVID-19 vaccine trial. A regional director employed at one of the trial sites in Texas, US, documented evidence that Pfizer falsified data, unblinded patients, employed inadequately controlled vaccinators and was slow to follow up on adverse events. The very same day that she emailed her complaint to the FDA she was fired from her position.[51] She subsequently commenced litigation under whistle-blower legislation for fraud against Pfizer on behalf of the American Government (and the people of the US). Pfizer's motion to dismiss the case (which apparently did not sway the judge) was based on the fact that the FDA had not acted on her (or any other) complaints, hence the allegations were not material to the Government.

In the US, Senator Ron Johnson conducted hearings with healthcare professionals who were presenting data on clear, substantial and very common adverse effects from the mRNA injections, and these deserved widespread public attention. He said 'the mainstream media are co-conspirators in this political dirty trick. Will they be held accountable for their role in this deception?'[52]

Social media platforms continue to be guilty of spreading misinformation. Their business model that focuses on increasing engagement at any cost makes society increasingly lose access to the truth and worsens our capacity for empathy as individuals, sowing even greater division and hostility. The so-called 'fact checkers' have censored anything that challenges the prevailing mainstream narrative (the establishment is trustworthy, and the vaccines are completely safe). They even labelled the BMJ's investigation

into potential fraud in Pfizer's pivotal trial as misinformation and stopped users sharing the story on their platform. A letter from the journal's current and former editor-in-chief to Mark Zuckerberg calls into question the integrity of Facebook's fact checkers:

> [R]ather than investing a proportion of Meta's substantial profits to help ensure the accuracy of medical information shared through social media, you apparently delegated responsibility to people incompetent in carrying out this crucial task.[53] (p. 1)

It has also come to light that Facebook has partnered with drug company Merck in deciding what content should be censored on its platform in relation to COVID-19 and the vaccine.[54] Is Facebook aware that Merck paid one of the largest fines in US history for being found guilty of fraud in relation to their pain killer Vioxx?[55] Not only did an investigation reveal that the drug did not reduce gastric bleeds (their original key selling point) in comparison with ibuprofen, but it significantly increased the risk of heart attacks and strokes, estimated to have caused excess deaths of between 40,000 and 60,000 Americans over a 5-year period.[56]

Improving metabolic health

Failure of public health messaging and policies to help people to improve their lifestyles during the pandemic represents a missed opportunity to mitigate harms from respiratory diseases such as COVID-19. After age, the biggest risk factor for worse COVID-19 outcomes has been obesity and conditions related to excess body fat. More than 90% of the deaths from COVID-19 occurred in countries where more than 50% of the population is overweight or obese. The United Kingdom's biobank data during the first wave revealed a more than fourfold higher risk in hospitalisation from COVID-19 depending on lifestyle factors. For example, a non-smoking adult in the mid-fifties with a normal body mass index (BMI) and obtaining adequate physical activity levels had a 1 in 1,521 chance of being admitted to hospital after contracting COVID-19, whereas an obese, smoking, sedentary person's risk was 1 in 327.[57]

Postulated pathophysiological mechanisms of risk and complications from infection include an array of markers that have insulin resistance and chronic inflammation at the root.

Even a single high blood-glucose reading in non-diabetics (a marker of insulin resistance) admitted to hospital has been shown to be associated with worse outcomes.[58] It has also recently emerged in the UK that of the 175,256 deaths associated with COVID-19 (2020–2021 inclusive),

fewer than 10% (17,371) had COVID-19 as the only cause on the death certificate, suggesting that the risk to those with optimal metabolic health from COVID-19 (Figure 2[59]) was notably smaller, as per the results of the aforementioned UK biobank study.[60]

The government and medical authorities should have made it a priority to emphasise the importance of eliminating ultra-processed foods and low-quality carbohydrates to reduce risk. They could have made the public aware that reversal of metabolic syndrome has been shown to occur in up to 50% of patients – independent of weight loss – within four weeks of dietary changes alone.[61]

The coronavirus disease 2019 was a momentary crisis that exploited a slow pandemic of poor metabolic health (see Figure 2[59]), which is also the predominant root cause behind the major chronic diseases that have been putting healthcare systems around the world under increasing strain for decades. It is estimated that healthier lifestyles would (in absolute terms) potentially eliminate 40% of cancers and 75% of cardiovascular disease and type 2 diabetes.[63]

Optimising metabolic health would not just improve immune resilience but also reduce the burden of heart disease, type 2 diabetes, cancer and dementia. Learning lessons from tobacco control, policy changes that target the availability, acceptability and affordability of ultra-processed food and drink and low-quality carbohydrates would substantially reduce the burden of obesity and related metabolic diseases, and also likely optimise immune resilience in populations within a few years (see Box 3[62]).

The solutions

There was never any evidence justifying any COVID-19 vaccine mandates, passports or any of the other coercive measures adopted by various governments worldwide. Every patient who was offered any COVID-19 vaccine should have been made aware of what the risk from COVID-19 is according to age and risk factors. In keeping with ethical medical practice, doctors should have informed patients of their absolute risk reduction for infection from previous more lethal variants being approximately 0.84% or 1 in 119 (based on non-transparent data) and that this level of protection only lasts for a few months. They should also have provided more precise and robust data on what the actual absolute individual risk reduction of COVID-19 death from the vaccine is, and also what the true rates are of serious adverse events (such as permanent disability, hospitalisation or death).

It is only when doctors and patients have all this information that they can

1. Taxation of all ultra-processed foods and drinks needs to be enforced with the money gained going directly to subsidise whole and minimally processed foods such as fruit and vegetables
2. All medical students and doctors need to have adequate training in nutrition and lifestyle medicine
3. Every doctor should be measuring the metabolic health of their patients and making lifestyle prescriptions specifically linked to diet, physical activity and stress reduction to improve those health markers as their first-line intervention before the use of medication
4. Compulsory nutrition education and cooking skills introduced into all school curriculums
5. All hospital chief executives need to be made accountable for allowing the sale of ultra-processed food on hospital grounds, as it continues to harm the health of staff and patients and legitimises the acceptability of such food consumption to the wider public
6. A ban on advertising of all ultra-processed food and drink on television and online demand services
7. A public education campaign is needed to help consumers understand what ultra-processed food is and the harm it causes
8. A complete ban and dissociation of ultra-processed food and drink sponsorship of sports teams and sporting events
9. Local authorities should encourage active travel and protect and increase green spaces in urban areas to make the healthy option the easy option
10. Medical staff, including doctors, nurses and dietitians, should themselves be assessed on their metabolic health and encouraged and helped to improve it, not just to set an example to patients but to optimise their own health and performance.

BOX 3: Policies to curb obesity and lifestyle-related disease.

Source: Malhotra A. The 21-day immunity plan. United Kingdom: Yellow Kite; 2021.

1. Is the application of individual clinical expertise with best available evidence and taking into consideration patient preferences and values in order to improve patient outcomes (relieve suffering and pain, treat illness and address risks to health)
2. Makes the ethical care of the patient its top priority
3. Demands individualised evidence in a format that clinicians and patients can understand
4. Is characterised by expert judgement rather than mechanical rule following
5. Shares decisions with patients through meaningful conversations
6. Builds on a strong clinician–patient relationship and the human aspect of care
7. Applies these principles at community level for evidence-based public health

Actions to deliver real evidence-based medicine

1. Although the pharmaceutical industry plays an important role in developing new drugs, they should play no role in testing them
2. All results of all trials that involve humans must be made publicly available
3. Regulators such as the FDA and MHRA must be publicly funded, and not receive any money from the pharmaceutical industry
4. Independent researchers must increasingly shape the production, synthesis and dissemination of high-quality clinical and public health evidence
5. Medical education should not be funded or sponsored by the pharmaceutical industry
6. Patients must demand better evidence, better presented (using absolute and not relative risk), better explained and applied in a more personalised way

BOX 4: Defining real evidence-based medicine and actions to deliver it.

Source: Adapted from Greenhalgh T, Howick J, Maskrey N. Evidence based medicine Renaissance Group. Evidence based medicine: A movement in crisis? BMJ. 2014;348:g3725. *https://doi.org/10.1136/bmj.g3725*

then be empowered to have frank decision-making conversations on whether any treatment – including this vaccine – is right for them.

The profession must explain that optimising metabolic health will give patients the best chance for ensuring they are not just resilient to infection but reducing their risk of chronic disease including heart disease, cancer and dementia.

The time has come to stop misleading evidence flowing downstream into media reporting and clinical decision-making and resulting in unethical and unscientific policy decisions. It is time for real evidence-based medicine (Box 4[64]).

There is also a strong scientific, ethical and moral case to be made that the current mRNA vaccine administration must stop until Pfizer releases all the raw data for independent scrutiny.[30] This will allow a more accurate understanding of which groups are more likely to potentially benefit from the vaccine *versus* those who are more likely to be harmed.

Given all the recent well-documented aforementioned shortcomings in medical research integrity (including that possibly half the published medical literature 'may simply be untrue'), the editor of the *Lancet* Richard Horton wrote in 2015 that science has taken a turn towards darkness and asked who is going to take the first step in cleaning up the system.[65] The unprecedented roll-out of an emergency use authorisation vaccine without access to the raw data, with increasing evidence of substantial harms, compounded by mandates that appear to serve no purpose other than to bolster profits of the drug industry, have highlighted modern medicine's worst failings on an epic scale, with additional catastrophic harms to trust in public health.

We must use this as an opportunity to transform the system to produce better doctors, better decision-making and healthier patients, and to restore trust in medicine and public health. Until all the raw data on the mRNA COVID-19 vaccines have been independently analysed, any claims purporting that they confer a net benefit to humankind cannot be considered to be evidence-based.

References

[1] Ioannidis JPA, Stuart ME, Brownlee S, Strite SA. How to survive the medical misinformation mess. Eur J Clin Invest. 2017;47(11):795–802. *https://doi. org/10.1111/eci.12834*

[2] Thacker PD. Pfizer's press release pandemic policy. The Disinformation Chronicle [serial online]. 2022 [cited 2022 Jun 5]. Available from: *https:// disinformationchronicle.substack.com/p/pfizers-press-release-pandemic-policy*

[3] Whitty C. With the Chief Nursing Officer, Chief Midwifery Officer, Medical Directors and others, I have written to NHS colleagues about the professional responsibility to protect patients from COVID-19. This includes getting vaccinated, as the great majority have [homepage on the Internet]. Twitter; 2022 [cited 2022 May]. Available from: *https://twitter.com/cmo_england/ status/1490975576676769794*

[4] Singanayagam A, Hakki S, Dunning J, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: A prospective, longitudinal, cohort study. Lancet Infect Dis. 2022;22(2):183–195. *https://doi.org/10.1016/S1473-3099(21)00648-4*

[5] CNBC News Release. First on CNBC: CNBC transcript: Pfizer chairman and CEO Albert Bourla speaks with CNBC's 'squawk box' today. CNBC [serial online]. 2022 [cited 2022 June]. Available from: *https://www.cnbc.com/2022/01/10/first-on-cnbc-cnbc-transcript-pfizer-chairman-and-ceo-albert-bourla-speaks-with-cnbcs- squawk-box-today.html*

[6] The MIT Press. Better doctors, better patients, better decisions [homepage on the Internet]. Cambridge: The MIT Press. 2011 [cited 2022 Jun 5]. Available from: *https://mitpress.mit.edu/9780262518529/better-doctors-better-patients-better- decisions/*

[7] BMJ. Peter C Gøtzsche: Prescription drugs are the third leading cause of death. The BMJ [serial online]. 2016 [cited 2022 Jun 5]. Available from: *https://blogs.bmj.com/bmj/2016/06/16/peter-c-gotzsche-prescription-drugs-are-the-third- leading-cause-of-death/*

[8] Jureidini J, McHenry L. The illusion of evidence based medicine. Adelaide: Wakefield Press; 2020.

[9] Heneghan C, Mahtani KR, Goldacre B, Godlee F, Macdonald H, Jarvies D. Evidence based medicine manifesto for better healthcare. BMJ. 2017;357:j2973. *https:// doi.org/10.1136/bmj.j2973*

[10] Malhotra A, Maughan D, Ansell J, et al. Choosing Wisely in the UK: The Academy of Medical Royal Colleges' initiative to reduce the harms of too much medicine. BMJ. 2015;350:h2308. *https://doi.org/10.1136/bmj.h2308*

[11] General Medical Council. Shared decision making is key to good patient care – GMC guidance [homepage on the Internet]. [cited 2022 Jun 5]. Available from: *https://www.gmc-uk.org/news/news-archive/shared-decision-making-is-key-to- good-patient-care---gmc-guidance*

[12] Braddock CH 3rd, Edwards KA, Hasenberg NM, Laidley TL, Levinson W. Informed decision making in outpatient practice: Time to get back to basics. JAMA. 1999;282(24):2313–2320. *https://doi.org/10.1001/jama.282.24.2313*

[13] Duties of a doctor registered with the General Medical Council [homepage on the Internet]. Royal College of Surgeons. [cited 2022 Feb]. Available from: *https:// www.rcseng.ac.uk/standards-and-research/gsp/duties-of-a-doctor-registered- with-the-general-medical-council/*

[14] Ioannidis JPA. Why most published research findings are false. PLoS Med. 2005;2(8):e124. https://doi.org/10.1371/journal.pmed.0020124

[15] Malhotra A. Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine - Part 1. J. insul. resist. 2022;5(1), a71. *https://doi.org/10.4102/jir.v5i1.71*

[16] Stacey D, Légaré F, Lewis K, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2017;4:CD001431. *https:// doi.org/10.1002/14651858.CD001431.pub5*

[17] Malhotra A. Finance trumps patients at every level – UK healthcare needs an inquiry. The Guardian [serial online]. The Guardian. 2017 [cited 2022 Feb]. Available from: *https://amp.theguardian.com/health-care-network/2017/nov/21/ finance-trumps-patients-uk-healthcare-needs-inquiry*

[18] Light DW, Lexchin J, Darrow JJ. Institutional corruption of pharmaceuticals and the myth of safe and effective drugs. J Law Med Ethics. 2013;41(3):590–600. *https:// doi.org/10.1111/jlme.12068*

[19] The Academy of Medical Sciences. Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines [homepage on the Internet]. 2017 [cited 2022 Mar]. Available from: *https://acmedsci.ac.uk/file- download/44970096*

[20] The Academy of Medical Sciences. Action needed to prevent confusion over medicines [homepage on the Internet]. [cited 2022 Jun 5]. Available from: *https://acmedsci.ac.uk/more/news/action-needed-to-prevent-confusion-over-medicines*

[21] Singh V. Pfizer hits deadlock with India over vaccine indemnity issue: Reuters [homepage on the Internet]. Yahoo!Finance; 2021 [cited 2022 Jun 5]. Available from: *https://finance.yahoo.com/news/pfizer-hits-deadlock-india-over-165353340.html*

[22] Das KN. Pfizer drops India vaccine application after regulator seeks local trial. Reuters [serial online]. 2021 [cited 2022 Jun 5]. Available from: *https://www.reuters.com/article/health-coronavirus-india-pfizer-idUSKBN2A50GE*

[23] Wilmshurst P. Research misconduct in pharmaceutical and medical devices industries [homepage on the Internet]. YouTube; 2014 [cited 2022 Jun 5]. Available from: *https://www.youtube.com/watch?v=-fLZ0sHOu8dE*

[24] Buntz B. GSK, Pfizer and J&J among the most-fined drug companies, according to study [homepage on the Internet]. Pharmaceutical Processing World; 2020 [cited 2022 Jun 5]. Available from: *https://www.pharmaceuticalprocessingworld.com/gsk-pfizer-and-jj-among-the-most-fined-drug-companies-according-to-study/*

[25] Houses of Parliament Parliamentary Office of Science and Technology. Integrity in research [homepage on the Internet]. Report No.: 544. 2017 [cited 2022 Mar]. Available from: h*ttps://researchbriefings.files.parliament.uk/documents/POST- PN-0544/POST-PN-0544.pdf*

[26] Rogers L. 800,000 'killed' by beta blockers. The Times [serial online]. 2014 [cited 2022 Jun 5]. Available from: *https://www.thetimes.co.uk/article/800000-killed- by-beta-blockers-ghsfrgrj6kb*

[27] Wilmshurst P. Written evidence [homepage on the Internet]. 2017 [cited 2022 Jun 5]. Available from: *http://data.parliament.uk/writtenevidence/committeeevidence. svc/evidencedocument/science-and-technology-committee/research-integrity/ written/68813.html*

[28] GBNews. Covid: Report reveals increase in risk of heart attack following the mRNA COVID vaccine [homepage on the Internet]. YouTube; 2021 [cited 2022 Jun 5]. Available from: *https://www.youtube.com/watch?v=gJ8t0qQ5R4I*

[29] Doshi P, Godlee F, Abbasi K. Covid-19 vaccines and treatments: We must have raw data, now. BMJ. 2022;376:o102. *https://doi.org/10.1136/bmj.o102*

[30] BMJ. Tamiflu campaign [homepage on the Internet]. [cited 2022 Jun 7]. Available from: *https://www.bmj.com/tamiflu*

[31] Demasi M. FDA to release Pfizer data but the devil could be in the detail [homepage on the Internet]. Investigative Journalism. 2022 [cited 2022 Jun 5]. Available from: *https://maryannedemasi.com/publications/f/fda-to-release- pfizer-data-but-the-devil-could-be-in-the-detail?blogcategory=COVID-19*

[32] Public Health and Medical Professionals for Transparency vs Food and Drug Administration. Civil Action No. 4:21-cv-01058-P public health and medical professionals for transparency [homepage on the Internet]. 2021 [cited 2022 Jun]. Available from: *https://www.sirillp.com/wp-content/uploads/2021/11/020- Second-Joint-Status-Report-8989f1fed17e2d919391d8df1978006e.pdf*

[33] US Food and Drug Administration (FDA) Fact sheet: FDA at a glance [homepage on the Internet]. Silver Spring, MD: FDA; 2019 [cited 2022 Jun]. Available from: *https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance*

[34] Gagnon MA, Lexchin J. The cost of pushing pills: A new estimate of pharmaceutical promotion expenditures in the United States. PLoS Med. 2008;5(1):e1. *https:// doi.org/10.1371/journal.pmed.0050001*

[35] Pfizer. BLA 125742 COVID-19 mRNA vaccine (BNT162/PF-07302048) part 1 of the original submission – Rolling Biologics License Application (BLA) request for priority review designation [homepage on the Internet]. 2021 [cited 2022 Jun]. Available from: *https://phmpt.org/wp-content/uploads/2022/03/125742_S1_ M1_cover.pdf*

[36] CONGRESS.GOV. Prescription Drug User Fee Act of 1992 [homepage on the Internet]. 5952 Sep 24, 1992 [cited 2022 Jun]. Available from: *http://www. congress.gov/*

[37] US Food and Drug Administration (FDA). FDA approves first COVID-19 vaccine [homepage on the Internet]. U.S. Food and Drug Administration. FDA; 2021 [cited 2022 Jun 5]. Available from: *https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine*

[38] Fromer MJ. Survey of FDA scientists shows they feel pressure to exclude or alter findings fear retaliation for voicing safety concerns. Oncol. times. 2006;28(16): 12–13, 16. *https://doi.org/10.1097/01.COT.0000295013.50300.69*

[39] Open letter to the MHRA regarding child death data [homepage on the Internet]. HART Group; 2022 [cited 2022 Jun 5]. Available from: *https://www.hartgroup. org/open-letter-to-the-mhra-regarding-child-death-data/*

[40] JCVI statement on COVID-19 vaccination of children aged 12 to 15 years: 3 September 2021 [homepage on the Internet]. GOV.UK. [cited 2022 Jun 5]. Available from: *https://www.gov.uk/government/publications/jcvi-statement-september-2021-covid-19-vaccination-of-children-aged-12-to-15-years/jcvi-statement-on-covid-19-vaccination-of-children-aged-12-to-15-years-3- september-2021*

[41] Healthcare products Regulatory Agency. The MHRA concludes positive safety profile for Pfizer/BioNTech vaccine in 12- to 15-year-olds [homepage on the Internet]. GOV.UK. 2021 [cited 2022 Jun 5]. Available from: *https://www.gov.uk/government/news/the-mhra-concludes-positive-safety-profile-for- pfizerbiontech-vaccine-in-12-to-15-year-olds*

[42] Demasi M. Are adverse events in Covid-19 vaccine trials under-reported? [homepage on the Internet]. Investigative journalism. [cited 2022 Jun 5]. Available from: *https://maryannedemasi.com/publications/f/are-adverse-events-in-covid-19-vaccine-trials-under-reported*

[43] Chua GT, Kwan MYW, Chui CSL, et al. Epidemiology of acute myocarditis/ pericarditis in Hong Kong adolescents following Comirnaty vaccination. Clin Infect Dis. 2021:ciab989. *https://doi.org/10.1093/cid/ciab98*

[44] McCoy D, Kembhavi G, Patel J, Luintel A. The Bill & Melinda Gates Foundation's grant-making programme for global health. Lancet. 2009;373(9675):1645–1653.

[45] Madureira Lima J, Galea S. Corporate practices and health: A framework and mechanisms. Global Health. 2018;14(1):21.

[46] Harcombe Z. JCVI conflicts of interest [homepage on the Internet]. 2022 [cited 2022 Jun 5]. Available from: *https://www.zoeharcombe.com/2022/02/jcvi- conflicts-of-interest/*

[47] British Thoracic Society: Professor Wei Shen Lim [homepage on the Internet]. [cited 2022 Jun 7]. Available from: *https://web.archive.org/web/20211213113812/ https://www.brit-thoracic.org.uk/about-us/committees-and-advisory-groups/ clinical-audit-leads/35589/*

[48] Kickbusch I, Allen L, Franz C. The commercial determinants of health. PloS Med. 2016;4(12):E895-E896. *https://doi.org/10.1016/S2214-109X(16)30217-0*

[49] McKee M, Stuckler D. Revisiting the corporate and commercial determinants of health. Am J Public Health. 2018;108(9):1167–1170.

[50] Samet JM. The bottom line or public health: Tactics corporations use to influence health and health policy and what we can do to counter them edited by William H. Wiist Merchants of Doubt: How a handful of scientists obscured the truth on issues from tobacco smoke to global warming by Naomi Oreskes and Erik M. Conway. Am J Epidemiol. 2012;175(9):971–972.

[51] Thacker PD. Covid-19: Researcher blows the whistle on data integrity issues in Pfizer's vaccine trial. BMJ. 2021;375:n2635.

[52] Johnson R. The mainstream media are co-conspirators in this political dirty trick. Will they be held accountable for their role in this deception? [homepage on the Internet]. Twitter; 2022 [cited 2022 Jun 5]. Available from: *https://twitter.com/ SenRonJohnson/ status/1493788283104604162*

[53] BMJ. Open letter from the BMJ to Mark Zuckerberg [homepage on the Internet]. 2022 [cited 2022 Jun 5]. Available from: *https://www. bmj.com/content/375/bmj. n2635/rr-80*

[54] Facebook, Merck commit $40 m for alliance for advancing health online [homepage on the Internet]. CSR Egypt; 2021 [cited 2022 Jun 5]. Available from: *https://www.csregypt.com/en/facebook-merck-commit-40-m-for-alliance-for- advancing-health-online/*

[55] Husten L. Merck pleads guilty and pays $950 million for illegal promotion of Vioxx. Forbes Magazine [serial online]. 2011 [cited 2022 Jun 5]; Available from: *https://www.forbes.com/sites/ larryhusten/2011/11/22/merck-pleads-guilty-and-pays- 950-million-for-illegal-promotion-of-vioxx/*

[56] Abraham C. Vioxx took deadly toll: Study. The Globe and Mail [serial online]. Available from: *https://www.theglobeandmail.com/life/vioxx-took-deadly-toll- study/article1113848/*

[57] Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. Brain Behav Immun. 2020;87:184–187.

[58] Morse J, Gay W, Korwek KM, et al. Hyperglycaemia increases mortality risk in non- diabetic patients with COVID-19 even more than in diabetic patients. Endocrinol Diabetes Metab. 2021;4(4):e00291.

[59] Araujo J, Cai J, Stevens J. Prevalence of optimal metabolic health in American adults: National Health and Nutrition Examination Survey 2009–2016. Metab Syndr Relat Disord. 2019;17(1):46–52. *https://doi.org/10.1089/met.2018.0105*

[60] ffice for National Statistics. Census 2021 - UK COVID-19 deaths by age with no underlying conditions [homepage on the Internet]. [cited 2022 Jun 5]. Available from: *https://www.ons.gov.uk/aboutus/transparencyandgovernance/freedomofinformationfoi/ukcovid19deathsbyagewithnounderlyingconditions*

[61] Hyde PN, Sapper TN, Crabtree CD, et al. Dietary carbohydrate restriction improves metabolic syndrome independent of weight loss. JCI Insight. 2019;4(12):e128308. *https://doi.org/10.1172/jci.insight.128308*

[62] Malhotra A. The 21-day immunity plan. United Kingdom: Yellow Kite; 2021.

[63] Marteau TM. Changing minds about changing behaviour. Lancet. 2018;391(10116):116–117.

[64] Greenhalgh T, Howick J, Maskrey N, Evidence Based Medicine Renaissance Group. Evidence based medicine: A movement in crisis? BMJ. 2014;348:g3725.

[65] Horton R. Offline: What is medicine's 5 sigma? Lancet. 2015;385(9976):1380.

Special Notes

Acknowledgements: I thank Dr Clare Craig for edits and data analysis, and Alex Starling for comments and suggestions. The author is also grateful for the assistance of a scientist who wishes to remain anonymous because of career pressure.

Competing interests: The author declares that he has no financial or personal relationships that may have inappropriately influenced him in writing this article.

Author's contribution: Aseem Malhotra is the sole author of this article.

Ethical considerations: This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability: Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer: The views and opinions expressed in this article are those of the author and do not necessarily reflect the official policy or position of any affiliated agency of the author.

Dr Aseem Malhotra, MBChB, MRCP, CCT Cardiology, is a consultant cardiologist and an international expert in prevention, diagnosis and management of heart disease. He is an honorary council member to the Metabolic Psychiatry Clinic at Stanford University School of Medicine, California. He is a founding member of Action on Sugar, highlighting the harm caused by excess sugar consumption in the United Kingdom, particularly in type 2 diabetes and obesity. In 2015 he helped co-ordinate the Choosing Wisely campaign by the Academy of Medical Royal Colleges as lead author in a *BMJ* paper to highlight the risks of overuse of medical treatments. In the same year he was appointed to the board of trustees of The King's Fund advising the UK government on health policy. A frequent expert commentator in print and broadcast media, he has written scores of articles for the *BMJ*, *British Journal of Sports Medicine*, *BMJ Open Heart*, *JAMA Internal Medicine*, *Prescriber*, *The Pharmaceutical Journal*, and T*he European Scientist.*

He has won awards for raising awareness of diet-related illness in the UK and internationally. In 2018 he was ranked by software company Onalytica as the number one doctor in the world influencing obesity thinking. In 2016 he was named in the *Sunday Times* Debrett's list as one of the most influential people in science and medicine in the UK in a list that included Professor Stephen Hawking. Award-winning American science journalist Gary Taubes describes Aseem Malhotra as someone who has 'probably done more in the UK to inject sanity into nutrition science and the pharmaceutical industry debate than any human being alive'.

Part 4

Australian data – with poor pharmacovigilance the safety signals go unrecognized

We human beings need data, so that we can recognize facts on a larger scale. Under-reporting is dangerous. The TGA's reporting system is passive and voluntary; it risks under-reporting which may conceal serious signals of harm. Comprehensive data collection and assessment are critical. This part provides a comprehensive analysis of pertinent excess mortality data which are not being evaluated for potential disturbing safety signals.

The World Health Organization says: 'a safety signal refers to information on a new or known side effect that may be caused by a medicine and is typically generated from more than a single report of a suspected side effect.'

Our authors in this section raise telling questions.

> No therapeutic agents (that is, drugs) are 'safe'…
>
> The Australian Therapeutic Goods Administration declared the COVID-19 vaccines (a more apt description is COVID gene-based spike injections) to be 'safe' without any qualification based, as we now know, on troublesome animal and clinical safety data. Such reckless advice had no equivalent in the history of the pharmaceutical industry. Furthermore, the TGA provisionally approved the use of these experimental gene-based injections for the entire population including healthy people, children, infants, and in pregnancy knowing full well that important safety data were

> lacking……..Post-marketing surveillance of adverse drug reactions is of particular importance when the safety and efficacy data for any drug under research are limited… (It) is necessary to have a transparent, efficient and dependable adverse drug reporting system to identify safety signals should they arise….One cannot have an expedited drug approval system which depends on very limited evidence of safety and, at the same time, have an unreliable and non-transparent adverse drug event reporting system which fails to identify and report important safety signals.
>
> – Dr Philip Altman

> Australia, like many other Western countries is currently experiencing excess mortality at a level not known of outside war times. Even after COVID deaths are taken into account, there is significant remaining excess mortality. Health authorities have no explanation for the cause of these Australian excess deaths above historical averages.
>
> – Dr Andrew Madry

> One must ask why death rates are at their highest in 2022 so long after the population was first exposed to the virus…. Results from three separate models show that a persistent trend of high excess deaths began in Australia in Spring, 2021, and continues in 2023.
>
> – Clare Pain

If evidence shows government COVID public health policy is causing an iatrogenic catastrophe rather than a measurable benefit, doctors and nurses have a moral, legal, and scientific duty to warn people. National and international laws, agreements, and regulation from Nuremberg to the Health Practitioners Regulation National Law reinforce the duty of physicians to serve humanity and to first do no harm. If policy created at the 'speed of science' appears to be neither safe nor effective, the community expects protective action and this involves free and open communication. For our medical authorities and political leaders to continue to enforce censorship in the face of an iatrogenic miscarriage of medical science causing untold harm shows a reckless indifference for the sufferings of Australians.

Doctors must be permitted to use their constitutional right of intellectual freedom, medical experience, clinical judgement and freedom of expression to save lives even from state-sanctioned policies.

Dr Philip Altman said, 'There appears to be a growing body of opinion that the COVID "vaccines" are doing more harm than good and they should be withdrawn.' This would seem a sensible move. Perhaps it might give rise to the next logical step, having serious medical attention being paid to providing proper treatment for the enormous numbers of those who have been damaged and whose suffering the medical system resolutely refuses to acknowledge.

Why all-cause mortality has become the most important COVID-19 statistic

by Phillip M. Altman
BPharm (Hons), MSc, PhD

No drug or vaccine is 'safe'. All have potentially serious and or fatal effects. Yet the Australian Therapeutic Goods Administration (TGA) declared the COVID-19 'vaccines', more appropriately described as COVID gene-based spike injections, to be 'safe' without any qualification based, as we now know, on troublesome animal and clinical safety data. Such reckless advice had no equivalent in the history of the pharmaceutical industry. Furthermore, the TGA released these experimental gene-based injections for use in the entire population including healthy people, children, infants and in pregnancy, knowing full well that important safety data were lacking.

After two and a half years of use, these COVID gene-based spike injections (they are not really vaccines because they do not prevent infection nor do they prevent transmission of the virus) have been reported to be associated with the highest incidence of serious adverse events and death of any drug ever released, according to multiple vaccine adverse event reporting systems, including the Vaccine Adverse Event Reporting System (VAERS) of the US Centers for Disease Control (CDC).[1] The latest VAERS report through August 4th 2023 reports 35,821 associated deaths and 207,715 hospitalisations. The true incidence of deaths due to serious adverse events in this US reporting system, following application of the widely acknowledged under-reporting factor of

1 Openvaers.com (last visited 28 June 2023)

about 50x, is 1.8 million.[2,3] These reported vaccine iatrogenic deaths exceed the number of declared US COVID deaths.[4] Even when compared to conventional vaccines the COVID so-called vaccines have been reported to cause more than 10 times the reported incidence of death, according to VAERS.

However, as of this time, the reported incidence of death in Australia caused by the COVID gene-based spike injections according to the TGA stands at 14.[5] The TGA says: 'The 14 deaths likely to be related to vaccination occurred in people aged 21–81 years old. There have been no deaths in children or adolescents determined to be linked to COVID-19 vaccination.'

So, why is there such a discrepancy between the overseas adverse event data and our TGA adverse event data?

The answer lies in the design of the voluntary adverse-event reporting systems and the way these systems are administered. Gross under-reporting may be a result of a lack of adequate staff to service the system and analyse the data in a timely fashion. However, other factors include: complex or cumbersome design which discourages reporting and searching, computer coding and or definition anomalies which make reporting or searching the database difficult. Failure to follow up important missing data in relation to deaths and other serious adverse events is another problem.[6]

Misclassification or deletion of records has been reported in relation to adverse drug reporting systems and important safety signals from these systems have been ignored.[7,8] In addition, health professionals are loath to report adverse drug reactions from the COVID injections because they fear being labelled as 'anti-vaxxers' or being seen as undermining the prevailing vaccine narrative promoted by the health regulators, and they fear being disciplined or even suspended for reporting. [9,3]

2 UK All Party Parliamentary Group – Pandemic Response and Recovery Group. 17 July 2023. https://appgpandemic.org/news/yellow-card

3 Kirsch, S., Rose, J. and Crawford, M. Estimating the number of COVID vaccine deaths in America. https://sunfellow.com/wp-content/uploads/2021/09/VAERS-Deaths-Kirsch-Rose-Crawford.pdf

4 Ourworldindata.org United States confirmed deaths. Last visited 21 Aug. 2023.

5 Australian Government – Dept. of Health and Aged Care. COVID-19 vaccine safety report 15-12-2022. https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-15-12-2022.

6 Rose, J.: Critical Appraisal of VAERS Pharmacovigilance: Is the U.S. vaccine Adverse Events Reproting System (VAERS) a Functioning Pharmacovigilance System". Science, Public Health Policy, and the Law. Vol 3:100-129, Oct. 2021. https://www.researchgate.net/publication/370158323_Critical_Appraisal_of_VAERS_Pharmacovigilance_Is_the_US_Vaccine_Adverse_Events_Reporting_System_VAERS_a_Functioning_Pharmacovigilance_System

7 Josh Guezknow Substack: CDC Finally Released its VAERS Safety Monitoring Analyses for COVID Vaccines via FOIA. 5 Jan. 2023. https://open.substack.com/pub/jackanapes/p/cdc-finally-released-its-vaers-safety?r=10pxn5&utm_campaign=post&utm_medium=email

8 Jessica Rose Substack: 19 June 2023. Scrub-a-dub-dub, is Janssen gettin' thrown off the sub? https://open.substack.com/pub/jessicar/p/scrub-a-dub-dub-is-janssen-gettin?r=10pxn5&utm_campaign=post&utm_medium=email

9 Josh Guezknow Substack: CDC Finally Released its VAERS Safety Monitoring Analyses for

Post-marketing adverse drug reporting systems have served a very important role in the past. This is because during the research and development of any new drug, depending on circumstances, usually only a few thousand people are studied in perhaps 10 to 30 clinical trials over 7 to 10 years.

While these clinical studies are highly monitored for adverse effects, the limited number of studied subjects in these R&D programs means that those adverse effects which occur, maybe one in a hundred or one in a thousand, will be difficult to identify as being caused by the drug tested rather than occurring by chance. For this reason, post-marketing surveillance in pharmacovigilance systems play an important and indispensable role. A total of 462 medicinal products have been withdrawn from the market between 1950 and 2013 using post-marketing surveillance.[10]

Post-marketing surveillance of adverse drug reactions is of particular importance when the safety and efficacy data for any drug under research are limited by the number of clinical trials conducted or limited by the types of patients studied. In the case of Provisional Approval in Australia or Emergency Use Authorisation in the US or Conditional Approval of the COVID 'vaccines' in the European Union, all these limitations applied.

In order to have a reliable estimate of safety a drug released under conditional approval where insufficient safety and efficacy data exist for full approval, it is necessary to have a transparent, efficient and dependable adverse drug reporting system to identify safety signals should they arise. Given the discrepancy between the large numbers of adverse events reported in relation to the COVID 'vaccines' overseas compared to Australia, it appears that Australia does not have a reliable and transparent adverse drug event reporting system to identify important safety signals and neither does the US Food and Drug Administration (FDA).[11]

For example, up to the writing of this paper, a reported total of nine children have died in relation to the administration of the COVID so-called vaccines[12] in the Australian TGA Drug Adverse Event Notification (DAEN) system. There is insufficient transparency to provide confidence to conclude these deaths are not related to the COVID vaccine. Indeed, there is considerable suspicion that

COVID Vaccines via FOIA. 5 Jan. 2023. https://open.substack.com/pub/jackanapes/p/cdc-finally-released-its-vaers-safety?r=10pxn5&utm_campaign=post&utm_medium=email

10 Onakpoya, I, J. et al: Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature. DOI 10.1186/s12916-016-0553-2

11 Demasi, M.: FDA urged o publish follow-up studies on Covid-19 vaccine safety signals. https://www.bmj.com/content/379/bmj.o2527

12 Personal communication: Case numbers 616124, 647663, 659048, 719838, 724023, 733723, 734187, 744306 and 762472

the TGA may be under-reporting and misclassifying deaths.[13,14] The full ADR records are not made publicly available to provide any level of assurance.

Reanalysis of the risk of serious adverse drug events which occurred in the Pfizer and Moderna COVID 'vaccine' clinical trials showed that about 1 in 800 people had a chance of a serious adverse event[15] representing a 16% higher risk of serious adverse events compared to placebo and far more than 1-2 for each million reported for vaccines in general.[16] The official reported TGA DAEN incidence for serious adverse events for COVID 'vaccines' fails even to come close to this statistic.

A practical example of the unreliability of adverse drug-event reporting systems is provided by the discrepancy between the official TGA-reported incidence of myocarditis and the incidence of myocarditis reported in clinical practice.

According to the TGA: 'Myocarditis is a known but very rare side effect' of the Pfizer and Moderna so-called vaccines. The TGA goes on to say: 'It is usually temporary, with most people getting better within a few days. Myocarditis is reported in around 1-2 in every 100,000 people who receive Comirnaty (Pfizer) and around 2 in every 100,000 of those who receive Spikevax (Moderna).'[17]

However, in a rare admission, one prominent Australian cardiologist revealed that he has seen about a hundred cases of myocarditis since the COVID so-called vaccines were rolled out.[18] Given that there are about 1200 cardiologists in Australia, this means there might have been 120,000 cases of symptomatic myocarditis – not around 500 cases as estimated by the TGA. This degree of discrepancy is unacceptable.

The problem is that insufficient safety data were generated prior to the release of the COVID so-called vaccines and the population is entirely dependent upon

13 Mercola, J.: Epoch Times 21 May 2022. Thousands of Deaths and Adverse Reactions Deleted from VAERS. https://www.theepochtimes.com/thousands-of-deaths-and-adverse-reactions-deleted-from-vaers_4481440.html?utm_source=Health&utm_campaign=health-2022-05-22&utm_medium=e-mail&est=7m17NiFo5EoGT1omDWz1WO3DSAnrvrbqvGJvEw%2BYltfW41BaiwbGVeQQ6zkYgn-niTyq%2FL7wEg7MbfdTV3MyrR1w%3D#Print

14 Mohanoor, A: A review of recent Creutzfeldt-Jakob disease VAERS reports. 17 April 2923. https://open.substack.com/pub/vaccinedatascience/p/a-review-of-recent-creutzfeldt-jakob?r=10px-n5&utm_campaign=post&utm_medium=email

15 Fraiman, J. et al: Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. Vaccine 40 (2022) 5798–5805. https://doi.org/10.1016/j.vaccine.2022.08.036

16 Office of Infectious Disease. HIV/AIDS Policy. Vaccine side effects. 2021. www.hhs.gov/immunization/basics/safety/side-effects/index.html

17 Australian Government – Dept. of Health and Aged Care. COVID-19 vaccine safety report 15-12-2022. https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-15-12-2022.

18 Radio Interview of Dr. Ross Walker 6 June 2023: 2HD 1143AM Newcastle. https://www.2hd.com.au/2023/06/06/dr-ross-walker-explains-the-importance-of-good-muscle-strength/?fbclid=IwAR2x-pd22lfXIuQRcHOYpEPU8o1_qzzPg3QDeOGM2zfGaOYIA_RuIONJkGsM_aem_th_AYsku5AtEg-bXgSaCfd6mJHWWNlaJbUNkNPjBn9WQ_Jyn0imbMS6CE-1Ia3bCRYf428E

an unreliable adverse drug event reporting system to prove safety. One cannot have an expedited drug approval system which depends on very limited evidence of safety, and, at the same time, have an unreliable and non-transparent adverse drug-event reporting system which fails to identify and report important safety signals. If safety signals such as cardiac arrest, pulmonary embolism, stroke, sudden death, cancer, diabetes and neurological disease such as dementia occur significantly above baseline values and are not duly recognised, there is no point in having an adverse drug-event reporting system.

There are other clues that our adverse drug-event reporting systems are under-reporting the real incidence of death associated with the so-called COVID vaccines. Life insurance companies around the world are reporting record numbers of unexpected deaths. These are not statistical fluctuations. For example, Lincoln National, the fifth largest insurance company in the US, reported a 153% increase in life insurance claims in 2021.[19]

It is becoming increasingly obvious that we cannot rely upon the various adverse drug-reaction reporting systems in order to assess the safety of the so-called COVID vaccines.

However, from time to time there is a substantial clue to the true and exceptionally high incidence of adverse events associated with the COVID 'vaccines.' One such clue was provided by Adverse Event Following Immunisation statistics released by the West Australian government for 2021. These data show in relative terms the rocketing numbers of adverse events reported for COVID 'vaccines.' Twice as many COVID 'vaccines' were injected as compared to all other vaccines – but forty times the number of adverse drug reactions were reported.[20]

But dangerous drugs can be identified in another way apart from adverse drug reporting systems. Most countries accurately measure a statistic termed the All-Cause Mortality and a statistic called Excess Deaths. The All-Cause Mortality is the number of deaths each year from all causes and Excess Deaths are the number of deaths from all causes above that normally expected based usually on recent years. The Australian Government publishes these data on a regular basis as Provisional Mortality Statistics.[21]

In Australia and around the world these All-Cause Mortality statistics have

19 Menge, M.: Crossroads Report. Fifth largest life insurance company in the US paid out 163% more for deaths of working people ages 18-64 in 2021 – total claims/benefits up $6 Billion. 16 June 2022. https://crossroadsreport.substack.com/p/breaking-fifth-largest-life-insurance?utm_source=substack&utm_medium=email

20 Western Australian Vaccine Safety Surveillance – Annual Report 2021. https://www.health.wa.gov.au/~/media/Corp/Documents/Health-for/Immunisation/Western-Australia-Vaccine-Safety-Surveillance-Annual-Report-2021.pdf

21 Australian Bureau of Statistics – Provisional Mortlity Statistics. Release 28.6.23. https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/latest-release

shown a disturbing trend of about 16-20% Excess Deaths since the rollout of the COVID 'vaccines' in 2021 but not in 2020 when there were no COVID 'vaccines' and the SARS-CoV-2 virus was at its most virulent. The majority of these excess deaths in 2021 and 2022 were non-COVID-19 deaths and include heart attacks, strokes, diabetes, dementia and other neurological conditions.

So, what caused most of the Excess Deaths if it was not COVID-19?

There is now evidence to show that an analysis of COVID vaccine use is strongly correlated with All-Cause Mortality over 31 European Union member states and Norway, Iceland, Liechtenstein and Switzerland.[22] The report shows that the more a country engages in COVID vaccination, the higher is the overall mortality from all causes. A Bradford Hill analysis of Excess Mortality in relation to the COVID 'vaccines' showed mass vaccination was strongly correlated with excess deaths.[23]

There appears to be a growing body of opinion that the COVID 'vaccines' are doing more harm than good[24] and they should be withdrawn.

Additional evidence that the COVID 'vaccines' are responsible for the majority of the excess deaths comes from a report by Rancourt et al.[25] The excess All-Cause Mortality following the COVID-19 vaccine rollout (31,000 deaths, mid-April 2021 through August 2022) is more than twice the total number of Australian deaths registered as being from or with COVID-19 (14,014 deaths, January 1st 2020 through August 29th 2022).

The Australian Government is currently attempting to minimise the number of excess deaths reported by the Australian Bureau of Statistics in their latest All-Cause Mortality statistics for 2022 first by ignoring the low number of excess deaths in 2020 used as a baseline and more recently by adjusting the number of excess deaths downwards by 12,000 using a mysterious statistical model[26] rather than actual Excess Death numbers. In reality, for 2022, there were about 10,000 COVID-19 deaths (as determined by PCR testing) and 20,000 unexplained non-COVID excess deaths.

---

22 Aarstad, J and Kvitastein, O.A.: Is there a Link between the 2021 COVID-19 vaccination uptake in Europe and 2022 Excess All-Cause Mortality? https://www.preprints.org/manuscript/202302.0350/v1

23 Sy, W.: Australian COVID-19 pandemic: A Bradford Hill Analysis of Iatrogenic Excess Mortality. J. Clin. Exp. Immunol. 2023, Vol 8, Issue 2, 542-556. 1 April 2023. https://www.opastpublishers.com/peer-review/australian-covid19-pandemic-a-bradford-hill-analysis-of-iatrogenic-excess-mortality-5339.html

24 Classen, J.B.: US COVID-19 Vaccines Proven to Cause More Harm than Good Based on Pivotal Clinical Trial Data Analyzed Using the Proper Scientific Endpoint, "All Cause Severe Morbidity". Trends int. Med. 2021, Vol 1, issue 1, pp1-6.

25 Correlation Research in the Public Interest. Rancourt, D.G. et al. 20 Dec. 2022. https://www.researchgate.net/publication/366445769_Probable_causal_association_between_Australia%27s_new_regime_of_high_all-cause_mortality_and_its_COVID-19_vaccine_rollout

26 Wilson Sy. Australian excess deaths: Moving the Goalposts. In print – Principia Scientific 2023 and phillipaltman.substack.com 24 Aug. 2023.

This is reprehensible. This needs investigation. This needs explaining.

The Australian government continues to insist that the so-called COVID vaccines are 'safe and effective' but evidence to support this claim is lacking. In addition, there is no credible or supportable explanation for the dramatic rise in the unexpected non-COVID excess deaths which have occurred only after the rollout of the COVID 'vaccines'.

One would have thought, given the magnitude of the COVID disaster, that it would be of utmost importance to determine what is causing more than 30,000 Australians to die non-COVID deaths above average since the COVID 'vaccines' were rolled out. A motion to investigate the possible causes of the unexpected non-COVID deaths was introduced into the Australian Federal Parliament in March 2023 and was defeated.

Dr Phillip Altman is an Australian authority on clinical trials and regulatory affairs with more than 40 years of experience in designing, managing and reporting of clinical trials and in working with the Australian Therapeutic Goods Administration in gaining new drug approvals.

He established Australia's first contract research organisations and served as a senior industry consultant for more than half of the pharmaceutical companies present in Australia. Involved in over a hundred clinical trials, he has been personally responsible for market approval of numerous new drugs since joining the pharmaceutical industry in 1974.

A graduate of Sydney University with an Honours degree in pharmacy, Master of Science and Doctor of Philosophy degrees (focusing on drug development, pharmacology and pharmaceutical chemistry), he co-founded and is a life member of the largest professional body of pharmaceutical industry scientists involved in clinical research and regulatory affairs. Most recently Dr Altman has provided expert reports in relation to both the Australian and NZ Judicial Review and High Court cases in relation to the COVID vaccines.

Excess deaths in Australia during the COVID period: the numbers

by Clare Pain

BSc Hons (Chemistry), MSc (Operational Research)

Abstract

The Australian Bureau of Statistics (ABS) is using two different models that estimate excess mortality over the COVID period, which are here called the simple and complex models. For 2022, using these models, the ABS has published estimates of 15.3% and 10.9% excess deaths in 2022 respectively and the corresponding figures to date for 2023 are 12.3% and 9.1%.

Examining data back to 1950, even the lower level of excess deaths in 2022 (10.9%, complex model) is unprecedented. Z-score analysis gives a highly significant value of 3.4 standard deviations from the mean. A pattern of two such high years in succession, (10.9% in 2022, 9.1% in 2023 to date, complex model) has not been seen before.

Similar trends of high excess deaths are evident in many other countries, which suggests that new factors may be causing substantial effects. Differences between the excess deaths pattern for Sweden, which had few restrictions, and other countries, suggests that patterns of excess deaths may be related to the ways governments intervened during the COVID period. Australia and New Zealand show very similar patterns. New Zealand and Sweden may represent two extremes, with an opposite sequence of vaccination and viral spread.

Results from three separate models show that a persistent trend of high excess deaths began in Australia in the Antipodean Spring of 2021, and continues in 2023.

An independent investigation is urgently needed, as is complete transparency about the ABS's complex model for excess deaths, and the excess death rates by age band and state that it produces.

1. Introduction - why measure excess deaths?

As Australia went through the COVID-19 period the population faced a novel virus, for which they were told there was no protection through existing immunity. Fear about this new virus became high, stoked by the media, seemingly with government support.

Australian Federal, State and Territory governments took unprecedented measures. Australia closed out the world, sealing its international borders, and citizens were told that they could not leave the country without permission. State and Territory borders were closed, opened, and closed again. Citizens learned a new word, lockdown, and were confined to their homes for most of the day for weeks and months. When people did encounter each other, they were told to keep apart and wear masks.

A completely new class of vaccination – genetic vaccines – was provisionally approved by the Therapeutic Goods Administration (TGA) and administered to almost the entire population. These new vaccinations were mandated by some States, Territories, and employers.

As we emerge from the COVID period it is important to examine the outcomes of the way it was managed in Australia. Did the decisions taken give better results than would have occurred with no interventions, or with different interventions? Did the governments' actions save thousands of lives, or have they, perhaps, cost thousands of lives? Have they caused economic effects[1] that have cost lives? One way to get a handle on this is to look at the pattern of deaths in Australia and in other countries, from any cause – known as 'all-cause mortality'.

There are strong arguments for looking at all-cause mortality rather than simply looking at the number of deaths from COVID.[2] Although the measures taken by governments such as lockdowns, treatment protocols, and vaccinations were intended to reduce COVID deaths, these measures and others may have affected the number of deaths from other causes too, making them higher or lower than normal.

Indeed, when the ABS released the first of its Provisional Mortality Statistics[3]

series on June 26th 2020, designed to report death statistics during the COVID period, they said: 'Examining mortality data across a broader range of causes provides a more comprehensive view of the impact of the pandemic on public health. This can give an indication of where "excess" mortality might occur beyond deaths directly from COVID-19.'

But how do we know whether the all-cause mortality data being reported is 'in excess' of what would be expected? For this we need to define an excess death.

1.1 What is an excess death?

The concept of excess mortality was used long before the COVID period, to measure how many extra deaths were caused by exceptional events such as influenza epidemics[2] and heatwaves. The idea is straightforward: compare the number of deaths that have occurred during an influenza epidemic or heatwave, with the number of deaths that would have been expected, had the exceptional event not happened.

Excess deaths are thus, $d_a - d_e$

And the excess deaths as a percentage is calculated as $(d_a - d_e)/d_e * 100$, where d_a is the actual number of deaths and d_e is the expected number of deaths.

An excess mortality *rate* (deaths per population) can be calculated in an analogous way. Using mortality rates may be preferable to simply using numbers of deaths especially in countries with high rates of migration like Australia. This is because the number of deaths in a country will increase as the population increases.[1]

1.2 Types of models used for estimating expected deaths

Many different modelling approaches for estimating the expected mortality can be used. A simple approach is to predict that mortality will continue at the same average level as it was for a certain number of years before the COVID period. The more years included, the less likely the prediction will be biased by a quirky year, but this must be balanced by the fact that recent years are more likely to be good predictors of the immediate future than older ones. For example, data for the year 2019 are more likely to be relevant when predicting 2020 deaths than are data from 2010.

The ABS began its Provisional Mortality Statistics series by choosing such a simple model to estimate expected deaths during the COVID period. The expected number of deaths in a particular week of the COVID period year was chosen to be the average of the number of deaths in the corresponding

1 Similarly, if a country has a declining population, perhaps through emigration, the number of deaths will decrease.

week in the five pre-COVID years, 2015-2019.

Other, more complicated approaches fit a trend line to a consecutive series of years of past data, often using least squares regression analysis, and modelling is sometimes extended to include higher-order (polynomial) terms in fitting the trend and the addition of sine and cosine terms to model seasonality. Many temperate countries, including Australia, have a seasonal pattern of high mortality in the winter months (driven by respiratory infections such as influenza) and lower mortality in summer.

1.3 The importance of model choice

The calculation of excess mortality is simple enough, but the choice of the model used to estimate the *expected* or predicted mortality (called 'baseline' in the ABS Provisional Mortality statistics) during the COVID period is crucial. As an example, using the Short-term Mortality Fluctuations (STMF) online tool[4] provided by the Human Mortality Database, one can choose different models that use either a simple average or a trend line through past data. One can also select the number of pre-COVID years to include in the model and choose to model using data for deaths or death rates.

Using these options, predictions for the expected deaths in 2022 in Australia range from 159,966 to 180,265 (Appendix A). This means that the number of calculated excess deaths in 2022 ranges from 9,671 to 29,970.

The choice of whether to model using data for deaths or for death rates can also make an important difference. For example, the STMF tool gives figures of 18.4% or 12.4% excess mortality for Australia in 2022, depending on whether the estimate is based on average deaths or average death rates for the years 2015-2019.

The concern here is that by careful or deliberate selection of a model, very different excess mortality statistics can be produced. This raises dangers, particularly when models are selected to calculate excess deaths *after* actual deaths data is known. This is because, should a particular spin be wanted on numbers of excess deaths, it would be quite possible to find a model that will produce the results required.[2]

It is important, then, to establish a model for predicted deaths in a period *before* one looks at the actual death numbers, using logic and principled reasoning.

2 Indeed, Professor John Gibson, Professor of Economics at Waikato University in New Zealand, has published a working paper[5] in which he criticises claims by Sir Ashley Bloomfield, former Director-General of Health in New Zealand, that over the COVID period there had been fewer deaths than expected (in other words a death deficit). The model on which the claims were based implicitly assumed that immigration would continue at the rates seen in 2015-2019 (thus inflating predictions of expected deaths) in a country with locked-down borders. When actual deaths were compared with inflated expected deaths, excess deaths appeared low.

To their credit, the ABS did this when they launched their Provisional Mortality Statistics series in mid-2020. If models are chosen after the actual deaths data have come out, (as was the case with the revised complex model the ABS has developed, see later), great care needs to be taken by the producer of the statistics to ensure that any such model is developed in as logical and as principled a way as possible.

1.4 How the ABS has measured Australian excess deaths over the COVID period

1.4.1 Provisional mortality statistics (ABS original and new simple models)

As already mentioned, in June 2020 the ABS took the initiative to provide monthly updates on provisional death figures during the pandemic, starting its Provisional Mortality Statistics series.[3]

In these statistics, the ABS provided measurements of deaths compared to the expected deaths from their model, terming the expected deaths 'baseline'. As mentioned earlier, their predictor was that deaths in each week during the pandemic would be the average of the deaths in the corresponding week in the five years before the pandemic (2015-2019). We will call this model for calculating excess deaths the ABS's 'original simple model'.

The simple model as used by the ABS in its Provisional Mortality Statistics in 2020 and 2021 can be justified in many ways. It makes sense to compare what happened during the COVID period with the years immediately preceding it. Further, using a reasonably long period of five years reduces the risk of the average being unduly influenced by years with unusually high or low deaths. (For example, 2017 and 2019 were years with bad influenza outbreaks.)

Importantly, this model was chosen before the actual death numbers came in. It was a sensible, principled model. One flaw, however, was that because deaths, rather than death rates, were modelled, it did not adjust for changes in the size of the Australian population; another was that any trend in the data was ignored.

However, on March 30th 2022, the ABS announced[6] it would be using a new model for the Provisional Mortality Statistics in 2022. For 2022 and 2023, deaths have been compared to the average of four years: 2017-2019 and 2021. This 'new simple model' is harder to defend than the original model for the following reasons:

3 As explained in the methodology section of the first Provisional Mortality Statistics release, the data differed from that in the existing series, published annually, called 'Deaths Australia' and 'Causes of Death, Australia' in several respects. For example, the Provisional Mortality Statistics do not include deaths certified by a coroner; and they are based on the date of death, not the date of registration of the death.

- Only four years of data were averaged (compared with five)
- There was a gap in the sequence of years
- Two of the included years were bad influenza years (2017 and 2019) and thus had high deaths (4.8% and 6.9% above the 2015-2019 average respectively)
- 2020, a year from the COVID period, was excluded – because, the ABS said: 'it included periods where numbers of deaths were significantly lower than expected.' Deaths in 2020 were -0.1% below the average for 2015-2019
- 2021, a year from the COVID period, in which Australia was not 'normal'– with border closures, lockdowns, a vaccination rollout and COVID outbreaks – was included. Deaths were 6.2% higher in 2021 than the 2015-2019 average

Of course, if the model uses years in which there were comparatively high rates of death, then it will predict high expected deaths in 2022 and 2023 – which, in turn, has the effect of reducing the calculated figure for excess deaths in those years.

Why did the ABS feel the need to switch from their logically rigorous original simple model, which used a consecutive series of pre-COVID data years from 2015-2019, to this new simple model, with its seemingly arbitrary choice of data years, 2017-2019 and 2021? The new simple model led to lower excess death figures being reported than would have been the case using the original model. It is noteworthy that when the choice of baseline was announced, excess deaths had been running at a high level for six months from October 2021.

1.4.2 Measuring Australia's Excess Mortality (ABS initial and revised complex models)

Since November 25th 2020, the ABS has also published occasional reports[7] entitled 'Measuring Australia's excess mortality during the COVID-19 pandemic' and using another model for excess deaths.

The more sophisticated mathematical model in these publications is an adaptation by the ABS of a model used by NSW Health to detect years of unusually high influenza. It uses death rates and has a constant term, a linear trend and sine and cosine terms to model seasonality. It also has 95% confidence intervals which provide a threshold level, above which an anomaly is assumed to have occurred (such as a COVID or influenza wave). We will call this the 'initial complex[4] model'.

4 This is unrelated to the concept of complex systems used in mathematics

This initial model was extensively revised[8] on July 17th 2023 in a report entitled 'Measuring Australia's excess mortality during the COVID-19 pandemic until the first quarter 2023'. While the initial version modelled national deaths and deaths from specific causes based on data for the five years before the COVID period, the revised model used age-specific death rates from 2013-2019. Age-specific death rates are deaths in a particular five-year age band (for example age 50-54 years) divided by the number of people in that age-band.

The methodology section of the July '23 release does not make it completely clear how the revised complex model has been done, but it appears that it is more granular – with death rate models for each age-band in each state to predict expected death rates by age band by state. It appears that these predictions have then been multiplied by population estimates for each age band during the COVID era and pooled to produce expected total numbers of deaths nationally.

Tantalisingly, this revised model presumably produces excess mortality rates by age-band and state by week, data which would be extremely illuminating about how COVID itself, and government interventions, have affected each age band throughout the COVID years. Sadly, the pooling of these data loses the insights it might have brought. It appears this information is not yet publicly available.

Good points about this revised complex model are: that a long period of data has been used (2013-2019); and all these data are from before the COVID period, when things were 'normal'. The use of death rates, rather than deaths, has the advantage that changes in population are accounted for, and using age-specific death rates allows for population changes in each age band to be modelled. For example, in the short term, an influx of younger people increases the population size with people who are unlikely to die in that year.

On the downside, to convert the age-specific death rate predictions into number of deaths, estimates of the populations of these age bands must be used, which may introduce inaccuracies. Populations are only known accurately on census nights.

Logically, this revised complex model has more credibility for establishing levels of excess deaths than the new simple model currently being used in the Provisional Mortality Statistics. However, one must also bear in mind that the revised complex model was chosen *after* the actual death numbers were known for the pandemic period up to at least the end of 2022. In view of this, and the potential for political pressure to be put on the ABS to reduce reported numbers of excess deaths, it is important that all aspects of the choice and

development of this model be brought into the public eye.

1.5 Other models

There are other models being used around the world to predict expected deaths, and thus to calculate excess deaths over the COVID period. Two are described below because their output is used in this analysis. Brief information on others is given in Appendix B.

1.5.1 Clarity on health models

The author's business, Clarity on Health (CoH) is engaged in a collaborative project to compare excess death patterns in different countries. However, the models used by the ABS are not used in all other countries. As a result, CoH has created a simple model that can be used across many countries. This model uses the average of annual death rates for the pre-COVID years 2015-2019 to estimate excess deaths during the COVID period. This model is only suitable for looking at annual data.

1.5.2 Rönning-Gulbrandsen model

Two researchers in Finland have developed a model[9] with a linear trend and a sine component which was used to analyse Finnish data. One of the authors, Tore Gulbrandsen, has used this model on ABS data and a graph showing his findings is presented later.

2. ABS estimates of excess deaths over the COVID period

As mentioned above, the choice of model can make a substantial difference to the excess death story over the COVID period, with the simple and complex ABS models giving a cumulative total of 42,208 and 19,064 excess deaths over the COVID period respectively.

The number of deaths in 2022 equates to thousands of Australian lives lost. Using the simple model, it is equivalent to a plane of the size of an Airbus 380-300 crashing roughly every four days, with the loss of everyone on board; with the complex model it is equivalent to such a plane crashing roughly every week.

3. What pattern of excess deaths should we expect after a pandemic?

Normally during an influenza epidemic, in the absence of intervention from governments and public health officials, there is a toll of deaths as the infection passes through the population, killing the vulnerable (mainly the frail and elderly

Table 1: Excess deaths (number and %) as calculated by ABS simple (original and new) and revised complex models						
Excess death predictions by model (numbers)	2020	2021	2022	2023 (part year)	Cumulative excess to date	Cumulative excess to end 2022
ABS 'simple' - Provisional Mortality Statistics (The original simple model applies to 2020 and 2021, the new simple model thereafter)	-108	8517	25235	8564	42208	33644
ABS 'revised complex' - Measuring Australia's Excess Mortality	-5228	2378	18634	3280	19064	15784
Excess death predictions by model (% excess)	2020	2021	2022	2023 (part year)	Cumulative excess to date	Cumulative excess to end 2022
ABS 'simple' - Provisional Mortality Statistics (The original simple model applies to 2020 and 2021, the new simple model thereafter)	-0.1%	6.0%	15.3%	13.2%	8.3%	7.5%
ABS 'revised complex' - Measuring Australia's Excess Mortality	-3.1%	1.4%	10.9%	9.1%	3.5%	3.1%

Notes:
Data for 2023 are not consistent as they are reported to different time points. The Provisional Mortality Statistics are to May 1st, and the Measuring Australia's Excess Mortality is to March 26th.

Sources: (Accessed 29 August 2023)

https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/latest-release
https://www.abs.gov.au/articles/measuring-australias-excess-mortality-during-covid-19-pandemic-until-first-quarter-2023

and others with weakened immunity). However, the next year there is typically a reduced number of deaths, known as a 'harvesting' or 'pull-forward' effect, and termed a mortality displacement[8] by the ABS.[5] COVID, we know, is most dangerous for a similar cohort.[6]

COVID became endemic in Australia in late 2021 and early 2022 when the Omicron variant reached the nation: lockdowns were ending and state and international borders were opened to vaccinated people. However, the compensatory decline in deaths expected a year later has not been seen in 2023. Instead, deaths remain in excess at 13.2% or 9.1%, depending on the ABS model used.

We must question the way the normal mortality displacement has not occurred with COVID. And we must ask why excess deaths are continuing with so many deaths assigned to COVID, despite the population being heavily vaccinated with vaccines that were billed as preventing death from the disease.

4. How unusual are the 2022-2023 excess deaths?

4.1 Visual inspection of history

The ABS does not seem to have addressed an important question. How unusual is it to have a 15.3% or 10.9% spike in deaths in a particular year?

This is something that Clarity on Health has examined, using data from the Australian Institute of Health and Welfare going back to 1950. The graph shows the percentage of excess deaths in a particular year, where the excess is calculated in comparison with the average number of deaths in the preceding five years. In the graph two lines are shown from 2020, namely the excess deaths calculated by the ABS simple and revised complex models.

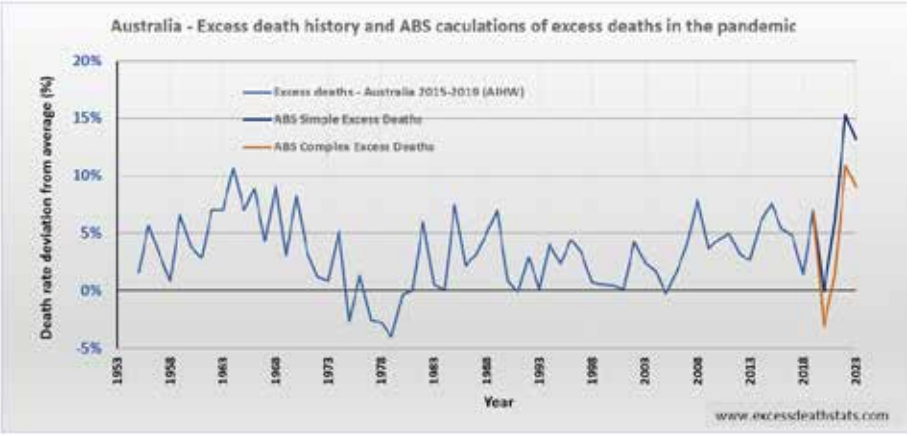
Looking back over history we see that the highest spike in deaths between 1955 and 2019 occurred in 1964, with a spike of 10.6%. The graph shows that the two-year pattern of excess deaths of 15.3% as reported by the ABS for 2022 using its new simple model, followed by 13.2% for 2023 (to the end of May), is unprecedented.

And using the revised complex model, even though the excess deaths are lower, the graph shows that a pattern of two years of 10.9% and 9.1% excess deaths has not been seen in the past 67 years.

Thus visual inspections show the annual 2022 and year-to-date 2023 excess

5 Similarly, after the deficit in deaths seen during lockdowns in 2020, one might expect a catch-up of deaths, particularly among older people, once Australia resumed normal life.

6 The median age of death from COVID was 86.9 years in 2020[10] and 79.1 years in 2021[11] (the most recent data available from the ABS). This lower age of deaths from COVID in 2021 than in 2020 has been ascribed to the Delta variant; however, normally variants tend to become not more but less virulent with time.

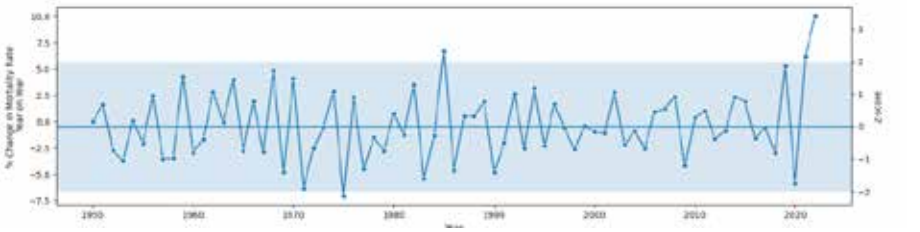


Graph 1.

death numbers give a clear signal that something very extraordinary has happened, regardless of which model one uses.

4.2 Z-scores

A more objective way to measure how unusual the excess death spikes in 2022 is to use z-scores, which measure how far a data point is from the mean in terms of the number of standard deviations. Graph 2 shows the z-scores of annual percentage changes in the death rate in Australia (year on year). The blue shaded band shows z-scores between +2 and -2 - and 95.45% of data points are expected to lie within this range. In 2022, the z-score was 3.39. The



Graph 2. Z-scores of year-on-year percentage changes in death rates, Australia

probability of getting such a z-score or higher by chance is 0.034%.

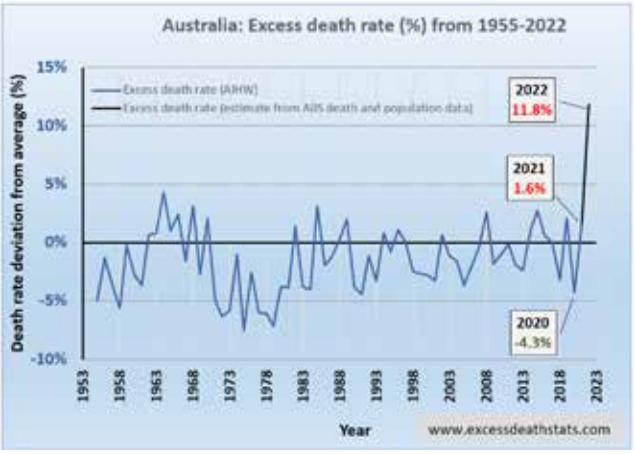
5. Excess deaths in other countries

Through a collaboration with Reignite World Freedom, Clarity on Health has been examining excess death statistics in other countries and posting results on www.excessdeathstats.com. The project relies on volunteers who are familiar with events in their own countries and who have been following their own statistical

office publications. For each country, a simple annual model of excess death rates during the pandemic is produced. The models use a predicted death rate of the average of the five pre-pandemic years (2015-2019). To put excess death rates during the COVID period in perspective, the results are displayed graphically, with the history going back as far as 1950 where possible. All data are taken from the country's official statistics office.

The project team has examined data from Australia, Philippines, New Zealand, Denmark, and Sweden so far and graphs for these countries are presented below.

Australia and New Zealand, which had very similar responses to the COVID period, aiming for zero COVID levels at times, have similar graphs. The virus only became widespread in 2022 in these countries - in January in Australia

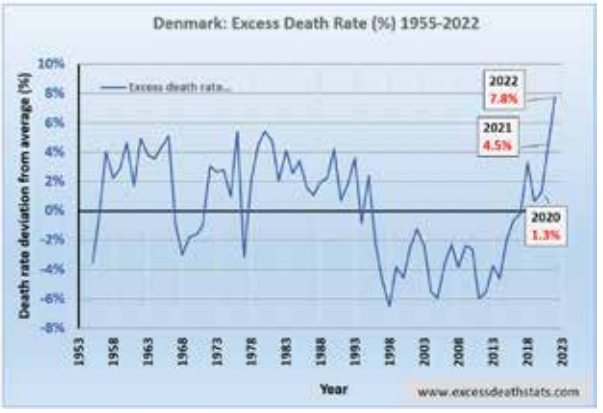


Graph 3.

Graph 4.

and March in New Zealand. For both countries 2022 shows the largest spike in death rate in 67 years.

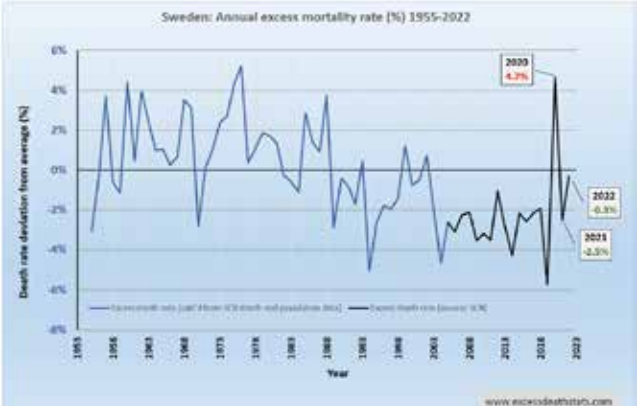
Denmark, with land borders, was not able to keep COVID out in 2020, but like Australia imposed lockdowns and rolled out COVID vaccines. It too



Graph 5.

shows a pattern of excess deaths, with 2022 having the biggest increase in death rate in 67 years. One must ask why death rates are at their highest in 2022, so long after the population was first exposed to the virus.

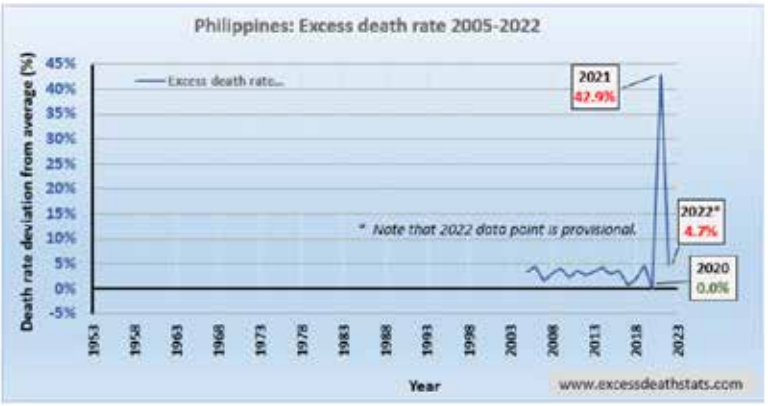
Sweden, which did not institute lockdowns, had a much more normal epidemic response with the virus spreading in 2020 and a 4.7% spike in death rate that year. Notably, the Swedish spike in death rates was smaller than that for any of the other countries discussed here, and it was not unprecedented



Graph 6.

in the post-war period (there was a 5.2% spike in 1976). The death rate had returned to normal by 2022 with a small 0.3% *deficit* of deaths. One might argue that Sweden's graph shows the spike-followed-by-harvesting effect, which would be expected after an epidemic.

In the Philippines, the spike was phenomenal: 42.9% in 2021. Final data have yet to come in for 2022, but provisional data suggest excess deaths have dropped down to 4.7% (this is still higher than pre-COVID averages). Of course, after such a large spike in deaths in 2021, a very large harvesting effect would be expected.



Graph 7.

The Philippines had strict lockdowns over an extended period and rolled out seven different COVID vaccines between March and August 2021, including Chinese and Russian vaccines. The reason for this huge spike in the death rate in 2021 should be investigated.

These graphs tell us that similar patterns to those found in Australia are being seen elsewhere in countries that responded to the COVID period in similar ways, with New Zealand being the most similar. Sweden and the Philippines show us though that different patterns of excess deaths can occur and it seems likely that this reflects different approaches to managing the response to COVID.

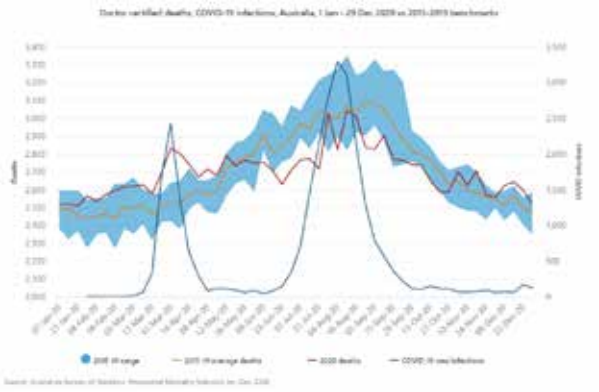
It is noteworthy that New Zealand and Sweden may represent opposite situations with regard to the relative timing of COVID injections and COVID infections. In New Zealand vaccinations preceded COVID spreading widely within the country. In Sweden it was probably the reverse.

6. In Australia, when did things start to go awry?

6.1 What the ABS's simple model tells us (Provisional Mortality Statistics)

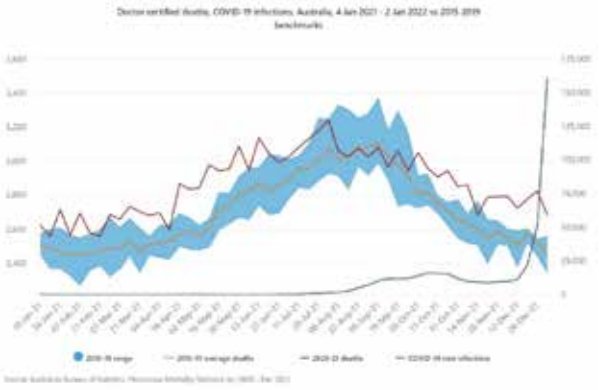
The provisional mortality statistics include a graph which shows average deaths in the years 2015-2019 (the predictor of expected deaths), and actual deaths. The blue shaded area gives the range of death numbers in those years.

As far as we know, no warning system was in place to alert the government or



Graph 8. ABS original simple model output 2020

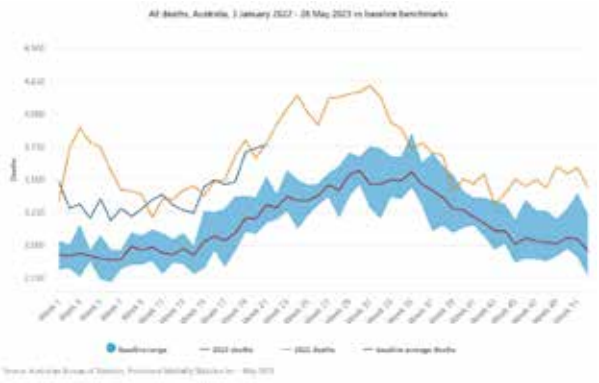
the public that deaths were reaching unusually high levels. Such a system could have been set up using excursions above the blue shaded area for a few weeks in succession.



Graph 9. ABS original simple model output 2021

The three graphs published by the ABS covering the COVID period demonstrate how often warning signals would have arisen. The first[12] shows 2020, the

second[13] 2021 (it appears that ABS mislabelled the red line 2020-21), and the third[14] shows 2022 and 2023 on the same graph.



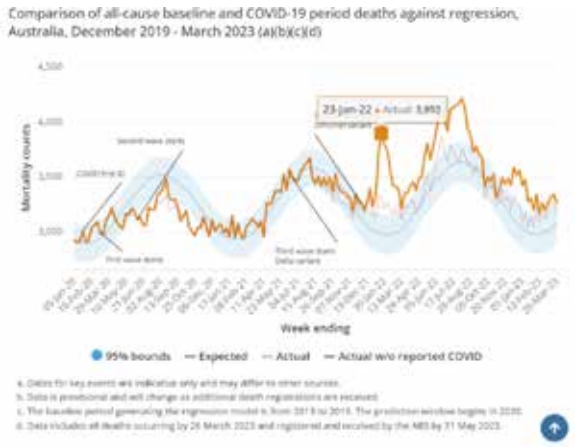
Graph 10. ABS new simple model output 2022-2023

In 2020 there was a brief spike in deaths above the blue shaded area that coincided with the first COVID wave. However, during the winter of 2020 there were periods where there is a deaths *deficit* even as a second COVID wave hit.

In 2021, there were extended periods where actual deaths (the red line) were above the blue shaded area in autumn and spring. Warnings would have been given in early October and, except for one week, they would have remained for the rest of the year.

Rather confusingly, the ABS swapped the colours of the lines in the third graph. In this graph actual deaths are shown in yellow-orange for 2022 and blue for 2023.

Except for three weeks in late winter and spring 2022, deaths remained



Graph 11. ABS revised complex model output 2020-2023

consistently above the blue-shaded area, and the curve remained stubbornly above the shaded region in 2023.

In summary, had excursions above the blue shaded area for a few weeks been taken as a warning signal, the ABS's simple model would have signalled that something was wrong from October 2021 to May 2022.

6.2 What the ABS's complex model tells us (measuring Australia's Excess Mortality)

In this model,[8] the blue shaded area shows 95% confidence intervals and the upper boundary is designed to act as a threshold.

Here is what the ABS said about interpreting the information in their report: 'When actual observations (counts of death) exceed the upper threshold or drop below the lower threshold this indicates a statistically significant change in the pattern of mortality. This should be used in conjunction with the percentage excess mortality.

'A single week above threshold does not necessarily suggest statistically significant excess mortality. Prolonged periods (2 or more weeks) where counts exceed thresholds suggest more strongly that the numbers of deaths are above or below normal.'

Examining the graph, the threshold was breached in the Australian Spring of 2021 and remained breached until late winter or early spring of 2022. Since mid-spring 2022 up to at least March 2023 the line has remained above the threshold.

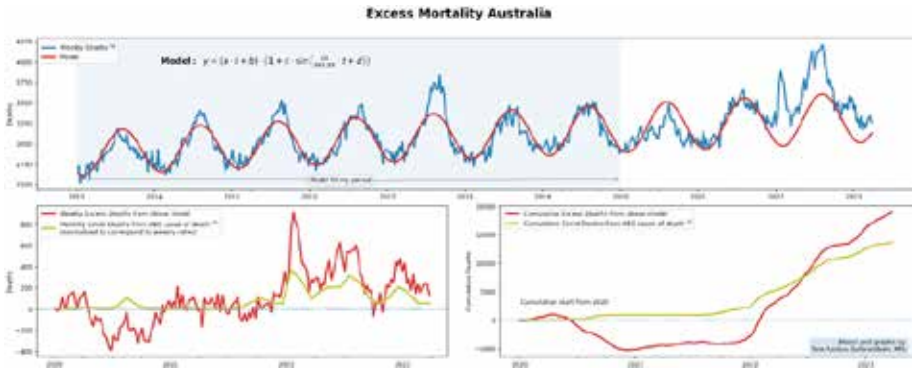
6.3 What the Rönning-Gulbrandsen model tells us

Like the ABS complex model, this model[9] uses a mathematical formula to model the data from 2013-2019 and to predict deaths over the COVID period. However, the formula (shown on the graph) is not the same as that used by the ABS.

In the graph below, actual deaths (in blue in the upper panel) can clearly be seen to depart from expected deaths in spring 2021, and except for a brief period in spring 2022, have remained in excess.

In the lower left panel, excess deaths are plotted in red and deaths due to COVID are plotted in green. Clearly, COVID death peaks and excess death peaks coincide in 2022.

The graph in the right lower panel shows cumulative excess deaths (in red) and cumulative deaths due to COVID (in green, derived from ABS monthly data). The fact that, from 2022, the slope of the excess deaths cumulative



Graph 12. Rönning-Gulbrandsen model output for 2020-2023

curve is steeper than the curve of deaths due to COVID suggests that COVID is not the only factor causing excess deaths.

This cumulative graph also raises intriguing questions: what caused the changes in slope of the cumulative excess deaths line in late 2020 and in early 2022?

In conclusion, three different models show excess deaths rising to levels that should trigger alarm from the Australian Spring of 2021 onwards.

7. Conclusion

7.1 Transparent publication of the details of the ABS 'revised complex model'

The model here called the revised complex model was produced after a trend of excess deaths had been established in Australia for nearly two years. Ideally such a model should be created using a logical and principled approach before any actual mortality data become available. The ABS needs to publish full details of the model, including coefficients and results for excess deaths by age band and state throughout the COVID period, to provide complete transparency.

7.2 An independent investigation

The Australian data discussed here show that Australians have been dying at rates approximately 10% greater than expected since the Spring of 2021. Yet it seems that no investigation has been set up into the causes of these excess deaths.

Notably, despite what the ABS tells us is "statistically significant excess mortality", Australian senators chose to vote against establishing a

committee to investigate excess deaths in March, 2023.

Since it is possible that some of these excess deaths may be the result of actions taken by public health officials and Australian governments during the COVID period, care needs to be taken in selecting a committee to investigate them. People who were involved in interventions such as lockdowns and vaccination rollouts may have a potential conflict of interest.

A truly independent investigation into the causes of these deaths is long overdue.

Thanks go to Ralph P, Terry Anderson, Tore Gulbrandsen, Jamie C and Colin M for their ideas and contributions to this paper.

References

[1] Foster, G. (2022) Do Lockdowns and Border Closures Serve the "greater Good"? A Cost-benefit Analysis of Australia's Reaction to COVID-19.

[2] Németh, L., Jdanov, D.A. and Shkolnikov, V.M. (2021) "An open-sourced, web-based application to analyze weekly excess mortality based on the Short-term Mortality Fluctuations data series," PLOS ONE, 16(2), p. e0246663. Available at: https://doi.org/10.1371/journal.pone.0246663.

[3] Provisional Mortality Statistics, Jan-Mar 2020 (2020). Available at: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-mar-2020 c) Provisional Mortality Statistics, Jan-Mar 2020 (2020). Available at: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-mar-2020

[4] https://mpidr.shinyapps.io/stmortality/

[5] Gibson, John. Cumulative Excess Deaths in New Zealand in the COVID-19 Era: Biases from Ignoring Changes in Population Growth Rates. Working Paper No. 23/02, Department of Economics, University of Waikato. 2023 e) Gibson, John. Cumulative Excess Deaths in New Zealand in the COVID-19 Era: Biases from Ignoring Changes in Population Growth Rates. Working Paper No. 23/02, Department of Economics, University of Waikato. 2023

[6] Provisional mortality Statistics, Jan 2020 - Dec 2021 (2022). Available at: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-2020-dec-2021.

[7] Measuring excess mortality in Australia during the COVID-19 pandemic (25/11/2020). Available at: https://www.abs.gov.au/articles/measuring-excess-mortality-australia-during-covid-19-pandemic.

[8] Measuring Australia's excess mortality during the COVID-19 pandemic until the first quarter 2023 (17/07/2023). Available at: https://www.abs.gov.au/articles/measuring-australias-excess-mortality-during-covid-19-pandemic-until-first-quarter-2023.

[9] Rönning, Kasper and Gulbrandsen, Tore A. (2022) "Excess death anomaly in Finland 2021," Available at: https://jarjenaani.fi/wp-content/uploads/2023/05/Excess_Death_Anomaly_Finland_2021.pdf

[10] Causes of Death, Australia, 2020 (2021). Available at: https://www.abs.gov.au/statistics/health/causes-death/causes-death-australia/2020.

[11] Causes of Death, Australia, 2021 (2022). Available at: https://www.abs.gov.au/statistics/health/causes-death/causes-death-australia/2021

[12] Provisional Mortality Statistics, Jan-Dec 2020 (no date). Available at: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-dec-2020

[13] Provisional mortality Statistics, Jan 2020 - Dec 2021 (2022b). Available at: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-2020-dec-2021.

[14] Provisional mortality statistics, Jan - May 2023 (2023). Available at: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-may-2023.

[15] Karlinsky, A. and Kobak, D. (2021) "Tracking excess mortality across countries during the COVID-19 pandemic with the World Mortality Dataset," eLife, 10. Available at: https://doi.org/10.7554/elife.69336.

[16] COVID-19 Data Explorer (no date). Available at: https://ourworldindata.org/explorers/coronavirus-data-explorer.

[17] *The Economist* (2022) 'Tracking covid-19 excess deaths across countries,' *The Economist*, 13 May. Available at: https://www.economist.com/graphic-detail/coronavirus-excess-deaths-tracker.

Appendix A

Estimates of excess deaths for Australia obtained using the Short-term Mortality Fluctuations Tool (STMF)					
Measure/Modelling approach	**Baseline Years**	**Reference mortality**	**Actual mortality**	**Excess mortality**	**Excess mortality**
Deaths/Week-specific averages	2015-2019	160,429	189,936	29,507	18.4%
	2016-2019	161,301	189,936	28,635	17.8%
	2017-2019	162,453	189,936	27,483	16.9%
	2018-2019	161,720	189,936	28,216	17.4%
	2019	164,370	189,936	25,566	15.6%
Deaths/Week-specific trends	2015-2019	168,470	189,936	21,466	12.7%
	2016-2019	167,928	189,936	22,008	13.1%
	2017-2019	159,966	189,936	29,970	18.7%
	2018-2019	180,265	189,936	9,671	5.4%
	2019	164,370	189,936	25,566	15.6%
Mortality Rate (Deaths/100,000 population)/Week-specific averages	2015-2019	652.86	733.95	81.09	12.4%
	2016-2019	651.35	733.95	82.60	12.7%
	2017-2019	650.98	733.95	82.97	12.7%
	2018-2019	643.08	733.95	90.87	14.1%
	2019	649.00	733.95	84.95	13.1%
Mortality Rate (Deaths/100,000 population)/Week-specific trends	2015-2019	635.29	733.95	98.66	15.5%
	2016-2019	633.38	733.95	100.57	15.9%
	2017-2019	615.39	733.95	118.56	19.3%
	2018-2019	684.71	733.95	49.24	7.2%
	2019	649.00	733.95	84.95	13.1%

Appendix B

Other models and data on excess deaths.

The Short-term Mortality Fluctuations Tool (SMFT)

Researchers from the Max Planck Institute in Germany and the University of Berkley in California developed an online tool[4] for modelling excess deaths. Users can choose the period of years used to estimate the baseline and whether to model deaths or death rates.

The World Mortality Dataset

A repository[15] collecting weekly, monthly or quarterly mortality data for 125 countries and territories from 2015 onwards.

Our World in Data

A portal[16] which has access to data on excess mortality that enables graphs to be plotted by country

The Economist

A webpage with underling model[17] tracking excess deaths by country.

Clare Pain is a medical journalist and science writer with over a decade's experience of writing for doctors and the general public.

After two years studying medicine, she completed a chemistry degree, followed by a Master's in operational research. She then worked for eight years in industry in the UK as a statistician. Clare Pain turned to science writing and medical journalism in 2011. She has written for the ABC, *New Scientist*, the Springer Nature publishing group, *Medical Observer, Australian Doctor* and *Spectator Australia*.

Since December 2021, she has run projects on www.ClarityonHealth.org to examine the response to COVID in Australia. Projects include the 'The Australian Survey of Reasons for COVID-19 Vaccination' and the Mandate Update project, which tracks which employers are (and are not) mandating COVID injections.

Clare Pain's current focus is to bring the phenomenon of worldwide excess deaths to the attention of ordinary people and their elected representatives. Her substack is clarityonhealth.substack.com.

Excess mortality in Australia — when were the warning signs apparent?

by Andrew Madry
BSc (Hons) PhD

1. Introduction

Australia, like many other Western countries, is currently experiencing excess mortality at a level unknown outside war times. Even after COVID deaths are taken into account, there is substantial remaining excess mortality. Health authorities have no explanation for the cause of these Australian excess deaths above historical averages.

We know in 2023 that excess mortality is well above estimated baselines, and has been so for some time: we consequently ask: were there trends apparent in mortality data, unrelated to COVID-19 disease, that should have raised early warnings to health authorities?

We take a statistical signal processing approach for detection of such phenomena. As well as classical time-series analysis approaches, we apply modern machine-learning methods to time series to investigate trends in detail.

The COVID vaccination campaign, in response to the COVID-19 disease, is the first time such a widespread effort has been made to deliver a novel pharmacological product to the Australian population.

We review the Therapeutic Goods Administration (TGA) reporting system

for adverse events related to COVID-19 vaccination. There are approximately 1,000 deaths reported following COVID vaccination. The TGA states that only 14 deaths were directly caused by COVID-19 vaccination with the implication being that all the other deaths are 'coincidental'.

This report focuses on data for the State of Queensland. COVID was kept out of the community in Queensland until January 2022 through hard border lockdowns. This allows mortality trends to be investigated for a longer period without the effects of COVID deaths.

Mortality in older ages exhibits a distinct change in trend in early 2021. This may not be another coincidence. The analysis in this report is based on a customised data set purchased from the Australian Bureau of Statistics ABS. ABS material was used as supplied. The analysis is the work of the author alone. The intention of this report is to demonstrate analytical techniques that can be applied to raw mortality data to track changes in trends of mortality.

2. Long-term mortality trends in Australia

The Australian Institute of Health and Welfare (AIHW) publication Deaths in Australia,[1] last updated in June 2022, describes rates of death progressively falling in Australia for both males and females. From reference[1] on trends in deaths over time:

> **In Australia, death rates have continued to decline since at least the early 1900s. Between 1907 and 2020, the crude death rate decreased by 42% (44% for males and 39% for females). When accounting for changes in the population age structure over this period, the age standardised death rate fell by 76% (74% for males and 78% for females). This was largely driven by the decline of infant and child deaths during this period; from 2,412 deaths per 100,000 children under 5 in 1907 to 71 per 100,000 in 2020 (decrease of 97%).**
>
> **As in many other developed nations, Australia has experienced a 'health transition' during the 20th century. While infectious diseases such as influenza and tuberculosis caused the most deaths in the early 1900s, from the 1930s onwards cardiovascular diseases and cancers were the leading causes of death.**

Figure 1 shows the age-standardised death rate in Australia for males and females from 1907 to 2020.

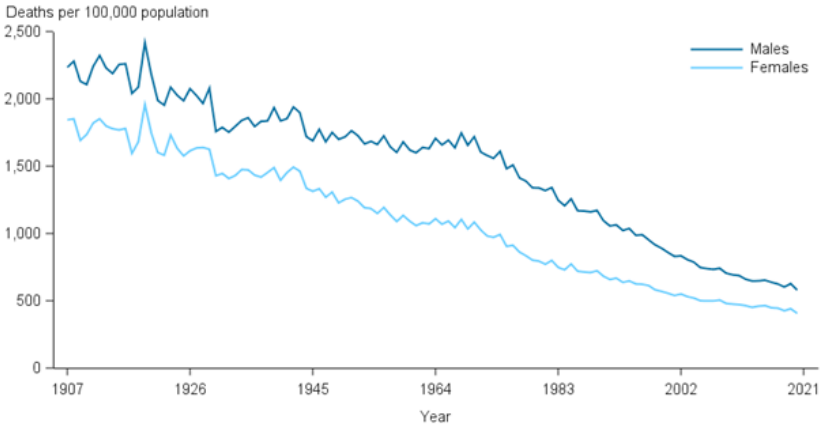


Figure 1. Source: Australian Institute of Health and Welfare (2022). 'Figure 5.1: Age-standardised death rates in Australia, by sex, 1907–2020.' *https://www.aihw.gov.au/reports/life-expectancy-death/deaths-in-australia/contents/trends-in-deaths*, accessed July 4th, 2023.[1]

2.1 Life expectancy

The following data are taken from Australian government websites.

From reference[2] (ABS):

> **Life expectancy at birth was 81.3 years for males and 85.4 years for females in 2019-21.**
>
> **In 2020, Australia recorded a lower than expected death rate as public health measures put in place to restrict the spread of COVID-19 also resulted in a reduction of deaths across a number of other causes. In 2021, the death rate increased but was still lower than pre-pandemic levels.[2]**

Further comments shall be made on the last statement above, regarding 2021, in Section 7.

From reference[3] (AIHW):

> **In 2020, there were 161,300 deaths registered in Australia (84,588 males; 76,712 females). The majority of deaths in Australia, like other developed countries, occur among older people (see Figure 2). Sixty-six per cent of deaths registered in Australia in 2020 were among people aged 75 or over (60% for males and 73% for females).**

> **The median age at death was 79 years for males and 85 years for females.**

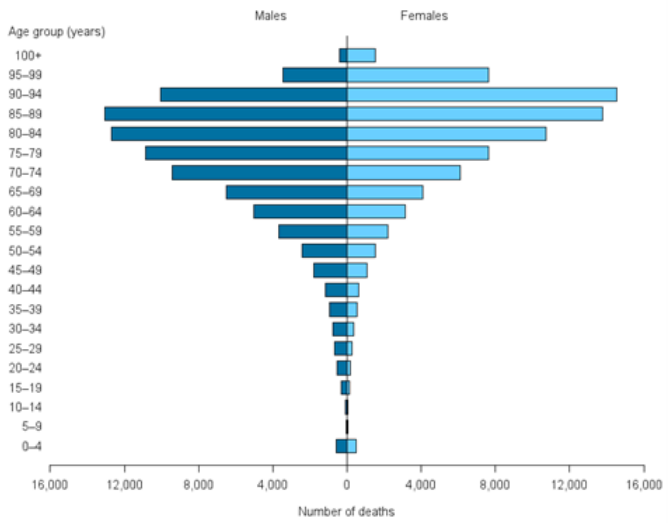


Figure 2. Source: Australian Institute of Health and Welfare (2022).
'Figure 2.1: Deaths in Australia by sex and age group, 2020.' *https://www.aihw.gov.au/reports/life-expectancy-death/deaths-in-australia/contents/age-at-death*, accessed July 4th, 2023.[3]

As of October 31st, 2022, the median age for those who had died from COVID-19 was 85.5 years (83.7 years for males, 87.5 years for females).[4] At this point there had been 13,201 deaths from or with COVID in Australia. 81.6% of these were from COVID, where it was considered the underlying cause of death.

3. Data sources used

Several data sources have been used to perform the analysis in this report and are listed in Table 1. The primary source is a dataset purchased from the Australian Bureau of Statistics (ABS) on mortality. This has finer-grained age categories than those provided on the public website. Fortunately, the ABS is a very professional organisation and provides carefully curated data. The same cannot be said of data provided publicly from health authorities in Australia. The COVID pandemic has highlighted the lack of rigorous data standards in government health reporting. The researcher is faced with challenges including: categorisation that changes over time, data only provided in graphics on websites, and data that are not updated in retrospect. Relevant data are sometimes only available through formal Freedom of Information (FOI) requests.

This has been unacceptable, particularly with the health of Australians at stake.

Table 1. Data sources used for this report.

Source	Description	Type of Data
ABS	Custom mortality dataset	Mortality, Australia and Queensland
ABS	Population from ABS Data Explorer	Quarterly by State and Age Group
covidbaseAU	3rd party aggregator site	COVID deaths, Vaccination rollout.
TGA	Database of Adverse Event Notifications (DAEN)	Reports of adverse events following COVID-19 vaccination.
TGA	Freedom of Information Requests	Cases resulting in death, Batch numbers

4. Analysis of excess mortality

In this section a brief review is provided on reporting of excess mortality in Australia.

4.1 Australian Bureau of Statistics

With each monthly release of mortality data, the ABS provides some commentary. The ABS is clear that its reporting of excess mortality uses very simple methods and it is not intended for providing health guidance. It makes a simple estimate of a baseline based on the average of a number of preceding years. In 2020 and 2021 the baseline was based on years 2015-2019. In 2022, years 2017-2019 and 2021 are used. There has been conjecture about whether the choice of years is appropriate, for example 2020 being a lower than normal year and 2021 being a higher year.

Simple estimates have their purpose. A graph from the ABS monthly report,[5] released at the end of May, 2023, covering the period up to February 2023, is shown in Figure 3.

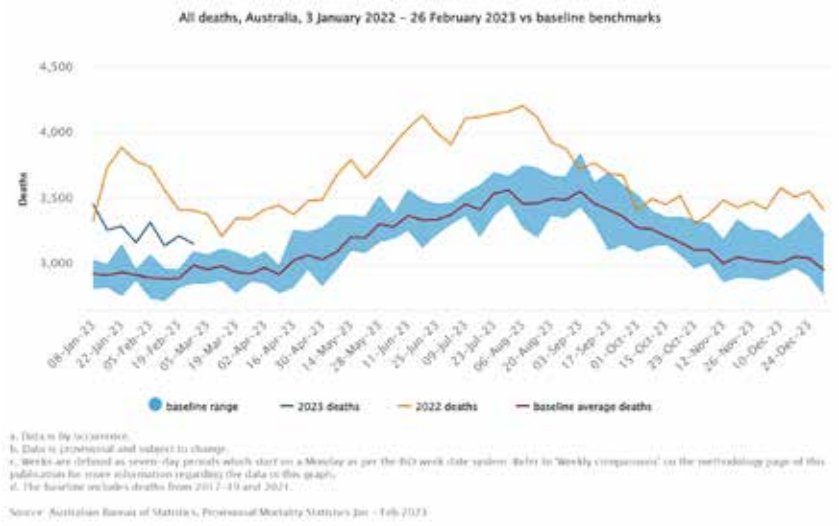


Figure 3. Australian Bureau of Statistics (2023): 'All deaths, Australia, 3 January 2022 – 26 February 2023 vs baseline Benchmarks.' *https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-feb-2023*, accessed July 4th 2023.[5] Deaths in 2022 are shown in orange. Deaths January-February 2023 are shown in blue. The estimated baseline is shown in red.

It is important to note that ABS data are marked as provisional. These are updated over time. The numbers for the last few months of the provisional reports always revise upwards as death reports are received late. The baseline shown in red in Figure 3 above is the average of the selected baseline years. The blue shading indicates the range of the values over those years.

In the report, covering the period up till December 2022, it is stated:

> In 2022, there were 190,394 deaths that occurred by 31 December and were registered by 28 February 2023, which is 25,235 (15.3%) more than the historical average.

By the February 2023 ABS report[5] that number revises up to 190,775 deaths. The ABS reports on the number of COVID deaths separately.[4]

4.2 Actuaries Institute

The Australian Actuaries Institute has a COVID-19 Working Group that provides analysis of excess deaths using their own methods. In the recent report, reference,[6] they estimate excess mortality for 2022 at 12%. They have used different methods for their analysis of mortality over the pandemic period. The most recent method uses Standardised Death Rates (SDR) that are published by the ABS. In the absence of detailed age breakdowns, this is a way to take

age differences into account. A simple rate of death can be computed by the number of deaths divided by the total population. But at different ages there are different numbers of deaths. A top-level description only of their method is provided in their reports and it is not possible to reproduce the analysis.

The Actuaries Institute goes to a lot of effort to subtract all COVID deaths ('from' and 'with') in coming up with an excess, had COVID not occurred. Unfortunately, this is too simplistic. Many of the COVID deaths that have occurred would unfortunately have occurred in the presence of the normal influenza seasonality, perhaps not the same people but typically in the same demographic, that is: older people with comorbidities.

They report that over half of the excess mortality in 2022 is due to deaths from COVID-19 (approximately 10,000 deaths). Subtracting all COVID deaths is not taking into account the normal seasonality of mortality. We know also that the median age of death due to COVID is greater than population median age of death. Those who die of COVID typically have several comorbidities. In this report we address this carefully, in Section 6 onwards.

They also make an attempt in the report to explain what could be causes of the non-COVID excess with a section titled: 'What could be causing the non-COVID-19 excess deaths?' They rate 'Post COVID-19 sequalae or interaction with other causes of death' as High and 'Delay in emergency care' as High with a caveat only during COVID-19 peaks. They rate lowest and negligible, 'Vaccine related deaths'. This is apparently based on the TGA having a 'very good' vaccine approval and safety monitoring process. They also base it on correlation of periods of excess mortality not being aligned with vaccine rollout, the logic being vaccine numbers were low in 2022 and excess deaths were high. There appears to have been no detailed analysis behind this assertion.

A further detailed critique of the methods used is outside the scope of this report.

4.3 TGA safety monitoring process

Data collected by the TGA have been used as another source of information. In an Appendix (see Section 12) we provide a detailed analysis of information gleaned from the TGA's safety monitoring system and through Freedom of Information requests made by the public. As at the time of writing (June 25th, 2023) 993 deaths have been reported following COVID-19 vaccination. The TGA attributes 14 only as being caused by COVID-19 vaccination. For a better understanding of the nature of the deaths reported, a visualisation from the work covered in the Appendix is provided in Figure 4.

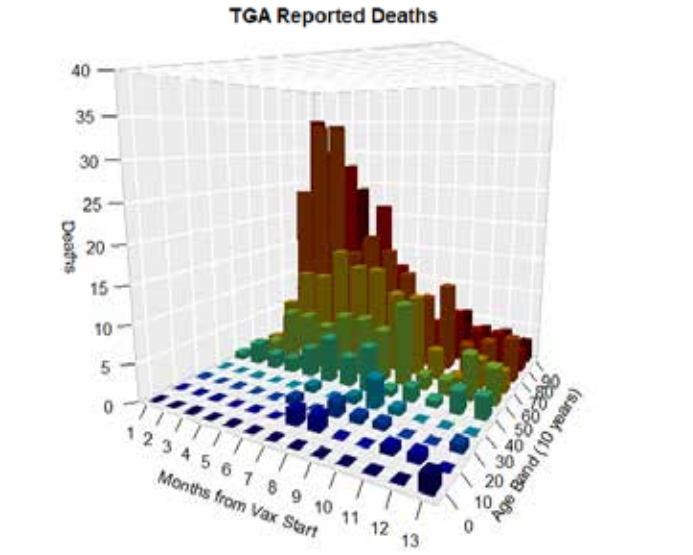


Figure 4. 3D histogram of TGA reported deaths following COVID-19 vaccination. Reported ages are shown in 10-year age bands, against time in months from the start of the rollout (Month one being March 2021).

As a result of FOI requests made by the public (see Section 12.4), it is known that the TGA was not transparent regarding deaths of children following vaccination. Deaths of two children under age 10 are represented in the foreground of the graphic (month 13, age 0-10).

The TGA monitoring system can be described as politically influenced or deficient, or both.

5 Other Australian mortality studies

Analyst Dr Wilson Sy has written insightful reports on Australia's excess mortality.[7,8] Useful graphics from reference[7] are reproduced in Figure 5, Australian monthly all-cause mortality, from reference.[7]

The lines drawn in Figure 5, Australian monthly all-cause mortality, from reference [7] show the approximate time of the mortality 'regime change'. It is clear that this occurs somewhere in 2021. Wilson Sy's analysis shows a correlation in excess mortality at a 5-month lag period from the time of vaccinations.

Other recent studies[9] highlight the need to revisit appropriate methods of estimating the baseline in the context of the pandemic, so as not to underestimate the excess. For example, bad influenza years should not necessarily be included in the 'normal' baseline estimates.

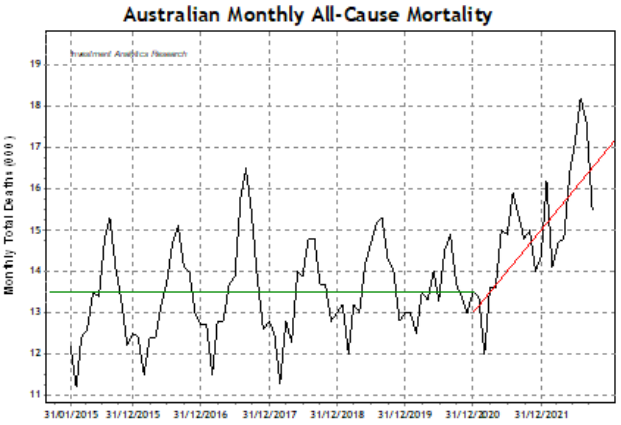


Figure 5. Australian monthly all-cause mortality, from reference.[7]

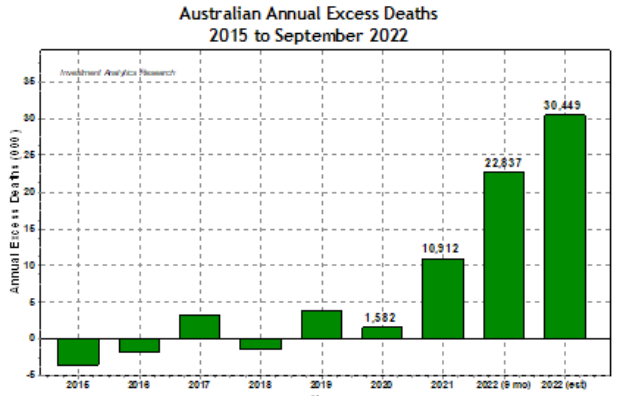


Figure 6. Australian annual excess deaths, from reference.[7]

6 Mortality analysis

In this section the methods used for mortality analysis in this report are described. Australian mortality data were available in five-year age bands. Narrow age bands mean we expect consistent behaviour within the group. With wide age bands a trend could be getting worse in one subgroup and better in another and then the trend can disappear. However, it is not acceptable to say overall the average is the same. When something has worsened in one subgroup it should be investigated. It would be like saying more children are dying by drowning but fewer teenagers are drowning so the average is the same and everything is all right.

We focus on mortality in the State of Queensland, where there was no locally-acquired COVID leading to death until January 2022.

We consequently avoid the approximations inherent in age-standardised approaches used in Section 4.2. We want to understand effects of pandemic measures on specific age groups. We know adverse outcomes from COVID have a strong age dependency. We know adverse effects from COVID-19 vaccines also have an age and gender dependency, for instance: myocarditis in young men.

We expect that some age ranges are more sensitive to external factors. Looking at the age distribution of deaths in Australia, Figure 2, we see the rapid rise as age increases. It is from around age 65 this increase is most rapid. As age increases, death obviously becomes more likely. We focus on ages over 60 in this report.

The example in the following sections steps through the methodology used.

6.1 Example: ages 80-84

We take an older age group, ages 80-84, in Queensland. Raw weekly mortality data from 2015 are shown in Figure 7.

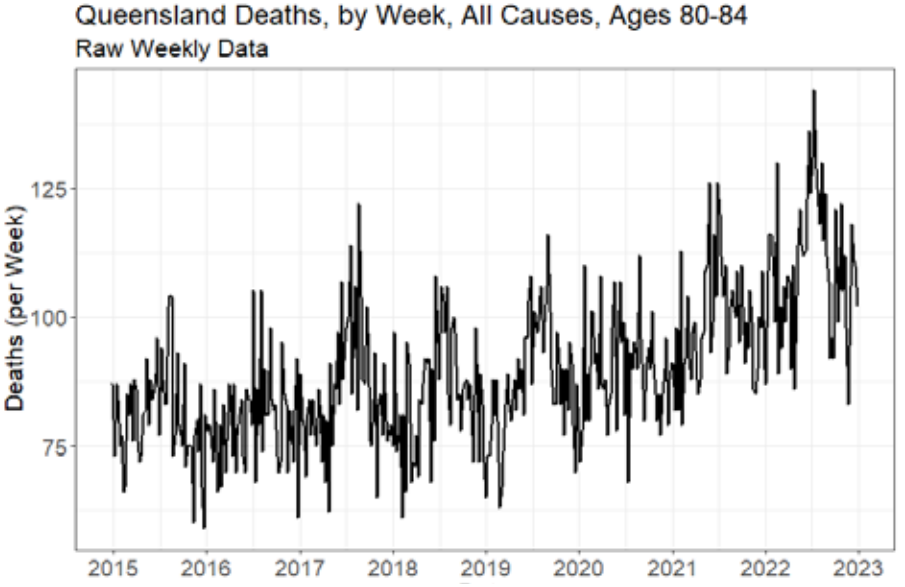


Figure 7. Queensland deaths by week, 2015-2022. Raw data.

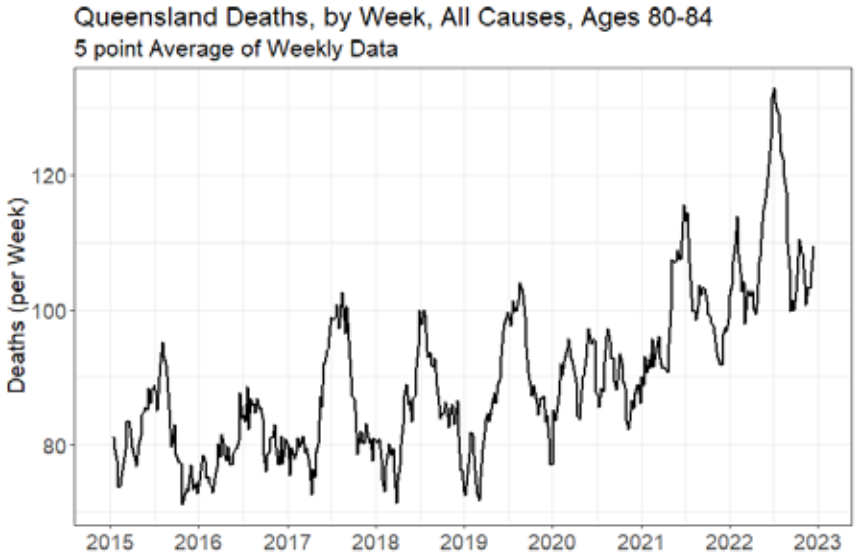


Figure 8. Smoothed 5-point average weekly deaths, in age group 80-84, for Queensland.

There is an inherent random variation embedded in the number of deaths, week to week. The deaths time series, week to week, is noisy. We find that simple smoothing cleans these data up, making trends and seasonality more apparent. See Figure 8. There are typically more deaths than the average in the Winter flu season. This is mid-year in the Southern Hemisphere. We see that in 2017 and 2019 there were worse flu seasons than other years. This was also shown previously in Figure 5. Australian monthly all-cause mortality, from reference. [7] for Australia all-ages mortality. Mortality following bad seasons sometimes tends to be lower. This is called a pull-forward effect. The bad flu season has pulled forward some deaths. Some people unfortunately die earlier in time than might otherwise have occurred, had they not succumbed to an infection. We see a much larger than normal number of deaths in 2022, of people in this age group, when the COVID Omicron wave reached Queensland after borders were opened. COVID is also expected to have a pull-forward effect. We will see whether this occurs in years to come.

What we see in these data is a gradual increase in raw numbers of deaths over time. This is called an increasing 'trend'. However, the total population in the group is changing over time and so, even though there are more deaths as time progresses, that can be expected because there is a bigger population. The rate of death can actually be falling.

Quarterly population data are available from the ABS. When weekly mortality data are used in this report, we interpolate between the available quarterly data points. The population for this age group is shown in Figure 9.

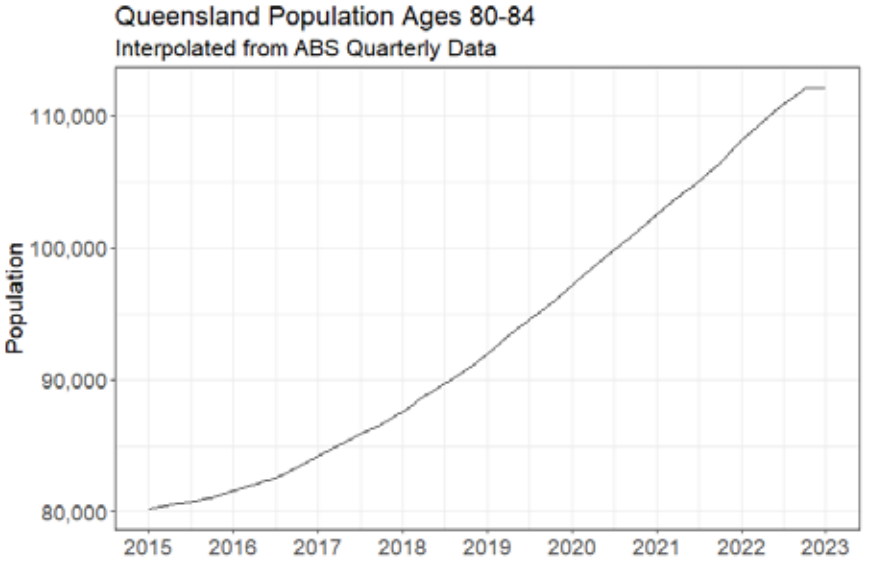


Figure 9. Population of Queensland residents, age 80-84, 2015 to 2022.

Population quarterly estimates were available up to Q3 2022. Rather than extrapolate to Q4 a constant value is used. This will have a minimal error given the typical change from quarter to quarter.

The population of this older age group increases by over 30% over the 8-year period shown. We can now scale the number of deaths by the population size at the time. There are several ways to do the scaling. In this report we do it by adjusting values so that the number of deaths remains the same at the end of the analysis period and all previous rates of death are appropriate to the population at the time. We thus show an 'estimated' number of deaths, given the most recent population estimate. These scaled data are shown in Figure 10.

This is now 'the signal' on which we perform analysis. We see that numbers of deaths in earlier years are larger than the actual numbers from Figure 8. There is now a trend that decreases from the start and turns upwards towards the end.

We can split these data and view them year on year in what is called a seasonal plot (see Figure 11).

This graph initially appears a little confusing with mortality for eight individual years overlaid. However, we can see that there is a seasonal variation in the

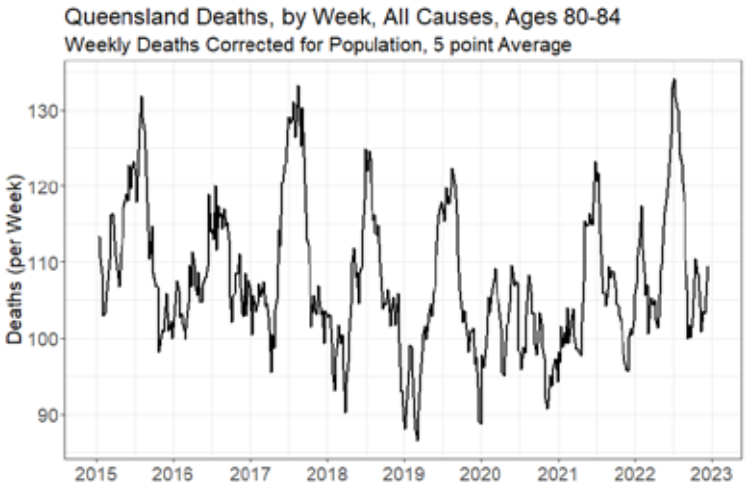


Figure 10. Population adjusted mortality for the 80-84 age group in Queensland.

pattern that repeats, within some bounds, year on year. In particular, we see a large number of deaths in Winter 2022 (black line) because of COVID-19 (peaking in week 29). We also see a similar size maximum, shifted slightly right (week 34), for the 2017 influenza season (green line). So, while COVID-19 had an adverse effect on mortality in this age group, it was similar in magnitude at its peak to the bad influenza season of Winter 2017, on a population-ad-

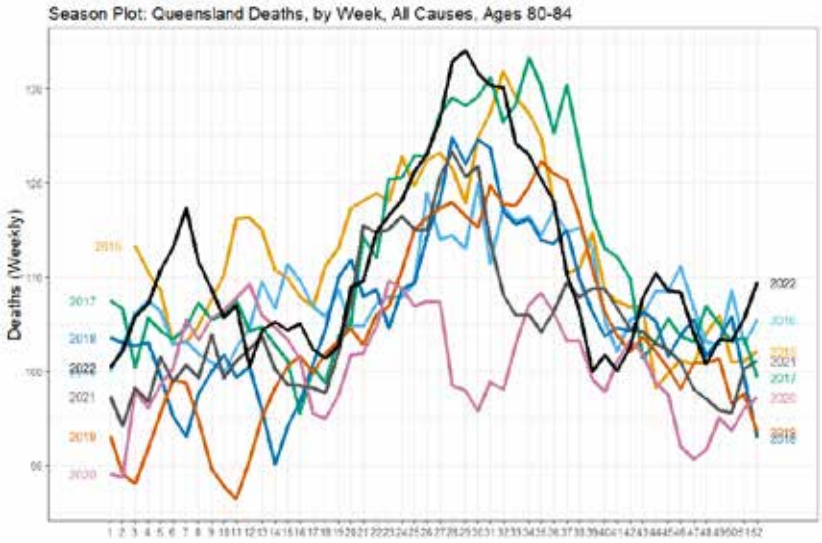


Figure 11. Seasonal mortality plot for Queensland, ages 80-84. Population is adjusted, and rolling 5-point average is applied.

justed basis. The 2022 COVID-19 Omicron peak, early in 2022, is abnormal, created upon the opening up from strict lockdowns to a community naïve to circulating virus.

One can ask how then is it that we are now experiencing an excess of mortality, if at the peak of a COVID wave mortality was similar to a previous influenza wave? The answer is complex in that the excess mortality calculation should take into account the trend of the data, trending down over time on a population-adjusted basis for this age group. What we should expect in a particular year is not necessarily the average of previous years. Taking the average of previous years, while intuitive, oversimplifies the dynamics. We should also not necessarily assume that a very bad previous influenza season is the norm.

Of note is that when it comes to medical resources available to deal with illness, if capacity to treat people has not increased over the intervening years to take into account population growth, then it can seem like systems are overflowing, when in fact it is bad health resource management.

2020 appears lower than other years but still with a seasonal variation. This is possibly partly a result of a pull-forward effect from 2019. It was also different, as a year of strict lockdowns.

From this data estimates can be made of a 'baseline' (see Section 4.1). This is an average estimate taken over previous years. When a subsequent year is above this baseline, we say there is an excess. However, baseline estimation can be too simplistic. If there is a trend where mortality is decreasing, year on year, and we have no reason to expect this trend not to continue, then this trend needs to be taken into account before we estimate an excess.

Care must also be taken, because it is easy to be deceived by these plots as a result of the random component. The overall mortality is the 'area under the curve,' that is, the sum of all the weekly deaths. One line can appear lower than others but when integrated turns out to be larger than expected. For the example above the annual mortality is shown in Table 2.

We see from Table 2 that the 2020 number of deaths was larger than the five previous years in raw death numbers, but when population-adjusted it follows a downwards trend until 2021. We see that 2020 is only 167 deaths fewer than the previous year, which was considered a bad flu season.

In Table 2, the annual, population-adjusted deaths decrease year on year (apart from a small uptick in 2017) until 2021 when something changed. It was stated by authorities (reference section 2.1) that the death rate in 2021 increased but was still lower than pre-pandemic years. We can see in Table 2 in the population adjusted column that we can go back in time to find a pre-pandemic

Table 2. Queensland, ages 80-84, annual number of deaths. Years marked * have 53 weeks using the ISO week convention. 52 weeks only are used.

Year	Deaths (raw numbers)	Population (as at Q2)	Adjusted Deaths
2015*	4,216	80,742	5,792
2016	4,159	82,559	5,588
2017	4,464	85,892	5,765
2018	4,418	89,681	5,465
2019	4,561	94,614	5,348
2020*	4,665	99,884	5,181
2021	5,145	105,049	5,433
2022	5,724	110,933	5,724

year higher than 2021. However, this ignores the fact that, had there not been external factors (that is, a pandemic and government interventions), we would have expected a continual downwards trend in mortality in this age group, albeit with small temporary increases for bad influenza seasons (as seen for 2017).

Note that 2015 and 2020 are 53-week years using the ISO Week convention. In Table 2 only 52 weeks are included for those years in the sum for consistency.

6.2 Time series decomposition

Time series analysis and forecasting is a mature field. There are also new techniques adapted from machine learning which can be applied.

A time series signal can be decomposed into components of:

- Seasonal
- Trend
- Random variation (also called error, remainder)

The decomposed components add together to equate to the actual time series. The aim of decomposition is to minimise the random component and make it truly random. From these components we obtain an understanding of a time series. We can also use these components to forecast forward in time. This assumes a trend continues and seasonal variation is similar.

There are also other components that can be embedded in time series. Seasonal means a variation on a fixed period. In this context, that is yearly. There is a

pattern that tends to repeat each year; for example, there are typically more deaths in Winter, and fewer in Summer. Another type of variation is called:

- Cyclical

Cyclical means variation over some other time period that may not be regular; for example, that could be due to economic variations.

There are also possible external shock components. These shocks are also referred to as exogenous impacts.

Exogenous describes an external effect, as opposed to endogenous for internal. These are unexpected events. Shock components make it difficult to predict data. Unless we know when they occur, they are unforecastable. For example, New Zealand mortality data need to take into account specific events. The Christchurch earthquake and mosque murders were both extreme mortality events. They would have disproportionately affected younger people compared to natural mortality. Reference[10] from New Zealand, looking at excess mortality associated with the booster rollout in New Zealand, deals with this.

Health authority-mandated COVID-19 measures, which may have had an effect on mortality, should be treated as exogenous effects.

So, one approach is to decompose a time series into components for time periods, where we know behaviour is what can be called 'typical.' We assume known trends continue in the absence of any interventions or new diseases. We use that to forecast the future and then we compare that forecast with what actually happened.

A decomposition of the time series from January 2015 to March 2021 is shown in Figure 12. Time series decomposition of the signal from Figure 10, population adjusted. The method used is known as Seasonal and Trend decomposition using Loess (stl). Tuning parameters control the allowable variation of the trend and seasonality. March 1st 2022 is chosen as the end-time for decomposition because this marked the start of the rollout of the novel COVID-19 vaccination.

With real-world data the decomposition is never perfect. In this decomposition there are some discrepancies in the seasonal component and the 2020 error part is larger.

The decomposition can be used to predict what will happen ahead. For the following period, from March 2021 to December 2022, the actual number of weekly deaths (smoothed and population adjusted) is shown as a solid line and the forecast of the same data is shown as a dotted line in Figure 13.

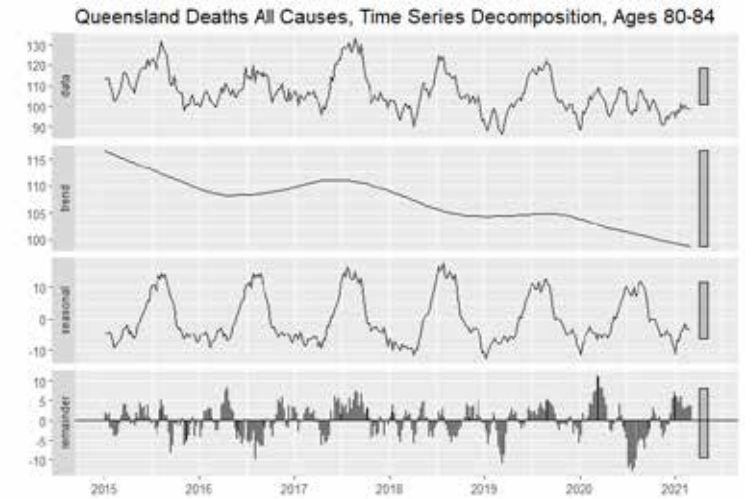


Figure 12. Time series decomposition of the signal from Figure 10 using the stl method.

The forecast (the dotted line) is what we would expect to occur had there been no external effects. We see that the forecast and the actual (solid line) mortality data distinctly diverge in level and shape during this period. The COVID-19 Omicron variant arrived in Australia in late 2021 and the first wave of deaths in Queensland occurred in January 2022. We see this in the actual deaths data, peaking in the middle of the graph in February 2022. The Winter 2022 COVID wave peaks in July 2022.

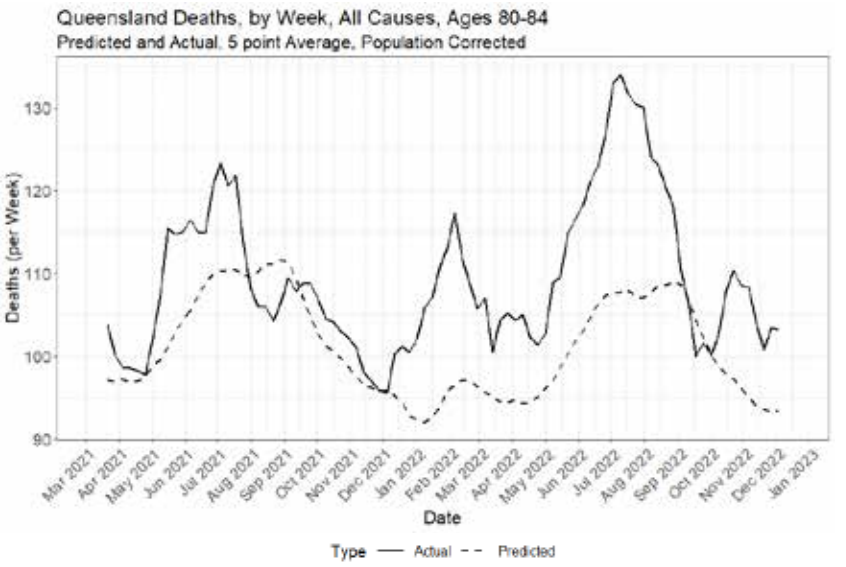


Figure 13. Forecast for period from March 2021 till Dec 2022.

However, near the start of the prediction period there is a peak that starts rising from April 2021, with maximum in July 2021. This is not predicted. We know this is not COVID-19 disease-related, as there was no locally-acquired COVID leading to death in Queensland until January 2022.

6.3 Alternative methods to determine trend

A trend component can be directly computed from the data. We propose a simple method for computing a trend based on a one-year running average. The one-year average runs across the seasonal variation that occurs over a year. It irons out the seasonal variation that goes up in Winter and down in Summer. For each week we take the average of the 52 weeks from that week backwards in time. This measure is potentially usable in a real time monitoring system as we do not rely on any values in the future, only values in the past. The result is shown in Figure 14 below for this age group.

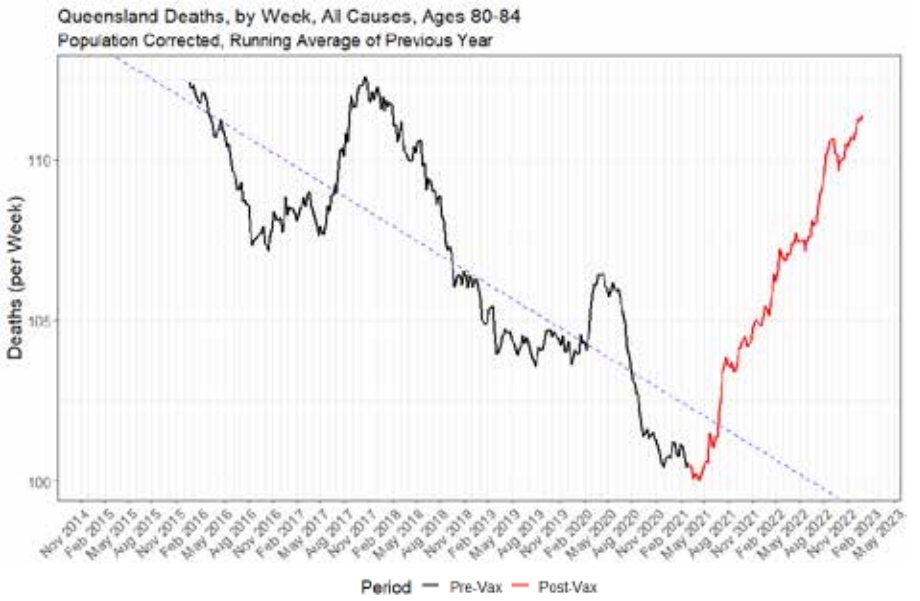


Figure 14. One-year running average of the signal from Figure 10. Population adjusted mortality for the 80-84 age group in Queensland. Linear regression line is fitted through values prior to March 2021, and is shown as the blue dashed line.

Available values start from one year after the first data point, when we have a full year to compute the average. In Figure 14 a linear regression line (blue dashed line) is fitted to the period prior to March 2021 (that is, the black line). In the absence of any exogenous effects, we would expect the computed trend to follow that line, tracking above and below it, slowly decreasing over time. This fitted line is like a longer-term trend that we expect the mortality to follow.

This running one-year average for computing the trend of the mortality has an intuitive interpretation. At any time, it is the average weekly number of deaths for the previous year. When it has increased by one unit it means that the number of deaths per week over the last year has increased by 1. If there are suddenly 52 extra deaths a year occurring, we will also see the one-unit increase. In Figure 14 above, there is a sharp increase of at least 2 units over a period of 1-2 weeks around July. Also, refer back to the time-series forecast in Figure 13 where we saw an increase in the actual value above the forecast around the same time.

At the onset of the 2017 flu season, we see the trend, computed by one-year running average, pick up, as there were more deaths starting to occur in that Winter season. Note that the peak in the running average is not necessarily at the same time as the peak in the raw data, as a result of the way the signal rises and falls. However, this method is still sensitive to onset of changes, picking up where mortality starts increasing. There is a very small local peak observed for the first Omicron wave and a larger one for the 2022 Winter COVID wave. To understand the change in trend upwards from April 2021 we can subtract the values of the regression line from the data and observe the variation from this line. This is shown in Figure 15.

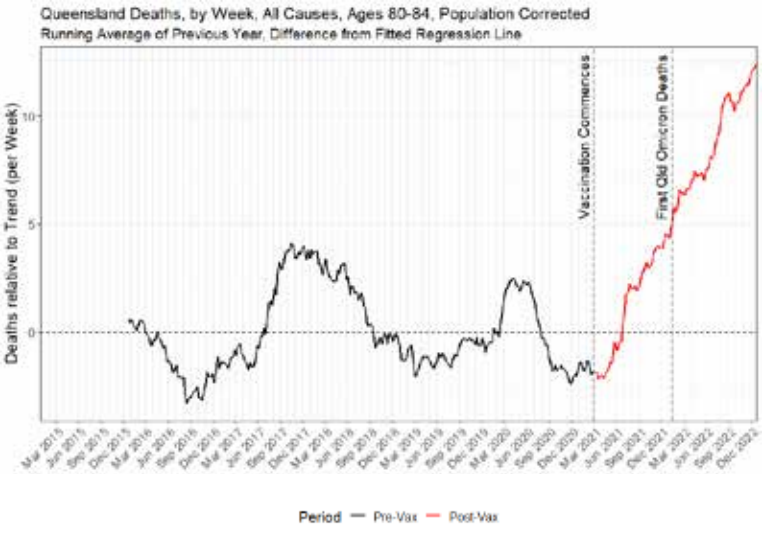


Figure 15. Data from Figure 14 for Queensland ages 80-84, with regression line through the trend values subtracted to show the variation.

The variation of the trend, above the fitted regression line, prior to March 2021 (marked by a vertical dashed line in Figure 15), is a maximum of 4 deaths per week, occurring in 2017 from the bad influenza season. After March 2021, and by January 2022 (marked with another vertical dashed line) it has reached approximately 5 deaths per week above the regression line. That is one death per week above the previous maximum value. If that value continued for a year, it would be 5x52 = 260 deaths per year above the line fitted through the trend.

The first vertical dashed line in Figure 15 shows the time of the start of the vaccination campaign in Australia. The second vertical dashed line shows the onset of the first major wave of COVID deaths in Queensland. There had only been 19 deaths in Queensland by mid-January 2022. See Section 8.1 for details on early COVID-19 deaths in Queensland. The very early COVID deaths registered for Queensland were of cruise-ship passengers and some died outside of Queensland. Clearly, in the time period of 10 months bounded by the vertical dashed lines, something has happened to take the trend above the previous high mark. To the end of 2022 there is no sign of any downturn.

Our interest in this work is in protecting and improving the health of Australians. Methods such as this could have been implemented in real time to detect historically large changes in mortality.

By the second half of 2021 we would have detected mortality in this age group trending above the worst previous influenza season, at a time when there was minimal influenza in the community and no COVID-19.

7 Analysis of Queensland mortality trends

We now plot the same mortality trend data for Queensland, as shown in Figure 14 (that is, prior to subtraction of the regression line through the trend), for multiple five-year age bands on the same graph. See Figure 16.

Inspection of Figure 16 shows what appears to be fairly flat lines over the eight-year time period (from 2015 to 2022) when plotted on a broad y scale. As previously discussed, the number of deaths is population-adjusted so that in earlier years, when population was less, that number is adjusted up to be relative to the value at the end of the time period. For the four highest lines, ages from 75-89, a decreasing trend is clear from the start followed by an upswing occurring somewhere in 2021. An upswing is not so obvious in age ranges 60-69.

For age 95+ the downwards trend is small, but the upswing is clear. Note also that the graph is showing an adjusted actual number of deaths and not a rate of deaths (that is, deaths per 1,000). So, for example, in the older

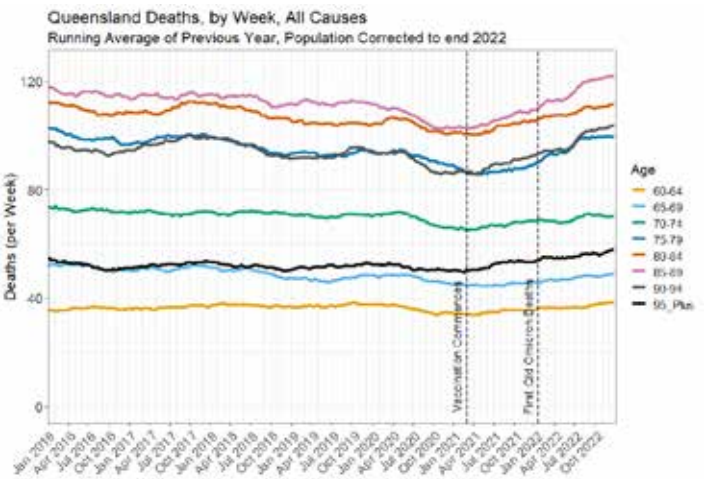


Figure 16. Queensland mortality trend, 5-year age bands from age 60 years up.

age range of 95+ there is a much smaller population (see Figure 2) and so numbers are smaller even though death is more likely.

To see the trends more clearly, we can adjust the vertical position of the lines so that they are all the same value at a particular date. Then we can look at what the number of deaths is, relative to what it was on that date. We choose the date of March 1st 2021, aligning with the vaccine rollout in Australia. The result is shown in Figure 17.

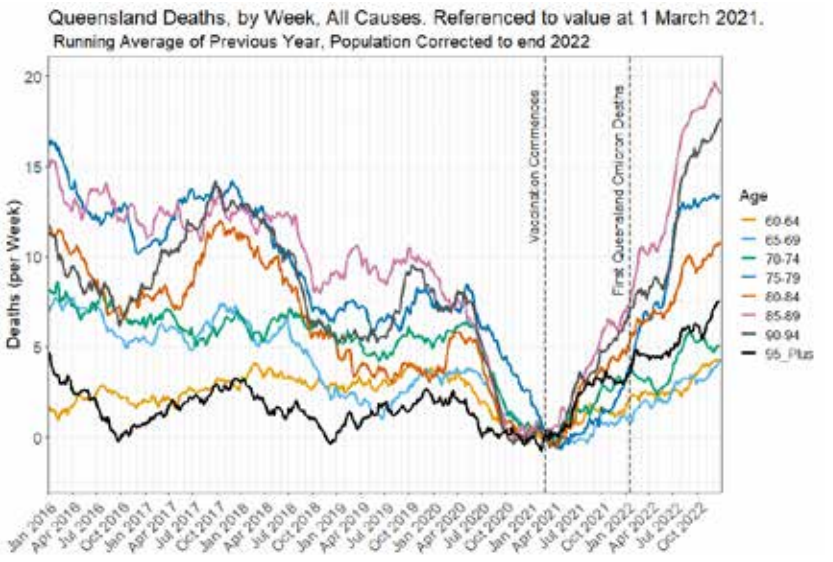


Figure 17. Queensland mortality trend, 5-year age bands from age 60 years up, referenced to value on March 1st 2021.

In Figure 17 small week-to-week variations are more apparent with the smaller y scale range. However, the most striking feature of this graph is that the historic downward trend, prior to March 2021, is turned around within months of the reference date, to an upward trajectory with no sign of plateauing. In the absence of any external input, such as the COVID-19 disease in the community, we would have expected a continuing downwards trend in each of the age groups, at their respective rates, with small natural variations up and down.

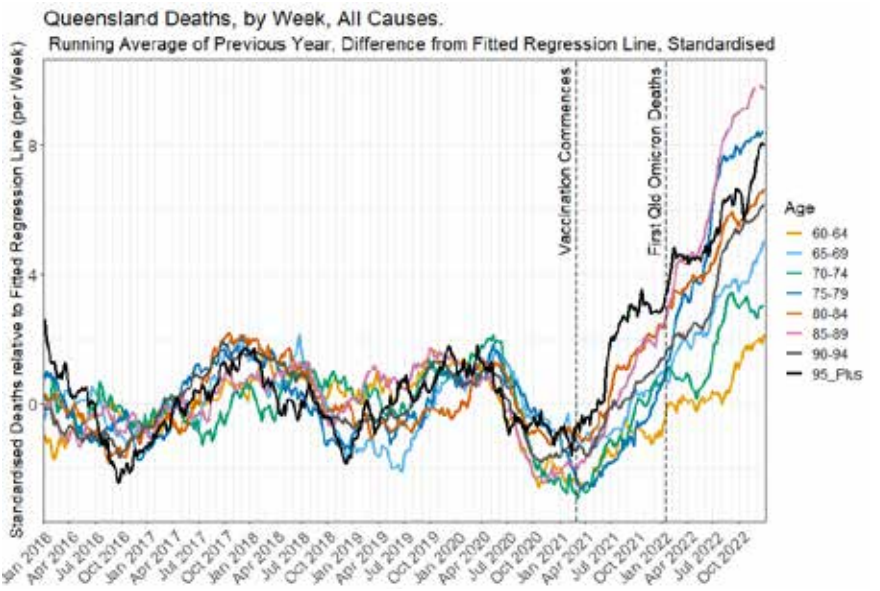


Figure 18. Mortality Queensland ages 60 up. one-year running average, difference from fitted regression line (up to 1 March 2021) and standardised.

The onset of the excess mortality phenomenon currently being experienced in Australia is identified. This upswing in all-cause mortality, occurring shortly after the rollout of COVID vaccines to the elderly population, could have been detected in real time.

It could be argued that the upswing occurs to compensate for a previous downswing in 2020. However, the upswing starting in 2021 should have already come down again to follow the historical decreasing trend prior to the point in 2022 when COVID-19 creates additional pressure upwards in Queensland.

We could subtract COVID-19 deaths from the start of 2022 onwards to monitor the increasing non-COVID excess. However, these data are not available for the age groups for Queensland.

The fitted linear regression through the trend prior to March 2021 can be subtracted for each age group, as was shown in the example in Figure 15. We assume that the trend should follow this downwards in the absence of any external influences. Each age group varies by a different amount about the fitted line for that age. We can standardise the values, so we look at standard deviations from the fitted line for each age group. This is computed and shown in Figure 18.

For the four oldest age groups we see that the standardised deviation from the trend, prior to any COVID-19 deaths occurring in the Queensland community (January 2022), is higher than the maximum deviation from trend encompassing the bad flu season of 2017.

Of concern is that for the younger age groups (for example, 60-64), while the creep upwards is slower, by the end of 2022 it exceeds previous maximum values. The effect of COVID-19 disease on younger ages is much less than for the older ages.

8 COVID-19 and vaccinations in Queensland

COVID deaths in Queensland were minimal until mid-January 2022. Consequently, it appears that interventions in 2021 did something to alter mortality trends.

The TGA Database of Adverse Event Notifications records approximately 1,000 deaths following COVID-19 vaccination. All but 14 of these are considered to be coincidences by the TGA. We therefore find another coincidence, that in a state in Australia, where COVID was not circulating, mortality suddenly increased in older age groups, starting from the time of introduction of novel pharmacological products to most of this community.

8.1 COVID deaths in Queensland

On November 1st 2021 Australian borders opened to vaccinated Australian citizens to return to Australia. Australia opened borders to vaccinated international tourists from February 21st, 2022. COVID had escaped quarantine only in sporadic outbreaks prior to this in Australia.

The state of Queensland maintained a hard border, not only for international travellers but also for travel from states outside of Queensland, with a motto 'Keeping Queenslanders Safe'. It is now known that the COVID-19 vaccines do not stop infection or transmission of the virus. Without enforced quarantine, the prevalent Omicron variant was released in Australia, leading to a major wave of COVID infections and death of the vulnerable, starting in January-February 2022.

Information on early COVID deaths in Queensland was found in documents uncovered during legal proceedings by Queensland doctors in mid-2022 against the Queensland Chief Health Officer's imposed vaccine mandates. The first locally-acquired infection leading to death in Queensland was of a vaccinated man in his 80s in the last weeks of December 2021. Early reported deaths after this date included a teenager who died in a car accident. Up to this point there had only been seven COVID-19 deaths of Queenslanders. These were primarily of cruise ship passengers (including three from the Ruby Princess). Some died outside of Queensland.

From the first locally-acquired case up to January 15th 2022 there were 19 COVID-19 deaths total for Queensland, predominantly in people above age 80. See Figure 19 below for a graph of the daily deaths in Queensland (all ages) up till September 2022. From September 2022 deaths were reported weekly. Note that these are messy data; spikes in bars shown may be due to delayed reporting of numbers, and deaths are not necessarily shown on date of death. However, the data give us an idea of the waves of death peaking in January for the first Omicron wave and then a Winter wave somewhere in July to August.

As a result of the late arrival of COVID-19 to Queensland, with a small number of deaths until mid-January (Figure 19. COVID deaths in Queensland, reported by day, January to September 2022. Data were obtained from aggregator website covidbaseau.com). We have a wider time-view of the effect of government-imposed health measures, not confounded by the effect of COVID-19 disease.

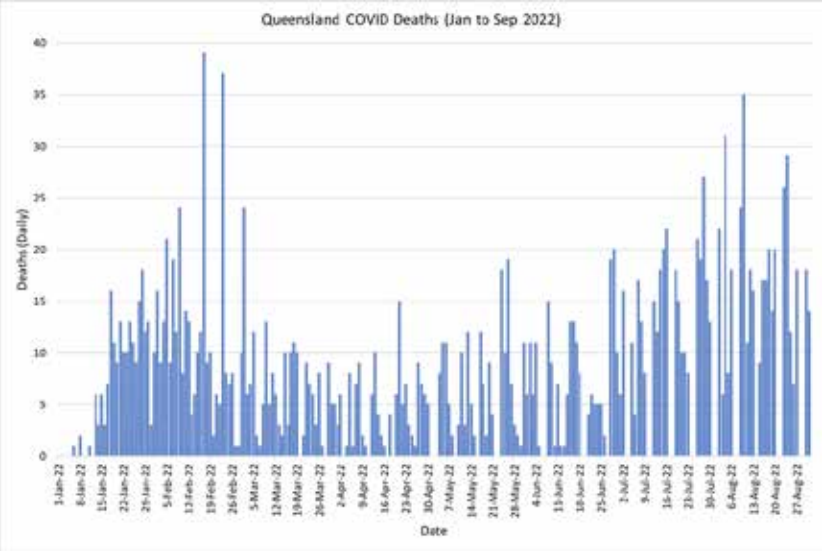


Figure 19. COVID deaths in Queensland, reported by day, Jan to Sep 2022. Data were obtained from aggregator website covidbaseau.com.

8.2 Vaccination rollout in Queensland

The cumulative vaccine rollout in Queensland is shown in Figure 20, The vaccine rollout in Queensland. The cumulative number of first, second, third and fourth doses is shown.

The doses per day, calculated from the cumulative number, are shown in Figure 21, Vaccine rollout in Queensland, daily number of doses shown. There are data points where quantities were reported irregularly, presumably because of backlogs in reporting. Poor data curation has unfortunately been typical of Health Department data reporting.

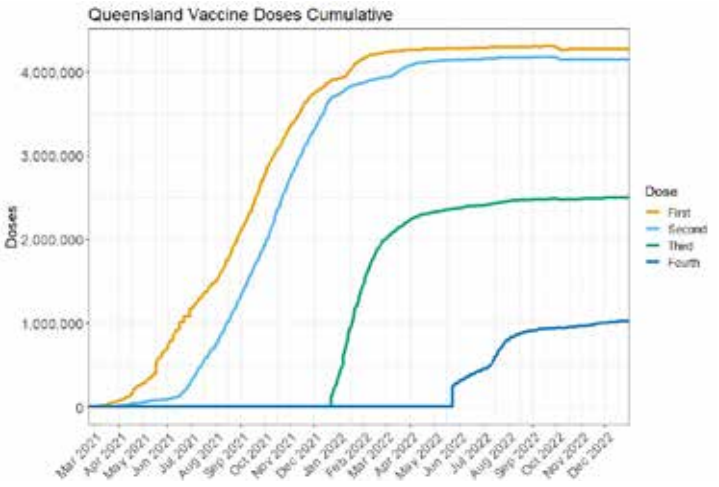


Figure 20. The vaccine rollout in Queensland. The cumulative number of doses is shown.

Features to notice in the daily doses are a push in the second half of 2021 to get first doses out. This was 'Operation COVID Shield' starting from August 2021, which included targeting Culturally And Linguistically Diverse (CALD) communities. First and second dose rollouts peak around the same time through older age groups receiving their second while younger were starting to get the first. The third dose was rolled out right in the midst of the onset of the Omicron wave. Demand had died out by mid-2022.

In the cumulative dose count in Figure 20, The vaccine rollout in Queensland, the cumulative is the fixed remaining difference between first and second doses.

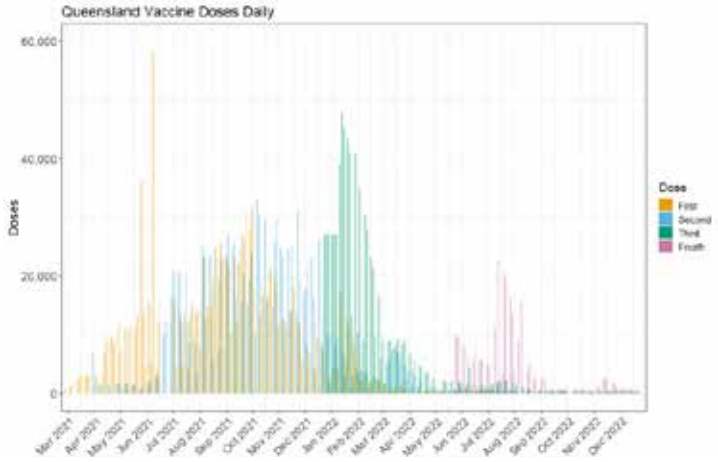


Figure 21. Vaccine rollout in Queensland. Daily number of Doses shown.

As at the end of December 2022, 4,267,680 people had received a first dose and 4,151,158 the second. This is out of 5,378,277 Queenslanders (ABS Dec 2022 figures). 116,553 persons therefore only took one injection. That means 97% of those receiving a first dose went on to a second. The 3% of people with only one dose are those who either sadly did not make it to a second dose because of death, or those who had a severe adverse reaction to the first and did not risk a second. Because of the Queensland mandates and restrictions placed on the unvaccinated (those who had not received the primary two doses), few people capable of receiving a second dose declined to do so voluntarily.

9 Machine Learning methods For Time Series forecasting

In this section we look at another specific age group and test other methods for tracking excess mortality, from TGA reports of death (see Figure 4. 3D histogram of TGA reported deaths following COVID-19 vaccination). Reported ages are shown in 10-year age bands, against time in months from the start of the rollout (Month one being March 2021), and Figure 31 in the Appendix. There are many reports of death in the 70s age group following COVID-19 vaccination.

Methods developed in recent years for Machine Learning have been applied to time series analysis. Machine Learning algorithms are the basis of Artificial Intelligence. An algorithm called Prophet, developed by researchers at Facebook, is used for time series forecasting. This algorithm has a feature of requiring minimal tuning and handling changes in trend within the data. It can identify what are known as changepoints.

In Figure 22 the time series of data for age 75-79 is used. The whole time series from 2015 till the end of 2022 is used to develop the model to predict data. The changepoint identified is shown in the first half of 2021.

The method used to generate data shown in Figure 22 allows us to determine, in retrospect, where trends changed, but we need future data to do this. The simple running average method, described in Section 6.3 and evaluated in Figure 17, detects the change in trend in real time.

We can train the algorithm only on data up to March 1st 2021, where we

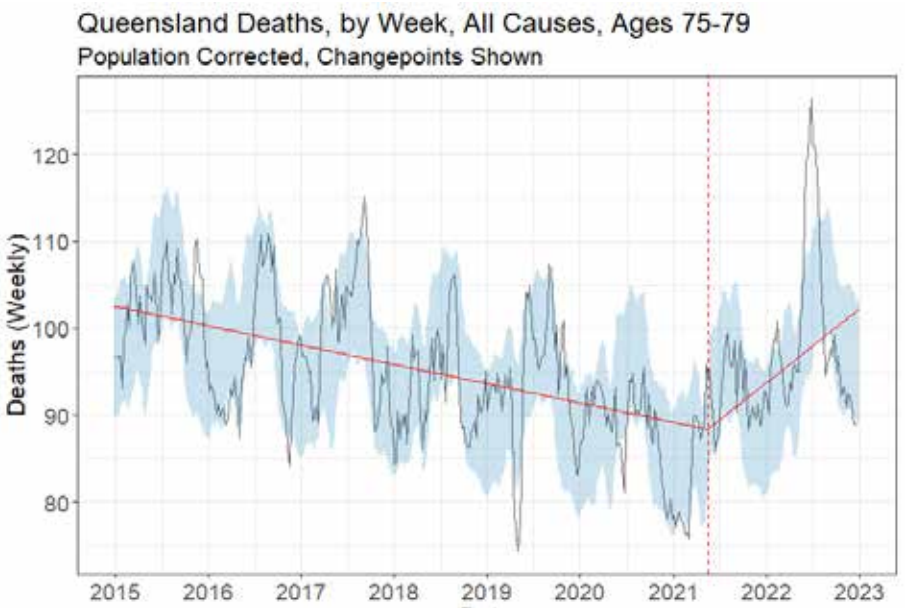


Figure 22. Changepoint identified using Prophet algorithm.

expect typical mortality patterns, and then base future predictions on the model generated. We then compare with the actual data and see if it diverges from what should be expected. This is shown in Figure 23. We can inspect where the actual deaths data go outside the error bounds. The actual values go outside the prediction bounds in the first half of 2021. A local peak observed in April-May 2021 is unusual, as this is prior to the normal seasonal variation peak.

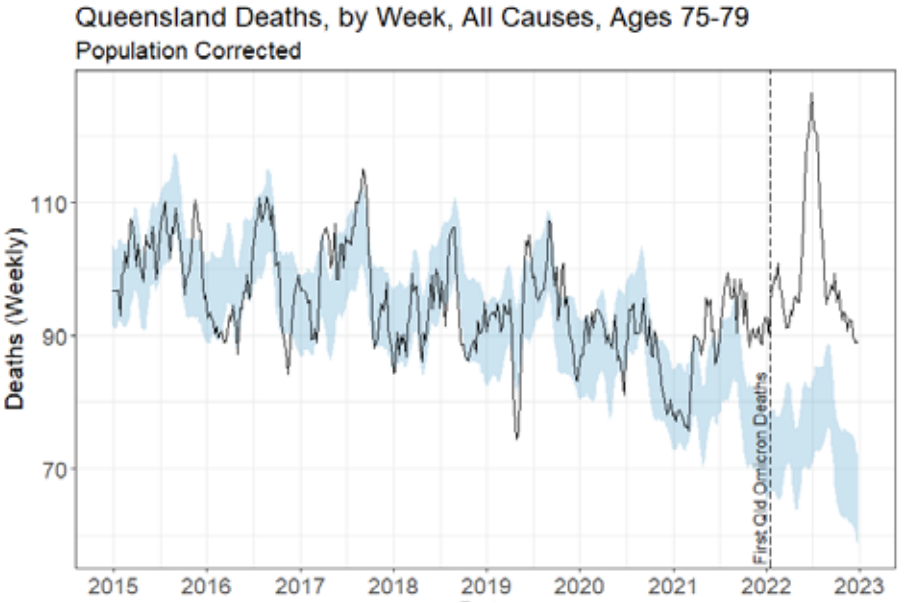


Figure 23. Algorithm trained on data prior to March 1st 2021. Error bounds of prediction are shown in shaded blue region. Actual data are the black line. Onset of COVID-19 in Queensland is shown with a vertical dashed line.

Dementia is typically a disease of the elderly. In Figure 24, ABS monthly data are shown for dementia as a cause of death for ages 75-79. These data are for all Australia and therefore are influenced by COVID deaths from the start of the pandemic. These data have not been population-adjusted. The data are for doctor-certified deaths only. The reason for this is that for 2022 coroner-certified deaths are not available. For dementia as a cause of death there is only a small number of coroner-certified deaths relative to the doctor-certified deaths. For example, in March 2021 there were 140 doctor-certified deaths and then three extra coroner-certified deaths.

The algorithm XGBoost has been shown to be effective for time series prediction.[11] Data prior to March 1st 2021 are used to train the algorithm. With this algorithm we need to first remove trend as it only predicts within the previously known data space. Figure 25 shows the actual values in black up to February 2021 and in red for contrast from February 2021. The predicted values (in grey), using the XGBoost algorithm, are shown from March 2021 onwards. Of note is a peak in the actual data in March 2021. Note that the value for a month is all deaths occurring in that month up to the end of the month. In Australia there was minimal COVID in 2021 from January up until July when the Delta wave started. This March 2021 peak is higher than all

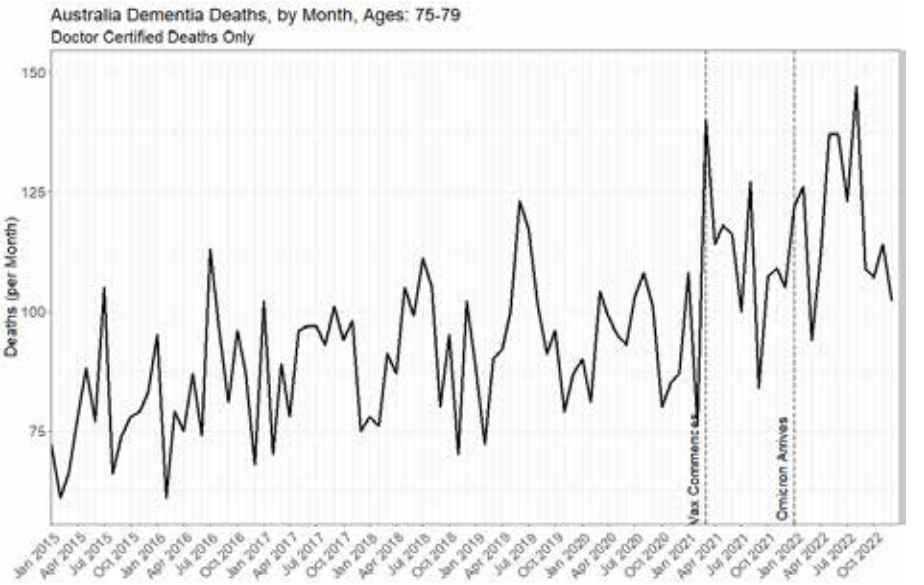


Figure 24. Deaths by cause Dementia, Australia, ages 75-79.

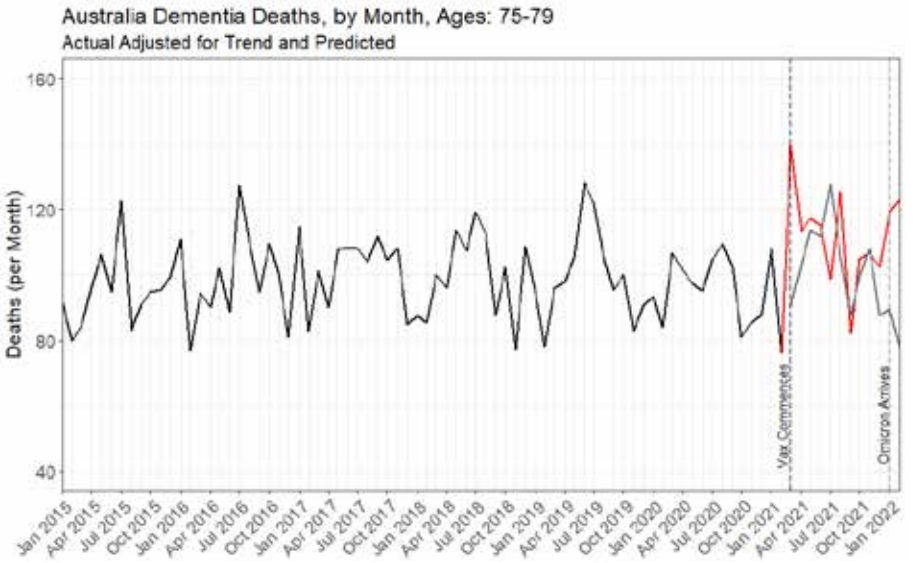


Figure 25. Deaths by Cause Dementia, ages 75-79, trend adjusted. Prediction shown in grey using XGBoost algorithm. Actual data shown in black prior to March 2021 and in red from March 2021.

previous historical peaks (relative to trend) and is at an unusual time of year, being before the Winter flu season.

There is a peak in August 2021, seen in Figure 25, which could have been influenced by COVID deaths. The Delta wave was waning at the end of 2021 prior to the onset of the Omicron wave in January 2022. Actual data are well above predicted values at the end of 2021. This is also traditionally when deaths are lowest in Australia (that is, Summer time).

People with dementia are a vulnerable cohort. They have difficulty caring for themselves. We had no prior information on the side effects of vaccination in this group from clinical trials; indeed, none was available. There were early warnings received by the TGA regarding deaths in nursing homes in Norway early in the vaccine rollout there in late 2020 (see section 12.3). It is therefore not surprising that we see a corresponding increase in deaths in a vulnerable cohort in Australia early in the rollout here, as seen in Figure 24 and Figure 25.

This brief overview of the application of some modern time series analysis method indicates that concerning trends in mortality are identified in vulnerable groups shortly after the rollout of COVID-19 vaccinations. It seems astounding that the TGA discounts all but 14 deaths following COVID-19 vaccination, out of one thousand deaths reported, given the historically unusual mortality patterns identified during times when there were no deaths from COVID-19 disease.

10 Summary

In this report we have looked at trends in mortality in Australia. Prior to the pandemic, in older ages, population-adjusted mortality had been slowly decreasing year on year, with older people living longer. We posed the question: when did the non-COVID excess mortality, currently being experienced in Australia since 2021, start?

In Queensland we have an extended time window to view mortality without the effects of COVID-19 disease. In the period from the start of the worldwide pandemic to the onset of COVID-19 disease in Queensland we can assess the effects of the numerous interventions imposed by health authorities. They include pharmacological, social and financial interventions.

We find an alarming upturn in the trend in mortality, in older age groups, starting from March 2021. Using data from Queensland means this is not confounded by any effect of COVID-19 disease. Two years later, at the end of 2022, there is no sign of mortality levelling out, let alone going back to a trend of slow decline in mortality in older age groups. A significant

proportion of the excess mortality is from 'unknown cause', with authorities suggesting it is COVID-19 disease-related.

Coincidentally the start of the upturn in mortality occurs shortly after the rollout of COVID-19 vaccinations to the elderly population. Almost 1,000 deaths have been reported, following COVID-19 vaccination, in the TGA Database of Adverse Event Notifications. The TGA considers all but 14 of these as 'coincidences.' It is disturbing that reported deaths of children following COVID-19 vaccination, with a possible causal link identified, appear to have been dismissed, and not disclosed to the public for fear of creating 'vaccine hesitancy.'

It would have been quite feasible to have implemented in real time the algorithmic methods described in this report. If that had been done the reporting of deaths following COVID-19 vaccination would have been witnessed, coincident with an upturn in mortality in the same age groups, in real time. That upturn reached a level above any previous deviation from the trend. This is in an environment where there was no COVID-19 disease to confound interpretation.

Clearly the health of Australians has been adversely affected by the panic promulgated and health measures applied by Australian government authorities.

11 References

[1] 'Deaths in Australia, Trends in Death,' Australian Institute of Health and Welfare, June 2022. [Online]. Available: *https://www.aihw.gov.au/reports/life-expectancy-death/deaths-in-australia/contents/trends-in-deaths*.

[2] 'Life tables. Statistics about life tables for Australia, states and territories and life expectancy at birth estimates for sub-state regions,' Australian Bureau of Statistics, 8 Nov 2022. [Online]. Available: *https://www.abs.gov.au/statistics/people/population/life-tables/2019-2021*.

[3] 'Deaths in Australia, Age at Death,' Australian Institute of Health and Welfare, 9 June 2022. [Online]. Available: *https://www.aihw.gov.au/reports/life-expectancy-death/deaths-in-australia/contents/age-at-death*.

[4] 'COVID-19 Mortality in Australia: Deaths registered until 31 October 2022,' Australian Bureau of Statistics, 25 11 2022. [Online]. Available: *https://www.abs.gov.au/articles/covid-19-mortality-australia-deaths-registered-until-31-october-2022*.

[5] 'Provisional Mortality Statistics', Australian Bureau of Statistics, 26 May 2023. [Online]. Available: *https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-feb-2023*.

[6] 'COVID-19 Mortality Working Group: Confirmation of 20,000 excess deaths for 2022 in Australia,' Actuaries Institute COVID-19 Mortality Working Group, 6 April 2023. [Online]. Available: *https://www.actuaries.digital/2023/04/06/covid-19-mortality-working-group-confirmation-of-20000-excess-deaths-for-2022-in-australia/*.

[7] W. Sy, 'Australian COVID-19 pandemic: A Bradford Hill analysis of iatrogenic excess mortality,' *J Clin Exp Immunol,* vol. 8, no. 2, pp. 542-556, 2023.

[8] W. Sy, 'Simpson's Paradox in the correlations between excess mortality and COVID-19 injections: a case study of iatrogenic pandemic for elderly Australians,' *Medical and Clinical Research (in Press).*

[9] V. Shkolnikov, 'What should be the baseline when calculating excess mortality? New approaches suggest that we have underestimated the impact of the COVID-19 pandemic and previous winter peaks,' *SSM - Population Health,* vol. 18, 2022.

[10] J. Gibson, 'The Rollout of the COVID-19 Booster Vaccines is Associated with Rising Excess Mortality in New Zealand,' *Working Paper in Economics, University of Waikato,* no. June, 2022.

[11] A. D. Lainder and R. Wolfinger, 'Forecasting with gradient boosted trees: augmentation, tuning, and cross validation strategies. Winning solution to the M5 uncertainty Competition.,' *International Journal of Forecasting,* vol. 38, pp. 1426-1433, 2022.

12 Appendix – TGA Safety Monitoring System

Prior to analysing mortality in Australia, which is currently above historic averages, we review the reporting of deaths following administration of pharmacological products.

The TGA Database of Adverse Event Notifications (DAEN) is a system to provide information about adverse events and incidents related to therapeutic goods used in Australia. Unfortunately, it is a is a poorly designed, clumsy system to use.

The system was updated during the pandemic (released temporarily as a 'beta' version) to allow export of datasets. The data export can be filtered to output adverse events from COVID vaccines only (Figure 26). Exported files have fields for:

- Case number
- Age
- Report entry data
- Gender
- Medicines reported as being taken
- MedDRA reaction terms.

The Medical Dictionary for Regulatory Activities (MedDRA) is an internationally used set of terms relating to medical conditions, medicines and medical devices. It was created to assist regulators with sharing information.

Unfortunately, the data in the DAEN do not indicate which cases resulted in death from a product. Death is not considered a medical reaction term. The TGA website states the total number of deaths reported following COVID-19 vaccination on a page where search is performed.

Figure 26. Search on web page: *https://daen.tga.gov.au/medicines-search/* (25 June 2023).

The public has to make Freedom of Information (FOI) requests to find out further information regarding the reported deaths.

12.1 Freedom of Information requests

Originally, FOI request 3586 obtained a redacted document with ages of persons where death was a result (921 deaths at the time). Unfortunately, this did not allow cross referencing with actual DAEN reports as it was just a list of ages left unredacted. Note also the Age field is sometimes left empty or null. This author submitted an FOI request, resulting in FOI 3785 (released June 23th 2022), where the Case number (field TGAICSRIdentifier) was also unredacted. This then allowed cross referencing with exported DAEN records. A similar request, FOI 3845, released August 1st 2022, provided the same information. The number of deaths was updated to 892 Deaths up to June 28th 2022. Analysis in this report uses data from the later FOI 3845.

A table with Case number and Age of death was joined with the table exported for all adverse events related to COVID-19 vaccines.

FOI 3545 provides an Excel spreadsheet with Batch number for Adverse events, on or before January 15th 2022. This table was joined with the table of deaths obtained. An extract of the first 25 entries of the resulting table is shown in Table 3. This covers deaths reported in the first month of vaccine rollout up to March 29th 2021. The COVID-19 vaccine was being delivered primarily to the elderly. However, a death of a person in their 60s occurred following vaccination in March 2021.

Table 3. First 25 TGA DAEN reports, by date, where death was an outcome.

Case number	Age	Report entry date	Gender	Vaccine	MedDRA reaction terms	Batch Number	Dose In Series
515141	46	21/12/2020	Female	Pfizer	Numerous reactions reported including renal failure, sepsis… See note.	-	-
520837	92	1/03/2021	Male	Pfizer	Adverse event following immunisation; Loss of consciousness	EP2163	1
521153	98	3/03/2021	Female	Pfizer	Decreased appetite	-	1
521302	81	4/03/2021	Female	Pfizer	Decreased appetite; Depressed level of consciousness; Dysphagia; Vomiting	-	1
521311	76	4/03/2021	Male	Pfizer	Cardiac arrest; Unresponsive to stimuli	NIL	1
521644	78	5/03/2021	Female	Pfizer	Dysphagia; Injection site reaction; Somnolence; Weight decreased	-	1
521667	67	5/03/2021	Male	Pfizer	Adverse event following immunisation	EP2163	-
521683	81	5/03/2021	Female	Pfizer	Aspiration; Sepsis; Vomiting	NIL	1
521743	90	6/03/2021	Male	Pfizer	Dyspnoea; Vomiting	-	-
521789	95	6/03/2021	Male	Pfizer	Pyrexia; Unresponsive to stimuli	EP2163	-
522108	92	9/03/2021	Male	Pfizer	Dyspnoea	EP2163	-
522391	92	11/03/2021	Female	Pfizer	Ischaemic stroke; Mydriasis	EP2163	-
522414	95	11/03/2021	Female	Pfizer	Diabetic ketoacidosis; Urosepsis	EP2163	-
522710	83	12/03/2021	Male	Pfizer	Cardiac arrest	-	1
522731	93	12/03/2021	Male	Not Specified	Pneumonia Respiratory failure	-	-
522739	83	12/03/2021	Female	Astra Zeneca	Multiple organ dysfunction syndrome; Pancreatitis; acute Rash macular	PV46672	-
523387	87	16/03/2021	Female	Pfizer	Pulmonary embolism	-	1
524083	77	18/03/2021	Male	Pfizer	General physical health deter ioration	EP2163	1
524247	96	19/03/2021	Male	Pfizer	Pneumonia viral	EP9602	1
524473	91	19/03/2021	Male	Pfizer	Malaise	EP9605	-
526002	77	24/03/2021	Male	Pfizer	Concomitant disease aggravated; Depressed level of consciousness; Lethargy; Pyrexia; Respiratory arrest	unknown	1
527357	90	26/03/2021	Male	Pfizer	Pneumonia	-	-
527413	86	26/03/2021	Male	Pfizer	Cerebral haemorrhage Cerebrovascular accident	ER7448/9	1
527894	78	28/03/2021	Male	Not Specified	General physical health deterioration	-	-
528345	93	29/03/2021	Male	Astra Zeneca	Chest pain General physical health deterioration	3001577	1

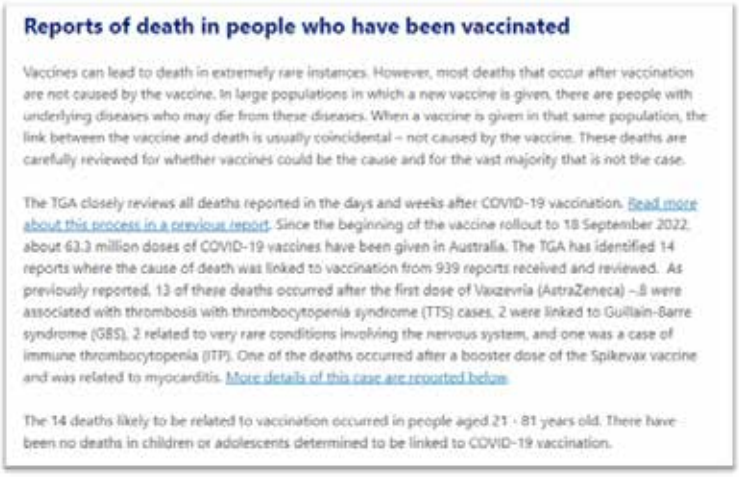
There is an odd report, case number 515141, of a 46-year-old female. Numerous reaction terms are reported, not all included in Table 3 for brevity. It did not appear in FOI 3785 but appeared two months later in FOI 3845. Perhaps it was from an Australian citizen overseas. The reported date of December 1st 2020 is prior to the rollout in Australia.

Later FOI 4077 provides a list of batch numbers and dose in series for adverse event cases where outcome was reported as fatal, from January 10th 2022 and November 8th 2022. It is disturbing that the batch number is only recorded for a small number of reported deaths. In many cases it is marked as unknown.

The TGA claims to be diligent in monitoring batches. It is hard to understand how this could be, given the lack of recording of batch numbers. The recording of batch numbers appears to have become laxer over time. While the recording of the batch number is not the TGA's responsibility at the point of entry, one would think there would be diligent follow-up particularly in the cases where death was an outcome.

12.2 COVID-19 vaccines in Australia

On February 15th a Singapore Airlines flight touched down in Sydney carrying 142,000 doses of the Pfizer-BioNTech vaccine. This was presumably Batch EP2163 (based on information in Table 30). The first doses were administered



Reports of death in people who have been vaccinated

Vaccines can lead to death in extremely rare instances. However, most deaths that occur after vaccination are not caused by the vaccine. In large populations in which a new vaccine is given, there are people with underlying diseases who may die from these diseases. When a vaccine is given in that same population, the link between the vaccine and death is usually coincidental – not caused by the vaccine. These deaths are carefully reviewed for whether vaccines could be the cause and for the vast majority that is not the case.

The TGA closely reviews all deaths reported in the days and weeks after COVID-19 vaccination. Read more about this process in a previous report. Since the beginning of the vaccine rollout to 18 September 2022, about 63.3 million doses of COVID-19 vaccines have been given in Australia. The TGA has identified 14 reports where the cause of death was linked to vaccination from 939 reports received and reviewed. As previously reported, 13 of these deaths occurred after the first dose of Vaxzevria (AstraZeneca) – 8 were associated with thrombosis with thrombocytopenia syndrome (TTS) cases, 2 were linked to Guillain-Barre syndrome (GBS), 2 related to very rare conditions involving the nervous system, and one was a case of immune thrombocytopenia (ITP). One of the deaths occurred after a booster dose of the Spikevax vaccine and was related to myocarditis. More details of this case are reported below.

The 14 deaths likely to be related to vaccination occurred in people aged 21 - 81 years old. There have been no deaths in children or adolescents determined to be linked to COVID-19 vaccination.

Figure 27. From TGA Vaccine Safety Report from September 2022: *https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-23-09-2022.* According to TGA FOI 3845 the last sentence in Figure 27. From TGA Vaccine Safety Report from September 2022: https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-23-09-2022. According to TGA FOI 3845 the last sentence in Figure 27 is questionable (see Section 12.4). is questionable (see Section 12.4).

on February 21st, including to Prime Minister Scott Morrison. The general COVID-19 vaccination in Australia program began on February 22nd 2021.

The first death following vaccination was reported on March 1st 2021, according to Table 3, of a 92-year-old man who lost consciousness following administration. This was a coincidence according to the TGA.

The TGA Vaccine Safety Report from September 2022 provides sparse information on the reported deaths (see Figure 27).

12.3 Early warnings of deaths in the elderly

On January 14th 2021, prior to the vaccine being available in Australia, the TGA received reports from Norway about the deaths of frail elderly people following vaccination with the Pfizer vaccine. The TGA concluded that there is no specific risk of vaccination with the Pfizer-BioNTech COVID-19 vaccine in elderly patients. Reference: https://www.tga.gov.au/news/media-releases/investigation-reveals-no-specific-risk-covid-19-vaccinations-elderly-patients. While noting that 'the clinical impact of even relatively mild systematic adverse events in the frail elderly should be carefully assessed on a case-by-case basis' the TGA assessed that these people were going to die anyway. TGA correspondence related to this warning is found in TGA FOI 4073 (9 documents).

Table 4. Top 25 by Occurrences (Occ) of MedDRA reaction terms in reported TGA deaths following COVID vaccination.

	MedDRA reaction term	Occ
1	Adverse event following immunisation	176
2	Cardiac arrest	87
3	Dyspnoea	81
4	Pulmonary embolism	70
5	Concomitant disease progression	68
6	Cerebrovascular accident	66
7	Malaise	53
8	Thrombocytopenia	48
9	Vomiting	47
10	Fibrin D dimer increased	46
11	Chest pain	42
12	Headache	41
13	Concomitant disease aggravated	40
14	Pneumonia	39
15	Deep vein thrombosis	37
16	Myocardial infarction	37
17	Pyrexia	32
18	Sepsis	28
19	Fatigue	27
20	Myocardial ischaemia	27
21	Multiple organ dysfunction syndrome	25
22	Lethargy	24
23	Fall	22
24	Acute myocardial infarction	21
25	Respiratory failure	21

Analysis of the reactions, in the cases reported leading to death, is summarised in Table 4 with the top 25 terms associated with death cases listed in the table.

The most common is the non-specific term 'Adverse event following immunisation'. 'Cardiac arrest' is the second.

12.4 Deaths of children

Of concern is that in known cases where children died following COVID vaccination, the process of the TGA has not been transparent.

Follow-up of specific cases by General Practitioner Dr Melissa McCann, using FOI request (FOI 3727), found internal TGA reports regarding deaths of 10 young people, two being children. Internal TGA reports show the text 'causal' with some of these reports. However, the TGA disputes that the term 'causal' uncovered in internal reports means causality was confirmed, but rather that it is 'template' text.

The TGA response to the FOI request was initially not uploaded to the TGA online disclosure log as would be the normal process. Senator Gerard Rennick has reported on this: https://gerardrennick.com.au/tga-cover-up-child-deaths/.

From our joined tables, constructed from different FOI data, we find details of these child cases:

The cases were reported in March 2022. A young boy and girl both suffered cardiac arrest following COVID-19 vaccination. It is disturbing that batch numbers were not recorded. The batches for these cases should have been found from FOI 4077. The FOI 4077 file contains one data row for each distinct report associated with a suspected interacting COVID-19 vaccine in an accepted adverse event case created between January 10th 2022 and November 8th 2022, where the outcome of the adverse event was reported as fatal. Those fields were empty for these cases.

Batch reporting clearly became laxer as rollout continued.

Table 5. Reported deaths of young children following COVID-19 vaccination.

Case number	Age	Report entry date	Gender	Vaccine	MedDRA reaction terms	Batch Number	Dose In Series
719838	7	11/03/2022	Male	Pfizer	Cardiac arrest Generalised tonic-clonic seizure	-	1
724023	9	25/03/2022	Female	Pfizer	Cardiac Arrest	-	-

12.5 DAEN deaths summary

A 3D visual showing the reported deaths as time progressed from rollout, for different age bands, based on our analysis is shown in Figure 28 (also shown in Figure 4 in the body of this report). We can see from this plot the deaths in the elderly, prioritised for vaccination first, progressing to middle ages as the rollout continued. Deaths of young people can be seen reported from month 6 of the rollout. The two sad deaths of children under 10, listed in Table 5, are represented in the foreground of the visual.

Slices can be taken through these data to see the effect on particular ages. See Figure 29, Figure 30 and Figure 31 for 5-year age bands from 95, 85 and 75 respectively. Counts in each bin (covering half a month) are separated by gender. Note that the date is the date of report which will be some time after the actual date of death. We do not have actual date-of-death data.

In the oldest age band age 95 and above (Figure 29), women are the most affected. However, the population of women in this age band is significantly larger than the men still left alive. In the age band 75-79, Figure 31, males

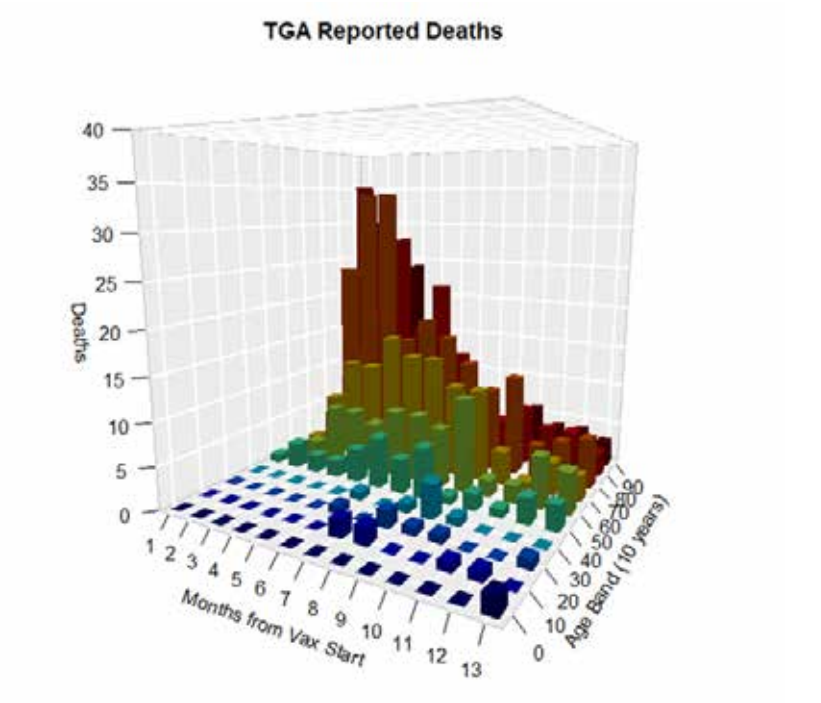


Figure 28. 3D Histogram of numbers of reported deaths for ages of death in 10-year bands, from the month of start of vaccination in Australia (March 2021-March 2022).

appear to be disproportionately affected.

Note these data were only available up to the date of data obtained via the FOI request from August 2022. There are other deaths, not shown, where age was not reported.

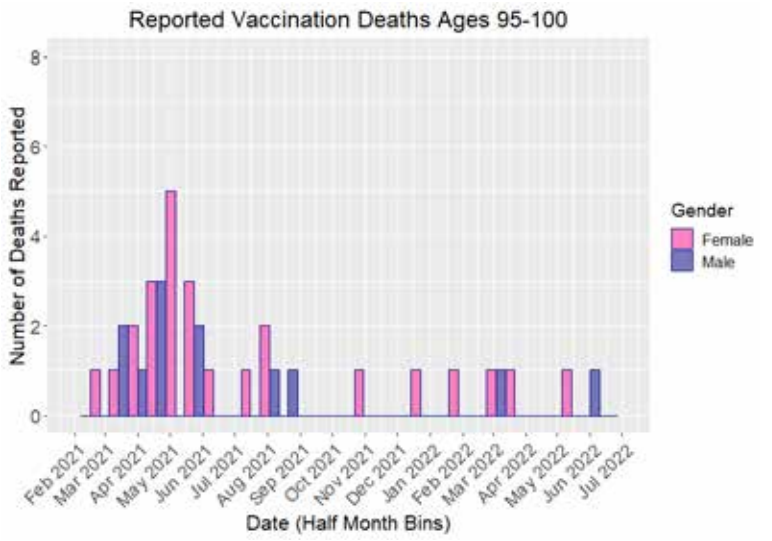


Figure 29. TGA reported deaths following COVID vaccination: Age band 95-100.

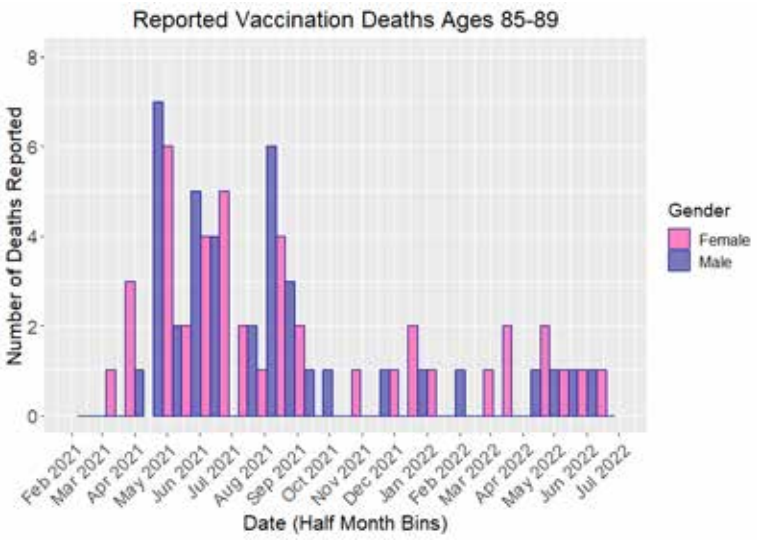


Figure 30. TGA reported deaths following COVID vaccination: Age band 85-89.

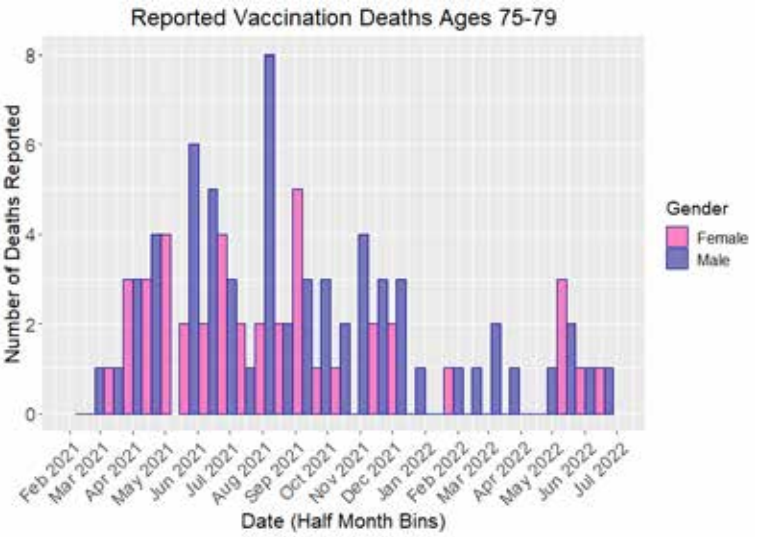


Figure 31. TGA reported deaths following COVID vaccination: Age band 75-79.

Andrew Madry has a degree in physics, a BSc (Hons) and PhD from the University of Sydney. His PhD work was in acoustics and signal processing. His early career was in the defence industry, developing and testing sonar systems for the Royal Australian Navy. This involved designing and testing transducers and developing signal detection algorithms.

He had a second career in medical devices, leading a team at a major Sydney hospital developing technology for treating abnormal heart rhythms. That led to a career-long interest in understanding abnormal electrical signals in the heart and developing algorithms for understanding mechanisms of atrial fibrillation.

A technical consultant since 2001, he has provided services to medical device companies including Cochlear and Resmed, as well as defence and industrial companies. Dr Madry developed a software product called Cardiac Electrophysiology Analysis System (CEPAS), used by researchers in cardiac electrophysiology, in the USA, Japan and Australia.

In the last five years he has focused on data science, providing customised training, based on years of experience in industry. Currently on the executive of the Systems Engineering Society of Australia, he has particular interest in applying Systems Thinking principles to data projects and healthcare.

Part 5

Global excess death – it's not just Australia

In the AMPS inquiry into the excess death rates it has become apparent that weak pharmacovigilance, poor data collection and excess all-cause mortality are being experienced not only in Australia but globally. This part now presents samples of reviews from European and American data sources.

> Based on analysis of the Vaccine Adverse Event Reporting System (USA) numbers, it may appear that adverse events are not currently imposing a significant burden on the fully vaccinated population; however, the weekly releases of VAERS data do not include all of the reports made to date – they are all the reports the CDC has processed to date – and the backlog is likely to be staggering. Thus, as a result of both the problems of under-reporting and the lag in report processing, this analysis reveals a strong signal from the VAERS data that the risk of suffering an SAE following injection is significant and the overall risk signal is high.
>
> – Dr Jessica Rose, USA

Concerning trends are also being noted in Finland:

> When the previously stable trend suddenly changes upwards, this represents unexpected increased mortality, that is, excess mortality… Finnish health authorities have thus far (April, 2022) either played

> down or altogether ignored these alarming data. In the light of the irrefutable evidence presented in this paper, it is high time health authorities stopped understating the severity of the situation and carried out a thorough and independent investigation of the cause for the dramatically elevated mortality.
>
> – Kasper Rönning, Finland

The Fenton et al. study of The Office for National Statistics (ONS) in the United Kingdom shows potential bias and misclassification which fail to provide evidence supporting the hypothesis that the vaccines reduced all-cause mortality.

> Overall, the ONS dataset is so compromised with inaccuracies, anomalies and biases that it cannot be used to reliably determine vaccine efficacy and safety. We recommend that the ONS adds full caveats to its future surveillance reports explaining the limitations and biases of its sample population. Also, any studies of vaccine efficacy or safety comparing vaccinated and unvaccinated which use whole population data of COVID cases, hospitalizations and death but which rely on the ONS estimates of proportion unvaccinated must be retracted.
>
> – Professor Norman Fenton, UK

The high excess death rates are now at more than fifteen per cent above baseline mortality. Australian and global data show a mass-casualty event, but our political and medical authorities seem to think there is nothing worth investigating

It is not as though there is any shortage of opinions of the depth and width of this silent crisis. It is simply that such opinions have been ignored, suppressed, diverted from public view and erroneously sent out to pasture, classified as conspiracy theory. To treat them this way is preposterous, yet the medical bureaucracy continues in the same way as the death toll rises.

> Analysis suggests that the vaccines are likely the cause of reported deaths, spontaneous abortions, anaphylactic reactions and cardiovascular, neurological and immunological adverse events. The precautionary principle promotes transparency and the adoption of preventative measures to address potential risks to the public in the arena of vaccination programs, and it is vital that people are informed of these potential risks before agreeing to participate in any medically involved treatment program.
>
> – Dr Jessica Rose, USA

What the ONS mortality COVID-19 surveillance data can tell us about vaccine safety and efficacy

by Norman Fenton[1], Martin Neil[1], Clare Craig[2], Scott McLachlan[3]

26 June 2023

Abstract

The UK has uniquely produced data deaths by vaccination status. These are critical data that should have been made public in every jurisdiction, but have not been. Unfortunately, the way the data were handled by the United Kingdom's Office for National Statistics (ONS) has meant that it is riddled with bias including failing to take account of various confounding factors which can thus be easily misinterpreted. The data presented here cover a report for England for the period January 1st 2021 to May 31st 2022 and a further report for the period April 1st 2021 to December 2022.

Those seeking evidence that the vaccines are unsafe might point to the overall all-cause mortality rate in the vaccinated (1,367 deaths per 100k person years) being much higher than in the unvaccinated (671 deaths per 100k person years). But this fails to take account of age confounding. Those seeking evidence that the vaccines are safe might point to the overall age-standardized mortality rate over the whole period being much higher in the unvaccinated (2,338 deaths per 100k person years) than the vaccinated (957 deaths per 100k

1 School of Electronic and Electrical Engineering and Computer Science, Queen Mary, University of London, UK
2 Independent researcher, UK
3 Faculty of Nursing, Midwifery & Palliative Care, King's College, London, UK

person years). But this fails to take account of major anomalies in the mis-categorization of deaths by vaccination status (especially in the first part of 2021), evidence for which can clearly be seen in the implausible differences in non-COVID mortality rates between different vaccination status categories. There is also now strong evidence that the ONS underestimates the proportion of unvaccinated, which leads to inflated mortality rates for the unvaccinated relative to the vaccinated. This underestimation is a major issue: the ONS claimed in May 2022 that 8% of adults are unvaccinated whereas the UKHSA estimated approximately 20% and an extensive and representative ICM survey estimated 26%.

Because the ONS data are based on a subset of England residents that excludes all those not registered with a GP and not registered in either the 2011 census (for the earlier dataset) or the 2021 census (for the later one), it is missing some 8 million adults who are not at all representative of those in the ONS sample. Hence, whilst it is conceivable that both the ONS 8% figure is correct for its sample, and the proportion of all adults in England unvaccinated is at least 20% as per the other sources, this means that at least 69% of adults missing from the ONS sample are unvaccinated. Hence, either the ONS is underestimating the proportion of unvaccinated in its sample or the sample is so unrepresentative of the whole population that any inferences made using the ONS data are worthless. Either way, the ONS estimate of the proportion unvaccinated must not be used for any comparisons of vaccine efficacy or safety of the whole England population. We also provide further evidence that the ONS are grossly underestimating mortality in their dataset, with their 18-39, 40-49 age groups showing approximately half the mortality rates published by the ONS in 2016, for both unvaccinated and vaccinated. We show that there are many missing deaths from their dataset with the eight million people suffering 30% of deaths despite comprising only 19% of the population, hence further compromising the accuracy and relevance of their data. Complaints to the UK Statistics Regulator about these issues were upheld but the ONS have not addressed these problems. Indeed, the more recent data release shows larger discrepancies in terms of the difference in mortality rates by vaccination status, the mortality by age and the proportion of real-world deaths included in their calculations.

1. Introduction

Shortly after the early 2021 rollout of the COVID vaccines in the UK, the Office for National Statistics (ONS) started to produce reports on mortality by vaccination status. These reports should, in principle, have enabled us to evaluate the overall risk-benefits of the vaccines by simply comparing – for each age group – the all-cause mortality rate of the vaccinated against the

unvaccinated. However, as we noted in our detailed analysis of the first year's data, http://dx.doi.org/10.13140/RG.2.2.28055.09124, the ONS data suffered from many obvious flaws and biases including the misclassification of many deaths shortly after vaccination as being unvaccinated. All of these flaws had the effect of underestimating the all-cause mortality of the vaccinated while overestimating the all-cause mortality of the unvaccinated. This was compounded by the fact that many vaccinated deaths were also simply missing from the ONS data, http://dx.doi.org/10.13140/RG.2.2.12472.42248. In November 2022 we produced a second detailed analysis of the most recent data which at that point was up to May 2022 – http://dx.doi.org/10.13140/RG.2.2.30898.07362. This study is based largely on that analysis. We found that many of the flaws and biases continued but that, with extremely conservative adjustments for these biases, there was strong evidence that in most age categories all-cause mortality was higher in the vaccinated than the unvaccinated. Nevertheless, we concluded that the data were so unreliable and biased that no definitive conclusions could be drawn. The ONS data were simply not fit for purpose. As explained in Section 10 below, we submitted a formal complaint about the data to the Statistics Regulator who agreed with two of our key recommendations, namely: 1) that the ONS sample was biased and unrepresentative of the England population (notably because it grossly underestimated the proportion of unvaccinated); and 2) that no conclusions about the efficacy or safety of the vaccines could be drawn from the ONS data because of its flaws and biases. Possibly because of our well-publicised criticisms, an update to the ONS data after May 2022 – which the ONS repeatedly promised during the fourth quarter of 2022 would be 'shortly forthcoming' – did not arrive until February, 2023. No data have been released for 2023. However, as described in Section 10, this latest update failed to address the concerns raised by ourselves and the Regulator. Moreover, because the ONS decided to use the new 2021 census data for the England population (a decision which did not actually address the problem of the biased sample) it was no longer possible to compare the results to the previous analyses. Hence, we believe these data were still unfit for purpose. Further problems surrounding this are highlighted in Section 11.

2. The ONS data up to May 2022

The Office for National Statistics (ONS) vaccine mortality surveillance reports including data up until May 2022 (the latest being[1]) are based on a subset of 39 million of the approximately 56 million population of England and are supposedly an authoritative source of data used by COVID-19 vaccine advocates and detractors alike. The ONS dataset can be easily misinterpreted in many ways by failing to take account of various confounding factors in the 'headline' results. Those seeking evidence that the vaccines are…

- … unsafe might point to the overall mortality being much higher in the vaccinated than the unvaccinated. But this fails to take account of age confounding;
- … safe might point to the age-standardized mortality rate over the whole period being much higher in the unvaccinated than the vaccinated. But this fails to take account of major anomalies in both the mis-categorization of deaths in the first part of 2021 and underestimates of the proportion of unvaccinated.

The report published in July 2022 in[1] covers the period January 2021 to May 2022 and claims that, over this full period, the age-standardised all-cause mortality of people vaccinated against COVID-19 is significantly lower than that of their unvaccinated counterparts (957 deaths per 100k person years compared to 2338). Figure 1 shows a plot of the overall age-standardised mortality rates by vaccination status for the period of the latest report. However, the ONS dataset has numerous anomalies which might bias its results toward underestimation of mortality rates of the vaccinated and overestimation of mortality rates of the unvaccinated. This includes miscategorising many vaccinated deaths as unvaccinated,[2] and the potential omission of many vaccinated deaths from the data.[3]

Another potential major anomaly in the ONS data that biases the results, the implications of which have not previously been thoroughly investigated, is an underestimation of the proportion of unvaccinated.

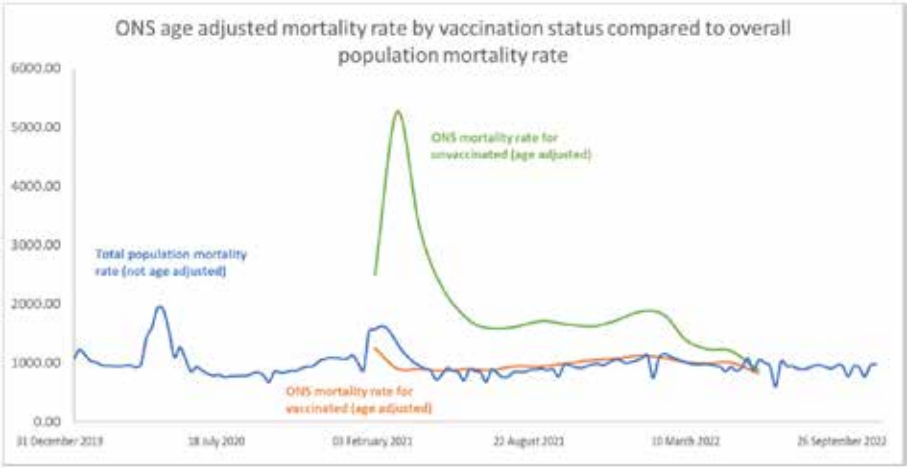


Figure 1 ONS age standardised mortality rate by vaccination status

There are competing claims about the percentage of adults who remain unvaccinated; at first glance this appears difficult to reconcile. The ONS claimed in May 2022 that 8% of adults were unvaccinated and indeed this was the headline figure on which the controversial BBC2 television program 'Unvaccinated' was based.[4] However, the problem with this 8% estimate is that it was completely at odds with other independent estimates. The UKHSA report at that time[5] was estimating 20% of those aged at least 18 as unvaccinated. More notably, in an extensive and highly representative survey undertaken by ICM in May 2022[6] that was used by the BBC for their documentary program, 26% of those aged at least 18 (664 out of 2570) were never vaccinated. The detailed survey spreadsheet, noted in reference[5], actually compares the survey results with the ONS estimates for all the population data (age, ethnicity, region, socio-economic class); the only attribute where there is any significant variation is the proportion of unvaccinated where it clearly states the ONS estimate as 8% compared to the 26% found.[4] Moreover, when the NHS uses ONS denominators to estimate vaccine coverage they report more than 100% of many older age groups have been vaccinated.[7]

This paper analyses the effect of these biases on the latest ONS data. In Section 2 we explain the limitations of the ONS dataset and how they arrived at the 8% adult unvaccinated in May 2022. We show it is conceivable that both the ONS 8% figure is correct for its sample, while the proportion of all adults in England unvaccinated is at least 20% as per the other sources. But we show in Section 3 that this would mean that at least 69% of adults missing from the ONS sample are unvaccinated. Hence, either the ONS is underestimating the proportion of unvaccinated in its sample or the sample is so unrepresentative of the whole population that any inferences made using the ONS data are worthless. Either way, the ONS estimate of proportion unvaccinated must not be used for any comparisons of vaccine efficacy or safety of the whole England population.

In Section 4, we review the raw mortality data in the ONS report and highlight some obvious problems with it. The raw mortality rates (which the ONS do not report) are higher in the vaccinated than the unvaccinated, but overall, these results are age confounded. Instead of reporting separate comparative mortality rates for each different age category to avoid age confounding, the ONS use overall age-standardised mortality rates (ASMR).

In Section 5 we identify the limitations and anomalies in the ASMR. We show that, even without adjusting for the previously observed anomalies and biases in references [2] and [3], the most recent monthly data (in contrast to the especially flawed data in 2021) provides no evidence that the vaccines reduce

4 A detailed analysis of this can be found in https://www.normanfenton.com/post/more-updates-on-bbc2-documentary-unvaccinated, and the linked video.

all-cause mortality once we make even minor adjustments for the possibility that the ONS has underestimated the proportion of unvaccinated. This is demonstrated in detail in Section 6 where we analyse the recent months' mortality data February to May 2022 for each of the different age categories.

Since all our analyses point toward errors in the claims made in support of vaccine safety and efficacy, it is unsurprising that vaccine advocates have sought alternative possible explanations for the anomalies in the ONS data beyond those already discussed and we address these in Section 7. The most common alternative explanations are directly contradictory, with some claiming a 'healthy vaccinee effect' and others claiming an 'unhealthy vaccinee effect'. Neither of these alternative explanations is supported either empirically or theoretically.

Our conclusions are presented in Section 8. We recommend that the ONS adds full caveats to its future surveillance reports explaining the limitations and biases of its sample population. Also, any studies of vaccine efficacy or safety comparing vaccinated and unvaccinated which use whole population data of COVID cases, hospitalisations, and deaths, but which rely on the ONS estimate of proportion unvaccinated must be retracted.

3. The ONS population sample: its limitations and estimates of number unvaccinated

The ONS vaccine mortality surveillance reports (the latest being[1]) relate to the population of England (it contains no data at all on Wales, Scotland or Northern Ireland). However, contrary to what many people assume, the data do not represent the whole population of England, but rather a biased subset of it. Specifically, people are in the database only if they were:

a) registered in England in the 2011 census, and

b) registered with a GP in England in 2019

In addition to all people not registered with a GP, this ONS dataset also excludes all people who arrived in the country after 2011 (believed to be around four million) and all children under the age of 10. The total number in the sample is about 39 million. We refer to Table 3 of the latest report[1] to source these numbers and to help understand how the ONS estimate the proportion unvaccinated. The report covers the 17 months from January 1st 2021 to May 31st 2022 and records the following:

- Total unvaccinated: 16,375,484 person-years
- Total ever vaccinated: 38,860,947 person-years

That is a total of 55,236,431 person-years. Since there are 516 days in the period

January 1st 2021 to May 31st 2022, to calculate the number of people in the dataset we must multiply by 365/516 since every person corresponds to 516/365 person-years**.** Hence, the number of people in the dataset is 39,072,282.

The current estimated England population is approximately 56 million of whom circa 49 million are aged at least 10. So, the sample excludes roughly 10 million people aged over 10. This missing 10 million are intrinsically different from those in the ONS dataset since they are either people who are new immigrants and or have refused, failed or are sufficiently healthy to have not needed to register with a GP. This means they are likely to be a much younger sub-population with a much higher proportion of people unvaccinated. In other words, the ONS dataset is not a representative sample of the population of England, aged at least 10. Indeed, we find very strong evidence of this underrepresentation when we look at the ONS estimates of the proportion unvaccinated.

First note that the reason the ONS uses person-years rather than number of people in their breakdown of vaccinated *versus* unvaccinated is that many people will only have been vaccinated for part of the previous 17-month period. By using the person-years data above, and by dividing the total unvaccinated by the total unvaccinated and ever vaccinated, we can calculate that 29.6% of the total person years were unvaccinated over the 17-month period. This does not mean that 29.6% of people remain unvaccinated at the end of the period, but rather that over the whole period, 29.6% of that time (for all people together) was spent unvaccinated. This includes people who spent the entire period unvaccinated as well as people who spent just a few days unvaccinated.

However, if we focus only on the latest available month, namely May 2022, from report [1], we can see how the ONS could arrive at their highly disputed estimate of 8% adult unvaccinated at this time.[8]

For any month the report provides (in its Table 1) the number of person years for the 'unvaccinated' and 'ever vaccinated'. If we multiply the person years 'unvaccinated' by 365 and divide by the number of days in the month we get the ONS estimate of the total number of people unvaccinated at that point.[5] Similarly, for the 'ever vaccinated'. So, for May 2022, there are:

- 448,434 unvaccinated person years, which corresponds to 5,279,949 people (we multiply by 365/31 as there are 31 days in May)
- 2,846,174 ever vaccinated years, which corresponds to 33,511,404 people.

Note that, as a consistency check, this totals just under 39 million people

5 Strictly speaking it is only an approximation of the number of people unvaccinated up to the end of the month because the person years contain a small number who were first vaccinated during that month

still alive in May 2022 from the original 39,072,282 in the ONS dataset in January 2021.

This means that, in the ONS dataset, 13.6% of the people were unvaccinated up to the end of May 2022. However, (as we explain in detail in the next section) if we remove those aged under 18 and account for the fact that a higher proportion of that age category are unvaccinated, we can see how that would result in a number close to the 8% adult unvaccinated claimed by the ONS (see below).

In a recent response to an FOI request, the ONS concede that 'it is difficult to identify exactly how many people in the population are unvaccinated'.[9] A plausible explanation for (at least part of) the difference in unvaccinated rates is that, compared to the others, the ONS sample is (as we have suspected all along) significantly biased. It does indeed seem reasonable that the England population who were not registered in the 2011 census and who were not registered with a GP will be a set of people much less likely to be vaccinated than those in the ONS sample.

While there is no dispute about the number of people (the 39 million) in the ONS dataset, the number 'ever vaccinated' is based on GP records which may not be accurate for reasons explained in [2]. There is also strong anecdotal evidence that many unvaccinated people are erroneously recorded as vaccinated with records that contain explicit dates and batch numbers.[10] However, such errors, should they be random, are assumed here not to make a major difference.

4. Estimating the proportion of unvaccinated in those missing from the ONS sample.

As explained above we know that in May 2022, in their sample of England residents (all aged 10+), the ONS estimate that there were:

- 5,279,949 unvaccinated
- 33,511,404 vaccinated

meaning that 13.6% were unvaccinated in May 2022. If we remove those aged 10-17 and account for the fact that a higher proportion of that age category are unvaccinated, we can get to the 8% figure estimated by ONS, if we assume 50% of the unvaccinated were aged less than 18 and that 10% of the vaccinated were aged less than 18, that is:

$$u_1 : number\ of\ unvaccinated\ adults\ in\ ONS\ sample\ = 2{,}639{,}975$$

$$v_1 : number\ of\ vaccinated\ adults\ in\ ONS\ sample\ = 30{,}160{,}264$$

This takes us to the 8% adult unvaccinated proportion claimed by the ONS for their sample.

But we also know that there are approximately 8,000,000 England residents aged 18+ who are missing from the ONS sample (specifically, the total number of England residents aged 10+ missing from the ONS sample is approximately 10,000,000 and approximately 80% of these are aged 18+).

Let

u_1 : *number of unvaccinated adults in ONS sample* $= 2{,}639{,}975$

v_1 : *number of vaccinated adults in ONS sample* $= 30{,}160{,}264$

This takes us to the 8% adult unvaccinated proportion claimed by the ONS for their sample.

But we also know that there are approximately 8,000,000 England residents aged 18+ who are missing from the ONS sample (specifically, the total number of England residents aged 10+ missing from the ONS sample is approximately 10,000,000 and approximately 80% of these are aged 18+).

Let

u_2 : *number of unvaccinated adults missing from ONS sample*

v_2 : *number of vaccinated adults missing from ONS sample*

Then $u_2 + v_2 = 8{,}000{,}000$ and the total number of adults overall is:

$$u_1 + u_2 + v_1 + v_2 = 8{,}000{,}000 + 2{,}639{,}975 + 30{,}160{,}264 = 42{,}800{,}239$$

But we know that, in May 2022, z was at least 20% based on the UKHSA (20%) and ICM (26%) estimates. Given such a value for z we are interested in knowing the proportion of unvaccinated in those missing from the ONS sample. Let α be the proportion of unvaccinated in those missing from the ONS sample. Then we know

$$u_2 = \alpha \times 8{,}000{,}000 \qquad (2)$$

Hence, by equations (1) and (2) we have:

$$z = \frac{2{,}639{,}975 + \alpha \times 8{,}000{,}000}{40{,}800{,}239}$$

So, if $z = 0.2$ we get:

$$0.2 \times 40{,}800{,}239 = 2{,}639{,}975 + \alpha \times 8{,}000{,}000$$

So

$$\alpha = \frac{8{,}160{,}048 - 2{,}639{,}975}{8{,}000{,}000} = 0.69$$

Hence, if the ONS estimate of 8% adult unvaccinated in their sample is correct and if there are at least 20% of adults unvaccinated in the whole of England, it follows that at least 69% of the adults missing from the ONS sample are unvaccinated.

But what if the 26% adult unvaccinated reported in the ICM survey for the BBC documentary was the true proportion for adult unvaccinated? Then substituting $z = 0.26$ above we get:

$$\alpha = \frac{10{,}608{,}062 - 2{,}639{,}975}{8{,}000{,}000} = 0.996$$

In other words, this would mean 99.6% of the adults missing from the ONS sample are unvaccinated.

So, if the ONS estimate of 8% adult unvaccinated for their sample is correct then, based on other independent estimates of the adult unvaccinated in the whole population, this would mean that between 69% and 99.6% of the 8,000,000 adults missing from the ONS sample were unvaccinated.

Is this feasible? It would mean the ONS sample is not at all representative of the whole England population. It is much more likely that the ONS population estimate and therefore their estimate of the size of the unvaccinated population is too low (the fact that NHS data show vaccination rates of greater than 100% using ONS denominators also confirms this). Yet the ONS are now claiming[11] that, as of end of August 2022 the number of unvaccinated has dropped even further despite extremely weak vaccine take-up during that period. Their latest report states: 'of those aged 12 years and over 93.6% had received a first dose of a COVID-19 vaccine'. Hence their latest estimate is that just 6.4% of those aged 12 and over are unvaccinated and this would mean even less (about 5%) of those aged 18+ are unvaccinated. It is highly unlikely that many of the 8,000,000 aged 18+ missing from the ONS sample have had the vaccine since May, 2022. This means the ONS sample is even more unrepresentative of the England population than originally thought.

If correct, then it means the ONS sample is such a highly biased subset of the England adult population that it should not be used to make any inferences about the entire population. Furthermore, any mortality analysis reliant on ONS estimates for proportion unvaccinated will significantly overestimate mortality rates for the unvaccinated and underestimate mortality rates for the vaccinated. This problem extends to the use of whole-population estimates of COVID case, hospitalisation, and mortality rates for vaccinated and unvaccinated. In other words, using the ONS estimate of 8% adult unvaccinated will likely result in a substantial exaggeration of the efficacy and safety of the vaccines.

So, while the vaccine might appear to support claims of safety and effectiveness for the ONS population dataset (and we will show in Section 6 that this is not the case of the ONS most recent data), this would certainly not mean any claims for safety and efficacy can be extended to the whole population. In fact, because of misclassification[2] and missing vaccine deaths,[3] as well as delays caused by post-mortems, there is even less support for any claims that the vaccine is safe and effective using the ONS's special population subset.

5. Understanding the ONS mortality dataset and its limitations

The following detailed analysis of the ONS dataset reveals evidence of further problems with it.[6] Table 3 in the ONS report[1] includes the aggregated mortality data for England over the 17-month period January 1st 2021 to May 31st 2022 shown in the left-hand side of Table 1. Note that the total number of deaths for the 17-month period is 641,009 which equates to an approximate annual mortality rate for the period of 1,163 deaths per 100k people (based on the sample size of 39 million and the 17 months equal to 516/365 years).

Note that there is a lower mortality rate for COVID-related deaths in the ever vaccinated, but a higher non-COVID mortality rate in the vaccinated, and overall, the all-cause mortality is substantially higher in the vaccinated.

Table 1: Age-confounded aggregated mortality rates
(with lowest death rates in each category italicised)

		Deaths			Death rate per 100k person years		
Vaccination status	Person years	Involving COVID	Non-COVID	All cause	Involving COVID	Non-COVID	All cause
Unvaccinated	1,991,761	24	265	289	1.2 (0.81, 0.79)	13.3 (11.7, 15.0)	14.5 (12.9, 16.2)
Ever vaccinated	1,458,465	7	225	232	0.5 (0.23, 0.99)	15.4 (13.5,17.6)	15.9 (14.0, 18.1)

Superficially this seems to suggest that, over this 17-month period, the risks of the vaccine outweigh the benefits overall. But this is not necessarily the case because these aggregated mortality data are age confounded, whereby a much higher proportion of young people in this population are unvaccinated and most deaths, of course, occur in the older population which has the highest proportion of vaccinated. Indeed, the ONS do not include the death rates shown on the right-hand side in Table 1 to avoid people drawing this inappropriate conclusion.

To determine the actual risk-benefit of vaccination (which may radically differ between age-groups), we need to look at the all-cause mortality rates within each age category. Helpfully, the ONS provide an age breakdown in Tables 5 and 6 in their reports. For example, for the 15-19 age category we can compute the mortality rates shown in Table 2.

6 This twitter thread also addresses these concerns about the ONS data: https://twitter.com/os51388957/status/1576204422857703424

Table 2: Age category 15-19 mortality rates (with lowest death rates in each category italicised and 95% confidence intervals in brackets)

		Deaths			Death rate per 100k person years		
Vaccination status	Person years	Involving COVID	Non-COVID	All cause	Involving COVID	Non-COVID	All cause
Unvaccinated	1,991,761	24	265	289	1.2 (0.81, 0.79)	13.3 (11.7, 15.0)	14.5 (12.9, 16.2)
Ever vaccinated	1,458,465	7	225	232	0.5 (0.23, 0.99)	15.4 (13.5,17.6)	15.9 (14.0, 18.1)

So, in the 15-19 age category, where there are few deaths overall, there is a higher mortality rate for COVID-related deaths in the unvaccinated but a lower non-COVID mortality rate in the unvaccinated. Overall, the all-cause mortality is lower in the unvaccinated because there are very few COVID related deaths in this age category[7] meaning that, for this age-group the risks of the vaccine might outweigh the benefits based on the whole 17-month period.[8] However, there may be a bias whereby the sickest 15–19 age group with the highest mortality rate might have been more likely to have been vaccinated.

However, things are very different for example in the 70-74 age category as shown in Table 3.

Table 3: Age category 70-74 mortality rates (with lowest death rates in each category italicised and 95% confidence intervals in brackets)

		Deaths			Death rate per 100k person years		
Vaccination status	Person years	Involving COVID	Non-COVID	All cause	Involving COVID	Non-COVID	All cause
Unvaccinated	1,991,761	24	265	289	1.2 (0.81, 0.79)	13.3 (11.7, 15.0)	14.5 (12.9, 16.2)
Ever vaccinated	1,458,465	7	225	232	0.5 (0.23, 0.99)	15.4 (13.5,17.6)	15.9 (14.0, 18.1)

In the 70-74 age category, where there are many deaths overall, the all-cause mortality is much lower in the vaccinated, meaning that, for this age-group, the benefits of the vaccine outweigh the risks based on the whole 17-month period.

However, Table 3 also reveals a major anomaly in the ONS dataset. While we would expect a lower COVID mortality rate in the vaccinated if the vaccine is effective, even if there were no serious adverse reactions from vaccination,

7 Moreover, we know that almost all the 31 deaths 'with COVID' reported here were not due to COVID. Based on an FOI request we know that only one person in this age category died up until 31 Dec 2021 with COVID as the only cause: https://www.ons.gov.uk/aboutus/transparencyandgovernance/freedomofinformationfoi/covid19deathsandautopsiesfeb2020todec2021

8 Because of the low numbers of deaths in this age category the difference is not highly significant with a 95% confidence Bayesian risk ratio of 0.77 to 1.08 and an 86% probability the rate is higher in the vaccinated.

we should not expect the non-COVID mortality rate in the vaccinated to be less than the unvaccinated. At best, if the vaccine was perfectly safe, these rates should be approximately equal. Yet the unvaccinated non-COVID mortality rate is 46% higher than the vaccinated. This is simply not credible.

As this is over the whole 17-month period it is instructive to look at the mortality rates for this age category in the latest month only, May 2022. Unfortunately, this is where we hit another inconsistency in the ONS dataset because, in contrast to their Tables 5 and 6, they only provide the monthly age categorised data (ONS Table 1) on a less granular level; we have the age category 70-79 and not 70-74 or 75-79. These May 2022 mortality data are shown in Table 4, which also distinguishes the different vaccination categories.

Table 4: Age category 70-79 mortality rates for May 2022

		Deaths			Death rate per 100k person years		
Vaccination status	Person years	Involving COVID	Non-COVID	All cause	Involving COVID	Non-COVID	All cause
Unvaccinated	10,216	20	216	236	196	2,114	2,310
First dose, less than 21 days ago	11	<3	<3	<3			
First dose, at least 21 days ago	1,163	<3	47	49		4,041	4,213
Second dose, less than 21 days ago	23	<3	<3	<3			
Second dose, at least 21 days ago	8,790	23	422	445	262	4,801	5,063
Third dose or booster, less than 21 days ago	273	<3	25	25		9,158	9,158
Third dose or booster, at least 21 days ago	349,100	250	6,130	6,380	72	1,756	1,828
Ever vaccinated	359,360	279	6,624	6,903	78	1,843	1,921

Note the following:

- The non-COVID mortality rate is still significantly higher in the unvaccinated compared to the ever vaccinated (2114 compared to 1843), meaning there is likely an ongoing mis-categorisation problem, but the difference has dropped dramatically – from 46% higher down to 15% higher.

- In each of the vaccination categories other than 'Third dose or booster, at least 21 days ago' the non-COVID mortality of the vaccinated is much higher than that of the unvaccinated, with wildly different values of 4041, 4801 and 9158. Even with only 273 person years for the 'Third dose or booster, less than 21 days ago' the non-COVID mortality rate is statistically significantly different from the other rates.

But, as mentioned above, assuming no significant adverse reactions, the non-COVID mortality rate for each of the different categories of vaccination status should be approximately equal, so the fact that they are wildly different is evidential support for misclassification in the data, as discussed in reference [2], namely that many of those who die shortly after their first dose are wrongly classified as unvaccinated and those who die shortly after their second dose are wrongly classified as single dose only.

6. Anomalies in the ONS age-standardised mortality rate

For risk-benefit analysis we would prefer to consider the separate all-cause mortality for each of the different age categories. As we already saw, in the 15-19 age category the all-cause mortality of the vaccinated was higher than that of the unvaccinated but in the older age categories the all-cause mortality of the unvaccinated was higher than that of the vaccinated. However, it is possible to provide an approximate whole population mortality rate that avoids the age-confounding problem. This is called the age-standardised metric[12] and it is the only mortality metric used by the ONS. The ONS dataset Table 3 provides this metric, and we summarise the results in Table 5 here:

Table 5: Whole period mortality rates with age-standardised metric

		Deaths			Age standardised mortality rate per 100k person years		
Vaccination status	Person years	Involving COVID	Non-COVID	All cause	Involving COVID	Non-COVID	All cause
Unvaccinated	16,375,484	38,285	71,606	109,891	863	1,474	2,338
First dose, less than 21 days ago	1,925,587	4,037	13,662	17,699	190	637	827
First dose, at least 21 days ago	5,536,696	7,270	69,930	77,200	122	1,167	1,289
Second dose, less than 21 days ago	1,878,686	200	11,786	11,986	8	504	513
Second dose, between 21 days and 6 months ago	13,454,401	5,462	151,075	156,537	30	838	868
Second dose, at least 6 months ago	2,664,983	6,664	65,126	71,790	198	1,909	2,107
Third dose or booster, less than 21 days ago	1,529,103	494	12,374	12,868	22	548	569
Third dose or booster, at least 21 days ago	11,871,491	12,048	170,990	183,038	59	825	883
Ever vaccinated	38,860,947	36,175	494,943	531,118	65	893	957

The whole point of the ASMR is that it is intended to take full account of the number of people and deaths in each age category so that age categories

with proportionally more deaths get a heavier weighting. This explains why, despite the deaths per person years being higher overall in the vaccinated, it is perfectly feasible for the ASMR to be higher in the unvaccinated. Also, because most deaths occur in the older age categories the ASMR is much 'closer' to the mortality rate of the older age-groups (such as those shown in Table 3) than the younger age-groups (such as those shown in Table 2).

The age-standardized metric is already adjusted to take account of the length of the reporting period, so although the time period in Table 5 is 17 months, the ASMR shown is an estimate of the number of people who die in a year (not 17 months). Hence, according to the estimate in the table, 1474 out of every 100k unvaccinated people would die per year from non-COVID causes, compared to just 893 out of every 100k ever vaccinated people.

But this means that the ASMR exhibit even stranger anomalies than seen in the mortality rates of the older age-groups for the whole period. In Table 5, the non-COVID mortality rate of the unvaccinated is 65% higher than the vaccinated. It suggests that such a gross anomaly might be disproportionately due to misclassification errors that occurred early in the 17-month period, because the latest month's figures (May 2022) shown in Table 6 are very different from those in Table 5.

Table 6: Latest month May 2022 age age-standardised mortality (x indicates number too low to reasonably estimate)

		Deaths			Age standardised mortality rate per 100k person years		
Vaccination status	Person years	Involving COVID	Non-COVID	All cause	Involving COVID	Non-COVID	All cause
Unvaccinated	448,434	82	935	1017	78	795	873
First dose, less than 21 days ago	2,291	0	1	1	x	x	x
First dose, at least 21 days ago	107,764	18	283	301	122	1,751	1,873
Second dose, less than 21 days ago	8,424	0	9	9	x	x	x
Second dose, between 21 days and 6 months ago	159,940	6	127	133	x	1,746	1,816
Second dose, at least 6 months ago	328,732	103	1,683	1,786	106	1,597	1,704
Third dose or booster, less than 21 days ago	13,292	0	96	96	x	2,056	2,056
Third dose or booster, at least 21 days ago	2,225,731	1,155	25,987	27,142	33	764	797
Ever vaccinated	2,846,174	1,282	28,186	29,468	36	787	823

So, in the May 2022 data there is no longer much difference between the age-standardised non-COVID mortality rate of the vaccinated, 787 per 100k people, and the unvaccinated, 795 per 100k people. The all-cause ASMR are also not too far apart (823 *versus* 873). Moreover, except for the category 'third dose or booster at least 21 days ago' the all-cause ASMR of the unvaccinated is much lower than that of each category of vaccinated. In other words, even with all the potential biases and misclassifications in the ONS data, in the latest available month's data there is no real evidence to support the hypothesis that the vaccine reduced all-cause mortality in May 2022.

To understand the extent of the anomaly with the full period data Table 5 we can compare them to the historical annual non-COVID mortality rates. The ONS provide age-standardised rates dating back to 1938 but for England &

Table 7: Age-standardised mortality rate (per 100k population)

* We are assuming the ASMR for the population of England is similar to that for England & Wales)

Year	England & Wales*
2020	1044
2019	925
2018	965
2017	965
2016	967
2015	993
2014	953
2013	986
2012	987
2011	979

Wales combined[13] as shown in Table 7, whereas Table 5 is for England only. However, we can estimate the England figures as shown.

As already discussed, there is no logical reason for the ASMR for non-COVID deaths to be higher in the unvaccinated since the vaccine cannot reduce non-COVID deaths. So, prior to the COVID year of 2020 the England ASMR is stable at around 974 deaths per 100k people. This means we should be seeing a similar yearly figure for both the latest unvaccinated and vaccinated non-COVID mortality rate. Yet, based on the whole 17-month period of the ONS dataset we have:

- Vaccinated rate is 893 (an 8% drop from what is expected)
- Unvaccinated rate is 1473 (a 51% increase from what is expected)

If we compare historical all-cause mortality, 974 ASMR, with the ONS dataset values, 2338 ASMR for the unvaccinated and 957 ASMR for the vaccinated, then we would conclude that in a period after the peak of the pandemic while the vaccinated now have a similar mortality rate to historical rates the unvaccinated are dying at an enormous rate, 240% higher than before. Hence, whether we focus on non-COVID deaths or all-cause deaths the ONS dataset cannot be correct. It is also important to compare the recent vaccinated and unvaccinated data, 823 and 873 respectively from Table 6, with historical rates, and this shows missing mortality and confirms that the ONS dataset is incorrect.

What was shown in [2] was that, in 2021 when the vaccine rollout began, the ONS data were showing peaks in non-COVID mortality among the unvaccinated at the very time the vaccine rollouts reached their peak in each different age category. Figure 2 shows this for the 60-69 age category. Later smaller peaks in non-COVID mortality were also seen in the unvaccinated when the second dose was rolled out.

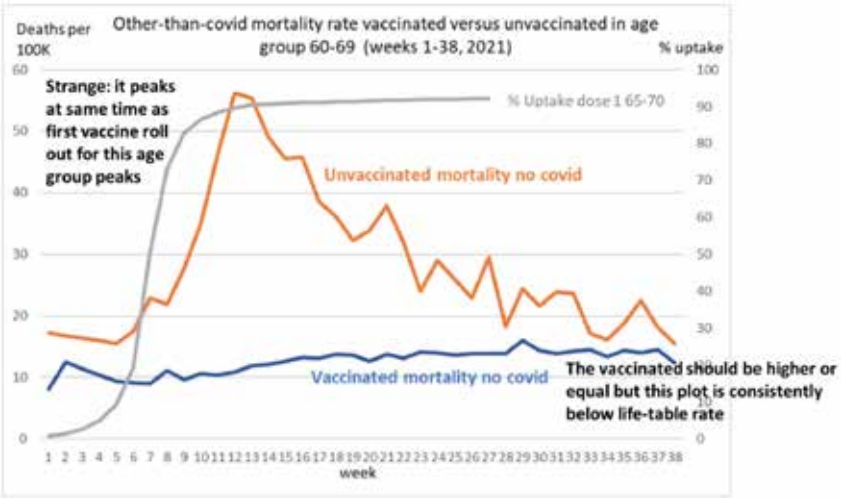


Figure 2: Non-COVID mortality rate in age category 60-69

That paper concluded that a possible plausible explanation for such an obvious anomaly was that people dying shortly after vaccination were being wrongly classified as unvaccinated. Whether through policy or error this certainly happens (indeed in Sweden a reply to an FOI[9] request confirms that those dying within 14 days of vaccination are routinely counted as unvaccinated). Once the ONS data were adjusted for these anomalies there was no evidence that the vaccines reduced all-cause mortality.

9 https://lakaruppropet.se/public-health-agency-reporting-has-distorted-mortality-rates-for-the-unvaccinated-and-vaccinated/

Using the data in the latest ONS report[1] Figure 3 shows the weekly non-COVID mortality rate in the unvaccinated and vaccinated over the whole period from January 1st 2021 to May 31st 2022. Note how the anomalies seen in the first half of 2021, when the major vaccine rollouts occurred, subside and the rates for both vaccinated and unvaccinated converge on the historical non-COVID mortality rates as they always should have done.

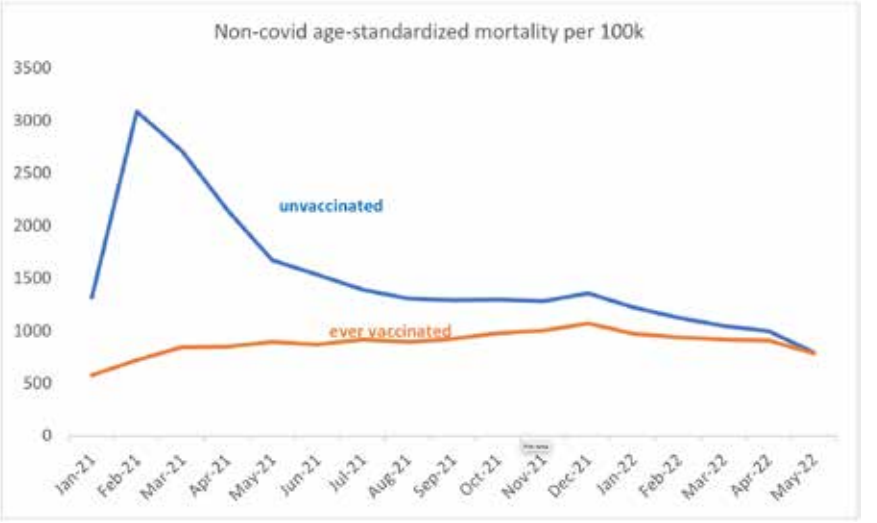


Figure 3: Non-COVID mortality rate January 2021 – May 2022

The fact that the vaccinated and unvaccinated non-COVID mortality rates have now converged, however, does not necessarily mean that claims of vaccine safety and efficacy can be supported. On the contrary, there are several reasons to believe that the non-COVID mortality in the vaccinated is being underestimated even in the ONS dataset:

- There is a large number of vaccinated deaths missing from the ONS dataset as explained in [3]
- It is likely that there is continued misclassification of those dying shortly after vaccination doses
- Even within the highly unrepresentative ONS sample of the England population the proportion of unvaccinated in the dataset is likely underestimated

Since we have argued that a much larger proportion of the whole England population is unvaccinated compared to the proportion in the ONS sample, it follows that if the whole population proportion is used as the denominator with the ONS mortality figures, the current non-COVID mortality rate (based on May 2022) would be significantly higher in the vaccinated.

7. Analysis of recent mortality data: 'dead presumed missing'

To best understand the current mortality rate of vaccinated and unvaccinated and to consider the effect of possible underestimation of proportion unvaccinated in the ONS data, we focus on the four most recent months (February to May 2022) and the mortality data in each separate age category. The most recent months should provide the most stable current estimate of differences in all-cause mortality between vaccinated and unvaccinated especially as there were no major waves of COVID mortality or vaccination during this period.

The relevant data for this come from Table 2 of the ONS dataset. There are, however, some curious omissions in this table that need to be noted that slightly compromise the analysis. Specifically:

- Whereas elsewhere in the dataset the ONS provide age categories (10-14, 15-19, 20-24, …, 85-89, 90+) the ONS only provide data for the age categories 18-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90+ in Table 2.
- Whereas elsewhere in the dataset the ONS provide the aggregated 'ever vaccinated' data in addition to all the individual vaccination status categories' data, this is omitted in Table 2. Of course, we can and do simply calculate the 'ever vaccinated' data by aggregating the data for all the individual vaccination status categories. However, while this enables us to calculate the mortality rate, it does not allow us to calculate the ASMR that ONS itself uses. Fortunately, because the data are already age-categorised (albeit quite coarsely) there is minimal age confounding, and these rates are close to the age-standardised rates.

Table 8 shows the aggregated mortality data and mortality rates (expressed as deaths per 100k person years) for the four most recent months of the ONS data. The last two columns show the reported percentages of unvaccinated by both ONS (which in each age category is simply the number of unvaccinated person years divided by the total person years in the age category) and the NIMS estimate for that period and age group.

Note that:

- For each of the younger age categories (18-39 and 40-49), as well as (curiously) the oldest age category 90+, the all-cause mortality rate of the unvaccinated is lower than that of the ever vaccinated.
- In each of the other age categories the all-cause mortality rate of the unvaccinated is higher than that of the ever vaccinated.

- In every age category the proportion of unvaccinated is significantly underestimated compared to the NIMS estimate. If we were to assume that the fatalities were accurately categorised but that the overall proportion was that of the NIMS estimate and not the ONS estimate, then the all-cause mortality would be significantly higher in the vaccinated in every age-group. In each of the age-groups where the unvaccinated mortality rate is higher than the vaccinated mortality rate, the NIMS estimate is at least 71% higher than the ONS estimate. A relative increase of between 20% and 40% over the reported unvaccinated mortality rate will result in a lower all-cause mortality rate for the unvaccinated category. However, these kinds of adjustments are questionable given that the unvaccinated, uncounted by the ONS, have no mortality represented within the ONS dataset.

However, these latest data provide some of the strongest evidence yet of how inaccurate the ONS dataset is when we compare the mortality rates with the

Table 8: Feb-May 2022 Mortality Rate by Age Category

Age Category	Total deaths	Person years	Mortality rate	Reported unvaccinated %	
			deaths per 100k person years	ONS	NIMS
18-39				19.3%	28.7%
Unvaccinated	151	706,779	21		
Ever vaccinated	730	2,952,830	25		
40-49				12.2%	19.6%
Unvaccinated	204	218,387	93		
Ever vaccinated	1,610	1,571,717	102		
50-59				6.9%	11.8%
Unvaccinated	560	144,459	388		
Ever vaccinated	5,712	1,960,002	291		
60-69				4.7%	8.2%
Unvaccinated	876	82,600	1,061		
Ever vaccinated	13,132	1,674,394	784		
70-79				2.8%	4.8%
Unvaccinated	1,178	39,319	2,996		
Ever vaccinated	31,064	1,388,370	2,237		
80-89				2.2%	4.4%
Unvaccinated	1,375	15,246	9,019		
Ever vaccinated	48,346	662,379	7,299		
90+				2.9%	4.4%
Unvaccinated	910	4,386	20,748		
Ever vaccinated	31,638	146,737	21,561		

historical rates up to 2016[14] as shown in Figure 4 reproduced from [14].

What we find is that the ONS mortality rates are much lower for both the vaccinated and unvaccinated in each age category (while a very small drop might be expected to account for February to May having slightly lower annual rates than a full year including January and December this should be more than compensated for the known increase in deaths in 2022 from the various effects of COVID-19 and lockdowns). For example, from Table 9, in the 18-39 age group the ONS data show mortality rates of 21 for the unvaccinated and 25 for the vaccinated, whereas historical rates are around 50. For the 40-49 age group there are ONS rates of 93 for the unvaccinated and 102 for the vaccinated, whereas historical rates are around 180. As the age categories increase the reported mortality rates for the unvaccinated and ever vaccinated converge.

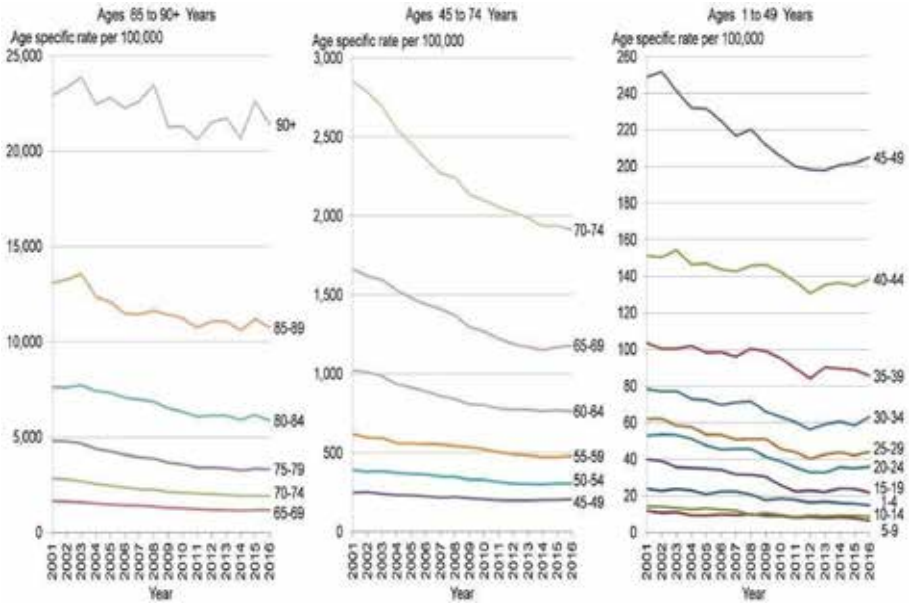


Figure 4: Historical mortality rates for England by age group

Where are these missing deaths? It might be that deaths reported by the ONS are only those registered with the authorities but deaths that require a coroner's investigation will not be included in the ONS death totals until the investigation is complete and the death is registered thereafter. Given coroners' investigations can take weeks or, in exceptional cases, months, a larger proportion of deaths will be missing in the most recent data from the ONS.[19] This creates a lag effect where actual mortality lags that which is reported and, over time, this lag effect self-corrects as deaths are registered and are then retrospectively added into the ONS data with the correct date

of occurrence. Clearly this lag effect would be more pronounced for younger age groups as the proportion of deaths that require investigation is higher in the young. However, given that the data are from February to May 2022 any backlog of deaths being investigated by the coroner should have cleared by the time of writing.

It would be possible to estimate the historical lag effect and, assuming it is representative of current processes, then estimate the total numbers of deaths missing for which self-correction is expected. However, the ONS have chosen not to do that and instead reported a misleading low mortality rate which will rise over time as the death data self-correct. Whereas the ONS had published updates to the data every two months or so, there has not been an update since July 2022 with no explanation as to why or when the next update is to be expected.

Table 9: February to May 2022 – age-standardized mortality rate compared with approximate historical mortality rate (deaths per 100k person years)

Age Category	Mortality rate	Historical Mortality rate in 2016 (approximate)
18-39		
Unvaccinated	21	50
Ever vaccinated	25	
40-49		
Unvaccinated	93	180
Ever vaccinated	102	
50-59		
Unvaccinated	388	400
Ever vaccinated	291	
60-69		
Unvaccinated	1,061	1,000
Ever vaccinated	784	
70-79		
Unvaccinated	2,996	3,000
Ever vaccinated	2,237	
80-89		
Unvaccinated	9,019	8,500
Ever vaccinated	7,299	
90+		
Unvaccinated	20,748	21,000
Ever vaccinated	21,561	

We have previously encountered this 'dead presumed missing' problem in ONS mortality data. In [3] we found that they had omitted 13,593 deaths from their dataset and as a result the mortality in the vaccinated was disproportionately low when compared to historical norms and those omitted from their dataset (but which appear in other government statistics). The ONS have

only acknowledged 1,436 deaths post vaccination whose vaccination record was not entered into the NIMS data system, thus originally categorising them as unvaccinated deaths, whilst stating that 71,318 people with inconsistent vaccination records were simply removed from the analysis.[20]

The ONS dataset continues to show grossly unrealistic discrepancies between the mortality rate of people within the ONS sample and the implied mortality rate of the remaining population. If we take the claimed ONS mortality rates for vaccinated and unvaccinated for the sample and extrapolate to the population, outside of their sample, we find there would have been over 150,000 deaths in the population that was not sampled (see below). That would mean those eight million people, while only 19% of the population of England and likely to be younger overall than those in the sample, accounted for 30% of all deaths in England and Wales.

In Section 3 we inferred that 69% of the 10+ population not in the ONS dataset are unvaccinated, and this gives us 5,520,000 unvaccinated people and 2,480,000 vaccinated people (a total of eight million not in the ONS dataset). Using the ONS unvaccinated and ever vaccinated all-cause mortality estimates for the whole period, 2337.5 and 957.4 (from Table 3 in[20]) and applying them to these ever vaccinated and unvaccinated populations results in 129,000 unvaccinated deaths and 23,700 vaccinated deaths (a grand total of 150,000 deaths in a year).

In England there are 42.8 million people aged 10+ and the eight million not in sample are approximately 19% of this population total. However, the total deaths recorded in England by ONS for 2021 are 496,309 and 150,000 deaths would be approximately 30% of that figure. Therefore, we can conclude that 19% of the aged 10+ population of England have generated 30% of the deaths. Rather than 69% if we assumed the upper limit of 99.6%, were unvaccinated then the total would be 187,000 deaths in the population that was not sampled, which would be 37% of the total deaths in whole population. How is this discrepancy explained? The obvious explanation is that the ONS dataset not only misrepresents the true proportion of the unvaccinated but also is selective in which deaths appear in the dataset and which do not.

8. Alternative explanations for the anomalous ONS data

Our analysis demonstrates that, even without any adjustments to take account of underestimates in the proportion of unvaccinated, the recent months of ONS data suggest that in the young (less than 50) and very old (90+) the all-cause mortality is higher among the vaccinated than the unvaccinated. Only very modest and realistic adjustments to the unvaccinated proportion indicate

the same may be true of all the other age groups. There is growing evidence elsewhere that the vaccines may lead to an increase in all-cause mortality across all age groups.[15]

Because of the potentially devastating effect of these conclusions on the vaccination program, and because it confirms the extent of the anomalies in the ONS data in the first half of 2021, there has been a concerted effort to invent alternative explanations for the anomalies in the ONS dataset. One persistent argument has been that the anomalies were the result of especially ill people being denied the vaccine; so, there was, they claimed, a 'healthy vaccinee effect' (or equivalently a 'moribund unvaccinated effect'). Indeed, as shown in [16] one of the harshest critics of the report [2] repeated that explanation while attacking the recent paper by Malhotra exposing problems with the COVID vaccines.[15]

The ONS even stated the 'healthy vaccinee effect' as an explanation in a subsequent report[17] after the anomalies in their data were identified. But the notion of the 'healthy vaccinee' was contradicted by the NHS guidelines[18] (which required the most critically ill people be prioritised for the vaccine, not denied it) and we know that even terminally ill patients in hospices and care homes were given the vaccine as a priority. Moreover, in[2] it was shown that the ONS data could not be explained by a 'healthy vaccinee' effect. From the mortality pattern across age categories in Table 9 there is no healthy vaccinee effect in evidence. Only the ever vaccinated in the middle to older age groups (50-59, 60-69, 70-70, 80-89) show lower mortality than the unvaccinated. Yet we see the opposite result in the very youngest (18-39, 40-49) and very oldest (90+) age groups, where the unvaccinated show lower mortality than the ever vaccinated. And in any case as we have already observed there is little evidence of any of these age groups containing substantial sub-populations of terminally ill or moribund people, given the mortality rates are less than or equal to historical figures across the board.

The most striking feature of Table 9 is that the mortality rates for the younger age groups in the ONS dataset are significantly less than we would reasonably expect given historical mortality rates. Given that ONS-reported mortality rates are adjusted to ensure that differences in population sizes are accounted for, by age-standardization, differences in population numbers cannot explain this. Neither can any hypothesis that unhealthy younger people, possibly more likely to die, are less likely to be in the ONS dataset because, if anything, such terminally ill young people would almost certainly be registered with a GP and thus be included in the ONS dataset.

Another alternative explanation for this observed reduced mortality effect is that there are fewer deaths in the ONS dataset than should be reported for these younger age categories.

9. Conclusions about the data up until May 2022

Previously discussed explanations for the anomalous differences between non-COVID mortality rates in the vaccinated and unvaccinated include miscategorising deaths shortly after vaccination as unvaccinated and omitting completely many vaccinated deaths. This paper considered an additional major source of bias that has not previously been widely discussed: possible underestimation of the proportion of unvaccinated people. The ONS estimate of 8% of adults unvaccinated in May 2022 contrasts starkly with two other independent sources which estimate the figure to be 20% and 26% respectively. Because the ONS data are based on a subset of England residents that excludes all those not registered with a GP and not registered in the 2011 census, it is missing some eight million adults who are not at all representative of those in the ONS sample. Hence, it is conceivable that both the ONS 8% figure is correct for its sample, while the proportion of all adults in England unvaccinated is at least 20% as per the other sources. But we showed this would necessarily imply that between 69% to 99.6% of adults missing from the ONS sample are unvaccinated. Hence, either the ONS is underestimating the proportion of unvaccinated in its sample or the sample is so unrepresentative of the whole population that any inferences made using the ONS data are worthless. Either way, the ONS estimate of proportion unvaccinated must not be used for any comparisons of vaccine efficacy or safety of the whole-England population. We also showed that even with these anomalies and biases the most recent monthly data (in contrast to the especially flawed data in 2021) provides no evidence that the vaccines reduce all-cause mortality. In fact, for each of the younger age categories (18-39 and 40-49), as well as (curiously) the oldest age category 90+, the all-cause mortality rate of the unvaccinated is lower than that of the ever vaccinated.

The ONS vaccine mortality surveillance reports for England have numerous anomalies which bias its results strongly toward underestimating mortality rates for the vaccinated and overestimating mortality rates for the unvaccinated. Clear evidence of the anomalies can be seen in the latest report by comparing the ONS reported age standardised mortality rates for non-COVID deaths in the vaccinated and unvaccinated. Assuming the vaccines do not cause many deaths from serious adverse reactions, there is no reason why these mortality rates for both vaccinated and unvaccinated should be significantly different from the pre-COVID era steady state figure of approximately 974 deaths per 100k person years. Yet, based on the whole period of vaccination from Jan 2021 to May 2022, the ONS data show a completely implausible non-COVID mortality rate of 1474 per 100k person years for unvaccinated people, compared to just 893 for vaccinated people. Moreover, when we analyse the recent months' data by age categories, we find that in both the vaccinated and unvaccinated the all-cause mortality rates are much lower than the historical rates. Likewise, the mortality

rate outside of the ONS dataset is significantly higher than that within the ONS dataset. The ONS data therefore suffers from deaths selection bias.

Overall, the ONS dataset is so compromised with inaccuracies, anomalies, and biases that it cannot be used to reliably determine vaccine efficacy and safety. We recommend that the ONS adds full caveats to its future surveillance reports explaining the limitations and biases of its sample population. Also, any studies of vaccine efficacy or safety comparing vaccinated and unvaccinated which use whole population data of COVID cases, hospitalisations, and deaths, but which rely on the ONS estimate of proportion unvaccinated must be retracted.

10. The follow-up report

We complained to the Statistics Regulator about the July 2022 report and he: (i) agreed with our recommendation to ignore any claims of vaccine safety or efficacy based on the data; and also (ii) that the ONS underestimates the true population proportion unvaccinated.

After a seven-month delay since the previous update on February 21st 2023, the ONS finally released a new version with data up to December 2022. So, there was great anticipation that the ONS would in the time available resolve the issues with their dataset and settle open questions about vaccine efficacy and safety. Unfortunately, this opportunity was missed.

To show how seriously they took their task, and despite all that time they had to get it right, a corrected version was issued 24 hours later after many people pointed out errors (more of that below; in fact, they only corrected some errors on month labels).

Inevitably, as in the previous report, the 'headline' figures are that the all-cause mortality rate – measured here by the age-standardised mortality rate (ASMR) – has been consistently lower among the vaccinated than the unvaccinated (although the difference is narrowing). If the data were accurate and reliable then, as we have always argued, the all-cause mortality rate is, indeed, the most objective measure of vaccine safety and efficacy. But, as in the previous version, it is easily shown that there are systemic flaws and biases in this latest version which make the stated ASMR figures meaningless.

Of course, this did not stop inevitable mainstream media publishing predictable pre-prepared stories ridiculing 'anti-vaxx myths'[10] claiming the data proved that death rates were lower among the vaccinated. An example of this, of the kind most readers will be used to seeing, can be found in the Mail Online headline, in the Appendix, on page 358.

A very quick look through the data revealed some obvious concerning changes from the previous version, namely:

- Data for those under 18 were removed.
- Data for January to March 2021; the later publication relied on census data from April 2021. Rather than extrapolate to include an estimate for January to March 2021 they removed that period altogether from the report
- There are many changes to the raw data for April 2021 to May 2022 between latest version and previous versions.

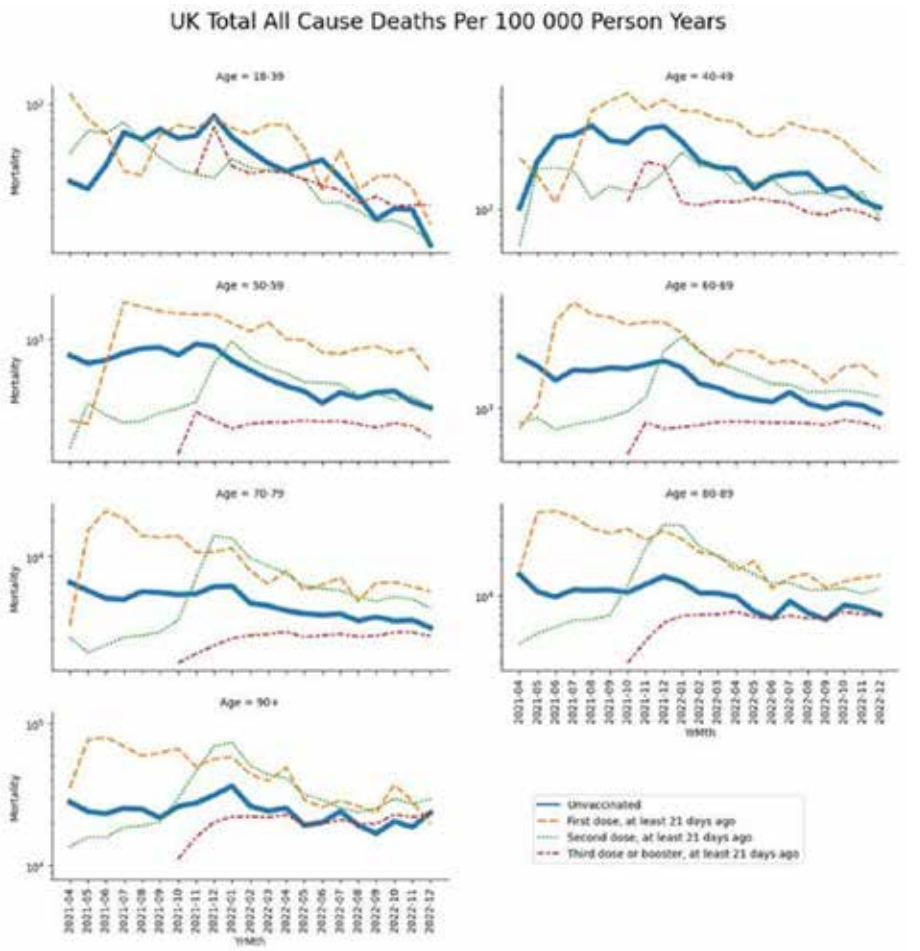
Before summarising some of the main complaints about the new data, it is important to note that the age-standardised mortality rate (ASMR) is a terrible metric for assessing vaccination safety (also it cannot be reproduced by the data provided in[1]). While it accounts for age-confounding, it obscures the information needed to determine risk-benefit for different specific age groups.

By looking at raw mortality rates within each age category there is no need for the complex, obfuscated ASMR. The ONS do provide age categorised breakdown:

18-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90+

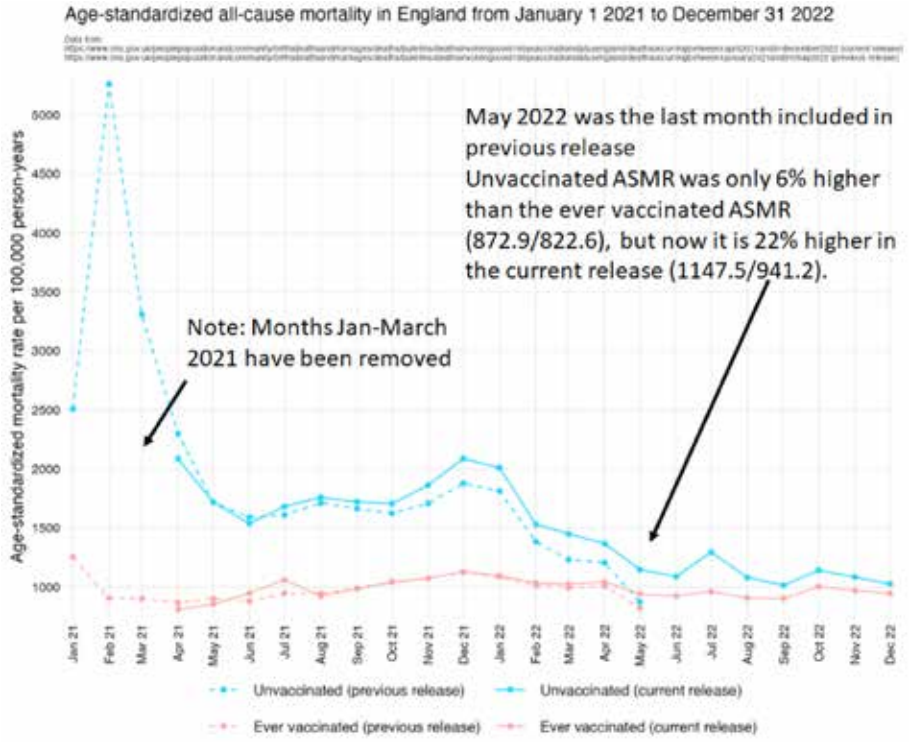
(The 18-39 category is rather coarse and, unlike the case with previous versions, those aged under 18 are no longer included so we have less information than before).

10 See the appendix.



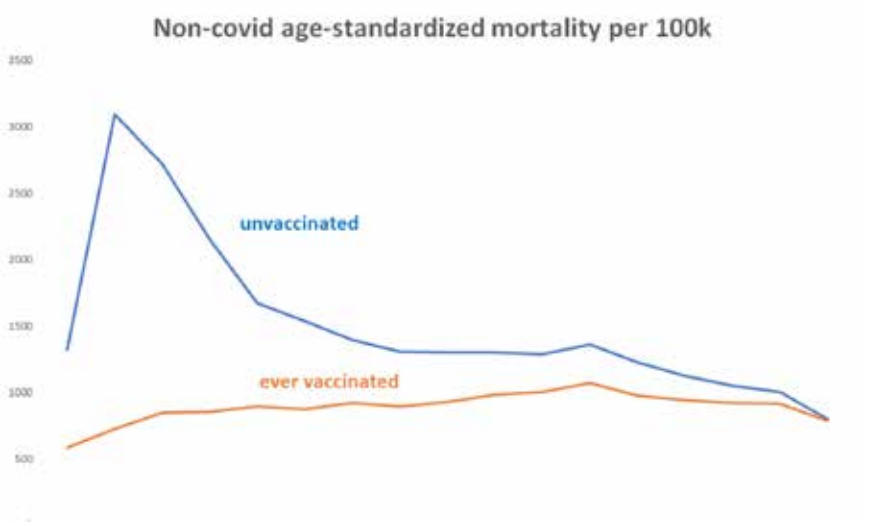
Tore Aarhus Gulbrandsen has produced the relevant all-cause mortality graphs for each of the age groups[11] (note the ONS uses person years rather than number of people). Note that, as in previous ONS releases, there are wild fluctuations in mortality rates for the different categories of vaccinated. But in no age group is there any strong evidence of reduced all-cause mortality for the vaccinated. The following chart summarises these (and the changes from the previous version):

11 https://twitter.com/saunasauen/status/1628138191642365958



Why would the ASMRs change so dramatically for the unvaccinated between releases? The ONS summary data was trumpeted by the mainstream media and those continuing to push the 'safe and effective' vaccine narrative, since it shows the ASMR for the unvaccinated higher than that of the ever vaccinated. But a deeper look into the data reveals the key problems with this.

Note that the January to March 2021 data have been removed (the ONS says this is because they are using the new 2021 census which only includes people alive after March 2021), so it is important to remind people of the following key graph of non-COVID mortality from the previous report's data:



Since this is non-COVID mortality the plots for unvaccinated and vaccinated should be similar. The sharp peak in unvaccinated non-COVID mortality in January to March 2021 (which was when the vaccine was rolled out) must have been the result of misclassifying those dying shortly after vaccination as unvaccinated. But the fact that there was a continued (albeit decreasing) difference proves there was systemic confounding of the data through one or more of:

- misclassification of vaccinated deaths as unvaccinated
- underestimating the population proportion of unvaccinated
- the 'healthy vaccinee effect'

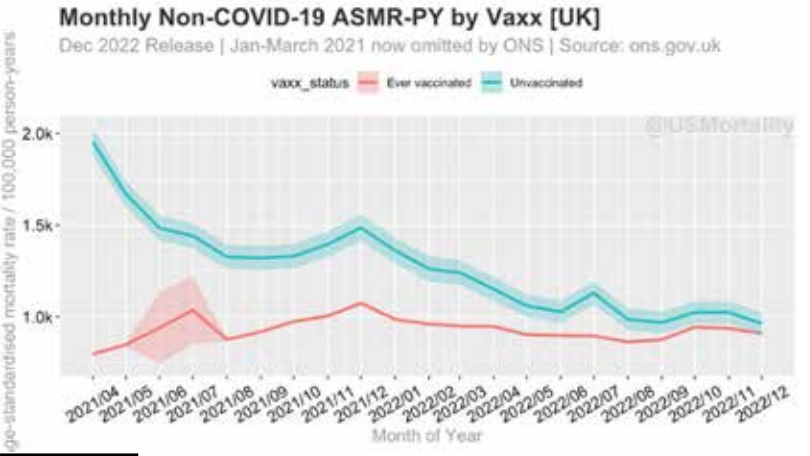
This bias influenced all of the mortality rates, but the ONS did not adjust for it at the time. They were however keen to assume a healthy vaccinee bias but presented no evidence to support this lazy assumption.

Similarly, in our latest report we pointed out that the ASMRs reported for February to May 2022 were significantly lower than historical rates from 2016, for younger age groups (59 and below), giving rise to what we dubbed the 'dead presumed missing' phenomenon. We suggested that this can be explained by deaths that are missing from their dataset. Comparing the ASMRs in the latest ONS release reveals this same problem, as shown in the table below. So, the mortality risk of people in the ONS dataset remains substantially different from that of the general population and we can see there are huge changes in the reported mortality rates between this ONS report and the last one, with percentage changes in mortality ranging from -31% to +38%. Why these dramatic changes?

Table 9a Feb-May 2022 Age-standardized Mortality Rate compared with approximate Historical Mortality Rate (deaths per 100k person years) with the addition of % Difference in reported Mortality

Age Category	Mortality rate	% Difference in reported Mortality	Historical Mortality rate in 2016 (approximate)
18-39			
Unvaccinated	21	38%	50
Ever vaccinated	25	0%	
40-49			
Unvaccinated	93	23%	180
Ever vaccinated	102	-18%	
50-59			
Unvaccinated	388	-8%	400
Ever vaccinated	291	-23%	
60-69			
Unvaccinated	1,061	-15%	1,000
Ever vaccinated	784	-27%	
70-79			
Unvaccinated	2,996	-19%	3,000
Ever vaccinated	2,237	-30%	
80-89			
Unvaccinated	9,019	-29%	8,500
Ever vaccinated	7,299	-31%	
90+			
Unvaccinated	20,748	-24%	21,000
Ever vaccinated	21,561	-65%	

How did mortality change in the latest release? USMortality provides the updated plot,[12] below. Clearly the systemic problems have not been resolved in the latest version. Comparing the latter months of the earlier report shows they have in fact become worse.



12 https://usmortality.substack.com/p/englands-all-cause-mortality-data

What about the critical problem with underestimation of the proportion of unvaccinated? Unfortunately, again, this problem has not been resolved even with the new census data. Clare Craig and Igor Chudov[13] have both analysed this. Here is the table provided by Clare Craig with the ONS estimates of proportions of unvaccinated in each group:

Unvaccinated proportion of population	18-39	40-49	50-59	60-69	70-79	80-89	90+	TOTAL
Apr-21	75.26	49.70	9.65	5.49	3.06	2.93	3.67	36.60
May-21	68.45	22.82	8.45	5.02	2.88	2.75	3.41	29.59
Jun-21	45.49	14.52	7.64	4.68	2.75	2.63	3.26	20.25
Jul-21	28.03	12.83	7.15	4.48	2.67	2.55	3.15	13.93
Aug-21	24.26	12.08	6.87	4.36	2.61	2.50	3.08	12.45
Sep-21	22.56	11.64	6.70	4.29	2.58	2.46	3.03	11.76
Oct-21	21.51	11.33	6.58	4.24	2.56	2.42	2.97	11.32
Nov-21	20.71	11.09	6.48	4.19	2.54	2.38	2.90	10.97
Dec-21	19.82	10.82	6.37	4.14	2.51	2.34	2.84	10.59
Jan-22	18.86	10.55	6.25	4.09	2.48	2.30	2.76	10.19
Feb-22	18.32	10.41	6.19	4.07	2.47	2.28	2.72	9.96
Mar-22	18.13	10.40	6.19	4.07	2.47	2.27	2.70	9.89
Apr-22	18.01	10.41	6.20	4.07	2.47	2.25	2.67	9.85
May-22	17.94	10.43	6.21	4.08	2.47	2.24	2.64	9.82
Jun-22	17.90	10.46	6.22	4.09	2.48	2.23	2.61	9.81
Jul-22	17.89	10.50	6.23	4.10	2.48	2.22	2.59	9.82
Aug-22	17.90	10.53	6.25	4.12	2.49	2.22	2.57	9.82
Sep-22	17.92	10.57	6.27	4.13	2.49	2.21	2.55	9.83
Oct-22	17.95	10.61	6.29	4.14	2.50	2.21	2.55	9.85
Nov-22	17.98	10.65	6.31	4.15	2.50	2.20	2.53	9.87
Dec-22	18.01	10.69	6.33	4.17	2.51	2.20	2.51	9.89

As Igor Chodov pointed out as an example, the March 2022 ONS estimate for the 50-59 age group is that there were just 6.19% in this age group unvaccinated, but according to the UKHSA Week 13 Vaccine Surveillance Report, (Page 17) 87% of the 50-59 age group were vaccinated in March 2022. So UKHSA say 13% were unvaccinated (a figure we know to be much more accurate). The ONS claim this is because their report is only from a subset of the population but it is clearly not a representative subset with this large discrepancy.

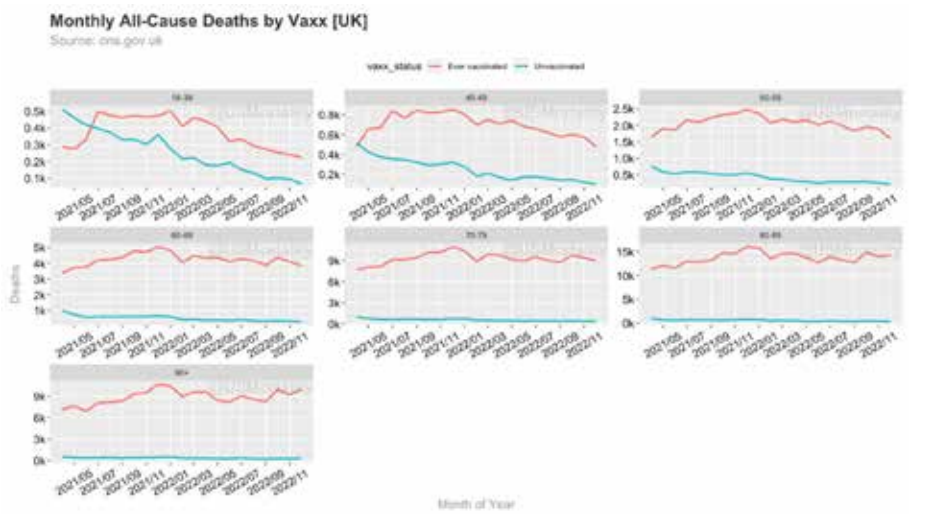
We also know that miscategorisation is still happening. Indeed, Note 17 of the ONS spreadsheet asserts:

> There were some people who were vaccinated but not included in the NIMS data as they died soon after vaccination. Of these, 1,029 linked to our 2021 Census linked dataset. We included the latest vaccination

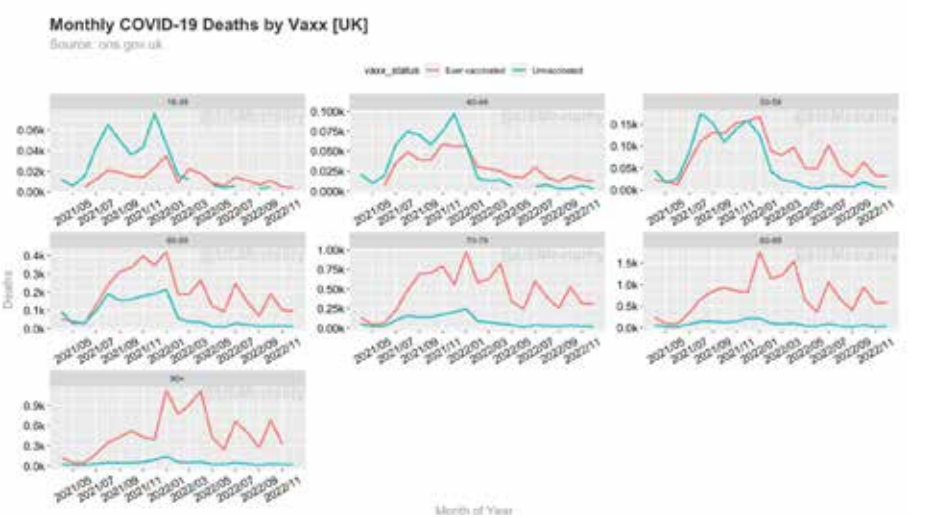
13 https://www.igor-chudov.com/p/ons-data-25-excess-mortality-among

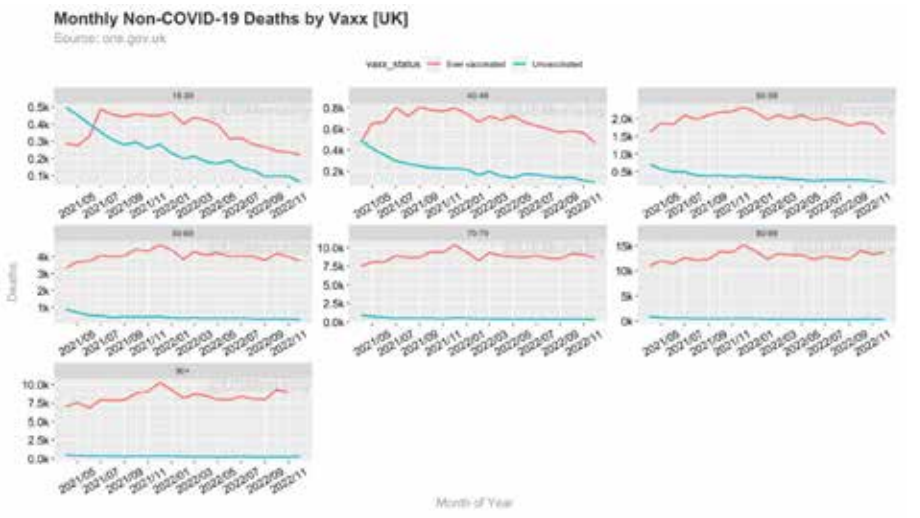
records for these people in our dataset. This data is provisional and extends up to the 1 November 2022. This will be updated in future releases.

USMortality also raised the concerns expressed in Screenshot 7, pointing out a series of important errors and omissions. Also produced were the following useful charts of absolute death counts in each age group:

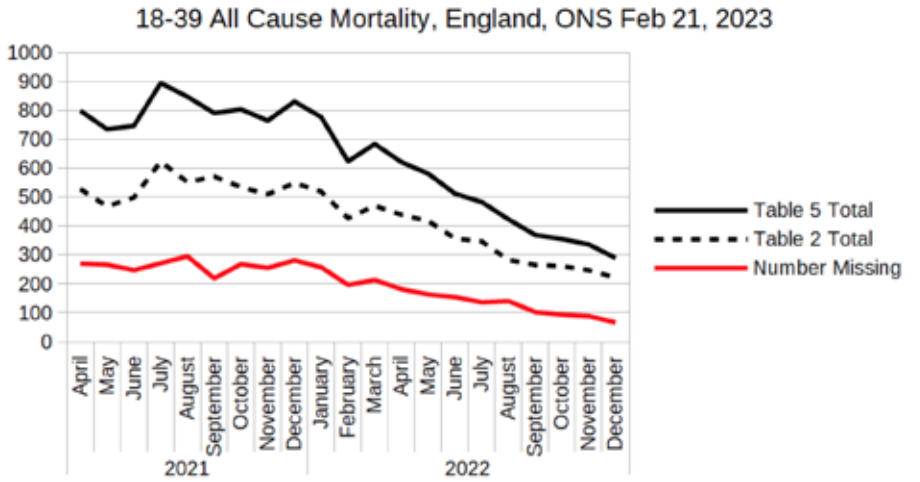


While obviously most people in the older age groups are vaccinated, the following plots do not exactly support the much-repeated mantra that the vaccinations 'stop people dying from COVID'.





A cursory analysis of the death counts in the ONS dataset shows that the death counts from Table 5 and Table 2 differ. @ExcessBurden has produced the following chart showing the dramatic differences in death counts reported in different tables of the same data release. The ONS said that table 5 contained all deaths regardless of a link to the census but any that could not be linked were removed for table 2.



Clare Craig asked the ONS about this discrepancy in death counts and explains how deaths can occur amongst the population 'ghosted' by the ONS (https://drclarecraig.substack.com/p/deaths-among-the-ghost-population). Others reached the same conclusion about the data and highlighted further concerns.

11. Postmodern science delivers immortality benefits

The ONS data show that the vaccines are delivering the prospect of immortality whether we take them or not. Consensus opinion across those who have looked in detail at the ONS deaths by vaccine status data[14] is that it is full of errors and biases and, as such, it is near useless for any inference we might wish to make about vaccine efficacy or safety.

In all of our deep-dive reports we have compared ONS data against historical actuarial mortality rates. We believe that only by comparing with expectations can we determine if there is a pandemic and whether the vaccines are putting a dent in it, or indeed adding to the mortality burden.

However, comparing mortality rates within the ONS data set does not clarify whether the data as a whole stand up to scrutiny. For that we need to test against historical data and previous reports. Let us turn again to this table from the previous section:

Table 9b Feb-May 2022 Age-standardized Mortality Rate compared with approximate Historical Mortality Rate (deaths per 100k person years) with the addition of % Difference in reported Mortality

Age Category	Mortality rate	% Difference in reported Mortality	Historical Mortality rate in 2016 (approximate)
18-39			
Unvaccinated	21	38%	50
Ever vaccinated	25	0%	
40-49			
Unvaccinated	93	23%	180
Ever vaccinated	102	-18%	
50-59			
Unvaccinated	388	-8%	400
Ever vaccinated	291	-23%	
60-69			
Unvaccinated	1,061	-15%	1,000
Ever vaccinated	784	-27%	
70-79			
Unvaccinated	2,996	-19%	3,000
Ever vaccinated	2,237	-30%	
80-89			
Unvaccinated	9,019	-29%	8,500
Ever vaccinated	7,299	-31%	
90+			
Unvaccinated	20,748	-24%	21,000
Ever vaccinated	21,561	-65%	

14 https://wherearethenumbers.substack.com/p/the-latest-ons-data-on-deaths-by

This table shows that between the old and new ONS reports the mortality rates changed substantially, with the mortality of unvaccinated and vaccinated older groups now exhibiting lower mortality figures, dropping by between -6% to -31%. How can this be? In contrast, for the unvaccinated younger age groups the mortality increased by between 23% and 38% between ONS reports. This is an extraordinary change that cannot be explained. It amounts to garbage.

So, comparing across ONS reports shows dramatic changes that cannot be accounted for. But much more important than this is the fact that the mortality rates are crazily different from those in 2016. How crazy? One would think in this age of data availability we would have the 2016 mortality rates at our fingertips. All we could find was this grainy image on an ONS web site:

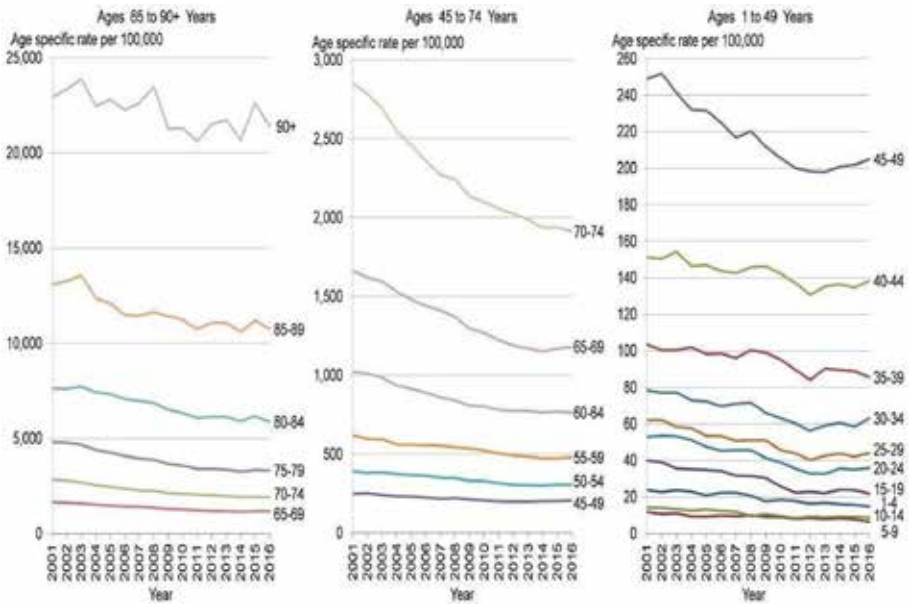
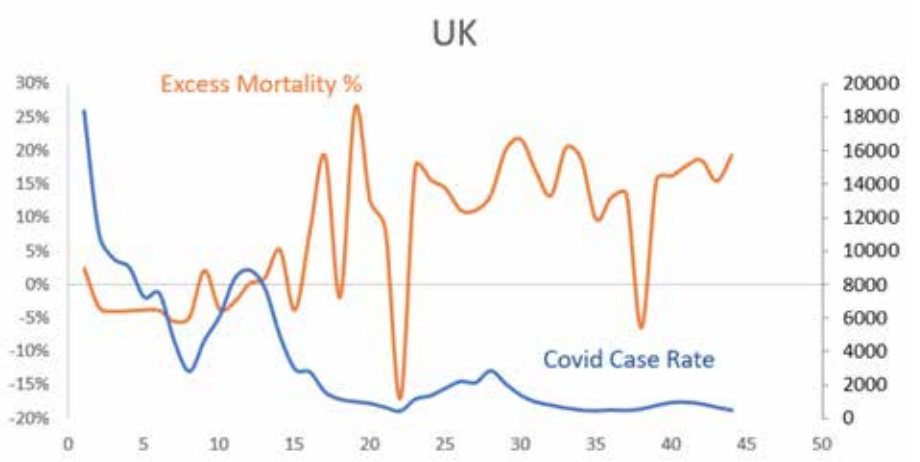


Figure 4a Historical mortality rates for England by age group

From this we can produce rough estimates of the mortality burden by age-group and compare them against the latest ONS mortality figures. The green line is the all-cause mortality rate per 100K people for that age group from 2016 and the red and blue lines are the all-cause mortality rates for the ever vaccinated and unvaccinated from the latest ONS report.

Plainly something is very wrong with these data. The most obvious thing is that, across all age groups, the all-cause mortality rate is significantly less from February 2022 than one would expect, compared to 2016, for both the vaccinated and unvaccinated. And this occurs at a time when excess deaths in the UK are starting to increase and the COVID case rate has plummeted, as can be seen from week eight in the chart below (the COVID case scale on the right-hand side is cases per 100,000 people):



So, more people are dying but in the ONS data set people are living longer. There are a few things we can conclude from this. Either deaths are not being recorded in the ONS dataset, and they do not bother to check (perhaps they are with the coroners' courts or in the post), or, if the data are correct then the vaccines are so good that they are improving mortality for everyone, whether we take them or not and the extra real-world total deaths came from elsewhere. Perhaps all of that vaccine shedding is a good thing after all, and with more of the vaccines we will achieve immortality.

It seems that detailed blow-by-blow takedowns of ONS are laboured, and this is the simplest and most obvious way of showing how useless the ONS data is. Nothing more than this is necessary to win the argument. These data are not representative of anything.

12. Final words

To date we have produced three exhaustive analyses of the ONS data, each of which has consumed very considerable time and effort. Recall that these data were said to be the gold standard produced by the best, most reliable official statistics department in the world.

Each time we looked at their data we, and many others, have discovered a litany of errors, oddities, missing data, inconsistencies, contradictions and under- or over-estimates. The ONS have either ignored our analyses or made lazy offhand assumptions that they believe explain these issues. None of the issues we have identified have been addressed and none of their assumptions have been justified.

We had, perhaps naïvely, hoped that the ONS would have responded to the criticism from the UK statistics regulator and improved their game, but it seems they have treated us, and the regulator, with contempt. Far from resolving all of the issues this report was replete with the same errors, was obviously hastily put together and even had to be amended and updated within hours of release. More importantly all of the original issues and biases remain unaddressed. These events raise many legitimate questions:

- If the regulator does not require the ONS to produce accurate or useful information about vaccine safety and efficacy, what is the ONS for? What are we paying our taxes for?
- If the regulator can be ignored, where the official statistics produced by the system are as bent before and after regulatory intervention, why do we need a regulator at all? Why are we paying for this?
- Why should we accept anything the UK government has historically claimed about the COVID vaccines based on these data? Why should we accept any of their public health claims in the future?

Acknowledgements

Thanks to Charlotte Bermingham of the ONS for clarifying some points about the ONS dataset.

13 References

[1] Office for National Statistics. Deaths by vaccination status, England - Office for National Statistics [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsbyvaccinationstatusengland

[2] Neil M, Fenton N, Smalley J, Craig C, Guetzkow J, McLachlan S, et al. Official mortality data for England suggest systematic miscategorisation of vaccine status and uncertain effectiveness of COVID-19 vaccination [Internet]. 2022. Available from: https://doi.org/http://dx.doi.org/10.13140/RG.2.2.12472.42248

[3] Craig C, Neil M, Fenton NE, McLachlan S, Smalley J, Guetzkow J, et al. Official mortality data for England reveal systematic undercounting of deaths occurring within first two weeks of COVID-19 vaccination [Internet]. 2022. Available from: http://dx.doi.org/10.13140/RG.2.2.12472.42248

[4] BBC Media Centre. BBC announces new documentary, Unvaccinated, with Professor Hannah Fry - Media Centre [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://www.bbc.co.uk/mediacentre/2022/unvaccinated-professor-hannah-fry

[5] UK Health Security Agency. Weekly national Influenza and COVID-19 surveillance report [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1088929/Weekly_Flu_and_COVID-19_report_w27.pdf

[6] ICM. Exploring attitudes towards COVID-19 vaccinations (for STV) - icmunlimited [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://www.icmunlimited.com/our-work/exploring-attitudes-towards-covid-19-vaccinations-for-stv/

[7] NHS England. COVID-19 vaccinations [Internet]. 2022 [cited 2022 Oct 27]. Available from: https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-vaccinations/

[8] Fenton NE. BBC wants to understand why 8% of the population remains unvaccinated against COVID [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://www.normanfenton.com/post/bbc-wants-to-understand-why-8-of-the-population-remains-unvaccinated-against-covid

[9] Office for National Statistics. Unvaccinated population of England and the UK - Office for National Statistics [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://www.ons.gov.uk/aboutus/transparencyandgovernance/freedomofinformationfoi/unvaccinatedpopulationofenglandandtheuk

[10] Smalley J. Evidence of Incorrect Vaccination Records [Internet]. 2022 [cited 2022 Oct 9]. Available from: https://metatron.substack.com/p/evidence-of-incorrect-vaccination

[11] Office for National Statistics. Coronavirus (COVID-19) latest insights - Office for National Statistics [Internet]. 2022 [cited 2022 Oct 6]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19latestinsights/vaccines

[12] Cochrane Org. The standardised mortality ratio and how to calculate it - Students 4 Best Evidence [Internet]. 2020 [cited 2022 Oct 6]. Available from: https://s4be.cochrane.org/blog/2020/08/26/the-standardised-mortality-ratio-and-how-to-calculate-it/

[13] Office for National Statistics. Annual deaths and mortality rates, 1838 to 2020 (provisional) - Office for National Statistics [Internet]. 2021 [cited 2022 Oct 6]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/adhocs/12735annualdeathsandmortalityrates1938to2020provisional

[14] Public Health England. Chapter 2: trends in mortality [Internet]. 2018. Available from: https://www.gov.uk/government/publications/health-profile-for-england-2018/c%0Ahapter-2-trends-in-mortality%0A

[15] Malhotra A. Journal of insulin resistance. [Internet]. Vol. 5, Journal of Insulin Resistance. AOSOS; 2016 [cited 2022 Oct 6]. 10 p. Available from: https://insulinresistance.org/index.php/jir/article/view/72/228

[16] Norman E Fenton. Can our detractors decide if vaccinees are especially healthy or especially unhealthy? [Internet]. 2022. Available from: https://www.normanfenton.com/post/can-our-detractors-decide-if-vaccinees-are-especially-healthy-or-especially-unhealthy

[17] Office for National Statistics. Deaths involving COVID-19 by vaccination status, England: deaths occurring between 1 January and 31 October 2021 [Internet]. 2021 [cited 2022 Oct 27]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingcovid19byvaccinationstatusengland/deathsoccurringbetween1januaryand31october2021

[18] JCVI. Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination [Internet]. 2020 [cited 2022 Oct 27]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/948353/Priority_groups_for_coronavirus__COVID-19__vaccination_-_advice_from_the_JCVI__2_December_2020.pdf

[19] Impact of registration delays on mortality statistics in England and Wales: 2020. [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths /articles/impactofregistrationdelaysonmortalitystatisticsinenglandandwales/2020

[20] Deaths involving COVID-19 by vaccination status, England: deaths occurring between 1 January 2021 and 31 May. [Online]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths /bulletins/deathsinvolvingcovid19byvaccinationstatusengland/latest Data: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths /datasets/deathsbyvaccinationstatusengland

14. Appendix


Mail Online

Home | News | U.S. | Sport | TV&Showbiz | Australia | Femail | Health | Science | Money

Strep A | Covid-19 | Cancer | NHS | Cold | Flu | Dementia | Fertility | UTI | Diabetes | Weight Loss | Diet

Death rates are NOT higher among Covid-vaccinated Brits, according to official stats debunking major anti-vaxx myth

- **The ONS analysed deaths recorded between April 2021 and December 2022**
- **Risk of dying was consistently lower for people who had ever been vaccinated**
- **Read more: Just a third of people in some parts of England had first Covid jab**

By EMILY STEARN, HEALTH REPORTER FOR MAILONLINE
UPDATED: 18:24, 21 February 2023

Norman Fenton is Professor Emeritus of Risk at Queen Mary University of London (retired as Full Professor Dec 2022) and a Director of Agena, a company that specialises in artificial intelligence and Bayesian probabilistic reasoning. He is a mathematician by training, with current focus on quantifying risk and uncertainty using causal, probabilistic models that combine data and knowledge (Bayesian networks). He has published seven books and over 350 peer-reviewed articles. His work covers multiple application domains including especially health, law and forensics (he has been an expert witness in major criminal and civil cases). Since 2020 he has been active in analysing data related to COVID risk.

A report on the US Vaccine* Adverse Events Reporting System (VAERS) of the COVID-19 messenger ribonucleic acid (mRNA) biologicals

by Jessica Rose
PhD, MSc, BSc

Abstract

Following the global roll-out and administration of the Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273) COVID-19 vaccines[1] on December 17, 2020 in the United States, and of the Janssen COVID-19 Vaccine PF (produced by Johnson & Johnson) on April 1st, 2021, tens of thousands of people have reported adverse events (AEs) using the American Vaccine Adverse Events Reports System (VAERS). This work summarizes these data to date and serves as information for the public, and as a reminder of the relevance of any adverse events, including deaths, that occur as a direct result of biologicals as prophylactic treatments. This is especially relevant in the context of technologically novel treatments in the experimental phase of development. Analysis suggests that the vaccines are likely the cause of reported deaths, spontaneous abortions, anaphylactic reactions and cardiovascular, neurological and immunological AEs. The precautionary principle promotes transparency and the adoption

1 mRNA biologicals are not true vaccines. True vaccines are a preparation of a weakened or killedpathogen, such as a bacterium or virus, or of a portion of the pathogen's structure that, upon administration to a person, stimulates antibody production or cellular immunity against the pathogen but is incapable of causing severe infection. Vaccines undergo an extremely rigorous time-dependent testing protocol to ensure safety and efficacy, typically enduring between 10 and 15 years. The mRNA biologicals do not satisfy either of these requirements and are thus more akin to experimental treatments.

of preventative measures to address potential risks to the public in the arena of vaccination programs, and it is vital that people are informed of these potential risks before agreeing to participate in any medically involved treatment program. VAERS reporting and recording is essential to the proper functioning of this system. It cannot be over-emphasized that the public should know how to use this system such that they actually do use it, and that once reports are made, responsible authorities enter each report into the database accordingly.

1. Background

The Vaccine Adverse Event Reporting System (VAERS) was created and implemented in 1990 in the United States by the Food & Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) to receive reports about adverse events that may be associated with vaccines. Most vaccine adverse event reports concern relatively minor events, such as injection site pain. Other reports describe serious events, such as hospitalizations, life-threatening illnesses, or deaths.[1] The reports of serious events are of greatest concern and are meant to receive the most careful scrutiny by VAERS staff and healthcare professionals. The primary purpose of maintaining the database is to serve as an early warning or signalling system for adverse events not detected during pre-market testing. In addition, the National Childhood Vaccine Injury Act of 1986 (NCVIA) requires healthcare providers and vaccine manufacturers to report to the DHHS specific adverse events following the administration of those vaccines outlined in the Act.[1] It must be noted that the adverse events reported to VAERS represent a fraction of the actual number of incidents. Studies have shown that the percentage of incidents reported can be quite low (1-10%) but, for the purposes of this report, in order to do the necessary calculations, VAERS numbers were used and the results should be considered to reveal trends.[1,2]

An Adverse Event (AE) is defined as any untoward or unfavourable medical occurrence in a human study participant, including any abnormal physical examination or laboratory finding, symptom, or disease, temporally associated with the participants' involvement in the research, whether or not it is considered related to participation in the research. A Serious or Severe Adverse Event (SAE) is defined as any adverse event that results in death, is life threatening, or places the participant at immediate risk of death from the event as it occurred, requires or prolongs hospitalization, causes persistent or significant disability or incapacity, results in congenital anomalies or birth defects, or is another condition which investigators judge to represent significant

hazards.[2, 3] The VAERS handbook states that approximately 15% of reported AEs are classified as severe.[1]

Ongoing collection of data in systems such as VAERS in the United States, the Coronavirus Yellow Card reporting site for the United Kingdom, as well as independent reports of AEs, merits further examination into both the safety and efficacy of the mRNA vaccines currently being rolled out globally in response to COVID-19, in particular those designed by Pfizer-BioNTech (BNT162b2, now known as the Pfizer-BioNTech COVID-19 Vaccine) and Moderna (mRNA-1273), which have been the most widely administered.[4] mRNA platforms are new in medical microbiology and have never before been implemented for use in human subjects on a global scale in the context of viruses. Safety is always a point of relevance with regard to new biological agents. As stated, the primary purpose for maintaining the VAERS database is to serve as an early warning system and one should be cautious in drawing conclusions regarding safety in its context. But since the number and range of side effects is vast and no long-term data of potential damaging effects such as autoimmune reactions exist, AE collection systems such as these are of utmost importance, not only to flag potential severe AEs not detected during premarket testing but also for weighing in on the potential safety of the biologicals themselves. The efficacy of a conventional vaccine is measured via explicit demonstration of broad-spectrum potent immune responses in the forms of both cellular and humoral responses as well as the establishment of enduring immunity.[3,4,5,6,7]

Although there are some studies claiming efficacy for these mRNA biologicals in humans,[4,5] that efficacy is not based on immunological assessment but rather on clinical assessment based on primary and secondary endpoints including confirmed or severe COVID-19. In these same studies, safety is assessed based on a maximum observation period of six months. This is not adequate to assess long-term safety outcomes. In this context, it is worth noting that the Pfizer-BioNTech, Moderna, and Janssen COVID-19 vaccines have *not* been approved or licensed by the FDA, having been authorized instead for

2 National Institute on Aging, Adverse Event and Serious Adverse Event Guidelines. https://www.nia.nih.gov/sites/default/files/2018-09/nia-ae-and-sae-guidelines-2018.pdf[40]

3 FDA. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm7frexternal%20icon

4 Messenger ribonucleic acid, first discovered in 1961 at Caltech, has been called the 'software of life.' Conventional vaccine types primarily use live-attenuated whole viruses or killed viruses as a means to elicit potent immune responses in the forms of both cellular and humoral responses and life-long immunity. Periodically, boosts are required in order to maintain longevity of immune responses, especially in the form of neutralizing antibodies.[42] mRNA treatment types use specific mRNA that encodes a particular protein, which is meant to be mass-produced by host cells as a means to trigger an appropriate immune response, primarily in the form of neutralizing antibodies, in order to provide a degree of protection upon challenge with the wild-type coronavirus. Although studies show cellular and humoral responses upon injection, it is not known how long immunity might last, and thus it has been suggested that many boosts will be required. It has also been detailed that these particular vaccines do not prevent transmission, and thus the effectiveness of these vaccines is very questionable.[8,9,10] Perhaps even more important is that it is unknown what the effect of non-neutralizing antibodies will be in the long term.

emergency use by the FDA under an Emergency Use Authorization (EUA) to prevent Coronavirus Disease 2019 (COVID-19), for use in people 16 years of age and older.[8,9,10] Ultimately, the roll-out of COVID-19 vaccines is actively being monitored, but all of the risks are not yet known.[9,10] In spite of this, real-world trials and administration of these biologicals into pregnant women and children are being pursued in countries around the world, such as Israel.[11] The VAERS dataset is currently the best (if not the only, albeit imperfect) way the public can monitor and be informed of the risks associated with administration of the COVID-19 injectables.

It is vital for the public to be aware of this reporting system and the valuable information therein so that informed decisions can be made and a risk-benefit analysis done. One of the ways that risk is assessed using findings from this study is by comparing the death rate reported in VAERS with the Infection Fatality Rate (IFR), which is a measure of the chance of dying from

the SARS-CoV-2 pathogen. All infected people, both symptomatic and asymptomatic, are accounted for in the IFR calculation, and data therein are based on serology. It is important for anyone analysing or comparing death statistics to use the IFR and not the Case Fatality Rate (CFR) — the ratio between confirmed deaths and confirmed cases[12,13] — because the CFR is based on potentially unreliable death and confirmed case accounts.[5] There is also a lag in time between when people are infected and when they die, and, most importantly, it does not capture the population with innate immunity. The major difference in the numbers, 1.8% (CFR) *versus* 0.15% (IFR), is due to a significantly larger denominator whereby infected persons with an effective innate immune response represent asymptomatic cases. The latter metric highlights the true risk of succumbing to the virus in the general population. It is more compelling to use the IFR as a metric for comparison for this and future studies.[12]

2. Methods

1. General methodology and descriptive statistics

To analyse the VAERS data set, R was used (a language and environment for statistical computing). The VAERS data set is available for download (https://vaers.hhs.gov/data/datasets) in three separate comma-separated values (csv) files representing i) general data for each report; ii) the reported AEs or 'symptoms'; and iii) vaccine data including vaccine manufacturer and lot number, as per report. The VAERS dataset is updated approximately once a week and the uploaded set is approximately one week behind the

5 The CFR is the fraction of reported deaths from SARS-CoV-2 to the reported confirmed cases of SARS-CoV-2. This gives an unreliable metric in that both the numerator and denominator may not be accurate (and have been reported not to be).[12,13]

reports. Upon individual reporting of vaccine side effects or adverse events, a VAERS ID number is provided to the person to preserve confidentiality, and a detailed description of the side effects is transcribed along with the person's age, residence by state, past medical history, allergies and gender and many other details. In addition, the vaccine lot number, place of vaccination and manufacturer details are included in the report. In order to maximize the input variables for my analysis, the three files were merged by VAERS ID that is included as a linking variable in all three files. The merged data set comprises data collected pertaining to all reported AEs associated with the Pfizer-BioNtech and the Moderna COVID-19 products. Data were sorted according to vaccine type (data reported for COVID-19) and relevant variables were sorted including VAERS ID, AEs, age, gender, state, vaccination date, date of death, incident of death, dose series, treatment lot number, treatment manufacturer, hospitalizations, emergency department visits and onset date of AEs. To determine the total number of AEs, multiple individually-reported AEs were aggregated into a single column vector. An additional column vector called AGE GROUPS was created to group the people who made reports according to age by decade. The grouped AE categories were created by selecting 'Y' in the case of the death, hospitalizations and emergency doctor visits while the cardiovascular, neurological and immunological groups were created by selecting key words indicative of an immunological medical issue such as 'lymphadenopathy', in the case of the immunological AE group, for example.

There are two primary vaccine manufacturers responsible for SARS-CoV-2 vaccines currently being administered, Pfizer-BioNTech and Moderna. Recently, a third, the Janssen COVID-19 Vaccine PF (produced by Johnson & Johnson), has begun to be administered. All three are included in this analysis, except where discrepancies were found by comparison between manufacturers.

Descriptive statistics on the incidence rates of relevant AEs were calculated as a percentage of the number of unique VAERS IDs and the fully vaccinated population in the United States.[6] Also calculated are the death rates by SARS- CoV-2 for each respective VAERS update date as reported by the Our World in Data collection.[14] It should be noted the death rate was reported from the SARS-CoV-2 virus report CFR, not IFR. Although a confirmed positive serological test should be conducted, according to the World Health Organization (WHO), the US Department of Health and Human Services, the CDC, the National Center for Health Statistics, and the National Vital Statistics System, it is acceptable to report COVID-19 on a death certificate without this confirmation.[7]

6 Our World in Data. https://ourworldindata.org/covid-vaccinations[14]

7 CDC. Guidance for Certifying Deaths Due to Coronavirus Disease 2019 (COVID–19). Vital Statistics Reporting Guidance, Report No. 3, April 2020. https://www.cdc.gov/nchs/data/nvss/vsrg/

2. Statistical testing and causation

Statistical analysis was done using the Student's t-Test to determine statistically significant differences between age groups in the context of grouped data, such as people who died *versus* people who did not die, for example. Causation implies that a change in one variable necessarily leads to a change in another variable. The three criteria for establishing causation are association, time ordering and non-spuriousness. Association is shown in the incidence-rate data and using heatmaps and is corroborated using Chi-Square Tests. Time ordering is presented in temporal relationship between vaccination date and the following onset of AE date or the date of death.

Non-spuriousness is more difficult to prove in real-world settings since it is not truly possible to rule out external influences as contributing factors for the associations. For example, it is possible that the people who died within 24 hours of being vaccinated did so not on account of the vaccine but because of underlying conditions such as heart defects. This challenge is met by looking at data available on potential third-variable causes such as medications taken at the time of vaccination, and existing medical conditions. Skewing in distribution of data is tested using Pearson's Skewness Index, I, which is defined as I = (mean-mode)/standard deviation. The data set is considered to be significantly skewed if III>1.

3 Results

1. General information

To date, approximately 15% of the total US population has been 'fully vaccinated' against COVID-19, with 183,467,709 million doses administered as of April 10, 2021; -0.5% of the total US population have been vaccinated against the flu, with 1,300,000 million doses administered as of March 26, 2021.[8] Based on the fact that the ratio of COVID-19 to flu vaccinations at the end of March was -100:1, then it is not surprising that 380 times more reports have been made in the context of the COVID-19 injections. 99% of all AEs reported in 2021 have been in the context of COVID-19 reports, while only 0.3% of all AEs reported to date have been in the context of the influenza vaccines. Of all vaccines administered in 2021, 0.7% have been influenza vaccines,[9] meaning that the higher percentage of reports made in the context of COVID-19 are due to more frequent reporting subsequent to more frequent administration of the COVID-19 products.

Figure 1.1 illustrates the total number of adverse events reported and uploaded

vsrg03-508.pdf

8 CDC. Seasonal Influenza Vaccine Supply & Distribution. https://www.cdc.gov/flu/prevent/vaccine-supplydistribution.htm

9 Ibid.

to the VAERS database per year. There is an increase in the number of reports being made each year over the past 30 years (possibly from increasing awareness and adoption of the reporting system). 20% of all reports were COVID-19 vaccinerelated in 2020 and this was due to only 14 days of the year since administration began on December 17th, 2020. Figure 1.2 shows reports for 2021 by week. The most recent updated data files have almost surpassed the sum total reports for the entire year in 2020 (and this includes reports for all vaccines, not just ones related to COVID-19). This is because reports relating to COVID-19 vaccines in 2021 to date are in the order of all vaccines in 2020.

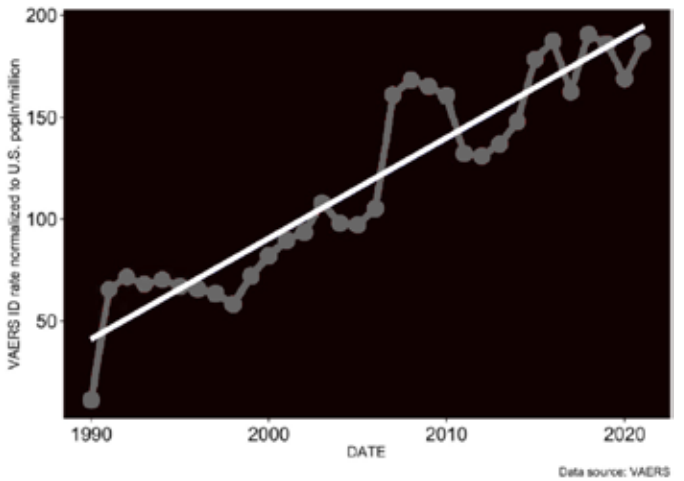


Figure 1.1 Time series plot – VAERS reporting rate normalized to US population by year

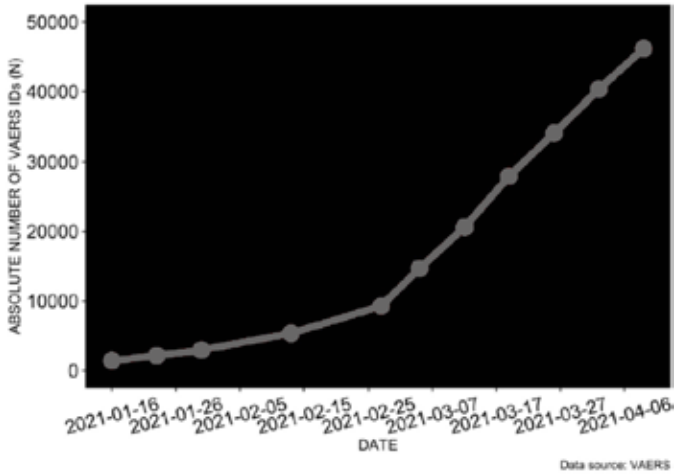


Figure 1.2 Time series plot – Absolute number of VAERS reports for the COVID-19 products for 2021

SAEs comprise 26% of all AEs, which is almost twice the estimate of SAEs documented in the VAERS handbook. Of all persons having received the first dose who reported an SAE, 74% did so after receiving the first dose. Similarly, of those who reported mild AEs, 81% did so after receiving the first dose. Of the total population of VAERS reports, 79% were made after receiving the first dose.

1.1 Incidence rates of AE groups by VAERS ID

As of mid-April 2021, a total of 4507 types of AEs have been reported and 46163 VAERS IDs have been assigned. Interestingly, of the reports, 74% came from females. This is likely due to a higher proportion of females reporting AEs but could stem from females succumbing to AEs more often than males. 5%, 12% and 16% of all AE reports involved death, hospitalization or an emergency doctor visit, respectively, as shown in Table 1. 18%, 12% and 35% of all AE reports involved cardiovascular, neurological or immunological events, respectively, also shown in Table 1.

Table 1. Summary table showing percentages of categories and COVID-19 cases by VAERS ID[10]

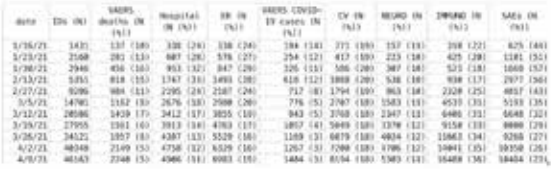
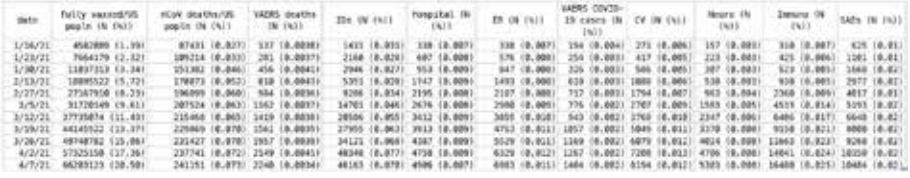


Table 2. Summary table showing percentages of categories and COVID-19 cases according to the fully vaccinated population in the US



1.2 Incidence rates of AE groups per fully vaccinated population

As shown in Table 2, presuming that the deaths are related to the injections, the incidence rate of VAERS-reported deaths with respect to the fully vaccinated population is quite low with 34 people dying per million. The fully-vaccinated population comprises 20.5% of people as reported by Our World in Data statistical group as of April 11, 2021.[11] This is comparable to the incidence rate

10 The SAEs total represents all emergency room visits, hospitalizations and deaths.

11 This is the death rate calculated by dividing the number of people who were reported to have died in the US

of SARS-CoV-2-reported deaths, which is 730 out of every million people as of April 11th, 2021. 74% of all who reported death using VAERS did so before receiving the second dose.

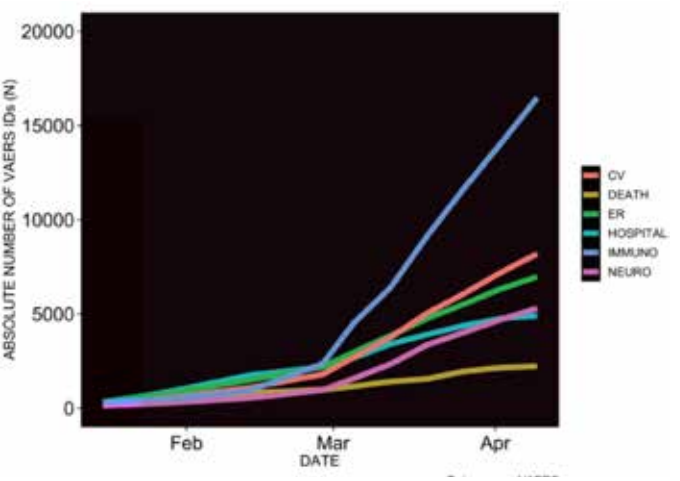


Figure 2.1 Time series plot — Increase in VAERS deaths, ER visits, hospitalizations, cardiovascular, neurological and immunological reports

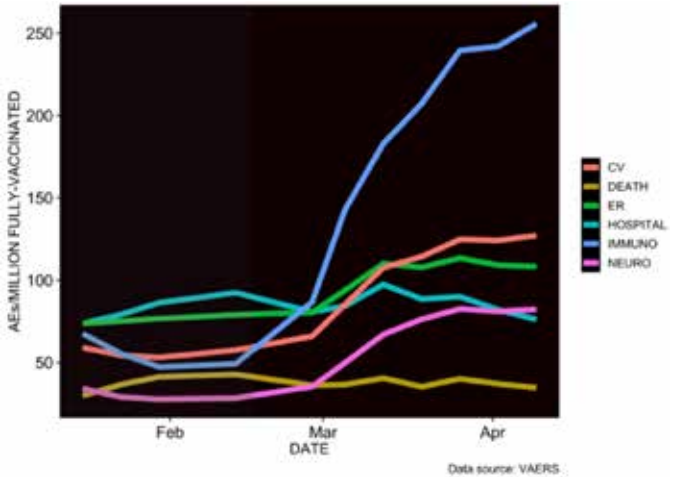


Figure 2.2 Time series plot — Relative change in deaths, ER visits, hospitalizations, cardiovascular, neurological and immunological reports with respect to the fully vaccinated population

In the context of the fully-vaccinated population, hospitalization and ER visit reports are at 70 and 110 per million, respectively, but as shown in Figures 2.1 and 2.2, the numbers of these reports are steadily increasing as the weeks pass. 68% of all people who reported being hospitalized and 77% of those who reported visiting an emergency room physician did so after the first dose.

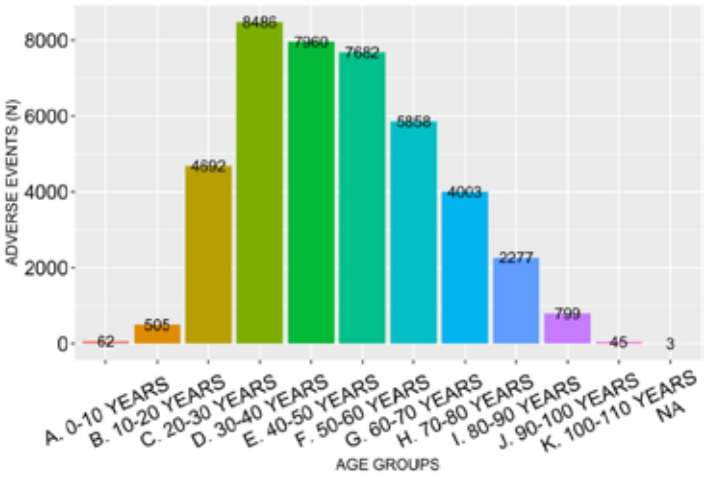


Figure 3. Distribution of age groups across all AEs

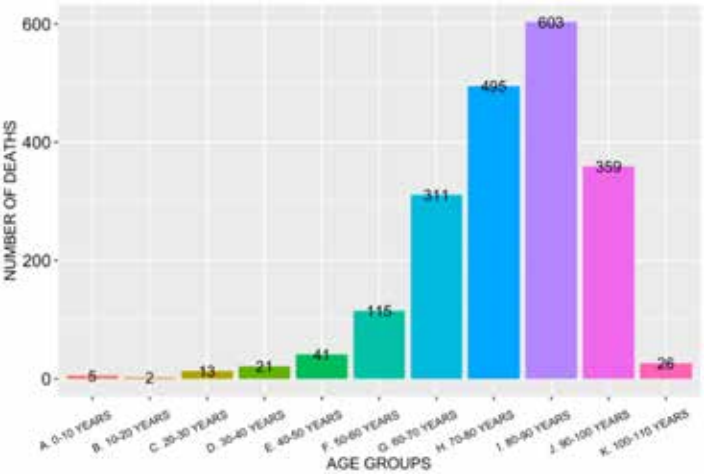


Figure 4.1 Distribution by VAERS ID according to age in individuals who died

With regard to AEs such as cardiovascular, neurological and immunological events, the number of reports when compared to the fully-vaccinated population are currently at 120, 80 and 250 people per million, respectively. It is important to remember that these reports likely under-estimate the true values by 10-100 times. Of those who reported cardiovascular AEs, 81% did so after the first dose. Similarly, 79% of those suffering neurological AEs did so after receiving the first dose, and 80% of the people who reported suffering an immunological AE did so after receiving the first dose as well.

Relative to the total number of reports, most of the trajectories of the AEs remain stable relative to the total number of IDs reported (Figure 2.2), with

the exception of the immunological AE trajectory, which continues to rise (relative to other AE categories). Interestingly, immunological AEs appear to dominate the AE cases, and this warrants investigation from the scientific community. Again, it is important to recall that we are very early on in the analysis: only four months' worth of data have been collected to date.

2. Distribution of data: age association with vaccine-associated AEs

The distribution of all VAERS reports according to age group is symmetric, unimodal and bell-shaped across all age groups with no significant skewing whereby 111=0.34. (Figure 3).

The highest absolute number of events reported are for people between 30 and 40 years of age (which account for 18% of all IDs), followed closely by people between the ages of 40 and 60 years of age (accounting for 17% in each age group, respectively). In general, the spread of data is normal and symmetric with low absolute numbers of persons between the ages of 0 and 10 and 100 and 110.

2.1 Deaths, hospitalizations and ER visits

Higher absolute numbers of VAERS deaths and hospitalization reports are associated with the elderly where the cut-off for the elderly is 65 years of age, and this is not surprising (Student's T-Test: $p<0.05$; $p<0.05$, respectively). However, emergency doctor visits are not associated with age (Student's T-Test: $p>0.05$).

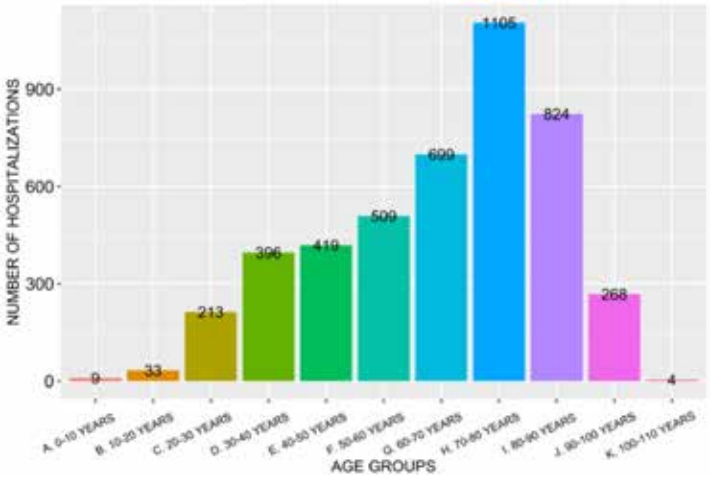


Figure 4.2 Distribution according to age in people who were hospitalized

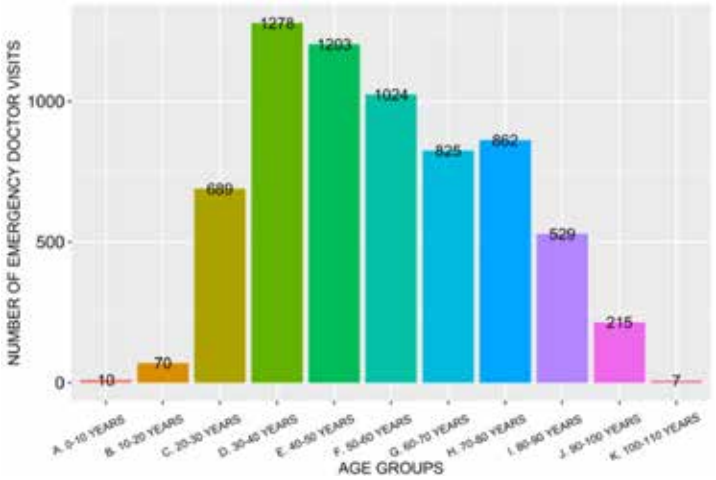


Figure 4.3 Distribution according to age in people who visited an emergency doctor

Absolute numbers of VAERS-reported deaths grouped according to age group reveal that 84% of those who were the subject of death reports were 70-90 years of age, as is shown in Figure 4.1. The death data are in fact left- skewed toward the elderly in a statistically significant way whereby the absolute value of I is 1.15 (abs(I)=1.15). The hospitalization spread is uniform over the age range, with 50% of reports made by people between the ages of 20 and 70. 43% of hospitalization reports were made by people between the ages of 70 and 90. Emergency doctor visit reports are even more uniform across middle-aged age groups, with more than half of the reports (61%) made by those aged 20 to 60 years. Neither are the distributions for the hospitalizations nor the ER visits skewed by age in a statistically significant way (abs(I)=0.59 and abs(I)=0.27, respectively).

2.2 Cardiovascular, neurological and immunological events

A substantial proportion of people reported having cardiovascular, neurological and or immunological events at 18%, 11% and 37%, respectively, of the total number of reports. In spite of the fact that people between the ages of 30 and 40 years comprise the largest subset of reports overall in the context of age grouping by decade, the highest frequency of cardiovascular reports were made by those between the ages of 20 and 30.

The highest frequencies of events occur in young and middle-aged people in all three categories, and this might be because they are the most vaccinated in absolute number. Neurological events were reported at the highest frequency in people between the ages of 40 and 50 years old. All histograms are unimodal and bell-shaped, with cardiovascular data appearing more uniform and neurological and immunological data being more symmetric. None of

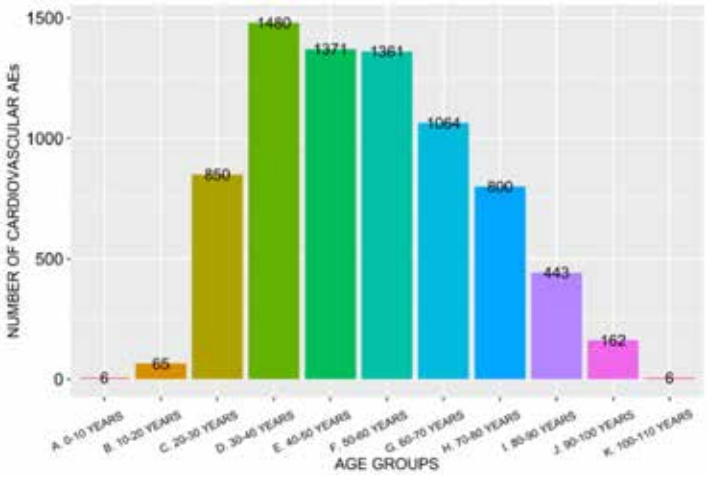


Figure 5.1 Distribution by VAERS ID according to age in people who reported cardiovascular adverse event

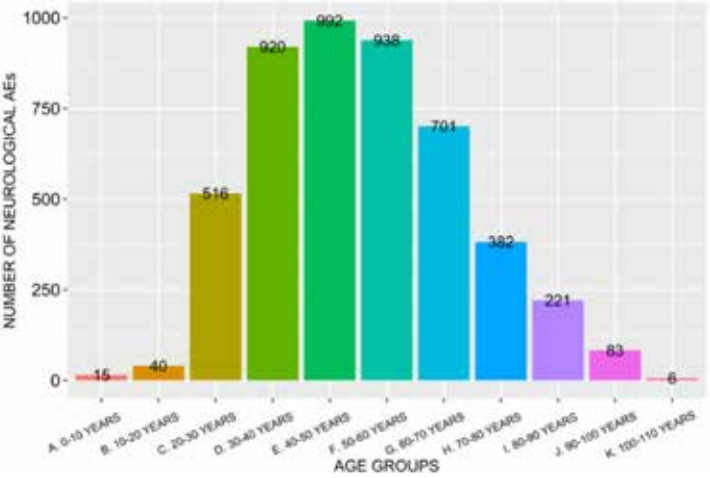


Figure 5.2 Distribution by VAERS ID according to age in people who reported neurological adverse events

the cardiovascular, neurological or immunological data are skewed toward a specific age group in a statistically significant way (abs(I)=0.34, abs(I)= 0.36, abs(I)=0.40, respectively).

2.3 Anaphylactic reactions

Anaphylactic reactions are reported in the VAERS database at a rate of 1%. Anaphylaxis was reported in people primarily between 30 and 60 years of age, yet distribution of the data is symmetric, unimodal and bell-shaped over the age

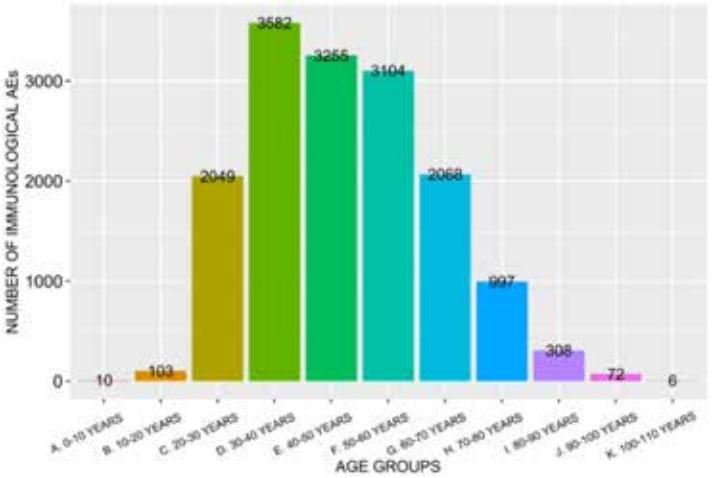


Figure 5.3 Distribution by VAERS ID according to age in people who reported immunological adverse events

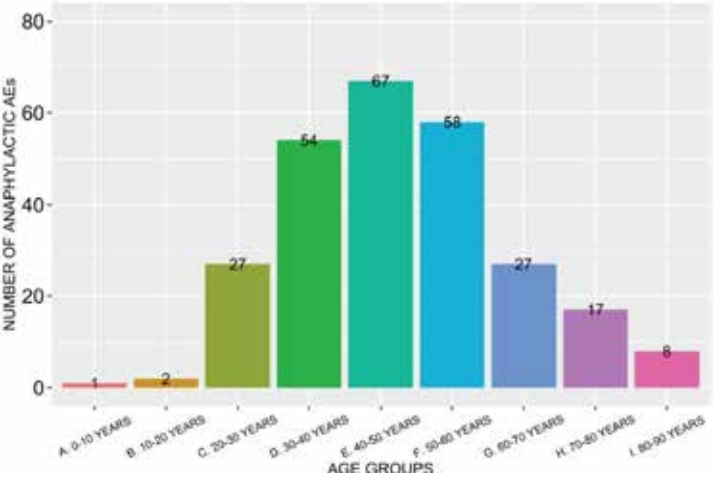


Figure 6. Distribution according to age in people who reported anaphylactic reactions

range, as shown in Figure 6. This particular AE is interesting to examine from a causation point of view since most reactions of this nature are known to be caused by specific triggers. It has been reported that one such trigger, poly-ethylene glycol (PEG), is an ingredient in the Moderna and Pfizer-BioNTech products. [15] It is also documented that polysorbate is an ingredient in the Janssen COVID-19 Vaccine PF product, and people are advised against using it if a known allergy exists for polysorbate. In many cases, they are unaware of the potential for an acute allergic response. It becomes clearer from time-series plots and heatmaps that causation is not only likely but probable.

Anaphylactic events are reported with highest frequency in people between the ages of 40 and 50. The distribution of data is not skewed toward a specific age group in a statistically significant way (abs(I)=0.29). Of those who reported an anaphylactic reaction, 76% did so after receiving the first dose.

2.4 Spontaneous abortions

Spontaneous abortions are not technically included as deaths as part of the VAERS data, but miscarriages involve foetal death. Since the number of these reports is increasing on average by six per week, it is included in this analysis as a stand-alone AE and classified as a severe adverse event. Spontaneous abortions were reported in females between the ages of 20 and 45 and were more frequent in women in their early 30s. This is likely due to more women in their early 30s being pregnant more frequently.

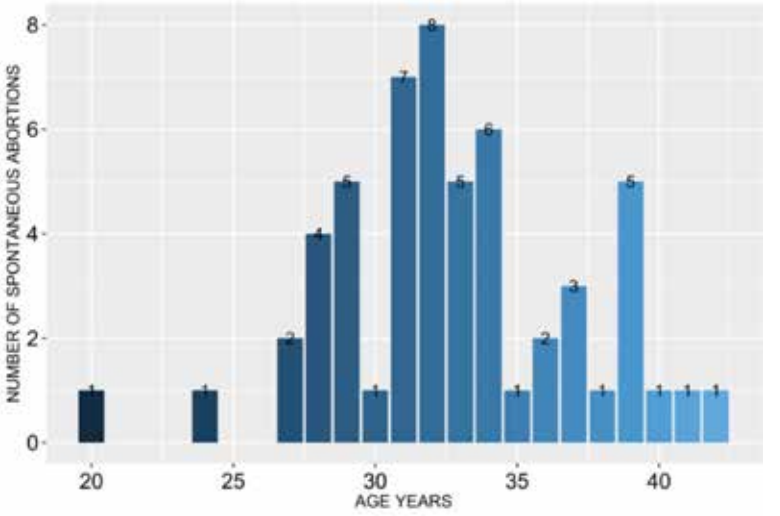


Figure 7. Distribution by age in individuals who reported spontaneous abortions

The distribution of data is not skewed toward a specific age in a statistically significant way (abs(I)=0.1). Of the women who reported having a spontaneous abortion, 65% did so after receiving the first dose. In the following section, the likelihood of causation is investigated since it is absolutely necessary to elucidate the conditions that induced miscarriage in these women, since plans for large-scale roll-out of these products into pregnant women are looming or currently active.

3. Evidence to support causation

A causal effect means that a change in one variable leads to change in another variable. In the context of all the AEs, 70% of all people had onset of symptoms

Table 3. Percentages of individuals reporting AEs following 24- and 48-hour periods

	AE within 24 hrs (% of cases)	AE within 48 hrs (% of cases)
Death	13	44
Hospital	15	47
ER	18	47

within 48 hours following first or second doses. Table 3 shows the percentages of those succumbing to particular AEs following a 24-hour or 48-hour period.

Figures 8.1-3 shows the number of days following injection as a percentage of the reported AEs with regard to deaths, hospitalizations and emergency doctor visits. The percentages of reported deaths, hospitalizations and emergency doctor visits are highest in the first two days post-injection.

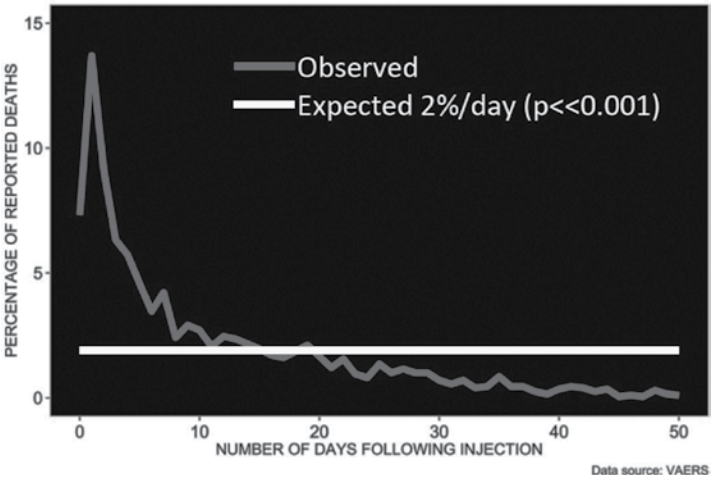


Figure 8.1 Time series plot — Percentage of reported deaths by time elapsed between the injection date and the reported adverse event

If deaths, for example, following COVID-19 injections are not causally linked, then the reported percentages of deaths should be equally distributed across days following injection: there should not be an excess of reports on days 0, 1 and 2, yet there are. Chi-square tests confirm association for each AE group with p-values less than 0.001 in each case. If risk is not accentuated by some immediate factor temporally, then that risk should necessarily plateau or diminish each day. This logic applies to each of the grouped AEs and each follows the same pattern: the percentages of Day 0 and 1 (time periods representing 0-24 hours and 24-48 hours) are much

higher than the percentages of other time periods post-injection.

This same reasoning applies to the grouped AEs representing cardiovascular,

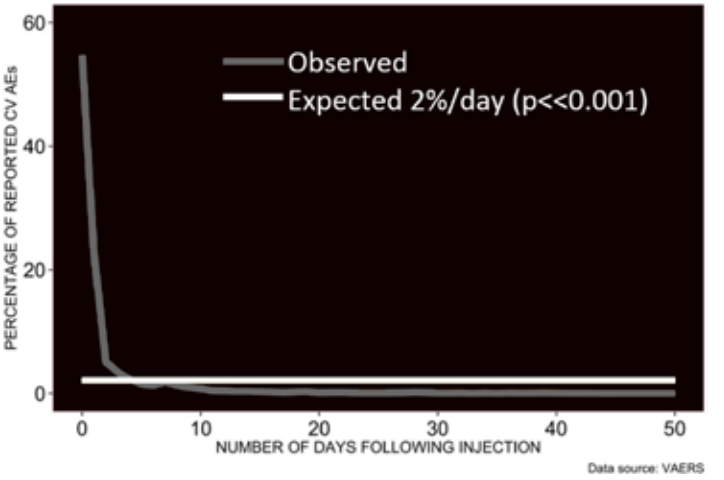


Figure 9.1 Time series plot — Percentage of reported cardiovascular AEs by time elapsed between injection date and adverse event

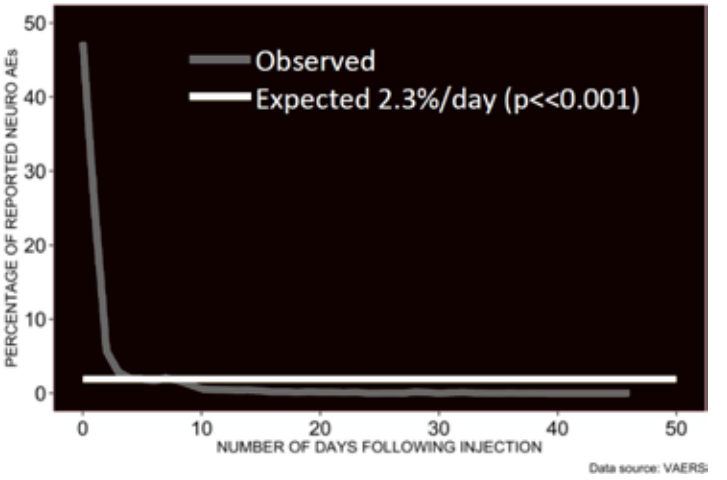


Figure 9.2 Time series plot — Percentage of reported neurological AEs by time elapsed between injection date and adverse event

neurological and immunological events as shown in Figures 9.1-3. The percentages of cardiovascular, neurological and immunological events are highest in the first two days post-injection. Again, if causation was absent, there should not be an excess of reports on days 0, 1 and 2. Chi-square tests confirm association for each AE group with p-values less than 0.001 in each case. Table 4 shows the percentages of people succumbing to particular AEs

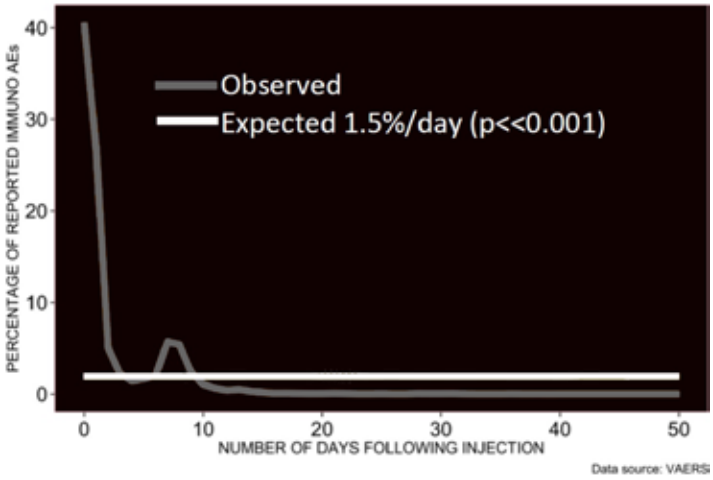


Figure 9.3 Time series plot — Percentage of reported immunological AEs by time elapsed between injection date and adverse event

following a 24-hour or 48-hour period.

There is a higher percentage (7%) of people who reported immunological events on the seventh day following injection, as shown in Figure 9.3. From an immunological point of view, this could be worth investigating in further studies.

Figures 10.1 and 10.2 show the same trend toward the highest percentages of anaphylactic reactions and spontaneous abortions occurring in the first two days post-injection. A staggering 87% of all anaphylactic reactions were reported within 48 hours and 76% were reported within 24 hours. This is not

Table 4. Percentages of individuals experiencing AEs following 24- and 48-hour periods

	AE within 24 hrs (% of cases)	AE within 48 hrs (% of cases)
Cardiovascular	13	44
Neurological	15	47
Immunological	18	47

surprising, considering the nature of this stand-alone AE. One would expect an anaphylactic reaction to occur quite immediately. More than half (61%) of all spontaneous abortions were reported within 48 hours of injection, and 42% within 24 hours.

These descriptive statistics give merit to association and time ordering post-injection in the contexts of these categorized AEs. In order to rule out spuriousness, there was examination of the potential contribution of additional variables, including pre-existing conditions and medications, that could have

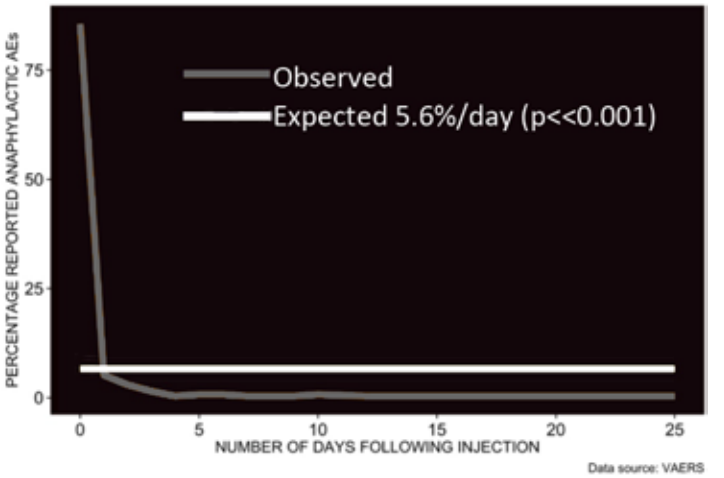


Figure 10.1 Time series plot — Percentage of reported anaphylaxis with respect to time elapsed between date of injection and AE

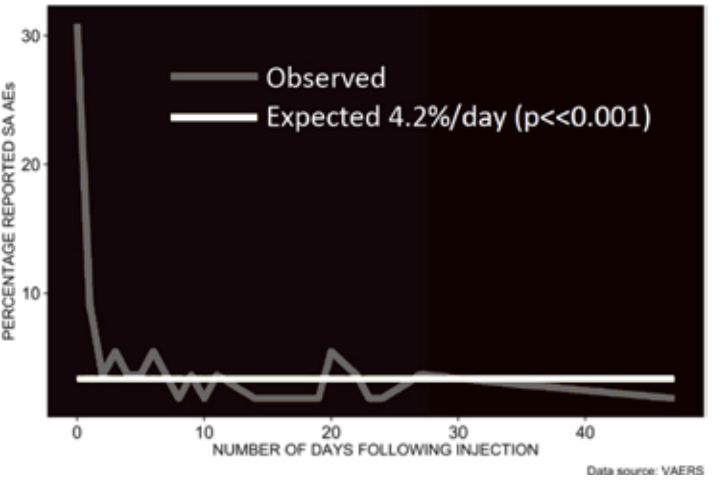


Figure 10.2 Time series plot — Percentage of reported spontaneous abortions by time elapsed between date of injection and AE

contributed to death. Of the medications, the most frequently reported occurred in ~6% of those people , and on the facet of prior conditions which may have led to death, only 8.5% of them had some heart-related incident reported in their prior history. This was the highest percentage of conditions reported in the

medical histories. It should be acknowledged that the VAERS-reported medical history is bound to be incomplete, and therefore it is possible that the AEs in question could be due to conditions not reported in VAERS data. Based on the data available, the three conditions of causation are satisfied, in general, but I leave it up to the reader to extrapolate beyond the data.

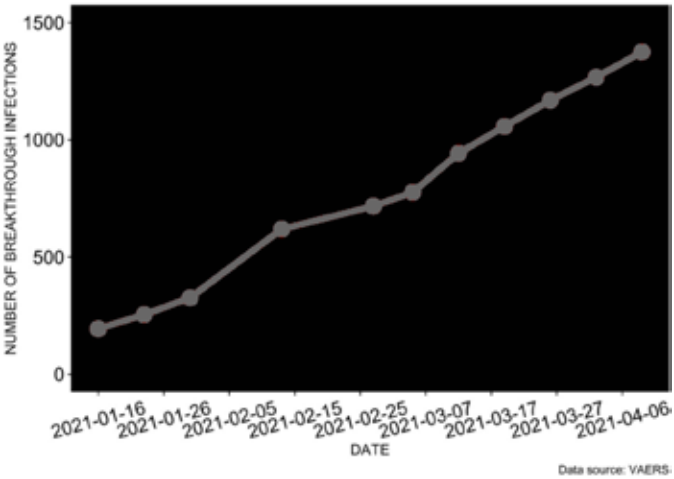


Figure 11. Time series plot — Increase in absolute number of COVID-19 confirmed cases from VAERS data

4. Confirmed COVID-19 cases post-vaccination

A total of 1267 COVID-19 cases have been reported to date with the Pfizer-BioNTech product representing a 3% rate and the Moderna product representing a 0.5% rate. Since the Janssen product first appeared in the VAERS system so recently, a low 0.007% rate is not surprising. The latter, included in Table 2, is data on the change in COVID-19 confirmed cases, which relative to the fully-vaccinated population is decreasing, but increasing absolutely. Figure 11 illustrates this increase over time, which appears to be a linear trajectory.

Distribution of COVID-19 cases in vaccinated people across age groups is uniform across the age groups between 30 and 90 years, as shown in Figure 12. No skewing was found relating a specific age group to COVID-19 cases that was statistically significant. The skewness should be compared *versus* the vaccinated and reporting population and not within the data subset itself, but this is for a future study.

When the COVID-19 data are examined by manufacturer, it stands out that 81% of all confirmed COVID-19 cases are associated with the Pfizer-BioNTech product. Without knowing the distribution proportions of

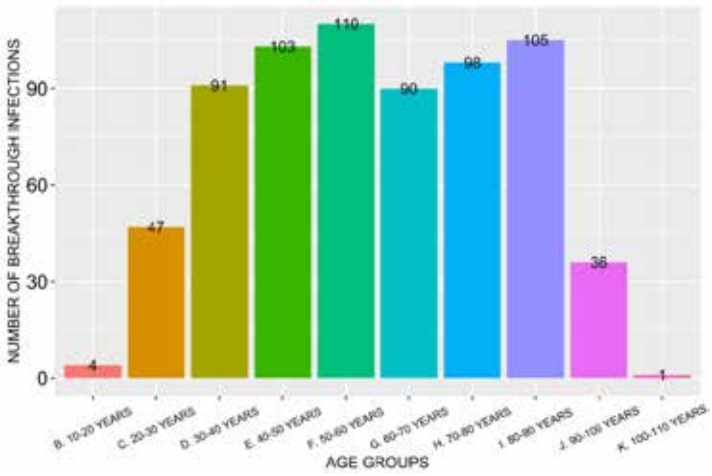


Figure 12. Distribution of COVID-19 confirmed cases from VAERS data by age

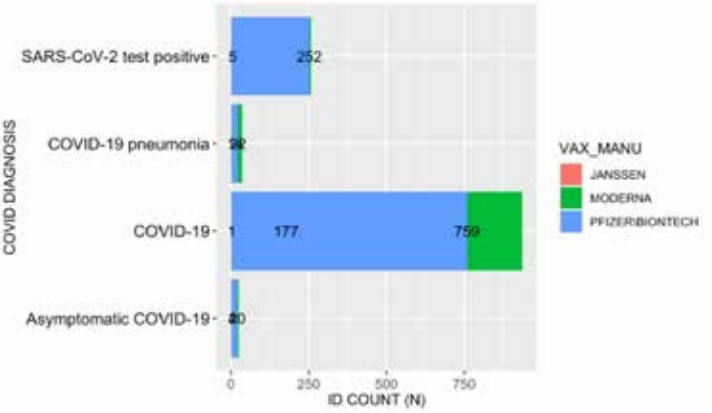


Figure 13. Distribution of COVID-19 cases according to vaccine manufacturer

the manufacturers in the population base, it is not possible to make claims about this sample with regard to any potential higher probability of getting COVID-19 in the context of the Pfizer-BioNTech product. If these data can be acquired, this question can be answered. This is reserved for a future study. Figure 13 shows the distribution of confirmed COVID-19 cases in VAERS reports across vaccine manufacturer.

4. Discussion

Safety and efficacy are the two requirements of any true vaccine. Based on this study, the risk of suffering an SAE following injection is minimal, with an average of 200 people succumbing to an SAE per million. By comparison, 1,500 people in every million die from to the virus. Of the SAEs in the data

reported so far, while taking the reported numbers at face value, the most undesirable reported is death. According to current VAERS data, 34 people per million will succumb to death. The rates are slightly higher at 120, 80 and 250 per million pertaining to specific AEs involving cardiovascular, neurological or immunological events. The risk overall, according to analysis of this data set, appears to be quite low. However, again, these data are very early and, in the context of a rushed, non-FDA-approved, continuing experimental roll-out, conclusions about long-term outcomes cannot be made yet. The VAERS data are very dynamic and new patterns may emerge at any time, depending on new reports.

The infection fatality rate (IFR), which is the number who died from COVID-19 among all those infected (both symptomatic and asymptomatic) is estimated to be 0.15% or 1500 people per million.[12,13] Thus, if compared to the death rate reported in the VAERS database in the context of the COVID-19 injections, which is 0.0034% or 34 people per million, the chance of dying from SARS-CoV-2 is greater than from the injections, based on data collected from the past four months. It is vital to remember here that the actual number of adverse events ongoing are likely being under-reported, and there are likely to be thousands more backlogged because of under-recording. If the estimated death rate is two orders of magnitude greater in reality, which it very well could be, this puts the death rate closer to 3,400 per million, which is higher than the IFR estimate. Despite the fact that 20.5% of the US population is fully vaccinated, the death count is still rising at a constant rate according to Our World in Data statistics. If one looks to Israel, the country with the most fully vaccinated people at 57.26%, it is clear to see that the death count remains on a steady upward trajectory.[14,16]

In a recent CDC report titled 'Local Reactions, Systemic Reactions, Adverse Events, and Serious Adverse Events: Pfizer-BioNTech COVID-19 Vaccine',[18,19] only the severity of the most frequently reported AEs in the VAERS database are reported in tabular form and not the SAEs themselves. They report that occurrence of severe adverse events involving system organ classes and specific preferred terms were balanced between vaccine and placebo groups and presented at a mere 0.5%. Although SAEs (grade >3, defined as interfering with daily activity) occurred more commonly in vaccine recipients than in placebo recipients, their claim is that no specific safety concerns were identified with regard to SAEs.[18,19]

Effective antiviral responses against the SARS-CoV-2 virus in the form of both cellular and humoral immune responses have been reported in peer-reviewed studies.[20,21,22,23,24, 25] Because of the combination of a

low IFR indicating effective and robust immune responses, it remains unclear why multiple experimental mRNA vaccines have been fast-tracked through conventional testing protocols and are also being fast-tracked through production and administration into the public. With repurposed drugs like Chloroquine and Ivermectin showing extremely positive results in patients,[26,27,28,29,30,31,32, 33,34,35,36] it is also unclear why these drugs are not being more extensively promoted as effective tools in the fight against this virus. One looming possibility is that EUA is not permissible if FDA-recognized, effective treatments exist.

5. Conclusion

This work summarizes VAERS data to date (April 9th, 2021) and serves as information for the public and a reminder of the relevance of any adverse events, including deaths, that likely occurred as a direct result of vaccine administration. Based on analysis of the VAERS numbers, it may appear that AEs are not currently imposing a significant burden on the fully vaccinated population; however, the weekly releases of VAERS data do not include all of the reports made to date — they are all the reports the CDC has processed to date — and the backlog is likely to be staggering. Thus, as a result of both the problems of under-reporting and the lag in report processing, this analysis reveals a strong signal from the VAERS data that the risk of suffering an SAE following injection is significant and that the overall risk signal is high.

Analysis suggests that the vaccines are likely the cause of reported deaths, spontaneous abortions and anaphylactic reactions in addition to cardiovascular, neurological and immunological AEs. Based on the precautionary principle, since there is currently no precedent for predictability with regard to long-term effects from mRNA injections, extreme care should be taken when making a decision to participate in this experiment. mRNA platforms are new to humans in terms of mass injection programs in the context of viruses. There is currently no way to predict potential detrimental outcomes with regard to SAE occurrences in the long-term. Also, concerning short-term analysis, these data are limited, based on reporting that likely substantially underestimates actual events.

It cannot be emphasized enough that these are very early data and that, based on the dynamic nature of the data, these conclusions may not be the same in a month's time. The efficacy of these products needs to be assessed by immunological assays, and long-term studies are required, while safety needs to be evaluated by rigorous clinical, laboratory and imaging assessments of severe reported adverse events. Autopsies should be done in cases of deaths temporally associated with COVID-19 injectables.

Overall, it is vital not to be hasty, and to make a proper risk assessment by being informed prior to making a decision as to whether or not to participate in experimental trials.

Treatments against SARS-CoV-2 and subsequent COVID-19 symptom formation are meant to minimize harm from the latter. It appears from this analysis that these treatments are, in fact, doing more harm than good when considering the points made herein, especially in the context of specific risk groups which are the very people we are claiming to want to protect.

Future work may include an investigation into potential correlations between SAE occurrences and frequencies and vaccine lot number, and of course updates should be made in accordance with the VAERS weekly update. In addition, investigation and focus on immunological issues certainly must be a priority in future studies with regard to adverse events reports related to COVID-19 biologicals.

Funding and Conflict of Interest information

This article received no specific funding.
No conflicts of interest are declared.

6. References

[1] US Department of Health & Human Services. VAERS Data Use Guide. November 2020. https://vaers.hhs.gov/docsAfAERSDataUseGuid e_ November2020.pdf

[2] Iannelli V. Underreporting of Side Effects to VAERS. September 17, 2017. https ://vaxopedia. org/2017/08/26/underreportin g-of-side-effects-to-vaers

[3] Demeure CE, Derbise A, Guillas C, Gerke C, Cauchemez S, Camiel E, Pizarro-Cerda J. Humoral and cellular immune correlates of protection against bubonic plague by a live Yersinia pseudotuberculosis vaccine. Vaccine. 2019 Jan 3;37(1): 123-129. doi:10.1016/j .vaccine.2018.11.022. Epub 2018 Nov 19. PMID: 30467064.

[4] Walsh EE, Frenck RW Jr, Falsey AR, Kitchin N, Absalon J, Gurtman A, Lockhart S, Neuzil K, Mulligan MJ, Bailey R, Swanson KA, Li P, Koury K, Kalina W, Cooper D, Fontes-Garfias C, Shi PY, Tiireci O, Tompkins KR, Lyke KE, Raabe V, Dormitzer PR, Jansen KU, §ahin U, Gruber WC. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. N Engl J Med. 2020 Dec 17;383(25):2439-2450. doi: 10.1056/NEJMoa2027906. Epub 2020 Oct 14. PMID: 33053279; PMCID: PMC7583697.

[5] Polack FP, et al. C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 31;383(27):2603-2615. doi:10.1056/NEJMoa2034577. Epub 2020 Dec 10. PMID: 33301246; PMCID: PMC7745181.

[6] McVey DS, Galvin JE, Olson SC. A review of the effectiveness of vaccine potency control testing. Int J Parasitol. 2003 May;33(5-6):507-doi: 10.1016/s0020-7519(03)00067-5. PMID: 12782051

[7] WHO. COVID-19 Global literature on corona virus disease. Last accessed: 5/16/2021. http://search.bvsalud.org/global-literature-on- novel-coronavirus-2019-ncov/

[8] CDC. Interim Public Health Recommendations for Fully Vaccinated People. May 13, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html

[9] Medicines.org.uk. 2021. Package leaflet: Information for the recipient: COVID-19 mRNA Vaccine BNT162b2 concentrate for solution for injection. https://www.medicines.org.uk/emc/files/pil. 124 35.pdf

[10] FDA. Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID- 19). 2021. Last accessed: 5/16/2021 (Revised 10 May 2021). https://www.fda.gov/media/144413/download

[11] Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, Pieman MA, Lipsitch M, Reis B, and Balicer RD. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. New England Journal of Medicine. February 24, 2021. DOI:10.1056/NEJMoa2101765

[12] Ioannidis JP. Reconciling estimates of global spread and infection fatality rates of COVID-19: an overview of systematic evaluations. Eur J Clin Invest. 2021. Accepted Author Manuscript el3554. https://doi.org/10. Ill 1/eci. 13554

[13] Noh J, Danuser G. Estimation of the fraction of COVID-19 infected people in U.S. states and countries worldwide. PLoS ONE 2021 16(2): e0246772. https://doi.org/10.1371/joumal.pone.0246772

[14] Our World in Data, https://ourworldindata.org

[15] CDC. Information about COVID-19 Vaccines for People with Allergies. Mar. 25, 2021. https://www.cdc.gov/coronavirus/2019- ncov/vaccines/recommendations/specific- groups/allergies.html

[16] Carmoz, D. 2021. Israeli Ministry of Health's COVID-19 data. Last Accessed, 5/16/2022. https://github.com/dancarmoz/israel_moh_covi d_dashboard_data

[17] Statista. Coronavirus (COVID-19) death rate in countries with confirmed deaths and over 1,000 reported cases as of May 12,2021, by country. https://www.statista.eom/statistics/l 105914/ coronavirus-death-rates-worldwide/

[18] CDC. Local Reactions, Systemic Reactions, Adverse Events, and Serious Adverse Events: Pfizer-BioNT ech COVID-19 Vaccine. https://www.cdc.gov/vaccines/covid-19/info- by-product/pfizer/reactogenicity.html

[19] CDC. The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNT ech COVID-19 Vaccine — United States, December 2020. https://www.cdc.gov/mmwr/volumes/69/wr/mm6950e2.htm?s_cid=mm6950e2_w

[20] Toor SM, Saleh R, Sasidharan Nair V, Taha RZ, Elkord E. T-cell responses and therapies against SARS-CoV-2 infection. Immunology. 2021 Jan;162(l):30-43. doi: 10.1111/imm. 13262. Epub 2020 Oct 27. PMID: 32935333; PMCID: PMC7730020

[21] Robbiani DF, et al. Convergent antibody responses to SARS-CoV-2 in convalescent individuals. Nature. 2020 Aug;584(7821):437- 442. doi: 10.1038/s41586-020-2456-9. Epub 2020 Jun 18. PMID: 32555388; PMCID: PMC7442695.

[22] Sun B, et al. Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients. Emerg Microbes Infect. 2020 Dec;9(l):940-948. doi: 10.1080/22221751.2020.1762515. PMID: 32357808; PMCID: PMC7273175.

[23] Le Bert N, et al. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. Nature. 2020 Aug;584(7821):457-462. doi: 10.1038/s41586- 020-2550-z. Epub 2020 Jul 15. PMID: 32668444.

[24] Mateus J, et al. Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. Science. 2020 Oct 2;370(6512):89-94. doi: 10.1126/science.abd3871. Epub 2020 Aug 4. PMID: 32753554; PMCID: PMC7574914.

[25] Lipsitch M, Grad YH, Sette A, Crotty S. Cross- reactive memory T cells and herd immunity to SARS-CoV-2. Nat Rev Immunol. 2020 Nov;20(ll):709-713. doi: 10.1038/s41577-020- 00460-4. Epub 2020 Oct 6. PMID: 33024281; PMCID: PMC7537578.

[26] Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. Int J Antimicrob Agents. 2020 Apr;55(4): 105932. doi: 10.1016/j.ijantimicag.2020.105932. Epub 2020 Mar 4. PMID: 32145363; PMCID: PMC7135139.

[27] Meo SA, Klonoff DC, Akram J. Efficacy of chloroquine and hydroxychloroquine in the treatment of COVID-19. Eur Rev Med Pharmacol Sci. 2020 Apr;24(8):4539-4547. doi: 10.26355/eurrev_202004_21038. PMID: 32373993.

[28] Ibanez S, Martinez O, Valenzuela F, Silva F, Valenzuela O. Hydroxychloroquine and chloroquine in COVID-19: should they be used as standard therapy? Clin Rheumatol. 2020 Aug;39(8):2461-2465. doi:10.1007/s 10067-020-05202-4. Epub 2020 JunPMID: 32495226; PMCID: PMC7267470.

[29] N, Esposito S. Chloroquine or hydroxychloroquine for prophylaxis of COVID-19. Lancet Infect Dis. 2020 Oct;20(10):1118. doi: 10.1016/ S1473- 3099(20)30296-6. Epub 2020 Apr 17. PMID: 32311322; PMCID: PMC7164862.

[30] Femer RE, Aronson JK. Chloroquine and hydroxychloroquine in Covid-19. BMJ. 2020 Apr 8;369:ml432. doi: 10.1136/bmj.ml432. PMID: 32269046.; Hernandez AV, Roman YM, Pasupuleti V, Barboza JJ, White CM. Hydroxychloroquine or Chloroquine for Treatment or Prophylaxis of COVID-19: A Living Systematic Review. Ann Intern Med. 2020 Aug 18;173(4):287-296. doi:10.7326/M20-2496. Epub 2020 May 27. PMID: 32459529.;

[31] Shah S, Das S, Jain A, Misra DP, Negi VS. A systematic review of the prophylactic role of chloroquine and hydroxychloroquine incoronavirus disease-19 (COVID-19). Int J Rheum Dis. 2020 May;23(5):613-619. doi:10.1111/1756-185X. 13842. Epub 2020 Apr 27. PMID: 32281213; PMCID: PMC7262257.

[32] Rizzo E. Ivermectin, antiviral properties and COVID-19: a possible new mechanism of action. Naunyn Schmiedebergs Arch Pharmacol. 2020 Jul;393(7): 1153-1156. doi: 10.1007/s00210-020-01902-5. Epub 2020 May PMID: 32462282; PMCID: PMC7251046.

[33] Heidary F, Gharebaghi R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. J Antibiot (Tokyo). 2020 Sep;73(9):593-602. doi: 10.1038/s41429-020-0336-z. Epub 2020 Jun 12. PMID: 32533071; PMCID: PMC7290143.

[34] Sharun K, Dhama K, Patel SK, Pathak M, Tiwari R, Singh BR, Sah R, Bonilla-Aldana DK, Rodriguez-Morales AJ, Leblebicioglu H. Ivermectin, a new candidate therapeutic against SARS-CoV-2/COVID-19. Ann Clin Microbiol Antimicrob. 2020 May 30;19(1):23. doi: 10.1186/sl2941 -020-00368-w. PMID: 32473642; PMCID: PMC7261036.

[35] Shih RD, Johnson HM, Maki DG, Hennekens CH. Hydroxychloroquine for coronavirus: The urgent need for a moratorium on prescriptions. Am J Med. 2020 Sep; 133(9): 1007-1008. doi: 10.1016/j.amjmed.2020.05.005. Epub 2020 Jun 2. PMID: 32502485; PMCID: PMC7265864.

[36] Lam S, Lombardi A, Ouanounou A. COVID- 19: A review of the proposed pharmacological treatments. Eur J Pharmacol. 2020 Nov 5;886:173451. doi:10.1016/j.ejphar.2020.173451. Epub 2020 Aug 6. PMID: 32768505; PMCID: PMC7406477.

[37] Drugs. Pfizer-BioNTech COVID-19 Vaccine FDA Approval Status. https://www.drugs.com/history/pfizer-biontech-covid-19-vaccine.html

[38] Drugs. mRNA-1273 FDA Approval Status. https://www.drugs.com/history/mrna-1273.html

[39] Drugs. Janssen Pharmaceuticals, Inc.. https://www.drugs.com/manufacturer/janssen- pharmaceuticals-inc-74.html

[40] National Institute on Aging. NIA Adverse Event and Serious Adverse Event Guidelines. https://www.nia.nih.gov/sites/default/files/2018 -09/nia-ae-and-sae-guidelines-2018.pdf

[41] FDA. Code of Federal Regulations — Title 21 — Food and Drugs. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?frextemal%20icon

[42] Poorolajal J, Hooshmand E. Booster dose vaccination for preventing hepatitis B. Cochrane Database Syst Rev. 2016 Jun 7;2016(6):CD008256. doi:10.1002/14651858.CD008256.pub3. PMID: 27271960; PMCID: PMC7154826.

[43] CDC. Guidance for Certifying Deaths Due to Coronavirus Disease 2019 (COVID-19). Vital Statistics Reporting Guidance. Report No. 3, April 2020. https://www.cdc.gov/nchs/data/nvss/vsrg/vsrgO3-508.pdf

[44] CDC. Seasonal Influenza Vaccine Supply & Distribution. https://www.cdc.gov/flu/prevent/vaccine-supply-distribution.htm

[45] Poon, L.L.M., Peiris, M. Emergence of a novel human coronavirus threatening human health. Nat Med 26, 317-319 (2020). https://d0i.0rg/l 0.1038/s41591-020-0796-5

[46] Galloway SE, Paul P, MacCannell DR, et al. Emergence of SARS-CoV-2 B.l.1.7 Lineage — United States, December 29, 2020-January 12, 2021. Morb Mortal Wkly Rep 2021;70:95-99.

[47] Harcourt J, Tamin A, Lu X, et al. Severe Acute Respiratory Syndrome Coronavirus 2 from Patient with Coronavirus Disease, United States. Emerging Infectious Diseases. 2020;26(6): 1266-1273.doi: 10.3201/eid2606.200516.

[48] Pfizer, Inc. https://www.pfizer.com

49] IPAK Report 2021-1. 2021. Post-vaccination Death Causality Likely Given Temporal Distribution of Deaths Following COVID19 Vaccinations. Interim results. http://ipaknowledge.org/resources/VAERS%20 deaths%20to%20 3%2010%202021%20update %203.pptx

[50] Tinari S. The EMA Covid-19 data leak, and what it tells us about mRNA instability. BMJ 2021; 372 :n627 doi:10.1136/bmj.n627

[51] UK Government Publishing Service. SPI-M-O: Summary of further modelling ofeasing restrictions-Roadmap Step 2. March 31, 2021. https://assets.publishing.service.gov.uk/govern ment/uploads/system/uploads/attachment_data/f ile/975909/S 1182_SPI-M-0_Summary_of_ modelling_of_easing_roadmap_step_2_restricti ons.pdf

[52] Corbett, K.S., Edwards, D.K., Leist, S.R. et al. SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness. Nature 586, 567-571 (2020). https://doi.org/10.1038/s41586-020-2622-0.

[53] Jaafar R, Aherfi S, Wurtz N, Grimaldier C, Van Hoang T, Colson P, Raoult D, La Scola B. Correlation Between 3790 Quantitative Polymerase Chain Reaction-Positives Samples and Positive Cell Cultures, including 1941 Severe Acute Respiratory Syndrome Coronavirus 2 Isolates. Clinical Infectious Diseases. 2020; ciaal491. https://doi.org/10.1093/cid/ciaal491

[54] Braunstein GD, Schwartz L, Hymel P, Fielding J. False Positive Results With SARS-CoV-2 RT-PCR Tests and How to Evaluate a RT- PCR-Positive Test for the Possibility of a False Positive Result. Journal of Occupational & Environmental Medicine. 2021 Mar I;63(3):el59-el62. doi: 10.1097/JOM.0000000000002138.

[55] Alroy KA, et al. Population-Based Estimates of Coronavirus Disease 2019 (COVID- 19)-like Illness, COVID-19 Illness, and Rates of Case Ascertainment, Hospitalizations, and Deaths—Noninstitutionalized New York City Residents, March-April 2020. Clinical Infectious Diseases. 2021; ciab038. https://doi.org/10.1093/cid/ciab038

Jessica Rose, PhD, MSc, BSc, is a Canadian researcher with a bachelor's degree in applied mathematics and a Master's degree in immunology from Memorial University of Newfoundland. She also holds a PhD in Computational Biology from Bar Ilan University and two post-doctoral degrees, one in molecular biology from the Hebrew University of Jerusalem, and the second in biochemistry from the Technion Institute of Technology. Her more recent research efforts are aimed at descriptive analyses of the Vaccine Adverse Event Reporting System (VAERS) data in efforts to make these data accessible to the public.

Excess death anomaly in Finland 2021

by Tore Aarhus Gulbrandsen, Kasper Rönning

Abstract

Total excess mortality statistics are a reliable metric for detecting changes in death rates at the population level. We present a model based on official statistics for death counts in Finland from the years 2008-2019 to evaluate the mortality in 2020 and 2021. Observed mortality for 2020 and early 2021 was at the expected level based on our model. However, our calculations show a substantial increase in mortality starting in early summer 2021 and continuing until present, totalling over 3000 excess deaths from May 2021 to February 2022, over 5% of yearly total deaths. We verify our finding of excess mortality by multiple independent metrics. Shorter periods of excess mortality are not uncommon, but the extended duration of the present observation represents a clear anomaly. In the period 1990-2019 mortality has consistently been at its lowest during the summer months and peaked during winter. During the weeks 25-42 of 2021 a total of 1752 excess deaths were observed, whereas only 231 COVID deaths were recorded during the same period. It is the duty of health and government officials to recognize this anomaly and initiate investigations to understand its cause.

Introduction

Population mortality statistics constitute a reliable metric for detecting significant events causing changes in death rate at the population level. The number of deaths is usually reported in weekly, monthly or yearly intervals, without attribution of causes of death. Excess mortality or mortality deficit means that, based on an inference from previous mortality, the currently observed mortality is higher or lower than expected.

The Finnish Institute for Health and Welfare (THL) in press releases and interviews has claimed that no notable changes have occurred in the mortality rates in Finland during the pandemic. The official Finnish institute for statistics, Statistics Finland, asserted in an interview in the major Finnish newspaper Helsingin Sanomat that the number of recorded deaths in 2021 was not exceptional, comparing it to the year 2020 and noting that there were a mere 500 deaths more.

The statements of THL and Statistics Finland are in conflict with both EuroMOMO and the most recent Population Prognosis published by Statistics Finland itself. In this paper we present a model for the expected number of deaths from 2020, relying on official statistics on deaths from the preceding 12 years. We demonstrate that the first year of the COVID pandemic 2020 shows completely normal mortality, whereas the year 2021 displays an extended period of excess mortality in the second half of the year. We also verify our model's correctness by comparing it to several independent data sources.

Materials and methods

Mathematical model

We present a mathematical function to predict the number of deaths per week, with no stratification by age or gender, and then use this function to compare pandemic death rates to those of previous years. Mortality is highly seasonal, peaking during the flu season in winter and bottoming out in summer. In Finland harsh heat waves are rare, but some years have seen excess mortality in summer from extended hot periods. On the other hand, some winters have brought quite large peaks of excess mortality from heavy flu seasons. Such winters are usually followed by periods of mortality deficit once the flu has subsided.

To model these patterns we apply a function consisting of a linear component for the long term trend in mortality and an oscillating cosine component to accommodate the seasonality (Figure 1). Similar mathematical functions underlie the models of EuroMOMO, although its focus is on short term excess mortality caused by epidemics.

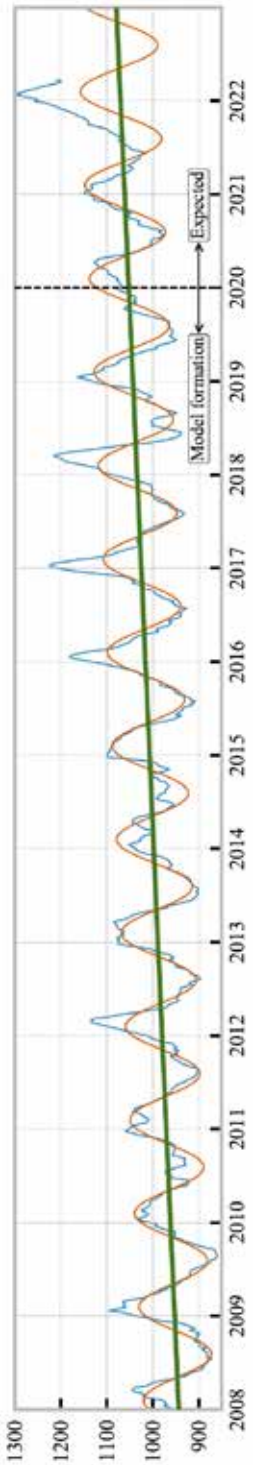


Figure 1. Weekly deaths are modelled by a linear trendline (green) modulated by a seasonal sine curve (orange). The blue line represents a 7 week moving average of the actual recorded deaths.

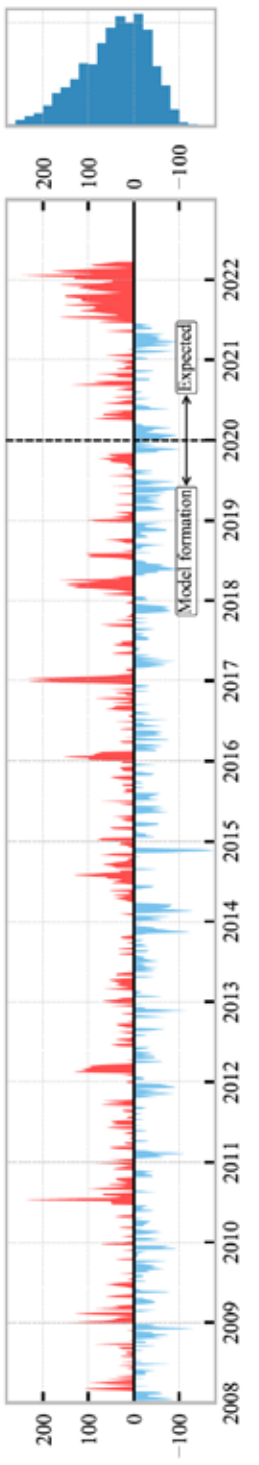


Figure 2. Weekly excess mortality in red, mortality deficit in blue.

The long-term trend has been highly linear during the entire reporting period of Statistics Finland, up until the summer of 2021. In the first half of the period, 1990-2006, it was decreasing mildly, and then gently increasing during 2007-2020. We applied our model to the period after 2008, where the trend has been consistently gently increasing.

The seasonal cosine component peaks in winter and bottoms out in summer. The amplitude of the cosine component is proportional to the total mortality, so that the seasonal variability would increase when total deaths increase. The mathematical function of our mortality model is thus:

$$f_b(t) = f_{trend}(t) + a\, f_{trend}(t)\, cos\left(\frac{2\pi}{365.24}t + \theta\right)$$
$$= f_{trend}(t)\left(1 + a\, cos\left(\frac{2\pi}{365.24}t + \theta\right)\right)$$

where:

- Parameter t is time.
- $f_{trend}(t)$ is a linear function running from $x_1 = 1Jan2008$ ja $x_2 = 31Dec2019$.
- Parameter a represents the amplitude and θ is the periodic shift of the of the cosine component.

The fitted parameters y_1, y_2, a and θ were established using the "curve fit"-function of SciPy, which utilizes non-linear least squares regression to minimize the difference between the model function $f_b(t)$ and the weekly deaths. The model was fitted for the time period 1 Jan 2008 - 31 Dec 2019, and the fit parameters were established as follows: $y_1 = 943.8$, $y_2 = 1044.6$, amplitude $a = 0.08$ and periodic shift $\theta = -35.37$ days.

Data sources

The source for total excess mortality was the weekly publication 'Kuolleet viikoittain pikaennakko' by Statistics Finland,[1] which contains the weekly number of deaths without cause of death or sex and gender information, available since 1990. In addition to this we used the monthly number of deaths from Statistics Finland[2] and EuroMOMO's Z-values[3] which represent excess mortality. The source for deaths ascribed to COVID-19 was THL's report 'Tartuntatautirekisterin COVID-19-tapaukset',[4] containing weekly COVID deaths.

Source code

The source code for the model and graphics was made with Python programming language, using SciPy and Matplotlib libraries. All source code

including PDF-graphics is available online at:

https ://github. com/k-ronning/acm_analyzer.

Results and discussion

Calculating the difference between weekly estimated deaths from our model and actual recorded numbers, we arrive at excess mortality numbers per week, illustrated in Figure 2. Nearly every year the flu season generates mortality numbers that exceed the normal range, followed usually by some months of mortality deficit.

Yearly cumulative excess mortality

The annual flu season varies in timing and may thus greatly skew the yearly mortality numbers depending on whether flu mortality peaks in December or January. To accommodate this variability, yearly cumulative deaths can be analysed by shifting the calculation starting point to after the flu season. We chose week 16 as the starting point of our cumulative values, as this is used by EuroMOMO as the week when the flu season is generally considered to have ended[5]. Figure 3 shows the shifted cumulative excess mortality curves for 2008-2021. Mortality patterns from spring, summer and autumn are seen on the left half of the graph, while the right side of the graph is dominated by the flu season and the high variability it brings. 2020 and 2021 are drawn with bold lines, and for these years an additional dashed line shows the excess mortality minus COVID deaths, by which one can evaluate excess deaths unrelated to COVID.

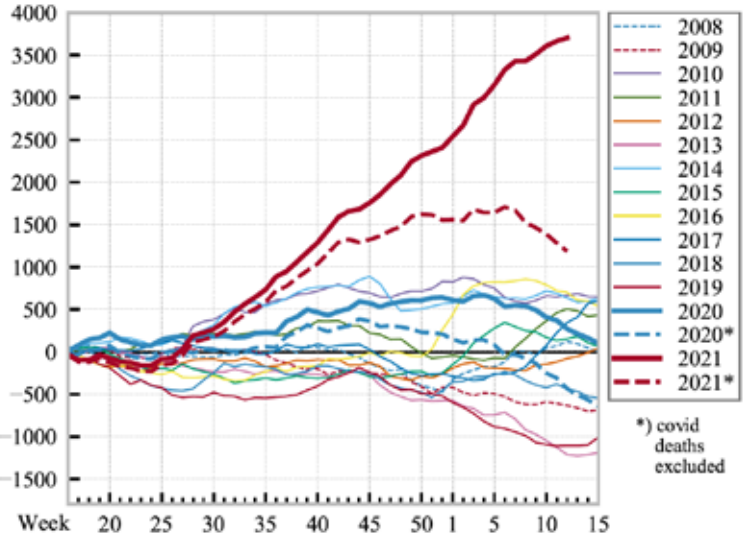


Figure 3. Yearly cumulative excess mortality 1990-2021.
Cumulation starts from week 16.

It is evident from the figure that 2020 does not stand out from previous years, regardless of whether we consider the total excess or the excess minus COVID deaths. In contrast, the year 2021 shows a dramatic departure from the other years; it starts out normally but then there is a steady increase from week 25 and it continues until the present (April 2022), totalling 35 weeks. Particularly noteworthy is the period between week 25 and week 42, during which we estimate 1752 excess deaths, while the same period saw only 231 COVID deaths.

Cumulative excess mortality of the entire time period

Figure 4 shows the cumulated excess mortality of the entire period used for the model. One can deduce from the figure that the linear model component represents the mortality reasonably well, considering that no extended period of excess or deficit mortality is seen, as is expected. If the linear component was a poor fit, the cumulative excess would deviate upwards or downwards for longer periods. While the above is true for the first years of the graph, such deviation does indeed happen in the summer of 2021. What could explain this abrupt change in the mortality pattern in summer 2021, given that the mortality has followed a stable downward trend since 2008? When the previously stable trend suddenly changes upwards, this represents unexpected increased mortality, that is, excess mortality. Our model estimates that from May 2021 until February 2022 there has been a total of over 3000 deaths more than expected in Finland, and only a part of these are COVID deaths.

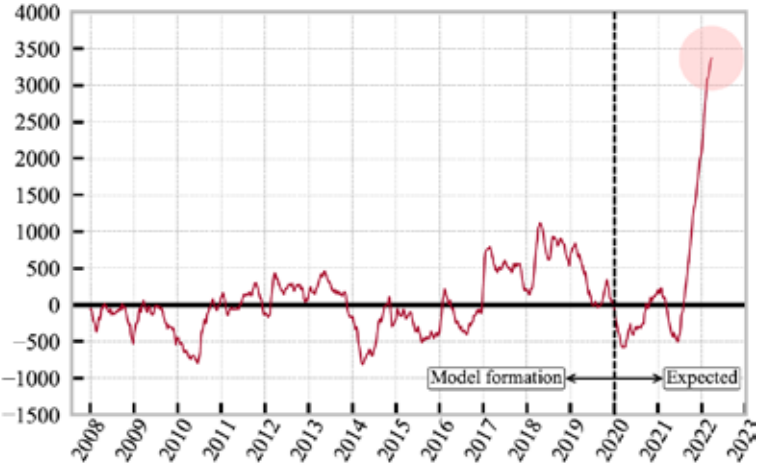


Figure 4. Excess mortality for the entire period 1 Jan 2008 - 20 Feb 2022.

Model verification

All models are based on assumptions, which may be wrong. To verify our model for correctness, we compared the outcome to three different data sources: EuroMOMO, Statistics Finland's monthly reported deaths and Statistics Finland's population forecast.

EuroMOMO

EuroMOMO is a mortality surveillance tool maintained by the Danish Statens Serum Institut. The underlying model for the excess death calculations is not in the public domain, but its Z-values refer to the standard normal distribution. $Z = 1$ refers to one standard deviation difference from the mean, and the mean in this case is the EuroMOMO expected number of deaths for the week, as given by the underlying model. EuroMOMO's Z-values serve as a process control chart for mortality, with an upper control limit of $4Z$. This control limit is often exceeded during harsh influenza seasons, indicating a sudden excess mortality as is often the case during influenza waves. However, in the domain of process control charts also extended periods of less pronounced deviations must be considered as possible anomalous events. Nelson's rules are often referred to when interpreting anomalies in control charts, and the EuroMoMo Z-values for 2021 trigger at least three of these rules:

A) Nine or more consecutive observations are on the same side of the mean line ($Z = 0$).

B) Four (or five) of five consecutive observations are farther than 1 standard deviation ($= 1Z$) in the same direction from the from the mean line.

C) Two (or three) of three consecutive observations are farther than 2 standard deviations ($= 2Z$) in the same direction from the mean line.

EuroMOMO's weekly Z-values since 2017 from Finland are shown in Figure 5. During the second half of 2021 the above-mentioned rules are violated numerous times:

- From Week 24, 2021 there are 20 consecutive weeks where $Z > 0$, and 33 of the subsequent 35 weeks $Z > 0$, so rule A is violated dozens of times.
- From Week 35, 2021 until Week 7, 2022, there are 9 occasions where four or more out of five consecutive weeks have $Z > 1$, so rule B is violated 9 times.
- From Week 27, 2021 until week 6, 2022 there are four occasions where two or more out of three consecutive weeks have $Z > 2$, so rule C is violated four times.

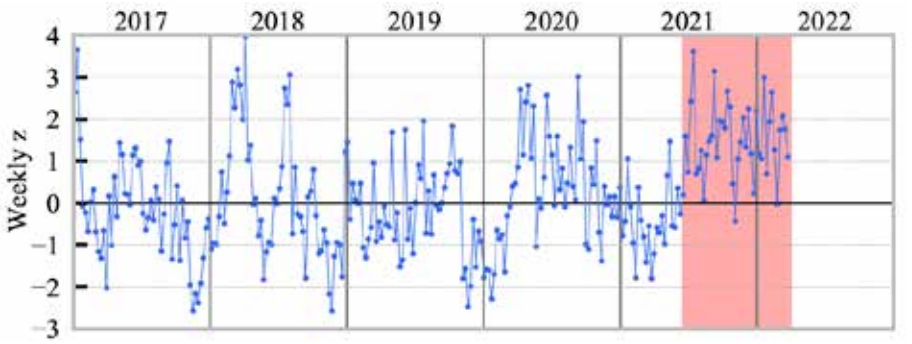


Figure 5. EuroMOMO's *Z*-values, where the *Z*-values in the red area violates Nelson's rules.

Together, these observations constitute a strong anomaly during the entire second half of 2021, fully in line with the excess deaths from our model.

Further validating the agreement between our model and EuroMOMO's *Z*-values, figure 6 shows a strong correlation between the two, with a correlation coefficient of r > 0.9. This demonstrates that the two models are well aligned and describe the same phenomenon.

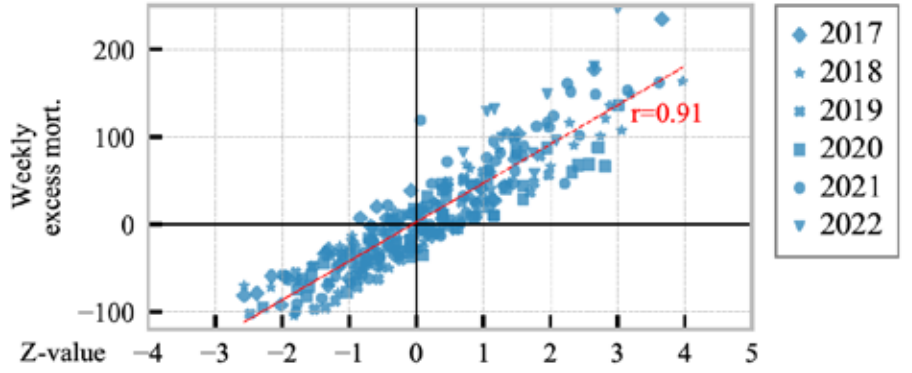


Figure 6. Correlation between EuroMOMO's *Z*-values and the excess deaths from our model.

Monthly distribution of deaths

As a second verification approach, we used monthly deaths statistics from Statistics Finland to calculate the relative distribution of deaths among the months of each year for the period 1990-2021. Figure 7 shows the mortality patterns for 1990-2020 as a blue area, with both 80% and 100% of the range per month indicated. This distribution is very repeatable from year to year, depending mainly on seasonal factors such as winter influenza and summer

heat waves. The roughly 10% drop for February is due to the fewer number of days in this month.

This figure shows clearly that already from May, the mortality pattern for 2021 was at the extremes of the range for 1990-2020, and that never during 1990-2020 did the months from July to November contain this high a proportion of total deaths of the year. The value for December 2021 was the third highest, with only 1993 and 2003 being higher, as a result of the influenza wave of these two years striking in December.

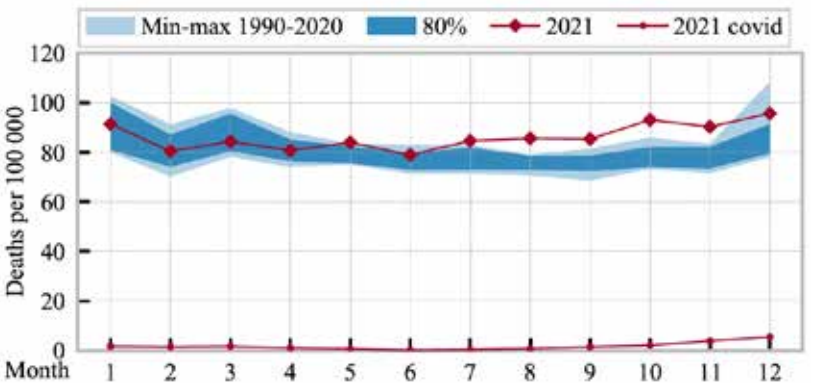


Figure 7. Monthly mortality 1990 – 2020. The second half of 2021 significantly exceeds the range of the previous 30 years. Covid explains only a small part of this pattern.

Distribution between first and second half of the year

In the methodology of control charts, another approach used is to compare the proportion of events per segment of time. Figure 8 shows the proportion of all deaths per year that happened during the second half of the year plotted as a function of the years. From 1990 to 2020, this proportion has meandered between 47.6% and 50.2%, with a standard deviation of 0.66%pt. Also in this comparison, 2021 deviates profoundly from the other years, with the

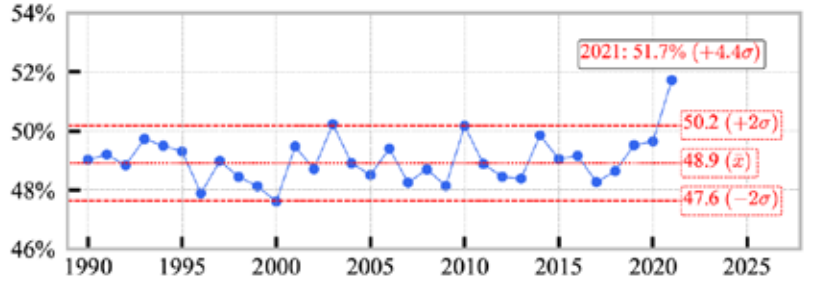


Figure 8. Proportion of deaths in second half of the year. 2021 clearly deviates from the entire previous 30 years.

proportion of deaths during the second half coming in at 51.7%, an astounding 4.4 standard deviations from the mean of 1990-2020. The probability that such an event would occur by pure chance without a special cause is p - 0.00001, or in other words once every 100,000 years.

Population forecasts

Every 1-3 years, Statistics Finland publishes a Population Forecast, which includes various metrics on the population, including expected deaths. The projections from the most recent publications of 2012, 2015, 2018 and 2019 are shown in Figure 9, and comparing to the actual number of deaths (blue line), one can see that these projections have been mostly slight underestimates. Since our model is fitted to the actual deaths of 2008-2019, it is expected to follow the actual number of deaths closely to the end of 2019. Of particular interest in this graph, however, is the forecast published on September 30th 2021, which estimates the deaths for 2021 at 1679 higher than the 2019 forecast predicted for the same year. In spite of being from the end of September and adjusting the 2019 clearly upwards, it still falls 1356 deaths short of the total number of deaths for the year, which came in only three months later. The total deaths in 2021 was 3035 more than the Statistics Finland 2019 prediction – an extreme deviation from a prediction only two years old.

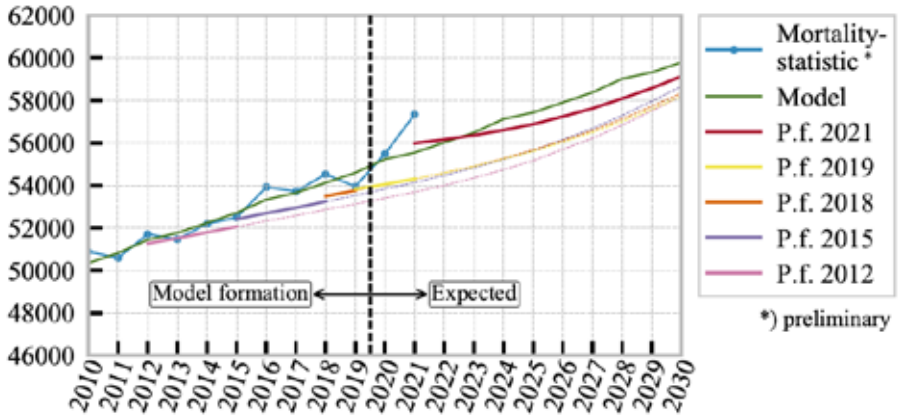


Figure 9. Yearly observed deaths in blue, our model's prediction in green, remaining colors are population forecasts.

Possible causes for the excess mortality

Healthcare backlog

The policies of the COVID period led to increases in healthcare backlogs, which could in part explain the excess mortality, but the effects of such backlogs would hardly lead to sudden changes in deaths, but would rather cause a

gradual increase. In other words, why would missing healthcare follow-up lead to no increased deaths from 2020 until May 2021 only to cause a sudden and persistent increase from Week 25,2021? The effect of healthcare backlogs must be must more gradual to be a feasible explanation.

COVID

If many people died of SARS-CoV2 without a diagnosed infection, this could explain excess deaths. The COVID deaths of 2021 were, however, at their lowest in summer – totalling a mere 31 deaths in June and July – when the number of excess deaths during the same period was +367. Correspondingly, the total COVID deaths in Weeks 25 through 42 were 231, but excess deaths during the same period were at +1752. If underdiagnosing of COVID was the explanation, COVID deaths and excess deaths should correlate. Furthermore, the tentative numbers of COVID deaths reported by the Finnish Institute for Health and Welfare (THL) from 2020 – 598 deaths – were adjusted down to 558 when the final cause of death statistics from Statistics Finland arrived. Thus, it is expected that THL's current estimate of 1136 COVID deaths for 2021 will be adjusted down. In other words, COVID deaths could at maximum explain one third of the excess deaths from our model, and mainly only the deaths from November and December. Also, considering that the roughly 500 COVID deaths in 2020 led to no observable excess mortality, this leaves nearly 2500 unexplained deaths for 2021.

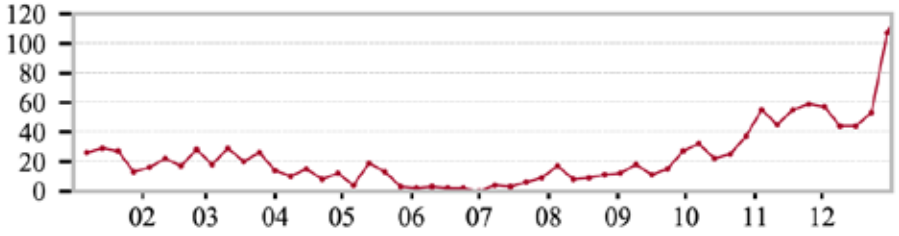


Figure 10. Deaths from covid per week 2021 (Month numbers on x-axis).

Ageing population

The older age cohorts in Finland have steadily been increasing during recent times, so it is expected that the total number of deaths will increase accordingly. This explains why the number of deaths per year in Finland has steadily increased over the last 10 years or more. If our model had underestimated this gradual increase, it could explain the observed excess deaths.

However, ageing is a slow process, the effects of which are also slow as a consequence. Our model takes into account such gradual effects, happening over decades. Our data show that the mortality patterns of 2021 are normal

until May, when the numbers suddenly rise and remain high for the entire second half of the year, and remained high when this paper was first published in Finnish (April, 2022).

Conclusions

In the present work, we have shown with multiple different approaches a highly anomalous pattern of excess deaths in Finland starting around June of 2021, currently totalling over 3,000 excess lives lost, and only partially explained by COVID infections. In particular, during the Weeks 24 through 42, 2021 there were 1,752 excess deaths, but only 231 COVID deaths, leaving 1521 non-COVID excess deaths.

While age stratification was not in the scope of this study, EuroMOMO indicates that the majority of the observed excess deaths appears to occur in the age cohorts above 80 years. Neither underdiagnosing of COVID infection, healthcare backlog nor ageing population explains this sudden and persistent excess mortality.

The excess mortality calculated from our model was cross-checked by three different methods: 1) Comparison with EuroMOMO; 2) Deviations in monthly distribution of each year's deaths; 3) Deviation from 2019 population forecast. All three approaches verified the observed anomaly. Given the strength of the statistical significance as established by EuroMoMo data, the anomaly cannot have arisen from random variation.

Finnish health authorities have thus far (April 2022) either played down or altogether ignored these alarming data. In the light of the irrefutable evidence presented in this paper, it is high time health authorities stop understating the severity of the situation and carry out a thorough and independent investigation of the cause for the dramatically elevated mortality.

References

[1] *Tilastokeskus: Kuolleet viikoittain sukupuolen, ian ja maakunnan mukaan (Pikaennakko).* Link: https://pxdata.stat.fi/PXWeb/pxweb/£i/Kokeelliset_tilastot/Kokeellise t_tilastot vamuu_koke/koeti_vamuu_pxt_12ng.px/.

[2] *Tilastokeskus: Vaestonmuutokset kuukausittain.* Link: https://pxweb2.stat.fi/PXWeb/pxweb/fi/StatFin/StatFin va muu/statfin_vamuu_pxt_llll.px.

[3] *EuroMoMo Graphs and Maps.* Link: https://www. eurom omo.eu/graphs-and-maps/.

[4] *THL: COVID-19 cases in the infectious diseases registry.* Link: https://sampo.thl.£i/pivot/prod/en/epirapo/covidl9case/fact_epirapo_covidl9case?row=dateweek20200101-509030&column=measure-444833.445356.492118.&fo=l.

[5] Bernadette Gergonne. *EuroMoMo Work Package 7 Report - A European algorithm for a common monitoring of mortality across Europe.* Link: https: //www. euromomo .eu/uploads/pdf/wp7_report.pdf. 2011.

Tore A. Gulbrandsen is a data scientist with over 10 years of experience in process and product development, and in supervising statistical analyses for regulatory submission. Having a passion for data and a slight suspicion for medical authorities based on personal experiences of failed treatment, he has followed key statistics with a critical eye from the start of the pandemic. One of his specialties is recognizing anomalous data patterns, which the last three years have seen in abundance; another is simulations and modelling. His focus has been on evaluating, modelling and predicting mortality statistics in the Nordics, but recently also other countries.

Part 6

From policy failure to iatrogenic crisis

Our authors have pointed consistently to the need for investigation. There are those who have argued that we are in actual policy-induced health crisis, and that it shows signs of continuing. 'Moreover, the injections appeared to have a cumulative effect on the immune system with the first booster campaign early in January 2022 having a devastating effect in Australia.' Thus, Dr Wilson Sy. And again: 'For the whole Australian population it has been shown that COVID-19 injections increase, not decrease as claimed, severe illness and death.'

Australians might be angered by being denied the basic level of objective scientific information. The government's reports demonstrate they knew or ought to have known using due skill, care, and diligence that these injections have not been proved safe or effective.

A preprint review of Australia's all-cause mortality data by Dr Wilson Sy, using the Bradford-Hill criteria, demonstrates a causal link with the COVID vaccination roll-out.

> Australian official mortality data show no clear evidence of significant excess deaths in 2020, implying from an older WHO definition that there was no COVID-19 pandemic. A seasonality analysis suggests

> that COVID-19 deaths in 2020 were likely misclassifications of influenza and pneumonia deaths. Australian excess mortality became significant only since 2021 when the level was high enough to justify calling a pandemic. Significant excess mortality was strongly correlated (+74%) with COVID-19 mass injections five months earlier. Strength of correlation, consistency, specificity, temporality, and dose-response relationship are foremost Bradford Hill criteria which are satisfied by the data to suggest the iatrogenesis of the Australian pandemic, where excess deaths were largely caused by COVID-19 injections. Therefore, a strong case has been presented for the iatrogenic origins of the Australian COVID-19 pandemic and, therefore, the associated mortality risk-benefit ratio for COVID injections is very high.
>
> – Dr Wilson Sy.

If these findings are accurate then there must be accountability and justice for this deceit that has gone beyond incompetence into the realm of malfeasance. Bureaucrats, politicians, directors of departments who oversaw the mandating of the largest vaccination trial ever, all played their part in undermining human rights and the Constitution. Offers to allow independent medical and scientific professionals to review and debate policy and data have been denied at every step of the process. Once a normal part of the participatory democratic model of governance, objectivity and transparency were squashed using censorship, fear and enforcement techniques.

Australian COVID-19 pandemic: A Bradford Hill analysis of iatrogenic excess mortality

by Wilson Sy[1]

1 Abstract

Australian official mortality data show no clear evidence of significant excess deaths in 2020, implying from an older WHO definition that there was no COVID-19 pandemic. A seasonality analysis suggests that COVID-19 deaths in 2020 were likely misclassifications of influenza and pneumonia deaths. Australian excess mortality became significant only since 2021 when the level was high enough to justify calling a pandemic. Significant excess mortality was strongly correlated (+74%) with COVID-19 mass injections five months earlier. Strength of correlation, consistency, specificity, temporality, and dose-response relationship are foremost Bradford Hill criteria which are satisfied by the data to suggest the iatrogenesis of the Australian pandemic, where excess deaths were largely caused by COVID-19 injections. Consequently, a strong case has been presented for the iatrogenic origins of the Australian COVID-19 pandemic and therefore, the associated mortality risk-benefit ratio for COVID injections is very high.

1 Revised 27 March 2023, PhD, Director, Biotechnology Unit, Investment Analytics Research. Lex Stewart and Jeremy Beck are thanked for useful comments. The author has no financial or political conflicts of interest and is not funded by external sources. This paper has appeared in the Journal of Clinical and Experimental Immunology. Sy, W. Australian COVID-19 pandemic: A Bradford Hill analysis of iatrogenic excess mortality, J Clin Exp Immunol, 8(2), 542-556.

2 Introduction

On 11 March 2020, the World Health Organization (WHO) declared[1] the COVID-19 pandemic based on 4,291 deaths, by 118,000 cases in 114 countries, with an average of about 1,000 cases in each country. Based on this very small sample, the WHO assumed that the COVID-19 disease is highly infectious and has an infection fatality rate (IFR) of at least 0.4 percent. Therefore, the COVID-19 pandemic was declared based on expectation and not on fact, as the WHO had previously defined for an influenza pandemic:[2]

> An influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in several, simultaneous epidemics worldwide with *enormous numbers of deaths* and illness.

Emphasis added. A pandemic should be justifiably declared only if there are 'enormous numbers of deaths', for otherwise seasonal influenza or even the common cold of the Rhinovirus could be declared as pandemics, that is, just based on numbers of cases of infection. By now, it is abundantly clear that the number of cases defined by the PCR tests may be grossly inflated (see section 2).

By assuming 'cases' would lead to 'enormous deaths', the WHO declared a pandemic based on supposition, not on scientific fact. The presumption of sound science by governments has allowed them to justify harsh public health measures which may have been counter-productive, ultimately causing more deaths. Based on objective data, this paper assesses whether there were enough excess deaths to warrant declaring a pandemic in Australia. By investigating those excess deaths, the probable cause of the Australian pandemic is deduced in this study.

In section 2, it is discussed that assessment of the pandemic based solely and quantitatively on COVID infection cases and deaths is questionable, because cases of COVID infection and deaths attributed to the SARS-CoV-2 virus have not been adequately proved. That is, the pandemic cannot be accurately assessed from COVID-19 data which are scientifically flawed (see discussion below). This paper assesses the COVID-19 pandemic in Australia based on all-cause mortality data, consistent with the earlier WHO definition of pandemics.

Since accurate and reliable data are critically important as inputs to the data analysis to draw valid conclusions, data methodology is discussed in section 3. In 2020, when many Victorian deaths were attributed to COVID-19, the effect on total mortality was insufficient to declare a pandemic in Australia. Details and possible explanations are discussed in section 4, to justify describing 2020 as the 'pre-pandemic' phase.

Australian excess deaths began to rise to a statistically significant level in 2021 to warrant the appellation of a 'pandemic.' Early increases in excess deaths accompanied the early rollout of mass COVID-19 injections. The injections were called 'vaccines,' but they do not prevent infections, nor were they tested to inoculate against infections, as admitted recently by Pfizer to the European Parliament.[3]

This paper rejects calling the COVID-19 injections 'vaccines'; they were never tested to be such. The public has been misinformed and misled to accept COVID-19 injections as 'vaccines.' When the injections clearly failed to reduce transmissions, the rhetoric of 'vaccine' benefit changed to reducing serious illnesses and deaths. This claim is also proved false in this paper, where the pandemic phase defined by elevated excess deaths is shown to be correlated with mass COVID-19 injections in section 5.

In section 5, the strong correlation between doses of injections administered and increased levels of excess deaths five months later suggest iatrogenic causality. This possibility is further strengthened by aspects of consistency and specificity in section 6 where the evidence of causality is seen by consistency across time and geography. Also, specificity is evident from the fact that the 'vaccinated' are more likely to die than the 'unvaccinated,' who are simply defined as those without any injections, rather than official definitions where the 'unvaccinated' may have had injections.

The main contributions of this paper, addressed in sections 5 and 6, are what we consider the five foremost criteria of Bradford Hill[4] causality for an iatrogenic pandemic. The remaining four aspects of Bradford Hill analysis are briefly reviewed from existing literature in section 7 on coherence and plausibility and in section 8 on experiment and analogy.

Essentially, iatrogenesis of the pandemic is coherent with, and does not violate, existing knowledge of pathology and epidemiology; the biological mechanisms are highly plausible, with some clinical experiments to validate them. In many ways, the current pandemic is analogous to the previous swine flu pandemic in 2009, except that the 2009 episode was not a pandemic, and it was without mass vaccination.

Section 9 contains a summary of preceding sections, with a tabulated synopsis of all nine Bradford Hill criteria discussed. The final section concludes that a strong case has been presented for the iatrogenic origins of the Australian COVID-19 pandemic.

2 COVID-19 data

This section explains why the Australian COVID-19 pandemic cannot be accurately assessed from COVID-19 data, because COVID-19 cases and infection were poorly defined. Therefore, COVID-19 data are scientifically flawed, but nevertheless they drove and continue to drive erroneous health policies.

A COVID infection has no definitive set of symptoms and was not detected by the presence of the SARS-CoV-2 virus, but was defined by a positive PCR test. However, a positive PCR test does not detect the presence of the SARS-CoV-2 virus which is the definitive pathogen of the COVID-19 disease. The CDC has explicitly made clear the following disclaimer:[5]

> *Since no quantified virus isolates of the 2019-nCoV were available for CDC use at the time the test was developed and this study conducted, assays designed for detection of the 2019-nCoV RNA were tested with characterized stocks of in vitro transcribed full-length RNA* (N gene; GenBank accession: MN908947.2) of known titer (RNA copies/µL) spiked into a diluent consisting of a suspension of human A549 cells and viral transport medium (VTM) to *mimic clinical specimen*.

Emphasis added. Consequently, COVID-19 cases may be cases of respiratory infections caused by other RNA viruses, which also implies that COVID cases and deaths may be wrongly attributed to the SARS-CoV-2 virus, wherever its controversial origin.

Deficiency of the PCR test has been acknowledged by the CDC in mid 2021 when it issued a Lab Alert[6] to plan a withdrawal of the test:

> After December 31, 2021, *CDC will withdraw* the request to the U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) of the CDC 2019-Novel Coronavirus (2019-nCoV) *Real-Time RT-PCR Diagnostic Panel*, the assay first introduced in February 2020 for detection of SARS-CoV-2 only.
>
> CDC encourages laboratories to consider *adoption of a multiplexed method* that can facilitate detection and *differentiation of SARS-CoV-2 and influenza viruses.*

Emphasis added. From 2022, instead of the PCR test which cannot differentiate between SARS-CoV-2 and influenza viruses, the CDC has suggested the use of a multiplexed method. A quadraplex method[7] was not discovered until early 2021, when the researchers claimed to have

simultaneously detected from clinical specimens two SARS-CoV-2 genes, as well as influenza A and influenza B viruses:

> To the authors' knowledge, *this is the first study to report a quadruplex rRT-PCR assay* for the detection of two SARS-CoV-2 genes, hIAV and hIBV with perfect clinical performance.

Emphasis added. It is unclear whether the research has been independently verified or whether commercial quantities of the quadraplex method for detecting SARS-CoV-2 have been produced or widely used since 2022. It is quite clear that COVID-19 data are scientifically flawed before 2022 everywhere and very likely since. Australian data continue to be flawed because PCR tests are still being used. The inability to distinguish between the detection of the SARS-CoV-2 and influenza viruses is a fundamental scientific uncertainty, which renders COVID-19 data scientifically flawed.

Adding to this uncertainty about what is identified in COVID infections and cases, there is also a substantial uncertainty about the titer (genetic fragments per unit volume) needed to define presence of the infection. Through a sufficient number of cycles of titer amplification, which is variable and not scientifically determined, the PCR test can nearly always return a positive result. Consequently, whether someone has a COVID infection at all is not clear from a PCR test.

For the first time in medical history, people who are perfectly healthy with no symptoms have been declared COVID cases, based solely on unreliable positive PCR tests. A person could have minute amounts of dead influenza viruses and be declared a COVID threat to public health.

On top of those fundamental uncertainties, there is a question of whether a particular COVID death is a death with COVID or from COVID in a typical case of the deceased having other comorbidities. Subjective judgement, distorted at times by financial incentives, creates uncertainties which can be removed objectively by autopsies, but they have been rarely performed.

Therefore, COVID cases and deaths cannot be used to characterize the pandemic, because the division of excess deaths into COVID and non-COVID causes appears arbitrary and inaccurate. Australian health policy has been based on misinformation from flawed COVID-19 data which are scientifically unsound.[9]

This paper focuses on all-cause mortality and excess deaths rather than COVID deaths as indicators of the severity of the Australian pandemic.

3 Data methodology

Even as unreliable as the COVID raw data are, Australian official COVID-19 data seen by the public are not even the raw data which are collated by state health authorities. They control and publish selected data in weekly and monthly reports without making available the raw data which are needed to independently verify the official data. These reports from health authorities may be misleading because of selection and classification biases, which have rendered invisible adverse events and deaths related to 'vaccines.'

For example, official reports allowed the national broadcaster ABC to claim falsely on prime-time television in July 2022 that the 'unvaccinated' are 16 to 37 times more likely to die than the doubly 'vaccinated'.[8] This misinformation was based on a key official data reporting flaw which came from classifying some deaths as 'unvaccinated' even though they had had COVID-19 injections and often multiple times.[9]

This paper avoids the processed data of health authority reports to eliminate their selection and classification biases. The main reliance is on data[10] from the national collector, the Australian Bureau of Statistics (ABS), which has the fewest conflicts of interest, but its data and reports are not accepted uncritically either, as will be illustrated below.

In scientific research the raw data and their sources should be publicly accessible or available and the methods of data analysis should be clearly disclosed so that

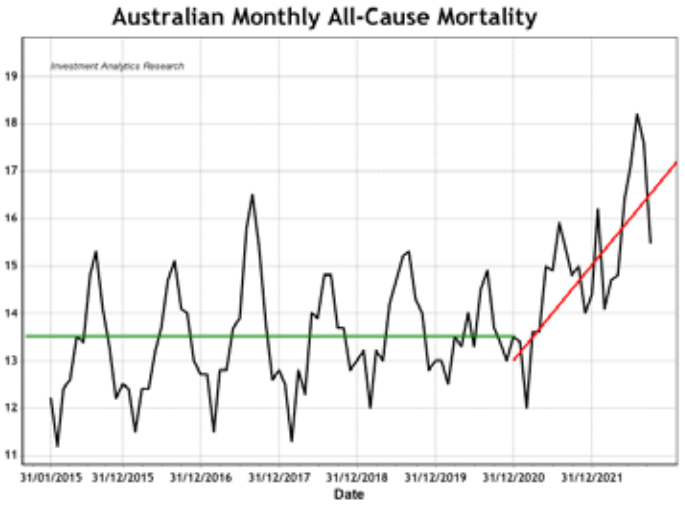


Figure 1

the conclusions of this or any other study can be reproduced precisely.

This study depends principally on the all-cause mortality data published by the ABS, from January 2015 to September 2022, the latest month of full reporting data. The raw data are shown in Figure 1, where the horizontal green line and the sloping red line have been added heuristically to suggest a 'regime change.'

The horizontal green line (for guidance) suggests that 2020 appears to be merely a continuation of the previous trend of relatively steady fluctuations in all-cause mortality. On a definition of pandemic based on excess mortality, there was no evidence of a pandemic in Australia in 2020, which could be called the pre-pandemic phase, followed by the pandemic phase starting in 2021 (the sloping red line).

The above raw data are used to calculate excess mortality in this paper, instead of simply accepting the official excess mortality data published by the ABS. The ABS has changed its baseline definitions (in other words, moved the goal posts) for calculating 2022 excess mortality in an inconsistent manner, without providing adequate justification.

Normally, the baseline for calculating excess mortality is the average of the previous five years, but the baseline for 2022 has been defined by the ABS as the average of four years, 2017-2019 and 2021, without adequate reasons :[10]

> Throughout this report, counts of deaths are compared to an average number of deaths for previous years. In this report, data for 2021 is compared to an average number of deaths recorded over the 5 years from 2015-2019 as was the case in previous publications. Data for 2022 is compared to a baseline comprising the years 2017-2019 and 2021. *2020 is not included in the baseline for 2022 data because it included periods where numbers of deaths were significantly lower than expected.*

Emphasis added. Note that the arbitrary exclusion of 2020, a year where 'numbers of deaths were significantly lower than expected', raises the baseline and therefore lowers excess mortality statistics for 2021 and 2022, creating a misleading impression of a less serious pandemic.

The five-year averages of 2015 to 2019 are used uniformly as the baseline throughout this study to assess the effect of COVID-19 on Australian mortality. Consequently, our excess mortality statistics for 2022 are different from official ABS statistics. Even though the differences are not great, a consistent baseline is used throughout in this paper for sake of scientific clarity.

The annual excess mortality for Australia from 2015 to the present is shown in Figure 2.

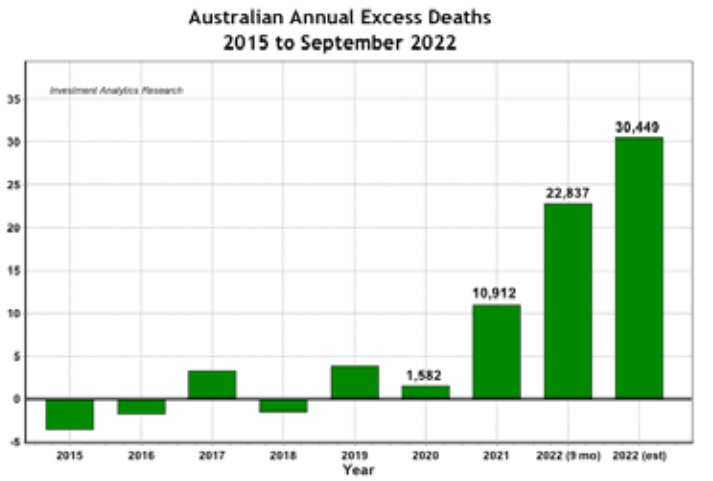


Figure 2

The annual excess mortality for 2020 was well within the range of normal statistical fluctuations and therefore validates the proposition that there was no pandemic in Australia, even though there were about 900 COVID-19 deaths (usually revised lower by the ABS over time) in 2020.

Clearly, dramatic rises in excess deaths have occurred since 2021, with the last bar (in Figure 2) being an annual estimate based on nine months of actual data.

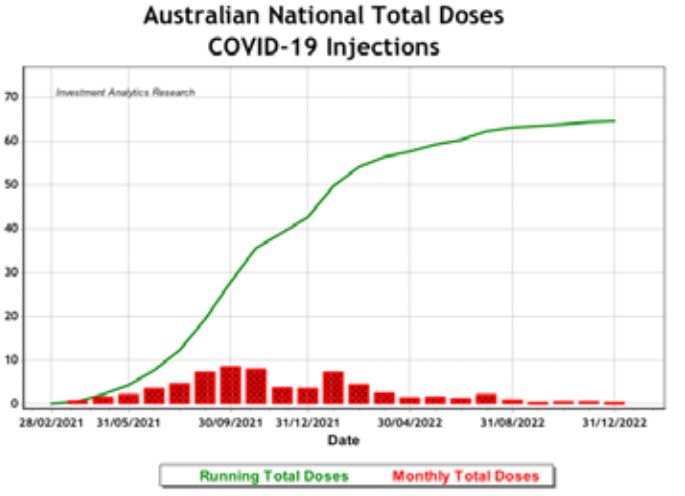


Figure 3

Relative to excess mortality in 2020, 2021 was nearly 7-fold and 2022 is already over 14-fold and potentially more than 19-fold. The data on excess mortality also validate that the Australian pandemic phase started in 2021, with the 2021 and 2022 total excess death toll likely to reach over 41,000, or 26 times that of 2020.

Obviously, the demarcation between the pre-pandemic phase in 2020 and the pandemic phase since 2021 is the elephant in the room – mass COVID-19 injections for most of the Australian population. To study their relationship to excess mortality, raw data on total national doses of COVID-injections administered over time have been obtained from a third-party data aggregator *CovidBaseAU*,[11] which also supplies data to international data providers such as *Our World in Data*. The data are shown in Figure 3.

Over 64 million doses have been administered to a population of 25.8 million. The two peaks of mass COVID injections occurred in September 2021 for the initial drive and in January 2022 for the first booster drive. These drives will be seen below to be correlated to peaks in excess deaths about five months later.

The above raw data in Figure 1-3, which are largely free from data manipulation, are the main sources from which data analysis is performed transparently in the rest of this paper to investigate the iatrogenesis of the Australian COVID pandemic.

4 The pre-pandemic phase

The iatrogenic hypothesis of the Australian pandemic depends necessarily on objective evidence that there was no significant excess mortality before government intervention with mass COVID-19 injections. The evidence is already apparent in Figure 2 above, where all-cause mortality in 2020 was well within normal expectations.

While there was no pandemic in 2020, could the 900 COVID-19 deaths recorded in 2020 presage a pandemic to develop from the novel coronavirus? A seasonality analysis with Australian mortality data raises serious doubt about just how 'novel' the SARS-CoV-2 virus is in Australia. Its closest relative, the 2003 SARS (now called SARS-CoV-1) was declared an 'outbreak,' not even a pandemic. Respiratory viruses mutate relatively frequently, so when is a mutation 'novel'? COVID-19 viruses had many variants; why are they not 'novel' viruses?

Respiratory diseases are seasonal, with most death occurring in late winter, the months of August and September in the Southern Hemisphere, when respiratory diseases commonly strike near the end stages of life. The typical pattern of seasonality is shown by the blue bars in Figure 4, based on five-year averages from 2015 to 2019.

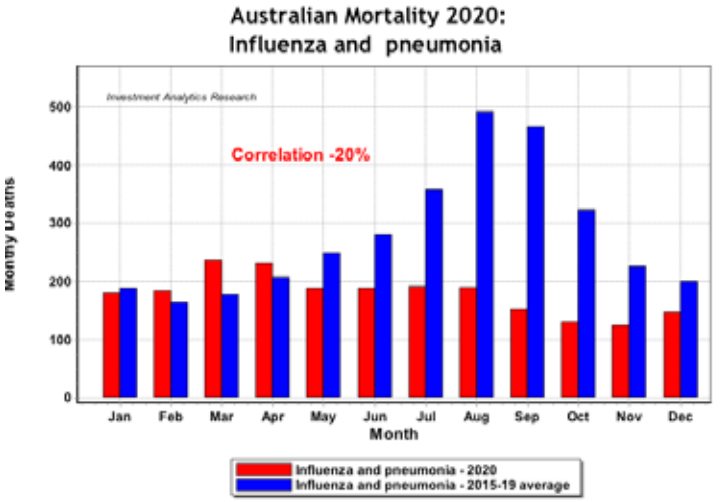


Figure 4

By comparison, 2020 was a very odd year, when deaths from influenza and pneumonia (red bars in Figure 4) substantially disappeared for several months around their normal peaks in late winter. The correlation between normal fluctuations and 2020 fluctuations was negative, at -20%, indicating a substantial seasonal anomaly.

However, COVID-19 is a respiratory disease, with similar symptoms to influenza and pneumonia (I&P) and there were surges in supposedly COVID

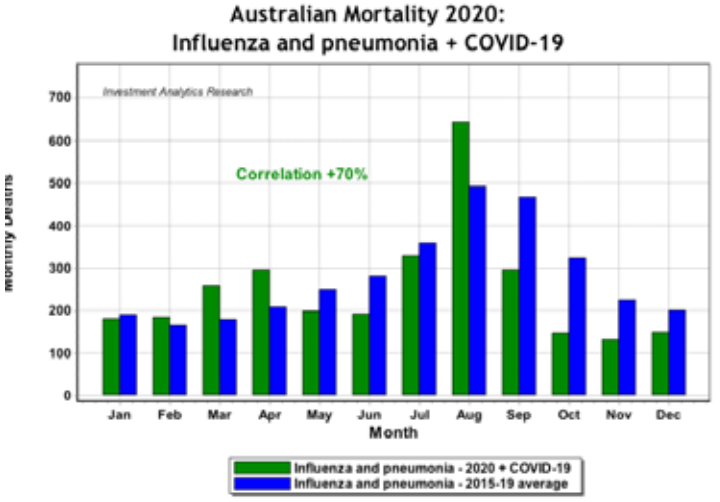


Figure 4

deaths around August in 2020, particularly in Victoria. If the deaths of I&P and COVID-19 are added together, then the comparison to normally-expected seasonality is shown in Figure 5.

In the I&P comparison in Figure 5, the green bars including COVID deaths are now consistent with the blue bars representing the expected seasonality pattern of previous years, with a positive correlation of +70%.

In view of the poorly-defined characteristics of COVID-19 infection and the subjective attribution of COVID-19 deaths as discussed in section 2, there is a strong possibility that COVID deaths may have been substantially misclassified from I&P deaths.

This likelihood of misclassification is very high because I&P deaths are themselves not clinically well-defined,[12] as evident in Table 1.

Table 1

CHAPTER X Diseases of the respiratory system (J00-J99)	2019	2020
Diseases of the respiratory system (J00-J99)	15,330	12,721
Influenza and pneumonia (J09-J18)	3,855	2,287
Influenza, virus not identified (J11)	249	7
Pneumonia, organism unspecified (J18)	2,721	2,157

Table 1 is a very small and partial extract from an extensive ABS data table listing detailed causes of doctor-certified deaths for 2019 and 2020 in Australia.[12] Note the codes in the brackets indicate categories and sub-categories (indented). In 2019, there were 3,855 deaths from influenza and pneumonia of which 2,970 deaths (77%) had no pathogen identified.

Note that this paper makes no assertion about whether the COVID-19 virus or disease exists or otherwise. The evidence suggests that COVID-19 symptoms and diagnosis are so imprecise and so much like cases of I&P that they may have been easily misclassified, as discussed in section 2.

Importantly, there are strong financial incentives for hospitals to reclassify I&P patients as COVID-19 patients, because the Australian Government had provided $4.8 billion for COVID-19 pandemic response, stating:[13] 'The full resources of our world-class health system – a blend of public and private systems – are needed to focus on treating COVID-19 patients', indicating more COVID-19 patients would mean more funding to hospitals.

Finally, the narrative that Australian public health measures such as masking and lockdowns were responsible for reducing excess deaths in 2020 has little credibility, for several reasons. First, it was against the recommendations of the global pandemic preparedness exercise conducted in 2019 Event 201, which

not only did not recommend lockdowns, but instead recommended open borders:[14]

> Countries, international organizations, and global transportation companies should work together to *maintain travel and trade during severe pandemics.* Travel and trade are essential to the global economy as well as to national and even local economies, and they should be maintained even in the face of a pandemic.

Emphasis added. Also, tens of thousands of highly credentialled medical researchers and doctors have signed *The Great Barrington Declaration*[15] recommending against masking and lockdowns, in favour of 'focused protection'. Overall, large amounts of research[16] have shown that there is no clear evidence that masking and lockdowns are effective, with countries such as Sweden ignoring such measures, performing overall none the worse when compared with other countries. If those public health measures were so good, why do governments even need 'vaccines'?

In summary, on statistics alone, there was no clear evidence of a new deadly coronavirus in Australia in 2020. Regardless of the precise nature or cause of COVID deaths, their effect on excess mortality in 2020 was insufficient to characterize that year as a pandemic.

5 The pandemic phase

The pandemic phase in Australia began in 2021 with rising all-cause mortality and excess mortality (see Figure 1 and Figure 2). Also, beginning in 2021 was the start of mass COVID-19 injections, which governments called 'safe and effective vaccines', for a pandemic just shown non-existent in 2020.

The coincidental increases in excess mortality and doses of injections administered (see Figure 3) are investigated here for possible iatrogenic causality. Essentially, the raw data shown in Figures 1-3 are reassembled into a new dataset to reveal the relationship between excess deaths and COVID injections as seen in Figure 6.

Overall, there was a negative correlation of -17% between monthly doses of injections and monthly excess mortality, with best evidence of correlation occurring in January 2022 and some evidence of correlation in the first half of 2021, when mass injections started. Contemporaneous correlation should not be expected because there is normally a time-lag between medication (the cause) and its effects, as will be shown below.

However, the close correlations observed in some periods suggest the existence of immediate effect of the injections on mortality probably due to anaphylaxis

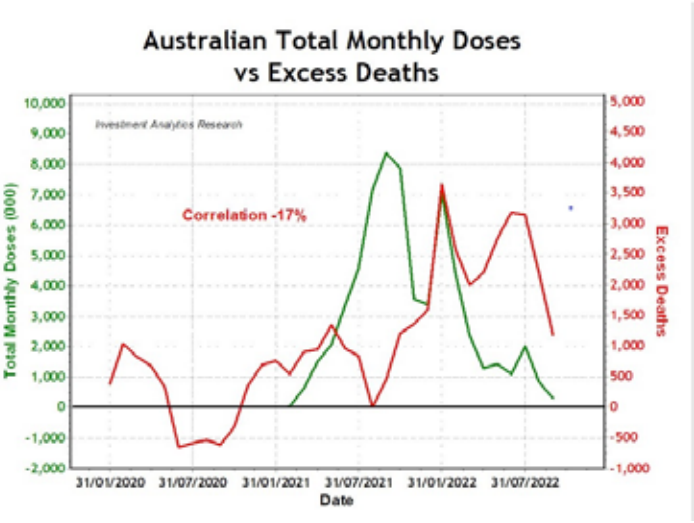


Figure 6

or other pre-conditions as reported in OpenVAERS in the USA.[17] There may be more than just a concurrent correlation between mass injection drives and deaths, which have been discussed in a previous paper.[9] The small peak in excess deaths in the first half of 2021, when COVID deaths were largely absent per ABS data,[10] has been attributed to non-COVID deaths, as seen as the first peak in Figure 7.

As mass injections were rolled out in 2021, there was a surge in deaths of the

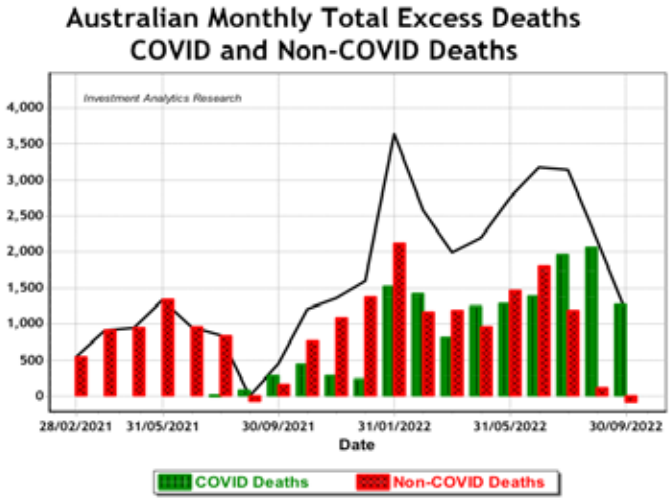


Figure 7

elderly, particularly those in the 85+ age group. Those who were already frail with chronic inflammation and numerous comorbidities easily succumbed to the extra challenge presented by the injections. Whether they had COVID infections or not, it was probably not unreasonable to assume they died from pre-conditions, even though an attribution to COVID deaths would have been inconvenient to the narrative of 'vaccine protection'.

The excess death peak in January 2022 may be due to the combined effects of both the initial doses of injection in September 2021 and the subsequent boosters in January 2022 owing to the phenomenon of 'pathogenic priming.'[18] There may be a combination of both a concurrent effect of fatal inflammation and a lagged effect of immune suppression, to be discussed below.

That is, the initial doses of injection may have weakened the immune system of the recipients to make them more vulnerable to subsequent challenges introduced for example by the boosters, a phenomenon also known as 'antibody dependent enhancement' of disease.[19,20] Indeed, if the data for total monthly doses were time shifted forward by five months, the two datasets (as Figure 6) now overlap well in Figure 8.

The rapid rise in excess mortality in January 2022, which coincided with

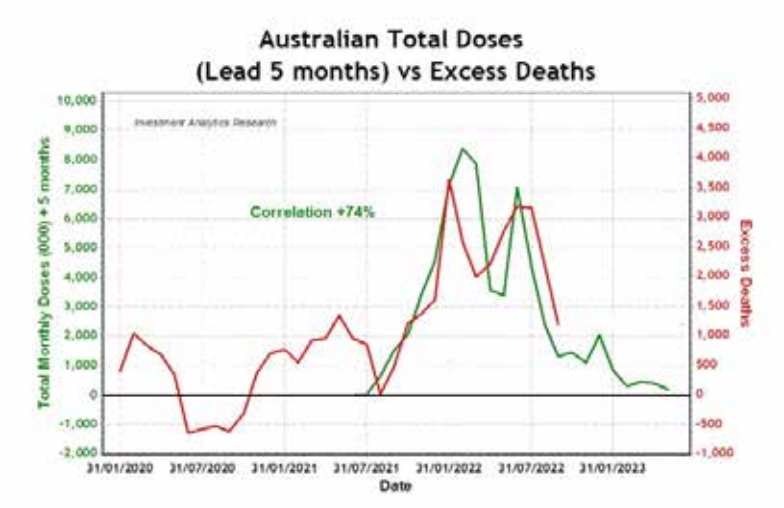


Figure 8

the first booster campaign, was correlated with the peak rate of COVID-19 injection, which occurred in September 2021. A secondary injection peak from the first booster campaign was correlated another five months later with a secondary peak in excess mortality in July 2022.

The maximum correlation between COVID-19 injections and excess deaths at +74% occurs for a five-month lag. From analysis, the correlation for a four-month lag is 61%, while for a six-month lag it is 64%. As a result, the evidence suggests that the five-month lagged effect on excess mortality is stronger than the concurrent effect or other lagged effects due to the COVID injections.

The five-month lag has been observed briefly in US and UK datasets, but has not been supported by more detailed investigations, as is being done here.

Metaphorically, the high correlation in January 2022 between the booster injections and deaths is likely to be the result of the second of a one-two knockout punch, where the first punch did the most damage five months earlier by immune suppression (see discussion below) and then by the second punch of the boosters which quickly delivered the *coup de grace* to their victims.

As an example, New South Wales data show[8] that the two-dose population was dying at a rapid rate of several hundred per week during the first booster campaign in January 2022, while very few deaths were recorded from the boosters. The boosters were lethal to some of the immune-suppressed two-dose population, but those deaths were wrongly registered as two-dose deaths through a flawed data reporting convention,[9] where injections were recognized only after weeks of delay.

Those who survived the first boosters would have had their immune system further weakened making them susceptible to viral infections and harm of the second boosters, which contributed later to the second peak in excess mortality in July 2022. The more injections anyone takes the more likely they will sustain iatrogenic injuries and death. Many Australians have learned from their actual experience, ignored official advice, and have become more hesitant of repeated injections.

Fortunately, because of falling rates of COVID-19 injections since July 2022, the empirical evidence may be predicting good news for lower rates of excess mortality (with data to be released) for the rest of 2022 per the injection data. Except for a blip in January 2023, excess mortality should continue to fall, as presaged by the tail-end of the green curve in Figure 8. (This prediction has been confirmed by the release of data[10] for October and November 2022, after the completion of the research for this paper.)

The data also suggest that the naïve proportional estimate of excess deaths for the whole of 2022 in Figure 2 is likely to be an over-estimate because of rapidly falling rates of injection five months earlier. The trend of falling excess mortality should continue, unless official advice succeeds in persuading the

public to accept more boosters, which would be the fifth dose for many.

The stronger correlation and temporality with the five-month lag satisfy two of the main criteria of Bradford Hill causality,[4] which are the 'strength' of high correlation and 'temporality' satisfied by a regular five-month lag of the excess mortality effect following the COVID-19 injection cause.

Another important Bradford Hill criterion is 'biological gradient' in medicine, which is the existence of an expected, monotonic dose-response relationship; that is, higher doses should lead to stronger responses. This criterion is met statistically in Figure 8, where excess mortality rises and falls with doses administered. The dose-response relationship can be made mathematically more precise by an ordinary-least-squares (OLS) regression which is statistically significant with a *p*-value of 0.0015 as shown in Figure 9.

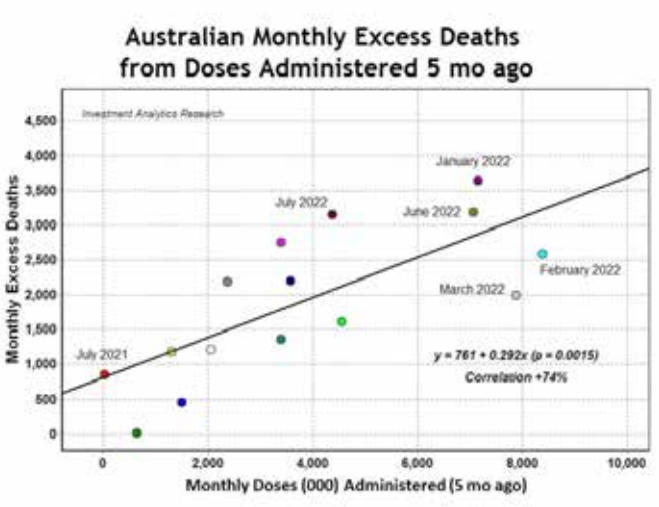


Figure 9

On average, the above dose-response relationship suggests, for example, that five million doses administered in a month nationally would lead on average to 2,221 excess deaths five months later, with a standard deviation of 705 excess deaths or a likely range between 1,516 and 2,926.

In summary, in meeting three main Bradford Hill criteria for causality a strong case, based on statistical data alone, has been made for the iatrogenesis of excess mortality in the Australian COVID-19 pandemic.

6 Consistency and specificity

As shown above, Australian data have displayed consistency in causal associations over time. Are similar associations observed in other places under similar conditions? Consistency is another criterion which Bradford Hill[4] thought was important to consider.

International comparisons of the relationship between COVID-19 injections and excess mortality are made difficult by heterogeneity of the data. Some countries, such as those in Africa, have largely avoided mass injections, while other countries, such as those in the Pacific Islands as well as Africa, have irregular excess mortality statistics. Even among those countries which have data both on doses of injection and on excess mortality, some report weekly, while others report monthly and their reporting dates and periods of available data are typically different.

From *Our World in Data*,[22] there are about two dozen countries, including most of the large developed countries, which have comparable abundance of data to perform a cross-sectional analysis. The level of COVID injection for any country is taken to be the latest reported total doses administered per hundred of the population. The average monthly excess mortality is calculated from the increase in cumulative excess mortality per million between the earliest injection start date and the latest report date, which vary between countries.

While the international dataset is far from complete and the data of selected

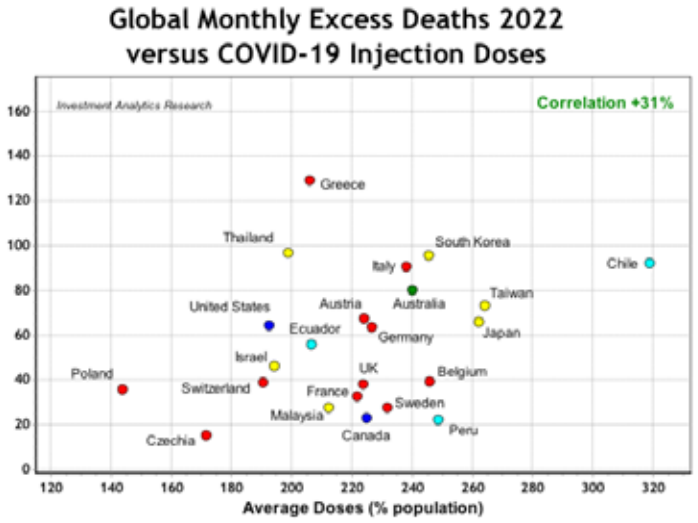


Figure 10

countries with sufficient quantity are likely inconsistent in quality, a positive dose-response relationship appears discernible across the selected countries as shown in Figure 10.

Country colours refer to their continents. So far in 2022 the Australian excess mortality per million population is about double that of the United Kingdom, but Australians are more highly 'vaccinated'. Australia with its higher dosage also leads its US, UK and Canadian partners in excess deaths. A clear dose-response relationship appears mildly consistent at +31% correlation across 23 countries.

Another useful criterion of Bradford Hill causality is 'specificity', which is related to the question of whether there are competing causes for the excess deaths, with similar strengths of association. Note that specificity is not a necessary criterion, but one which, if satisfied, helps to draw conclusions for the most probable cause. Is iatrogenesis the strongest and most specific explanation for the observed excess mortality?

Bradford Hill[4] gave the example of smoking causing lung cancer, which has potentially many possible causes, but smokers have statistically significant higher incidences of lung cancer than non-smokers. Therefore, smoking is an important specific cause of lung cancer. The close association between COVID injections and excess deaths shown above suggests a similar argument prevails for iatrogenesis.

Classification bias has resulted in flawed data reported by the health authorities,

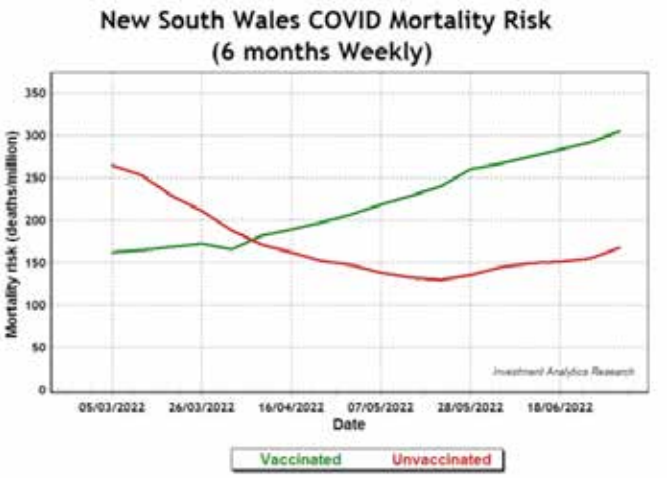


Figure 11

which have misled the public to believe most excess deaths are from the 'unvaccinated'.[8,9] As mentioned above, the national broadcaster ABC wrongly stated on prime-time television that the 'unvaccinated' are 16-37 times more likely to die than the 'doubly vaccinated'.

Australian adults (age 16+) nearly all (97.5%) have had at least one dose of the injection.[11] Is it likely that the remaining 2.5% of the adult population are responsible for most of the excess deaths?

New South Wales Health has COVID death data segregated by 'vaccination status' which is defined by the number of doses.[8,9] The data permit the 'unvaccinated' to be properly defined as those without any injections. The data show that, by mid 2022, the 'vaccinated' had about double the COVID mortality risk compared to the 'unvaccinated', as seen in Figure 11.

This COVID injection enhancement of COVID deaths extends to excess mortality and as the fifth dose or the third booster rolls out across Australia from March 2023, excess mortality is expected to remain elevated. As Bradford Hill noted,[4] this is a 'specificity in the magnitude of association.'

7 Coherence and plausibility

On Bradford Hill's coherence and plausibility, the suggestion of iatrogenic origin of excess deaths following five months after COVID injections does not contradict any research on 'vaccine safety'. The clinical trials conducted were much shorter than five months. For example, the Pfizer BNT162b2 trial[23] was between July 27th 2020 and November 14th 2020, with a data cut-off date of October 9th 2020.

That is, the Pfizer trial data analysed were conducted over eleven weeks or 77 days, about half of the time necessary for fatalities to occur per the above empirical findings, so the suggested iatrogenesis is coherent and not in conflict with any known facts.

Are there any plausible biological mechanisms which could explain the causal effect of COVID-19 injections on the excess mortality of the young and healthy? In the past three years, there has been a deluge of research published on how the spike protein, either from the assumed SARS-CoV-2 virus infection or generated from the mRNA injections, could lead to inflammation in various organs causing death.

Most of the proposed mechanisms are evidential, plausible and coherent with existing knowledge on the cutting edge of medical research. However, the 'speed of science' requires many more years of replication and validation of the research to sort out the best explanations for the ever-accumulating evidence. It is beyond

our knowledge or the scope of this paper to comment on the vast literature, except to mention some research findings which may be relevant to the statistical observations presented in this paper.

Most theories of the iatrogenesis of the COVID injections revolve around mechanisms for how the spike protein can cause a suppression of the immune system called 'pathogenic priming'[18] or 'antibody dependent enhancement'.[19, 20] Essentially, after repeated infections or mRNA injections, the body adjusts to the pathogen, or similar ones, by down-regulating the immune system.

In a recently published clinical study[21] of the mRNA injections, production of neutralizing IgG3 antibodies against the spike protein was observed to switch over time to the production of non-neutralizing IgG4 antibodies. Thus, the class switching may reduce the rate of clearance of the toxic spike protein which may accumulate sufficient titers to cause pathogenesis and mortality.

The five-month lag between injections and mortality found in this paper may be related to the switching time between the classes of antibodies; this was not the focus of the cited clinical study, but it provides some useful indications. The levels of IgG antibodies were measured 10 days and 210 days after the second mRNA dose.

Class switching did not occur at 10 days, but was observed at 210 days, which suggests that it is a relatively slow process.[21] However, some cases of breakthrough infection 70 days after the second dose suggest the immuno-suppression effect may already occur meaningfully much earlier.

The recommended interval between the first and second dose of mRNA injections in Australia is between 8 to 12 weeks. If the antibody class switching mechanism were responsible for the excess deaths five months later, then the mechanism would suppress immunity significantly after about 100 days. In summary, the class switching to IgG4 antibodies is a plausible, but not a proven, mechanism to explain the observed immune suppression of COVID-19 injections, a topic worthy of further research.

8 Experiment and analogy

By 'experiment', Bradford Hill [4] refers to any laboratory (*in vitro*) or clinical (*in vivo*) evidence to support the epidemiological association between cause and effect. In the current context of causes of excess mortality, 'experiment' should be taken to mean post-mortems and autopsies to show the connection between COVID injections and deaths.

Australian governments have deliberately discouraged such 'experiments' because they may lead to findings which cause 'vaccine hesitancy'. For example,

Australian doctors have been threatened with fines of up to $20,000 for using serological tests to verify the results of the PCR tests for COVID-19 diagnosis.[24] Nevertheless, the scientific imperative is strong enough to have led to several post-mortem studies[26,29] to discover the smoking-gun evidence of spike proteins from COVID injections.

The SARS-Cov-2 virus is defined by a full genome sequence published by the Wuhan Institute of Virology.[25] Without any claim having been independently validated, no virus has ever been isolated from COVID-19 patients which matches exactly the genome sequence, nor has the spike protein from infections been exactly matched to that of the SARS-CoV-2 virus. The messenger RNA which is synthesized and manufactured to go inside the lipid nanoparticles (LNP) of the mRNA injections is presumably conformal to the relevant part of the published sequence.

The spike proteins found in tissues from autopsies may originate, *a priori*, from infections and or from injections. In view of the way the PCR test was developed, as discussed in the introduction of this paper, without genetic analysis, the spike proteins from a COVID-infected person may have come from an influenza virus, which differs from a coronavirus mainly in having a segmented, rather than continuous, genome.

If COVID injections suppress the immune system and hinder the clearance of the pathogenic spike proteins, and, indeed, manufacture even more spike proteins by the body's own cells, then post-mortems and autopsies should provide the evidence from significant quantities of spike proteins.

Indeed, from autopsies, the absence of the nucleocapsid IgG/IgM and their characteristic morphological features of COVID-19 is the indicator of mRNA injection origin of the spike proteins.[26-29] The observed time lags after injections of deaths occurring within days to several months are consistent with the combination of a short-term causality and a long-term causality discussed above.

The autopsy experiments, where COVID morphologies are absent, without viral nucleocapsid protein and the antibodies associated with them, have largely deprecated the explanation that the COVID disease or 'long COVID' is the cause of those deaths. The young have often died suddenly from myocarditis and pericarditis, on the sporting fields or in their sleep, after mRNA injections, but without any signs of infections.[29] An analogy to the current COVID-19 pandemic is the 2009 Swine flu pandemic from the H1N1 influenza virus. Then, as now, the pandemic was called, based not on fact, but on expectations of a highly infectious and very deadly disease projected by the Oxford computer models. The main difference is that the 2009 'pandemic' was never allowed to be

transformed to an iatrogenic pandemic and it quickly died out on its own accord, amounting ultimately to a weaker form of the seasonal influenza. The episode had more cases worldwide, but fewer deaths (about 18,000) and a much lower case-fatality rate than a seasonal flu.[30] On an excess mortality definition, the 2009 Swine flu season was not a pandemic.

The main difference between then and now is that mass 'vaccination' did not play a significant role in 2009, thus avoiding an iatrogenic pandemic, as now. In 2009, production of 'vaccines' and their injections into the population were not fast enough or widespread enough before the Swine flu infections died out on their own accord.

Between 2009 and 2020, governments were 'educated' for 'pandemic preparedness', which meant preparation for legally-declared emergency measures, unimpeded by the 'speed of science'. For example, lockdowns were enforced everywhere without scientific justification,[16] and this also had the effect of preventing the development of herd immunity from isolation, thus prolonging the period of infection. In the extended time available, 'vaccines' were developed under 'Operation Warp Speed' and rushed to the market, side-stepping standard procedures of longer-term testing to ensure safety.

The analogy to the 2009 swine flu is that the COVID-19 pandemic might not have continued or even existed (in such as the 2003 SARS outbreak), had there not been mass mRNA injections to cause and perpetuate the COVID-19 pandemic.

9 Bradford Hill analysis

Austin Bradford Hill suggested[4] his nine 'viewpoints' to be aspects considered for causality. He did not call them 'criteria', a term which has been used in this paper for simplicity and convenience. Bradford Hill refrained from calling them nine criteria, because they are neither necessary nor sufficient conditions to make hard and fast decisions on causality. They are aspects to address when examining alternative causal hypotheses.

In science, the set of available facts at any time determines what is the best explanation and Bradford Hill has suggested some objective aspects to help deciding on alternative explanations. This paper has reported some highly significant facts which may not have been recognized yet. These facts have come from epidemiological data when they have been presented without obfuscation by manipulation and classification, as in official health authority reports.

Previous sections of this paper have been devoted to addressing Bradford Hill 'criteria' for assessing the iatrogenic hypothesis for Australian excess mortality since 2021. The analysis in previous sections is summarized in Table 2.

The main contributions to existing knowledge of the Australian COVID-19 pandemic are contained in sections 5 and 6, where the first five Bradford Hill criteria are addressed. These criteria are probably foremost because they apply equally to hard sciences such as physics. Criteria 6 to 9 are reviewed in Sections 7 and 8 through existing literature, which can be seen to support generally the iatrogenic hypothesis advanced in this paper.

Criterion	Evidence	Comment
1. Strength	Section 4, Figure 8	Monthly correlation between doses of injections and excess deaths at +74%
2. Consistency	Section 4, Figure 9; Section 5, Figure 10	Strong correlations between injections and excess deaths exist over time and across many countries.
3. Specificity	Section 5, Figure 11	Iatrogenic excess deaths have few other competing explanations, with the "vaccinated" having higher mortality risk than the "unvaccinated".
4. Temporality	Section 4, Figures 6 & 8	Consistent five-month lag of excess deaths following COVID injections.
5. Biological gradient	Section 4, Figure 9	Consistent dose-response relationship found in data.
6. Plausibility	Section 6	Abundant research indicates the injections suppress immunity. Antibody class switching from IgG3 to IgG4 leads to non-neutralization of spike proteins.
7. Coherence	Section 6	Neither the safety signals found here, nor the suggested underlying pathology contradicts any existing facts.
8. Experiment	Section 7	Autopsies show the pathology of spike proteins produced explicitly by mRNA injections.
9. Analogy	Section 7	Swine flu 2009 petered out naturally without mass "vaccination".

On the basis that the Australian pandemic is iatrogenic, which caused the observed excess mortality, then it follows also that harm, or risk of harm, outweighs any benefit of the COVID injections. This can be shown formally by the equation for mortality risk and benefit which is expressed as follows:

$$\textit{Lives lost (L) from side effects of injection} - \textit{Lives saved (S) from disease mitigation} = \textit{Excess Deaths (X)}$$

or $L-S=X$. Excess deaths X are known to be large, but L and S are unknown from the data. Since $X >> 0$, it follows that $L-S >> 0$ or $L >> S$, hence $L/S >> 1$. A mortality risk-benefit ratio which may be defined by L/S is very high.

Therefore, because of the very large excess deaths following Australia's policy of mass COVID injections, lives lost far exceed lives saved; the mortality risk-benefit ratio is very high. Further research is needed to quantify this ratio for health authorities.

10 Conclusion

Australian health policy has been based on misinformation from flawed COVID-19 data which are scientifically unsound. Based on sound mortality data, the Australian COVID-19 pandemic did not begin until the advent of mass mRNA injections in 2021. It is ironic that mass injections which were introduced to mitigate a non-existent pandemic in fact created a real iatrogenic pandemic. This study, backed by a Bradford Hill analysis, has shown that more injections administered to reduce the pandemic had the opposite effect of causing more excess deaths to increase the pandemic.

The very large excess deaths observed from the data imply that the mortality risk-benefit ratio from COVID injections is very high. That is, the harm or risk realized has far outweighed any benefit from COVID injections.

This study has introduced a very simple, but robust, methodology, which should be used by other countries, particularly those in Figure 10 which appear to have adequate data, to replicate and investigate the likely iatrogenic origins of their own pandemics. Billions of lives in the world are at stake from the potential findings of the research.

References

[1] World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020, News releases. Retrieved from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 (accessed 23 January 2023)

[2] World Health Organization. Pandemic Preparedness, Communicable Disease Surveillance & Response (CSR), 2 February 2003. Retrieved from: http://web.archive.org/web/20030202200410/http:/www.who.int/csr/disease/influenza/pandemic/en/index.html

[3] Roos R. Pfizer exec laughs when asked whether they knew their product stopped transmission prior to release. Retrieved from: https://www.youtube.com/watch?v=2YagXbprzFE

[4] Hill AB, The environment and disease: association or causation? Proceedings of the Royal Society of Medicine (1965) 58, 295–300. Retrieved from: https://journals.sagepub.com/doi/epdf/10.1177/003591576505800503

[5] Centers for Disease Control and Prevention. CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel, FDA News Release. Retrieved from: https://www.fda.gov/media/134922/download

[6] Centers for Disease Control and Prevention. 07/21/2021: Lab Alert: Changes to CDC RT-PCR for SARS-CoV-2 Testing, CDC's Laboratory Outreach Communication System (LOCS). Retrieved from: https://www.cdc.gov/locs/2021/07-21-2021-lab-alert-Changes_CDC_RT-PCR_SARS-CoV-2_Testing_1.html

[7] Ni M, Xu H, Luo J, Liu W, Zhou D. Simultaneous detection and differentiation of SARS-CoV-2, influenza A virus and influenza B virus by one-step quadruplex real-time RT-PCR in patients with clinical manifestations. Int J Infect Dis. 2021;103:517-524. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7836965/pdf/main.pdf

[8] Sy W. Mortality risk of COVID-19 injections: evidence from New South Wales and England, Academia, 30 July 2022. Retrieved from: https://www.academia.edu/83924771/Mortality_risk_of_COVID_19_injections_evidence_from_New_South_Wales_and_England

[9] Sy W. Data reporting flaw in plain sight distorting COVID-19 mortality statistics, Academia, 25 August 2022. Retrieved from: https://www.academia.edu/85597731/Data_reporting_flaw_in_plain_sight_distorting_COVID_19_mortality_statistics

[10] Australian Bureau of Statistics, Provisional Mortality Statistics, Released 22/12/2022. Retrieved from: https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-sep-2022

[11] CovidbaseAU, Australia COVID-19 Vaccinations. Retrieved from: https://covidbaseau.com/vaccinations/

[12] Australian Bureau of Statistics, Causes of Death, Australia, Released 24/06/2020 and 29/09/2021, Retrieved from: https://www.abs.gov.au/statistics/health/causes-death/causes-death-australia

[13] Department of Health. Supporting our Hospitals – COVID-19 pandemic response. Australian Government Budget 2020-2021. Retrieved from: https://www.health.gov.au/sites/default/files/documents/2020/10/budget-2020-21-supporting-our-hospitals-covid-19-pandemic-response.pdf

[14] Event 201, Public-private cooperation for pandemic preparedness and response, Recommendations. Retrieved from: https://www.centerforhealthsecurity.org/our-work/exercises/event201/recommendations.html

[15] Kulldorff M, Gupta S and Bhattacharya J, The Great Barrington Declaration. Retrieved from: https://gbdeclaration.org/#read

[16] Herby J, Jonung L and Hanke S, A Literature Review and Meta-Analysis of the Effects of Lockdowns on COVID-19 Mortality, Johns Hopkins Institute for Applied Economics, Global Health, and the Study of Business Enterprise. Retrieved from: https://sites.krieger.jhu.edu/iae/files/2022/01/A-Literature-Review-and-Meta-Analysis-of-the-Effects-of-Lockdowns-on-COVID-19-Mortality.pdf

[17] OpenVAERS, VAERS COVID Vaccine Mortality Reports. Retrieved from: https://www.openvaers.com/covid-data/mortality

[18] Lyons-Weiler J. Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity, J Transl Autoimmun, 3 (2020), p. 100051, Retrieved from: https://reader.elsevier.com/reader/sd/pii/S2589909020300186?token=DFCD78FD4DC4E-12CAAFB482AB98C6FA67E0CEC94AA372FE8B36DEE61E8B80A99558B4A611752EE8E6B189B4130EDABA1&originRegion=us-east-1&originCreation=20230128052337

[19] Wen J, Cheng Y, et al., Antibody-dependent enhancement of coronavirus, Int J of Infect Dis 100 (2020) 483–489. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7483033/pdf/main.pdf

[20] Ricke D, Two Different Antibody-Dependent Enhancement (ADE) Risks for SARS-CoV-2 Antibodies, Frontiers Immun, Vol. 12, 640093. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943455/pdf/fimmu-12-640093.pdf

[21] Irrgang P, Gerling J, et al., Class switch towards non-inflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination, Sci. Immunol. 8, eade2798 (2023) 27 January 2023. Retrieved from: https://www.science.org/doi/pdf/10.1126/sciimmunol.ade2798

[22] Ritchie H, Mathieu E, et al. Data on COVID-19 (coronavirus) by Our World in Data, OurWorldInData.org. Retrieved from: https://github.com/owid/covid-19-data/tree/master/public/data

[23] Polack FP, Thomas SJ et al. Safety and efficacy of BNT162b2 mRNA Covid-19 vaccine, The New England Journal of Medicine, December 16, 2020, Vol. 383, No. 27. Retrieved from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa2034577?articleTools=true

[24] Calafiore S, GPs face $20k fines for using serology tests to diagnose coronavirus, AUSTRALIAN DOCTOR NEWS, 15/04/2020. Retrieved from: https://www.rcpa.edu.au/Library/COVID-19-Updates/COVID-19-Useful-Resources/Docs/GPs-face-$20k-fines-for-using-serology-tests-to-di.aspx

[25] Wu F, Zhao S et al. Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome, National Library of Medicine, NCBI Reference Sequence: NC_045512.2. Retrieved from: https://www.ncbi.nlm.nih.gov/nuccore/NC_045512

[26] Hansen T, Titzea U, et al., First case of postmortem study in a patient vaccinated against SARS-CoV-2, Int. J. of Infectious Diseases 107, 172–175 (2021). Retrieved from: https://www.sciencedirect.com/science/article/pii/S1201971221003647

[27] Hirschbühl K, Schaller T, et al., High viral loads: what drives fatal cases of COVID-19 in vaccinees? – an autopsy study. Mod Pathol 35, 1013–1021 (2022). Retrieved from: https://www.nature.com/articles/s41379-022-01069-9

[28] Palmer M and Bhakdi S, Vascular and organ damage induced by mRNA vaccines: irrefutable proof of causality, Publications of Doctors for COVID Ethics, August 19, 2022. Retrieved from: https://doctors4covidethics.org/vascular-and-organ-damage-induced-by-mrna-vaccines-irrefutable-proof-of-causality/

[29] Schwab, C., Domke, L.M., Hartmann, L. et al. Autopsy-based histopathological characterization of myocarditis after anti-SARS-CoV-2-vaccination. Clin Res Cardiol (2022). Retrieved from: https://link.springer.com/article/10.1007/s00392-022-02129-5

[30] Klemm C, Das E and Hartmann T. Swine flu and hype: a systematic review of media dramatization of the H1N1 influenza pandemic, Journal of Risk Research, 19:1, 1-20. Retrieved from: https://www.researchgate.net/publication/272591281_Swine_flu_and_hype_A_systematic_review_of_media_dramatization_of_the_H1N1_influenza_pandemic

Simpson's Paradox in the correlations between excess mortality and COVID-19 injections: a case study of iatrogenic pandemic for elderly Australians

by Wilson Sy[1]
BPharm (Hons), MSc, PhD

Abstract

Background: Conflicting findings in correlation studies between COVID-19 injections and excess deaths have been published. Negative correlations with 2021 data appear to justify the official claim that COVID-19 injections reduce illness and death and therefore should be prioritized for vulnerable elderly (over-75s) Australians. This claim needs to be reviewed including 2022 data.

Method: Simpson's Paradox is illustrated to explain how the negative correlations, supporting injection effectiveness, can come from 2021 data, while positive correlations, suggesting injection ineffectiveness, have come from inclusion of 2022 data. Excess deaths of Australian elderly in the COVID pandemic are analysed in detail for their statistical significance.

Results: Negative correlations from 2021 data are refuted in this paper as false causality, because the results have insufficient temporal separation between cause and effect. Strong positive correlation (69 to 74 percent) in Australian data is confirmed when the effects of excess mortality are lagged

1 18 June 2023. PhD, Director, Biotechnology Unit, Investment Analytics Research. Lex Stewart, Julian Gillespie and Jeremy Beck are thanked for useful comments. The author has no financial or political conflicts of interest and is not funded by external sources.

optimally by 21 weeks after COVID-19 injections.[1] A strong statistical signal (2.5 standard deviations) is shown in this paper in the mortality of elderly Australians, who suffered the greatest relative harm from the injections, even when adjusted for age-dependent high expected mortality.

Conclusions: Earlier epidemiological evidence that COVID injections reduce illness and death is now methodologically invalidated, and the claim that the injections are beneficial for the vulnerable is refuted. The injections explain the mystery of substantial numbers of non-COVID excess deaths. The Australian pandemic is shown to be iatrogenic particularly for the elderly, who have suffered disproportionate harm. Deliberately ignoring this clear evidence is tantamount to iatrogenic geronticide.

1. Introduction

Early in the COVID pandemic, the stated purpose of a vaccine was to immunize against, or protect from, the infectious disease. Medicines which do not sufficiently prevent infection and transmission should not be labelled 'vaccines,' because only those with safe and high preventative properties should be widely used or mandated for the collective social benefit of stopping a pandemic by blocking spread.

With the pandemic continuing after more than two years of mass 'vaccination,' a 'vaccine' has now been demoted to require merely to stimulate an immune response, rather than actually to provide immunity. A 'vaccine' has been redefined as 'a preparation that is used to stimulate an immune response against diseases'[2] or redefined functionally as 'the most effective way to reduce deaths and severe illness from infection. The protective benefits of vaccination far outweigh the potential risks.'[3]

This mislabelling of COVID-19 injections as 'vaccines' has continued to mislead most of the public to accept coercive injections for expected immunity in order to travel, keep employment, protect Grandma and do other public good. Even though Pfizer and Moderna have still been mislabelling theirs 'preventative vaccines', the FDA has not adequately clarified[4] to the public that infection prevention is officially not needed for authorized use of the injections:

> It is important to note that *FDA's authorization and licensure standards for vaccines do not require demonstration of the prevention of infection or transmission*. A vaccine can meet the licensure standard if *the vaccine's benefits of protecting against disease outweigh the vaccine's risks* for the licensed use.

Emphasis added. Vaccines now do not have to meet the immunity definition of vaccines that most of the public and the media still misguidedly assume. The COVID-19 injections, whatever their commercial-in-confidence content, are now defined by health authorities to be a therapy to mitigate the effects of infection. However, even this therapeutic benefit has not been tested or demonstrated before they were authorized for use. The COVID-19 injections were assumed axiomatically to be so beneficial that they were prioritized for the most vulnerable, the elderly Australians, as Australian policy endorses a recent CDC and WHO recommendation:[5]

> *COVID-19 vaccines are safe and reduce COVID-19 mortality. The World Health Organization (WHO) recommends that countries prioritize populations at increased risk, e.g., older adults*, for COVID-19 vaccination with a goal of 100% coverage with a completed primary series for populations at-risk."

Emphasis added. What are the facts? It is the purpose of this paper to establish simple, robust, and verifiable facts to assess whether COVID-19 injections provide the said therapeutic benefit, especially for elderly Australians.

Three main sources of *a priori* evidence for safety and therapeutic effectiveness of COVID-19 injections in reducing severe illness and death are briefly discussed in the next section, where real-world epidemiological data will be established as the most valid source of evidence, being most free from data flaws and official conflicts of interest.[6,7] The main epidemiological evidence indicating therapeutic effectiveness consists of a large number of studies with 2021 data, finding negative correlation between COVID-19 injections and excess deaths,[8] thus apparently supporting the effectiveness of the injections in reducing deaths.

It is a typical fallacy in medical research as seen in footnote 8 that a meta-analysis of a large number of papers, shown to be invalid here, appears to have determined the consensus. Whilst there are far fewer publications of positive correlation between COVID-19 injections and excess deaths, the conflict of evidence is explained in section 3 by Simpson's Paradox,[9] which is resolved in section 4 in favour of the minority view of positive correlation between COVID-19 injections and Australian excess deaths. The resolution is based on the important requirement of temporality of correlation to imply valid causality – that is, the cause must precede the effect by a reasonable amount of time.

If COVID-19 injections actually caused excess deaths, then why should they be prioritized for vulnerable elderly Australians? This policy could be rational only if the positive correlation found for the whole Australian population does

not somehow apply to the elderly subpopulation, as an exceptional case of Simpson's Paradox.[9] That is, could the elderly subpopulation exhibit negative correlations between injections and deaths, through unknown confounding factors, even though the whole population exhibits positive correlation? This possibility is refuted in section 5.

While sudden deaths among the young and healthy have attracted worldwide attention, less recognized is the plight of the elderly who have borne the brunt of most Australian excess mortality. Section 6 provides an analysis of the statistical significance of excess mortality by age-group and shows that elderly Australians have suffered disproportionate harm from COVID-19 injections, suggesting geronticide.

Section 7 summarizes the strong evidence for the iatrogenesis of the COVID-19 pandemic for elderly Australians, thus contra-indicating the official assumption that the COVID-19 injections are beneficial for the vulnerable. The concluding section indicates the need to investigate the possibility of iatrogenic geronticide.

2. Safety and therapeutic effectiveness

A priori evidence for COVID-19 safety and effectiveness in reducing severe illness and death may come potentially from three data sources: (1) clinical trials (2) surveillance reports of health authorities and (3) epidemiological data of statistical agencies.

The double-blind clinical trials, on which emergency use authorization (EUA) was granted, were unblinded within weeks after EUA and full safety investigation of the COVID-19 injections was never possible. Moreover, recently the interim datasets accompanying the EUA process were independently re-analysed[10] for serious adverse events of special interest (AESI). From the analysis,[10] Pfizer and Moderna injections were found to have excess risk of serious AESI compared to placebo.

Similarly, the Australian TGA recently released, under Freedom of Information (FOI) requests, a nonclinical evaluation report[11] submitted by Pfizer Australia as a part of its application for approval. The report admitted no human studies were done on most types of toxicity and that in animal models the toxic lipid nanoparticles were not localized at the site of injection, but were slowly and importantly distributed to major organs, particularly to the liver.

Therefore, to date, clinical studies and laboratory experiments have only raised serious safety concerns and have only provided worrying evidence of increased safety risk of the COVID-19 injections, casting doubt on their therapeutic benefit.

After rollout of the 'vaccines,' safety and effectiveness have been monitored through weekly and monthly surveillance reports of health authorities which provided numbers on COVID cases, hospitalizations, ICU admissions and deaths, and selective comparisons based on 'vaccination status'. Unfortunately, these reports are misleading because they are based on flawed COVID data, which were not collected for scientific accuracy, but for managing public perception.[12]

Flaws in official COVID data originate from two main fundamental defects. First, PCR test does not detect the presence of the SARS-CoV-2 virus, the attributed pathogen of the COVID disease. It is unclear whether a COVID infection or other infection is even detected by a positive PCR result, which itself depends on arbitrary numbers of amplification cycles. A PCR-defined COVID infection merely indicates the fragmentary presence of any number of unknown RNA strands,[13,14] but not necessarily presence of any virus of the COVID disease or of any actual infection or disease. Even whole genome sequencing of the SARS-CoV-2 virus in faecal samples of a few positive PCR subjects[15] has not established an association with the disease.

It is clear that certification of deaths during COVID is not an exact science, as the guidance for reporting and financial incentives leave room for bias and subjective judgement in the raw data, as discussed in.[1] For example, a person without COVID symptoms could go to a hospital with a heart attack, while there receive a false positive PCR test result and when having died a day later then be declared a COVID death. In some cases, to declare a COVID death, a positive PCR test is not even necessary for registration by CDC:[16]

> Ideally, *testing for COVID-19 should be conducted, but it is acceptable to report COVID-19 on a death certificate without this confirmation* if the circumstances are compelling within a reasonable degree of certainty.

Emphasis added. Consequently, the distinction between COVID and non-COVID deaths would be inaccurate and COVID data on the numbers of cases and deaths are likely inaccurate measurements of the COVID pandemic.

Secondly, on data defects, attributions of COVID deaths according to 'vaccination status' are also likely to be inaccurate, because 'vaccination status' is not a precise record of the number of injections someone had at a particular date. The recorded status depends on the number of days since last injection. [17] For example, if someone had their first injection less than 14 days ago, they are recorded as 'unvaccinated.' Should the person die in less than 14 days, it is counted as the death of an 'unvaccinated' person. Generally, death numbers of 'vaccinated' and 'unvaccinated' are confused.

Consequently, reports of lower COVID death rates among the 'vaccinated' than 'unvaccinated,' using official COVID data, have been shown[7] to be misleading evidence of the therapeutic effectiveness of COVID injections. Independent replication of results of surveillance reports to discover the exact sources of errors in the Australian databases has been made extremely difficult because the raw data have not been collected accurately in databases, as discussed in the Appendix. Australian COVID data being flawed do not, and cannot, show correctly the therapeutic effectiveness of COVID injections.

In summary, based on official admissions, neither clinical trials nor surveillance reports can be relied upon to provide accurate raw data to support the therapeutic effectiveness of the COVID-19 injections. There remain only epidemiological data which might provide the needed real-world evidence. The mortality data collected by national statistical agencies are data which are more difficult to manipulate to justify government policies and their public pronouncements. Hence, epidemiological data are the most legitimate source to assess the therapeutic effectiveness of COVID-19 injections.

3. Simpson's Paradox in epidemiology

Epidemiological data used for Australian all-cause mortality are published by the Australian Bureau of Statistics (ABS) since 2015.[18] Obviously excess mortality data depend on how the baseline is calculated. The ABS has arbitrarily excluded 2020 as a low mortality year for calculating 2022 excess mortality, thus including only 2017-2019 and 2021 in its baseline.

Other methods of calculating the baseline include that of Actuaries Institute Australia[19] which used extrapolation of linear regression models fitted to standardized death rates. The main adjustments of this baseline are demographic changes in ageing and population. The need to adjust for two years of demographic changes is unclear and the method renders the replication of the calculated results unnecessarily complicated and difficult to use for a variety of analytical purposes.

Computer models of excess mortality are not about statistical facts, but are theoretical models hypothesized to estimate or predict excess mortality based on assumed causes of mortality;[20] their usefulness depends on the assumptions they make.[21,22] In contrast, our excess mortality is a calculated statistic to quantify deviations from expectation to indicate anomalous statistical signals.

To investigate the COVID era, excess mortality is calculated in this paper from the average of five years from 2015 to 2019, as the baseline of the pre-COVID era, which is used throughout our analysis. Therefore, our excess

mortality data are slightly different from those published by the ABS which has an *ad hoc* baseline stated above.[18]

The main methodological strength of the current study is its economical use of data of highest quality and integrity; essentially only two variables are used. The new insightful contributions, which are largely statistical, will come from a more rigorous and thorough analysis of limited data. Conclusions will be fewer, but will be more robust and trustworthy. No direct contribution is made about the underlying science of the COVID virology or vaccinology.

Apart from all-cause mortality data, the only other variable used is the total numbers of doses of COVID-19 injections over time in Australia.[23] The two variables have data collected independently by two separate agencies which are largely free from any known conflicts of interests. The relationships between these two variables have not been investigated together or reported by the health authorities, thus allowing new and unbiased findings to be discovered.

Currently, the number of research publications finding negative correlations between COVID-19 injections and COVID deaths have far exceeded the number finding positive correlations, which have only started to appear since 2023. The reason for this imbalance will be explained below. Our recent paper[1] found strong positive correlations in Australian data, which imply probable causality based on Bradford Hill analysis. This is only one peer-reviewed paper with positive correlation against a large number of other peer-reviewed papers with negative correlations. Health authorities would conclude that the numerical consensus sides with negative correlations and therefore the overall evidence supports therapeutic effectiveness of COVID-19 injections. This fallacy is explained by Simpson's Paradox in this section.

Simpson first discovered[9] a paradox in the interpretation of (2 x 2 x 2) contingency tables for the association between two variables. Generally, the paradox is a statistical phenomenon where an association between two variables in a population may be different from, and possibly contradictory to, those of its subpopulations. The implication is: statistical associations cannot be generalized from one data sample to others without a proper understanding and interpretation of the results. This is illustrated in our current epidemiological context. It is the duty of science to falsify formally any contradictory evidence or at least reconcile with it to establish true scientific consensus.

Our previous paper[1] found strong positive correlation for the whole dataset only when the COVID injection cause leads the excess mortality effect by five months. Virtually all journal-published papers[8] have ignored this temporality, making causal inference likely invalid. If temporality is ignored, then the weekly data (rather than monthly data) are shown in Figure 1.

Visually, it is easy to see (green: doses; red: excess deaths) that there were alternating periods of positive and negative correlation in the Australian data. For the first few months of mass injection till the end of May 2021, there was positive correlation and excess deaths which were largely attributed to 'unvaccinated' deaths, because the sick elderly in nursing homes died too soon after injection to be considered 'vaccinated. The sudden rise in elderly deaths was considered coincidental, unrelated to 'vaccination'.

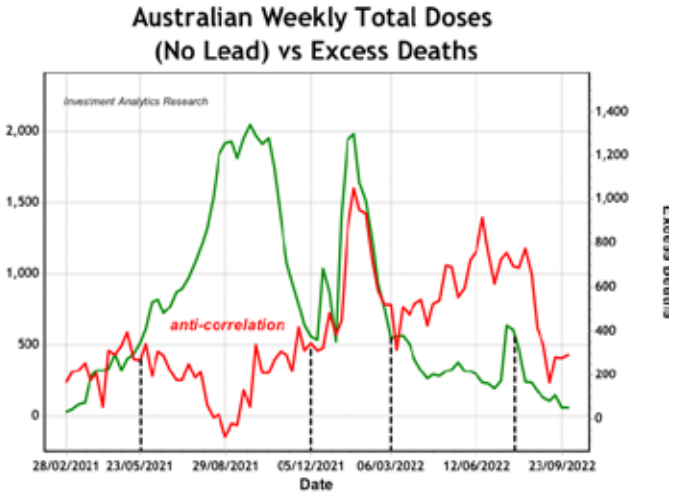


Figure 1

For the three months to the end of August 2021, strong negative correlations were attributed to the 'vaccines reducing illness and death', but excess deaths started to rise again from September 2021, the concept of 'waning' was invented. By the end of 2021, more than 50 studies from different countries were published showing that the injections[8] 'were associated with a favourable effectiveness against SARS-CoV2 incidence rate, hospitalization, and mortality rate in the first and second doses in different populations'.

However, the correlation turned strongly positive from December 2021 to March 2022, with the advent of the first boosters, but by then, about five months after the initial 'vaccination' drive, 'vaccine effectiveness' was considered established beyond doubt and the new data emerging were considered with suspicion, as misinformation, not 'peer-reviewed research'. After March 2022, 'vaccine hesitancy' increased understandably and the rates of injections declined while excess deaths continued to rise. In this period, the correlation turned from positive to negative again.

A scatter plot of Figure 1 is shown in Figure 2, where first and last periods of

anti-correlation are shown as red points and fuchsia points respectively, while positive correlation periods are shown as green points.

Thus, depending on which data period is selected to obtain the correlation between COVID-19 injections and excess deaths, it is possible to obtain

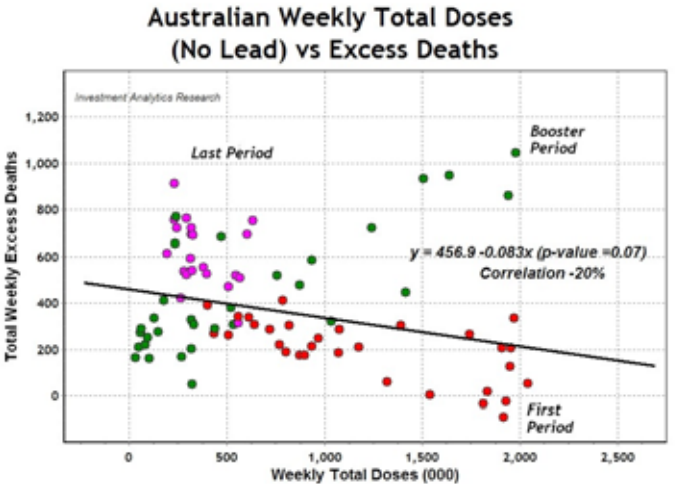


Figure 2

statistically significant positive or negative correlation, as shown in Table 1, in an illustration of Simpson's Paradox.

Colours refer to the data points for each period in Figure 2 and Table 1. The

Table 1: Correlation and Regression of Selected Periods

Period Start	Period End	Sample (Weeks)	Correlation (%)	Slope (Deaths/Doses)	*p*-value
23 May 2021	5 Dec 2021	29	-60.5	-0.143	0.001
5 Dec 2021	6 Mar 2022	14	84.6	0.415	0.000
6 Mar 2022	24 Jul 2022	21	-31.7	-0.317	0.161
28 Feb 2021	30 Sep 2022	83	-20.0	-0.083	0.07

total data sample of 83 points shows (bottom row) a negative correlation of -20 percent with moderate statistical significance (*p*-value 0.07). However, subsamples (top row, red) have higher negative correlation of -60.5 percent with higher statistical significance (*p*-value 0.001) with 29 data points in the first period and have highest positive correlation of +84.6 percent (second row, green) with highest significance (*p*-value 0.000), but with

only 14 data points in the second period.

Most research for the first period was published in 'peer-reviewed' journals,[8,24,25] which favoured the official narrative that 'vaccines' were therapeutically effective. This evidence was assumed universally valid. Later research[26,27] including 2022 data from the second period (see Figure 1) effectively exposed some of the lagged effects of the injections. Such findings contradict those of the earlier published papers and would likely be rejected for journal publication because they do not suit the official narrative. This has created a bias in the literature. Who is right? Should the result of the total Australian data sample be taken as the correct result for the population? Or, should it be the common practice in medical research of reaching a conclusion from a meta-analysis, averaging all results?

Existence of Simpson's Paradox suggests there may be one or more confounding factors important in interpreting and validating the results. Conflicting results have been shown, which require science rather than authorities (or the law courts) to resolve. This paper resolves this Simpson's Paradox by showing that causality requires temporality of correlation on account of inherent time delays for medical treatments to cause observable therapeutic effects.

4. Temporality of correlation

If a healthy youth without medical conditions dies immediately after a COVID-19 injection, it could be caused by an anaphylactic reaction. Or, if the youth dies one or two days later, the injection would still be the likely cause, and can be confirmed by finding spike proteins in affected organs from an autopsy. In these cases, the immediate adverse events are most likely reported and recorded in databases, but others are unlikely to be reported and therefore appear rare, because CDC data reporting convention[17] assumes the injection does not take effect until after 14 days.

On the other hand, for the sick elderly who are close to death, the additional challenge of a synthetic infection from the injections could immediately push them over the edge. The cause of death would be attributed to one or more of their existing comorbidities. From March to May 2021 (see Figure 1), a positive correlation was seen between injections and non-COVID deaths.

Situations with pre-conditions are where COVID injections could have an immediate effect on mortality. Except for the elderly, existence of pre-conditions is relatively uncommon, where, for most people of average health, the COVID injection takes time to affect metabolic processes of pathogenesis.

The lipid nanoparticles (LNP) of the mRNA injections, observed from studies with animal models,[11] take 48 hours to spread to most parts of the body,

particularly to the major organs. From those sites, the LNPs have to transfect into body cells to deliver the genetic material into the cytoplasm, which then initiates processes to manufacture the SARS-CoV-2 spike proteins; the antigens when expressed from the cell provoke the production of antibodies.

Pathologies originate from the way the spike proteins, manufactured or acquired from infection, normally interact with antibodies and body tissues over weeks and months. If the COVID injection were to cause severe illness and death through acquired immune dysfunction, then it would also normally take weeks and months, potentially through down-regulation,[31,32] to see pathology manifested. Even the convention of 14-day delay in reporting 'vaccination status' tacitly acknowledges the requirement of temporality.

Consequently, many studies reporting negative correlations between COVID injections and deaths from 2021 data have misleadingly inferred immediate therapeutic effectiveness in preventing death (for example, see the first period in Table 1). The inferred causality violates temporality with insufficient lag between cause and effect, and needs 2022 data to be included. That is, those research publications should not be used by the health authorities to infer therapeutic effectiveness of the injections in reducing severe illness and death. The opposite conclusion is the case, by correct statistical analysis with more data, as shown in the previous paper.[1]

Complementing monthly data analysis,[1] weekly data of Figure 1 are shifted optimally with doses of injection temporally leading excess deaths by 21 weeks, and are shown in Figure 3.

From the whole dataset, the overlap period with temporal shift was from August 2021 to November 2022. The peaks in excess deaths coincided approximately with two booster peaks which were five to six months apart. Over this period the correlations between COVID injections and Australian excess deaths are consistently high, as shown in Figure 4.

The linear regression is statistically significant with p-value essentially zero and a positive correlation of +69 percent. On average, one million doses administered in a week would lead to 460 weekly excess deaths 21 weeks later. The correlation of the whole dataset is largely free from Simpson's Paradox, because only very small subpopulations show any sign of negative correlation, as indicated by data points in red and blue.

The temporal separation between COVID injections and observed deaths, five months or 21 weeks later, as distribution peaks, has been suggested from simple observations and anecdotes from US and European data.[28]

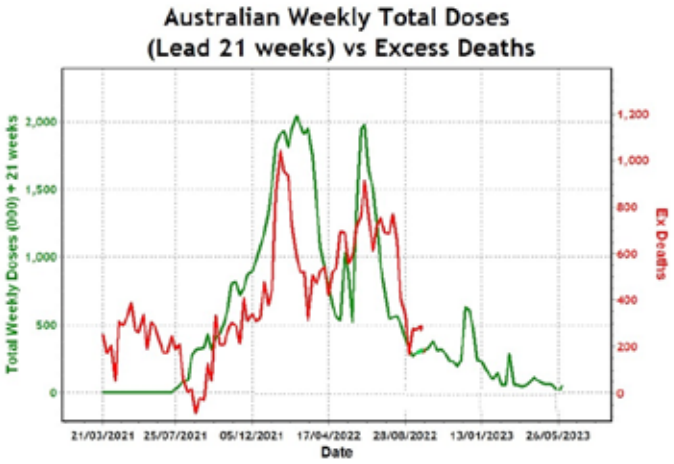


Figure 3

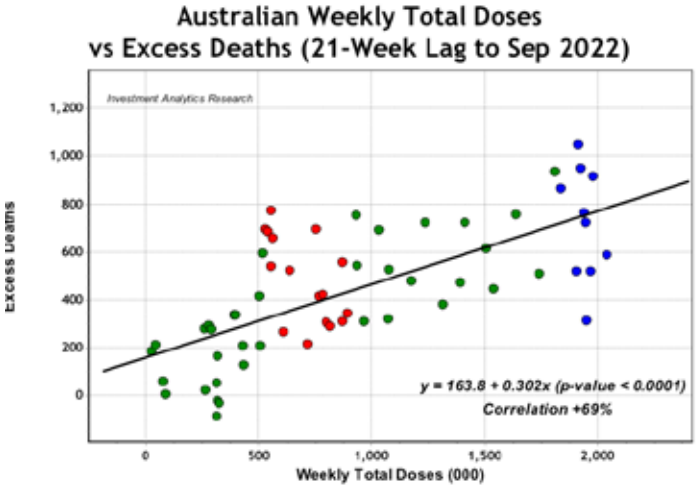


Figure 4

5. Age-group therapeutic effect

While Australian data show the COVID injections have a negative therapeutic effect on the whole population, increasing excess deaths, it may be possible *a priori* that the COVID injections have a positive therapeutic effect on subpopulations, such as the elderly, as another example of the Simpson's Paradox.

For the whole Australian population, it has been shown that COVID-19 injections increase, not decrease as claimed, severe illness and death. Yet, COVID-19 injections have continued to be recommended by health authorities

for the elderly and the vulnerable. Could Simpson's Paradox provide a rational explanation to justify the counter-factual claim that COVID-19 injections reduce severe illness and death specifically for the vulnerable elderly?

Theoretically, one way the elderly Australians could statistically escape the conclusion of iatrogenic excess deaths observed in the total Australian population is for that subpopulation to exhibit Simpson's Paradox by having a negative correlation between doses of injection and excess deaths. This possibility is examined here.

The ABS monthly all-cause mortality data stratified by age-groups since 2015 are shown in Figure 5.

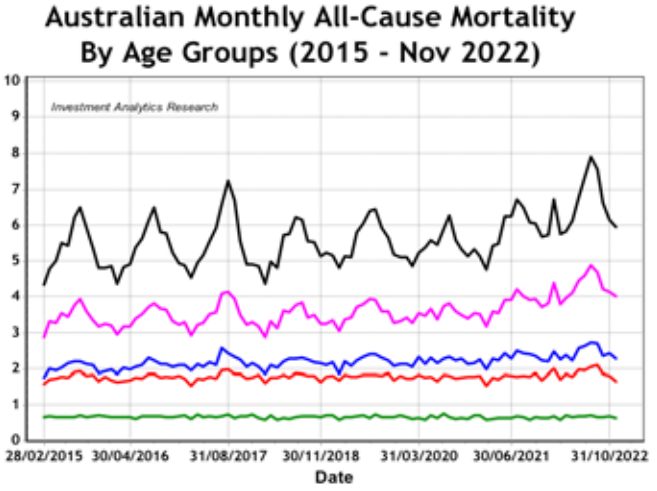


Figure 5

As expected, mortality increases strongly and monotonically with age. Visually, from Figure 5, it is evident that notable increases in all-cause deaths above expectation in the older age-groups have occurred since 2021, when mass injections started. Is this statistically significant?

Age-standardized mortality statistics used in most published studies mask information on different effects of COVID-19 injections on different age-groups, because the data are standardized to fixed age distributions. Consistent with our aim of clearly exposing the outcomes of the COVID era, excess deaths for each age-group are calculated from their own baselines using their own respective averages of the years 2015-2019, of the pre-COVID era. To simplify discussion, the elderly are defined by an over-75 or 75+ age-group by aggregating the 75-84 age-group and the 85+ age-group. The rest of the Australian population is referred to as the under-75 or 75- age-group.

Whether Simpson's Paradox occurs with the 75+ age-group depends empirically on the correlation between the doses injected into that age-group and the resulting excess deaths. Accurate dose-statistics for different age-groups are not available in Australia, as explained in the Appendix. Therefore, total national dose-statistics are used as proxy, since their variations are expected to closely reflect the variations of the 75+ and 75- age-groups.

The relationship between monthly total doses and monthly excess mortality for the 75+ age-group is shown in Figure 6, which closely resembles Figure 8 of the previous paper[1] and is consistent with the weekly version in Figure 3 above.

The first peak in excess deaths in January 2022 is particularly anomalous because it was during the height of the Australian Antipodean summer, when fewer elderly normally die from respiratory diseases. The second peak in July and August may appear seasonally more normal, but it too is anomalous because registered deaths from influenza and pneumonia were unusually low relative to pre-pandemic averages. Eliminating natural causes at those peaks suggests that the excess deaths in the elderly were likely caused by COVID-19 injections administered five months earlier, given the Bradford Hill analysis in the previous paper.[1]

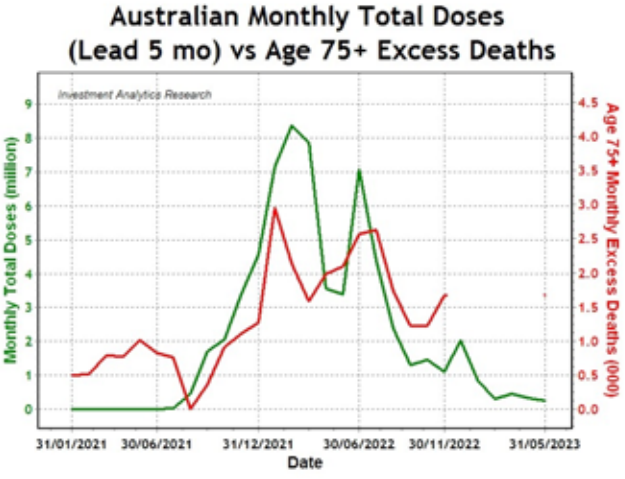


Figure 6

A similar conclusion is reached for the under-75 age-group with the same Bradford Hill analysis. Hence, in the current dataset, Simpson's Paradox has been eliminated for the elderly and it has been verified that COVID injections do not reduce, but increase, excess deaths for the elderly, as well as for the whole population.

The remaining question is: are the elderly excess deaths caused by the injections statistically significant? What is their relative harm compared to other age-groups?

6. Age-group comparison

In the COVID era, the annual excess deaths as percentages of baseline expectations for various age-groups are shown in Figure 7, where it is evident that the Australian pandemic as defined by excess deaths only started in 2021, with the advent of mass injections.

In the next three months after the data analysed in this paper, monthly total Australian deaths have been 15,300, 14,500 and 12,700 to February 2023, with baseline expected mortality of 12,800, 12,600 and 11,500 giving respectively excess death tolls of 2,540, 1,950 and 1,270 or 19.9, 15.5, and 10.4 percent above expectation. These statistics (rounded for ease of reading) have similar magnitudes to those to November 2022 in Figure 7 (last group), suggesting still significant excess deaths.

The previous paper[1] showed that 2020 was pre-pandemic in Australia, because there was no evidence of significant excess deaths to warrant calling a pandemic, according to traditional WHO definitions. This applies to all age-groups.

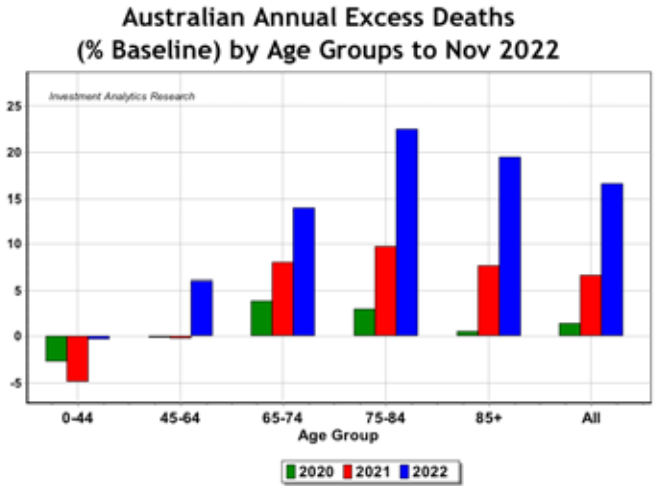


Figure 7

As shown in Table 2 below, the percentages of excess deaths for all age-groups compared to baseline expectations are all less than four percent (column 5), substantially less than historical fluctuations, resulting in low sigmas (units of

standard deviation). That is, there were no statistically significant signals for a pandemic for any age-group in Australia in 2020.

The second last column shows that annualized volatility of percentage excess deaths and the last column shows sigmas (standard deviations) less than 0.3 percent, indicating statistical insignificance.

For those over 65 years, the 65+ age-group excess deaths (1,980) account for more than 100 percent of excess deaths (1,690) in 2020 (column 4, shaded), because the youngest age-groups had lower deaths than expectation. This resulted in higher COVID-19 deaths attributed to the elderly, giving the misleading impression that the elderly were particularly vulnerable to COVID-19 mortality, and this was false because of statistical insignificance.

Table 2: Pre-Pandemic 2020 Age-Group Excess Deaths

Group	All-Cause Baseline	All-cause 2020	Excess 2020	Excess % 2020	Excess % Volatility	Sigma
0-44	8,000	7,770	-230	-2.88	12.5	-0.23
45-64	21,200	21,100	-60	-0.28	8.4	-0.03
65-74	25,400	26,400	937	3.69	13.0	0.28
75-84	41,200	42,300	1,070	2.60	9.7	0.27
85+	65,100	60,100	-30	-0.05	12.2	0.00
All	161,000	158,000	1,690	1.05	6.9	0.15

The situation changed markedly after 2021 with mass COVID injections. Excess mortality climbed substantially, particularly in the elderly. Australian COVID injection drives generally lagged the rest of the world by a few months, partly as a result of global health directives and partly through ordering and supplying issues, as seen in Figure 8.

The temporal separation between cause and effect meant that the effect of COVID-19 injections was not fully felt until 2022 in Australia, at least a few months after completing mass injections of the primary series in the Australian population. Moreover, the injections appeared to have a cumulative effect on the immune system with the first booster campaign early in January 2022 having a devastating effect in Australia.[1]

On account of Australian injections lagging other countries such as the US and UK, Australian deaths would lag the rest of the world, making Australian relative 2022-2021 death tolls higher than those of most other countries,

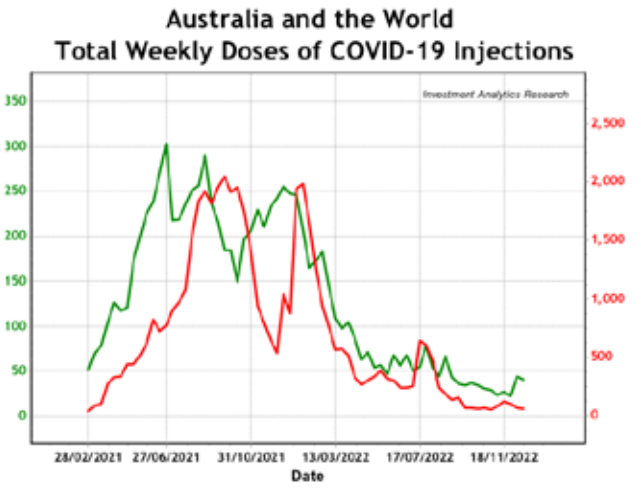


Figure 8

which had more injections and deaths earlier. The Australian excess deaths to November 2022 by age-groups is shown in Table 3.

All numbers have been rounded to three significant figures, for ease of reading and adjusted for 11 months of data for 2022. Before the excess mortality of the elderly is discussed, and this is a main focus of this paper, the surprisingly low 2022 excess mortality (first row) of the youngest group needs to be discussed to allay any fears about the quality and integrity of the data.

Table 3: Age-Group Excess Deaths to November 2022

Group	Population (m)	Pop (%)	All-Cause Baseline	All-cause 2022	Excess 2022	Excess % 2022	Excess % Volatility	Sigma
0-44	14.8	58.2	7,300	7,270	-29	-0.4	12.5	0.0
45-64	6.26	24.6	19,400	20,700	1,290	6.6	8.4	0.8
65-74	2.46	9.7	23,400	26,900	3,570	15.3	13.0	1.2
75-84	1.38	5.4	37,900	47,200	9,240	24.4	9.7	2.5
85+	0.54	2.1	60,100	72,700	12,500	20.8	12.2	1.7
All	25.4	100	148,000	175,000	26,600	18.0	6.9	2.6

The current focus of most research has been generally on the young who normally have very low rates of mortality, but are now appearing to die at higher rates (see Figure 7). With dramatic statistical signals and with many years of lifespan at risk for every young person, it is reasonable to urgently investigate diagnosis, causes and treatments.

Young and fit athletes collapsing and dying suddenly during training or in

sports events in front of crowds of spectators provide visually powerful evidence of unexpected deaths. Most of these deaths have been shrugged off as rare, perhaps due to asymptomatic COVID infections, but statistically insignificant, as seen above. The contradiction between anecdotes and mortality data needs explanation.

In the youngest age-group (0-44), deaths from medical causes are normally rare (about 0.014 percent per annum – see Table 4). This makes highly conspicuous any sudden rise in medically-caused deaths from a very small to a larger number. That is, sudden rises in cardiac arrests and strokes relative to their virtual absence normally have raised statistical alarms. However, in absolute terms, those deaths may not have overall significance on total excess mortality in Australia's youngest age-group, because of large numbers of non-medical deaths.

For the youngest age-group (0-44), broad categories of causes of deaths are shown for different age subgroups in Table 4. Top-10 medical causes mainly include neonatal deaths, malignant cancers and cerebral palsy, with heart disease and strokes only starting to occur after 25 years. The top-10 non-medical causes exceed medical causes, leading by intentional self-harm, followed by accidents which involve misadventure, car, motorcycle and other transport.

Table 4: Causes of Death in Youngest Age-Groups

Cause/Age (Years)	< 1	1 to 14	15 to 24	25 to 34	35 to 44	Total
Population (million)		4.64	3.04	3.62	3.49	14.8
Top-10 Medical	801	113	69	216	944	2,140
Top-10 Non-medical		108	739	1,050	971	2,870
Intentional Self-harm		32	402	581	567	1,580
Accidental Harm		76	337	473	404	1,290
Top-10 Total	801	221	808	1,270	1,920	5,020
All-cause Total	1,010	425	1,170	1,950	3,250	7,740

That is, statistical signals in the rise of medically-caused deaths in the youngest age-group may be masked by a significantly larger number of non-medical deaths, as seen in the above table (see rows 2 and 3). For example, lockdowns during the pandemic, particularly before 2022, might have had an unintended consequence of reducing traffic and other accidents in the young (for example, ages 15 to 34). Reduced traffic accidents alone may have more than compensated for any rise in medically-caused deaths.

Over the short term, the aggregate data have not shown significant increased

mortality in the youngest age-group, though 2022 has faintly hinted at an emerging upward trend. The long-term effect of COVID injections on future mortality on the mostly healthy young age-group is as yet unpredictable from published data.

The main concern of this paper is the bulk of excess deaths in the over-75 age group. Table 3 shows Australian elderly (75+ years) are nearly two million, or 7.5 percent of the population (third column, shaded). Normally they are responsible for about 66 percent of baseline all-cause mortality of the Australian population (fourth column). Yet they represented 82 percent excess deaths in the year to November 2022 (sixth column, shaded).

The excess deaths for 75-84 age group and the 85+ group were 24.4 percent and 20.8 percent above expectation (seventh column). Such percentages of increase in excess deaths are statistically significant, because when measured against historic volatilities of percentages of excess deaths (eighth column), their sigmas (or z-scores) were 2.5 and 1.7 (last column) or p-values of 0.006 and 0.045 respectively, indicating chance is improbable. Volatilities are calculated based on scaling of percentage monthly excess deaths over 2015-2019.

Note that the statistical significance of excess deaths is even higher with a sigma of 2.6 (p-value of 0.005) for the whole Australian population, because the overall volatility of percentage excess deaths is lower for a larger sample. The statistical significance is greatest for the nation as a whole, which is another example of Simpson's Paradox. Each age group may have confounding factors adding 'noise' to affect their dose-response relationship. With different idiosyncrasies of each age group having been washed out, the main factor affecting all groups becomes clearer statistically.

The high statistical significance of the 2022 excess deaths in the Australian elderly is very clear, even without population adjustments. The Australian economy grows by around one percent per annum simply from immigration. It may appear that demographic changes could affect our interpretation of the data on excess mortality of the elderly. However, Australian immigration is heavily biased in favour of the young because of skill shortages in various sectors and the need to fill high levels of job vacancies. Immigration would have little numerical effect on the elderly population.

The fact that COVID-19 injections have substantially accelerated the mortality rates of the Australian elderly can be shown clearly and precisely in monthly percentage excess mortality data since 2015 in Figure 9, which eliminates seasonal fluctuations (not usually done).

Between 2015-2019 of the baseline, the monthly excess mortality of the 75-84

age-group rarely exceeded plus or minus five percent of the baseline, with an annualized volatility of 9.7 percent, shown by the horizontal green line in Figure 9. In 2022, the monthly excess deaths were well in excess of 15 percent (as high as 36 percent), about three times (as high as seven times) the baseline. On an annual-average basis, 2022 was 24.4 percent above baseline compared to 9.7 percent annualized volatility of the baseline. The statistical signal for high excess deaths in the Australian elderly is very strong, suggesting the presence of a potent cause.

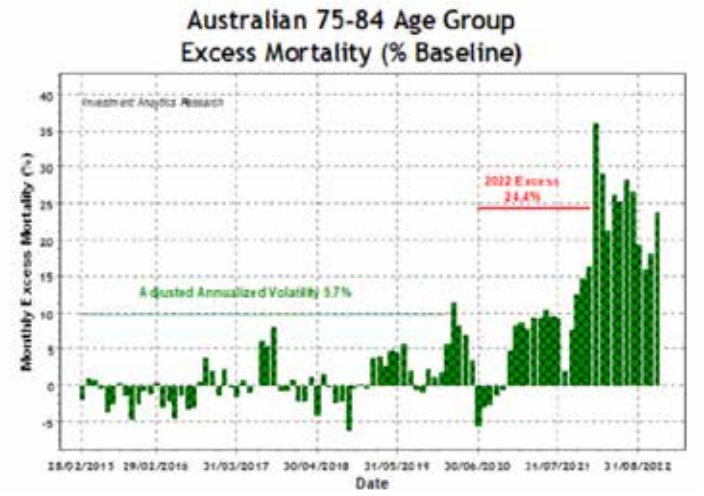


Figure 9

Obviously, excess deaths have potentially many different *a priori* causes and are unlikely to be caused entirely by a single factor such as COVID-19 injections, which may statistically provide 70 percent of the causality. For example, it is difficult to dismiss the direct evidence from an autopsy of a 76-year-old man[29] who had an unnatural death from improbable simultaneous multiple organ failures linked to injection-associated spike proteins.

Unless there is another explanation which has better causal credentials, then from the mortality data of this paper, the strong association between excess deaths and COVID-19 injections would suggest probable causality, given that other aspects of Bradford Hill analysis[1] are also supportive. Consequently, this probable causality warrants serious attention and further investigation to justify continued COVID injections.

7. Summary discussion

This paper has examined the Australian official claim that COVID 'vaccines' reduce severe illness and death. After eliminating the empirical evidence from other methods, which suffer from poor-quality source data,[3,6,7] this paper has used more reliable real-world epidemiological data to analyse in detail whether the official claim could be justified. Many published papers supporting this claim were also based on epidemiological data, but have been shown to be invalid in their interpretation mainly because of Simpson's Paradox. Their supposed causal associations would wrongly fluctuate randomly between positive and negative effects over different time periods. The correlations of those studies are therefore temporally inconsistent, because of incorrect temporal separation between cause and effect to attribute consistent medical causality – they are examples of correlation not being causation.

A temporal separation of 21 weeks or five months between the COVID injections to cause the mortality effect has been proposed[1] as necessary to explain consistently the Australian data. This suggests clinical trials needed, but have not been provided with, at least five months to observe serious adverse effects. As the temporal separation from Australian data is consistent with those observed in other datasets from many countries,[28] it may reflect a genuine scientific fact: the time required for as-yet-unknown processes of pathogenesis to cause most of the deaths. Consequently, the observed temporality warrants further pathological investigation.[31,32]

Of course, there may also be other processes and temporalities which result in death, but these have yet to be observed as empirical facts. Indeed, the lethality of the injections could have a long tail, judging anecdotally by reported instances of heart disease, cancer, neuropathy and more, many months following the COVID injections, particularly in the younger age-groups. Data need to be accurately and systematically collected for future research.

This paper has provided further proof to confirm the previous hypothesis[1] that the COVID injections are the main cause of excess deaths reaching pandemic levels in Australia. The injections explain the mystery of substantial numbers of non-COVID deaths. This finding falsifies and contradicts the sole rationale of current official recommendation for the injections which are purported to reduce severe illness and death. On the contrary, this paper has shown clearly that empirically the COVID injections substantially increase deaths, particularly in the elderly. Thus, COVID-19 injections do more harm than good for the vulnerable.

While these serious findings may not be surprising to those who read widely in the available research, it is important to have established formally and scientifically the occurrence of statistically significant iatrogenic excess mortality, which should not be dismissed as misinformation.

8. Conclusion

Earlier epidemiological evidence that COVID injections reduce illness and death has been refuted as an example of Simpson's Paradox; instead, the evidence has shown increased iatrogenic deaths. Without taking the precaution of investigating the abnormally high excess deaths, Australia has continued to prioritize the elderly for COVID injections which the elderly cannot usually refuse if they are in residential aged-care facilities.

The longer the authorities delay stopping widespread injections to conduct a thorough investigation into the causes of excess deaths in Australia, the stronger is the implication that the excess deaths in the elderly are deliberate policy, which is in effect iatrogenic geronticide. Geronticide is a serious violation of human rights, because it is a morally reprehensible criminal act to target intentionally older adults based on their age.

References

[1] Sy, W. Australian COVID-19 pandemic: A Bradford Hill analysis of iatrogenic excess mortality, J Clin Exp Immunol, 8(2), 542-556. https://www.opastpublishers.com/open-access-articles/australian-covid19-pandemic-a-bradford-hill-analysis-of-iatrogenic-excess-mortality.pdf

[2] Centers for Disease Control and Prevention. Definition of Terms, Vaccines & Immunizations. https://www.cdc.gov/vaccines/vac-gen/imz-basics.htm

[3] Therapeutic Goods Administration. COVID-19 vaccine safety report – 12-01-2023. https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-12-01-23

[4] U.S. Food and Drug Administration, Reply to Citizen Petition (Docket Number: FDA-2023-P-0360) from Coalition Advocating for Adequately Labeled Medicines (CAALM) https://www.documentcloud.org/documents/23786932-fda-letter-on-covid-19-vaccine-labeling

[5] Center for Disease Control and Prevention, Morbidity and Mortality Weekly Report, February 3, 2023, COVID-19 Mortality and Progress Toward Vaccinating Older Adults —World Health Organization, Worldwide, 2020–2022. https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7205-H.pdf

[6] Sy W, Mortality risk of COVID-19 injections: evidence from New South Wales and England, Academic.edu. https://www.academia.edu/83924771/Mortality_risk_of_COVID_19_injections_evidence_from_New_South_Wales_and_England (accessed 30 July 2022).

[7] Sy W. Data reporting flaw in plain sight distorting COVID-19 mortality statistics, Academia, 25 August 2022. https://www.academia.edu/85597731/Data_reporting_flaw_in_plain_sight_distorting_COVID_19_mortality_statistics

[8] Rahmani K, Shavaleh R, Forouhi M et al. The effectiveness of COVID-19 vaccines in reducing the incidence, hospitalization, and mortality from COVID-19: A systematic review and meta-analysis, Front. Public Health, 26 August 2022, Sec. Infectious Diseases: Epidemiology and Prevention Volume 10 - 2022. https://doi.org/10.3389/fpubh.2022.873596

[9] Simpson E. The Interpretation of Interaction in Contingency Tables, Journal of the Royal Statistical Society: Series B (Methodological), 13(2): 238–241. doi:10.1111/j.2517-6161.1951.tb00088.x. http://math.bme.hu/~marib/bsmeur/simpson.pdf

[10] Fraiman J, Erviti J, Jones M et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. Vaccine, 40(40), 5798-5805, 22 September 2022. https://www.sciencedirect.com/science/article/pii/S0264410X22010283

[11] Therapeutic Goods Administration. Nonclinical evaluation report, Document 6, Submission No. PM-2020-05461-1-2, Pfizer Australia Pty Ltd. https://www.tga.gov.au/sites/default/files/foi-2389-06.pdf

[12] Igoe M. Deborah Birx: US COVID-19 data was 'worse than what I found overseas', Devex 15 July 2022, (See video, quotes at 11.30 and 8.20 min). https://www.devex.com/news/deborah-birx-us-covid-19-data-was-worse-than-what-i-found-overseas-103640

[13] Centers for Disease Control and Prevention. CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel, FDA News Release. https://www.fda.gov/media/134922/download

[14] Corman V, Landt O, Kaiser M et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR, Euro Surveill. 2020;25(3):pii=2000045. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6988269/pdf/eurosurv-25-3-5.pdf

[15] Papoutsis A, Borody T, Dolai S, et al. Detection of SARS-CoV-2 from patient fecal samples by whole genome sequencing, Gut Pathog (2021) 13:7 https://doi.org/10.1186/s13099-021-00398-5

[16] Center for Disease Control and Prevention, Guidance for Certifying Deaths Due to Coronavirus Disease 2019 (COVID-19),Vital Statistics Reporting Guidance Report No. 3, Released April 2020 – Expanded February 2023. https://www.cdc.gov/nchs/data/nvss/vsrg/vsrg03-508.pdf

[17] Centers for Disease Control and Prevention, COVID-19 Vaccine Breakthrough Case Investigation and Reporting (Updated June 23, 2022), https://www.cdc.gov/coronavirus/2019-ncov/php/hd-breakthrough.html#report

[18] Australian Bureau of Statistics, Provisional Mortality Statistics, Released 24/02/2023. https://www.abs.gov.au/statistics/health/causes-death/provisional-mortality-statistics/jan-nov-2022

[19] Actuaries Institute Australia, Catch up on the Actuaries Institute's COVID-19 Mortality Working Group's latest analysis of excess deaths, COVID-19 Mortality Working Group, 6 March 2023. https://www.actuaries.digital/2023/03/06/almost-20000-excess-deaths-for-2022-in-australia/

[20] Sy, W. A critique of estimates of excess mortality from COVID-19 pandemic, March 29, 2022, Principia Scientific International, https://principia-scientific.com/a-critique-of-estimates-of-excess-mortality-from-covid-19-pandemic/

[21] Watson O, Barnley G, Toor J et al. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study, Lancet Infect Dis, June 23, 2022; 22: 1293–302. https://doi.org/10.1016/S1473-3099(22)00320-6

[22] Wang H, Paulson K, Pease S et al. Estimating excess mortality due to COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-2021, The Lancet, March 10, 2022. https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2902796-3

[23] CovidbaseAU, Australia COVID-19 Vaccinations. https://covidbaseau.com/vaccinations/

[24] Suthar A, Wang J, Seffren V et al. Public health impact of covid-19 vaccines in the United States: observational study, BMJ 2022;377:e069317. http://dx.doi.org/10.1136/bmj-2021-069317 https://www.bmj.com/content/bmj/377/bmj-2021-069317.full.pdf

[25] Haas E, Angulo F, McLaughlin J et al., Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data, Lancet.2021 May 15;397(10287):1819-1829. doi: 10.1016/S0140-6736(21)00947-8. Epub 2021 May 5. https://pubmed.ncbi.nlm.nih.gov/33964222/

[26] Redert A. Causal effect of covid vaccination on mortality in Europe, ResearchGate Preprint, February 2023. https://www.researchgate.net/publication/368777703_Causal_effect_of_covid_vaccination_on_mortality_in_Europe

[27] Aarstad J and Kvitastein O. Is there a Link between the 2021 COVID-19 Vaccination Uptake in Europe and 2022 Excess All-Cause Mortality? 18, February 2023. https://www.preprints.org/manuscript/202302.0350/v1

[28] Kirsch S. Vaccines are taking an average of 5 months to kill people, 1 September 2022. https://stevekirsch.substack.com/p/this-one-graph-tells-you-everything

[29] Mörz M. A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against COVID-19. Vaccines 2022, 10, 1651. https://doi.org/10.3390/vaccines10101651

[30] Department of Health and Aged Care, COVID-19 vaccination – vaccination data, Australian Government. https://www.health.gov.au/resources/collections/covid-19-vaccination-vaccination-data

[31] Irrgang P, Gerling J, et al., Class switch towards non-inflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination, Sci. Immunol. 8, eade2798 (2023) 27 January 2023. Retrieved from: https://www.science.org/doi/pdf/10.1126/sciimmunol.ade2798

[32] Uversky VN, Redwan EM, et al., IgG4 Antibodies Induced by Repeated Vaccination May Generate Immune Tolerance to the SARS-CoV-2 Spike Protein. Vaccines. 2023; 11(5):991. https://doi.org/10.3390/vaccines11050991

Appendix: official data flaws

Among Australian health authorities, there is an absence of raw-data-download facilities available to the public for COVID research. The published data in weekly and monthly surveillance reports are based on selections of flawed COVID data[6,7] which are unprofessionally assembled. Inconsistent reports which have misled the public cannot be corrected and resolved without accurate raw data. A few examples of problematic official 'vaccination' data are given here.

Official data on COVID-19 'vaccination' are assembled by the Department of Health and Aged Care[30] collated from the data of eight state and territories health departments. The data are made available to the public in approximately 170 separate, individually-named weekly EXCEL files.

Those EXCEL files do not satisfy the basic requirements of data tables according to basic principles of data science because they are two-column or three-column tables (since April 2023) consisting of arbitrary lists of descriptive items with their associated numerical values, without data structure.

There are insurmountable problems to extract data reliably and accurately from the source. For example, to get the weekly time series of a particular item, say, cumulative total adult doses administered, one would have to open individually about 170 files and look up the values for the item. Even this theoretically simple task is impossible because item descriptors are inconsistent, as Table 5 shows.

In Table 5, the first column is the date, which specifies the filename, for

example: "covid-19-vaccination-vaccination-data-31-July-2022.xlsx", for the data in the second and third column of the first row. The second and third columns of Table 5 are the contents from data files specified in the first column.

Table 5: Sample of Official Data on 'Vaccination'

Date	Measure Name	Value
31/07/2022	National - Number of people 16 and over with 1 dose	20,160,781
31/08/2022	National - Number of people 16 and over who have received at least 1 dose	20,203,639
28/02/2022	Age group - 75-79 - Number of people with 1 dose	836,978
28/02/2022	Age group - 75-79 - Number of people fully vaccinated	827,310
28/02/2022	Age group - 75-79 - Population	773,742
28/02/2023	Age group - 75-79 - Number of people who have received at least 1 dose	890,892
28/02/2023	Age group - 75-79 - Number of people who have received at least 2 doses	885,026
28/02/2023	Age group - 75-79 - Population	807,195

The first two rows of Table 5 are from two data files one month apart; the field descriptor has changed from adults 'with 1 dose' to adults 'who have received at least 1 dose', without any notification or explanation. It is highly probable they are the same data with their item names arbitrarily changed, since only one or the other item exists in each data file. Such inconsistencies prevent meaningful data extraction.

The next three data rows in Table 5 show the numbers of people vaccinated is greater than the population, which is nonsensical. Moreover, it is unclear what 'fully vaccinated' means – for instance, do they include the first boosters?

The last three data rows in Table 5 also show the numbers of people vaccinated is greater than the population, which is also nonsensical. In the 75-79 age-group, the number 'with 1 dose' is 836,978 and the number 'who have received at least 1 dose' is 890,892. Do we conclude that 53,914 have two or more doses? Is this number included in those 'who have received at least 2 doses'? These simple

questions cannot be answered from the data provided. It is possible that the person entering the data also did not know.

There are many more examples of ambiguity and inconsistency in the data provided by the national health authority. For example, the data entry convention of 14-day lag to register injection would imply inconsistencies[7] in the raw data between persons dosed and total doses administered. From what has been provided, it is impossible to reconstruct a proper relational database which satisfies professional standards of data consistency and integrity.

Extraction of valid data from what is available would be a very hazardous and tedious exercise, prone to errors and inconsistencies. Having to interpret dodgy data leads inevitably to making up data, opening the door to data manipulation and fabrication. This may explain the poor quality of official surveillance data and reports – garbage in, garbage out. Importantly, deliberate data fraud in reports cannot be easily proved or ruled out.[6,7]

Suffice to say, government agencies collecting data to support and justify government policies[12] have inherent conflicts of interests, which can only be managed if strict measures are in place to ensure data integrity. This has not been the case for Australian COVID-19 data, which have serious flaws resulting from inaccurate data collection and which are not organized in professional databases, making impossible the extraction of reliable data.

Dr Wilson Sy has held senior positions in academia, industry and government. He is a quantitative and statistical analyst with several dozens of journal publications in physics, finance, economics, biology and medicine. He is highly experienced in data analysis in business and government. He has held positions as Principal Researcher at the Australian Prudential Regulation Authority (APRA) and as senior adviser to the Australian Treasury for the Super System Review. Recently, he has published several journal articles on epidemiological data analysis of the COVID pandemic.

Excess mortality and bereavement

by Monique O'Connor

MBBS FRANZCP

Introduction

Every death has a profound human cost at the individual, family and societal level, particularly if that death is premature or unexpected. Excess mortality in Australia and around the world translates to an excess prevalence of people who are bereaved. This is directly associated with increased personal and societal burden of psychosocial, mental health and economic harms and needs.

Normal bereavement

The death of a loved one automatically causes bereavement and a period of acute grief[1] that is typically associated with functional impairment and profound emotional pain.

Grief is a natural and expected process. In most bereavements well-being and normal function resume, albeit with permanent but less troublesome residual grief, after a period of mourning.

The death of a close loved one is known to be a major life stressor. Bereavement is recognised to be associated with elevated physical and mental health risks.[2]

Premature or unexpected death can be a damagingly transformative life event

for those left behind (spouses, children or parents). Close bereavement may bring about enduring detrimental developmental, psychosocial and economic changes.

Prolonged Grief Disorder

If grief does not attenuate naturally over time (at least a year), the impairment and intense emotional pain can persist indefinitely. When this occurs, a recognised mental health condition is identifiable, classified as Prolonged Grief Disorder (PGD) in DSM5-TR and ICD-11.[3,4]

Definition

Prolonged Grief Disorder (PGD) is a recognised psychiatric condition that is impairing; when present, it is associated with serious risks, including suicide, and requires treatment. The impairment in function can have negative consequences on the ability to work, parent, carry out responsibilities, study and so forth. The hallmark of PGD is debilitating grief that persists longer than expected in social, cultural or religious norms. The grief is preoccupying and characterised by longing and yearning for the deceased. It is often associated with intense emotional pain, a sense of disbelief, emotional numbness, social disconnection, profound loneliness and identity confusion.

Risk of Prolonged Grief Disorder

There are many recognised factors that place the bereaved at risk of developing PGD. These include adversity in childhood, prior losses, trauma, a history of mental illness and an unexpected or premature death. Also, a very close relationship or difficult circumstance surrounding the death increase the risk of PGD.[1,2]

It is noteworthy that deaths which occurred during COVID-19 pandemic restrictions likely have an elevated risk of Prolonged Grief Disorder. The inability to visit the sick or dying, difficulty or inability to travel to be with family, isolation in quarantine whilst bereaved, the inability to attend funerals and wakes, to follow religious or cultural practices and exposure to traumatic deaths in which PPE or ventilation of patients was used will have contributed to this elevated risk.

Prevalence

PGD occurs in at least 7-10% of close bereavements;[5,6,7] it is probably higher with bereavements complicated by pandemic measures that inhibited normal grieving.

Comorbidity

High rates of comorbidity occur with PGD, including PTSD, depression, substance abuse and suicidality.[1,8,9,10]

Management of Prolonged Grief Disorder

The treatment of choice is condition-specific psychotherapy, delivered by a therapist trained in Prolonged Grief Therapy.[11,12,13,14]

Societal costs of Prolonged Grief Disorder

The serious nature of PGD equates to individual and societal costs.[2] The number of bereaved following each death varies. Those closely bereaved are at risk of PGD, especially following spousal or child death. The number of closely bereaved (that is, those with a close, important and loving relationship) is roughly five or six for each death. The number of bereaved negatively affected by a sudden or premature death can be substantially higher. A study by Cerel et al.[15] found 135 people affected by a single suicide bereavement.

The expected number of cases of PGD can be estimated in broad terms by the following equation:

[Number of deaths] x 5 (the closely bereaved) x 10%

The Australian Bureau of Statistics deaths and mortality data[16,17] can be used to estimate expected cases of Prolonged Grief Disorder.

- Expected new cases of PGD caused by deaths in 2022

There were 190,939 registered deaths in Australia in 2022[16]

5 x 190,939 = 954,695

10% of 954,695 (that is, the expected number of cases of PGD following 2022 deaths) = 95,467 cases of PGD in 2022

- Expected new cases of PGD Caused by Excess deaths in 2022 compared to 2021

There were 19,470 more deaths in Australia in 2022 compared to 2021[16]

5 x 19,470 = 97350 closely bereaved excess bereavements in 2022.

10% x 97350 = 9,735 expected excess cases of PGD resulting from excess death in 2022

A more accurate number of excess deaths in 2022 would be to compare the number of deaths in 2022 with a pre-pandemic measure baseline number rather than the 2021 number, but that unfortunately has not been provided by the ABS. However, my calculations are for illustrative purposes. It is noteworthy that the death rate for males and females aged 25-44 increased by 8.0% and 5.1% respectively in 2022, and death rates for those aged 45-64 years were the highest in the 10 years.[17] These represent premature deaths likely to have been unexpected. Sudden cardiac deaths are an example of a premature death in which the following risk of PGD is high.

Discussion

Grief caused by excess deaths burden the already overloaded mental health services and contribute to additional harm and suffering of the Australian population.

Australia has a severe shortage of mental health services and skilled clinicians. The management of Prolonged Grief Disorder is a specialised area of mental health service delivery, which is not widely available in Australia.

It is essential to recognise and prioritise the high human cost of bereavement and consequent grief, together with the need for specialist clinical services to care for those bereaved. This is especially so in the context of the present where there are concerning numbers of excess deaths in Australia.

References

[1] Szuhany KL, Malgaroli M, Miron CD, Simon NM. Prolonged Grief Disorder: Course, Diagnosis, Assessment, and Treatment. Focus (Am Psychiatr Publ). 2021 Jun;19(2):161-172. doi: 10.1176/appi.focus.20200052. Epub 2021 Jun 17. PMID: 34690579; PMCID: PMC8475918.

[2] Shear MK, Simon N, Wall M, Zisook S, Neimeyer R, Duan N, Reynolds C, Lebowitz B, Sung S, Ghesquiere A, Gorscak B, Clayton P, Ito M, Nakajima S, Konishi T, Melhem N, Meert K, Schiff M, O'Connor MF, First M, Sareen J, Bolton J, Skritskaya N, Mancini AD, Keshaviah A. Complicated grief and related bereavement issues for DSM-5. Depress Anxiety. 2011 Feb;28(2):103-17. doi: 10.1002/da.20780. PMID: 21284063; PMCID: PMC3075805.

[3] American Psychiatric Association (2022) Diagnostic and statistical manual of mental disorders, 5th Edition, text revision. https://doi.org/10.1176/ appi.books.9780890425787

[4] World Health Organization (2018) International Statistical Classification of Diseases and Related Health Problems, 11th Edition. Geneva: World Health Organization.

[5] Djelantik AAAMJ, Smid GE, Kleber RJ, Boelen PA. Early indicators of problematic grief trajectories following bereavement. Eur J Psychotraumatol. 2018 Jan 19;8(sup6):1423825. doi: 10.1080/20008198.2018.1423825. PMID: 29372008; PMCID: PMC5774421.

[6] Nielsen MK, Carlsen AH, Neergaard MA, Bidstrup PE, Guldin MB. Looking beyond the mean in grief trajectories: A prospective, population-based cohort study. Soc Sci Med. 2019 Jul;232:460-469. doi: 10.1016/j.socscimed.2018.10.007. Epub 2018 Oct 19. PMID: 31230666.

[7] Lundorff M, Holmgren H, Zachariae R, Farver-Vestergaard I, O'Connor M. Prevalence of prolonged grief disorder in adult bereavement: A systematic review and meta-analysis. J Affect Disord. 2017 Apr 1;212:138-149. doi: 10.1016/j.jad.2017.01.030. Epub 2017 Jan 23. PMID: 28167398.

[8] Keyes KM, Pratt C, Galea S, McLaughlin KA, Koenen KC, Shear MK. The burden of loss: unexpected death of a loved one and psychiatric disorders across the life course in a national study. Am J Psychiatry. 2014 Aug;171(8):864-71. doi: 10.1176/appi.ajp.2014.13081132. PMID: 24832609; PMCID: PMC4119479.

[9] Tal I, Mauro C, Reynolds CF 3rd, Shear MK, Simon N, Lebowitz B, Skritskaya N, Wang Y, Qiu X, Iglewicz A, Glorioso D, Avanzino J, Wetherell JL, Karp JF, Robinaugh D, Zisook S. Complicated grief after suicide bereavement and other causes of death. Death Stud. 2017 May-Jun;41(5):267-275. doi: 10.1080/07481187.2016.1265028. Epub 2016 Nov 28. PMID: 27892842.

[10] O'Connor MM. Response to: Media depictions of possible suicide contagion among celebrities: A cause for concern and potential opportunities for prevention - The role of grief. Aust N Z J Psychiatry. 2020 Apr;54(4):438. doi: 10.1177/0004867419893430. Epub 2019 Dec 7. PMID: 31813233.

[11] Shear MK, Wang Y, Skritskaya N, Duan N, Mauro C, Ghesquiere A. Treatment of complicated grief in elderly persons: a randomized clinical trial. JAMA Psychiatry. 2014 Nov;71(11):1287-95. doi: 10.1001/jamapsychiatry.2014.1242. PMID: 25250737; PMCID: PMC5705174.

[12] Shear K, Frank E, Houck PR, Reynolds CF 3rd. Treatment of complicated grief: a randomized controlled trial. JAMA. 2005 Jun 1;293(21):2601-8. doi: 10.1001/jama.293.21.2601. PMID: 15928281; PMCID: PMC5953417.

[13] Shear MK, Reynolds CF 3rd, Simon NM, Zisook S, Wang Y, Mauro C, Duan N, Lebowitz B, Skritskaya N. Optimizing Treatment of Complicated Grief: A Randomized Clinical Trial. JAMA Psychiatry. 2016 Jul 1;73(7):685-94. doi: 10.1001/jamapsychiatry.2016.0892. PMID: 27276373; PMCID: PMC5735848.

[14] American Psychiatric Association: Prolonged Grief Disorder webpage: https://www.psychiatry.org/patients-families/prolonged-grief-disorder (accessed 05 October 2023).

[15] Cerel J, Brown MM, Maple M, Singleton M, van de Venne J, Moore M, Flaherty C. How Many People Are Exposed to Suicide? Not Six. Suicide Life Threat Behav. 2019 Apr;49(2):529-534. doi: 10.1111/sltb.12450. Epub 2018 Mar 7. PMID: 29512876.

[16] Australian Bureau of Statistics webpage: Statistics about deaths and mortality rates for Australia, states and territories, and sub-state regions. Released 27/09/2023: https://www.abs.gov.au/statistics/people/population/deaths-australia/latest-release (accessed 05 October 2023)

[17] Australian Bureau of Statistics webpage: Statistics on the number of deaths, by sex, selected age groups, and cause of death classified to the International Classification of Diseases (ICD). Released 27/09/2023: https://www.abs.gov.au/statistics/health/causes-death/causes-death-australia/latest-release (accessed 05 October 2023)

Dr Monique O'Connor MBBS FRANZCP graduated in medicine from Kings College, University of London, and trained in psychiatry in Western Australia. A consultant psychiatrist and Australian expert in grief, she has had broad experience in clinical psychiatry, with special interest in Psychiatry of Old Age and Palliative Care. She was the Director of Advanced Training in Psychiatry of Old Age in WA for five years. In 2017 she established a private practice specialising in grief and providing Prolonged Grief Disorder Therapy.

Dr O'Connor shares her expertise through teaching, supervision and academic publication. She is an advocate of grief education promotion in health sciences. Her ambition is to improve management of high-risk bereavements, with the aim of reducing the burden of chronic mental illness and suicide risk associated with prolonged grief.

Conclusion

This book has been assembled by an aggregation of highly-qualified and experienced doctors and researchers who take their ethics seriously. Here, information has not been withheld, or, worse, blocked.

In a letter to AMPS, in January of 2023, the then-Australian Secretary of the Department of Health and Aged Care, Brendan Murphy, wrote: 'Regarding excess mortality statistics, there is no credible evidence to suggest that excess mortality is related to COVID-19 vaccination either in Australia or internationally. The Actuaries Institute's COVID-19 Mortality Working Group are independently publishing regular analysis of excess deaths. The Working Group have concluded that vaccination impacts on excess mortality are negligible and do not fit with the timing or shape of excess mortality.' It is very telling that Murphy thereby skirts the issue. If the excess mortality rates are not being grossly raised by the mRNA injections, what are they being raised by? Would not this be the central concern? Or is denial more important?

'No credible evidence….' These are very peculiar words. On the day this book was launched, AMPS had access to well over three thousand five hundred studies casting extreme doubt on the integrity of the COVID-19 injections, and pointing to untold damage from them. All of these studies have been written by highly-qualified people; only a few of them could be selected for

this book. They offer vast scientific evidence about the inappropriateness, the damage and the danger found in the Australian government's slavish adaptation and succumbing to what can be distilled into the demands of the world's biggest pharmaceutical companies. Drug-company medicine has overtaken the medical institutions, and rammed its methods home to the point where those students trained in them are finally ejected into practice believing in pharmaceutical products to the extent of religious evangelism. The money expended in purchase and disbursement of these products, now shown never to have worked, has crippled economies worldwide as it has passed to the drug companies.

'No credible evidence'?

For three years Australia succumbed to the will of corporate ideologues in big pharma, big media, big finance, and big government who seem to prioritise profit over people. This enslavement, and it is nothing less, may help to explain these high excess death rates being witnessed now at more than 15 per cent above baseline mortality. Put another way, AMPS and all ethical and informed doctors are horrified at the ten or twenty or thirty thousand excess deaths in this country in the time since March, 2021. Australian and other Western data show a mass casualty event; peculiarly, the higher figures are occurring in the countries that are highly injected, but our political and medical authorities seem to think there is nothing worth scrutiny. Now, with this book, it has been probed. This investigation has had to cut straight across the lockstep media messaging, the medical misinformation and the censorship.

Big pharma has created a fine business model for itself, but what has been the cost to humanity? Until Australia's policymakers become more aware of the influence of big pharma and the technological big food and private industrial complex, policies will continue to reflect decisions not grounded in medical thinking. Big pharma ought not to be allowed to continue funding medical journals and university chairs because the end result of this is high profit combined with weak medicine. Considering the criminal records and the level of penalties (in the form of extraordinary fines) on multinational drug companies, the TGA needs to focus on the integrity of the drug companies. Their databases accordingly need to be transparent. Is a peak body of pharmacovigilance called for?

In the presence of unprecedented death rates and adverse reactions, and the ignoring of safety signals, why has the Therapeutic Goods Administration, the body meant to stand guard, not withdrawn the COVID vaccines, pending a full investigation? It defies logic. Is this wilful blindness?

Australians have endured relentless psychological manipulation through

media and propaganda, misinformation from authorities, and medical censorship designed to create an illusion of consensus by our own government and authorities entrusted with our protection. It became obvious quickly that this was not about 'following the science' or 'keeping people safe'. It was about the establishment and the enforcement at any cost of a system imposed from above by people misusing their authority. The nation has been through dark times and there now needs to be an accounting.

Australian people were tracked, traced, quarantined, shamed, and finally threatened into submitting to a vaccination-only strategy. On the streets to protest they were shot with rubber bullets. Governmental figures have shown how these gene-based pharmaceuticals were ineffective from the start. Now the health system continues to advocate perpetual boosters, which in themselves and by their repetition show how incompetent the novel vaccine platform is in the protection of patients from contracting COVID. The public health system appears to have been used against a trusting population for what seems financial benefit in terms of corporate profits, and all with the assistance of misinformed politicians. Australians have a right to feel violated. If medical regulators believe their job is primarily to protect the government public health messaging rather than to protect the public then the corruption of medicine is complete.

The Australian Medical Professionals Society is joining hands with more and more of the likeminded, people who believe in first doing no harm, in having informed valid voluntary consent, and protecting bodily autonomy in accordance with the longest-standing principles of civilized medical practice. We believe medicine in Australia exists to serve the people, and it should never be as it is now, the other way around.

The Australian Health Practitioner Registration Agency (AHPRA) has many perceived negatives and has demonstrated no adequate ability for oversight, as this book has amply shown. If it continues to exist then that should be solely as a registering body. This of course cannot be said by individual practitioners who see through the holes in the present system, because the system will immediately punish them and so they will be suspended. Practitioners must regain the right to speak freely, for this reason, and also to be able to call out research fraud.

Regulatory agencies should not be in a position to take money from the big pharmaceutical companies. Australian people need protection from predatory corporate bodies, those in pharmaceuticals, in food and in agriculture. In particular, AMPS finds that the regulators' job is to assess the information presented by vested interests. Data have to be released, and need to be open-sourced in the raw form to independent researchers. Otherwise,

censorship is too easily applied, to the detriment of the facts.

This present book is finding its way to medical and political authorities both in Australia and overseas. The introduction to the book ended with a quotation from Winston Churchill. The Australian Medical Professionals Society has every intention of driving forward this debate to the point of prompting substantial governmental action to rectify serious problems within our health system, and it may be appropriate to finish with another. 'Now, this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning.'