National Academies Committee on Review of Relevant Literature Regarding Adverse Events Associated with Vaccines March 30 2023: Written material accompanying oral remarks.

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National Academies Committee on Review of Relevant Literature Regarding Adverse Events Associated with Vaccines March 30 2023: Written material accompanying oral remarks.

Submitted March 31 2023 to: vaccines@nas.edu

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Oral remarks at: https://player.vimeo.com/video/809903500#t=84m37s

Capsule

A committee of the National Academies convened on March 30 2023 to *"review relevant literature regarding adverse events associated with* [Covid-19] *vaccines."* To supplement oral remarks delivered at the meeting and to assist the committee's deliberations, further detail is provided here along with a summary (with original documents) of our written comments submitted to FDA and CDC advisory committees on Covid-19 Vaccines. These comments contain a number of novel analyses conducted relating to Covid-19 vaccine safety. This document further discusses:

- Hasty vaccine development, undisclosed sequences and kinetics of modRNA and spike protein
- Novel heterotrimers formed after bivalent vaccination
- Gene therapy nature of the Pfizer, Moderna and Janssen Covid-19 vaccines
- VAERS underreporting
- Safety signal analysis
- Masking of safety signals
- Ischemic stroke
- Negative efficacy: an indicator of immune suppression?
- All-cause mortality and vaccination
- Concerning cancer reports
- Transparency, scientific engagement, rebuilding trust in public health

We show here a number of instances of FDA or CDC analyses being unreliable or highly limited.

According to a recent article in Nature,(1) Covid-19 vaccine hesitancy has spilled over to other vaccinations reaching their lowest point since 2008 and jeopardizing the health of millions. This is attributed an erosion of trust and confidence in governments and public-health institutions exacerbated with the advent of COVID-19 vaccines.

Restoring trust in public health institutions must surely be your highest priority. Unless the setting of parameters that will determine whether someone is eligible for compensation for alleged vaccine-injury is seen as just, there will be further erosion in trust of public health institutions, exacerbated as the specter of unknown long-term harms related to the hastily deployed novel gene therapy, becomes appreciated.

Restoration in trust can only be begin if your work is transparent and open to scientific dialog. Yours cannot be another exercise in "going through the motions" of the kind we have seen with FDA and CDC committees. My colleagues and I are ready to participate in meaningful and necessary scientific discourse.

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1. Original oral remarks

"Thank you. I am a PhD with a background in experimental pathology, pharmacy and pharmacology. I led a research program at Johnson and Johnson where my duties included pharmacovigilance. I focus on fibrosis and pain, running my own company since 1996. I joined Dr. McCullough on Senator Johnson's panel.

These expedited and still experimental vaccines are the most complicated medical products ever deployed. Sequences remain undisclosed and questions about the persistence of mRNA and spike have been evaded despite reports that they linger many months. The Moderna, and likely Pfizer bivalents elicit up to four distinct spike proteins, including two novel heterotrimers with likely new toxicology.

Despite meeting FDAs biologic definition of gene therapy products, these vaccines are excluded from the gene therapy guidance, with no public comment from FDAs gene therapy infectious disease vaccine labs. Concerns for autoimmune, neurological, hematological and other diseases must remain on the table. We see cancer signals.

VAERS is underreported (2), up to 14 times for myocarditis. FDA have ignored their own estimates for underreporting up to 36 times (3) when dismissing the now three fold excess of death reports for covid vaccines over all other vaccines for all years.

I will provide our 17 submissions to FDA and CDC. PRR signal analysis is useful but limited. Using vaccination coverage, we found more accurate age stratified normalized event ratios up to 7 for GBS, 34 for serous events, 370 for coagulopathies, 98 for deaths and 403 for myocardial infarction.

Significant PRR ratios for events of interest are published in NIH funded work (4)
Kwan (5) found elevations in POTS and other diagnoses. FDA's Harpaz (6) despite finding masking also hinted at signals for events on your list.

In their recent discussion of ischemic stroke, CDC and FDA claimed that they found a transient signal in VSD and nowhere else. And yet, in CDC's own FOIA disclosure appeared significant PRR signals for ischemic stroke in VAERS form last July. We obtained a similar result from an online PRR calculator funded by NIH. (7)

Most concerning are data, including CDCs', showing negative vaccine efficacy, indicating immune suppression. A Cleveland clinic study (8) recently remarked that theirs was not the only one to find "a possible association with more prior vaccine doses and higher risk of COVID-19.

We have found from European data, correlations between vaccination coverage and all cause mortality. There is a time dependency critical to understand the effect of these vaccines with mostly periods of detrimental associations, punctuated by briefer periods of benefit.

Your work must be open to scientific dialog that is not just "going through the motions" we have seen with FDA and CDC. I welcome your further interaction."

2. Introduction

Per its web site:[1] The National Academies of Sciences, Engineering, and Medicine has convened an ad hoc committee to review the epidemiological, clinical, and biological evidence regarding the relationship between:

• COVID-19 vaccines and specific adverse events i.e. Guillain-Barrè Syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), transverse myelitis (TM), Bell's palsy, hearing loss, tinnitus, chronic headaches, infertility, sudden death, myocarditis/pericarditis, thrombosis with thrombocytopenia syndrome (TTS), immune thrombocytopenic purpura (ITP), thromboembolic events (e.g., cerebrovascular accident (CVA), myocardial infarction (MI), pulmonary embolism, deep vein thrombosis (DVT)), capillary leak syndrome, and

• intramuscular administration of vaccines and shoulder injuries.
The committee will make conclusions about the causal association between vaccines and specific adverse events.

This document provides further detail to assist the committee's deliberations.

[1] https://www.nationalacademies.org/our-work/review-of-relevant-literature-regarding-adverse-events-associated-with-vaccines

This document is not all encompassing with many areas requiring further consideration, most notably the effects of Covid-19 on reproductive function.

Further it is to stressed that any discussion of safety reports, present of a signal does not prove causality.

3. Summary of written comments submitted to FDA and CDC on Covid-19 Vaccines

Below are summarized our written comments on adverse event related topics contained within made to FDA or CDC. The files are provided as attachments to this document and numbered according to their citation n this document.

Date	Year	Agency	Committee	AE related topics/ filename	Ref
8/29	2021	CDC	ACIP	• Disproportionality Signal Analysis discussion. Calculation of Normalized Event Ratio • Calculation of VAERS under reporting for death • Covid-19 and non-Covid-19 deaths after vaccination • Wiseman09-CDC-2021-0089-0023_attachment_1.pdf	(9)
8/29	2021	CDC	ACIP	• Supplement to (9) • Full approval of COMIRNARY – vaccine hesitancy • Waning immunity • Wiseman10-CDC-2021-0089-0039_attachment_1.pdf	(10)
9/17	2021	FDA	VRBPAC	• Disproportionality Signal Analysis discussion. Calculation of Normalized Event Ratio (similar to (9)) • Wiseman11-FDA-2021-N-0965-0016_attachment_1.pdf	(11)
10/15	2021	FDA	VRBPAC	• Cases and deaths increase in Israel after booster rollout. • Evidence of immunosuppression from our analysis of early Israeli published (12) and MoH data. • Wiseman13-FDA-2021-N-0965-0146.pdf	(13)
10/15	2021	FDA	VRBPAC	• Critique of disproportionality analyses. Calculation of Normalized Event Ratio (NER) vs. PRR • Wiseman14-FDA-2021-N-0965-0164-SUPPLEMENT.pdf	(14)
10/21	2021	CDC	ACIP	• Additional NER/ vs. PRR calculations. Ineffectiveness (negative efficacy?) from Israeli data presented at 10/15/21 VRBPAC • Wiseman15-CDC-2021-0098-FDA-2021-N-1088.pdf	(15)
11/19	2021	CDC	ACIP	• VAERS underreporting for myocarditis by 4.8x according to Pfizer • Wiseman16-CDC-2021-0125-0003_attachment_1.pdf	(16)
12/16	2021	CDC	ACIP	• Coagulopathies with mRNA vs DNA vaccines • All-cause mortality with vaccination coverage: lag analysis of European data. Need to analysis data by lag time. • NER/PRR for various AEs. • Inconsistent treatment of TTS for Janseen vs. other coagulopathies/ thromboembolic evets with mRNA products • Wiseman17-CDC-2021-0133-0002_attachment_1.pdf	(17)
1/5	2022	CDC	ACIP	• Manipulation of UK graphs to conceal waning v Omicron • Waning and negative efficacy, evidence of immunosuppression? • Wiseman18-CDC-2022-0002-0002_attachment_1.pdf	(18)
2/4	2022	CDC	ACIP	• CDC fails to inform ACIP of negative efficacy data – evidence of immune suppression? • Inaccurate risk-benefit analysis. • Discrepancies of CDC reports for rates of myocarditis provided at ACIP, VRBPAC meetings vs. CDC's published work.(19) • Comments by EMA official and ACIP members on possible harms of boosting. • Wiseman20-CDC2022-0022-0009-Feb4ACIP-FDA-2022-N-0082-FINAL.pdf	(20)
4/6	2022	FDA	VRBPAC	• Update waning VE vs. Omicron • All population booster COVID19 vaccine injections are associated with all-cause mortality amidst limited periods of benefit in all ages: European and US data • Consistent data found with CDC data • Gene therapy concerns • Wiseman21-FDA-2022-N-0336-2500_attachment_1.pdf	(21)
4/20	2022	CDC	ACIP	• Very high rates of myocarditis after booster presented by Israeli MoH	(22)

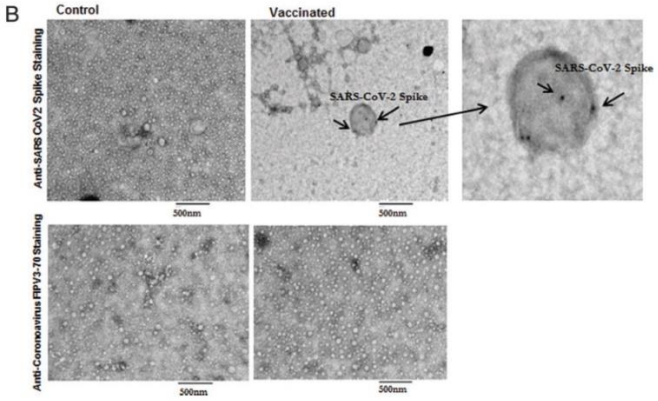
				• Other information similar to VRBPAC 4/6/22 • Wiseman22-CDC-2022-0051-0260_attachment_1.pdf	
5/19	2022	CDC	ACIP	• Estimates of VAERS underreporting, including by Kaiser Permanente – of 6-14 times for myocarditis.(23) • Wiseman24-CDC2022-0065-ACIP051922-corrected2.pdf	(24)
6/10	2022	FDA	CTGTAC	• Cell Therapy Gene Therapy Advisory Committee • C19 vaccines meet FDA's biological definition of a gene therapy product. Safety concerns discussed relating to gene therapy, as well as lack of genotoxicty and carcinogenicity studies. • Wiseman25-FDA-2022-N-0470-June10-CTGTAC-LINKS.pdf	(25)
6/23	2022	CDC	ACIP	• Stunningly poor data for infants < 5years: Negative VE in some scenarios. • High rates of myocarditis found in VSD vs VAERS by about 6x in some cases • Evasion of questions concerning persistence of mRNA and spike. • Wiseman26-CDC-2022-0085-0017_attachment_2.pdf	(26)
7/19	2022	CDC	ACIP	• High rates of myocarditis for Novavax glossed over by CDC. • CDC fail to provide PRR analysis per protocol(27) • Guo et al., publish a PRR analysis(4) • Wiseman28-CDC-2022-0085-0017_attachment_1.pdf	(28)
9/1	2022	CDC	ACIP	• Disclosure by Moderna of novel heterotrimers • Wiseman29-CDC-2022-0103-0049_attachment_1.pdf	(29)
10/19	2022	CDC	ACIP	• Unethical pregnancy studies by CDC • Evasive answers to question about mRNA and spike distribution and persistence. • Early (May 2021) indications of negative efficacy from Denmark.(30) • Discussion of novel heterotrimer • Wiseman31-CDC-2022-0111-126227-OCT19-ACIP.pdf	(31)
1/26	2023	FDA	VRBPAC	• Analysis of FDA briefing document re: new strain selection. • Wiseman32-2023-VRBPACJan23-FDA-2022-N-2810-CommentsonBrefingDocument-TRACKING.pdf	(32)
2/24	2023	CDC	ACIP	• Ischemic stroke signal – FDA/CDC ignore its own PRR signal i VAERS. • Consideration of bivalent vaccines as primary series. • Wiseman33-CDC-2023-0007-0496_attachment_1.pdf	(33)

4. Expanded detail of oral remarks

4.1. Hasty vaccine development, undisclosed sequences and kinetics of modRNA and spike protein

These expedited and still experimental vaccines are the most complicated medical products ever deployed. Pfizer's recently retired head of vaccine research, Dr. Kathrin Jansen, was quoted as saying *""We flew the aeroplane while we were still building it."* (34) Much about the pharmacology and toxicology of this novel class of vaccine remain to be discovered, but should have been known prior to roll out, or even now. A review of the preclinical investigations performed or not performed by Pfizer and Moderna is helpful in assessing plausibility of an adverse event, but is beyond the scope of this document.

Sequences remain undisclosed. Questions about the persistence of modRNA and spike have been evaded (see discussion in 20)) despite reports that they linger many months. Bansal et al., (35) found that exosomes demonstrated spike protein antigens on their surface and that *"Exosomes with spike protein and antibodies decreased in parallel after four months."*



This persistence, far longer than that popularly communicated to be in the order of a few days, is a key factor in analyzing the causality of adverse events.

The potential toxicity of LNP components has been reviewed recently(36) and was already anticipated in the above mentioned 2016 paper from Langer's group: (37)

"Among the most problematic are the potential toxicity of LNP components, including cationic lipids, phospholipids or combinations thereof. The immunogenicity of PEG and the decreased interaction of the LNPs with the endosomal membranes that hinders endosomal escape are also important issues for both siRNA and mRNA delivery."

A further consideration in assessing the toxicity of the Covid-19 vaccines relates to the Lipid Nanoparticles (LNPs) used to deliver the modRNA payload. Contrary to popular misconception that the Covid-19 vaccines stay close to the site of injection in the arm, LNPs distribute widely around the body.

Study 18530 released by FOIA and conducted by Pfizer[2] looked at the distribution of Lipid Nanoparticles (LNP) in rats following intramuscular injection. The study only proceeded for 48 hours, but the LNPs accumulated in a number of tissues, including (highlighted below), adrenal glands, bone marrow, liver, lymph nodes, ovaries, spleen, and to a smaller extent, testes. This indicates that we should be particularly vigilant for possible adverse effects in these tissues. The study should have been continued to determine the point at which the LNPs (or their breakdown products), were eliminated from the body.

Report Number: 185350

Species (Strain):	Rat (Wistar Han)
Sex/Number of Animals:	Male and female/3 animals/sex/timepoint (21 animals/sex total for the 50 µg dose)
Feeding Condition:	Fed ad libitum
Method of Administration:	Intramuscular injection
Dose:	50 µg [^{3}H]-08-A01-C0 (lot # NC-0552-1)
Number of Doses:	1
Detection:	Radioactivity quantitation using liquid scintillation counting
Sampling Time (hour):	0.25, 1, 2, 4, 8, 24, and 48 hours post-injection

Sample	Mean total lipid concentration (µg lipid equivalent/g (or mL) (males and females combined)							% of administered dose (males and females combined)						
	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h	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	0.271	1.48	2.72	2.89	6.80	13.8	18.2	0.001	0.007	0.010	0.015	0.035	0.066	0.106
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365	0.000	0.001	0.001	0.001	0.001	0.002	0.002
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687	--	--	--	--	--	--	--
Bone marrow (femur)	0.479	0.960	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	0.007	0.013	0.020	0.016	0.011	0.010	0.009
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112	0.000	0.001	0.001	0.002	0.002	0.002	0.003
Heart	0.282	1.03	1.40	0.987	0.790	0.451	0.546	0.018	0.056	0.084	0.060	0.042	0.027	0.030
Injection site	128	394	311	338	213	195	165	19.9	52.6	31.6	28.4	21.9	29.1	24.6
Kidneys	0.391	1.16	2.05	0.924	0.590	0.426	0.425	0.050	0.124	0.211	0.109	0.075	0.054	0.057
Large intestine	0.013	0.048	0.093	0.287	0.649	1.10	1.34	0.008	0.025	0.065	0.192	0.405	0.692	0.762
Liver	0.737	4.63	11.0	16.5	26.5	19.2	24.3	0.602	2.87	7.33	11.9	18.1	15.4	16.2
Lung	0.492	1.21	1.83	1.50	1.15	1.04	1.09	0.052	0.101	0.178	0.169	0.122	0.101	0.101

[2] https://phmpt.org/wp-content/uploads/2022/03/125742_S1_M2_26_pharmkin-tabulated-summary.pdf

Sample	Total Lipid concentration (µg lipid equivalent/g [or mL]) (males and females combined)							% of Administered Dose (males and females combined)						
	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h
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	1.37	--	--	--	--	--	--	--
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	12.3	0.001	0.009	0.008	0.016	0.025	0.037	0.095
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599	0.003	0.007	0.014	0.015	0.015	0.011	0.019
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694	0.000	0.001	0.001	0.001	0.000	0.000	0.001
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170	0.001	0.001	0.002	0.003	0.003	0.004	0.003
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264	0.003	0.007	0.008	0.008	0.005	0.006	0.009
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	1.28	1.30	1.47	0.024	0.130	0.319	0.543	0.776	0.906	0.835
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112	0.001	0.002	0.002	0.003	0.001	0.001	0.001
Spleen	0.334	2.47	7.73	10.3	22.1	20.1	23.4	0.013	0.093	0.325	0.385	0.982	0.821	1.03
Stomach	0.017	0.065	0.115	0.144	0.268	0.152	0.215	0.006	0.019	0.034	0.030	0.040	0.037	0.039
Testes (males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320	0.007	0.010	0.017	0.030	0.034	0.074	0.074
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331	0.004	0.007	0.010	0.012	0.008	0.007	0.008
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.00	0.000	0.001	0.001	0.001	0.001	0.001	0.001
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.456	0.002	0.011	0.015	0.008	0.016	0.018	0.022
Whole blood	1.97	4.37	5.40	3.05	1.31	0.909	0.420	--	--	--	--	--	--	--
Plasma	3.97	8.13	8.90	6.50	2.36	1.78	0.805	--	--	--	--	--	--	--
Blood:Plasma ratio[a]	0.815	0.515	0.550	0.510	0.555	0.530	0.540	--	--	--	--	--	--	--

4.2. Novel heterotrimers

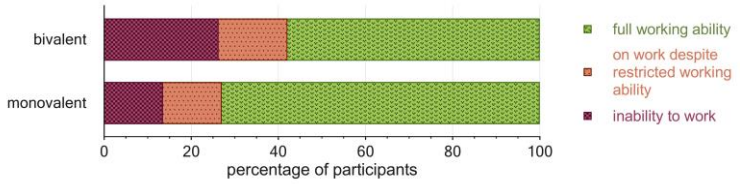
The Moderna, and likely Pfizer bivalents elicit up to four distinct spike proteins, including two novel heterotrimers with likely new toxicology.

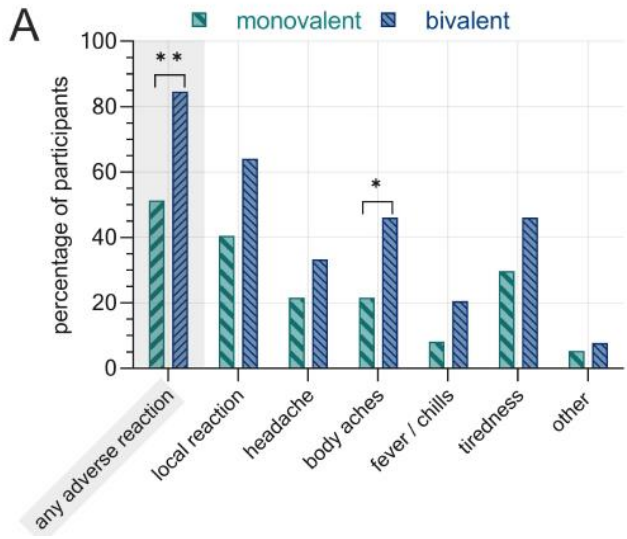
As we discuss (31) Moderna revealed at the Sept 1st ACIP (29,31) that their bivalent vaccine elicits the formation of novel spike protein heterotrimers to produce a superior immunological response. This would mean that these vaccines might have a different toxicological profile, as yet untested.

Based on EMA documents, it is likely that the same occurs for the Pfizer bivalent vaccine. This represents novel chemistry, novel pharmacology and potentially novel toxicology.

Indeed Wagenhauser et al. recently reported (38) that the *"rate of adverse reactions for the second booster dose was significantly higher among participants receiving the bivalent 84.6% (95% CI 70.3%-92.8%; 33/39) compared to the monovalent 51.4% (95% CI 35.9-66.6%; 19/37) vaccine (p=0.0028)."*

Graphical results from Wagenhauser et al. (38)





4.3. Gene therapy nature of the Pfizer, Moderna and Janssen Covid-19 vaccines

"FDA generally considers human gene therapy products to include all products that mediate their effects by transcription or ***translation of transferred genetic material*** *or by specifically altering host (human) genetic sequences. Some examples of gene therapy products include* ***nucleic acids*** *(e.g., plasmids,* ***in vitro transcribed ribonucleic acid (RNA)****),…."* (39)

Despite meeting FDAs biologic definition of gene therapy products, these vaccines are excluded from the gene therapy guidance, with no public comment from FDAs gene therapy infectious disease vaccine labs. Concerns for long term effects of autoimmune, neurological, hematological and other diseases must remain on the table, especially cancer (see 4.10). Indeed FDA's guidance on long term follow up for gene therapy products (39) suggests follow up times of 5-15 years. The long-term studies committed to by Pfizer and Moderna have not yet been completed or reported. Accordingly, it may not be possible for this committee to rule out many effects of these vaccines.

The mRNA vaccines are more properly described in FDA documents as "nucleoside modified mRNA" (modRNA) vaccines. mRNA has been modified by codon optimization and by substitution of N1-methylpseudouridine. There are two proline amino acid substitutions and the modRNA contains Untranslated Regions (UTR) with gene sequences of human origin. This is critical in understanding the toxicology of these products. We discuss this matter more fully in our submission to FDA's Cell Therapy and Gene Therapy Advisory Committee. (25)

Along with the finding by European regulators of residual DNA (from the plasmid vector used in manufacturing), these issues recall the concerns expressed by FDA in its 2007 guidance for plasmid vectored vaccines for infectious diseases (40):
"Plasmid biodistribution, persistence and integration studies were initially recommended to examine whether subjects in DNA vaccine trials were at heightened risk from the long-term expression of the encoded antigen, either at the site of injection or an ectopic site, and/or plasmid integration. Theoretical concerns regarding DNA integration include the risk of tumorigenisis if insertion reduces the activity of a tumor suppressor or increases the activity of an oncogene. In addition, DNA integration may result in chromosomal instability through the induction of chromosomal breaks or rearrangements.

FDA's own staff have addressed concerns about residual DNA in vaccines,(41) which are surely heightened with a study that suggests that vaccinal mRNA can be reversed transcribed.(42) Transcriptionally competent DNA carried by exosomes can enter spermatozoa and inherited extra-chromasomally.(43)

4.4. VAERS underreporting

FDA have acknowledged that VAERS is mis- and underreported (2), up to 14 times for myocarditis from FDA, Israel MoH and Kaiser-Permanente sources, as we discuss mor fully. (24)

The disproportionately large number of death reports for Covid-19 vaccines in VAERS is well known. A search of VAERS (3/30/23) for reports of death with any Covid-19 vaccine in the US and Territories revealed 17,185 reports, compared with 5539 reports for all other vaccines, all years combined. Flu vaccine accounted for 1361 of these reports.

VAERS 3/30/23 Covid vax

Messages:

- VAERS data in CDC WONDER are updated every Friday. Hence, results for the same query can change from week to week.
- These results are for 17,185 total events.

Event Category	Events Reported	Percent (of 17,185)
Death	17,185	100.00%
Total	**17,185**	**100.00%**

All other vaccines

Event Category	Events Reported	Percent (of 5,539)
Death	5,539	100.00%
Total	**5,539**	**100.00%**

Flu vaccine

Messages:

- VAERS data in CDC WONDER are updated every Friday. Hence, results for the same query can change from week to week.
- These results are for 1,361 total events.

Event Category	Events Reported	Percent (of 1,361)
Death	1,361	100.00%
Total	**1,361**	**100.00%**

FDA's Day et al. (3) have attempted to dismiss this sort of discrepancy by comparing the death rates with those normally expected with data we excerpted here:

			Observed reporting rates			
	Expected all-cause deaths†		All COVID-19 vaccines			
	7-day‡	42-day	7-day	URF	42-day	URF
Sex						
Female	159.3	956	14.5	11.0	23.4	40.9
Male	172	1,031.7	20.5	8.4	32.7	31.6
Age (years)						
5-14	2.6	15.6	0.3	8.7	0.8	19.5
15-24	14.2	85.1	1.8	7.9	2.8	30.4
25-34	25.5	152.7	2.8	9.1	4	38.2
35-44	37.4	224.5	4.6	8.1	7.3	30.8
45-54	77	461.7	8.1	9.5	12.4	37.2
55-64	169.8	1,018.6	16	10.6	24.6	41.4
65-74	343.2	2,059.4	27.8	12.3	44.7	46.1
75-84	857.2	5,143.0	51.1	16.8	86.3	59.6
≥85	2,601.40	15,608.3	178	14.6	292.3	53.4
Total	**165.6**	**993.3**	**17.3**	**9.6**	**27.8**	**35.7**
Min-Max by age range						
Min				**7.9**		**19.5**
Max				**16.8**		**59.6**

These data show, despite mandatory reporting, that the VAERS Under Reporting Factor (URF) for deaths associated with Covid-19 vaccines is about 10 for a 7-day window and 36 for a 42-day window. This certainly does not rule out any association between deaths and vaccination, but highlights the severe shortcomings of the VAERS database.

In August 2021 we (9) used CDC published methodology (44) to estimate the degree of under-reporting of in VAERS for the Pfizer product, by comparing the death of AEs published in clinical trials, with death rates normalized for population found in VAERS. Using a 30 day window, our estimate of 4.9-15 times underreporting is highly consistent with the figure of 9.6 derived from FDA's Day et al. (3)

4.5. Safety signal analysis

Disproportionality Signal Analysis (DSA) is commonly used in pharmacovigilance. The use of the Proportional Reporting Ratio (PRR) is described in the VAERS SOP for analyzing safety signals for the Covid-19 vaccines.(27) As we discuss extensively (11,14,15) the flaws of the PRR method are well known. It was developed to detect small single or low double digit increases in the numbers of a reported event after use of a particular drug, using the surrogate denominator of the total number events reported. This surrogate was necessary because the exact number of drug doses administered is not known.

This problem does not exist for the Covid-19 vaccines, as CDC maintains updated statistics on vaccine coverage, including how many doses of any given vaccine were actually administered, stratified by age.

We therefore used CDC's vaccination coverage statistics to calculate a more accurate "normalized event ratio" (NER), using flu vaccines as the comparator. This removes masking type artifacts that can lead to underestimates of an event frequency.(6) (see 4.6) The NER appears far more sensitive than the PRR, shown below.

We conducted a number of analyses in the Fall of 2021 which we reported to FDA and CDC committees. In this analysis (11) we show high NER values, despite small PRR values by event category, for all Covid-19 vaccines. The same calculation is also shown for H1N1 vaccines, collected at a time when AE reporting was encouraged by CDC as an example as "stimulated reporting." The ratios calculated for the Covid-19 far exceed those for a vaccine whose reporting was considered to be "stimulated."

	NER or PPR				
	C19 vs Flu			C19 vs H1N1	
Event Category	NER people[a]	NER Doses[b]	PRR[c]	NER People[d]	PRR[e]
Death	176.7	97.5	5.2*	35.1	0.4
Life Threatening	58.9	32.5	1.7	13.2	1.1
Permanent Disability	29.6	16.3	0.9	19.5	0.7
Congenital Anomaly / Birth Defect *	47.0	26.0	1.4	0.0	0.0
Hospitalized	53.8	29.7	1.6	13.5	1.1
Existing Hospitalization Prolonged	44.3	24.5	1.3	1.3	11.3
Emergency Room * (note)	42.1	32.3	1.7	18.2	0.8
Office Visit * (note)	22.4	17.2	0.9	13.1	1.1
None of the above	37.8	20.9	1.1	15.7	0.9
Serious	51.4	28.3	1.5	14.8	0.97
Not serious	33.1	18.3	1.0	14.9	0.96

We used estimates from CDC for the number of doses delivered/ people vaccinated.[14] We used USAFACTS[15] for age-related population figures for various years, and CDC figures on numbers of people vaccinated [16]for seasonal flu or H1N1 vaccines. Original figures obtained from VAERS 7/30/21 using "USA Territories, unknown"" as the location filter.

[a] Normalized Event Ratio (NER) of number of events in each event category (denominator number of unique events) adjusted for number of people given at least one dose of C19 (all dates) or Flu vaccine for 2016/7, 17/18 or 18/19 seasons
[b] NER of number of events in each event category adjusted for number of doses given of C19 (all dates) or Flu vaccine for 2016/7, 17/18 or 18/19 seasons
[c] PRR, C19, vs. flu (using unique events as denominator)
[d] Ratio of number of events in each event category adjusted for number of people given at least one dose of C19 (all dates) or H1N1 vaccine for 2009/10 season

In the next analysis (11) for all Covid-19 vaccines we show NER values exceeding the PRR equivalent value in five major event categories, by age. We find NER value up to 7 for GBS, up to 34 for serious events, up to 370 for coagulopathies, up to 98 for deaths and up to 403 for myocardial infarction. In most cases these values correspond to a statistically significant PRR value.

*Table 2: **COVID-19 vs. Flu Vaccines: Normalized Event Ratio vs. Disproportionality Signal Analysis as Proportion of All Reports or events***

	SERIOUS EVENTS			DEATHS			GBS			COAGULOPATHY			Myocardial Infarction		
Ages	NER dose	PRR event	PRR report	NER dose	PRR event	PRR report	NER dose	PRR event	PRR report	NER dose	PRR event	PRR report	NER dose	PRR event	PRR report
10-17	34	1.66	1.35	32	1.52	1.24	7	0.34	0.28	74	3.56	2.89	n.e.	n.e.	n.e.
18-49	25	0.87	0.99	64	2.22	2.52	3	0.09	0.1	226	7.78	8.82	403	13.92	15.78
50-64	26	1.23	1.45	85	4.01	4.74	3	0.12	0.14	239	11.19	13.22	121	5.68	6.71
65+	30	2.34	2.76	98	7.77	9.16	3	0.22	0.26	370	31.34	36.97	88	7.01	8.27
10+	28	1.31	1.52	91	4.24	4.93	3	0.13	0.15	276	12.77	14.84	126	5.83	6.78

Note: The PRR is the ratio of the proportion of a particular event or event type out of all reports (or events) for COVID-19 to the proportion of all reports (or events) for the combined 2015-2019 flu seasons. Orange shading indicates a statistically significant difference between the proportion of COVID-19 proportion of COVID-19 and flu reports for that age group and event type (chi squared test. Flu reporting rates represent the total reports to VAERS across the 2015/16-2019/20 flu seasons for each age group. Covid-19 reporting rates include all reports to VAERS for COVID-19 vaccines for each age group as of Aug. 6, 2021. The Normalized Event Ratio shown is calculated according to the number of doses given.
The "coagulopathy" category includes a set of 26 preferred terms (PT) for thromboembolic events (although the category does not include coagulopathy PT). The full list of PT's for GBS, coagulopathy and acute myocardial infarctions can be found in Table 4.6 of the VAERS SOP document.(21)

(also in (17))

Of note is the apparent reduction in GBS assessed by PRR, in the face of an increase by NER.

We then (14,15,17) stratified by vaccine type and more granular event type. We found greater NER values for coagulopathy and embolic/thrombotic events for Janssen than Pfizer or Moderna, which are nonetheless high. NERs for death and myocardial infarction are high for all three vaccines. This means that reporting of deaths after Covid-19 vaccination is 119-297 times the rate than after flu vaccination.

Table 1: ***Normalized Event Ratio (NER) for Covid-19 quasi-Vaccines Compared with Seasonal Flu Vaccines***

	JANSSEN		MODERNA		PFIZER\BIONTECH	
	By dose	By person	By dose	By person	By dose	By person
Death	297	297	170	316	119	225
Life Threatening	110	110	39	72	32	60
Permanent Disability	57	57	24	44	20	38
Congenital Anomaly/Birth Defect	112	112	58	108	51	95
Hospitalized	101	101	43	80	37	70
GBS	19	19	3	5	2	4
Coagulopathy	1427	1428	286	531	218	413
Myocardial Infarction	411	412	232	431	180	339
Myo/peri carditis	181	181	170	317	217	410
Embolic Thrombotic	610	610	151	280	113	213
Serious	92	92	41	76	34	65
Not serious	46	46	27	51	16	31

Using VAERS data as of 10/13/21, we obtained the numbers of reports for various event types and categories using the "USA/Territories/Unknown" filter and for ages 6 and above. We stratified by Covid q-vaccine type and compared event rates with those for seasonal flu vaccines from the 2015/16 to 2019/20 seasons. Flu and Covid-19 (q-)vaccine coverage data were obtained from CDC, and population estimates where needed from https://usafacts.org/. We calculated NER for the Covid-19 q-vaccines against seasonal flu vaccine. We normalized both for the number of doses administered and the number of people having at least one dose.

Montano used similar method to ours (45) and remarked:
"The largest absolute risks were observed for allergic, constitutional reactions, dermatological, gastrointestinal, neurological reactions, and localised and non-localised pain. The largest relative risks between COVID-19 vs. influenza vaccines were observed for allergic reactions, arrhythmia, general cardiovascular events, coagulation, haemorrhages, gastrointestinal, ocular, sexual organs reactions, and thrombosis."

Significant PRR ratios for events of interest are published in NIH funded work (4) excerpted here.

TABLE 3 | (*Continued*) Statistically signant AEs associatenssen, ModernID-19 vacci

Adverse Event	Vaccine	Count	PRR	x^2
	Pfizer	740	2.35	345.59
Cerebrovascular accident	Janssen	439	2.94	498.29
	Pfizer	1,391	2.11	511.72
Epistaxis	Janssen	309	2.17	178.72
Contusion	Janssen	644	2.03	311.33
Pulmonary embolism	Janssen	584	4.57	1,351.53
	Pfizer	1,339	2.30	599.16
Thrombosis	Janssen	1,004	6.66	3,716.05
	Pfizer	1737	2.38	830.80
Pulmonary thrombosis	Janssen	139	5.76	433.54
Deep vein thrombosis	Janssen	524	5.85	1,667.82
	Pfizer	943	2.15	361.52

Of note are a number of neurological events in the same study.

TABLE 3 | Statistically significant medically relevant AEs associated with the Janssen, Moderna, and Pfizer COVID-19 vaccines.

Adverse Event	Vaccine	Count	PRR	x^2
Behavioral and neurological AE (38) Janssen (22) Moderna (6) Pfizer (23)				
Ageusia	Janssen	439	2.13	241.48
	Moderna	1866	2.08	654.59
	Pfizer	2,381	3.26	1944.30
Anosmia	Janssen	344	2.18	199.33
	Pfizer	2007	3.92	2070.10
Anxiety	Pfizer	4,279	2.21	1763.70
Cold sweat	Janssen	659	2.50	535.31
Dysgeusia	Pfizer	3,391	2.64	1985.12
Fatigue	Janssen	10,913	2.01	5,538.40
	Moderna	47,860	2.00	16,620.00
Impaired work ability	Janssen	656	2.20	393.88
	Moderna	2,714	2.09	964.26
Nervousness	Pfizer	1,212	2.05	411.43
Night sweats	Janssen	314	2.04	151.81
Panic attack	Janssen	139	2.13	76.22
	Pfizer	672	2.64	391.61
Bell's palsy	Moderna	1,384	2.21	558.43
	Pfizer	1728	3.36	1,467.30
Facial paralysis	Janssen	274	2.10	144.77
	Pfizer	1,333	2.61	761.59
Seizure	Janssen	650	2.50	527.36
	Pfizer	2,373	2.10	860.96
Chills	Janssen	11,387	2.31	8,299.80
	Moderna	12,512	19.19	15,573.00

Using a different method with electronic health records, Kwan et al. (5) (below) found elevations in POTS, dysautonomia, and myocarditis. and other diagnoses. Statistically significant but smaller (14-30%) elevations in a number of other diagnoses were also found, which may be clinically significant.

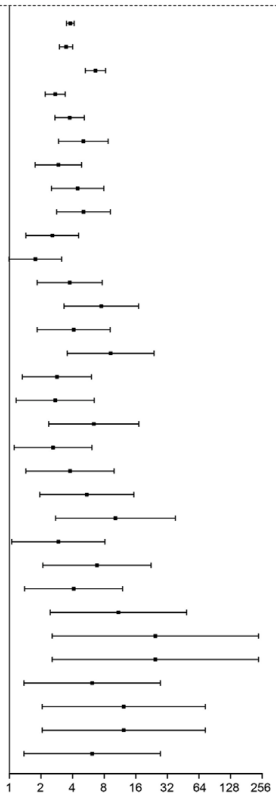
Table 1 | Diagnoses within 90 days of exposure for study sample with documented COVID-19 vaccination (*n*=284,592)

Diagnosis	No. new diagnoses	New diagnosis before exposure	New diagnosis after exposure	Post-exposure risk		Diagnostic group
	n (per 100,000)	*n* (per 100,000)	*n* (per 100,000)	Odds (95% CI)	*P* value	
Myocarditis	25 (8.78)	7 (2.46)	18 (6.32)	2.57 (1.02–6.77)*	0.046	Myocarditis
Dysautonomia	68 (23.89)	21 (7.38)	47 (16.51)	2.24 (1.30–3.87)†	0.002	POTS
POTS	1,264 (444.14)	501 (176.04)	763 (268.10)	1.52 (1.36–1.71)‡	<0.001	POTS
Mast cell disorders	64 (22.49)	27 (9.49)	37 (13.00)	1.37 (0.81–2.32)	0.26	POTS
UTI	2,038 (716.11)	879 (308.86)	1,159 (407.25)	1.32 (1.21–1.44)‡	<0.001	CPC
Dizziness	2,191 (769.87)	954 (335.22)	1,237 (434.66)	1.30 (1.19–1.41)‡	<0.001	CPC
Lumbago	2,845 (999.68)	1,256 (441.33)	1,589 (558.34)	1.27 (1.17–1.36)‡	<0.001	CPC
Fatigue	3,090 (1,085.76)	1,377 (483.85)	1,713 (601.91)	1.24 (1.16–1.34)‡	<0.001	POTS
Edema	1,196 (420.25)	533 (187.29)	663 (232.97)	1.24 (1.11–1.40)‡	<0.001	CPC
Hyperlipidemia	4,373 (1,536.59)	1,952 (685.89)	2,421 (850.69)	1.24 (1.17–1.32)‡	<0.001	CPC
Hypertension	4,639 (1,630.05)	2,080 (730.87)	2,559 (899.18)	1.23 (1.16–1.30)‡	<0.001	CPC
Iron deficiency anemia	1,688 (593.13)	757 (265.99)	931 (327.13)	1.23 (1.12–1.36)‡	<0.001	CPC
Anxiety	2,929 (1,029.19)	1316 (462.42)	1,613 (566.78)	1.23 (1.14–1.32)‡	<0.001	CPC
Depression	1,737 (610.35)	795 (279.35)	942 (331.00)	1.18 (1.08–1.30)‡	<0.001	CPC
GERD	2,795 (982.11)	1,308 (459.61)	1,487 (522.50)	1.14 (1.05–1.23)‡	<0.001	CPC
Cellulitis	1,799 (632.13)	844 (296.56)	955 (335.57)	1.13 (1.03–1.24)*	0.01	CPC

Using CMS data FDA staff (Wong et al. (46)) reported:
"Four outcomes met the threshold for a statistical signal following BNT162b2 vaccination including pulmonary embolism (PE; RR = 1.54), acute myocardial infarction (AMI; RR = 1.42), disseminated intravascular coagulation (DIC; RR = 1.91), and immune thrombocytopenia (ITP; RR = 1.44). After further evaluation, only the RR for PE still met the statistical threshold for a signal; however, the RRs for AMI, DIC, and ITP no longer did. No statistical signals were identified following vaccination with either the mRNA-1273 or Ad26 COV2.S vaccines."

From VAERS, Yan et al (47) calculated Reporting Odds Ratios, a metric related to PRR, finding signals for a number of thrombo-embolic events.

Thrombus and embolic events	BNT162b2 (a/b)	Comparators (c/d)	ROR	95% CI	Height
Arterial thrombosis events	**792 /445,134**	**1,707 /3,715,735**	**3.87**	**(3.56−4.21)**	**10.06**
Myocardial infarction	260 /445,666	615 /3,716,827	3.53	(3.05−4.08)	5.84
Acute myocardial infarction	141 /445,785	175 /3,717,267	6.72	(5.38−8.39)	3.80
Transient ischaemic attack	107 /445,819	321 /3,717,121	2.78	(2.23−3.46)	3.85
Ischaemic stroke	54 /445,872	118 /3,717,324	3.82	(2.76−5.26)	2.59
Retinal artery occlusion	21 /445,905	34 /3,717,408	5.15	(2.99−8.87)	1.49
Coronary arterial stent insertion	20 /445,906	56 /3,717,386	2.98	(1.79−4.96)	1.59
Arteriogram carotid abnormal	18 /445,908	33 /3,717,409	4.55	(2.56−8.08)	1.40
Cerebral artery occlusion	18 /445,908	29 /3,717,413	5.17	(2.87−9.32)	1.36
Coronary artery occlusion	15 /445,911	48 /3,717,394	2.61	(1.46−4.65)	1.39
Thrombotic thrombocytopenic purpura	14 /445,912	65 /3,717,377	1.80	(1.01−3.20)	1.39
Lacunar infarction	11 /445,915	24 /3,717,418	3.82	(1.87−7.80)	1.10
Peripheral artery thrombosis	11 /445,915	12 /3,717,430	7.64	(3.37−17.32)	0.93
Coronary artery bypass	9 /445,917	18 /3,717,424	4.17	(1.87−9.28)	0.96
Percutaneous coronary intervention	9 /445,917	8 /3,717,434	9.38	(3.62−24.31)	0.77
Stress cardiomyopathy	9 /445,917	26 /3,717,416	2.89	(1.35−6.16)	1.02
Angioplasty	7 /445,919	21 /3,717,421	2.78	(1.18−6.54)	0.88
Arterial thrombosis	7 /445,919	9 /3,717,433	6.48	(2.41−17.41)	0.73
Carotid artery occlusion	7 /445,919	22 /3,717,420	2.65	(1.13−6.21)	0.89
Basal ganglia infarction	6 /445,920	13 /3,717,429	3.85	(1.46−10.12)	0.75
Cerebral artery thrombosis	6 /445,920	9 /3,717,433	5.56	(1.98−15.61)	0.69
Carotid artery thrombosis	5 /445,921	4 /3,717,438	10.42	(2.80−38.81)	0.49
Ischaemic cerebral infarction	5 /445,921	14 /3,717,428	2.98	(1.07−8.27)	0.70
Peripheral artery occlusion	5 /445,921	6 /3,717,436	6.95	(2.12−22.76)	0.57
Thromboembolectomy	5 /445,921	10 /3,717,432	4.17	(1.42−12.20)	0.66
Aortic thrombosis	4 /445,922	3 /3,717,439	11.12	(2.49−49.67)	0.40
Arterial stent insertion	3 /445,923	1 /3,717,441	25.01	(2.60−240.44)	0.18
Basilar artery occlusion	3 /445,923	1 /3,717,441	25.01	(2.60−240.44)	0.18
Carotid endarterectomy	3 /445,923	4 /3,717,438	6.25	(1.40−27.94)	0.40
Intra−aortic balloon placement	3 /445,923	2 /3,717,440	12.50	(2.09−74.84)	0.29
Renal artery thrombosis	3 /445,923	2 /3,717,440	12.50	(2.09−74.84)	0.29
Vertebral artery occlusion	3 /445,923	4 /3,717,438	6.25	(1.40−27.94)	0.40



Applying sequential testing (Poisson Maximized Sequential Probability Ratio Test - PMaxSPRT) and near real time surveillance to data from three medical databases, FDA's Lloyd et al., (48) compared outcomes of 17 AESIs after Covid-19 vaccination with a historical dataset. The AESIs were:

- unusual site thrombosis (broad) with thrombocytopenia (tp)
- common site thrombosis with thrombocytopenia (tp)
- acute myocardial infarction
- deep vein thrombosis
- pulmonary embolism#
- disseminated intravascular coagulation
- non-hemorrhagic stroke
- hemorrhagic stroke
- immune thrombocytopenia
- myocarditis/pericarditis
- Guillain-Barré syndrome
- Bell's palsy
- encephalomyelitis/encephalitis
- transverse myelitis
- narcolepsy
- appendicitis
- anaphylaxis

15/17 outcomes evaluated failed to meet the statistical signal threshold in any database. Myocarditis/pericarditis failed to met the threshold after use of the Pfizer product in one of the databases. Anaphylaxis met the threshold in all three databases for both the Pfizer and Moderna products. These somewhat surprisingly non-uniform findings for events well-recognized to be associated with vaccination highlight the limitations in datasets considered more reliable than VAERS. It is worth reproducing here the limitations described by Lloyd et al. as they might apply to a number of studies that analyze health record databases:

1. Signal may not persist in a fully adjusted epidemiologic study. Historical comparator group selected without selection criteria to ensure comparability. Did not adjust for confounding factors other than age and sex.

2. Events identified by reimbursement codes in claims databases, subject to coding errors. Only conditions triggering a health encounter were captured.
3. Risk intervals prespecified based on literature and clinical input - subject to misclassification or are incorrect for C19 vaccines, e.g. with delayed risk or longer intervals.
4. Although the overall population in RCA provides greater precision to detect rare AEs, AESI risk of certain subgroups may be masked.
5. Differences in population for each health plan may result in different findings, possibly explaining missing signal for myocarditis/pericarditis in 1/3 data sources.
6. Covid-19 vaccination administration data are not fully captured (linked) in claims data. [this is reflected in a separate paper by FDA authors, who, on using algorithmic methods increased by 16.8% identification of vaccine administration compared with use of unstructured data alone. (49)]
7. Sequential testing requires a wide range of prespecified parameters, and their misspecification could result in errors in either direction.
8. While some uptake of booster doses in late 2021 was captured in the all-dose mRNA vaccine analyses, this study did not include third or booster dose specific analyses.
9. Results from these commercially insured populations may not be generalizable to those uninsured or covered by other plans.

4.6. Masking of safety signals

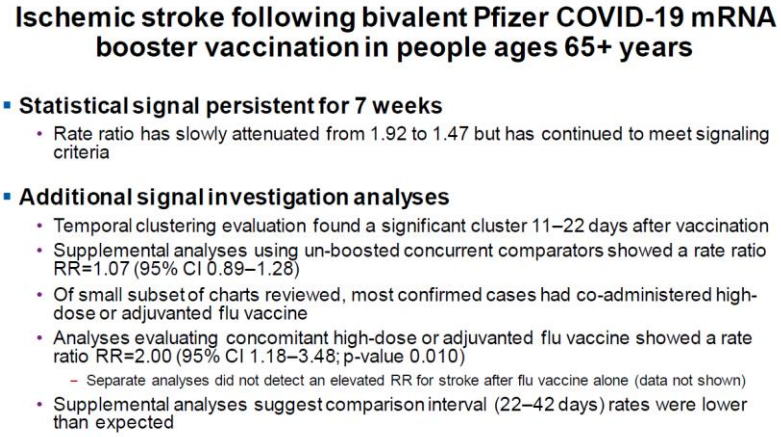
FDA's Harpaz et al. (6) describe the problem of masking with disproportionality signal methods:
"Signals […] are hidden by the presence of other reported products. Due to vaccine novelty, and an unprecedented dynamic of reporting, statistical signals […] related to]…] COVID-19 vaccines are more prone to masking and, therefore, to being undetected or delayed. The results also suggest that properly identifying and addressing the masking effect exposes strong statistical associations that would otherwise be deemed uninteresting."

Harpaz further commented on signals where there is likely a high masking component: Bell's palsy, appendicitis, pulmonary embolism, Herpes Zoster, tinnitus.

4.7. Ischemic stroke signal in more than one database

In their recent discussion of ischemic stroke, CDC and FDA claimed that they found a transient signal in VSD and nowhere else. And yet, in CDC's own FOIA disclosure appeared significant PRR signals for ischemic stroke in VAERS form last July. We obtained a similar result from an online PRR calculator funded by NIH. (7)

At the January 26th VRBPAC meeting, data were presented (selected slides shown below) by CDC's Dr. Shimabukuro [3] and FDA's Dr. Forshee[4] regarding a signal found in the VSD system relating to ischemic stroke and the Pfizer bivalent Covid-19 vaccine. They suggested that if this was a true signal, it was only in those over 65, and likely associated with injection of a flu vaccine on the same day as the Covid-19 vaccine.



CDC described a number of follow up actions, including what sort of further evaluation they would be conducting:

[3] https://www.fda.gov/media/164811/download
[4] https://www.fda.gov/media/164815/download

Further evaluation

- Continue to monitor weekly and explore potential data-related explanations for the statistical signal in VSD
- Consider expanding chart review to all VSD sites
- Consult with other surveillance systems to better understand:
  - Possible role of concomitant high-dose or adjuvanted flu vaccination with COVID-19 vaccination
  - Possible decreased rate of stroke in the 3-6 weeks following vaccination

FDA provided analyses from the BEST and other systems.

Data Suggesting Absence of Safety Risk for the Bivalent Boosters in Age 65y+

1) No excess reports of stroke from VAERS
2) CMS database with about 4.25 million doses shows no increase in stroke
3) VA database run shows no increase in stroke on preliminary query
4) Various countries in Europe as well as Israel indicate no increased risk of stroke in their surveillance systems
5) Pfizer notes no increase in signal in their global safety database or when comparing the monovalent to bivalent vaccines

In any case, a formal epidemiologic study is being initiated by FDA to prepare for potential vaccine coadministration in 2023-2024

However, it was not felt that this signal warranted any change to CDC's recommendations regarding the use of the vaccine.

Key next steps

- CDC continues to recommend that everyone eligible for a COVID-19 mRNA bivalent booster or a flu vaccine get vaccinated
- CDC and FDA are engaged in epidemiologic analyses regarding co-administration of COVID-19 mRNA bivalent booster and flu vaccines

There were extensive comments from FDA and CDC extolling the robustness of the various safety monitoring systems, for example those of FDA's Dr. Marks:[5]

≫ DR. PETER MARKS: This is Peter Marks . Dr. Gans, this is actually I can answer for you and Dr. Forshee can help, as well .We during the pandemic have been working with a network through the international conference of medicine regulators . It's about 60 countries that have been exchanging pharmacovigilance information and that's why when a safety signal comes up, we can actually query the other countries. And it was very re -- it was reassuring with the latest stroke question that that was not seen in millions of doses given overseas I couldn't agree with you more that this is a fantastic opportunity to collaborate with VAERS other regulators to be able to put together the maximum amount of safety information that we can

The overall impression from these remarks, particularly that of FDA's Dr. Forshee, is that *"with the multiple systems in place, it is not at all surprising that we sometimes get signals in one system but not in another"* In other words, the signal for stroke could not be found in any other system queried.

This is inaccurate.

Recently, pursuant to a FOIA request, CDC's PRR analyses were released from July 29 2022. The data files have been made available online.[6]

The "Evans" criteria(50) adopted by the VAERS SOP(27) applied to determine if a signal is present is that the PRR value should be ≥2 with a chi-square value of ≥4. There must be 3 or more cases of the AE following receipt of the specific vaccine of interest. The screen shot below shows the output for ischemic stroke with all mRNA vaccines, ages 18+.Here the Evans criteria have been met with PRR = 4.83, and chi-square = 103.61.

[5] https://youtu.be/ZjULNuSYfd0?t=31115
[6] https://childrenshealthdefense.org/defender/cdc-safety-signals-pfizer-moderna-covid-vaccines-et/

PREFERRED Medical Dictionary for Regulatory Activities (MedDRA) Terms (VAERS-1 Box 7, VAERS 2.0 Box 18)
For Current Week and Past Week Comparison
Following **ALL 12/14/2020-07/29/2022 COVID19 mRNA Vaccines (AGES 18+ YEARS)**
Compared to **ALL 01/01/2009-07/29/2022 NON-COVID19 Vaccines (AGES 18+ YEARS)**
AGES 18+ YEARS Excludes missing ages, Initial domestic reports only, VAERS reports as of 07/29/2022
Vaccination, Received, and Completed Date: 12/14 - 07/29 (Current Week) and 12/14 - 07/22 (Past Week)
N>=3 (Current Week), PRR>=2.00 (Ratio of Proportions), Chi-Square>=4.00
MedDRA PTs sorting based on lower confidence limit and COVID19 mRNA adverse event count from 12/14/2020-07/29/202

MedDRA Codes ALL Reports (18+)	12/14/2020-07/29/2022 COVID19 mRNA N=660643	01/01/2009-07/29/2022 NON-COVID19 N=242091	12/14-07/29 Chi-Square	12/14-07/29 PRR	12/14-07/29 LCL	12/14-07/29 UCL
ISCHAEMIC STROKE	488	37	103.61	4.83	3.46	6.75

A similar picture is obtained examining only serious events, with PRR = 2.64 and chi-square of 29.95/

PREFERRED Medical Dictionary for Regulatory Activities (MedDRA) Terms (VAERS-1 Box 7, VAERS 2.0 Box 18)
For Current Week and Past Week Comparison
Following **ALL 12/14/2020-07/29/2022 COVID19 mRNA Vaccines (SERIOUS AGES 18+ YEARS)**
Compared to **ALL 01/01/2009-07/29/2022 NON-COVID19 Vaccines (SERIOUS AGES 18+ YEARS)**
SERIOUS AGES 18+ YEARS Excludes missing ages, Initial domestic reports only, VAERS reports as of 07/29/2022
Vaccination, Received, and Completed Date: 12/14 - 07/29 (Current Week) and 12/14 - 07/22 (Past Week)
N>=3 (Current Week), PRR>=2.00 (Ratio of Proportions), Chi-Square>=4.00
MedDRA PTs sorting based on lower confidence limit and COVID19 mRNA adverse event count from 12/14/2020-07/29/2022

MedDRA Codes ALL Reports (SERIOUS 18+)	12/14/2020-07/29/2022 COVID19 mRNA N=73178	01/01/2009-07/29/2022 NON-COVID19 N=13287	12/14-07/29 Chi-Square	12/14-07/29 PRR	12/14-07/29 LCL	12/14-07/29 UCL
ISCHAEMIC STROKE	465	32	29.95	2.64	1.84	3.77

As a further check, we interrogated Cov19VaxKB, an online database[7] described by Huang et al.(7) some of whom were affiliated with NIH, and which work was funded partly by NIH-NIAID. This database calculates PRR values, but adds to the Evans criteria the condition that the number of cases must be >0.2% of the total number. This is a condition not used in the original Evans criteria(50) nor in the VAERS SOP.(27) The imposition of this criterion contradicts the intent of the Evans method to detect small changes in numbers of unusual events.

Here is the screen shot showing that for ischemic stroke, the Pfizer vaccine exceeds the Evans criteria (ignoring the added 0.2% criterion) with PRR = 2.4 and chi-square = 93.3

[7] http://www. violinet.org/cov19vaxkb/

violinet.org/cov19vaxkb/cov19vaxafe/stat_analysis.php

Cov19VaxKB
COVID-19 VACCINES

Search: Vaxquery for GO Clear Help

Statistical Test Results

	COVID19 (COVID19 (PFIZER-BIONTECH))	Other Vaccines
Ischaemic stroke	211	275
Other Adverse Events	397240	1220761

Adverse Event Frequency:

Total cases of this event for the vaccine: 211
Total case reports associated with this vaccine: 397451
Percentage of this event out of the total case reports for this vaccine: 0.05%

Proportional Reporting Ratio (PRR) Test Result:

PRR = 2.3571902494098

Note: The proportional reporting ratio (PRR) statistical method calculates the proportions of specific adverse events for a vaccine (or a group of vaccines) of interest where the comparator is all other vaccines in the VAERS database.

Chi-squared Test Result:

X-squared = 93.325, df = 1, p-value < 2.2e-16

Is this adverse event stastically significant for this vaccine based on our results and criteria?

NO

Note: Our default statistical analysis cutoffs are PRR > 2, Chi-square score > 4, and the number of cases > 0.2% of total reports.

References:

- **PRR:** Evans SJ, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. *Pharmacoepidemiol Drug Saf.* Oct-Nov 2001;10(6):483-6. doi: 10.1002/pds.677. PMID: 11828828.
- **Chi-square tests:**
  - https://stat.ethz.ch/R-manual/R-devel/library/stats/html/chisq.test.html
  - https://www.bmj.com/about-bmj/resources-readers/publications/statistics-square-one/8-chi-squared-tests.
  - *Note:* The shortcut Chi-square test formula described in the above document is equivalent to the R *chisq.test* function with no correction. Also, see the description in our own paper: Xie J, He Y. Ontology-Based Vaccine Adverse Event Representation and Analysis. *Advances in Experimental Medicine and Biology*, 2017;1028:89-103. PMID: 29058218.
- **Statistical cutoffs:** Sarntivijai S, Xiang Z, Shedden KA, Markel H, Omenn GS, Athey BD, and He Y. Ontology-based combinatorial comparative analysis of adverse events associated with killed and live influenza vaccines. *PLoS ONE*. 2012, 7(11): e49941. doi:10.1371/journal.pone.0049941. PMID: 23209624. PMCID: PMC3509157.

For Moderna, the same analysis for ischemic stroke, yields PRR = 1.6 and chi-square = 24.4. Although this does not meet the Evans criteria, the result is highly statistically significant with $p = 7 \times 10^{-7}$. Since the Evans criteria were established to detect small absolute changes in event frequency (e.g. 4 "control" events and 8 "new drug" events), those limits were appropriate to provide sufficient power. However, where there are over 100 events in this case, the PRR shown here, supports the result from the Pfizer analysis.

Cov19VaxKB
COVID-19 VACCINES

Search: Vaxquery for GO Clear Help

Statistical Test Results

	COVID19 (COVID19 (MODERNA))	Other Vaccines
Ischaemic stroke	163	323
Other Adverse Events	387687	1230314

Adverse Event Frequency:

Total cases of this event for the vaccine: 163
Total case reports associated with this vaccine: 387850
Percentage of this event out of the total case reports for this vaccine: 0.04%

Proportional Reporting Ratio (PRR) Test Result:

PRR = 1.6012209166114

Note: The proportional reporting ratio (PRR) statistical method calculates the proportions of specific adverse events for a vaccine (or a group of vaccines) of interest where the comparator is all other vaccines in the VAERS database.

Chi-squared Test Result:

X-squared = 24.463, df = 1, p-value = 7.577e-07

Is this adverse event stastically significant for this vaccine based on our results and criteria?

NO

Note: Our default statistical analysis cutoffs are PRR > 2, Chi-square score > 4, and the number of cases > 0.2% of total reports.

References:

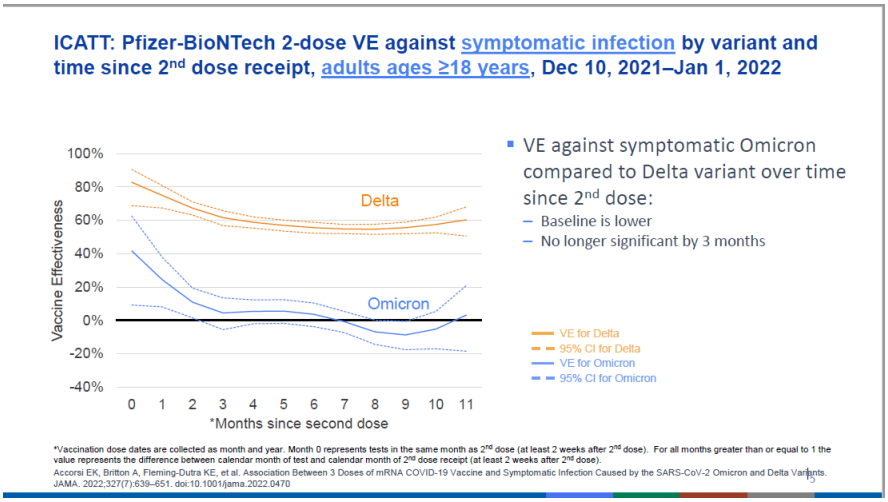
- **PRR:** Evans SJ, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. *Pharmacoepidemiol Drug Saf.* Oct-Nov 2001;10(6):483-6. doi: 10.1002/pds.677. PMID: 11828828.
- **Chi-square tests:**
  - https://stat.ethz.ch/R-manual/R-devel/library/stats/html/chisq.test.html
  - https://www.bmj.com/about-bmj/resources-readers/publications/statistics-square-one/8-chi-squared-tests.
  - *Note:* The shortcut Chi-square test formula described in the above document is equivalent to the R *chisq.test* function with no correction. Also, see the description in our own paper: Xie J, He Y. Ontology-Based Vaccine Adverse Event Representation and Analysis. *Advances in Experimental Medicine and Biology*, 2017;1028:89-103. PMID: 29058218.
- **Statistical cutoffs:** Sarntivijai S, Xiang Z, Shedden KA, Markel H, Omenn GS, Athey BD, and He Y. Ontology-based combinatorial comparative analysis of adverse events associated with killed and live influenza vaccines. *PLoS ONE*. 2012, 7(11): e49941. doi:10.1371/journal.pone.0049941. PMID: 23209624. PMCID: PMC3509157.

Evidently, the impression left by the CDC and FDA presentations that a signal for ischemic stroke was only found in one system is incorrect. It is seen here in VAERS, both with CDC's PRR analysis, and that obtained using the Cov19VaxKB systems.

4.8. Negative Efficacy: an indicator of immune suppression?

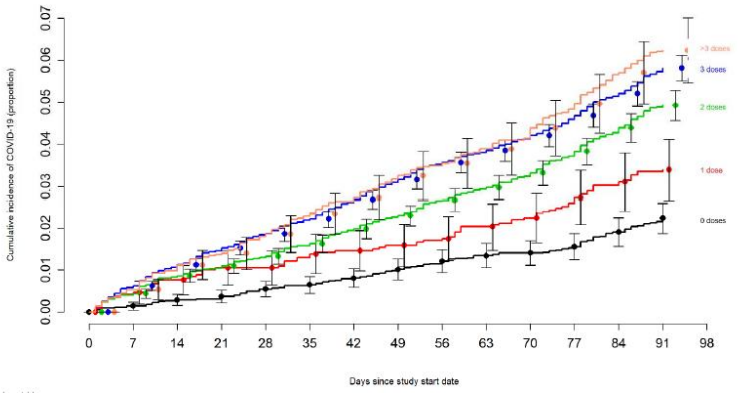
Data showing negative vaccine efficacy are most concerning as they may indicate immune suppression. Prominent among the several studies reporting this finding (which we discuss in more depth (18) (20)) is this work from CDC showing no statistical effect of the vaccine by 3 months, becoming negative by 7 months.

Slide 5 presented by Dr. Ruth Link-Gelles at VRBPAC Meeting of June 14 2022[8]



Other studies for example from Canada (51) and Denmark (52) reported greater negative vaccine efficacy.

A Cleveland clinic study (8) recently remarked that theirs was not the only one to find "*a possible association with more prior vaccine doses and higher risk of COVID-19.* Alarmingly, the authors found that the risk *"of COVID-19 increased with time since the most recent prior COVID-19 episode and with the number of vaccine doses previously received."*

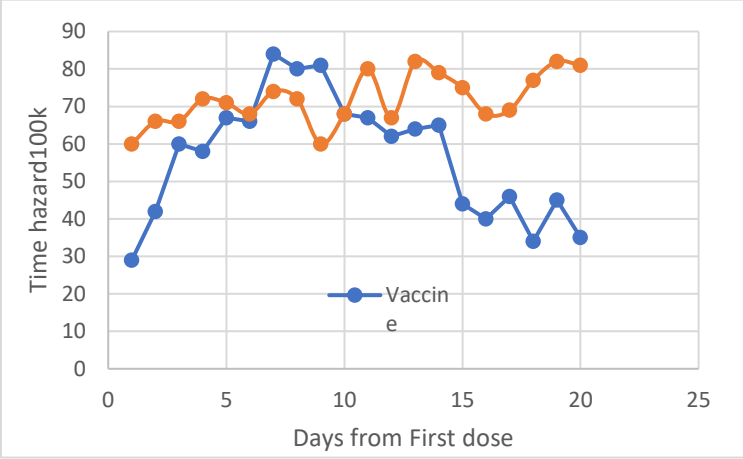


Shrestha et al., (8) further remarked: *"it is important to examine whether multiple vaccine doses given over time may not be having the beneficial effect that is generally assumed."*

There were early suggestions of negative efficacy after vaccination, which we discussed in a submission to CDC in August 2021.(9) In an analysis of the data from the initial use (first 44 days) in 596,000 subjects of the Pfizer vaccine in Israel reported by Dagan et al. in NEJM (12), one of us (HS) observed an early (<7 days) uptick in Covid-19 cases following vaccination.

[8] www.fda.gov/media/159225/download

Covid-19 cases following vaccination in Dagan et al.



A letter to NEJM (March 11 2021) was rejected but described in an article in France Soir – May 5.[9] There, the incidences of Covid-19 tripled from day 1 to 7 among the vaccinated,[10] and decreased to the initial rate 20 days after 1st injection, remaining at that level until day 28.The letter continues: "*This suggests a weakened immunity of the vaccinees which causes other, unreported, short-term (non-COVID-19) adverse effects, including some deaths. This analysis should have influenced decisions about who to vaccinate and when. Long-term risks can be expected with age and sex factors."*

Combining data in Dagan et al., with statistics from the Israeli Ministry of Health, an increase in the number of Covid-19 deaths in vaccinated subjects could be found following vaccination. These Israeli data were particularly informative because by the cut-off date, 54% of adult Israelis had been vaccinated, mitigating to some degree biases due to early vaccination of those most at risk. Further, by combining these data sources, we could see what was happening **among vaccinated patients**. There are a number of limitations as to causality and potential time biases, but this analysis suggested that there may have been at that time 121-413 excess deaths/million associated with vaccination, in those vaccinated (>= 1 dose), equating to about 25,000-85,000 deaths in the USA at that time. Again, we cannot ascribe cause, merely association. The finding from a large Israeli cohort of and increased risk of Herpes zoster infection(53) may also indicate immunosuppression related to vaccination in some subjects. In one study naïve vaccinees had a 13.06-fold (95% CI, 8.08 to 21.11) increased risk for breakthrough infection with the Delta variant compared to those previously infected.(54)

Results from Denmark also from Spring 2021 are consistent with the findings in the Israeli data. The Danish Statens Serum Institut,(30) found in priority vaccination groups (LTCF, FLHW) negative VE (unadjusted) for Covid-19 related death up to the 2nd dose.

Priority groups for vaccination / Time period	VE COVID-19 related death								
	No. of events	PYRS	IR	Unadjusted			Adjusted*		
				VE	95% CI		VE	95% CI	
All priority groups									
Unvaccinated	445	153179.6	0.003						
0-14 days after 1st dose	69	17667.0	0.004	-0.34	-1.42	0.25	0.76	0.68	0.82
>14 days after 1st dose until 2nd ddose	203	12470.8	0.016	-4.6	-7.24	-2.81	0.07	-0.15	0.25
0-7 days after 2nd dose	0	7429.7	0	-	-	-	-	-	-
>7 days after second dose	25	37631.7	0.001	0.77	0.42	0.91	0.94	0.90	0.96

[9] francesoir.fr/societe-sante/le-new-england-journal-medecine-refuse-une-lettre-davertissement-du-dr-seligman-sur
[10] The imbalance between the two groups on initiation poses a separate problem as to the matching of the two groups.

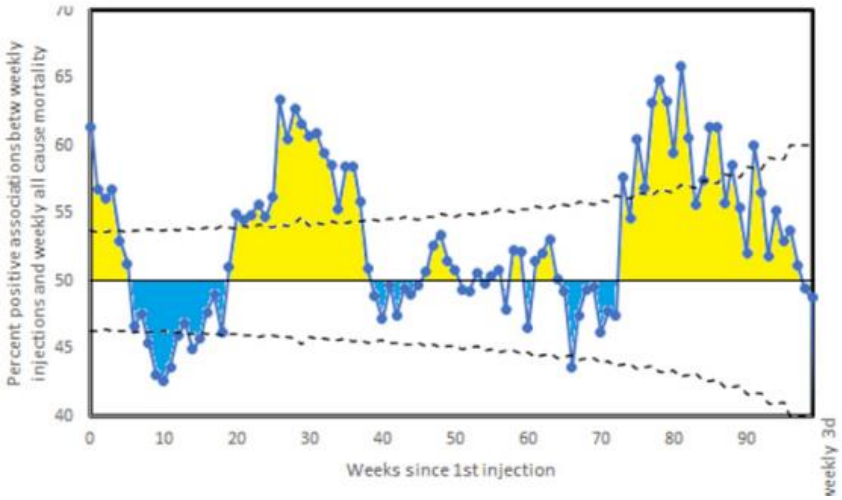
Upon adjustment, these estimates became positive. However, the large swings between unadjusted and adjusted estimates necessitate detailed examination of the raw datasets to assuage concern that there is an association between vaccination and ACM.

Assessing data for all-cause mortality (ACM) avoids the problem of mischaracterization of cause of death, as discussed below.

4.9. All cause mortality (ACM) and vaccination

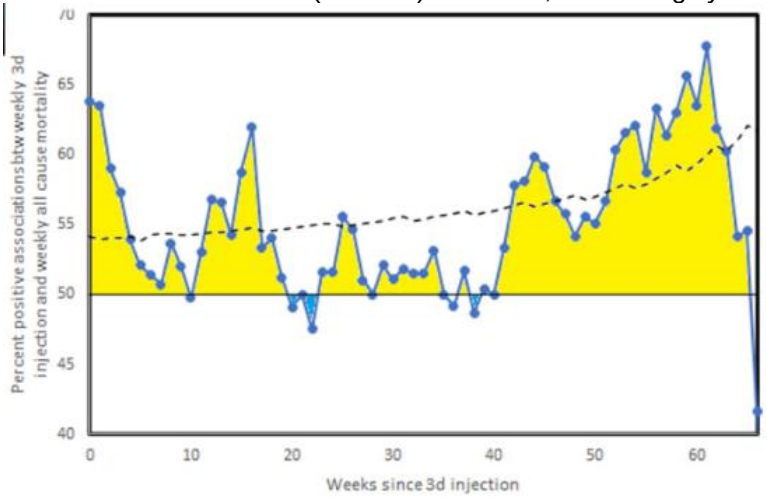
We have found from European and CDC data, correlations between vaccination coverage and all-cause mortality, which we describe more fully in (21) for the booster doses, but consistent with earlier work on the primary series.(55)

Rather than take static snapshots in time common in other analyses, this analysis constructs correlations across 23 European countries using Euromomo data for every lag in time (by week) between vaccination and an estimate of ACM. The most recent version of this analysis (3/25/23) is shown here (courtesy Dr. H. Seligmann). Yellow and blue areas indicate detrimental and beneficial associations between vaccination coverage and ACM. The dotted lines indicate significance boundaries, outside of which denotes statistical significance. They are wider for the longer lag times, where there are fewer data points. The analysis aggregates time lags of the same length regardless of the calendar data when vaccination occurred.



This analysis shows an early (~0-6 weeks) detrimental effect of Covid-19 vaccination, followed by a brief (~6-20w) beneficial period. Another detrimental period (20-40w) is then followed by a mostly neutral period (40-75w), again followed by a detrimental period. At longer lag times, a number of people will receive booster doses.

The following analysis of correlations between booster (3rd dose) and ACM, shows largely detrimental associations.



We are unaware of other work that uses a lag analysis which is essential to understanding the obviously time dependent effects of the Covid-19 vaccines.

The subject of the effect of vaccination on ACM requires detailed review beyond the scope of this document.

Suffice to say that there were indications as early as Spring 2021 about the association between the two. The table below from same Danisg study cited above,(30) shows estimates for negative VE (unadjusted) for ACM for priority vaccination groups (LTCF, FLHW) for all time periods except 0-7 days after 2nd dose.

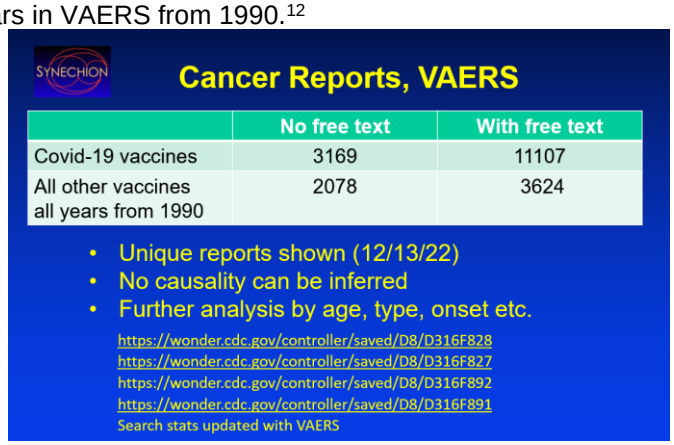
Priority groups for vaccination	VE all cause death								
	No. of	PYRS	IR	Unadjusted			Adjusted*		
Time period	events			VE	95% CI		VE	95% CI	
All priority groups									
Unvaccinated	6419	153179.6	0.042						
0-14 days after 1st dose	843	17667.0	0.048	-0.14	-0.32	0.02	0.47	0.43	0.51
>14 days after 1st dose until 2nd ddose	1580	12470.8	0.127	-2.02	-2.39	-1.7	0.06	0.00	0.12
0-7 days after 2nd dose	252	7429.7	0.034	0.19	-0.05	0.38	0.66	0.61	0.70
>7 days after second dose	2952	37631.7	0.078	-0.87	-1.05	-0.71	0.49	0.46	0.52

*Adjusted for calendar time, age, sex, co-morbidities and hospital admission

Upon adjustment, these estimates become positive. However, the large swings between unadjusted and adjusted estimates necessitate detailed examination of the raw datasets to assuage concern that there is an association between vaccination and ACM.

4.10. Concerning cancer reports

It is particularly concerning that according to the package insert (eg for COMIRNATY), *"no carcinogenicity or genotoxicity studies were done"*[11] We searched VAERs for cancer signals and found an excess for the Covid-19 vaccines compared with all other vaccines for all years in VAERS from 1990.[12]



Additional cancer signals were found CDC's PRR analyses disclosed after a FOIA request,[13] shown below.

[11] fda.gov/media/151707/download
[12] Search parameters are saved in VAERS, but data update automatically.
https://wonder.cdc.gov/controller/saved/D8/D316F828
https://wonder.cdc.gov/controller/saved/D8/D316F827
https://wonder.cdc.gov/controller/saved/D8/D316F892
https://wonder.cdc.gov/controller/saved/D8/D316F891
[13] www.theepochtimes.com/exclusive-cdc-finds-hundreds-of-safety-signals-for-pfizer-and-moderna-covid-19-vaccines_4956733.html

MedDRA Codes ALL Reports (18+)	12/14/2020-07/29/2022 COVID19 mRNA N=660643	01/01/2009-07/29/2022 NON-COVID19 N=242091	12/14-07/29 Chi-Square	12/14-07/29 PRR	12/14-07/29 LCL	12/14-07/29 UCL
COLON CANCER	47	2	11.77	8.61	2.09	35.45
BREAST CANCER METASTATIC	22	1	4.83	8.06	1.09	59.81
METASTASIS	43	6	4.59	2.63	1.12	6.17
THYROID CANCER	13	1	1.85	4.76	0.62	36.42
METASTASES TO LIVER	34	3	5.68	4.15	1.28	13.52
BREAST MASS	444	36	90.33	4.52	3.22	6.35
METASTASES TO BONE	32	1	8.34	11.73	1.60	85.81
METASTASES TO CENTRAL NERVOUS SYSTEM	29	2	5.56	5.31	1.27	22.27
METASTASES TO LYMPH NODES	22	1	4.83	8.06	1.09	59.81
CHRONIC LYMPHOCYTIC LEUKAEMIA	74	10	8.77	2.71	1.40	5.25
B-CELL LYMPHOMA	36	4	4.94	3.30	1.17	9.27
FOLLICULAR LYMPHOMA	20	1	4.14	7.33	0.98	54.61

There are a number of mechanisms published that provide biological plausibility to causation, a discussion of which is beyond the scope of this reveiew.

4.11. Transparency, scientific engagement, restoring trust in public health institutions

To date (3/30/23) according to CDC,[14] only 16.5% of those eligible have received the bivalent booster doses of the Covid-19 vaccine. According to a recent article in Nature,(1) Covid-19 vaccine hesitancy has spilled over to other vaccinations reaching their lowest point since 2008 and jeopardizing the health of millions.

OUTLOOK | 19 December 2022

Vaccination rates are falling, and its not just the COVID-19 vaccine that people are refusing

Society's best defence against childhood diseases is waning. What needs to be done to help it recover?

Michael Eisenstein

The article attributes this alarming trend to an erosion of trust and confidence in governments and public-health institutions exacerbated with the advent of COVID-19 vaccines. One of no doubt many reasons for this mistrust is the opacity of government agencies.(56)

The New York Times

The C.D.C. Isn't Publishing Large Portions of the Covid Data It Collects

https://www.nytimes.com/2022/02/20/health/covid-cdc-data.html

Apoorva Mandavilli

11-14 minutes

The agency has withheld critical data on boosters, hospitalizations and, until recently, wastewater analyses.

Vaccine injury is among the most controversial topics related to the use of the Covid-19 vaccines. At its open public session, (3/30/23) the committee heard from a number of vaccine-injured patients, many of whom were among the first to become vaccinated to "do their part" in the pandemic. A theme common to many of those remarks was the feeling of abandonment and betrayal by public health institutions they had trusted.

Restoring trust in public health institutions must surely be your highest priority. Most of all, unless the setting of parameters that will determine whether someone is eligible for compensation for alleged vaccine-injury is seen as just, there will be further erosion in trust of public health institutions in general and in vaccine acceptance in particular. This will only be

[14] https://covid.cdc.gov/covid-data-tracker

exacerbated as the specter of unknown long-term harms related to the hastily deployed novel gene therapy, becomes appreciated. I need not spell out the medical and economic consequences of such mistrust.

Restoration in trust can only be begin if your work is transparent and open to scientific dialog. Yours cannot be another exercise in "going through the motions" of the kind we have seen with FDA and CDC committees where public comment from patients and scientists passes unidirectionally without engagement or reaction. My colleagues and I are ready to participate in meaningful and necessary scientific discourse.

5. Bio

I am an experimental pathologist with a background in pharmacy, pharmacology and immunology. At Johnson & Johnson, as one of only 66 Research Fellows, I led a research program in the prevention of post-operative adhesions where my duties included pharmacovigilance. I focus on fibrosis and pain, running my own company providing R&D services for the development of medical products since 1996. I was invited to participate in Senator Johnson's expert Covid-19 panels in January and December 2022.

6. List of files provided

Files (20) are provided containing written comments submitted to FDA or CDC advisory committees. They are numbered as per the citation list.
Wiseman09-CDC-2021-0089-0023_attachment_1.pdf
Wiseman10-CDC-2021-0089-0039_attachment_1.pdf
Wiseman11-FDA-2021-N-0965-0016_attachment_1.pdf
Wiseman13-FDA-2021-N-0965-0146.pdf
Wiseman14-FDA-2021-N-0965-0164-SUPPLEMENT.pdf
Wiseman15-CDC-2021-0098-FDA-2021-N-1088.pdf
Wiseman16-CDC-2021-0125-0003_attachment_1.pdf
Wiseman17-CDC-2021-0133-0002_attachment_1.pdf
Wiseman18-CDC-2022-0002-0002_attachment_1.pdf
Wiseman20-CDC2022-0022-0009-Feb4ACIP-FDA-2022-N-0082-FINAL.pdf
Wiseman21-FDA-2022-N-0336-2500_attachment_1.pdf
Wiseman22-CDC-2022-0051-0260_attachment_1.pdf
Wiseman24-CDC2022-0065-ACIP051922-corrected2.pdf
Wiseman25-FDA-2022-N-0470-June10-CTGTAC-LINKS.pdf
Wiseman26-CDC-2022-0085-0017_attachment_2.pdf
Wiseman28-CDC-2022-0085-0017_attachment_1.pdf
Wiseman29-CDC-2022-0103-0049_attachment_1.pdf
Wiseman31-CDC-2022-0111-126227-OCT19-ACIP.pdf
Wiseman32-2023-VRBPACJan23-FDA-2022-N-2810-CommentsonBrefingDocument-TRACKING.pdf
Wiseman33-CDC-2023-0007-0496_attachment_1.pdf

7. References

1. Eisenstein M. Vaccination rates are falling, and its not just the COVID-19 vaccine that people are refusing. Nature 2022; 612:S44-s6. Epub Dec 19 http://doi.org/10.1038/d41586-022-04341-9
2. Funk PR, Yogurtcu ON, Forshee RA, et al. Benefit-risk assessment of COVID-19 vaccine, mRNA (Comirnaty) for age 16-29 years. Vaccine 2022. Epub 2022/04/05 http://doi.org/10.1016/j.vaccine.2022.03.030
3. Day B, Menschik D, Thompson D, et al. Reporting Rates for VAERS Death Reports Following COVID-19 Vaccination, December 14, 2020-November 17, 2021. medRxiv 2022:2022.05.05.22274695. Epub May 7 http://doi.org/10.1101/2022.05.05.22274695
4. Guo W, Deguise J, Tian Y, et al. Profiling COVID-19 Vaccine Adverse Events by Statistical and Ontological Analysis of VAERS Case Reports. Frontiers in pharmacology 2022; 13:870599. Epub 2022/07/12 http://doi.org/10.3389/fphar.2022.870599
5. Kwan AC, Ebinger JE, Wei J, et al. Apparent risks of postural orthostatic tachycardia syndrome diagnoses after COVID-19 vaccination and SARS-Cov-2 Infection. Nature Cardiovascular Research 2022. Epub http://doi.org/10.1038/s44161-022-00177-8
6. Harpaz R, DuMouchel W, Van Manen R, et al. Signaling COVID-19 Vaccine Adverse Events. Drug safety 2022; 45:765-80. Epub 20220623 http://doi.org/10.1007/s40264-022-01186-z

7. Huang PC, Goru R, Huffman A, et al. Cov19VaxKB: A Web-based Integrative COVID-19 Vaccine Knowledge Base. Vaccine X 2021:100139. Epub 2022/01/05 http://doi.org/10.1016/j.jvacx.2021.100139
8. Shrestha NK, Burke PC, Nowacki AS, et al. Effectiveness of the Coronavirus Disease 2019 (COVID-19) Bivalent Vaccine. medRxiv 2022:2022.12.17.22283625. Epub Dec 19 http://doi.org/10.1101/2022.12.17.22283625
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