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Article

# Multiple Increasing Vaccine Adverse Events Safety Signals for Older Adults

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## Abstract

Immune responses naturally decline with age in the elderly; this process is named immunosenescence. The risks for adverse events (AEs) can increase, decrease, or be uncorrelated with increasing age. Safety signals associated with vaccines can be detected within the Vaccine Adverse Event Reporting System (VAERS). Herein, VAERS was retrospectively examined for safety signals associated with the elderly. In general, common AEs include normal immune responses and also injection site-related AEs. For multiple COVID-19 vaccines, breakthrough infections and COVID-19-related AEs had unexpectedly high normalized frequencies. The normalized frequency for AE death was elevated for multiple vaccines, including COVID-19 vaccines; the associated risk appears to be additive for coadministered combinations of the COVID-19 Janssen vaccine with either the COVID-19 Pfizer-BioNTech BNT162b2 or the COVID-19 Moderna mRNA-1273 vaccine. Multiple manufacturing lots for the COVID-19 Janssen, COVID-19 Pfizer-BioNTech BNT162b2, and Moderna mRNA-1273 vaccines have high AE death normalized frequencies. These observations, combined with rapid AE death onset following vaccination, likely point to possible manufacturing contamination of specific manufacturing lots; endotoxins are a possible causative constituent. The sensitivity to these causative constituent(s) increases with age in the elderly.

**Keywords:** death; fall; endotoxin; mRNA vaccine; COVID-19 vaccine; breakthrough infection

## 1. Introduction

Aging-associated declines in immune system responses, a process named immunosenescence, result in weaker immune responses to new pathogens and vaccines. For improved protection against influenza, multiple high-dose vaccines are provided to the elderly. Immune responses to vaccines are reflected in associated adverse events. The Vaccine Adverse Event Reporting System (VAERS) collects population samples of adverse events (AEs) for the detection of associated safety signals. Safety signals specific to vaccine constituents can be detectable above expected background occurrence frequencies by comparing AE frequencies between different vaccines.

Characteristics of immunosenescence for antibody and T-cell responses have been observed in multiple studies for COVID-19 vaccines. Lower neutralization of SARS-CoV-2 infection was observed for IgA and IgG serum from elderly recipients, accompanied by lower T cell responses after the first dose of the Pfizer-BioNTech BNT162b2 vaccine [1]. Similar results were observed for 71 and 149 elderly COVID-19 Pfizer-BioNTech BNT162b2 vaccine recipients in two studies [2,3]. A study including 105 older long-term care facility residents found dramatically impaired humoral and cellular memory responses three months after the first COVID-19 Pfizer-BioNTech BNT162b2 mRNA vaccine dose [4]. A study of 138 nursing home residents found lower neutralization for residents receiving the COVID-19 Pfizer-BioNTech BNT163b2 vaccine (4-fold lower) and the COVID-19 Moderna mRNA-1273 vaccine (2-fold lower) [5]. A study of 165,755 nursing home residents in Sweden found higher mortality for unvaccinated residents and residents with no prior COVID-19 infection who had not received a COVID-19 vaccine or booster dose within the last 90 days [6]. Lower mortality is observed for COVID-19 vaccinated compared to unvaccinated individuals [7].

To detect possible safety signals in the elderly, AEs were retrospectively examined in VAERS for 10-year age groups for all vaccines. As anticipated, multiple AEs were observed with frequencies that correlate with increasing age, likely associated with immunosenescence. Unexpectedly, the AE death appears to have additive risks for coadministered vaccines with higher frequencies; this may indicate unknown causative constituents like manufacturing contaminants within specific vaccines. It is strongly recommended that COVID-19 vaccines not be coadministered with other vaccines without prior clinical trials of these vaccine combinations that include elderly individuals.

## 2. Materials and Methods

### *Materials*

State all the materials used in the study, and include the manufacturer's name, city and country of origin.

The VAERS database [8] was retrospectively examined for AEs with the Ruby program `vaers_tally_age10.rb` [9]; this program summarizes AEs by 10-year age groups. The download of VAERS data includes all AEs reported from 1990 to October 31, 2025. This program calculates the frequencies of reported AEs normalized to 100,000 VAERS reports:  $\text{AE normalized frequency} = (\text{age group observed AEs} / \text{all vaccine AEs}) * 100,000$  for each single administered vaccine or coadministered vaccines. For reference, the names of coadministered vaccines are joined with the plus symbol. Vaccines and vaccine combinations including the text "no brand name", "foreign", "unknown", and "vaccine not specified" were excluded to avoid possible reporting biases due to the possibility of underrepresentation of less severe AEs resulting in increased normalized frequency estimates. This retrospective study examines the age groups 50-59, 60-69, 70-79, 80-89, 90-100, and 100-109. VAERS AE names and spelling have not been changed. The day of onset data was examined with the Ruby program `vaers_slice5.rb` [9]. Microsoft Excel was used for median calculations, data sorting, and creating figures.

## 3. Results

For the age group 80 to 89 and vaccines with at least 1,000 VAERS AEs, the top AEs are illustrated for five COVID-19 vaccines (Table 1A) and Influenza seasonal (Fluzone high-dose), Pneumo (Pneumovax), Pneumo (Prevnar13), Zoster (Shingrix), and Zoster live (Zostavax) (Table 1B); AEs selected were in the top 50 by normalized frequency for at least two vaccines. Multiple AEs in the COVID-19 AEs list (Table 1A) do not overlap with the top AE list for the other five vaccines; these AEs are illustrated in Table 2. Other top AEs for the five non-COVID-19 vaccines did not overlap the COVID-19 top list: back pain, blister, cellulitis, herpes zoster, hypoaesthesia, injected limb mobility decreased, injection site induration, injection site inflammation, injection site pruritus, injection site rash, injection site reaction, injection site warmth, mobility decreased, muscular weakness, musculoskeletal pain, neck pain, oedema peripheral, paraesthesia, rash erythematous, rash pruritic, skin warm, swelling, tenderness, tremor, and urticaria. The AE death normalized frequencies are illustrated in Figure 1, and AE fall in Figure 2 for multiple vaccines. The AE death normalized frequencies by manufacturing lot number are illustrated for selected lots for three COVID-19 vaccines (Figure 3). The day of onset for AE death is illustrated in Table 3.

**Table 1.** Top 50 adverse events for vaccines with at least 1,000 VAERS adverse events for ages 80 to 89 (A) COVID-19 vaccines and (B) five other vaccines. The table is sorted by descending average mean value of the normalized frequencies. COVID-19 vaccines (A) top 50 list letter designators: J – COVID-19 (Janssen), m - COVID-19 (Moderna), M - COVID-19 (Moderna bivalent), p - COVID-19 (Pfizer-BioNTech), and P - COVID-19 (Pfizer-BioNTech bivalent). Additional vaccines (B) top 50 list letter designators: I – Influenza seasonal (Fluzone high-dose), O - Pneumo (Pneumovax), P - Pneumo (Prevnar13), S - Zoster (Shingrix), and Z - Zoster live (Zostavax).

Adverse event	COVID-19 (Janssen)	COVID-19 (Moderna)	COVID-19 (Moderna bivalent)	COVID-19 (Pfizer-BioNTech)	COVID-19 (Pfizer-BioNTech bivalent)	Top 50
COVID-19	30,540	15,462	15,502	20,500	18495	JmMpP
SARS-CoV-2 test positive	25,263	12,054	12,816	15,586	17651	JmMpP
Dyspnoea	13,588	6752	4834	9652	6680	JmMpP
Fatigue	8707	9157	8902	8036	4571	JmMpP
Asthenia	9234	7476	5679	7848	8509	JmMpP
Pyrexia	7387	8229	6983	8085	5555	JmMpP
Death	13,588	7147	1995	8089	3445	JmMpP
Cough	9036	4045	6753	5746	7383	JmMpP
Expired product administered	791	5410	11,588	1603	9845	mM P
Product storage error	1451	3903	4297	2342	13994	mMpP
Headache	4815	6305	5602	5334	2812	JmMpP
Pain	4617	4903	5909	4134	3445	JmMpP
Pain in extremity	4881	6088	5141	4615	2039	JmMpP
Acute respiratory failure	4089	2061	3146	2873	9704	JmMpP
Dizziness	4485	4638	3607	5142	2672	JmMpP
Chills	3891	5895	3146	4215	3305	JmMpP
Nausea	4485	4839	3530	4538	3023	JmMpP
Malaise	3759	2889	4758	4522	3305	JmMpP
Hypoxia	5343	2173	2686	2836	5977	JmMpP
Condition aggravated	4815	2647	2609	3224	4992	JmMpP
Vaccine breakthrough infection	5277	2539	2609	3048	2742	JmMpP
Arthralgia	2572	3549	3914	3273	1828	JmMpP
Fall	3627	2606	2302	3309	2953	JmMpP
COVID-19 pneumonia	5540	1961	1074	3485	2672	Jm pP
Vomiting	3166	3009	2455	3416	2531	JmMpP
Diarrhoea	3562	3180	2302	3428	1969	JmMpP

Chest X-ray abnormal	4485	1771	1688	2424	3375	JmMpP
Extra dose administered	1121	1334	4451	1285	4219	M P
Myalgia	1781	3419	2686	2489	1195	mMp
Rash	1385	3501	1611	2461	1969	mMpP
Pneumonia	3166	1879	1381	2718	1687	Jm pP
Confusional state	2770	1886	1534	2167	2461	JmMpP
Decreased appetite	2968	2382	1611	2767	984	Jm pP
Atrial fibrillation	2506	1659	1458	2424	2390	JmMpP
Injection site pain	1978	2457	1841	906	2109	JmM P
Gait disturbance	2044	1588	1841	1881	1687	JmMpP
Peripheral swelling	2440	2158	1995	1424	984	JmM
Feeling abnormal	1583	2102	2302	1816	1125	mM
Pulmonary embolism	2836	1107	997	1787	1898	J P
Pruritus	857	3818	1074	2028	843	m p
Chest pain	1715	1487	1841	1954	1336	mMp
Cerebrovascular accident	2440	1510	690	1848	1687	Jm pP
Acute kidney injury	2506	1017	920	1477	1969	J P
Erythema	1187	3143	1458	1461	632	mM
Anticoagulant therapy	2638	913	1151	1073	2039	J P
Unevaluable event	2968	1856	383	1885	703	Jm p
Inappropriate schedule of product administration	395	1935	1688	2301	1476	mMp
Oropharyngeal pain	1319	820	1918	1020	2672	M P
Sepsis	2308	816	1074	1048	2109	J P
Injection site erythema	263	3161	1841	624	914	mM
Respiratory tract congestion	791	678	1611	722	2039	M
Injection site swelling	329	1979	1688	453	1195	mM

Table 1B.

Adverse event	Influenza seasonal (Fluzone high-dose)	Pneumo (Pneumovax)	Pneumo (Prevnar13)	Zoster (Shingrix)	Zoster live (Zostavax)	Top 50
Injection site erythema	9978	25,530	28,231	13,499	12,782	IOPSZ
Erythema	7749	21,378	19,391	9769	8134	IOPSZ

Injection site pain	11,093	18,074	16,444	14,068	4770	IOPSZ
Injection site swelling	8439	21,472	17,395	9010	5932	IOPSZ
Pain in extremity	12,951	12,364	12,452	15,333	3363	IOPSZ
Pain	10,350	10,382	10,076	12,867	11,192	IOPSZ
Pyrexia	11,677	11,845	9410	9895	2568	IOPSZ
Rash	4299	3445	7889	10,907	15,902	IOPSZ
Herpes zoster	106	235	95	7556	32,782	SZ
Pruritus	3980	4907	9885	7714	10,275	IOPSZ
Injection site warmth	4989	10,335	11,501	5153	4036	IOPSZ
Chills	11,411	2642	5893	9326	1039	IOPSZ
Peripheral swelling	3237	9202	8935	5026	366	IOPS
Headache	6157	1793	4372	8409	3792	IOPSZ
Fatigue	5414	1840	4847	10,116	1834	IOPSZ
Skin warm	4299	6606	7414	3446	1896	IOPSZ
Injection site pruritus	2388	2501	8935	4331	4403	IOPSZ
Asthenia	5732	2737	3992	5501	2568	IOPSZ
Swelling	3078	6984	5513	3035	1651	IOPSZ
Nausea	5891	2548	3707	6165	1773	IOPSZ
Dizziness	4670	2595	3231	4552	3302	IOPSZ
Malaise	3397	3303	3326	4204	2385	IOPSZ
Myalgia	3343	2312	3897	5279	1590	IOPSZ
Arthralgia	2600	1604	3422	4805	1773	IOPSZ
Mobility decreased	3556	2878	2756	3793	733	IOPS
Cellulitis	636	7126	4182	885	550	OP
Dyspnoea	3927	2548	3802	1549	1345	IOPSZ
Injection site rash	1433	1179	4277	2402	3608	I PSZ
Rash erythematous	1804	1226	2756	2971	4036	I PSZ
Vomiting	5520	1321	1996	2307	856	I PS
Urticaria	2388	1038	2091	2655	2507	I PSZ
Diarrhoea	3450	566	2281	2845	978	I PS
Tremor	4989	943	855	2655	672	I S
Injection site reaction	1645	2925	1615	1517	2140	IOP Z
Musculoskeletal pain	3237	1793	1901	1738	1039	IOPSZ
Injected limb mobility decreased	2282	2831	2091	1896	122	IOPS
Oedema peripheral	796	6134	665	126	1406	O Z

Extra dose administered	3450	519	1235	2877	672	I S
Tenderness	1008	3445	1996	1201	978	OP
Blister	265	330	380	2023	5382	SZ
Back pain	1698	1274	1045	2023	2140	I SZ
Rash pruritic	1008	188	1330	2529	3058	PSZ
Cough	2813	1415	2376	758	550	IOP
Pneumonia	583	3916	2661	316	428	OP
Decreased appetite	1910	1179	2376	1802	550	I PS
Muscular weakness	1804	991	2091	1960	795	I PS
Injection site induration	690	1746	2756	695	1590	OP Z
Neck pain	1645	991	1996	1738	795	I PS
Feeling abnormal	1380	802	1235	2307	795	I PS
Paraesthesia	1433	519	570	1580	2262	I SZ
Condition aggravated	955	991	475	1580	1896	SZ
Hypoaesthesia	1857	849	570	1738	856	I S
Gait disturbance	1273	471	1520	1612	856	PS
Death	902	1746	1520	252	1039	OP Z
Injection site inflammation	424	1604	2186	663	489	OP
Fall	1645	755	380	1612	611	I S

Table 2. COVID-19 selected adverse events normalized frequencies.

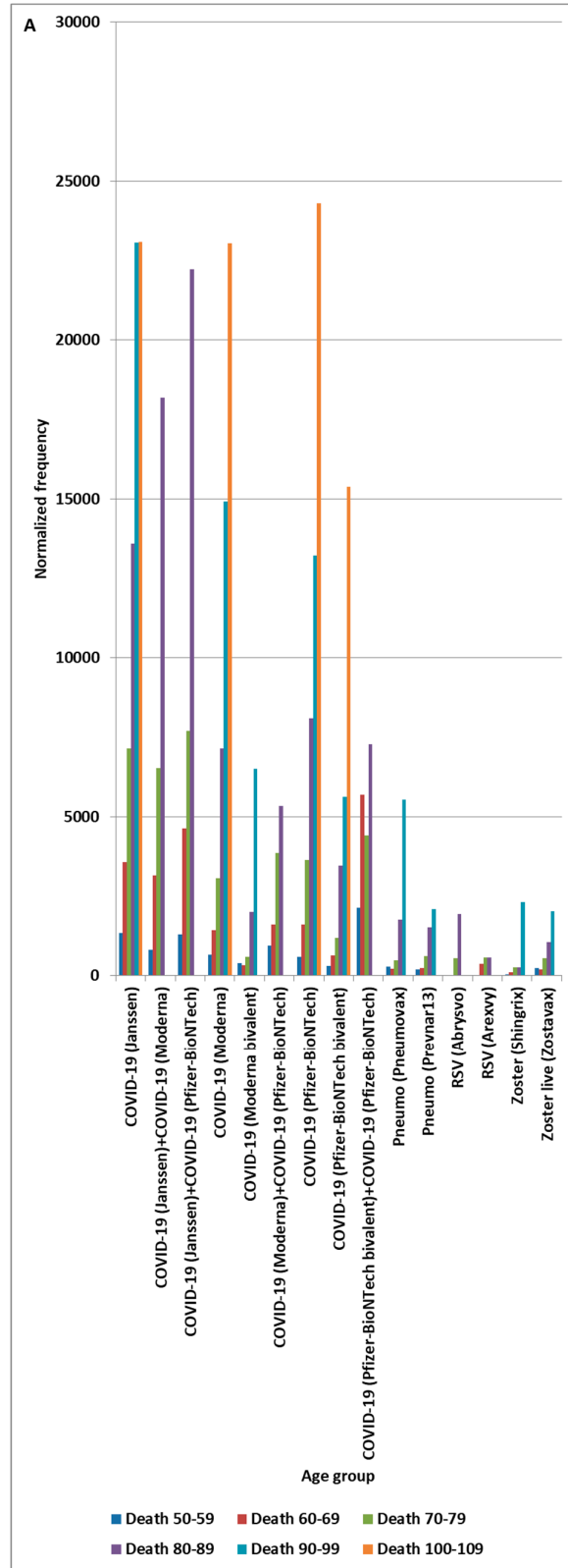
Adverse event	Age group	COVID-19 (Janssen)	COVID-19 (Moderna)	COVID-19 (Moderna bivalent)	COVID-19 (Pfizer-BioNTech)	COVID-19 (Pfizer-BioNTech bivalent)
Acute kidney injury	50-59	428	154	108	212	247
	60-69	829	326	201	465	344
	70-79	1430	629	425	1045	789
	80-89	2506	1017	920	1477	1969
Acute respiratory failure	50-59	714	200	325	379	949
	60-69	1469	463	717	955	1895
	70-79	2861	957	1567	1862	3996
	80-89	4089	2061	3146	2873	9704
Atrial fibrillation	50-59	436	407	595	508	289
	60-69	965	746	1091	1017	1033
	70-79	1379	1223	1461	1726	1934
	80-89	2506	1659	1458	2424	2390

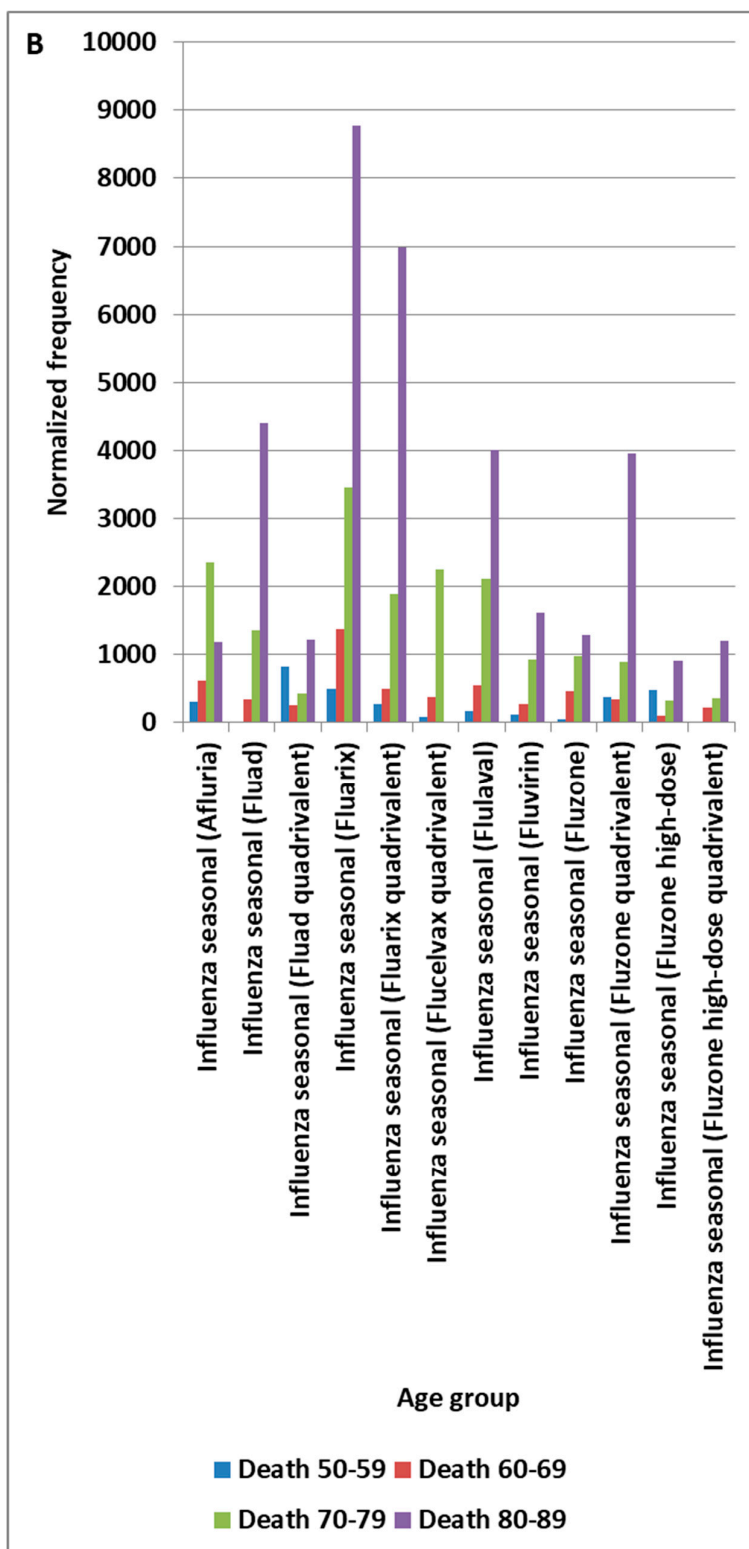
Cerebrovascular accident	50-59	1045	463	325	601	371
	60-69	1280	630	229	832	590
	70-79	1788	900	478	1224	1272
	80-89	2440	1510	690	1848	1687
Chest pain	50-59	3683	2669	2329	3379	2105
	60-69	3222	1880	1608	2680	1624
	70-79	3193	1554	1567	2254	1374
	80-89	1715	1487	1841	1954	1336
Chest X-ray abnormal	50-59	729	257	270	393	660
	60-69	1605	524	660	735	812
	70-79	2989	926	1036	1362	1960
	80-89	4485	1771	1688	2424	3375
Confusional state	50-59	766	547	433	632	578
	60-69	923	669	717	738	541
	70-79	1379	1085	744	1130	1069
	80-89	2770	1886	1534	2167	2461
COVID-19	50-59	7352	6030	12,026	7911	12,262
	60-69	12,248	7494	20,017	11,670	19,374
	70-79	20,975	10,033	18,841	15,991	22,683
	80-89	30,540	15,462	15,502	20,500	18,495
COVID-19 pneumonia	50-59	1075	232	108	432	165
	60-69	1994	557	201	936	492
	70-79	3960	1045	451	2129	1145
	80-89	5540	1961	1074	3485	2672
Hypoxia	50-59	781	214	54	405	743
	60-69	1458	545	459	801	1452
	70-79	2938	970	876	1662	2316
	80-89	5343	2173	2686	2836	5977
Oropharyngeal pain	50-59	1714	1673	4767	2216	4830
	60-69	1700	1719	7495	2099	6794
	70-79	1303	1452	5793	1938	5804
	80-89	1319	820	1918	1020	2672
Pulmonary embolism	50-59	1278	730	325	746	495
	60-69	1731	859	373	977	861
	70-79	2120	916	558	1408	763
	80-89	2836	1107	997	1787	1898
Sepsis	50-59	293	121	270	198	289
	60-69	472	253	258	322	295
	70-79	919	456	558	733	992
	80-89	2308	816	1074	1048	2109
	50-59	699	740	812	731	1321

Unevaluable event	60-69	1143	946	459	1019	713
	70-79	1328	1259	558	1498	636
	80-89	2968	1856	383	1885	703
Vaccine breakthrough infection	50-59	714	447	1083	559	660
	60-69	1721	866	1062	1077	960
	70-79	2887	1228	1222	1851	2163
	80-89	5277	2539	2609	3048	2742

Table 3. Death adverse event day of onset.

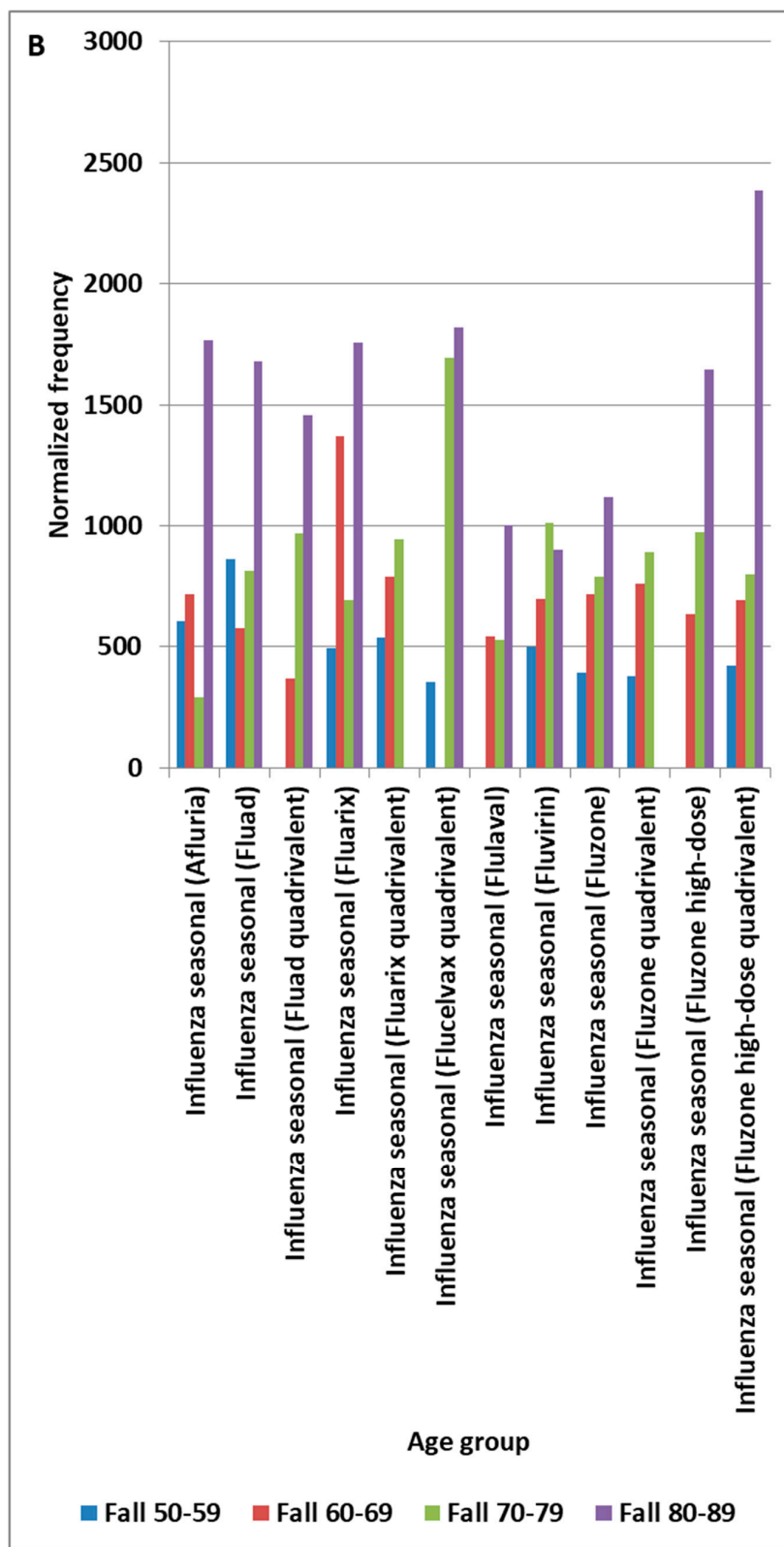
Vaccine name	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
COVID-19 (Janssen)	62	73	32	34	20	16	20	23
COVID-19 (Moderna)	567	649	289	170	124	129	84	124
COVID-19 (Moderna bivalent)	11	19	9	2	2	4		3
COVID-19 (Pfizer-BioNTech)	1022	795	404	287	216	201	138	131
COVID-19 (Pfizer-BioNTech bivalent)	15	30	11	7	3	4	5	2
Pneumo (Pneumovax)	56	19	15	11	5	4	3	2
Pneumo (Prevnar13)	138	189	67	49	34	9	13	11
RSV (Abrysvo)	4	2	3	1				1
RSV (Arexvy)	7	7	3	3	1			1
Zoster (Shingrix)	40	36	7	5	3	6	1	4
Zoster live (Zostavax)	13	7	10	2	1	2	4	3



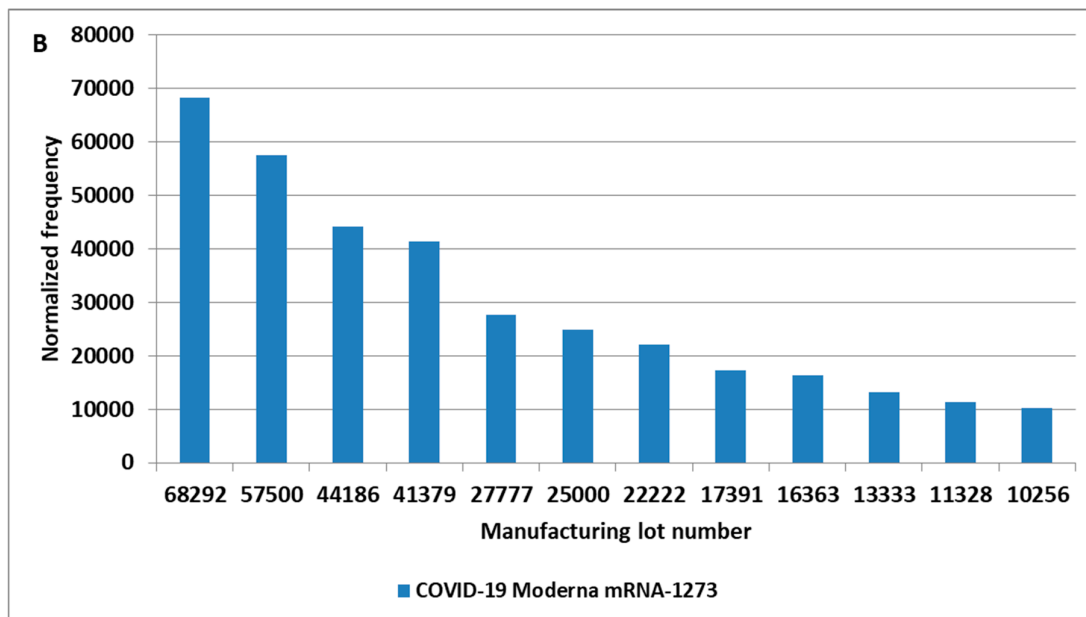
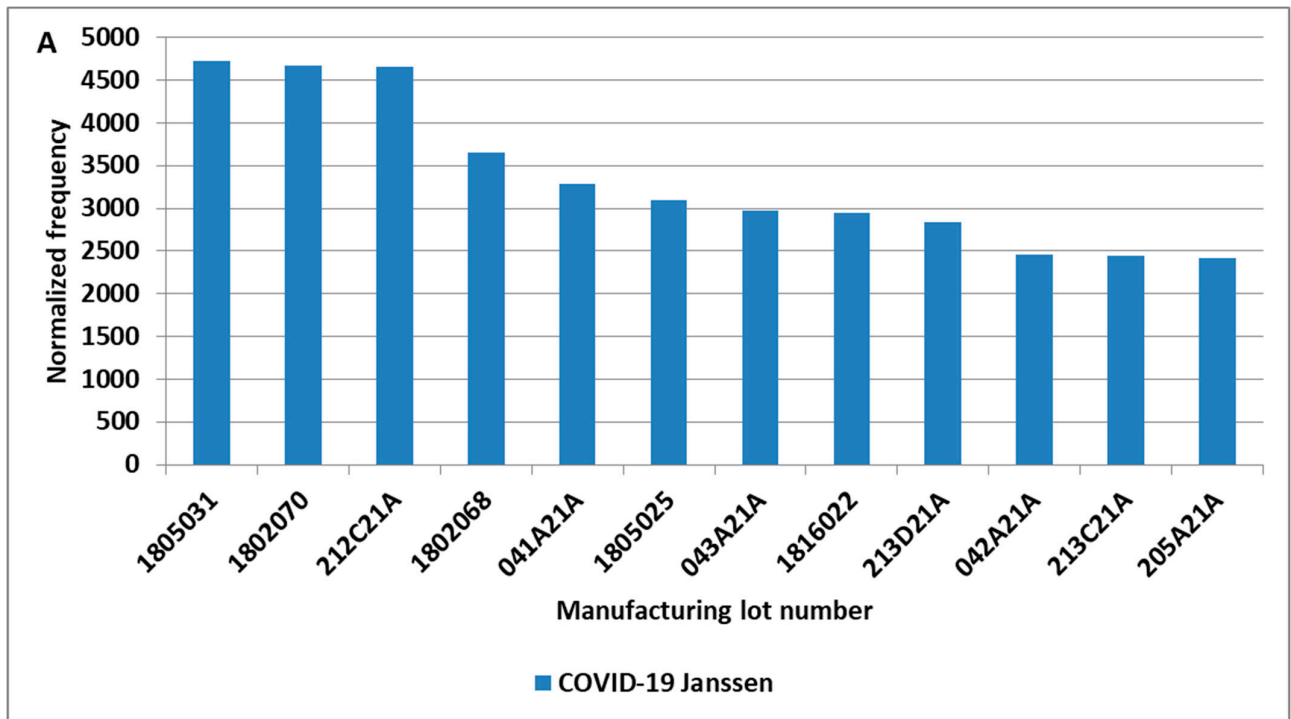


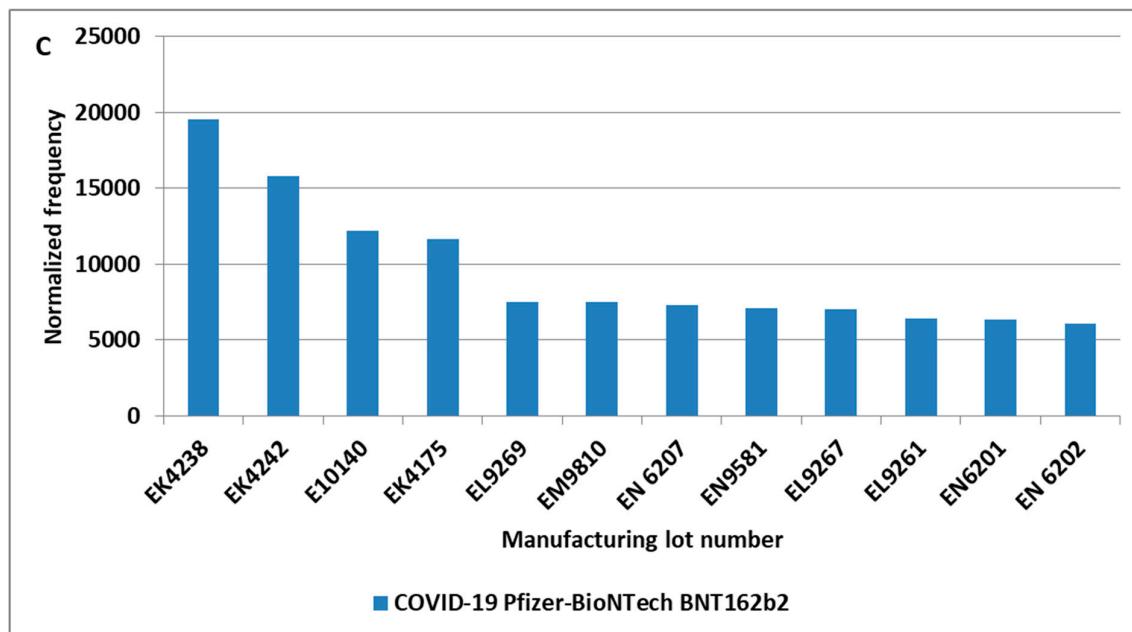
**Figure 1.** Death adverse event normalized frequencies by age group. A) COVID-19, Streptococcus pneumonia (Pneumo), Respiratory Syncytial virus (RSV), and Herpes Zoster vaccines; B) Influenza vaccines.





**Figure 2.** Fall adverse event normalized frequencies by age group. A) COVID-19, Streptococcus pneumonia (Pneumo), Respiratory Syncytial virus (RSV), and Herpes Zoster vaccines; B) Influenza vaccines.





**Figure 3.** Death adverse event normalized frequency for selected manufacturing lots (A) COVID-19 Janssen, (B) COVID-19 Moderna mRNA-1273, and (C) COVID-19 Pfizer-BioNTech BNT162b2 vaccines.

## 4. Discussion

### 4.1. Frequent Adverse Events in the Age Group 80 to 89

Aging likely negatively impacts AEs following immunizations. The top AEs for vaccines with more than 1,000 VAERS reports are shown in Table 1. For COVID-19 vaccine recipients, COVID-19 infection and associated AEs are only seen associated with the COVID-19 vaccines (Table 1); age group comparisons for these AEs are illustrated in Table 2. For the age group 80 to 89 vaccine recipients of the COVID-19 Janssen vaccine, 1 in 3.3 (30.5%) reported COVID-19 infection, and 1 in 7.4 (13.6%) died (Table 1A). The normalized frequency for AE death for the COVID-19 vaccines was 1829 for the COVID-19 (Janssen), 1409 for the COVID-19 (Moderna), 646 for the COVID-19 (Moderna bivalent), 1260 for the COVID-19 (Moderna Mnexspike), 629 for the COVID-19 (Novavax), 1063 for the COVID-19 (Pfizer-BioNTech), and 887 for the COVID-19 (Pfizer-BioNTech bivalent). For all ages, higher numbers of deaths were reported following the second dose compared to the first dose of the COVID-19 Pfizer-BioNTech vaccine (3487 first dose and 4654 second dose) and the COVID-19 Moderna vaccine (2931 first dose and 3749 second dose). For the age group 80 to 89 vaccine recipients of the COVID-19 Pfizer-BioNTech vaccine, 1 in 4.9 (20.5%) reported COVID-19 infection, and 1 in 12.4 (8.1%) died (Table 1A). For the COVID-19 AEs illustrated in Table 2, the majority fit the pattern of increasing normalized frequency by increased age, except for chest pain and oropharyngeal pain. Note the chest pain AE may have associations with myocarditis and pericarditis AEs with inverse age risks following COVID-19 immunization for both genders [10].

Multiple COVID-19 lots exhibit higher normalized frequencies than the overall average for all ages for the AE death (Figure 3 and Supplemental Table S1). For the COVID-19 Janssen lots 1805031 (4731), 1802070 (4676), and 212C21A (4651), plus 14 additional lots, were higher than the overall 1829 (Supplemental Table S1). A total of 175 COVID-19 Moderna lots with at least 4 death AEs exceed the overall 1260, including lots 207H23-2A (68,292), 3043159 (57,500), and 3046731 (44,186), with the normalized frequency for 12 lots higher than 10,000 (> 1 in 10) (Supplemental Table S1). Five COVID-19 Moderna bivalent lots had at least four AEs, including AS7184B (6756), AS7180B (4938), and 020H22A (3478), which were higher than the overall 646 (Supplemental Table S1). A total of 174 COVID-19 Pfizer-BioNTech lots exceed the overall AE death normalized frequency of 1063, including

EK4238 (19,512), EK4242 (15,789), and E10140 (12,195) (Supplemental Table S1). While normal distributions are expected, the very high normalized frequencies for the COVID-19 Moderna, COVID-19 Moderna bivalent, COVID-19 Pfizer-BioNTech, and possibly COVID-19 Janssen vaccines are consistent with manufacturing contaminants as likely causative components [11].

Endotoxins are one possible manufacturing contaminant. Lipopolysaccharides (LPS), also known as endotoxins or pyrogens, are constituents of the outer membrane of gram-negative bacteria. Endotoxins are a common manufacturing contaminant of vaccines. Endotoxin levels can vary widely by vaccine [12,13]. To minimize endotoxin contaminants, nanoparticles should be manufactured under endotoxin-free conditions [14].

#### 4.2. COVID-19 Breakthrough Infection

Individuals are getting the COVID-19 immunization to avoid COVID-19. It seems counterintuitive that the top AE associated with COVID-19 immunization (**Table 1A**) is COVID-19. The coronavirus family is well-known for infecting phagocytic immune cells using Fc receptor binding to infect additional host cells [15]. The process of antibody-dependent enhancement of disease (ADE) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has been proposed [16] and supported by clinical evidence [17]. The proposed ADE infection of immune cells has been demonstrated to be sensitive to the antibody titer level for the SARS-CoV-1 virus [18]. Hence, until COVID-19 vaccine recipients reach very high Spike protein antibody titer levels, the vaccine recipients have possibly higher infectivity potential than non-vaccinated individuals. Likewise, as the Spike antibody titers naturally decrease after several months, breakthrough infections of fully vaccinated and boosted individuals are being observed. The current recommendations for COVID-19 booster shots every six months should maintain ongoing very high levels of Spike protein antibodies.

#### 4.3. Death Adverse Event

The risk of death increases with increased age. For comparison purposes, an upper limit for background AE death can be estimated roughly as 252 per 100,000 VAERS reports using the value for Zoster (Shingrix) (**Table 1B**); given this, the normalized frequency for COVID-19 Janssen is 81 times higher than this background rate (20,500 / 252), and COVID-19 Pfizer-BioNTech is 32 times higher than this background rate (8,089 / 252). The background deaths per 7 days per 100,000 individuals in the United States is 109 [19]. Normalized frequencies for AE death for age groups 50-59, 60-69, 70-79, and 80-89 for multiple vaccines and several coadministered vaccines are illustrated in **Figure 1**. The normalized frequencies for death appear additive for COVID-19 Janssen and COVID-19 Moderna (18.2%), COVID-19 Janssen and COVID-19 Pfizer-BioNTech (22.2%), and COVID-19 Pfizer-BioNTech bivalent + Influenza seasonal (Fluzone high-dose quadrivalent) (6.9%) (**Figure 1**). The normalized frequency for the COVID-19 Janssen vaccine is 1829 (1.8%), and the COVID-19 Pfizer-BioNTech vaccine is 1063 (1.1%). The normalized frequency for the COVID-19 Janssen vaccine age group 80 to 89 is 11.2 times higher than for all ages; the normalized frequency for ages 80 to 89 for the COVID-19 Pfizer-BioNTech vaccine is 7.6 times higher than for all ages. The majority of deaths AEs are reported with an onset of a few days (**Table 3**); it is well-known that as time increases, the likelihood of reporting AEs to VAERS decreases. The normalized frequencies for AE death for COVID-19 vaccine recipient age groups 70 to 79 and 80 to 89 represent multiple safety signals (**Figure 1**). The normalized frequencies for AE death for Pneumo (Pneumovax), Pneumo (Prevnar13), RSV (Abrysvo), and Zoster live (Zostavax) age group 80 to 89 may also represent safety signals (**Figure 1**). Top overlapping AEs with death that do not overlap the COVID-19 top AEs (**Table 1A**) include autopsy, cardiac arrest, cardio-respiratory arrest, endotracheal intubation, general physical health deterioration, hypotension, loss of consciousness, mechanical ventilation, mental status changes, myocardial infarction, oxygen saturation decreased, positive airway pressure therapy, pulse absent, respiratory arrest, respiratory distress, respiratory failure, resuscitation, septic shock, syncope, unresponsive to stimuli, and vaccination failure. Deaths have been linked with the COVID-19 Pfizer-

BioNTech vaccine [20]. Excess deaths have been observed after repeated COVID-19 vaccination in Japan [21]. Florida residents who received the COVID-19 Pfizer-BioNTech BNT162b2 vaccine were observed with significantly higher risk for 12-month all-cause mortality compared to matched COVID-19 Moderna mRNA-1273 vaccine recipients [22].

**Hypothesis 1:** *Immunization with a COVID-19 vaccine correlates with SARS-CoV-2 infection in elderly individuals.*

Multiple days are anticipated for a SARS-CoV-2 infection post-immunization, followed in some individuals by COVID-19-associated death, with COVID-19-associated death occurring multiple days after infection. Defining any individual receiving a COVID-19 vaccine as vaccinated, these cases all represent COVID-19 vaccine breakthrough infections; many cases in VAERS are reported after the first of two paired mRNA vaccine doses, but more cases follow the second dose. ADE may be contributing to the severity of COVID-19 in elderly individuals [16].

**Hypothesis 2:** *Novel safety signal detected is associated with multiple vaccines, including the COVID-19 Moderna, COVID-19 Pfizer-BioNTech, COVID-19 Moderna bivalent, and COVID-19 Janssen for AE death; elevated normalized frequencies associated with manufacturing lots are supportive of unknown manufacturing contamination as a likely causative component.*

VAERS data indicate elevated additive risks for coadministration of two or more vaccines with elevated AE death normalized frequencies. VAERS data are consistent with a rapid onset in days for this safety signal. Deaths associated with the **Hypothesis 2** model are likely independent of SARS-CoV-2 infection, but overlaps between these two independent etiology models can occur randomly. Note that both the COVID-19 Pfizer-BioNTech BNT162b2 and the COVID-19 Moderna Spikevax mRNA-1273 vaccines were found to have residual plasmid DNA and SV40 promoter-enhancer sequences in some vaccine batches [23]; while this is of major concern with regards to long-term expression of the Spike protein within vaccine recipient bacteria cells, any relationship to immediate-onset adverse event death is unknown. This does illustrate contamination of vaccine batches with unintended constituents.

#### 4.4. Fall Adverse Event

The risk of falling following immunization has been previously identified [24]. The AE fall is in the top 50 ranked AEs for multiple vaccines (**Table 1**). This study demonstrates an undetected age risk factor for the fall AE (**Figure 2**). The normalized frequencies for the AE fall are much higher for COVID-19 vaccines and coadministered combinations including a COVID-19 vaccine than for non-COVID-19 vaccines (**Figure 2**). There may be some signature overlaps with the AE death signatures by vaccine and coadministered vaccines, pointing to possible overlapping etiologies worthy of further investigation. Immediate onset of fall AEs has been previously reported [24].

## 5. Conclusions

Informed consent considers risks versus benefits for vaccines and coadministered vaccines. This study identifies clear safety signals that increase with age for death associated with specific vaccines. Multiple safety signals associated with increased mortality risks were identified and are worthy of follow-up studies.

The risk of falling within two days post-immunization increases with age. Reiterating: "Avoidance of activities like driving, operating heavy machinery, with increased risks of falling, etc., for one to two days following immunization provides an opportunity to reduce the frequency of falls, injuries, and other rare accidents" [24].

**Supplementary Materials:** The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

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