

# Supplementary Materials for

# SARS-CoV-2 vaccine protection and deaths among US veterans during 2021

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#### **Materials and Methods**

We examined SARS CoV-2 infections and death due to any cause in U.S. Veterans age  $\geq 18$ years and receiving care in the Veterans Health Administration (VHA), the largest integrated health system in the country. After the U.S. Food and Drug Administration issued an emergency use authorization for the Pfizer-BioNTech vaccine in December 2020, the Department of Veterans Affairs (VA) first provided vaccinations to front-line health care workers and Veterans residing in long-term care facilities in 37 of its medical centers across the U.S. As vaccine supplies increased, additional Veterans received vaccinations based on age, existing health conditions, and other factors for increased risk of severe illness or death from COVID-19, and as of October 21, 2021, more than 3.5 million Veterans have been fully vaccinated (available at:

https://www.accesstocare.va.gov/Healthcare/COVID19NationalSummary).

We used the VA Corporate Data Warehouse (CDW) to identify vaccination status (fully vaccinated vs. unvaccinated), vaccine type (Pfizer-BioNTech, Moderna, Janssen), SARS CoV-2 infections, and deaths due to any cause during the period February 1, 2021 to October 1, 2021.We focused on this time period because it encompasses the time when many Veterans became fully vaccinated (i.e., vaccine eligibility extended beyond long-term care facilities) and the mid-summer 2021 surge in cases in the U.S. The VA CDW provides discrete, individual-level data, including demographics, administrative claims-based diagnosis and procedure codes, prescriptions, anthropometric measures, and free-text data including procedure notes and pathology reports; data include all 50 states and U.S. territories.

Fully vaccinated was defined as two doses of Pfizer-BioNTech or Moderna or one dose of Janssen vaccines, administered at the appropriate intervals. We excluded partial vaccinations and vaccinations that were administered off-label and/or not according to recommendation. We did not consider booster vaccines as the study period largely precedes authorization for boosters in the U.S. SARS-CoV-2 infection was defined as the detection of SARS-CoV-2 on most recent reversetranscriptase–polymerase-chain-reaction (RT-PCR) assay, regardless of symptoms or test setting. The reason for RT-PCR assay is not provided in the VA CDW. Veterans may have received a RT-PCR assay for many reasons, including but not limited to, concern about exposure, symptoms, as a requirement of a clinic visit or in advanced of a medical procedure, or as part of a hospital admission. We included assays received for any reason or in any clinical setting.

Deaths due to any cause (n=22,345) were identified using a combination of data from the Master Veteran Index, vital status files, and medical records (hierarchical in that order). These data include deaths that occurred both inside and outside the VHA.

Vaccine effectiveness (1- adjusted hazard ratio [aHR] x 100) against infection was estimated using Cox proportional hazards models, overall and by vaccine type (Pfizer-BioNTech vs. Moderna vs. Janssen), with vaccination status modeled as time-varying. Modeling vaccination as time-varying assigns follow-up time for Veterans before the date of full vaccination (defined as 14 days after receipt of the second dose of Pfizer-BioNTech or Moderna or one dose of Janssen vaccines) as unvaccinated time and time after the date of full vaccination as vaccinated time; those never vaccinated contribute only unvaccinated time We required Veterans to receive a RT-PCR assay to contribute vaccinated and/or unvaccinated follow-up time, such that Veterans who received a recent RT-PCR assay before vaccination contributed unvaccinated time only. Veterans in both groups were followed from February 1, 2021 until their most recent RT-PCR assay or October 1, 2021. We used calendar time as the underlying time scale to allow the baseline hazard to vary flexibly as vaccine eligibility, testing practices, non-pharmaceutical interventions, and infection transmission changed over time. As noted by others (31), models with calendar time as the underlying time scale compare those who are unvaccinated on each calendar date to those who are vaccinated on that same date.

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We report aHR and 95% confidence intervals (CI), adjusted for age, sex and comorbidity. Comorbidity was measured using the Charlson comorbidity index (*26*), and a diagnosis of diabetes, chronic obstructive pulmonary disease, bronchitis, acute respiratory failure, chronic lung disease, cardiovascular disease in the two years prior to the RT-PCR assay. We also examined time dependence by including product terms for vaccination status by the log of follow-up time, with p<0.01 indicating statistical significance.

To illustrate findings, we plotted cumulative risk of infection using Kaplan-Meier estimation to account for censoring, overall and by vaccination status and age group (<50 years, 50-64 years, and  $\geq$ 65 years). We used the same time-varying assignment described above allowing individuals to contribute time before and after vaccination and allowing for changes in RT-PCR status. Thus, as described above for Cox models, the time scale compares those who are unvaccinated on each calendar date to those who are vaccinated on that same date. We selected these age groups because they correspond to the phased-in eligibility for vaccination.

We examined vaccine effectiveness against death in a nested sample (n=775,536) of Veterans who were: 1) unvaccinated and received an RT-PCR assay from February 1, 2021 to September 30, 2021; or 2) fully vaccinated and received an RT-PCR assay after the date of full vaccination during the same period. We plotted cumulative risk of death due to any cause using Kaplan-Meier estimation, separately by age group <65 vs.  $\geq$ 65 years) and comorbidity score (Charlson Comorbidity Index, <3 vs.  $\geq$ 3) (*26*). Follow-up was accrued from the date of RT-PCR assay until death or October 1, 2021. In addition, we used Cox proportional hazards models to examine vaccine effectiveness against death during the period corresponding to the emergence and dominance of the Delta variant in the U.S. We limited the nested sample for this analysis to RT-PCR assays on or after July 1, 2021 (n=312,829) and report aHR and 95% CI. All analyses were conducted using SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC). This study was approved by the Institutional Review Board at the University of California San Francisco and the Public Health Institute, as well as the San Francisco VA Research and Development Committee.

Supplementary Table 1. Distribution of SARS-CoV-2 infection by demographics and
vaccination status in 780,225 U.S. Veterans, February 1, 2021 to October 1, 2021

	Most recent RT-PCR <sup>1</sup>							
	Negative	Positive (%)						
Vaccination status <sup>2</sup>								
Unvaccinated	209,439	72,638 (25.8%)						
Janssen	28,717	6,945 (19.5%)						
Moderna	206,420	24,342 (10.6%)						
Pfizer-BioNTech	204,044	27,680 (12.0%)						
Sex								
Female	91,535	20,424 (18.2%)						
Male	557,085	111,181 (16.6%)						
Ethnicity								
Hispanic	49,050	10,753 (18.0%)						
Non-Hispanic	599,570	120,852 (16.8%)						
Race								
American Indian/Alaska Native	4,884	1,087 (18.2%)						
Asian	6,816	1,147 (14.4%)						
Black or African American	142,197	26,282 (15.6%)						
Native Hawaiian/Other Pacific Islander	5,563	1,206 (17.8%)						
White	421,726	86,332 (17.0%)						
Age at RT-PCR (years)								
<50	144,338	41,099 (22.2%)						
50-64	185,155	37,831 (17.0%)						
≥65	319,127	52,675 (14.2%)						
Comorbidity score <sup>3</sup> (Charlson Comorbidity Index)								
0	253,896	60,263 (19.2%)						
1-2	218,042	41,595 (16.0%)						
3-4	102,372	16,988 (14.2%)						
≥5	74.310	12.759 (14.6%)						

<sup>1</sup>For vaccinated Veterans, RT-PCR assessed 15 days after last dose that established full vaccination status; for unvaccinated Veterans, RT-PCR assessed beginning in February 1, 2021, coincident with broadscale vaccine eligibility in the VA. <sup>2</sup>Vaccination status defined as: 1) a single Janssen vaccine; 2) two Moderna vaccines or 3) two Pfizer-BioNTech vaccines.<sup>3</sup>Pre-existing morbidity as represented by the Charlson Co-Morbidity Index reported within 2 years of first RT-PCR test or hospitalization related to first RT-PCR test.

# Supplementary Table 2. Distribution of vaccine type by demographics among 498,148 fully vaccinated U.S. Veterans, February 1, 2021 to October 1, 2021

		Vaccine Type <sup>1</sup>	
	Janssen (%)	Moderna (%)	Pfizer (%)
Total Vaccinated	35,662 (7.2%)	230,762 (46.3%)	231,724 (46.5%)
February	30 (0.0%)	32,114 (41.3%)	45,675 (58.7%)
March	5,862 (3.6%)	86,107 (52.2%)	72,828 (44.2%)
April	10,732 (7.6%)	65,530 (46.1%)	65,852 (46.3%)
May	4,057 (7.0%)	27,986 (48.5%)	25,651 (44.5%)
June	5,844 (24.0%)	9,176 (37.7%)	9,305 (38.3%)
July	3,358 (29.6%)	3,694 (32.5%)	4,305 (37.9%)
August	3,645 (37.4%)	2,491 (25.5%)	3,621 (37.1%)
September	2,143 (20.8%)	3,664 (35.6%)	4,487 (43.6%)
Sex			
Female	3,884 (8.1%)	19,752 (41.2%)	24,295 (50.7%)
Male	31,778 (7.1%)	211,010 (46.9%)	207,429 (46.1%)
Ethnicity			
Hispanic	2,703 (6.7%)	19,659 (48.9%)	17,842 (44.4%)
Non-Hispanic	32,959 (7.2%)	211,103 (46.1%)	213,882 (46.7%)
Race			
American Indian/Alaska Native	316 (8.5%)	1,746 (47.0%)	1,657 (44.6%)
Asian	349 (6.4%)	2,382 (43.4%)	2,753 (50.2%)
Black or African American	7,499 (6.4%)	44,476 (38.2%)	64,425 (55.4%)
Native Hawaiian/Other Pacific Islander	295 (6.7%)	1,973 (44.8%)	2,131 (48.4%)
White	24,900 (7.4%)	166,448 (49.3%)	146,199 (43.3%)
Age (years)			
<50	8,855 (12.8%)	26,253 (38.0%)	33,981 (49.2%)
50-64	13,823 (10.0%)	59,240 (43.0%)	64,644 (46.9%)
≥65	12,984 (4.5%)	145,269 (49.9%)	291,352 (58.5%)

<sup>1</sup>Vaccination status defined as: 1) a single Janssen vaccine; 2) two Moderna vaccines or 3) two Pfizer-BioNTech vaccines

Supplementary Table 3A: RT-PCR Assays by Vaccination Status and Week, February 1 – October 1, 2021 (used for Figure 2A): All Ages

	Unvac	cinated	Vaccinated										
			Jans	sen		Mod	erna		Pfizer-Bi	oNTech			
Week	PCR+	PCR-	PCR+	PCR-		PCR+	PCR-		PCR+	PCR-			
1	6543	17817	0	0		31	83		24	113			
2	4557	16543	0	0		32	171		45	329			
3	5132	20736	0	1		86	650		124	866			
4	4548	18848	0	0		111	1062		146	1448			
5	3176	18010	0	0		109	1402		179	1978			
6	3639	16699	1	6		180	1992		236	2536			
7	3739	16623	9	79		261	2611		272	2935			
8	3615	14775	29	137		293	3221		330	3297			
9	3607	14534	38	189		348	3853		391	4015			
10	3619	13969	55	259		408	4555		485	4498			
11	3231	13401	67	369		454	5009		530	5029			
12	2915	11258	104	406		475	5481		569	5609			
13	1608	9855	50	458		176	5513		196	5606			
14	1388	9350	26	425		158	5762		183	5900			
15	1178	8425	27	458		173	5920		153	6018			
16	968	7427	29	462		147	5491		133	5605			
17	772	6884	32	449		150	5498		147	5563			
18	754	7689	30	583		135	6312		123	6384			
19	675	7178	31	553		162	5984		130	6368			
20	699	7284	32	626		129	6320		144	6166			
21	703	6663	34	591		136	5788		145	5685			
22	835	6681	39	613		150	5982		180	5831			
23	1378	8265	72	794		230	7215		376	6822			
24	1989	9216	91	841		371	7592		503	7187			
25	2923	10112	158	874		471	7860		711	7563			
26	3840	11371	258	996		756	8699		1077	8410			
27	4621	11740	285	1068		896	8942		1268	8792			
28	4721	6532	321	629		989	4980		1353	4568			
29	4632	5112	333	525		1149	3752		1378	3252			
30	4488	4574	330	478		1054	3477		1305	3012			
31	3486	4015	263	439		855	3344		1009	2774			
32	3136	4494	268	481		880	3696		1037	3221			
33	2452	4154	180	465		758	3536		803	3081			
34	1966	3993	162	462		649	3280		646	2937			

Supplementary Table 3B: RT-PCR Assays by Vaccination Status and Week, February 1 – October 1, 2021 (used for Figure 2B): Age <50 years

	Unvaco	inated			Vac	Vaccinated					
			Jans	sen	Mod	erna	Pfizer-	BioNTech			
Week	PCR+	PCR-	PCR+	PCR-	PCR+	PCR-	PCR+	PCR-			
1	1598	4162	0	0	3	21	2	12			
2	1136	3582	0	0	3	28	5	16			
3	1316	4542	0	0	6	53	6	48			
4	1266	4098	0	0	6	53	9	70			
5	995	4016	0	0	9	81	8	86			
6	1093	4006	0	1	10	97	13	93			
7	1236	4183	1	11	23	135	18	122			
8	1241	4151	9	20	18	154	25	149			
9	1337	4174	6	37	20	168	23	212			
10	1335	4357	11	39	33	243	43	286			
11	1289	4487	12	71	43	307	35	365			
12	1053	3929	18	93	28	344	63	485			
13	627	3520	11	104	10	397	14	546			
14	488	3447	5	83	11	475	20	575			
15	411	2934	3	90	14	493	18	643			
16	343	2672	2	84	16	427	19	599			
17	279	2406	4	95	10	489	23	620			
18	262	2691	5	134	10	524	12	733			
19	240	2488	6	117	17	513	20	703			
20	263	2559	7	117	16	535	23	687			
21	296	2313	11	115	19	502	19	605			
22	371	2437	9	118	18	521	23	716			
23	631	3127	19	165	23	709	55	852			
24	974	3742	21	167	48	720	77	896			
25	1458	4186	36	199	65	805	106	1068			
26	1870	5025	73	242	104	1002	210	1256			
27	2153	5315	84	267	112	1086	204	1251			
28	2104	2966	84	149	117	591	218	718			
29	2082	2311	94	132	128	491	180	527			
30	2032	2089	96	129	129	435	179	522			
31	1528	1805	61	104	100	419	157	451			
32	1342	2012	61	109	86	454	157	526			
33	987	1833	43	115	76	433	115	478			
34	798	1639	46	100	59	389	71	469			

Supplementary Table 3C: RT-PCR Assays by Vaccination Status and Week, February 1 – October 1, 2021 (used for Figure 2C): Age 50-64 years

	Unvacc	inated			Vaccinated				
			Jan	ssen	Mod	erna		Pfizer-E	BioNTech
Week	PCR+	PCR-	PCR+	PCR-	PCR+	PCR-		PCR+	PCR-
1	1838	5223	0	0	9	24		5	21
2	1368	4621	0	0	8	49		4	57
3	1501	5677	0	0	24	124		23	125
4	1377	5360	0	0	23	177		29	183
5	945	5335	0	0	22	209		34	293
6	1172	5165	1	3	31	275		32	340
7	1218	5277	5	29	35	367		42	434
8	1176	4967	15	61	56	478		60	514
9	1108	4985	15	78	60	595		79	748
10	1165	4921	24	119	89	808		116	971
11	982	4726	22	158	113	975		141	1148
12	916	3863	39	156	111	1233		158	1453
13	477	3290	18	182	43	1215		46	1464
14	432	3047	10	169	39	1377		38	1562
15	370	2705	8	195	36	1422		36	1627
16	289	2359	17	184	27	1345		25	1432
17	231	2220	10	180	31	1334		38	1524
18	212	2463	13	225	31	1573		37	1657
19	193	2201	12	216	39	1494		24	1729
20	214	2333	10	260	31	1545		38	1693
21	199	2125	12	236	27	1341		36	1566
22	249	2128	20	267	38	1510		44	1589
23	405	2645	17	321	45	1757		103	1869
24	567	2930	37	338	88	1953		139	1997
25	839	3319	72	355	113	2047		203	2090
26	1072	3701	99	412	178	2230		284	2345
27	1412	3760	107	438	209	2365		339	2559
28	1432	1990	111	245	236	1247		324	1265
29	1355	1519	125	212	266	906		341	890
30	1259	1365	115	181	244	833		345	769
31	1020	1204	111	164	198	838		234	689
32	904	1348	113	177	190	895		249	843
33	758	1205	72	170	165	824		203	794
34	605	1207	64	178	128	775		148	759

Supplementary Table 3D: RT-PCR Assays by Vaccination Status and Week, February 1 – October 1, 2021 (used for Figure 2D): Age >65 years

	Unvac	cinated						
			Jans	sen	Mo	derna	Pfizer-B	ioNTech
Week	PCR+	PCR-	PCR+	PCR-	PCR+	PCR-	PCR+	PCR-
1	3107	8432	0	0	19	38	17	80
2	2053	8340	0	0	21	94	36	256
3	2315	10517	0	1	56	473	95	693
4	1905	9390	0	0	82	832	108	1195
5	1236	8659	0	0	78	1112	137	1599
6	1374	7528	0	2	139	1620	191	2103
7	1285	7163	3	39	203	2108	212	2379
8	1198	5657	5	56	219	2589	245	2634
9	1162	5375	17	74	268	3090	289	3055
10	1119	4691	20	101	286	3504	326	3241
11	960	4188	33	140	298	3727	354	3516
12	946	3466	47	157	336	3904	348	3671
13	504	3045	21	172	123	3901	136	3596
14	468	2856	11	173	108	3910	125	3763
15	397	2786	16	173	123	4005	99	3748
16	336	2396	10	194	104	3719	89	3574
17	262	2258	18	174	109	3675	86	3419
18	280	2535	12	224	94	4215	74	3994
19	242	2489	13	220	106	3977	86	3936
20	222	2392	15	249	82	4240	83	3786
21	208	2225	11	240	90	3945	90	3514
22	215	2116	10	228	94	3951	113	3526
23	342	2493	36	308	162	4749	218	4101
24	448	2544	33	336	235	4919	287	4294
25	626	2607	50	320	293	5008	402	4405
26	898	2645	86	342	474	5467	583	4809
27	1056	2665	94	363	575	5491	725	4982
28	1185	1576	126	235	636	3142	811	2585
29	1195	1282	114	181	755	2355	857	1835
30	30 1197		119	168	681	2209	781	1721
31	938	1006	91	171	557	2087	618	1634
32	890	1134	94	195	604	2347	631	1852
33	707	1116	65	180	517	2279	485	1809
34	563	1147	52	184	462	2116	427	1709

Supplementary Table 3E: Vital Status by Vaccination Status, RT-PCR Assay, and from RT-PCR Assay, Beginning February 1, 2021 (used for Figure 3A): Age <65 years

	Unvaccinated						Vaccinated				
		I	PCR-		Р	CR +	I	PCR-		Р	CR +
Weeks from RT-PCR Assay		Deaths	Non- Deaths		Deaths	Non- Deaths	Deaths	Non- Deaths		Deaths	Non- Deaths
1		95	3932		74	1811	55	3747		11	677
2		164	3002		192	1731	92	2839		14	673
3		133	3285		173	2217	107	3068		9	853
4		120	2923		126	2497	91	2729		11	861
5		119	3297		88	3203	97	2990		17	1101
6		102	3622		43	3329	89	3315		4	1129
7		80	4648		27	3380	87	4457		7	1082
8		78	8459		23	3397	83	8480		5	1048
9		68	8036		15	2778	74	8075		3	937
10		64	6770		8	2157	66	7172		1	594
11		44	5949		8	1413	62	6678		1	404
12		50	5024		9	950	71	6266		3	258
13		43	3845		8	562	41	5276		4	149
14		33	3669		7	453	33	4941		0	124
15		29	4015		9	427	32	5466		2	122
16		25	3741		4	380	31	5513		0	117
17		21	4035		5	403	32	5674		1	106
18		21	3502		6	417	24	5048		3	114
19		12	3672		4	519	28	5028		1	105
20		20	3951		8	638	19	5668		1	114
21		18	4394		4	731	15	5747		1	122
22		18	4301		3	848	22	5737		0	139
23		20	4562		1	1404	14	5989		1	414
24		12	4845		4	1554	10	5869		1	362
25		12	4476		4	1634	14	5935		0	307
26		9	4255		3	1522	15	5556		0	198

NOTE: Numbers in table correspond to Kaplan-Meier curves shown in Figure 3 which were truncated at 26 weeks to avoid incomplete follow-up and sparse data. Therefore, the total number of observations in the table does not represent the total nested sample given in Materials and Methods.

Supplementary Table 3F: Vital Status by Vaccination Status, RT-PCR Assay, and Week from RT-PCR Assay, Beginning February 1, 2021 (used for Figure 3B): Age  $\geq$ 65 years

	Unvaccinated						Vaccinated				
	I	PCR-	P	PCR +		PCR-			PCR +		
Weeks from RT-PCR Assay	Deaths	Non- Deaths	Deaths	Non- Deaths		Deaths	Non- Deaths		Deaths	Non- Deaths	
1	390	1542	348	708		459	5760		102	1241	
2	698	1100	725	661		996	4267		237	1046	
3	614	1102	670	821		959	4360		210	1300	
4	530	953	401	852		813	3870		128	1210	
5	436	1038	227	1059		756	4114		82	1508	
6	355	1190	147	1032		665	4368		63	1648	
7	301	1405	92	1011		564	5961		29	1488	
8	276	2367	58	872		500	10820		19	1330	
9	216	2280	63	729		449	10616		23	1084	
10	192	2166	40	477		375	9777		17	692	
11	180	2097	41	348		324	9563		13	517	
12	163	2033	46	260		300	9179		16	395	
13	114	1691	24	175		254	7676		17	203	
14	113	1719	26	160		222	7698		13	170	
15	87	1820	30	179		219	8341		12	166	
16	67	1854	28	193		191	8207		7	197	
17	65	1822	25	213		173	8563		8	167	
18	55	1564	21	188		129	7364		8	195	
19	56	1557	22	244		134	7657		12	186	
20	50	1784	16	276		112	8222		10	220	
21	52	1710	16	307		103	8228		8	230	
22	44	1732	16	332		103	8179		10	259	
23	33	1777	17	523		92	8422		6	682	
24	28	1761	13	515		70	8391		2	646	
25	28	1821	10	559		73	8179		2	585	
26	15	1637	15	513		48	7925		5	541	

NOTE: Numbers in table correspond to Kaplan-Meier curves shown in Figure 3 which were truncated at 26 weeks to avoid incomplete follow-up and sparse data. Therefore, the total number of observations in the table does not represent the total nested sample given in Materials and Methods.

Beginning February 1, 2021 (used for Figure 3C): Charlson Comorbidity Index score <3												
			Unvac	cinated				Vaco	cina	ated		
		F	PCR-	P	CR +		F	PCR-		Р	CR +	
Weeks from RT-PCR Assay		Deaths	Non- Deaths	Deaths	Non- Deaths		Deaths	Non- Deaths		Deaths	Non- Deaths	
1		238	4881	209	2203		195	7051		31	1239	
2		382	3725	485	2080		384	5387		80	1133	
3		339	3953	462	2656		375	5588		80	1454	
4		294	3515	294	2945		292	4982		46	1362	
5		236	3961	178	3766		296	5372		27	1787	
6		202	4375	103	3902		261	5795		17	1841	
7		179	5423	60	3897		219	7462		10	1723	
8		164	9542	34	3792		196	13031		5	1593	
9		120	9084	35	3153		174	12549		8	1390	
10		122	7782	18	2374		148	11097		9	866	
11		105	6890	23	1580		123	10559		6	630	
12		106	5954	18	1078		114	9972		2	423	
13		63	4620	10	651		102	8305		4	214	
14		69	4401	15	514		95	8069		5	189	
15		53	4856	18	524		87	8871		3	185	
16		49	4602	10	482		79	8953		1	208	
17		44	4854	10	513		76	9263		2	181	
18		41	4199	7	509		60	8090		2	192	
19		38	4388	11	651		69	8288		3	186	
20		32	4778	10	777		44	9218		1	196	
21		38	5230	8	878		42	9298		3	198	
22		24	5155	8	1025		53	9298		5	248	
23		22	5385	8	1666		37	9615		1	637	
24		23	5656	6	1769		33	9503		0	605	
25		21	5339	7	1879		27	9610		1	504	
26		14	5047	7	1747		21	9078		1	410	

Supplementary Table 3G: Vital Status by Vaccination Status, RT-PCR Assay, and Week from RT-PCR Assay,

NOTE: Numbers in table correspond to Kaplan-Meier curves shown in Figure 3 which were truncated at 26 weeks to avoid incomplete follow-up and sparse data. Therefore, the total number of observations in the table does not represent the total nested sample given in Materials and Methods.

Supplementary Table 3H: Vital Status by Vaccination Status, RT-PCR Assay, and Week from RT-PCR Assay, Beginning February 1, 2021 (used for Figure 3D): Charlson Comorbidity Index score  $\geq$ 3

	Unvaccinated					Vaccinated				
	I	PCR-	F	PCR +			PCR-		Р	CR +
Weeks from RT-PCR Assay	Deaths	Non- Deaths	Deaths	Non- Deaths		Deaths	Non- Deaths		Deaths	Non- Deaths
1	247	593	213	316		319	2456		82	679
2	480	377	432	312		704	1719		171	586
3	408	434	381	382		691	1840		139	699
4	356	361	233	404		612	1617		93	709
5	319	374	137	496		557	1732		72	822
6	255	437	87	459		493	1888		50	936
7	202	630	59	494		432	2956		26	847
8	190	1284	47	477		387	6269		19	785
9	164	1232	43	354		349	6142		18	631
10	134	1154	30	260		293	5852		9	420
11	119	1156	26	181		263	5682		8	291
12	107	1103	37	132		257	5473		17	230
13	94	916	22	86		193	4647		17	138
14	77	987	18	99		160	4570		8	105
15	63	979	21	82		164	4936		11	103
16	43	993	22	91		143	4767		6	106
17	42	1003	20	103		129	4974		7	92
18	35	867	20	96		93	4322		9	117
19	30	841	15	112		93	4397		10	105
20	38	957	14	137		87	4672		10	138
21	32	874	12	160		76	4677		6	154
22	38	878	11	155		72	4618		5	150
23	31	954	10	261		69	4796		6	459
24	17	950	11	300		47	4757		3	403
25	19	958	7	314		60	4504		1	388
26	10	845	11	288		42	4403		4	329

NOTE: Numbers in table correspond to Kaplan-Meier curves shown in Figure 3 which were truncated at 26 weeks to avoid incomplete follow-up and sparse data. Therefore, the total number of observations in the table does not represent the total nested sample given in Materials and Methods.

Supplementary Table 3I: Vital Status by Vaccination Status, RT-PCR Assay, and Week from RT-PCR Assay, Beginning July 1, 2021 (used for Figure S1A): Age <65 years

			Unvad	nated		Vaccinated					
	PCR- PCR +			CR +	PCR-			PCR +			
Weeks from RT-PCR Assay		Deaths	Non- Deaths		Deaths	Non- Deaths	Deaths	Non- Deaths		Deaths	Non- Deaths
1		30	3932		35	1811	19	3747		10	677
2		33	3002		127	1731	42	2839		11	673
3		17	3285		104	2217	32	3068		7	853
4		27	2923		85	2497	34	2729		6	861
5		19	3297		44	3203	24	2990		13	1101
6		19	3622		24	3329	33	3315		1	1129
7		16	4648		9	3380	17	4457		5	1082
8		12	8459		5	3397	22	8480		2	1048

NOTE: Numbers in table correspond to Kaplan-Meier curves shown in Supplementary Figure 1 which included RT-PCR results beginning July 1, 2021 onward to examine the time period corresponding to the dominance of the Delta variant. Owing to the shorter follow-up period these curves were truncated at 8 weeks to avoid incomplete follow-up and sparse data. Supplementary Table 3J: Vital Status by Vaccination Status, RT-PCR Assay, and Week from RT-PCR Assay, Beginning July 1, 2021 (used for Figure S1B): Age  $\geq$ 65 years

	Unvaccinated						Vaccinated					
		PCR-		PCR +			PCR-			PCR +		
Weeks from RT- PCR Assay	Deaths	Non- Deaths		Deaths	Non- Deaths		Deaths	Non- Deaths		Deaths	Non- Deaths	
1	79	1542		131	708		178	5760		64	1241	
2	133	1100		345	661		383	4267		185	1046	
3	86	1102		323	821		333	4360		149	1300	
4	105	953		177	852		255	3870		92	1210	
5	75	1038		83	1059		230	4114		51	1508	
6	55	1190		38	1032		182	4368		27	1648	
7	58	1405		25	1011		158	5961		15	1488	
8	40	2367		8	872		119	10820		10	1330	

NOTE: Numbers in table correspond to Kaplan-Meier curves shown in Supplementary Figure 1 which included RT-PCR results beginning July 1, 2021 onward to examine the time period corresponding to the dominance of the Delta variant. Owing to the shorter follow-up period these curves were truncated at 8 weeks to avoid incomplete follow-up and sparse data.

**Supplementary Figure 1**. Kaplan-Meier curves illustrating cumulative risk of death due to any cause by vaccination status and RT-PCR assay for the period beginning July 1, 2021, corresponding to the emergence and dominance of the Delta variant in the U.S.: A) age <65 years; B) age  $\geq$ 65 years



### A. Age <65 years

## B. Age <u>></u>65 years





### **References and Notes**

- 1. T. Pilishvili, K. E. Fleming-Dutra, J. L. Farrar, R. Gierke, N. M. Mohr, D. A. Talan, A. Krishnadasan, K. K. Harland, H. A. Smithline, P. C. Hou, L. C. Lee, S. C. Lim, G. J. Moran, E. Krebs, M. Steele, D. G. Beiser, B. Faine, J. P. Haran, U. Nandi, W. A. Schrading, B. Chinnock, D. J. Henning, F. LoVecchio, J. Nadle, D. Barter, M. Brackney, A. Britton, K. Marceaux-Galli, S. Lim, E. C. Phipps, G. Dumyati, R. Pierce, T. M. Markus, D. J. Anderson, A. K. Debes, M. Lin, J. Mayer, H. M. Babcock, N. Safdar, M. Fischer, R. Singleton, N. Chea, S. S. Magill, J. Verani, S. Schrag, A. Yousaf, Y. Chung, J. Onukwube, W. Xing, B. Clinansmith, L. Uribe, K. E. Poronsky, D. M. Hashimoto, M. Bahamon, M. St. Romain, E. Kean, A. Stubbs, S. Roy, G. Volturo, J. Galbraith, J. C. Crosby, M. R. Fuentes, M. Mulrow, J. Lee, H. Johnston, A. J. Hansen, S. K. Fridkin, L. E. Wilson, S. Lovett, M. Christian, C. Myers, V. L. S. Ocampo, K. Talbot, J. Seidelman, A. M. Milstone, M. Hayden, M. Samore, J. H. Kwon, D. Shirley, D. Dillard, J. Dobson; Vaccine Effectiveness Among Healthcare Personnel Study Team, Interim Estimates of Vaccine Effectiveness of Pfizer-BioNTech and Moderna COVID-19 Vaccines Among Health Care Personnel - 33 U.S. Sites, January-March 2021. MMWR Morb. Mortal. Wkly. Rep. 70, 753–758 (2021). doi:10.15585/mmwr.mm7020e2 Medline
- A. Christie, S. J. Henley, L. Mattocks, R. Fernando, A. Lansky, F. B. Ahmad, J. Adjemian, R. N. Anderson, A. M. Binder, K. Carey, D. L. Dee, T. Dias, W. M. Duck, D. M. Gaughan, B. C. Lyons, A. D. McNaghten, M. M. Park, H. Reses, L. Rodgers, K. Van Santen, D. Walker, M. J. Beach, Decreases in COVID-19 Cases, Emergency Department Visits, Hospital Admissions, and Deaths Among Older Adults Following the Introduction of COVID-19 Vaccine United States, September 6, 2020-May 1, 2021. *MMWR Morb. Mortal. Wkly. Rep.* **70**, 858–864 (2021). <u>doi:10.15585/mmwr.mm7023e2 Medline</u>
- M. G. Thompson, J. L. Burgess, A. L. Naleway, H. L. Tyner, S. K. Yoon, J. Meece, L. E. W. Olsho, A. J. Caban-Martinez, A. Fowlkes, K. Lutrick, J. L. Kuntz, K. Dunnigan, M. J. Odean, K. T. Hegmann, E. Stefanski, L. J. Edwards, N. Schaefer-Solle, L. Grant, K. Ellingson, H. C. Groom, T. Zunie, M. S. Thiese, L. Ivacic, M. G. Wesley, J. M. Lamberte, X. Sun, M. E. Smith, A. L. Phillips, K. D. Groover, Y. M. Yoo, J. Gerald, R. T. Brown, M. K. Herring, G. Joseph, S. Beitel, T. C. Morrill, J. Mak, P. Rivers, K. M. Harris, D. R. Hunt, M. L. Arvay, P. Kutty, A. M. Fry, M. Gaglani, Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers Eight U.S. Locations, December 2020-March 2021. *MMWR Morb. Mortal. Wkly. Rep.* 70, 495–500 (2021). doi:10.15585/mmwr.mm7013e3 Medline
- 4. C. M. Brown, J. Vostok, H. Johnson, M. Burns, R. Gharpure, S. Sami, R. T. Sabo, N. Hall, A. Foreman, P. L. Schubert, G. R. Gallagher, T. Fink, L. C. Madoff, S. B. Gabriel, B. MacInnis, D. J. Park, K. J. Siddle, V. Harik, D. Arvidson, T. Brock-Fisher, M. Dunn, A. Kearns, A. S. Laney, Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings Barnstable County, Massachusetts, July 2021. *MMWR Morb. Mortal. Wkly. Rep.* **70**, 1059–1062 (2021). doi:10.15585/mmwr.mm7031e2 Medline

- 5. R. Herlihy, W. Bamberg, A. Burakoff, N. Alden, R. Severson, E. Bush, B. Kawasaki, B. Berger, E. Austin, M. Shea, E. Gabrieloff, S. Matzinger, A. Burdorf, J. Nichols, K. Goode, A. Cilwick, C. Stacy, E. Staples, G. Stringer, Rapid Increase in Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant Mesa County, Colorado, April-June 2021. *MMWR Morb. Mortal. Wkly. Rep.* **70**, 1084–1087 (2021). doi:10.15585/mmwr.mm7032e2 Medline
- 6. S. J. Thomas, E. D. Moreira Jr., N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, J. L. Perez, G. Pérez Marc, F. P. Polack, C. Zerbini, R. Bailey, K. A. Swanson, X. Xu, S. Roychoudhury, K. Koury, S. Bouguermouh, W. V. Kalina, D. Cooper, R. W. Frenck Jr., L. L. Hammitt, Ö. Türeci, H. Nell, A. Schaefer, S. Ünal, Q. Yang, P. Liberator, D. B. Tresnan, S. Mather, P. R. Dormitzer, U. Şahin, W. C. Gruber, K. U. Jansen; C4591001 Clinical Trial Group, Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months. *N. Engl. J. Med.* 10.1056/NEJMoa2110345 (2021). doi:10.1056/NEJMoa2110345 Medline
- N. Doria-Rose, M. S. Suthar, M. Makowski, S. O'Connell, A. B. McDermott, B. Flach, J. E. Ledgerwood, J. R. Mascola, B. S. Graham, B. C. Lin, S. O'Dell, S. D. Schmidt, A. T. Widge, V.-V. Edara, E. J. Anderson, L. Lai, K. Floyd, N. G. Rouphael, V. Zarnitsyna, P. C. Roberts, M. Makhene, W. Buchanan, C. J. Luke, J. H. Beigel, L. A. Jackson, K. M. Neuzil, H. Bennett, B. Leav, J. Albert, P. Kunwar; mRNA-1273 Study Group, Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19. *N. Engl. J. Med.* 384, 2259–2261 (2021). doi:10.1056/NEJMc2103916 Medline
- H. M. El Sahly, L. R. Baden, B. Essink, S. Doblecki-Lewis, J. M. Martin, E. J. Anderson, T. B. Campbell, J. Clark, L. A. Jackson, C. J. Fichtenbaum, M. Zervos, B. Rankin, F. Eder, G. Feldman, C. Kennelly, L. Han-Conrad, M. Levin, K. M. Neuzil, L. Corey, P. Gilbert, H. Janes, D. Follmann, M. Marovich, L. Polakowski, J. R. Mascola, J. E. Ledgerwood, B. S. Graham, A. August, H. Clouting, W. Deng, S. Han, B. Leav, D. Manzo, R. Pajon, F. Schödel, J. E. Tomassini, H. Zhou, J. Miller; COVE Study Group, Efficacy of the mRNA-1273 SARS-CoV-2 Vaccine at Completion of Blinded Phase. *N. Engl. J. Med.* 10.1056/NEJMoa2113017 (2021). doi:10.1056/NEJMoa2113017 Medline
- 9. J. M. Polinski *et al.*, Effectiveness of the Single-Dose Ad26.COV2.S COVID Vaccine. *medRxiv*, 2021.2009.2010.21263385 (2021). doi:10.1101/2021.09.10.21263385.
- E. S. Rosenberg, D. R. Holtgrave, V. Dorabawila, M. Conroy, D. Greene, E. Lutterloh, B. Backenson, D. Hoefer, J. Morne, U. Bauer, H. A. Zucker, New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status New York, May 3-July 25, 2021. *MMWR Morb. Mortal. Wkly. Rep.* **70**, 1306–1311 (2021). doi:10.15585/mmwr.mm7037a7 Medline
- 11. S. Nanduri, T. Pilishvili, G. Derado, M. M. Soe, P. Dollard, H. Wu, Q. Li, S. Bagchi, H. Dubendris, R. Link-Gelles, J. A. Jernigan, D. Budnitz, J. Bell, A. Benin, N. Shang, J. R. Edwards, J. R. Verani, S. J. Schrag, Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant National Healthcare Safety Network, March 1-August 1, 2021. *MMWR Morb. Mortal. Wkly. Rep.* 70, 1163–1166 (2021). <u>doi:10.15585/mmwr.mm7034e3 Medline</u>

- A. Fowlkes, M. Gaglani, K. Groover, M. S. Thiese, H. Tyner, K. Ellingson; HEROES-RECOVER Cohorts, Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance - Eight U.S. Locations, December 2020-August 2021. MMWR Morb. Mortal. Wkly. Rep. 70, 1167–1169 (2021). doi:10.15585/mmwr.mm7034e4 Medline
- 13. M. W. Tenforde, W. H. Self, E. A. Naioti, A. A. Ginde, D. J. Douin, S. M. Olson, H. K. Talbot, J. D. Casey, N. M. Mohr, A. Zepeski, M. Gaglani, T. McNeal, S. Ghamande, N. I. Shapiro, K. W. Gibbs, D. C. Files, D. N. Hager, A. Shehu, M. E. Prekker, H. L. Erickson, M. N. Gong, A. Mohamed, D. J. Henning, J. S. Steingrub, I. D. Peltan, S. M. Brown, E. T. Martin, A. S. Monto, A. Khan, C. L. Hough, L. W. Busse, C. C. Ten Lohuis, A. Duggal, J. G. Wilson, A. J. Gordon, N. Qadir, S. Y. Chang, C. Mallow, C. Rivas, H. M. Babcock, J. H. Kwon, M. C. Exline, N. Halasa, J. D. Chappell, A. S. Lauring, C. G. Grijalva, T. W. Rice, I. D. Jones, W. B. Stubblefield, A. Baughman, K. N. Womack, C. J. Lindsell, K. W. Hart, Y. Zhu, M. Stephenson, S. J. Schrag, M. Kobayashi, J. R. Verani, M. M. Patel, N. Calhoun, K. Murthy, J. Herrick, A. McKillop, E. Hoffman, M. Zayed, M. Smith, N. Settele, J. Ettlinger, E. Priest, J. Thomas, A. Arroliga, M. Beeram, R. Kindle, L.-A. Kozikowski, L. De Souza, S. Ouellette, S. Thornton-Thompson, P. Tyler, O. Mehkri, K. Ashok, S. Gole, A. King, B. Poynter, N. Stanley, A. Hendrickson, E. Maruggi, T. Scharber, J. Jorgensen, R. Bowers, J. King, V. Aston, B. Armbruster, R. E. Rothman, R. Nair, J.-T. T. Chen, S. Karow, E. Robart, P. N. Maldonado, M. Khan, P. So, J. Levitt, C. Perez, A. Visweswaran, J. Roque, A. Rivera, T. Frankel, M. Howell, J. Friedel, J. Goff, D. Huynh, M. Tozier, C. Driver, M. Carricato, A. Foster, P. Nassar, L. Stout, Z. Sibenaller, A. Walter, J. Mares, L. Olson, B. Clinansmith, C. Rivas, H. Gershengorn, E. J. McSpadden, R. Truscon, A. Kaniclides, L. Thomas, R. Bielak, W. D. Valvano, R. Fong, W. J. Fitzsimmons, C. Blair, A. L. Valesano, J. Gilbert, C. D. Crider, K. A. Steinbock, T. C. Paulson, L. A. Anderson, C. Kampe, J. Johnson, R. McHenry, M. Blair, D. Conway, M. LaRose, L. Landreth, M. Hicks, L. Parks, J. Bongu, D. McDonald, C. Cass, S. Seiler, D. Park, T. Hink, M. Wallace, C.-A. Burnham, O. G. Arter; IVY Network Investigators; IVY Network, Sustained Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Associated Hospitalizations Among Adults -United States, March-July 2021. MMWR Morb. Mortal. Wkly. Rep. 70, 1156–1162 (2021). doi:10.15585/mmwr.mm7034e2 Medline
- 14. H. M. Scobie, A. G. Johnson, A. B. Suthar, R. Severson, N. B. Alden, S. Balter, D. Bertolino, D. Blythe, S. Brady, B. Cadwell, I. Cheng, S. Davidson, J. Delgadillo, K. Devinney, J. Duchin, M. Duwell, R. Fisher, A. Fleischauer, A. Grant, J. Griffin, M. Haddix, J. Hand, M. Hanson, E. Hawkins, R. K. Herlihy, L. Hicks, C. Holtzman, M. Hoskins, J. Hyun, R. Kaur, M. Kay, H. Kidrowski, C. Kim, K. Komatsu, K. Kugeler, M. Lewis, B. C. Lyons, S. Lyons, R. Lynfield, K. McCaffrey, C. McMullen, L. Milroy, S. Meyer, L. Nolen, M. R. Patel, S. Pogosjans, H. E. Reese, A. Saupe, J. Sell, T. Sokol, D. Sosin, E. Stanislawski, K. Stevens, H. Vest, K. White, E. Wilson, A. MacNeil, M. D. Ritchey, B. J. Silk, Monitoring Incidence of COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Status 13 U.S. Jurisdictions, April 4-July 17, 2021. *MMWR Morb. Mortal. Wkly. Rep.* 70, 1284–1290 (2021). doi:10.15585/mmwr.mm7037e1 Medline
- 15. W. H. Self, M. W. Tenforde, J. P. Rhoads, M. Gaglani, A. A. Ginde, D. J. Douin, S. M. Olson, H. K. Talbot, J. D. Casey, N. M. Mohr, A. Zepeski, T. McNeal, S. Ghamande, K.

W. Gibbs, D. C. Files, D. N. Hager, A. Shehu, M. E. Prekker, H. L. Erickson, M. N. Gong, A. Mohamed, D. J. Henning, J. S. Steingrub, I. D. Peltan, S. M. Brown, E. T. Martin, A. S. Monto, A. Khan, C. L. Hough, L. W. Busse, C. C. Ten Lohuis, A. Duggal, J. G. Wilson, A. J. Gordon, N. Qadir, S. Y. Chang, C. Mallow, C. Rivas, H. M. Babcock, J. H. Kwon, M. C. Exline, N. Halasa, J. D. Chappell, A. S. Lauring, C. G. Grijalva, T. W. Rice, I. D. Jones, W. B. Stubblefield, A. Baughman, K. N. Womack, C. J. Lindsell, K. W. Hart, Y. Zhu, L. Mills, S. N. Lester, M. M. Stumpf, E. A. Naioti, M. Kobayashi, J. R. Verani, N. J. Thornburg, M. M. Patel, N. Calhoun, K. Murthy, J. Herrick, A. McKillop, E. Hoffman, M. Zayed, M. Smith, N. Seattle, J. Ettlinger, E. Priest, J. Thomas, A. Arroliga, M. Beeram, R. Kindle, L.-A. Kozikowski, L. De Souza, S. Ouellette, S. Thornton-Thompson, O. Mehkri, K. Ashok, S. Gole, A. King, B. Poynter, N. Stanley, A. Hendrickson, E. Maruggi, T. Scharber, J. Jorgensen, R. Bowers, J. King, V. Aston, B. Armbruster, R. E. Rothman, R. Nair, J.-T. T. Chen, S. Karow, E. Robart, P. N. Maldonado, M. Khan, P. So, J. Levitt, C. Perez, A. Visweswaran, J. Roque, A. Rivera, L. Angeles, T. Frankel, L. Angeles, J. Goff, D. Huynh, M. Howell, J. Friedel, M. Tozier, C. Driver, M. Carricato, A. Foster, P. Nassar, L. Stout, Z. Sibenaller, A. Walter, J. Mares, L. Olson, B. Clinansmith, C. Rivas, H. Gershengorn, E. J. McSpadden, R. Truscon, A. Kaniclides, L. Thomas, R. Bielak, W. D. Valvano, R. Fong, W. J. Fitzsimmons, C. Blair, A. L. Valesano, J. Gilbert, C. D. Crider, K. A. Steinbock, T. C. Paulson, L. A. Anderson, C. Kampe, J. Johnson, R. McHenry, M. Blair, D. Conway, M. LaRose, L. Landreth, M. Hicks, L. Parks, J. Bongu, D. McDonald, C. Cass, S. Seiler, D. Park, T. Hink, M. Wallace, C.-A. Burnham, O. G. Arter; IVY Network, Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions -United States, March-August 2021. MMWR Morb. Mortal. Wkly. Rep. 70, 1337-1343 (2021). doi:10.15585/mmwr.mm7038e1 Medline

- 16. Y. Goldberg *et al.*, Waning immunity of the BNT162b2 vaccine: A nationwide study from Israel. *medRxiv*, (2021). doi:10.1101/2021.08.24.21262423.
- 17. N. Dagan, N. Barda, E. Kepten, O. Miron, S. Perchik, M. A. Katz, M. A. Hernán, M. Lipsitch, B. Reis, R. D. Balicer, BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. *N. Engl. J. Med.* 384, 1412–1423 (2021). doi:10.1056/NEJMoa2101765 Medline
- 18. "Israel expands COVID vaccine booster campaign to over 50s, health workers., *Reuters*, 13 August 2021.
- Y. M. Bar-On, Y. Goldberg, M. Mandel, O. Bodenheimer, L. Freedman, N. Kalkstein, B. Mizrahi, S. Alroy-Preis, N. Ash, R. Milo, A. Huppert, Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. *N. Engl. J. Med.* 385, 1393–1400 (2021). doi:10.1056/NEJMoa2114255 Medline
- 20. J. Lopez Bernal, N. Andrews, C. Gower, E. Gallagher, R. Simmons, S. Thelwall, J. Stowe, E. Tessier, N. Groves, G. Dabrera, R. Myers, C. N. J. Campbell, G. Amirthalingam, M. Edmunds, M. Zambon, K. E. Brown, S. Hopkins, M. Chand, M. Ramsay, Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. *N. Engl. J. Med.* 385, 585–594 (2021). doi:10.1056/NEJMoa2108891 Medline

- 21. K. B. Pouwels *et al.*, Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. *medRxiv*, 2021.2008.2018.21262237 (2021). doi:10.1101/2021.08.18.21262237.
- 22. FDA, "FDA Authorizes Booster Dose of Pfizer-BioNTech COVID-19 Vaccine for Certain Populations" (www.fda.gov/news-events/press-announcements/fda-authorizes-booster-dose-pfizer-biontech-covid-19-vaccine-certain-populations).
- 23. FDA, "Coronavirus (COVID-19) Update: FDA Takes Additional Actions on the Use of a Booster Dose for COVID-19 Vaccines" (www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-additional-actions-use-booster-dose-covid-19-vaccines).
- 24. P. R. Krause, T. R. Fleming, R. Peto, I. M. Longini, J. P. Figueroa, J. A. C. Sterne, A. Cravioto, H. Rees, J. P. T. Higgins, I. Boutron, H. Pan, M. F. Gruber, N. Arora, F. Kazi, R. Gaspar, S. Swaminathan, M. J. Ryan, A.-M. Henao-Restrepo, Considerations in boosting COVID-19 vaccine immune responses. *Lancet* **398**, 1377–1380 (2021). doi:10.1016/S0140-6736(21)02046-8 Medline
- CDC COVID-19 Vaccine Breakthrough Case Investigations Team, COVID-19 Vaccine Breakthrough Infections Reported to CDC - United States, January 1-April 30, 2021. MMWR Morb. Mortal. Wkly. Rep. 70, 792–793 (2021). Medline
- 26. N. Brusselaers, J. Lagergren, The Charlson Comorbidity Index in Registry-based Research. *Methods Inf. Med.* 56, 401–406 (2017). <u>doi:10.3414/ME17-01-0051</u> <u>Medline</u>
- 27. Y. Young-Xu, C. Korves, J. Roberts, E. I. Powell, G. M. Zwain, J. Smith, H. S. Izurieta, Coverage and Estimated Effectiveness of mRNA COVID-19 Vaccines Among US Veterans. JAMA Netw. Open 4, e2128391 (2021). doi:10.1001/jamanetworkopen.2021.28391 Medline
- 28. Y. Wang, R. Chen, F. Hu, Y. Lan, Z. Yang, C. Zhan, J. Shi, X. Deng, M. Jiang, S. Zhong, B. Liao, K. Deng, J. Tang, L. Guo, M. Jiang, Q. Fan, M. Li, J. Liu, Y. Shi, X. Deng, X. Xiao, M. Kang, Y. Li, W. Guan, Y. Li, S. Li, F. Li, N. Zhong, X. Tang, Transmission, viral kinetics and clinical characteristics of the emergent SARS-CoV-2 Delta VOC in Guangzhou, China. *EClinicalMedicine* 40, 101129 (2021). doi:10.1016/j.eclinm.2021.101129 Medline
- 29. K. Bruxvoort *et al.*, Effectiveness of mRNA-1273 against Delta, Mu, and other emerging variants. *medRxiv*, (2021). doi:10.1101/2021.09.29.21264199.
- 30. A. Puranik *et al.*, Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence. *medRxiv*, (2021). doi:10.1101/2021.08.06.21261707.
- 31. S. Y. Tartof, J. M. Slezak, H. Fischer, V. Hong, B. K. Ackerson, O. N. Ranasinghe, T. B. Frankland, O. A. Ogun, J. M. Zamparo, S. Gray, S. R. Valluri, K. Pan, F. J. Angulo, L. Jodar, J. M. McLaughlin, Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: A retrospective cohort study. *Lancet* **398**, 1407–1416 (2021). <u>doi:10.1016/S0140-6736(21)02183-8 Medline</u>
- 32. H. Chemaitelly, P. Tang, M. R. Hasan, S. AlMukdad, H. M. Yassine, F. M. Benslimane, H. A. Al Khatib, P. Coyle, H. H. Ayoub, Z. Al Kanaani, E. Al Kuwari, A. Jeremijenko, A.

H. Kaleeckal, A. N. Latif, R. M. Shaik, H. F. Abdul Rahim, G. K. Nasrallah, M. G. Al Kuwari, H. E. Al Romaihi, A. A. Butt, M. H. Al-Thani, A. Al Khal, R. Bertollini, L. J. Abu-Raddad, Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. *N. Engl. J. Med.* 10.1056/NEJMoa2114114 (2021). doi:10.1056/NEJMoa2114114 Medline

- 33. H. Chemaitelly, H. M. Yassine, F. M. Benslimane, H. A. Al Khatib, P. Tang, M. R. Hasan, J. A. Malek, P. Coyle, H. H. Ayoub, Z. Al Kanaani, E. Al Kuwari, A. Jeremijenko, A. H. Kaleeckal, A. N. Latif, R. M. Shaik, H. F. Abdul Rahim, G. K. Nasrallah, M. G. Al Kuwari, H. E. Al Romaihi, M. H. Al-Thani, A. Al Khal, A. A. Butt, R. Bertollini, L. J. Abu-Raddad, mRNA-1273 COVID-19 vaccine effectiveness against the B.1.1.7 and B.1.351 variants and severe COVID-19 disease in Qatar. *Nat. Med.* 27, 1614–1621 (2021). doi:10.1038/s41591-021-01446-y Medline
- 34. T. Tada *et al.*, Comparison of Neutralizing Antibody Titers Elicited by mRNA and Adenoviral Vector Vaccine against SARS-CoV-2 Variants. *bioRxiv*, 2021.2007.2019.452771 (2021). doi:10.1101/2021.07.19.452771.
- 35. R. R. Goel, M. M. Painter, S. A. Apostolidis, D. Mathew, W. Meng, A. M. Rosenfeld, K. A. Lundgreen, A. Reynaldi, D. S. Khoury, A. Pattekar, S. Gouma, L. Kuri-Cervantes, P. Hicks, S. Dysinger, A. Hicks, H. Sharma, S. Herring, S. Korte, A. E. Baxter, D. A. Oldridge, J. R. Giles, M. E. Weirick, C. M. McAllister, M. Awofolaju, N. Tanenbaum, E. M. Drapeau, J. Dougherty, S. Long, K. D'Andrea, J. T. Hamilton, M. McLaughlin, J. C. Williams, S. Adamski, O. Kuthuru, I. Frank, M. R. Betts, L. A. Vella, A. Grifoni, D. Weiskopf, A. Sette, S. E. Hensley, M. P. Davenport, P. Bates, E. T. Luning Prak, A. R. Greenplate, E. J. Wherry, S. Adamski, Z. Alam, M. M. Addison, K. T. Byrne, A. Chandra, H. C. Descamps, N. Han, Y. Kaminskiy, S. C. Kammerman, J. Kim, A. R. Greenplate, J. T. Hamilton, N. Markosyan, J. H. Noll, D. K. Omran, A. Pattekar, E. Perkey, E. M. Prager, D. Pueschl, A. Rennels, J. B. Shah, J. S. Shilan, N. Wilhausen, A. N. Vanderbeck; UPenn COVID Processing Unit<sup>‡</sup>, mRNA vaccines induce durable immune memory to SARS-CoV-2 and variants of concern. *Science* 10.1126/science.abm0829 (2021). doi:10.1126/science.abm0829 Medline
- 36. K. B. Pouwels, E. Pritchard, P. C. Matthews, N. Stoesser, D. W. Eyre, K.-D. Vihta, T. House, J. Hay, J. I. Bell, J. N. Newton, J. Farrar, D. Crook, D. Cook, E. Rourke, R. Studley, T. E. A. Peto, I. Diamond, A. S. Walker, Effect of Delta variant on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. *Nat. Med.* 10.1038/s41591-021-01548-7 (2021). doi:10.1038/s41591-021-01548-7 Medline
- 37. R. M. Anderson, C. Vegvari, T. D. Hollingsworth, L. Pi, R. Maddren, C. W. Ng, R. F. Baggaley, The SARS-CoV-2 pandemic: Remaining uncertainties in our understanding of the epidemiology and transmission dynamics of the virus, and challenges to be overcome. *Interface Focus* **11**, 20210008 (2021). <u>doi:10.1098/rsfs.2021.0008</u>
- 38. D. W. Eyre *et al.*, The impact of SARS-CoV-2 vaccination on Alpha & amp; Delta variant transmission. *medRxiv*, 2021.2009.2028.21264260 (2021). doi:10.1101/2021.09.28.21264260.

- 39. M. J. M. Niesen *et al.*, COVID-19 vaccines dampen genomic diversity of SARS-CoV-2: Unvaccinated patients exhibit more antigenic mutational variance. *medRxiv*, 2021.2007.2001.21259833 (2021). doi:10.1101/2021.07.01.21259833.
- 40. C. H. Sudre, B. Murray, T. Varsavsky, M. S. Graham, R. S. Penfold, R. C. Bowyer, J. C. Pujol, K. Klaser, M. Antonelli, L. S. Canas, E. Molteni, M. Modat, M. Jorge Cardoso, A. May, S. Ganesh, R. Davies, L. H. Nguyen, D. A. Drew, C. M. Astley, A. D. Joshi, J. Merino, N. Tsereteli, T. Fall, M. F. Gomez, E. L. Duncan, C. Menni, F. M. K. Williams, P. W. Franks, A. T. Chan, J. Wolf, S. Ourselin, T. Spector, C. J. Steves, Attributes and predictors of long COVID. *Nat. Med.* 27, 626–631 (2021). doi:10.1038/s41591-021-01292-y Medline
- 41. B. van den Borst, Recovery after Covid-19. *Lancet Reg. Health West. Pac.* **12**, 100208 (2021). <u>doi:10.1016/j.lanwpc.2021.100208</u> <u>Medline</u>
- 42. J. L. Hirschtick, A. R. Titus, E. Slocum, L. E. Power, R. E. Hirschtick, M. R. Elliott, P. McKane, N. L. Fleischer, Population-based estimates of post-acute sequelae of SARS-CoV-2 infection (PASC) prevalence and characteristics. *Clin. Infect. Dis.* 10.1093/cid/ciab408 (2021). <u>Medline</u>
- 43. R. L. Atmar *et al.*, Heterologous SARS-CoV-2 Booster Vaccinations Preliminary Report. *medRxiv*, 2021.2010.2010.21264827 (2021). doi:10.1101/2021.10.10.21264827.
- 44. L. SAAD., Americans Getting Out More, but Cautiously (2021). Accessed October 22, 2021. https://news.gallup.com/poll/350666/americans-getting-cautiously.aspx
- 45. K. L. Bajema, R. M. Dahl, M. M. Prill, E. Meites, M. C. Rodriguez-Barradas, V. C. Marconi, D. O. Beenhouwer, S. T. Brown, M. Holodniy, C. Lucero-Obusan, G. Rivera-Dominguez, R. G. Morones, A. Whitmire, E. B. Goldin, S. L. Evener, M. Tremarelli, S. Tong, A. J. Hall, S. J. Schrag, M. McMorrow, M. Kobayashi, J. R. Verani, D. Surie, G. Ahmadi-Izadi, J. Burnette, R. Deovic, L. Epstein, A. Hartley, E. Morales, T. Tanner, N. Patel, A. Tunson, K. Elliot, I. Graham, D. Lama, I. Pena, A. Perea, G. A. Perez, J. Simelane, S. Smith, G. Tallin, A. Tisi, A. A. Lopez, M. C. Gonzalez, B. Lengi, D. Mansouri, M. V. Tamez, B. Aryanfar, I. Lee-Chang, C. Jeong, A. Matolek, C. Mendoza, A. Poteshkina, S. Naeem, M. Agrawal, J. Lopez, T. Peters, G. Kudryavtseva, J. Cates, J. M. Folster, A. Kambhampati, A. Kelleher, Y. Li, H. J. Ng, Y. Tao; SUPERNOVA COVID-19; Surveillance Group; Surveillance Platform for Enteric and Respiratory Infectious Organisms at the VA (SUPERNOVA) COVID-19 Surveillance Group, Effectiveness of COVID-19 mRNA Vaccines Against COVID-19-Associated Hospitalization - Five Veterans Affairs Medical Centers, United States, February 1-August 6, 2021. MMWR Morb. Mortal. Wkly. Rep. 70, 1294–1299 (2021). doi:10.15585/mmwr.mm7037e3 Medline
- 46. P. Cirillo, N. Krigbaum, Code for Methods for SARS-CoV-2 Vaccine Protection and Deaths among U.S. Veterans during 2021. Zenodo (2021); doi:10.5281/zenodo.5609444.