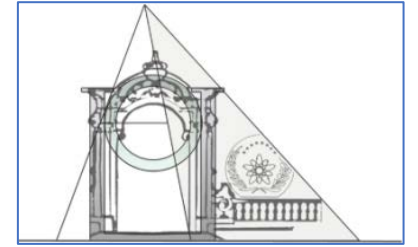


**WEBINAR FORMATIVO
AMD SID CAMPANIA BASILICATA**

**DARE CERTEZZE PER SCIOGLIERE I DUBBI
“Il vaccino contro il COVID-19”**



I Vaccini anti-COVID-19: le evidenze scientifiche

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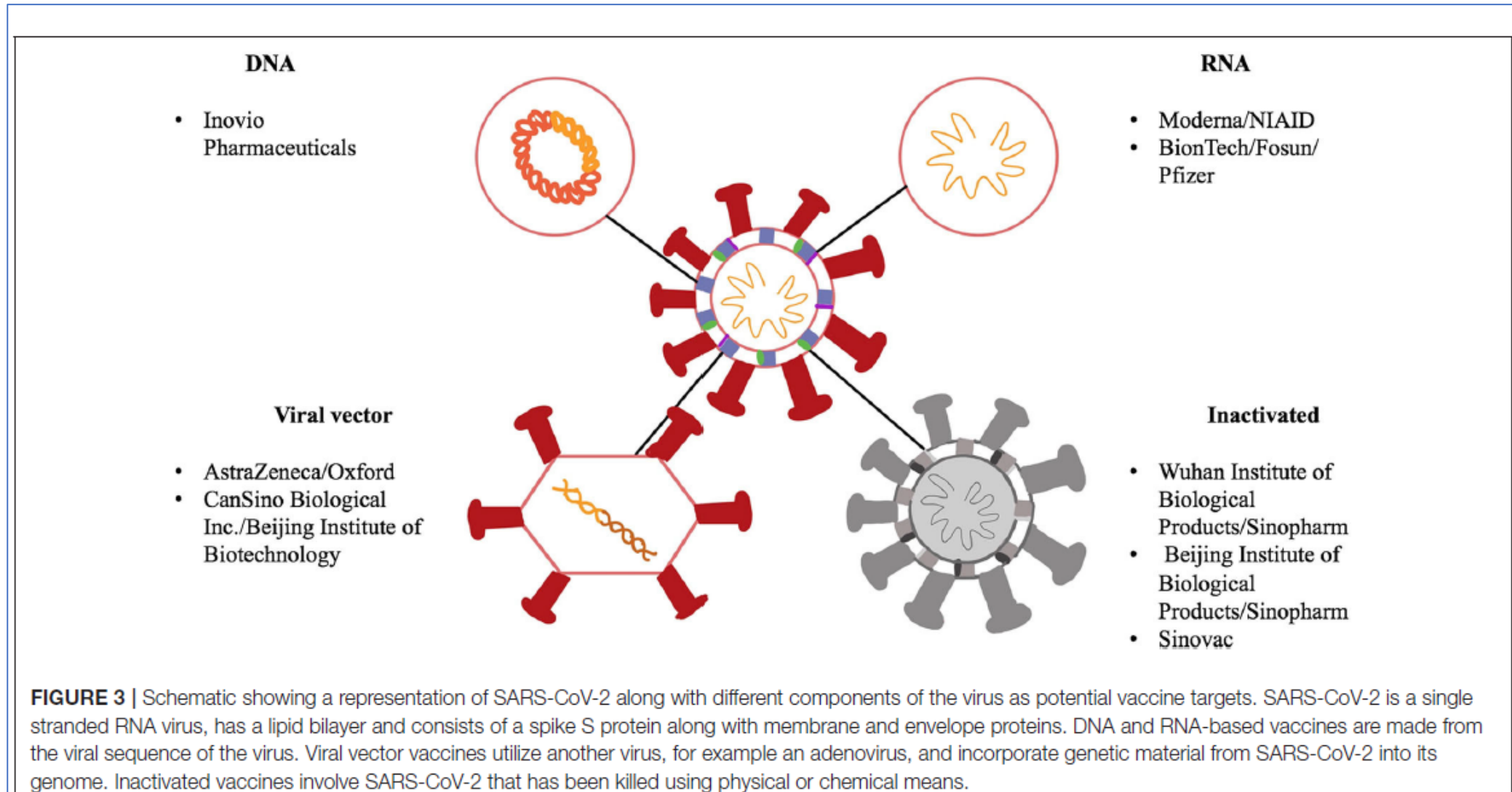
Disclosures

NC reports:

- grants from ViiV Healthcare, Janssen-Cilag and Gilead Science
- personal fees from Gilead Sciences, Abbvie, Bristol-Myers Squibb, Correvio and Merk-Sharp & Dohme, Angelini

Specific disclosure





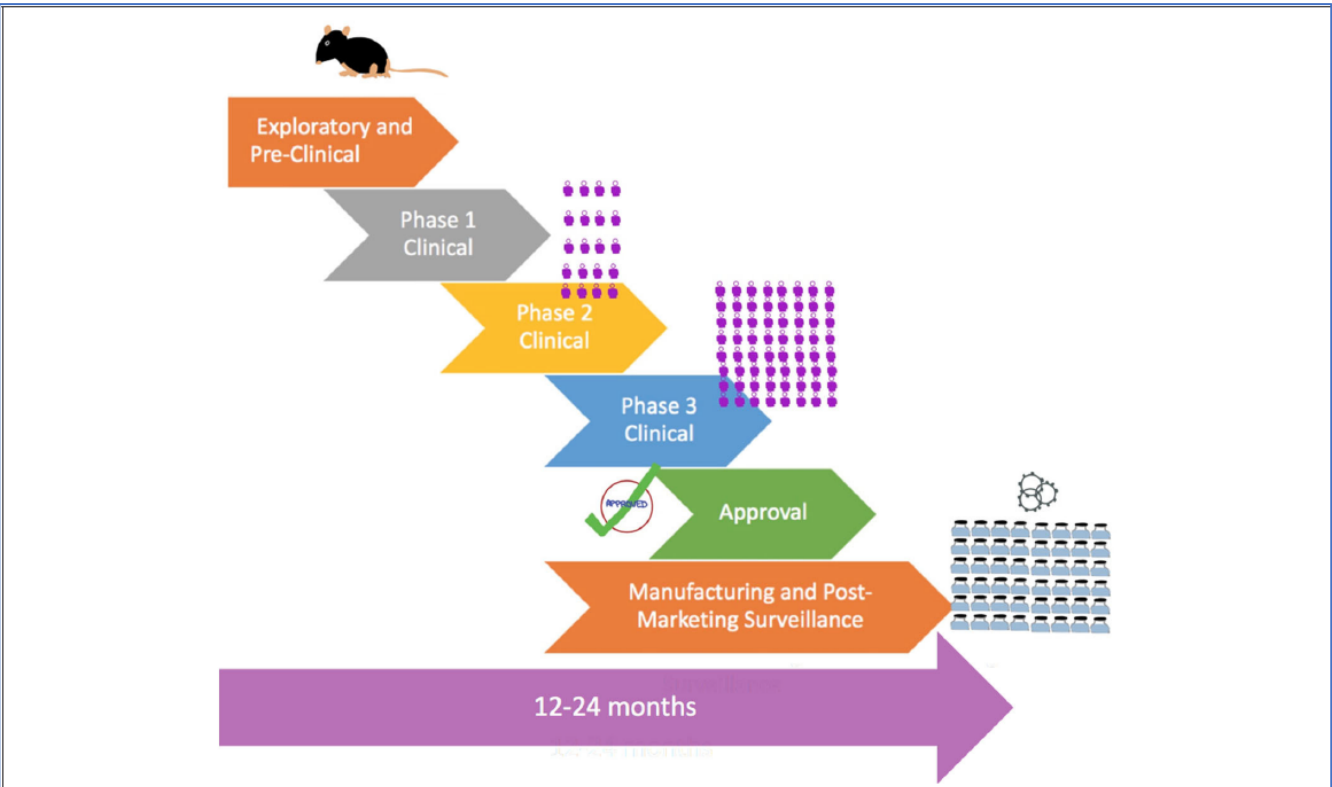
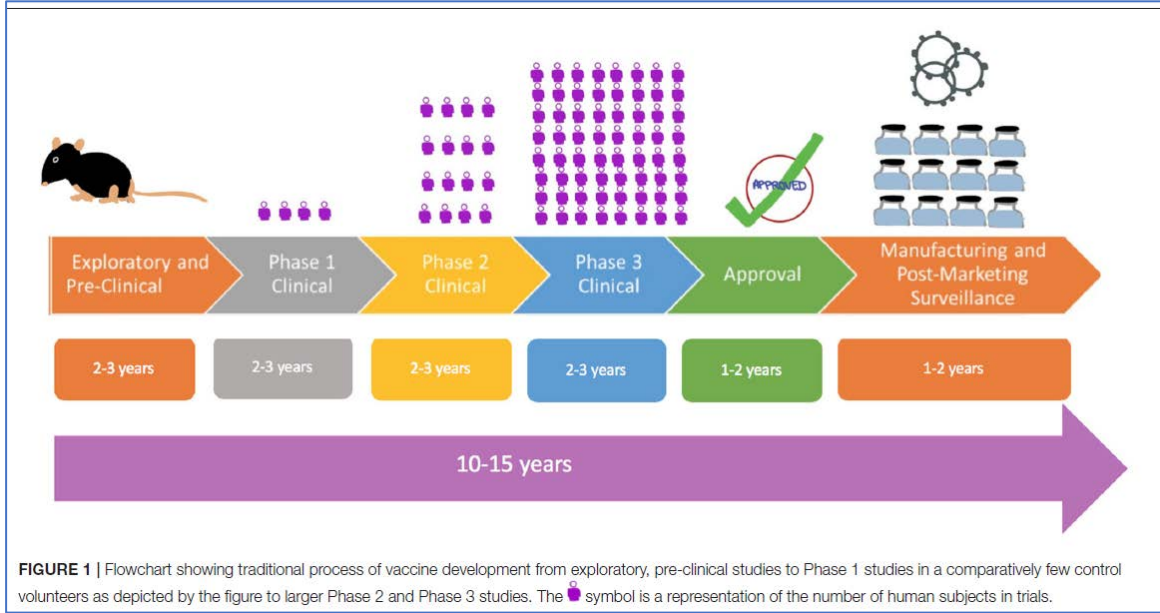
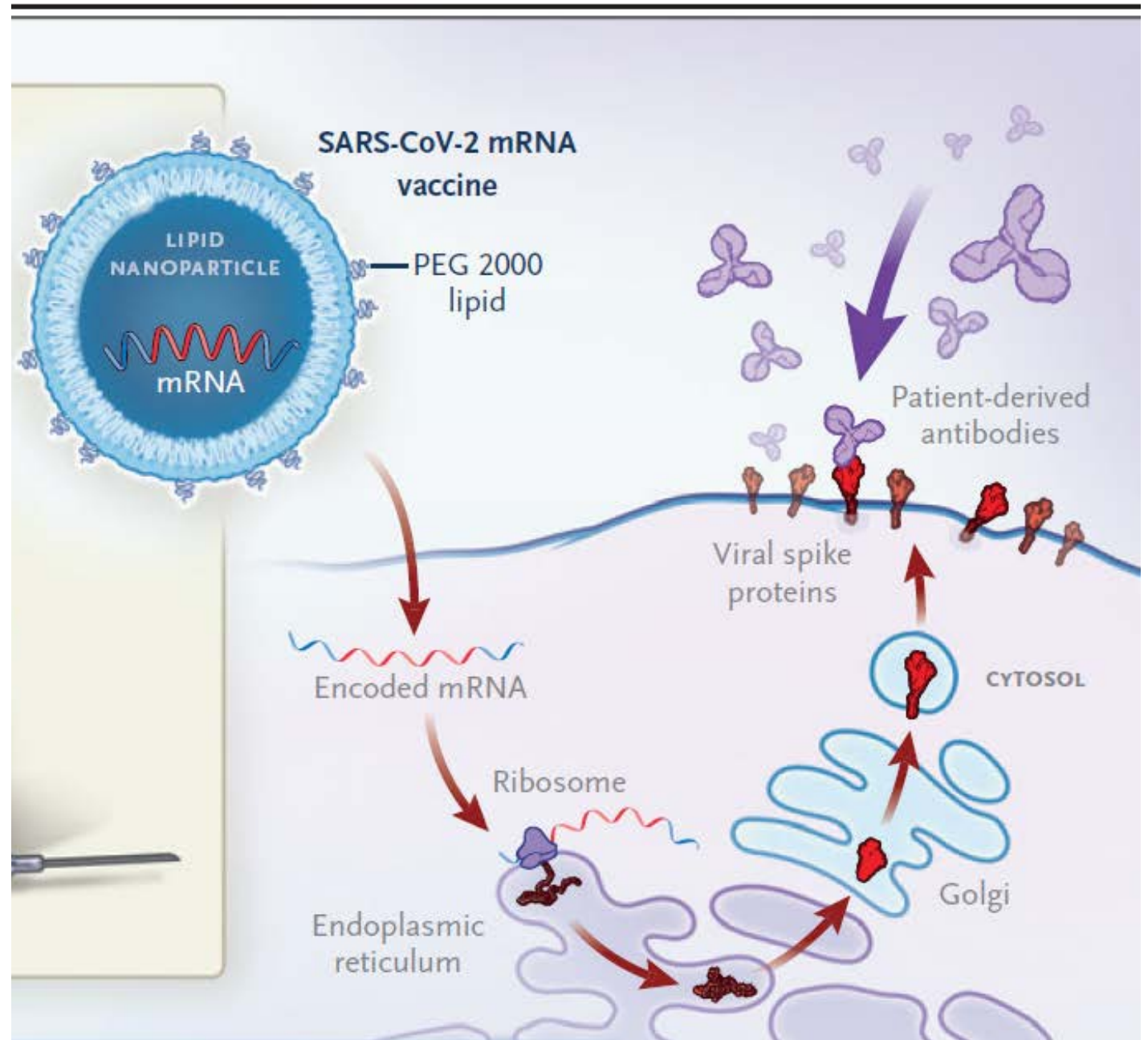


Table 1. SARS-CoV-2 Vaccines under Emergency Use Authorization (EUA) or in Late-Phase Studies.

Vaccine Platform	Type of Vaccine and Immunogen	Developer (Name of Vaccine)	Dose Schedule and Administration	Phase*	Excipients†
RNA-based vaccine	mRNA encoding spike protein (30 µg)	BioNTech–Pfizer (BNT162b2)	Two doses (day 0, day 21) Intramuscular	Post-EUA	0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol, 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% sodium chloride Injection) contributes an additional 2.16 mg sodium chloride per dose
RNA-based vaccine	mRNA encoding spike protein (100 µg)	Moderna (mRNA-1273)	Two doses (day 0, day 28) Intramuscular	Post-EUA	Lipids (SM-102; 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 [PEG 2000-DMG]; cholesterol; and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose
Adenovirus vector (nonreplicating)	ChAdOx1-Sn Cov-19 Nonreplicating chimpanzee AdV5 expressing spike protein	AstraZeneca and University of Oxford (AZD1222)	One (day 0) or two (day 0, day 28) doses Intramuscular	Phase 3	10 mM histidine, 7.5% (w/v) sucrose, 35 mM sodium chloride, 1 mM magnesium chloride, 0.1% (w/v) polysorbate 80, 0.1 mM edetate disodium, 0.5% (w/v) ethanol, at pH 6.6
Adenovirus vector (nonreplicating)	Ad26.COV2.S Adenovirus 26 vectored vaccine using AdVac and PER.C6 technology	Janssen	One (day 0) or two (day 0, day 56) doses Intramuscular	Phase 3	Sodium chloride, citric acid monohydrate, polysorbate 80, 2 hydroxypropyl-β-cyclodextrin (HBCD), ethanol (absolute), sodium hydroxide
Protein subunit	Full-length recombinant SARS-CoV-2 glycoprotein nanoparticle with Matrix M adjuvant Spike prefusion protein	Novavax	Two doses (day 0, day 21) Intramuscular	Phase 3	Matrix M1 adjuvant Full-length spike protein formulated in polysorbate 80 detergent and Matrix M1 adjuvant
Protein subunit	SARS-CoV-2 vaccine formulation with adjuvant (S-protein) (Baculovirus production) Spike protein	Sanofi Pasteur and GSK	Two doses (day 0, day 21) Intramuscular	Phase 1–2	Sodium phosphate monobasic monohydrate, sodium phosphate dibasic, sodium chloride polysorbate 20, disodium hydrogen phosphate, potassium dihydrogen phosphate, potassium chloride

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RNA-based vaccine	mRNA encoding spike protein (100 µg)	Moderna (mRNA-1273)	Two doses (day 0, day 28) Intramuscular	Post-EUA	Lipids (SM-102; 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 [PEG 2000-DMG]; cholesterol; and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose
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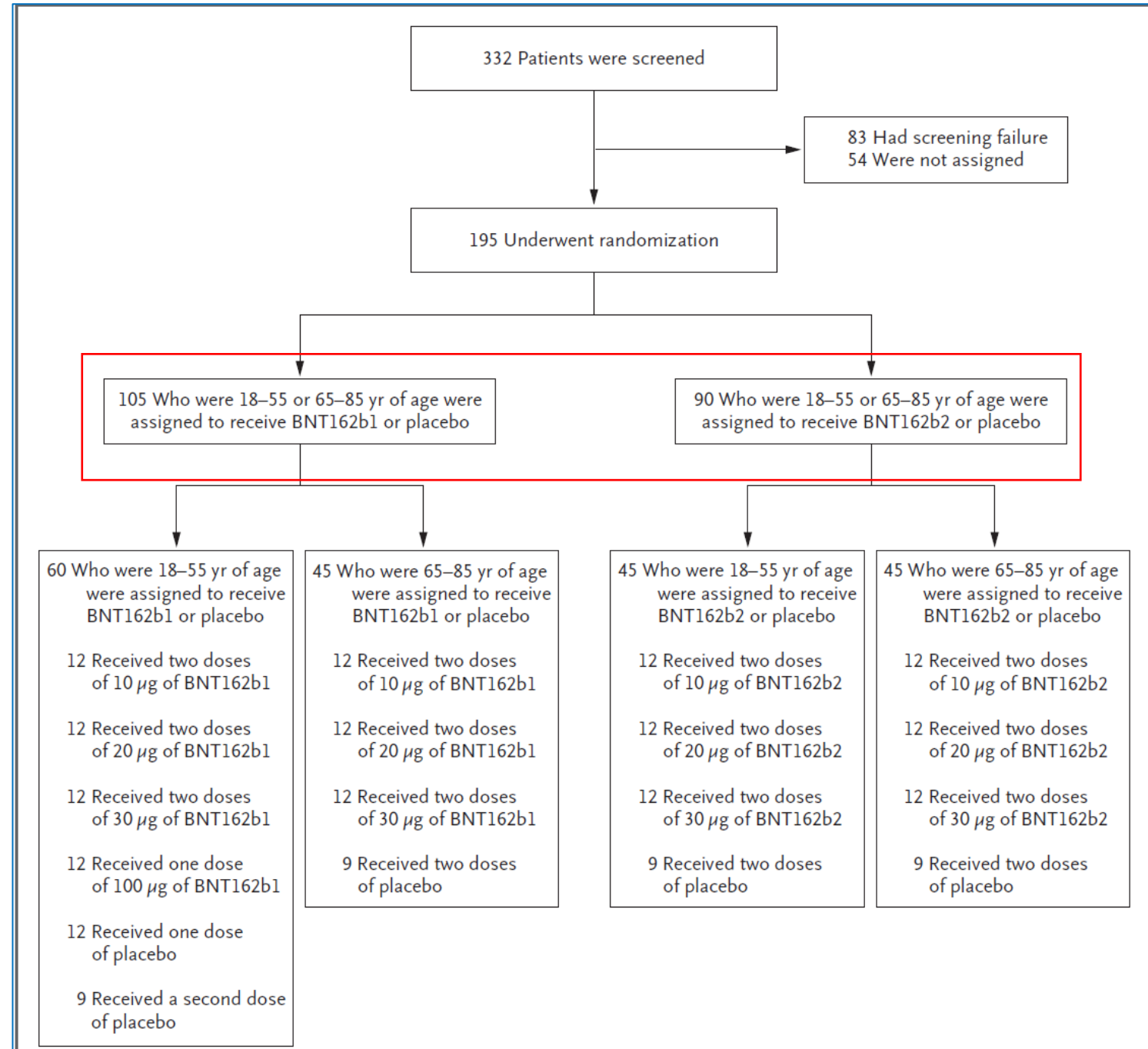
Phase 1 trials on mRNA vaccines

Vaccine	First author	Journal	Type of study	N° of subjects	Placebo group	Dose vaccine	Age groups
BNT162b1 (Pfizer)	Mulligan MJ	Nature (August, 12)	observer-blinded, dose-escalation trial	45	yes	10, 30, 100ul	18-55 years old
BNT162b1 (Pfizer) BNT162b2 (Pfizer)	Walsh E	NEJM (December, 17)	observer-blinded, dose-escalation trial	195	yes	10, 20, 30, 100ul	18-55 years old 65-85 years old
mRNA-1273 (Moderna)	Jackson LA	NEJM (November, 12)	dose-escalation, open-label trial	45	no	25, 100, 250ul	18-55 years old
mRNA-1273 (Moderna)	Anderson EJ	NEJM (December, 17)	dose-escalation, open-label trial	40	no	25,100 ul	>55 years old

ORIGINAL ARTICLE

Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates

Edward E. Walsh, M.D., Robert W. Frenck, Jr., M.D., Ann R. Falsey, M.D.,



ORIGINAL ARTICLE

Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates

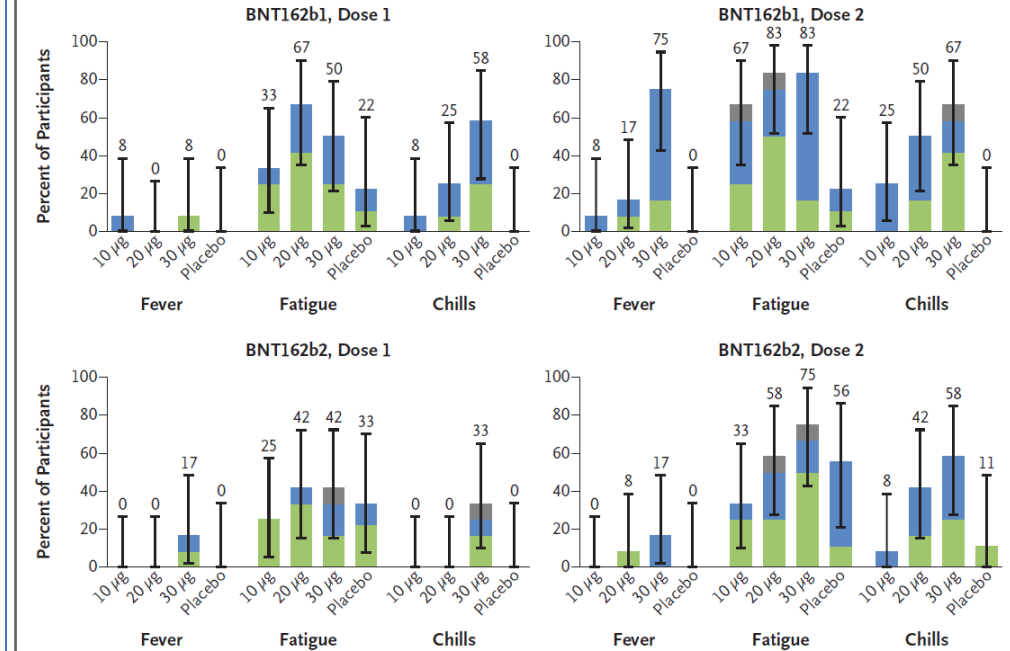
Edward E. Walsh, M.D., Robert W. Frenck, Jr., M.D., Ann R. Falsey, M.D.,

Adverse events

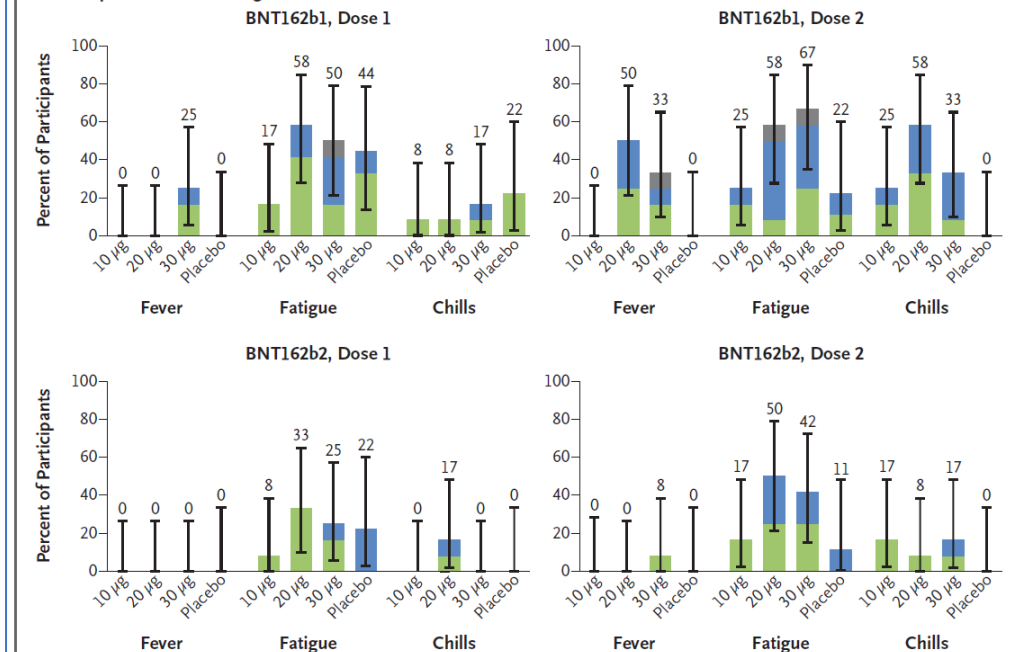
CONCLUSIONS

The safety and immunogenicity data from this U.S. phase 1 trial of two vaccine candidates in younger and older adults, added to earlier interim safety and immunogenicity data regarding BNT162b1 in younger adults from trials in Germany and the United States, support the selection of BNT162b2 for advancement to a pivotal phase 2–3 safety and efficacy evaluation. (Funded by BioNTech and Pfizer; ClinicalTrials.gov number, NCT04368728.)

A Participants 18–55 Yr of Age



B Participants 65–85 Yr of Age



ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA
Covid-19 Vaccine

An ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose)

Inclusion criteria: Adults 16 years of age or older who were healthy or had stable chronic medical conditions

Exclusion criteria: medical history of Covid-19, treatment with immunosuppressive therapy, or diagnosis with an immunocompromising condition

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA
Covid-19 Vaccine

An ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose)

End- point: efficacy of the vaccine against laboratory-confirmed Covid-19 and safety

Where: 152 sites worldwide (United States, 130 sites; Argentina, 1; Brazil, 2; South Africa, 4; Germany, 6; and Turkey, 9)

When: between July 27, 2020, and November 14, 2020

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

End- point: efficacy of the vaccine against laboratory-confirmed Covid-19 and safety

Efficacy:

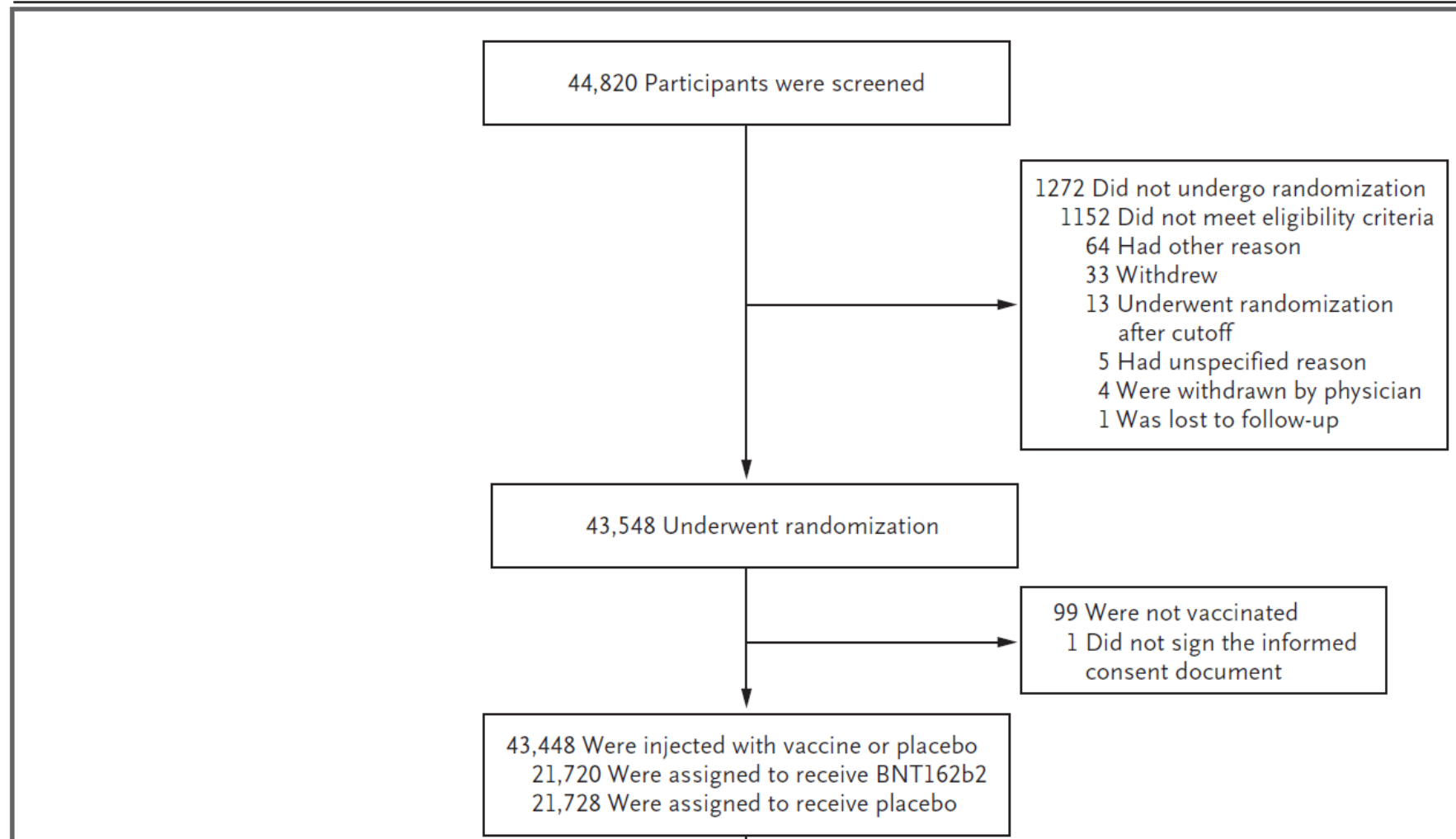
- confirmed Covid-19 (symptomatic) with onset at least 7 days after the second dose
- severe Covid-19

Safety:

- solicited, specific local or systemic adverse events and use of antipyretic or pain medication within 7 days after the receipt of each dose of vaccine or placebo recorded in an electronic diary in a subset of participants
- unsolicited adverse events (those reported by the participants without prompts from the electronic diary) through 1 month after the second dose and unsolicited serious adverse events through 6 months after the second dose.

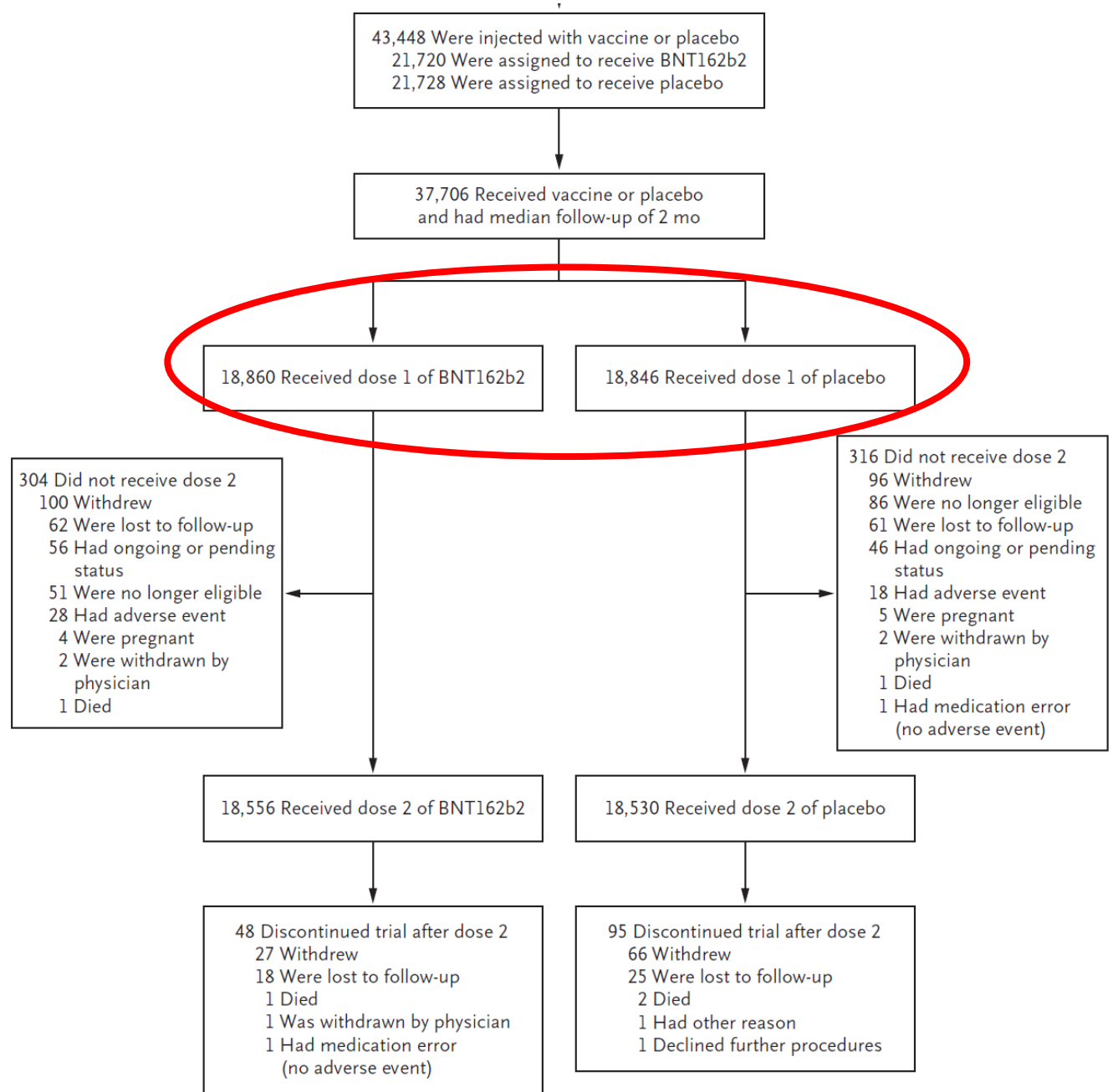
ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine



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Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine



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Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Polack FP, NEJM 2020

Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16–89	16–91	16–91
Body-mass index‡			
≥30.0: obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

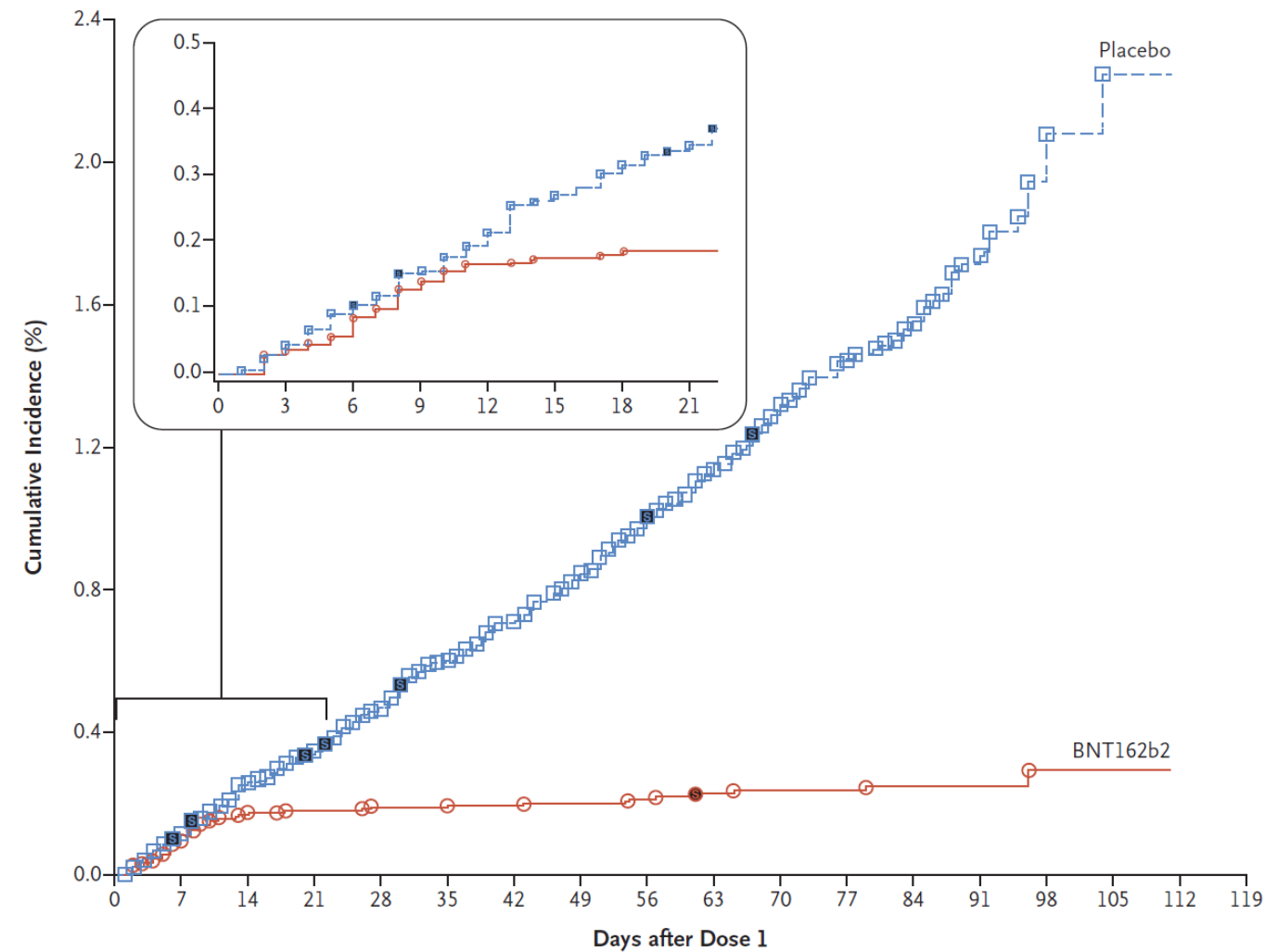
ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

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Safety and Efficacy of the BNT162b2 mRNA
Covid-19 Vaccine

Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time <i>person-yr (no. at risk)</i>	No. of participants	Surveillance time <i>person-yr (no. at risk)</i>	
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI) [†]
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr	3	0.980 (7,500)	48	0.983 (7,543)	93.7 (80.6–98.8)
≥65 yr	1	0.508 (3,848)	19	0.511 (3,880)	94.7 (66.7–99.9)
≥75 yr	0	0.102 (774)	5	0.106 (785)	100.0 (–13.1–100.0)
Sex					
Male	3	1.124 (8,875)	81	1.108 (8762)	96.4 (88.9–99.3)
Female	5	1.090 (8,536)	81	1.114 (8,749)	93.7 (84.7–98.0)
Race or ethnic group [‡]					
White	7	1.889 (14,504)	146	1.903 (14,670)	95.2 (89.8–98.1)
Black or African American	0	0.165 (1,502)	7	0.164 (1,486)	100.0 (31.2–100.0)
All others	1	0.160 (1,405)	9	0.155 (1,355)	89.3 (22.6–99.8)
Hispanic or Latinx	3	0.605 (4,764)	53	0.600 (4,746)	94.4 (82.7–98.9)
Non-Hispanic, non-Latinx	5	1.596 (12,548)	109	1.608 (12,661)	95.4 (88.9–98.5)
Country					
Argentina	1	0.351 (2,545)	35	0.346 (2,521)	97.2 (83.3–99.9)
Brazil	1	0.119 (1,129)	8	0.117 (1,121)	87.7 (8.1–99.7)
United States	6	1.732 (13,359)	119	1.747 (13,506)	94.9 (88.6–98.2)

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Safety and Efficacy of the BNT162b2 mRNA
Covid-19 Vaccine

Efficacy Endpoint Subgroup	BNT162b2 (30 µg) (N ^a =18198)		Placebo (N ^a =18325)		VE (%)	(95% CI ^e)
	n1 ^b	Surveillance Time ^c (n2 ^d)	n1 ^b	Surveillance Time ^c (n2 ^d)		
Overall	8	2.214 (17411)	162	2.222 (17511)	95.0	(90.0, 97.9)
At risk ^f						
Yes	4	1.025 (8030)	86	1.025 (8029)	95.3	(87.7, 98.8)
No	4	1.189 (9381)	76	1.197 (9482)	94.7	(85.9, 98.6)
Age group (years) and at risk						
16–64 and not at risk	4	0.962 (7671)	69	0.964 (7701)	94.2	(84.4, 98.5)
16–64 and at risk	3	0.744 (5878)	74	0.746 (5917)	95.9	(87.6, 99.2)
≥65 and not at risk	0	0.227 (1701)	7	0.233 (1771)	100.0	(29.0, 100.0)
≥65 and at risk	1	0.281 (2147)	12	0.279 (2109)	91.7	(44.2, 99.8)
Obese ^g						
Yes	3	0.763 (6000)	67	0.782 (6103)	95.4	(86.0, 99.1)
No	5	1.451 (11406)	95	1.439 (11404)	94.8	(87.4, 98.3)
Age group (years) and obese						
16–64 and not obese	4	1.107 (8811)	83	1.101 (8825)	95.2	(87.3, 98.7)
16–64 and obese	3	0.598 (4734)	60	0.609 (4789)	94.9	(84.4, 99.0)
≥65 and not obese	1	0.343 (2582)	12	0.338 (2567)	91.8	(44.5, 99.8)
≥65 and obese	0	0.165 (1265)	7	0.173 (1313)	100.0	(27.1, 100.0)

Table S4 | Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities among Participants without Evidence of Infection Prior to 7 Days after Dose 2. Time period for

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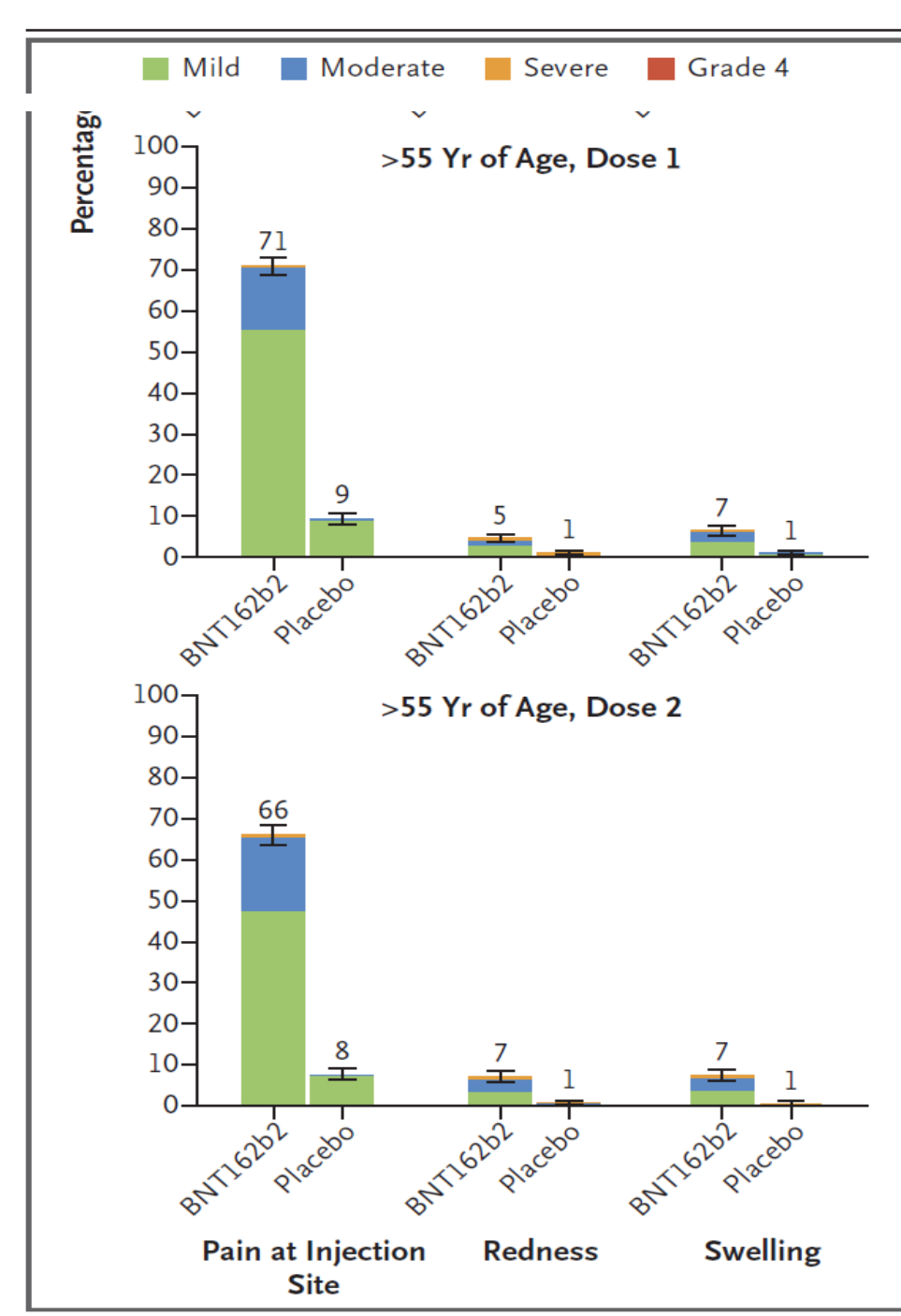
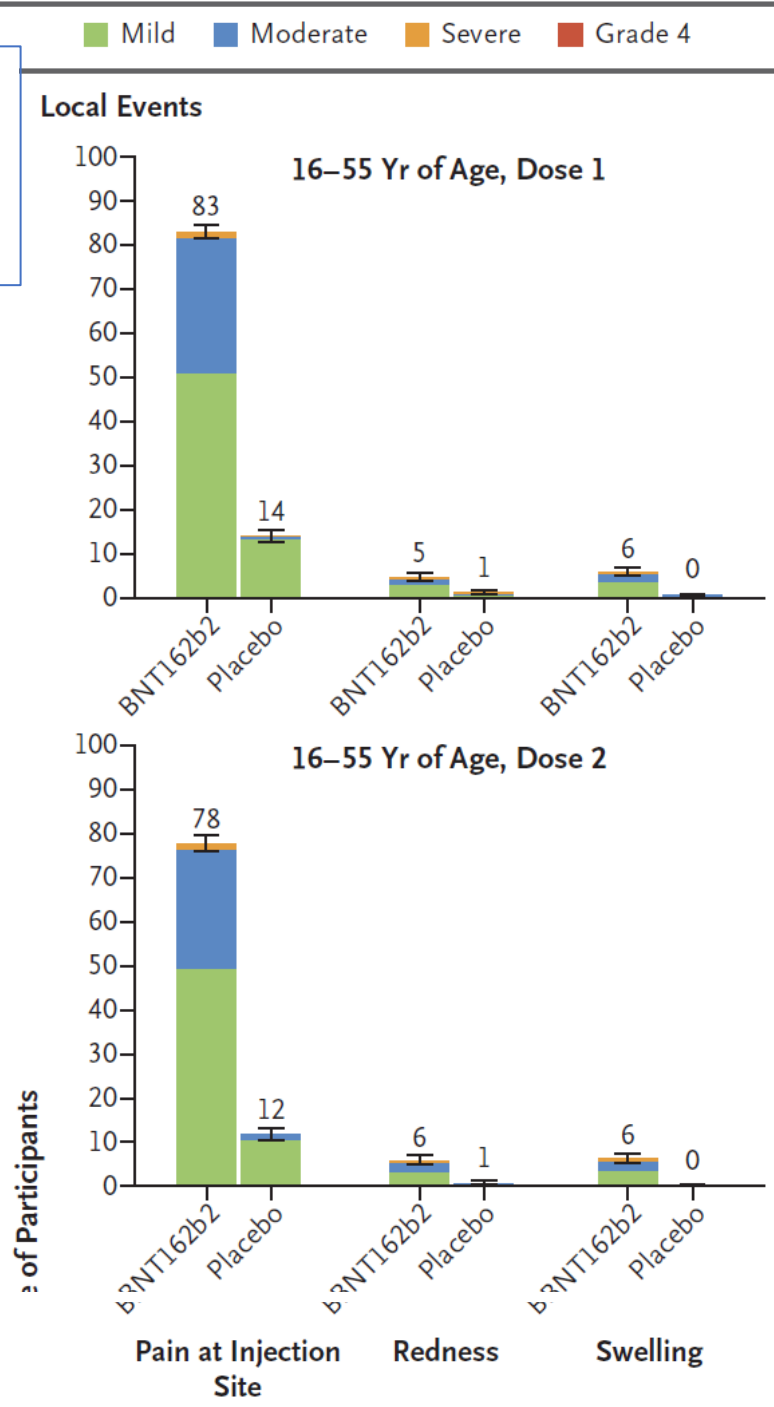
Safety and Efficacy of the BNT162b2 mRNA
Covid-19 Vaccine

Efficacy Endpoint Subgroup	BNT162b2 (30 µg) (N ^a =21669)		Placebo (N ^a =21686)		VE (%)	(95% CI ^e)
	n1 ^b	Surveillance Time ^c (n2 ^d)	n1 ^b	Surveillance Time ^c (n2 ^d)		
Severe COVID-19 occurrence after Dose 1	1	4.021 (21314)	9	4.006 (21259)	88.9	(20.1, 99.7)
After Dose 1 to before Dose 2	0		4		100.0	(-51.5, 100.0)
Dose 2 to 7 days after Dose 2	0		1		100.0	(-3800.0, 100.0)
≥7 Days after Dose 2	1		4		75.0	(-152.6, 99.5)

Table S5 | Vaccine Efficacy of Severe COVID-19 Occurrence after Dose 1 (Modified Intention-to-Treat). a. N = number of participants in the specified group. b. n1 = Number of

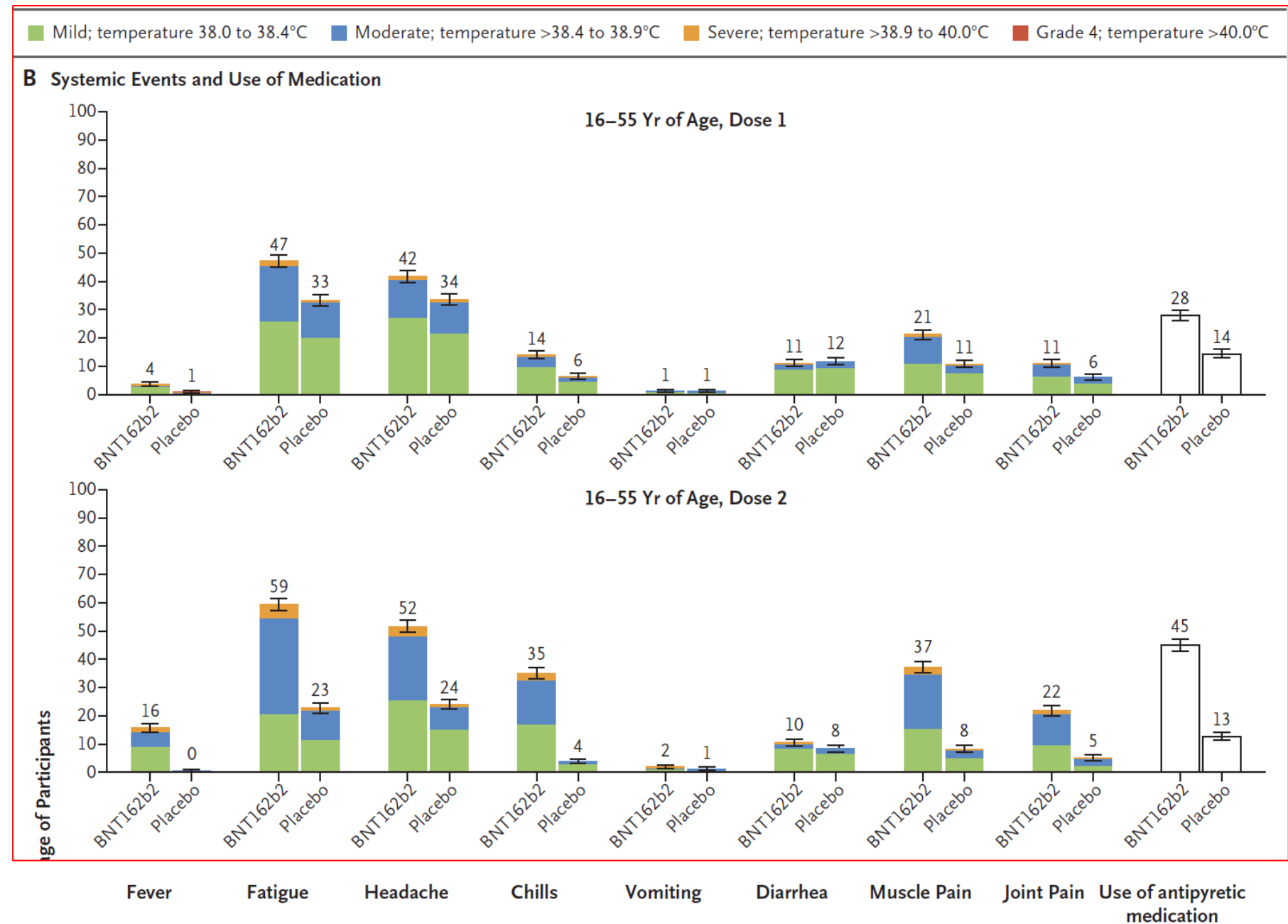
Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Local adverse events



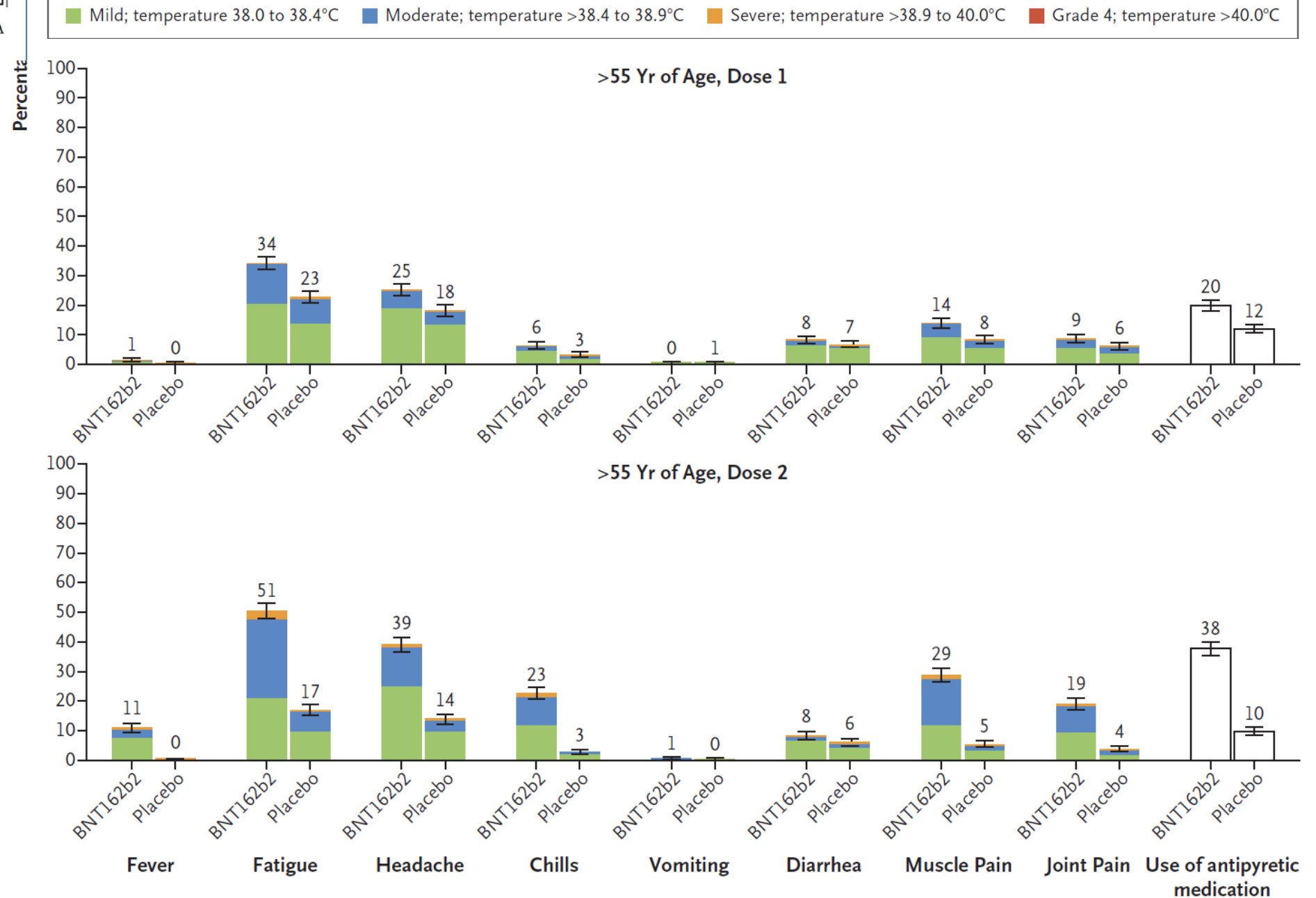
Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Systemic adverse events in young population



Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Adverse events in older age



Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Adverse events

	BNT162b2 (30 µg) (N^a=21621)	Placebo (N^a=21631)
Adverse Event	n^b (%)	n^b (%)
Any event	5770 (26.7)	2638 (12.2)
Related ^c	4484 (20.7)	1095 (5.1)
Severe	240 (1.1)	139 (0.6)
Life-threatening	21 (0.1)	24 (0.1)
Any serious adverse event	126 (0.6)	111 (0.5)
Related ^c	4 (0.0)	0
Severe	71 (0.3)	68 (0.3)
Life-threatening	21 (0.1)	23 (0.1)
Any adverse event leading to withdrawal	37 (0.2)	30 (0.1)
Related ^c	16 (0.1)	9 (0.0)
Severe	13 (0.1)	9 (0.0)
Life-threatening	3 (0.0)	6 (0.0)
Death	2 (0.0)	4 (0.0)

Table S3 | Participants Reporting at Least 1 Adverse Event from Dose 1 (All Enrolled Participants). The ‘all enrolled’ population included all participants who received at least 1 dose

Table 1. SARS-CoV-2 Vaccines under Emergency Use Authorization (EUA) or in Late-Phase Studies.

Vaccine Platform	Type of Vaccine and Immunogen	Developer (Name of Vaccine)	Dose Schedule and Administration	Phase*	Excipients†
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RNA-based vaccine	mRNA encoding spike protein (100 µg)	Moderna (mRNA-1273)	Two doses (day 0, day 28) Intramuscular	Post-EUA	Lipids (SM-102; 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 [PEG 2000-DMG]; cholesterol; and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose
Adenovirus vector (nonreplicating)	ChAdOx1-Sn Cov-19 Nonreplicating chimpanzee AdV5 expressing spike protein	AstraZeneca and University of Oxford (AZD1222)	One (day 0) or two (day 0, day 28) doses Intramuscular	Phase 3	10 mM histidine, 7.5% (w/v) sucrose, 35 mM sodium chloride, 1 mM magnesium chloride, 0.1% (w/v) polysorbate 80, 0.1 mM edetate disodium, 0.5% (w/v) ethanol, at pH 6.6
Adenovirus vector (nonreplicating)	Ad26.COV2.S Adenovirus 26 vectored vaccine using AdVac and PER.C6 technology	Janssen	One (day 0) or two (day 0, day 56) doses Intramuscular	Phase 3	Sodium chloride, citric acid monohydrate, polysorbate 80, 2 hydroxypropyl-β-cyclodextrin (HBCD), ethanol (absolute), sodium hydroxide
Protein subunit	Full-length recombinant SARS-CoV-2 glycoprotein nanoparticle with Matrix M adjuvant Spike prefusion protein	Novavax	Two doses (day 0, day 21) Intramuscular	Phase 3	Matrix M1 adjuvant Full-length spike protein formulated in polysorbate 80 detergent and Matrix M1 adjuvant
Protein subunit	SARS-CoV-2 vaccine formulation with adjuvant (S-protein) (Baculovirus production) Spike protein	Sanofi Pasteur and GSK	Two doses (day 0, day 21) Intramuscular	Phase 1–2	Sodium phosphate monobasic monohydrate, sodium phosphate dibasic, sodium chloride polysorbate 20, disodium hydrogen phosphate, potassium dihydrogen phosphate, potassium chloride

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Phase 3 randomized, observer-blinded, placebo-controlled trial on subjects at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 µg) or placebo 28 days apart

Inclusion criteria: persons 18 years of age or older with no known history of SARS-CoV-2 infection and with locations or circumstances that put them at an appreciable risk of SARSCoV-2 infection, a high risk of severe Covid-19, or both

Exclusion criteria: medical history of Covid-19, fever in the last 72h, pregnancy or breastfeeding, treatment with immunosuppressive therapy, or diagnosis with an immunocompromising condition

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Phase 3 randomized, observer-blinded, placebo-controlled trial on subjects at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 µg) or placebo 28 days apart

End- point: efficacy of the vaccine against laboratory-confirmed Covid-19 and safety

Where: 99 sites in United States

When: between July 27 and October 23, 2020

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

End- point: efficacy of the vaccine against laboratory-confirmed Covid-19 and safety

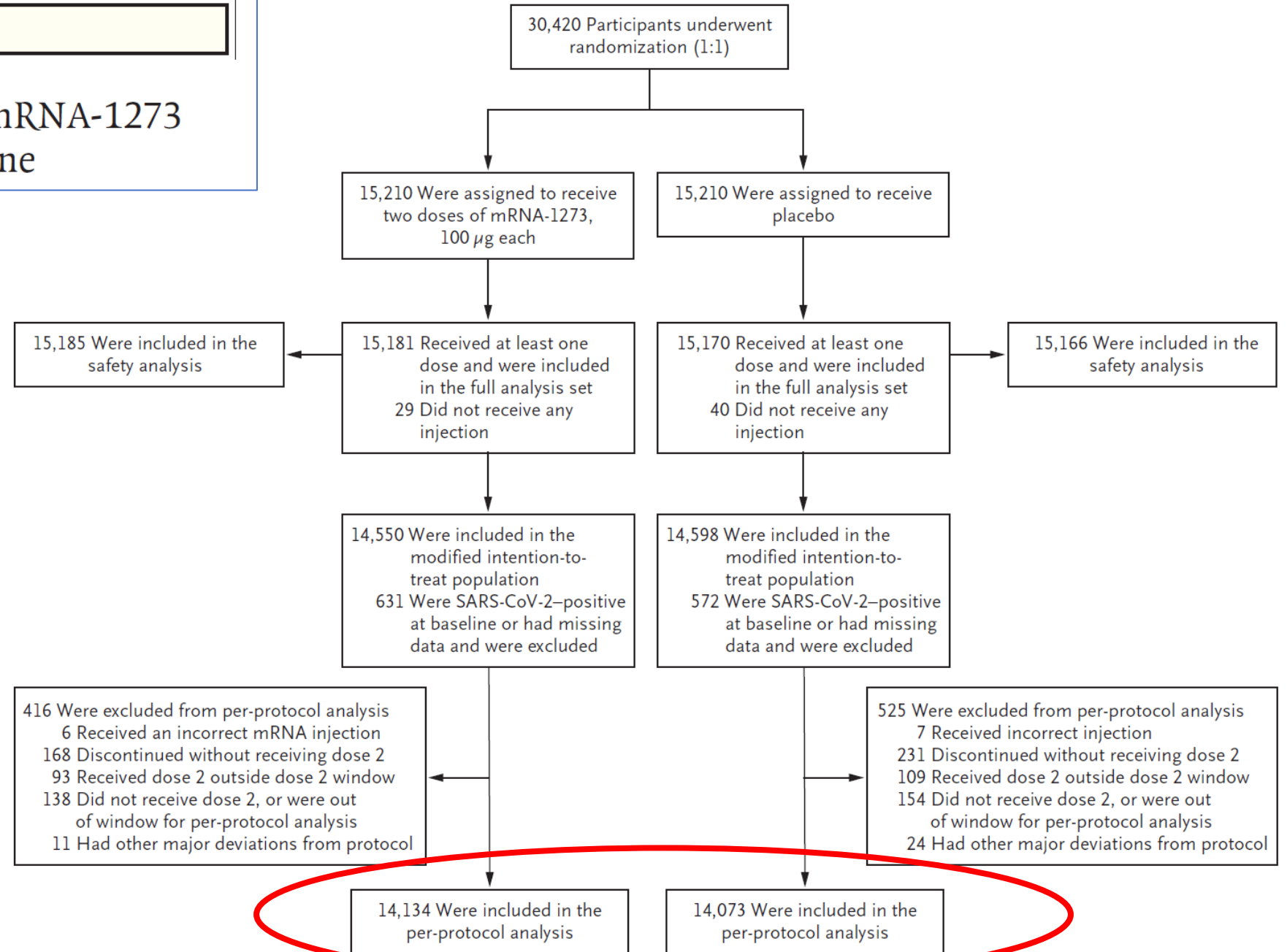
Efficacy:

- preventing a first occurrence of symptomatic Covid-19 with onset at least 14 days after the second injection
- Prevention of severe Covid-19

Safety:

- Solicited local and systemic adverse events for 7 days after each injection;
- unsolicited adverse reactions for 28 days after each injection;

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine



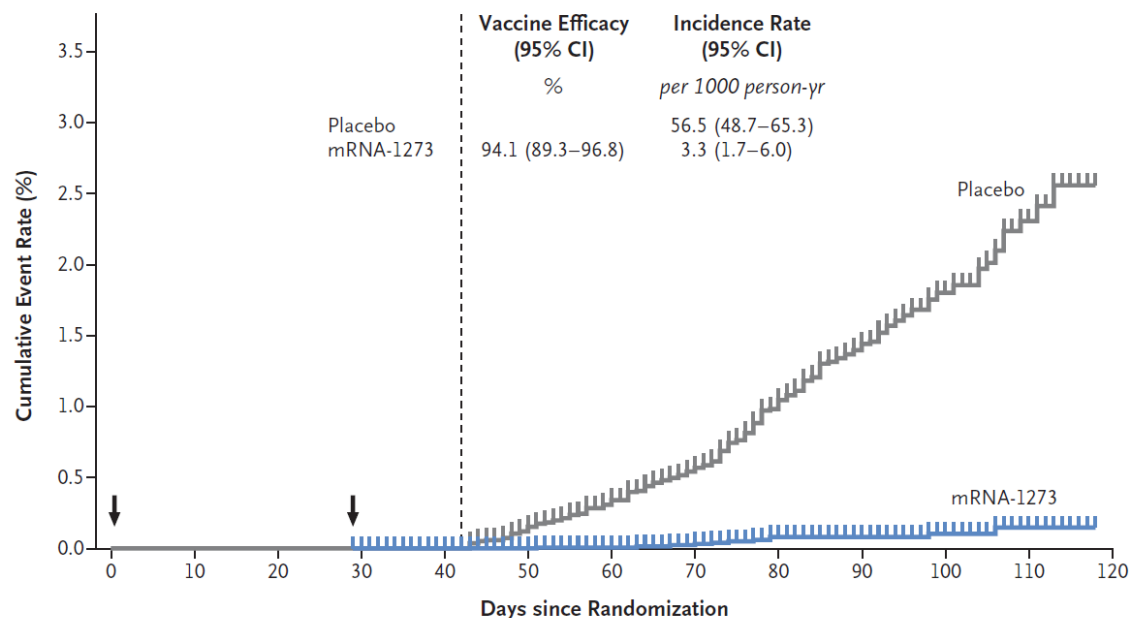
Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Table 1. Demographic and Clinical Characteristics at Baseline.*

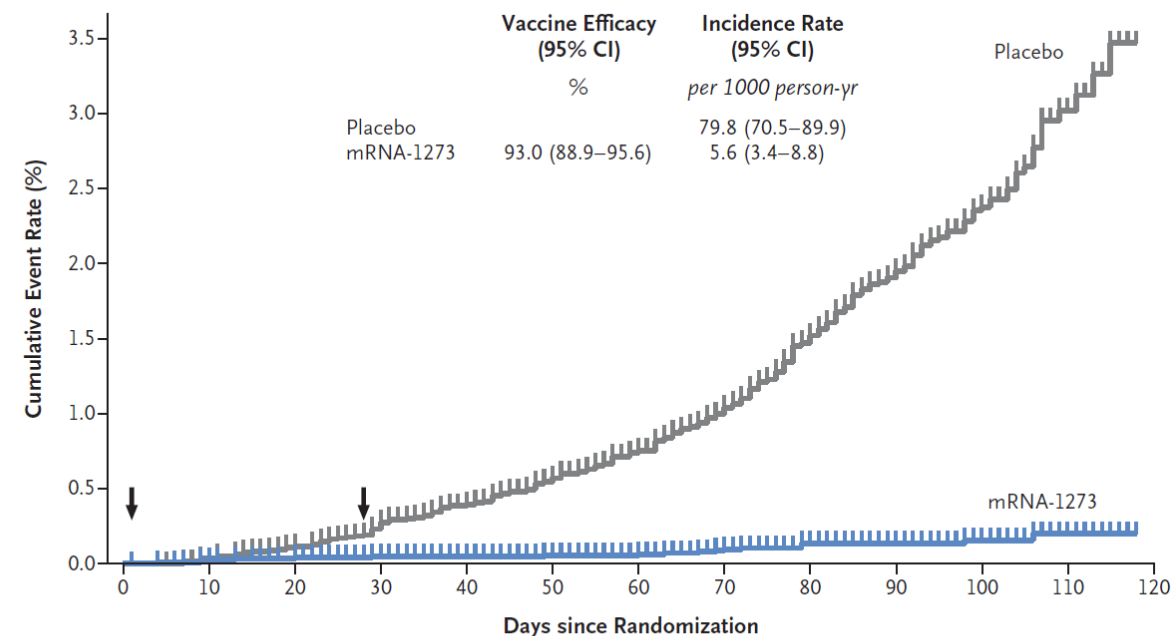
Characteristics	Placebo (N=15,170)	mRNA-1273 (N=15,181)	Total (N=30,351)
Sex — no. of participants (%)			
Male	8,062 (53.1)	7,923 (52.2)	15,985 (52.7)
Female	7,108 (46.9)	7,258 (47.8)	14,366 (47.3)
Mean age (range) — yr	51.3 (18–95)	51.4 (18–95)	51.4 (18–95)
Age category and risk for severe Covid-19 — no. of participants (%)†			
18 to <65 yr, not at risk	8,886 (58.6)	8,888 (58.5)	17,774 (58.6)
18 to <65 yr, at risk	2,535 (16.7)	2,530 (16.7)	5,065 (16.7)
≥65 yr	3,749 (24.7)	3,763 (24.8)	7,512 (24.8)
Hispanic or Latino ethnicity — no. of participants (%)‡			
Hispanic or Latino	3,114 (20.5)	3,121 (20.6)	6,235 (20.5)
Not Hispanic or Latino	11,917 (78.6)	11,918 (78.5)	23,835 (78.5)
Not reported and unknown	139 (0.9)	142 (0.9)	281 (0.9)
Race or ethnic group — no. of participants (%)‡			
White	11,995 (79.1)	12,029 (79.2)	24,024 (79.2)
Black or African American	1,527 (10.1)	1,563 (10.3)	3,090 (10.2)
Asian	731 (4.8)	651 (4.3)	1,382 (4.6)
American Indian or Alaska Native	121 (0.8)	112 (0.7)	233 (0.8)
Native Hawaiian or Other Pacific Islander	32 (0.2)	35 (0.2)	67 (0.2)
Multiracial	321 (2.1)	315 (2.1)	636 (2.1)
Other	316 (2.1)	321 (2.1)	637 (2.1)
Not reported and unknown	127 (0.8)	155 (1.0)	282 (0.9)

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

A Per-Protocol Analysis



B Modified Intention-to-Treat Analysis



Covid-19 Onset

Randomization to 14 days after dose 1
14 Days after dose 1 to dose 2
Dose 2 to 14 days after dose 2
Starting 14 days after dose 2
Total (any time after randomization)

Placebo
(N=14,598)

mRNA-1273
(N=14,550)

11

5

35

2

19

0

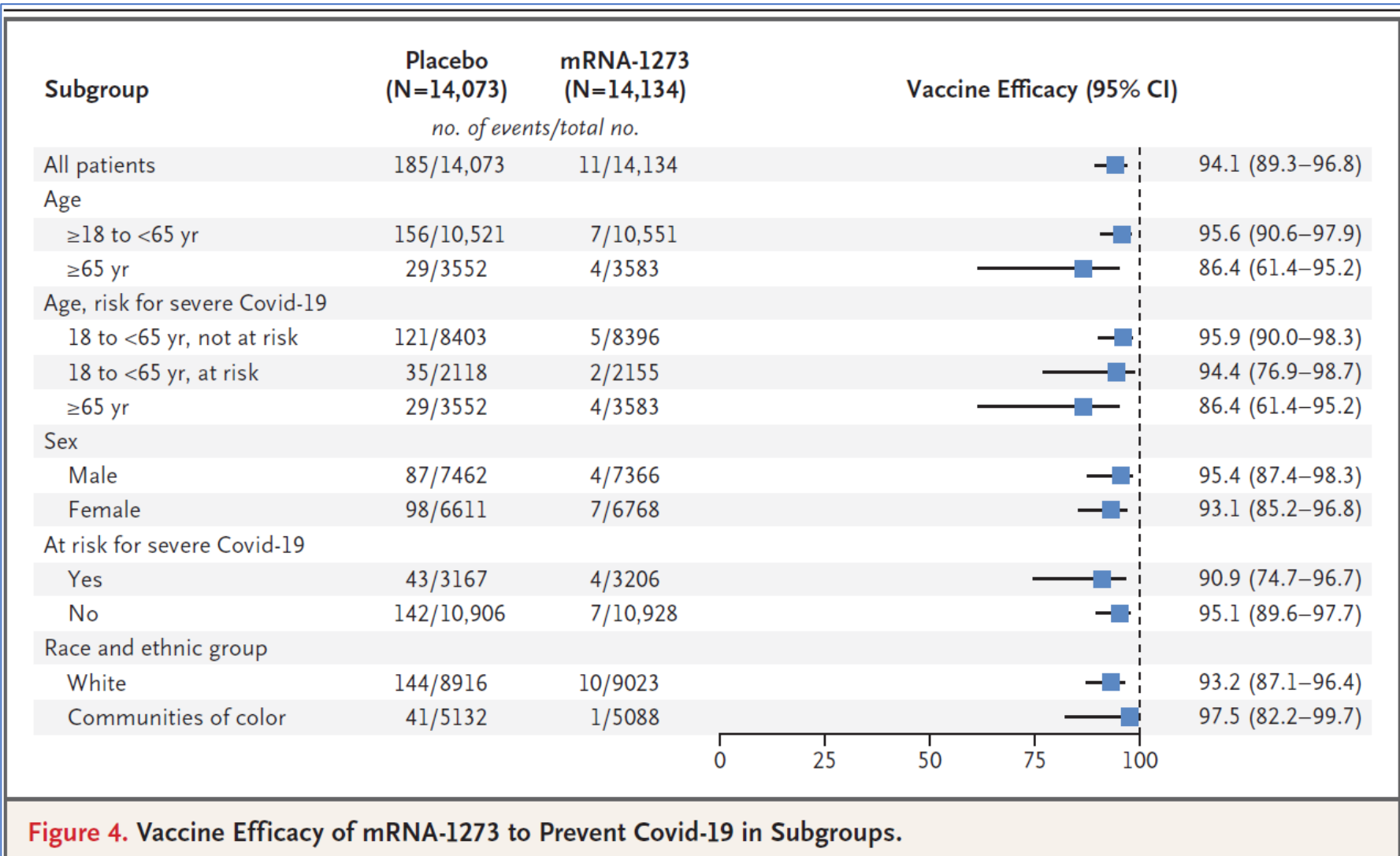
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269

19

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine



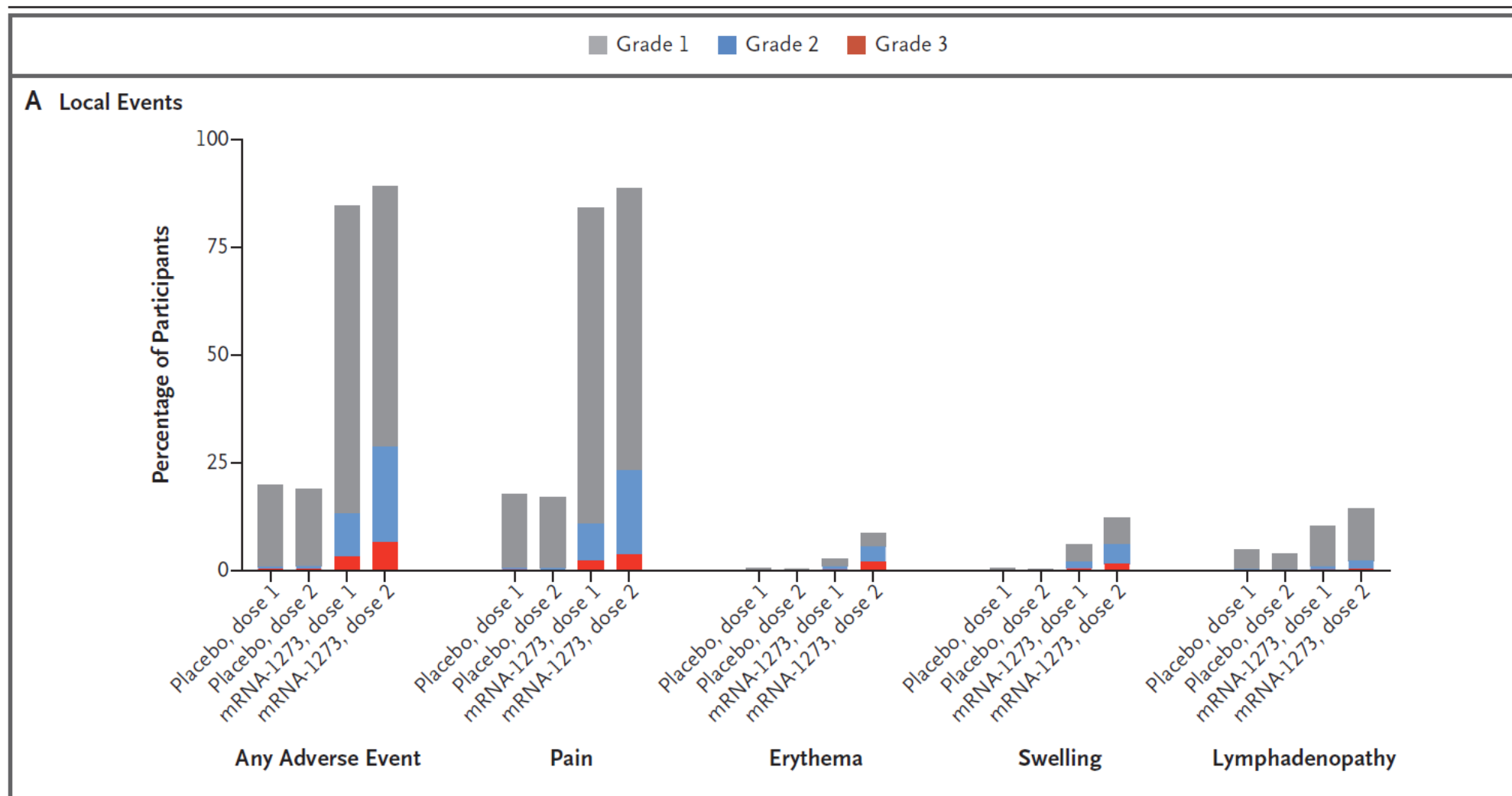
Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Table S16. Efficacy of Key Secondary Endpoints, Per-protocol Set

Secondary endpoint	Placebo	mRNA-1273
	(N=14073)	(N=14073)
Severe Covid-19 starting 14 days after second injection, adjudicated		
n, events, PP	30	0
VE Based on Hazard Ratio (95% CI)*		1.00 (NE-1.00)
Covid-19 after the first dose†		
n, events, PP	225	11
VE Based on Hazard Ratio (95% CI)		0.952 (0.912-0.974)
Secondary definition of Covid-19 starting 14 days after second injection‡		
n, events, PP	221	11
VE Based on Hazard Ratio (95% CI)		0.951 (0.911-0.973)
Covid-19 after the second injection regardless of prior SARS-CoV-2 infection, adjudicated		
n/N events§ FAS	187/15170	12/15181
VE Based on Hazard Ratio (95% CI)		0.936 (0.886-0.965)

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Local adverse events



Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Systemic adverse events

B Systemic Events

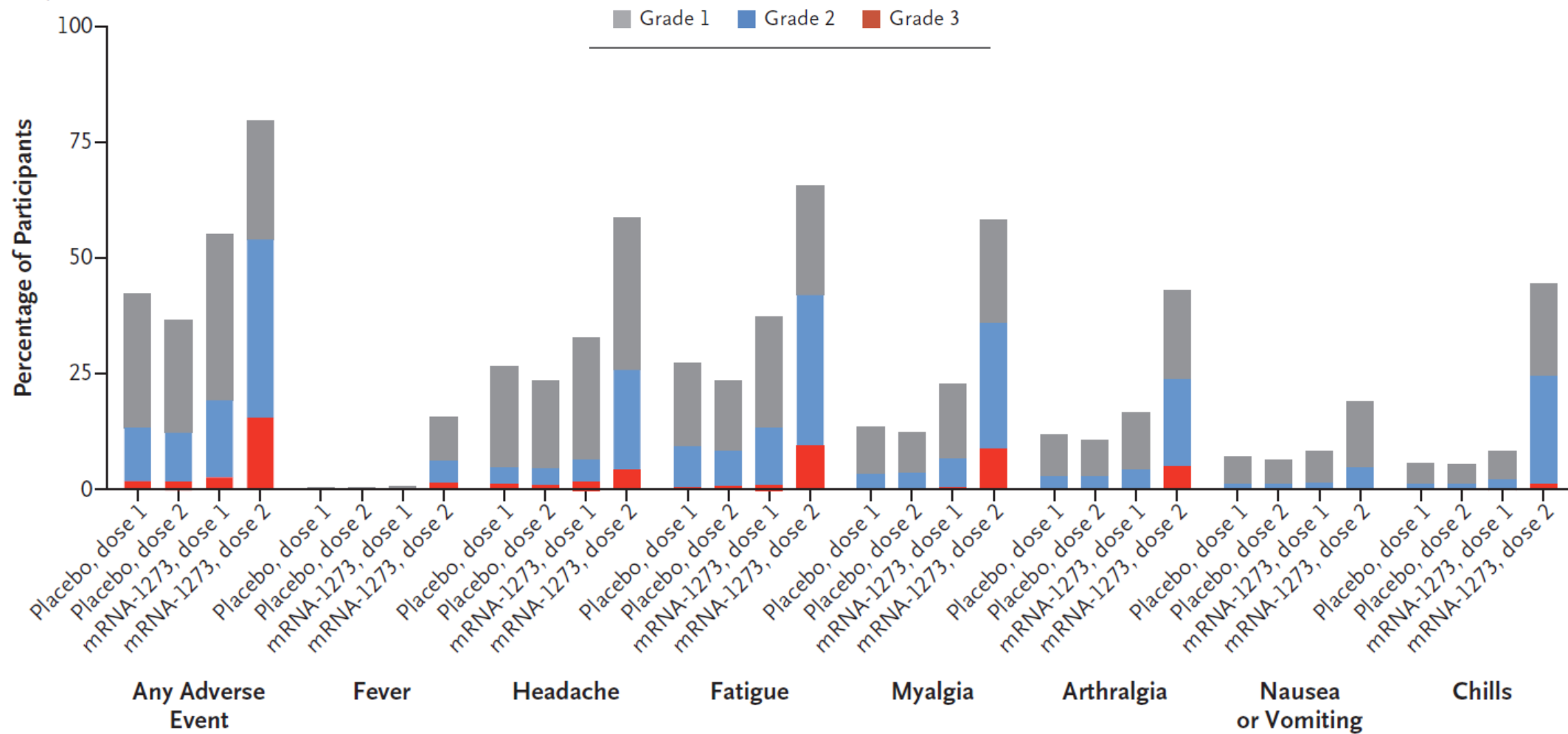


Table 1. SARS-CoV-2 Vaccines under Emergency Use Authorization (EUA) or in Late-Phase Studies.

Vaccine Platform	Type of Vaccine and Immunogen	Developer (Name of Vaccine)	Dose Schedule and Administration	Phase*	Excipients†
RNA-based vaccine	mRNA encoding spike protein (30 µg)	BioNTech–Pfizer (BNT162b2)	Two doses (day 0, day 21) Intramuscular	Post-EUA	0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol, 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% sodium chloride Injection) contributes an additional 2.16 mg sodium chloride per dose
RNA-based vaccine	mRNA encoding spike protein (100 µg)	Moderna (mRNA-1273)	Two doses (day 0, day 28) Intramuscular	Post-EUA	Lipids (SM-102; 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 [PEG 2000-DMG]; cholesterol; and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose
Adenovirus vector (nonreplicating)	ChAdOx1-Sn Cov-19 Nonreplicating chimpanzee AdV5 expressing spike protein	AstraZeneca and University of Oxford (AZD1222)	One (day 0) or two (day 0, day 28) doses Intramuscular	Phase 3	10 mM histidine, 7.5% (w/v) sucrose, 35 mM sodium chloride, 1 mM magnesium chloride, 0.1% (w/v) polysorbate 80 , 0.1 mM edetate disodium, 0.5% (w/v) ethanol, at pH 6.6
Adenovirus vector (nonreplicating)	Ad26.COV2.S Adenovirus 26 vectored vaccine using AdVac and PER.C6 technology	Janssen	One (day 0) or two (day 0, day 56) doses Intramuscular	Phase 3	Sodium chloride, citric acid monohydrate, polysorbate 80 , 2 hydroxypropyl-β-cyclodextrin (HBCD), ethanol (absolute), sodium hydroxide
Protein subunit	Full-length recombinant SARS-CoV-2 glycoprotein nanoparticle with Matrix M adjuvant Spike prefusion protein	Novavax	Two doses (day 0, day 21) Intramuscular	Phase 3	Matrix M1 adjuvant Full-length spike protein formulated in polysorbate 80 detergent and Matrix M1 adjuvant
Protein subunit	SARS-CoV-2 vaccine formulation with adjuvant (S-protein) (Baculovirus production) Spike protein	Sanofi Pasteur and GSK	Two doses (day 0, day 21) Intramuscular	Phase 1–2	Sodium phosphate monobasic monohydrate, sodium phosphate dibasic, sodium chloride polysorbate 20 , disodium hydrogen phosphate, potassium dihydrogen phosphate, potassium chloride

5 phase 1/2, single-blind, randomised controlled trials

Healthy adults aged 18–55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 at a dose of 5×10^{10} viral particles or MenACWY as a single intramuscular injection

COV002 (UK; LD/SD; N=2741)		COV002 (UK; SD/SD; N=4807)		COV003 (Brazil; all SD/SD; N=4088)	
ChAdOx1 nCoV-19 (n=1367)	MenACWY (n=1374)	ChAdOx1 nCoV-19 (n=2377)	MenACWY (n=2430)	ChAdOx1 nCoV-19 (n=2063)	MenACWY plus saline (n=2025)

Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK



	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (CI*)
		n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	
All LD/SD and SD/SD recipients	131	30/5807 (0.5%)	44.1 (248 299)	101/5829 (1.7%)	149.2 (247 228)	70.4% (54.8 to 80.6)†
COV002 (UK)	86	18/3744 (0.5%)	38.6 (170 369)	68/3804 (1.8%)	145.7 (170 448)	73.5% (55.5 to 84.2)
LD/SD recipients	33	3/1367 (0.2%)	14.9 (73 313)	30/1374 (2.2%)	150.2 (72 949)	90.0% (67.4 to 97.0)‡§
SD/SD recipients	53	15/2377 (0.6%)	56.4 (97 056)	38/2430 (1.6%)	142.4 (97 499)	60.3% (28.0 to 78.2)
COV003 (Brazil; all SD/SD)	45	12/2063 (0.6%)	56.2 (77 930)	33/2025 (1.6%)	157.0 (76 780)	64.2% (30.7 to 81.5)‡
All SD/SD recipients	98	27/4440 (0.6%)	56.4 (174 986)	71/4455 (1.6%)	148.8 (174 279)	62.1% (41.0 to 75.7)
Other non-primary symptomatic COVID-19 disease¶	18	7/5807 (0.1%)	10.3 (248 299)	11/5829 (0.2%)	16.3 (247 228)	36.4% (−63.8 to 75.3)‡
Any symptomatic COVID-19 disease	149	37/5807 (0.6%)	54.4 (248 299)	112/5829 (1.9%)	165.5 (247 228)	67.1% (52.3 to 77.3)
Asymptomatic or symptoms unknown (COV002)	69	29/3288 (0.9%)	69.8 (151 673)	40/3350 (1.2%)	96.0 (152 138)	27.3% (−17.2 to 54.9)
LD/SD recipients	24	7/1120 (0.6%)	41.4 (61 782)	17/1127 (1.5%)	100.6 (61 730)	58.9% (1.0 to 82.9)‡
SD/SD recipients	45	22/2168 (1.0%)	89.4 (89 891)	23/2223 (1.0%)	92.9 (90 408)	3.8% (−72.4 to 46.3)
Any NAAT-positive swab	221	68/5807 (1.2%)	100.0 (248 299)	153/5829 (2.6%)	226.0 (247 228)	55.7% (41.1 to 66.7)

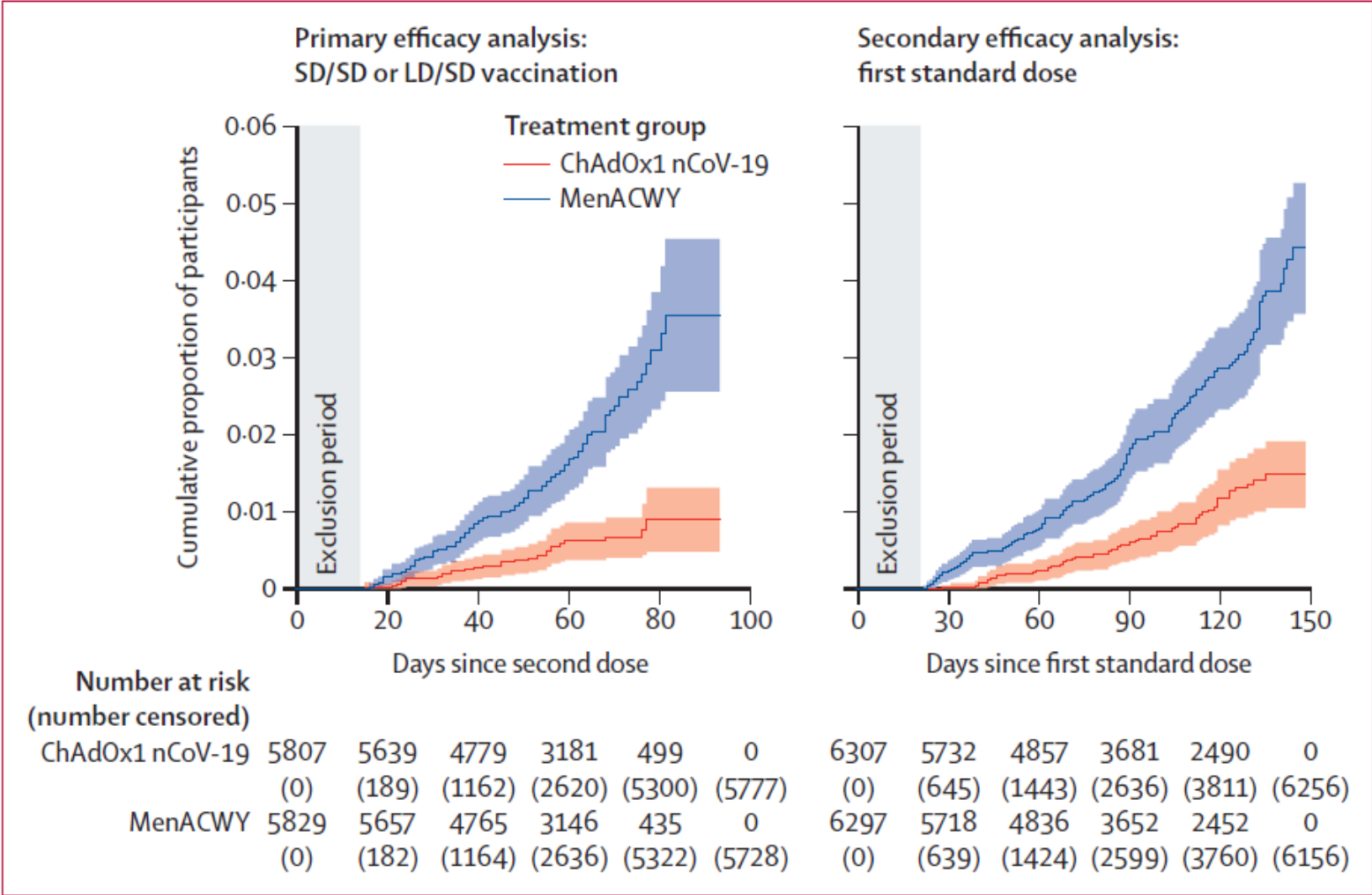


Table 1. SARS-CoV-2 Vaccines under Emergency Use Authorization (EUA) or in Late-Phase Studies.

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Phase 1–2 Trial of a SARS-CoV-2 Recombinant
Spike Protein Nanoparticle Vaccine

Randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5- μ g and 25- μ g doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults

A Vaccine Regimens

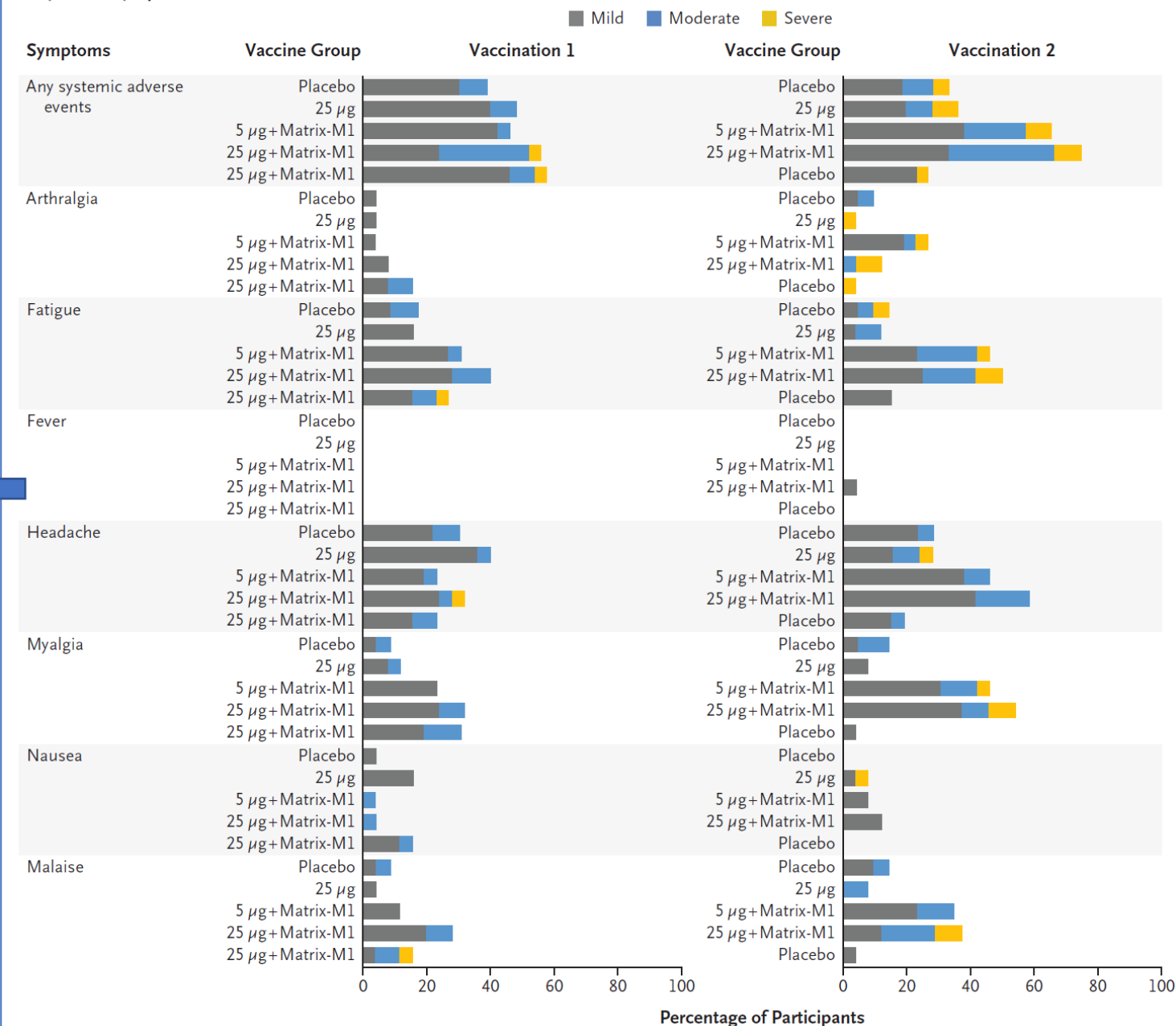
Vaccine Group	No. of Participants		Day 0		Day 21 (+5 days)	
	Randomized	Sentinel	rSARS-CoV-2	Matrix-M1 adjuvant	rSARS-CoV-2	Matrix-M1 adjuvant
A	25	—	0	0	0	0
B	25	—	25 μ g	0	25 μ g	0
C	25	3	5 μ g	50 μ g	5 μ g	50 μ g
D	25	3	25 μ g	50 μ g	25 μ g	50 μ g
E	25	—	25 μ g	50 μ g	0	0

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

CONCLUSIONS

At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype. (Funded by the Coalition for Epidemic Preparedness Innovations; ClinicalTrials.gov number, NCT04368988).

B Systemic Symptoms



Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia



Denis Y Logunov*, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatullin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg

On 76 subjects in Russia

Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial



Feng-Cai Zhu*, Xu-Hua Guan*, Yu-Hua Li, Jian-Ying Huang, Tao Jiang, Li-Hua Hou, Jing-Xin Li, Bei-Fang Yang, Ling Wang, Wen-Juan Wang, Shi-Po Wu, Zhao Wang, Xiao-Hong Wu, Jun-Jie Xu, Zhe Zhang, Si-Yue Jia, Bu-Sen Wang, Yi Hu, Jing-Jing Liu, Jun Zhang, Xiao-Ai Qian, Qiong Li, Hong-Xing Pan, Hu-Dachuan Jiang, Peng Deng, Jin-Bo Gou, Xue-Wen Wang, Xing-Huan Wang, Wei Chen

On 603 subjects in China

Open questions

- Clinical and virological efficacy
- Long-term efficacy
- Efficacy on viral quasi-species
- Large-wide tolerability
- Vaccination of subjects with a COVID-19 history

Open questions

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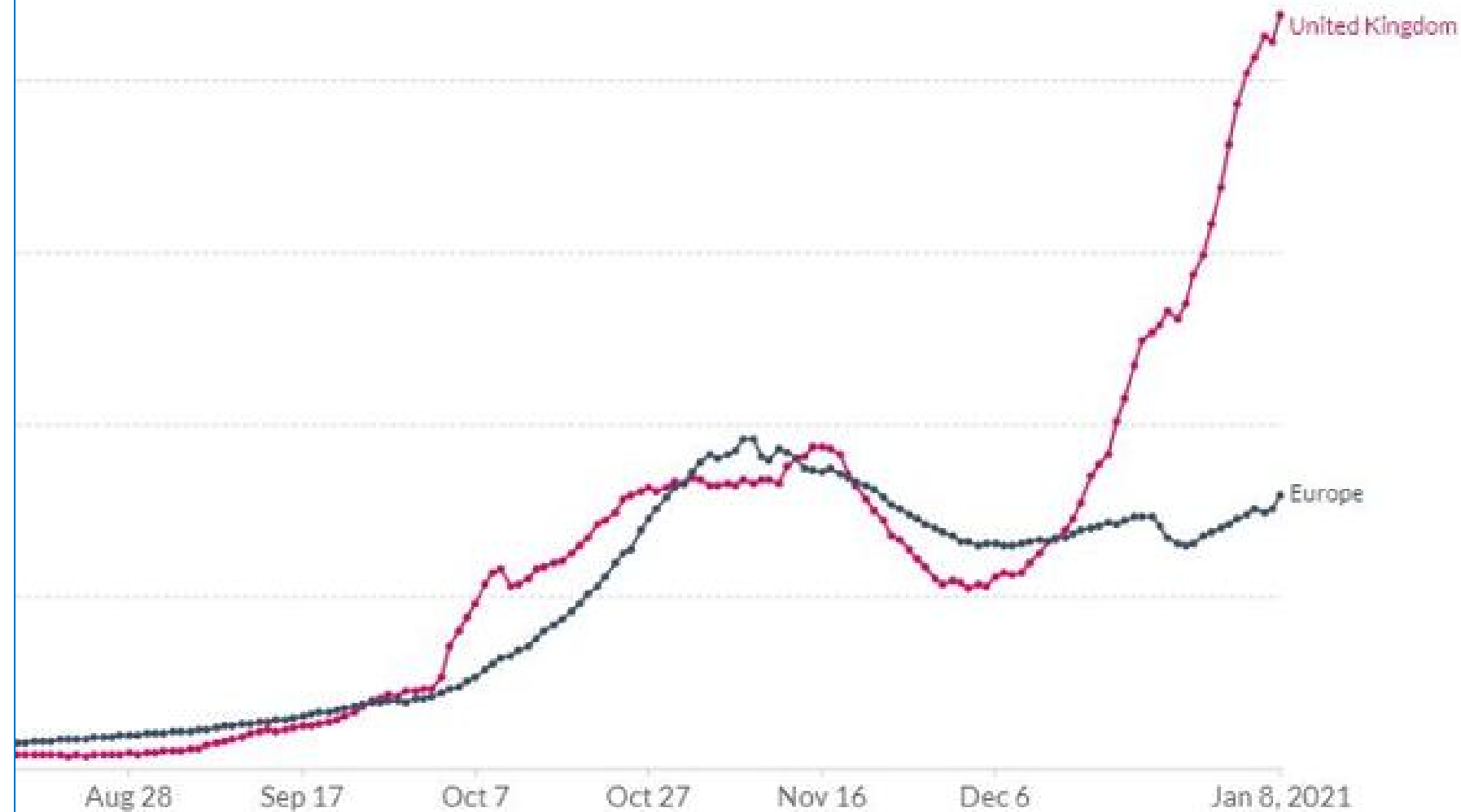
Open questions

- Clinical and virological efficacy
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- Tlarge-wide olerability
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COVID-19 cases per million people

The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

Our World
in Data



COVID-19 Data - Last updated 9 January, 06:07 (London time)

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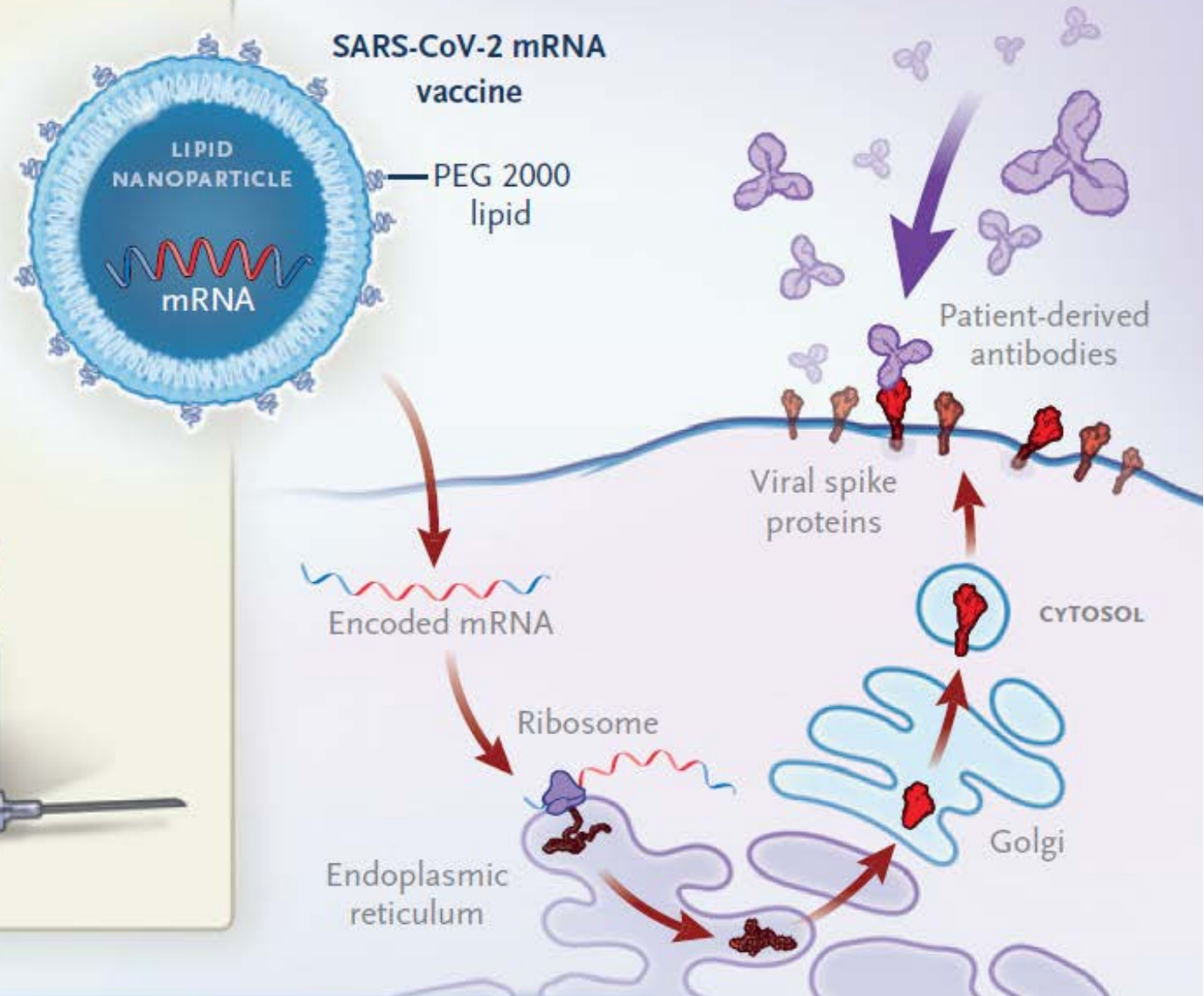
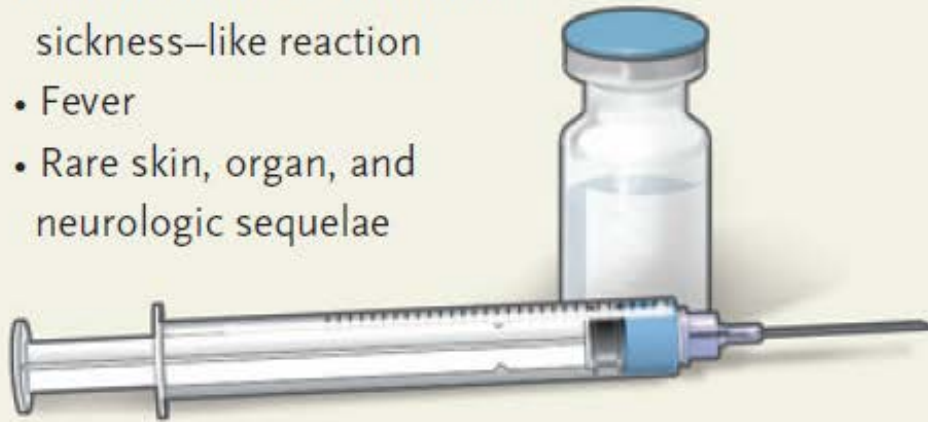
Jan 8, 2021

Open questions

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Vaccine Reactions

- Immediate
 - IgE
 - Non-IgE
 - Nonimmune (vasovagal syncope)
- Delayed
 - Site reactions
 - Urticaria or benign exanthem
 - Serum sickness and serum sickness–like reaction
 - Fever
 - Rare skin, organ, and neurologic sequelae



Science

Pfizer's vaccine raises allergy concerns

Jop de Vrieze

Science 371 (6524), 10-11.
DOI: 10.1126/science.371.6524.10

COVID-19

Pfizer's vaccine raises allergy concerns

Polymer in mRNA's "packaging" may cause rare anaphylactic reactions

By Jop de Vrieze

Severe allergy-like reactions in at least 12 people who received the COVID-19 vaccine produced by Pfizer and BioNTech may be due to a compound in the packaging of the messenger RNA (mRNA) that forms the vaccine's main ingredient, scientists say. A similar mRNA vaccine developed by Moderna also contains the compound, polyethylene glycol (PEG).

Anaphylactic reactions can occur with any vaccine but are extremely rare—about one per 1 million doses. As of 23 December 2020, the United States had seen 10 cases of anaphylaxis among 614,117 people who received the COVID-19 vaccine; the United Kingdom had recorded two. Because the Pfizer and Moderna mRNA vaccines use a new platform, the reactions call for careful scrutiny, says Elizabeth Phillips, a drug hypersensitivity researcher at Vanderbilt University Medical Center who attended an NIAID meeting on 16 December. "This is new."

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Maintaining Safety with SARS-CoV-2 Vaccines

Mariana C. Castells, M.D., Ph.D., and Elizabeth J. Phillips, M.D.

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Protein subunit	SARS-CoV-2 vaccine formulation with adjuvant (S-protein) (Baculovirus production) Spike protein	Sanofi Pasteur and GSK	Two doses (day 0, day 21) Intramuscular	Phase 1–2	Sodium phosphate monobasic monohydrate, sodium phosphate dibasic, sodium chloride polysorbate 20, disodium hydrogen phosphate, potassium dihydrogen phosphate, potassium chloride

Open questions

- Clinical and virological efficacy
- Long-term efficacy
- Efficacy on viral quasi-species
- Large-wide tolerability
- **Vaccination of subjects with a COVID-19 history**

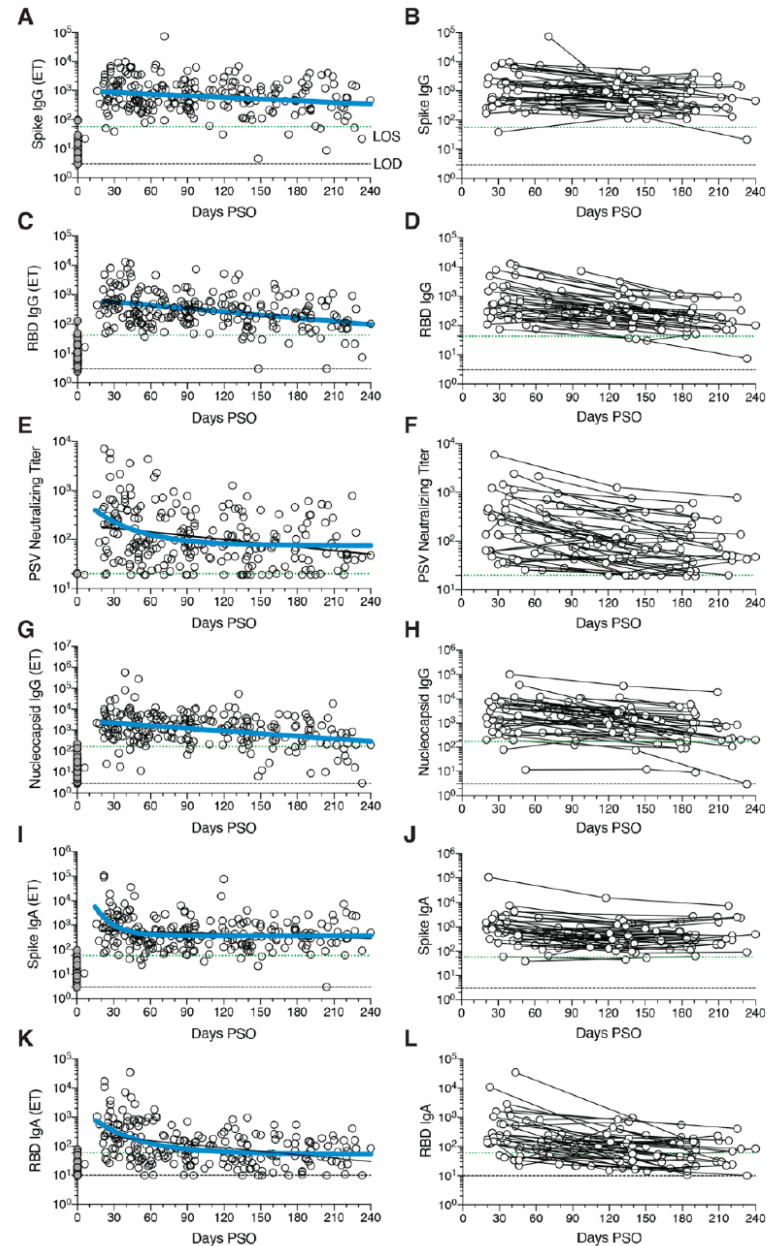
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Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection

Jennifer M. Dan^{1,3*}, Jose Mateus^{1*}, Yu Kato^{1*}, Kathryn M. Hastie¹, Esther Dawen Yu¹, Caterina E. Faliti¹, Alba Grifoni¹, Sydney I. Ramirez^{1,3}, Sonya Haupt¹, April Frazier¹, Catherine Nakao¹, Vamseedhar Rayaprolu¹, Stephen A. Rawlings³, Bjoern Peters^{1,2}, Florian Krammer¹, Viviana Simon^{1,3,6}, Erica Ollmann Saphire^{1,3}, Davey M. Smith³, Daniela Weiskopf^{1†}, Alessandro Sette^{1,3†}, Shane Crotty^{1,3†}

Multiple compartments of circulating immune memory to SARS-CoV-2 in 254 samples from 188 COVID-19 cases, including 43 samples at ≥ 6 months post-infection, were analyzed.

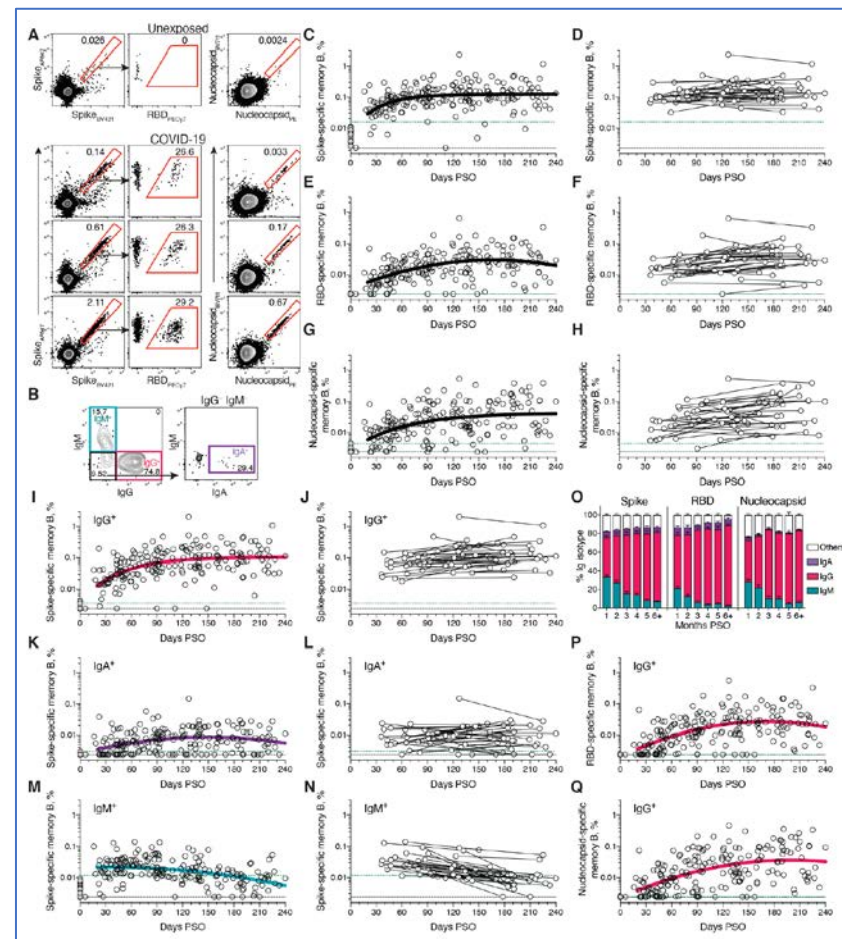
Circulating antibodies to SARS-CoV-2 over time.



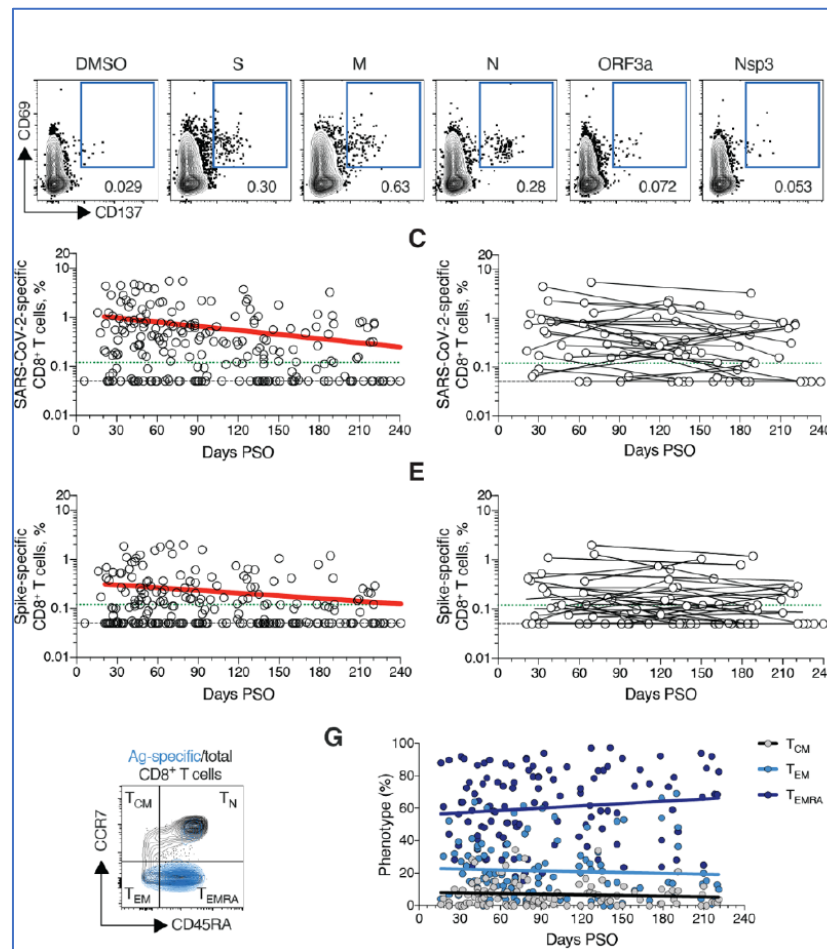
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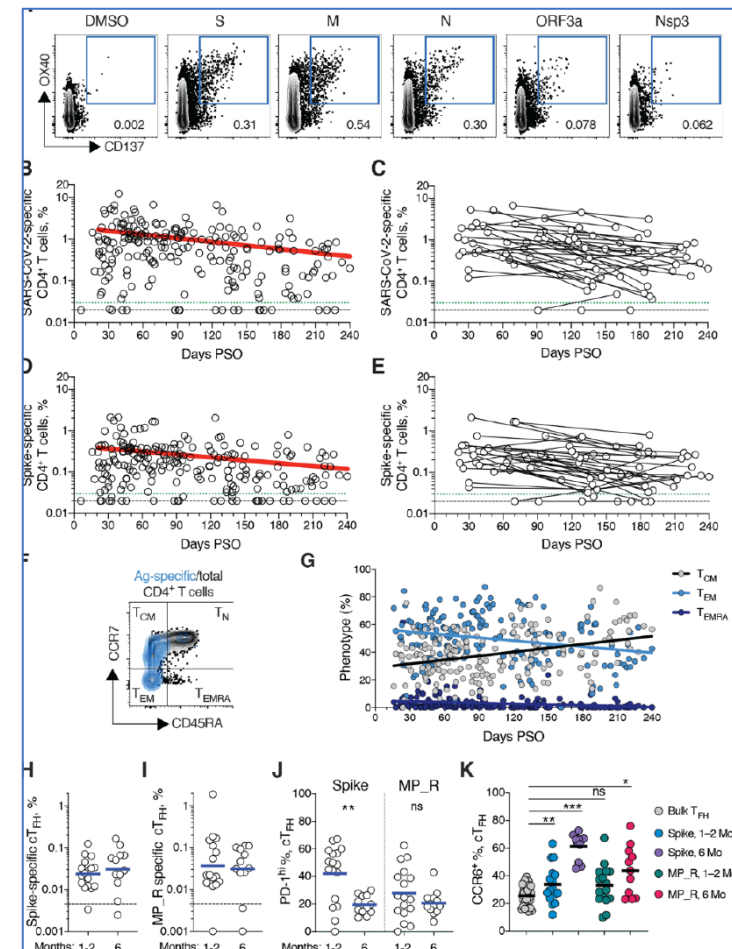
Kinetics of SARS-CoV-2 memory B cell responses.



SARS-CoV-2 circulating memory CD8⁺ T cells.



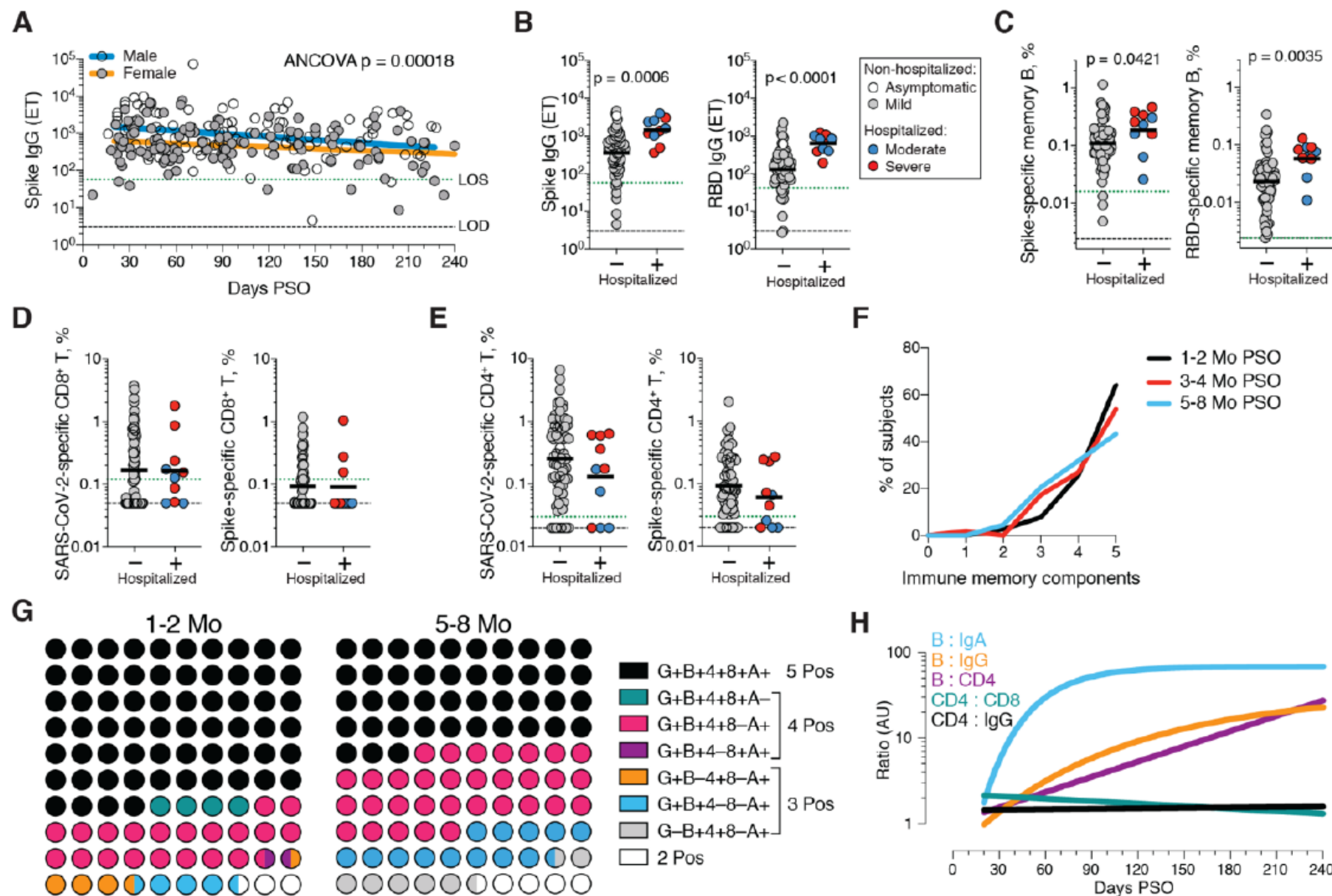
SARS-CoV-2 circulating memory CD4⁺ T cells.



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Immune memory relationships.

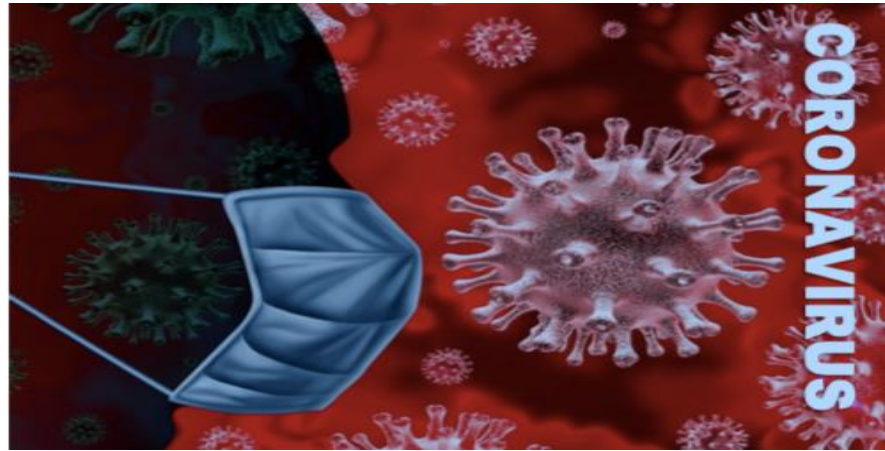


Conclusions

- EBM supports the use of COVID-19 vaccines
- Some open questions remain







Grazie per l'attenzione!

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

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Journal of Thrombosis and Haemostasis

Patients with	28-day mortality		Univariate analysis	
	Treating with Heparin	Non-treating with heparin	Odds ratio (95% CI)	P value
D-dimer >6 ULN (n=161)	32.8%	52.4%	0.442 (0.226-0.865)	0.017
D-dimer >8 ULN (n=150)	33.3%	54.8%	0.412 (0.207-0.817)	0.011