COREB
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VACCINES

Scientific update on COVID-19

Updated on 24th July 2021

anRS
MALADIES INFECTIEUSES ÉMERGENTES

https://reacting.inserm.fr/

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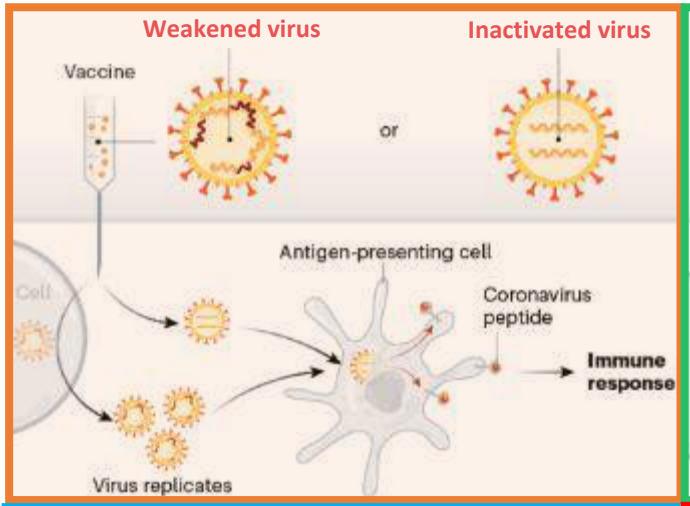
VACCINES

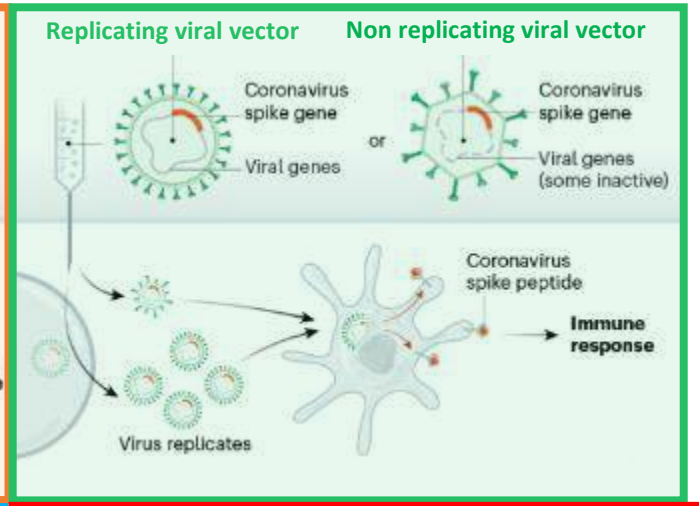
Question:

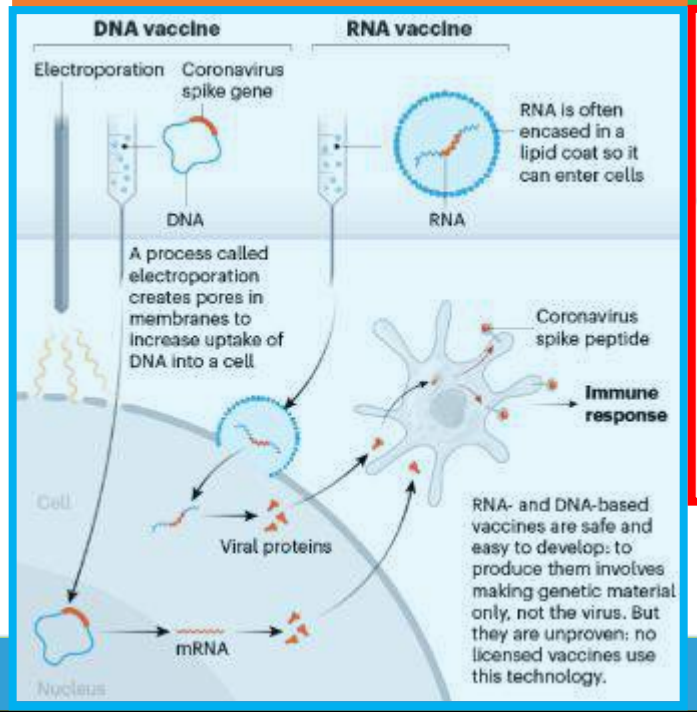
- What are the types of vaccines in clinical evaluation?
- Which are the results of immunogenicity safety and efficacy of SARS CoV-2 vaccines?
- Can they protect against arising viral variants?
- Is there any security issues related to authorised vaccines

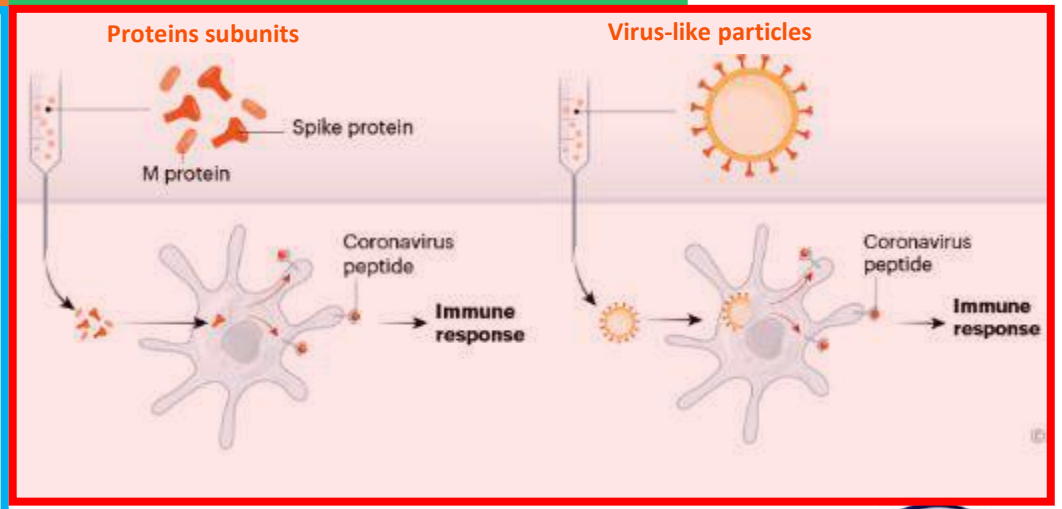
Vaccines

- **Vaccines aims**: expose the immune system to an antigen that won't cause disease, provoke an immune response (able to block/kill the virus)
- **Eight types of vaccines**:
  - virus (inactivated, weakened),
  - viral vector (replicating, non replicating)
  - nucleic acid (DNA, RNA)
  - protein based (protein subunit, virus like particles)









Callaway E. *Nature* Apr 2020

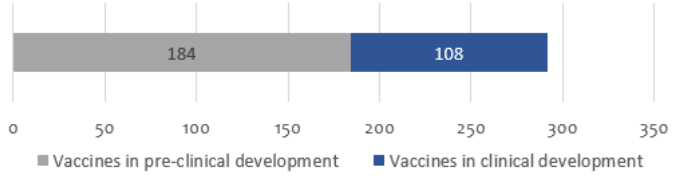
Vaccines

- **R&D landscape**: WHO lists 184 candidates in preclinical development, 105 candidate vaccines in clinical evaluation (July 22nd 2021); update available at :

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

Summary Information on Vaccine Products in Clinical Development

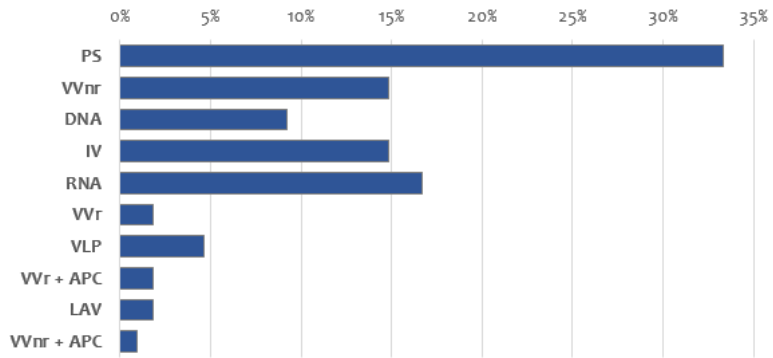
1. - Number of vaccines in clinical development	108
2. - Number of vaccines in pre-clinical development	184



3. - Candidates in clinical phase

Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	36	33%
VVnr	Viral Vector (non-replicating)	16	15%
DNA	DNA	10	9%
IV	Inactivated Virus	16	15%
RNA	RNA	18	17%
VVr	Viral Vector (replicating)	2	2%
VLP	Virus Like Particle	5	5%
VVr + APC	VVr + Antigen Presenting Cell	2	2%
LAV	Live Attenuated Virus	2	2%
VVnr + APC	VVnr + Antigen Presenting Cell	1	1%
		108	



5 vaccines abandoned after trials: MSD-IAVI, MSD-Pasteur, Imperial College, University of Queensland, Altimmune

From WHO COVID19 vaccine tracker

Phase III/IV COVID-19 Vaccines (July 22nd 2021)

Institutes	Phase	Vaccine	Platform	Location	Start date	Primary completion date	Trial number	Status
Janssen Pharmaceutical Companies	Phase III	Janssen Ad26.COV2.S	Vector (non-replicating)	South Africa	18/02/2021	31/03/2022	NCT04838795	Recruiting
Center for Genetic Engineering/and Biotechnology (peptide #1)	Phase III	CIGB CIGB-66/Abdala	Protein subunit	Cuba	22/03/2021	31/07/2021	IG/CIGB-66I/CVI	Pending
Beijing Institute of Biological Products/Wuhan Institute of Biological Products/Sinopharm	Phase III	WIBP/BIBP vaccines	Inactivated	Bahrain, Jordan, Egypt, UAE	16/07/2020	16/06/2021	NCT04510207	Recruiting
Janssen Pharmaceutical Companies	Phase III	Janssen Ad26.COV2.S	Vector (non-replicating)	USA, Argentina, Brazil, others	07/09/2020	22/01/2021	NCT04505722	Active, not recruiting
Instituto Finlay de Vacunas (peptide #2)	Phase III	Instituto Finlay de Vacunas Soberana 2	Protein subunit	Cuba	05/03/2021	07/11/2021	IFV/COR/09	Pending
BioNTech/Pfizer/Fosun Pharma	Phase II/III	BioNTech BNT162 (b1/b2/b2SA)	RNA	USA, Argentina, Brazil, others	29/04/2020	02/11/2021	NCT04368728	Recruiting
Erciyes University (inactivated)	Phase III	Erciyes TURCOVAC	Inactivated	Turkey	22/06/2021	01/09/2022	NCT04942405	Recruiting
CanSino Biological Inc/Beijing Institute of Biotechnology	Phase III	Cansino Ad5-nCoV	Vector (non-replicating)	Argentina, Chile, Mexico, others	15/09/2020	30/12/2021	NCT04526990	Recruiting
West China Hospital,/Sichuan University	Phase III	West China Hospital protein subunit va	Protein subunit	China	18/06/2021	28/02/2022	NCT04887207/N	Enrolling by invitation
Moderna/NIAID	Phase III	Moderna mRNA-1273	RNA	USA	24/03/2021	22/12/2021	NCT04811664	Recruiting
Sanofi Pasteur/GSK	Phase III	Sanofi/GSK CoV2 preS dTM	Protein subunit	USA, Honduras, Japan	26/05/2021	26/01/2023	NCT04904549	Recruiting
CureVac	Phase II/III	CureVac CVnCoV	RNA	Argentina, Belgium, Colombia, others	14/12/2020	16/04/2021	NCT04652102	Active, not recruiting
Institute of Medical Biology,/Chinese Academy of Medical Sciences	Phase III	CAMS vaccine	Inactivated	Brazil, Malaysia	28/01/2021	30/09/2021	NCT04659239	Enrolling by invitation
Gamaleya Research Institute	Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	Russia	07/09/2020	01/05/2021	NCT04530396	Active, not recruiting
Novavax	Phase III	Novavax NVX-CoV2373	Protein subunit	USA, Mexico, Puerto Rico	27/12/2020	30/06/2023	NCT04611802	Recruiting
University of Oxford/AstraZeneca	Phase III	Oxford ChAdOx1-S	Vector (non-replicating)	USA, Argentina, Chile, others	28/08/2020	05/03/2021	NCT04516746	Active, not recruiting
Janssen Pharmaceutical Companies	Phase III	Janssen Ad26.COV2.S	Vector (non-replicating)	USA, Belgium, Brazil, others	16/11/2020	10/05/2022	NCT04614948	Active, not recruiting

Phase III/IV COVID-19 Vaccines (July 22nd 2021)

Institutes	Phase	Vaccine	Platform	Location	Start date	Primary completion date	Trial number	Status
Medicago Inc	Phase II/III	Medicago CoVLP	Virus-like particle	USA, Canada, UK	19/11/2020	31/12/2021	NCT04636697	Recruiting
Moderna/NIAID	Phase III	Moderna mRNA-1273	RNA	USA	27/07/2020	27/10/2022	NCT04470427	Active, not recruiting
Anhui Zhifei Longcom Biopharmaceutical/Chinese Academy of Sciences	Phase III	AZLB ZF2001	Protein subunit	China, Ecuador, Indonesia, others	16/12/2020	30/04/2022	NCT04646590	Recruiting
Zydus Cadila Healthcare Limited (DNA)	Phase III	Zydus Cadila ZyCoV-D	DNA	India	20/01/2021	20/09/2022	CTRI/2021/01/03	Recruiting
Shenzhen Kangtai Biological Products Co Ltd	Phase III	Shenzhen Kangtai KCONVAC	Inactivated	Pending	01/05/2021	30/11/2021	NCT04852705	Not yet recruiting
Walvax Biotech/PLA Academy of Military Sciences/Suzhou Abogen Biosciences	Phase III	Walvax ARCoV	RNA	Pending	28/05/2021	30/10/2021	NCT04847102	Not yet recruiting
Bharat Biotech/ICMR/National Institute of Virology	Phase III	Bharat Covaxin	Inactivated	India	16/11/2020	08/01/2021	NCT04641481	Active, not recruiting
Clover Biopharmaceuticals Inc/GSK/Dynavax	Phase II/III	Clover SCB-2019	Protein subunit	Belgium, Brazil, Colombia, others	01/03/2021	31/07/2022	NCT04672395	Not yet recruiting
Shifa Pharmed	Phase II/III	Shifa Pharmed COVIran	Inactivated	Iran	14/03/2021		IRCT2020120204	Recruiting
Novavax	Phase III	Novavax NVX-CoV2373	Protein subunit	UK	28/09/2020	31/01/2021	NCT04583995	Recruiting
Nanogen Biopharmaceutical	Phase III	Nanogen Nanocovax	Protein subunit	Vietnam	07/06/2021	07/07/2022	NCT04922788	Recruiting
Sinovac	Phase III	Sinovac CoronaVac	Inactivated	Turkey	14/09/2020	15/02/2021	NCT04582344	Recruiting
Sinovac	Phase III	Sinovac CoronaVac	Inactivated	Brazil	21/07/2020	17/12/2020	NCT04456595	Active, not recruiting
University of Oxford/AstraZeneca	Phase II/III	Oxford ChAdOx1-S	Vector (non-replicating)	UK	28/05/2020	30/09/2021	NCT04400838	Active, not recruiting
Beijing Institute of Biological Products/Wuhan Institute of Biological Products/Sinopharm	Phase III	WIBP/BIBP vaccines	Inactivated	Peru	09/09/2020	19/02/2021	NCT04612972	Active, not recruiting
ReiThera/Leukocare/Univercells	Phase II/III	ReiThera GRAd-COV2	Vector (non-replicating)	Italy	15/03/2021	30/10/2021	NCT04791423	Active, not recruiting
University of Oxford/AstraZeneca	Phase III	Oxford ChAdOx1-S	Vector (non-replicating)	Brazil	02/06/2020	30/09/2021	NCT04536051	Recruiting

Phase III/IV COVID-19 Vaccines (July 22nd 2021)

Institutes	Phase	Vaccine	Platform	Location	Start date	Primary completion date	Trial number	Status
BioNTech/Pfizer/Fosun Pharma	Phase III	BioNTech BNT162 (b2)	RNA	USA	28/06/2021	06/02/2022	NCT04955626	Not yet recruiting
Vaxxinity	Phase II/III	Vaxxinity UB-612	Protein subunit	Pending	01/02/2021	22/03/2023	NCT04683224	Not yet recruiting
Moderna/NIAID	Phase II/III	Moderna mRNA-1273	RNA	USA	15/03/2021	12/06/2023	NCT04796896	Recruiting
Gamaleya Research Institute	Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	Russia	19/02/2021	31/12/2021	NCT04741061	Recruiting
BioNTech/Pfizer/Fosun Pharm	Phase I/II/III	BioNTech BNT162 (b2)	RNA	USA, Finland, Poland, S	24/03/2021	04/03/2022	NCT04816643	Recruiting
University of Oxford/AstraZeneca/Beijing Institute of Biological Products/Sinopharm	Phase II/III	ChAdOx1-S/BBIBP-CorV	Vector (non-replicating)/Inactiv	Egypt	23/02/2021	01/10/2021	NCT04885764	Recruiting
Valneva/Dynavax/University of Oxford/AstraZeneca	Phase III	VLA2001/ChAdOx1-S	Inactivated/Vector (non-replica	UK	26/04/2021	15/07/2021	NCT04864561	Active, not recruiting
Moderna/NIAID	Phase II/III	Moderna mRNA-1273	RNA	USA	09/12/2020	30/06/2022	NCT04649151	Active, not recruiting
Beijing Institute of Biological Products/Sinopharm	Phase III	BIBP BBIBP-CorV	Inactivated	Argentina	16/09/2020	01/12/2021	NCT04560881	Active, not recruiting
Research Institute for/Biological Safety Problems (inactivated)	Phase III	RIBSP QazCovid-in	Inactivated	Kazakhstan	25/12/2020	20/07/2021	NCT04691908	Active, not recruiting
Vector Institute (peptide)	Phase III	Vector Institute EpiVacCorona	Protein subunit	Russia	18/11/2020	31/08/2021	NCT04780035	Active, not recruiting
CureVac	Phase III	CureVac CVnCoV	RNA	Germany	23/12/2020	30/06/2021	NCT04674189	Active, not recruiting
Sinovac	Phase III	Sinovac CoronaVac	Inactivated	Chile	27/11/2020	31/01/2022	NCT04651790	Recruiting
Gamaleya Research Institute	Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	Venezuala	01/11/2020	31/10/2021	NCT04642339	Not yet recruiting
Sinovac	Phase III	Sinovac CoronaVac	Inactivated	Indonesia	10/08/2020	09/01/2021	NCT04508075	Active, not recruiting
Gamaleya Research Institute	Phase II/III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	India	30/11/2020	30/08/2021	NCT04640233	Active, not recruiting
University of Oxford/AstraZeneca	Phase II/III	Oxford ChAdOx1-S	Vector (non-replicating)	India	24/08/2020	24/03/2021	CTRI/2020/08/02	Completed
BioNTech/Pfizer/Fosun Pharma	Phase III	BioNTech BNT162 (b2/b2.B.1.351)	RNA	USA	15/02/2021	22/07/2021	NCT04713553	Recruiting
CureVac	Phase III	CureVac CVnCoV	RNA	Belgium	22/04/2021	15/09/2021	NCT04860258	Recruiting
Sinovac	Phase III	Sinovac CoronaVac	Inactivated	China	31/10/2020	28/11/2020	NCT04617483	Recruiting
CureVac	Phase III	CureVac CVnCoV	RNA	Argentina, Colombia, Peru	01/10/2021	30/11/2021	NCT04848467	Not yet recruiting
Gamaleya Research Institute	Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	UAE	01/12/2020	31/08/2021	NCT04656613	Not yet recruiting
BioNTech/Pfizer/Fosun Pharma/Sinovac/University of Oxford/AstraZeneca	Phase III	BNT162/CoronaVac/ChAdOx1-S	RNA/Inactivated/Vector (non-re	Hong Kong	08/05/2021	31/03/2025	NCT04800133	Recruiting

Phase III/IV COVID-19 Vaccines (July 22nd 2021)

Institutes	Phase	Vaccine	Platform	Location	Start date	Primary completion date	Trial number	Status
Valneva/Dynavax	Phase III	Valneva VLA2001/VLA2101	Inactivated	Pending	01/07/2021	31/12/2021	NCT04956224	Not yet recruiting
BioNTech/Pfizer/Fosun Pharma	Phase II/III	BioNTech BNT162 (b2)	RNA	USA, Brazil, South Africa, others	16/02/2021	25/07/2022	NCT04754594	Recruiting
BioNTech/Pfizer/Fosun Pharma	Phase III	BioNTech BNT162 (lyophilised b2)	RNA	USA	01/04/2021	06/07/2021	NCT04816669	Active, not recruiting
BioNTech/Pfizer/Fosun Pharma	Phase III	BioNTech BNT162 (b2) +/- 20vPnC	RNA	USA	20/05/2021	29/11/2021	NCT04887948	Recruiting
Wuhan Institute of Biological Products/Sinopharm	Phase III	WIBP vaccine	Inactivated	Morocco	02/09/2020	31/12/2020	ChiCTR20000390	Recruiting
Bharat Biotech/ICMR/National Institute of Virology	Phase II/III	Bharat Covaxin	Inactivated	India	26/05/2021	15/08/2021	NCT04918797	Recruiting
CanSino Biological Inc/Beijing Institute of Biotechnology	Phase III	Cansino Ad5-nCoV	Vector (non-replicating)	Russia	11/09/2020	30/05/2021	NCT04540419	Active, not recruiting
Osaka University/AnGes/Takara Bio	Phase II/III	AnGes AG0302-COVID19	DNA	Japan	23/11/2020	02/04/2021	NCT04655625	Active, not recruiting
BioNTech/Pfizer/Fosun Pharma/Moderna/NIAID	Phase III	BNT162/mRNA-1273	RNA	Switzerland	19/04/2021	31/07/2022	NCT04805125	Active, not recruiting
Inovio Pharmaceuticals/International Vaccine Institute	Phase II/III	Inovio INO-4800	DNA	USA	30/11/2020	30/09/2022	NCT04642638	Active, not recruiting
Gamaleya Research Institute	Phase II/III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	Russia	06/07/2021	06/10/2022	NCT04954092	Recruiting
Moderna/NIAID	Phase II/III	Moderna mRNA-1273.211	RNA	USA	28/05/2021	05/06/2022	NCT04927065	Active, not recruiting
Moderna/NIAID	Phase III	Moderna mRNA-1273	RNA	USA	16/04/2021	26/08/2021	NCT04860297	Recruiting
Moderna/NIAID	Phase III	Moderna mRNA-1273	RNA	Canada	11/03/2021	13/06/2021	NCT04806113	Active, not recruiting
CureVac	Phase III	CureVac CVnCoV	RNA	Pending	14/05/2021	31/08/2021	NCT04838847	Not yet recruiting
Gamaleya Research Institute	Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Vector (non-replicating)	Belarus	28/09/2020	28/03/2021	NCT04564716	Active, not recruiting
University of Oxford/AstraZeneca/Gamaleya Research Institute	Phase III	Oxford ChAdOx1-S	Vector (non-replicating)	Russia	02/09/2020	11/05/2021	NCT04540393	Suspended
University of Queensland/CSL/Seqirus	Phase II/III	Queensland Sclamp	Protein subunit	Not applicable	15/12/2020	15/12/2020	NCT04806529	Withdrawn

mRNA vaccine

BNT162 b2

IMMUNOGENICITY AND SAFETY DATA

BioNTech/Pfizer

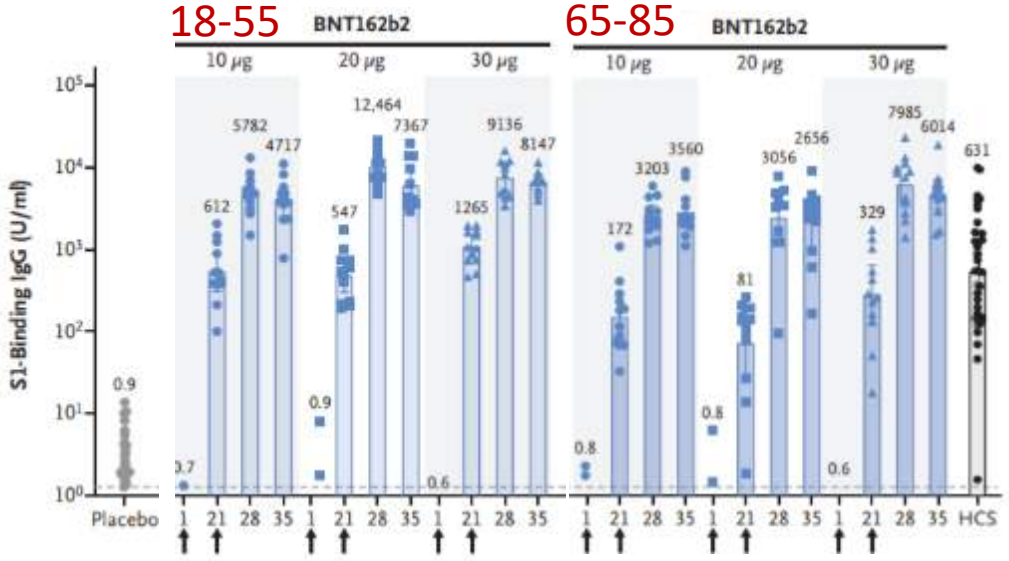
Phase I: NCT04368728

Study Designw	Phase I randomized controlled, dose-finding trial
Age range	18 – 55 or 65 – 85
Nb of participants	195
Nb of doses/route	2 (days 1/21)-IM
Vaccine groups	10 µg BNT162b2 (S) 18–55y (n = 12) 20 µg BNT162b2 (S) 18–55y (n = 12) 30 µg BNT162b2 (S) 18–55y (n = 12) 10 µg BNT162b2 (S) 65–85y (n = 12) 20 µg BNT162b2 (S) 65–85y (n = 12) 30 µg BNT162b2 (S) 65–85y (n = 12) *+BNT1621b (not used in Phase III)*
SAE	None
Local AE	Injection site pain, swelling
Systemic AE	Headache, fatigue, chills, muscle pain, fever, joint pain, diarrhoea

IMMUNOGENICITY 1/2

1. S1 specific binding responses

Assay: Luminex immunoassay
Units: Geometric mean concentration, U/mL (95% CI)



Antigen-binding IgG and virus-neutralizing responses to vaccination with 10 µg to 30 µg of BNT162b2 **boosted by the second dose** in both the younger adults and the older adults (**lower** antigen-binding **IgG in elderly** group)

Walsh EE et al. NEJM Oct 2020

mRNA vaccine

BNT162 b2

IMMUNOGENICITY AND SAFETY DATA

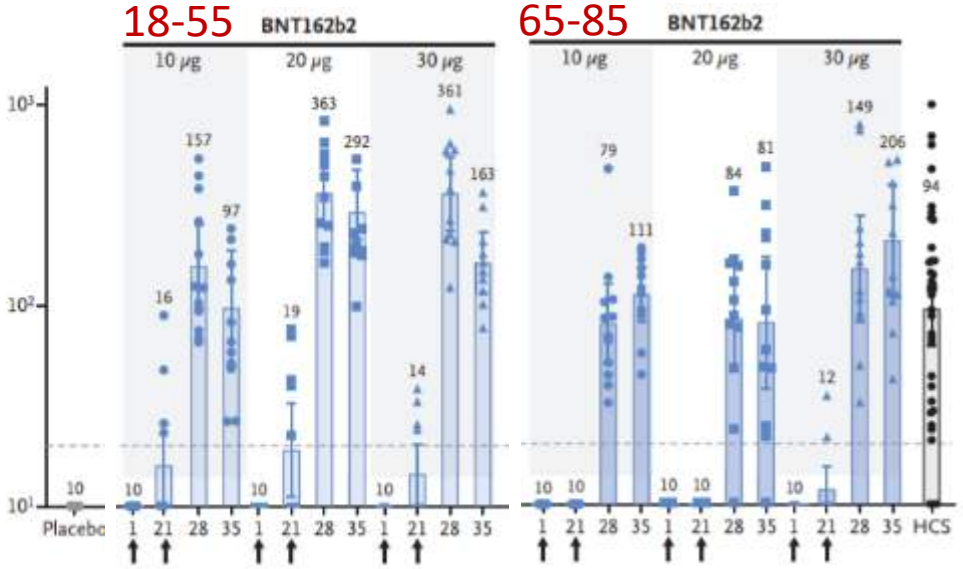
IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: SARS-CoV-2 virus neutralisation test (mNeonGreen reporter strain), 50% inhibitory dilution

Units: Geometric mean response, ID50 (95% CI)

The **50% neutralizing** at the 30-µg dose level on day 28 or day 35 ranged from **1.7 to 4.6 times the GMT of the convalescent serum panel** among participants **18 to 55** years of age and from 1.1 to 2.2 times the GMT of the convalescent serum panel among those **65 to 85** years of age.



Walsh EE et al. NEJM Oct 2020

mRNA vaccine

mRNA 1273

IMMUNOGENICITY AND SAFETY DATA

Moderna-NIH

Phase I: NCT04283461

Study Design	Phase I open-label, non-randomised, dose-finding trial
Age range	18 – 55
Nb of participants	45
Nb of doses/route	2 (days 1/29)-IM
Vaccine groups	25 µg (n = 15) 100 µg (n = 15) 250 µg (n = 15)
SAE	None
Local AE	Injection site pain *(67–100% at ds1, 77–100% at ds 2)*
Systemic AE	Headache *(20–47% at ds1, 23–100% at ds2)*, myalgia *(7–27% at ds1, 23–93% at ds2)*, chills *(8–86% at ds2)*, fatigue *(27–33% at ds1, 39–80% at ds2)*, fever *(0–57% at ds2)*, nausea *(0–47% at ds 2)*

IMMUNOGENICITY 1/2

1. GMHI* assay to spike protein in trial participants.

Assay: ELISA
Units: Geometric mean titre (95% CI)

Time Point	25-µg Group		100-µg Group		250-µg Group		Convalescent Serum	
	no.	GMT (95% CI)	no.	GMT (95% CI)	no.	GMT (95% CI)	no.	GMT (95% CI)
ELISA anti–S-2P							38	142,140 (81,543–247,768)
Day 1	15	116 (72–187)	15	131 (65–266)	15	178 (81–392)		
Day 15†	15	32,261 (18,723–55,587)	15	86,291 (56,403–132,016)	15	163,449 (102,155–261,520)		
Day 29	15	40,227 (29,094–55,621)	15	109,209 (79,050–150,874)	14	213,526 (128,832–353,896)		
Day 36	13	391,018 (267,402–571,780)	15	781,399 (606,247–1,007,156)	14	1,261,975 (973,972–1,635,140)		
Day 43	13	379,764 (281,597–512,152)	14	811,119 (656,336–1,002,404)	14	994,629 (806,189–1,227,115)		
Day 57	13	299,751 (206,071–436,020)	14	782,719 (619,310–989,244)	13	1,192,154 (924,878–1,536,669)		

Binding antibody IgG geometric mean titers (GMTs) to S protein: **seroconversion in all participants by day 15.**

A recent study shows that mRNA 1273 vaccine induces specific IgG responses and NAbs in adults older than 70 years of age. *(Anderson EJ, NEJM 2020)*

Jackson LA et al. *NEJM.* Jul 2020

COREB mission nationale Coordination Opérationnelle Risque Epidémique et Biologique

anrs MALADIES INFECTIEUSES ÉMERGENTES

mRNA vaccine

mRNA 1273

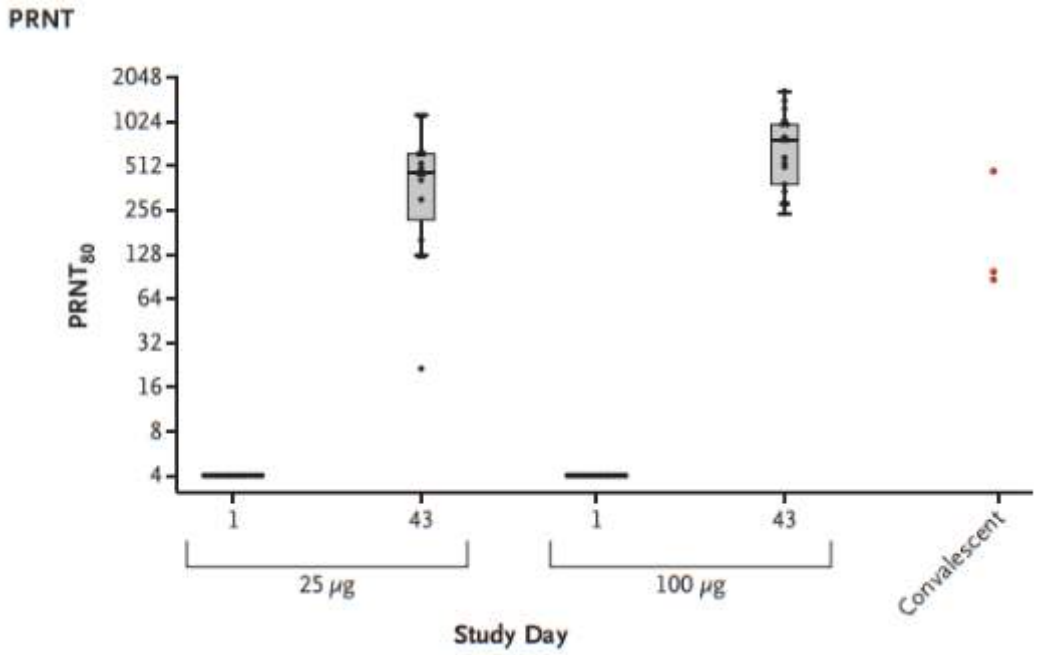
IMMUNOGENICITY AND SAFETY DATA

IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: Plaque-reduction neutralization test (80% inhibitory dilution)
Units: Geometric mean response, ID80 (95% CI)

At day 43, **wild-type virus–neutralizing activity capable of reducing SARS-CoV-2 infectivity by 80%** or more ($PRNT_{80}$) detected in all participants, with geometric mean $PRNT_{80}$ responses of 339.7 (95% CI, 184.0 to 627.1) in the 25-µg group and 654.3 (95% CI, 460.1 to 930.5) in the 100-µg group



3. Cellular responses: 25-µg and 100-µg doses elicit CD4 T-cell responses **biased toward expression of Th1** cytokines (TNFα > IL2> IFNγ).

Adenoviral vector vaccine

AZD1222

IMMUNOGENICITY AND SAFETY DATA

AstraZeneca-Oxford University

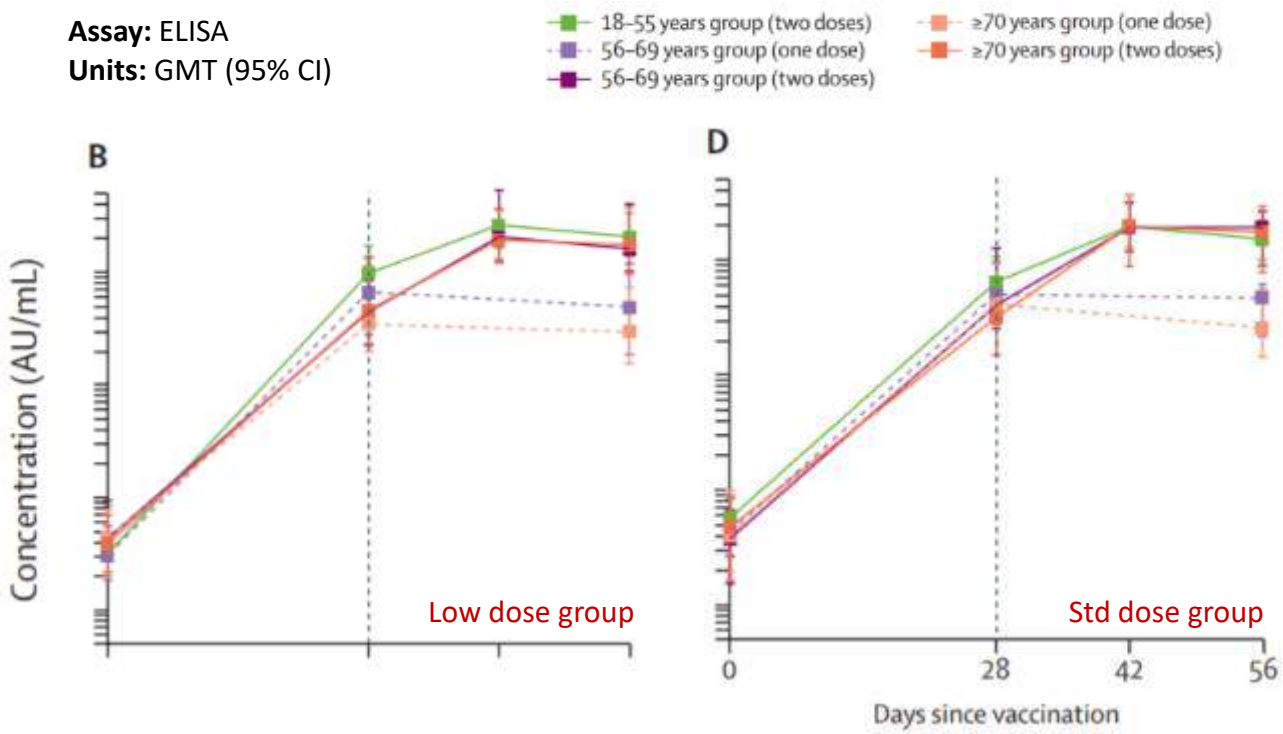
Phase II: NCT04400838

Study Design	Phase II randomised controlled trial
Age range	1: 18–55; 2: 56–69; 3: ≥70
Nb of participants	560
Nb of doses/route	1 (day 0) or 2 (days 0/28)- IM
Vaccine groups	18–55y: 2 x low dose (n = 50) 56–69y: 1 x low dose (n = 30) 56–69y: 2 x low dose (n = 30) ≥70y: 1 x low dose (n = 50) ≥70y: 2 x low dose (n = 50) 18–55y: 2 x std dose (n = 50) 56–69y: 1 x std dose (n = 30) 56–69y: 2 x std dose (n = 30) ≥70y: 1 x std dose (n = 50) ≥70y: 2 x std dose (n = 50) **Control group:** MenACWY (n = 534)
SAE	13 serious adverse events have occurred none of which are considered related to either study vaccine as assessed by the investigators *(Ph III trial suspended and resumed in Sep 2020 due to 2 cases of tranverse myelitis among participants, found not to be related to vaccination)*
Local AE	Tenderness, injection site pain; reported for participants who received 2 doses of vaccine; adverse events were less frequent in older adults (≥56y)
Systemic AE	Fatigue, headache, muscle ache, malaise, feverish, chills, joint pain; reported for participants who received 2 doses of vaccine; adverse events were less frequent in older adults (≥56y)

IMMUNOGENICITY 1/2

1. SARS-CoV-2 IgG response to spike protein

Assay: ELISA
Units: GMT (95% CI)



Total IgGs against the Spike protein **were similar in all age groups regardless the dose.**
Responses at day 28 **decreased with increasing age** (low: 18–55 years, median 6439[AU]/mL; 56–69 years, 4553 AU/mL; ≥70 years, 3565 AU/mL. Std: 18–55 years, median 9807 AU/mL; 56–69 years, 5496 AU/mL; ≥70 years, 4156 AU/mL)

Ramasamy MN *et al*. Lancet Nov 2020

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Adenoviral vector vaccine

AZD1222

IMMUNOGENICITY AND SAFETY DATA

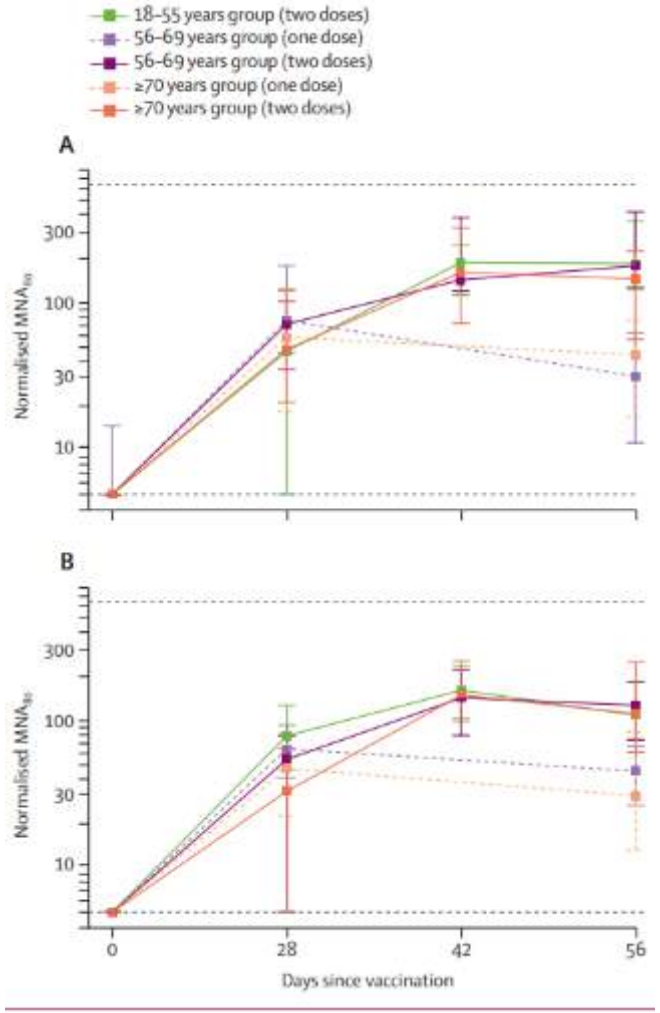
IMMUNOGENICITY 2/2

2. Live SARS-CoV-2 microneutralisation assay (MNA_{80})

Assay: Microneutralisation test (80% inhibitory dilution) tion)
Units: Median titre, ID80 (IQR)

Neutralizing antibody responses: Median titres peaked by day 42 in groups receiving two vaccinations.

There are **no significant differences** in normalized titers **between age groups at day 42** (low: 18–55 years, median 161; 56–69 years, 143; ≥70 years, 150. Std: 18–55 years, median 193; 56–69 years, 144; and ≥70 years, 161.



3. Induction of T cell responses and increase of IFN-γ expression

IFN-γ ELISpot responses against SARS-CoV-2 spike protein peaked 14 days after the prime vaccination

Ramasamy MN *et al*. Lancet Nov 2020

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Adenoviral vector vaccine

Sputnik V

IMMUNOGENICITY AND SAFETY DATA

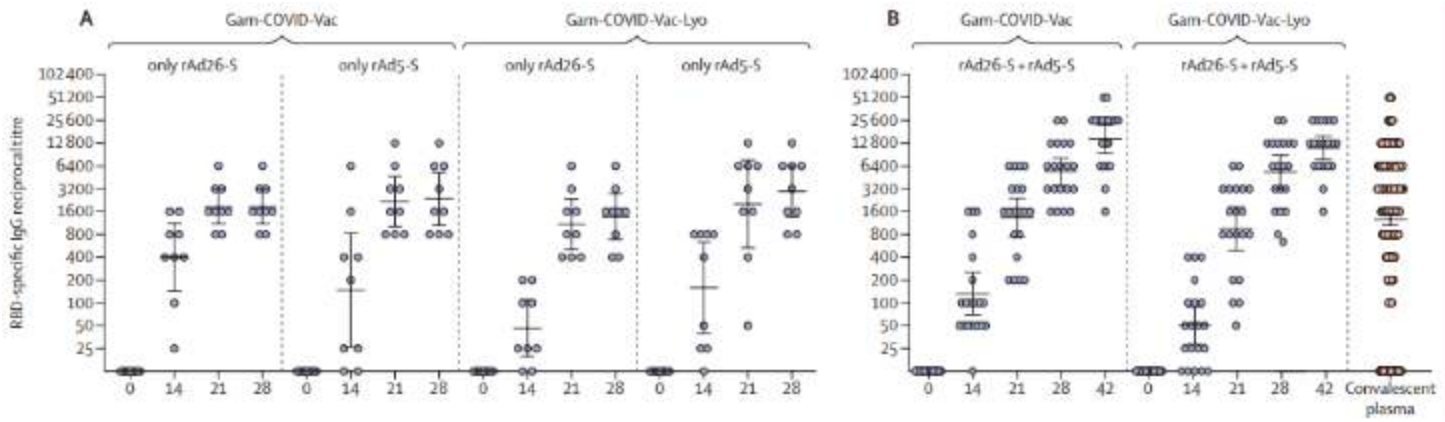
Phase I/II: NCT04436471 *(frozen product)*
NCT04437875 *(lyo product)*

Study Design	Phase I/II open-label, non-randomised trial
Age range	18 – 60
Nb of participants	76
Nb of doses/route	1 (day 0) or 2 (rAd26 on day 0, rAd5 on day 21) -IM
Vaccine groups	Frozen 1 x 10^{11} rAd26 (n = 9) Frozen 1 x 10^{11} rAd5 (n = 9) Frozen 10^{11} rAd26/10^{11} rAd5 (n = 20) Lyo 1 x 10^{11} rAd26 (n = 9) Lyo 1 x 10^{11} rAd5 (n = 9) Lyo 10^{11} rAd26/10^{11} rAd5 (n = 20)
SAE	None
Local AE	Injection site pain *(40–78%)*
Systemic AE	Changes in laboratory variables *(67–100%),* hyperthermia *(11–100%),* headache *(25–67%),* asthenia *(0–55%),* muscle or joint pain *(11–33%),* subjective heartbeat palpitation *(0–33%)*

IMMUNOGENICITY 1/2

1. SARS-CoV-2 RBD-specific IgGs

Assay: ELISA
Units: Geometric mean titre (95% CI)



Anti-RBD IgG responses detected **from day 14** for both products and in all vaccine administration schemes . At **day 21** RBD-specific IgGs were detected in **100% of vaccinated** participants. ([GMT] 1629 with the frozen formulation and 951 with the lyophilized one). **Heterologous boosting** with rAd5-S led to an **increase in SARS-CoV-2 RBD specific IgG** titres; 7 days after boost.

Logunov DY et al *Lancet*. Sep 2020

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Adenoviral vector vaccine

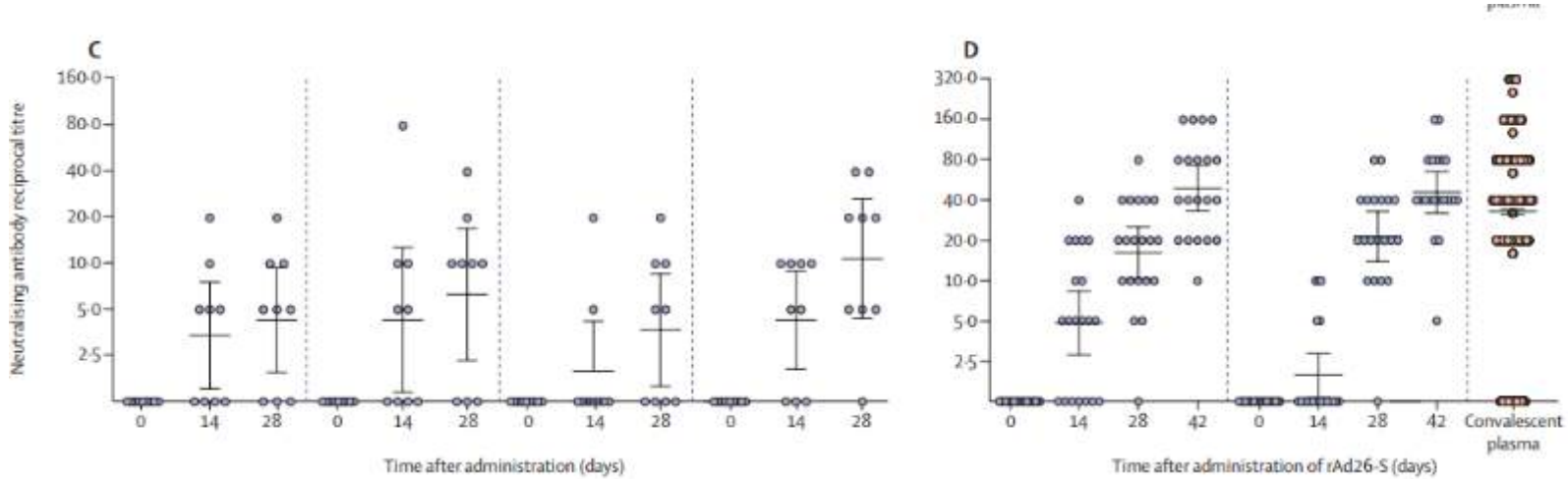
Sputnik V

IMMUNOGENICITY AND SAFETY DATA

IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: Microneutralisation assay (50% inhibitory dilution, Vero E6 cells)
Units: Geometric mean titre, ID50 (95% CI)



Administration of **both rAd26-S and rAd5-2** led to production of **neutralizing antibodies in 100% of participants**, whereas administration of only rAd26-S led to a lower seroconversion rate

3. T cell response: induction of **CD4+** and **CD8+** cells and an increase in the concentration of **interferon-γ secretion**

Logunov DY et al *Lancet*. Sep 2020

Adenoviral vector vaccine

Ad26COVS1

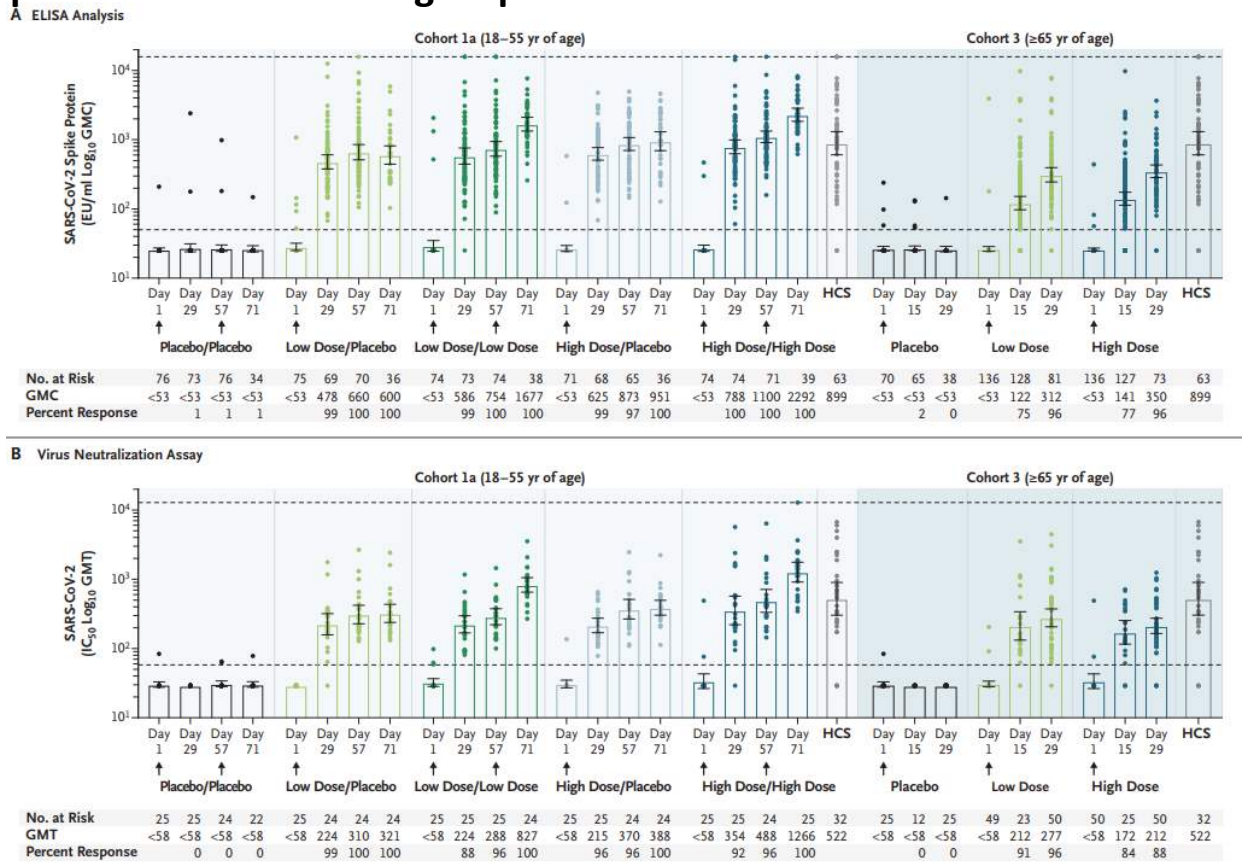
IMMUNOGENICITY AND SAFETY DATA

Janssen Pharmaceuticals

Phase I/IIa: NCT04436276

Study Design	Phase I/IIa randomised controlled trial
Age range	18 – 55; ≥65
Nb of participants	805
Nb of doses/route	1 (day 1) or 2 (day 1 and 57) ; IM
Vaccine groups	18–55y : low dose at d1/57 (n = 75) 18–55y : low dose at d1 (n = 75) 18–55y : high dose at d1/57 (n = 75) 18–55y : high dose at d1 (n = 75) 18–55y : low dose at d1/57 (n = 5) 18–55y : low dose at d1 (n = 5) 18–55y : high dose at d1/57 (n = 5) 18–55y : high dose at d1 (n = 5) ≥65y : low dose at d1/57 (n = 75) ≥65y : low dose at d1 (n = 75) ≥65y : high dose at d1/57 (n = 75) ≥65y : high dose at d1 (n = 75)
SAE	1SAE, participant recovered within 24h
Local AE	Injection site pain
Systemic AE	Fatigue, headache, myalgia, pyrexia (fever), nausea

Spike protein and neutralizing responses



A single dose of Ad26.COV2.S elicited a strong humoral response, with the presence of S-binding and neutralizing antibodies in more than **90% of the participants**, regardless of either age group or vaccine dose.

At **day 71** after the first dose, antibody titers **further increased and stabilized**

Sadoff J et al.; NEJM 2020, Jan 2021

Protein Subunit vaccine

NVX-COV-2373

IMMUNOGENICITY AND SAFETY DATA

NOVAVAX

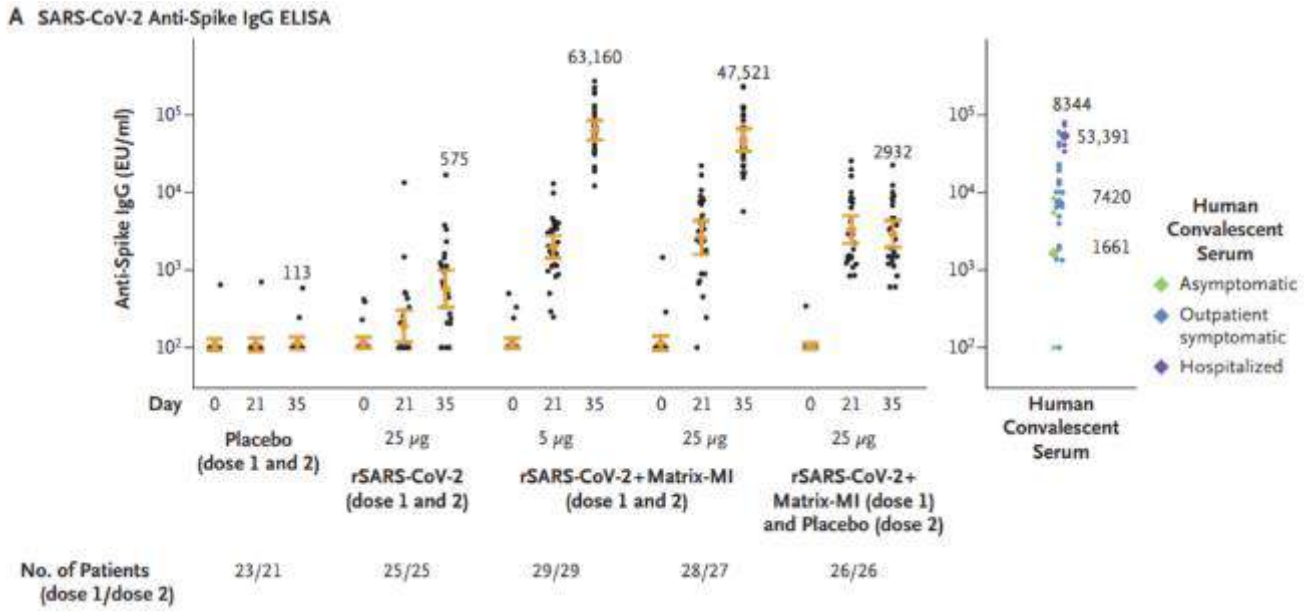
Phase I: NCT04368988

Study Design	Phase I randomised controlled, dose-finding trial
Age range	18 – 59
Nb of participants	131
Nb of doses/route	1 (day 0) or 2 (days 0/21) - IM
Vaccine groups	2 x 25 µg (n = 25) 2 x 5 µg + 50 µg Matrix-M1 (n = 28) 2 x 25 µg + 50 µg Matrix-M1 (n = 28) 1 x 25 µg + 50 µg Matrix-M1 (n = 25) 2 x 5 µg and 2 x 25 µg included 3 sentinel participants who were vaccinated in an open-label manner and observed for reactogenicity **Control group:** 0.9% saline placebo (n = 25)
SAE	None
Local AE	Tenderness *(20–65% at ds1, 12–81% at ds2)*, injection site pain *(24–54% at ds1, 8–63% at ds 2)*
Systemic AE	Headache *(23–40% at dose 1, 28–58% at dose 2),* muscle pain/myalgia *(12–32% at dose 1, 8–54% at dose 2)*, fatigue *(16–40% at dose 1, 12–50% at dose 2)*, malaise *(4–28% at dose 1, 8–38% at dose 2),* joint pain *(4–27% at dose 2)*

IMMUNOGENICITY 1/2

1. SARS-CoV-2 Anti-Spike IgGs

Assay: ELISA
Units: Geometric mean titre (95% CI)



By day 21 after 1st vaccination, **IgG specific responses** occurred for all adjuvant regimens (**10-fold of non adjuvant).** IgGs concentrations **further increased after 2nd dose** vaccination (day 29 and day 35)

Keech C et al. *NEJM.* Sep 2020

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Protein Subunit vaccine

NVX-COV-2373

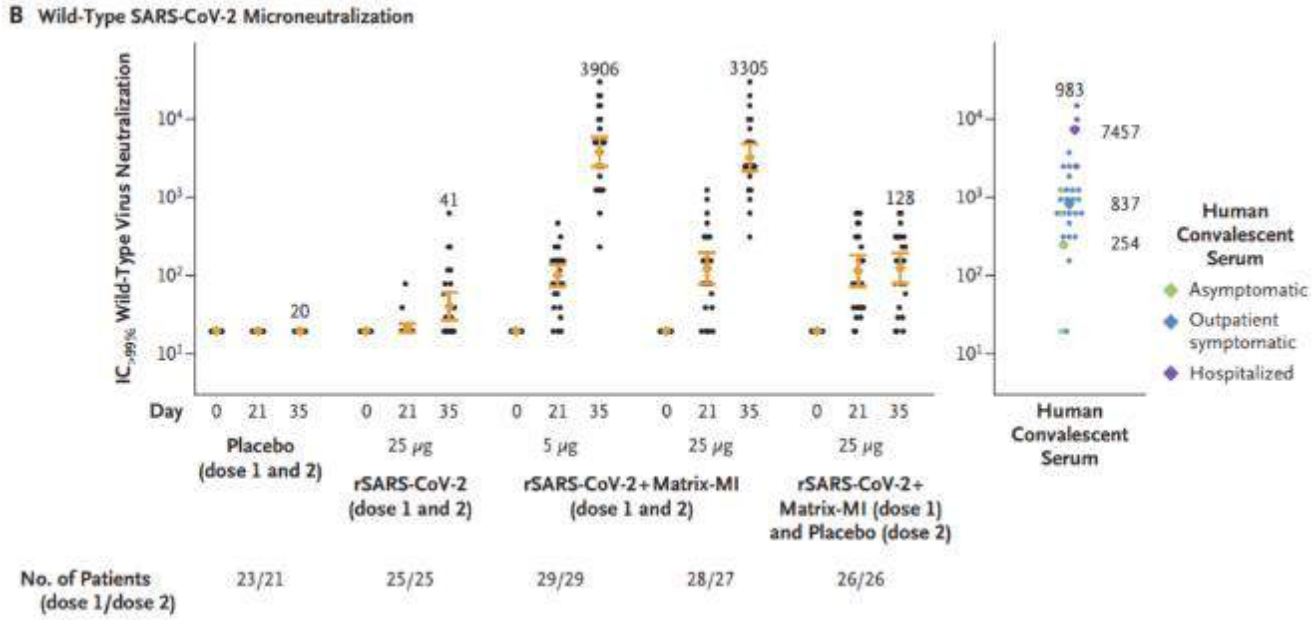
IMMUNOGENICITY AND SAFETY DATA

IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: Microneutralisation assay (99% inhibitory dilution, Vero E6 cells)
Units: Geometric mean titre, ID99 (95% CI)

Two doses of adjuvant vaccine induced an increase on the concentration of neutralizing antibodies more than **100 times greater** than single vaccinations without adjuvant.



3. Induction of T-cell responses: antigen-specific induction of CD4+ T-cell responses A strong bias toward this Th1 phenotype observed

Keech C et al. *NEJM.* Sep 2020

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Heterologous vaccination regimen

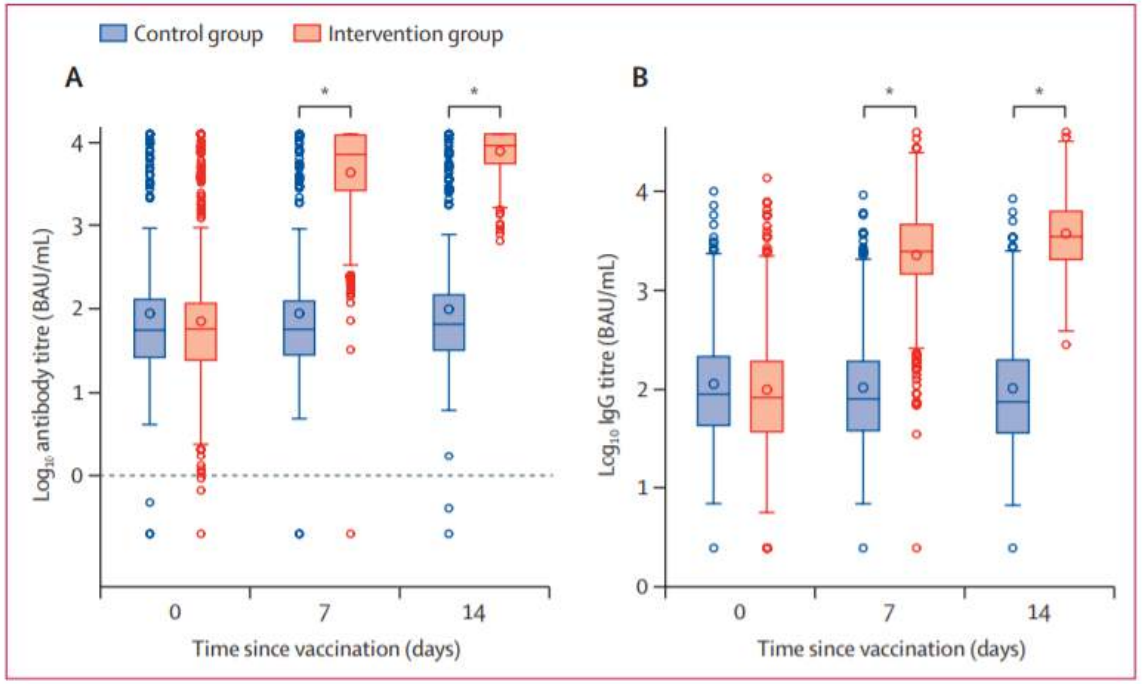
Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS)

Methods:

- Phase 2 open-label, randomised, controlled trial
- Participants: 676 adults aged 18–60 years vaccinated with a single dose of ChAdOx1-S 8–12 weeks before screening, and no history of SARS-CoV-2 infection.
- Participants were randomly assigned (2:1) to receive either BNT162b2 (one single injection) or continue observation (control group).
  - intervention group (n=450)
  - control group (n=226)

Primary outcome: 14-day immunogenicity

SAFETY: Reactions were mild (68%) or moderate (30%), (injection site pain, induration, headache and myalgia) No serious adverse events were reported.



IMMUNOGENICITY

Intervention group: GMT of RBD antibodies increased from 71.46 BAU/mL (95% CI 59·84–85·33) at baseline to 7756.68 BAU/mL (7371·53–8161·96) at day 14.

Vaccine Summary results on immunogenicity

Vaccine & Developer	Phase III regimen	Specific IgG titers (14 - 28 days after 2nd dose) *as per Phase I or II published results*	NAb titers (14 - 28 days after 2nd dose) *as per Phase I or II published results*
BNT162b2 BioNTech – Pfizer – Fosun Pharma	2 doses (d1 and d22) 30µg/dose	8147 GMT *Test: Luminex anti S1 IgG*	163 GMT *Test: $wtVNA_{50}$*
mRNA-1273 Moderna – NIAID	2 doses (d1 and d29) 100µg/dose	782 719 GMT *Test: ELISA anti S IgG*	654.3 GMT *Test: $PRNT_{80}$*
Ad5-nCoV CanSino Biologicals Inc –Beijing Institute of Biotechnology	1 dose $5x10^{10}$ vp	571.0 GMT *Test: ELISA anti RBD IgG*	18.3 GMT *Test: WT virus neutralization*
SputnikV Gamaleya Research Institute	d1 0,5 mL rAd26 d21 0,5 mL rAd5	14 703 GMT *Test: ELISA anti RBD IgG*	49.25 GMT *Test: MNA_{50}*
Ad26COVS1 Janssen Pharmaceutical Companies Beth Israel Deaconness Medical Center	1 dose $5x10^{10}$ vp	478 GMC *Test: ELISA anti S IgG*	224 GMT *Test: MNA_{50}*
ChAdOx1 nCoV-19 University of Oxford – AstraZeneca	2 doses (d1 and d29) $5x10^{10}$ vp	639 EU *Test: ELISA anti S IgG*	136 MT *Test: MNA_{80}*
NVX COV2373 Novavax	2 doses (d0 and d28) 25µg+Matrix M/ dose	47 521 GMEU *Test: ELISA anti S IgG*	3305 GMT *Test: MNA_{99}*
CoronaVac Sinovac – Institut Butantan	2 doses (d1 and d14)	1094,3 GMT *Test: ELISA anti RBD IgG*	27,6 GMT *Test: Micro cytopathic effect assay*
BBIBP-CorV Beijing Inst. Biological Products –Sinophram	2 doses (d0 and d21)	*Not reported*	219,9 GMT *Test: MNA_{50}*
SARS-CoV-2 Vaccine Wuhan Inst. Biological products– Sinopharm	2 doses (d0 and d21)	215 GMT *Test: ELISA anti S IgG*	247 GMT *Test: $PRNT_{50}$*

NOTE:

COMPARISONS SHOULD NOT BE MADE AS ASSAYS ARE NOT STANDARDIZED

VACCINE EFFICACY DATA

First data regarding vaccine efficacy has been made public by the means of **PRESS RELEASES** by pharmaceutical companies

Date of Press release	Company	Vaccine	Analysis
November 9th 2020	BioNTech/Pfizer	BNT162b2	1st interim analysis; 28 days after 1st dose 94 confirmed cases of COVID19 • **> 90% Efficacy**
November 11th 2020	Gamaleya	Sputnik V	1st interim analysis; 21 days after 1st dose 20 confirmed cases of COVID19 • **> 92% Efficacy**
November 16th 2020	Moderna	mRNA 1273	1st interim analysis; 42 days after 1st dose 95 confirmed cases of COVID19 • **94.5% Efficacy**
November 18th 2020	BioNTech/Pfizer	BNT162b2	**Final analysis**; 28 days after 1st dose 170 confirmed cases of COVID19 • **95% Efficacy**
November 23rd 2020	AstraZeneca/Oxford	AZD1222	**1st interim analysis** 14 days after 2nd dose 131 confirmed cases of COVID19 • **90% Efficacy when given as half dose/full dose** • **62% Efficacy when given as full dose/full dose** • **Overall 70% efficacy**
November 24th 2020	Gamaleya	Sputnik V	**2nd interim analysis**; 42 days after 1st dose 39 confirmed cases of COVID19 *(10 severe)* • **95% Efficacy**
November 30th 2020	Moderna	mRNA 1273	**Final analysis**; 42 days after 1st dose 196 confirmed cases of COVID19 *(30 severe)* • **94.1% Efficacy**

VACCINE EFFICACY DATA

First data regarding vaccine efficacy has been made public by the means of **PRESS RELEASES** by pharmaceutical companies

Date of press release	Company	Vaccine	Analysis
January 28th 2021	NOVAVAX	NVX-COV2373:	1st interim analysis; Onset of COVID 7 days after 2nd dose 28 days after 1st dose (one dose vaccine) 62 confirmed cases of COVID19 (56 on the placebo group) • Efficacy by strain was calculated to be **95.6% against the original COVID-19** strain and **85.6% against the UK variant strain**
January 29th 2021	Janssen	Ad26COVS1	1st interim analysis 28 days after vaccination (one dose) Etude multinational ENSEMBLE. • **72% Effective** in the US and **66% Effective** Overall at Preventing Moderate to Severe COVID-19 • **85% Effective** overall in preventing severe disease. • **Complete protection** against COVID-19 related Hospitalisation and Death • Protection against the SARS-CoV-2 Variant from the B.1.351 Lineage Observed in South Africa
February 2nd 2021	Sinovac	CoronaVac	1st interim analysis; 14 days after 2nd dose vaccination 253 confirmed cases of COVID19 Efficacy rate against diseases caused by COVID-19 for: • **all** cases: **50.65%** • cases requiring **medical treatment:** 83.70% **hospitalized, severe** and **fatal** cases: **100%** Efficacy by strain: • **85.6%** against the **UK variant** strain

mRNA vaccine

BNT162 b2

EFFICACY AND SAFETY DATA

- Efficacy data from ongoing double blind, randomized phase III trial across Argentina, Brazil, South Africa and USA (43 548 participants randomized 1:1)
- Two 30 µg doses of BNT162b2 vaccine, 21 days apart
- **Inclusion criteria:** healthy adults or stable chronic medical conditions, including HIV, HBV or HCV aged of 16y or more.
- **Exclusion criteria:** medical history of Covid-19, treatment with immunosuppressive therapy, or diagnosis with an immunocompromising condition
- Primary **efficacy** endpoint: efficacy of BNT162b2 against confirmed Covid-19 with onset at least 7 days after the second dose
- Primary **safety** end points: solicited, specific local or systemic adverse events and use of antipyretic or pain medication within 7 days after the receipt of each dose

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)

* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

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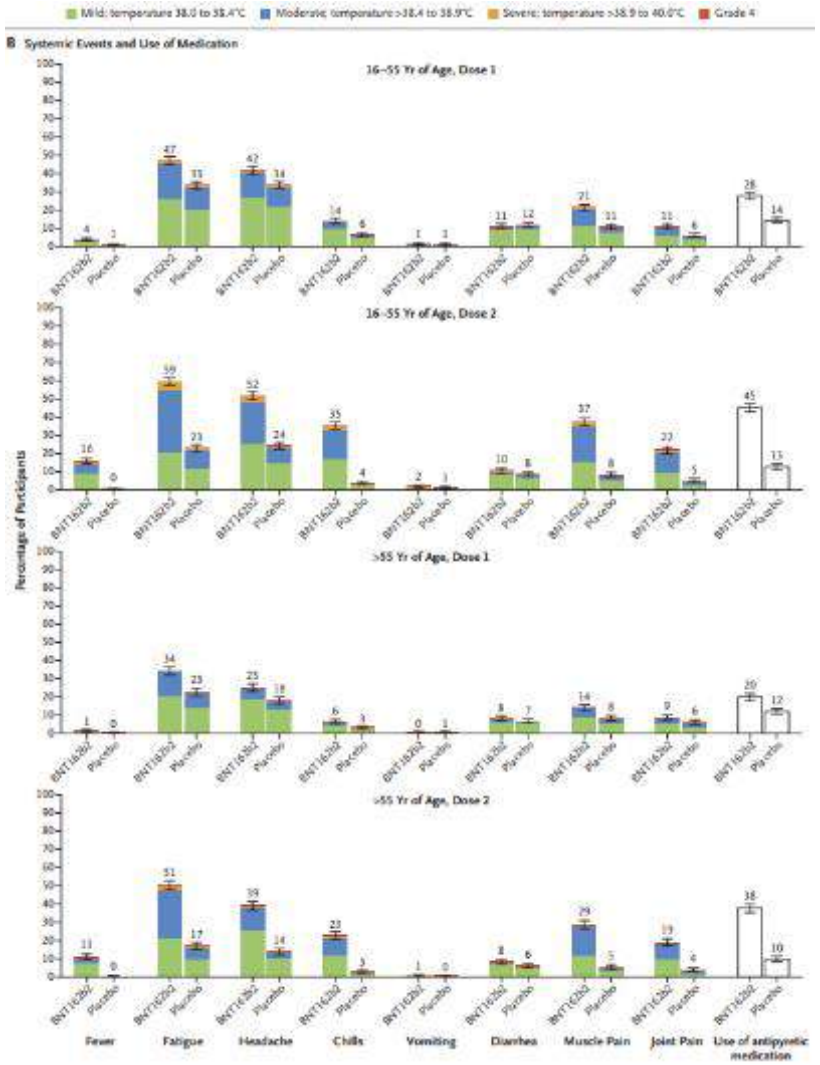
Polack FP *et al. NEJM* Dec 2020

MALADIES INFECTIEUSES ÉMERGENTES

mRNA vaccine

BNT162 b2

EFFICACY AND SAFETY DATA



- The BNT162b2 vaccine is reactogenic, but the side effects remain acceptable in all populations studied.
- The short-term safety profile of the BNT162b2 vaccine is characterized by mild to moderate pain at the injection site, fatigue and headache. These manifestations disappear after 24 to 48 hours.
- The only grade 3 adverse events with a frequency greater than 2% after the second vaccine administration are fatigue (97/2405 participants; 4.6%) and headache (7/2015; 3.2%).
- No grade 4 adverse side effects observed.

Six deaths were reported during the clinical trials, including four in the placebo group, but no relation with vaccination was found.

<u>Limits :</u>

Just 2 month follow up safety data

Data for over 75 is scarce and absent for children, pregnant women or immunocompromised

Polack FP *et al. NEJM* Dec 2020

mRNA vaccine

BNT162 b2

EFFICACY AND SAFETY DATA

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 (1,7411)	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

TOTAL OF CASES: 170

- 8 in the BNT162b2 group/162 in the Control
- 10 severe cases, 9 within the Placebo group

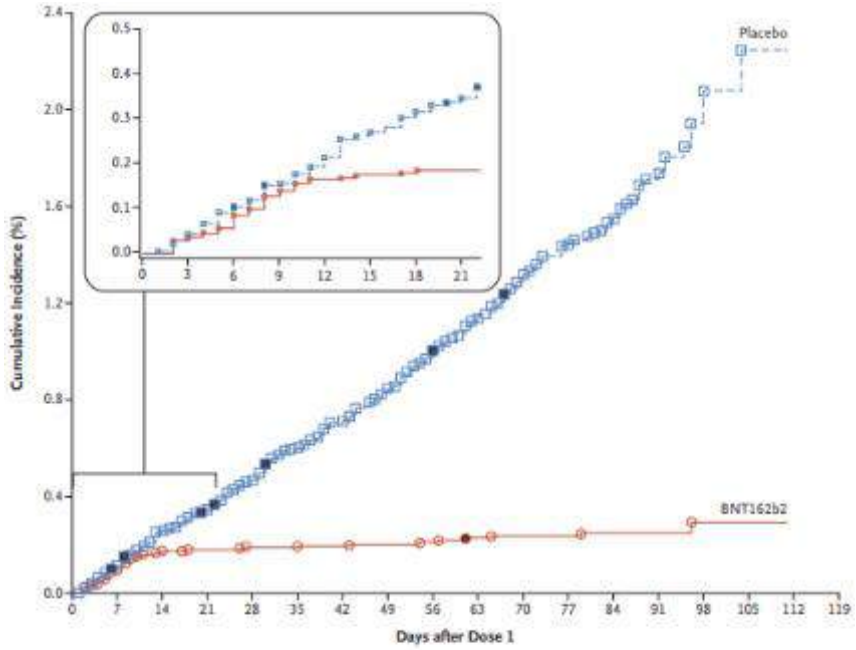
Vaccine efficacy: 95%

Limits:

Efficacy measured in symptomatic patients

No evidence of an potential effect against viral shedding

- Protection occurs as early as the second week after the first vaccine administration, with an increase of protection level up to 95% after the second administration



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669) No. of participants	BNT162b2, 30 μg (N=21,669) Surveillance time person-yr (no. at risk)	Placebo (N=21,686) No. of participants	Placebo (N=21,686) Surveillance time person-yr (no. at risk)	VE (95% CI) percent
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)

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Polack FP *et al. NEJM* Dec 2020

anRS MALADIES INFECTIEUSES ÉMERGENTES

mRNA vaccine

mRNA 1273

EFFICACY AND SAFETY DATA

- Efficacy data from Phase III blinded, randomized, controlled trials at 99 US sites
- 2 doses of 100 µg of mRNA 1273 or placebo 28 days apart
  - 30 420 participants randomized (1:1)
  - >96% received 2nd dose
- Inclusion criteria: healthy adults aged of 18y or more with no history of SARS CoV 2 and high risk of severe COVID19

Primary endpoint: efficacy of the mRNA-1273 vaccine in preventing a first occurrence of symptomatic Covid-19 with onset at least 14 days after the second injection (virologically confirmed, symptomatic COVID-19: positive swab combined with at least two qualifying symptom)

Secondary end point: efficacy of mRNA-1273 in the prevention of severe Covid-19

Safety assessments: monitoring of solicited local and systemic adverse events for 7 days after each injection; unsolicited adverse reactions for 28 days after each injection

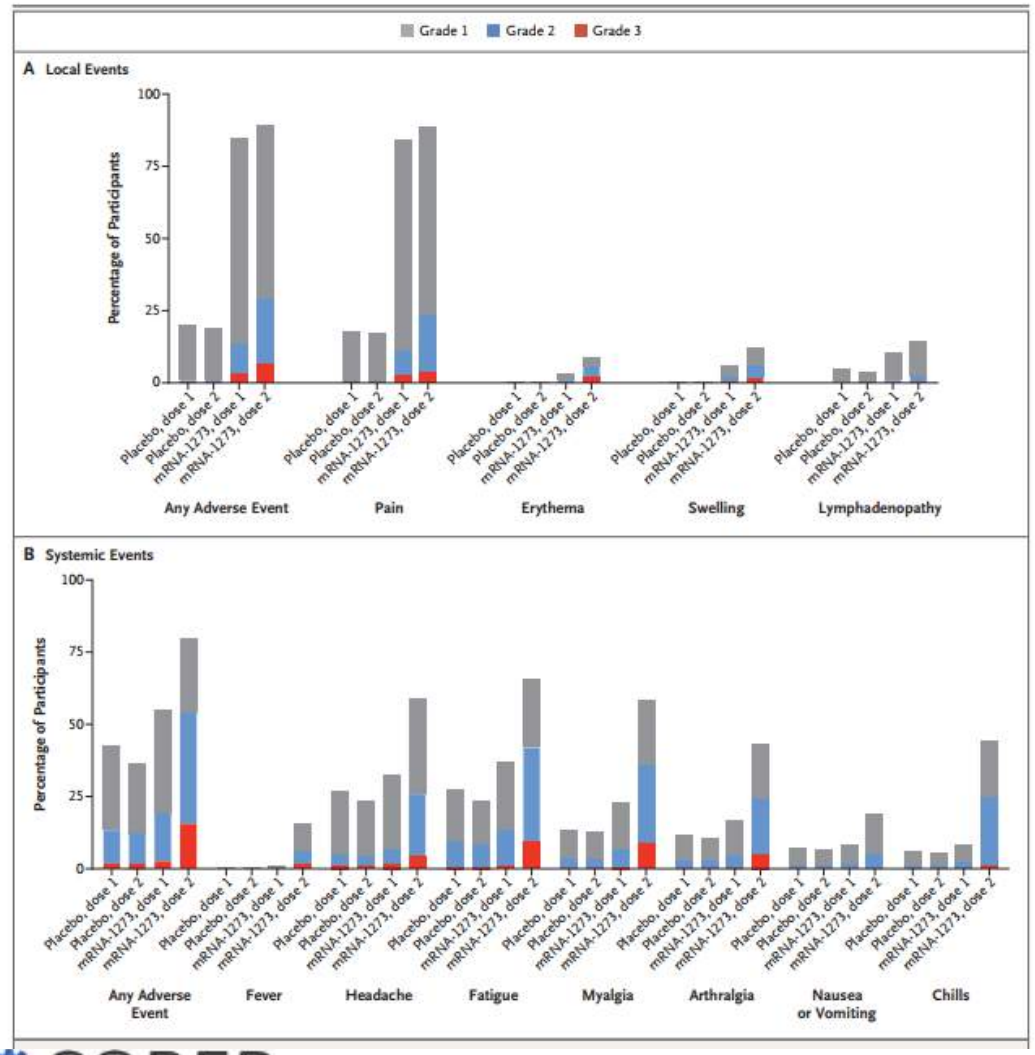
Table 1. Demographic and Clinical Characteristics at Baseline.*

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)
Baseline SARS-CoV-2 status — no. of participants (%)§			
Negative	14,598 (96.2)	14,550 (95.8)	29,148 (96.0)
Positive	337 (2.2)	343 (2.3)	680 (2.2)
Missing data	235 (1.5)	288 (1.9)	523 (1.7)
Baseline RT-PCR test — no. of participants (%)			
Negative	14,923 (98.4)	14,917 (98.3)	29,840 (98.3)
Positive	95 (0.6)	87 (0.6)	182 (0.6)
Missing data	152 (1.0)	177 (1.2)	329 (1.1)
Baseline bAb anti–SARS-CoV-2 assay — no. of participants (%)			
Negative	14,726 (97.1)	14,690 (96.8)	29,416 (96.9)
Positive	303 (2.0)	305 (2.0)	608 (2.0)
Missing data	141 (0.9)	186 (1.2)	327 (1.1)
Risk factor for severe Covid-19 — no. of participants (%)			
Chronic lung disease	744 (4.9)	710 (4.7)	1,454 (4.8)
Significant cardiac disease	744 (4.9)	752 (5.0)	1,496 (4.9)
Severe obesity	1,021 (6.7)	1,025 (6.8)	2,046 (6.7)
Diabetes	1,440 (9.5)	1,435 (9.5)	2,875 (9.5)
Liver disease	96 (0.6)	100 (0.7)	196 (0.6)
Human immunodeficiency virus infection	87 (0.6)	92 (0.6)	179 (0.6)

mRNA vaccine

mRNA 1273

EFFICACY AND SAFETY DATA



- **Solicited adverse events at the injection site:** more frequent in the mRNA-1273 group after both the 1st (84.2%, vs. 19.8%) and the 2nd dose (88.6%, vs. 18.8%). Mainly grade 1 or 2
- **Solicited systemic adverse events:** more often in the mRNA-1273 group after both the 1st (54.9%, vs. 42.2%) and the 2nd dose (79.4%, vs. 36.5%). Increase proportions of grade 2 and 3 events after 2nd Dose (from 16.5% vs 38.1% and from 2.9% to 15.8%).
- Both solicited injection-site and systemic adverse events were more common among younger participants (18 to <65y) than among older participants (≥65 y)
- The frequency **of unsolicited adverse events, unsolicited severe adverse events, and serious adverse events** 28 days after injection similar among age groups
- **Hypersensitivity reactions** reported in 1.5% and 1.1% of participants in the vaccine and placebo groups. 3 **Bell's palsy** in the vaccine group and 1 in the placebo group
- 5 deaths, including 3 in the mRNA 1273 group with no link to vaccine

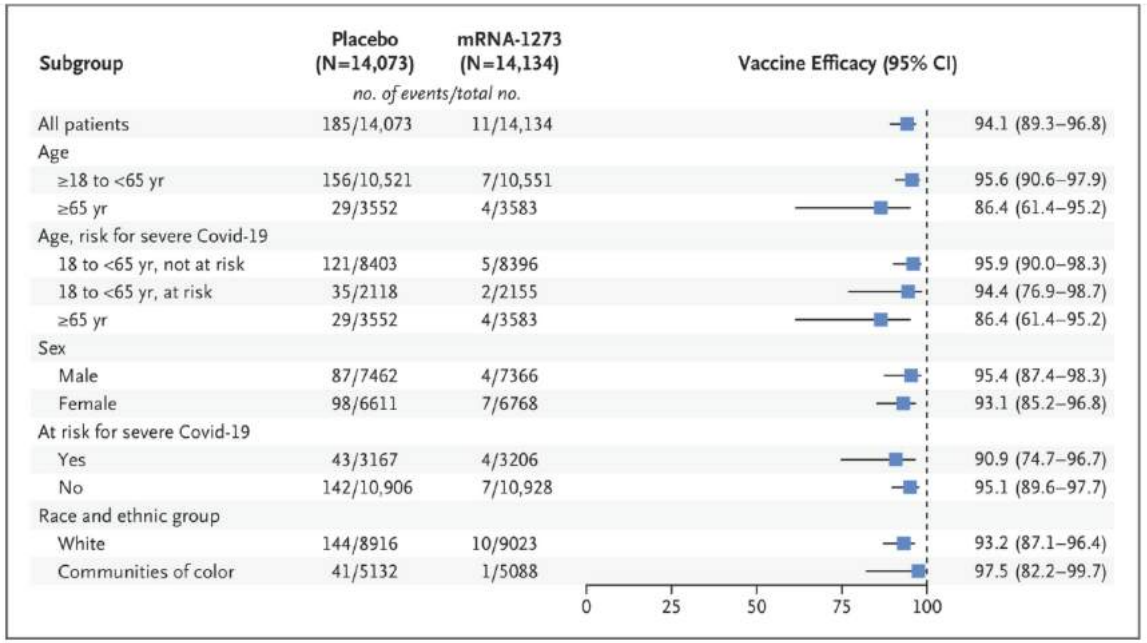
Key limitations: short duration of safety and efficacy follow-up

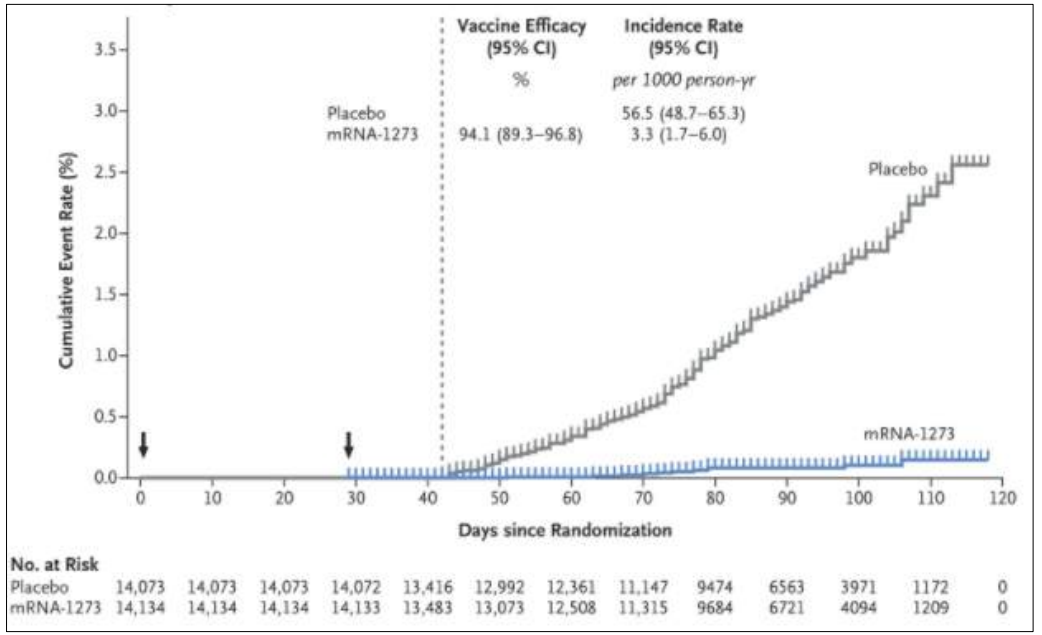
mRNA vaccine

mRNA 1273

EFFICACY AND SAFETY DATA

Subgroup	Placebo (N=14,073)	mRNA-1273 (N=14,134)	Vaccine Efficacy (95% CI)
	no. of events/total no.		
All patients	185/14,073	11/14,134	94.1 (89.3–96.8)
Age			
≥18 to <65 yr	156/10,521	7/10,551	95.6 (90.6–97.9)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Age, risk for severe Covid-19			
18 to <65 yr, not at risk	121/8403	5/8396	95.9 (90.0–98.3)
18 to <65 yr, at risk	35/2118	2/2155	94.4 (76.9–98.7)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Sex			
Male	87/7462	4/7366	95.4 (87.4–98.3)
Female	98/6611	7/6768	93.1 (85.2–96.8)
At risk for severe Covid-19			
Yes	43/3167	4/3206	90.9 (74.7–96.7)
No	142/10,906	7/10,928	95.1 (89.6–97.7)
Race and ethnic group			
White	144/8916	10/9023	93.2 (87.1–96.4)
Communities of color	41/5132	1/5088	97.5 (82.2–99.7)





TOTAL OF CASES: 196

- 11 in the mRNA 1273 group /185 in the placebo group
- 30 severe cases all within the placebo group

Vaccine efficacy: 94.1% (100% protection against severe cases)

data not sufficient to assess asymptomatic infection

Limits: efficacy tested in a setting of national recommendations for masking and social distancing, which may have translated into lower levels of infectious inoculum.

Adenoviral vector vaccine

AZD1222

EFFICACY AND SAFETY DATA

- Efficacy data from ongoing blinded, randomized, controlled trials across UK and Brazil
  - **COV 002:**Phase II/III study in UK. Two dosage groups:
    - LD/SD: prime **$2{,}2\times10^{10}$** vp; boost **5×10^{10}** vp at **28 days**
    - SD/SD: prime **5×10^{10}** vp; boost **5×10^{10}** vp at **28 days**
  - **COV 003:**Phase III study in Brazil. Dosage:
    - SD/SD: prime/boost **$3{\cdot}5–6{\cdot}5\times10^{10}$** vp up to **12 weeks** apart (target 4 weeks)
- **Inclusion criteria:** healthy adults aged of 18y or more.
  - **COV 002:** healthy adults
  - **COV 003:** healthy and stable pre-existing health conditions individuals
- **Main outcome**: virologically confirmed, symptomatic COVID-19 (positive swab combined with at least one qualifying symptom)
- The interim **efficacy** is assessed by **combining data from COV002 and COV003**

	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)
Age, years						
18–55	1367 (100·0%)	1374 (100·0%)	1879 (79·0%)	1922 (79·1%)	1843 (89·3%)	1833 (90·5%)
56–69	0	0	285 (12·0%)	293 (12·1%)	209 (10·1%)	187 (9·2%)
≥70	0	0	213 (9·0%)	215 (8·8%)	11 (0·5%)	5 (0·2%)
Sex						
Female	886 (64·8%)	927 (67·5%)	1378 (58·0%)	1437 (59·1%)	1261 (61·1%)	1156 (57·1%)
Male	481 (35·2%)	447 (32·5%)	999 (42·0%)	993 (40·9%)	802 (38·9%)	869 (42·9%)
BMI, kg/m²	25·2 (22·8–28·7)	25·3 (22·7–28·8)	25·4 (22·9–28·7)	25·5 (22·9–29·1)	25·6 (22·8–29·1)	25·6 (23·1–29·0)
Ethnicity						
White	1257 (92·0%)	1278 (93·0%)	2153 (90·6%)	2214 (91·1%)	1357 (65·8%)	1366 (67·5%)
Black	6 (0·4%)	2 (0·1%)	17 (0·7%)	14 (0·6%)	230 (11·1%)	210 (10·4%)
Asian	76 (5·6%)	59 (4·3%)	137 (5·8%)	138 (5·7%)	54 (2·6%)	53 (2·6%)
Mixed	19 (1·4%)	22 (1·6%)	48 (2·0%)	42 (1·7%)	410 (19·9%)	386 (19·1%)
Other	9 (0·7%)	13 (0·9%)	22 (0·9%)	22 (0·9%)	12 (0·6%)	10 (0·5%)
Health and social care setting workers	1236 (90·4%)	1253 (91·2%)	1441 (60·6%)	1513 (62·3%)	1833 (88·9%)	1775 (87·7%)
Comorbidities						
Cardiovascular disease	104 (7·6%)	92 (6·7%)	264 (11·1%)	266 (10·9%)	271 (13·1%)	244 (12·0%)
Respiratory disease	158 (11·6%)	176 (12·8%)	285 (12·0%)	316 (13·0%)	215 (10·4%)	210 (10·4%)
Diabetes	18 (1·3%)	15 (1·1%)	58 (2·4%)	60 (2·5%)	59 (2·9%)	60 (3·0%)

Data are n (%) or median (IQR). The primary efficacy population (LD/SD and SD/SD) includes randomly assigned participants who were seronegative at baseline and received LD/SD or SD/SD or were in the corresponding control group, and remained on study more than 14 days after their second dose without having had a previous virologically confirmed severe acute respiratory syndrome coronavirus 2 infection. In addition, for groups in COV002, only efficacy groups (ie, groups 4, 6, 9, and 10) are included. LD/SD=low-dose prime plus standard-dose boost. SD/SD=two standard-dose vaccines given. MenACWY=meningococcal group A, C, W, and Y conjugate vaccine. BMI=body-mass index.

Table 1: **Baseline characteristics of participants included in the primary efficacy population, by study and dosing strategy**

Limits:

Immunocompromised volunteers not included in the trial

Elderly participants are low represented

Heterogenicity between trials (concentration and schedule)

Adenoviral vector vaccine

AZD1222

EFFICACY AND SAFETY DATA

	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)

Vaccine efficacy was calculated from the robust Poisson model. The primary efficacy population (LD/SD and SD/SD) includes randomly assigned participants who were seronegative at baseline and received LD/SD or SD/SD or were in a corresponding control group, and remained on study more than 14 days after their second dose without having had a previous virologically confirmed SARS-CoV-2 infection. In addition, for groups in COV002, only efficacy groups (ie, groups 4, 6, 9, and 10) are included. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. LD/SD=low-dose prime plus standard-dose boost. SD/SD=two standard-dose vaccines given. NAAT=nucleic acid amplification test. *CIs are 95% unless indicated otherwise. †95·8% CI used for primary analysis. ‡Vaccine efficacy calculated from a reduced robust Poisson model that was not adjusted for age. All other models included an adjustment for age. §p value for interaction term comparing LD/SD with SD/SD is p=0·010. ¶Other non-primary symptomatic COVID-19 disease includes cases who have symptoms other than the five main symptoms that are required for inclusion in the primary analysis (eg, a participant who has diarrhoea and malaise but no fever, cough, shortness of breath, anosmia, or ageusia).

Table 2: Efficacy against SARS-CoV-2 more than 14 days after a second dose of ChAdOx1 nCoV-19 vaccine in the primary efficacy population

Primary Efficacy Analysis: 2weeks after second dose

- 98 cases in the ***SD/SD*** group (2 trials)
  - 27 within the ChAdOx1 nCov19 group
  - 71 within the Control group
  - ***Vaccine Efficacy in SD/SD: 62,1%***
- 33 cases in the ***LD/SD*** group
  - 3 within the ChAdOx1 nCov19 group
  - 33 within the Control group
  - ***Vaccine Efficacy in LD/SD: 90%***

TOTAL OF CASES: 131
30 in the ChAdOx1 nCov /101 in the Control
Vaccine efficacy: 70,4%

Limits:

Is aggregation of SD/LD and SD/SD data for efficacy analysis possible? (different doses, different vaccination schedules schedules)

Adenoviral vector vaccine

AZD1222

EFFICACY AND SAFETY DATA

	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (95% CI)
		n/N (%)	Incidence per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence per 1000 person-years (person-days of follow-up)	
COV002 (UK)	90	28/3060 (0·9%)	35·4 (288 955)	62/3064 (2·0%)	78·5 (288 395)	55·0% (29·7 to 71·1)
COV003 (Brazil)	102	23/3247 (0·7%)	46·7 (179 743)	79/3233 (2·4%)	162·4 (177 693)	71·2% (54·2 to 81·9)
Primary symptomatic COVID-19*	192	51/6307 (0·8%)	39·7 (468 698)	141/6297 (2·2%)	110·5 (466 088)	64·1% (50·5 to 73·9)
Other non-primary symptomatic COVID-19†	21	12/6307 (0·2%)	9·4 (468 698)	9/6297 (0·1%)	7·1 (466 088)	−32·8% (−214·8 to 44·0)‡
Any symptomatic COVID-19	213	63/6307 (1·0%)	49·1 (468 698)	150/6297 (2·4%)	117·5 (466 088)	58·3% (44·0 to 68·9)
Asymptomatic or symptoms unknown (COV002)	71	34/2751 (1·2%)	46·8 (265 142)	37/2760 (1·3%)	51·0 (264 994)	7·8% (−46·7 to 42·1)
Any NAAT-positive swab	291	102/6307 (1·6%)	79·5 (468 698)	189/6297 (3·0%)	148·1 (466 088)	46·3% (31·8 to 57·8)

Vaccine efficacy was calculated from the robust Poisson model. The first-standard-dose efficacy population includes participants seronegative at baseline who received only standard dose vaccines or were in the corresponding control group, and remained on study 22 days after their first dose without having had a previous virologically confirmed SARS-CoV-2 infection. In addition, for groups in COV002, only efficacy groups (ie, groups 4, 6, 9, and 10) are included. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. NAAT=nucleic acid amplification test. *NAAT-positive swab plus at least one of cough, shortness of breath, fever higher than 37·8°C, anosmia, or ageusia. †Other non-primary symptomatic COVID-19 disease includes cases that have symptoms other than the five main symptoms required for inclusion in the primary analysis (eg, a participant who has diarrhoea and malaise but no fever, cough, shortness of breath, anosmia, or ageusia). ‡Vaccine efficacy was calculated from a reduced robust Poisson model (excluding the age group category due to the full model failing to converge). Participants with a low-dose prime were excluded.

Table 4: **Efficacy against SARS-CoV-2 more than 21 days after the first standard dose in seronegative participants who received only standard doses**

Primary Efficacy Analysis at more than 21 days after second dose

TOTAL OF CASES: 192
(only SD/SD group; two trials, *different vaccination schedules*)
51 in the ChAdOx1 nCov / 141 in the Control
Vaccine efficacy: 64,1%

Limits: No evidence of an potential effect against viral shedding

From 21 days after the first dose: there were ten cases hospitalized for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death

	ChAdOx1 nCoV-19 (n=12 021)	MenACWY or saline control (n=11 724)
Hospitalisation (WHO clinical progression score ≥4)		
≤21 days after the first dose	2*	6
>21 days after the first dose and ≤14 days after the second dose	0	5
>14 days after the second dose	0	5
Severe COVID-19 (WHO clinical progression score ≥6)		
≤21 days after the first dose	0	0
>21 days after the first dose and ≤14 days after the second dose	0	1
>14 days after the second dose	0	1

The safety population includes all randomisation participants who received at least one dose of vaccine. Severe COVID-19 (WHO score ≥6) is a subset of hospitalisations (WHO score ≥4). Cases were eligible for inclusion in efficacy if the first symptom or first NAAT-positive result was on or before the data cutoff date (Nov 4, 2020). Two cases appear in this table that do not appear in the table for serious adverse events in appendix 1 (pp 15–20) as the adverse event reporting date was after the data cutoff date. MenACWY=meningococcal group A, C, W, and Y conjugate vaccine. NAAT=nucleic acid amplification test. *One case on the day of the first vaccination and one case 10 days after the first dose.

Table 5: **Hospitalisation for COVID-19 and severe COVID-19 in the safety population**

COREB mission nationale
Coordination Opérationnelle Risque Epidémique et Biologique

Voysey M *et al. The Lancet* Dec 2020

MALADIES INFECTIEUSES ÉMERGENTES

Adenoviral vector vaccine

Sputnik V

EFFICACY AND SAFETY DATA

- Sputnik vaccine comprises two vector components, rAd26-S and rAd5-S.
- Efficacy data from Phase III blinded, randomized, controlled trials at 25 sites in Moscow-Russia
- 2 doses of 10^{11} recombinant vp each at 21 d interval (d26 first, Ad5 later)
  - 21 977 participants randomized (3:1)
  - >90% received 2nd dose
- Inclusion criteria: healthy adults aged of 18y negative for HIV, Hepatitis B and C and no history of SARS CoV 2

Primary outcome: proportion of participants with COVID-19 confirmed by PCR from day 21 after receiving the first dose

Secondary outcomes: end point: severity of COVID-19; changes in antibody levels against SARS-CoV-2 glycoprotein S; proportion of participants with antibodies against SARS-CoV-2 N-protein; changes in SARS-CoV-2 neutralising antibody titres; changes in antigen-specific cellular immunity level; and incidence and severity of adverse events

	Vaccine (n=14 964)	Placebo (n=4902)
Sex		
Female	5821 (38·9%)	1887 (38·5%)
Male	9143 (61·1%)	3015 (61·5%)
Race		
White	14 741 (98·5%)	4830 (98·5%)
Asian	217 (1·5%)	69 (1·4%)
Other*	6 (<0·1%)	3 (<0·1%)
Age group, years		
18–30	1596 (10·7%)	521 (10·6%)
31–40	3848 (25·7%)	1259 (25·7%)
41–50	4399 (29·4%)	1443 (29·4%)
51–60	3510 (23·5%)	1146 (23·4%)
>60	1611 (10·8%)	533 (10·9%)
Age, years	45·3 (12·0)	45·3 (11·9)
Bodyweight, kg	81·3 (17·5)	81·6 (17·7)
Height, cm	173·1 (9·1)	173·3 (9·0)
Body-mass index, kg/m²	26·75 (4·56)	26·75 (4·55)
Concomitant diseases (diabetes, hypertension, ischaemic heart disease, obesity)†	3687/14 944 (24·7%)	1235/4892 (25·2%)
Risk of infection in volunteers†‡		
High	65/14 567 (0·4%)	23/4778 (0·5%)
Medium	3853/14 567 (26·5%)	1280/4778 (26·8%)
General	10649/14 567 (73·1%)	3475/4778 (72·7%)

Data are n (%) and mean (SD). *Includes Black or African American, Native Hawaiian or other Pacific Islander, or undefined. †Denominator shows number of participants for whom these data were available. ‡High risk denotes those whose work involves interaction with patients with a confirmed diagnosis of COVID-19; medium risk is those who have professional contact with a large number of people, such as general practitioners, social workers, and shop assistants; and general risk denotes those with no additional risks associated with their professional activities.

Table 1: Baseline characteristics of participants who received two doses of assigned treatment and were included in primary outcome analysis

Adenoviral vector vaccine

Sputnik V

EFFICACY AND SAFETY DATA

Primary Efficacy Analysis

	Total cases	Vaccine group	Placebo group	Vaccine efficacy (95% CI)	p value
First COVID-19 occurrence from 21 days after dose 1 (day of dose 2)*					
Overall	78	16/14 964 (0·1%)	62/4902 (1·3%)	91·6% (85·6–95·2)	<0·0001
Age group (years)					
18–30	5	1/1596 (0·1%)	4/521 (0·8%)	91·9% (51·2–99·3)	0·0146
31–40	17	4/3848 (0·1%)	13/1259 (1·0%)	90·0% (71·1–96·5)	<0·0001
41–50	19	4/4399 (0·1%)	15/1443 (1·0%)	91·3% (73·7–96·9)	<0·0001
51–60	27	5/3510 (0·1%)	22/1146 (1·9%)	92·7% (81·1–97·0)	<0·0001
>60	10	2/1611 (0·1%)	8/533 (1·5%)	91·8% (67·1–98·3)	0·0004
Sex					
Female	32	9/5821 (0·2%)	23/1887 (1·2%)	87·5% (73·4–94·2)	<0·0001
Male	46	7/9143 (0·1%)	39/3015 (1·3%)	94·2% (87·2–97·4)	<0·0001
Moderate or severe cases	20	0/14 964	20/4902 (0·4%)	100% (94·4–100·0)	<0·0001
First COVID-19 occurrence after dose 1†					
Any time after dose 1	175	79/16 427 (0·5%)	96/5435 (1·8%)	73·1% (63·7–80·1)	<0·0001
From 14 days after dose 1	109	30/14 999 (0·2%)	79/4950 (1·6%)	87·6% (81·1–91·8)	<0·0001
First COVID-19 occurrence after dose 2 (28 days after dose 1)*					
All	60	13/14 094 (0·1%)	47/4601 (1·0%)	91·1% (83·8–95·1)	<0·0001

Data are n/N (%), unless otherwise stated. *Includes those who received both doses. †Includes participants who received at least one dose.

Table 2: Interim results on vaccine efficacy

Limitations of the interim analysis: the small sample sizes within age strata

From 21 days after the first dose of vaccine (the day of dose 2)

TOTAL OF CASES: confirmed cases78
16 in the vaccinated group /62 in the Placebo
20 moderate of severe cases all in the Placebo
4 deaths unrelated to vaccine
Vaccine efficacy: 91,6%
(greater that 87% for all studied groups including >60)

SAFETY:

- Most of the reported adverse events (7485 [94·0%] of 7966) were grade 1; 451 were grade 2 (5·66%) and 30 were grade 3 (0·38%) (*flu-like illness, injection site reactions, headache, and asthenia).*
- 122 rare adverse events (91 in the vaccine group and 31 in the placebo group
- 70 episodes of serious adverse events, considered not related to COVID-19 (68 participants, 45 from the vaccine group and 23 from the placebo group)

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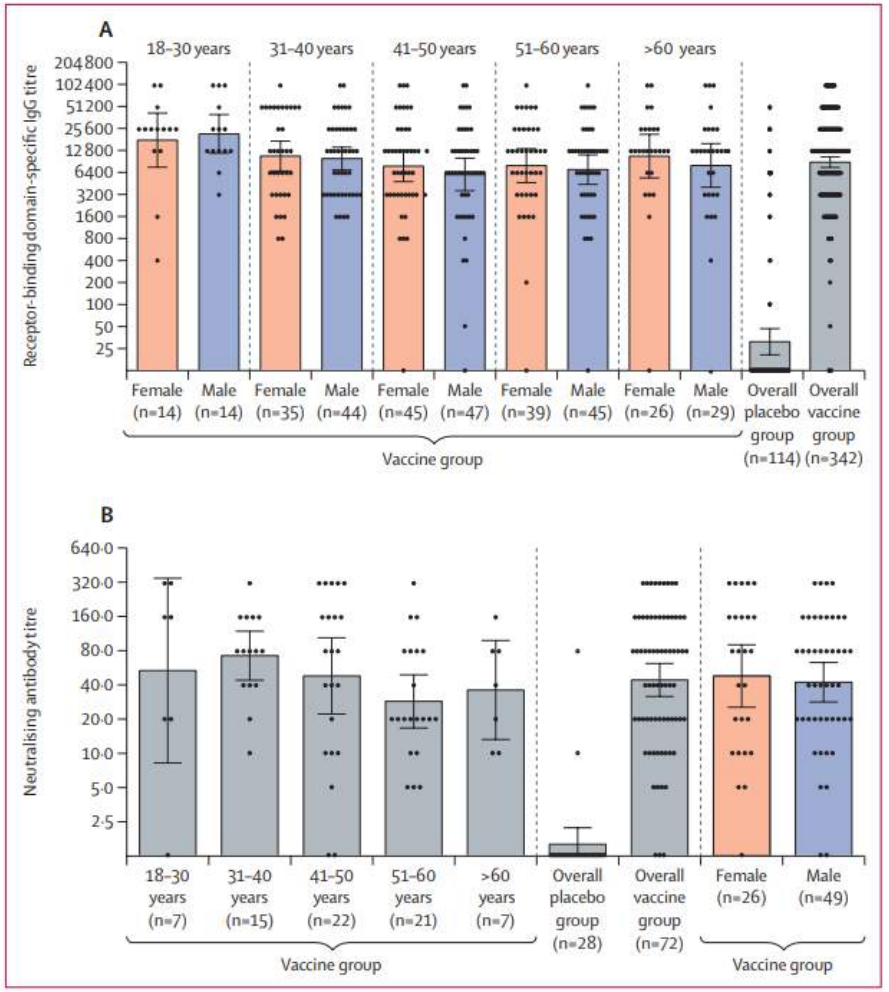
Logunov Denis Y., *et al. The Lancet* Feb 2021

anrs MALADIES INFECTIEUSES ÉMERGENTES

Adenoviral vector vaccine

Sputnik V

EFFICACY AND SAFETY DATA



- **Presence of IgGs** specific to RBD 42 days from the start of vaccination
  - In the vaccine group, : detected in 336 (98%) of 342 samples, with a GMT of 8996 (95% CI 7610–10 635). Seroconversion rate: 98·25%.
  - In the placebo group: detected in 17 (15%) of 114 samples, with a GMT of 30,55 (20,18–46,26), and a seroconversion rate of 14·91%
  - 18–30 years group had a significantly higher GMT than the other age groups
- **Presence of neutralizing antibodies** on day 42 after first vaccination
  - In vaccine group: GMT of 44,5 (95% CI 31,8–62,2) and the seroconversion level was 95,83%
  - In the placebo group: GMT 1,6 (1,12–2,19) and the seroconversion rate was 7·14%

- All participants in the vaccine group had significantly higher levels of IFN-γ secretion upon antigen stimulation

Adenoviral vector vaccine

Ad26COVS1

EFFICACY AND SAFETY DATA

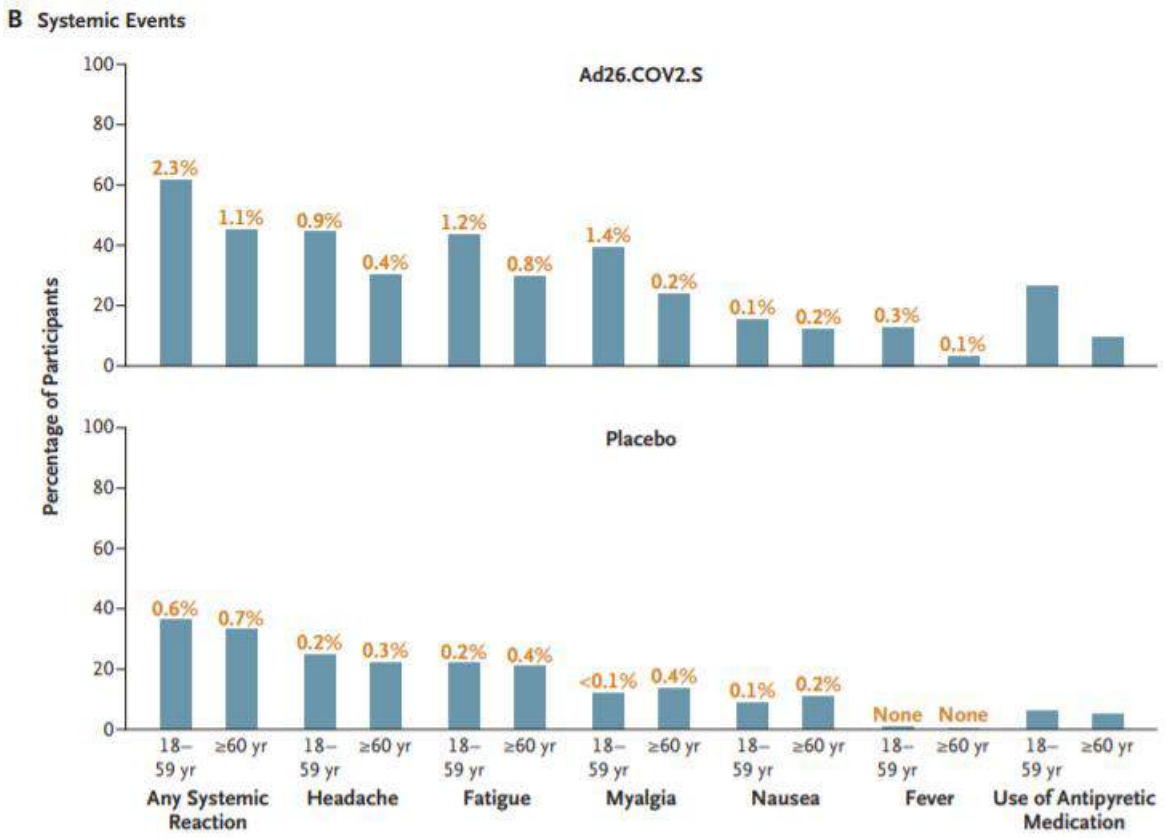
- **Phase 3:** Multicenter, randomized, double-blind, placebo-controlled, in Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United States.

- Randomisation in a 1:1 ratio to receive a single dose of Ad26.COV2.S (5×1010 viral particles) or placebo. 43786 participants vaccinated

Primary end points: vaccine efficacy against moderate to severe–critical Covid-19 with an onset at least 14 days and at least 28 days after administration.

Safety subpopulation: 3356 participants in the vaccine group and 3380 in the placebo group.

> Reactogenicity higher with Ad26.COV2.S but mild to moderate and transient.



Sadoff J et al.; NEJM, Jun 2021

Adenoviral vector vaccine

Ad26COVS1

EFFICACY AND SAFETY DATA

Table 2. Vaccine Efficacy against Covid-19 with Onset at Least 14 Days and at Least 28 Days after the Administration of Vaccine or Placebo (Per-Protocol at-Risk Population).*

Variable	≥14 Days after Administration†					≥28 Days after Administration‡				
	Ad26.COV2.S (N=19,514)		Placebo (N=19,544)		Vaccine Efficacy (95% CI)	Ad26.COV2.S (N=19,306)		Placebo (N=19,178)		Vaccine Efficacy (95% CI)
	no. of cases	*person-yr*	*no. of cases*	*person-yr*	%	*no. of cases*	*person-yr*	*no of cases*	*person-yr*	%
Moderate to severe–critical Covid-19	116	3116.6	348	3096.1	66.9 (59.0–73.4)	66	3102.0	193	3070.7	66.1 (55.0–74.8)
18–59 yr	95	2106.8	260	2095.0	63.7 (53.9–71.6)	52	2097.6	152	2077.0	66.1 (53.3–75.8)
≥60 yr	21	1009.8	88	1001.2	76.3 (61.6–86.0)	14	1004.4	41	993.6	66.2 (36.7–83.0)
Symptomatic Covid-19 of any severity	117	3116.5	351	3095.9	66.9 (59.1–73.4)	66	3102.0	195	3070.5	66.5 (55.5–75.1)
Mild	1	3116.5	3	3095.9	NC§	0	3102.0	2	3070.5	NC§
Moderate	102	3116.6	288	3096.1	64.8 (55.8–72.2)	61	3102.0	159	3070.7	62.0 (48.7–72.2)
Severe–critical	14	3125.1	60	3122.0	76.7 (54.6–89.1)	5	3106.2	34	3082.6	85.4 (54.2–96.9)
Severity-adjusted symptomatic Covid-19¶	117	3116.5	351	3095.9	68.1 (60.3–74.3)	66	3102.0	195	3070.5	69.0 (56.7–77.6)
18–59 yr	95	2106.8	260	2095.0	65.8 (56.2–73.1)	52	2097.6	152	2077.0	69.3 (57.4–77.7)
≥60 yr	22	1009.6	91	1001.0	74.5 (57.9–84.3)	14	1004.4	43	993.5	67.9 (38.2–82.8)
Moderate to severe–critical Covid-19, including noncentrally confirmed cases	173	3113.9	509	3089.1	66.3 (59.9–71.8)	113	3100.3	324	3065.9	65.5 (57.2–72.4)
Covid-19, according to FDA harmonized definition‖	114	3116.6	345	3,096.3	67.2 (59.3–73.7)	65	3102.0	193	3070.6	66.7 (55.6–75.2)
Moderate to severe–critical Covid-19, according to Cox proportional-hazards model**	116	3116.6	348	3,096.1	66.9 (59.1–73.2)	66	3102.0	193	3070.7	66.2 (55.3–74.4)

TOTAL OF CASES: 468

28 days after administration - moderate to severe cases

> 66 the vaccine group

> 193 in the placebo group

Global Vaccine Efficacy : 66.1 (95% CI 55.0-74.8)

Vaccine efficacy against severe cases: 85.4% (95% CI 54.2-96.9)

Efficacy against disease with an onset at least 28 days after administration was similar across age groups

VOC: 512 RT-PCR–positive samples

> Prototypic strain in 96% of US samples

> Prototypical strain in 30.6% and Gamma strain in 69.4% of the Brazilian samples.

> Beta strain in 94.5% of South African samples.

VE in south African context: 64.0% against moderate to severe–critical disease and 81.7% against severe–critical disease with onset

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Sadoff J et al.; NEJM, Jun 2021

anrs MALADIES INFECTIEUSES ÉMERGENTES

Adenoviral vector vaccine

NVX-CoV2373

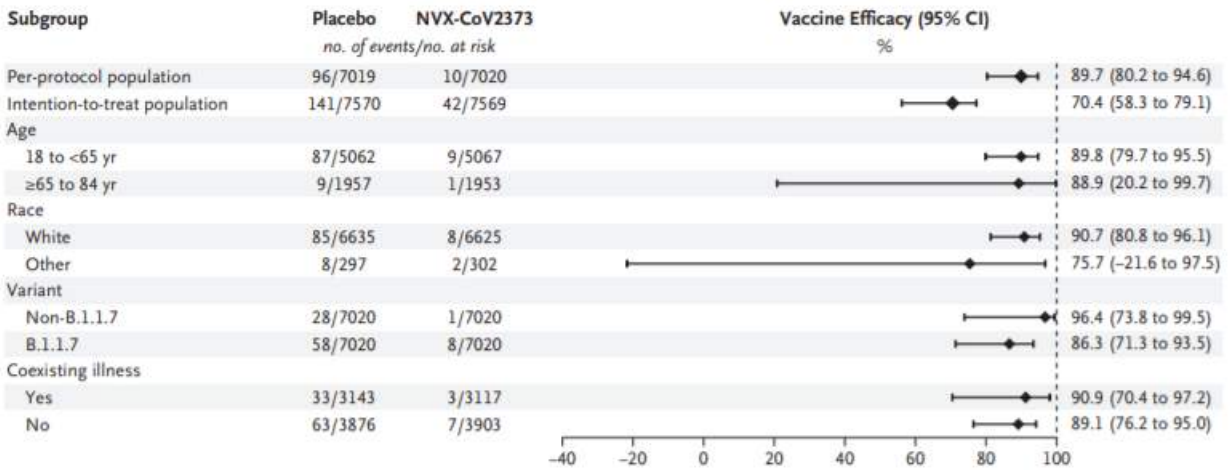
EFFICACY AND SAFETY DATA

- **Phase 3:** 33 sites in UK. 18-84 years of age. Healthy or stable chronic medical condition.
- 15 187 participants randomly assigned in a 1:1 ratio to receive two 5µg doses of NVX-CoV2373 (+50µg Matrix M) or placebo (normal saline) administered 21 days apart.

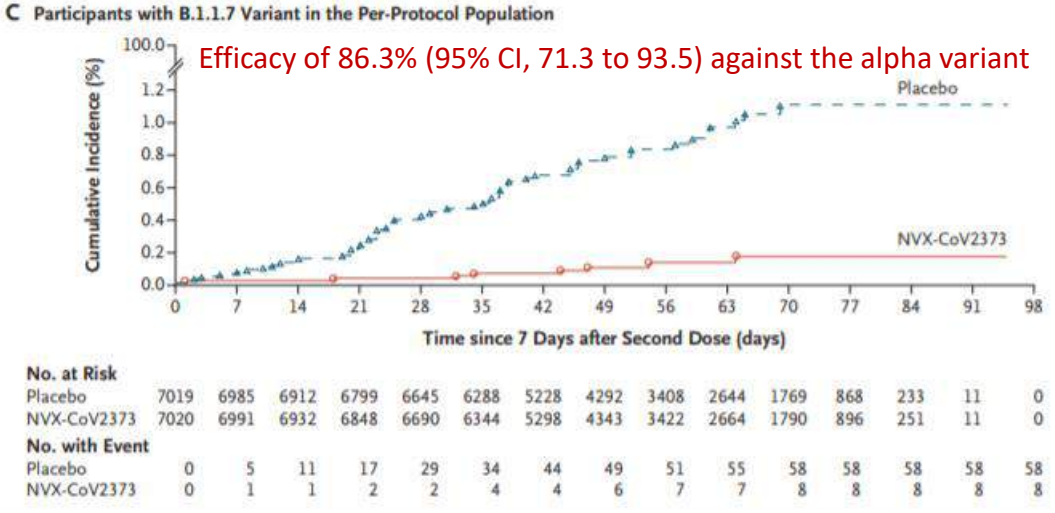
Primary end point: efficacy of the NVX-CoV2373 vaccine against the first occurrence of virologically confirmed symptomatic mild, moderate, or severe Covid-19 with onset at least 7 days after the second dose

SAFETY: Reactogenicity was generally mild and transient. The incidence of serious adverse events was low and similar in the two groups.

Cases from 7 days after administration - moderate to severe cases
> 10 in the vaccine group
> 96 in the placebo group
Global Vaccine Efficacy : 89.97% (95% CI 80.2. - 94.6)
100% protection against severe cases



Subgroup	Placebo (no. of events/no. at risk)	NVX-CoV2373 (no. of events/no. at risk)	Vaccine Efficacy (95% CI) %
Per-protocol population	96/7019	10/7020	89.7 (80.2 to 94.6)
Intention-to-treat population	141/7570	42/7569	70.4 (58.3 to 79.1)
Age			
18 to <65 yr	87/5062	9/5067	89.8 (79.7 to 95.5)
≥65 to 84 yr	9/1957	1/1953	88.9 (20.2 to 99.7)
Race			
White	85/6635	8/6625	90.7 (80.8 to 96.1)
Other	8/297	2/302	75.7 (−21.6 to 97.5)
Variant			
Non-B.1.1.7	28/7020	1/7020	96.4 (73.8 to 99.5)
B.1.1.7	58/7020	8/7020	86.3 (71.3 to 93.5)
Coexisting illness			
Yes	33/3143	3/3117	90.9 (70.4 to 97.2)
No	63/3876	7/3903	89.1 (76.2 to 95.0)



No. at Risk															
Placebo	7019	6985	6912	6799	6645	6288	5228	4292	3408	2644	1769	868	233	11	0
NVX-CoV2373	7020	6991	6932	6848	6690	6344	5298	4343	3422	2664	1790	896	251	11	0
No. with Event															
Placebo	0	5	11	17	29	34	44	49	51	55	58	58	58	58	58
NVX-CoV2373	0	1	1	2	2	4	4	6	7	7	8	8	8	8	8

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Heath PT et al. NEJM, Jun 2021

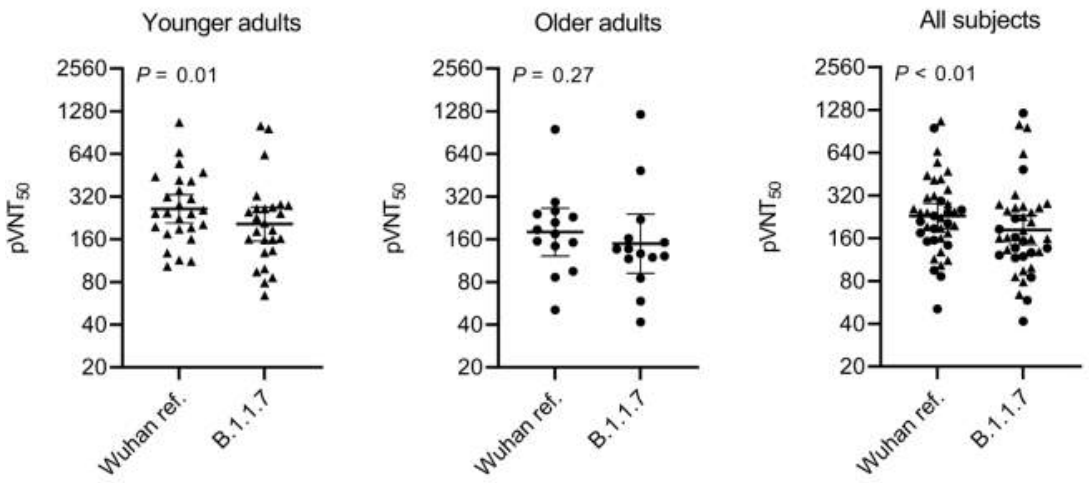
MALADIES INFECTIEUSES ÉMERGENTES

Neutralization of viral variants

Sera of BNT162b2 vaccinated subjects tested against lab generated VSV pseudovirus bearing B.1.1.7 SARS CoV2 mutations

Description of tested sera:

- 40 participants from Phase I
  - 26 younger (23-55 years of age)
  - 14 older (57-73 years of age)
- 7 or 21 days after booster immunization



The 50% neutralization GMT of the sera against the SARS-CoV-2 lineage B.1.1.7 pseudovirus were slightly, statistically significantly reduced compared to the GMTs against the Wuhan reference pseudovirus

The largely preserved neutralization of pseudoviruses bearing the B.1.1.7 spike by BNT162b2-immune sera makes it unlikely that the UK variant virus will escape BNT162b2-mediated protection.

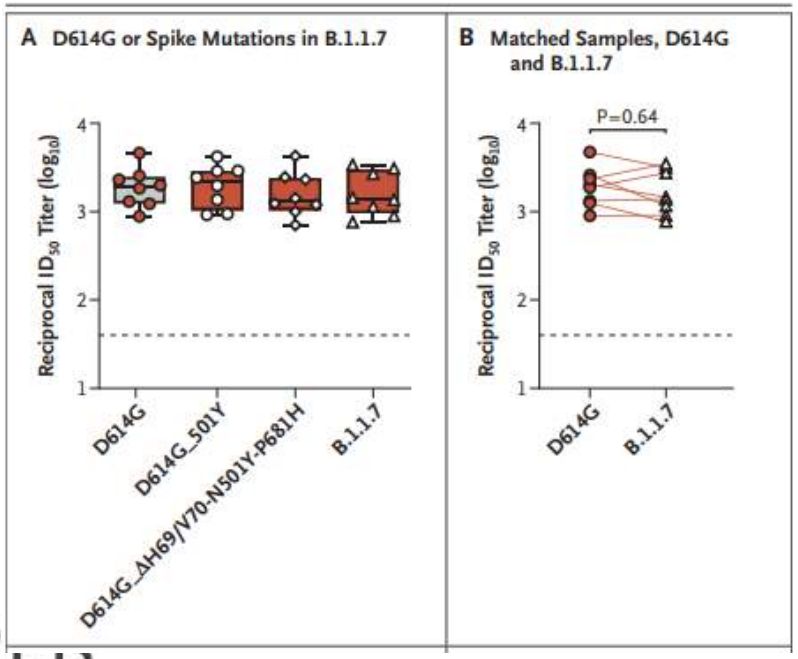
Limitation of the work: use of a non-replicating pseudovirus system

Neutralization of viral variants

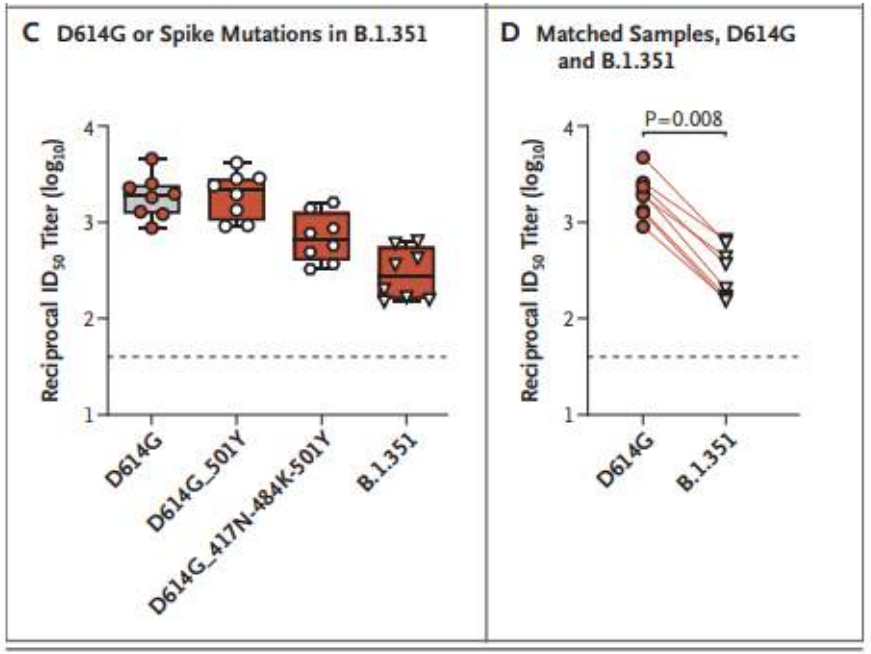
Serum neutralizing activity against recombinant vesicular stomatitis virus (rVSV)–based SARS-CoV-2 bearing the spike protein from the original Wuhan-Hu-1 isolate, the D614G variant, the B.1.1.7 and B.1.351 variants

Description of tested sera: participants from Phase I trial of the mRNA-1273 vaccine, 7 days after second dose

Full panel of mutations and a subset of mutations affecting the RBD of the B.1.1.7 variant had no significant effect on neutralization by serum from vaccinated patients



Decrease in titers of neutralizing antibodies against the B.1.351 variant and a subset of its mutations affecting the RBD.



Wu K., *et al NEJM* April 2021.

Efficacy of AZD1222 vaccine against SARS-CoV-2 Alpha variant

Population: Volunteers enrolled in the phase 2/3 vaccine efficacy studies in the UK (>18)

Methods: Upper airway swabs on a weekly basis and if symptoms of COVID-19 disease. NAAT for SARS-CoV-2 sequencing if positive

Efficacy analysis included symptomatic COVID-19 in seronegative participants with a NAAT positive swab more than 14 days after a second dose of vaccine

Primary outcome : symptomatic COVID-19 disease, defined as a positive NAAT from upper airway swab in a participant with at least one symptom, including cough, fever of 37·8°C or higher, shortness of breath, anosmia, or ageusia

	Cases*	ChAdOx1 nCoV-19 vaccine (n=4244)	Control vaccine (n=4290)	ChAdOx1 nCoV-19 vaccine efficacy (95% CI)
Primary symptomatic COVID-19				
B.1.1.7	52 (19%)	12	40	70·4% (43·6 to 84·5)
Other variants	95 (35%)	15	80	81·5% (67·9 to 89·4)
No sequence result†	30 (11%)	5	25	80·2% (48·3 to 92·4)
Not sequenced‡	92 (34%)	27	65	59·1% (36·0 to 73·9)
Total cases	269	59	210	72·3% (63·1 to 79·3)
Asymptomatic or unknown infection				
B.1.1.7	19 (9%)	8	11	28·9% (−77·1 to 71·4)
Other variants	34 (16%)	8	26	69·7% (33·0 to 86·3)
No sequence result†	64 (31%)	36	28	−27·0% (−108·1 to 22·5)
Not sequenced‡	92 (44%)	45	47	5·6% (−42·3 to 37·3)
Total cases	209	97	112	14·6% (−12·1 to 34·9)
Any NAAT positive infection§				
B.1.1.7	75 (14%)	21	54	61·7% (36·7 to 76·9)
Other variants	144 (28%)	27	117	77·3% (65·4 to 85·0)
No sequence result†	101 (19%)	44	57	23·7% (−13·0 to 48·5)
Not sequenced‡	200 (38%)	81	119	32·9% (11·0 to 49·5)
Total cases	520	173	347	50·9% (41·0 to 59·0)

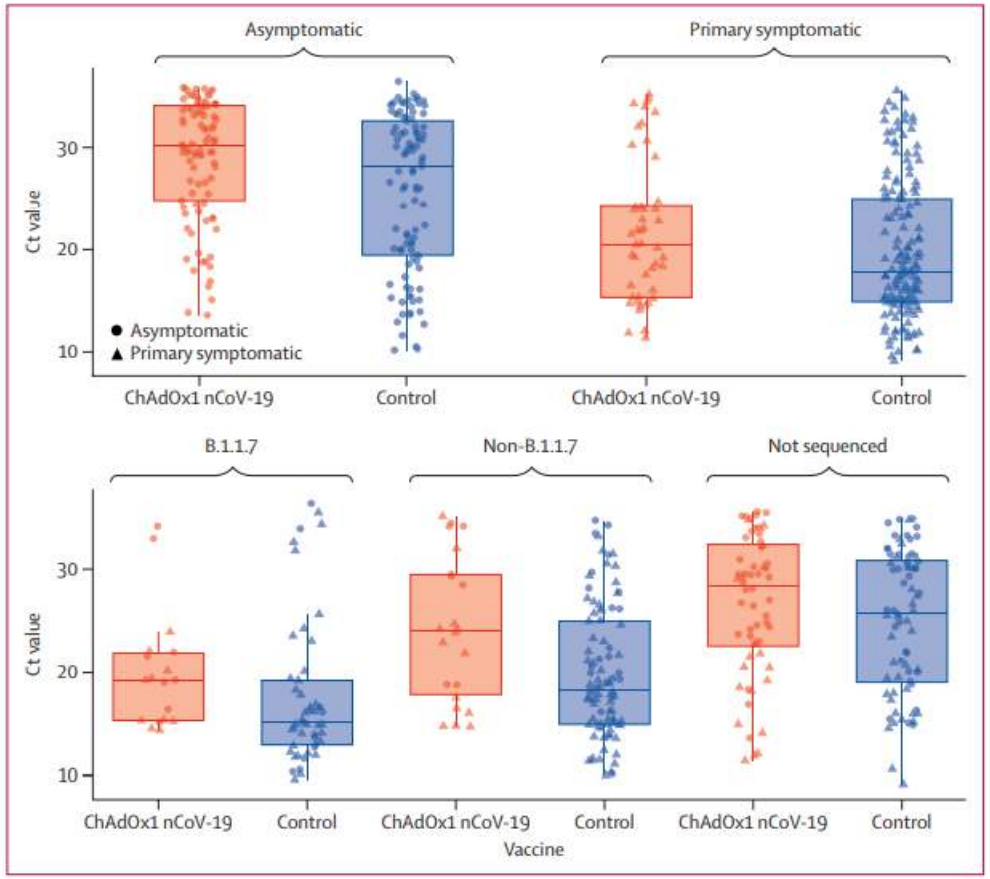
Data include SD/SD and LD/SD seronegative efficacy cohorts only. NAAT=nucleic acid amplification test. SD=standard dose. LD=low dose. *Data in this column are n (%) or n. †No viable sequence obtained or unprocessed due to cycle threshold >30. ‡Sample did not enter sequencing pipeline, was destroyed, or sequencing results are yet to be obtained. §Includes primary symptomatic cases, non-primary symptomatic cases (those with other symptoms such as nausea or diarrhoea; not shown separately), asymptomatic cases, and cases for which symptoms were unknown.

Table: Vaccine efficacy against B.1.1.7 and non-B.1.1.7 variants

TOTAL OF CASES: 520
21 caused by B.1.1.7 variant in the vaccinated group;
54 caused by B.1.1.7 variant in the control group
Vaccine efficacy against B1.351: 61.7%

Emary KRW, et al. *The Lancet* March 2021

Efficacy of AZD1222 vaccine against SARS-CoV-2 Alpha variant



The viral load among NAAT-positive swab in the AZD 1222 vaccinated group was statistically significantly lower than among those who were in the control group.

> vaccinees showing a NAAT-positive swab could be less likely to transmit the virus than an unvaccinated NAAT

Emary KRW, et al. *The Lancet* March 2021

Efficacy of AZD1222 vaccine against SARS-CoV-2 Alpha variant

Population: Volunteers enrolled in the phase 2 trial in South Africa (>18, HIV-)

Methods: Serum samples obtained from 25 participants after the second dose were tested by pseudovirus and live-virus neutralization assays against the original D614G virus and the B.1.351 variant.

Primary endpoints: Safety and efficacy of the vaccine against laboratory-confirmed symptomatic cases more than 14 days after the second dose.

Table 2. Vaccine Efficacy against Mild-to-Moderate Symptomatic Covid-19 Confirmed by Nucleic Acid Amplification Test.*

End Point	Baseline Serologic Status†	Total No. of Cases	Placebo	Incidence Risk	Vaccine	Incidence Risk	Vaccine Efficacy‡
			no./total no. (%)	*per 1000 person-yr (person-days)*	*no./total no. (%)*	*per 1000 person-yr (person-days)*	*% (95% CI)*
Mild-to-moderate illness with onset >14 days after second injection	Seronegative	42	23/717 (3.2)	93.6 (89,714)	19/750 (2.5)	73.1 (94,881)	21.9 (−49.9 to 59.8)
Mild-to-moderate illness associated with B.1.351 variant with onset >14 days after second injection	Seronegative	39	20/714 (2.8)	81.6 (89,448)	19/750 (2.5)	73.1 (94,881)	10.4 (−76.8 to 54.8)
Mild-to-moderate illness with onset >14 days after second injection, regardless of baseline serostatus	Any	46	24/865 (2.8)	81.9 (106,898)	22/884 (2.5)	73.2 (109,659)	10.6 (−66.4 to 52.2)
Mild-to-moderate illness with onset >14 days after one dose until October 31, 2020, a proxy for non-B.1.351 variant infection	Overall	15	12/938 (1.3)	31.1 (140,774)	3/944 (0.3)	7.6 (143,140)	75.4 (8.9 to 95.5)

TOTAL OF CASES 42
39 cases caused by B.1.351 variant;
Vaccine efficacy against B1.351: 10.4%
(95% CI, −76.8 to 54.8).

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Madhi, S.A. et al. *NEJM.* April 2021

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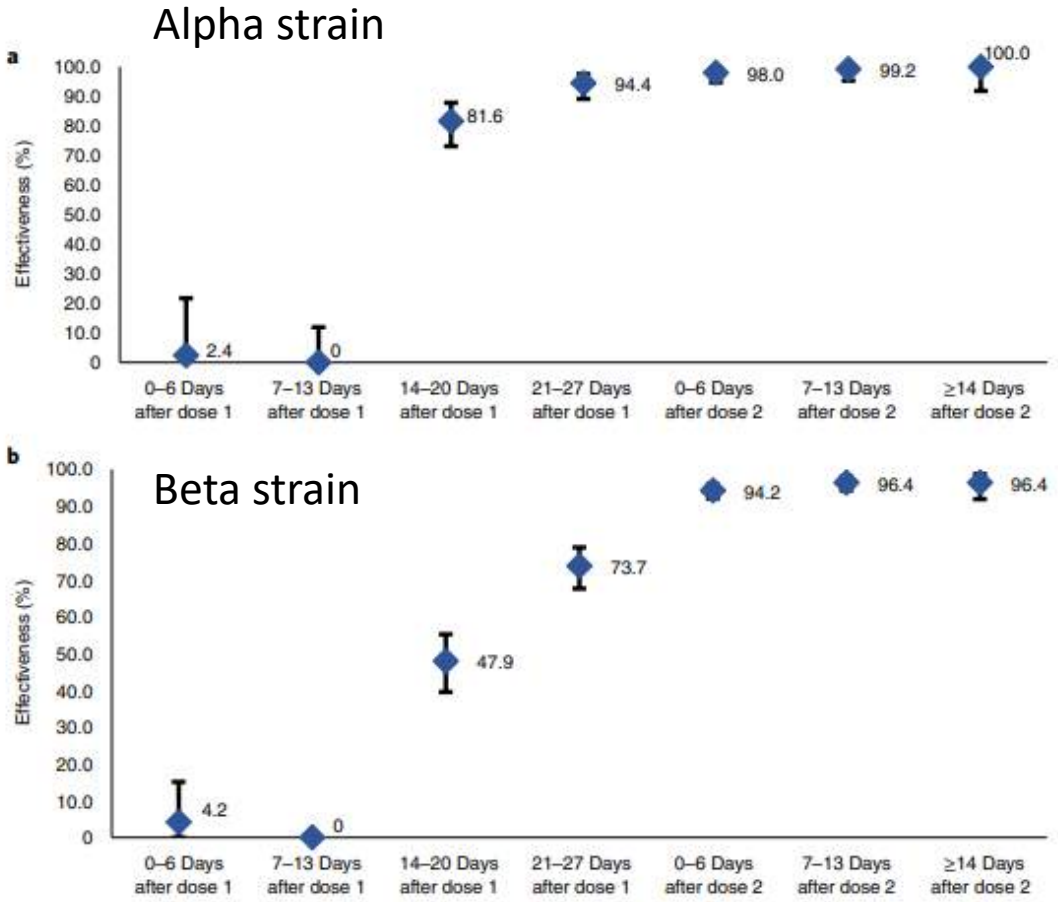
mRNA-1273 vaccine effectiveness against Alpha and Beta variants

- mRNA-1273 (Moderna) vaccine efficacy: 94.1% at preventing symptomatic COVID-19 due to infection with 'wild-type' variants

- Real life effectiveness against Alpha and Beta variants in Qatar, a population that comprises mainly working-age adults

- Effectiveness against alpha infection:
  - 88.1% (95% CI 83.7–91.5%) ≥14 days after the first dose but before the second dose,
  - 100% (95% CI: 91.8– 100.0%) ≥14 days after the second dose.
- Effectiveness against beta infection:
  - 61.3% after the first dose (95% CI: 56.5–65.5%)
  - 96.4% after the second dose (95% CI: 91.9–98.7%).

- Effectiveness against any severe, critical or fatal COVID-19 disease due to any SARS-CoV-2 infection
  - 81.6% (95% CI: 71.0–88.8%) after the first dose
  - 95.7% (95% CI: 73.4–99.9%) after the second dose



Chemaitelly, H. et al. *Nature medcine*. July2021

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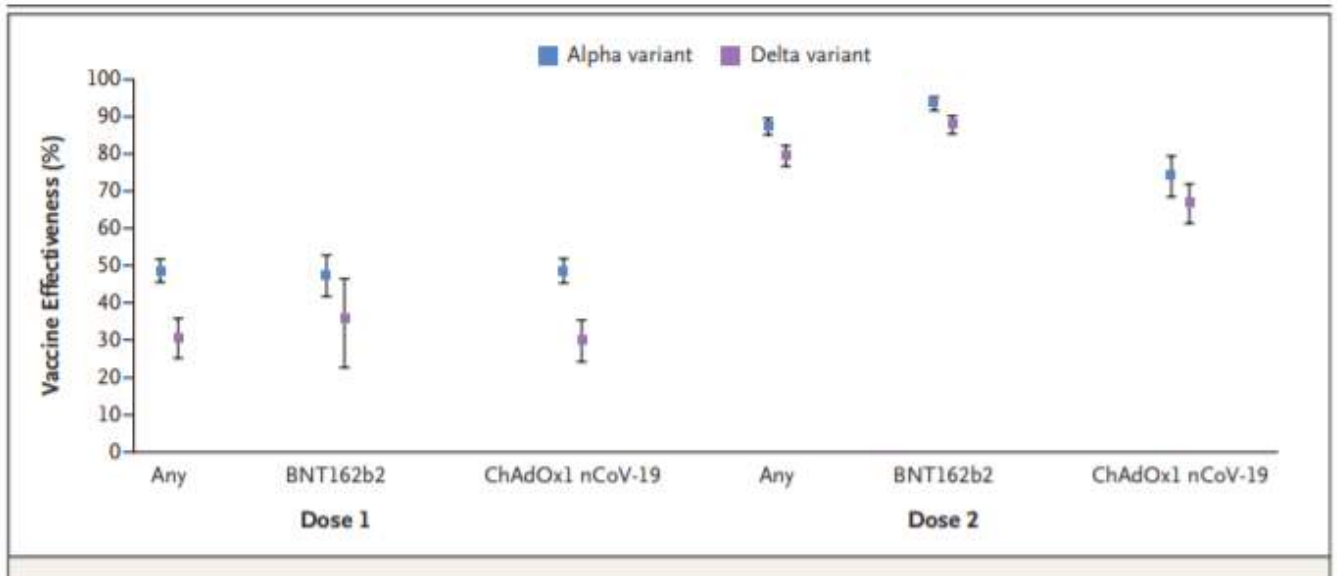
anrs MALADIES INFECTIEUSES ÉMERGENTES

Effectiveness of Covid-19 Vaccines against Delta Variant

- Effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) was notably lower among persons with the delta variant (30.7%; 95% confidence interval [CI], 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7

- BNT162b2 > the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant.

- ChAdOx1 nCoV-19 vaccine > the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant.



Negative case control: Vaccine effectiveness estimation against symptomatic disease caused by the delta variant, as compared with the alpha variant

Effectiveness of SARS-CoV-2 vaccination: Real Life Data

GENERAL POPULATION

Mass vaccination campaigns against COVID19 in Israel

- Estimated **vaccine effectiveness:**
  > 7 days after the second dose: 92% for documented infection, 94% for symptomatic Covid-19, 87% for hospitalization, and 92% for severe Covid-19

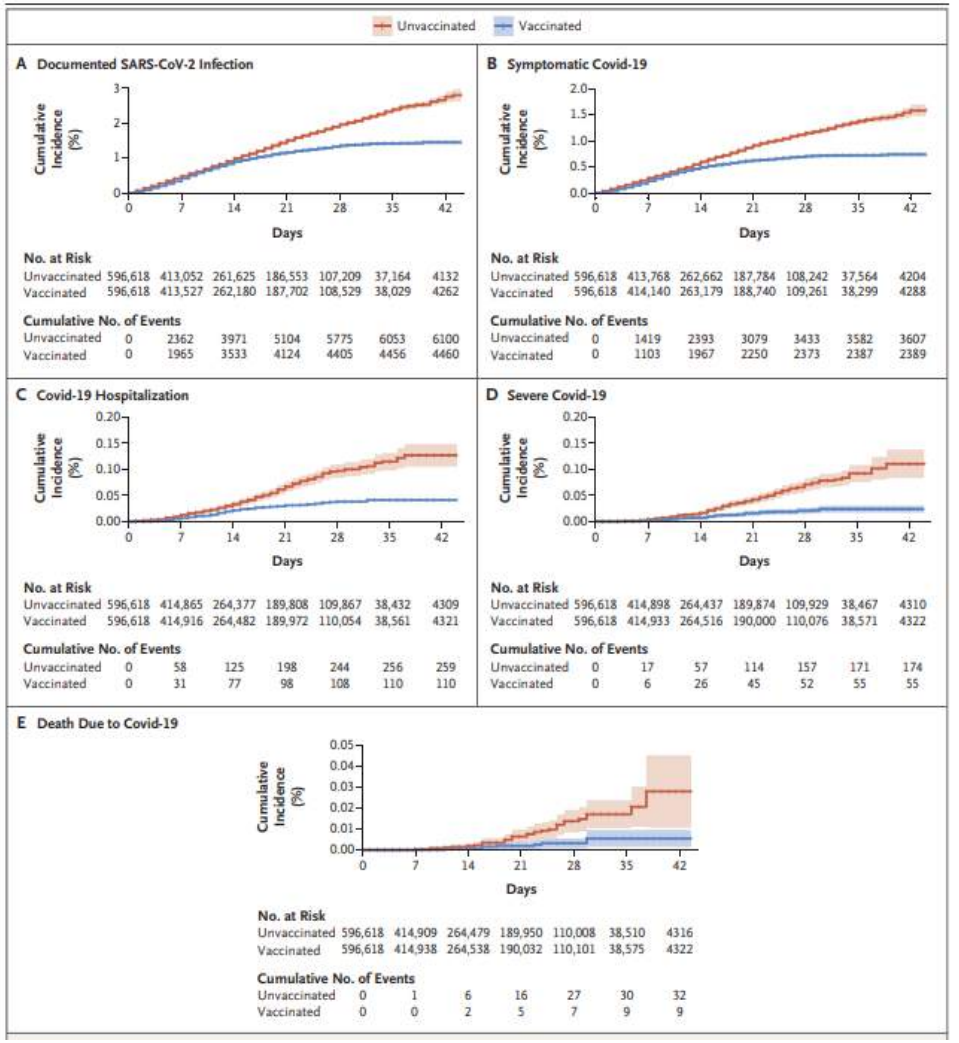
  > During days 14 through 20 and days 21 through 27: 46% and 60% for documented infection, 57% and 66% for symptomatic Covid-19, 74% and 78% for hospitalization, 62% and 80% for severe Covid-19, and 72% and 84% for Covid-19–related death, respectively

- BNT162b2 vaccine is effective for a wide range of Covid-19–related outcomes

Table 2. Estimated Vaccine Effectiveness against Covid-19 Outcomes during Three Time Periods.*

Period	Documented Infection		Symptomatic Illness		Hospitalization		Severe Disease		Death	
	1–RR	Risk Difference	1–RR	Risk Difference	1–RR	Risk Difference	1–RR	Risk Difference	1–RR	Risk Difference
	% (95% CI)	*no./1000 persons (95% CI)*	% (95% CI)	*no./1000 persons (95% CI)*	% (95% CI)	*no./1000 persons (95% CI)*	% (95% CI)	*no./1000 persons (95% CI)*	% (95% CI)	*no./1000 persons (95% CI)*
14 to 20 days after first dose	46 (40–51)	2.06 (1.70–2.40)	57 (50–63)	1.54 (1.28–1.80)	74 (56–86)	0.21 (0.13–0.29)	62 (39–80)	0.14 (0.07–0.21)	72 (19–100)	0.03 (0.01–0.07)
21 to 27 days after first dose	60 (53–66)	2.31 (1.96–2.69)	66 (57–73)	1.34 (1.09–1.62)	78 (61–91)	0.22 (0.13–0.31)	80 (59–94)	0.18 (0.10–0.27)	84 (44–100)	0.06 (0.02–0.11)
7 days after second dose to end of follow-up	92 (88–95)	8.58 (6.22–11.18)	94 (87–98)	4.61 (3.29–6.53)	87 (55–100)	0.22 (0.08–0.39)	92 (75–100)	0.32 (0.13–0.52)	NA	NA

* Confidence intervals were estimated using the percentile bootstrap method with 500 repetitions. Estimates were calculated only for cells with more than 10 instances of an outcome across the two groups. NA denotes not available, and RR risk ratio.



Dagan, N., et *al.* NEJM. April 15 2021

Effectiveness of SARS-CoV-2 vaccination: Real Life Data

VACCINATION OF HCW

Israel (BNT162b2 mRNA)

Week since First Dose	Received a First Dose of Vaccine†	Incidence of Covid-19 among Vaccinated HCWs: HCWs Tested at HHUMC	Incidence of Covid-19 among Vaccinated HCWs: HCWs Tested at HHUMC or Community Clinics§
		no./1000 workers	
Week 1	5297	32.1	9.4
Week 2	5247	32.9	9.0
Week 3	5200	19.5	5.6
Week 4	5164	16.1	2.1
Received second dose	4864	11.5	1.4
Did not receive second dose	300	51.3	13.3
Week 5	5050	4.4	0.6
Received second dose	4934	4.6	0.6
Did not receive second dose	116	0	0
Week 6	4947	0	0.4
Received second dose	4793	0	0.4
Did not receive second dose	154	0	0
Week 7	4079	19.1	1.2
Received second dose	4069	19.9	1.0
Did not receive second dose	10	0	100.0

Benenson S et *al. NEJM. March* 2021

Decrease number of positive test result among vaccinated HCW.

Efficacy of these vaccines is maintained outside the trial settings.

Suggest that widespread and effective vaccination among health care workers provides a safe environment

California (mRNA 1273 & BNT162b2 mRNA)

Days after Vaccination	Vaccinated Persons: With New Infection (N=379)	Vaccinated Persons: Tested (N=14,604)*
	number	
Dose 1		
Days 1–7	145	5794
Days 8–14	125	7844
Days 15–21	57	7958
Day 22 or later, before dose 2	15	4286
Dose 2		
Days 1–7	22	5546
Days 8–14	8	4909
Day 15 or later	7	4167

Keehner J et *al. NEJM. March* 2021

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SARS-CoV-2 viral load after BNT162b2 vaccine: Real Life data

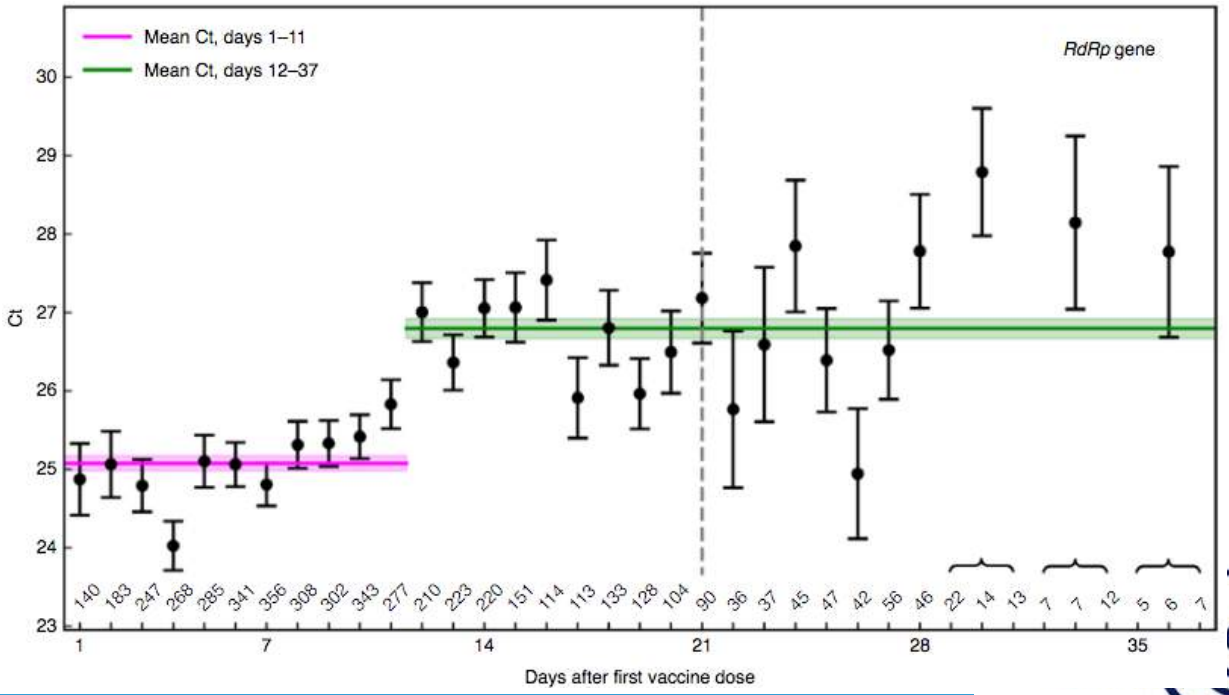
Effect of vaccination on viral load in COVID-19 post-vaccination infections ?

Retrospective study – December 21, 2020 to February 11, 2021

Analyse the RT–qPCR test measurements of three SARS-CoV-2 genes, from positive post-vaccination tests (4938 patients) → analysis of the infection cycle threshold (Ct).

Decrease viral load after 12d post-vaccination

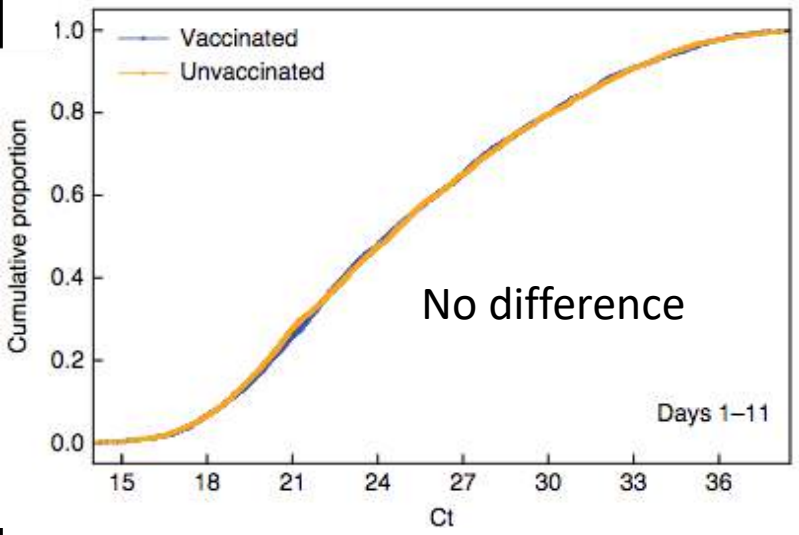
Ct values of positive samples collected 12–37 d after were higher than the Ct values of positive samples taken during the first 11 d after vaccination

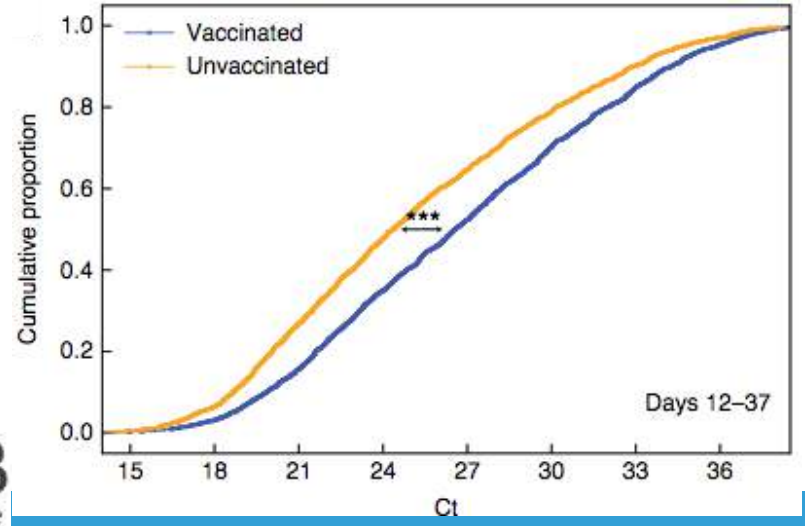


Levine-Tiefendrun M et *al. Nature Medicine. March* 2021

SARS-CoV-2 viral load after BNT162b2 vaccine: Real Life data

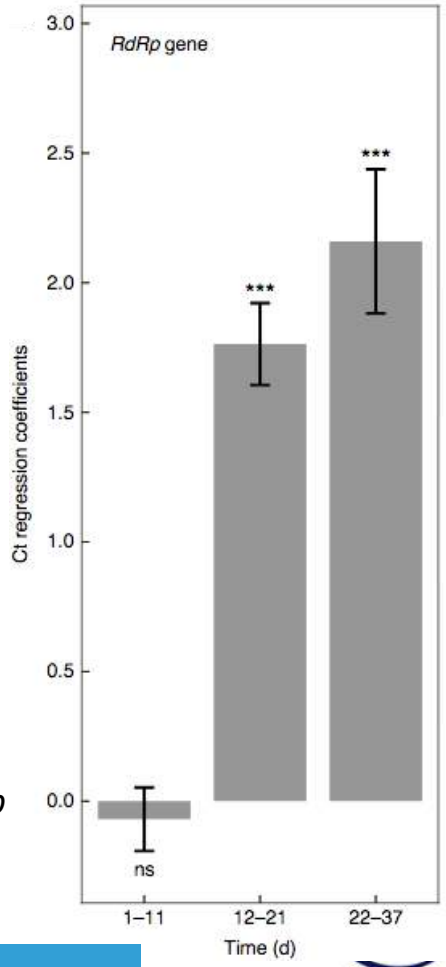
Ct values of positive sample of vaccinated patients versus Ct values of positive tests of unvaccinated patients.





A difference of 1 Ct unit is approximately equivalent to a factor of 2 in the number of viral particles per sample,
These Ct differences represent a decrease of 2.8–4.5-fold in viral load in vaccinated individuals

→ Infection occurring 12 d or longer after vaccination have significantly reduced viral loads.
→ affecting viral shedding and contagiousness ?



Coefficient for the association of Ct of the RdRp gene with vaccination at different vaccination-to-sample time bins in comparison to unvaccinated patients

Levine-Tiefendrun M et *al. Nature Medicine. March* 2021

Safety of SARS-CoV-2 vaccination: Real Life data

BLOOD CLOT RELATED EVENTS

Thrombotic Thrombocytopenia after AZ1222 Vaccination

- Vaccination with ChAdOx1 nCov-19 can result in the rare development of immune thrombotic thrombocytopenia
- This can be mediated by platelet activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia.

Norway cases:

- five patients with venous thrombosis and thrombocytopenia 7 to 10 days after receiving the first dose of the AZ1222 vaccine (32 to 54 years)
- Four of the patients had severe cerebral venous thrombosis with intracranial hemorrhage, and the outcome was fatal in three.

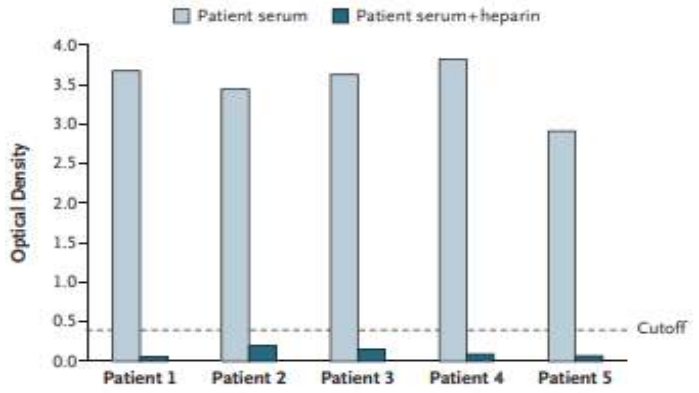


Figure 2. IgG PF4–Polyanion Detection in Serum.

Nina H. Schultz *et al* NEJM April 2021

Germany and Austria cases:

- 11 patients (9 women). Median age of 36 years (22 to 49).
- 10 patients with one or more thrombotic events beginning 5 to 16 days after vaccination
- 1 patients with fatal intracranial hemorrhage

Table 2. Clinical and Laboratory Summary of 11 Patients with Available Clinical Information.*

Variable	Patient Number										
	1	2	3	4	5	6	7	8	9	10	11
Platelet nadir (per mm³)	13,000	107,000	60,000	9,000	23,000	75,000	29,000	16,000	13,000	8,000	NA because of death
CVT	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Pending†
Splanchnic-vein thrombosis‡	Yes	No	No	No	Yes	No	No	No	No	Yes	No
Pulmonary embolism	Yes	Yes	No	No	Yes	No	No	No	No	No	No
Other thrombosis	Aortoiliac	No	No	No	Right intraventricular, iliofemoral vein, IVC	No	No	Widespread microvascular (brain, lungs, kidneys)§	Multiple organ thrombi§	No	Cerebral hemorrhage†
Symptom onset (no. of days after vaccination)	5	6	9	7	13	7	8	8	16	11	12¶
INR peak	1.40	1.12	NA	1.66	1.25	1.05	1.34	NA	1.70	NA	NA
PTT peak (sec)	41.6	29.0	NA	46.6	64.8	23.0	45.0	NA	46.1	NA	NA
D-dimer peak (mg/liter)	142.0	1.8	13.0	NA	NA	2.6	>33.0	NA	21.0	>35.0	NA
Fibrinogen nadir (mg/dl)	78	568	NA	NA	173	NA	210	NA	40	80	NA
PF4–heparin ELISA (optical density)	3.16	3.08	3.50	3.40	1.20	NA	NA	2.02	3.51	2.35	2.16
PF4-dependent platelet-activation assay	Pos	Pos	Pos	Pos	Pos	NA	NA	Pos	Pos	Pos	Pos
Heparin treatment	Yes	LMWH**	Unknown	Yes	Yes	Unknown	Yes	No	No	No	No
Other medical condition	No	No	No	CND	VWD-I; FVL ACL-Abs	No	No	No	No	No	Unknown
Outcome	Fatal	Recovering	Unknown	Fatal	Recovering	Recovering	Recovering	Fatal	Fatal	Fatal	Fatal

Greinacher, A., *et al*. NEJM April 2021

A case report Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination

Muir, KL., *et al*. NEJM April 2021

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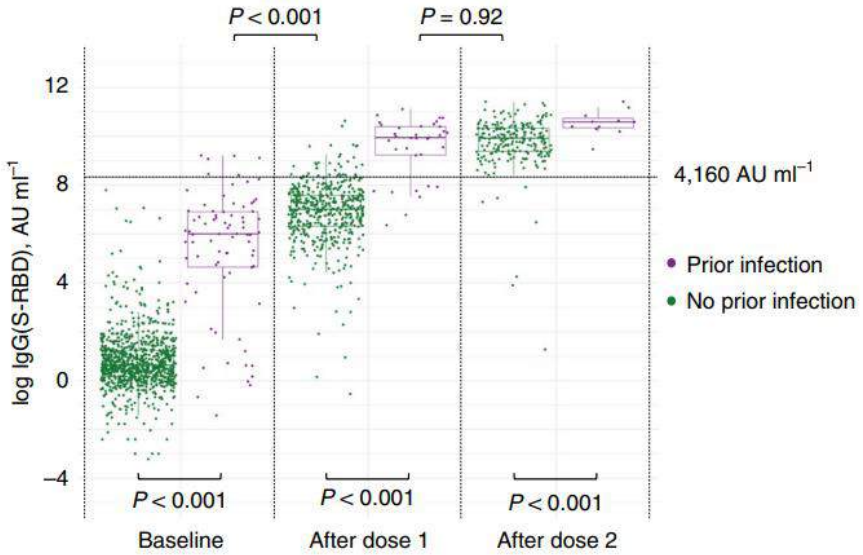
Vaccination of particular populations

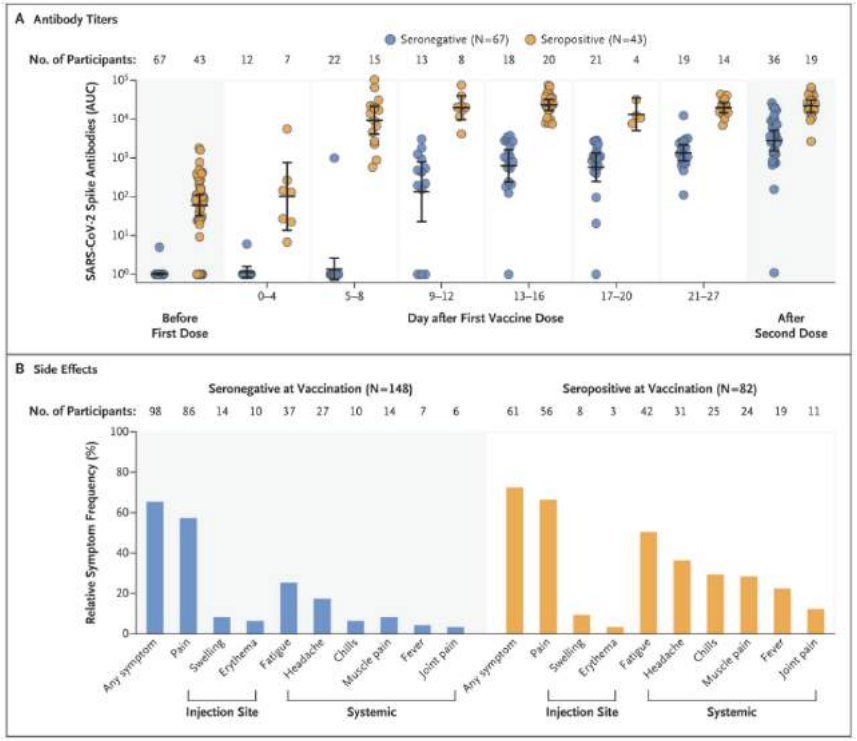
COVID 19 PATIENTS

Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccines

- A single dose of mRNA vaccine (either BNT162b2 or mRNA 1273) elicited rapid immune responses in seropositive participants, with postvaccination antibody titers similar to or exceeded titers found in seronegative participants who received two vaccinations.

- Post-vaccine symptoms were more prominent for those with prior infection after the first dose, but symptomology was similar between groups after the second dose





Ebinger ,JE., *et al* Nature Medicine March 2021.

Krammer, F., et al NEJM April 2021

Vaccination of particular populations

PREGNANT WOMEN

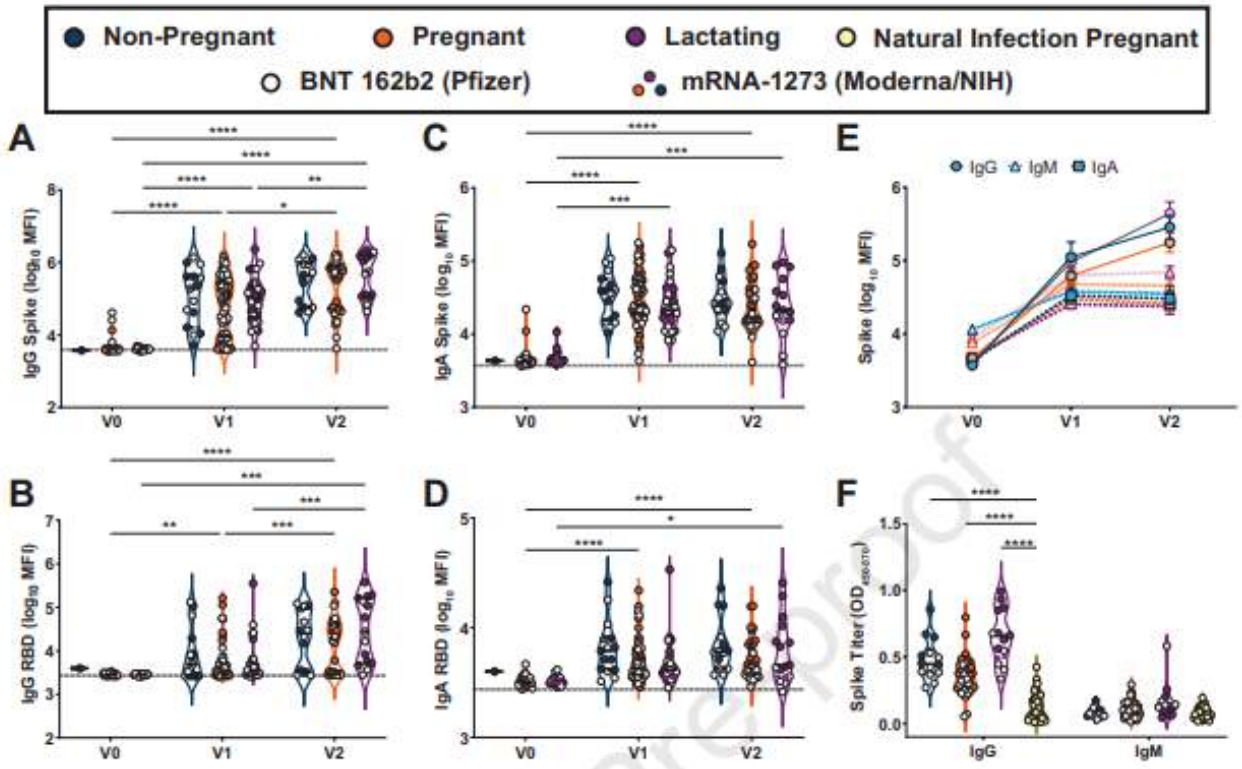
Population: pregnant (n=84; 13 deliveries); lactating (n=31); or non-pregnant woman of reproductive age (18-45) (n=16)

Type of COVID-19 vaccine received: (BNT162b2 Pfizer/BioNTech or mRNA-1273 Moderna/NIH)

- Mean gestational age at 1st dose: 23.2 weeks
- 13% vaccinated at 1st trimester (1st dose)
- 46% vaccinated at 2nd trimester (1st dose)
- 40% vaccinated at 3rd trimester (1st dose)

Sampling: Blood and breastmilk collected at: V0 (at the time of first dose), V1 (at the time of second vaccine dose) V2 (2-6 weeks following the 2nd dose) and at delivery.
Umbilical cord blood was also collected at delivery

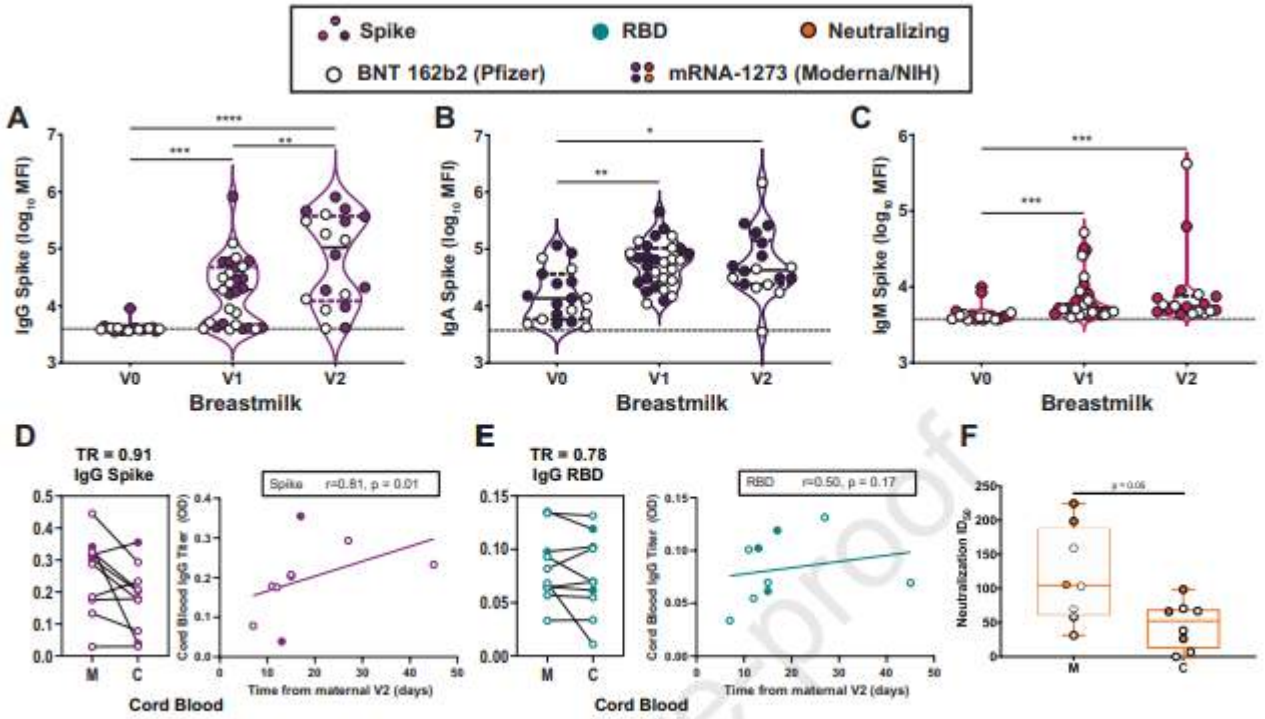
SAFETY: low cumulative symptoms score with no significant differences between groups



MATERNAL VACCINE RESPONSE: significant rise of both S and RBD specific IgGs and IgAs from V0 to V2. Higher levels of SARS-CoV-2 antibodies were observed in all 268 vaccinated women compared to pregnant women with natural infection.

Vaccination of particular populations

PREGNANT WOMEN



BREASTMILK ANTIBODY TRANSFER

- Anti-S specific antibodies were found in maternal breastmilk.
- Spike and RBD-specific IgG were detectable in 10/10 umbilical cords after maternal vaccination
- NAb titers tending to be lower in umbilical cord than maternal serum

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Gray K., *et al AJOG* March 2021.

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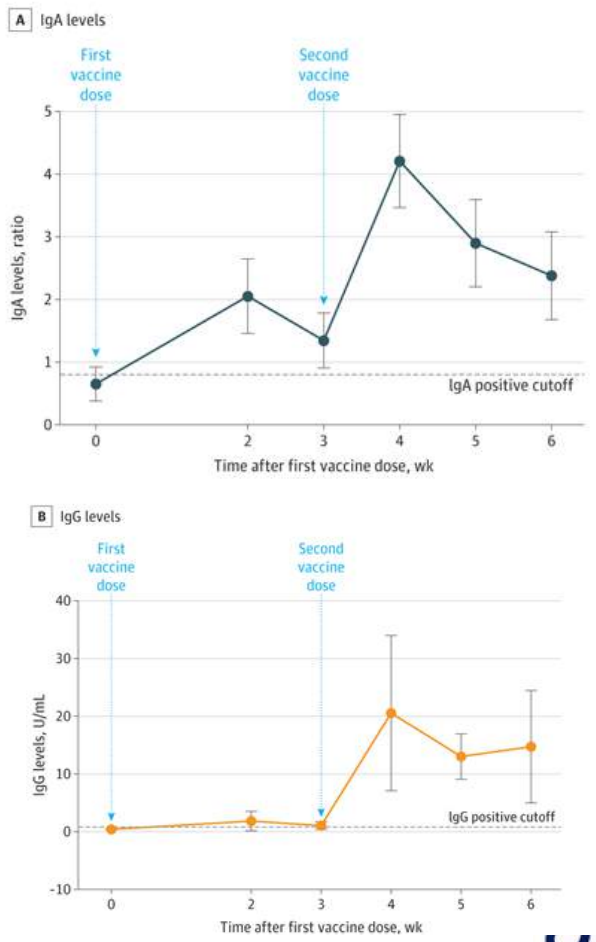
Vaccination of particular populations

PREGNANT WOMAN

SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women

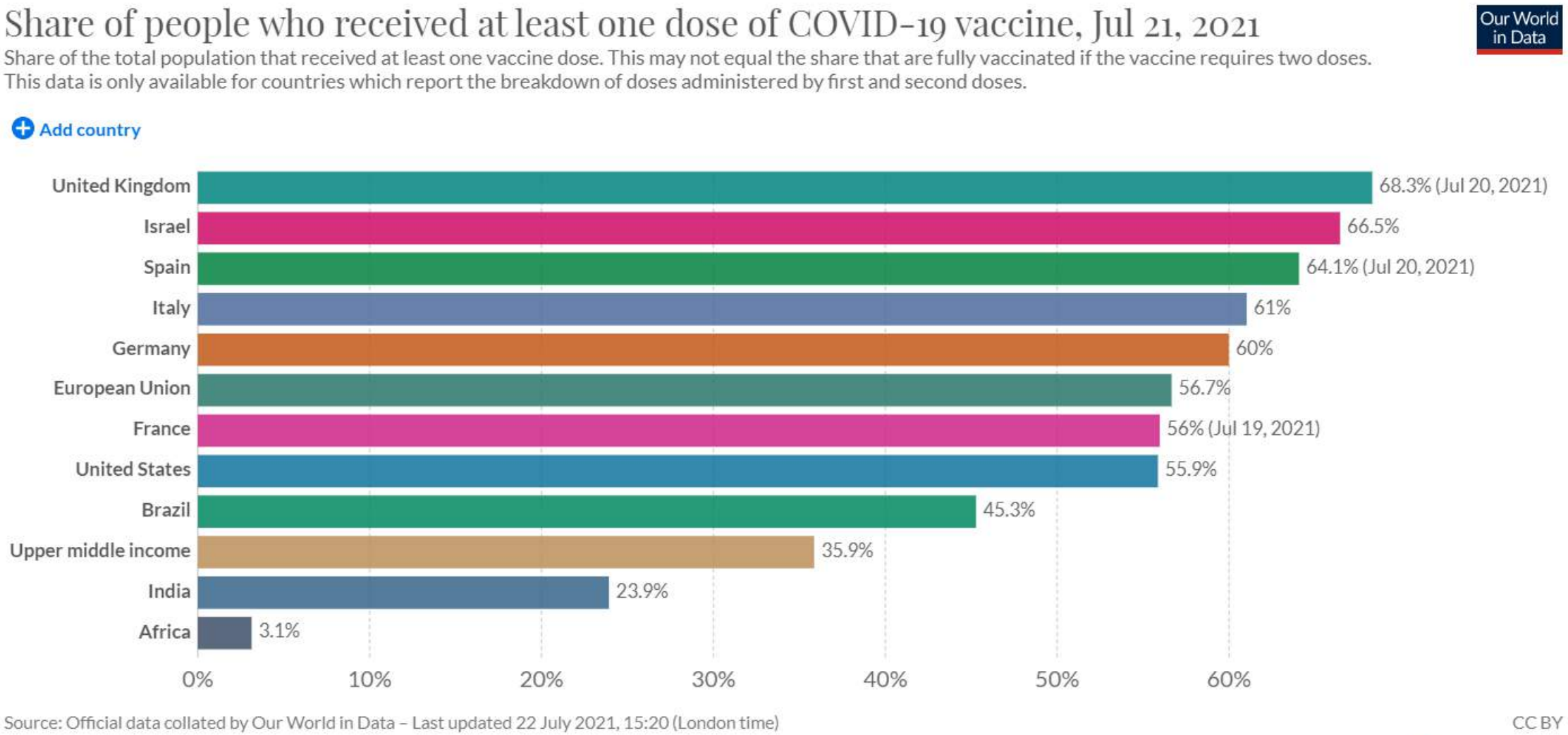
Population: Eighty-four women receving 2 doses of BNT162b2; 504 breast milk samples

- Anti–SARS-CoV-2-specific IgA antibodies in the breast milk increased rapidly and were significantly elevated at 2 weeks after the first vaccine.
- Mean levels remained elevated for the duration of follow-up, and at week six, 65.7% of samples tested positive.
- Anti–SARS-CoV-2-specific IgG antibodies remained low for the first 3 weeks, with an increase at week 4



Perl, SH., *et al.* JAMA April 2021.

Cumulative vaccination doses administered



VACCINES - SUMMARY

(July 2021)

- 88 vaccine candidates are ongoing clinical evaluation. 11 have received authorization from national or international medicines agencies
- Published Phase I/II data suggests that vaccine candidates on trial are immunogenic and mostly well tolerated in young adults. Data is emerging in elderly and children, globally keeping the trend described in young adults
- Induced titers of NAb are variable depending on the vaccine candidate. Comparison of Nab titers among vaccines is not possible. Yet, emerging data suggest that NAb are likely to be considered as correlates of protection.
- Published data do not show increased risk of ADE in vaccinees
- Overall vaccines efficacy results are good and rang between 50% and 95% depending on the vaccine, with mRNA vaccines performing the best.
- Individuals already seropositive for SARS-CoV-2 develop strong humoral responses after one dose of mRNA vaccine
- SARS-COV-2 variants represent a challenge for current vaccines with preliminary results showing variable level of cross-reaction depending on the viral strain. However, protection seems to remain at reasonably high levels.

References

1. Ewen Callaway. The race for coronavirus vaccines: a graphical guide. Nature 2020 Apr;580(7805):576-577. doi: 10.1038/d41586-020-01221-y.
2. Walsh EE et al. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. N Engl J Med. 2020 Dec 17;383(25):2439-2450. doi: 10.1056/NEJMoa2027906. Epub 2020 Oct 14.
3. Jackson LA et al. An mRNA Vaccine against SARS-CoV-2 - Preliminary Report. N Engl J Med. 2020 Nov 12;383(20):1920-1931. doi: 10.1056/NEJMoa2022483. Epub 2020 Jul 14.
4. Anderson E et al. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. N Engl J Med. 2020 Dec 17;383(25):2427-2438. doi: 10.1056/NEJMoa2028436. Epub 2020 Sep 29.
5. Ramasamy MN *et al*. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet. 2021 Dec 19;396(10267):1979-1993. doi: 10.1016/S0140-6736(20)32466-1. Epub 2020 Nov 19.
6. Logunon DY et al. 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. Lancet. 2020 Sep 26;396(10255):887-897. doi: 10.1016/S0140-6736(20)31866-3. Epub 2020 Sep 4.
7. Sadoff J et al. Interim Results of a Phase 1-2a Trial of Ad26.COV2.S Covid-19 Vaccine. N Engl J Med. 2021 Jan 13;NEJMoa2034201. doi: 10.1056/NEJMoa2034201
8. Keech C et al. Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. N Engl J Med. 2020 Dec 10;383(24):2320-2332. doi: 10.1056/NEJMoa2026920. Epub 2020 Sep 2.
9. Polack FP et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 31;383(27):2603-2615. doi: 10.1056/NEJMoa2034577. Epub 2020 Dec 10.
10. Muik A et al. Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera. Science. 2021 Mar 12;371(6534):1152-1153. doi: 10.1126/science.abg6105. Epub 2021 Jan 29.

References

11. Baden LR et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021 Feb 4;384(5):403-416. doi: 10.1056/NEJMoa2035389. Epub 2020 Dec 30.
12. Wu K et al. Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine. N Engl J Med . 2021 Mar 17. doi: 10.1056/NEJMc2102179.
13. Voysey M et al. 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. Lancet. 2021 Jan 9;397(10269):99-111. doi: 10.1016/S0140-6736(20)32661-1. Epub 2020 Dec 8.
14. Emary KRW et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. Lancet . 2021 Apr 10;397(10282):1351-1362. doi: 10.1016/S0140-6736(21)00628-0. Epub 2021 Mar 30.
15. Madhi SA et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. N Engl J Med . 2021 Mar 16;NEJMoa2102214. doi: 10.1056/NEJMoa2102214.
16. Logunov DY et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. Lancet. 2021 Feb 20;397(10275):671-681. doi: 10.1016/S0140-6736(21)00234-8. Epub 2021 Feb 2.
17. Dagan N et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. N Engl J Med. 2021 Apr 15;384(15):1412-1423. doi: 10.1056/NEJMoa2101765. Epub 2021 Feb 24.
18. Beneson S et al. BNT162b2 mRNA Covid-19 Vaccine Effectiveness among Health Care Workers. N Engl J Med. 2021 Mar 23;NEJMc2101951. doi: 10.1056/NEJMc2101951
19. Keehner J et al. SARS-CoV-2 Infection after Vaccination in Health Care Workers in California. N Engl J Med. 2021 Mar 23;NEJMc2101927. doi: 10.1056/NEJMc2101927.
20. Levine-Tiefendrun M et al. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. Nat Med. 2021 Mar 29. doi: 10.1038/s41591-021-01316-7.

References

21. Schultz NH et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. N Engl J Med. 2021 Apr 9. doi: 10.1056/NEJMoa2104882.
22. Greinacher A et al. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. N Engl J Med. 2021 Apr 9. doi: 10.1056/NEJMoa2104840.
23. Muir KL et al. Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination. N Engl J Med. 2021 Apr 14. doi: 10.1056/NEJMc2105869.
24. Ebinger JE et al. Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2. Nat Med. 2021 Apr 1. doi: 10.1038/s41591-021-01325-6.
25. Krammer F et al. Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine. N Engl J Med. 2021 Apr 8;384(14):1372-1374. doi: 10.1056/NEJMc2101667. Epub 2021 Mar 10.
26. Gray KJ et al. COVID-19 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol. 2021 Mar 24;S0002-9378(21)00187-3. doi: 10.1016/j.ajog.2021.03.023.
27. Perl SH et al. SARS-CoV-2-Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women. JAMA. 2021 Apr 12. doi: 10.1001/jama.2021.5782.
28. Chemaitelly H et al. 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 2021 july 09. . https://doi.org/10.1038/s41591-021-01446-y
29. Heath PT et al. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine N Engl J Med. 2021 June 30 DOI: 10.1056/NEJMoa2107659
30. Borobia AM et al. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. The Lancet. 2021 July 10. https://doi.org/10.1016/S0140-6736(21)01420-3
31. Sadoff Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. N Engl J Med. 2021 April 21. DOI: 10.1056/NEJMoa2101544
32. Lopez Bernal, J et al. Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. N Engl J Med. 2021 July 21. DOI: 10.1056/NEJMoa210889

Draft landscape and tracker of COVID-19 candidate vaccines https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

COVID19 vaccine Tracker (LSHTM) https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/#

Covid tracker: https://covidtracker.fr/vaccintracker/

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