COREB
mission nationale
Coordination Opérationnelle
Risque Epidémique et Biologique

https://www.coreb.infectiologie.com/

# VACCINES

# Scientific update on COVID-19

**Updated on April 19th 2021**

anRS
MALADIES INFECTIEUSES ÉMERGENTES

https://reacting.inserm.fr/

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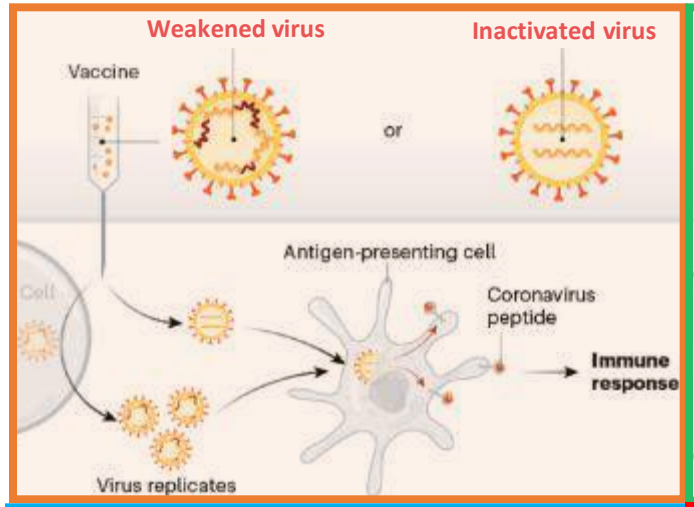
# VACCINES

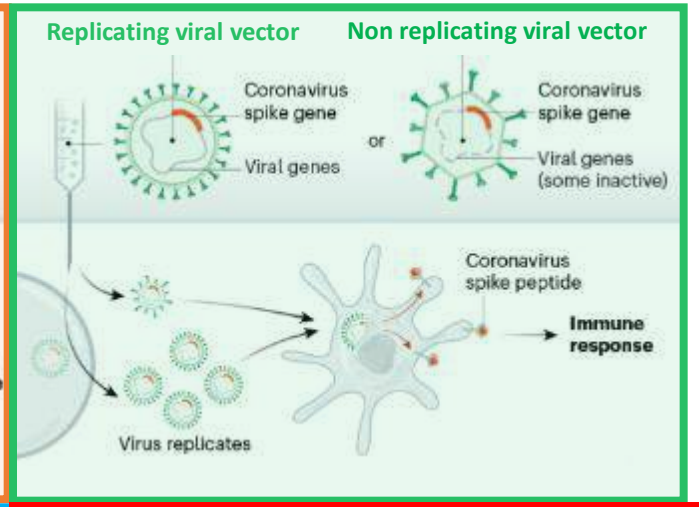
**Question:**

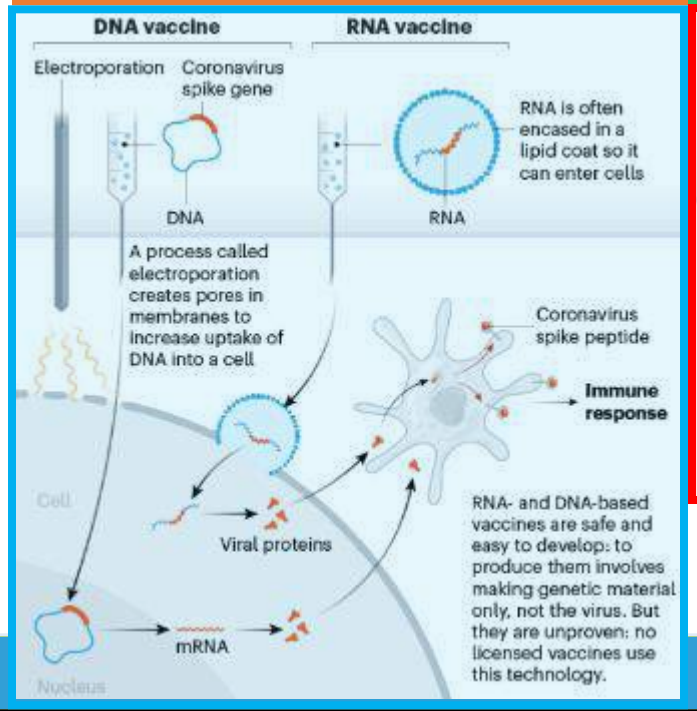
- What are the types of vaccines in clinical evaluation?
- Which are the results of immunogenicity safety and efficacy of SARS CoV-2 vaccines?
- May they protect against arising viral variants?
- Is there any security issues related to authorised vaccines

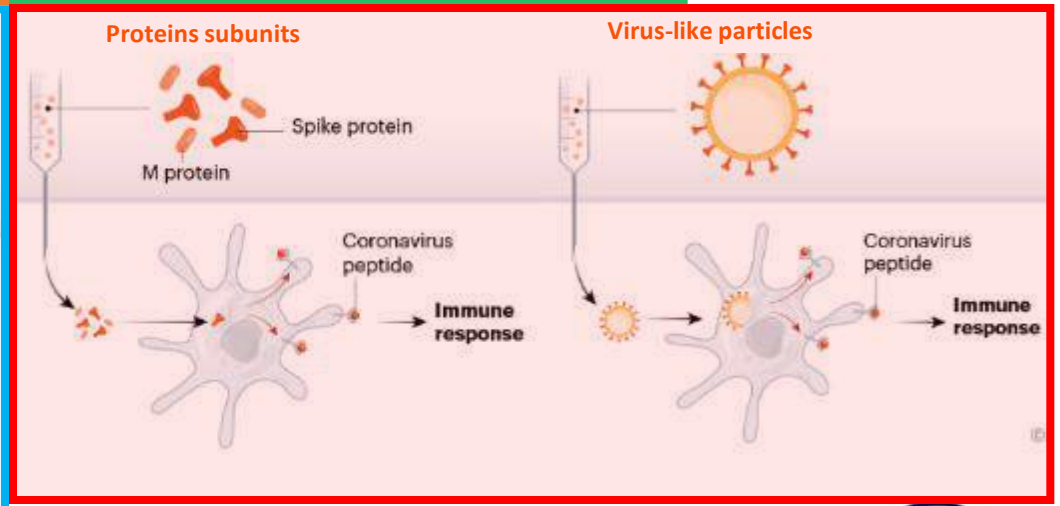
# Vaccines

- **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)



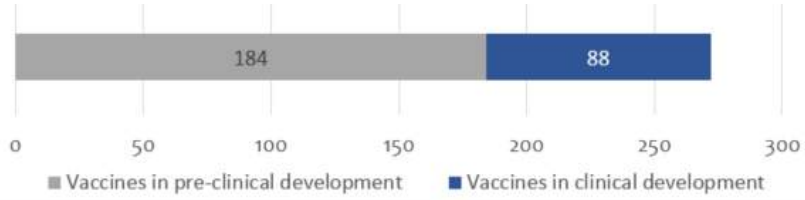

Callaway E. *Nature* Apr 2020

# Vaccines

- **R&D landscape**: WHO lists 184 candidates in preclinical development, 85 candidate vaccines in clinical evaluation (April 5th 2021); update available at :

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

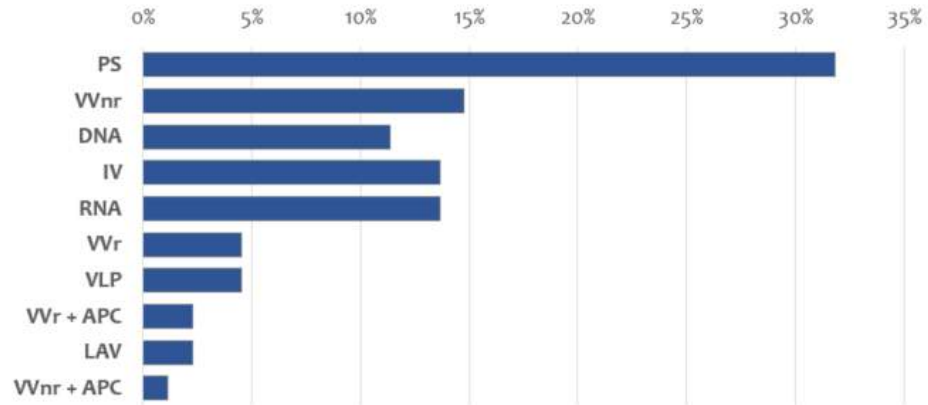
| | |
|---|---|
| 1. - Number of vaccines in clinical development | 88 |
| 2. - Number of vaccines in pre-clinical development | 184 |




3. - Candidates in clinical phase

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

| Platform | | Candidate vaccines (no. and %) | |
|---|---|---|---|
| PS | Protein subunit | 28 | 32% |
| VVnr | Viral Vector (non-replicating) | 13 | 15% |
| DNA | DNA | 10 | 11% |
| IV | Inactivated Virus | 12 | 14% |
| RNA | RNA | 12 | 14% |
| VVr | Viral Vector (replicating) | 4 | 5% |
| VLP | Virus Like Particle | 4 | 5% |
| VVr + APC | VVr + Antigen Presenting Cell | 2 | 2% |
| LAV | Live Attenuated Virus | 2 | 2% |
| VVnr + APC | VVnr + Antigen Presenting Cell | 1 | 1% |
| | | 88 | |




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

*From WHO COVID19 vaccine tracker*

# Phase III/IV COVID-19 Vaccines (April 19th 2021)

| Developer | Vaccine Platform | Description |
|---|---|---|
| **BioNTech – Pfizer – Fosun Pharma** | RNA | **BNT162b2*:** Lipid nanoparticle-formulated, nucleoside **modified mRNA** vaccine encoding **full-length spike (S) protein** |
| **Moderna – NIAID** | RNA | **mRNA-1273:** Lipid nanoparticle encapsulated, mRNA vaccine encoding **pre fusion spike (S) protein** |
| **CureVac** | RNA | **CVnCoV:** Lipid nanoparticle encapsulated, mRNA (non modified) vaccine encoding **pre fusion spike (S) protein** |
| **Inovio-IVI** | DNA | **INO-4800:** DNA plasmid vaccine with electroporation |
| **Osaka University-Takara Bio** | DNA | **AG0302-COVID19:** DNA plasmid vaccine + Adjuvant |
| **CanSino Biologicals Inc – Beijing Institute of Biotechnology** | Non replicating viral vector | **Ad5-nCoV:** Replication-deficient **Ad5** vector containing optimised **full-length spike (S) protein** |
| **Gamaleya Research Institute** | Non replicating viral vector | **Spoutnik V:** Recombinant **Ad26 (prime)** and recombinant **Ad5 (boost)** viruses expressing the gene for **spike (S) protein** |
| **Janssen Pharmaceutical Companies – Beth Israel Deaconness Medical Center** | Non replicating viral vector | **Ad26COVS1:** Recombinant adenovirus vaccine **(Ad26)** incorporating SARS-CoV-2 full stabilized **Spike (S)** protein |
| **University of Oxford – AstraZeneca** | Non replicating viral vector | **AZD1222:** Replication-deficient **simian adenovirus (ChAdOx1)** vector containing **codon-optimised spike (S) protein** |

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*FDA approved* *EMA approved* *Approved by other national regulatory agencies*

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| Developer | Vaccine Platform | Description |
|---|---|---|
| **ReiThera - Univercells** | Non replicating viral vector | **GRAd-CoV2.S:** replication defective **Simian adenovirus** (GRASd) encoding SARS COV 2 **S prot**ein |
| **Novavax** | Protein subunit | **NVX-COV2373:** Recombinant **nanoparticle** vaccine consisting of **full-length spike (S) protein**, with or without **Matrix-M1 adjuvant** |
| **Medicago Inc** | Protein subunit | **CoVLP: Plant-derived** VLP **adjuvanted** with AS03 |
| **Anhui Zhifei Logcom Biopharmaceutical-Chinese Academy of Sciences** | Protein subunit | **ZF2001: Adjuvanted** recombinant protein (**RBD-Dimer**) expressed in CHO cells |
| **Clover – GSK– Dynavax** | Protein subunit | **SCB-2019: Native** like **trimeric subunit Spike** Protein (AS03 or CpG1018 plus alum **adjuvanted**) |
| **Covaxx<br>University of Nebraska** | Protein subunit | **UB-6212: Multiepitope** peptide based **S1-RBD** protein based vaccine |
| **Center for genetic engineering and Biotcehnology** | Protein subunit | **CIGB-66: RBD+aluminium** hydroxide |
| **Instituto Finlay de Vacunas** | Protein subunit | **FINLAY-FR-2/Soberana2:** Anti-SARS CoV 2 (**RBD chemically conjugated to tetanus toxoid)+adjuvant** |
| **Sanofi Pasteur** | Protein subunit | **VAT00002:** Anti-SARS CoV 2 **(S)+adjuvant** |
| **Vector Institute** | Protein subunit | **EpiVacCorona: peptide** based vaccine for COVID19 **prevention** |

| Developer | Vaccine Platform | Description |
|---|---|---|
| **Sinovac – Institute Butantan** | Inactivated | **CoronaVac: β-propiolactone inactivated** vaccine adiministered with **aluminium hydroxide adjuvant** |
| **Beijing Institute of Biological Products – Sinophram** | Inactivated | **BBIBP-CorV**: **β-propiolactone i**nactivated vaccine adiministered with **aluminium hydroxide adjuvant** |
| **Wuhan Institute of Biological products– Sinopharm** | Inactivated | **SARS-CoV-2 Vaccine: β-propiolactone inactivated** vaccine adsorbed to 0.5-mg **aluminum** |
| **Bharat Biotech- ICMR- National Institut of Virology** | Inactivated | **COVAXIN:** whole-virion inactivated vaccine |
| **Research Institute for Biological Safety Problems** | Inactivated | **QazCovid-in:** Inactivated vaccine |
| **Institute of Medical Biology Chine Academy of Medical Sciences** | Inactivated | Inactivated Vaccine |
| **Shifa Pharmed** | Inactivated | Inactivated Vaccine |

mRNA vaccine

# BNT162 b2

IMMUNOGENICITY AND SAFETY DATA

## BioNTech/Pfizer

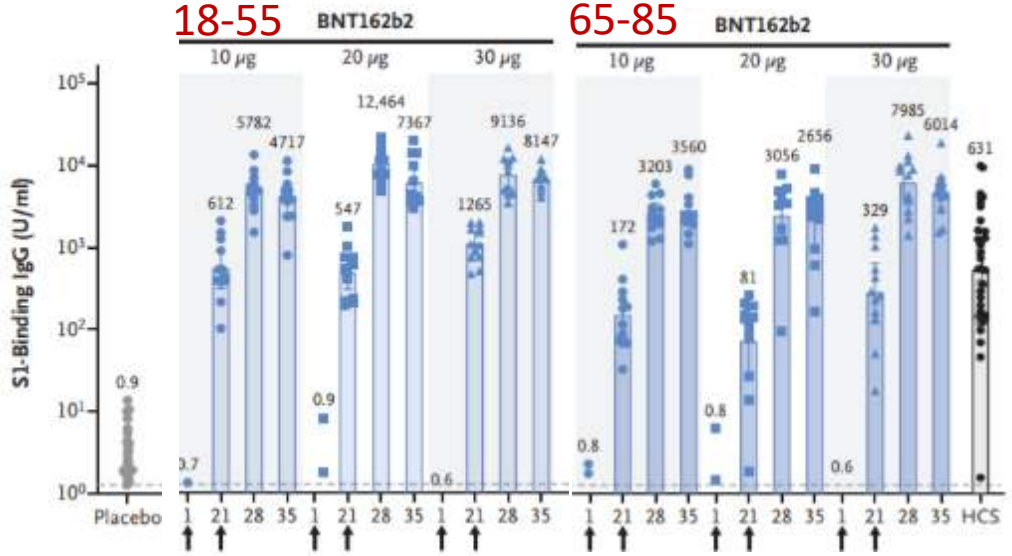
**Phase I:** NCT04368728

| | |
|---|---|
| **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)<br>20 µg BNT162b2 (S) 18–55y (n = 12)<br>30 µg BNT162b2 (S) 18–55y (n = 12)<br>10 µg BNT162b2 (S) 65–85y (n = 12)<br>20 µg BNT162b2 (S) 65–85y (n = 12)<br>30 µg BNT162b2 (S) 65–85y (n = 12)<br>*+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

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mRNA vaccine

# BNT162 b2

IMMUNOGENICITY AND SAFETY DATA

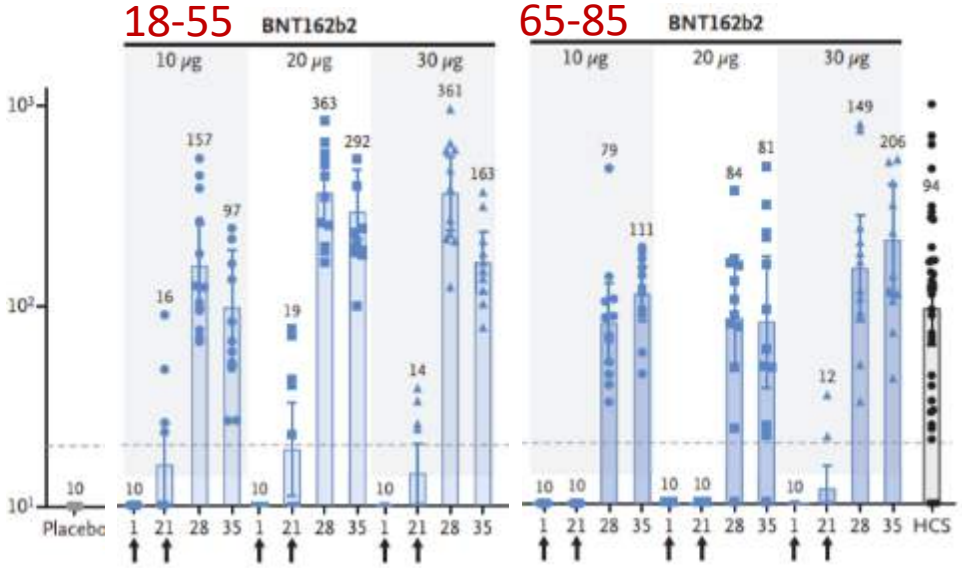
## IMMUNOGENICITY 2/2

### 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.



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)<br>100 µg (n = 15)<br>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

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mRNA vaccine

# mRNA 1273

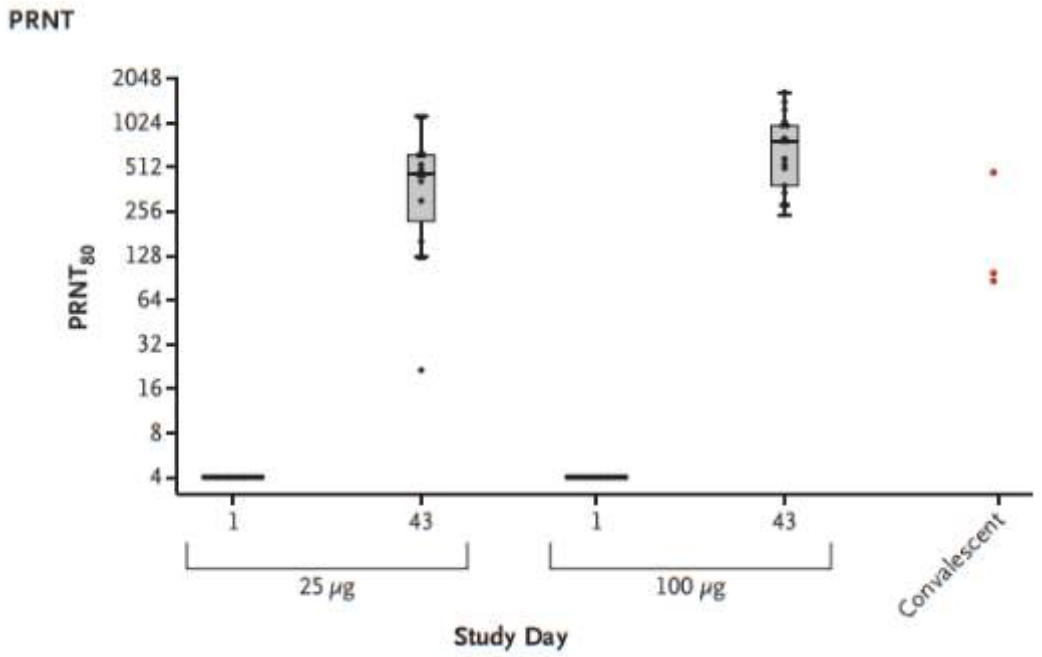
IMMUNOGENICITY AND SAFETY DATA

## 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

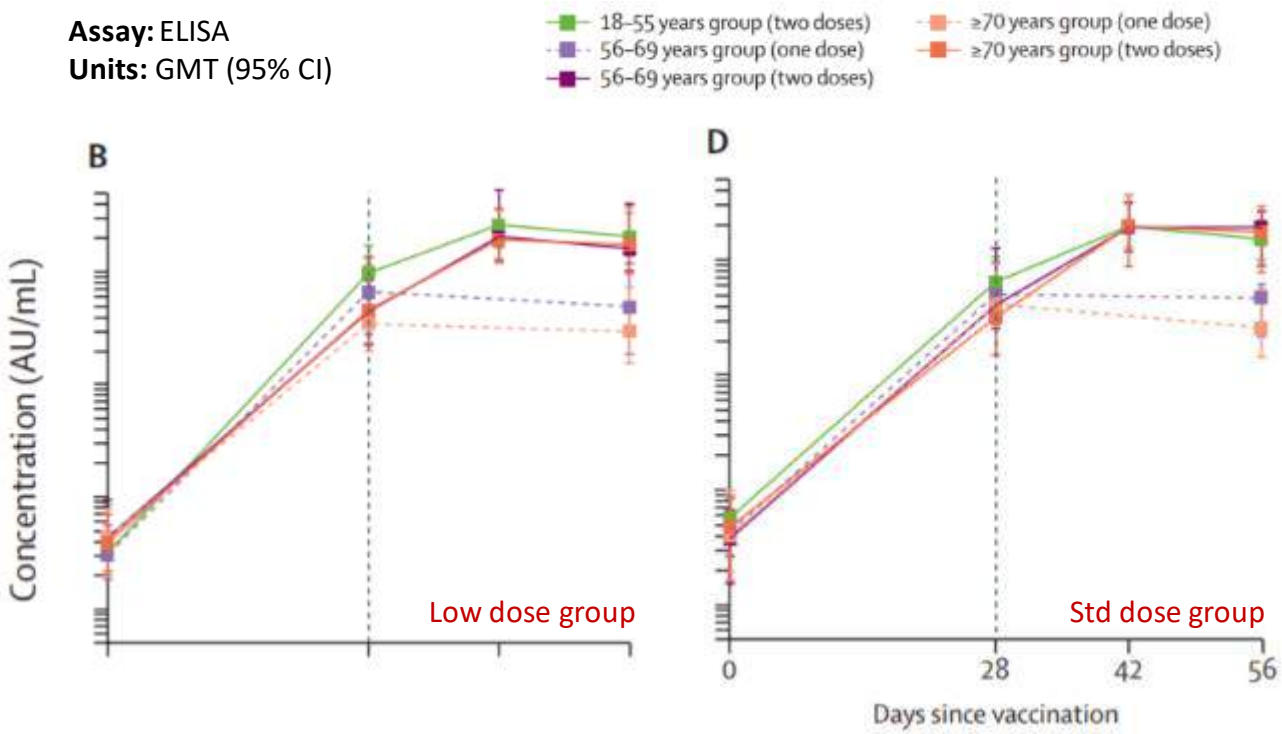
## AstraZeneca-Oxford University Phase II: NCT04400838

| | |
|---|---|
| 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)<br>56–69y: 1 x low dose (n = 30)<br>56–69y: 2 x low dose (n = 30)<br>≥70y: 1 x low dose (n = 50)<br>≥70y: 2 x low dose (n = 50)<br>18–55y: 2 x std dose (n = 50)<br>56–69y: 1 x std dose (n = 30)<br>56–69y: 2 x std dose (n = 30)<br>≥70y: 1 x std dose (n = 50)<br>≥70y: 2 x std dose (n = 50)<br>**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<br>*(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

Adenoviral vector vaccine

# AZD1222

IMMUNOGENICITY AND SAFETY DATA

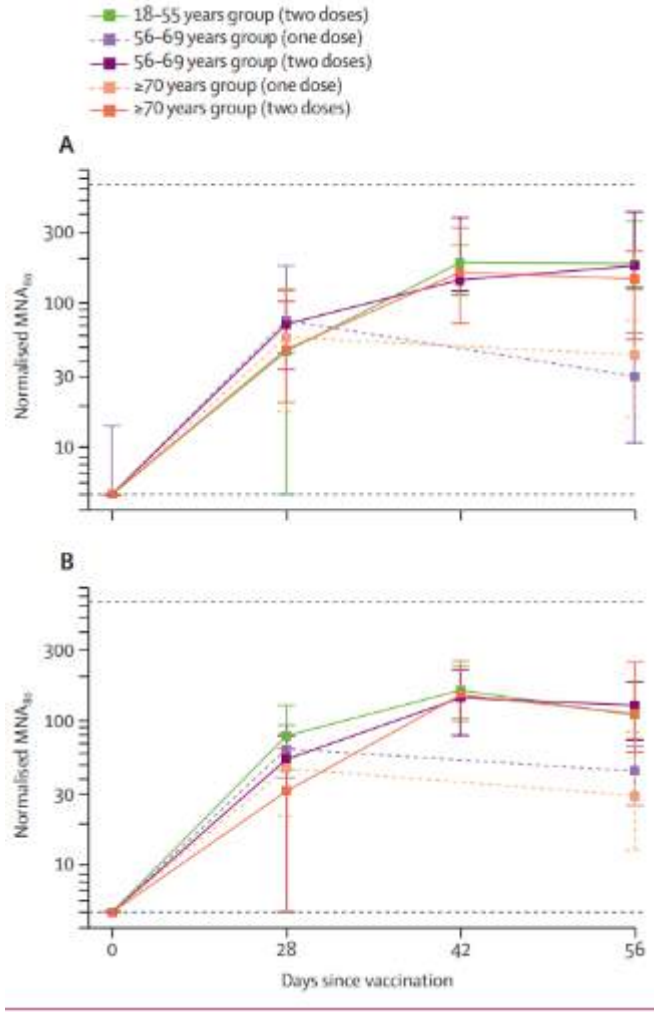
## IMMUNOGENICITY 2/2

### 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

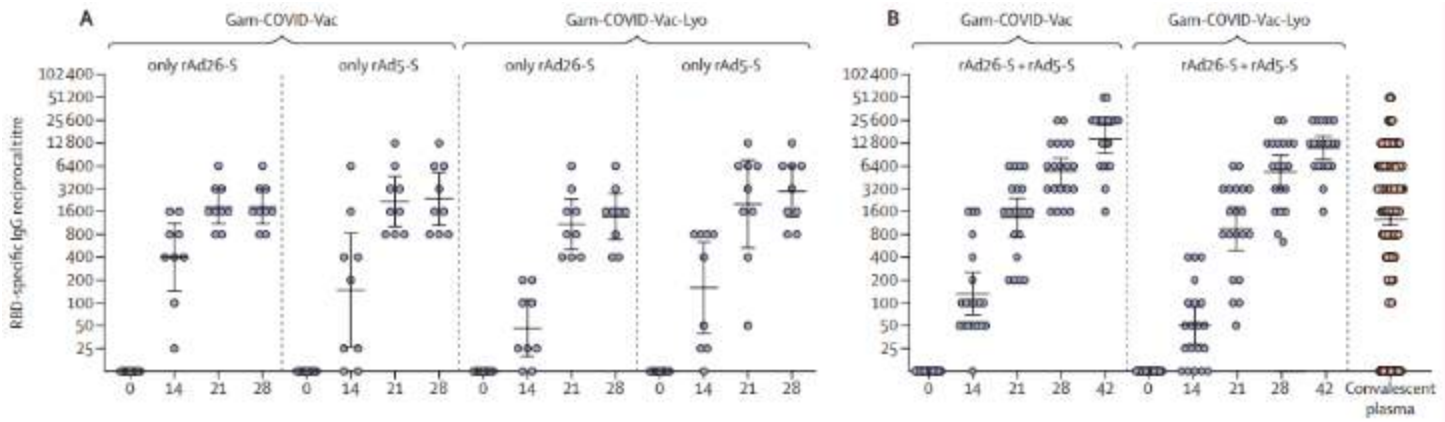
**Phase I/II:** NCT04436471 *(frozen product)*
NCT04437875 *(lyo product)*

| | |
|---|---|
| **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)<br>Frozen 1 x $10^{11}$ rAd5 (n = 9)<br>Frozen $10^{11}$ rAd26/$10^{11}$ rAd5 (n = 20)<br>Lyo 1 x $10^{11}$ rAd26 (n = 9)<br>Lyo 1 x $10^{11}$ rAd5 (n = 9)<br>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

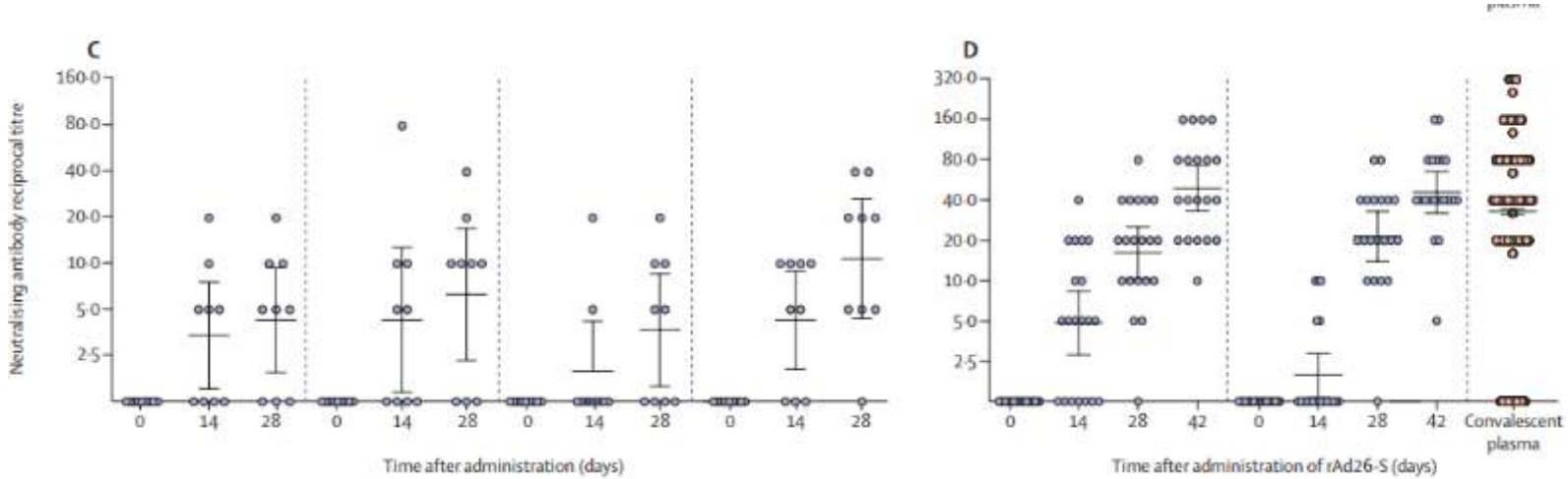
# Sputnik V

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

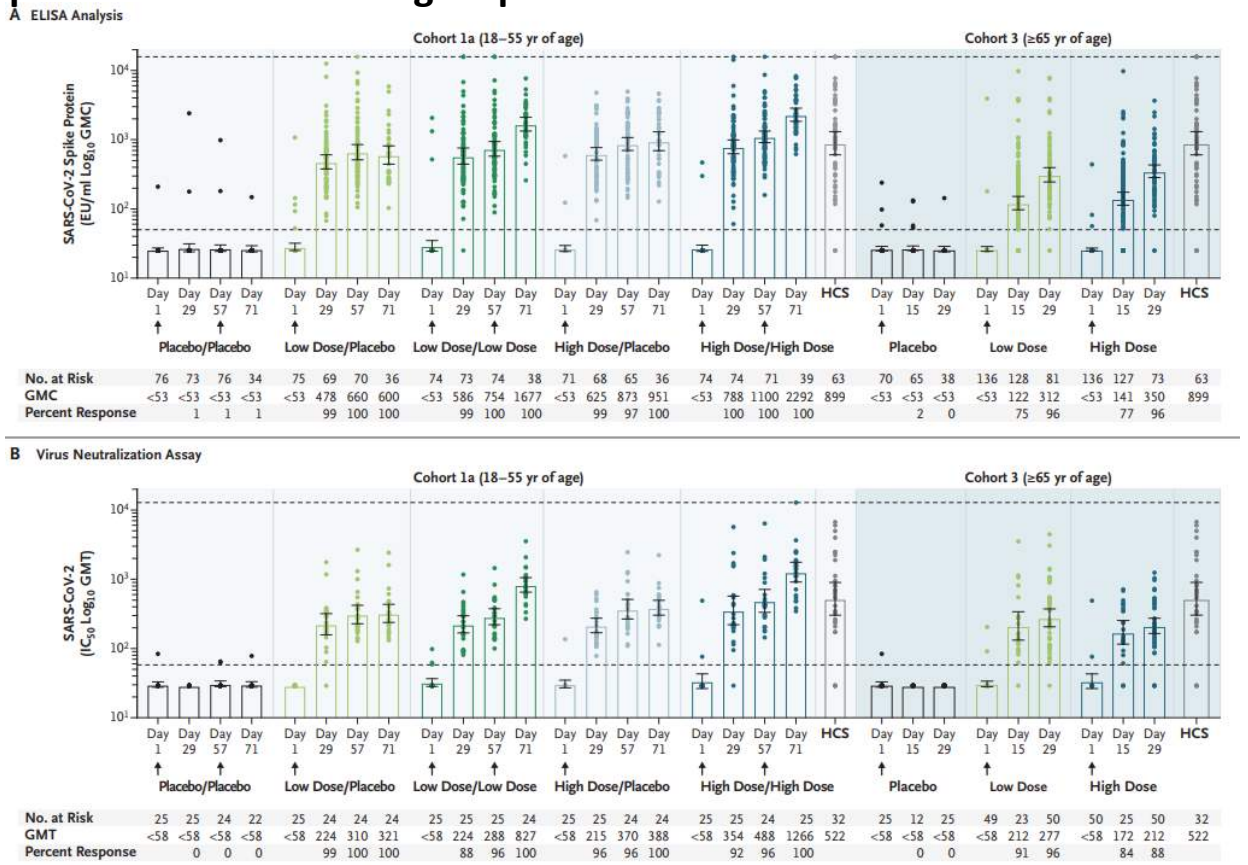
IMMUNOGENICITY AND SAFETY DATA

## 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)<br>18–55y : low dose at d1 (n = 75)<br>18–55y : high dose at d1/57 (n = 75)<br>18–55y : high dose at d1 (n = 75)<br>18–55y : low dose at d1/57 (n = 5)<br>18–55y : low dose at d1 (n = 5)<br>18–55y : high dose at d1/57 (n = 5)<br>18–55y : high dose at d1 (n = 5)<br>≥65y : low dose at d1/57 (n = 75)<br>≥65y : low dose at d1 (n = 75)<br>≥65y : high dose at d1/57 (n = 75)<br>≥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

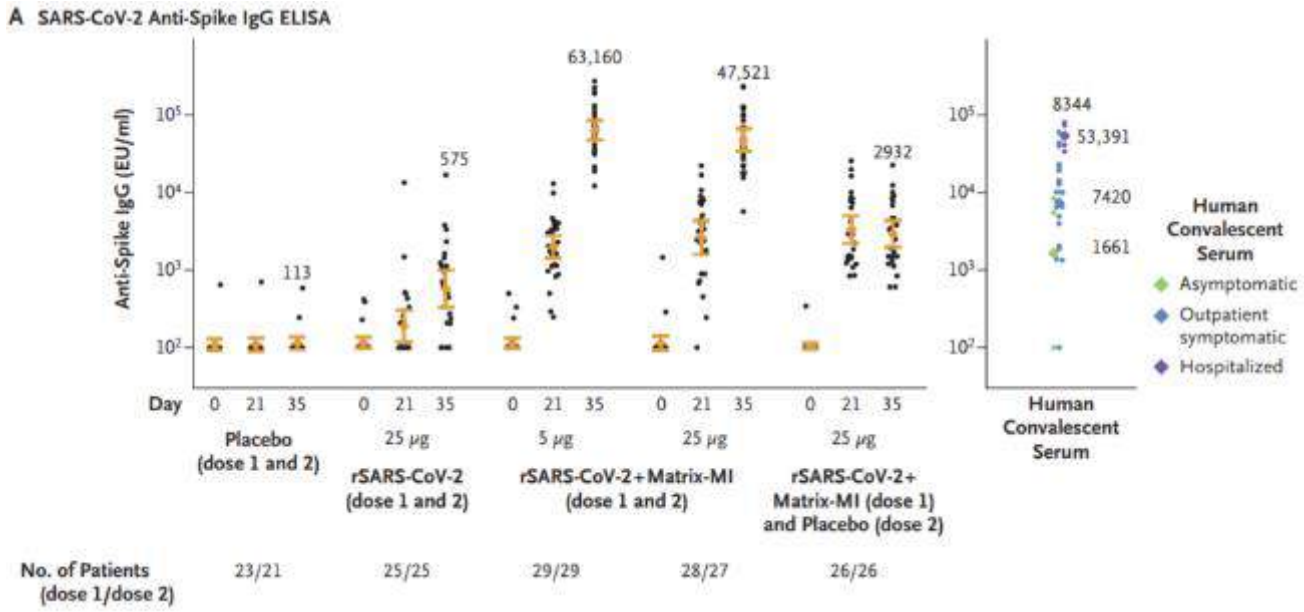
**Phase I:** NCT04368988

| | |
|---|---|
| **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)<br>2 x 5 µg + 50 µg Matrix-M1 (n = 28)<br>2 x 25 µg + 50 µg Matrix-M1 (n = 28)<br>1 x 25 µg + 50 µg Matrix-M1 (n = 25)<br>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<br>**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

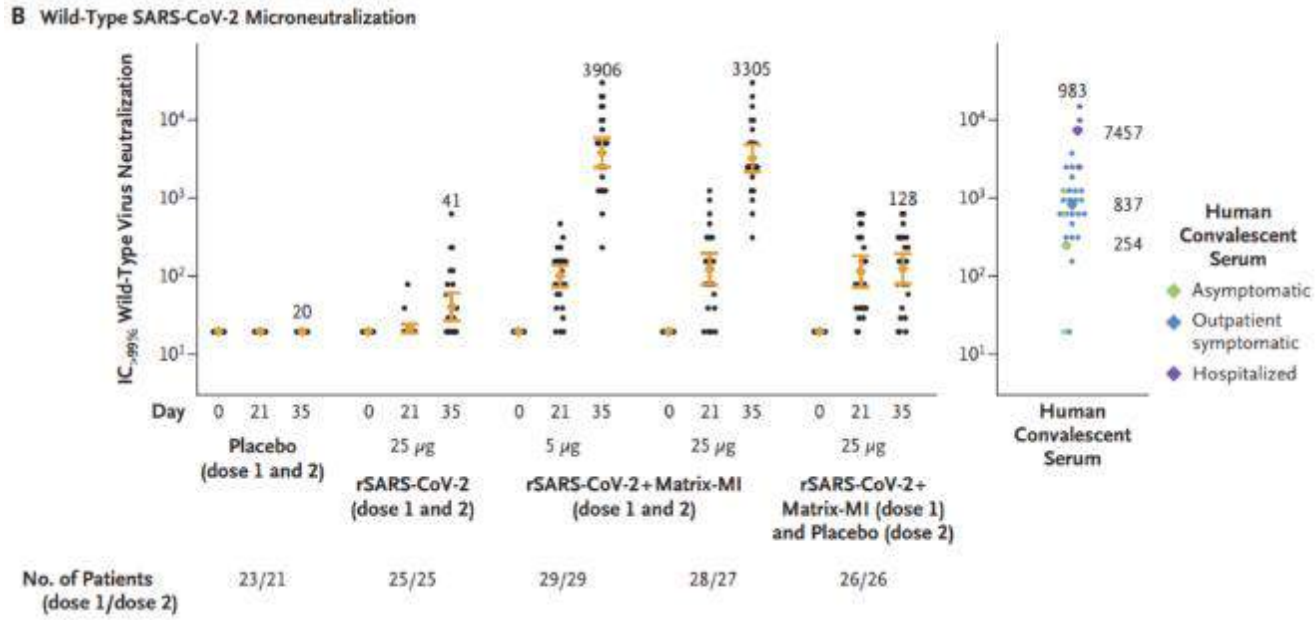
IMMUNOGENICITY AND SAFETY DATA

## 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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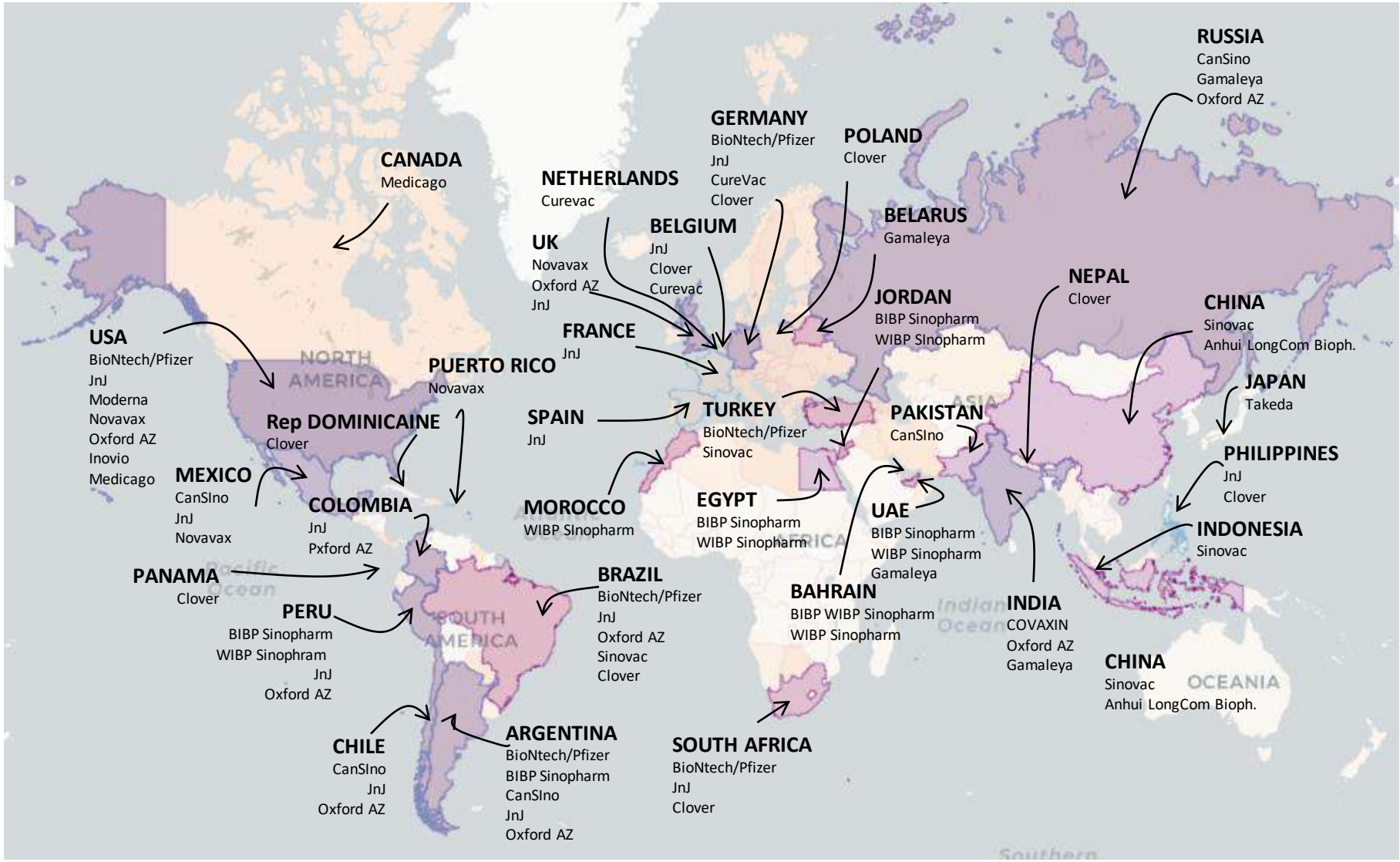
# Vaccine Summary results on immunogenicity

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

**NOTE:**

**COMPARISONS SHOULD NOT BE MADE AS ASSAYS ARE NOT STANDARDIZED**

# Efficacy Trial Map (April 19th 2021)




*Adapted from LSHTM COVID19 vaccine tracker* https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

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# 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<br>94 confirmed cases of COVID19<br>• **> 90% Efficacy** |
| November 11th 2020 | Gamaleya | Sputnik V | 1st interim analysis; 21 days after 1st dose<br>20 confirmed cases of COVID19<br>• **> 92% Efficacy** |
| November 16th 2020 | Moderna | mRNA 1273 | 1st interim analysis; 42 days after 1st dose<br>95 confirmed cases of COVID19<br>• **94.5% Efficacy** |
| November 18th 2020 | BioNTech/Pfizer | BNT162b2 | **Final analysis**; 28 days after 1st dose<br>170 confirmed cases of COVID19<br>• **95% Efficacy** |
| November 23rd 2020 | AstraZeneca/Oxford | AZD1222 | **1st interim analysis** 14 days after 2nd dose<br>131 confirmed cases of COVID19<br>• **90% Efficacy when given as half dose/full dose**<br>• **62% Efficacy when given as full dose/full dose**<br>• **Overall 70% efficacy** |
| November 24th 2020 | Gamaleya | Sputnik V | **2nd interim analysis**; 42 days after 1st dose<br>39 confirmed cases of COVID19 *(10 severe)*<br>• **95% Efficacy** |
| November 30th 2020 | Moderna | mRNA 1273 | **Final analysis**; 42 days after 1st dose<br>196 confirmed cases of COVID19 *(30 severe)*<br>• **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<br>28 days after 1st dose (one dose vaccine)<br>62 confirmed cases of COVID19 (56 on the placebo group)<br>• 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)<br>Etude multinational ENSEMBLE.<br>• **72% Effective** in the US and **66% Effective** Overall at Preventing Moderate to Severe COVID-19<br>• **85% Effective** overall in preventing severe disease.<br>• **Complete protection** against COVID-19 related Hospitalisation and Death<br>• 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<br>253 confirmed cases of COVID19<br>Efficacy rate against diseases caused by COVID-19 for:<br>• **all** cases: **50.65%**<br>• cases requiring **medical treatment:** 83.70%<br>**hospitalized, severe** and **fatal** cases: **100%**<br><br>Efficacy by strain:<br>• **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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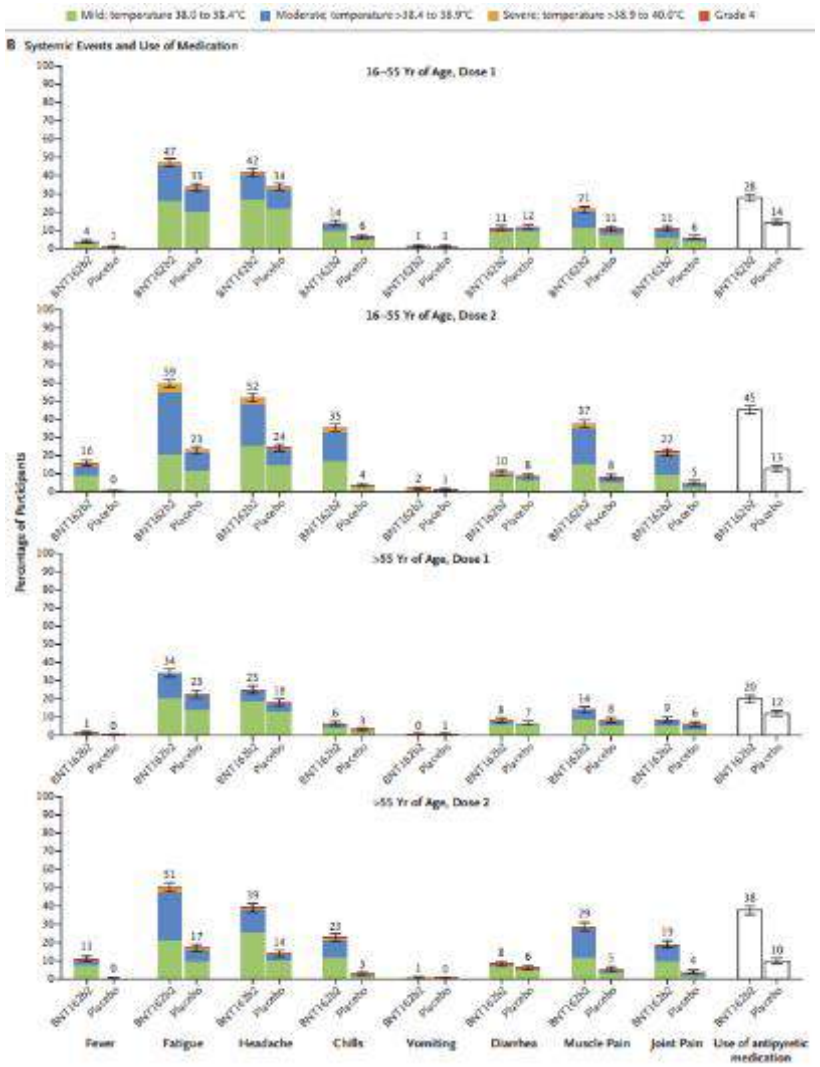
Polack FP *et al. NEJM* Dec 2020

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

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# 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

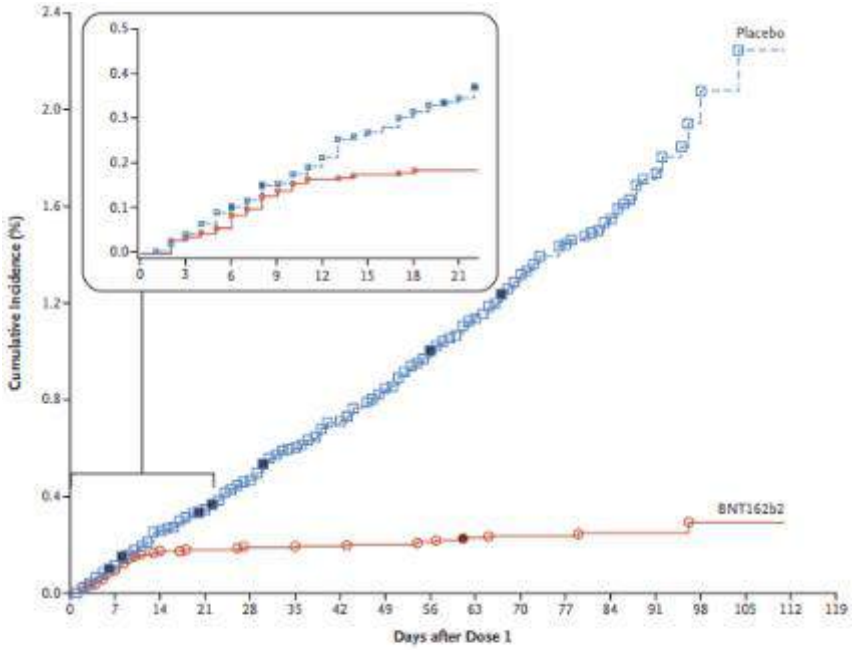
**Vaccine efficacy: 95%**

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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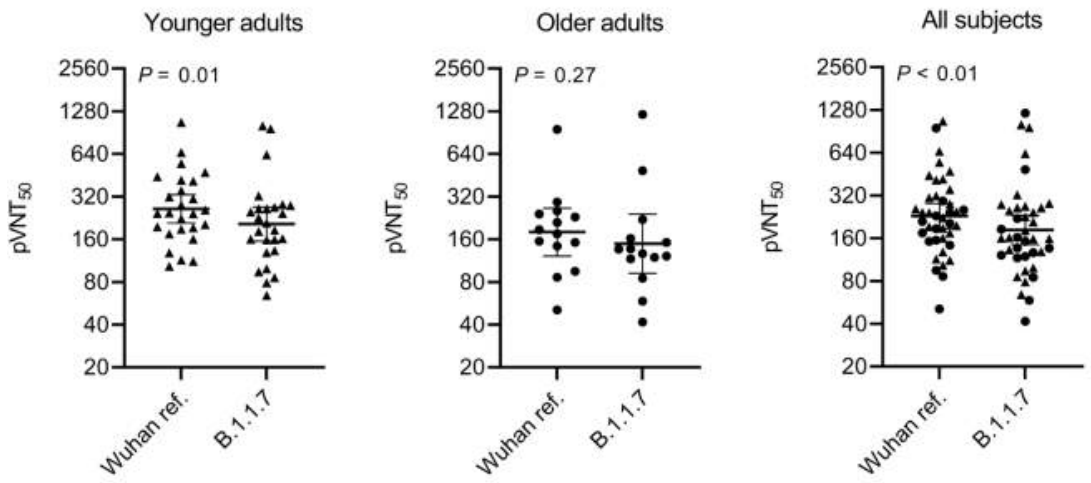
# BNT162 b2

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

Muik A *et al. Science FEB* 2021

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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

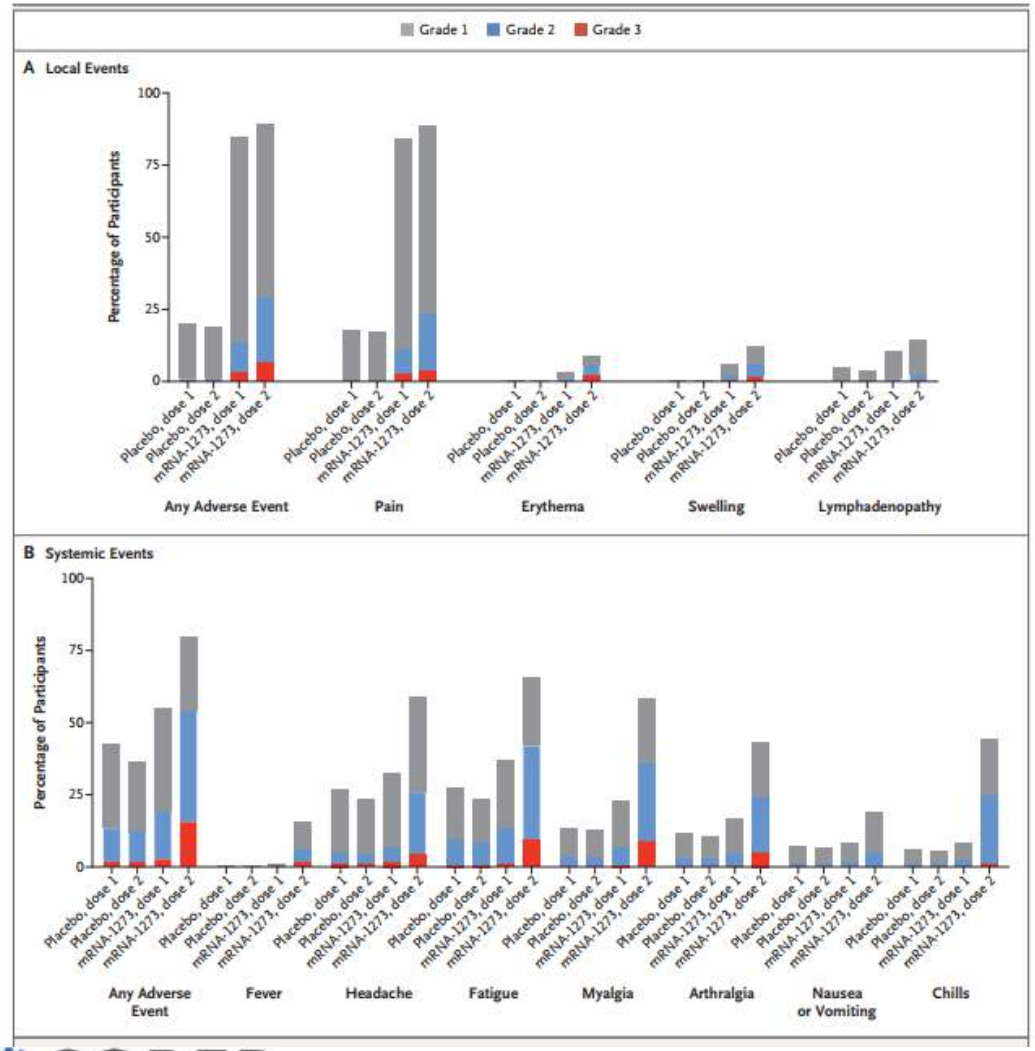
Table 1. Demographic and Clinical Characteristics at Baseline.*

| 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

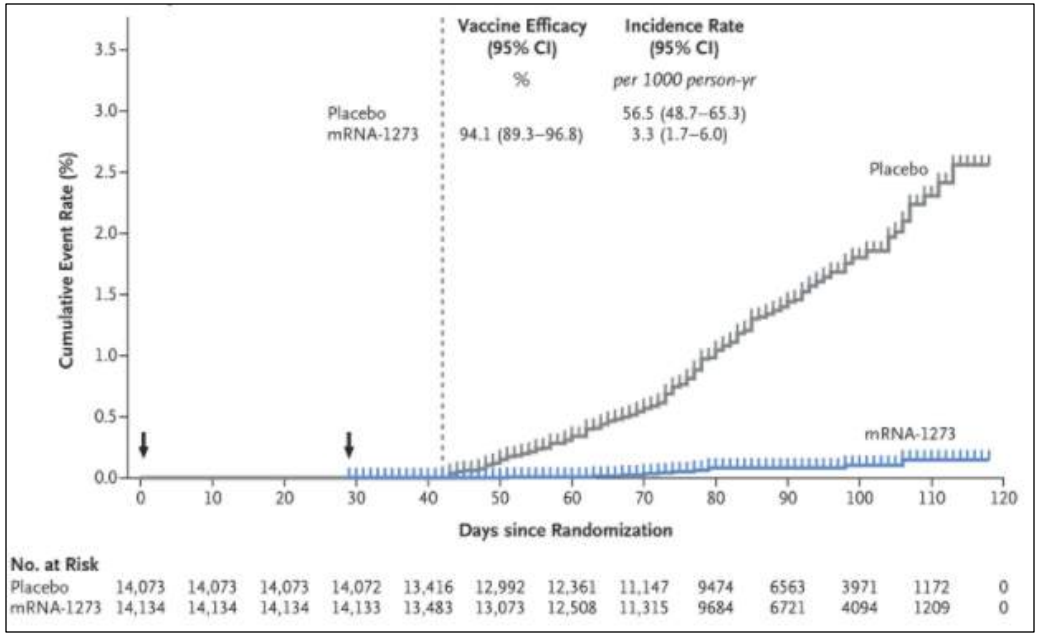
Key limitations: short duration of safety and efficacy follow-up

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.

mRNA vaccine

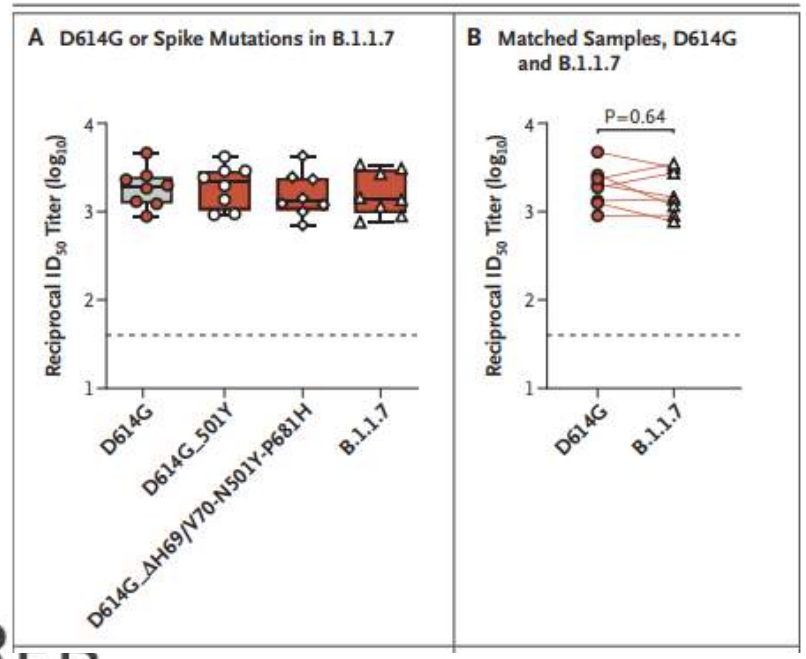
# mRNA 1273

NEUTRALIZATION OF VIRAL VARIANTS

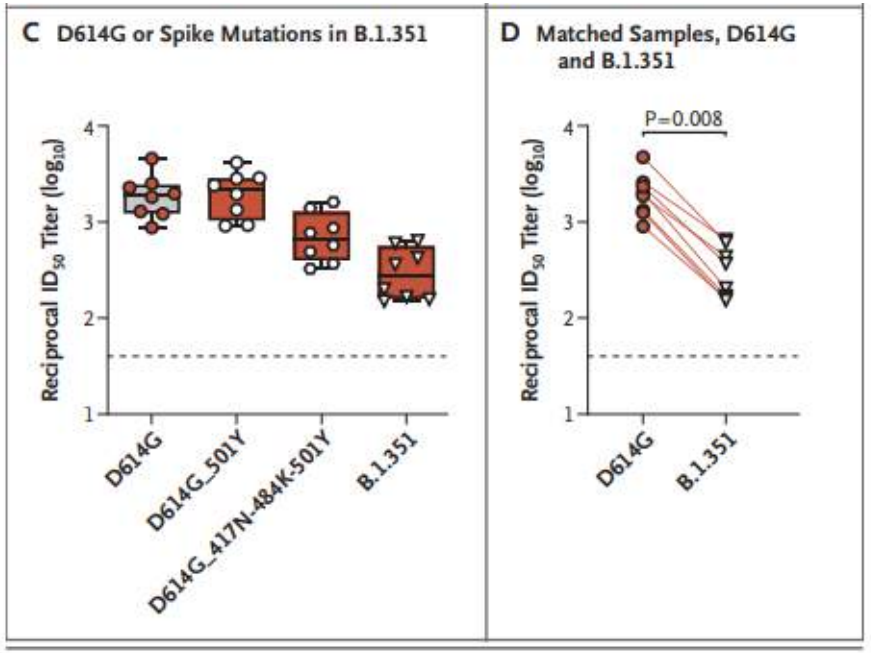
Serum neutralizing activity against recombinant vesicular stomatitis virus (rVSV)–based SARS-CoV-2 bearing the spike protein from the original Wuhan-Hu-1 isolate, the D614G variant, the B.1.1.7 and B.1.351 variants

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.

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 **$5\times10^{10}$** vp at **28 days**
    - SD/SD: prime **$5\times10^{10}$** vp; boost **$5\times10^{10}$** 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

# AZD1222

EFFICACY AGAINST VIRAL VARIANTS

## Efficacy of AZD1222 vaccine against SARS-CoV-2 VOC 202012/01 (B.1.1.7)

**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

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%**

| | 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

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

COREB mission nationale Coordination Opérationnelle Risque Epidémique et Biologique

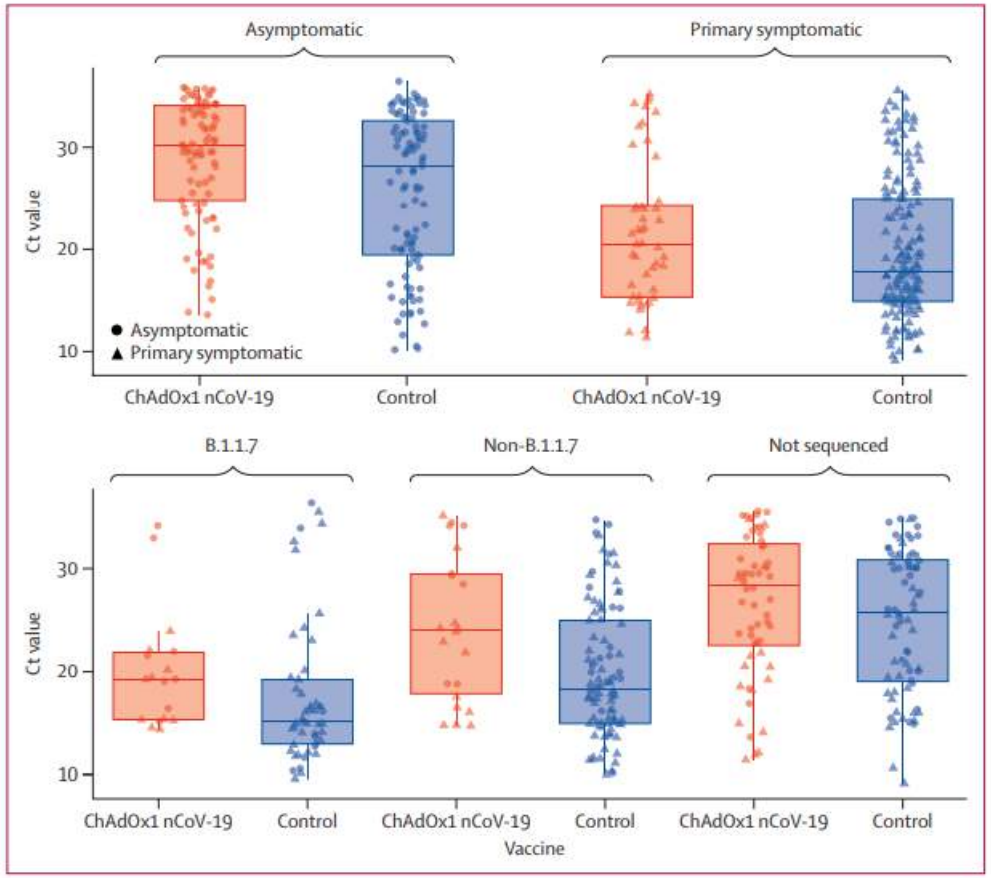
MALADIES INFECTIEUSES ÉMERGENTES

Adenoviral vector vaccine

# AZD1222

EFFICACY AGAINST VIRAL VARIANTS

## Efficacy of AZD1222 vaccine against SARS-CoV-2 VOC 202012/01 (B.1.1.7)




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

Adenoviral vector vaccine

# AZD1222

EFFICACY AGAINST VIRAL VARIANTS

## Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 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).*

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

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

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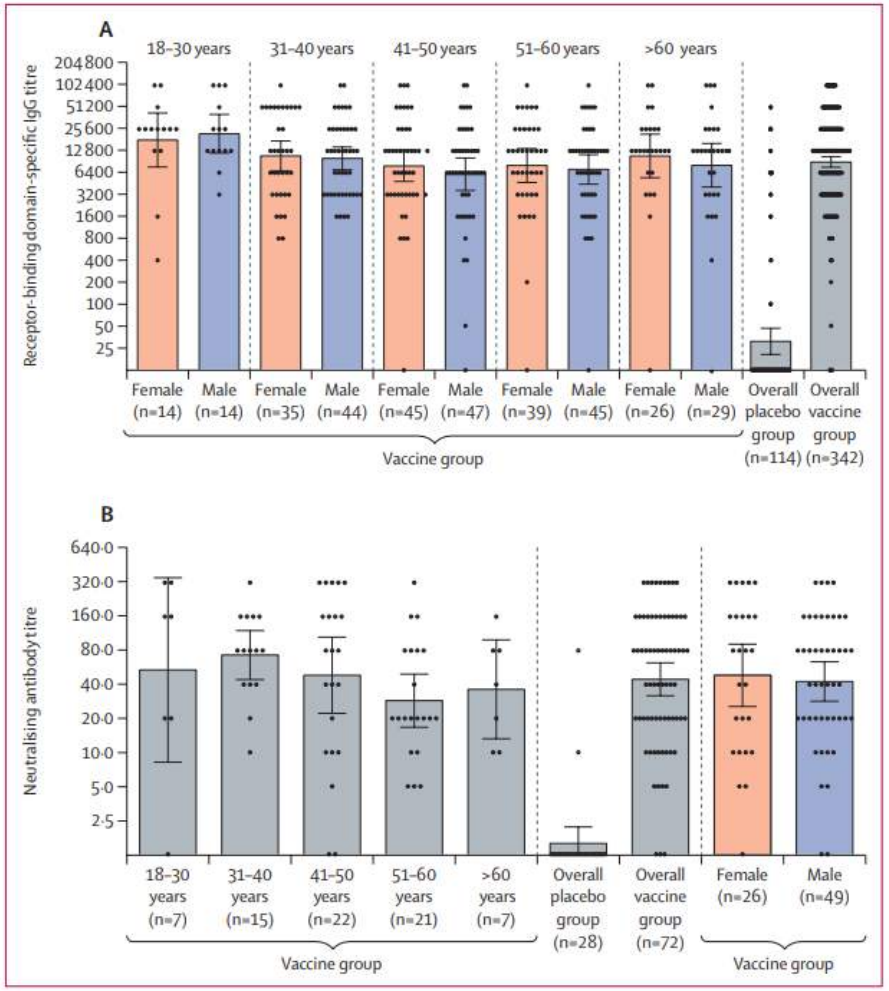
Adenoviral vector vaccine

# 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

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

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# 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

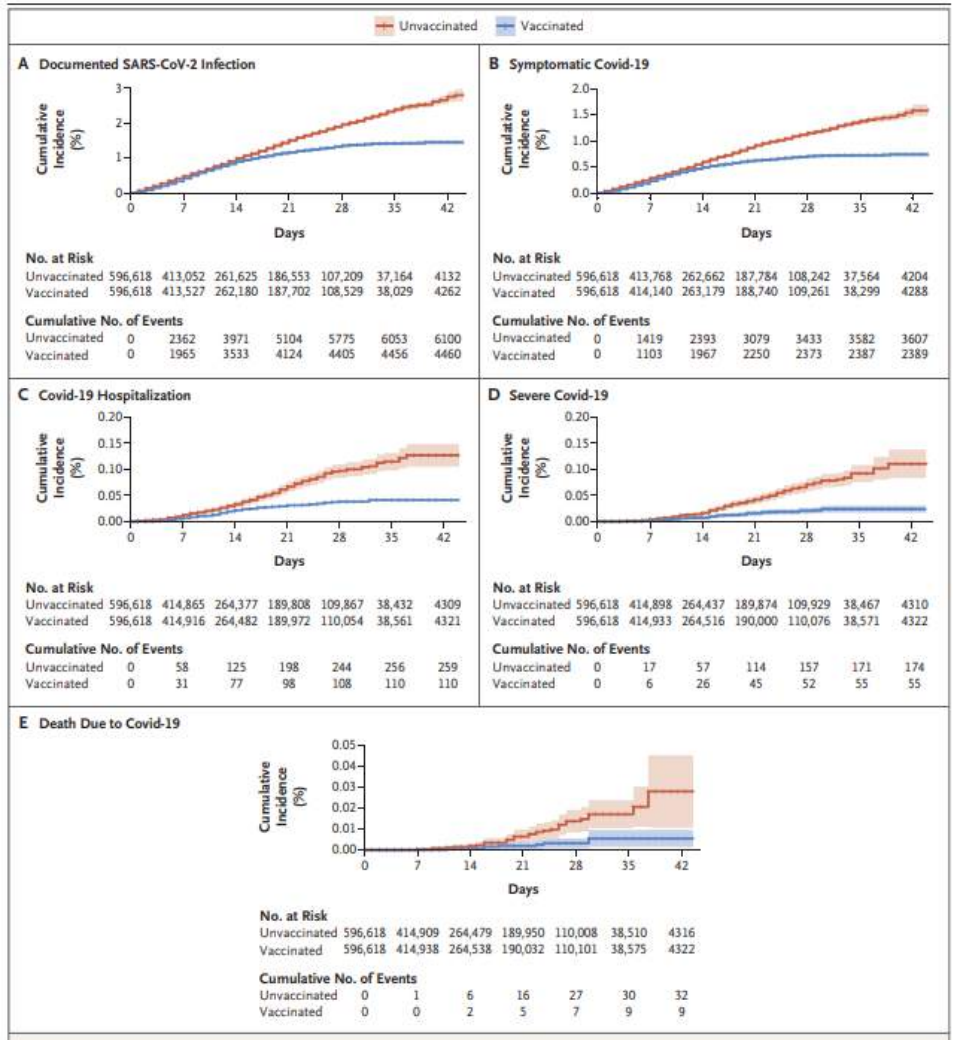
  > During days 14 through 20 and days 21 through 27: 46% and 60% for documented infection, 57% and 66% for symptomatic Covid-19, 74% and 78% for hospitalization, 62% and 80% for severe Covid-19, and 72% and 84% for Covid-19–related death, respectively

- 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 vaccineted 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

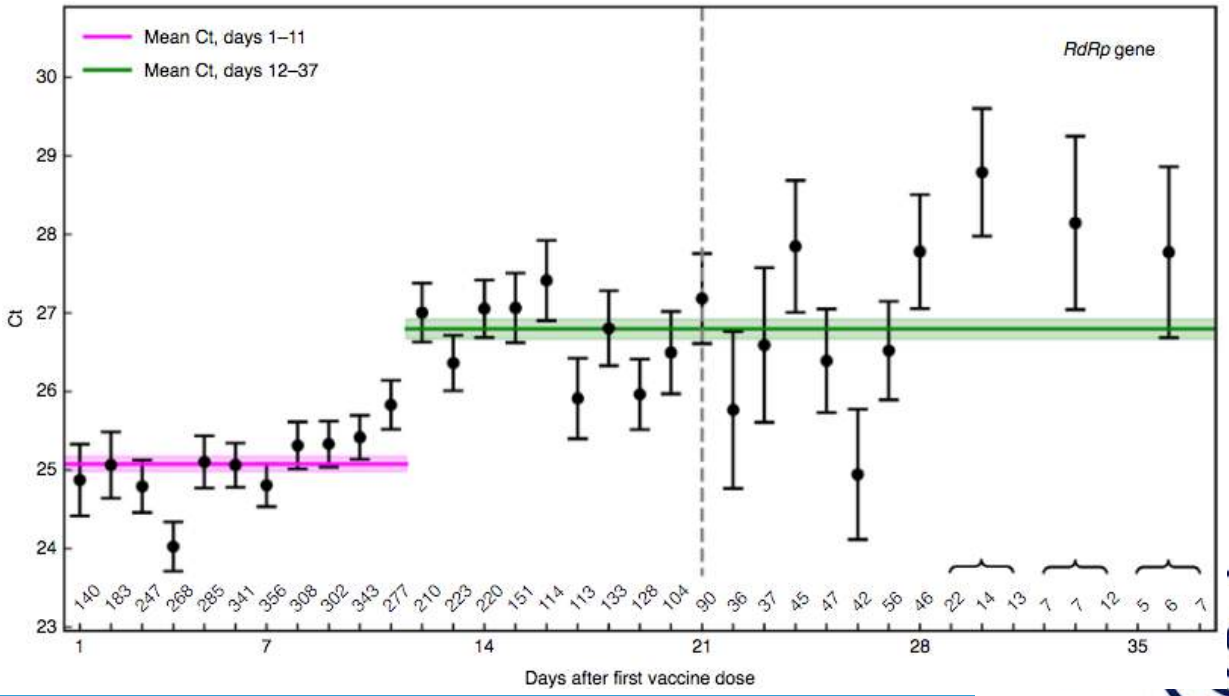
**Effect of vaccination on viral load in COVID-19 post-vaccination infections ?**

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**

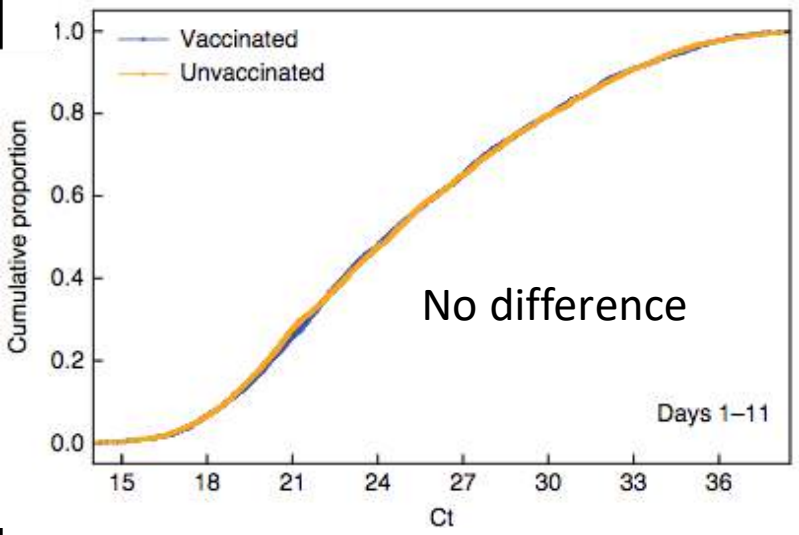
Ct values of positive samples collected 12–37 d after were higher than the Ct values of positive samples taken during the first 11 d after vaccination

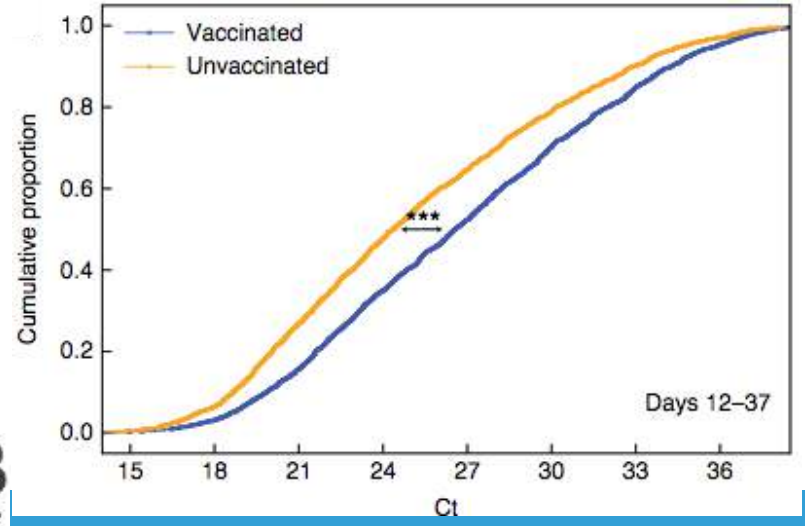



Levine-Tiefendrun M et *al. Nature Medicine. March* 2021

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

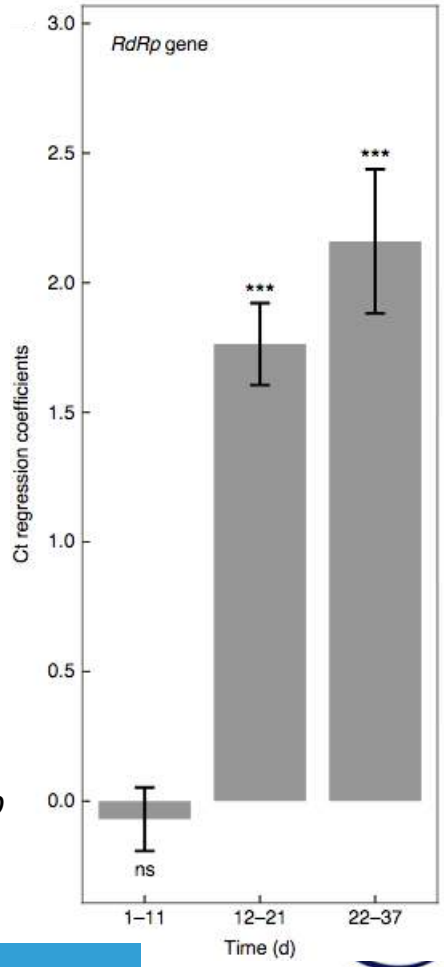
Ct values of positive sample of vaccinated patients versus Ct values of positive tests of unvaccinated patients.




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

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# 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.

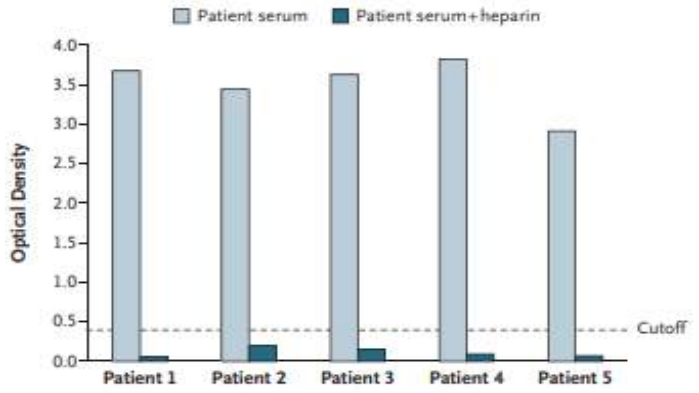


Figure 2. IgG PF4–Polyanion Detection in Serum.

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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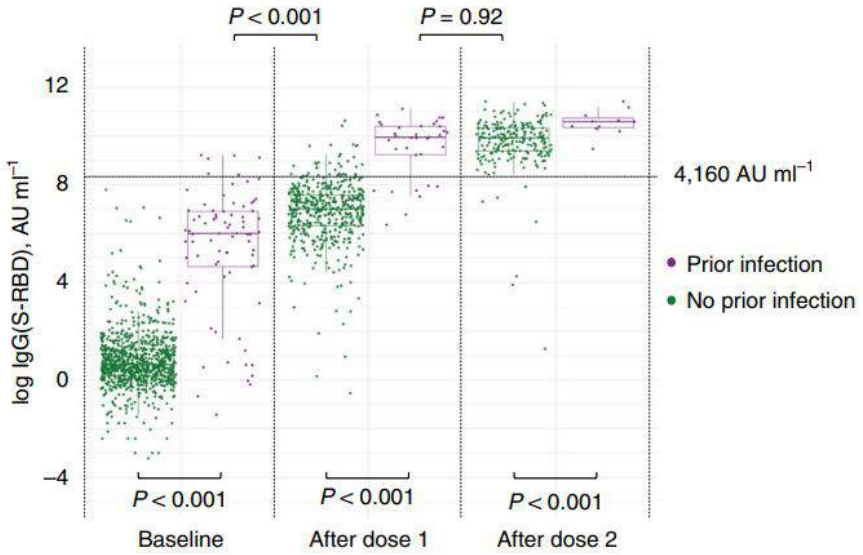
# Vaccination of particular populations

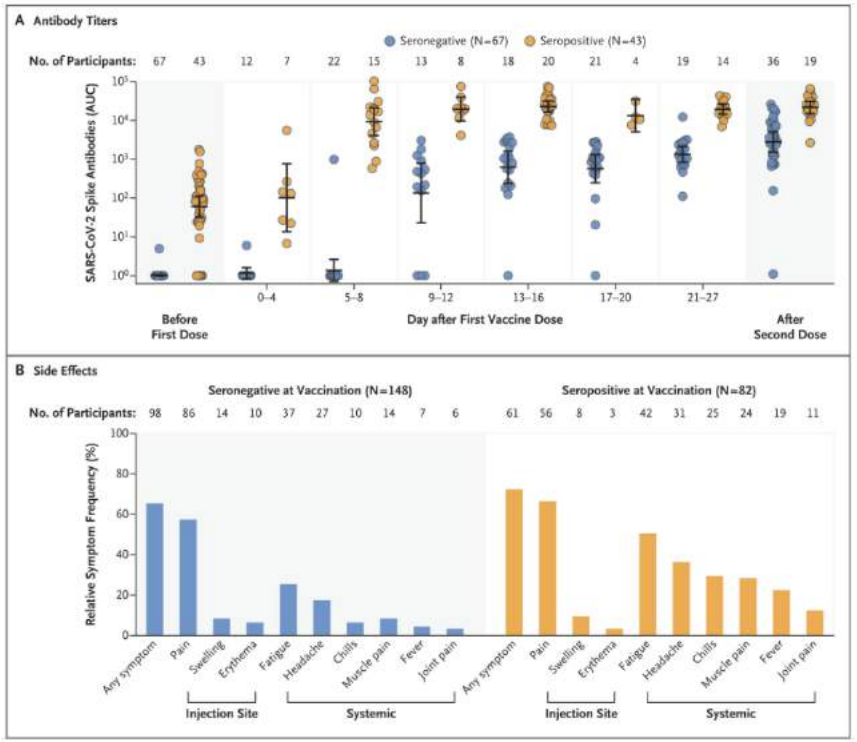
COVID 19 PATIENTS

## 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 WOMAN

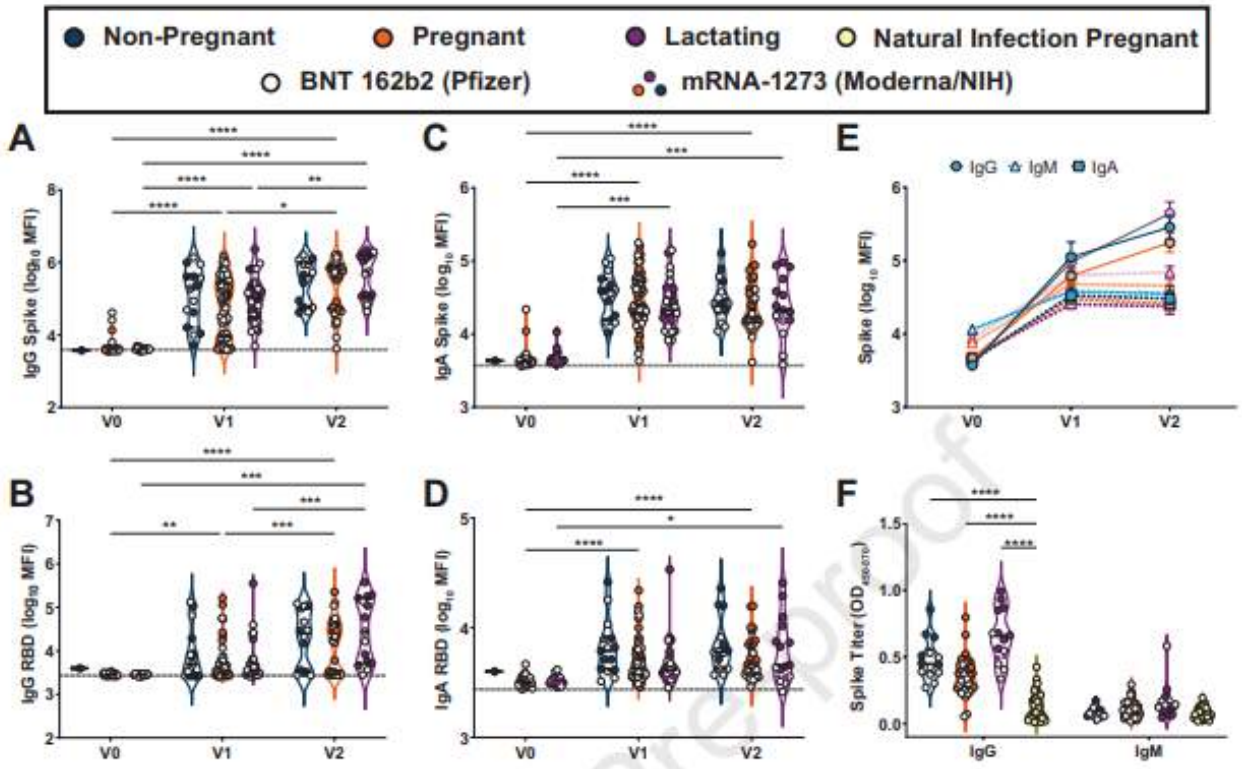
**Population:** pregnant (n=84; 13 deliveries); lactating (n=31); or non-pregnant woman of reproductive age (18-45) (n=16)

**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

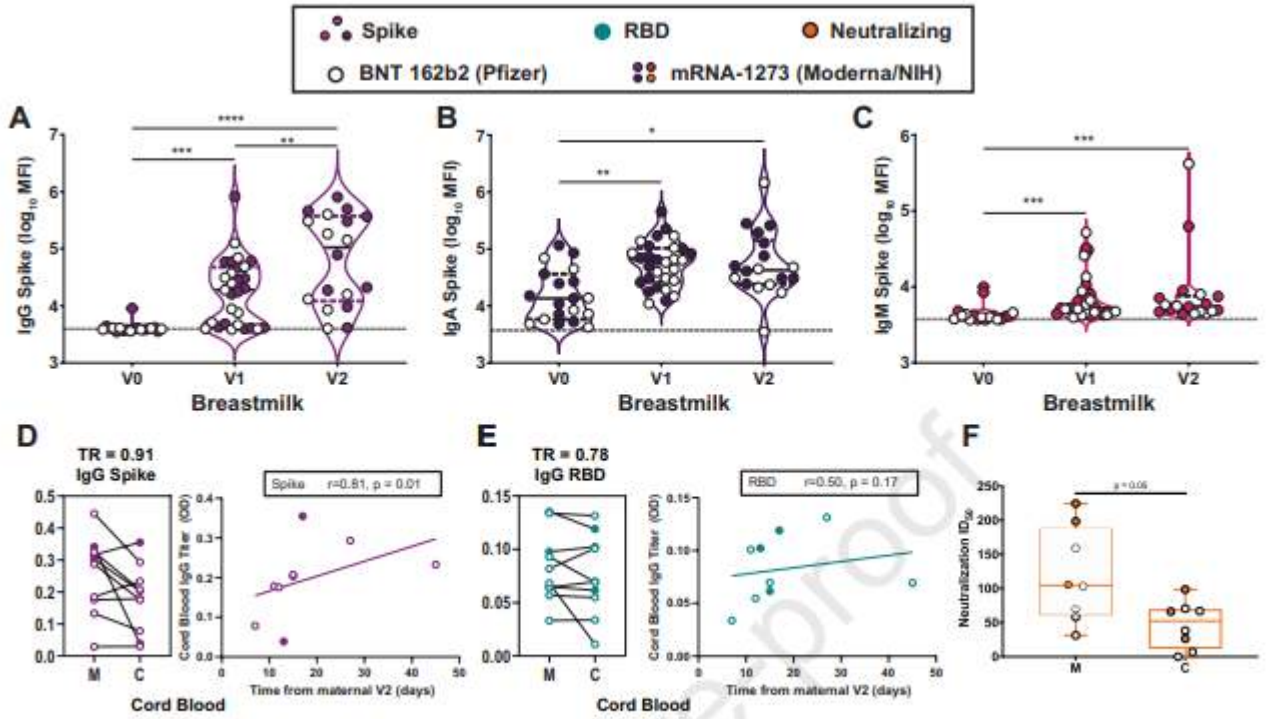
**SAFETY:** low cumulative symptoms score with no significant differences between groups




**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 WOMAN




**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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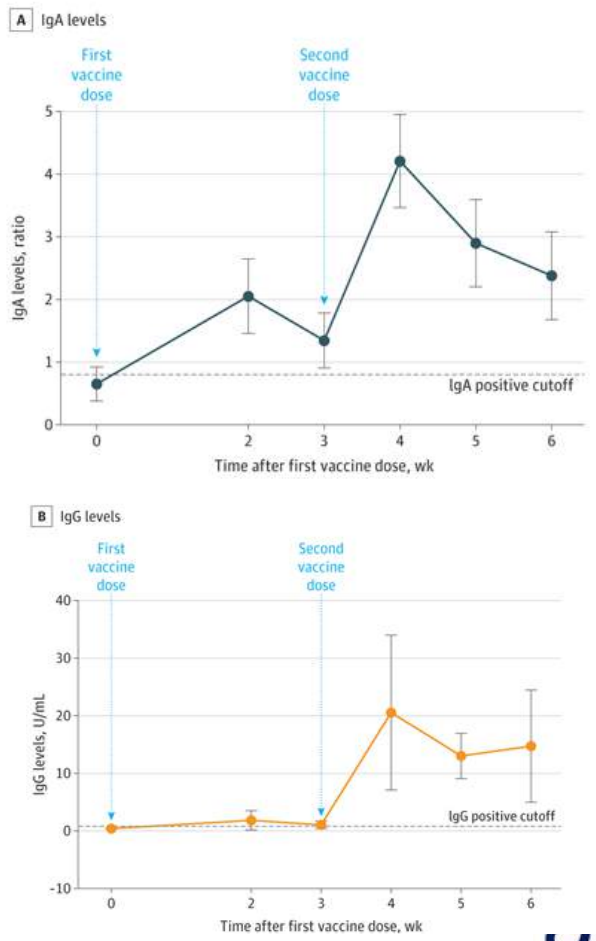
# Vaccination of particular populations

PREGNANT WOMAN

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

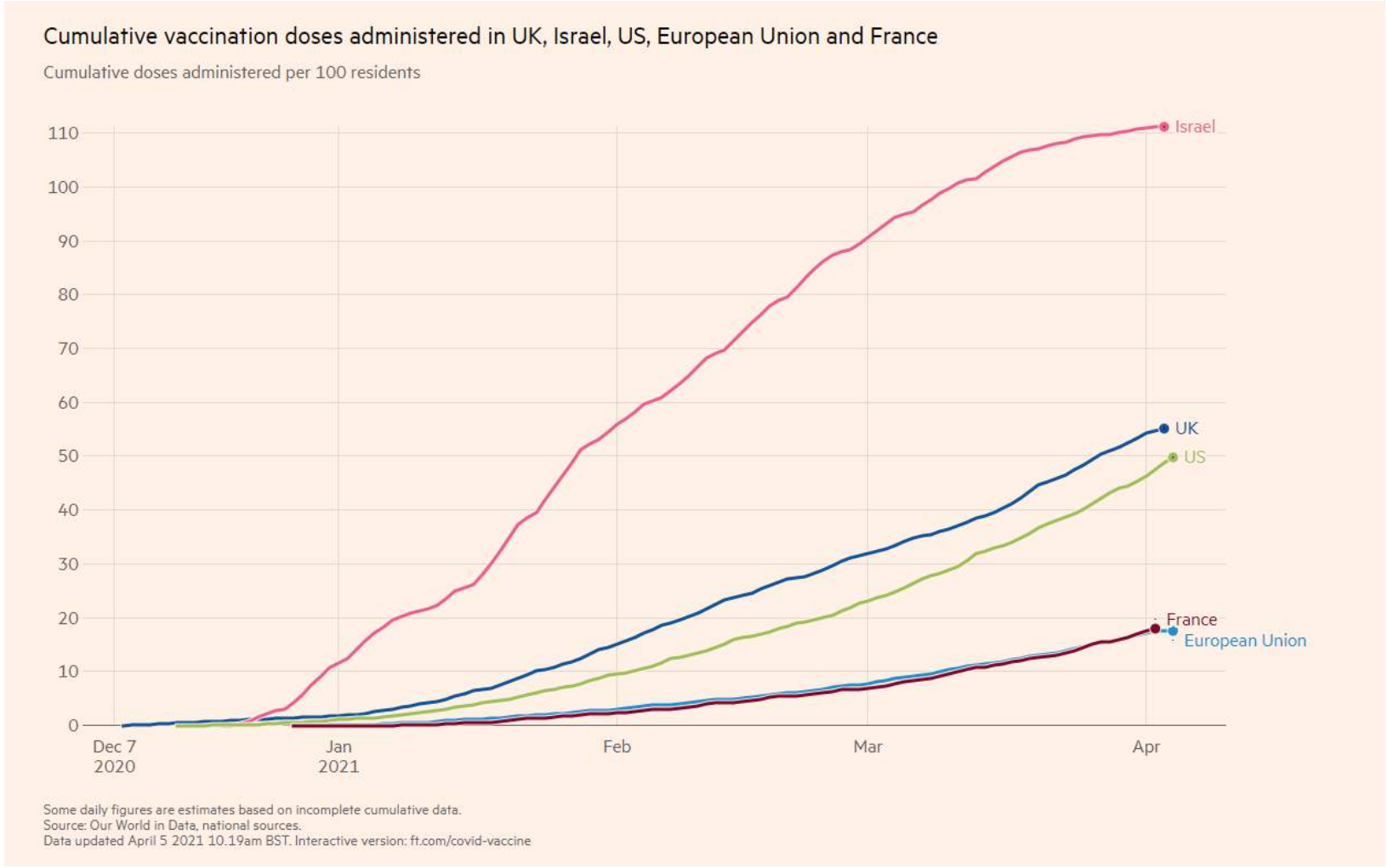
Population: Eighty-four women receving 2 doses of BNT162b2; 504 breast milk samples

- 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 (April 1st 2021)




*The Financial Times*

# Testing and implementation status of front-running candidates


*The Financial Times*

# VACCINES (April 19th 2020)

- 88 vaccine candidates are in an ongoing clinical evaluation. 11 have received authorisation from national or international medicine agencies
- Published Phase I/II data suggests that vaccine candidates on trial are immunogenic and mostly well tolerated in young adults. Data is emerging on elderly, 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 protection correlates.
- 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 studies with mRNA vaccines performing the best.
- COVID19 patients elicit strong Humoral responses after one doses of mRNA vaccines
- SARS COV 2 variants represent a challenge for current vaccines with preliminary results showing and variable level of cross-reaction depending on the viral strain.

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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/#

Financial time vaccine tracker:
https://ig.ft.com/coronavirus-vaccine- tracker/?areas=gbr&areas=isr&areas=usa&areas=eue&cumulative=1&populationAdjusted=1

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