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Evidence Assessment:
Updates for the mRNA vaccines developed by Pfizer-BioNTech and Moderna

FOR RECOMMENDATION BY THE STRATEGIC ADVISORY GROUP OF EXPERTS (SAGE) ON IMMUNIZATION

Prepared by the SAGE Working Group on COVID-19 vaccines and the VE studies WG

EVIDENCE ASSESSMENT: Updates for Pfizer and Moderna mRNA vaccines

The SAGE Working Group specifically considered the following questions:

1. What is the rationale and evidence for recommending the Pfizer vaccine to adolescents aged 12-15?
2. What is the rationale and evidence for the use of mRNA vaccines in pregnancy?
3. Should persons with prior SARS-CoV-2 infection receive one or two doses of mRNA vaccines?
4. What is the evidence on post-introduction VE? In settings of Variants of Concern?
5. What is the current evidence to use mix-and match?
6. In settings with limited vaccine supply and high disease burden, should the second dose of an mRNA vaccine be deferred to allow a higher first dose coverage?

EVIDENCE ASSESSMENT: Updates for Pfizer and Moderna mRNA vaccines

The SAGE Working Group specifically considered the following questions:

1. What is the rationale and evidence for recommending the Pfizer vaccine to adolescents aged 12-15? Melanie Marti, Sarah Pallas
2. What is the rationale and evidence for the use of mRNA vaccines in pregnancy? Saad Omer
3. Should persons with prior SARS-CoV-2 infection receive one or two doses of mRNA vaccines? Annelies W-S, Minal Patel
4. What is the evidence on post-introduction VE? In settings of Variants of Concern? Minal Patel
5. What is the current evidence to use mix-and match? Annelies Wilder-Smith
6. In settings with limited vaccine supply and high disease burden, should the second dose of an mRNA vaccine be deferred to allow a higher first dose coverage? Adam Finn, Mary Ramsay, Nick Grassly

Pediatric indication (Pfizer); individual benefit : risk vs global considerations

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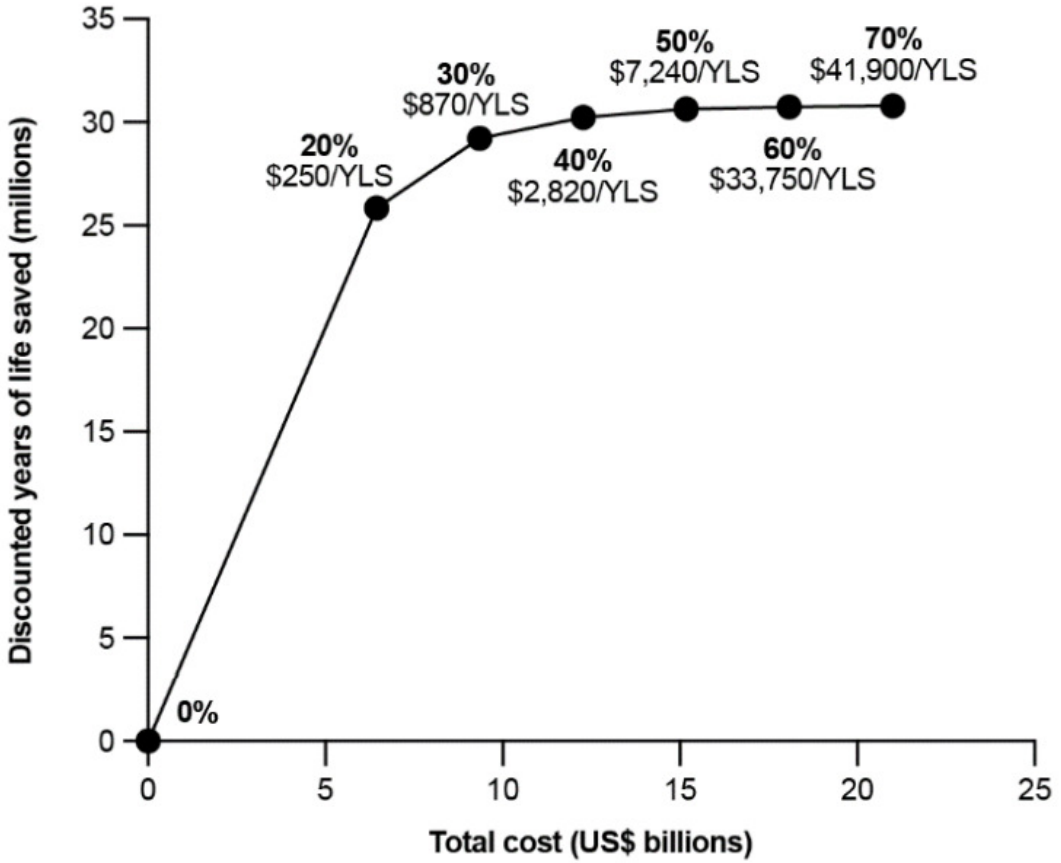
Individual level:

- Safety: *We have low confidence in the quality of evidence that the risk of serious adverse events in children following one or two doses of BNT162b2 vaccine is low*
- Efficacy: *We are confident that 2 doses of BNT162b2 vaccine are efficacious in preventing PCR-confirmed COVID-19 in children (12-15 years)*
- Benefit- harm: *Based on limited safety data, the balance of benefits and harms is highly context-specific and remains unclear to date*

Population and global level:

- Equity: *may increase inequity*
- *"As a matter of global equity, as long as many parts of the world are facing extreme vaccine shortage, WHO recommends that countries that have achieved high vaccine coverage in the high risk populations consider global sharing of BNT162b2 vaccine before proceeding to vaccination of children and adolescents who are at low risk for severe disease. "*

Decreasing efficiency of expanding vaccination coverage in age-descending prioritization strategy



Siedner et al. (2021) https://www.medrxiv.org/content/10.1101/2021.04.28.21256237v1.full.pdf

- Panel shows incremental cost-effectiveness ratios of increasing COVID-19 vaccination coverage per year of life saved (YLS) for **91 COVAX AMC countries from donor perspective**
  - Study uses Janssen COVID-19 vaccine
  - Panel shows R=1.2; higher R makes vaccination more cost-effective
- Similar diminishing marginal returns seen for averted hospitalizations and infections
  - Model assumes homogenous mixing, i.e., no increased contact rates among younger ages
- Results sensitive to assumptions about extent of natural immunity and duration of protection
- Analysis does not capture broader value of expanding vaccination coverage on other outcomes (e.g., slowing emergence of variants, facilitating social and economic reopening)

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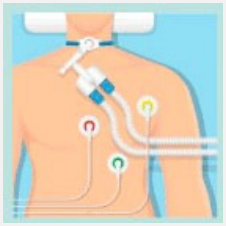
Rationale and Evidence for updating the Recommendations for mRNA vaccines in pregnant women

Saad Omer

Increased risk of severe COVID-19 disease

Meta-analysis of 192 studies published

ICU Admission
OR 2.13
95%CI: 1.53 to 2.95



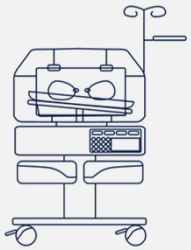
Invasive Ventilation
OR 2.59
95%CI: 2.28 to 2.94

Maternal Death
OR 2.85
95%CI: 1.08 to 7.52

Allotey et al. BMJ 2020

Risk to fetus

Preterm birth
OR 1.82
95%CI: 1.38 to 2.39



NICU Admission
OR 3.69
95%CI: 1.39 to 9.82

Meta-analysis of 42 studies with 438 548 pregnant women

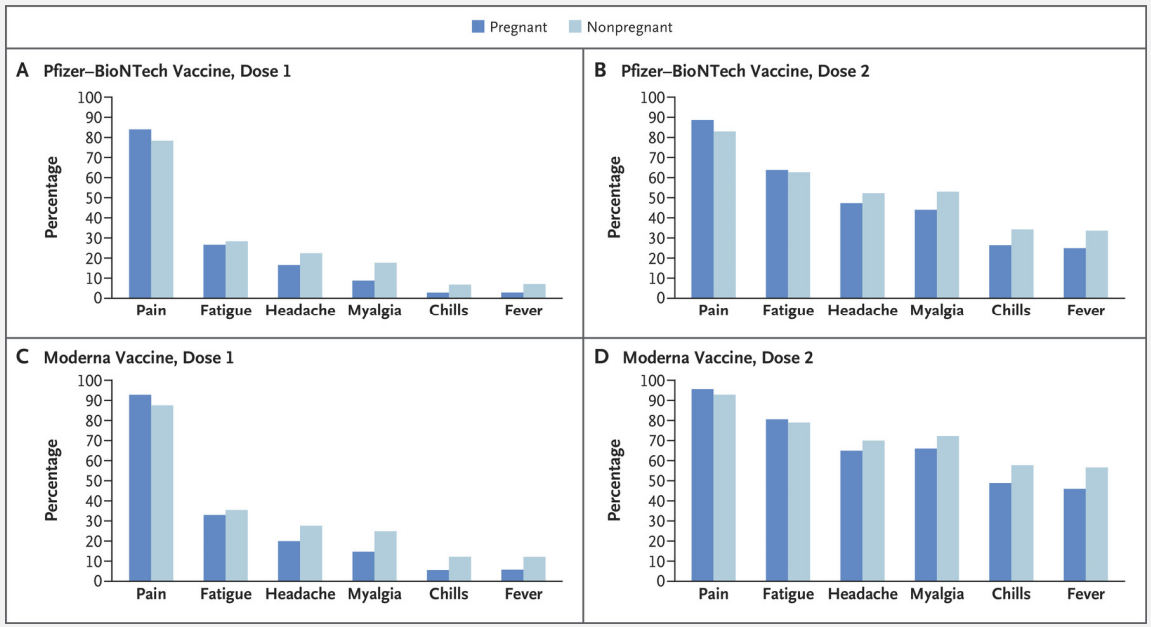
Neonatal SARS-CoV-2
1.8% to 2.0%

PAN-COVID (UK) & AAP-SONPM National Perinatal COVID-19 (USA) registries

Wei et al. CMAJ 2021; Mullins et al. Ultrasound Obstet Gynecol 2021

Safety of mRNA vaccines in pregnancy (AEs)

CDC v-safe data



35,691 v-safe participants identified as pregnant
Similar adverse events in pregnant & non-pregnant women

Shimabukuro et al. NEJM 2021

Yale Institute for Global Health

Safety of mRNA vaccines in pregnancy (outcomes)

V-safe pregnancy registry

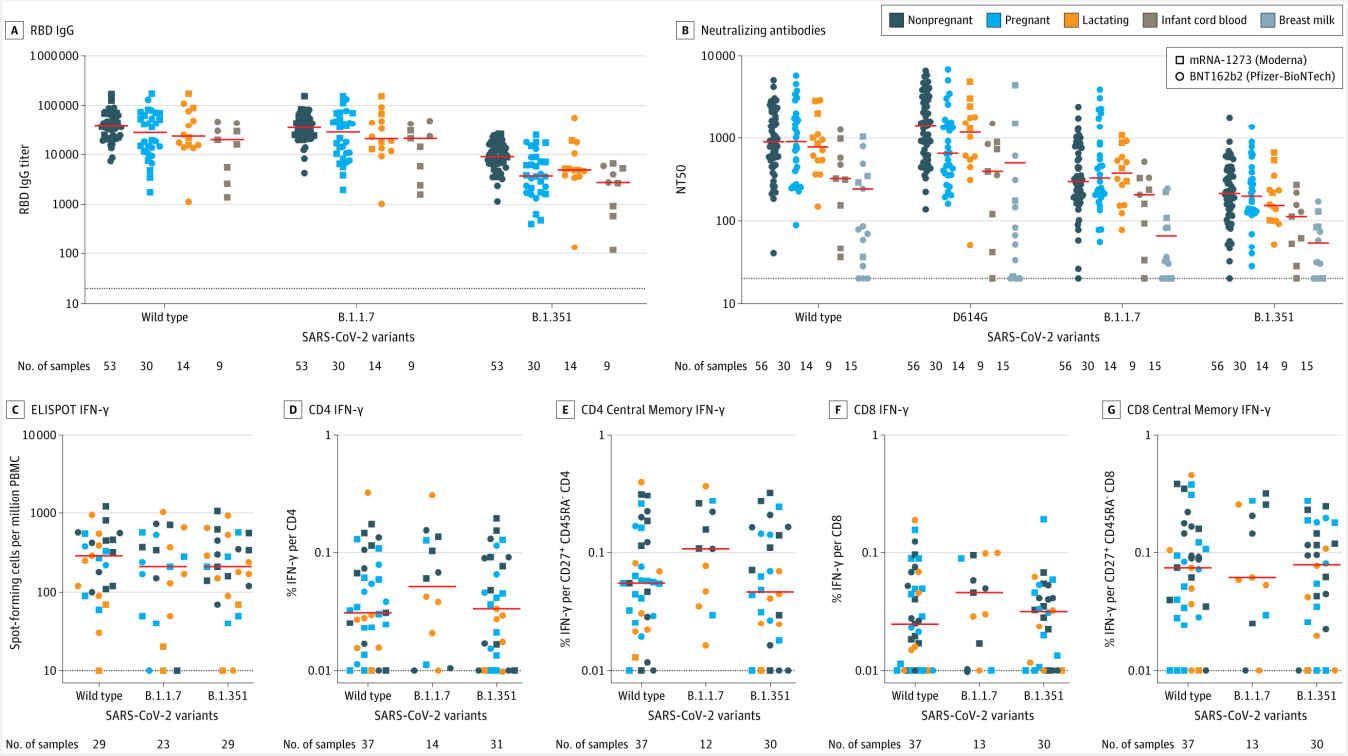
Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†
	%	*no./total no. (%)*
Pregnancy loss among participants with a completed pregnancy		
Spontaneous abortion: <20 wk[15-17]	10–26	104/827 (12.6)‡
Stillbirth: ≥ 20 wk[18-20]	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk[21,22]	8–15	60/636 (9.4)¶
Small size for gestational age[23,24]‖	3.5	23/724 (3.2)
Congenital anomalies[25]**	3	16/724 (2.2)
Neonatal death[26]††	<1	0/724

3,958 pregnant women of which 827 had outcomes

Shimabukuro et al. NEJM 2021

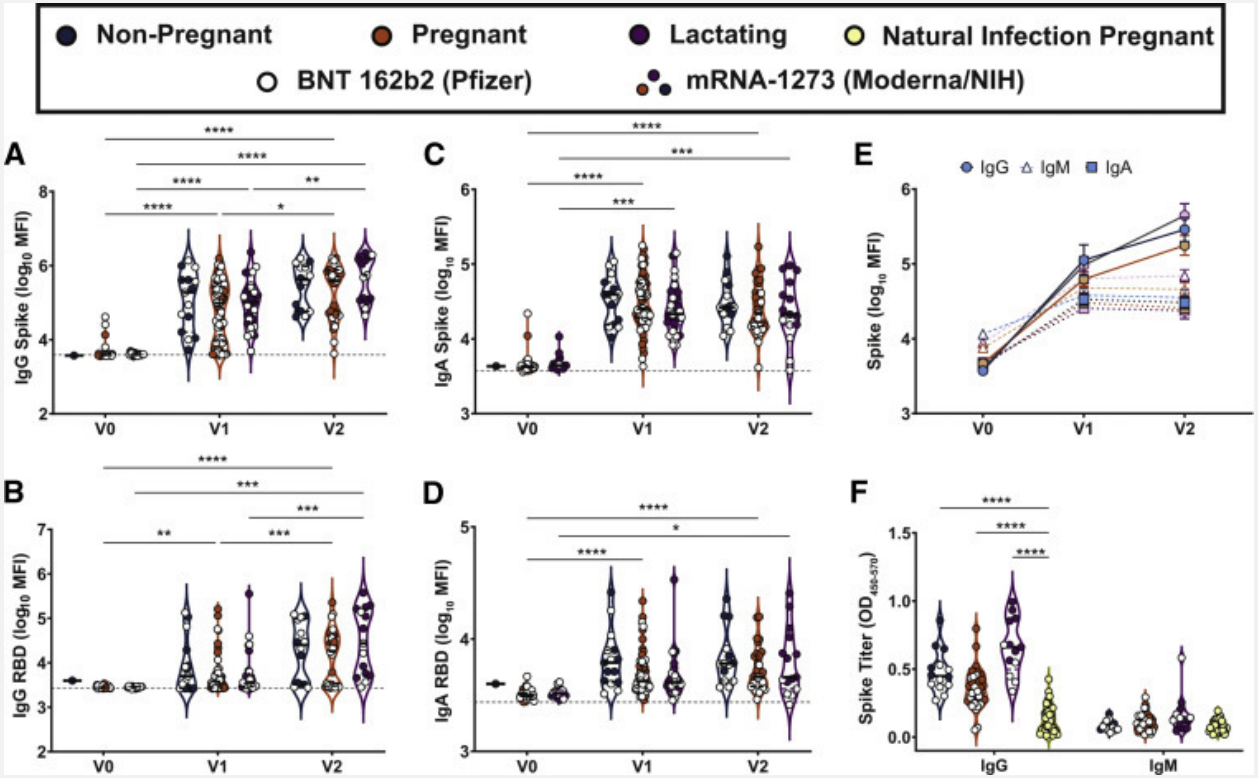
Immunogenicity of mRNA vaccines in pregnancy



COVID-19 mRNA vaccine is immunogenic in pregnant women, and vaccine-elicited antibodies are transported to infant cord blood and breast milk.

Collier et al. JAMA 2021

Immunogenicity of mRNA vaccines in pregnancy



mRNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to nonpregnant women

Gray et al. Am J Obstet Gynecol 2021

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Persons with a history of PCR confirmed SARS-CoV-2 infection

Delay vaccination for 6 months (earlier in areas with circulating VOC

One or two doses of mRNA vaccines?

COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study

*Victoria Jane Hall, Sarah Foulkes, Ayoub Saei, Nick Andrews, Blanche Oguti, Andre Charlett, Edgar Wellington, Julia Stowe, Natalie Gillson, Ana Atti, Jasmin Islam, Ioannis Karagiannis, Katie Munro, Jameel Khawam, Meera A Chand, Colin S Brown, Mary Ramsay, Jamie Lopez-Bernal, Susan Hopkins, and the SIREN Study Group**

Lancet 2021; 397: 1725–35

	Total person-time, days	Number of PCR positives	Incidence density per 10 000 person-days	Unadjusted hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
Full cohort					
Unvaccinated	710 587	977	14	1 (ref)	1 (ref)
Dose 1	87 278	71	8	0·43 (0·23–0·64)	0·30 (0·15–0·45)
Dose 2	20 978	9	4	0·23 (0·06–0·40)	0·15 (0·04–0·26)
Negative cohort					
Unvaccinated	442 605	902	20	1 (ref)	1 (ref)
Dose 1	59 748	66	11	0·33 (0·17–0·49)	0·28 (0·14–0·42)
Dose 2	14 746	8	5	0·18 (0·04–0·31)	0·14 (0·03–0·24)
Positive cohort					
Unvaccinated	267 982	75	3	..	..
Dose 1	27 530	5	2	..	..
Dose 2	6232	1	2	..	..

We calculated cumulative vaccine effectiveness after suitable intervals (21 days post-first dose and 7 days post-second dose) to focus on infections acquired since vaccination after a sufficient interval for biological protection. Unadjusted includes vaccine effect (period) only. The full model was adjusted for site as a random effect, period, and eight fixed effects: age, gender, ethnicity, comorbidities, job role, frequency of contact with COVID-19 patients, employed in a patient facing role, and occupational exposure. There was insufficient information to model the positive cohort separately so stratified hazard ratios are not available for the positive cohort.

Table 2: Effectiveness of the BNT162b2 COVID-19 vaccine, between Dec 7, 2020, and Feb 5, 2021 (n=23 324)

Summary of the VE Literature for on Vaccine Impact in Persons with PCR confirmed Prior SARS-CoV-2 infection

5 studies identified with results stratified vaccine effectiveness by prior history

- No studies are designed to answer this question
- 3/5 studies preprint
- Challenging to compare studies: VOCs, different limitations in each study, different definitions for partial/fully vaccinated
- Misclassification of prior infection
  - Failure to test
  - Challenges with antibody testing
- Length of follow up <2 months in most cases—unsure duration of protection from natural infection
- Impact of VOCs on reinfection risk

Summary of Studies

VIVALDI study[1]: Prospective cohort of 10,412 ≥65 in 310 LTCF in England (11% prior infection)

Pfizer/AZ VE against infection	AZ	Pfizer	Both Vaccines
#/% Vaccinated with 1 dose	6138 (59%)	3022 (29%)	9160 (88%)
Day 34-48 post dose 1	68% (34-85%)	65% (29-83%)	62% (23-81%)
No prior infection: Day 34-48 post dose 1			64% (27-82%)
Prior Infection: Day 34-48 post dose 1			-66% (-615%-61%)
Prior infection unvaccinated vs naïve unvaccinated			81% (70-88%)

Monge et al[2]: Administrative database cohort study in Spain of 299,209 ≥65 LTCF (17.5% prior infection)

- Pre-post vaccination risk analysis: infections in 2nd wave compared to 3rd wave
- 99.8% Pfizer/0.2% Moderna

Pfizer VE against infection	2 doses (day >28)	Unvaccinated 3rd vs 2nd wave
No prior infection	81.8 (81.0-82.7%)	
Prior infection	56.8 (47.1-67.7%)	86.6 (85.2-87.8%)

[1]Shrotri et al. Vaccine Effectiveness o f the first dose o f ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of Long-Term Care Facilities (VIVALDI study). *MedRxiv*. Retrieved from https://www.medrxiv.org/content/10.1101/2021.03.26.21254391v1

[2]Monge. Direct and indirect effectiveness of mRNA vaccination against SARS-CoV-2 infection in long-term care facilities in Spain. *MedRxiv*, 2021.04.08.21255055. http://doi.org/10.1101/2021.04.08.21255055VE

Summary of Studies

Lumley et al[1]: Longitudinal cohort study of 13,109 HCWs in 4 hospitals in UK (10% seropositive)

- AZ+Pfizer combined: Pfizer 52% got 1 dose; 11% got 2 doses
- Compared to unvaccinated seronegative HCWs

AZ/Pfizer VE against infection /risk reduction	Symptomatic PCR+	Infection
1 dose (>14 days post dose 1)	67% (48-79%)	64% (50-74%)
2 dose (>14 days post dose 2)	None	90% (62-98%)
1-2 dose among previous seropositive (>14 days post dose 1)	93% (49-99%)	96% (63-99%)
Unvaccinated seropositive	98% (82-99%)	85% (74-92%)

Pritchard et al[2]: Prospective cohort study of 373,402 in the UK (11% prior infection)

Pfizer VE against infection	Infection (any)	Symptomatic disease	Asymptomatic infection
Dose 1 (≥21 days) (irrespective of prior history)	67% (61-72%)	75% (68-81%)	56% (45-64%)
Dose 2 (≥0 days) (irrespective of prior history)	72% (64-79%)	91% (83-95%)	52% (34-64%)
Not vaccinated, with prior history	70% (62-76%)	87% (79-92%)	49% (35-60%)

[1]Lumley et al. An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status. http://doi.org/10.1101/2021.03.09.21253218

[2]Pritchard et al. Impact of vaccination on SARS-CoV-2 cases in the community: a population-based study using the UK COVID-19 Infection Survey. *MedRxiv*, 2021.04.22.21255913. http://doi.org/10.1101/2021.04.22.21255913

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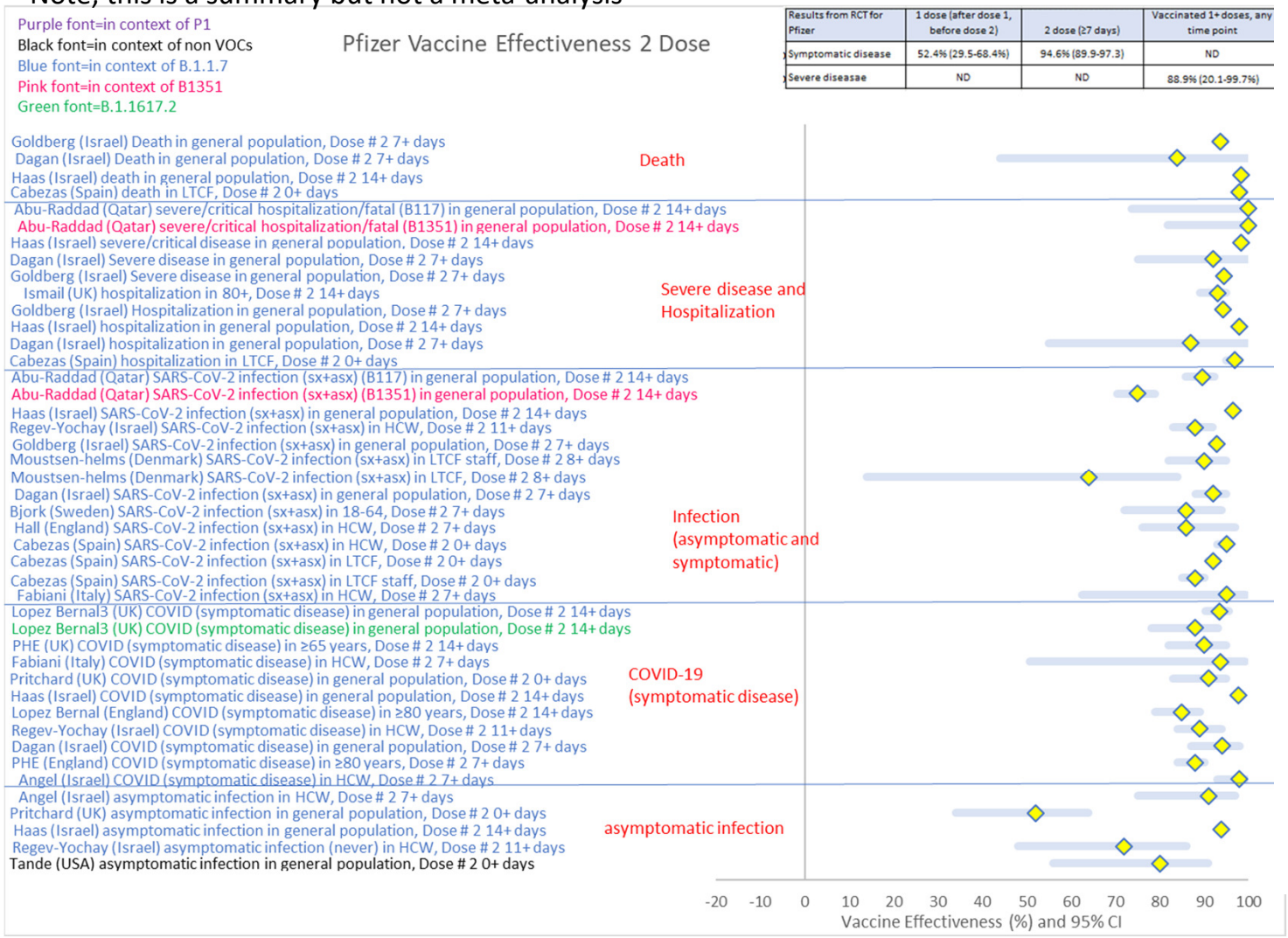
Post-introduction Vaccine effectiveness studies (including against Variants of Concern

Minal Patel

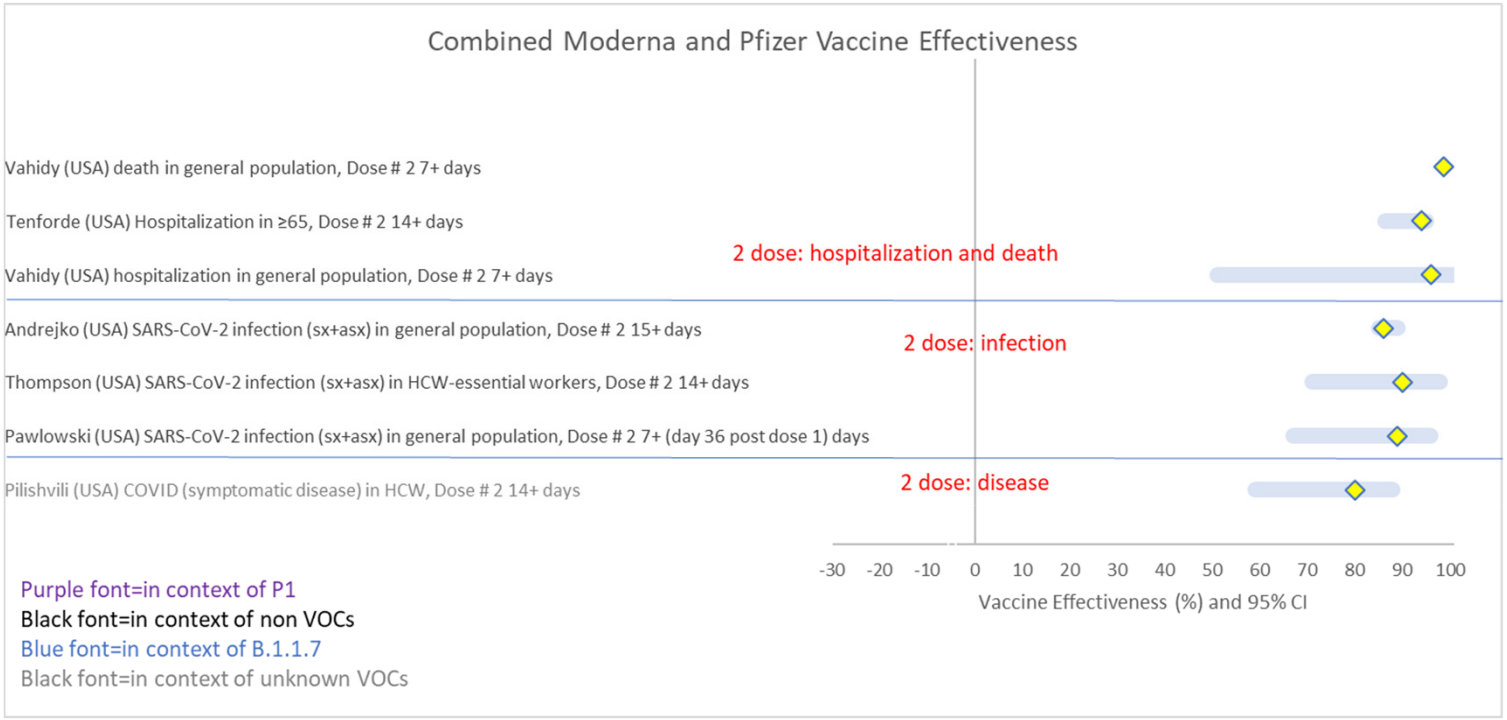
Summary of Pfizer VE literature

Note, this is a summary but not a meta-analysis



- Asymptomatic infection
  - 5 studies
  - Mix of asymptomatic and presymptomatic
  - Range of VE 52-94%
- Symptomatic disease
  - 8 studies
  - Range: 85-98%
- Infection
  - 10 studies
  - Range 64-97%
  - 75% of data points >86%
- Hospitalization
  - 5 studies
  - Range 87-98%
- Severe disease
  - Different definitions
  - 4 studies
  - 92-100%
- Death
  - 4 studies
  - 84-98%

Summary of Pfizer/Moderna VE literature



- 7 studies combining Pfizer/Moderna VE, all in USA
  - Most of the authors acknowledge not ideal to combine→interim analysis/small sample size
- Symptomatic disease: 1 study, 80%
- Infection: 3 studies, 86-90%
- Hospitalization: 2 studies, 94-96%
- Death: 1 study, 99%

Pfizer VE and VOCs

B117

- Many VE studies from Israel, UK, and other European countries showing VE similar to RCT findings

P1

- No studies

B1351

- Abu-Raddad et al Qatar study: slightly lower VE for infection for B1351

VE ≥14 days post dose 2	B1351	B117
Infection	75 (70.5-78.9)	89.5 (85.9-92.3)
Severe, critical, fatal disease	100.0 (81.7–100.0)	100.0 (73.7–100.0)

- Kustin et al Israel study
  - -Case-only analysis assessing breakthrough
  - -Assess odds of a variant being detected comparing vaccinated to unvaccinated case patients
  - -Unadjusted OR 8 (no CI) for fully vaccinated (n=149) to have B1351 (5.4%) vs unvaccinated (0.7%)

B1617.2

- similar VE against symptomatic disease for 2 dose

	B1617.2	B117
1 dose (21+)	33.2% (8.3-51.4)	49.2% (42.6-55)
2 dose (14+)	87.9% (78.2-93.2)	93.4% (90.4-95.5)

- Case only analysis: OR 1.17 (0.82-1.67) for detection of B.1.617.2 relative to B.1.1.7 in vaccinated compared to unvaccinated case patients

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Mix-and-match studies: No results available to be presented today, but likely next week

Various mix-and-match studies in various combinations ongoing.

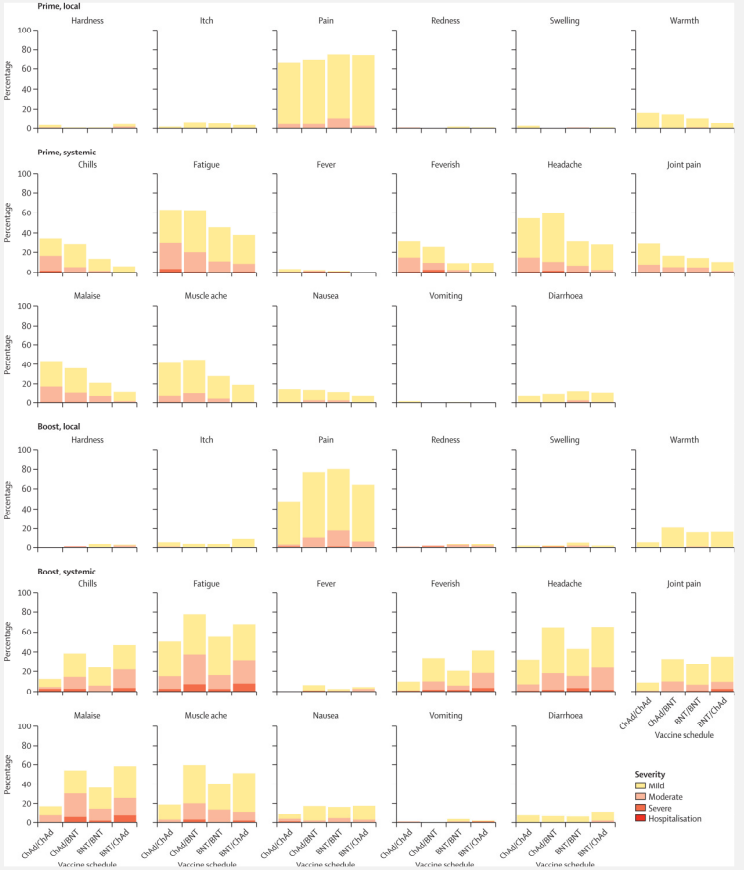
Most advanced studies include the combination AZ-Pfizer.

Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data

Robert H Shaw, Arabella Stuart, Melanie Greenland, Xinxue Liu, Jonathan S Nguyen Van-Tam, Matthew D Snape

The Lancet

DOI: 10.1016/S0140-6736(21)01115-6



The Lancet DOI: (10.1016/S0140-6736(21)01115-6)
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What is the evidence for deferring the second dose in settings with high disease burden and limited vaccine supply?
Immunology, Vaccine effectiveness data, Modelling

Mary Ramsay, Nick Grassly

UK programme

- Commenced with Pfizer vaccine on 8th December, initially delivered in hospitals (because of ULT requirements)
  - Health care workers
  - Community dwelling over 80s
- Initial scheduled at 3 week interval in line with market authorisation
- In late December, transmission of B1.1.7 (Kent variant) recognised
- From 4th January, UK went into lockdown, and AZ vaccine authorised
  - Accelerated vaccination programme to deliver first dose to care homes, clinically vulnerable and over 70s by mid February
  - Both vaccines recommended at 12 week interval

24

Overview of vaccine effectiveness studies

- Routine surveillance
  - Routine community PCR testing data England (self initiated) with symptoms

    Linked to emergency admissions and death registration data
  - Hospitalisations – admissions for ARI in sentinel NHS hospitals
- SIREN – study of ~35,000 healthcare workers of known antibody status, undergoing regular PCR screening (twice per week)
- VIVALDI – study of care home residents and staff of known antibody status, undergoing regular PCR screening (twice per week)
- All linked to national vaccination register (NIMs) on NHS number

25

Analytical approaches

- Data on testing, emergency admission and deaths
  - Test negative case control design was used to estimate the odds of vaccination in symptomatic individuals PCR positive compared to negative.
  - Screening (case-coverage) method in hospitalised cases compared to population
  - Adjustment for five-year age group, gender, NHS region, whether they were a care home resident and week of symptom onset
- Cohort studies (SIREN / VIVALDI)
  - Proportional hazards cohort model
  - HCW model also adjusted for ethnicity, comorbidities, region, job role, frequency of COVID-19 patient contact, patient-facing role, and workplace setting
- Odds ratios compared to unvaccinated and by period after vaccination

26

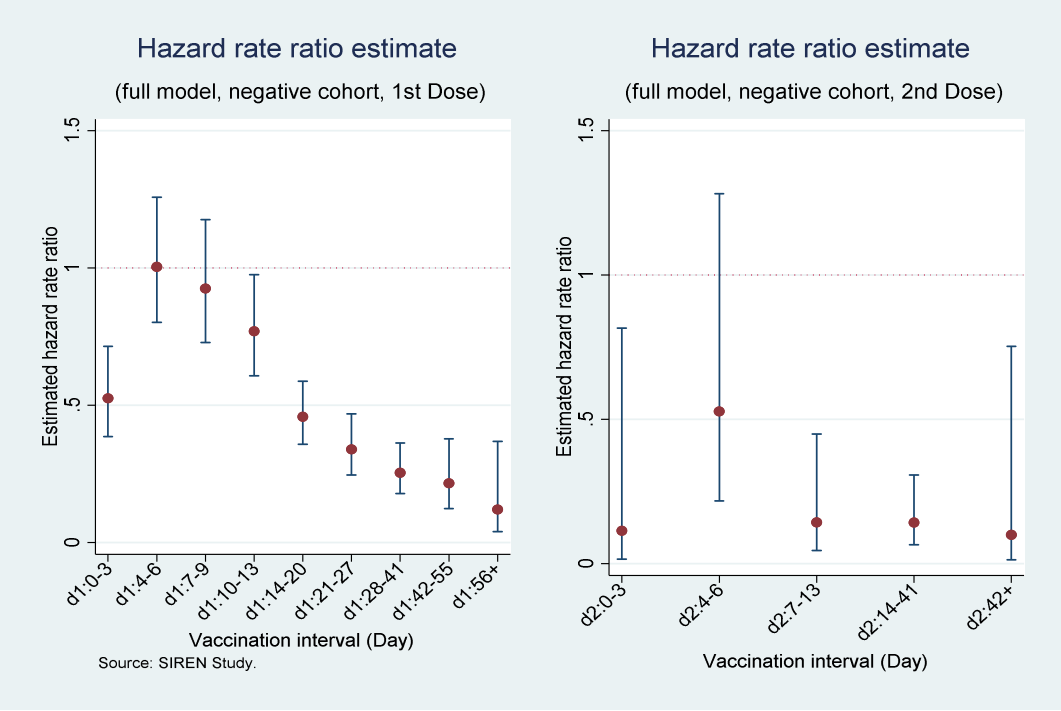
Asymptomatic and symptomatic infection

SIREN (health care workers)

- 72% (95% CI 63-78%) from ≥21 days post-dose 1
- no evidence of a decline from first dose protection beyond 56 day (to day 95)
- Dose 2 - 85% (95% CI 73-92%)

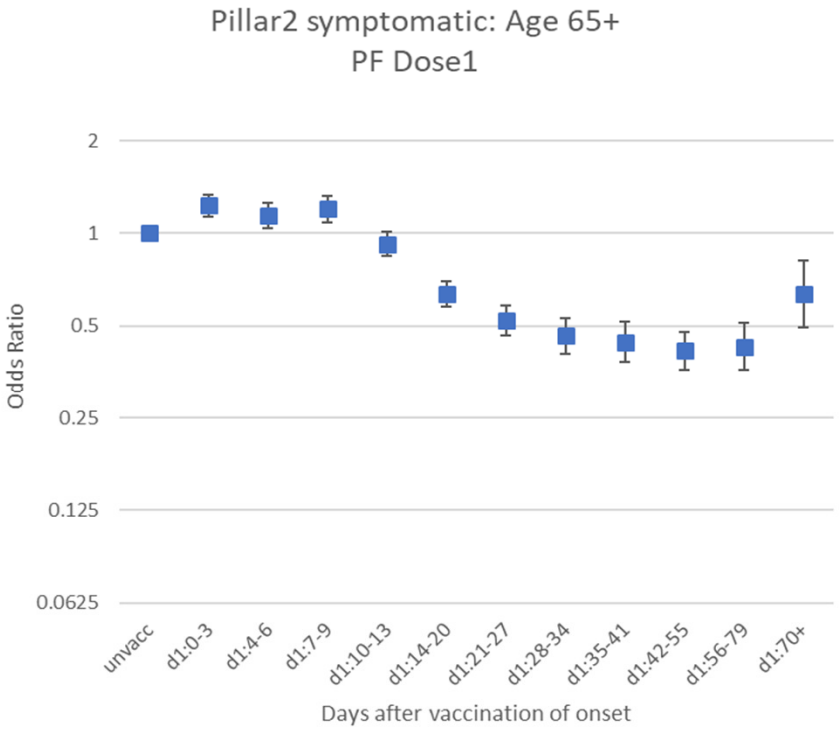
VIVALDI (care home residents)

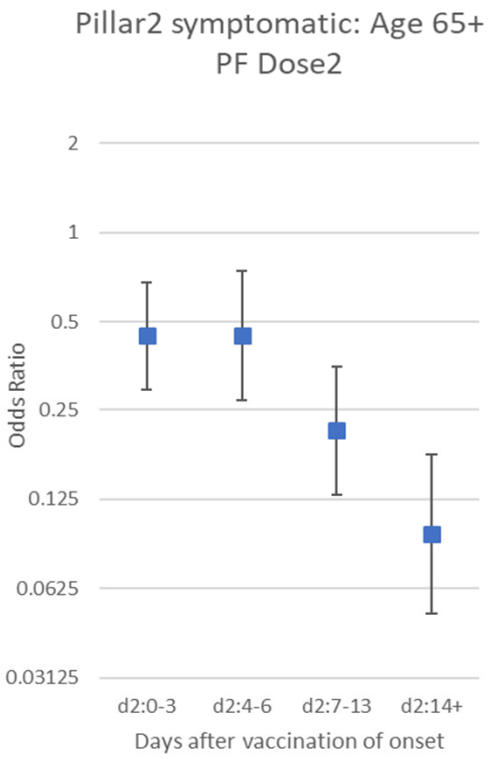
- 65% (95% CI 29-83%) from 35 days post first dose of Pfizer



27

Age 65+ vaccinated from Jan 4th 2021





One dose VE

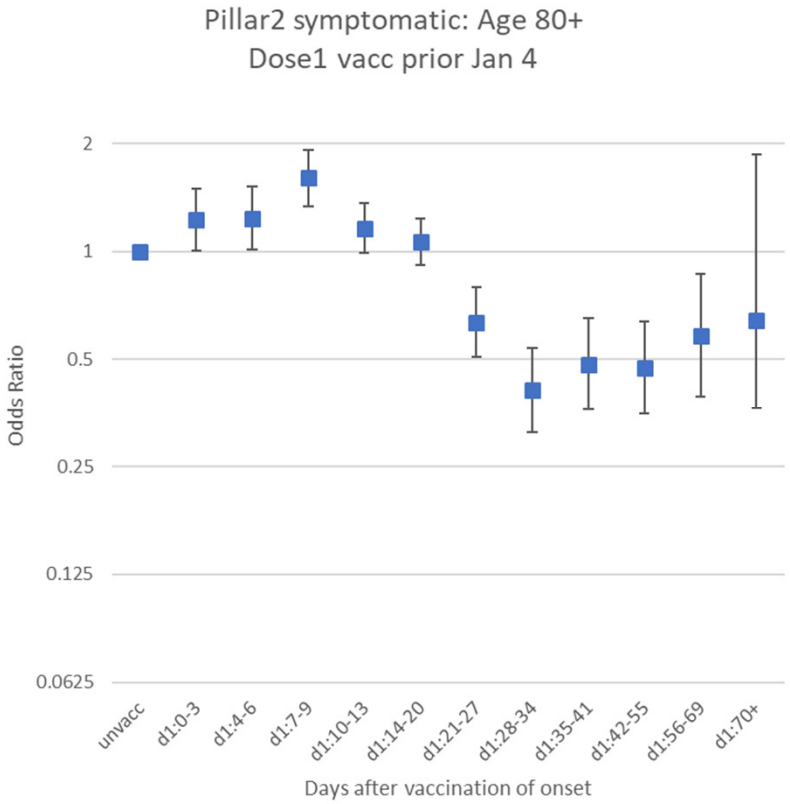
- 54%
- (95% CI 50-58%)

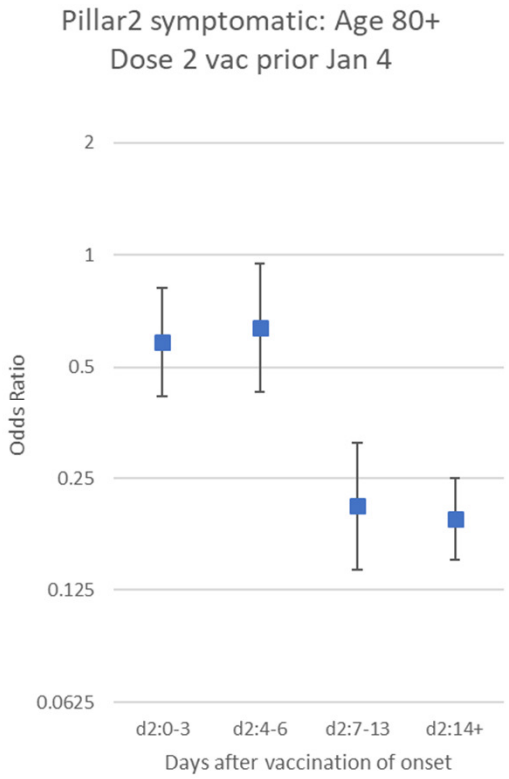
Two dose VE

- 90%
- (95%CI 82-95%)

28

80+ vaccinated before Jan 4th 2021 - Pfizer





Additional protection of ~60% from the second dose

Comparing from 14 days after dose 2 to 28+ after dose 1

OR= 0.4 (0.31-0.52)

29

Pfizer – protection from a single (second) dose

Effectiveness against infection from day 21/28

- 65%-72% against all infections – increases to 85%
- 35-50% reduced risk of transmission to a confirmed case in household

Effectiveness against symptomatic disease

- 57% in over 65s - increases to 85% - no significant decline to 10 weeks
- additional 42% protection against death in vaccinated cases (increases to 59%)

Effectiveness against hospitalisation (over 80s)

- Dose 1: 81% (76-85%)
- Dose 2: 93% (89-95%)

In over 80s vaccinated before January 4th higher VE at longer schedule

- 80% (75-85%) vs 92% (66-98%) (*non-significant*)
- Consistent with better immunogenicity

30

Protection against symptomatic disease due to B1.617.2

Single dose of Pfizer BNT162b2 vaccine effectiveness reduced from

- B.1.1.7 51.1% (95%CI: 47.3 to 54.7)
- B.1.617.2 33.2% (95%CI: 8.3 to 51.4)

Two doses of Pfizer BNT162b2 vaccine effectiveness reduced from

- B.1.1.7 93.4% (95%CI: 90.4 to 95.5) to
- B.1.617.2. 87.9% (95%CI: 78.2 to 93.2)

- NB. first dose B1.1.7 protection against hospitalisation is 81%
- Difference first and second dose may be exaggerated due to use of more immunogenic schedule (at 12 weeks)

31

Key links / references

https://www.gov.uk/government/publications/phe-monitoring-of-the-effectiveness-of-covid-19-vaccination

https://www.gov.uk/government/publications/covid-19-vaccine-surveillance-report

https://www.bmj.com/content/373/bmj.n1088

https://khub.net/documents/135939561/430986542/Effectiveness+of+BNT162b2+mRNA+and+ChAdOx1+adenovirus+vector+COVID-19+vaccines+on+risk+of+hospitalisation+among+older+adults+in+England.pdf/9e18c525-dde6-5ee4-1537-91427798686b

https://www.gov.uk/government/news/vaccines-highly-effective-against-b-1-617-2-variant-after-2-doses

32

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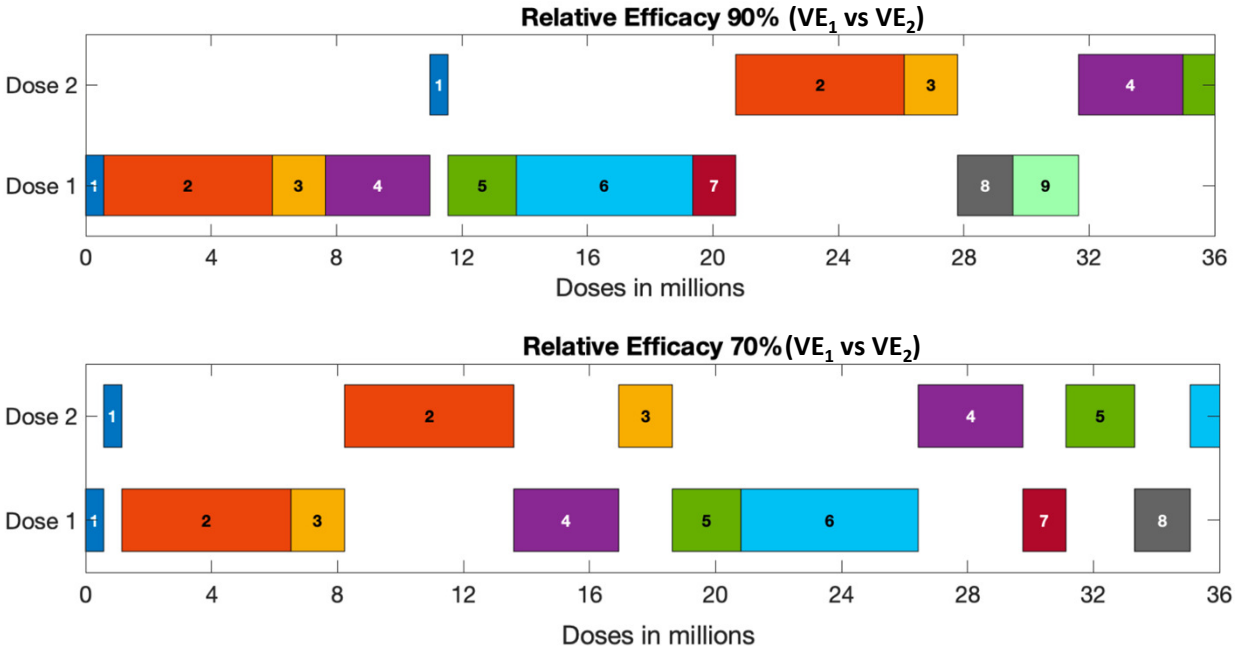
Summary of modelling work on vaccination strategies that prioritise 1st dose coverage

Nick Grassly

Delaying the second dose beyond 3-4 weeks

- Simple insight: if $VE_1 > 0.5*VE_2$, prioritise first dose if all individuals equal
- But, all individuals are not equal: second dose given to most vulnerable gives greater benefit than first dose given to less vulnerable group once coverage reaches a certain level



Optimal deployment in UK of 1 and 2 doses

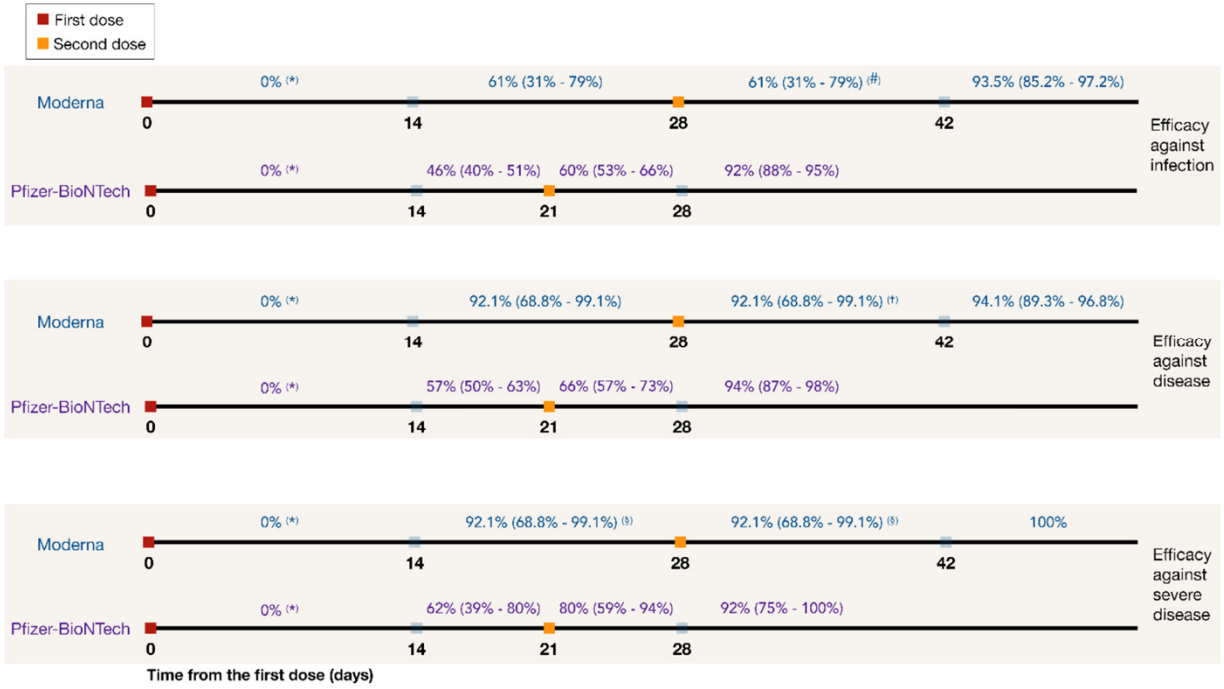
- Care homes
- HCWs & 80+
- 75-79
- 70-74 & CEV
- 65-69
- UHC
- 60-64
- 55-59
- 50-54

HCW = Healthcare Worker
CEV = Clinically Extremely Vulnerable
UHC = Underlying Health Condition

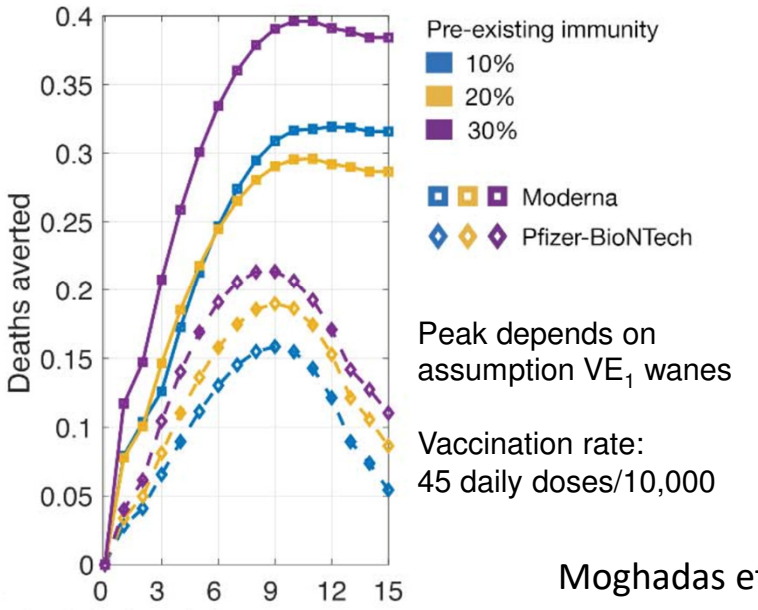
Hill and Keeling 2021 *medrxiv*

Delaying the second dose beyond 3-4 weeks

- Waning immunity after one dose can affect recommendation, especially if VE_1 low
- Product-specific recommendations may be required if evidence for true differences in VE_1 among products
- Currently uncertain impact of VoCs on relative efficacy of dose 1 vs. 2 against severe outcomes



Illustrative example only



Peak depends on assumption VE_1 wanes

Vaccination rate:
45 daily doses/10,000

Delay in second dose from recommended schedule

Moghadas et al. 2021 *PloS Biol*

Results for Pfizer vaccine in Qatar (manuscript in print)

	15-21 days after dose 1					≥14 days after second dose				
	Cases (PCR positive)		Controls (PCR negative)		Effectiveness in % (95% CI)*	Cases (PCR positive)		Controls (PCR negative)		Effectiveness in % (95% CI)*
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Effectiveness against infection										
Any infection with the B.1.1.7 variant†	148	17,380	422	17,106	65.5 (58.2-71.5)	50	16,354	465	15,939	89.5 (85.9-92.3)
Any infection with the B.1.351 variant‡	338	19,400	623	19,115	46.5 (38.7-53.3)	179	19,396	698	18,877	75.0 (70.5-78.9)
Effectiveness against disease										
Any severe, critical, or fatal disease with the B.1.1.7 variant§	7	434	24	417	72.0 (32.0-90.0)	0	401	20	381	100.0 (81.7-100.0)
Any severe, critical, or fatal disease with the B.1.351 variant¶	9	336	20	325	56.5 (0.0-82.8)	0	300	14	286	100.0 (73.7-100.0)
Any severe, critical, or fatal disease with any SARS-CoV-2 infection**	23	1,845	83	1,785	73.2 (56.8-84.0)	3	1,692	109	1,586	97.4 (92.2-99.5)

*Vaccine effectiveness was estimated using the test-negative, case-control study design.[1] Cases and controls were matched one-to-one by age, sex, nationality, and reason for polymerase chain reaction (PCR) testing. Vaccine effectiveness is given by[1] $\text{Vaccine effectiveness} = 1 - \frac{\text{vaccinated among cases} \times \text{unvaccinated among controls}}{\text{vaccinated among controls} \times \text{unvaccinated among cases}}$.

†Any B.1.1.7 PCR-confirmed infection. A B.1.1.7 infection is proxied as an S-gene "target failure" case using the TaqPath COVID-19 Combo Kit platform (Thermo Fisher Scientific, USA), applying the criterion of PCR cycle threshold value ≤30 for both the N and ORF1ab genes, but a negative outcome for the S-gene. The median date of vaccination was March 1 for the cases and February 28 for their matched controls.

‡Any B.1.351 PCR-confirmed infection. With only B.1.351 and B.1.1.7 cases identified in the viral genome sequencing after March 7, 2021, a B.1.35 1infection is proxied as the complement of the B.1.1.7 criterion, that is any infection with a Ct value ≤30 for the N, ORF1ab, and S genes between March 8-31. The median date of vaccination was March 7 for the cases and March 1 for their matched controls.

§Any B.1.1.7 PCR-confirmed infection that led to severe, critical, or fatal disease. Severe disease, critical disease, and COVID-19 death were defined based on the World Health Organization criteria for classifying SARS-CoV-2 infection severity[2] and COVID-19-related death.[3]

¶Any B.1.351 PCR-confirmed infection that led to severe, critical, or fatal disease. Severe disease, critical disease, and COVID-19 death were defined based on the World Health Organization criteria for classifying SARS-CoV-2 infection severity[2] and COVID-19-related death.[3]

**Any PCR-confirmed infection that led to severe, critical, or fatal disease. With the dominance of both B.1.1.7 and B.1.351 variants during the study period, this effectiveness is a combined measure against both of these variants. Severe disease, critical disease, and COVID-19 death were defined based on the World Health Organization criteria for classifying SARS-CoV-2 infection severity[2] and COVID-19-related death.[3]