從英國防疫經驗到真實世界證據

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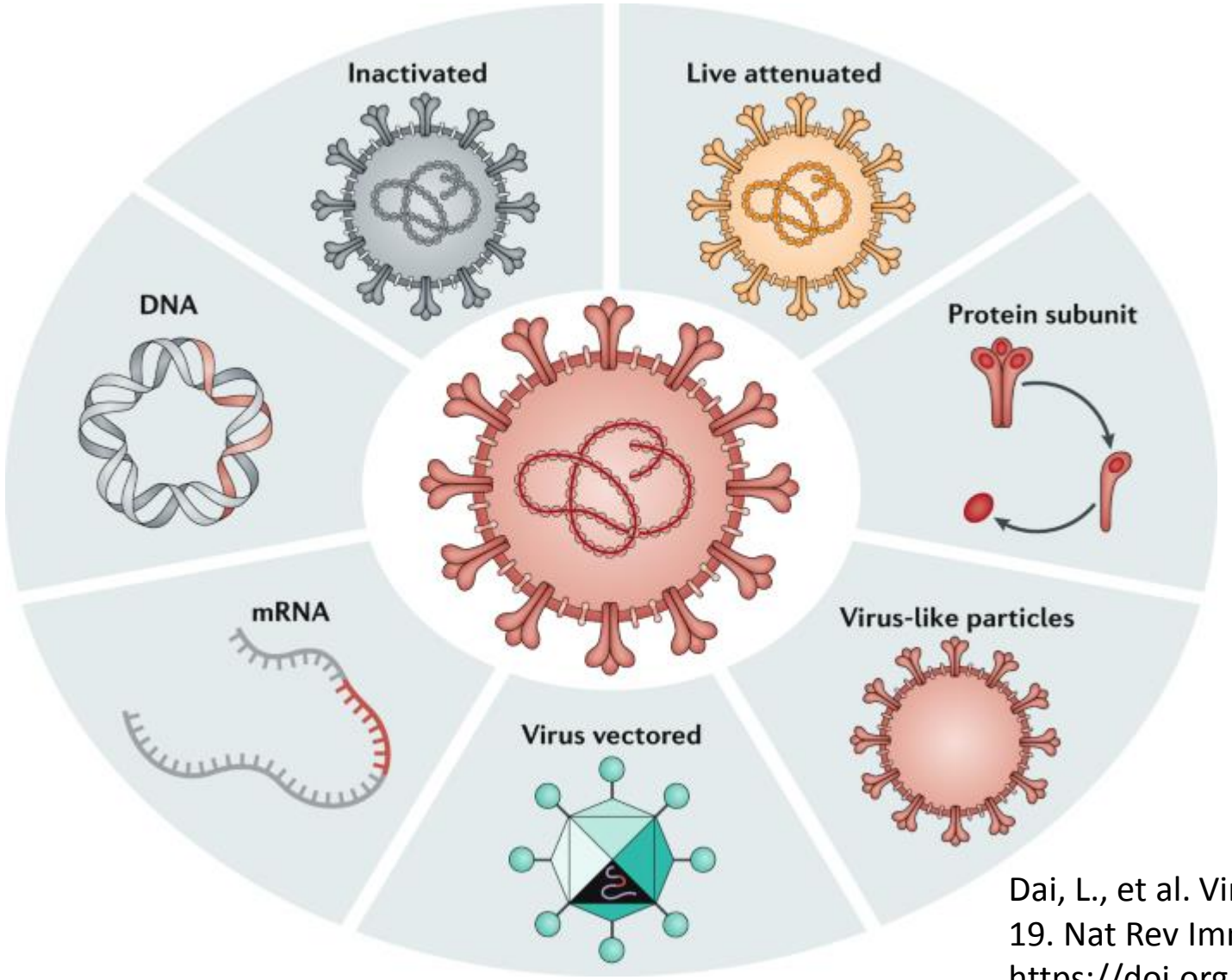
Topics

- 介紹
- 臨床試驗簡要總結
- 真實證據：有效性
- 真實證據：傳播和免疫反應
- 安全概況
- 結論

Disclaimers

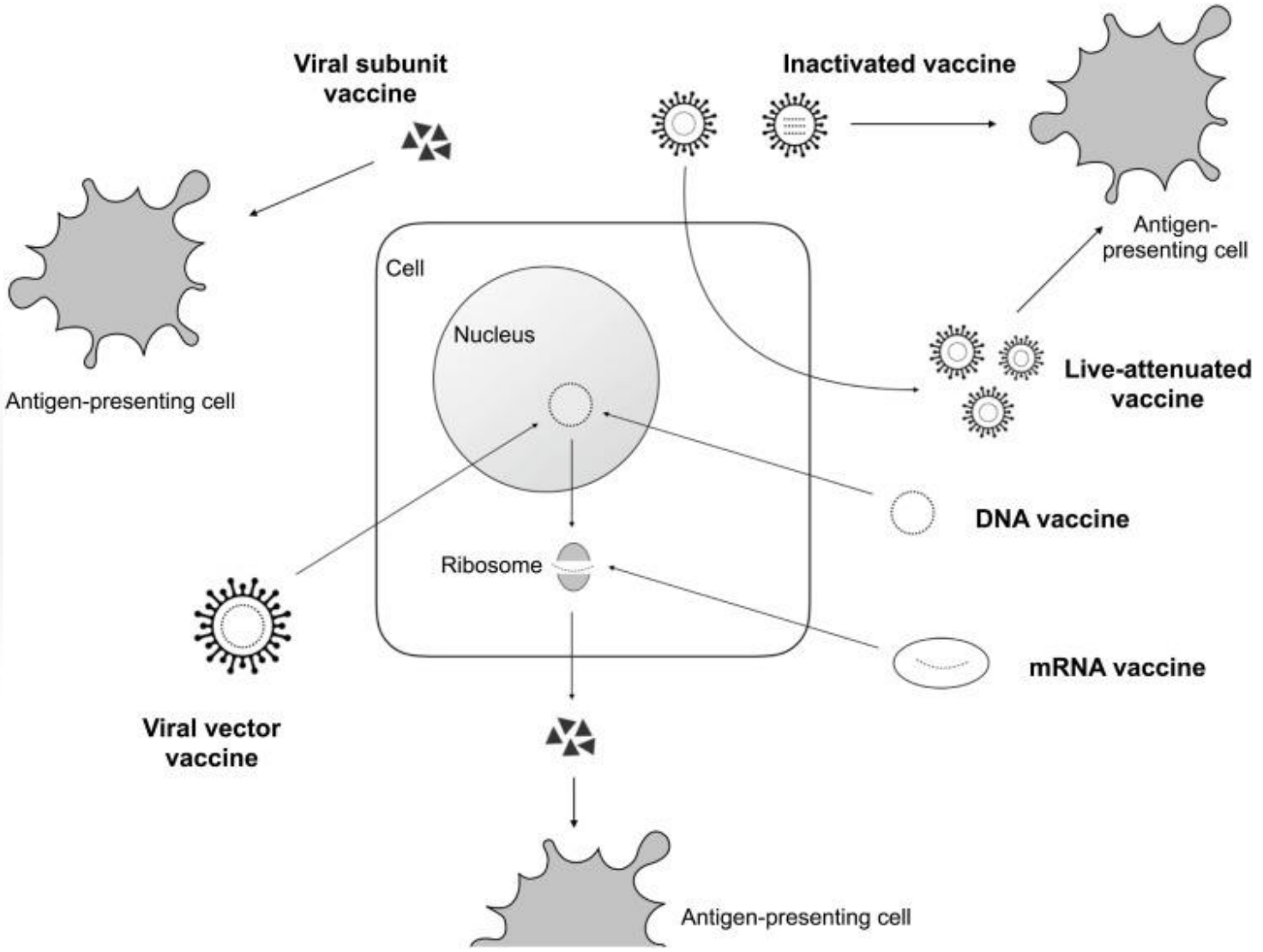
- This meeting has been organised and funded by AstraZeneca
- AstraZeneca products will be discussed at this meeting
- For further medical information or adverse event reporting, please visit https://www.azcovid-19.com/

COVID-19 疫苗候選者
疫苗策略



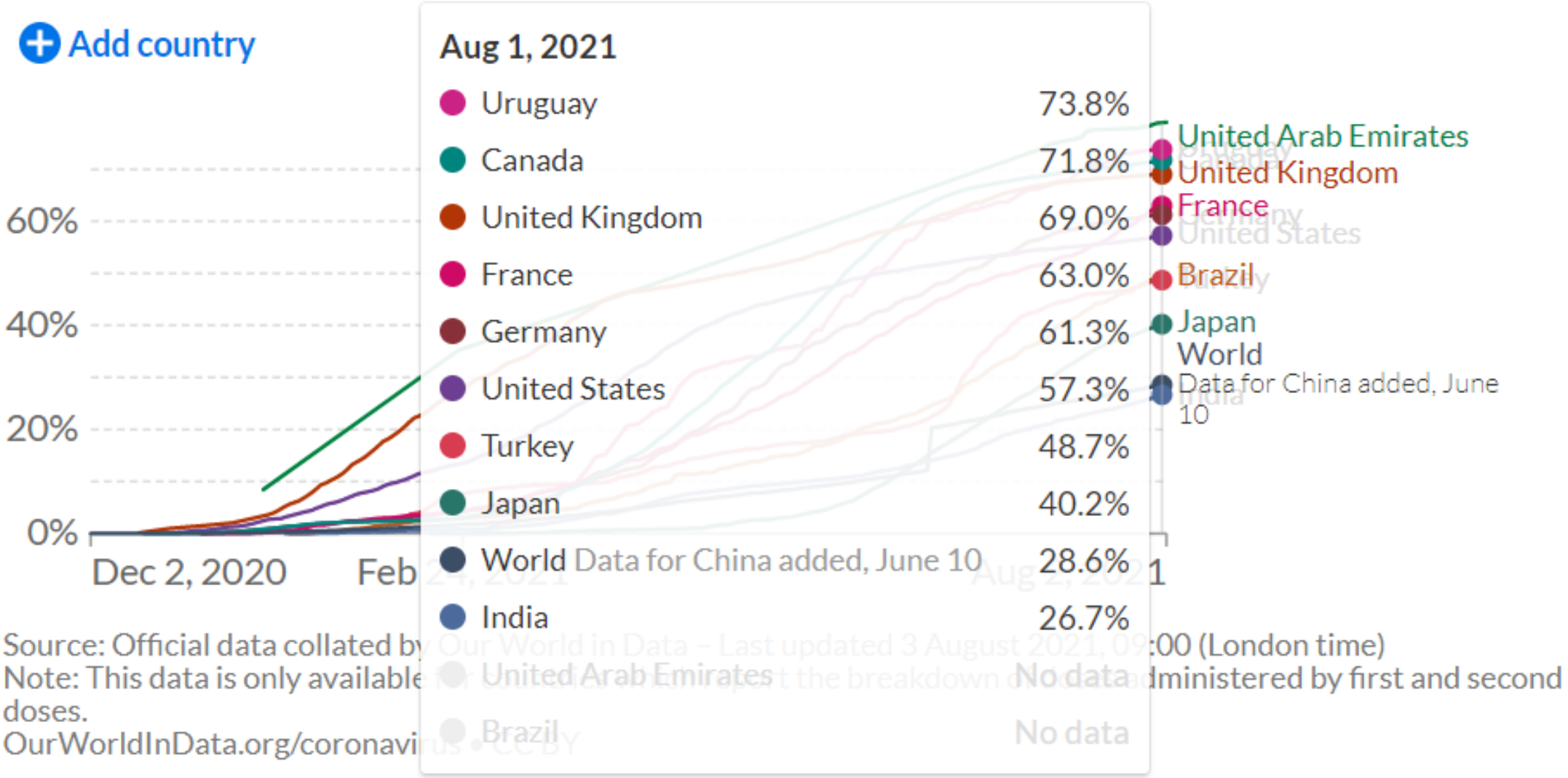
Dai, L., et al. Viral targets for vaccines against COVID-19. Nat Rev Immunol (2020). https://doi.org/10.1038/s41577-020-00480-0

每個疫苗平台的機制



Respir Med.2021;180:106355.

接受至少一劑COVID-19疫苗的人的比率



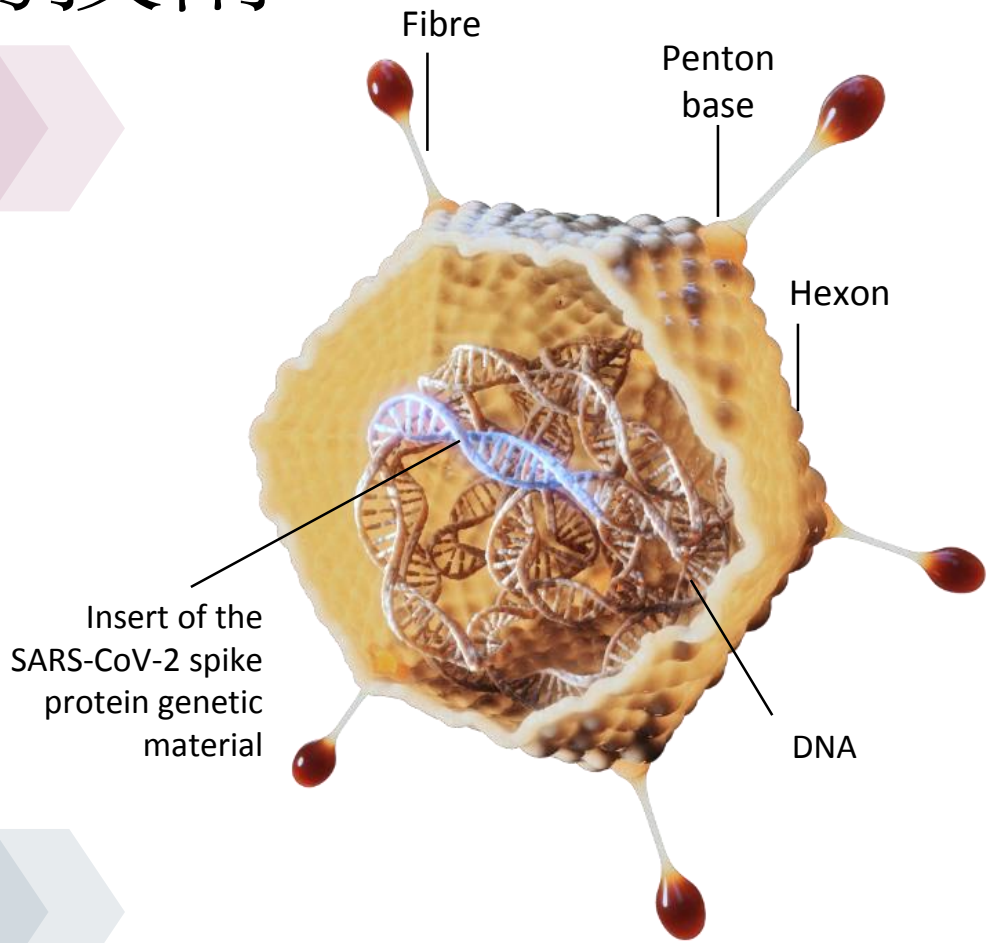
COVID-19 Vaccine AstraZeneca

COVID-19 Vaccine AstraZeneca: 疫苗候選背後的技術

Based on existing simian recombinant adenovirus vaccine vector (ChAdOx1)[1]

- Non-replicating[2]
- Simian adenovirus vector circumvents the pre-existing immunity to human adenoviruses[3]
- Adenovirus vectors do not integrate into host genomes, remaining as episomal DNA in the nucleus of host cells[4]
- Vector induces strong immune cell responses against the vaccine antigen[5]
- ChAdOx1 MERS showed encouraging early clinical safety[2]

SARS-CoV-2 S-protein is expressed in the prefusion conformation[6]

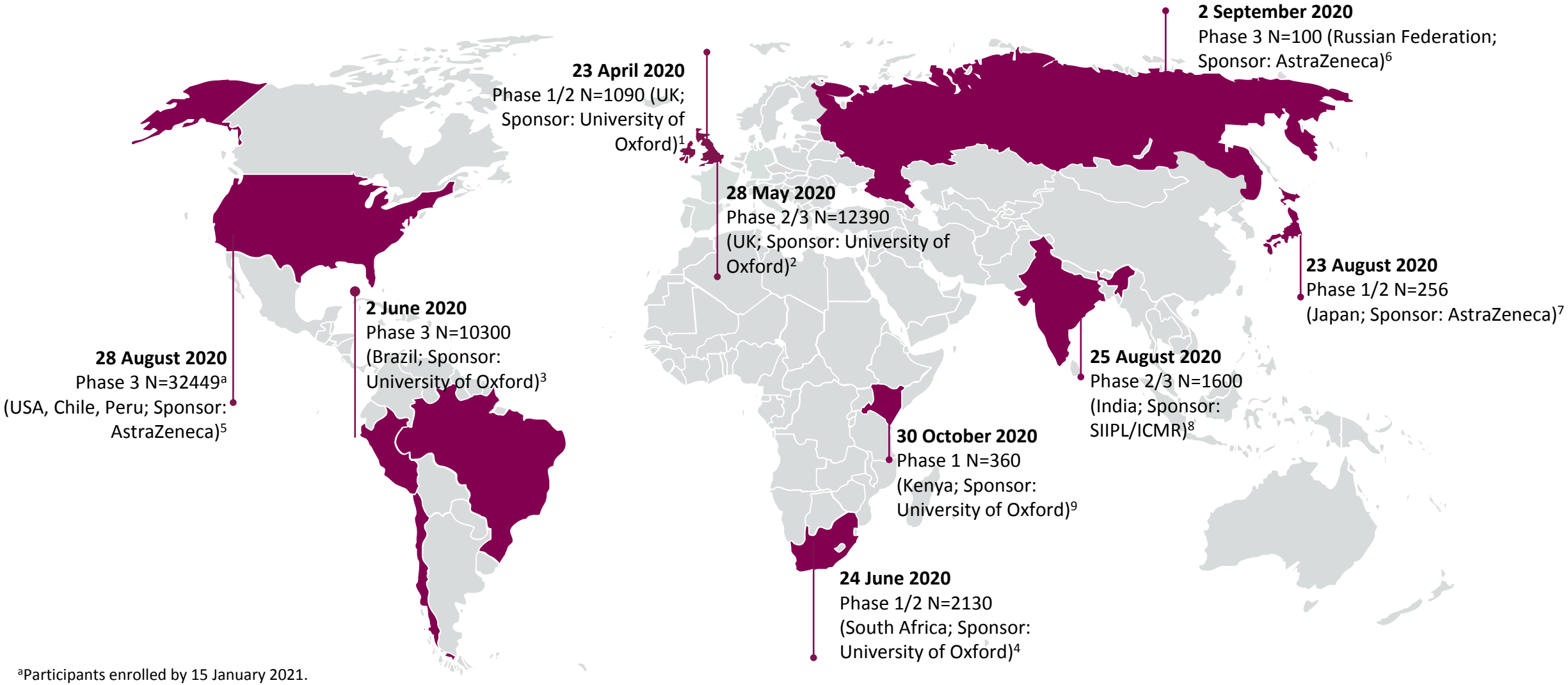


Representation of a COVID-19 Vaccine AstraZeneca virus particle

DNA = deoxyribonucleic acid; MERS = Middle East respiratory syndrome; S = spike; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2.

1. van Doremalen N et al. Online ahead of print. *bioRxiv.* 2020; 2. Folegatti PM et al. Published correction in *Lancet Infect Dis.* 2020. http://dx.doi.org/10.1016/S1473-3099(20)30160-2;
3. Morris SJ et al. *Future Virol.* 2016;11:649-659; 4. Singh S. Adenoviral Vector-Based Vaccines and Gene Therapies: Current Status and Future Prospects. 2018:53-91;
5. van Doremalen N et al. *Sci Adv.* 2020. http://dx.doi.org/10.1126/sciadv.aba8399; 6. Watanabe Y et al. *bioRxiv.* 2021.01.15.426463. https://doi.org/10.1101/2021.01.15.426463

COVID-19 Vaccine AstraZeneca
臨床發展方案



[a]Participants enrolled by 15 January 2021.

1. Study NCT04324606. ClinicalTrials.gov website; 2. Study NCT04400838. ClinicalTrials.gov website; 3. Study NCT04536051. ClinicalTrials.gov website; 4. Study NCT04444674. ClinicalTrials.gov website; 5. Study NCT04516746. ClinicalTrials.gov website; 6. Study NCT04540393. ClinicalTrials.gov website; 7. Study NCT04568031. ClinicalTrials.gov website; 8. AstraZeneca. Data on File; 9. University of Oxford press release: published 30 October 2020: https://www.research.ox.ac.uk/Article/2020-10-30-trials-of-oxford-coronavirus-vaccine-begin-in-kenya (Accessed 27 March 2021)

COVID-19 Vaccine AstraZeneca
美國第三階段分析確認安全性和有效性

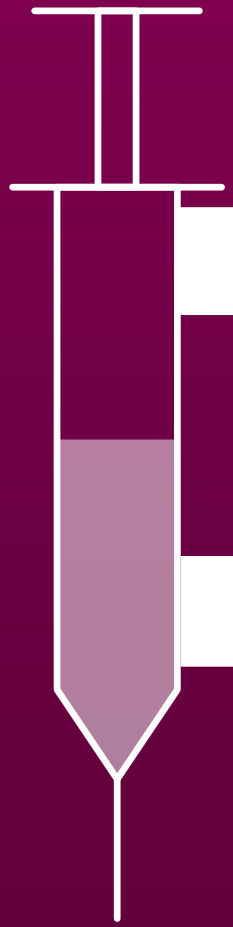
- 32449 participants accruing 190 symptomatic cases of COVID-19[1]
- 2:1 randomisation of vaccine to placebo[1]
- Two doses evaluated **4 weeks apart**[1]

- No safety concerns related to the vaccine[1]
- No increased risk of thrombosis or events characterised by thrombosis[2]

- Among participants in the analysis, ~79% were white / Caucasian, 8% black / African American, 4% Native American and 4% Asian[2]
- 22% of participants were Hispanic[2,a]

- Full primary analysis being submitted for EUA and to scientific journal for peer-review publication

100% efficacy against severe or critical disease and hospitalisation[1]



Overall vaccine efficacy[1]

76%

Confidence interval 68% to 82%

Efficacy in 65 years and over[1]

85%

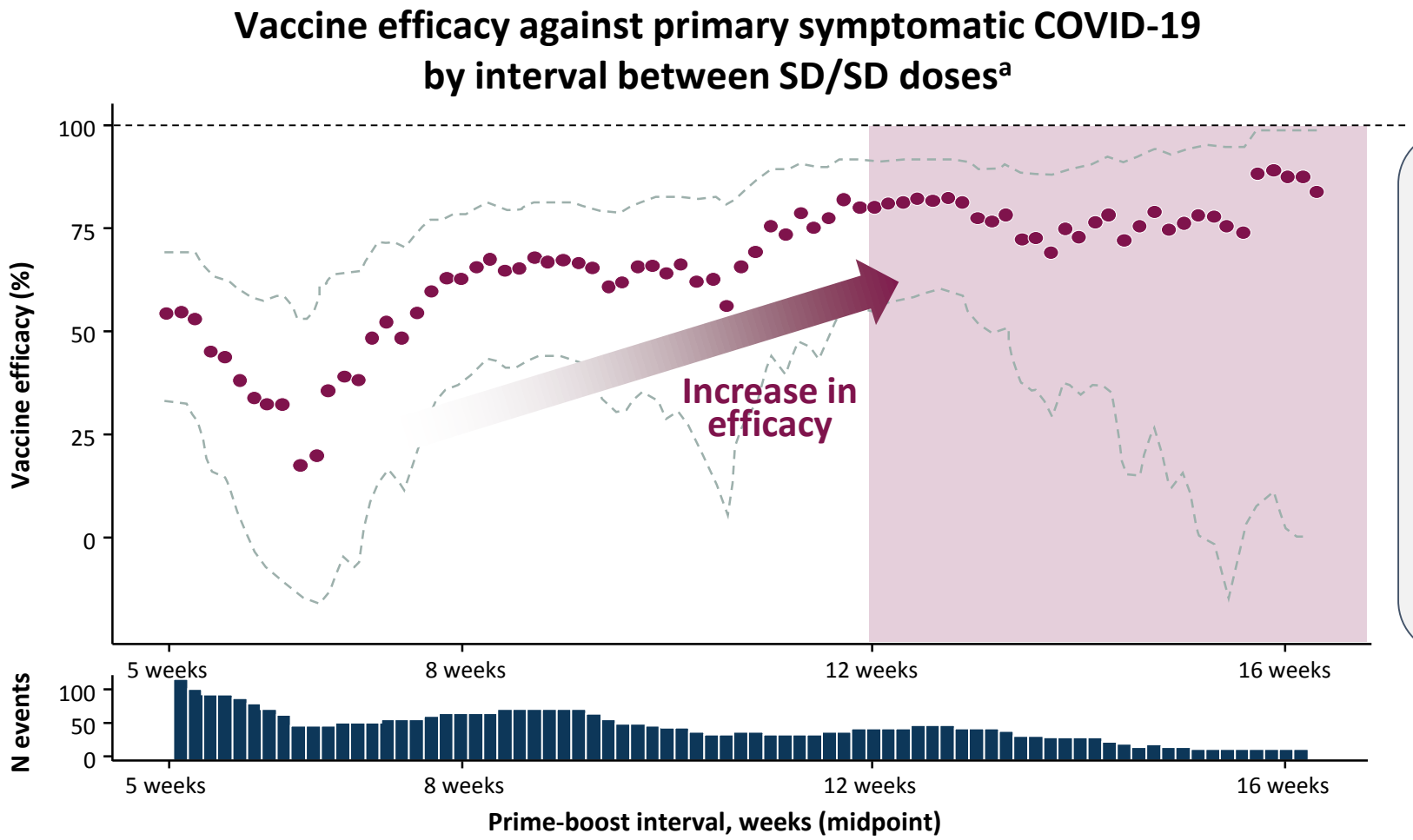
Confidence interval 58% to 95%

Efficacy was consistent across ethnicity and age[1]

[a]Participants may include themselves in more than one category
COVID-19 = coronavirus disease 2019; EUA = Emergency Use Authorisation

1. AstraZeneca Pharmaceuticals LP. Press release. 25 March 2021. Available from: https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/azd1222-us-phase-iii-primary-analysis-confirms-safety-and-efficacy.html (Accessed 25 March 2021);
2. AstraZeneca Pharmaceuticals LP. Press release. 22 March 2021. Available from: https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/astrazeneca-us-vaccine-trial-met-primary-endpoint.html (Accessed 25 March 2021)

當第一次和第二次劑量之間的間隔延長到≥12周時 阿斯利康COVID-19疫苗的療效提高到81%



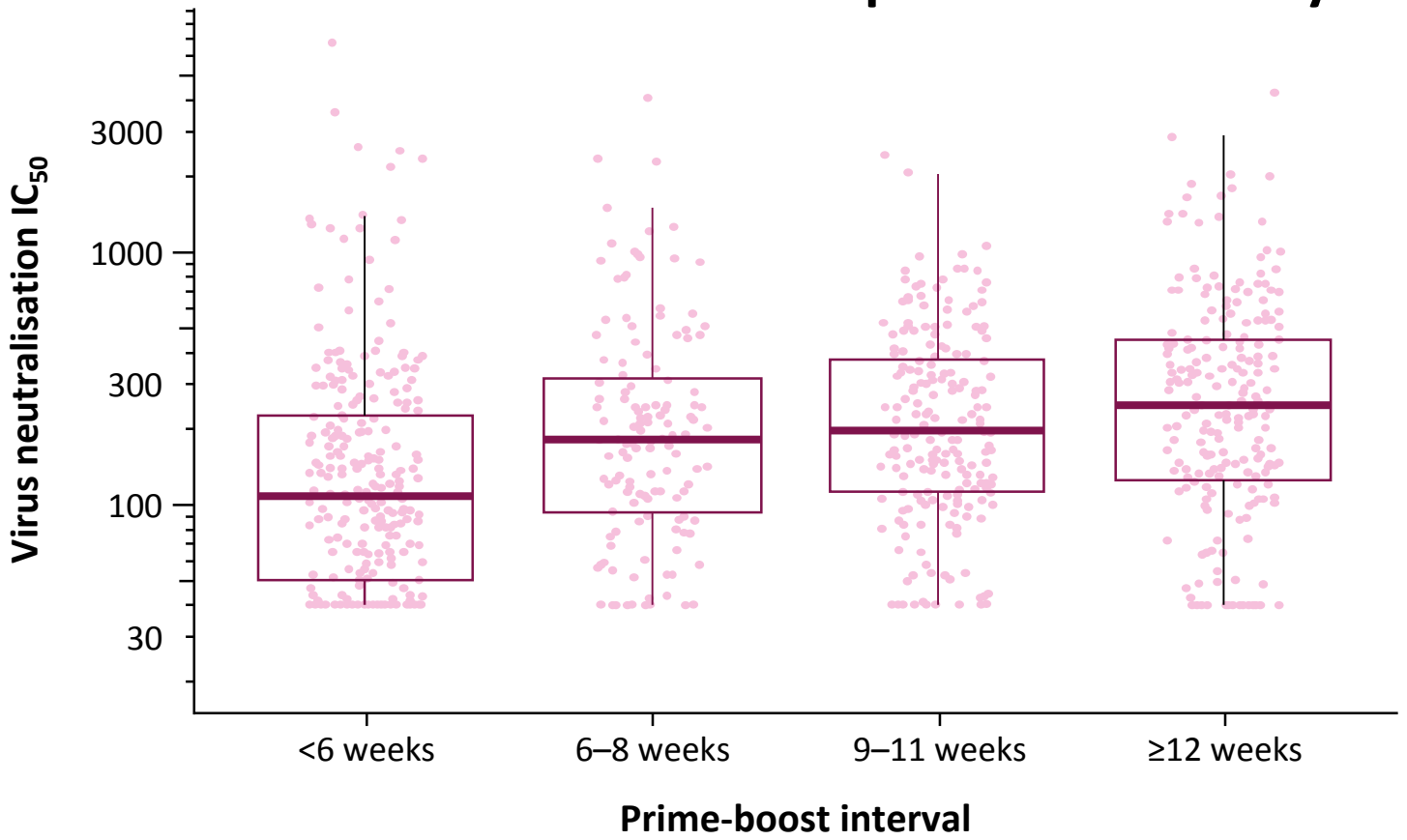
Efficacy after two SDs with interval between:

- <6 weeks: 55.1% (95% CI 33.0%, 69.9%)[b]
- >12weeks: 81.3% (95% CI 60.3%, 91.2%)[c]

[a]Each dot represents one estimate of VE in a subset of participants who received two doses of COVID-19 Vaccine AstraZeneca with a gap between first and second dose within a 20-day range;
the x-axis shows the midpoint of the 20-day range for dosing; dotted lines show 95% CI for each point estimate of VE. [b]111 confirmed cases. [c]53 confirmed cases.
CI = confidence interval; COVID-19 = coronavirus disease 2019; SD = standard dose (5×10^{10} virus particles); VE = vaccine efficacy.
Voysey M, et al. Lancet 2021;doi 10.1016/S0140-6736(21)00432-3: 19 Feb [Epub ahead of print]

劑量間隔更長中和抗體反應增加

Neutralising antibodies 28 days after a second dose, measured in pseudovirus assay[a,b]

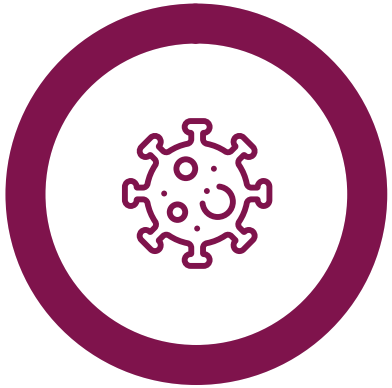


'slow burner'

Neutralising antibodies increased with an increased interval before the second dose

[a]Participants who tested positive for SARS-CoV-2 by PCR prior to the blood sample taken at Day 28 after the second dose were removed from the analysis. [b]This includes both SD/SD and LD/SD.
IC_{50} = half maximal inhibitory concentration; LD = low dose (2.2×10^{10} virus particles); PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; SD = standard dose (5×10^{10} virus particles).
Voysey M, et al. Lancet 2021;doi 10.1016/S0140-6736(21)00432-3: 19 Feb [Epub ahead of print] Supplementary Appendix

阿斯利康COVID-19 疫苗耐受性良好
在臨床試驗中表現出對有症狀的COVID-19的防護



100% protective against severe disease, hospitalisation and death >22 days after the **first dose**[1]

76% efficacy >21 days after the first dose, that is maintained to the second dose[2]

Increased efficacy up to **>80%** with an interval between doses of at least 12 weeks[2]

1. Voysey M et al. Lancet. 2021;397:99-111; 2. Voysey M et al. Online ahead of print. Lancet. 2021;

真實證據：有效性

獨立的實際效果研究

Public Health Scotland (EAVEII)[1]

Determine **first-dose vaccine effectiveness** of BNT162b2 and COVID-19 Vaccine AstraZeneca vaccines against **hospital admissions** for COVID-19

Public Health England[2]

Estimate the real-world effectiveness of BNT162b2 and COVID-19 Vaccine AstraZeneca vaccines against **confirmed COVID-19, hospitalisations and deaths.**

Bristol study (AvonCAP)[3]

Vaccine effectiveness of **first dose** against **hospital admission** with either a clinical or radiological diagnosis of acute LRT disease and/or signs and symptoms of that disease, ≥14 days after vaccination

Welsh LTCF study[4]

Vaccine effectiveness of first dose of BNT162b2 and COVID-19 Vaccine AstraZeneca against **SARS-CoV-2 infection** in older people living in care homes, with adjustment for frailty

Public Health England (VIVALDI)[5]

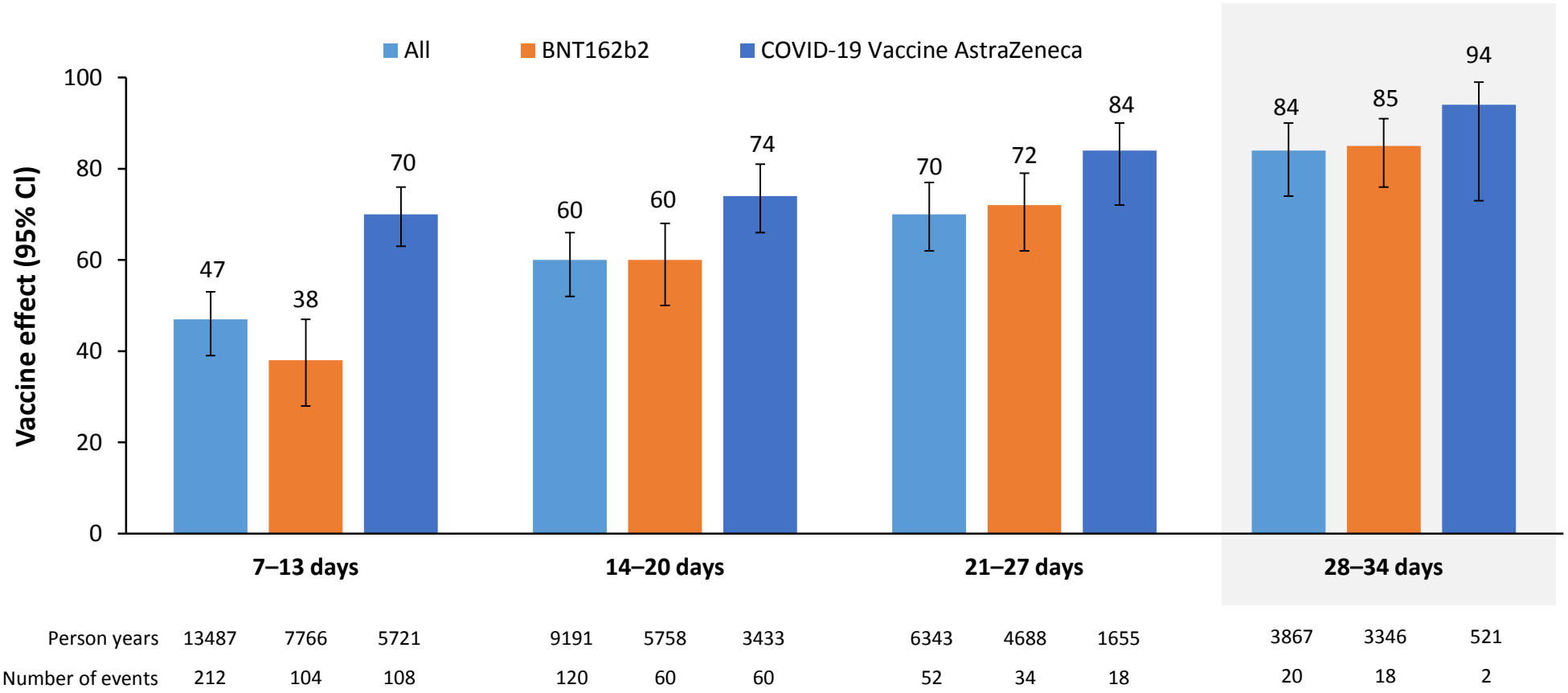
Vaccine effectiveness of first dose of BNT162b2 and COVID-19 Vaccine AstraZeneca against **SARS-CoV-2 infection** in long-term care facilities

COVID-19 = coronavirus disease 2019; LRT = lower respiratory tract; LTCF = long-term care facility; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

1. Vasileiou E, et al. Preprint published online. Lancet 2021; 2. Bernal JL, et al. Preprint published online. medRxiv 2021; 3. Hyams C, et al. Preprint published online. Lancet 2021; 4. Hollinghurst, et al. Preprint published online. medRxiv 2021; 5. Shrotri M, et al. Preprint published online. medRxiv 2021

第一次劑疫苗的有效性隨著時間而提高
兩種疫苗的接種時間達到28-34天高峰

Vaccine effect in hospitalisation for COVID-19 according to days after the first dose for both BNT162b2 and COVID-19 Vaccine AstraZeneca and by vaccine type[a]



	7–13 days			14–20 days			21–27 days			28–34 days		
Person years	13487	7766	5721	9191	5758	3433	6343	4688	1655	3867	3346	521
Number of events	212	104	108	120	60	60	52	34	18	20	18	2

The highest vaccine effect against COVID-19 hospitalisation was

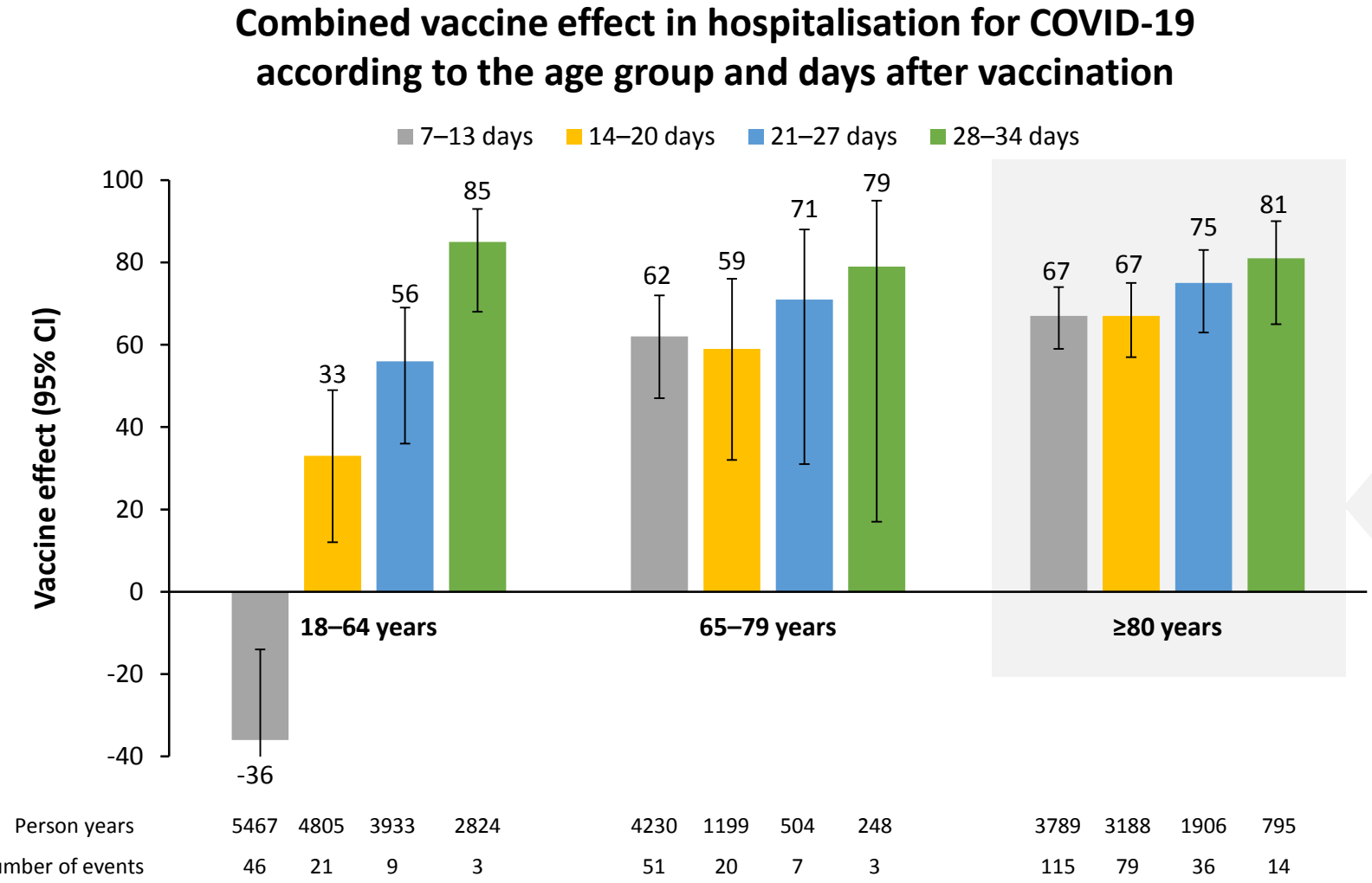
85% (95% CI 76%, 91%) for **BNT162b2**

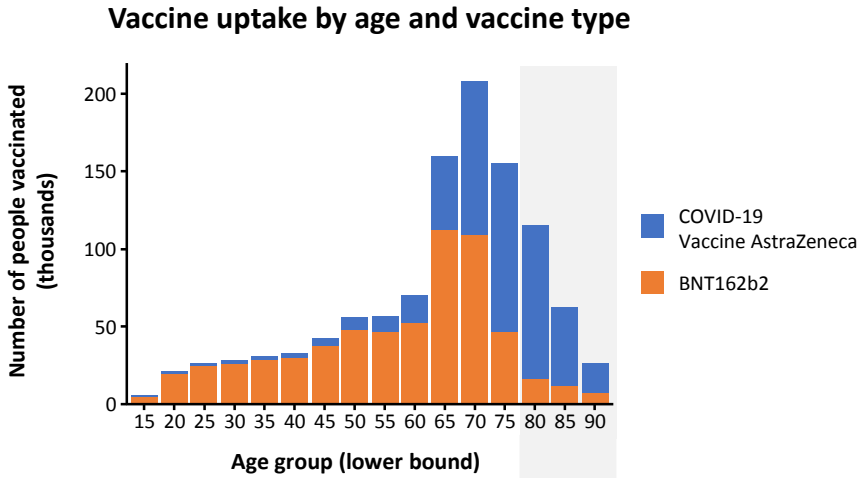
and

94% (95% CI 73%, 99%) for **COVID-19 Vaccine AstraZeneca**

[a]Omitting individuals who had previously tested positive. CI = confidence interval; COVID-19 = coronavirus disease 2019.
Vasileiou E et al. Preprint published online. *Lancet*. 2021

預防COVID-19相關住院的效果在各年齡組相似
疫苗對老年人有效

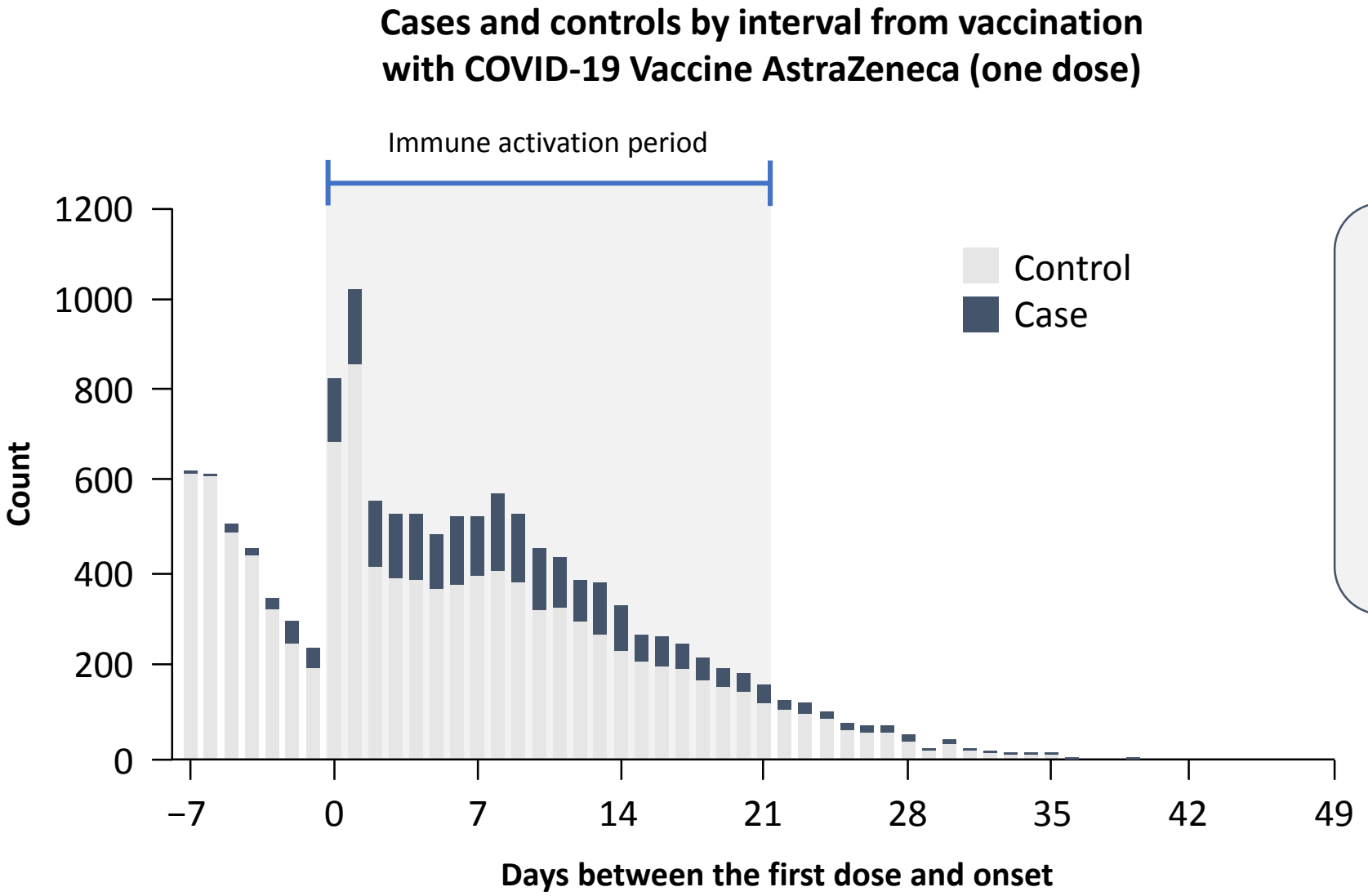




- In those aged ≥80 years, the peak vaccine effect against COVID-19-related hospitalisations was **81%** (95% CI 65%, 90%)
- Data in that age group are primarily driven by COVID-19 Vaccine AstraZeneca

CI = confidence interval; COVID-19 = coronavirus disease 2019; VE = vaccine effect.
Vasileiou E et al. Preprint published online. *Lancet*. 2021

一劑COVID-19疫苗的影響隨著時間的推移

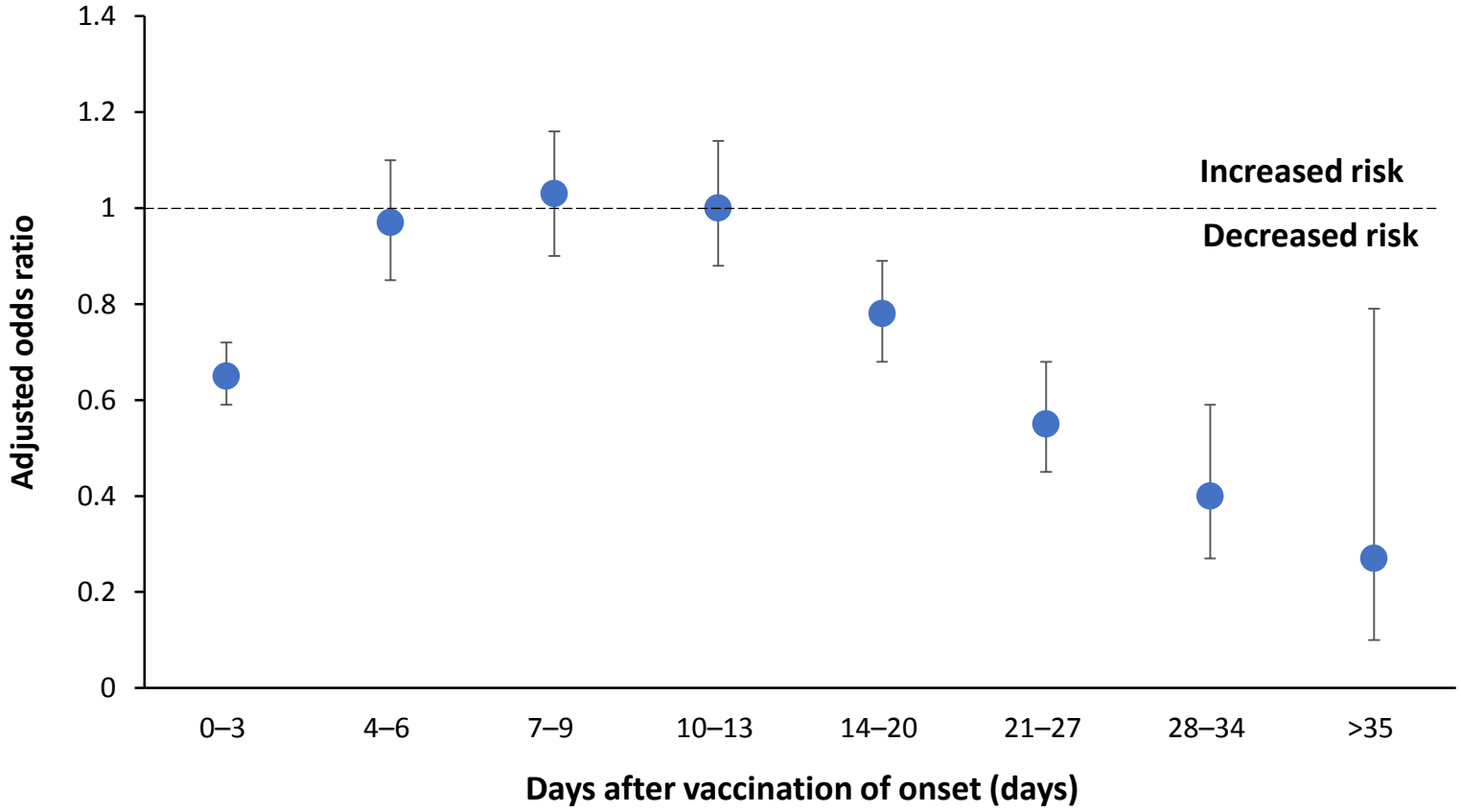


隨著疫苗引起的免疫活化的發生，觀察到病例的減少

Bernal JL et al. medRxiv 2021.03.01.21252652; doi: https://doi.org/10.1101/2021.03.01.21252652 [Preprint published online]

COVID-19 阿斯利康疫苗在 ≥ 70 歲老人第一次接種疫苗 35 天內達到 73% 的有效性

Adjusted odds ratios[a] for confirmed case by interval after the first dose of COVID-19 Vaccine AstraZeneca (from 4 January 2021, age ≥70 years)



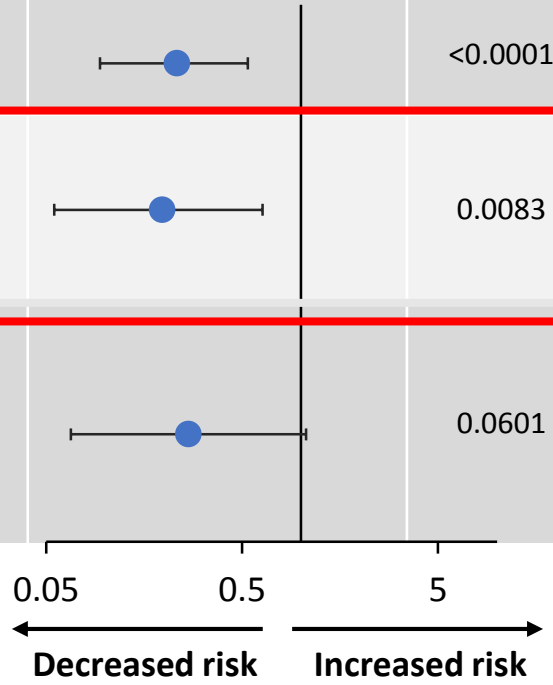
- There was no significantly increased risk during the early post-vaccination period
- Data suggest a vaccine effectiveness against hospitalisation of at least 80% following a **single dose** of COVID-19 Vaccine AstraZeneca

[a]Odds ratio adjusted for age, period, sex, region, ethnicity, care home, IMD quintile.
CI = confidence interval; IMD = index of multiple deprivation; OR = odds ratio.
Bernal JL et al. medRxiv 2021.03.01.21252652; doi: https://doi.org/10.1101/2021.03.01.21252652 [Preprint published online]

一劑COVID-19疫苗阿斯利康疫苗對≥80歲成人住院的疫苗有效率為80.4%

Vaccine effectiveness for one dose of COVID-19 Vaccine AstraZeneca in adults ≥80 years based on different analyses[a,b]

Analysis	Factor	Vaccine effectiveness 95% (CI)	OR (95% CI)	P-value
Unadjusted	-	76.7 (46.5, 90.6)	0.233 (0.094, 0.535)	<0.0001
Logistic regression model	One dose	**80.4 (36.4, 94.5)**	0.196 (0.055, 0.636)	0.0083
Matched conditional regression model	One dose	73.3 (−6.1, 93.2)	0.267 (0.067, 1.061)	0.0601



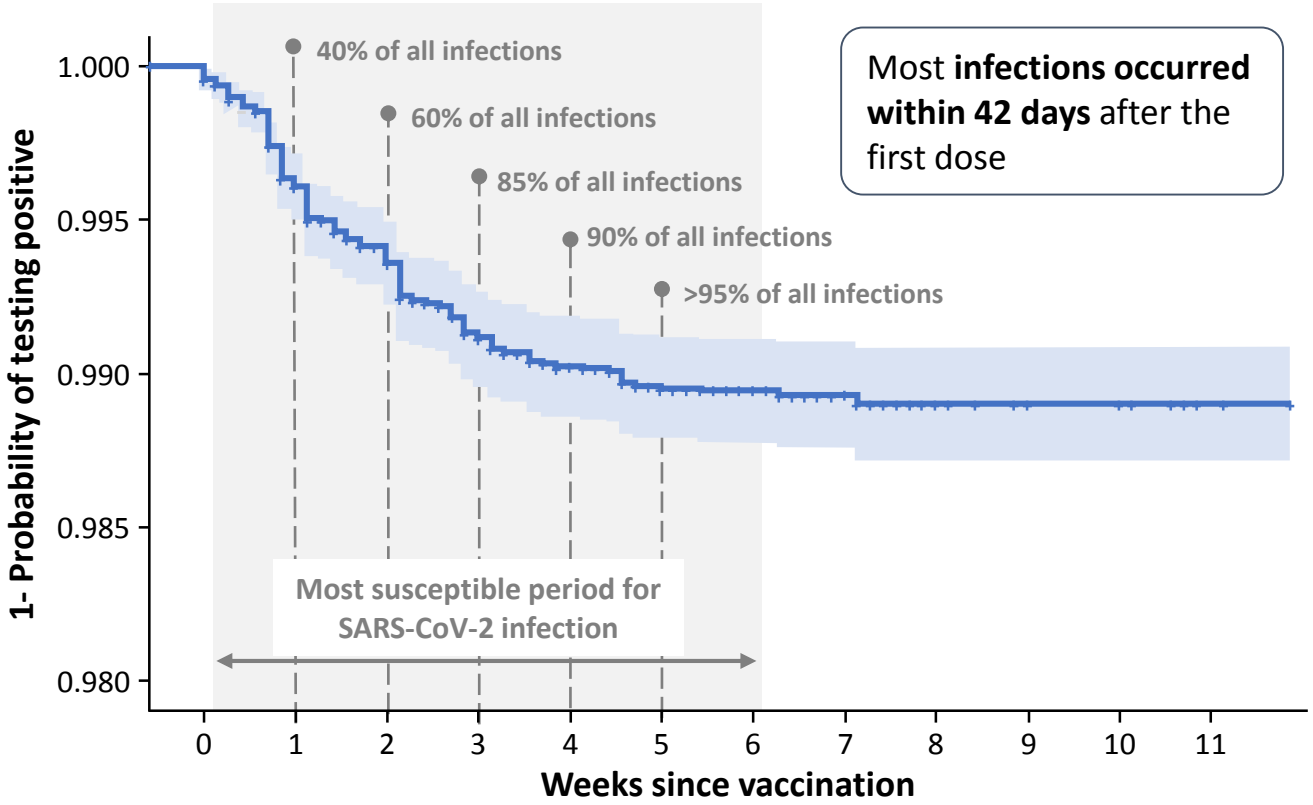
- 9/36 (25%) cases with SARS-CoV-2 infection and 53/90 (58.9%) controls received one dose of COVID-19 Vaccine AstraZeneca, resulting in an unadjusted effectiveness of 76.7% and an adjusted effectiveness of 80.4%

Vaccine effectiveness for one dose of COVID-19 Vaccine AstraZeneca calculated from 8 January 2021 to 26 February 2021.
[a]The follow-up period ranged between 19 and 64 days. [b]The median age was 88.3 years.
CI = confidence interval; COVID-19 = coronavirus disease 2019; IMD = index of multiple deprivation; OR = odds ratio.
Hyams C et al. Preprint published online. *Lancet*. 2021

在威爾士住在LTCFs的 >60歲成年人接種了疫苗減少了SARS-CoV-2感染

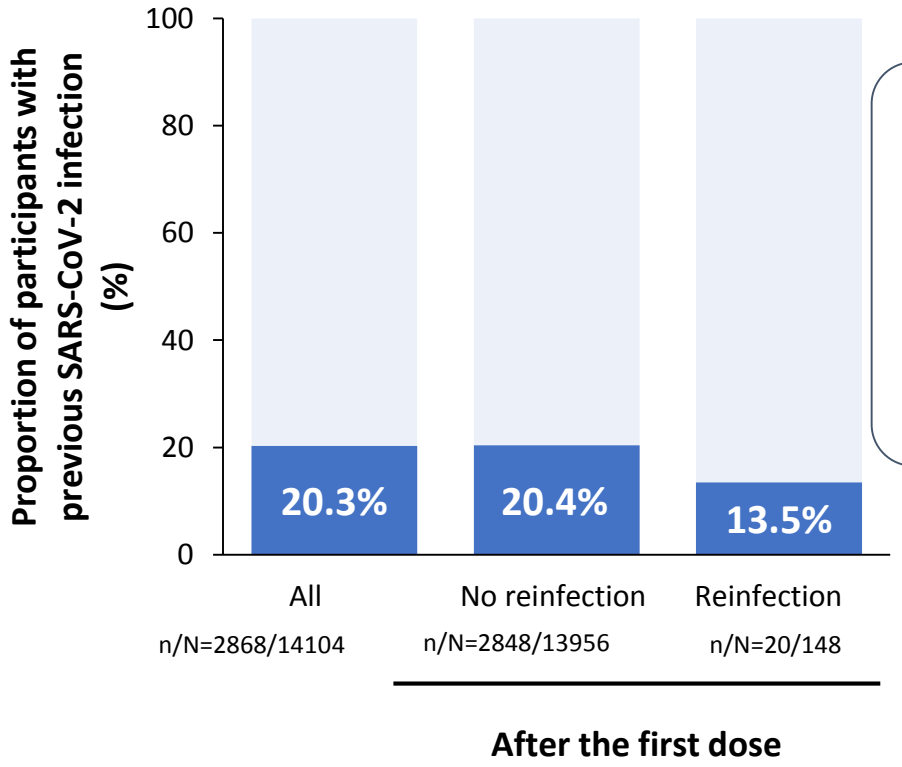
1.05% of participants tested positive for SARS-CoV-2 after vaccination

Time to first positive SARS-CoV-2 PCR test following the first dose



Most **infections occurred within 42 days** after the first dose

Patients with previous SARS-CoV-2 infection in the overall and subgroup analysis



7 days after the first dose of the vaccine, those with previous SARS-CoV-2 infection had a **decreased risk of reinfection**

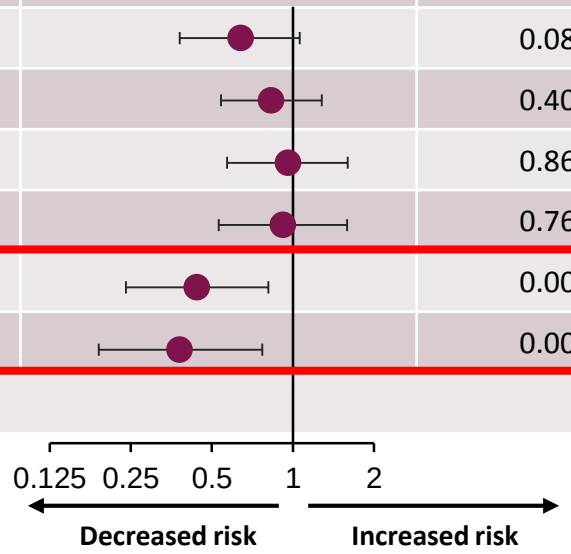
HR 0.54 (95% CI: 0.30, 0.95)

PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Hollinghurst J, et al. Preprint published online. medRxiv 2021

在英格蘭65歲≥成年人的單劑量疫苗對症狀和無症狀疾病的綜合有效性

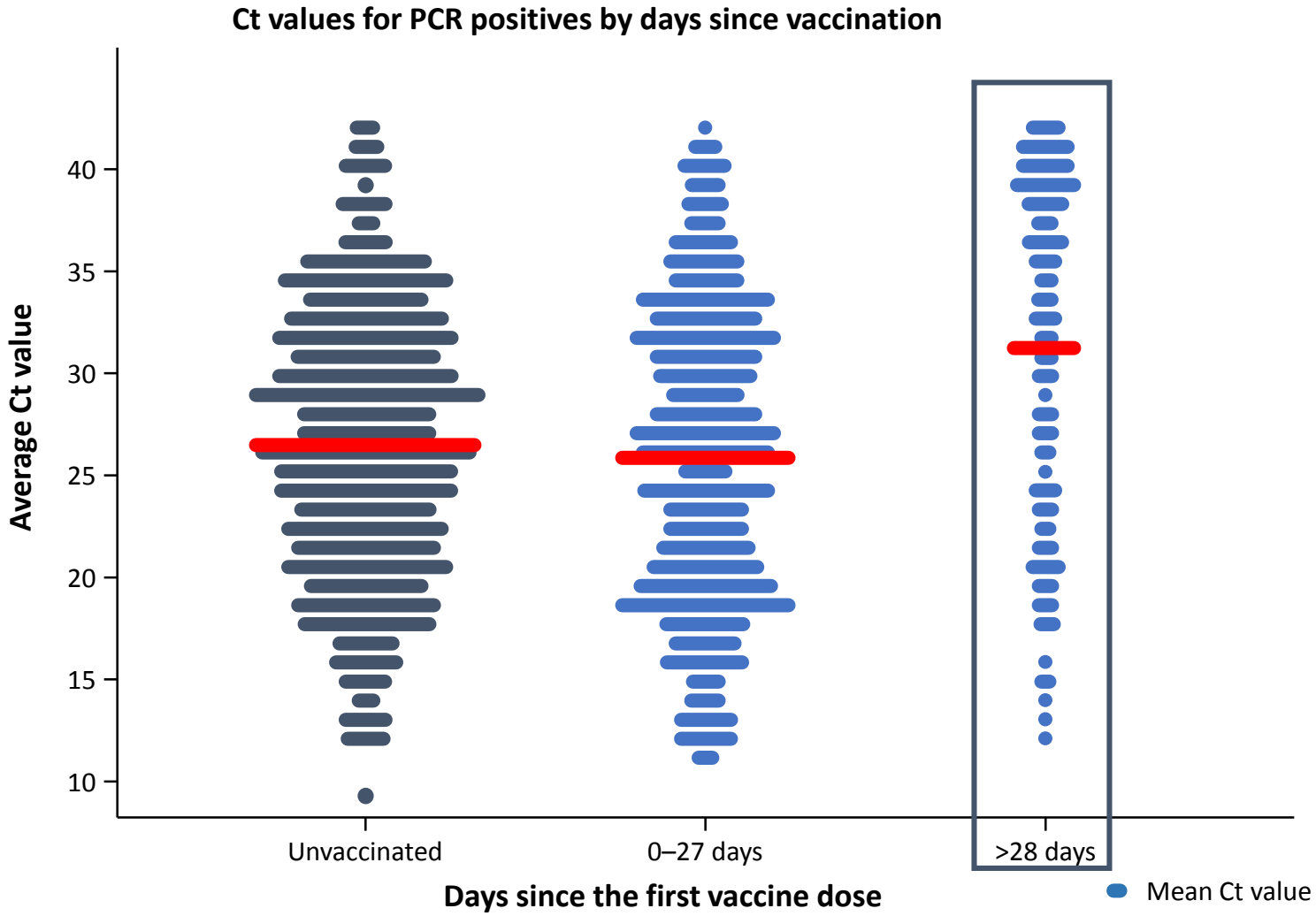
	Person days at risk	PCR tests	PCR testing rate per 1000 person days	Infection events	Infection rate per 10000 person days	Adjusted[a] HR (95% CI)		P-value
Unvaccinated	338003	15392	45.54	723	21.39	1		
0–6 days	47591	2482	52.15	105	22.06	0.64 (0.38, 1.06)		0.083
7–13 days	53511	3189	59.60	139	25.98	0.83 (0.54, 1.28)		0.404
14–20 days	50362	2462	48.89	132	26.21	0.96 (0.57, 1.60)		0.866
21–27 days	47514	2478	52.15	95	19.99	0.92 (0.53, 1.59)		0.762
28–34 days	43136	2078	48.17	42	9.74	0.44 (0.24, 0.81)		0.009
35–48 days	63012	4681	74.29	59	9.36	0.38 (0.19, 0.77)		0.007
Overall	670628	36352	54.21	1335	19.91			



- At ≥49 days after vaccination, the estimates were less precise and no longer significantly different to the unvaccinated group
- In this model, prior infection was associated with a reduced risk of subsequent infection (HR 0.19 [95% CI 0.12, 0.30])

[a]Adjusted HR was estimated using a Cox proportional hazard regression model with an interaction term between vaccination status and prior infection status; the comparator is the unvaccinated group with evidence of prior infection. 95% CIs were calculated using robust standard errors for LTCF-level effects
CI = confidence interval; HR = hazard ratio; LTCF = long-term care facility; PCR = polymerase chain reaction
Shrotri M, et al. Preprint published online. medRxiv 2021

接種疫苗 大於28天感染的參與者的病毒載量顯著減少 代表傳播能力降低



The Ct value is inversely proportional to the viral load

No difference was observed when comparing the mean Ct value of PCR tests from the unvaccinated group with those who became infected with SARS-CoV-2 within 0–27 days of the first vaccine dose (P=0.158)

The mean Ct value of those infected with SARS-CoV-2 >28 days after the first dose was significantly higher (*P*<0.001) than that observed in those from the unvaccinated group who became infected

Ct = cycle threshold; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Shrotri M, et al. Preprint published online. medRxiv 2021

單次劑量疫苗有效性的真實證據與臨床試驗數據一致

Public Health Scotland (EAVEII)[1]

94% effective in preventing hospitalisation in an **enriched elderly population**

Public Health England[2]

73% effective against symptomatic COVID-19 from Day 35 onwards in **older adults (≥70 years)** Vaccine effectiveness against **hospitalisation of at least 80%** following a single dose of **COVID-19 Vaccine AstraZeneca**

Bristol study (AvonCAP)[3]

80% effective in preventing hospitalisation in elderly and frail real-world adults (≥80 years) with extensive comorbid disease

Welsh LTCF study[4]

1.05% residents had a SARS-CoV-2-positive test following vaccination, with 90% of infections within 28 days

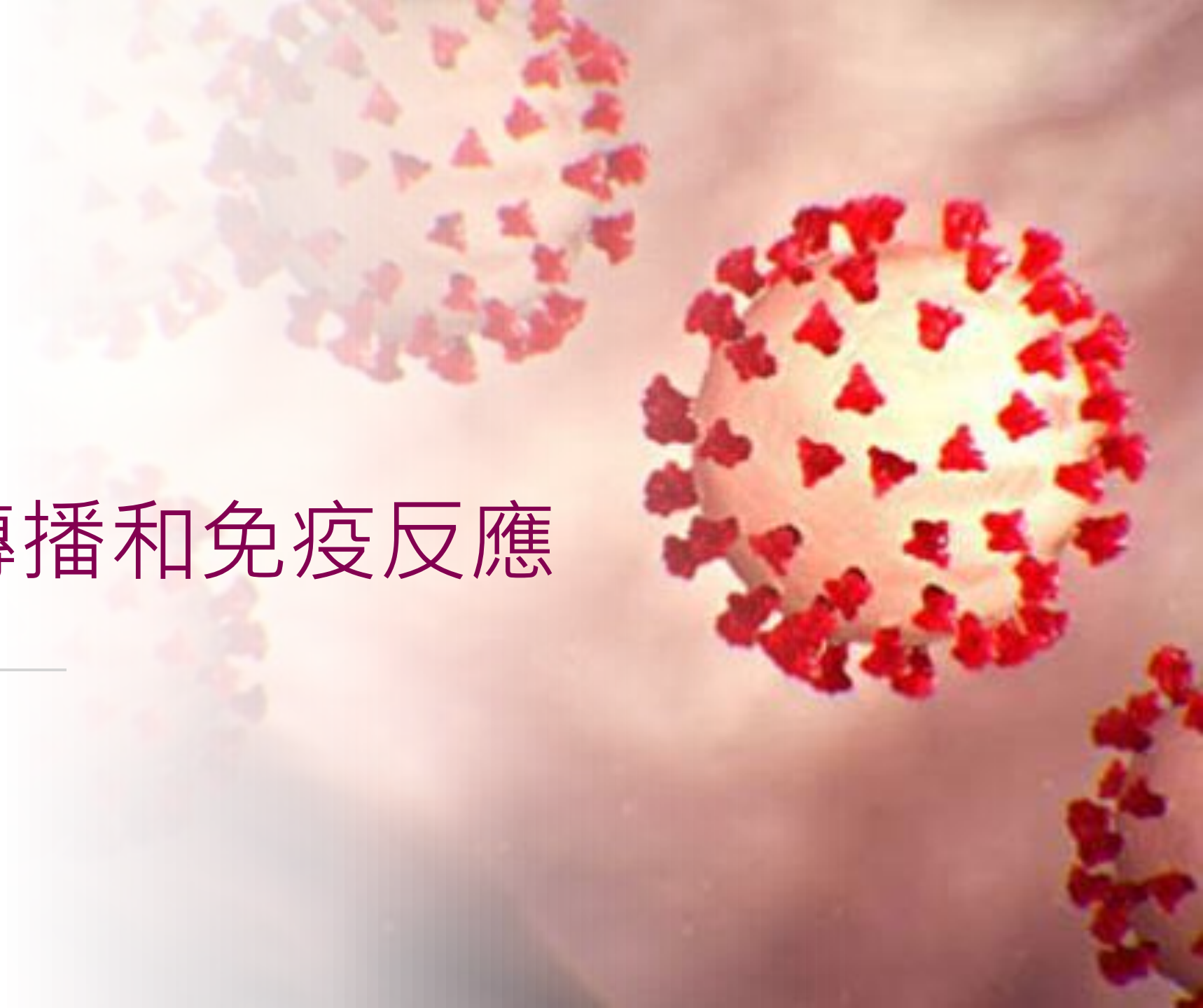
Public Health England (VIVALDI)[5]

Reduced SARS-CoV-2 infection risk from **4 to at least 7 weeks.** **Estimated 56% vaccine effectiveness reported at 28–34 days**, and **62% at 35–48 days**

COVID-19 = coronavirus disease 2019; HR = hazard ratio; LTCF = long-term care facility; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

1. Vasileiou E, et al. Preprint published online. Lancet 2021; 2. Bernal JL, et al. Preprint published online. medRxiv 2021; 3. Hyams C, et al. Preprint published online. Lancet 2021; 4. Hollinghurst, et al. Preprint published online. medRxiv 2021; 5. Shrotri M, et al. Preprint published online. medRxiv 2021

真實證據：傳播和免疫反應



關於傳播和免疫反應
現實世界有效性獨立的研究

Scotland transmission study[1]

National record linkage study to examine **COVID-19 cases and hospitalisations** and the **transmission** in **HCWs** and their **households** before and after vaccination

UK transmission study[2]

A **prospective cohort study** to assess the effectiveness of **COVID-19 vaccination in preventing SARS-CoV-2 infection** in the **community**

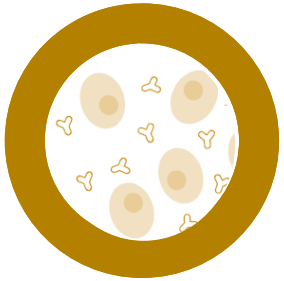
England transmission study[3]

A study to assess the **impact of one dose of COVID-19 vaccine** on **transmission** of SARS-CoV-2 to **unvaccinated household contacts** after a positive test

Public Health England study[4]

Study to explore adaptive **immune responses** after 5 weeks of a single dose of BNT162b2 or COVID-19 Vaccine AstraZeneca in adults >80 years of age

UK study[5]



Study to investigate **anti-trimeric spike IgG antibody responses** after vaccination by time since vaccination, considering vaccine type, number of doses received and whether there was evidence of prior SARS-CoV-2 infection

COVID-19 = coronavirus disease 2019; HCW = healthcare worker; IgG = immunoglobulin G; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

1. Shah ASV, et al. Preprint published online. medRxiv 2021; 2. Pritchard E, et al. Preprint published online. medRxiv 2021; 3. Harris RJ, et al. Preprint published online. 2021; 4. Parry H, et al. Preprint published online. Lancet 2021; 5. Wei J, et al. Preprint published online. medRxiv 2021

疫苗接種對COVID-19傳播的影響：對醫護人員及其家屬的觀察性研究

Study design:

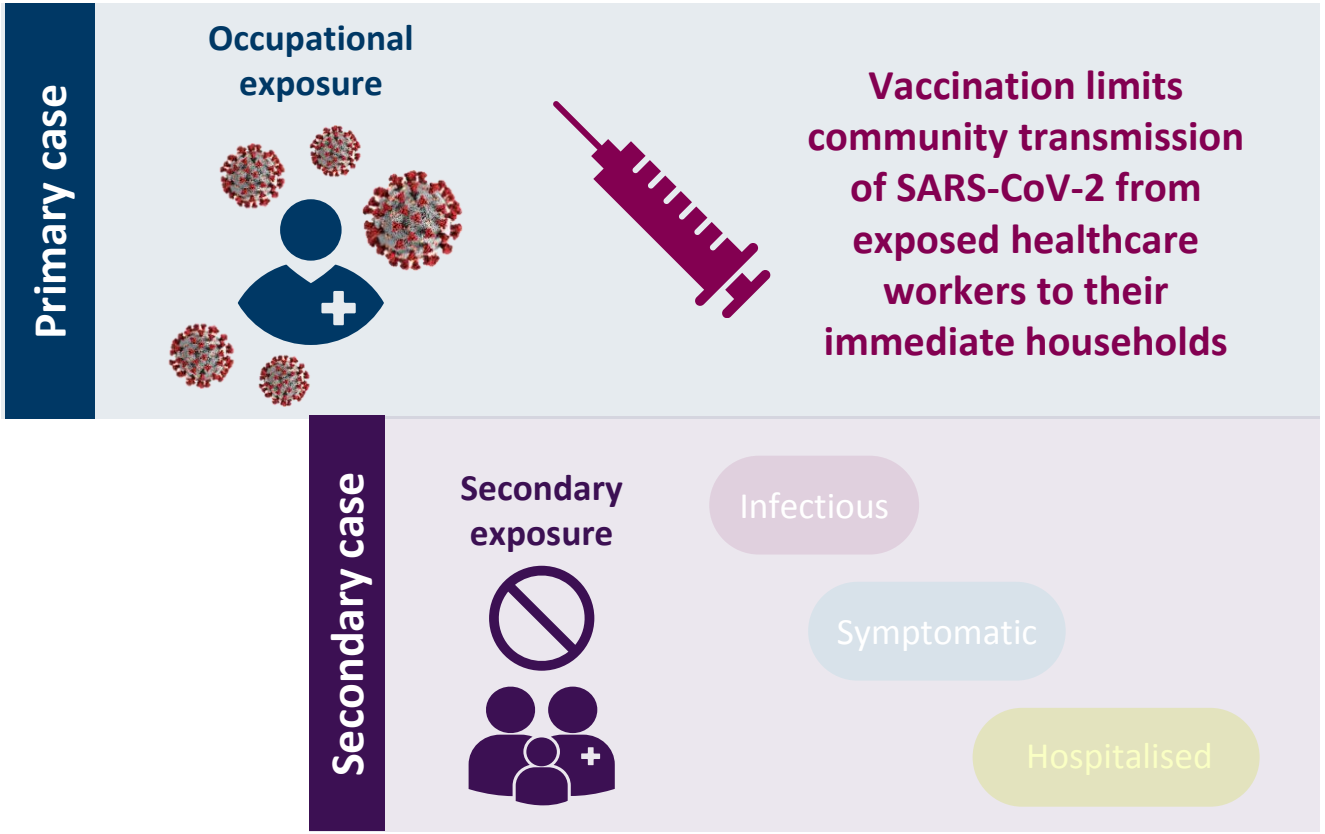
- National record linkage study analysing COVID-19 cases and hospitalisations in unvaccinated household members of vaccinated and unvaccinated healthcare workers (HCW)

Population

- HCW employed by the National Health Service in Scotland on or before 1 March 2020 and still employed on 1 November 2020
- Those with a positive COVID-19 PCR test before 8 December 2020 were excluded
- 113,253 (78.3%) HCWs received ≥1 dose of COVID-19 Vaccine AstraZeneca or BNT162b2 and 36227 (25.1%) received a second dose

Exposure

- 8 December 2020 to 3 March 2021



COVID-19 = coronavirus disease 2019; HCW = healthcare worker; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Shah ASV et al. Preprint published online. medRxiv. 2021

醫護人員COVID-19 感染及相關住院的風險從第 14 天開始降低 從第一次劑量的第 20 天起更加顯著

Effect of vaccination in healthcare workers and their households on COVID-19 cases and COVID-19 hospitalisations

Unvaccinated period vs time period following the **first dose**[a]

Days after vaccination		COVID-19 cases (Hazard ratio)	COVID-19 hospitalisations (Hazard ratio)
1–6 days	HCWs	0.81 (0.72, 0.90)	0.48 (0.25, 0.92)
	Household	0.73 (0.61, 0.87)	0.95 (0.53, 1.69)
7–13 days	HCWs	1.11 (1.02, 1.22)	0.78 (0.48, 1.27)
	Household	1.08 (0.94, 1.25)	1.25 (0.78, 2.02)
14–20 days	HCWs	**0.54 (0.47, 0.61)**	**0.16 (0.06, 0.43)**
	Household	0.85 (0.73, 0.99)	0.96 (0.56, 1.63)
20–27 days	HCWs	0.42 (0.36, 0.49)	0.13 (0.04, 0.40)
	Household	0.68 (0.58, 0.81)	0.83 (0.47, 1.46)
≥28 days	HCWs	0.43 (0.39, 0.47)	0.17 (0.09, 0.32)
	Household	0.64 (0.56, 0.73)	0.64 (0.40, 1.01)

Immune activation period

55% lower risk of COVID-19 among vaccinated **HCWs** (≥14 days after the first dose);
84% reduction in risk of COVID-19 related hospitalization after the first dose

[a]Adjusted for age, sex, SIMD, ethnicity, HCW role, occupation, part-time status and comorbidity.
COVID-19 = coronavirus disease 2019; HCW = healthcare worker; SIMD = Scottish Index of Multiple Deprivation.
Shah ASV et al. Preprint published online. medRxiv. 2021

第二劑疫苗後
醫護人員及家人COVID-19 感染的風險進一步降低

Effect of vaccination in HCWs and their households on COVID-19 cases and COVID-19 hospitalisations

Unvaccinated period vs ≥14 days after the **second dose**

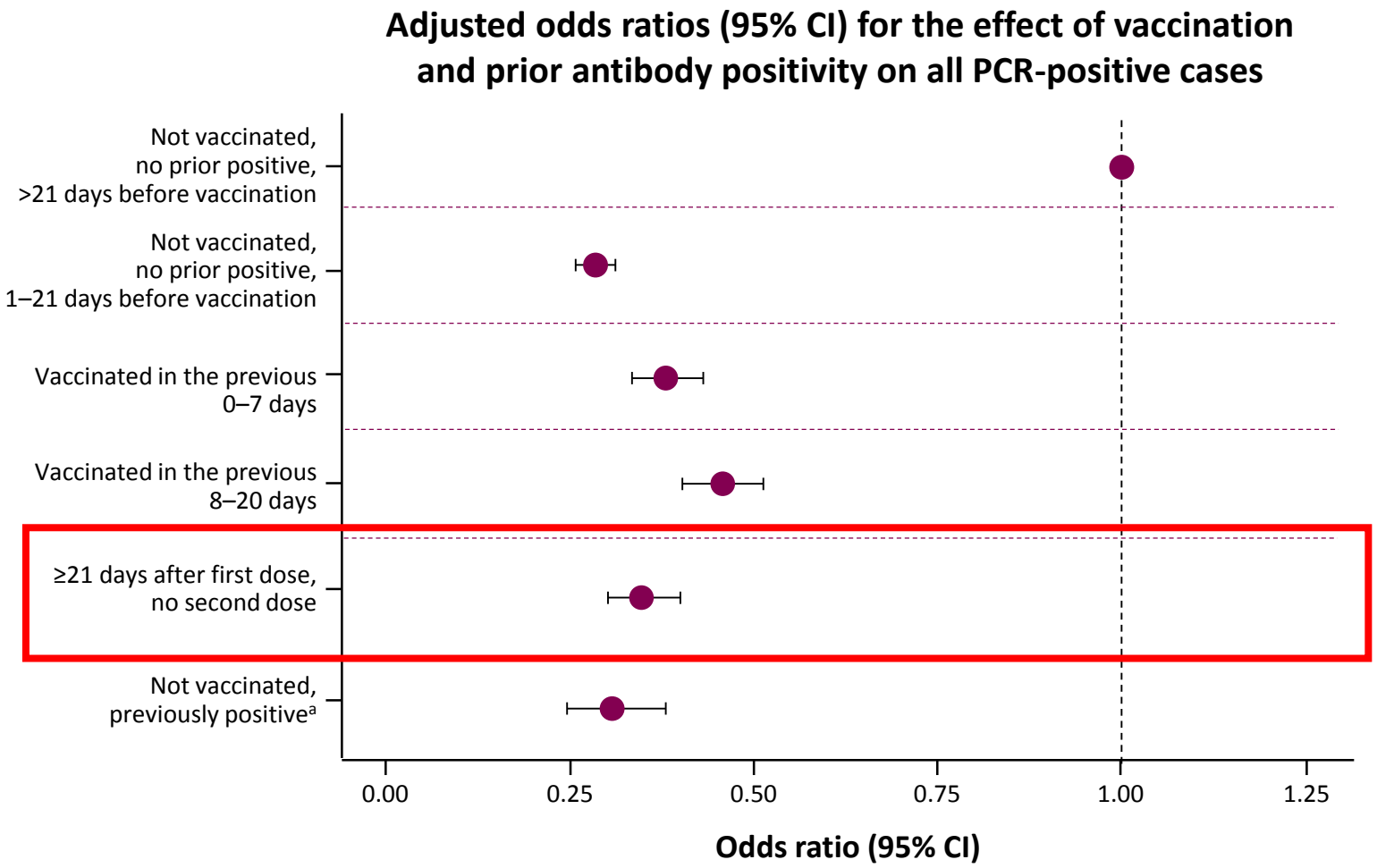
		COVID-19 cases (Hazard ratio)	COVID-19 hospitalisations (Hazard ratio)
Unadjusted	HCWs	0.10 (0.05, 0.19)	-
	Household	0.48 (0.32, 0.73)	0.71 (0.17, 2.92)
Adjusted for age and sex	HCWs	0.10 (0.05, 0.20)	-
	Household	0.47 (0.31, 0.72)	0.68 (0.17, 2.84)
Adjusted for age, sex, SIMD and ethnicity	HCWs	0.11 (0.05, 0.22)	-
	Household	0.50 (0.33, 0.76)	0.78 (0.19, 3.24)
Adjusted for age, sex, SIMD, ethnicity, HCW role, occupation and part-time status	HCWs	0.08 (0.04, 0.17)	-
	Household	0.46 (0.30, 0.70)	0.69 (0.17, 2.83)
Adjusted for age, sex, SIMD, ethnicity, HCW role, occupation, part-time status and comorbidity	HCWs	0.08 (0.04, 0.17)	-
	Household	0.46 (0.30, 0.70)	0.68 (0.17, 2.83)

- 36227 HCWs received the second dose:
  - 368 COVID-19 Vaccine AstraZeneca
  - 35859 BNT162b2
- There were **no hospitalisations** in HCWs who received the second dose of the vaccine
- **54%** lower risk of COVID-19 in **household** contacts (≥14 days after the second dose) with a **92%** reduction in risk of COVID-19 in vaccinated **HCWs** after the second dose

COVID-19 = coronavirus disease 2019; HCW = healthcare worker; SIMD = Scottish Index of Multiple Deprivation.

Shah ASV et al. Preprint published online. medRxiv. 2021

第一劑疫苗≥21天
新的PCR陽性病例的幾率降低了65%

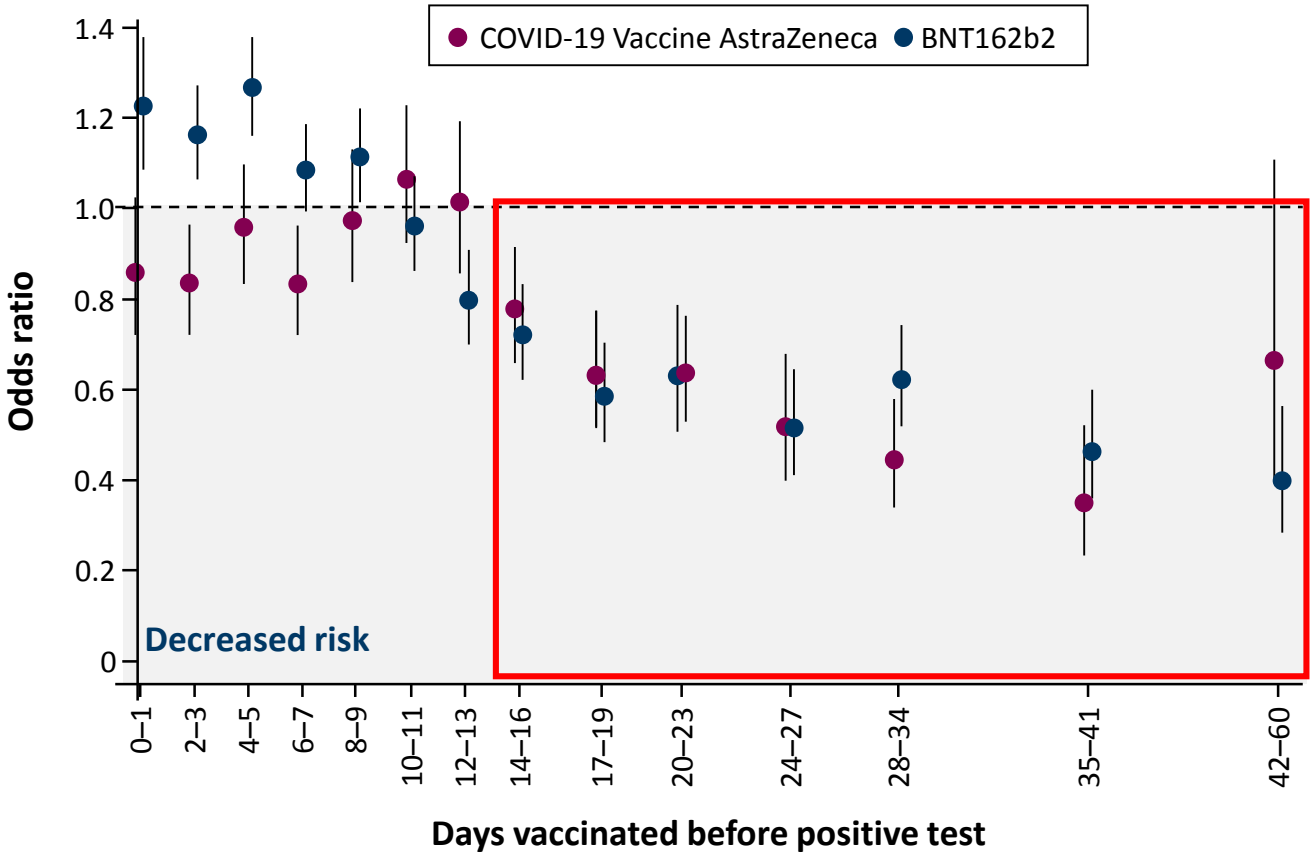


- The **odds of a new PCR-positive case were reduced by 65% (P<0.001)** in those vaccinated ≥21 days before with no second dose, a significant difference compared with those vaccinated in the prior 8–20 days (*P*=0.004)
- The **odds of a new PCR-positive case were reduced by 55% (95% CI 49, 60) in the 8–20 days** after vaccination versus those not vaccinated or no previously positive and ≥21 days before vaccination

[a]Not vaccinated, but with a positive antibody result in the study >45 days previously or a previous positive episode in the study
CI = confidence interval; PCR = polymerase chain reaction
Pritchard E, et al. Preprint published online. medRxiv 2021

從接種疫苗14天後觀察到傳播減少

Odds ratios for secondary cases according to vaccination timing of the index case by type of vaccine vs contacts where the index case was not vaccinated[a,b]



The odds of secondary cases were reduced if the index case was vaccinated ≥14 days before testing positive

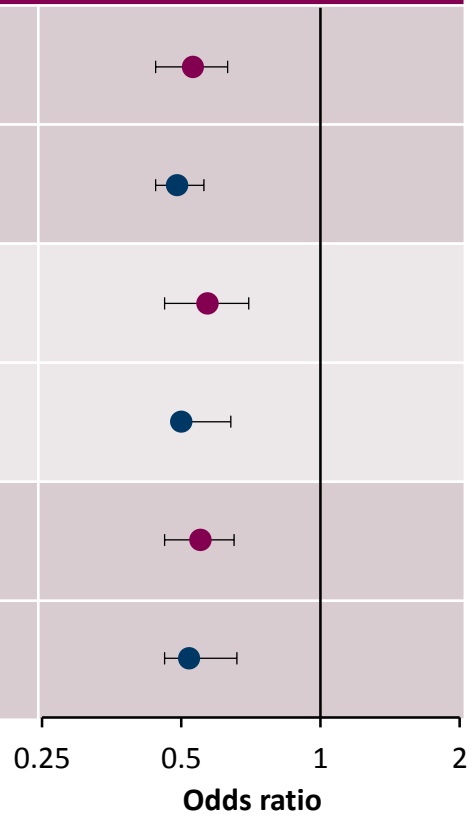
[a]Results from multivariable logistic regression; [b]this analysis also includes households where the index case was vaccinated <21 days before testing positive, which due to the timing of the rollout and data under consideration, are a larger group than those vaccinated ≥21 days before testing positive

Harris RJ, et al. Preprint published online. 2021

第一次劑後 21-35 天
接觸成為次發病例的機率降低一半

Odds ratios for contacts being a secondary case according to vaccination timing of the index case (21–35 vs 1–10 days) before testing positive[a]

	Vaccine	N[b]	Percentage of data, %[c]	OR (95% CI)
Logistic regression	COVID-19 Vaccine AstraZeneca	13169	100.0	0.53 (0.44, 0.63)
	BNT162b2	25688	100.0	0.49 (0.44, 0.56)
Matched case control **Age of index case and contact at week of index case vaccination**	COVID-19 Vaccine AstraZeneca	1218	99.4	0.57 (0.46, 0.70)
	BNT162b2	2930	99.8	0.55 (0.48, 0.64)
Stratified cohort **Age of index case and contact at week of index case vaccination**	COVID-19 Vaccine AstraZeneca	12296	93.4	0.55 (0.46, 0.65)
	BNT162b2	24937	97.1	0.52 (0.46, 0.68)



All three methods showed reductions in transmission for vaccination 21–35 days before a positive test

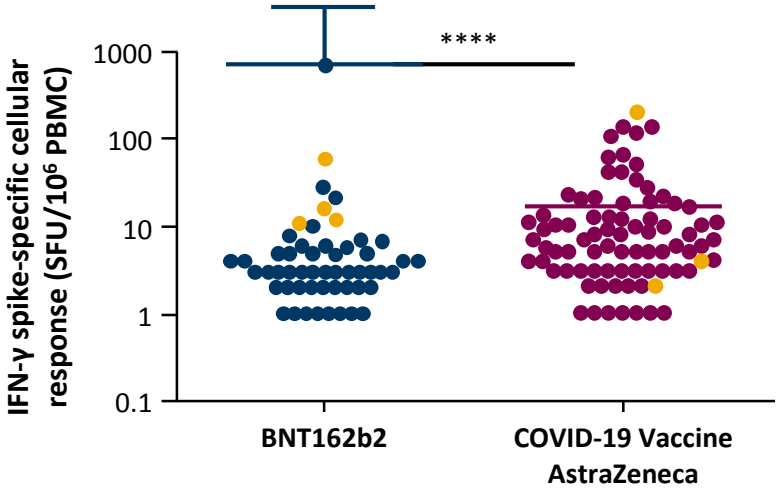
These results lend confidence to the overall conclusion that **vaccination reduces transmission**

[a]Multivariable logistic regression and matched case control and stratified cohort designs by age; [b]the N column is the sample size, except for the matched case control, which is the number of matched secondary cases; [c]the proportion of all available data that could be used in the model (either matched, or having usable strata)
CI = confidence interval; OR = odds ratio
Harris RJ, et al. Preprint published online. 2021

阿斯利康COVID-19 疫苗誘導T細胞反應比 BNT162b2 更大

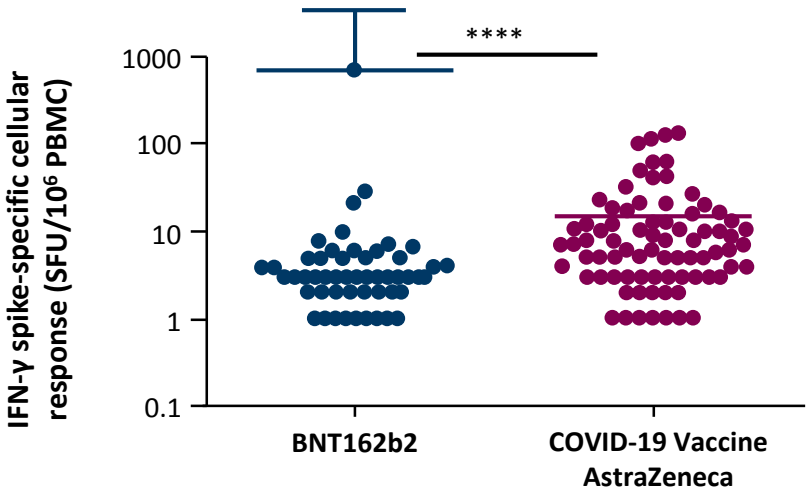
S-specific cellular responses after the first dose

Whole cohort



Cellular responses were detectable in 12.3% and 30.7% of participants at 5 weeks after the first dose of BNT162b2 and COVID-19 Vaccine AstraZeneca, respectively

Participants without previous SARS-CoV-2 infection



The magnitude of cellular responses was three-fold greater in those who received COVID-19 Vaccine AstraZeneca compared with those who received BNT162b2, regardless of previous SARS-CoV-2 infection (P<0.0001)

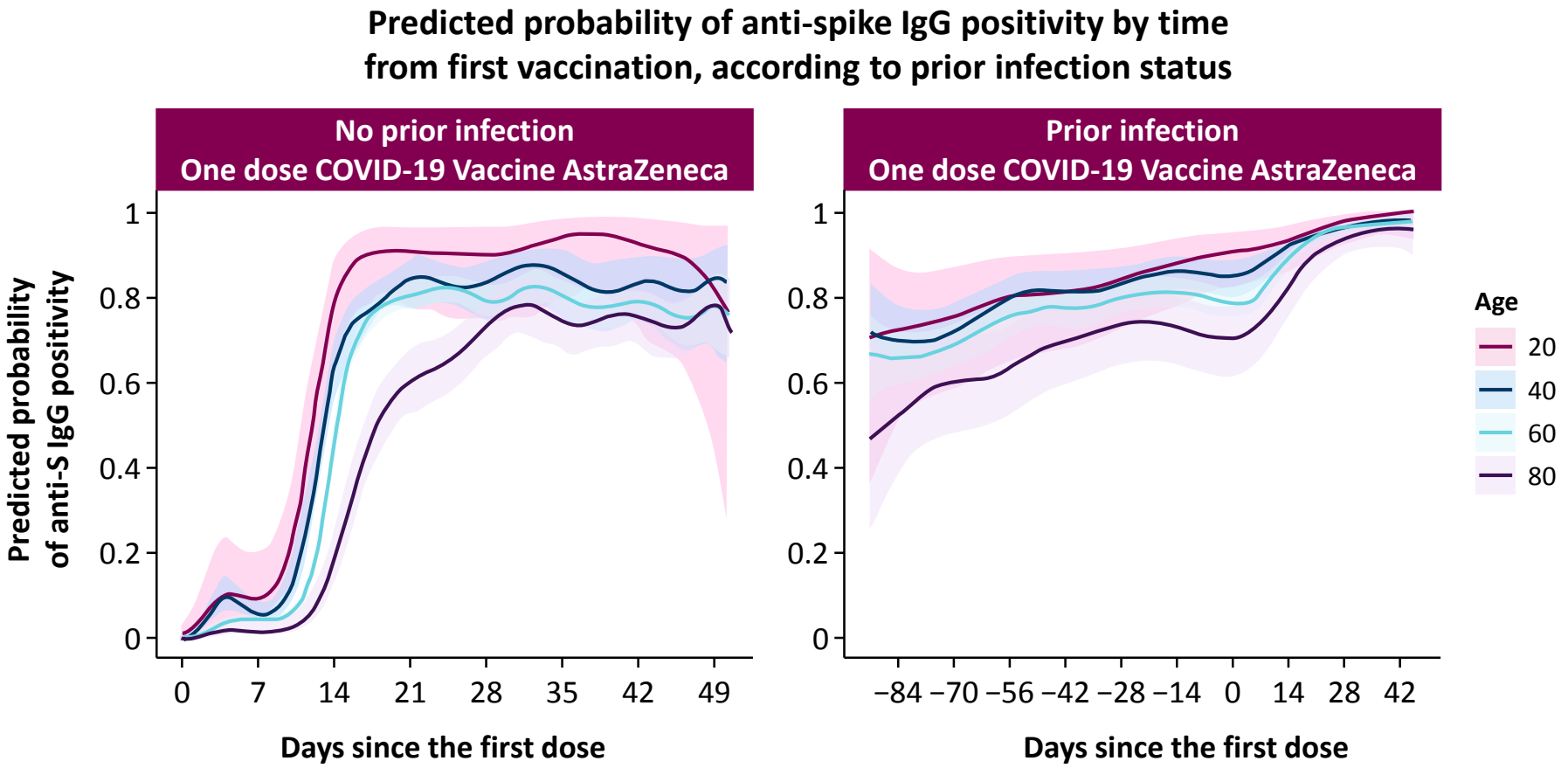
Participants with previous SARS-CoV-2 infection COVID-19 Vaccine AstraZeneca BNT162b2

*P<0.5; ****P<0.0001

IFN = interferon; PBMC = peripheral blood mononuclear cell; S = spike; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SFU = spot-forming unit

Parry H, et al. Preprint published online. Lancet 2021

在沒有感染證據的參加者接種疫苗抗S Abs的估計百分比隨著時間而增加且因年齡而異



- **Older participants had lower seropositivity rates than younger participants after the first dose of either vaccine**
- There was no evidence of Ab level decline following first dose of COVID-19 Vaccine AstraZeneca in individuals aged >20 years

Ab = antibody; IgG = immunoglobulin G; S = spike

Wei J, et al. Preprint published online. medRxiv 2021

關於傳播和免疫反應
現實世界有效性獨立的研究

Scotland transmission study[1]

Vaccination of HCWs was **associated with a substantial reduction in COVID-19 cases in their household members** (30% and 54% lower risk of documented cases after the first and the second dose, respectively)

UK transmission study[2]

Reduction in the odds of new PCR-positive cases afforded **by vaccination was similar to that provided by natural immunity** and the results highlighted the **potential for limited ongoing transmission** in vaccinated individuals

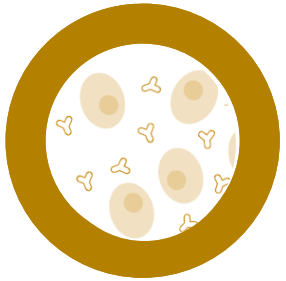
England transmission study[3]

Transmission was reduced by 40–50% in households in which the index case was vaccinated ≥21 days before testing positive compared with those not vaccinated
A reduction in transmission **was observed from 14 days** after vaccination

Public Health England study[4]

Cellular immune responses were **stronger** in those who received **COVID-19 Vaccine AstraZeneca** compared with BNT162b2

UK study[5]



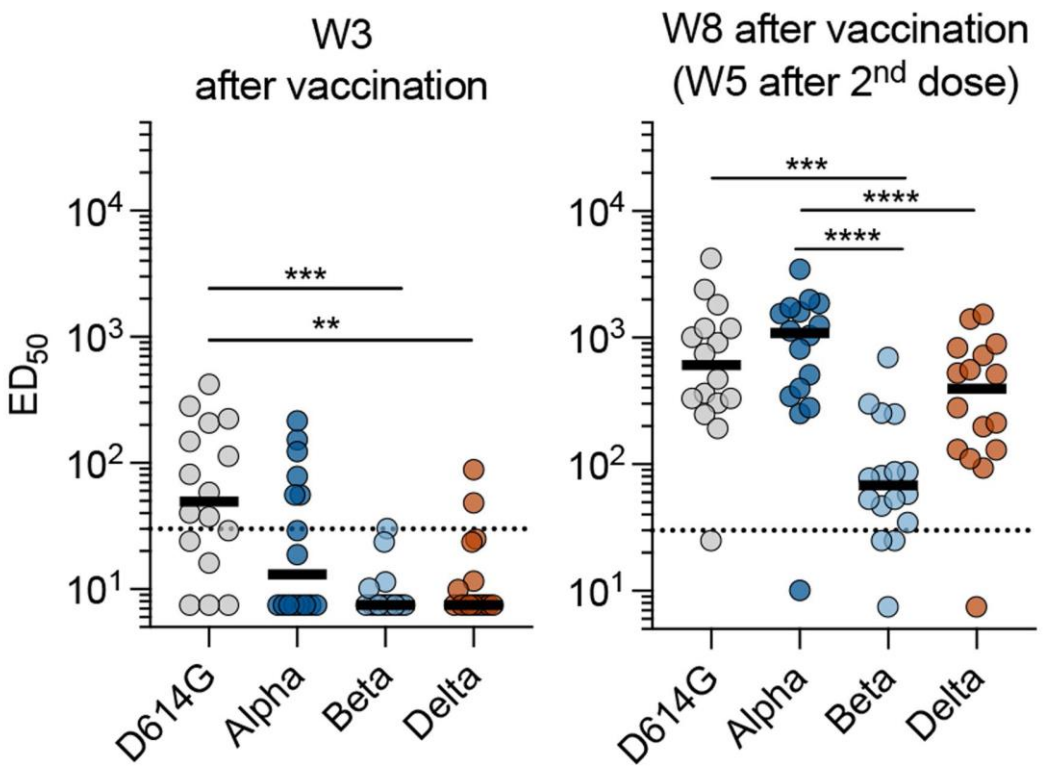
Antibody levels in those who received one dose of COVID-19 Vaccine AstraZeneca **varied by prior infection status, age and sex**
Without prior infection, **seroconversion rates and antibody levels after a single dose were lower in those >60 years** than in younger individuals

COVID-19 = coronavirus disease 2019; HCW = healthcare worker; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

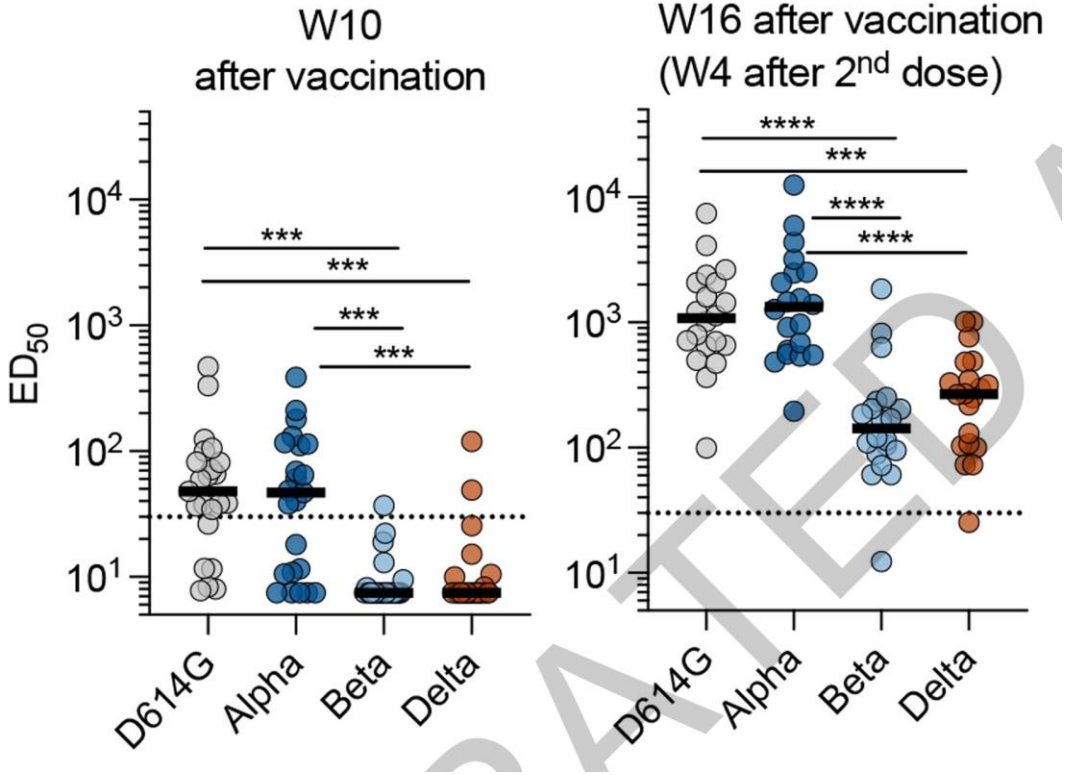
1. Shah ASV, et al. Preprint published online. medRxiv 2021; 2. Pritchard E, et al. Preprint published online. medRxiv 2021; 3. Harris RJ, et al. Preprint published online. 2021;
4. Parry H, et al. Preprint published online. Lancet 2021; 5. Wei J, et al. Preprint published online. medRxiv 2021

Sensitivity of SARS-CoV-2 variants to sera from vaccine recipients

Pfizer vaccinated recipients



AstraZeneca vaccinated recipients

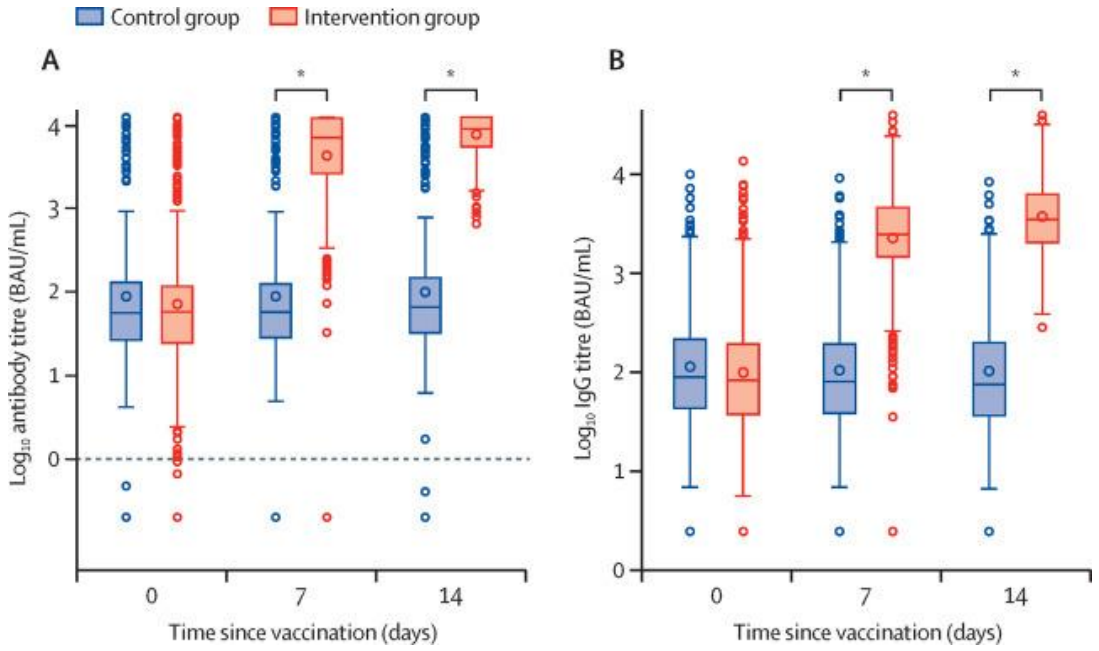


Nature. 2021 Jul 8. doi: 10.1038/s41586-021-03777-9.

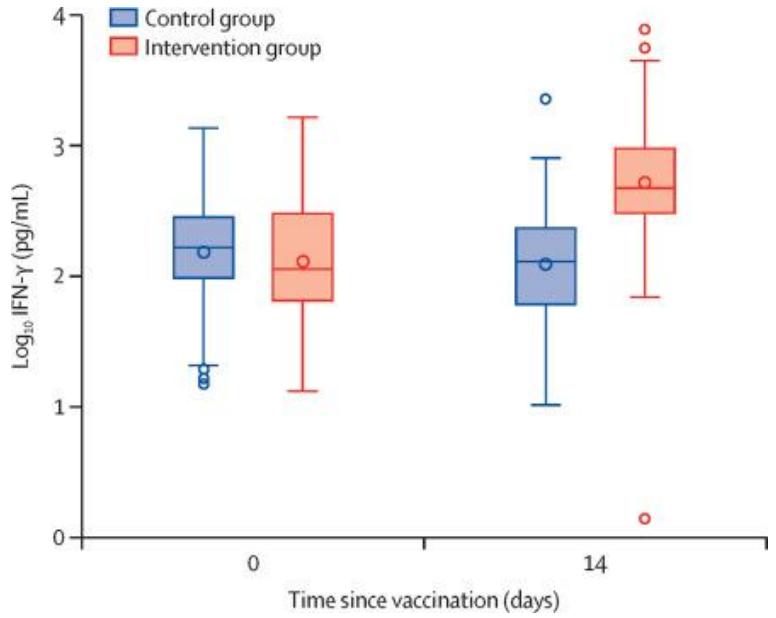
Heterologous vaccine regimens against COVID-19

BNT162b2 given as a second dose in individuals prime vaccinated with ChAdOx1-S induced a robust immune response, with an acceptable and manageable reactogenicity profile

Antibody titres



IFN-γ concentrations



Lancet 2021; 398: 121–30

安全概况

英國數據

Public Health England(PHE)

Medicines and Healthcare Products Regulatory Agency (MHRA)

REUTERS FACT CHECK MARCH 13, 2021 / 2:50 AM / UPDATED 3 MONTHS AGO

Fact Check-Deaths reported under UK 'Yellow Card' scheme aren't confirmed to be linked to COVID-19 vaccination

By Reuters Fact Check 4 MIN READ

[2021.3.13 Reuters報導]

英國藥品和醫療產品監管署(Medicines and Healthcare Products Ragulatory Agency, MHRA)收到456例接種疫苗後的死亡案例

- 212例接種Pfizer/BNT疫苗
- 244例接種AZ疫苗

MHRA已經對這些接種報告進行調查，迄今為止未發現因接種疫苗而導致死亡的案例。

"456 U.K. deaths so far immediately after having 'vaccines'", the posts read. "MHRA has received 212 UK reports of suspected ADRs to the Pfizer/BioNTech vaccine in which the patient died shortly after vaccination, 244 reports for the Oxford University/AstraZeneca vaccine."

One role of the UK's Medicines and Healthcare products Regulatory Agency (MHRA) is to monitor vaccine safety by receiving reports of suspected side effects.

Any health professional or member of the public can report suspected side effects through the Yellow Card scheme.

As the post correctly notes, there has been more than 400 reports of suspected adverse reactions to the Pfizer-BioNTech and Oxford University-AstraZeneca vaccines in which the patient died shortly after vaccination (here).

For the purpose of monitoring, these reports (here) (here) document all the suspected adverse reactions that have happened after vaccination.

It is not, however, a list of those who died because of the vaccine.

"The nature of Yellow Card reporting means that reported events are not always proven side effects", the MHRA says. "Some events may have happened anyway, regardless of vaccination."

Reference：https://www.reuters.com/article/factcheck-vaccine-statistics-idUSL1N2LA28C

英國Yellow Card Report 2020.12.9-2021.6.9

Table 1: Number of people who have received the first dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 9 June 2021.

Country	Number of doses
England	34,148,547
Wales	2,195,485
Northern Ireland	1,101,629
Scotland	3,422,431

Table 2: Number of people who have received the second dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 9 June 2021.

Country	Number of doses
England	24,461,363
Wales	1,314,368
Northern Ireland	736,190
Scotland	2,345,181

As of 9 June, an estimated 15.6 million first doses of the Pfizer/BioNTech vaccine and 24.6 million first doses of the COVID-19 Vaccine AstraZeneca had been administered, and around 10.8 million and 17.7 million second doses of the Pfizer/BioNTech vaccine and COVID-19 Vaccine AstraZeneca respectively. An approximate 0.56 million first doses of the COVID-19 Vaccine Moderna have also now been administered.

第一劑

AZ：大約 24,600,000 劑

Pfizer：大約 15,600,000 劑

Moderna：大約 560,000 劑

第二劑

AZ：大約 17,700,000 劑

Pfizer：大約 10,800,000 劑

The MHRA has received 421 UK reports of suspected ADRs to the Pfizer/BioNTech vaccine in which the patient died shortly after vaccination, 885 reports for the COVID-19 Vaccine AstraZeneca, four for the COVID-19 Vaccine Moderna and 22 where the brand of vaccine was unspecified. The majority of these reports were in elderly people or people with underlying illness. Usage of the COVID-19 Vaccine AstraZeneca has increased rapidly and as such, so has reporting of fatal events with a temporal association with vaccination however, this does not indicate a link between vaccination and the fatalities reported. Review of individual reports and patterns of reporting does not suggest the vaccine played a role in the death.

接種後死亡案例

AZ：885人，死亡率: 0.002%(接種：約4,230萬人次)

Pfizer：421人，死亡率: 0.001% (接種：約2,640萬人次)

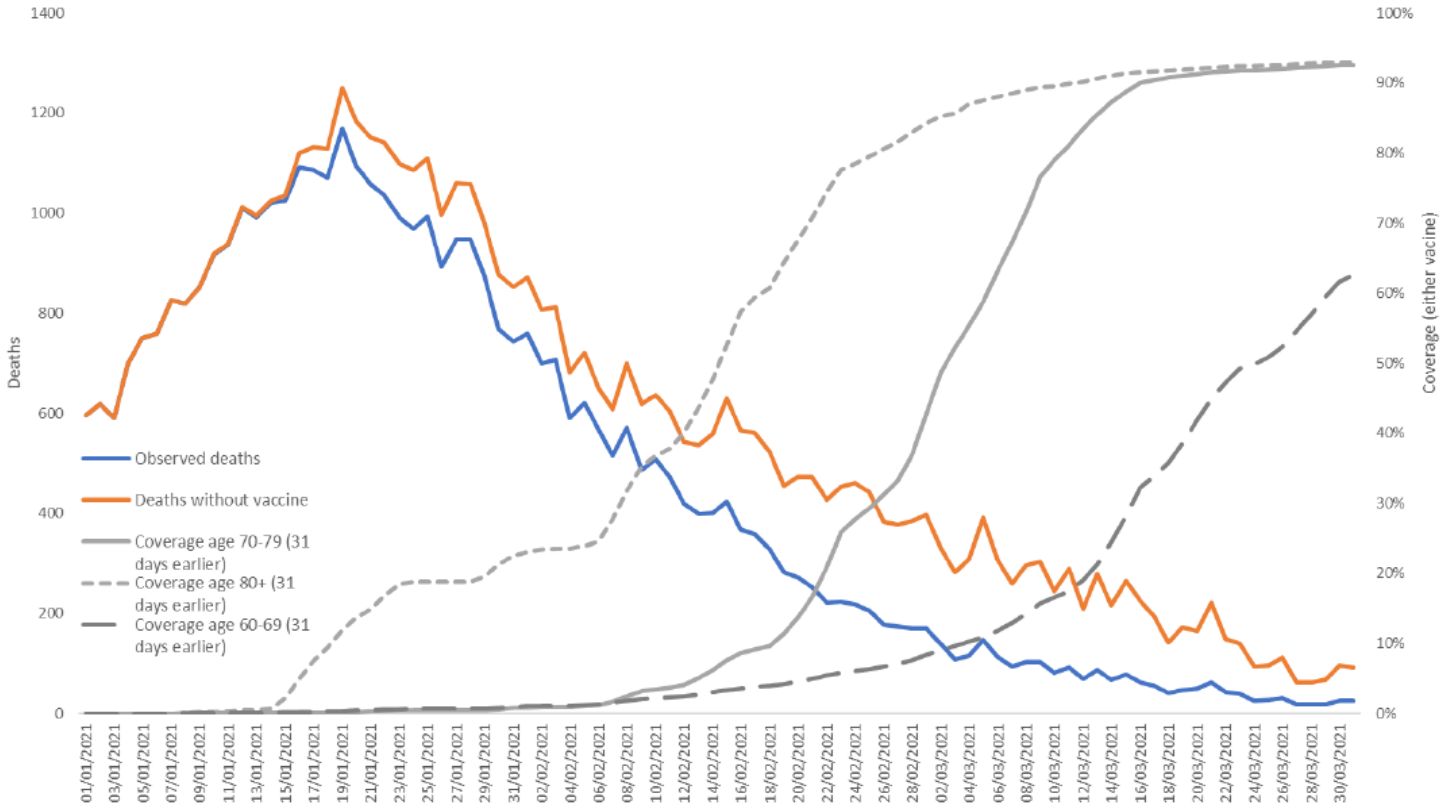
Moderna：4人，死亡率: 0.0007% (接種：約56萬人次)

Reference：https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/994726/20210616_Coronavirus_vaccine_-_summary_of_Yellow_Card_reporting__v2_-_clean.pdf

Public Health England(PHE)：英國COVID-19疫苗接種對死亡率的影響 2020.12 - 2021.03

Impact of COVID-19 vaccines on mortality in England: December 2020 to March 2021

Figure 1: Daily Observed COVID-19 deaths aged 60+ and expected numbers in the absence of vaccination using the back calculation method



根據英國PHE估計(疫苗開始接種直到2021 年 3 月底)：

- 預防了 9,100位 80 歲以上族群死亡
- 預防了 1,200位 70 至 79 歲族群死亡
- 預防了 100位60 至 69 歲族群死亡

總共避免了 10,400 位 60 歲或以上人的死亡。

因COVID-19導致死亡定義：SARS-CoV-2檢測陽性後28天內的任何死亡

Reference：https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/977249/PHE_COVID-19_vaccine_impact_on_mortality_March.pdf

Taiwan FDA: COVID-19 疫苗不良事件 (ADR)通報摘要報告 Updated to 2021/7/28

自 110 年 3 月 22 日起，COVID-19 疫苗接種計畫開始。截至 110 年 7 月 28 日止，全國共施打 COVID-19 疫苗總數為 **7,617,682** 劑，共接獲疫苗不良事件通報 3928 件，平均每千劑注射通報數約為 **0.5** 件

不良事件總體評估如下:

1. 接獲之疫苗不良事件通報案件中，大多數(**2199 件**)屬於「**非嚴重不良事件**」通報。主要通報症狀為發燒、肌肉痛、頭痛、發寒、接種部位紅腫痛、疲倦、嘔吐、皮膚紅疹等。
2. 另有 **1729 件**屬於「嚴重不良事件」通報，其中含 **530 件死亡通報案件**(280 位男性及 249 位女性，個案年齡介於 26 歲至 101 歲，70 歲以上個案占 78.5%，接種至死亡日距介於 0 至 58日間；另有 1 件為母親接種疫苗後當日以母乳哺餵女嬰，隔日發現嬰兒死亡之通報案例)及65 件危及生命通報案件。依現有通報資訊之不良事件症狀及歷程、既有疾病等資訊比對分析，暫未觀察到疫苗安全疑慮，相關資訊持續追蹤調查中。
3. 上述通報案件中包含**疑似過敏性反應(anaphylaxis) 17 件**、心律不整 10 件、急性心肌梗塞 59件、血管炎 4 件、顏面神經麻痺 23 件、癲癇 12 件、心肌炎 5 件、特發性血小板減少紫斑症23 件、腦血管中風 136 件、橫斷性脊髓炎 1 件、急性瀰漫性腦脊髓炎 2 件、**格林-巴利症候群(Guillain–Barre´ Syndrome) 6 件**、脊髓炎 1 件、**血栓併血小板低下症候群(thrombosis withthrombocytopenia syndrome) 13 件**、視神經炎 2 件、急性胰臟炎 3 件、橫紋肌溶解症 4 件、急性肝損傷 2 件、多形性紅斑 2 件、關節炎 2 件、流產 6 件、死產 4 件、視網膜靜脈阻塞 4 件、視網膜動脈阻塞 2 件、深層靜脈栓塞 23 件、肺栓塞 27 件、腦靜脈竇栓塞 5 件、其他血栓相關疾患(other thrombotic disorder) 7 件(通報症狀包含左腎梗塞、缺血性腸道疾病、肝門靜脈血栓及腸骨靜脈、腸道血管靜脈栓塞、上腸繫膜動脈栓塞、腎臟靜脈栓塞及脾梗塞)，皆為接種疫苗後曾被零星報告過的不良事件，將持續進行監測。

綜合目前疫苗不良事件通報資料之評估結果，**尚未觀察到須採取相關措施之安全疑慮**。衛 生福利部食品藥物管理署與全國藥物不良反應通報中心將持續針對疫苗不良事件通報進行安全 訊號偵測，以積極執行藥品安全監視機制，保障民眾之用藥安全。

Source: FDA (https://www.fda.gov.tw/TC/siteList.aspx?sid=1571)

台灣疾病管制署COVID-19疫苗日報表 2021/6/28

年齡	AZ接種人次[1]	死亡通報[1]	接種後死亡率* (%)	全因死亡背景值** (%)
Age	No. of Persons Vaccinated	Reported Deaths	Post-VC Mortality Rate	Expected Mortality Rate
<75	1,314,438	54	0.004%	0.35%
>75	524,886	186	0.035%	6.62%
總數 Total	1,839,324	240	0.013%	6.97%

Source:

1. Taiwan CDC COVID-19疫苗日報表 https://www.cdc.gov.tw/Category/Page/9jFXNbCe-sFK9EImRRi2Og (Access on 2021/6/28)
2. 內政部主計處 死亡人數 (Age >75):https://statis.moi.gov.tw/micst/stmain.jsp?sys=220&ym=9700&ymt=10900&kind=21&type=1&funid=c0120202&cycle=4&outmode=0&compmode=0&outkind=1&fld0=1&codspc0=0,1,85,1,91,1,97,1,103,1,109,1,115,1,121,1,&rdm=ireedypr ；內政部主計處 死亡人數 (Age <75) https://statis.moi.gov.tw/micst/stmain.jsp?sys=220&ym=9700&ymt=10900&kind=21&type=1&funid=c0120202&cycle=4&outmode=0&compmode=0&outkind=1&fld0=1&codspc0=0,2,7,1,13,1,19,1,25,1,31,1,37,1,43,1,49,1,55,1,61,1,67,1,73,1,79,1,85,1,&rdm=mdmWyetq (Access on 2021/6/24)
3. 內政部主計處 人口數年齡別 https://statis.moi.gov.tw/micst/stmain.jsp?sys=220&ym=10905&ymt=11005&kind=21&type=1&funid=c0110203&cycle=41&outmode=0&compmode=0&outkind=1&fldspc=0,1,76,26,&cod00=1&cod10=1&rdm=Kmfemmnj (Access on 2021/6/24)

*接種後死亡率 = 死亡通報/AZ接種人次
**全因死亡背景值 = 死亡人數(Ref.2)/人口數年齡別(Ref.3)- 如下

全因死亡背景值計算：
2020 Age >75 Deaths / 2020 Age >75 Population
= 95,322 / 1,439,127 = 6.62 %

2020 Age <75 Deaths / 2020 Age <75 Population
= 77,830 / 22,122,109 = 0.35%

COVID-19 疫苗接種後不良事件通報

(通報資料截止點: 110/8/5 16:00)

疫苗廠牌		疫苗接種量(劑)	疫苗接種後不良事件	疫苗接種後非嚴重不良事件[a]	疑似疫苗接種後嚴重不良事件			
					小計	死亡	疑似嚴重過敏反應[b]	其他疑似嚴重不良事件[c]
總計	新增	256,777	100	47	53	14	2	37
	累計	8,875,048	4,723[f]	2,621	2,102[f]	578[e]	19	1,505
AstraZeneca	新增	247,085	81	39	42	9[d]	2	31
	累計	5,824,943	3,903	2,271	1,632	486	14	1,132
Moderna	新增	9,692	19	8	11	5[d]	0	6
	累計	3,050,105	820	350	470	92	5	373

COVID-19 疫苗

- 來自大型 RCT 的數據進一步證實了其有效性和安全性
- 已知較長的間隔會導致更好的免疫反應
- 真實數據表明保護水準很高
- 數據在研究中一致;證明老年人住院保護水準高（≥70歲）
- 數據顯示傳播減少的可能性
- COVID-19疫苗的益處遠遠大於風險

Discussion

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