Vaccine effectiveness and impact – measurement using linked data

Australian Vaccinology Course
28 August 2025

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Outline

- Why do we measure vaccine effectiveness?
- How can we use data-linkage to do this efficiently in Australia?
- Examples of how this has been applied for COVID-19

Why do we measure vaccine effectiveness?

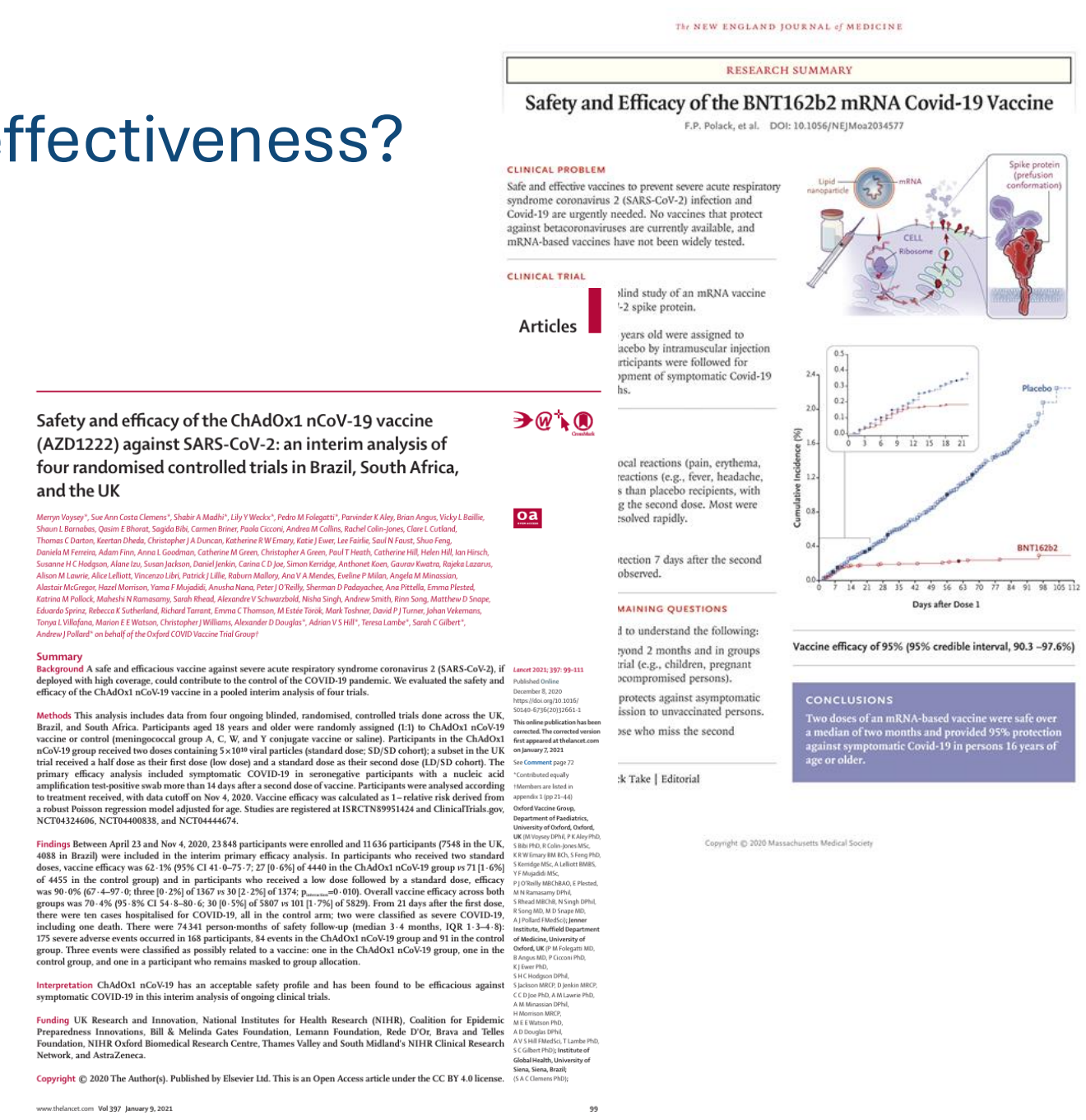
Clinical trials provide evidence on efficacy and safety of vaccines to enable vaccine registration

BUT

- may exclude certain populations
- lack power for severe disease endpoints
- insufficient duration of follow-up
- pathogen (antigen) may evolve
- not designed to compare different vaccines

Could design new trials to address these issues but $$$$

Vaccine effectiveness which measures performance of vaccine in the field can be used



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

F.P. Polack, et al. DOI: 10.1056/NEJMoa2034577

CLINICAL PROBLEM

Safe and effective vaccines to prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 are urgently needed. No vaccines that protect against betacoronaviruses are currently available, and mRNA-based vaccines have not been widely tested.

CLINICAL TRIAL

lind study of an mRNA vaccine
-2 spike protein.

years old were assigned to
lacebo by intramuscular injection
rticipants were followed for
opment of symptomatic Covid-19
hs.

ocal reactions (pain, erythema,
reactions (e.g., fever, headache,
s than placebo recipients, with
g the second dose. Most were
esolved rapidly.

tection 7 days after the second
observed.

MAINING QUESTIONS

d to understand the following:
yond 2 months and in groups
rial (e.g., children, pregnant
ocompromised persons).
protects against asymptomatic
ission to unvaccinated persons.
ose who miss the second

k Take | Editorial

Lipid nanoparticle
mRNA
Spike protein (prefusion conformation)
CELL
Ribosome

Cumulative Incidence (%)
Placebo
BNT162b2
Days after Dose 1

Vaccine efficacy of 95% (95% credible interval, 90.3 –97.6%)

CONCLUSIONS

Two doses of an mRNA-based vaccine were safe over a median of two months and provided 95% protection against symptomatic Covid-19 in persons 16 years of age or older.

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Articles

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

Merryn Voysey*, Sue Ann Costa Clemens*, Shabir A Madhi*, Lily Y Weckx*, Pedro M Folegatti*, Parvinder K Aley, Brian Angus, Vicky L Baillie, Shaun L Barnabas, Qasim E Bhorat, Sagida Bibi, Carmen Briner, Paola Cicconi, Andrea M Collins, Rachel Colin-Jones, Clare L Cutland, Thomas C Darton, Keertan Dheda, Christopher J A Duncan, Katherine R W Emary, Katie J Ewer, Lee Fairlie, Saul N Faust, Shuo Feng, Daniela M Ferreira, Adam Finn, Anna L Goodman, Catherine M Green, Christopher A Green, Paul T Heath, Catherine Hill, Helen Hill, Ian Hirsch, Susanne H C Hodgson, Alane Izu, Susan Jackson, Daniel Jenkin, Carina C D Joe, Simon Kerridge, Anthonet Koen, Gaurav Kwatra, Rajeka Lazarus, Alison M Lawrie, Alice Lelliott, Vincenzo Libri, Patrick J Lillie, Raburn Mallory, Ana V A Mendes, Eveline P Milan, Angela M Minassian, Alastair McGregor, Hazel Morrison, Yama F Mujadidi, Anusha Nana, Peter J O'Reilly, Sherman D Padayachee, Ana Pittella, Emma Plested, Katrina M Pollock, Maheshi N Ramasamy, Sarah Rhead, Alexandre V Schwarzbold, Nisha Singh, Andrew Smith, Rinn Song, Matthew D Snape, Eduardo Sprinz, Rebecca K Sutherland, Richard Tarrant, Emma C Thomson, M Estée Török, Mark Toshner, David P J Turner, Johan Vekemans, Tonya L Villafana, Marion E E Watson, Christopher J Williams, Alexander D Douglas*, Adrian V S Hill*, Teresa Lambe*, Sarah C Gilbert*, Andrew J Pollard* on behalf of the Oxford COVID Vaccine Trial Group†

Summary

Background A safe and efficacious vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), if deployed with high coverage, could contribute to the control of the COVID-19 pandemic. We evaluated the safety and efficacy of the ChAdOx1 nCoV-19 vaccine in a pooled interim analysis of four trials.

Methods This analysis includes data from four ongoing blinded, randomised, controlled trials done across the UK, Brazil, and South Africa. Participants aged 18 years and older were randomly assigned (1:1) to ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugate vaccine or saline). Participants in the ChAdOx1 nCoV-19 group received two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort); a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort). The primary efficacy analysis included symptomatic COVID-19 in seronegative participants with a nucleic acid amplification test-positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to treatment received, with data cutoff on Nov 4, 2020. Vaccine efficacy was calculated as 1 – relative risk derived from a robust Poisson regression model adjusted for age. Studies are registered at ISRCTN89951424 and ClinicalTrials.gov, NCT04324606, NCT04400838, and NCT04444674.

Findings Between April 23 and Nov 4, 2020, 23 848 participants were enrolled and 11 636 participants (7548 in the UK, 4088 in Brazil) were included in the interim primary efficacy analysis. In participants who received two standard doses, vaccine efficacy was 62·1% (95% CI 41·0–75·7; 27 [0·6%] of 4440 in the ChAdOx1 nCoV-19 group *vs* 71 [1·6%] of 4455 in the control group) and in participants who received a low dose followed by a standard dose, efficacy was 90·0% (67·4–97·0; three [0·2%] of 1367 *vs* 30 [2·2%] of 1374; $p_{\text{heterogeneity}}$=0·010). Overall vaccine efficacy across both groups was 70·4% (95·8% CI 54·8–80·6; 30 [0·5%] of 5807 *vs* 101 [1·7%] of 5829). From 21 days after the first dose, there were ten cases hospitalised for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death. There were 74 341 person-months of safety follow-up (median 3·4 months, IQR 1·3–4·8): 175 severe adverse events occurred in 168 participants, 84 events in the ChAdOx1 nCoV-19 group and 91 in the control group. Three events were classified as possibly related to a vaccine: one in the ChAdOx1 nCoV-19 group, one in the control group, and one in a participant who remains masked to group allocation.

Interpretation ChAdOx1 nCoV-19 has an acceptable safety profile and has been found to be efficacious against symptomatic COVID-19 in this interim analysis of ongoing clinical trials.

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This online publication has been corrected. The corrected version first appeared at thelancet.com on January 7, 2021

See Comment page 72

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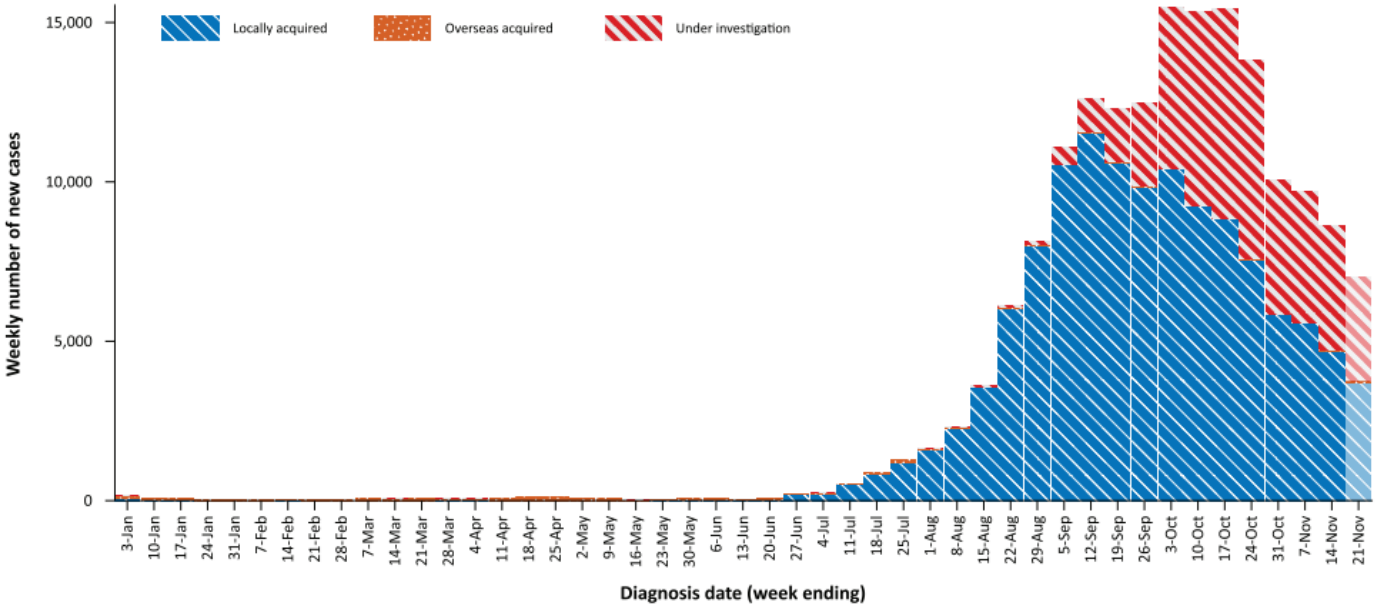
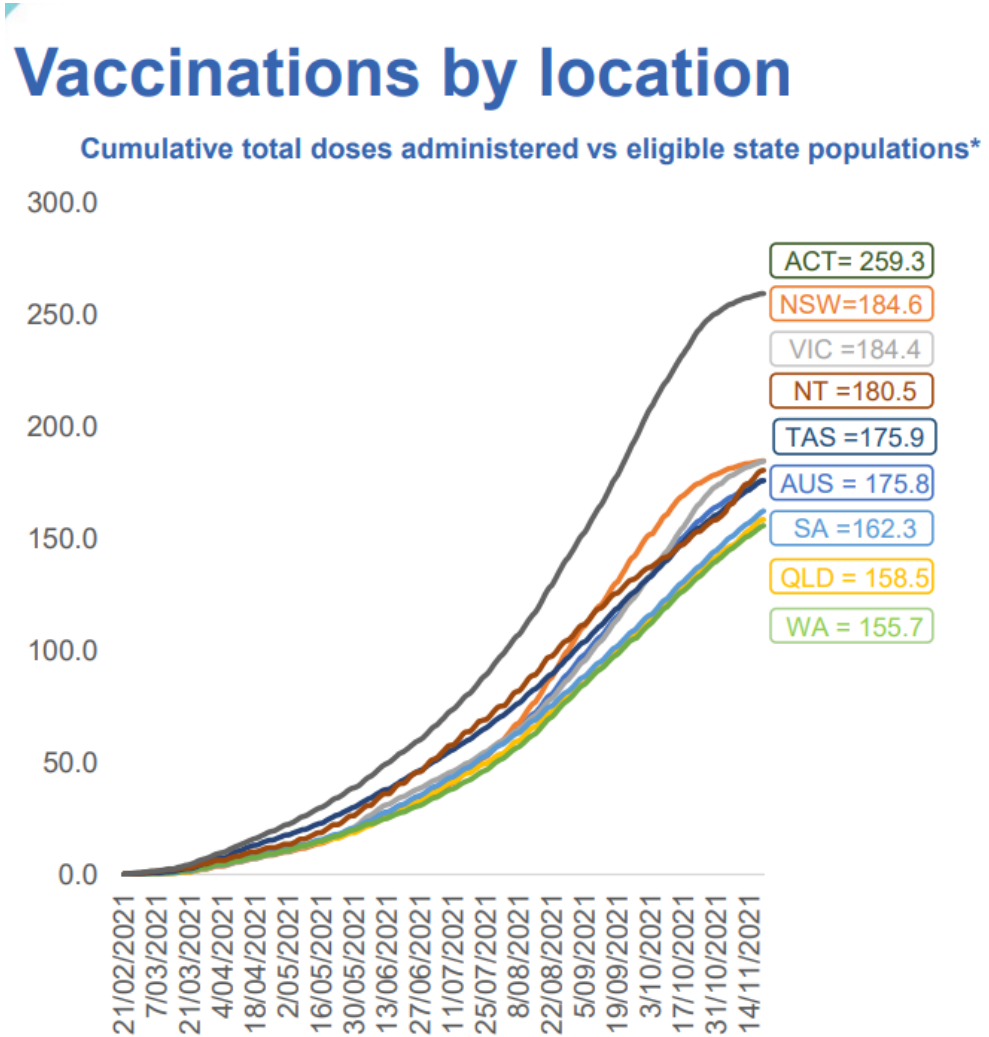
COVID-19 case rates compared to vaccine uptake during 2021*

Figure 1: COVID-19 notified cases by source of acquisition and diagnosis date, 28 December 2020 – 21 November 2021[a,b]



a Source: NINDSS, extract from 23 November 2021 for notifications to 21 November 2021.

b The lighter bar at the right represents the most recent reporting week and should be interpreted with caution as additional cases may be identified in the coming week that have a diagnosis date during this period.



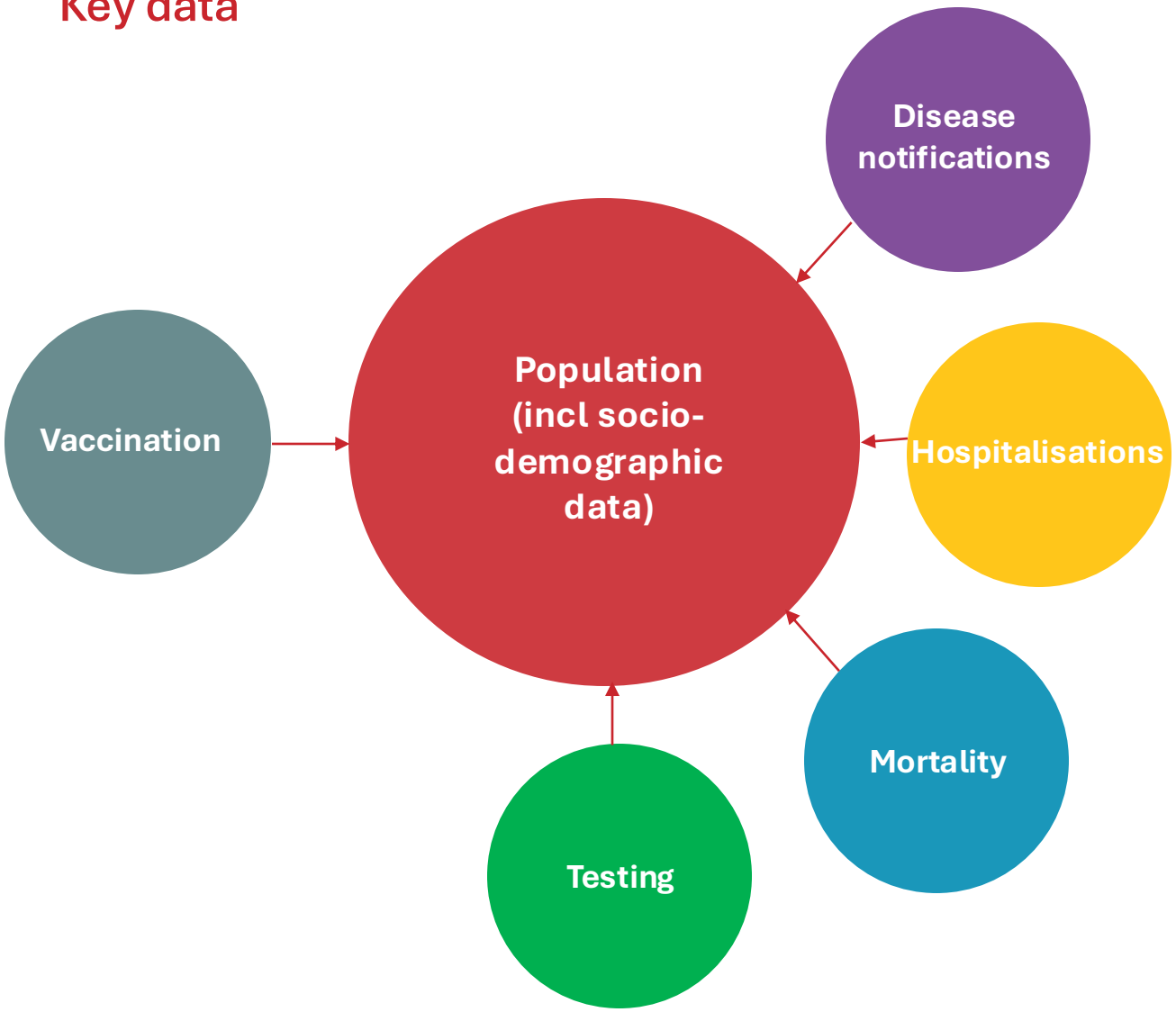
*To November 2021

Communicable Diseases Intelligence 2022 - COVID-19 Australia: Epidemiology Report 57 - Reporting period ending 16 January 2022 (health.gov.au)

COVID-19 vaccine rollout update – 31 January 2022 (health.gov.au)

Linked data required for vaccine effectiveness studies

Key data



Different epidemiological study designs enable estimates to be made with more limited data

Linkage is not necessary but can be more efficient and more generalisable

- Case-control studies
- e-Medical records

Data linkage process in Australia

Governance and ethics

- Data from different sources and custodians
- Does it require ethics

Data	Data custodian	Use
Hospital data	Health district; state health department	Provision of healthcare, statistics/reporting
Australian Immunisation Register	Commonwealth Department of Health and Aged Care	Governed by Australian Immunisation Register Act 2015; Recording of immunisation events, provision of healthcare, research

Practical process

Need a unique ID in each of the separate data sources

Number or combination of name, DoB, sex, number

For privacy protection, data linkage is typically conducted in a sequence

- Splitting
- Linking
- Integration
- Research

ACCOUNTABILITY IN RESEARCH
2025, VOL. 32, NO. 5, 741–761
HTTPS://DOI.ORG/10.1080/08989621.2025.2460521

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Is my project research? Determining which projects require review by a research ethics committee

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ABSTRACT

Background: Deciding which types of activities require an ethics review is a critical component of research regulation. Reviews conducted by research ethics committees consider the rights and safety of potential research participants, and occur as part of a wider set of governance reviews. However, to save time and resources, projects that do not raise ethical issues, or

ARTICLE HISTORY
Received 11 October 2024
Accepted 27 January 2025.

KEYWORDS
Ethics; governance; research; review; classification

Data linkage process in Australia

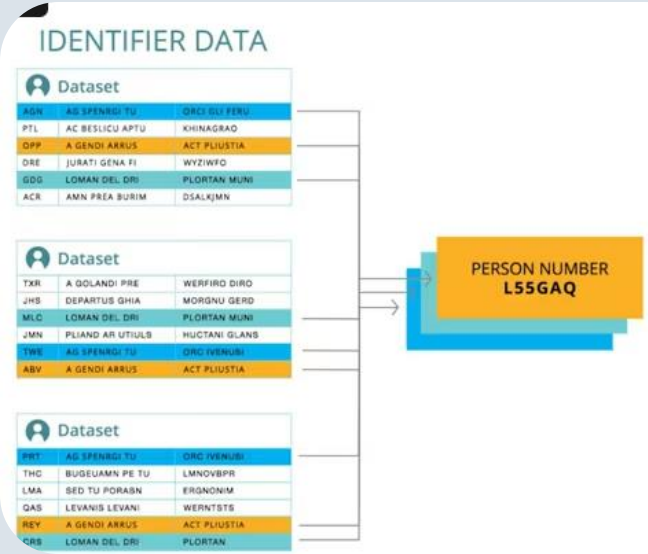
1. Splitting

2. Linking

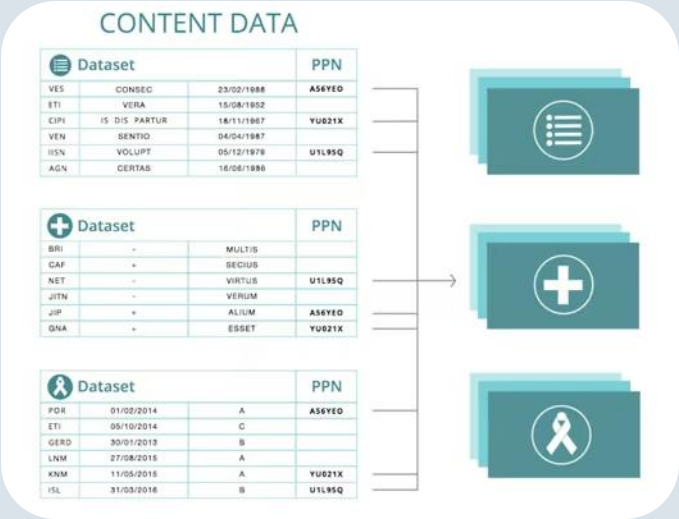
Probabilistic,

deterministic,

clerical review



3. Integration

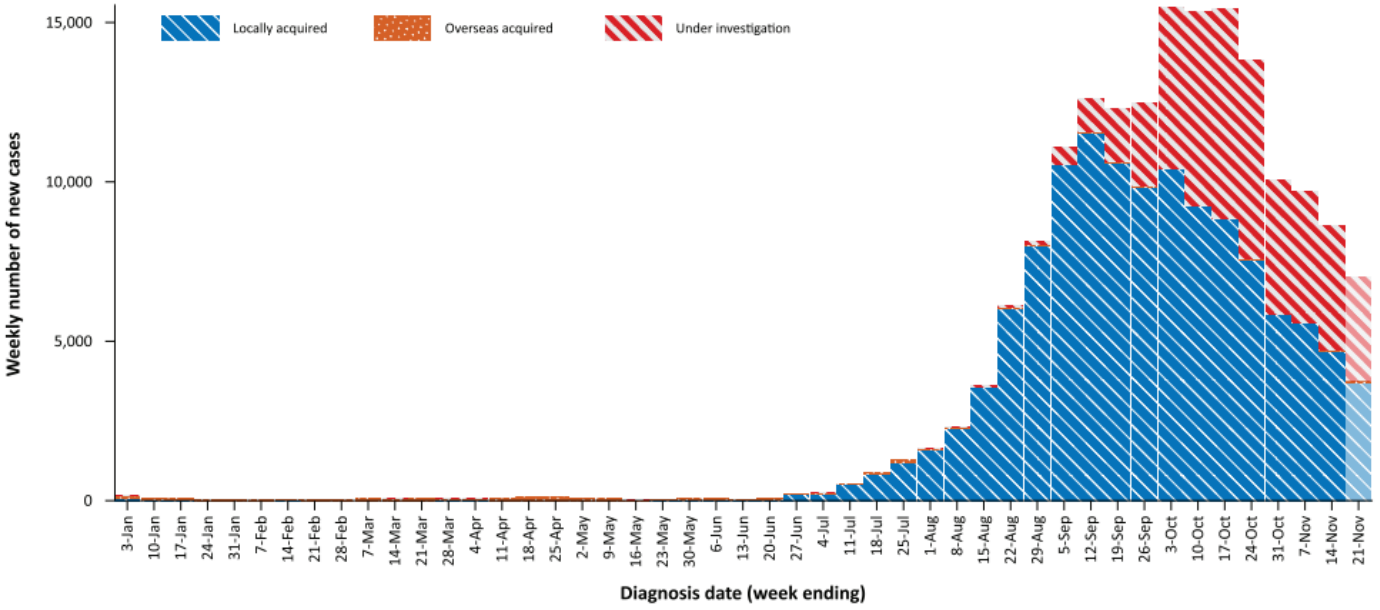


4. Research

NSW Centre for Health Record Linkage

COVID-19 case rates compared to vaccine uptake during 2021*

Figure 1: COVID-19 notified cases by source of acquisition and diagnosis date, 28 December 2020 – 21 November 2021[a,b]



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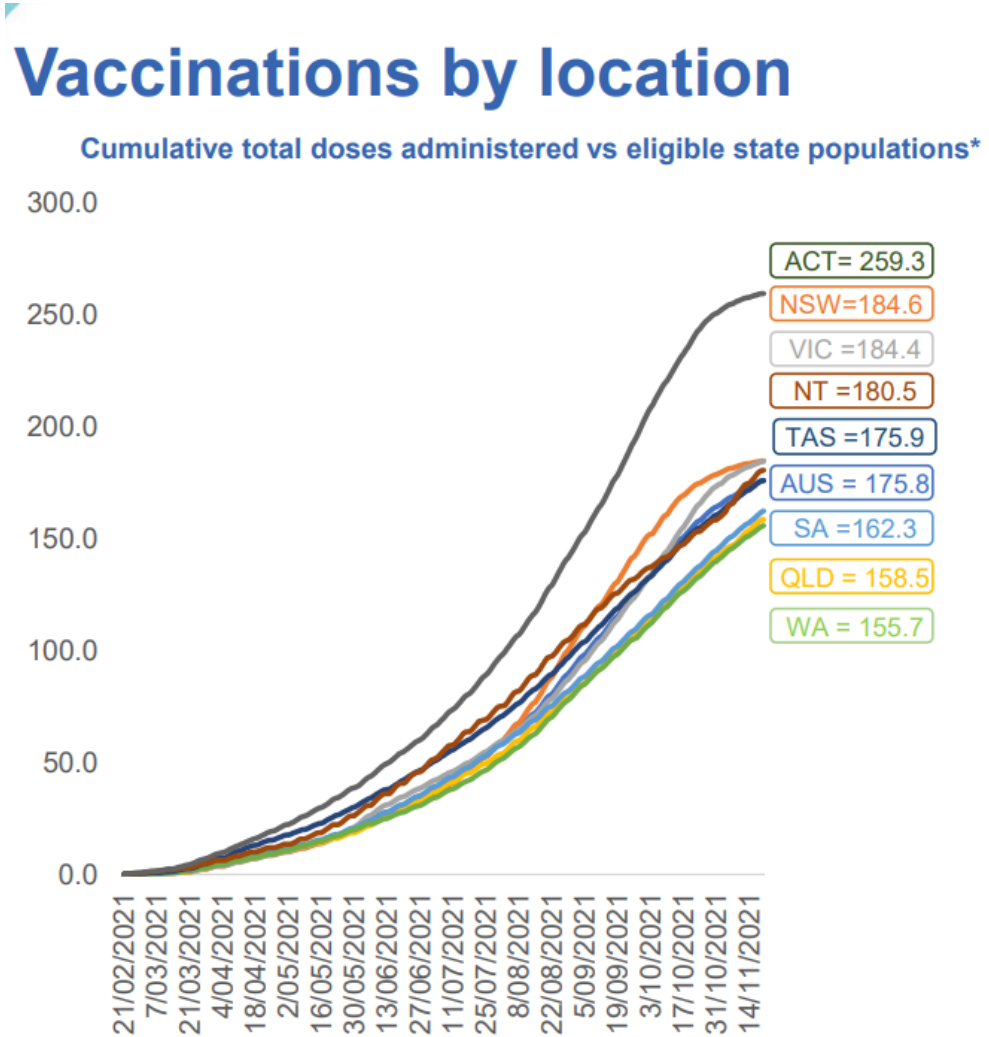

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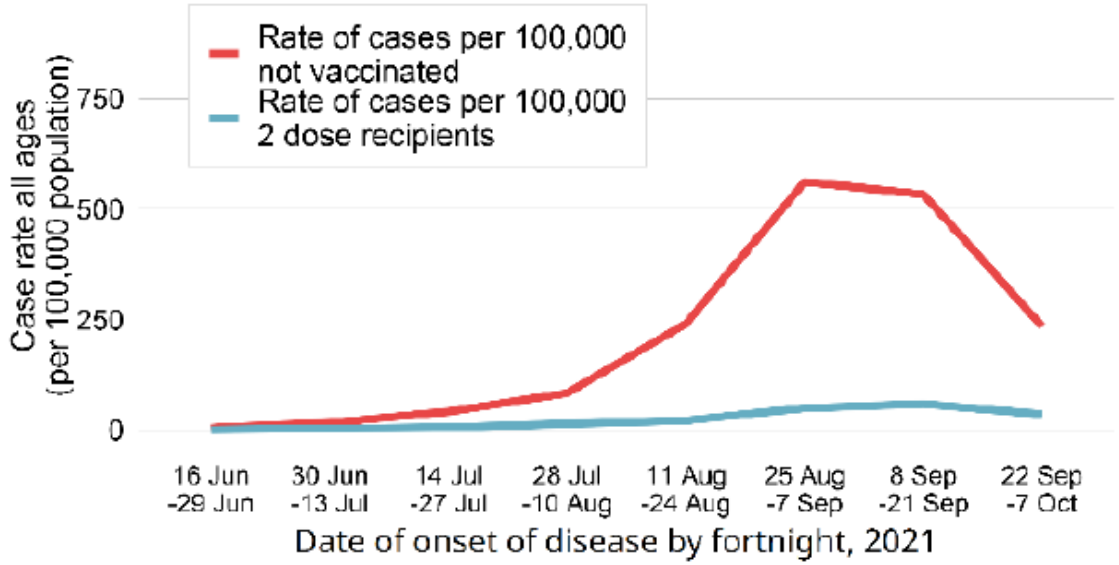
Communicable Diseases Intelligence 2022 - COVID-19 Australia: Epidemiology Report 57 - Reporting period ending 16 January 2022 (health.gov.au)

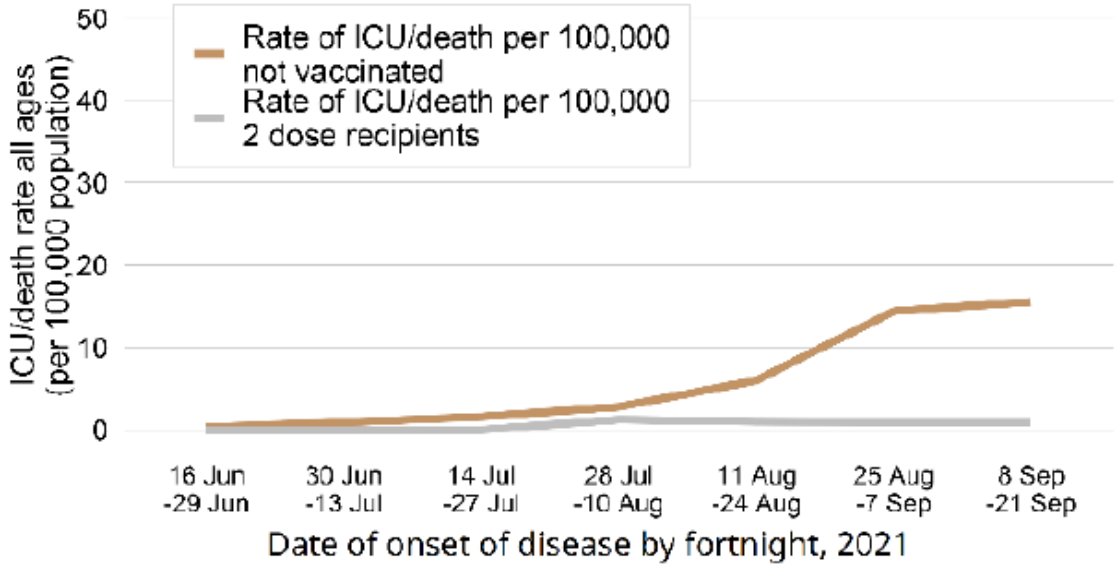
COVID-19 vaccine rollout update – 31 January 2022 (health.gov.au)

COVID-19 cases linked to vaccine register data in NSW, 2021

COVID-19 case rates by vaccination status

Rate of COVID-19 cases and ICU admissions/deaths amongst two dose vaccine recipients and the population who had not received a vaccine by fortnight†





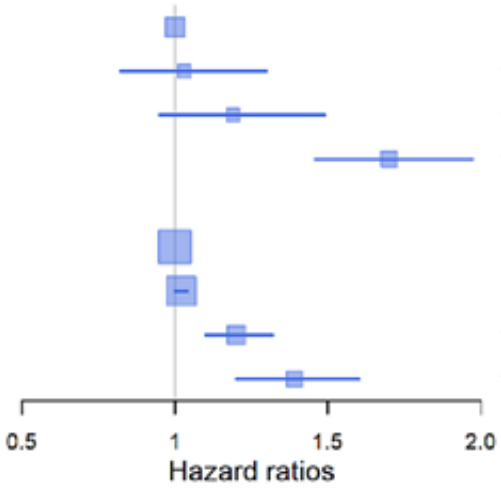
Notes: Population and cases restricted to 12 years and older resident in Greater Sydney.

† Cases with an unknown vaccination status are categorised as unvaccinated. Cases who received a single dose of vaccine, regardless of when it was given, or two doses but it was less than 14 days since receipt at the time of onset, are not included in the rate analyses.

https://www.health.nsw.gov.au/Infectious/covid-19/Documents/in-focus/covid-19-vaccination-case-surveillance-051121.pdf

Comparative effectiveness of different COVID-19 vaccines against COVID-19 notification, March – May 2022 in NSW

	Number of infections	%PCR confirmed	Person Years	Person-time rate (per 100-Person-Year) (95% CI)	Adjusted HRs (95% CI)	P value
Primary course; dose 2 14-63 days						
BNT162b2 mRNA	635	49%	1530	42 (36; 49)	Ref.	
mRNA-1273	84	45%	193	43 (28; 67)	1.03 (0.82-1.30)	0.77
ChAdOx-1 nCov-19	83	46%	185	45 (29; 69)	1.19 (0.95-1.49)	0.14
NVX-CoV2373	231	53%	410	56 (43; 73)	1.70 (1.46-1.97)	<0.001*
Booster; dose 3 14-63 days						
BNT162b2 mRNA	73,373	50%	122,731	60 (59; 61)	Ref.	
mRNA-1273	19,517	48%	31,083	63 (61; 64)	1.02 (1.00-1.04)	0.01
ChAdOx-1 nCov-19	503	51%	899	56 (47; 66)	1.20 (1.10-1.32)	<0.001*
NVX-CoV2373	187	58%	271	69 (53; 91)	1.39 (1.20-1.60)	<0.001*



Infection more likely →

Limitations of observational studies: insufficient power for hospitalisation outcomes, potential confounders

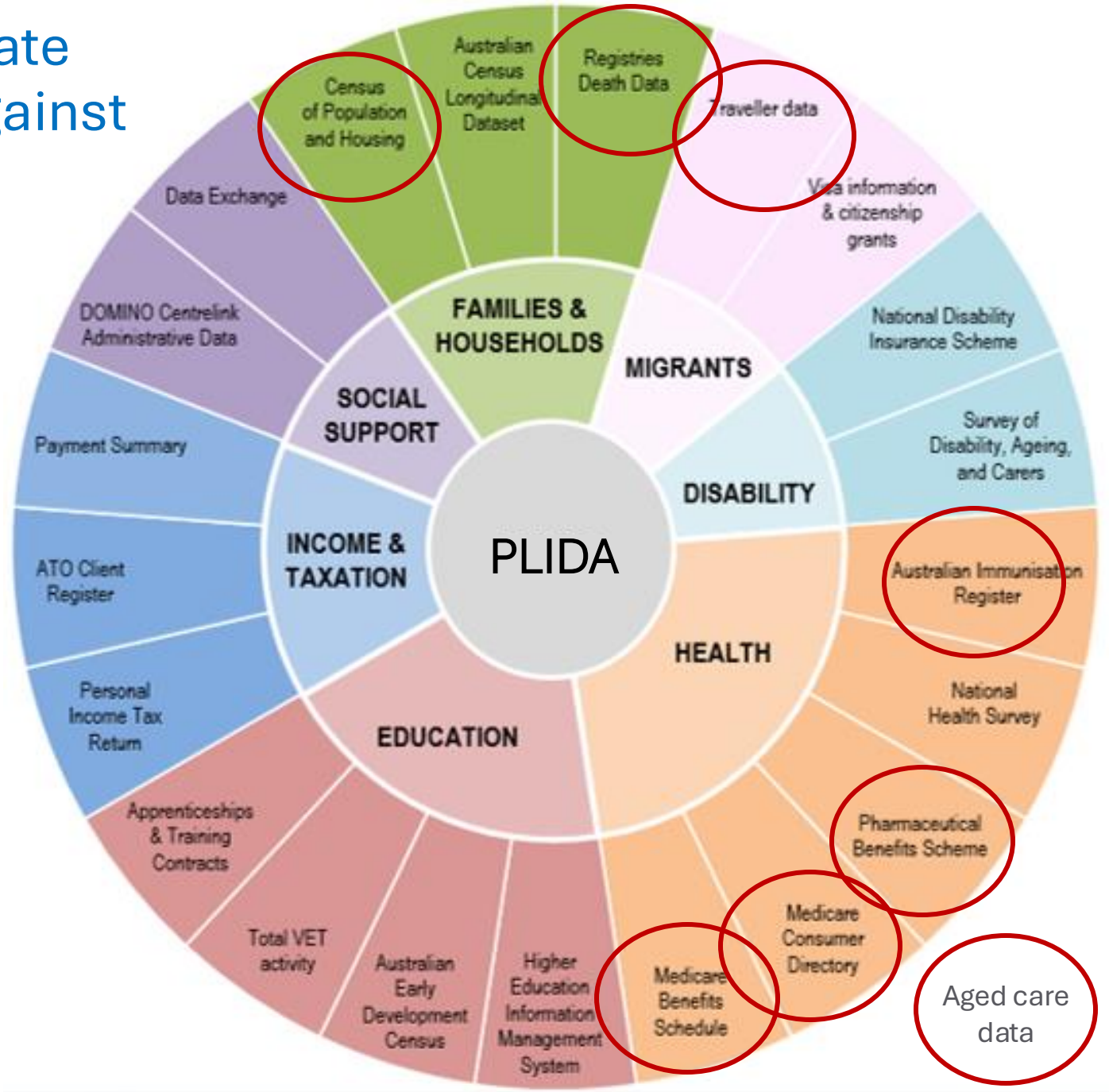
https://pubmed.ncbi.nlm.nih.gov/37524631/

Using national linked data to estimate COVID-19 vaccine effectiveness against COVID-19 mortality

Methods:

- Used AIR-PLIDA
- Survival analysis
- 65+ years
- Certified deaths
- Time-varying vaccination
- Adjusted for confounders

- Repeat in different waves:
- **B.A.1/2 (1 Jan 2022 – 31 May 2022)*;**
- **B.A.4/5 (1 June 2022 – 30 Nov 2022)*;**
- **B.A.2.75, X's (1 Nov 2022 – 31 May 2023)****
- **XB, XBB (1 March 2023 – 30 Sept 2023)**
- **XB, XBB, EG.5 (1 Aug 2023 – 28 Feb 2024)*****
- **JN.1, KP3 (01 Mar 2024 – 30 Nov 2024)**
- **XEC, KP.3.1.1 (01 Dec 2024 – 15 May 2025)**

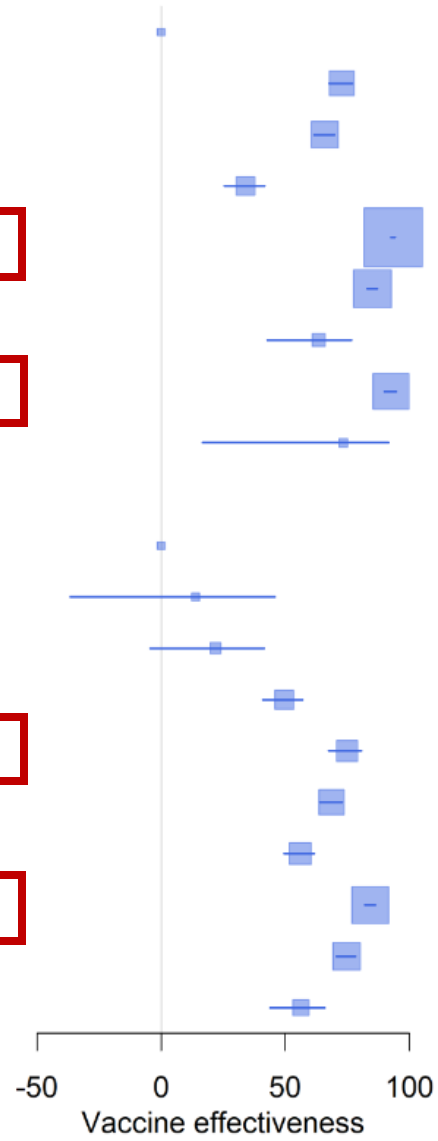


*https://www.thelancet.com/pdfs/journals/lanwpc/PIIS2666-6065(23)00246-8.pdf
**https://pmc.ncbi.nlm.nih.gov/articles/PMC10668254/
***https://pubmed.ncbi.nlm.nih.gov/40703004/

COVID-19 vaccine effectiveness-against mortality by dose, time since receipt 2022

Age 65+ years

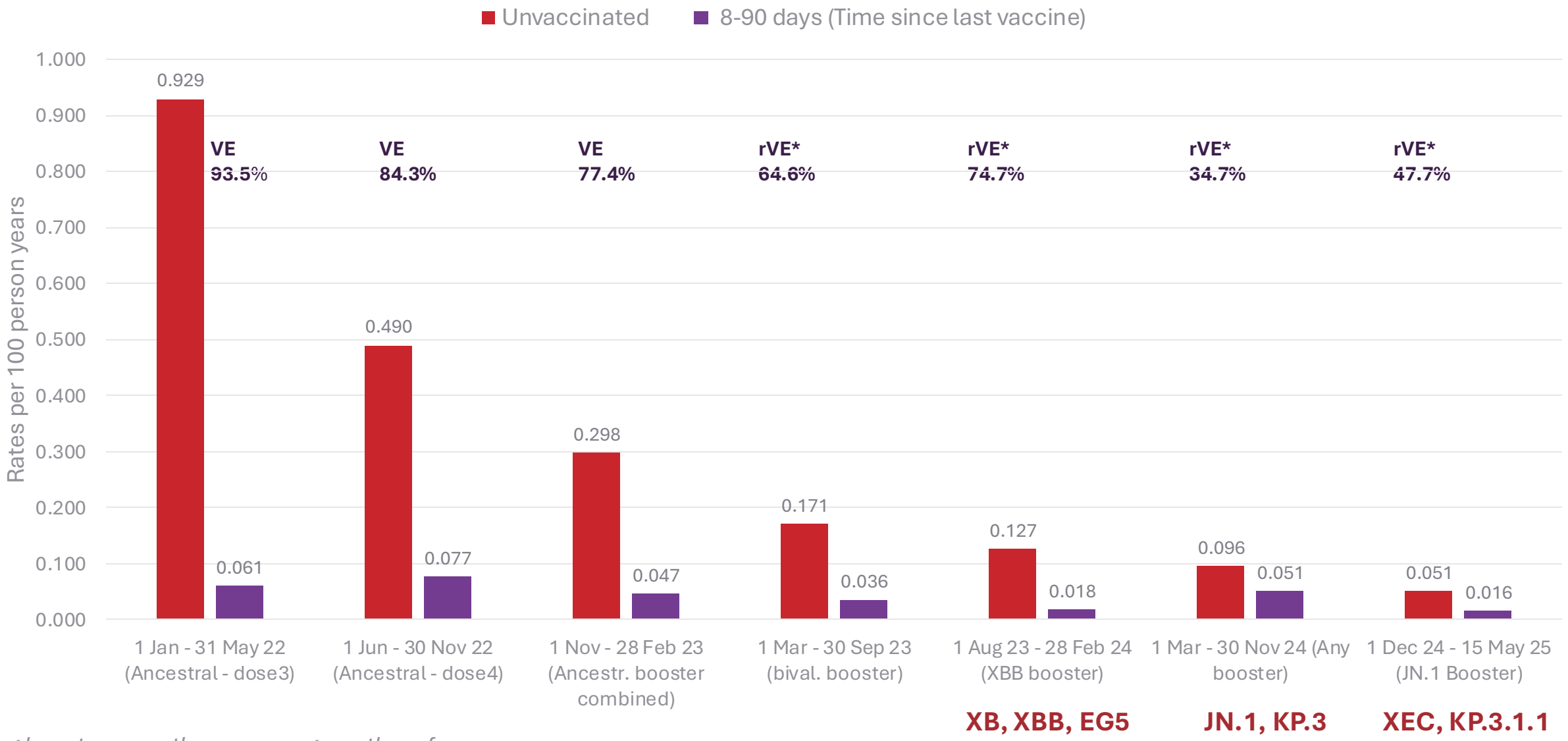
	Rate (per 100-PY) (95% CI)	VE (%) (95%CI)
01JAN22 – 31MAY22		
Unvaccinated	0.929 (0.812; 1.063)	ref
Dose2 8-90 days	0.279 (0.217; 0.359)	72.7 (67.8; 76.9)
Dose2 91-180 days	0.326 (0.285; 0.373)	65.9 (61.7; 69.7)
Dose2 >180 days	0.927 (0.794; 1.082)	34.0 (25.5; 41.6)
Dose3 8-90 days	0.070 (0.060; 0.081)	93.4 (92.6; 94.2)
Dose3 91-180 days	0.164 (0.141; 0.191)	85.1 (82.9; 86.9)
Dose3 >180 days	1.139 (0.536; 2.417)	63.4 (42.9; 76.6)
Dose4 8-90 days	0.094 (0.058; 0.151)	92.6 (90.0; 94.5)
Dose4 >90 days	0.386 (0.053; 2.831)	73.3 (16.8; 91.4)
01JUN22 – 30NOV22		
Unvaccinated	0.490 (0.399; 0.601)	ref
Dose2 8-90 days	1.218 (0.471; 3.149)	13.9 (-36.6; 45.7)
Dose2 91-180 days	0.595 (0.337; 1.051)	21.8 (-4.3; 41.4)
Dose2 >180 days	0.209 (0.162; 0.269)	49.6 (41.0; 56.9)
Dose3 8-90 days	0.232 (0.142; 0.381)	74.9 (67.5; 80.6)
Dose3 91-180 days	0.207 (0.172; 0.248)	68.6 (63.9; 72.7)
Dose3 >180 days	0.205 (0.172; 0.245)	56.0 (49.6; 61.6)
Dose4 8-90 days	0.134 (0.114; 0.156)	84.3 (82.0; 86.2)
Dose4 91-180 days	0.094 (0.078; 0.113)	74.7 (70.7; 78.2)
Dose4 >180 days	0.128 (0.086; 0.189)	56.3 (44.0; 65.9)



Vaccine effectiveness adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2022 flu vaccine receipt

https://www.thelancet.com/pdfs/journals/lanwpc/PIIS2666-6065(23)00246-8.pdf

COVID-19 mortality rates due to COVID-19 for 65+ years population, Jan 2022 to May 2025



** Using booster more than a year ago as the reference*

Summary

- Vaccine effectiveness studies are important as part of monitoring of vaccine programs following implementation.
- Data linkage can be a powerful tool to bring together data that gives insights needed to assess vaccine effectiveness and impact to inform policy
- Australia has good core datasets and the capacity to undertake data linkage of these, but timeliness of data is key to unlocking potential for policy and program support
- Appropriate epidemiological study designs need to be used to monitor vaccine effectiveness and program impact
- Detailed monitoring of COVID-19 vaccine impact throughout pandemic has been possible through having individual level linked data

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Australian Government
Department of Health, Disability and Ageing

NSW

Australian Bureau of Statistics

Questions