IMMUNISATION COALITION

The history and future of respiratory viral disease surveillance

7:50 pm

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Respiratory virus surveillance: past, present and future

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Surveillance pre-2000

National Influenza Surveillance Scheme

- laboratory diagnosis (virus isolation, detection or serological evidence)
- consultation rates for influenza-like illness by sentinel general practitioners (ASPREN)
- absenteeism data from a “national employer” (Australia Post)

Figure 3. Influenza laboratory reports, by virus type and week of specimen collection, Australia, 1998

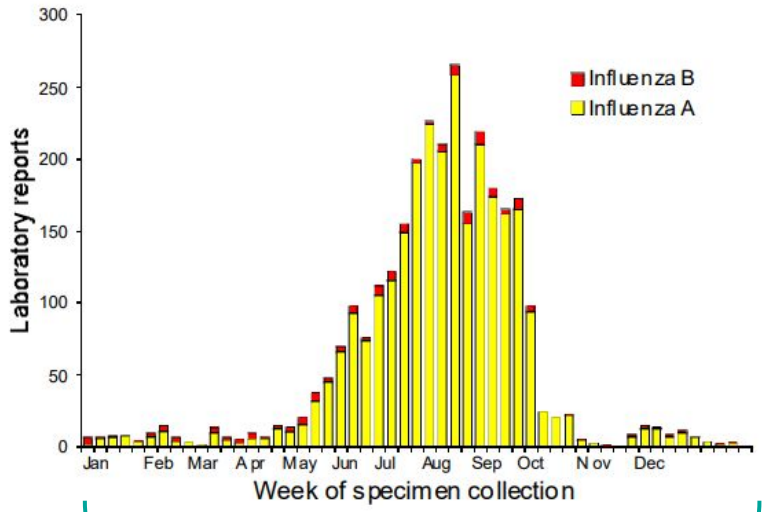


Figure 10. Sentinel general practitioner consultation rates, influenza-like illness, by week and scheme, 1998

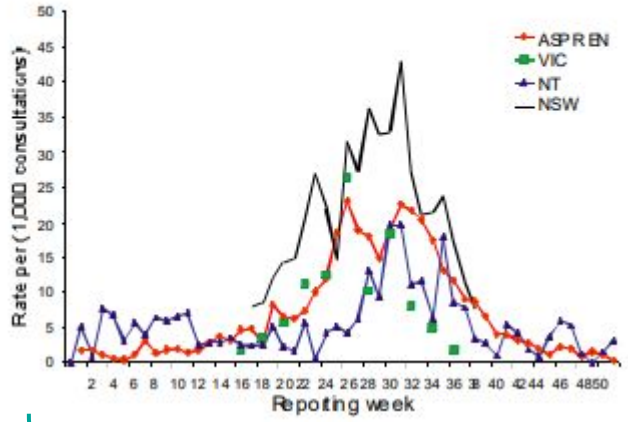
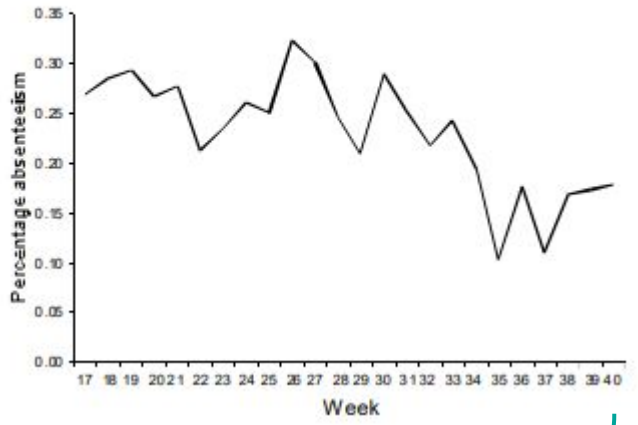


Figure 13. Absenteeism rates in Australian Post, May to September, by week of the year, 1998



Notifications data

Indirect data on illness

Annual report of the National Influenza Surveillance Scheme, 1998
https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-pubs-cdi-1999-cdi2307-cdi2307a.htm

National Influenza Surveillance Scheme

- Indirect measures of activity
  - ILI and absenteeism not specific to influenza
  - Lab diagnostics not widely used (pre-PCR)
- Mostly consistent over time but clearly not true indicator of burden of disease
  - 1998 n=2943 vs 2023 n=251,095 notifications!
- Limited data on severe disease

Global surveillance - GISRS

- global mechanism of surveillance, preparedness and response for seasonal, pandemic and zoonotic influenza
- global platform for monitoring influenza epidemiology and disease
- global alert for novel influenza viruses and other respiratory pathogens

Developments in 2000s

- Hospitalisation data
- Telephone surveys to assess vaccine coverage (2002-4, 2009, 2014)
- Increasing use of diagnostic tests
- Improved genomic characterization of viral strains
- Other data sources
  - Death certificates (NSW, ABS)
  - Paediatric ICU admissions (APSU)
  - ED presentations (NSW, WA)

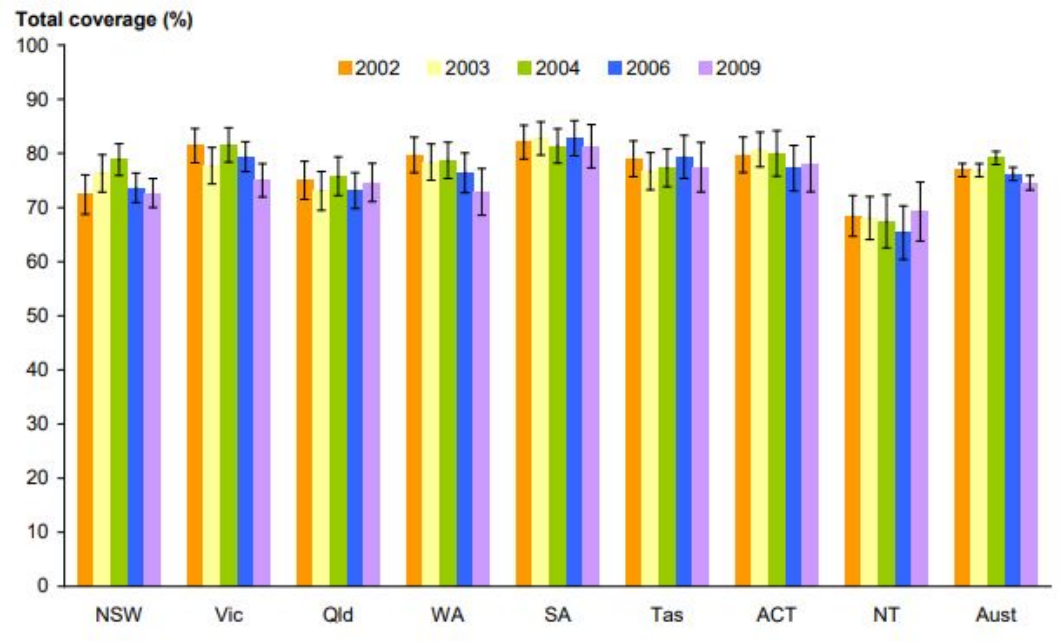


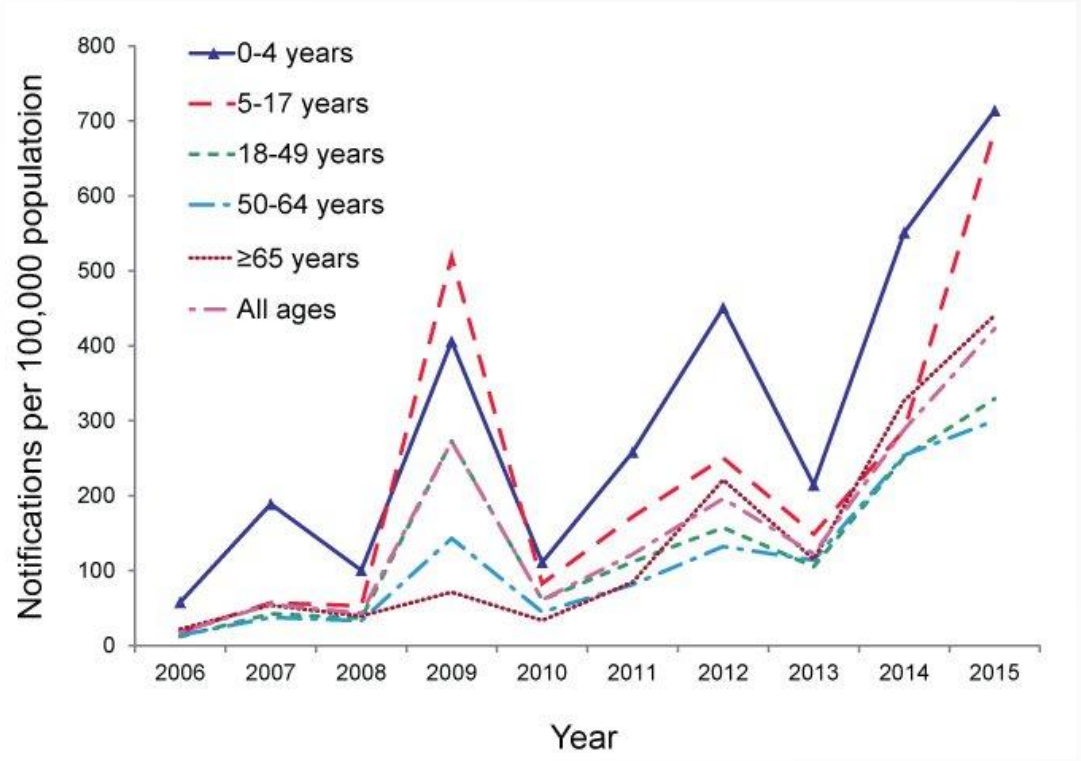
Figure 2.1: Estimated seasonal influenza vaccination total coverage rates and 95% confidence intervals, persons aged 65 years or older, Australia, 2002 to 2009

Estimated influenza vaccine coverage in 65+ (AIHW, 2009)

AIHW adult vaccination survey: https://www.aihw.gov.au/reports/primary-health-care/2009-adult-vaccination-survey-summary-results/summary
Newspoll Omnibus Survey:
https://www.health.gov.au/topics/immunisation/immunisation-data/childhood-immunisation-coverage/immunisation-coverage-data-surveys-and-reports

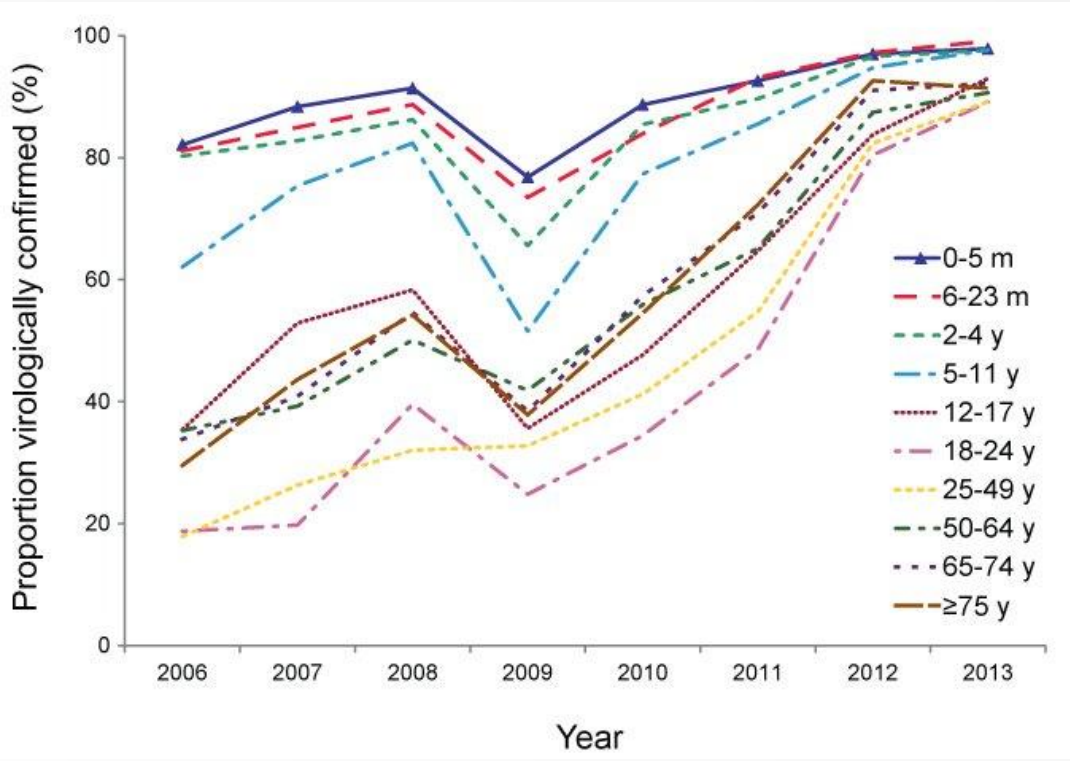
Swine flu 2009

- Increasing utilization of sensitive diagnostics
- FluTracking (2006-)
- FluCAN (2009-)
- PHREDSS (NSW) - Public Health Rapid Emergency Disease Syndromic Surveillance
- Excess mortality
- Vaccine effectiveness



Notification rate of influenza – 2006-2015

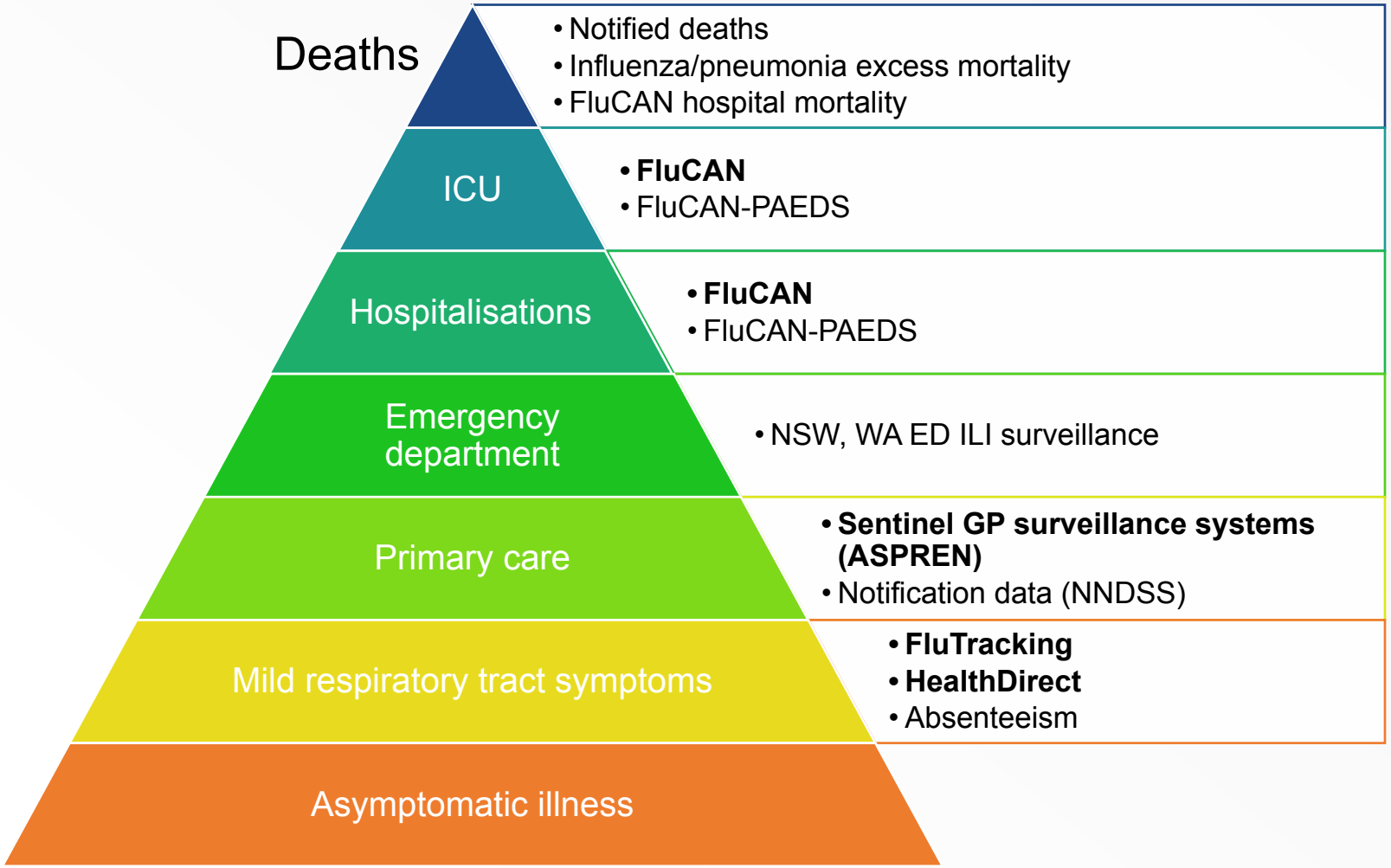
- Overall increase unlikely to represent true increase in infections



Proportion of hospitalisations with confirmed influenza 2006-2013

- Virologically confirmed (J9-10) of total (any diagnosis: J09-J11)
- Increasing utilisation of diagnostic testing esp in adults
- (or coding issues?)

Surveillance pyramid



Dimensions of influenza

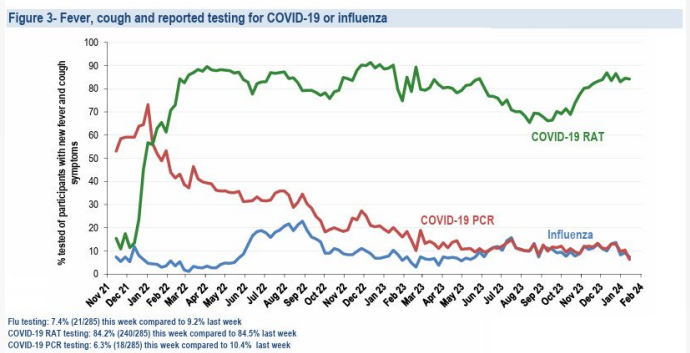
WHO Pandemic Influenza Severity Assessment (PISA) - 2017

- **Transmission** - How many people in a population get sick from influenza on a weekly basis
- **Seriousness** - How severely sick individual people get when infected with the influenza virus
- **Impact** - How the influenza epidemic or pandemic affects the healthcare system and society

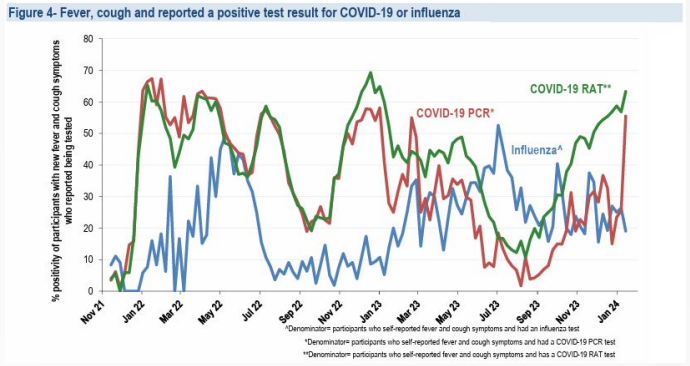
PISA - https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/pandemic-influenza-severity-assessment/frequently-asked-questions

FluTracking – community-based surveillance

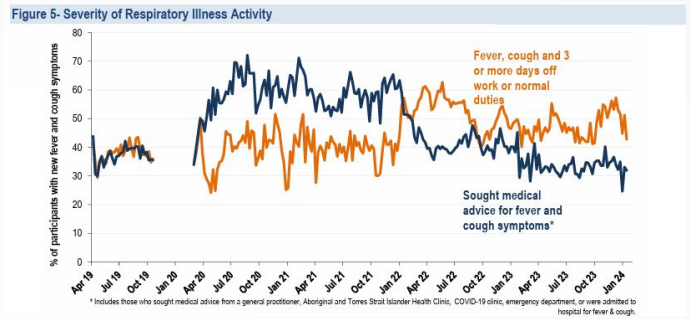
In operation since 2006
N=~110,000 participants, 23M surveys



Testing

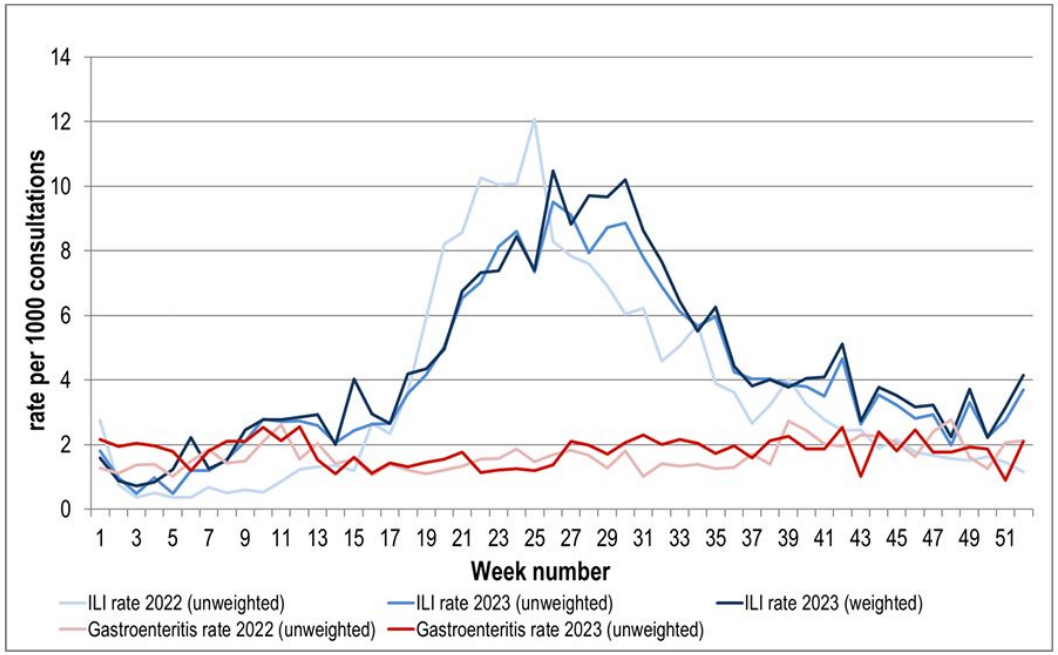


Positive tests

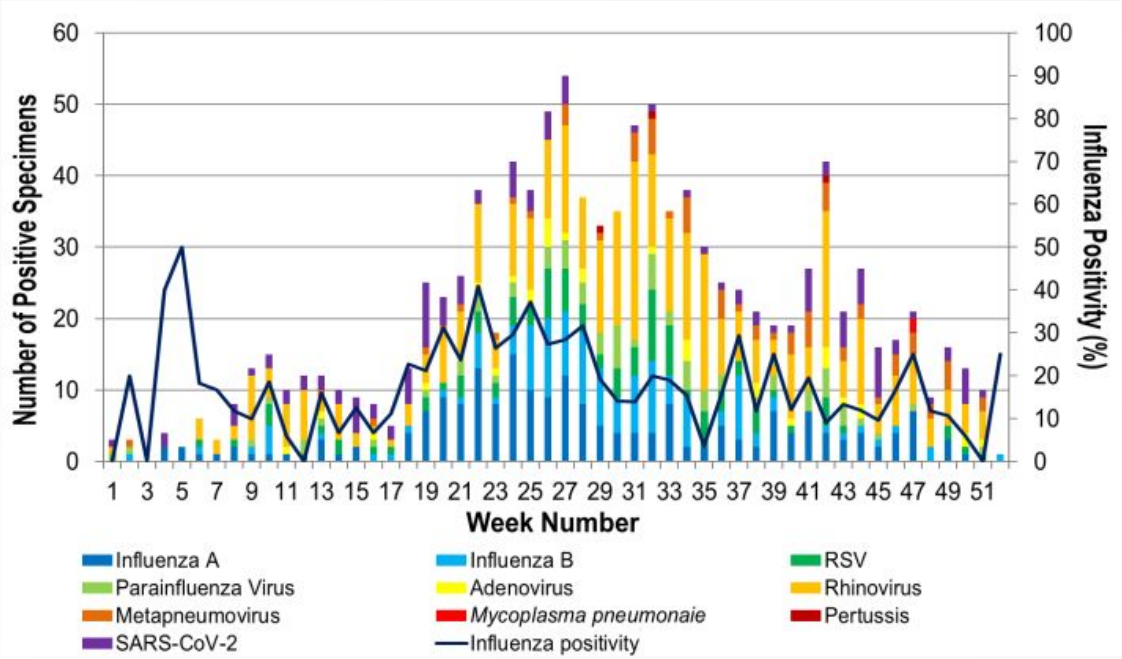


Impact

ASPREN – GP surveillance

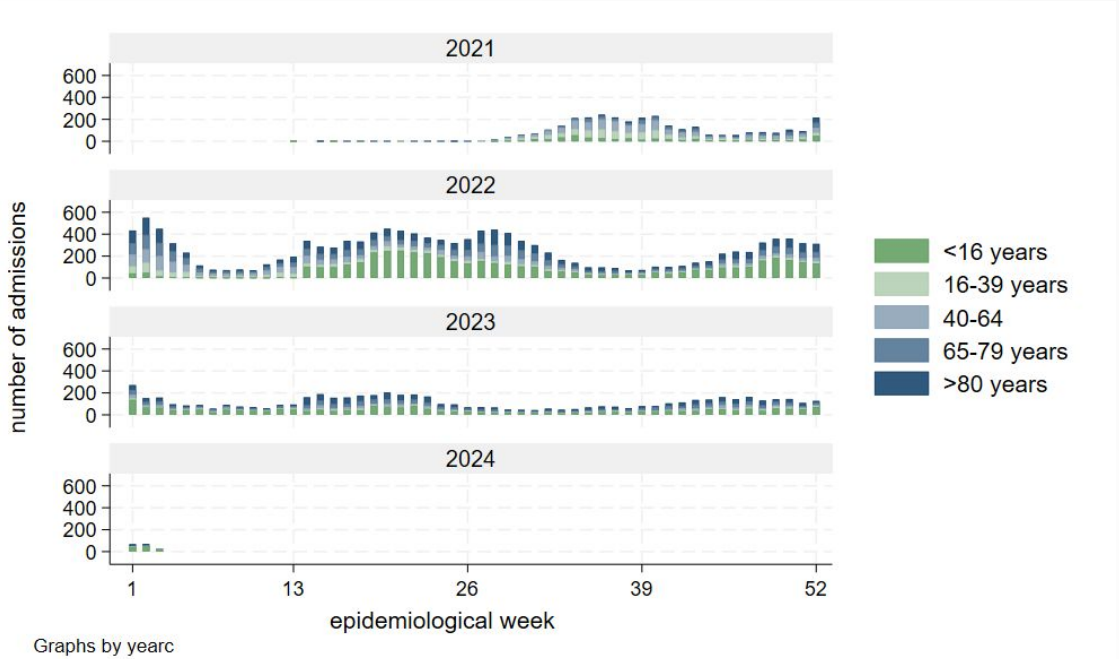


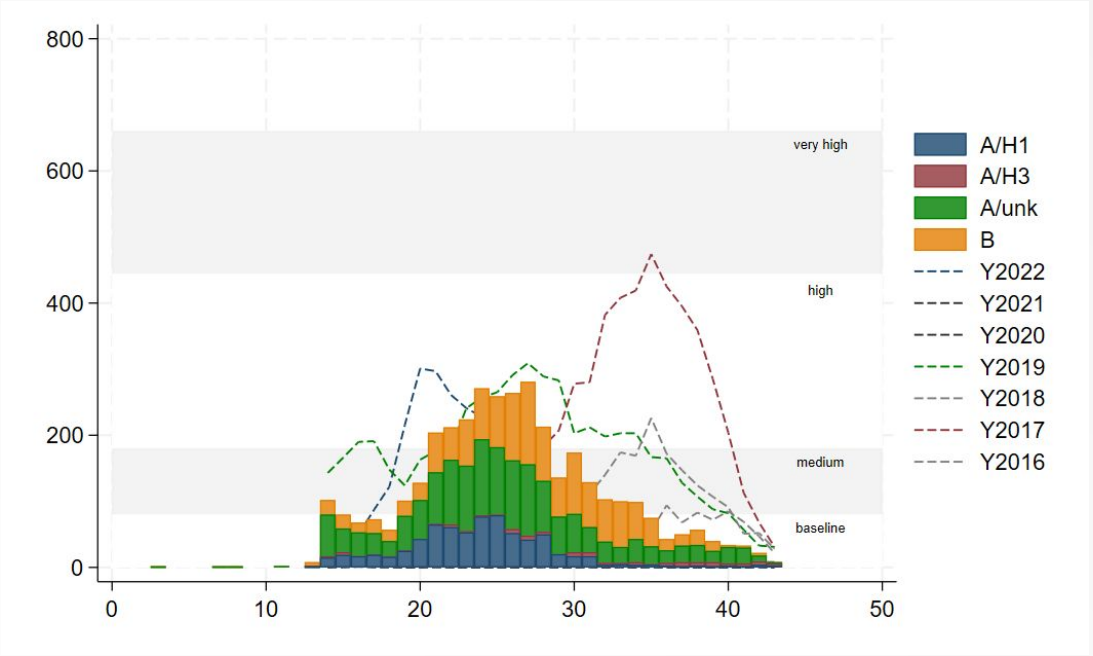
Syndromes: Influenza-like illness and gastroenteritis rate



Pathogens: influenza and other respiratory pathogens

Hospitalisations with COVID and influenza (FluCAN)





COVID-19

- 6084 admissions Jan 2023-19 Jan 2024
- 5.9% directly admitted to ICU
- Hospitalisation-fatality 166/5317 (3.1%)

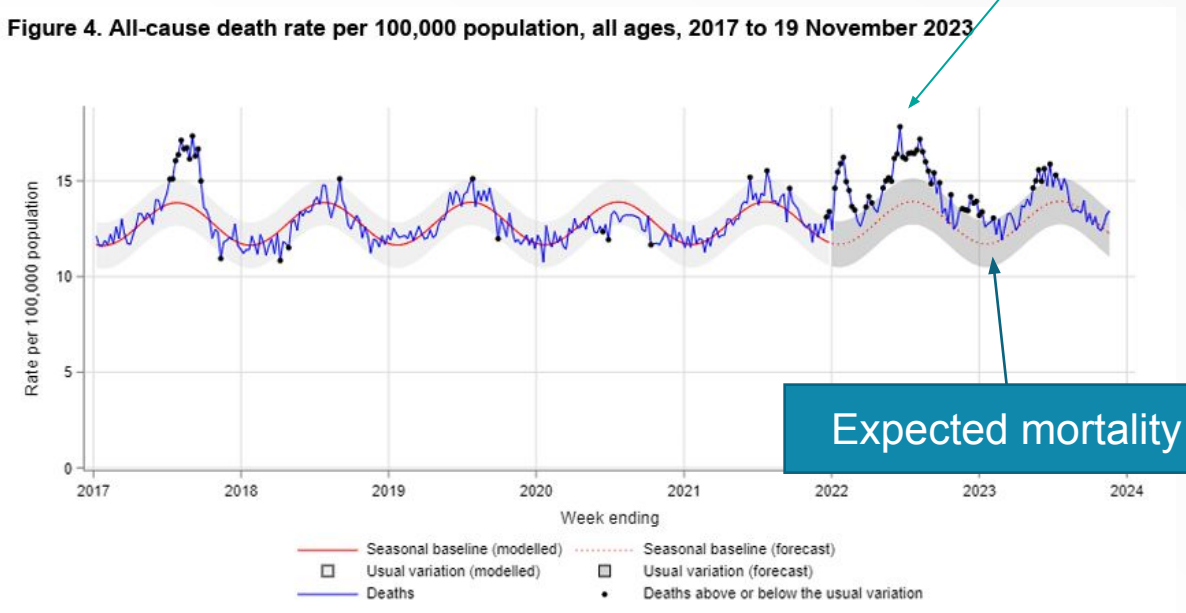
Influenza

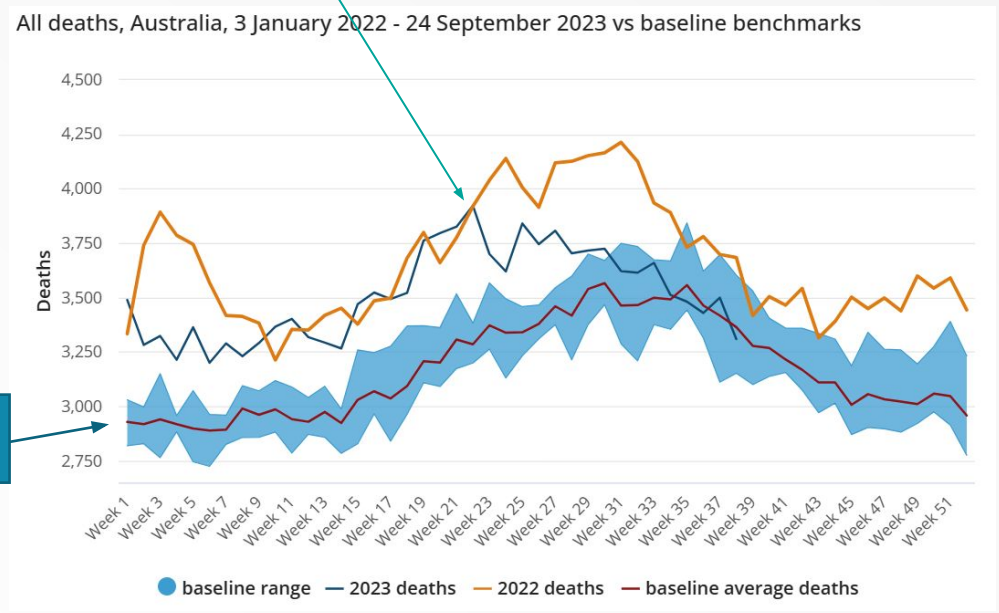
- 3757 admissions April-Oct
- 36% influenza B
- 7% directly admitted to ICU
- 13 paediatric deaths

Excess mortality

Observed mortality

Expected mortality





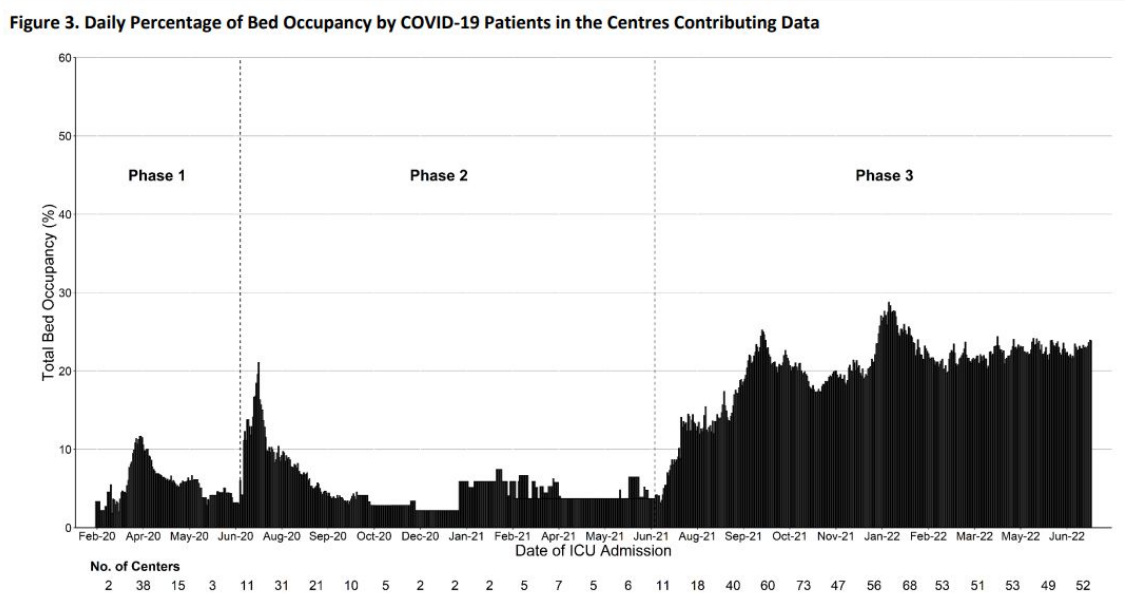
NSW respiratory surveillance report

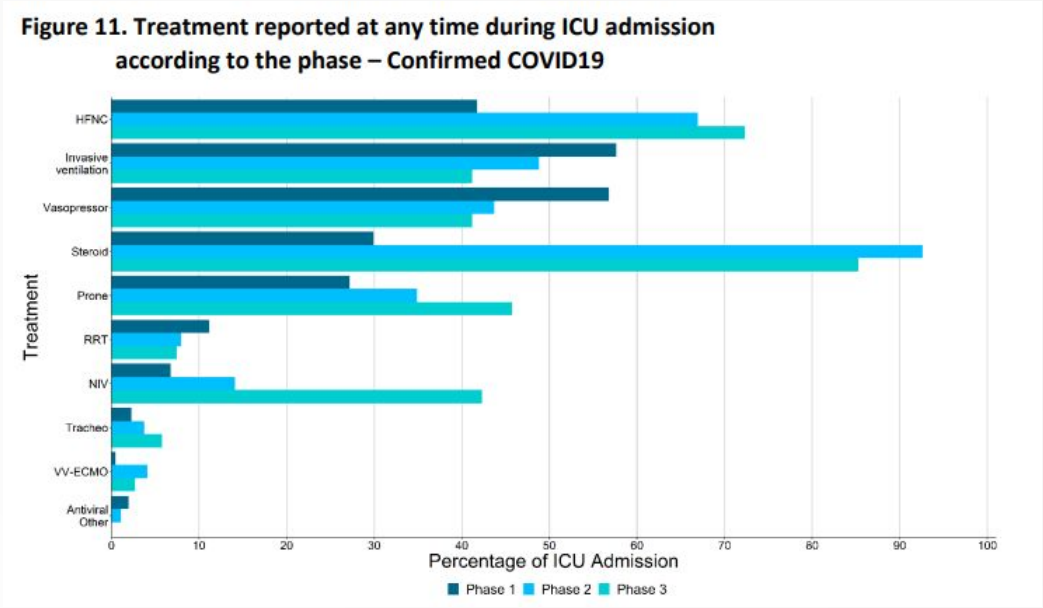
ABS provisional mortality statistics

COVID-19

- ICU data
- Wastewater surveillance
- Social and behavioural indicators; modelling and forecasting
- Genomic data
- Vaccine registries - explore differences in coverage
- Linked data for cases, vaccine coverage, vaccine effectiveness
- *First few hundred studies*
- *Clinical characterization protocol*

ICU surveillance – ANZIC-RC SPRINT-SARI

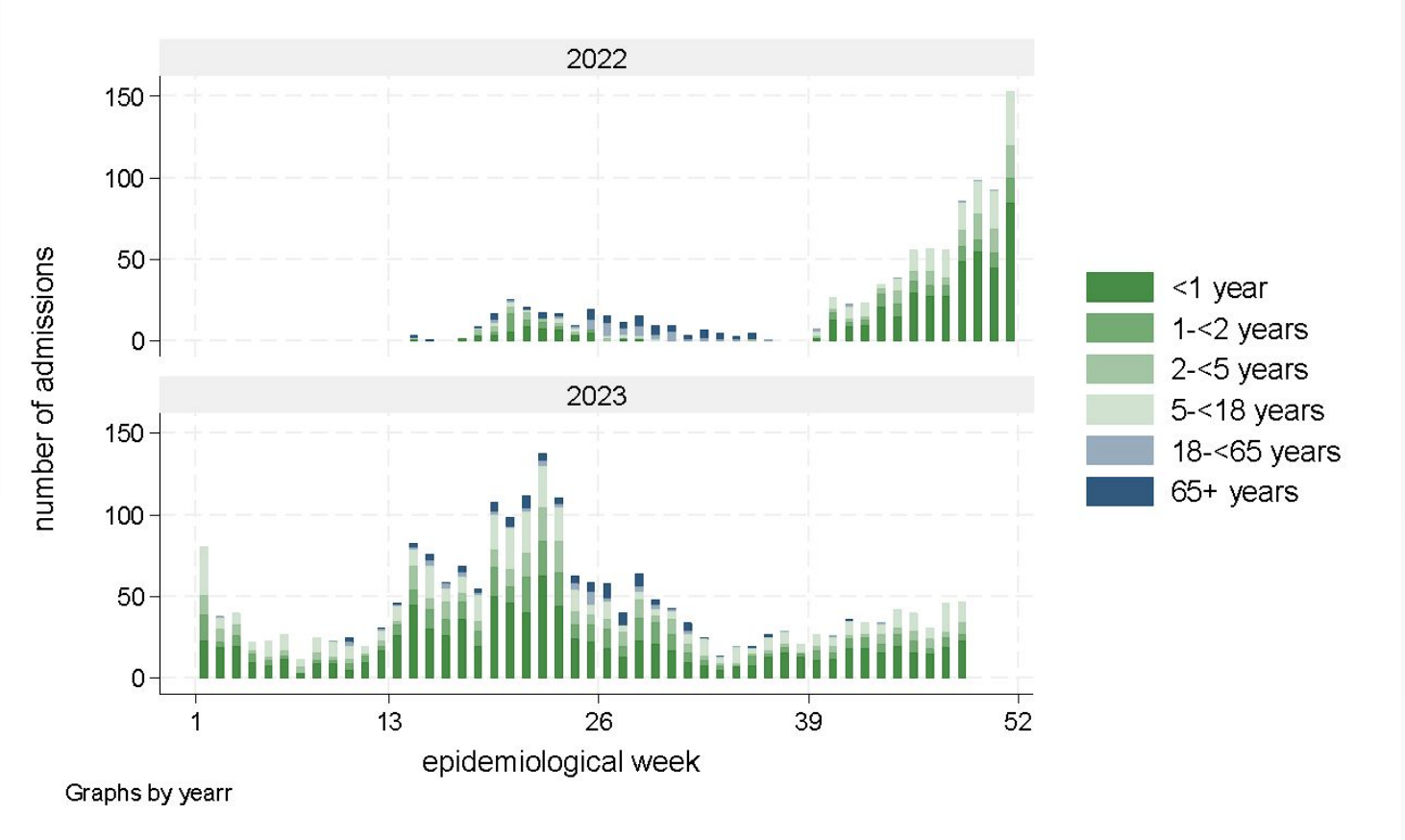




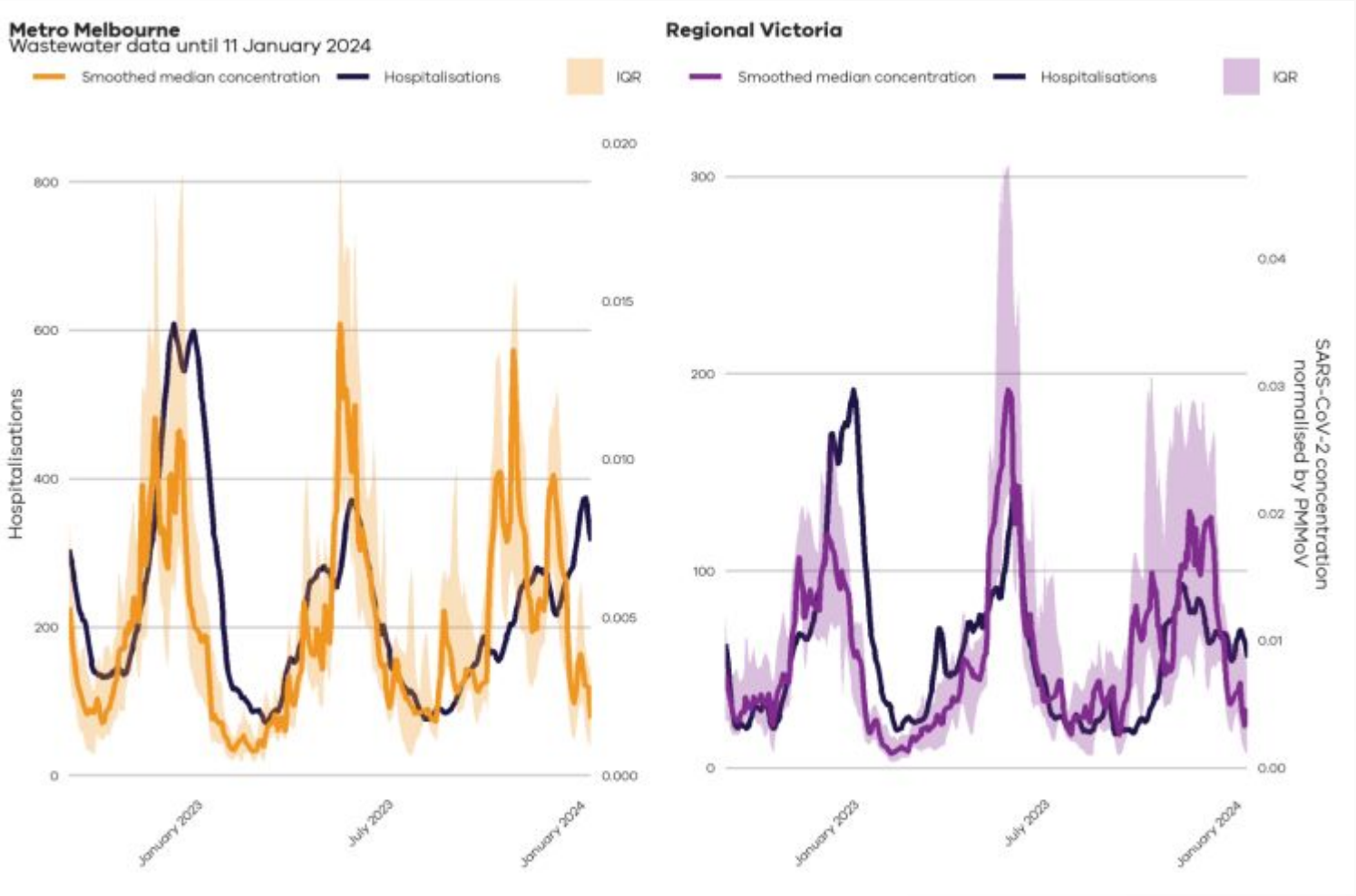
Short PeRiod IncideNce sTudy of Severe Acute Respiratory Infection – ISARIC
International protocol – modular case report form
Australia: 71 ICUs in all jurisdictions - COVID
Comprehensive data on risk factors and treatments

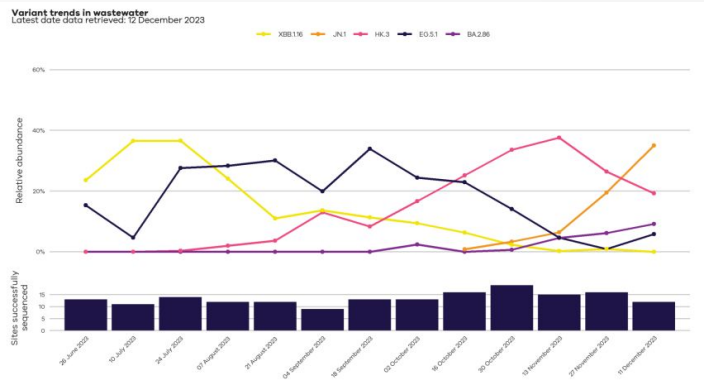
RSV pilot

- Opportunistic sample in FluCAN
- 976 patients in 2022
- 2264 patients in 2023
  - 965 (43%) were in infants <1 year of age
  - 1611 (71%) were in children <5 years of age.
  - 7% of cases were in adults



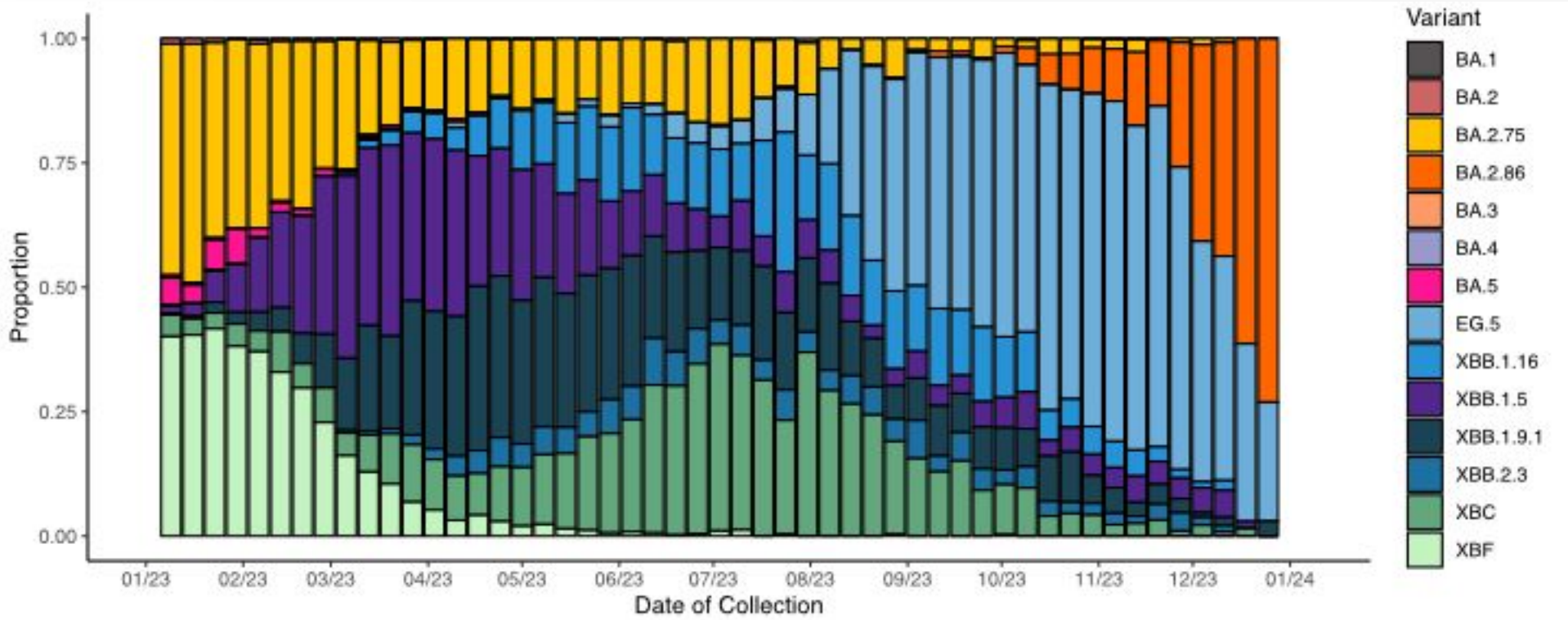
Wastewater surveillance



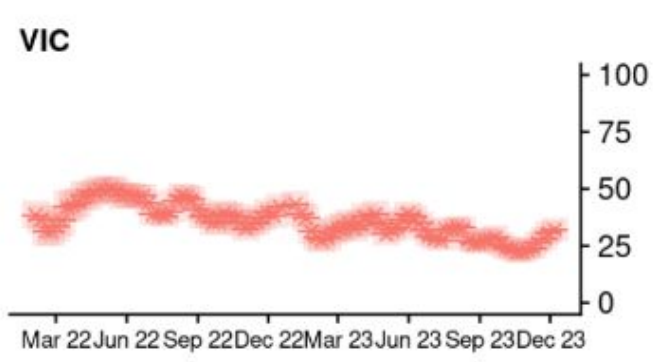


Variant trends

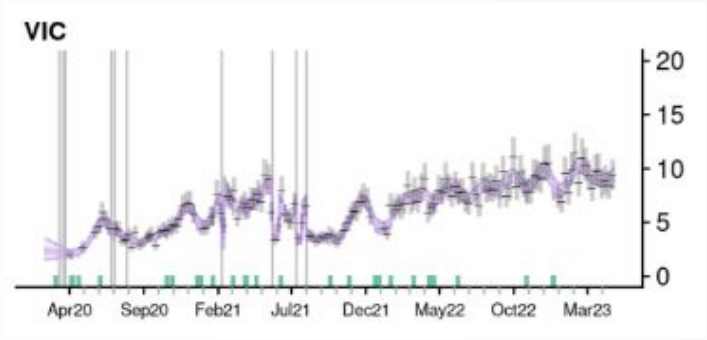
Genomic data - AusTrakka



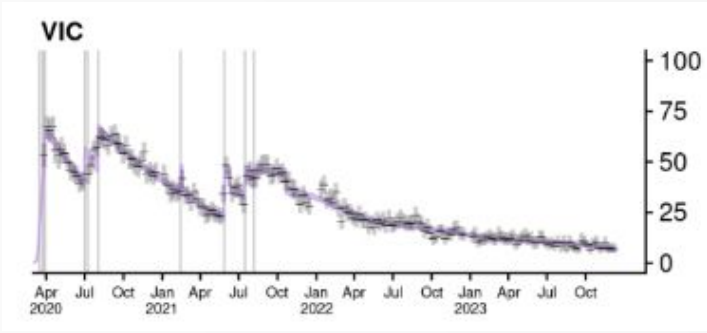
Behavioural data – public health measures



Test seeking behaviour
Proportion of respondents with symptoms reporting seeking PCR or RAT

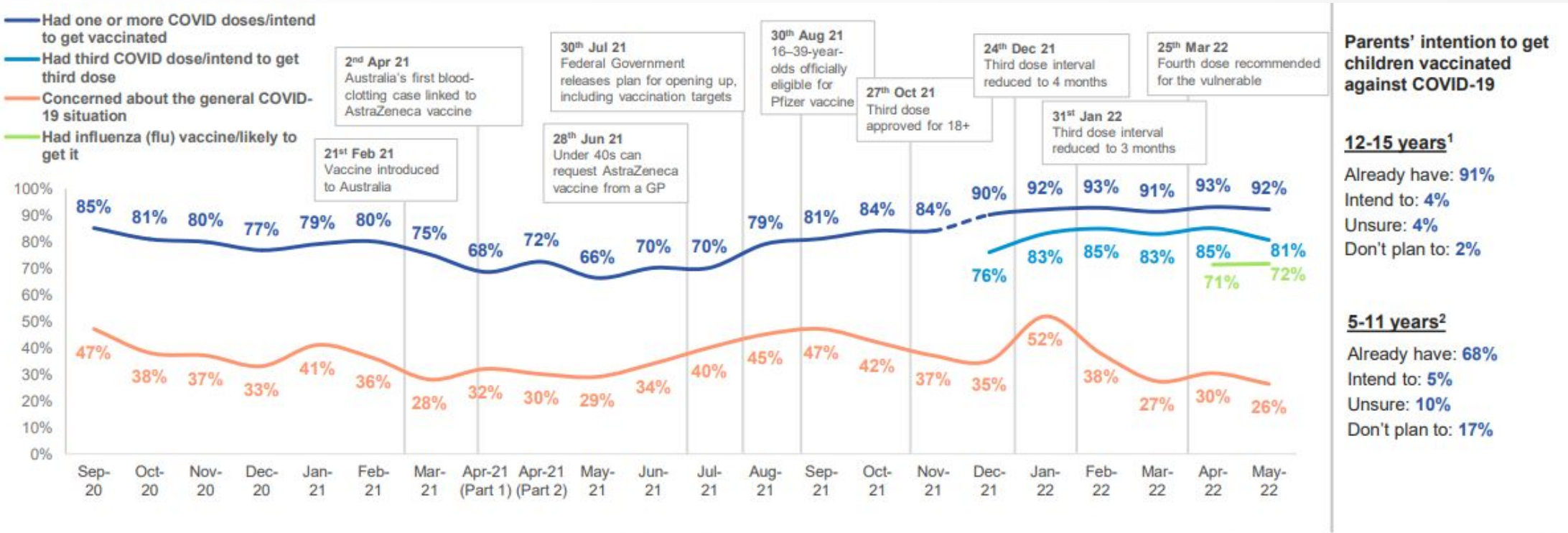


“Macro-distancing”
Estimated mean number of non-household contacts



“Micro-distancing”
Proportion reporting “always” keeping 1.5m distance

Behavioural data - immunisation



Parents' intention to get children vaccinated against COVID-19

12-15 years[1]

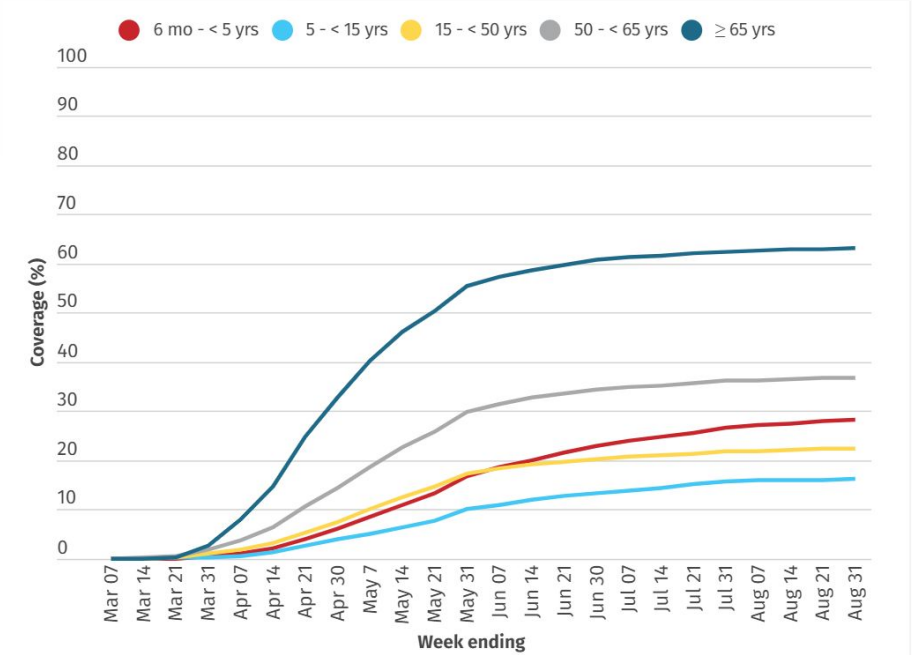
Already have: **91%**
Intend to: **4%**
Unsure: **4%**
Don't plan to: **2%**

5-11 years[2]

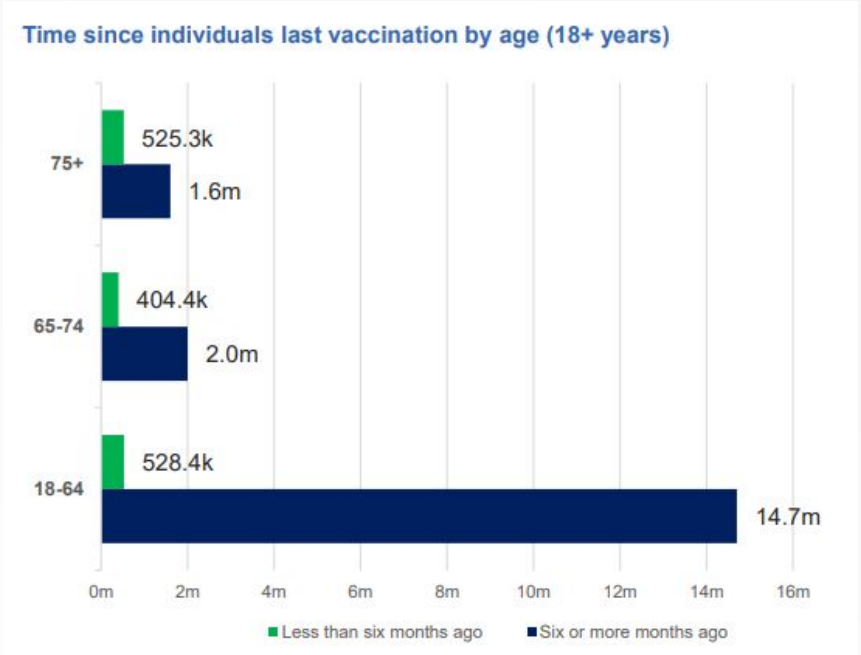
Already have: **68%**
Intend to: **5%**
Unsure: **10%**
Don't plan to: **17%**

*Base (if not indicated otherwise): All Australian adults, n=1,000 per wave, measured in the **first week of the month** (in Apr-21 data was collected in the first two weeks). Note: Vaccination behaviour/intentions question wording was changed between Nov-21 and Dec-21 to highlight the 'already vaccinated' options. Wording change in May-22 to add third dose or more. [1]Base: Parents of 12-15 year olds (n=109 May-22) [2]Parents of 5-11 year olds (n=139 May-22).*

Vaccine coverage – Australian Immunisation Register



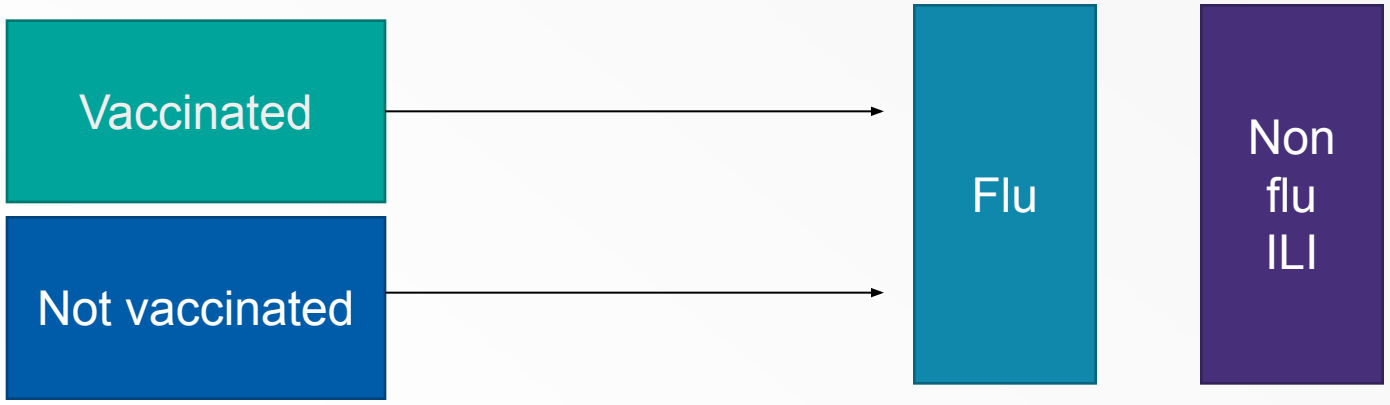
Influenza vaccine coverage – 2023 (NCIRS)



COVID – recent doses – Jan 2024 (Australian Dept of Health)

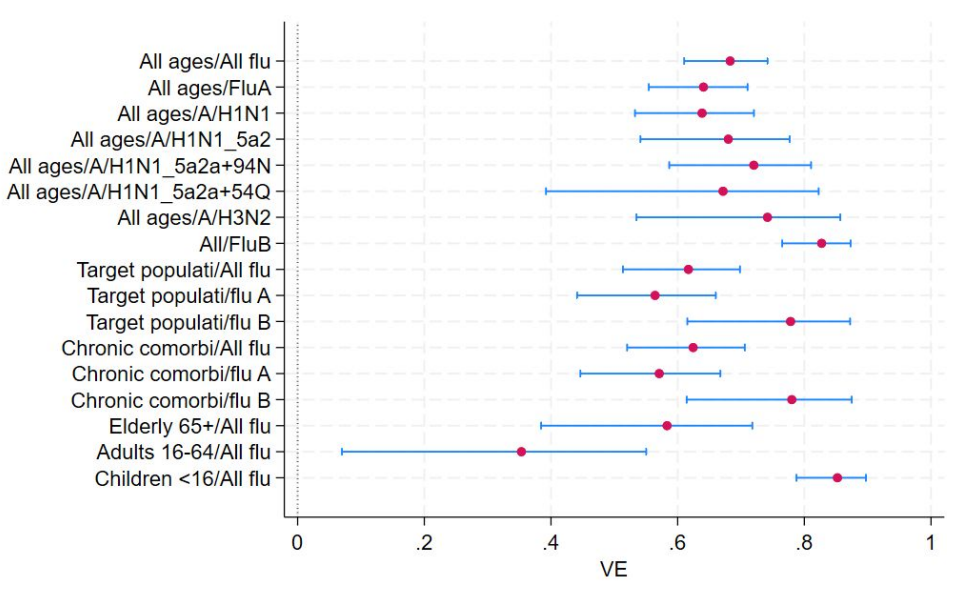
Influenza vaccination coverage data: https://ncirs.org.au/influenza-vaccination-coverage-data
COVID-19 Vaccine Rollout https://www.health.gov.au/sites/default/files/2024-01/covid-19-vaccine-rollout-update-12-january-2023.pdf

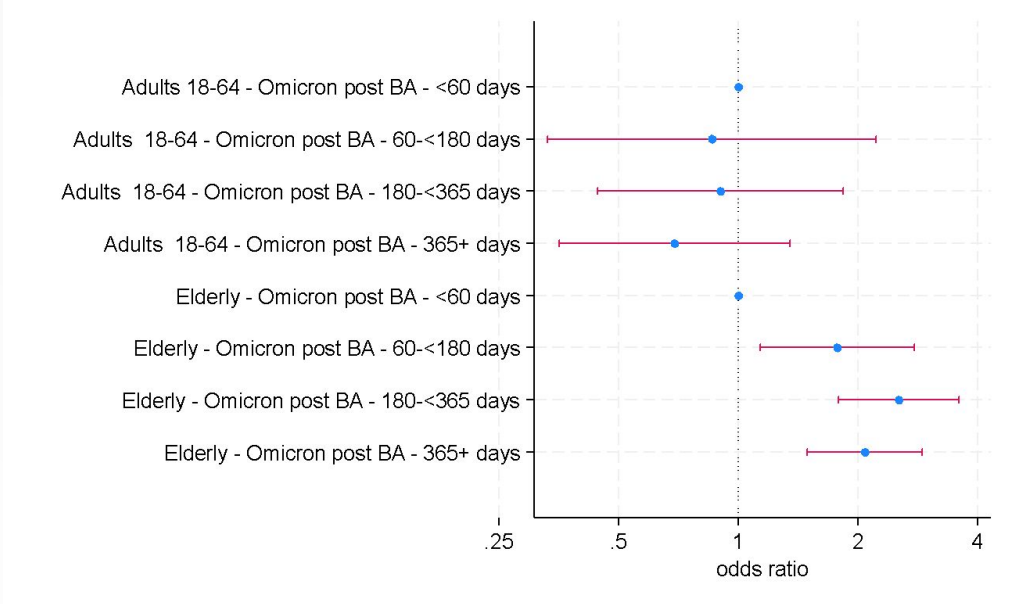
Incidence density test-negative studies



Case = influenza
Control = non influenza ILI stratified by date of presentation
Case/control status assigned when test result known
Adjust for confounders

Vaccine effectiveness – FluCAN 2023





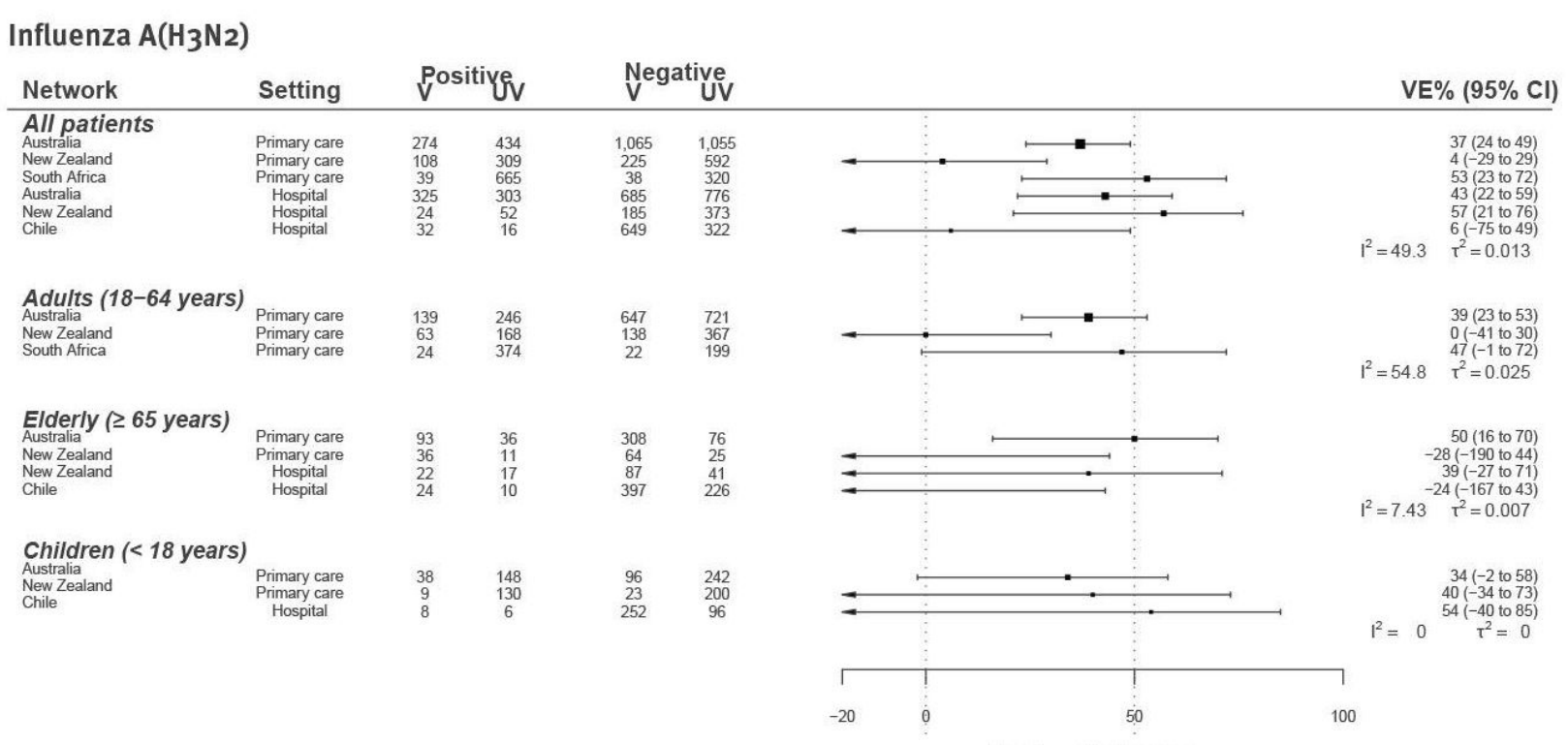
Influenza VE against hospitalization

- High overall VE than usual
- Early season, more children, well matched strains

COVID-19 rVE against hospitalization

- Increased protection with recent dose in elderly, but not in non-elderly

Vaccine effectiveness – Southern Hemisphere systems



Global Influenza VE (GIVE) collaboration

- SH 2019 data
- Moderate VE against influenza in Australia, South Africa
- Lower VE in NZ primary care and Chile

Sullivan S et al Euro Surveill. 2019 Nov 7; 24(45): 1900645.
doi: 10.2807/1560-7917.ES.2019.24.45.1900645

Study designs for VE

Specific cohort or case control studies

- Smaller/lower statistical power
- More detailed clinical data eg smoking, weight
- Confirmed (specific) outcome
- Potential issues with control group – test negative controls

Large linked datasets

- Population level datasets – high statistical power
- Feasible since registration of COVID and flu vaccines now required in AIR
- Potential differential ascertainment of some information eg previous hospitalisations
- Some outcomes may not be coded accurately eg COVID hospitalisations
- Difficulty in defining cohort; “inactive” patients, border issues

COVID vaccine effectiveness - NSW linked data

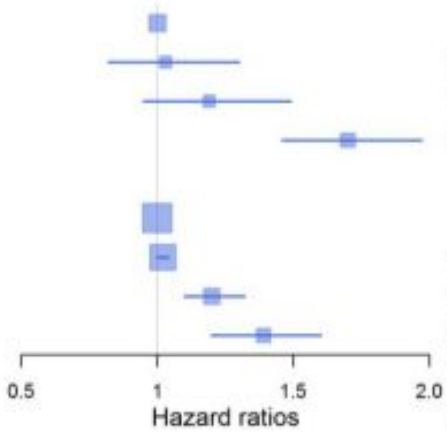
- Sydney and HNE region data (1 March-27 May 2021 – BA.1, BA.2)
- Linked AIR to NSW COVID notifications and death registrations
- Vaccination – time varying covariate
- Adjusted for age, gender, SES of resident address, number of comorbidities (based on coded hospitalisations in 2y prior to analysis start date)

Liu B et al, Vaccine 2023 Aug 31;41(38):5587-5591. doi: 10.1016/j.vaccine.2023.07.050

NSW linked data

Figure 1: Rate and hazard ratio for SARS-CoV-2 infection by primary course and booster vaccine type in interval 14-63 days following receipt of dose, March-May 2022

	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

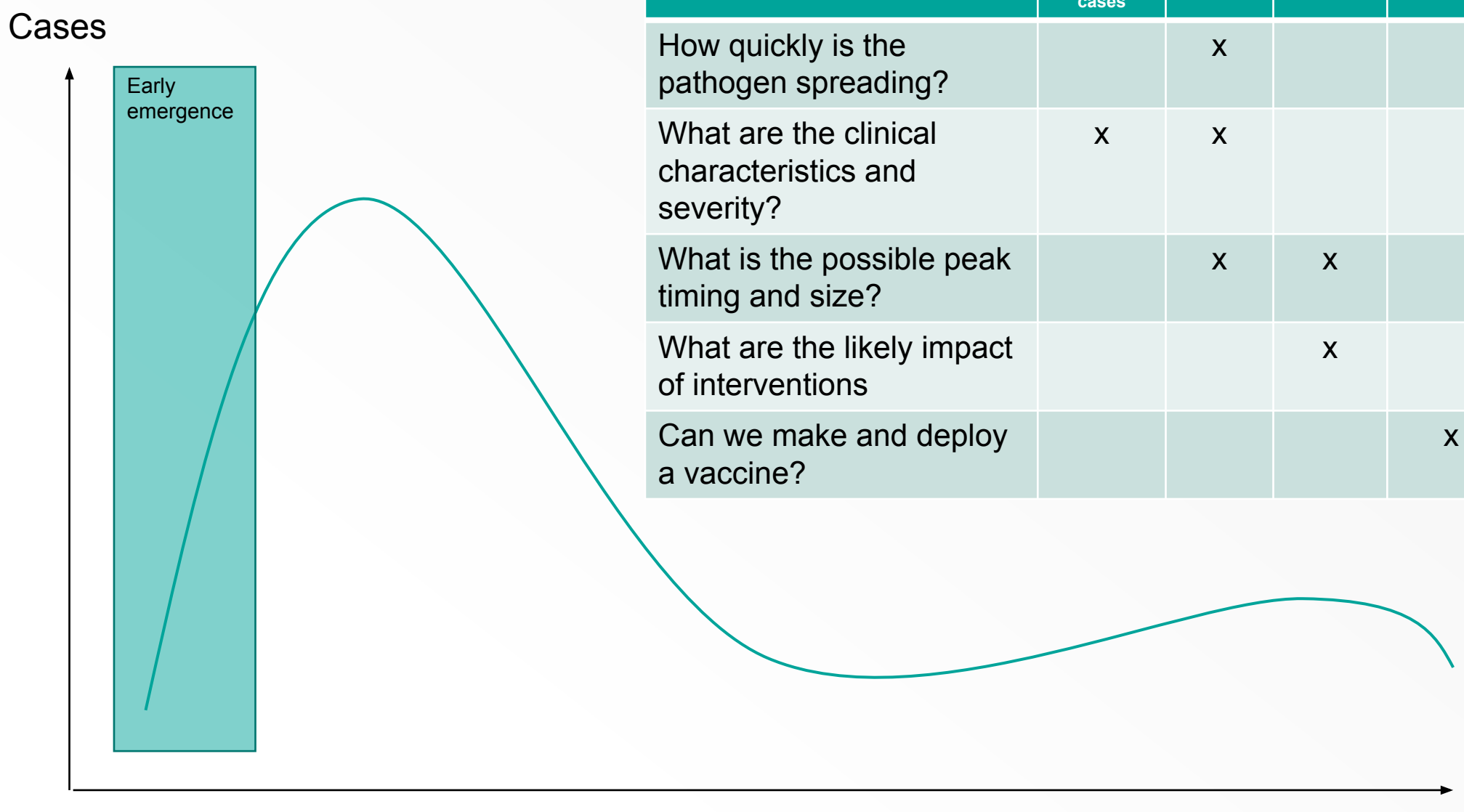


Hazard ratios adjusted for age, gender, socioeconomic status and comorbidity. Boxes in plot are proportional to the amount of data and lines represent the 95% confidence intervals of the hazard ratio. Analyses included only individuals without a prior COVID-19 diagnosis. Total study population included in primary course analysis N=2,273,324; booster analysis N=4,610,877.

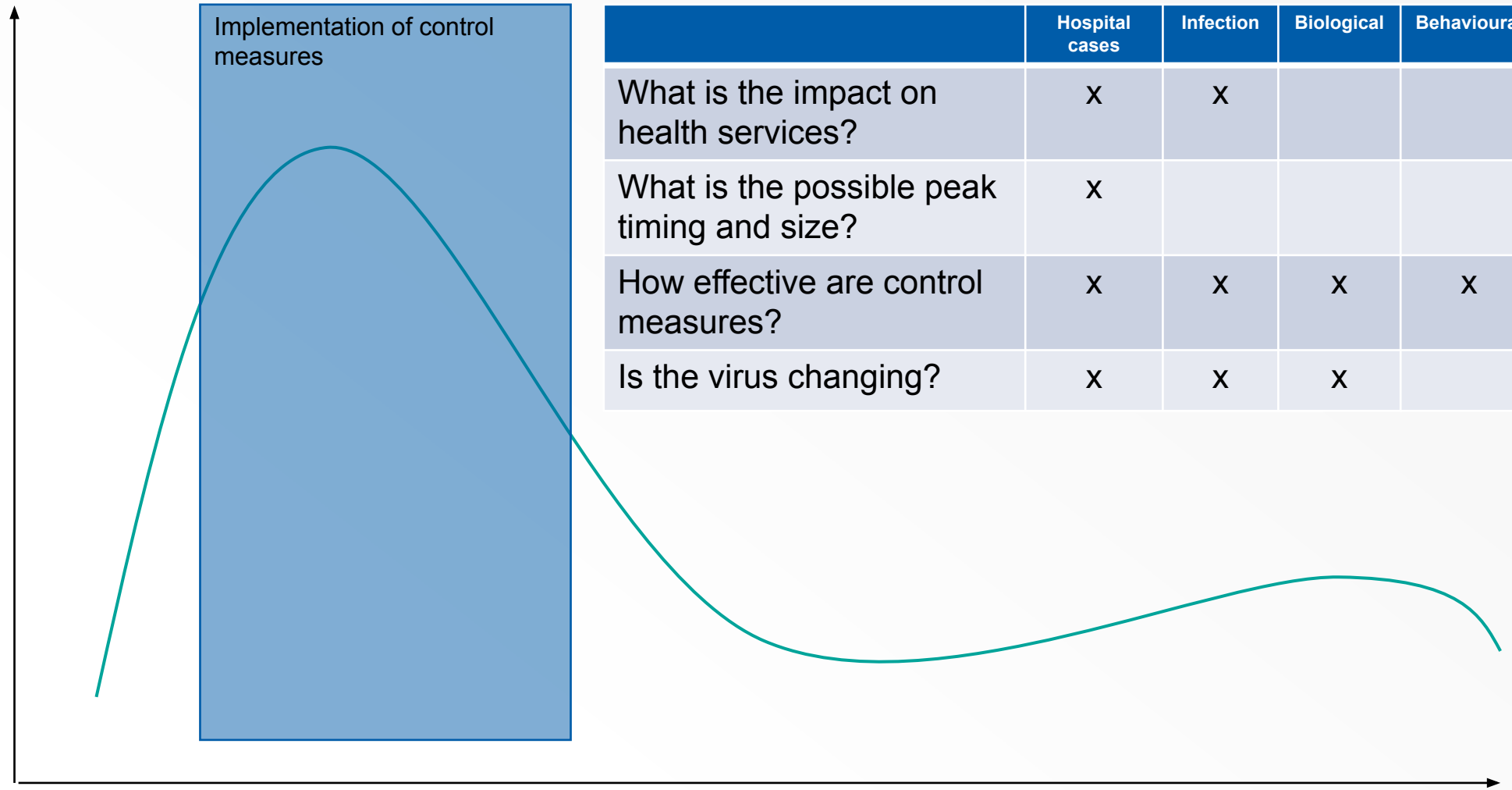
Liu B et al, Vaccine 2023 Aug 31;41(38):5587-5591. doi: 10.1016/j.vaccine.2023.07.050

Comprehensive respiratory surveillance

- Provides information on transmission, severity and impact
  - Combination of big data and sentinel surveillance; broader range of data sources
  - Complementary data on control measures and socio-behavioural context
- Adaptable to new pathogens
  - Rapidly scalable – upwards and downwards
  - Integrated with clinical trials
- Targeted at vaccine preventable viruses (IAV/IBV, COVID, RSV) and those potentially preventable in future (eg hMPV)
- Detection of new strains
  - Wastewater, clinical data
  - Trans-national sharing of genomic data

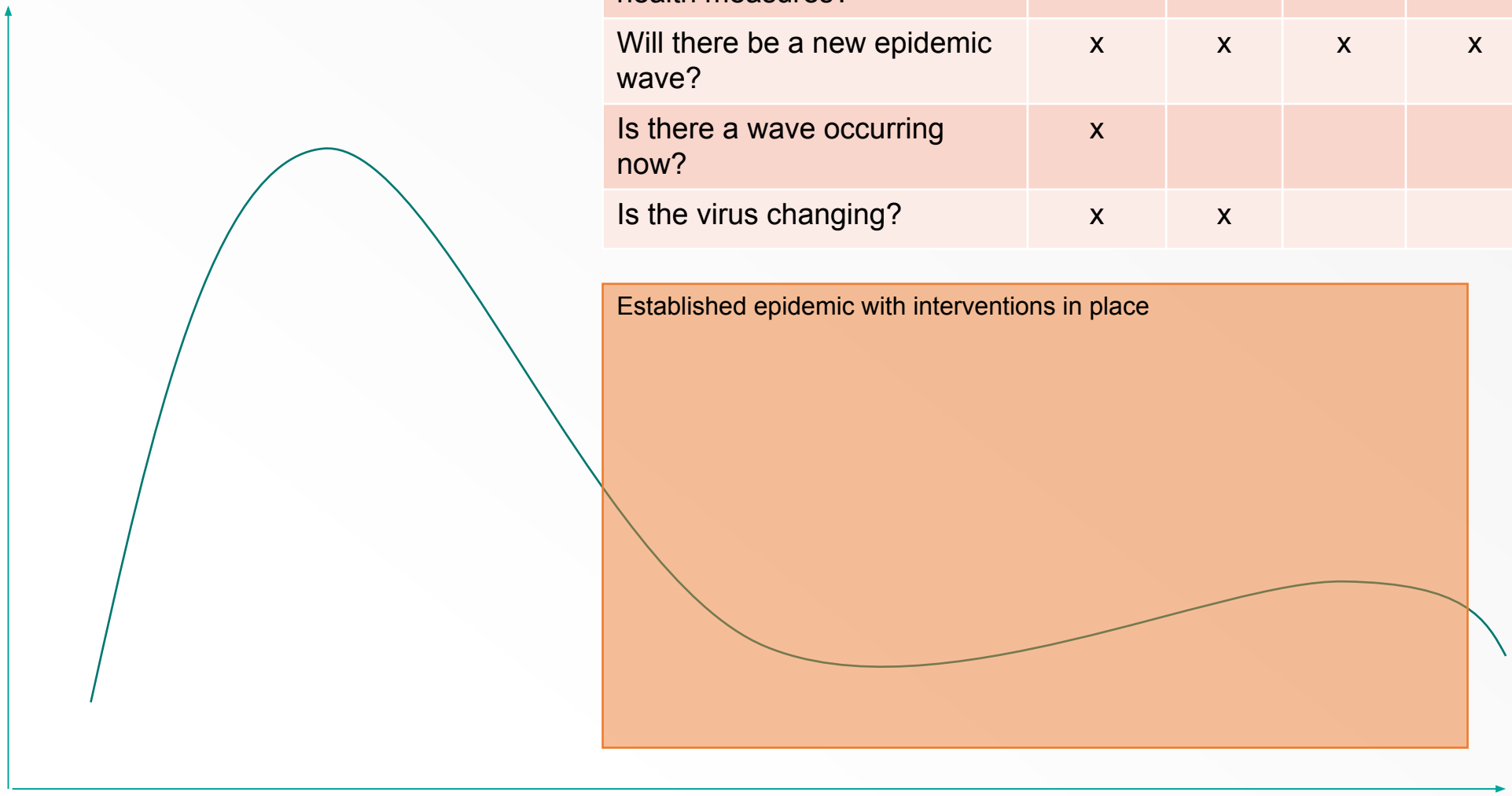


	Hospital cases	Infection	Biological	Behavioural	Virological
How quickly is the pathogen spreading?		x			
What are the clinical characteristics and severity?	x	x			
What is the possible peak timing and size?		x	x		
What are the likely impact of interventions			x		
Can we make and deploy a vaccine?				x	x



	Hospital cases	Infection	Biological	Behavioural	Virological
What is the impact on health services?	x	x			
What is the possible peak timing and size?	x				
How effective are control measures?	x	x	x	x	
Is the virus changing?	x	x	x		x

	Hospital cases	Infection	Biological	Behavioural	Virological
What was the impact of public health measures?	x	x		x	
Will there be a new epidemic wave?	x	x	x	x	x
Is there a wave occurring now?	x				
Is the virus changing?	x	x			x



Workshop outcomes

- what to measure
  - Establish protocols for monitoring biological and epidemiological characteristics affecting transmission.
  - Establish systems for monitoring infections (as distinct from cases).
  - Ensure systematic collection of behavioural data related to disease transmission and control.
- how to measure
  - Build Australia's local surveillance capabilities and infrastructure to ensure that public health response can be tailored to the Australian context.
  - Implement appropriate statistical designs to maximise the efficiency and utility of surveillance systems.

Respiratory virus surveillance

Past

- Uni-dimensional indicators
- Focus on viral activity
- Virus specific (influenza) surveillance

Future

- Multi-dimensional indicators of transmission, severity, impact
- Timely integrated surveillance with multiple complementary sources of data
- Assessment of disease control measures eg vaccine effectiveness, public health interventions
- Multiple viruses; adaptable to disease X
- *Non-respiratory syndromes? Encephalitis*

Acknowledgements

- FluCAN investigators
- Sheena Sullivan - WHOCC
- Bette Liu
- Aiden Burrell, Andrew Udy – SPRINT-SARI
- Freya Shearer, James McCaw and workshop participants