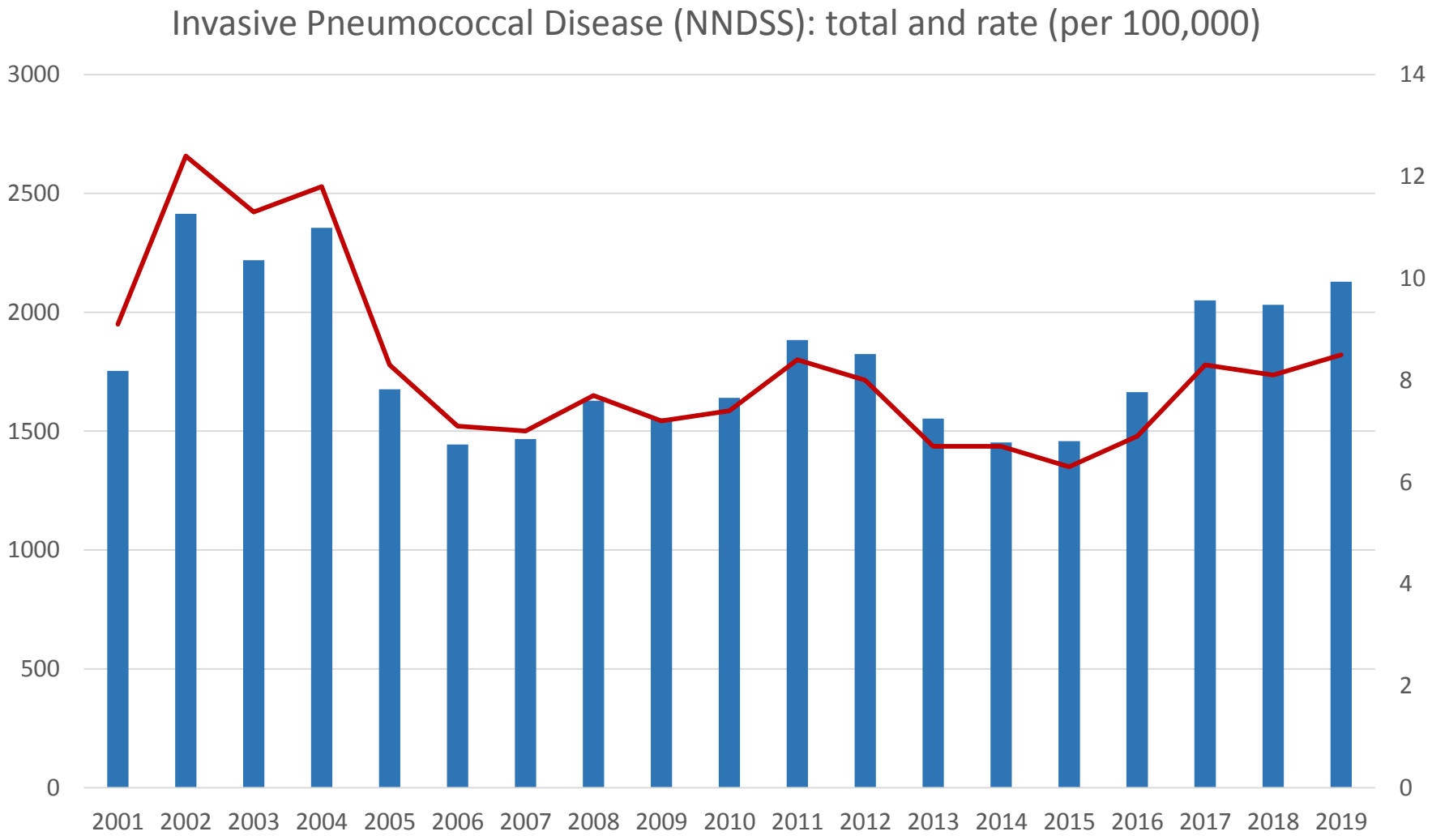
Pneumococcal disease: Immunisation strategies to improve protection for those at greatest risk

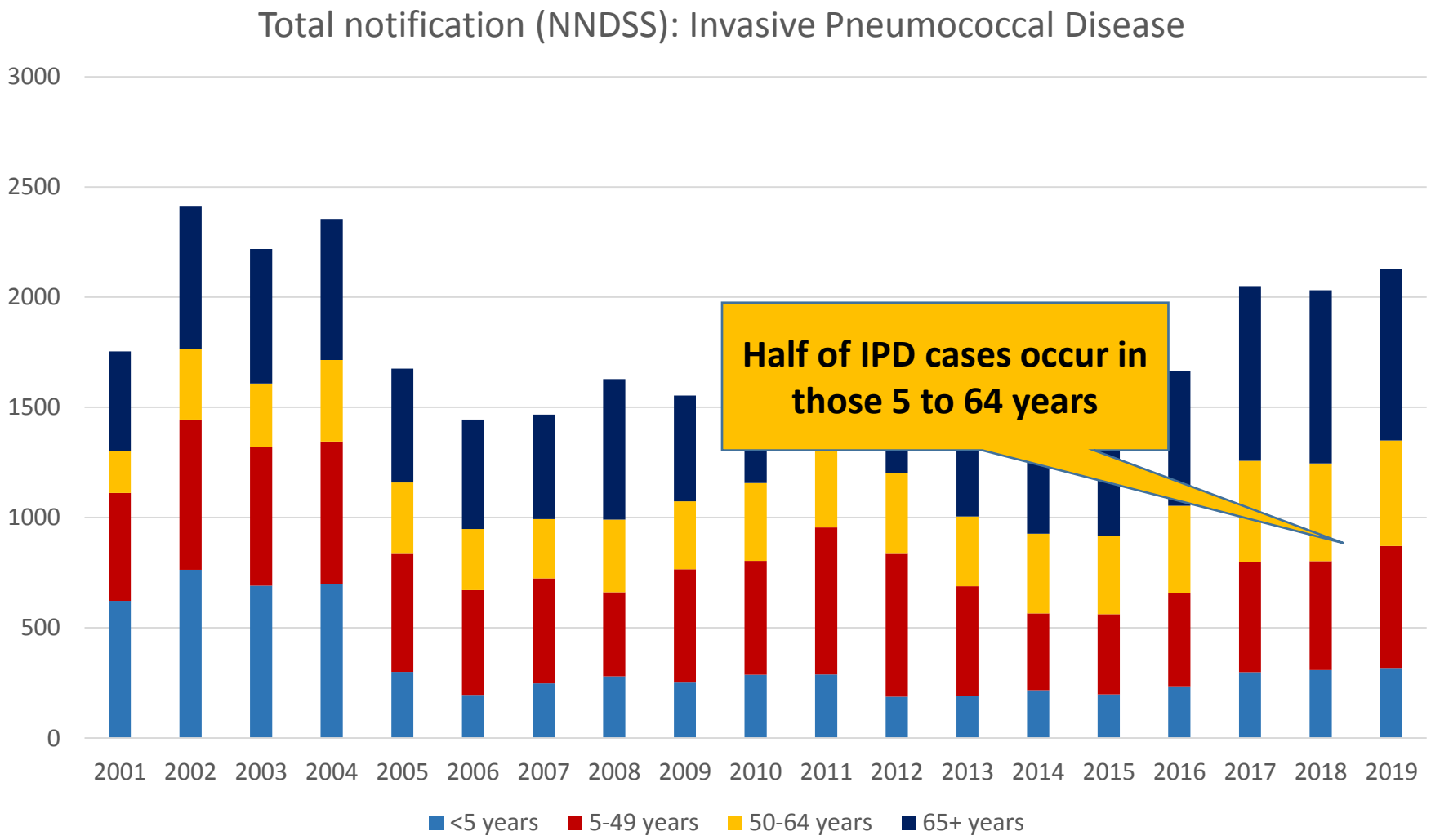
Chris Blyth

Associate Professor, School of Medicine, University of Western Australia
Co-director, Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute
Infectious Diseases Physician, Department Infectious Diseases, Perth Children's Hospital
Clinical Microbiologist PathWest Laboratory Medicine WA, QEII Medical Centre
Emerging Leadership Fellow, National Health and Medical Research Council
christopher.blyth@uwa.edu.au
@ChrisBlyth74

Current state of play



Current state of play

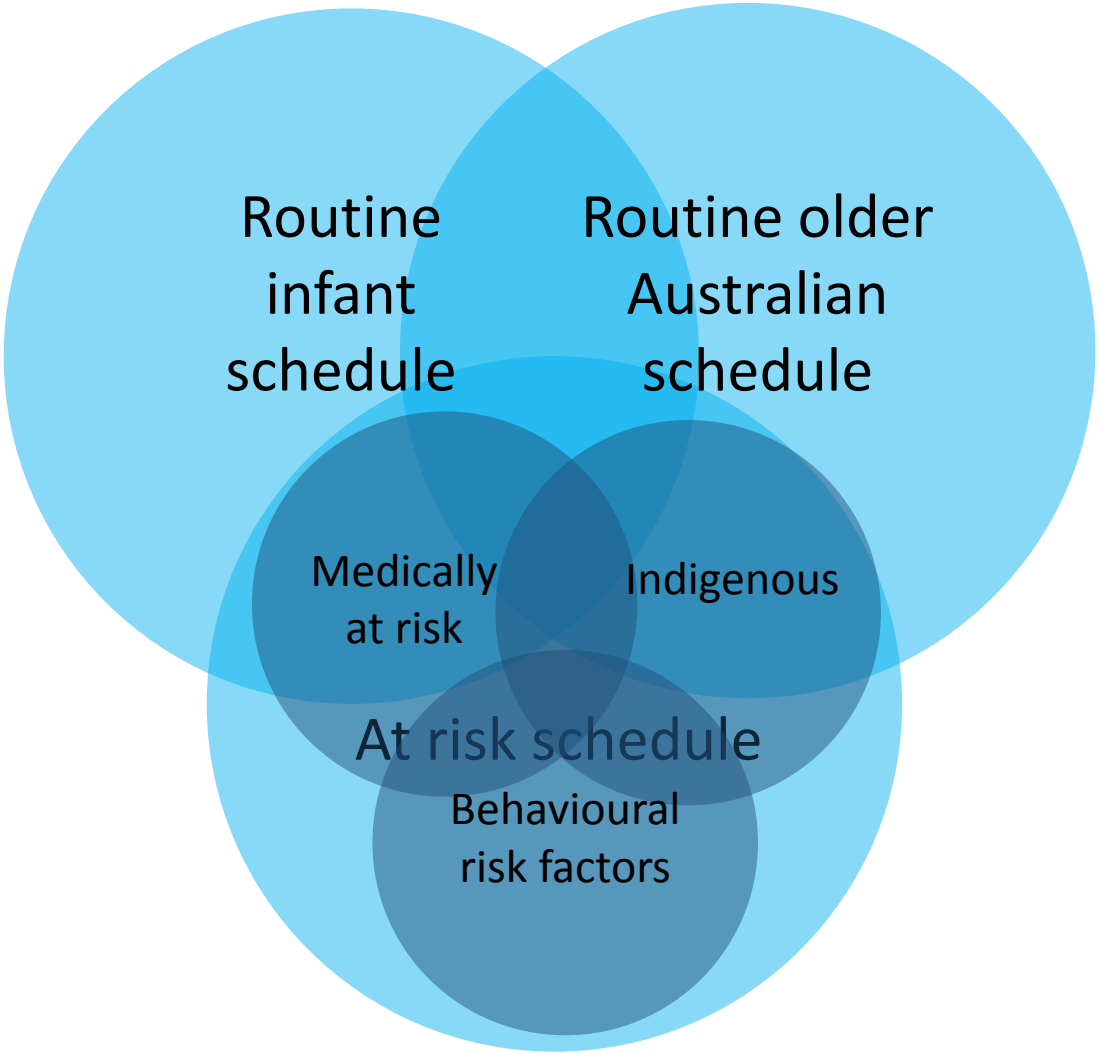


Take home message

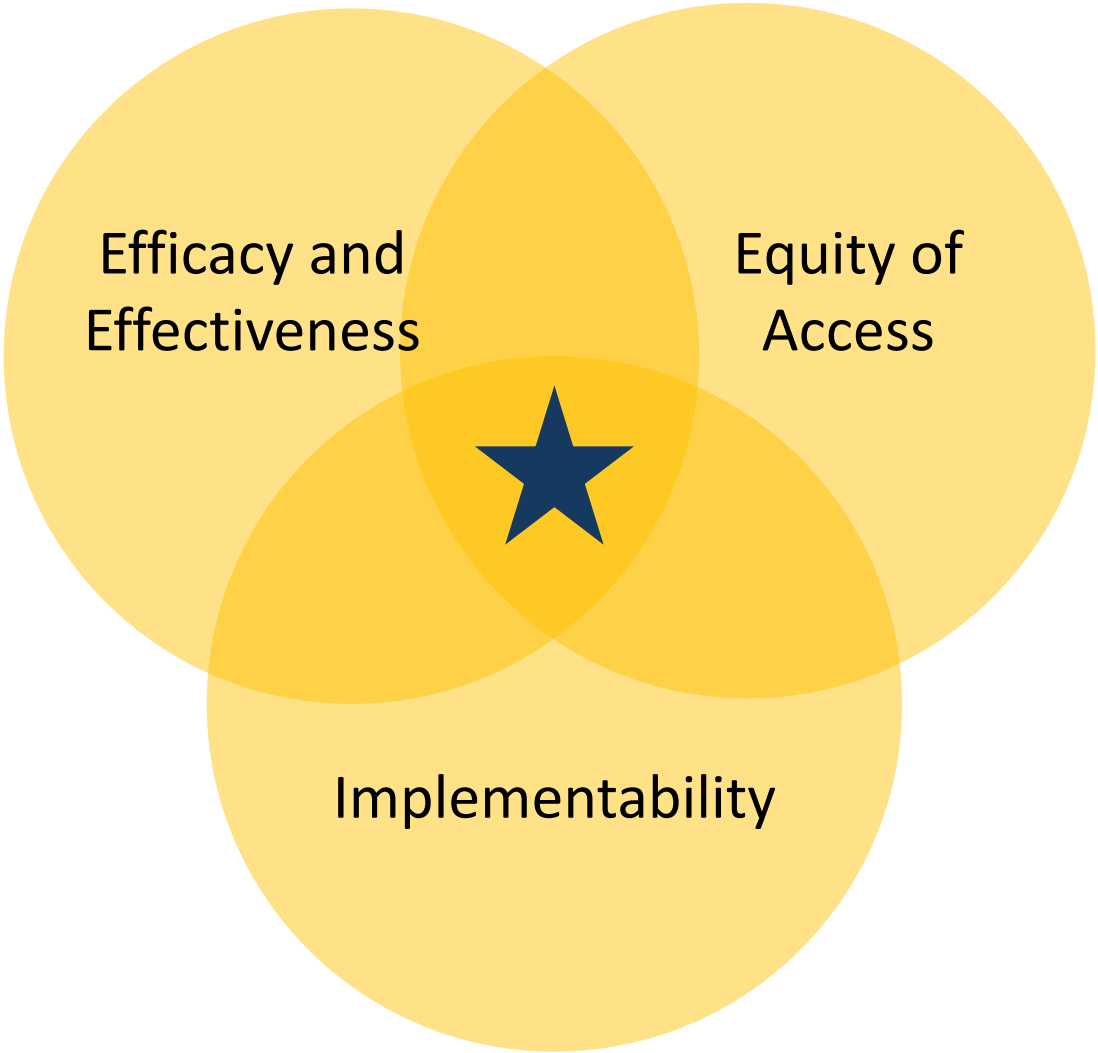
- The overall impact of current policies on pneumococcal disease control has been suboptimal
- A significant burden of disease occurs in those between 5 and 64 years, most of whom have risk factors for IPD and yet are under vaccinated
- IPD in those 65+years is mostly observed in those with risk factors for disease. This is occurring despite the current vaccination program.

What we are doing now is not working very well

Pneumococcal program



Principles guiding reforms



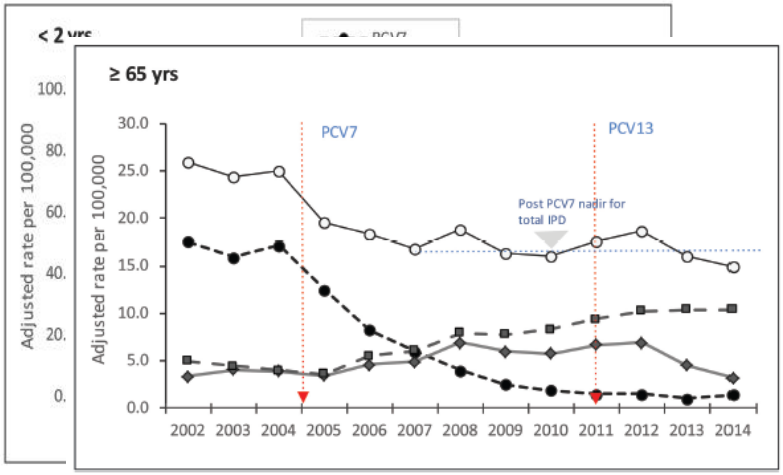
Infant schedule

Routine infant schedule

Routine infant vaccines recommended in 2005:
7vPCV in a 3+0 schedule

Routine schedule changed in 2011:
PCV13 in a 3+0 schedule
Three dose coverage: ≈94%

Significant impact on IPD due to serotypes contained in PCV13



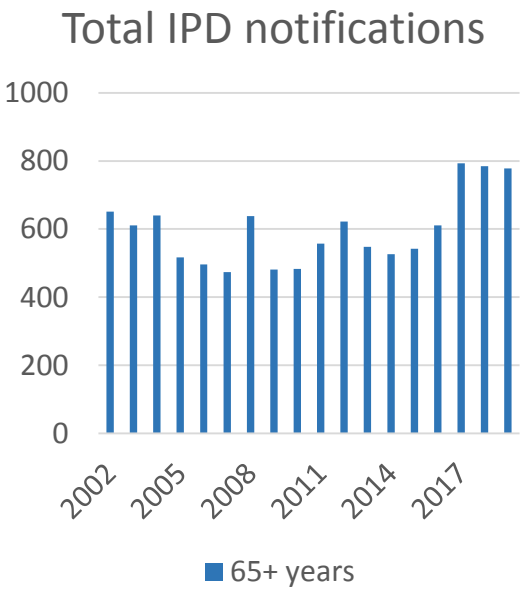
48% reduction in 13 valent types post introduction of PCV13

Jayasinghe S et al, CID 2017

Schedule for older Australians

Older vaccination program funded since 1999-2000 (NIP since 2005):
Non-Indigenous: PPV23 at 65 years
Indigenous: PPV23 at 50 years
Coverage: ≈55% (2009)

Routine older Australian schedule



Overall impact of this program is challenging to assess given infant program and absence of data prior to 2000.

VE against vaccine-type IPD: 61% (95% CI: 55-68)

VE against vaccine-type pneumonia more difficult to estimate:
Limited evidence of randomised controlled trials
Much of these data are from observational studies conducted in regions without mature infant conjugate programs

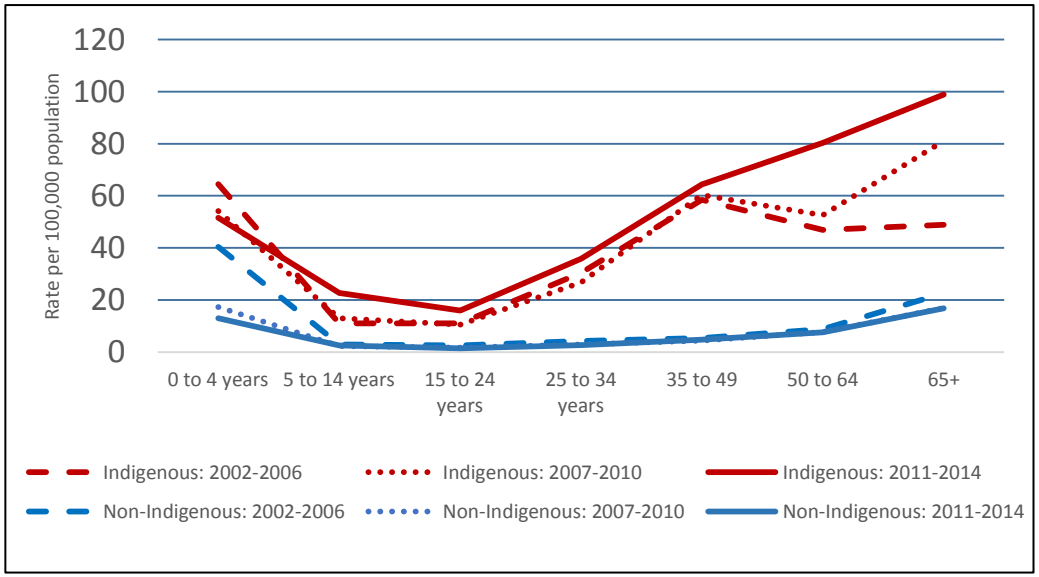
This is in contrast to 13vPCV – demonstrated VE against vaccine-type pneumonia

Menzies R et al MJA 2014; AIHW 2009 Adult vaccination survey;

At risk schedule

Complex recommendations and funding arrangements resulting in poor coverage in those at risk

IPD in Indigenous Australians:



NIP funded Indigenous program:
PPV23 (2 doses) from 50 years
Additional infant dose of PCV13 in four states

Jayasinghe S et al, ISPPD 2018

At risk schedule

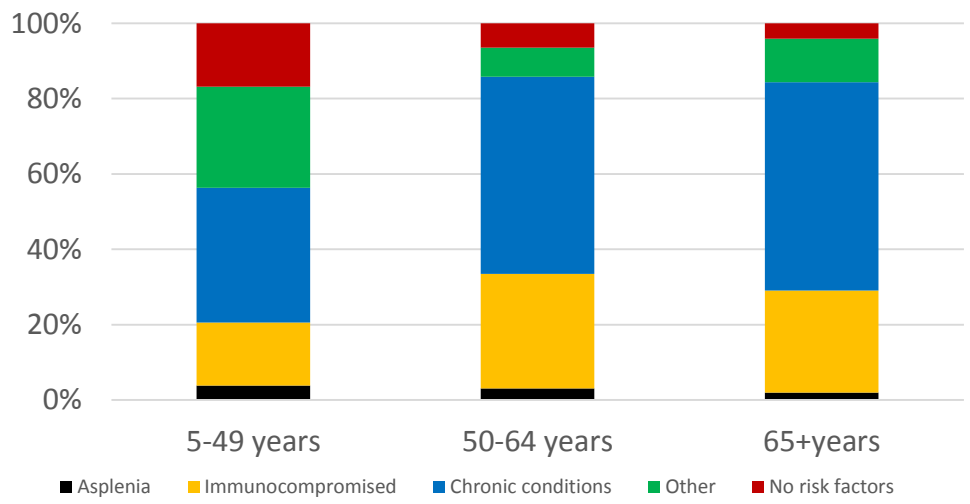
Complex recommendations and funding arrangements resulting in poor coverage in those at risk

Complex recommendations
Category A: PCV13 + PPV23
Category B: PPV23
(number of doses of PPV23 varying by risk factor)
Coverage: uncertain

Pneumococcal vaccines have <u>not</u> been NIP funded for those with comorbid conditions (PBS only):

This is despite the majority of cases of IPD occurring in those with risk factors

IPD in non-indigenous populations by comorbid condition and age (2011 to 2014):



NNDSS data: unpublished

Pneumococcal score card: 2016

What we are doing now is not working very well

Lower than expected reductions in adult diseases
Rising gap between Indigenous and non-Indigenous adults
Most populations at greatest risk not able to access funded pneumococcal vaccine
Inadequate coverage in those at greatest risk

In 2016, ATAGI sought to conduct a comprehensive review of pneumococcal vaccination to inform the NIP and handbook

Changes to the infant schedule

Routine infant schedule

Vaccine failures observed with PCV13

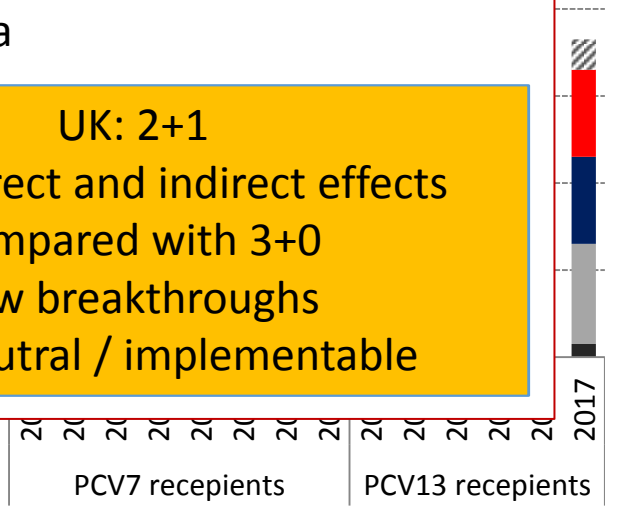
First noted in 2013:
reviewed and monitored

Reviewed in 2016: prompted more urgent review in schedule

Local and international epidemiological data were reviewed to inform optimal infant schedules for Australia

US: 3+1
Better direct and indirect effects compared with 3+0
Significant cost implication

UK: 2+1
Better direct and indirect effects compared with 3+0
Few breakthroughs
Cost neutral / implementable



Blyth CC et al, CID 2019

Changes to the at-risk schedule

- **Previous episode of invasive pneumococcal disease**
- **Immunocompromising conditions including ……**
- **Chronic respiratory conditions including ……**
- **Harmful use of alcohol**

- Previous episode of invasive pneumococcal disease
- Functional or anatomical asplenia, including sickle cell disease or other haemoglobinopathies, congenital or acquired asplenia or hyposplenia
- Immunocompromising conditions, including
  - congenital or acquired immune deficiency, including symptomatic IgG subclass or isolated IgA deficiency
  - haematological malignancies
  - solid organ and haematopoietic stem cell transplant
  - HIV infection
  - immunosuppressive therapy, where sufficient immune reconstitution for vaccine response is expected
  - non-haematological malignancies receiving chemo or radiotherapy
- Proven or presumptive CSF leak, including cochlear implants and intracranial shunts
- Chronic respiratory disease, including suppurative lung disease, bronchiectasis, cystic fibrosis, severe asthma, chronic lung disease in preterm infants
- Chronic renal disease, including relapsing or persistent nephrotic syndrome and chronic renal impairment (eGFR <30 mL/min)
- Cardiac disease, including congenital heart disease, coronary artery disease and heart failure
- Children born less than 28 weeks gestation
- Trisomy 21
- Chronic liver disease, including chronic hepatitis, cirrhosis, biliary atresia
- Diabetes
- Smoking (current or in the immediate past)
- Harmful use of alcohol

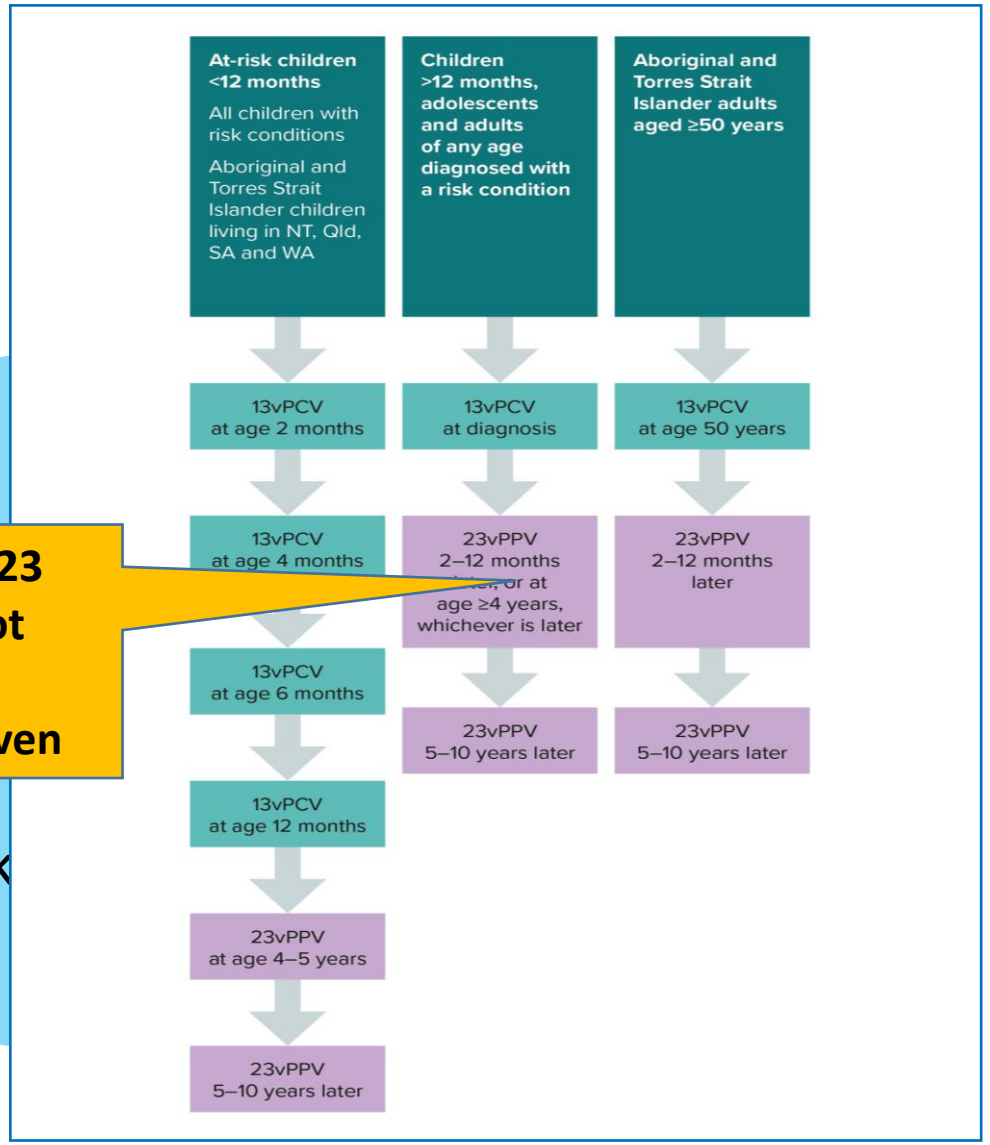
Changes to the at-risk schedule

Feedback from providers were that previous recommendations were too complex

A review of pneumococcal dosing schedules to simplify existing recommendations or those with risk factors

- **If previously doses of PPV23 given, repeating dosing not required**
- **If not documented, not given**

At risk



Changes for older Australians

The role of PCV13, PPV23 or mixed schedules in older populations

Pfizer PCV13 application to replace a dose of PPV23 with PCV13 in older Australians based primarily on data from the CAPiTA trial (PCV13 vs placebo against pneumococcal CAP)
PBAC commissioned independent review of the cost effectiveness of PPV23

Conclusions of the PBAC

Replacing one dose of PPV23 with PCV13 was likely to be cost effective in older Australians.
PPV23 is unlikely to be cost-effective when provided to the total population ≥65 years.

Upon further consideration by the PBAC

PCV13 followed by up to two doses of PPV23 is likely to be cost-effective in Indigenous Australians ≥ 50 years given low opportunity cost and overall cost to government.
The same schedule is expected to be cost effective in specific at-risk populations.

PBAC public summary documents: http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes/recommendations-pbac-july-2019

Changes to the at-risk schedule

Feedback from providers were that previous recommendations were too complex

Extensive literature review to inform creation of a “single” at risk table

- **PCV13 + PPV23 + PPV23 funded for many very high risk patients previously unable to access funded pneumococcal vaccine**

At risk

- Previous episode of invasive pneumococcal disease
- Functional or anatomical asplenia, including sickle cell disease or other haemoglobinopathies, congenital or acquired asplenia or hyposplenia
- Immunocompromising conditions, including
  - congenital or acquired immune deficiency, including symptomatic IgG subclass or isolated IgA deficiency
  - haematological malignancies
  - solid organ and haematopoietic stem cell transplant
  - HIV infection
  - immunosuppressive therapy, where sufficient immune reconstitution for vaccine response is expected
  - non-haematological malignancies receiving chemo or radiotherapy
- Proven or presumptive CSF leak, including cochlear implants and intracranial shunts
- Chronic respiratory disease, including suppurative lung disease, bronchiectasis, cystic fibrosis, severe ashtma and chronic lung disease in preterm infants
- Chronic renal disease, including relapsing or persistent nephrotic syndrome and chronic renal impairment (eGFR <30 mL/min)
- Cardiac disease, including congenital heart disease, coronary artery disease and heart failure
- Children born less than 28 weeks gestation
- Trisomy 21
- Chronic liver disease, including chronic hepatitis, cirrhosis, biliary atresia
- Diabetes
- Smoking (current or in the immediate past)
- Harmful use of alcohol

Changes to the at-risk schedule

Feedback from providers were that previous recommendations were too complex

Extensive literature review to inform creation of a “single” at risk table

At risk sc

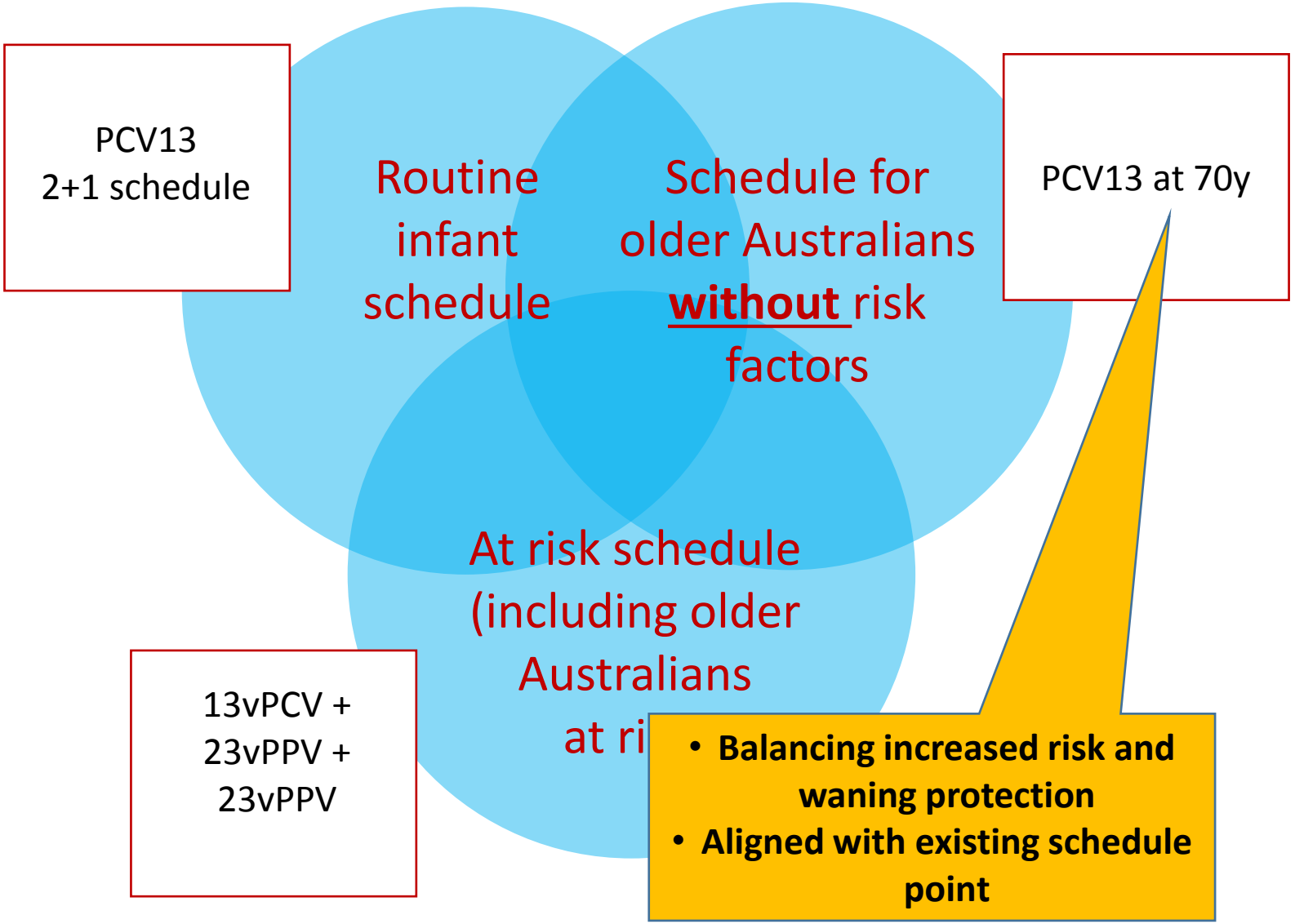
List. Updated list of risk conditions for pneumococcal vaccine recommendations and their eligibility for funding under the national immunisation program (NIP)

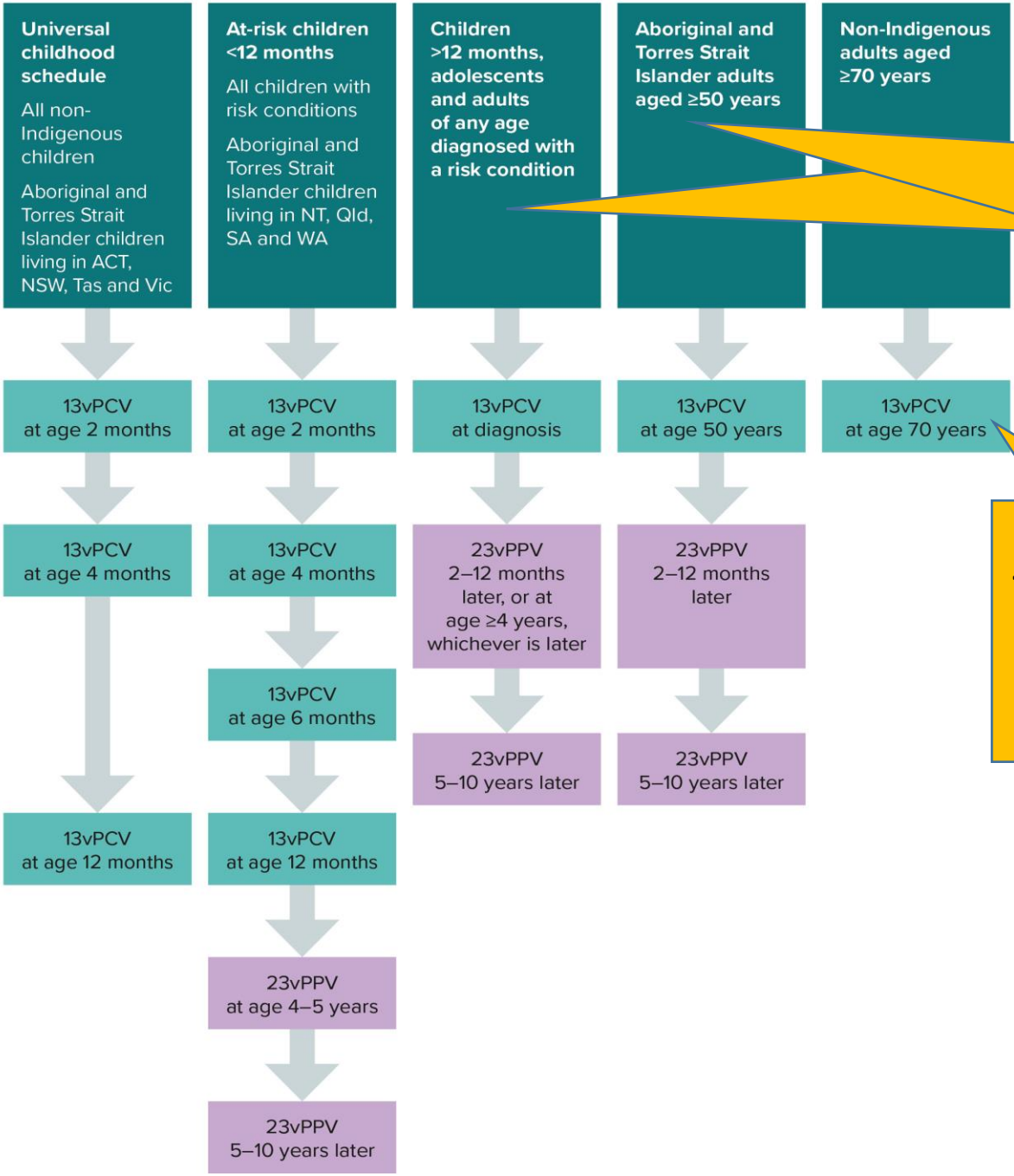
Risk condition	Eligibility for NIP funding	
	<5 years of age	≥5 years of age
Previous episode of invasive pneumococcal disease	✓	✓
Functional or anatomical asplenia, including		
– sickle cell disease or other haemoglobinopathies	✓	✓
– congenital or acquired asplenia (for example, splenectomy) or hyposplenia	✓	✓
Immunocompromising conditions, including		
– congenital or acquired immune deficiency, including symptomatic IgG subclass or isolated IgA deficiency	✓	✓
– haematological malignancies	✓	✓
– solid organ transplant	✓	✓
– haematopoietic stem cell transplant	✓	✓
– HIV infection	✓	✓
– immunosuppressive therapy, where sufficient immune reconstitution for vaccine response is expected; this includes those with underlying conditions requiring but not yet receiving immunosuppressive therapy		
– non-haematological malignancies receiving chemotherapy or radiotherapy (currently or anticipated)		
Proven or presumptive cerebrospinal fluid (CSF) leak, including		
– cochlear implants	✓	✓
– intracranial shunts	✓	✓
Chronic respiratory disease, including¶		
– suppurative lung disease, bronchiectasis and cystic fibrosis	✓	✓
– chronic lung disease in preterm infants	✓	✓
– chronic obstructive pulmonary disease (COPD) and chronic emphysema		
– severe asthma (defined as requiring frequent hospital visits or the use of multiple medications)		
– interstitial and fibrotic lung disease		
Chronic renal disease		
– relapsing or persistent nephrotic syndrome	✓	✓
– chronic renal impairment – eGFR <30 mL/min (stage 4 or 5 disease)	✓*	✓*
Cardiac disease, including¶		
– congenital heart disease	✓	
– coronary artery disease	✓	
– heart failure	✓	
Children born less than 28 weeks gestation	✓	
Trisomy 21	✓	
Chronic liver disease, including¶		
– chronic hepatitis		
– cirrhosis		
– biliary atresia		
Diabetes		
Smoking (current or in the immediate past)		
Harmful use of alcohol (Defined as consuming on average ≥60 g of alcohol (6 Australian standard drinks) per day for males and ≥40 g of alcohol (4 Australian standard drinks) per day for females)		

* Funded under the NIP for eGFR <15 mL/min only (including patients on dialysis)
¶ Individual conditions listed beneath or those that are similar based on clinical judgment

Note: All children and adults with above conditions are recommended to receive additional pneumococcal vaccine doses but they are funded under the NIP for those with the shaded conditions

Proposed pneumococcal program




Universal childhood schedule
All non-Indigenous children
Aboriginal and Torres Strait Islander children living in ACT, NSW, Tas and Vic
At-risk children <12 months
All children with risk conditions
Aboriginal and Torres Strait Islander children living in NT, Qld, SA and WA
Children >12 months, adolescents and adults of any age diagnosed with a risk condition
Aboriginal and Torres Strait Islander adults aged ≥50 years
Non-Indigenous adults aged ≥70 years
13vPCV at age 2 months
13vPCV at age 4 months
13vPCV at age 12 months
13vPCV at age 2 months
13vPCV at age 4 months
13vPCV at age 6 months
13vPCV at age 12 months
23vPPV at age 4–5 years
23vPPV 5–10 years later
13vPCV at diagnosis
23vPPV 2–12 months later, or at age ≥4 years, whichever is later
23vPPV 5–10 years later
13vPCV at age 50 years
23vPPV 2–12 months later
23vPPV 5–10 years later
13vPCV at age 70 years
Many at risk populations may have previously received 23vPPV but unlikely to have received 13vPCV. Please check and give catch up!
This includes those who have previously received 23vPPV

Looking forward

What ever we are doing now is not working very well

- NIP funding of PCV13 + PPV23 for those at greatest risk of disease will improve compliance and reduce IPD
- Simplification of the pneumococcal schedules will make implementation easier
- Infant changes will enhanced indirect effects
- Pneumococcal epidemiology will need to be monitored to assess impact and evitable changes in pneumococcal serotypes and disease