Benefits of schedule switch from 3+0 to 2+1 for 13vPCV in Australian children

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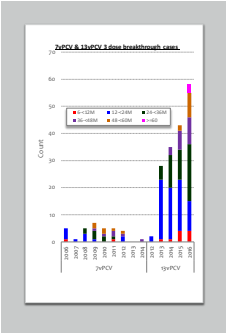
Background

- "3p+0" schedule (doses at 2,4 and 6 months, no booster) introduced in 2005 when 7vPCV was included on the NIP
- "3p+0" continued when 13vPCV replaced 7vPCV in 2011
  - Decision based on experience with 7vPCV providing adequate protection in infancy
- Increase in 13vPCV vaccine failures from 2013 in children > 12 months of age triggered exploration of a booster dose
- Comparing "3p+0" with other schedules, it was noted:
  - Lower rates of VFs are being observed with alternative schedules which include a 2nd year of life booster
  - Greater reductions in disease in un-vaccinated individuals (herd effects) are observed with alternative schedules with 2nd year of life booster
- ATAGI recommended moving 3rd dose to age 12 months
  - NHMRC endorsed post public consultation in Sep 2017
  - PBAC positive recommendation in April 2018



Results - Breakthrough cases

Schedule	Age <12 months		Age ≥12 months		Total	
	Severe IPD[†]	All IPD	Severe IPD[†]	All IPD	Severe IPD[†]	All IPD
AUS (observed, 3+0 schedule)	1	7	24	101	25	108
UK (observed, 2+1 schedule)	19	41	18	28	37	69
AUS (imputed, 2+1 schedule[‡])	8	18	8	12	16	30

Rate of breakthrough IPD in children ≥12 months of age
- 3.4 cases/10^6 in Australia
- 0.7 cases/10^6 in UK

Total numbers over the first 4 years of the program presented

Key assumption: differential 13vPCV effect attributable to schedule

[†]Includes pneumococcal meningitis and pneumonia with empyema/effusion
[‡]Crude extrapolation to estimate number expected if 2+1 schedule was used instead of 3+0 schedule in this period by accounting for the difference in birth cohort sizes of 700,000 in the UK and 300,000 in Australia [n=37], rounded to nearest whole number

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AUS (difference between imputed and observed)	+7	+11	−16	−89	−9	−78

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Total numbers over the first 4 years of the program presented

Cases that could have been averted in four years of 13vPCV if 2+1 was used
- 89 in children aged ≥12 months
  - may have been offset by 11 more cases in age 6-12 months (~3/ Yr)
- Nett cases averted 78

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Results - Population impact

Age group (years)	Cases averted if 2+1 used
< 2 years	-23
2-4 years	-49
5-14 years	-28
15-44 years	-50
45-64	-65
65+	-53
Age adjusted total	-268

Any residual disease (including that in young infants), is expected to be further reduced by population impacts

- IRR for 13v serotypes for the 5 years post 13vPCV substantially higher in UK than Australia
- Had the 2+1 schedule been used in Australia a total of ~270 fewer cases of 13vPCV serotype IPD would have been observed in fifth post-13vPCV introduction year

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Conclusion

- Substantial reductions in vaccine type IPD across all age groups with 13vPCV using a 3p+0 schedule has been observed
- Unlike 7vPCV 3p+0 which appeared comparable to booster dose schedules (2p+1), 13vPCV 3p+0 appears inferior
  - ? VE waning
  - ? Less impact on carriage
- 2p+1 schedule likely result in less breakthrough & greater herd benefit
  - Potential small increase in 2 dose VFs between 6-12 months age likely to be only transient
- No change to 4 dose (3p+1) 13vPCV schedule in at risk groups
  - Including Indigenous children in NT, QLD, SA & WA
- Post schedule change essential to
  - Carefully monitor IPD incidence in routine surveillance
  - Undertake comprehensive evaluation at pre-determined time point to ensure expected benefits achieved