This house believes that a 2+1 PCV schedule is preferable to a 3+0 PCV schedule in LMICs.
Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years

O’Brien et al, Lancet 2009
Philosophy

a theory or attitude that acts as a guiding principle for behaviour
This house believes that a 2+1 PCV schedule is preferable to a 3+0 PCV schedule in LMICs.
Pneumococcal schedules

- 3+0 = 6, 10 and 14 weeks
- 2+1 = 6, 14 weeks and 9 months
- 2+1 = 2, 4 months and 9/12 months
Timeliness of vaccination in 45 LMIC/LICs

Clark and Sanderson, Lancet 2009
Pneumococcal Conjugate Vaccine (PCV) Review of Impact Evidence (PRIME)
Summary of Findings from Systematic Review

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**Table 1: Summary of evidence from head to head comparisons at the post-primary time point**

<table>
<thead>
<tr>
<th>Result</th>
<th>GMC: Similar</th>
<th>GMC: Favors 3p</th>
<th>GMC: Favors 3p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%Response: Similar</td>
<td>%Response: Similar</td>
<td>%Response: Favors 3p</td>
</tr>
<tr>
<td>Serotypes</td>
<td>3</td>
<td>1</td>
<td>6A*</td>
</tr>
<tr>
<td></td>
<td>19F</td>
<td>5</td>
<td>6B*</td>
</tr>
</tbody>
</table>

*Prevalence Ratio (PR) For % response 2p vs 3p = 0.93 for 6A and 0.77 for 6B*
Post-primary in 2+1 vs 3+0

GMC

Hamaluba et, Lancet ID al 2015
**Table 2: Summary of evidence from head to head comparisons at the post-dose 3 time point**

<table>
<thead>
<tr>
<th>Result</th>
<th>GMC: Similar %Response: Similar</th>
<th>GMC: Favors 2+1 %Response: Similar</th>
<th>GMC: Favors 2+1 %Response: Favors 2+1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotypes</td>
<td>3*</td>
<td>1</td>
<td>6B**</td>
</tr>
<tr>
<td></td>
<td>19A</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

*2 studies, 1 with GMC 2+1<<GMC 3+0, 1 with GMCs equal

**Prevalence Ratio (PR) for % response 2+1 vs 3+0 = 1.13**

Ratio of proportions above cut-off for 2+1 vs. 3+0 schedule

**RCTs Post-3rd dose % responders**
Antibody at 10 months of age after booster in 2+1 vs persistence in 3+0

Hamaluba et, Lancet ID al 2015
Post-booster persistence

Hamaluba et, Lancet ID al 2015
**Figure 9:** Head-to-head trials comparing PCV10-type carriage in children who received 3+0 vs 2+1 schedules

Footnote: In the Finland trial, the 3+0 arm was assessed at 11.5m of age while the 2+1 arm was assessed 3 months later at 14.5m of age where carriage was higher in the control arm (carriage increased with age in this trial, shown here for both ages in RCTS Carriage post “booster”).
Other studies Carriage post "booster"
Figure 11: Vaccine-type NP carriage before and after PCV10/13 introduction in countries using 3+0 (blue lines) vs 2+1 schedules (red lines), for all studies

- Pre-PCV7 Carriage
- PCV10/13 Introduced (Year=0)
- Malawi 3+0 PCV13 post-only data
- Malawi 3+0 PCV13 <1yrs
- *Gambia 3+0 PCV13 <1yrs (Roca, 2015)
- Australia 3+0 PCV13 <3y (Moi, 2016)
- Aboriginal (Wigler, 2014)
- Burkina Faso 3+0 PCV13 <5y (Mois, 2016)
- Malawi 3+0 CU PCV13 3-5y (Swarthout, 2016)
- Cambodia 3+0 PCV13 0-11m (Sonkuong, 2016)
- *France 2+1 PCV13 <2yrs (Dumas, 2015)
- *Norway 2+1 PCV13 <2yrs (Steens, 2016)
- *Israel 2+1 CU PCV13 <5 yrs (Dahlo; Ben Shimol, 2016)
- *UK 2+1 PCV13 <5y (Devine; Jones, 2016)
- So.Af. 2+1 PCV13 <2yrs (Nzente, 2016)
- *UK 2+1 CU PCV13 <S yrs (Van Hoek)
- So.Af. 2+1 CU PCV13 <2yrs (Nzente, 2016)
- Mozambique 3+0 PCV10 <2y (Sigaque, 2015)
- *Kenya 3+0 CU PCV10 <2y (Hammitt, 2016)
- *Kenya 3+0 PCV10 <5y (Kim, 2016)
- *Kenya 3+0 PCV10 <5y (Kim, 2016)
- Fiji 3+0 PCV10 <2y (Dunne, 2016)
- Sweden 2+1 PCV13 < (Galana, 2016)

Post-implementation Carriage observational data

*Statistically significant reduction in carriage

**Grey triangles represent prior use of PCV7, but no pre-PCV7 carriage data are available so the slope of the line is unknown. The triangle's left edge extends to the year of PCV7 intro.
Figure 20: Percent change in prevalence of PCV10 VT carriage compared to the pre PCV period by schedule

Median of 2 year post-PCV10, years 2011-2015
**Prior use of PCV7

*** Jokinen 2016: comparison is between 3 years post-PCV10 and 1 year post-PCV10 among siblings of controls

Indirect effects on carriage
**Figure 21: Carriage prevalence of PCV10 serotypes over time among adults in pre-post survey studies by schedule**

Indirect effects on carriage in adults
Figure 23: Impact on PCV13 IPD types vs pre PCV period by schedule

Figure 24: Impact on PCV13-type IPD vs PCV7 period by schedule

Impact on IPD

*Post PCV13 data are an average rate combining all PCV13 years
**Country with PCV13 use following interim period of PCV10 use
PCV10/13 period were very heterogeneous, ranging from a 59% decrease to a 16% increase (Figure 27 and Figure 30: Impact on clinical pneumonia in countries without prior PCV7 use)
3+0 and 2+1 schedules are similar in impact
WHO Position- Schedule

For administration of PCV to infants, WHO recommends a 3-dose schedule administered either as 2p+1 or as 3p+0, starting as early as 6 weeks of age.
Philosophy vs Evidence

• Scientists generate evidence to challenge beliefs and make rational decisions