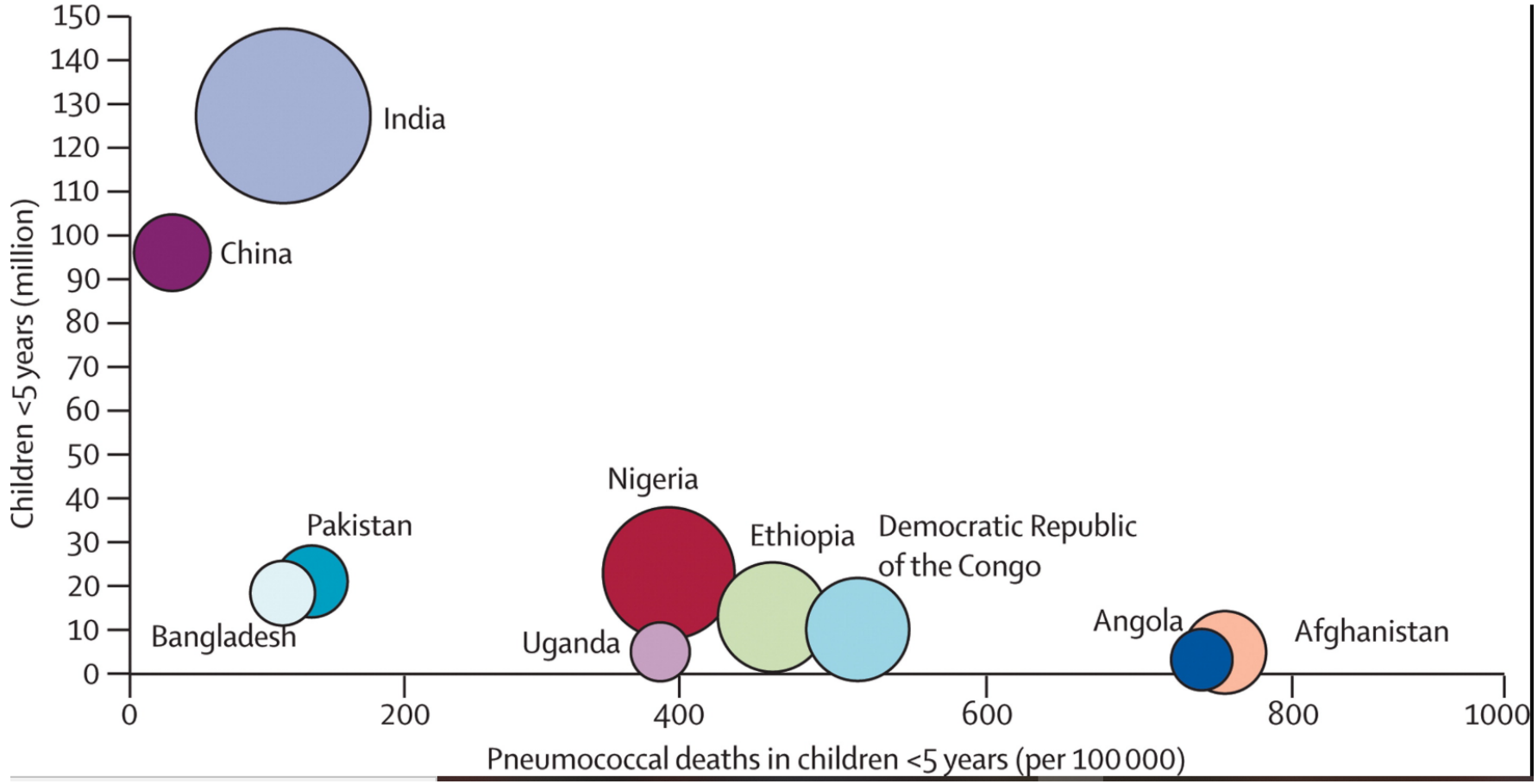
This house believes that a 2+1 PCV schedule is preferable to a 3+0 PCV schedule in LMICs

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

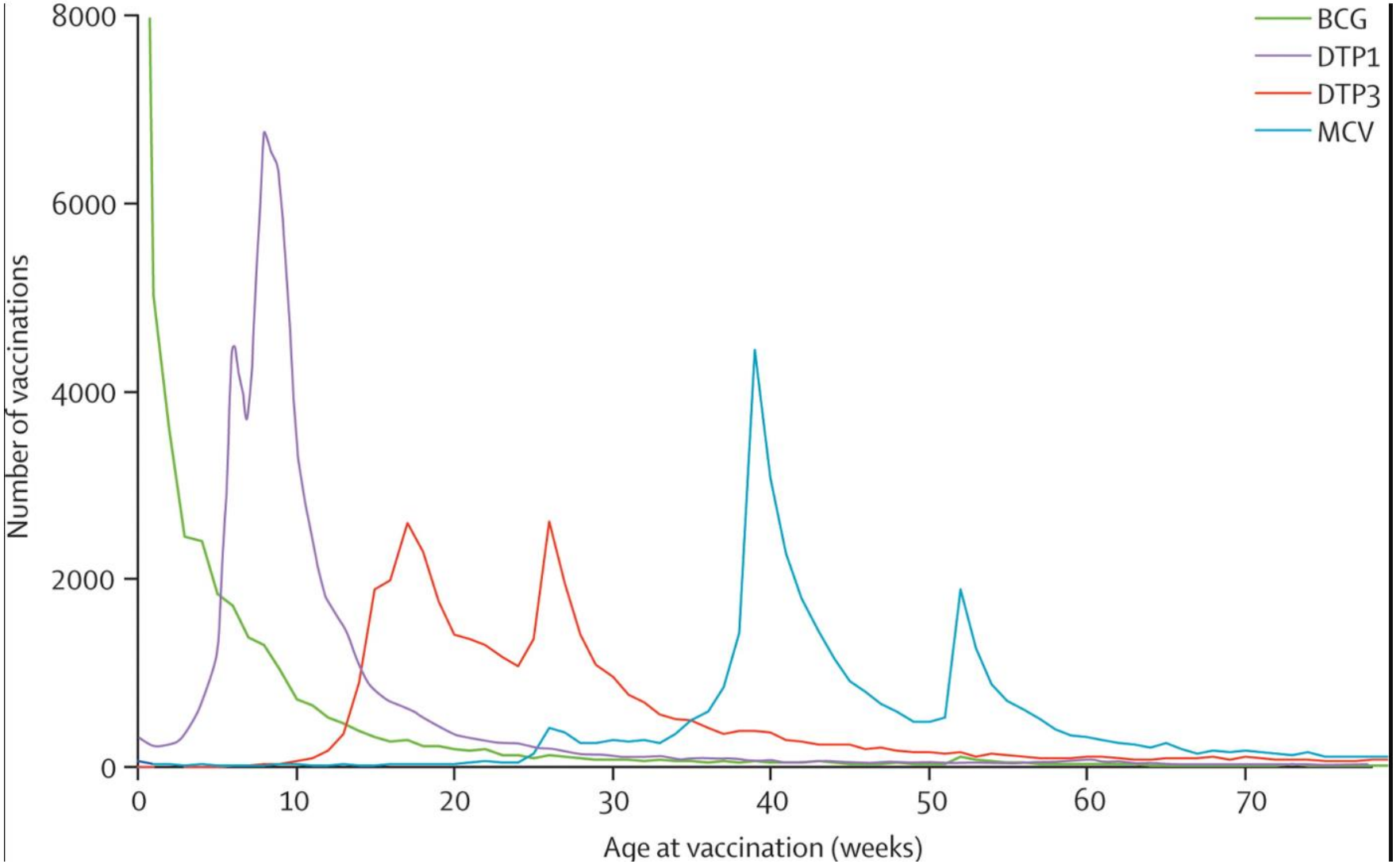
No

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

International Vaccine Access Center

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Pan-American Health Organization

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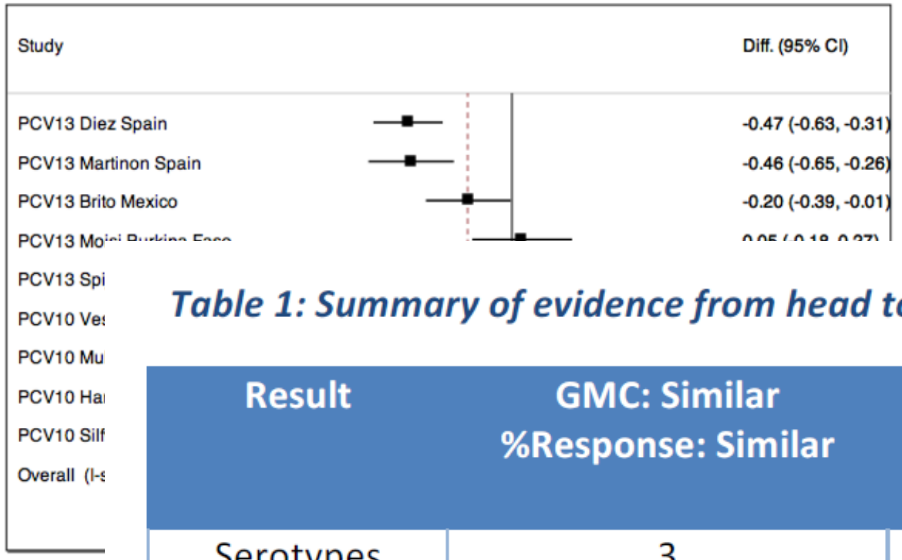
https://www.who.int/immunization/sage/meetings/2017/october/3_FULL_PRIME_REPORT_2017Sep26.pdf

https://www.who.int/immunization/sage/meetings/2017/october/02_Knoll_FINAL_PRIME_SAGEpres2017Oct16.pdf?ua=1

SEROTYPE 1:



SEROTYPE 6B:

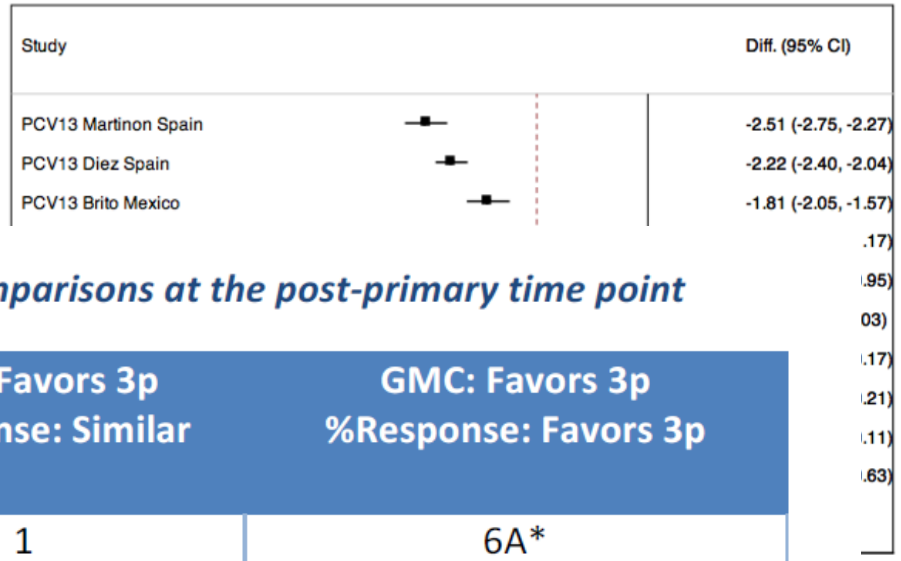
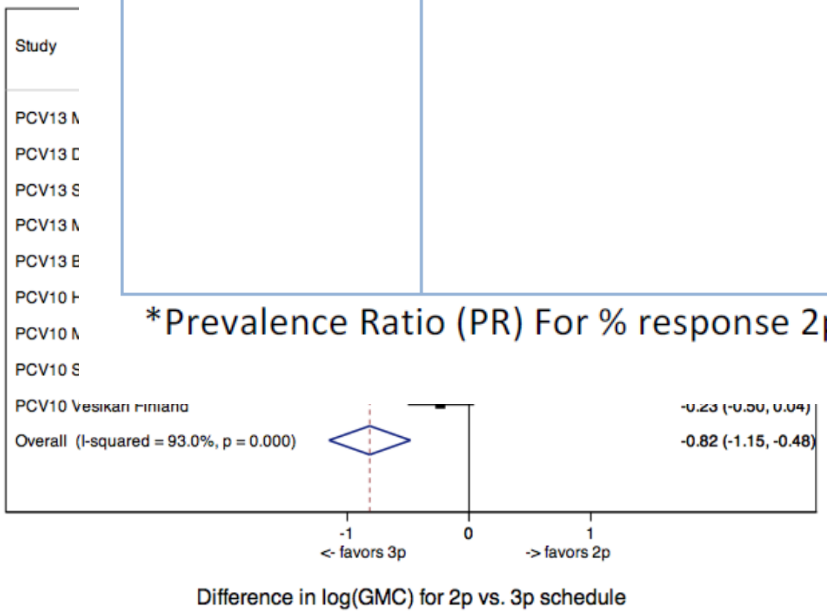


Table 1: Summary of evidence from head to head comparisons at the post-primary time point

Result	GMC: Similar %Response: Similar	GMC: Favors 3p %Response: Similar	GMC: Favors 3p %Response: Favors 3p
Serotypes	3 19F	1 5 7F 14 19A 23F	6A* 6B*

*Prevalence Ratio (PR) For % response 2p vs 3p =0.93 for 6A and 0.77 for 6B

SEROTYPE 23

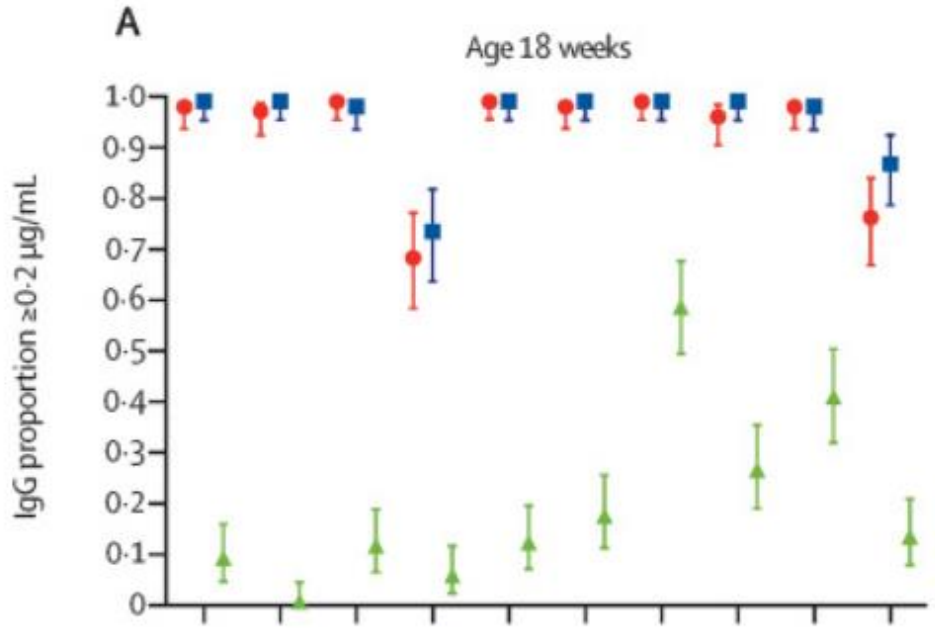


Difference in log(GMC) for 2p vs. 3p schedule

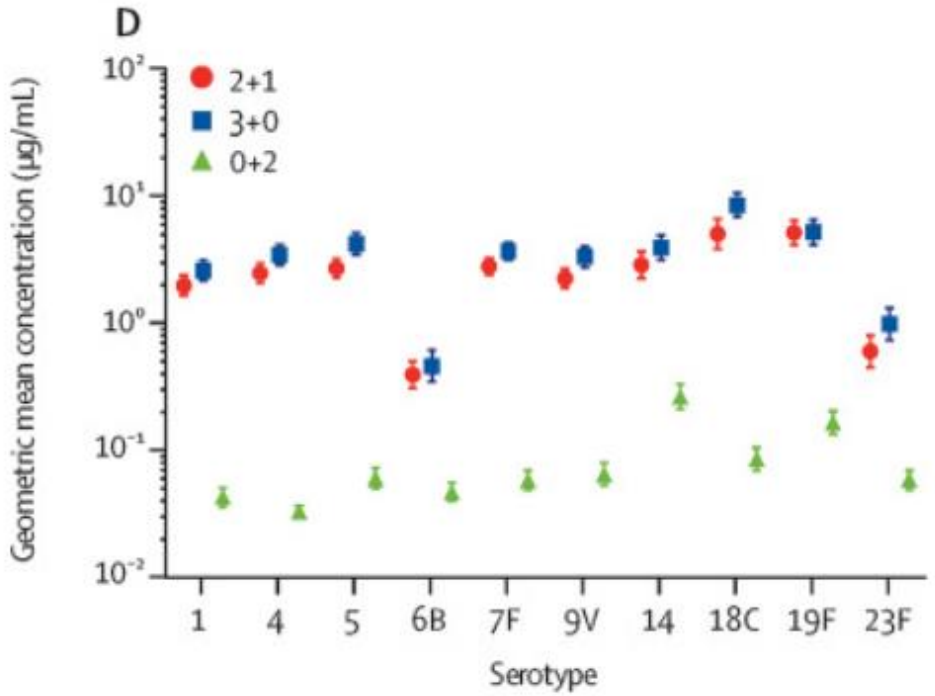
RCTs Post-primary GMC

Post-primary in 2+1 vs 3+0

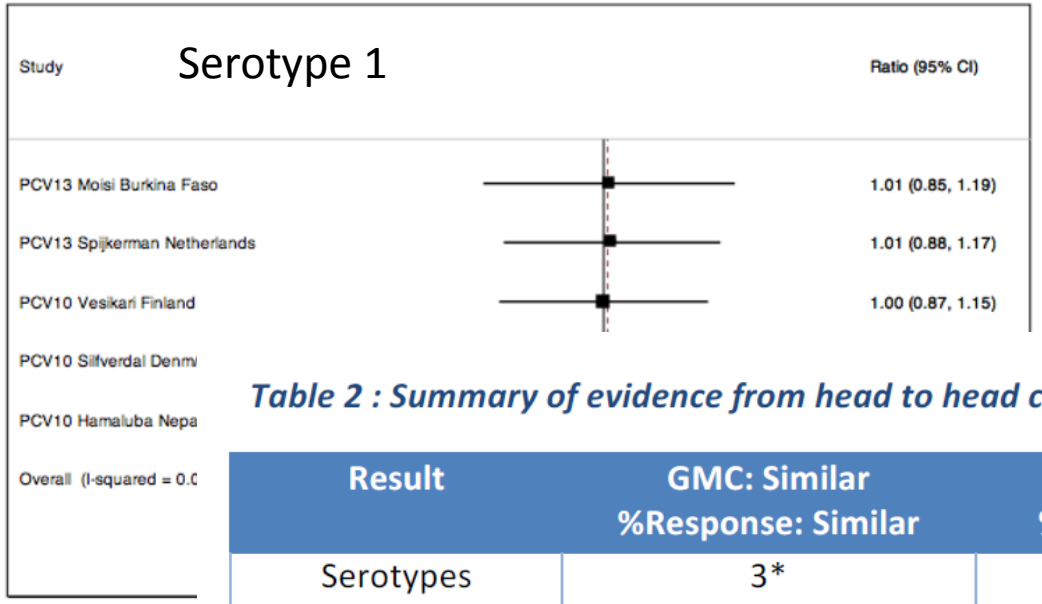
%>0.2



GMC



Hamaluba et, Lancet ID al 2015



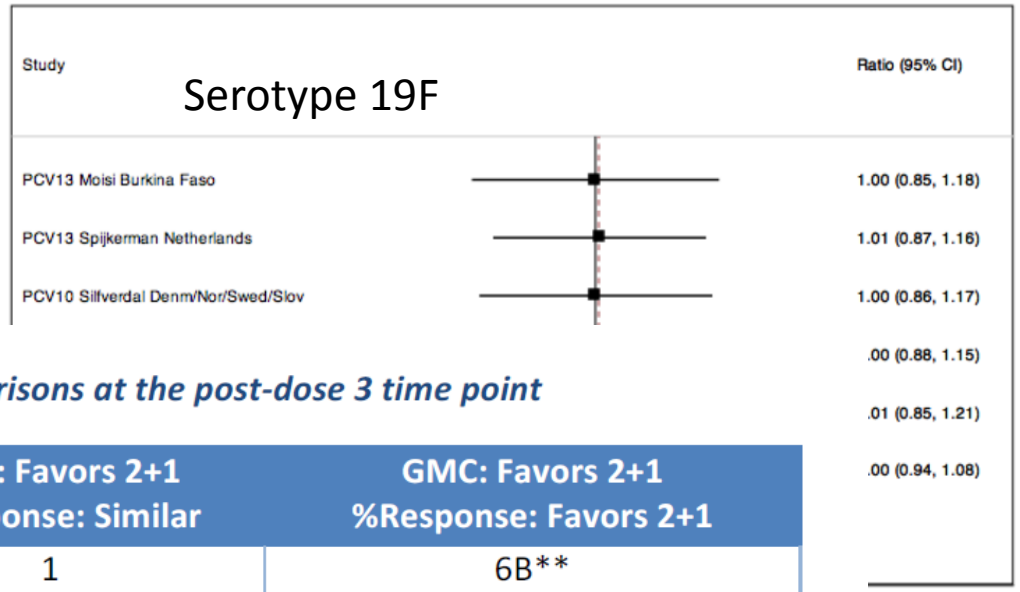


Table 2 : Summary of evidence from head to head comparisons at the post-dose 3 time point

Result	GMC: Similar %Response: Similar	GMC: Favors 2+1 %Response: Similar	GMC: Favors 2+1 %Response: Favors 2+1
Serotypes	3* 19A	1 5 6A 7F 14 19F 23F	6B**

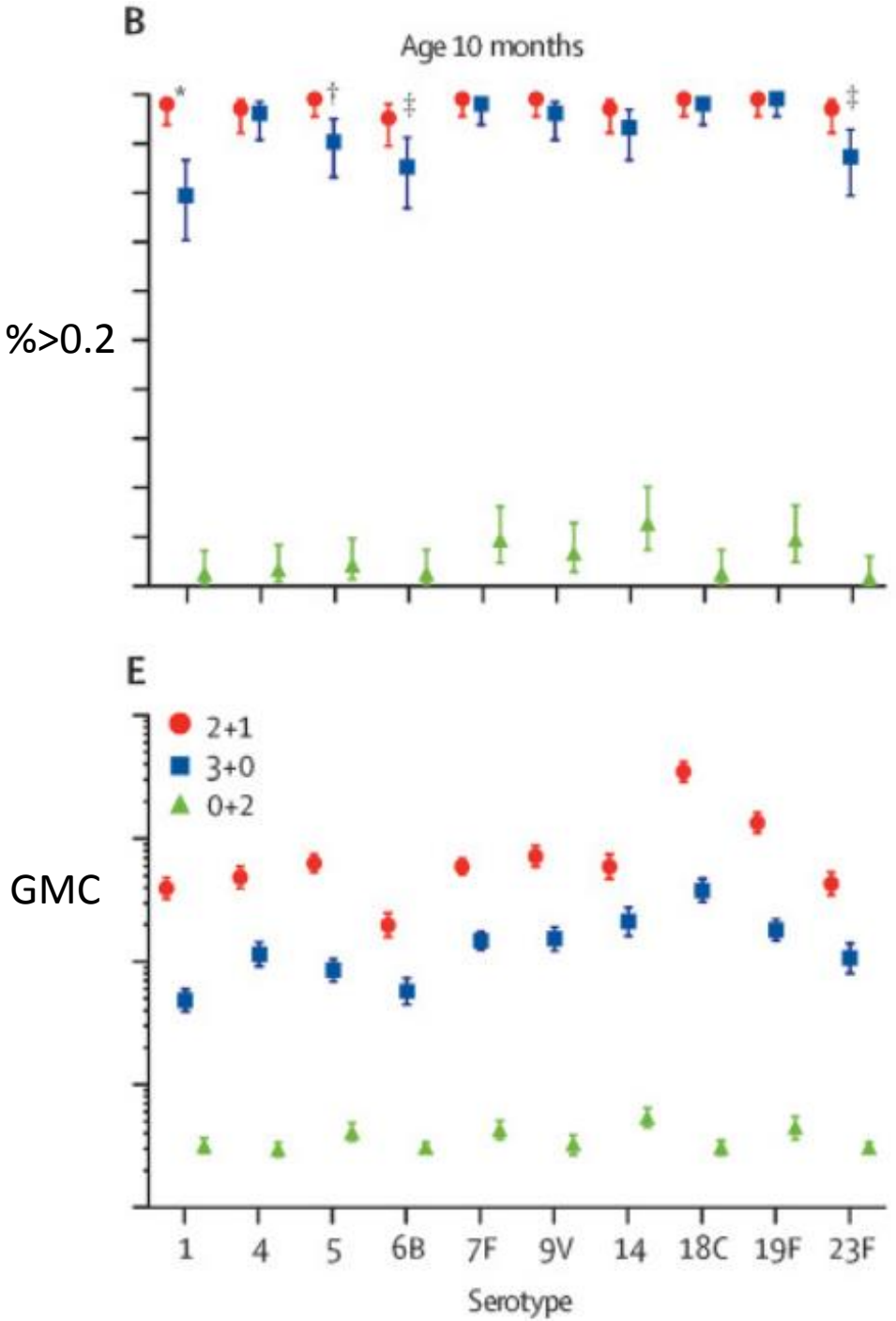
*2 studies, 1 with GMC 2+1<<<GMC 3+0, 1 with GMCs equal

**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

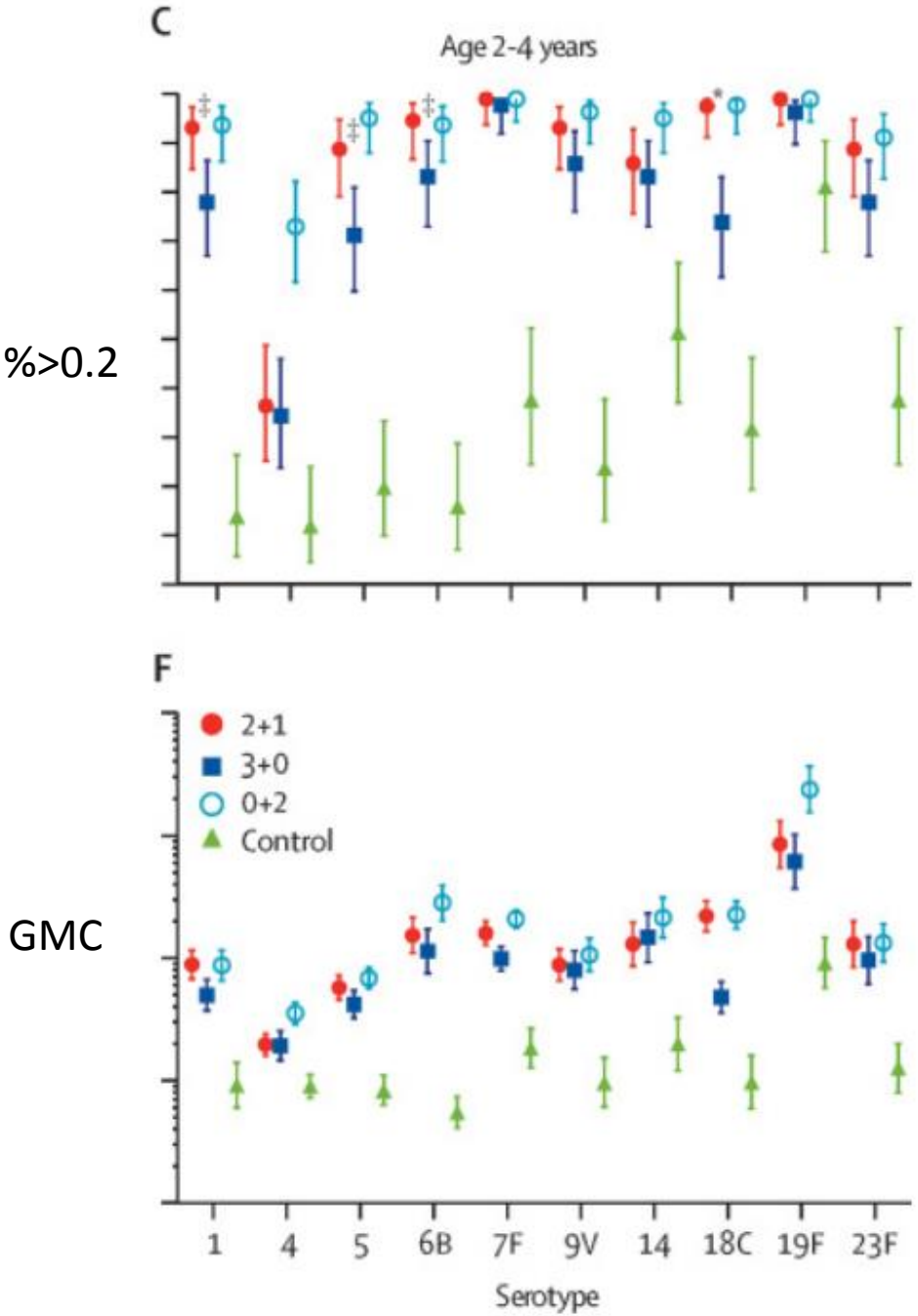
RCTs Post-3rd dose % responders

Antibody at 10 months of age after booster in 2+1 vs persistence in 3+0



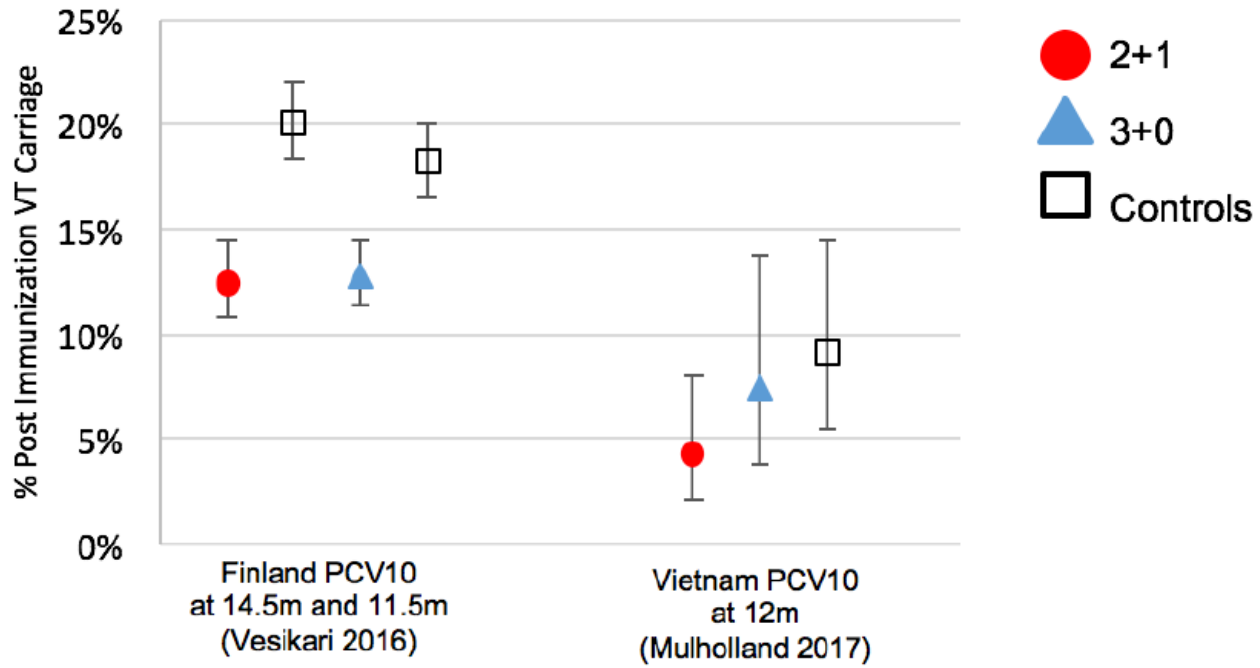
Hamaluba et, Lancet ID al 2015

Post-booster persistence



Hamaluba et, Lancet ID al 2015

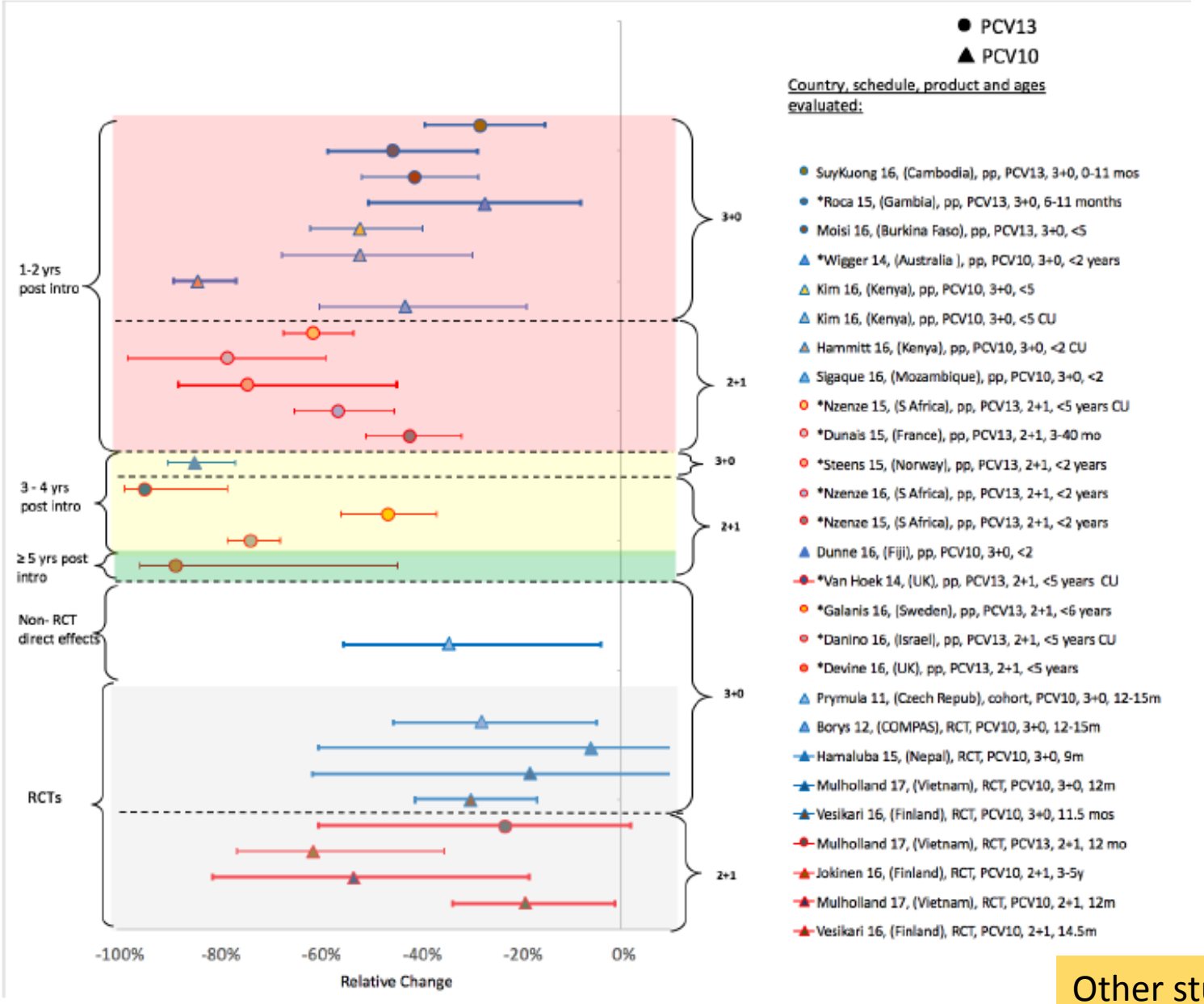
Figure 9: Head-to-head trials comparing PCV10-type carriage in children who received 3+0 vs 2+1 schedules



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

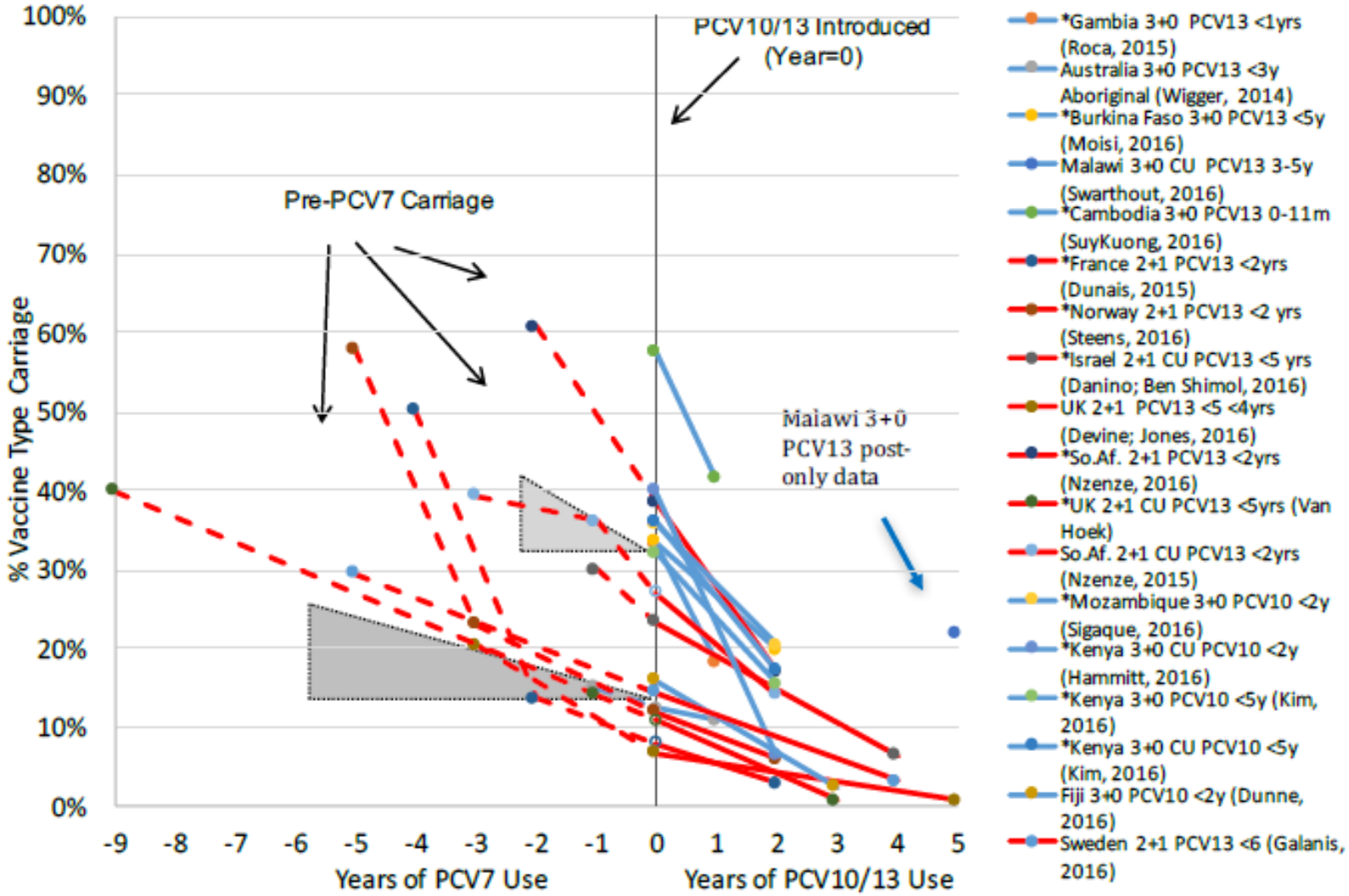
RCTS Carriage post”booster”

Figure 10: Clinical trials and observational studies evaluating impact on vaccine-type carriage in children who received 3+0 (blue points/lines) vs 2+1 schedules (red points/lines)



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

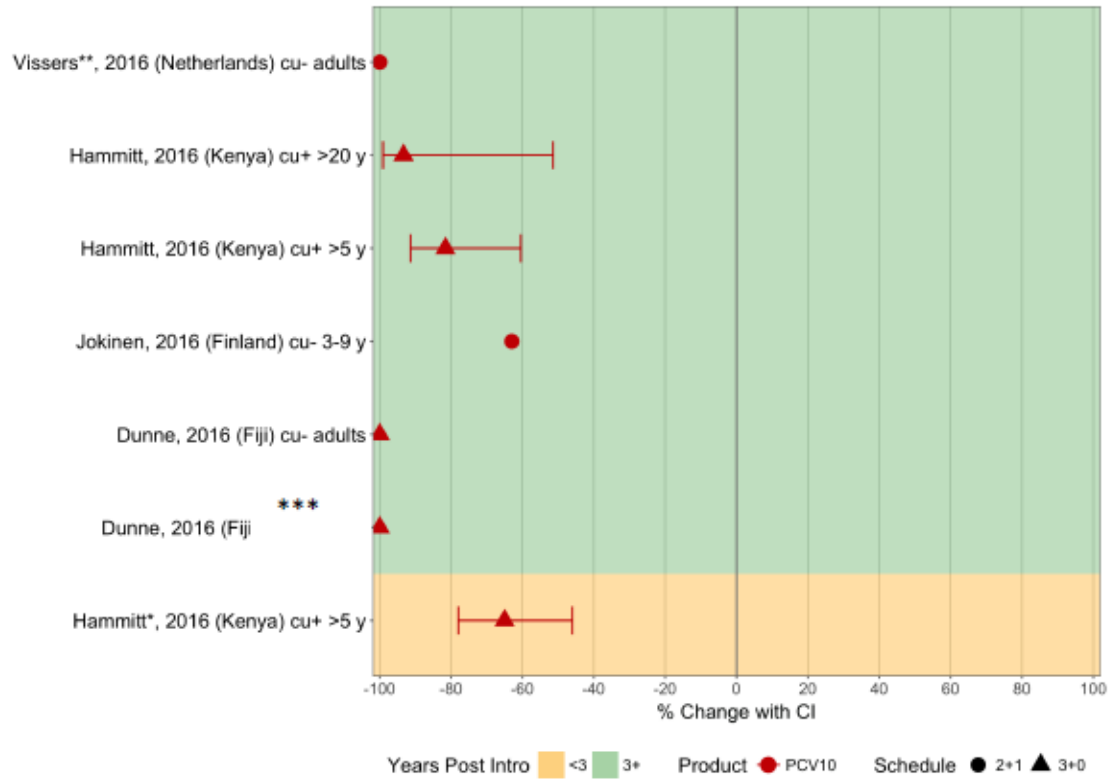


*statistically significant reduction in carriage

**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.

Post-implementation Carriage observational data

Figure 20: Percent change in prevalence of PCV10 VT carriage compared to the pre PCV period by schedule



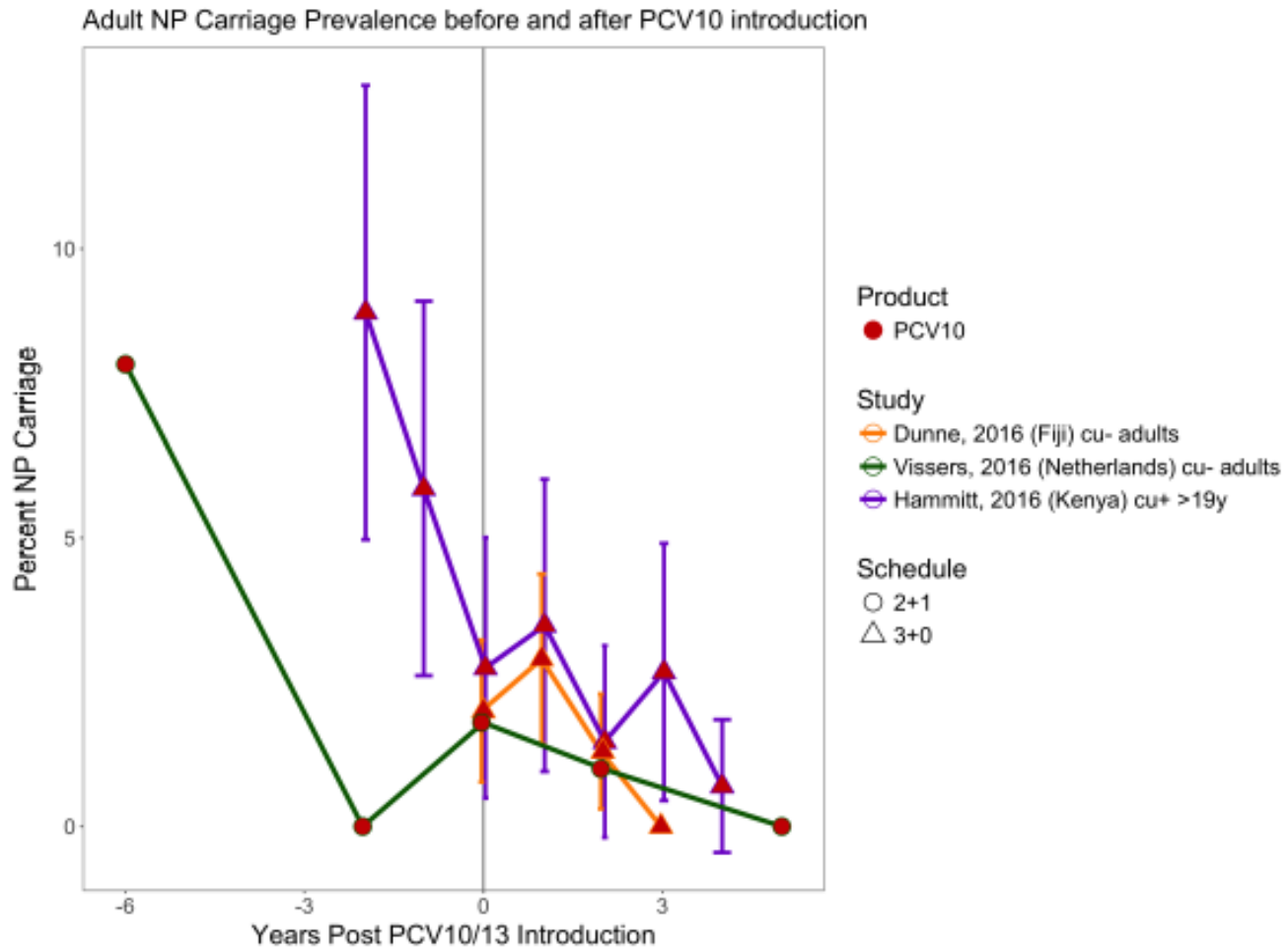
*Median of 2 year post-PCV10, years 2011-2015

**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

igure 23: Impact on PCV13 IPD types vs pre PCV period by schedule

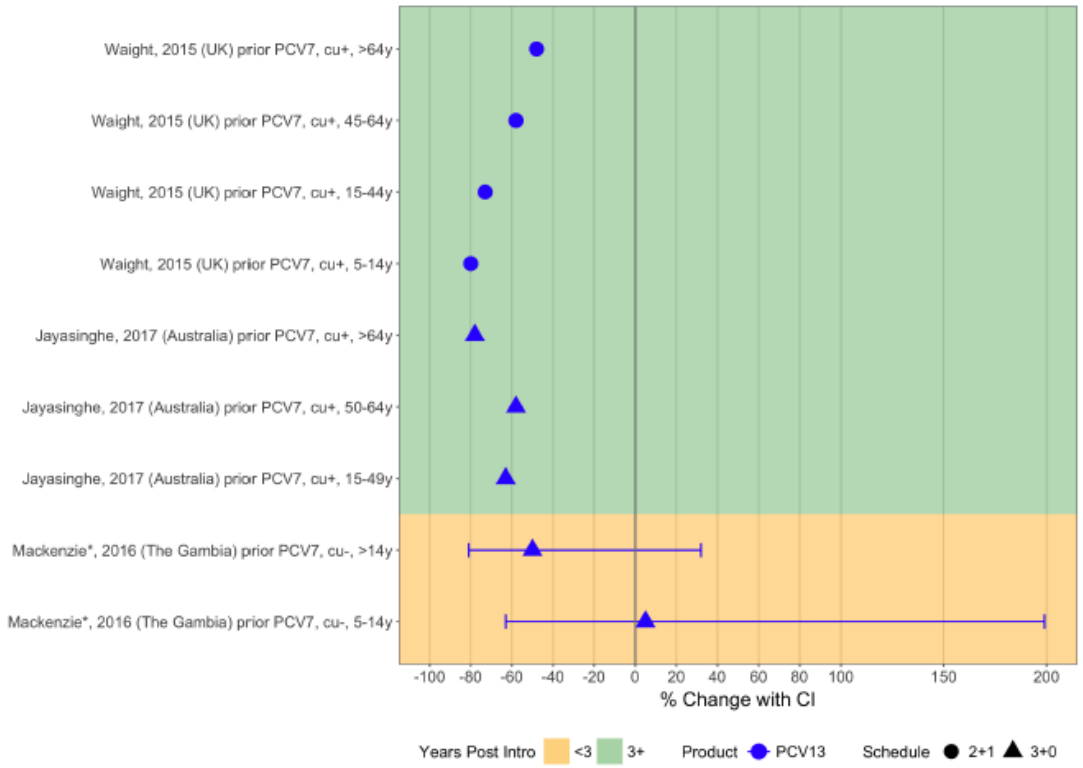
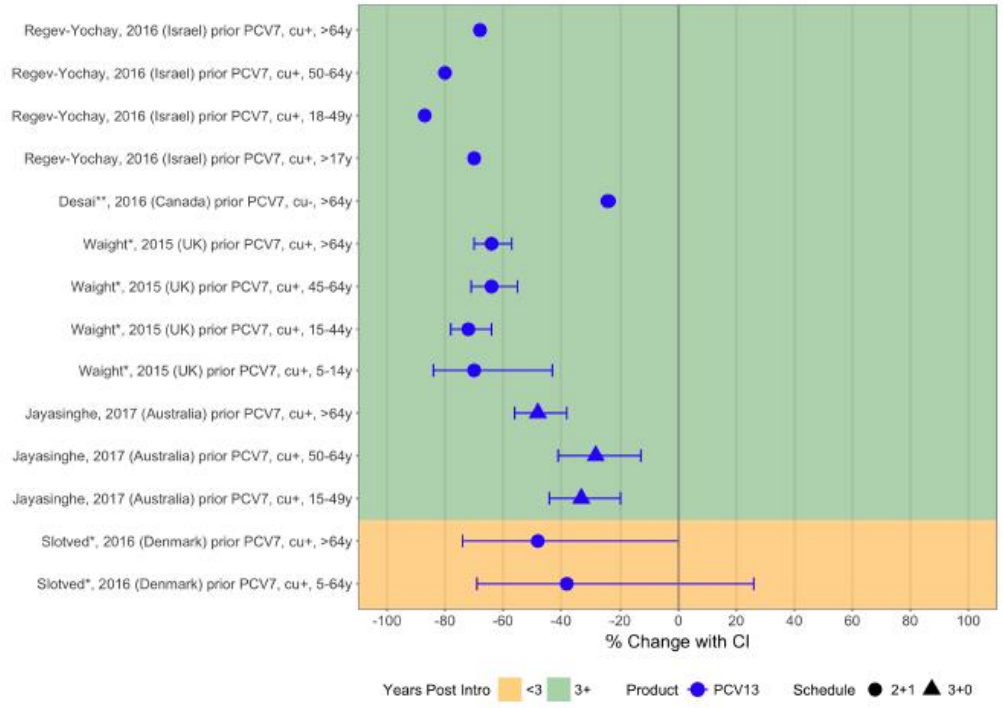


Figure 24: Impact on PCV13-type IPD vs PCV7 period by schedule



*Post PCV13 data are an average rate combining all PCV13 years
**Country with PCV13 use following interim period of PCV10 use

Impact on IPD

PCV10/13 period were very heterogeneous, ranging from a 59% decrease to a 16% increase (**Figure 27** and

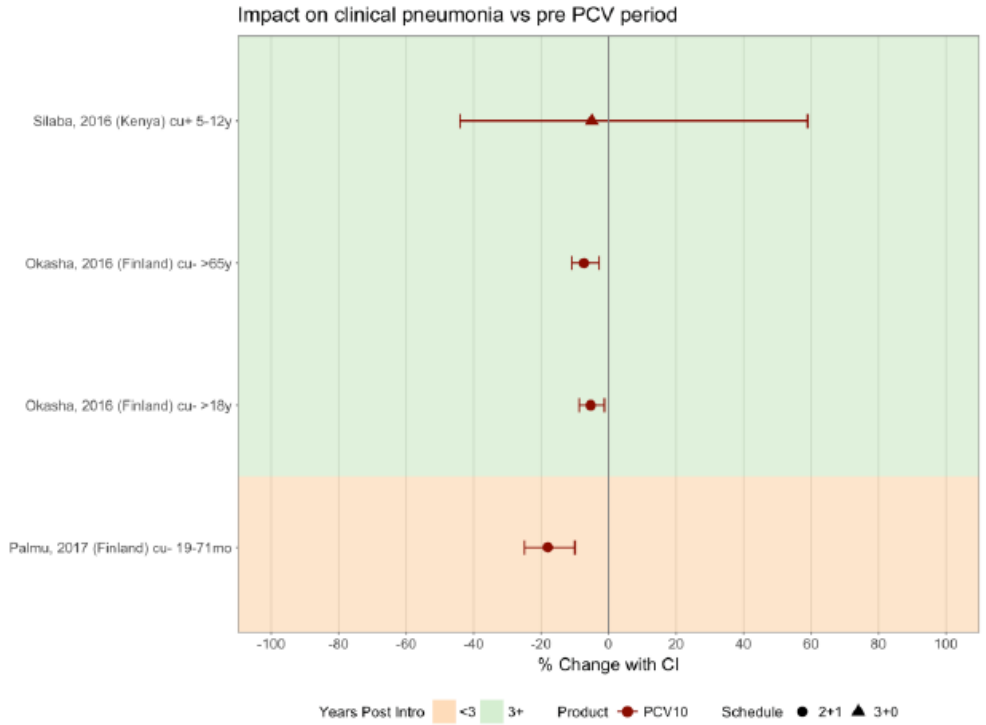
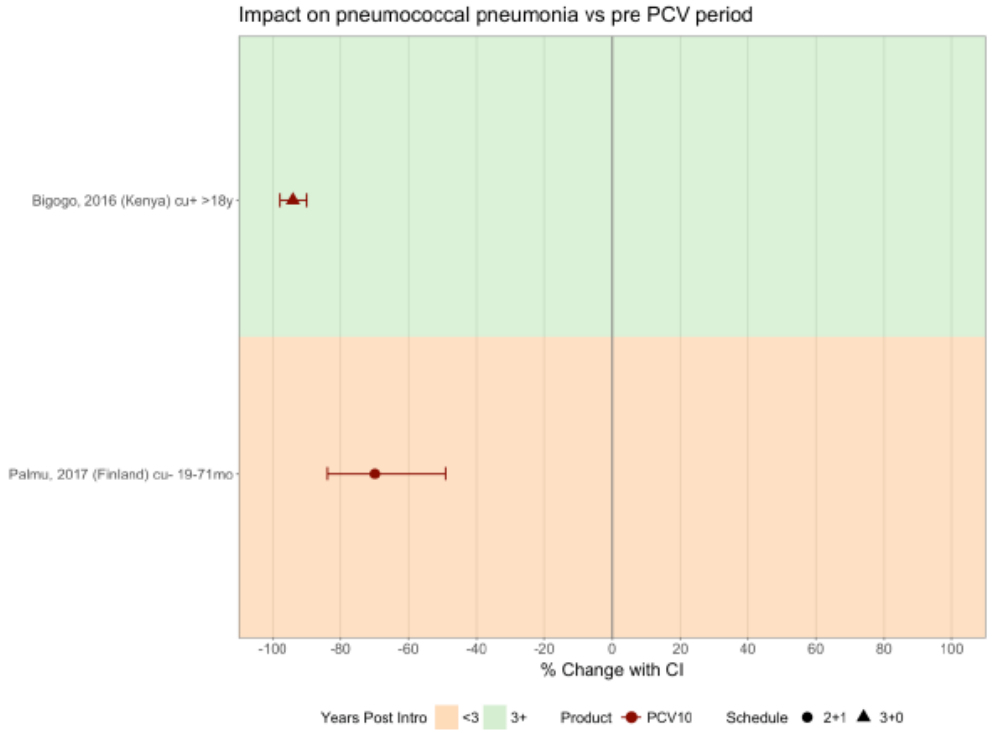


Figure 30: Impact on clinical pneumonia in countries without prior PCV7 use



Impact on pneumonia

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