

Pertussis vaccination schedules

Session 10 - Thursday 16th April, 11:00am

Modelling of impact of different DTP schedules

Andy Clark, LSHTM

**Modelling the direct impact
...of alternative primary wP schedules
...on pertussis deaths <5yrs
...in low and middle income countries**

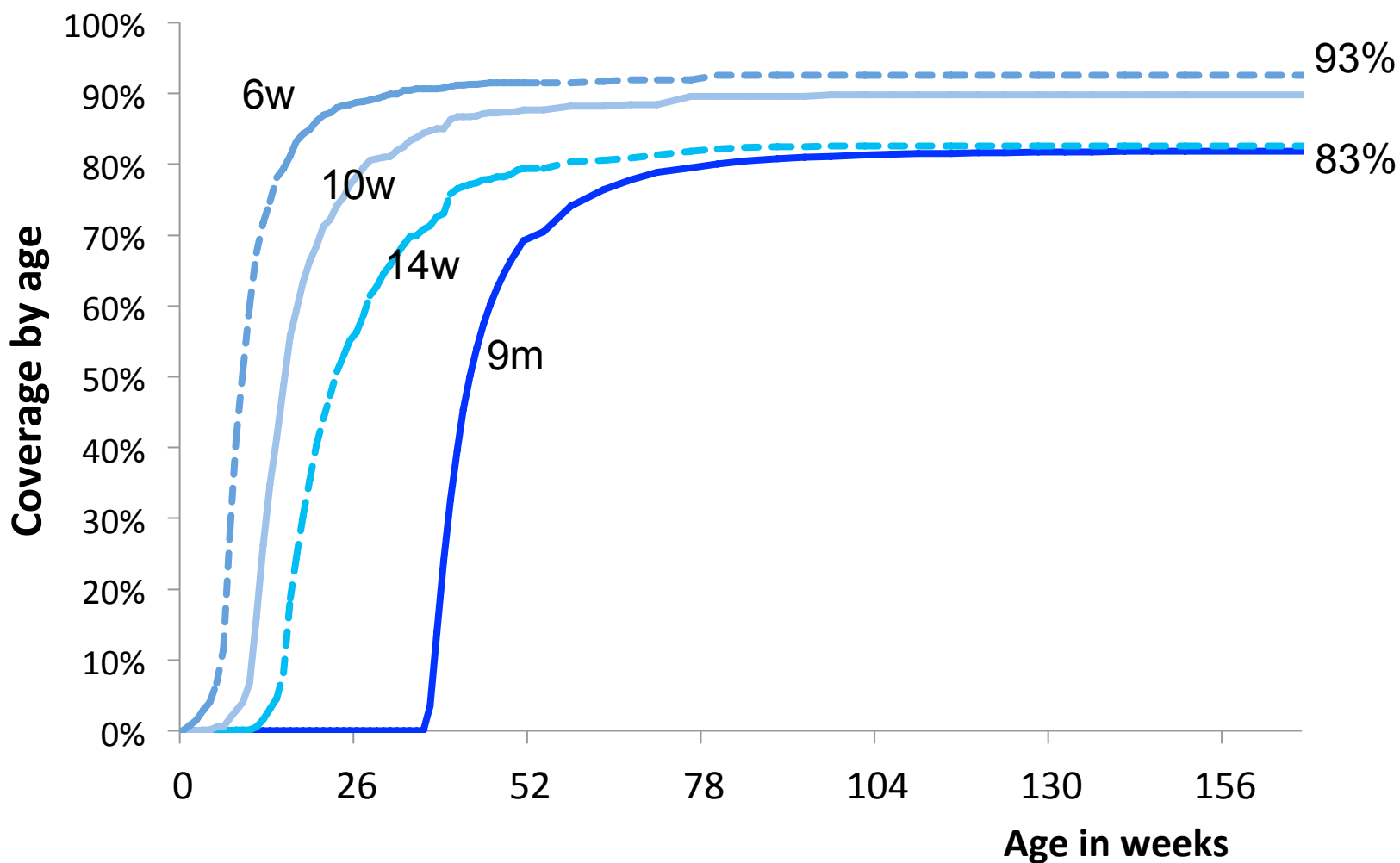
Example: Senegal

Pre-vaccine era age distribution of pertussis deaths <5yrs in Senegal (1986)



Source: Preziosi et al, *Am J Epidemiol* 2002

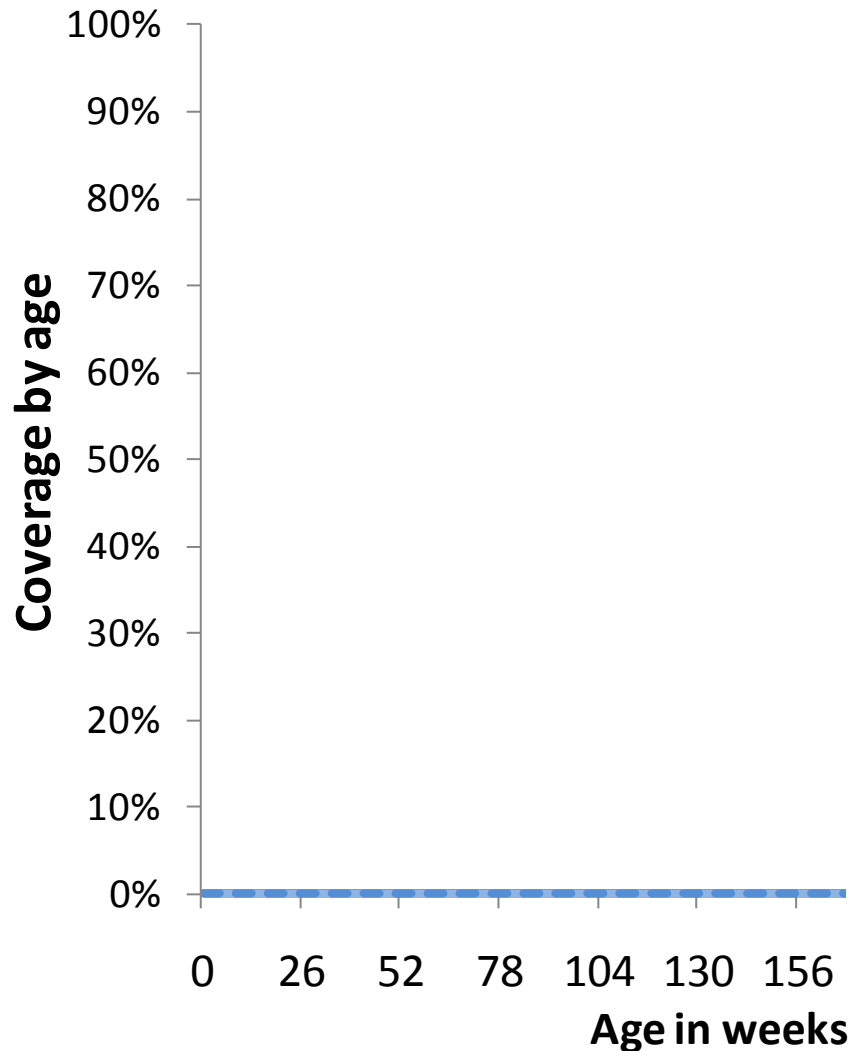
Coverage and timeliness of vaccination in Senegal



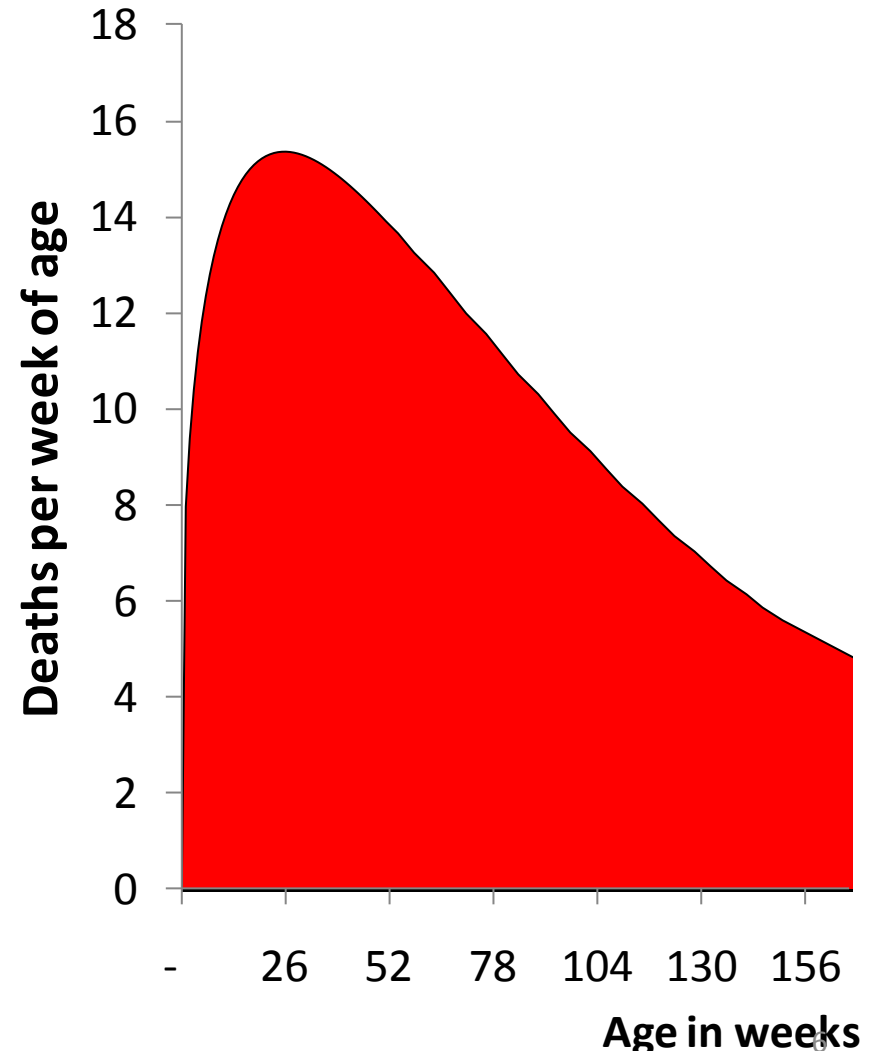
Estimating coverage of different doses among potential deaths

Potential pertussis deaths covered by each dose by age

Coverage by age

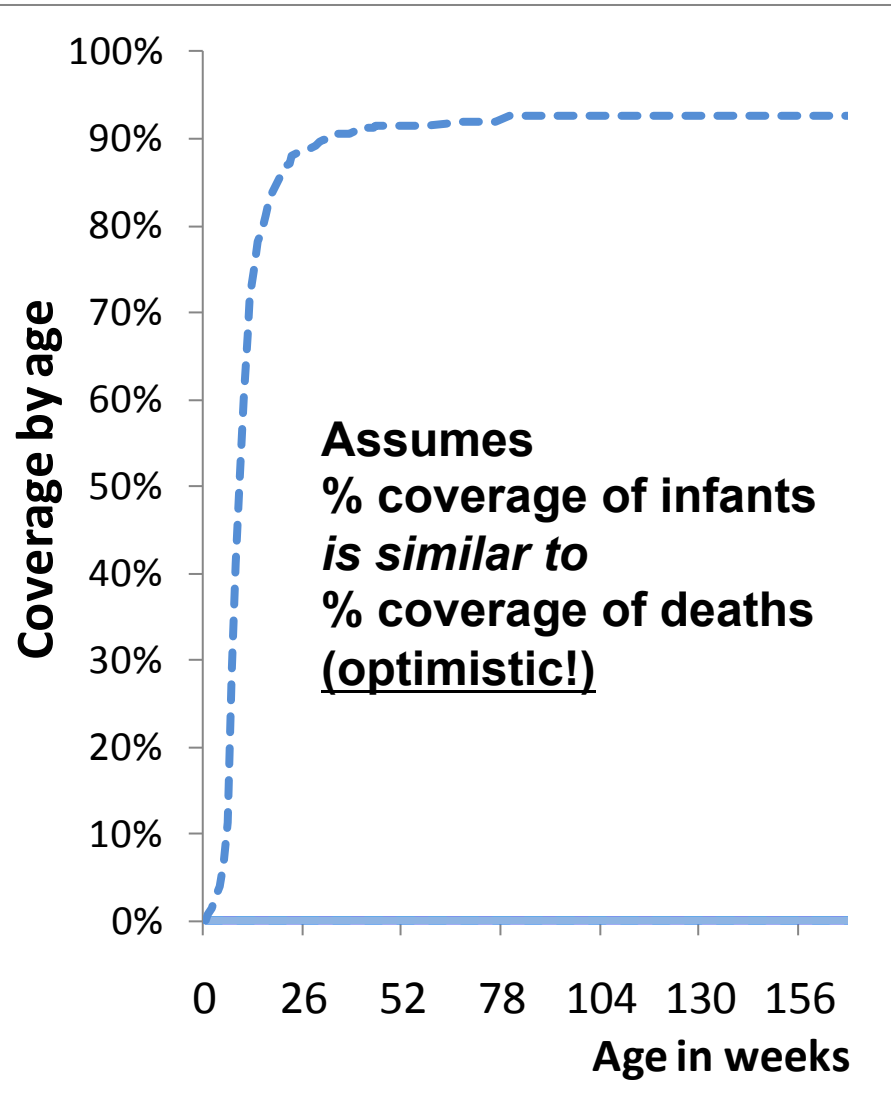


Deaths/deaths covered by age

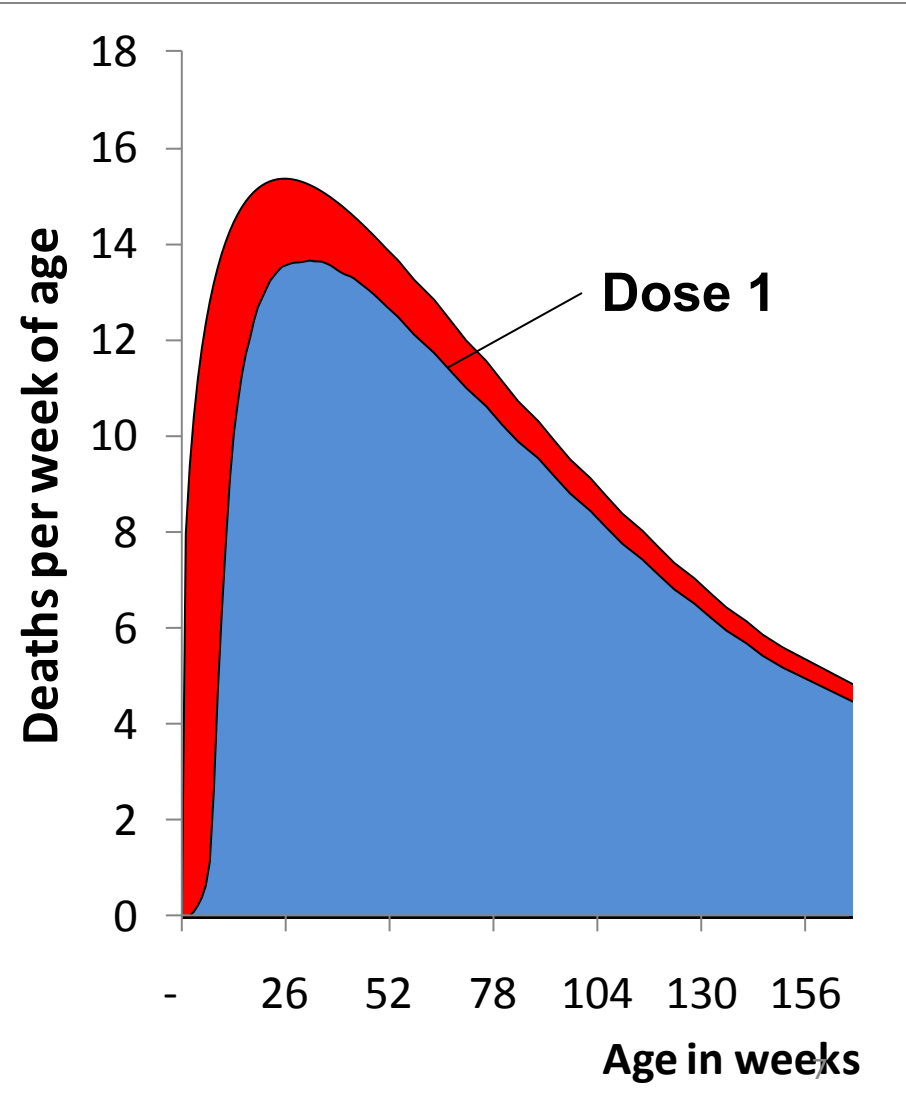


Potential pertussis deaths covered by each dose by age

Coverage by age

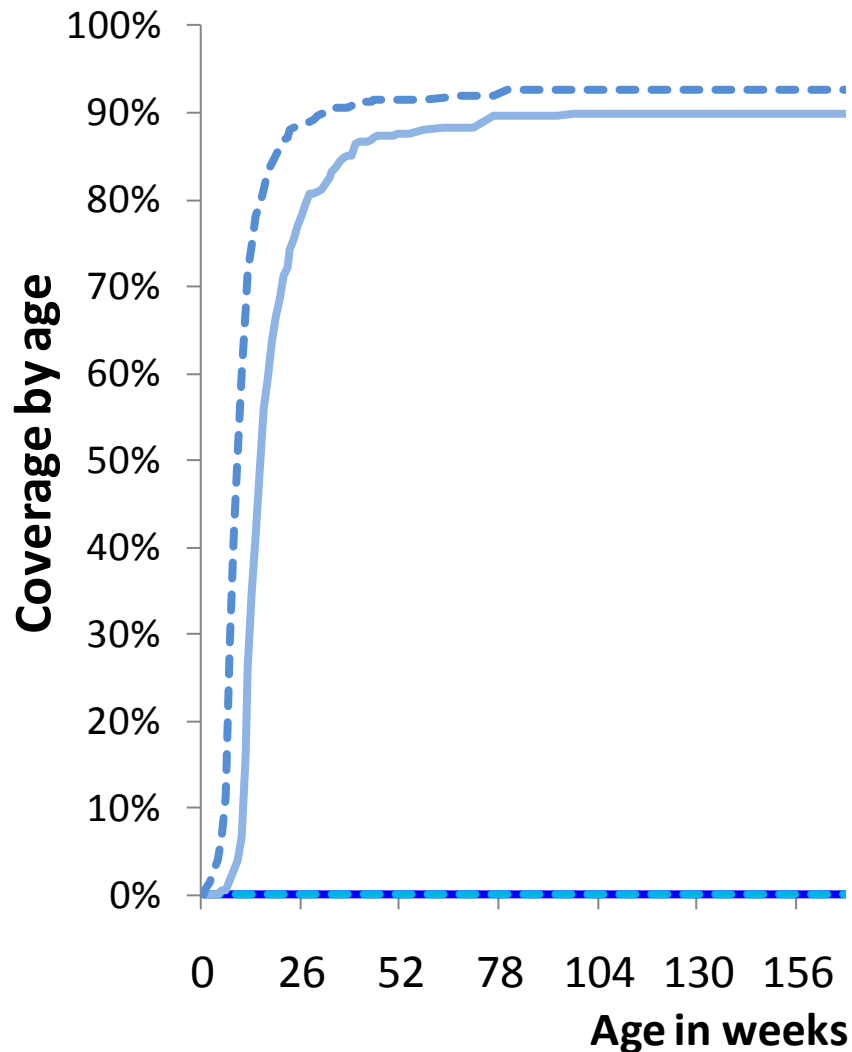


Deaths/deaths covered by age

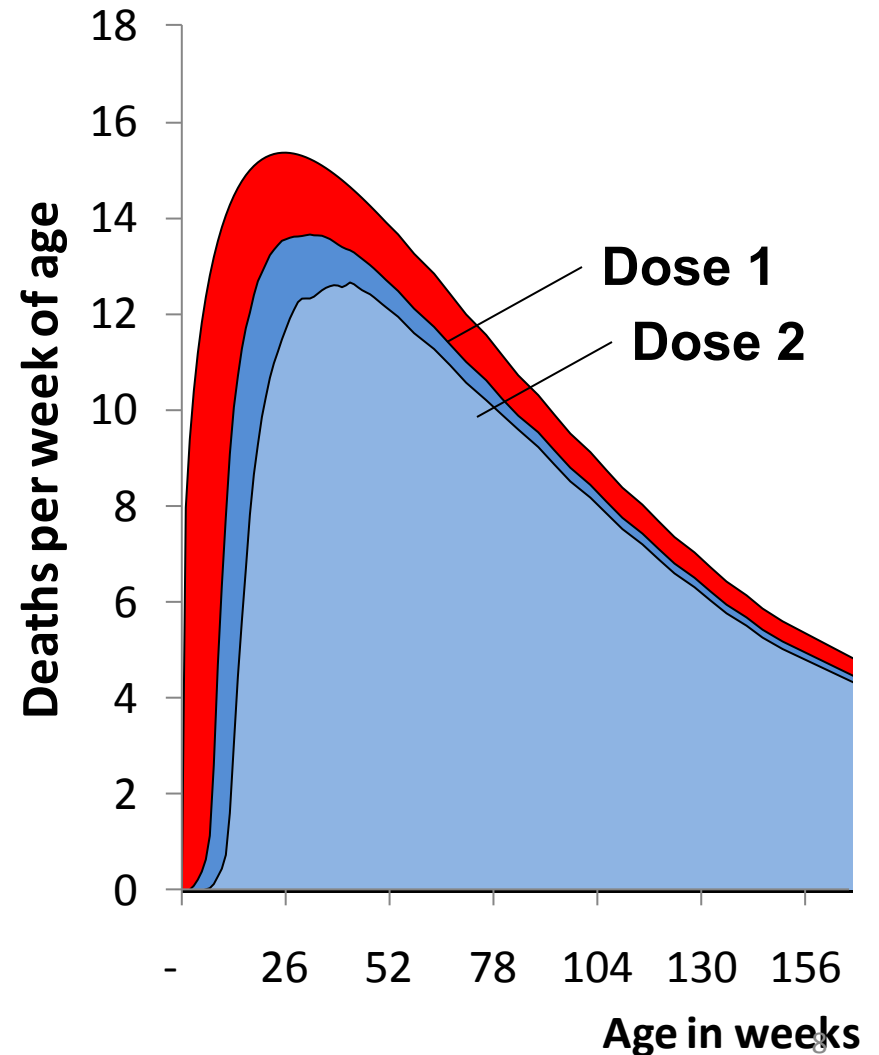


Potential pertussis deaths covered by each dose by age

Coverage by age

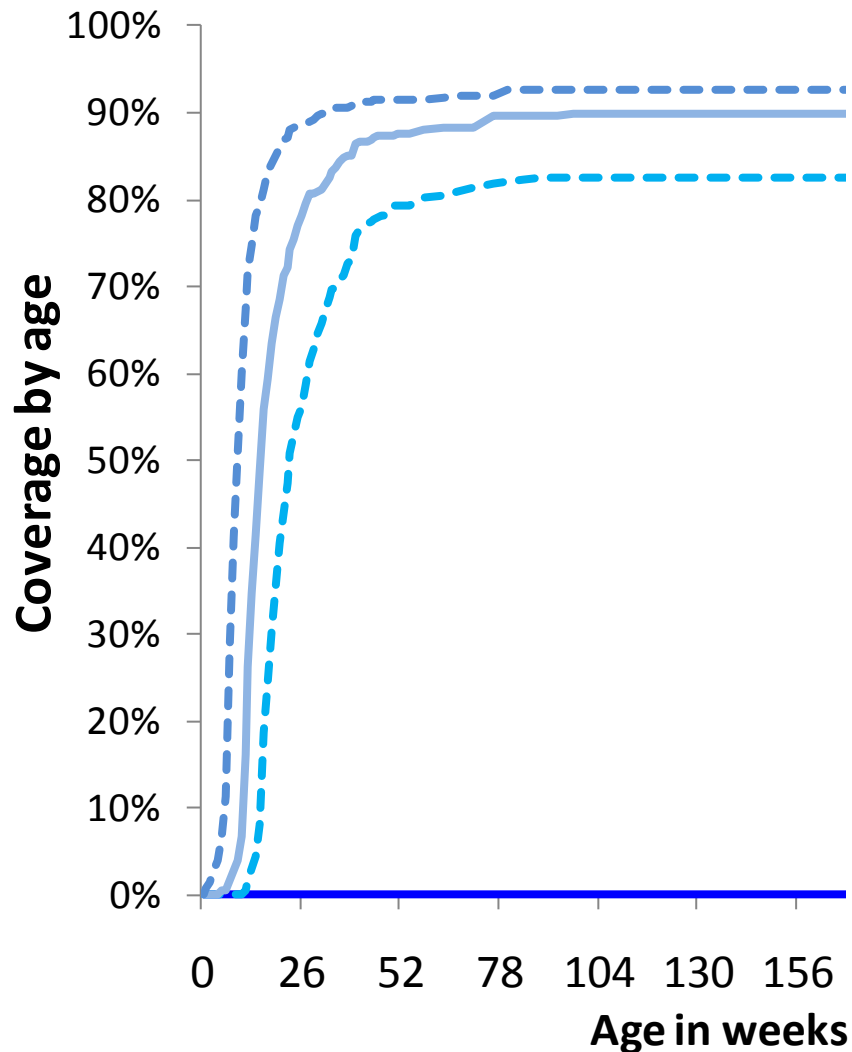


Deaths/deaths covered by age

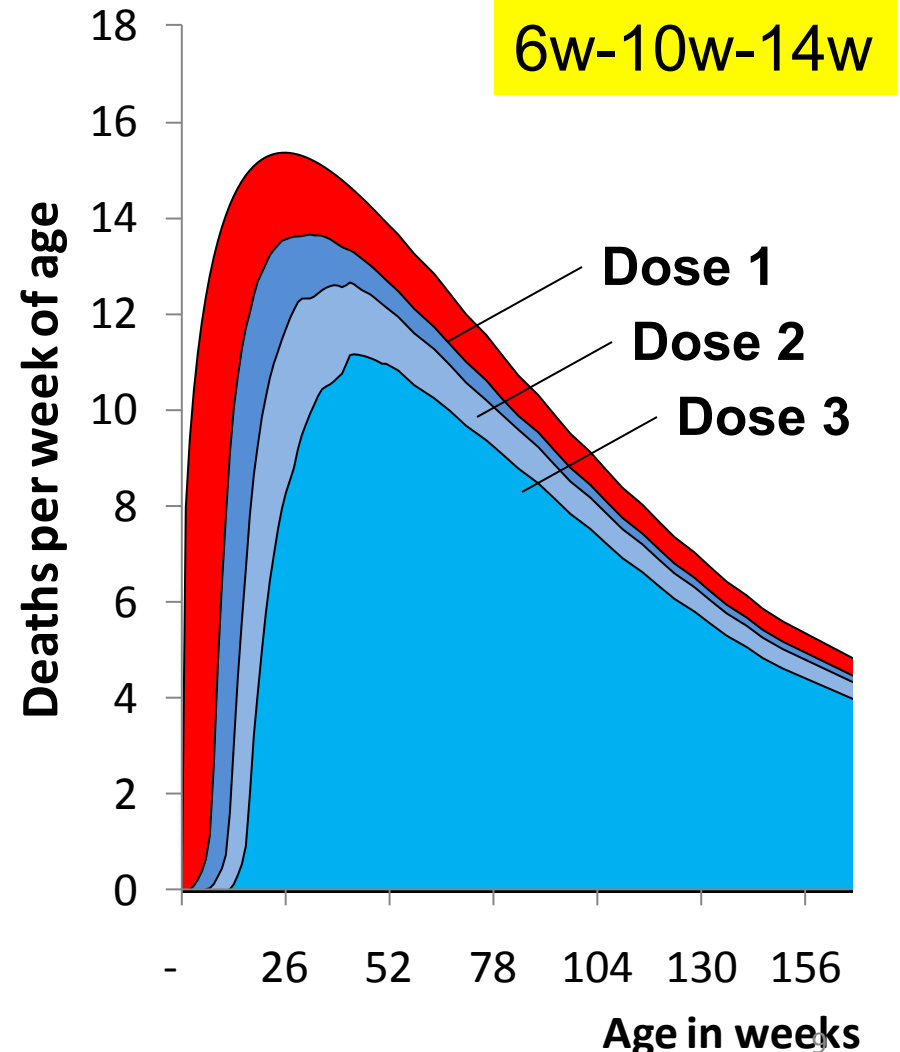


Potential pertussis deaths covered by each dose by age

Coverage by age

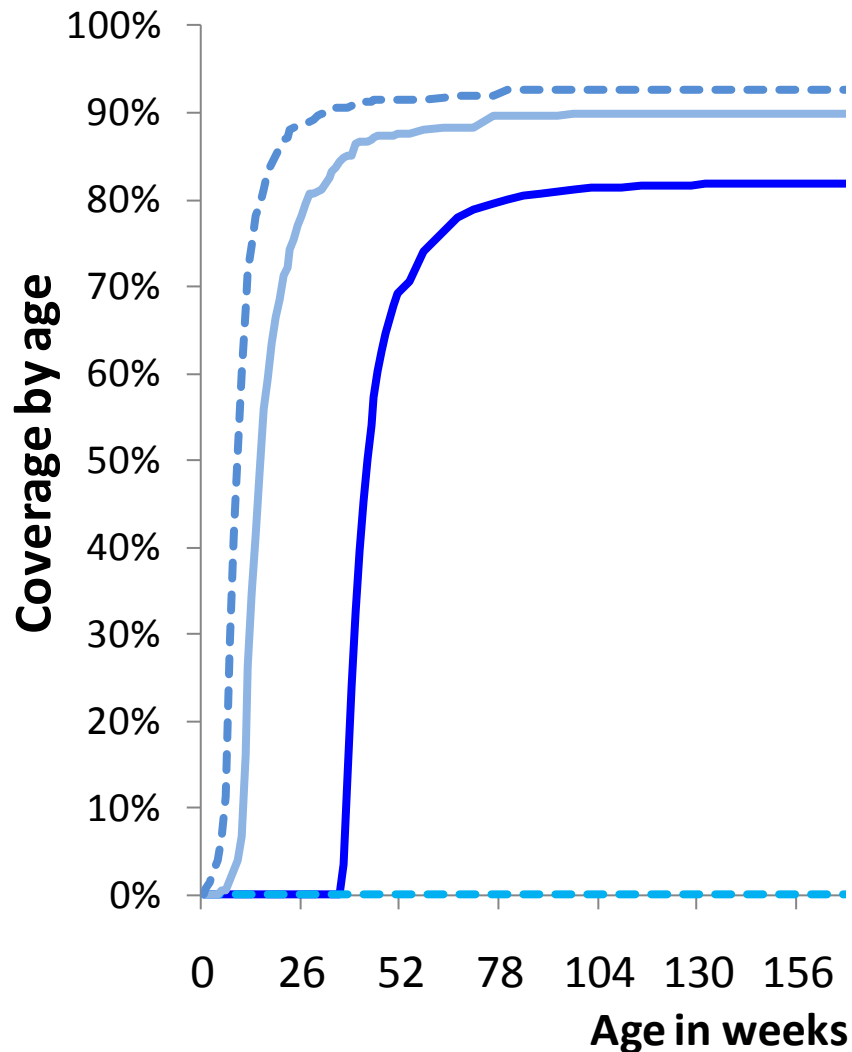


Deaths/deaths covered by age

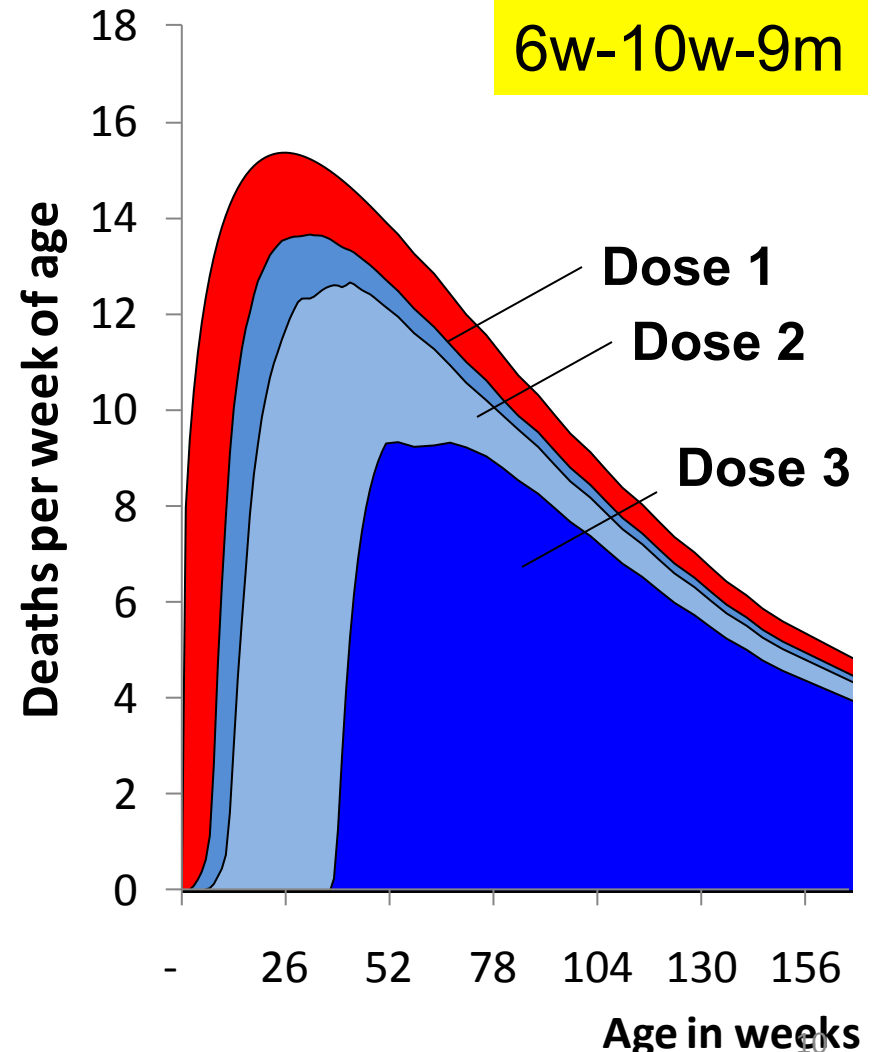


Potential pertussis deaths covered by each dose by age

Coverage by age

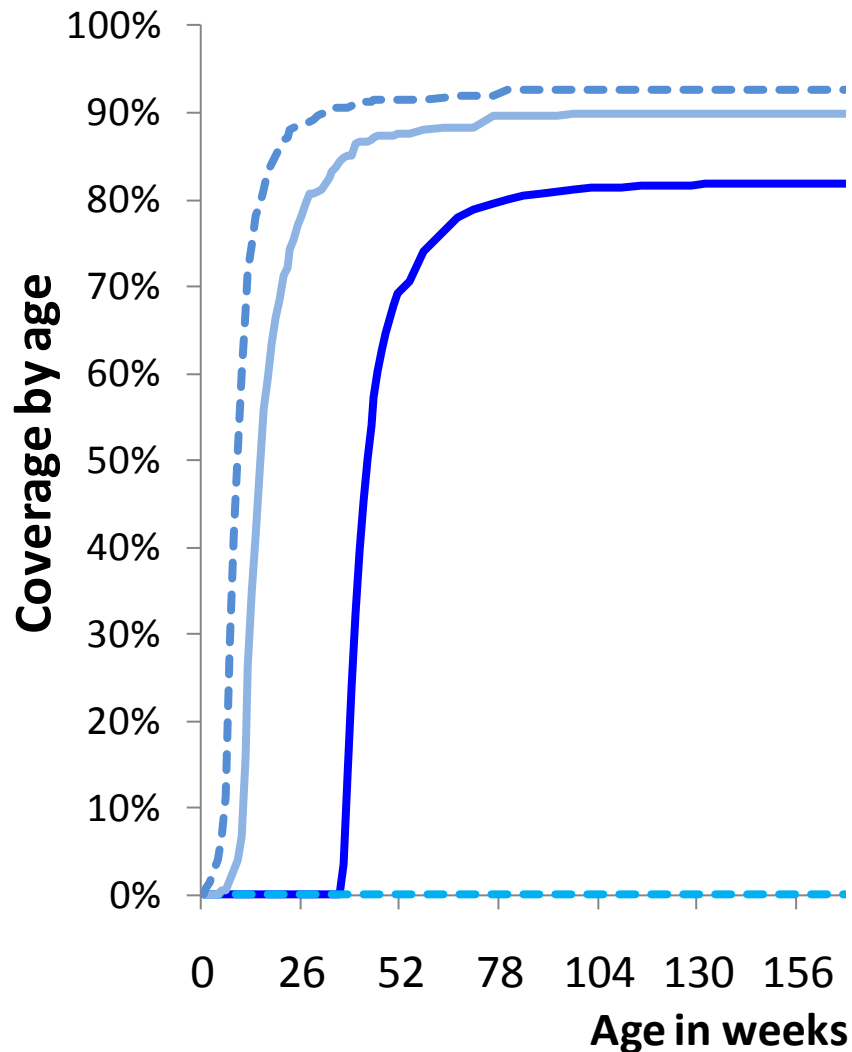


Deaths/deaths covered by age

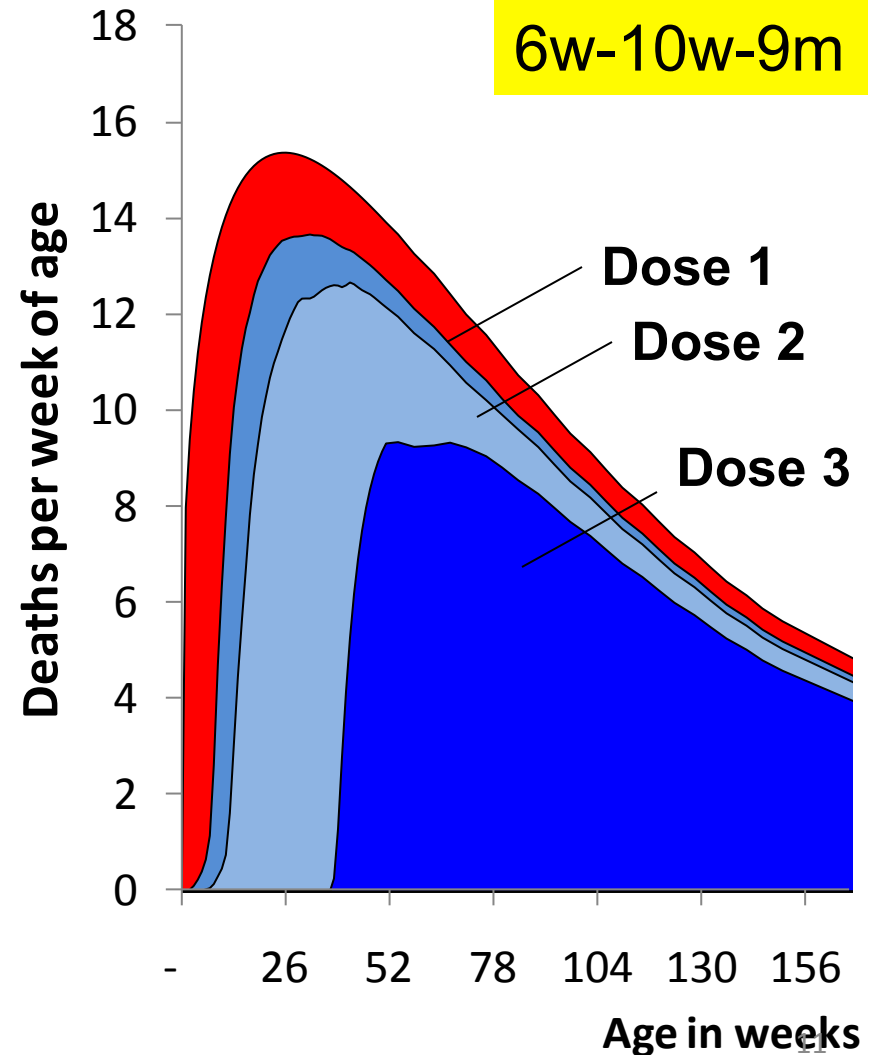


Potential pertussis deaths covered by each dose by age

Coverage by age



Deaths/deaths covered by age



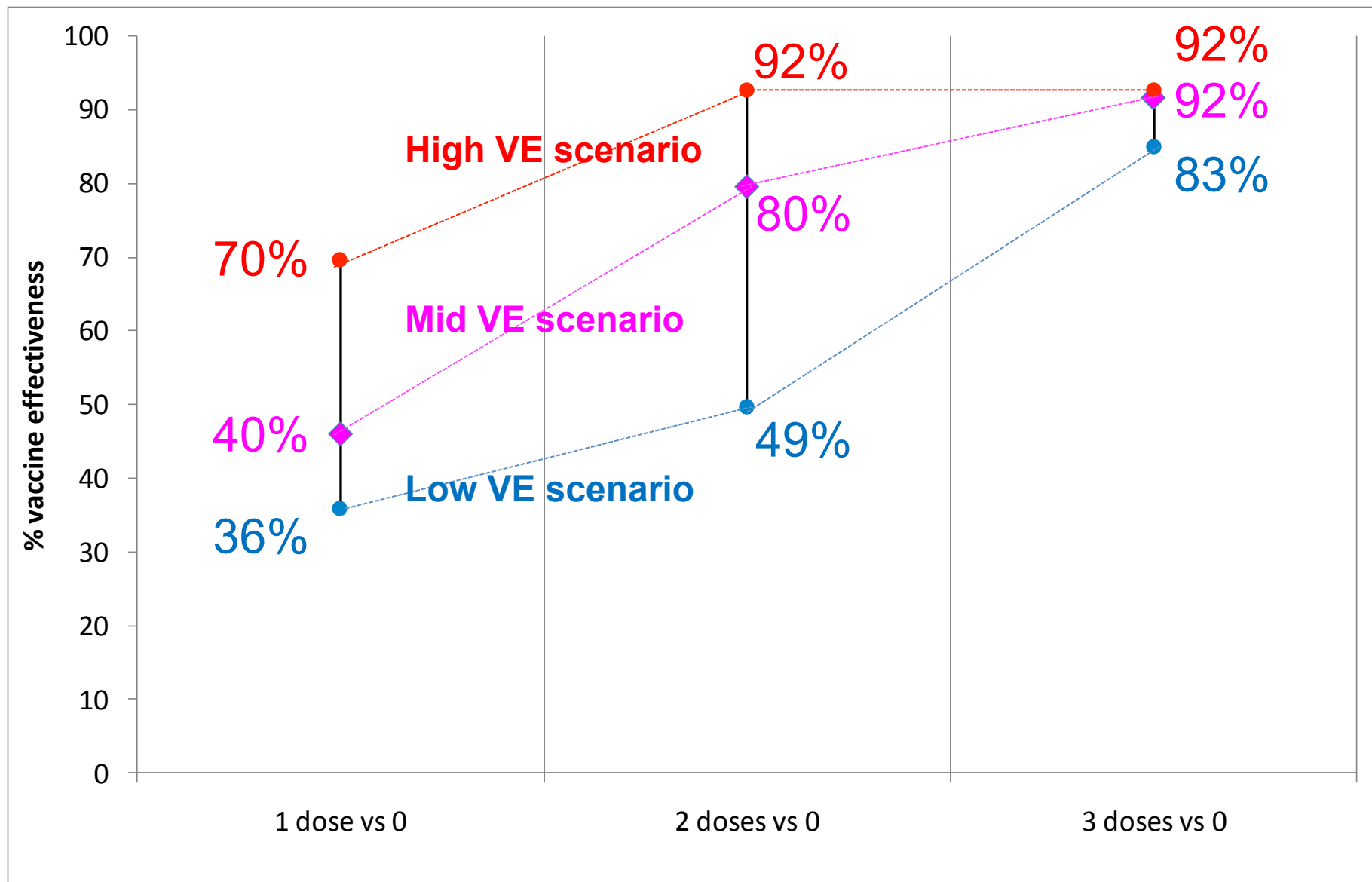
How does coverage translate into direct vaccine impact?

Focus on wP vaccines

1. Protection after each dose
2. Duration of protection after each dose

Protection after each dose of wP

Dose-specific VE of wP: studies reporting on all 3 doses



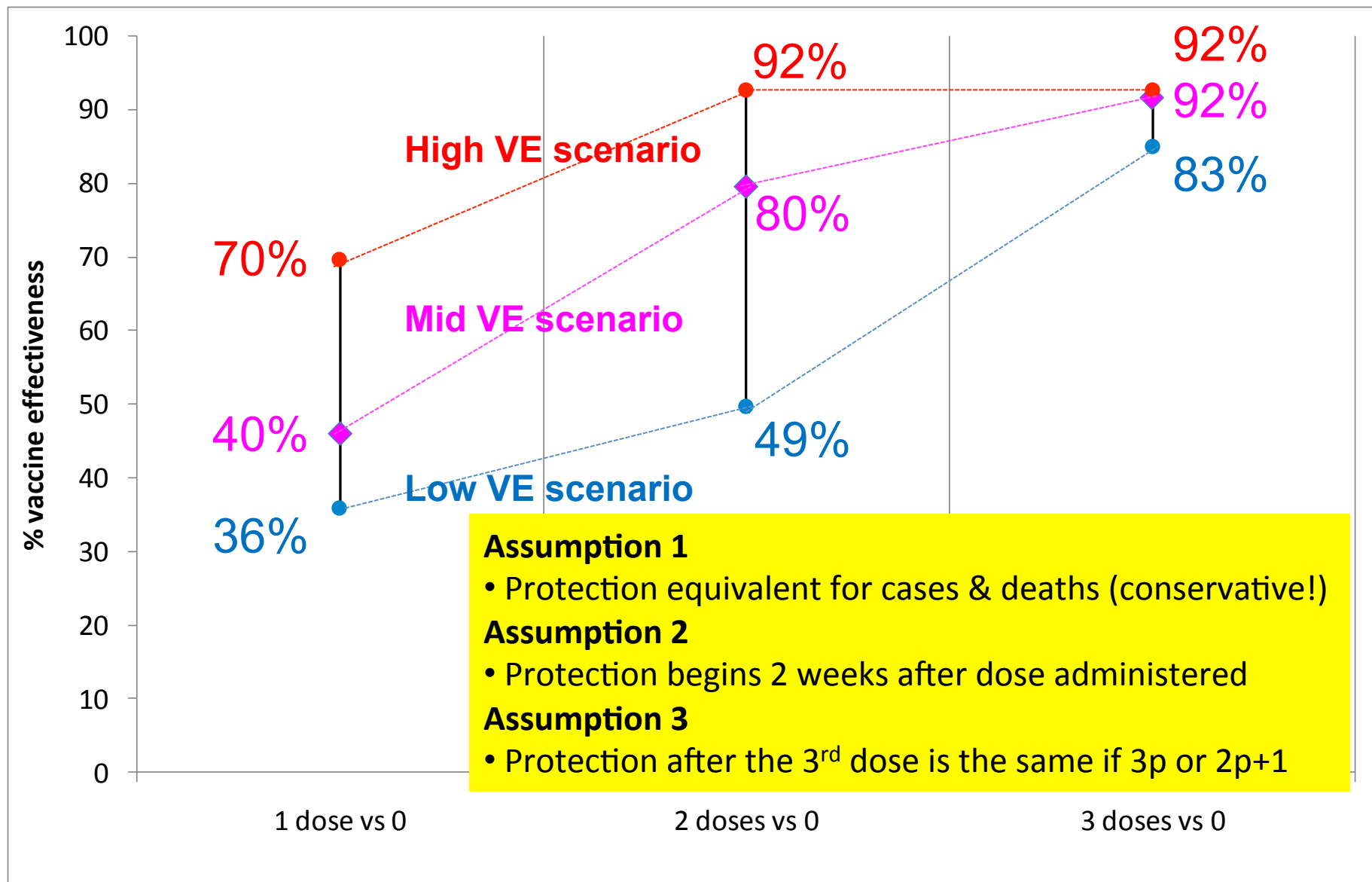
■ RCT

● Cohort

◆ Case control

● Screening

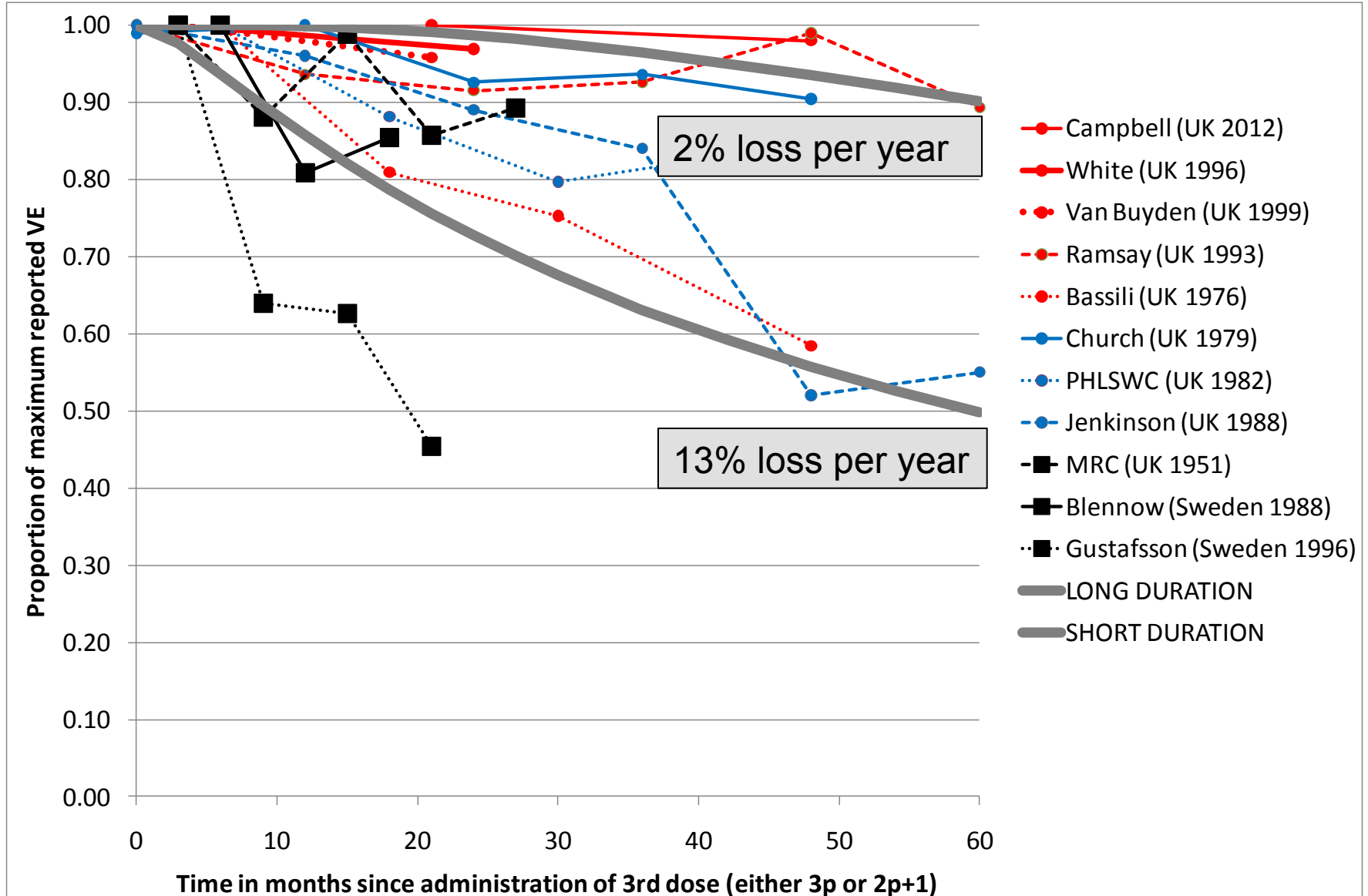
Dose-specific VE of wP: studies reporting on all 3 doses



Duration of clinical protection

Relative clinical protection by time since 3 doses of wP:

VE expressed as a proportion of the highest reported VE in studies with multiple follow-up points



■ RCT

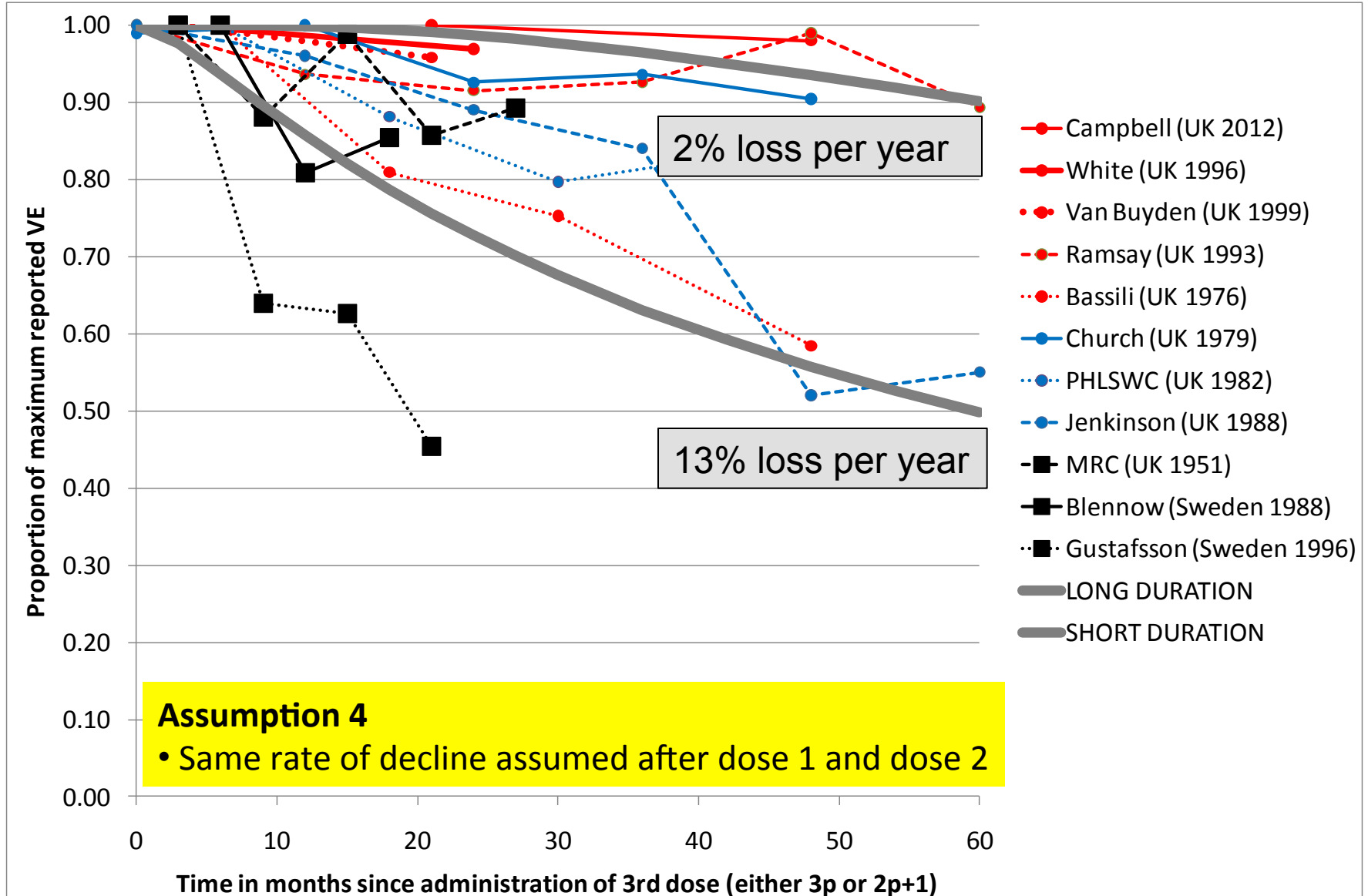
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Relative clinical protection by time since 3 doses of wP:

VE expressed as a proportion of the highest reported VE in studies with multiple follow-up points



■ RCT

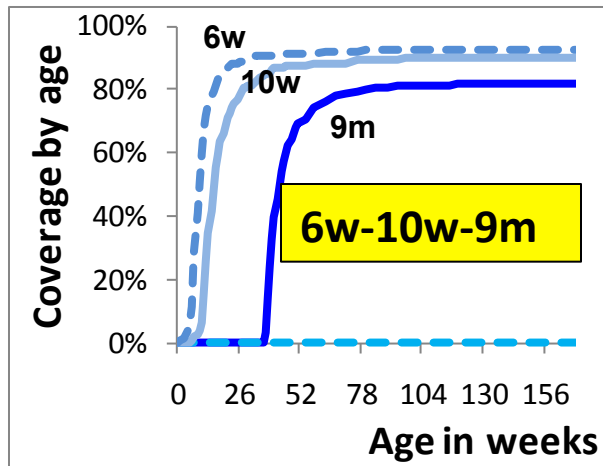
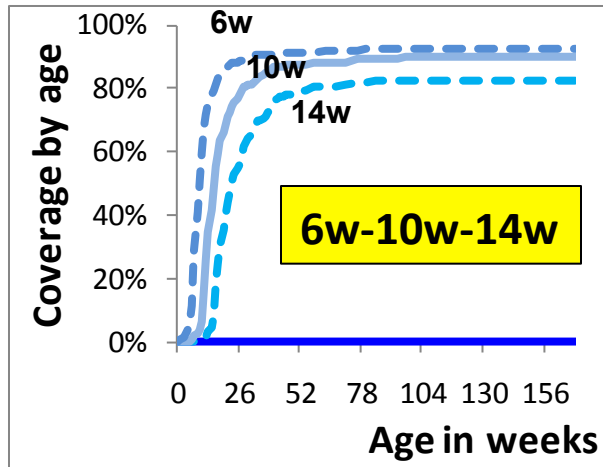
● Cohort

◆ Case control

● Screening

Direct impact of wP vaccination in Senegal:

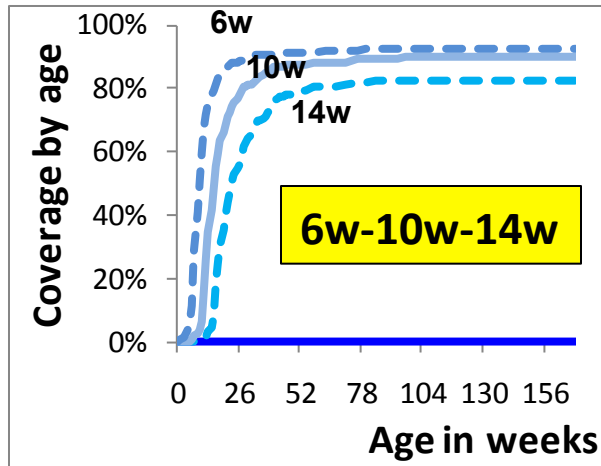
(a) Coverage by age



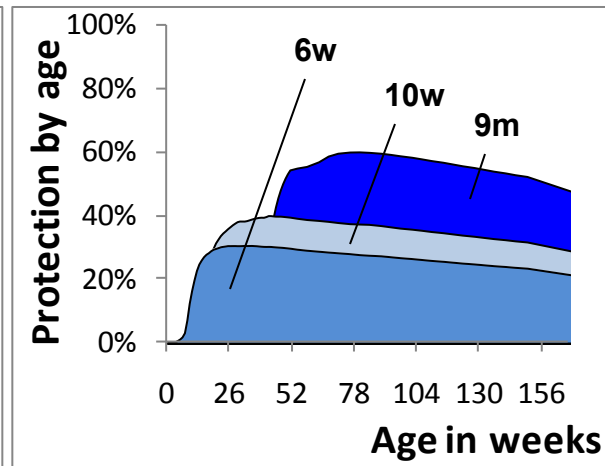
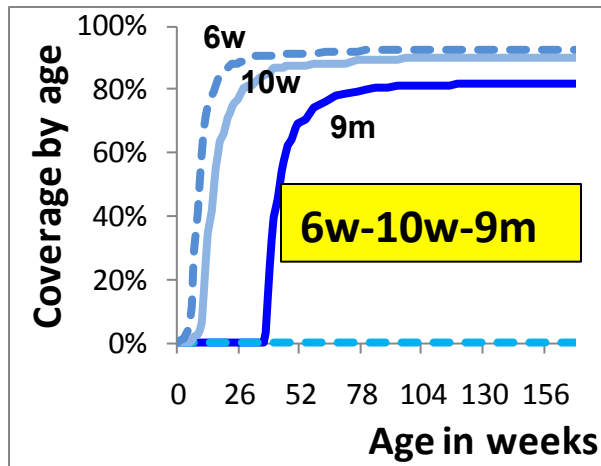
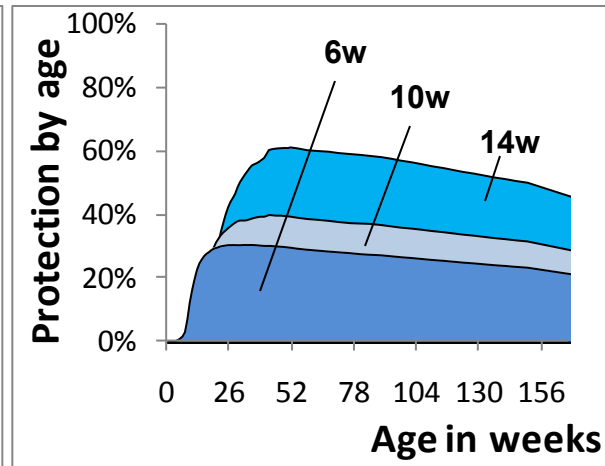
Direct impact of wP vaccination in Senegal:

Low VE scenario (36%→49%→83%), 13% waning per year

(a) Coverage by age



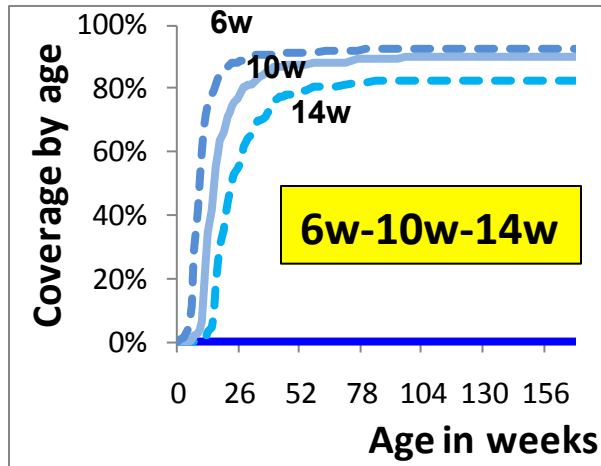
(b) Protection by age



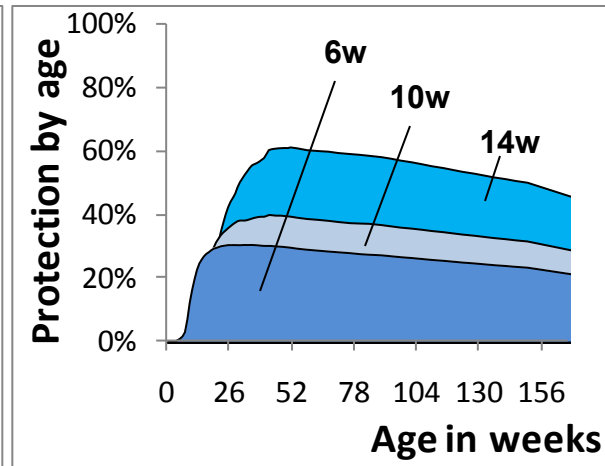
Direct impact of wP vaccination in Senegal:

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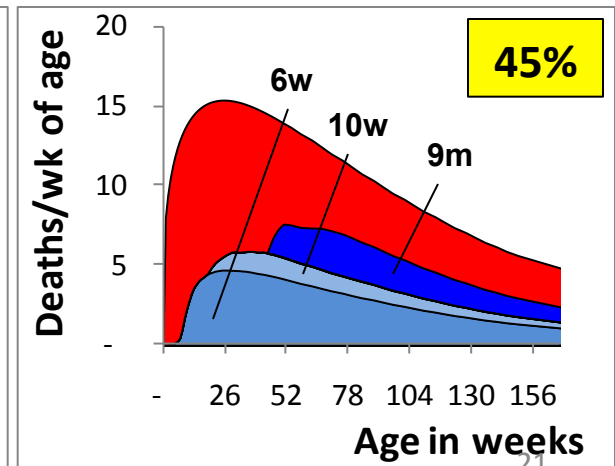
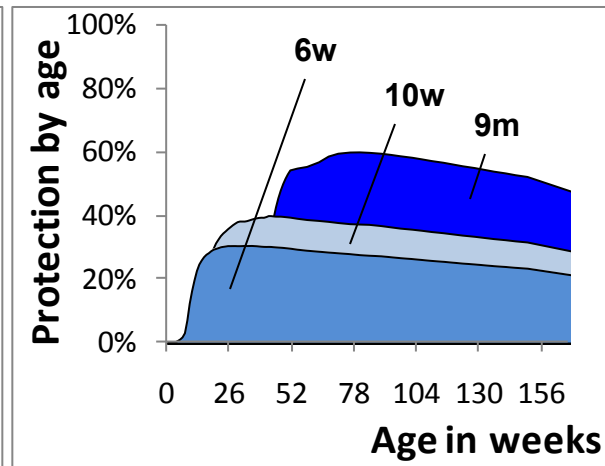
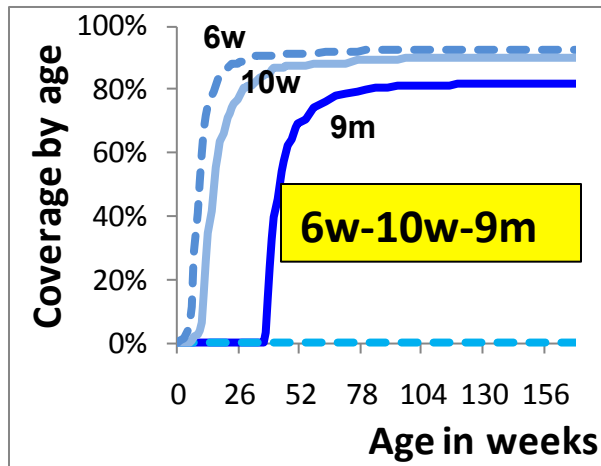
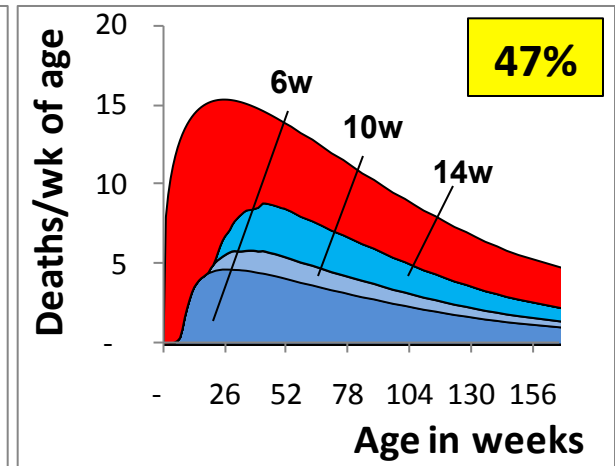
(a) Coverage by age



(b) Protection by age



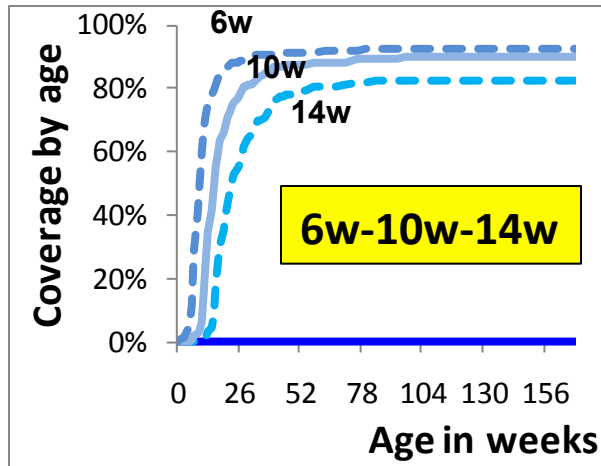
(c) Direct impact by age



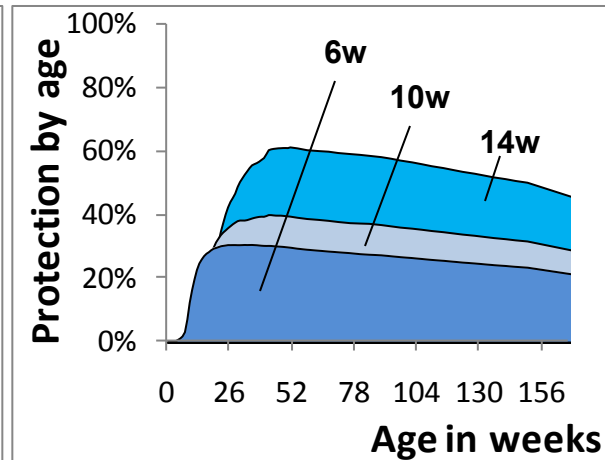
Direct impact of wP vaccination in Senegal:

Low VE scenario (36%→49%→83%), 13% waning per year

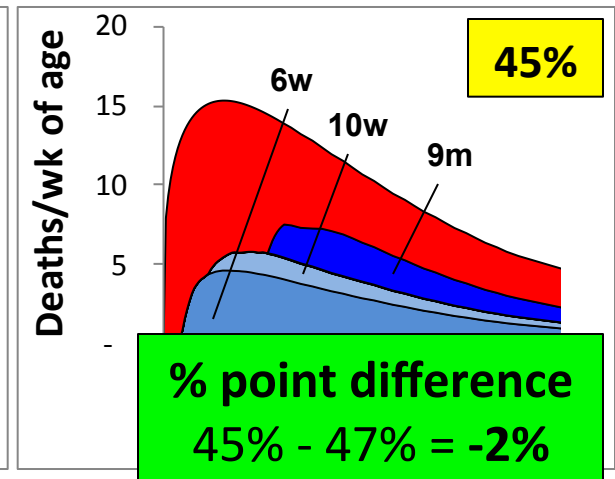
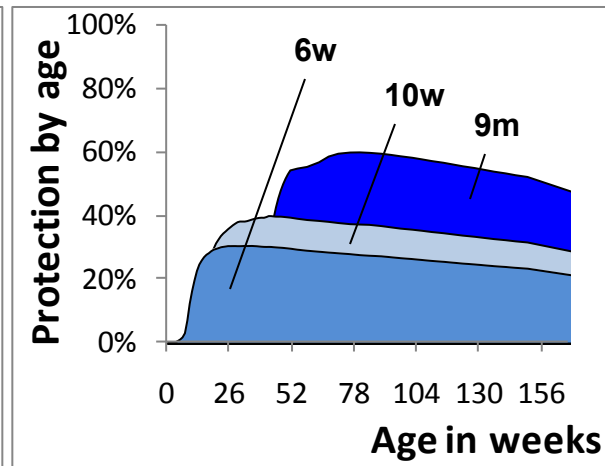
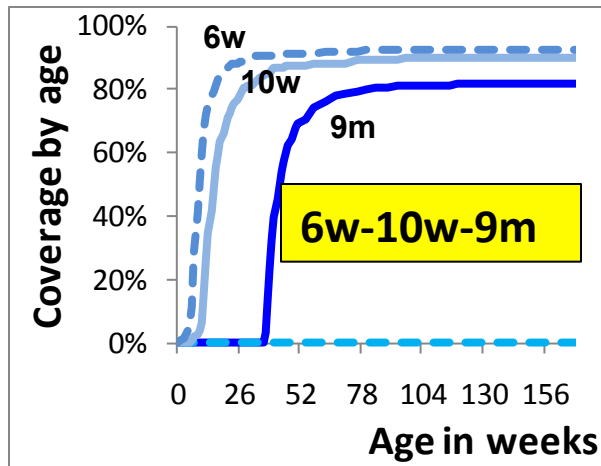
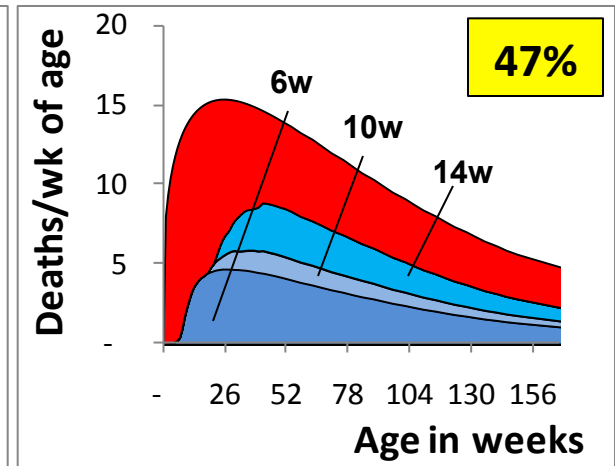
(a) Coverage by age



(b) Protection by age



(c) Direct impact by age



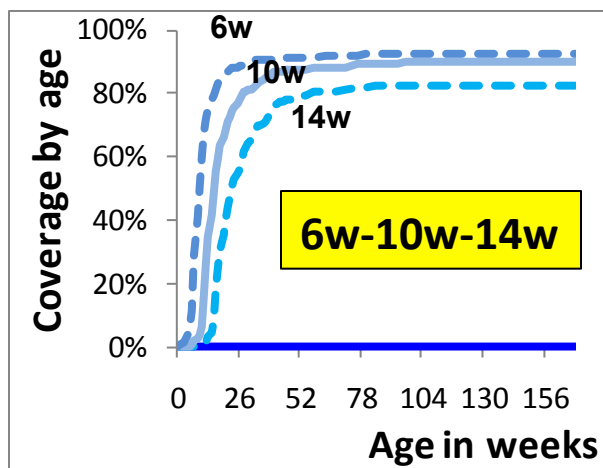
% point difference
45% - 47% = -2%

**What if protection after the 2nd dose
is higher (80%+)?**

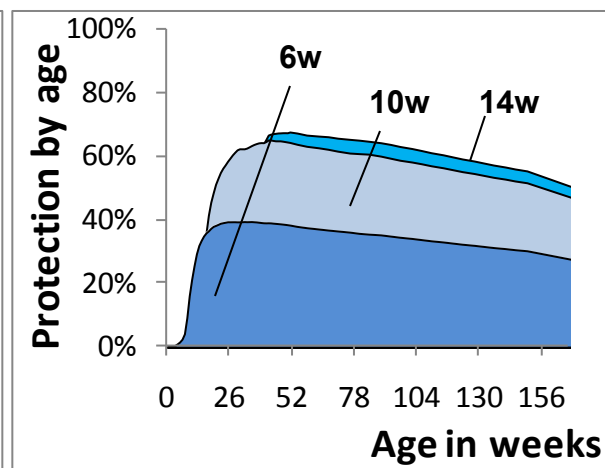
Direct impact of wP vaccination in Senegal:

Mid VE scenario (40%→80%→92%), 13% waning per year

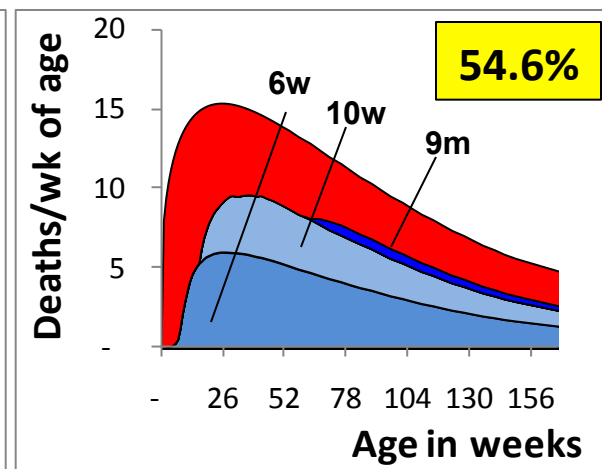
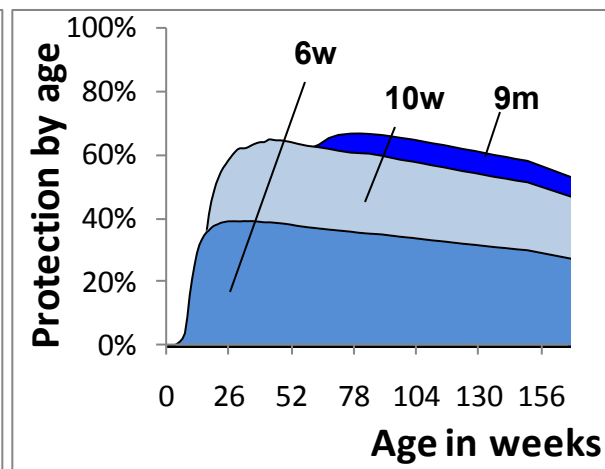
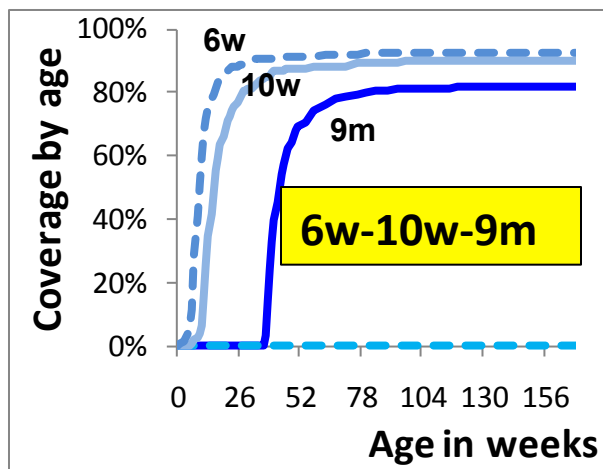
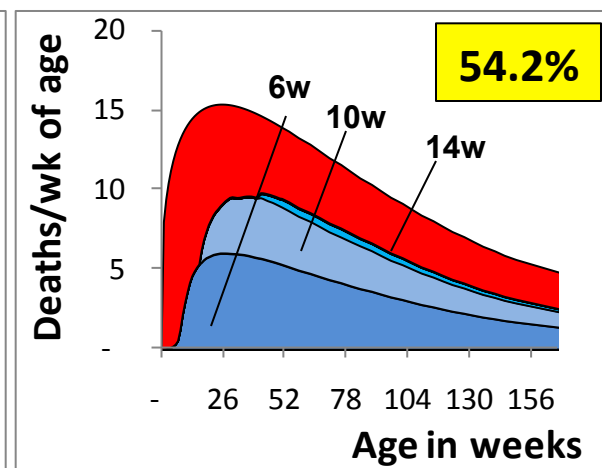
(a) Coverage by age



(b) Protection by age



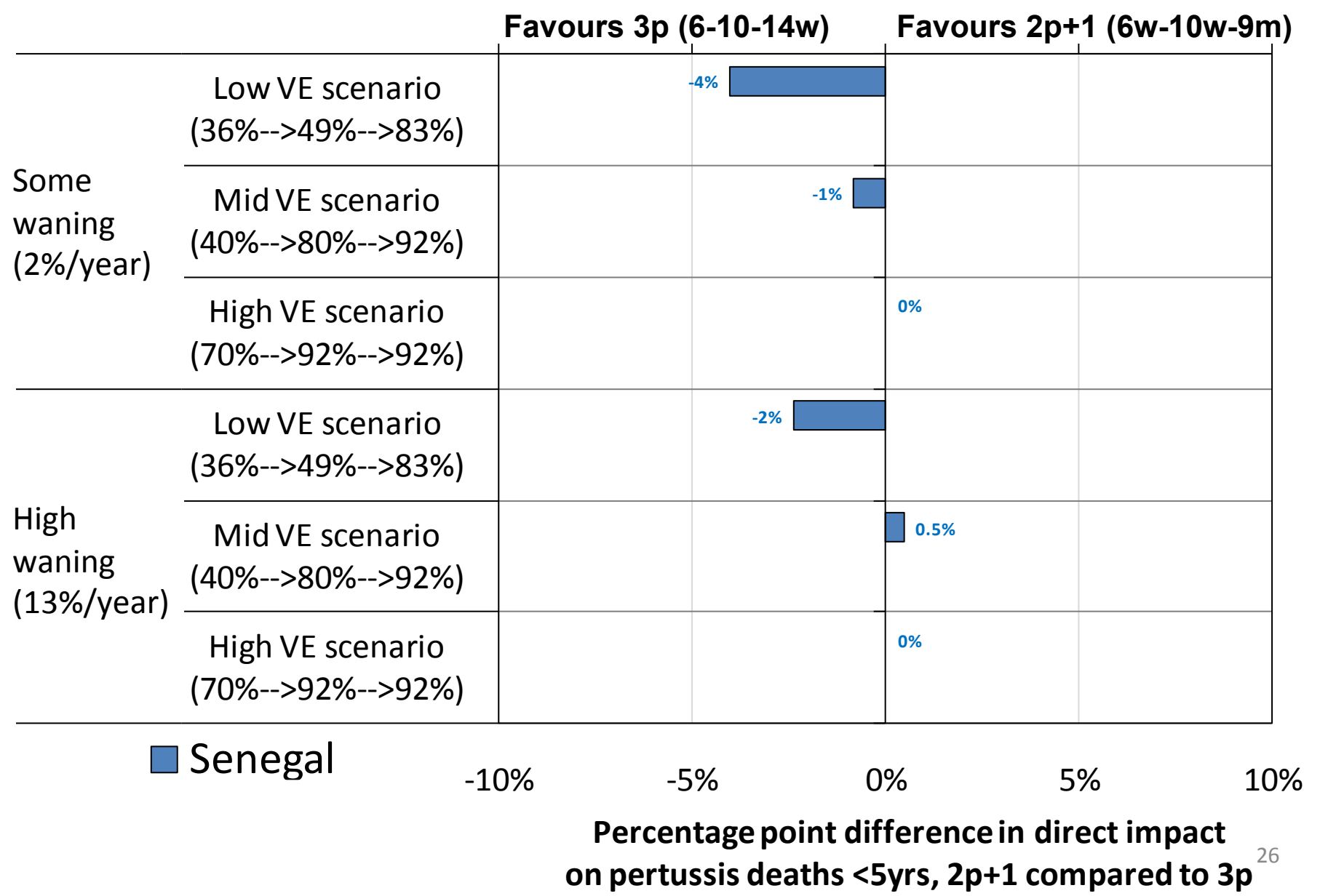
(c) Direct impact by age



For both schedules the effect of the 3rd dose is small because: a) 2 dose VE is high; b) 3rd dose coverage is low

Alternative scenarios...

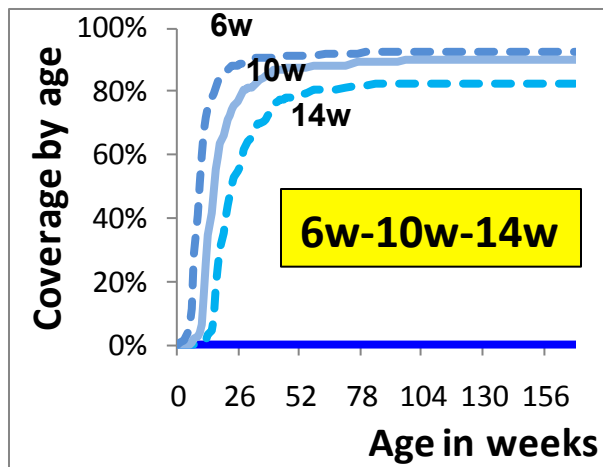
Percentage point difference in direct impact vs pertussis deaths <5yrs: 2p+1 compared to 3p in Senegal



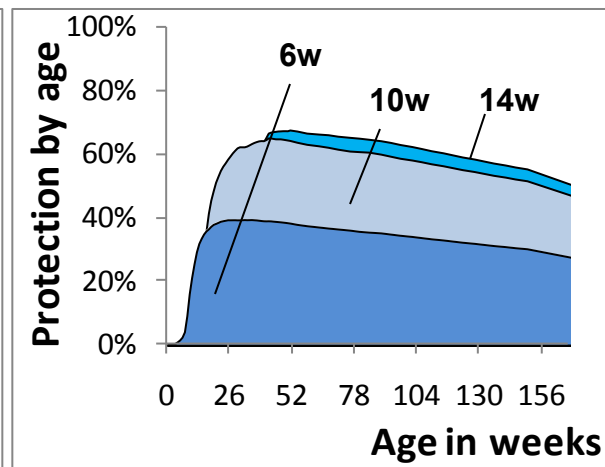
What about other LMICs?

Direct impact of wP vaccination in Senegal: Mid VE scenario (40%→80%→92%), 13% waning per year

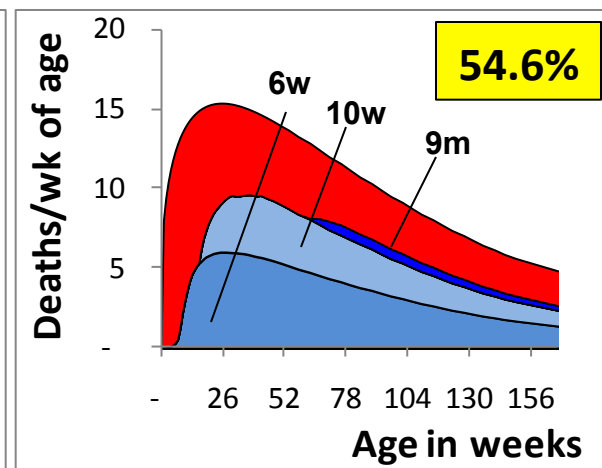
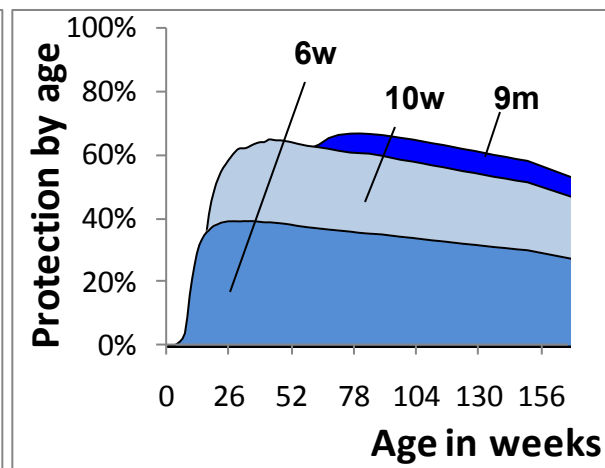
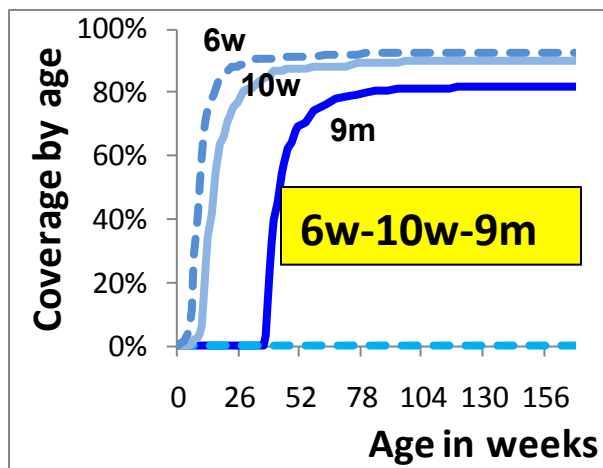
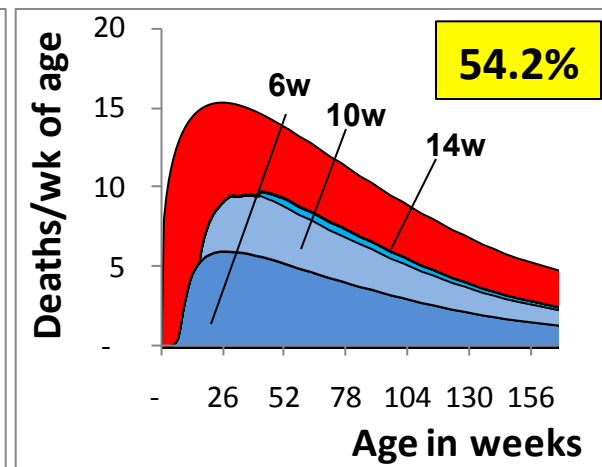
(a) Coverage by age



(b) Protection by age



(c) Direct impact by age

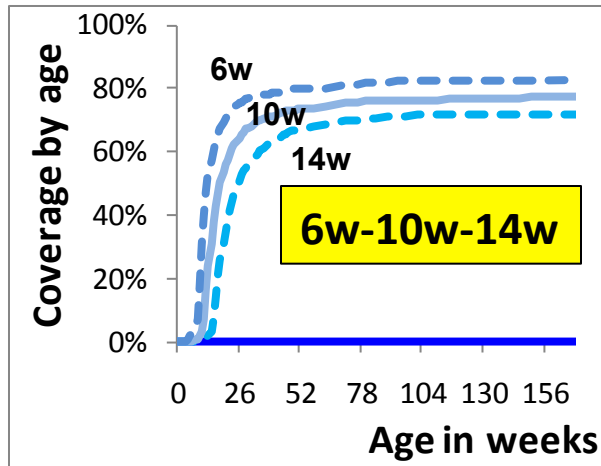


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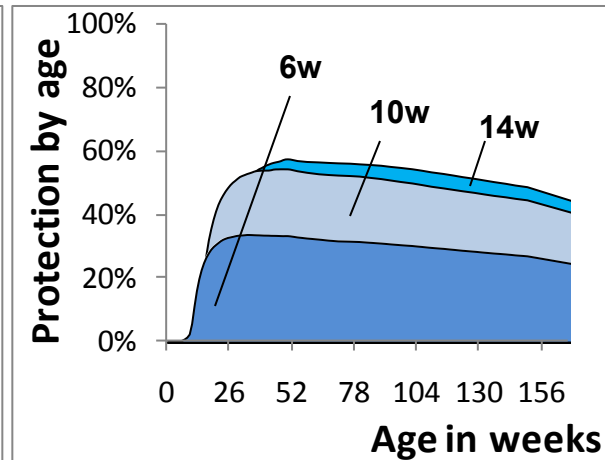
Direct impact of wP vaccination in India:

Mid VE scenario (40%→80%→92%), 13% waning per year

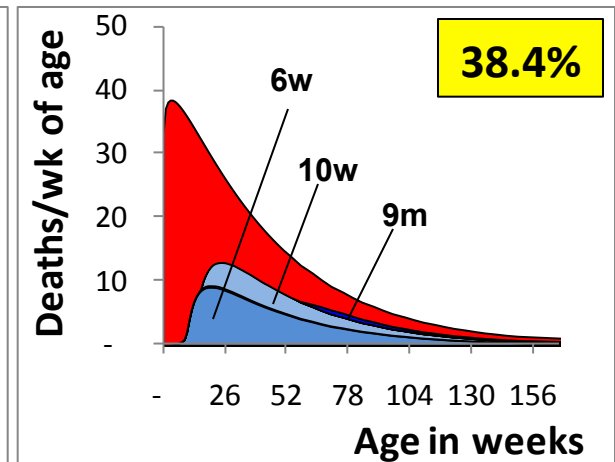
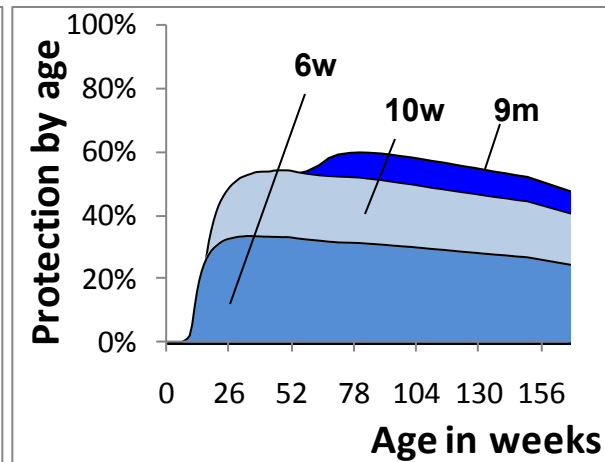
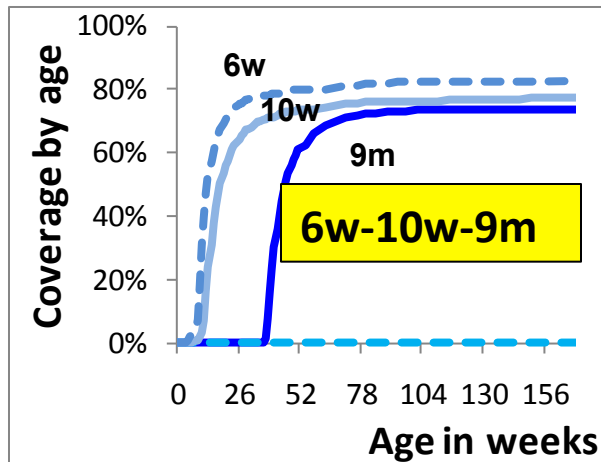
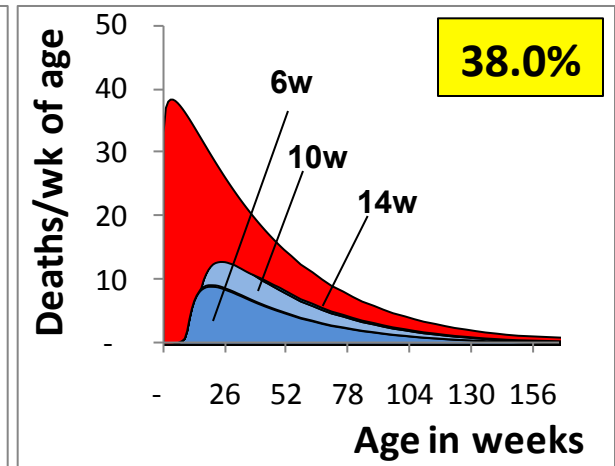
(a) Coverage by age



(b) Protection by age

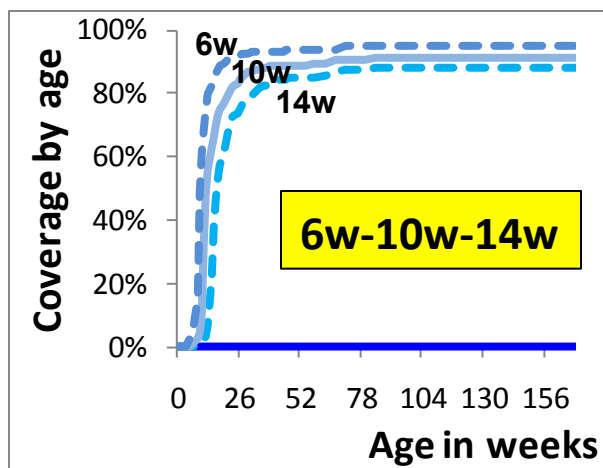


(c) Direct impact by age

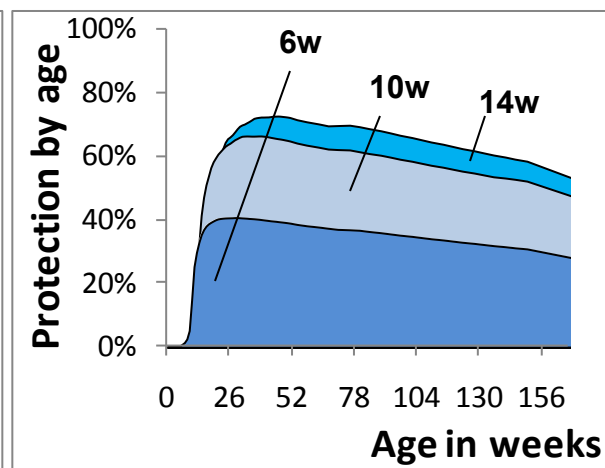


Direct impact of wP vaccination in Kenya: Mid VE scenario (40%→80%→92%), 13% waning per year

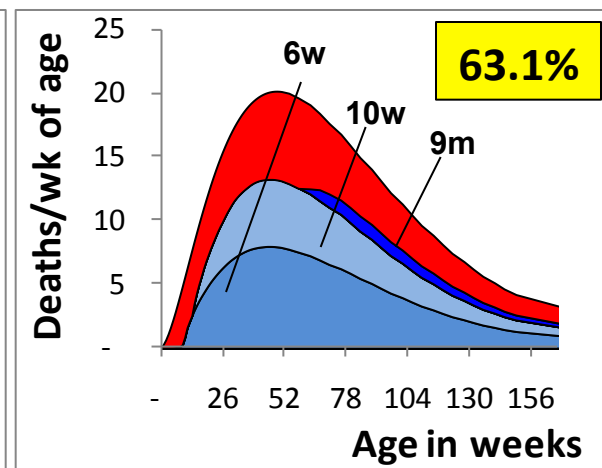
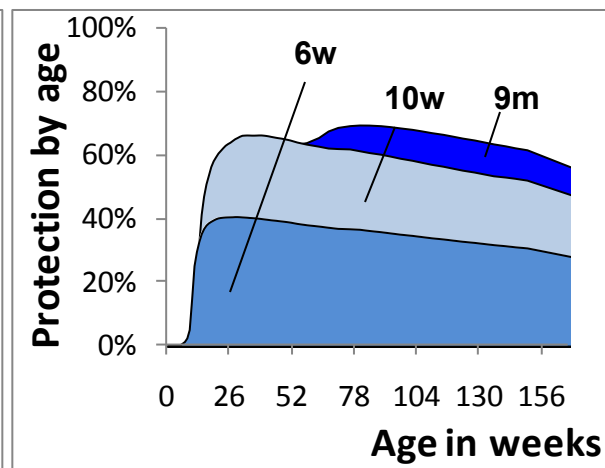
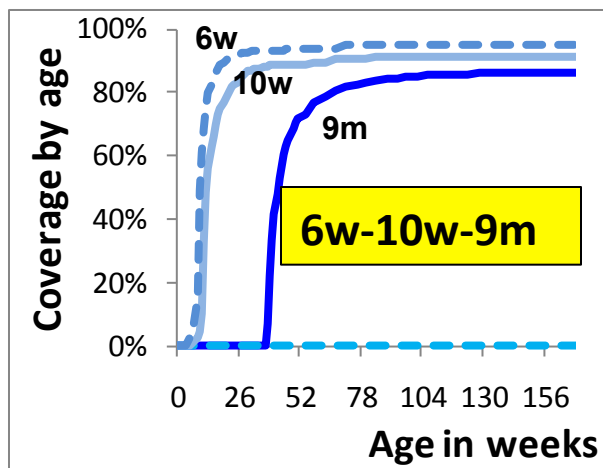
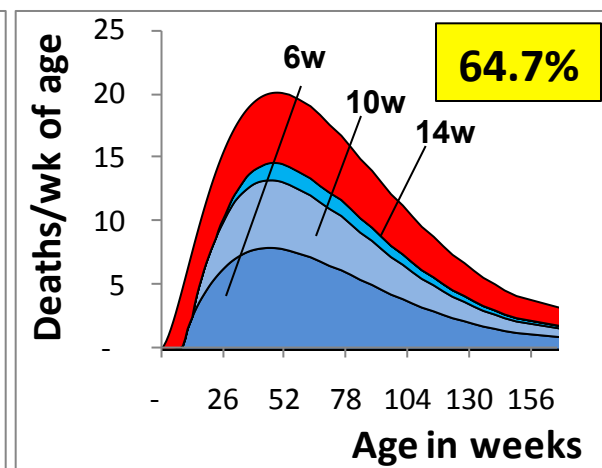
(a) Coverage by age



(b) Protection by age

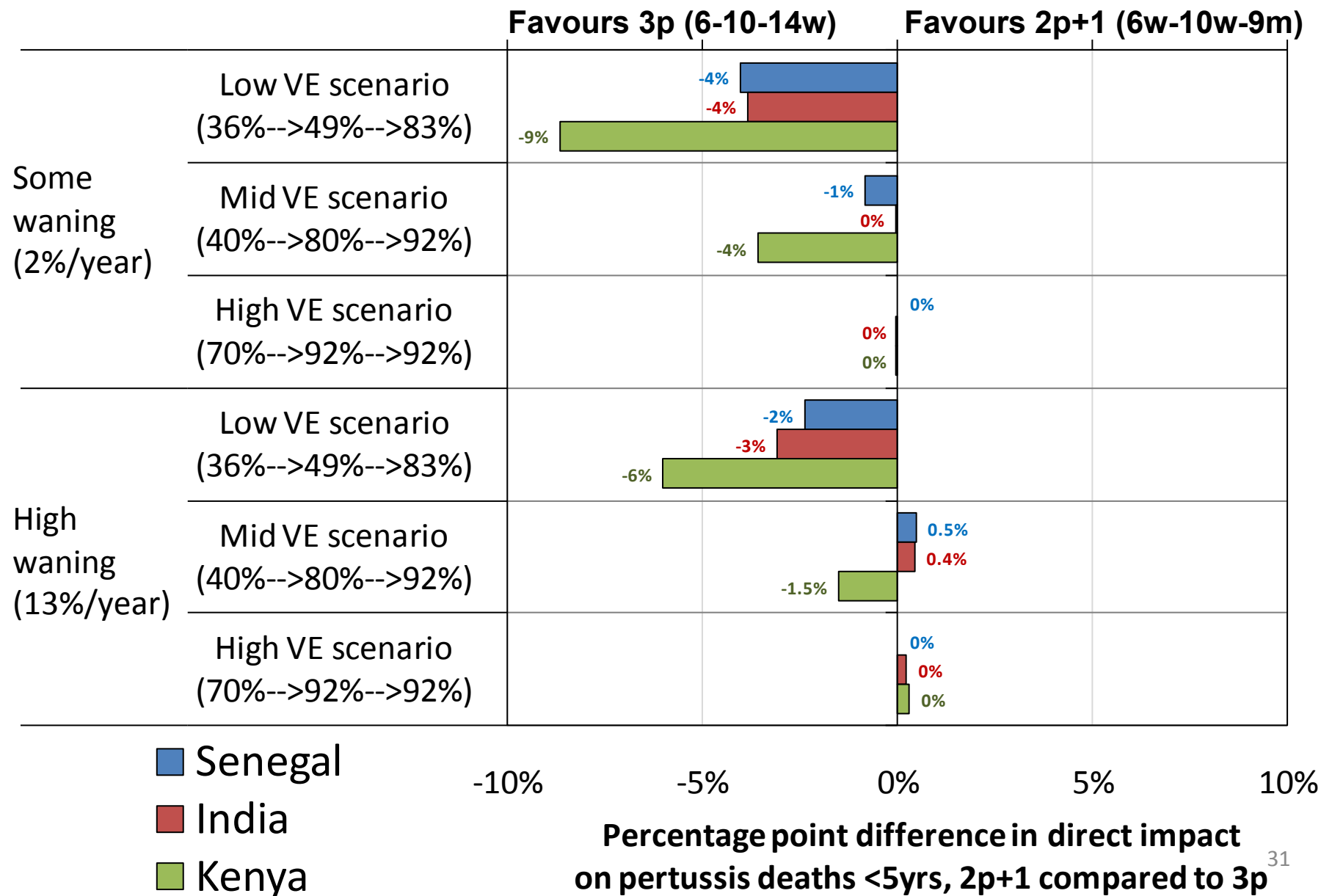


(c) Direct impact by age

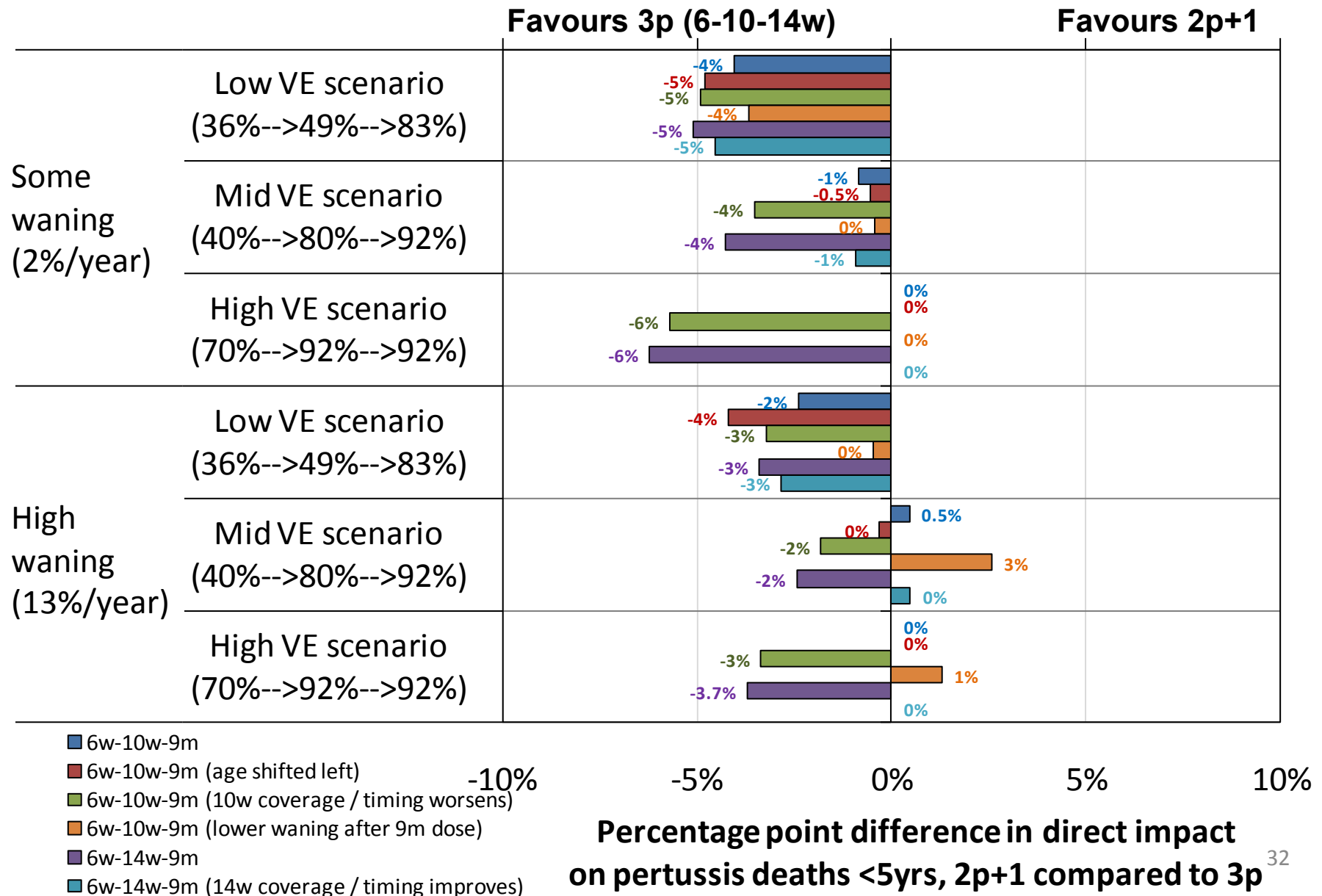


In Kenya, mortality starts to peak in the window between 14w and 9m, so a 14w dose is preferable.

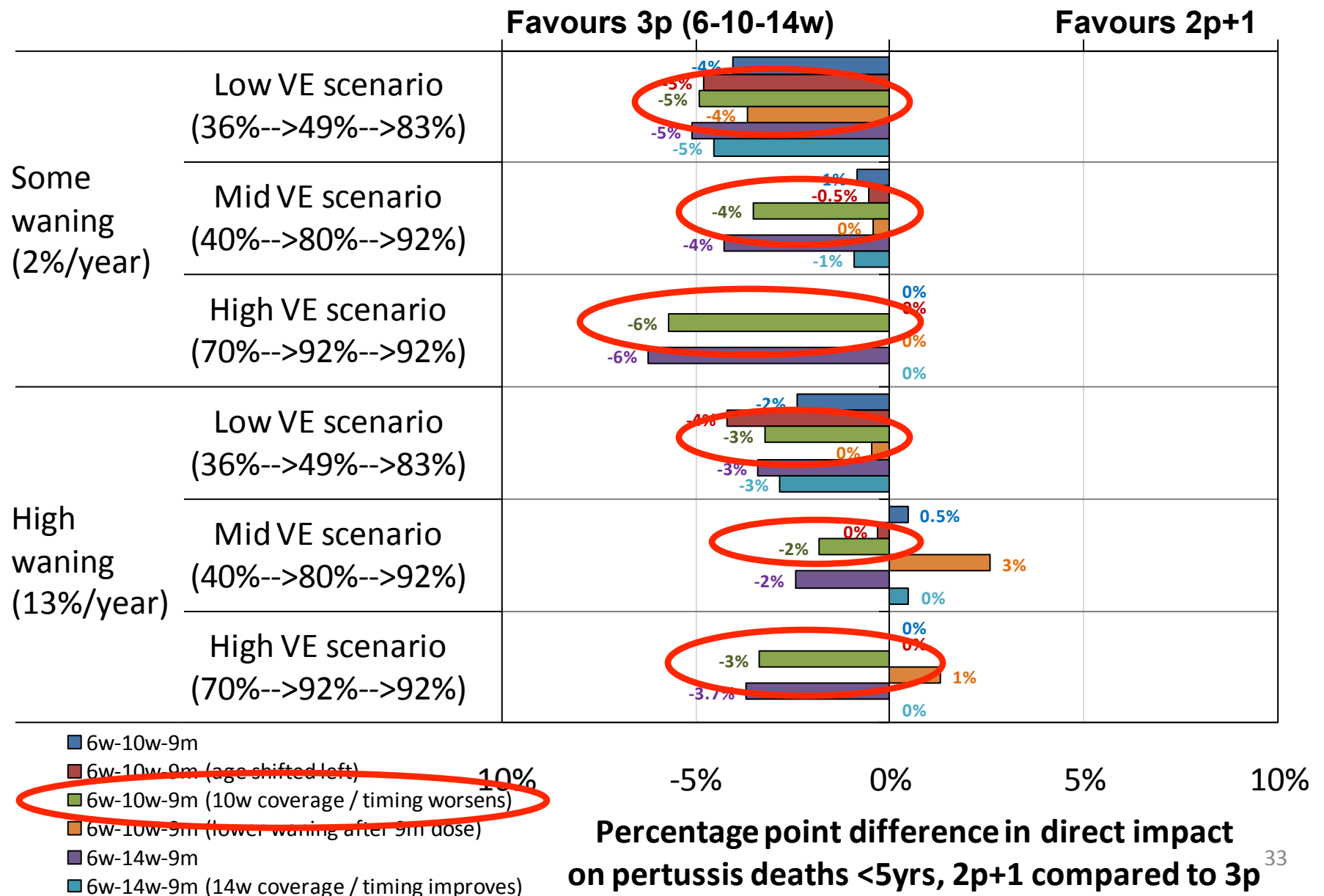
Percentage point difference in direct impact vs pertussis deaths <5yrs: 2p+1 compared to 3p in Senegal, India and Kenya



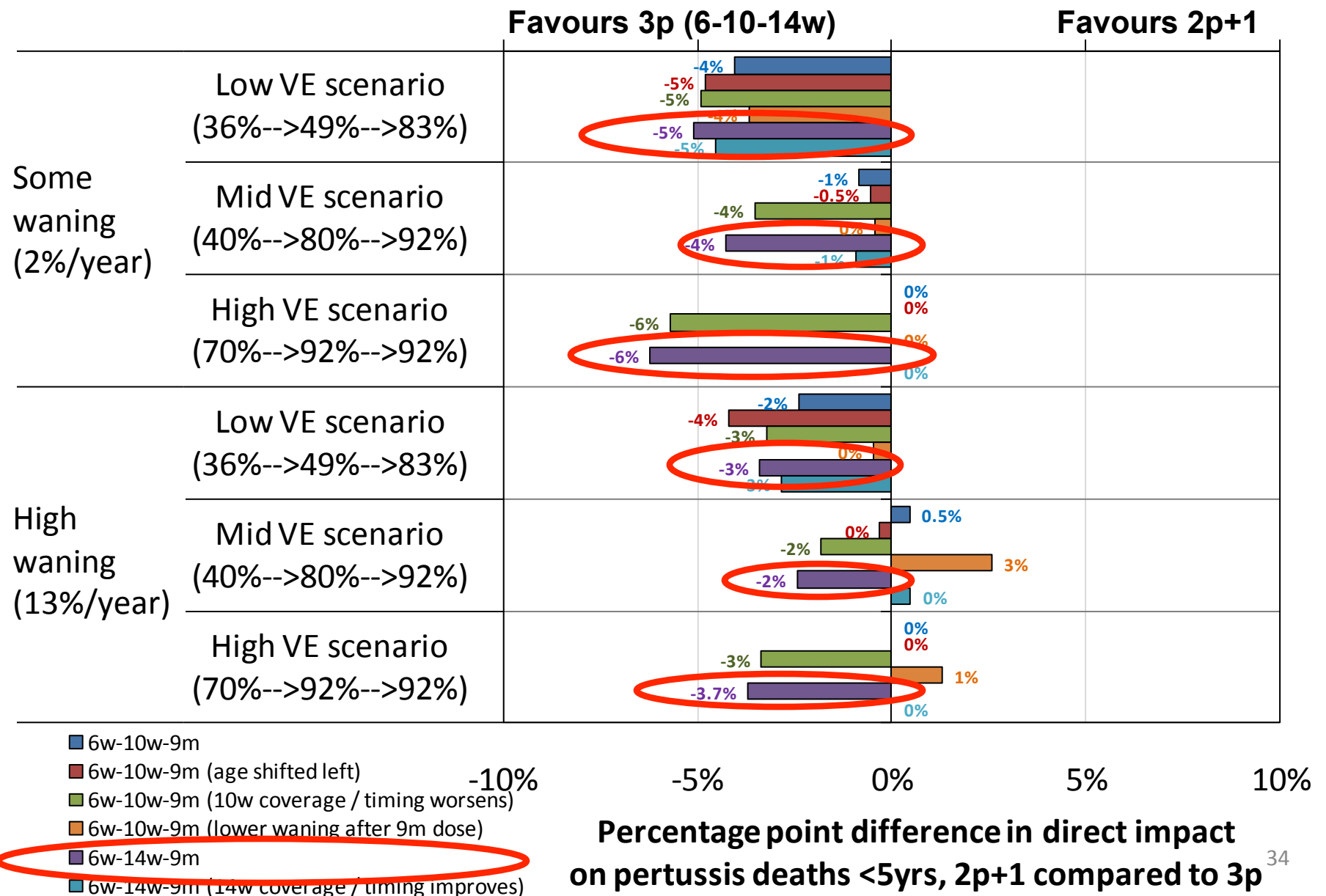
Percentage point difference in direct impact vs pertussis deaths <5yrs: 2p+1 compared to 3p in [Senegal – alternative scenarios](#)



Percentage point difference in direct impact vs pertussis deaths <5yrs: 2p+1 compared to 3p in [Senegal – alternative scenarios](#)



Percentage point difference in direct impact vs pertussis deaths <5yrs: 2p+1 compared to 3p in [Senegal – alternative scenarios](#)



Conclusions (in selected LMICs)

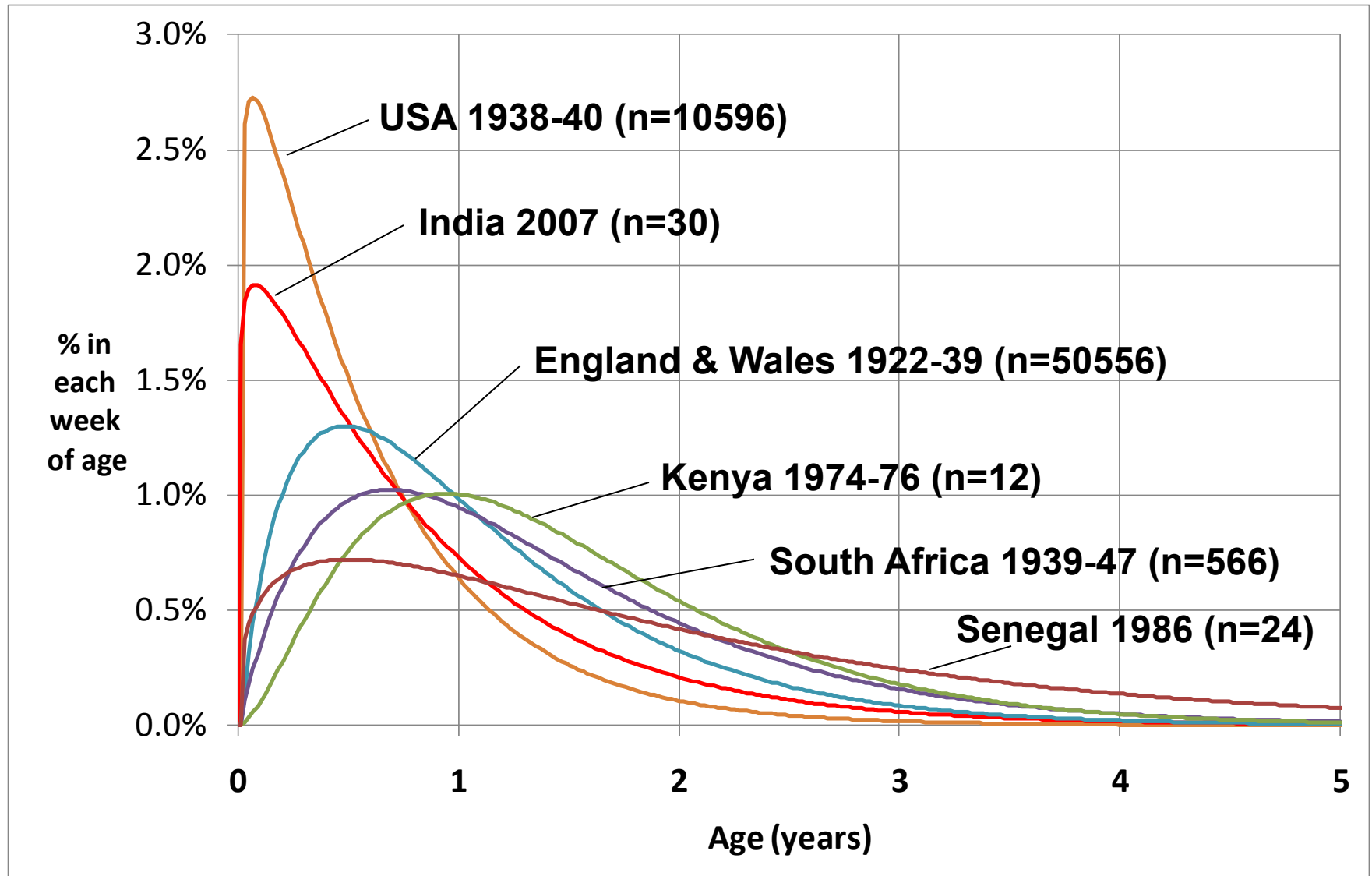
- Direct impact is likely to be similar for 6w-10w-14w and 6w-10w-9m schedules *if* protection after the 2nd dose is high (80%+)
- Current evidence is not strong enough to preclude a move to 6w-10w-9m should this be advantageous for other antigens administered as part of the same combined vaccine.

However:

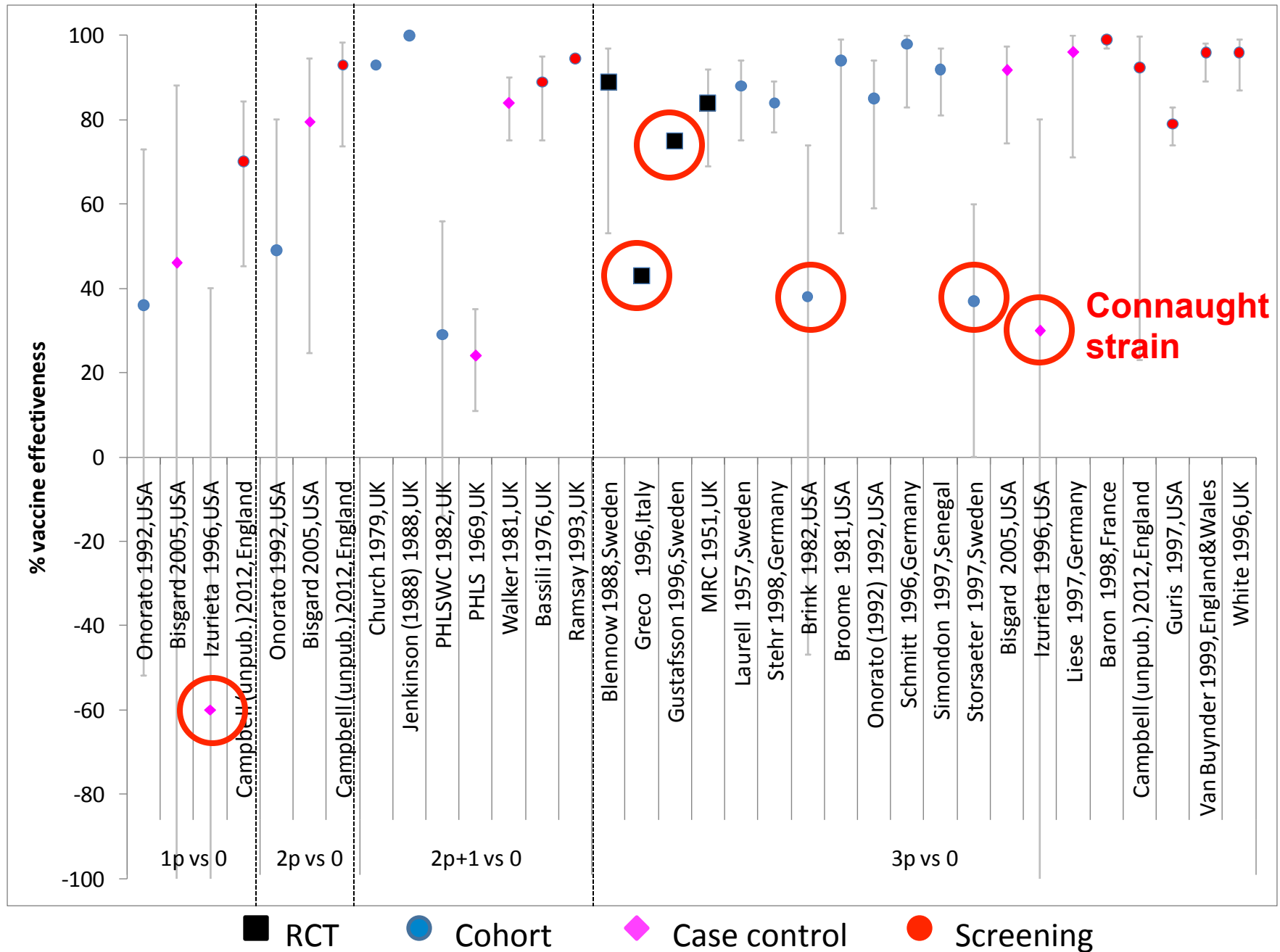
- it depends on the local situation e.g. in Kenya there is a stronger case for 6-10-14w as the 14wk dose is timely/high and covers peak age of death;
- moving to a 6w-10w-9m schedule could be detrimental if 10w coverage and timeliness are adversely affected;
- uncertainty about the influence of herd effects (not modelled/included)
- 6w-14w-9m is likely to be inferior to 6w-10w-9m, particularly in countries where the 14w dose is less timely and has lower coverage than the 10w dose.

Backup slides

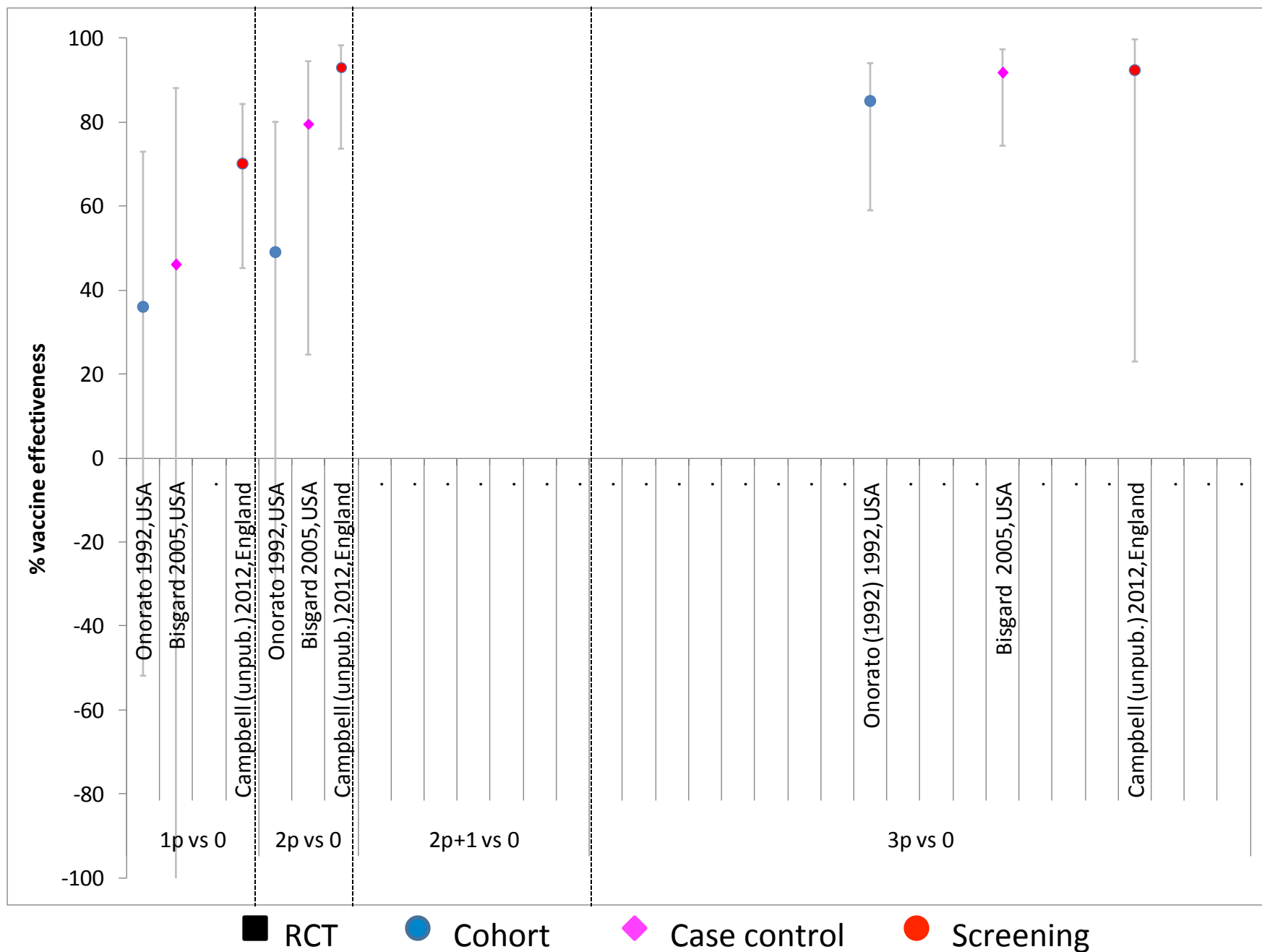
Variation in the age distribution of pertussis deaths <5yrs in the pre-vaccine era: curves fitted to available datasets



Dose-specific VE of wP: earliest reported follow-up

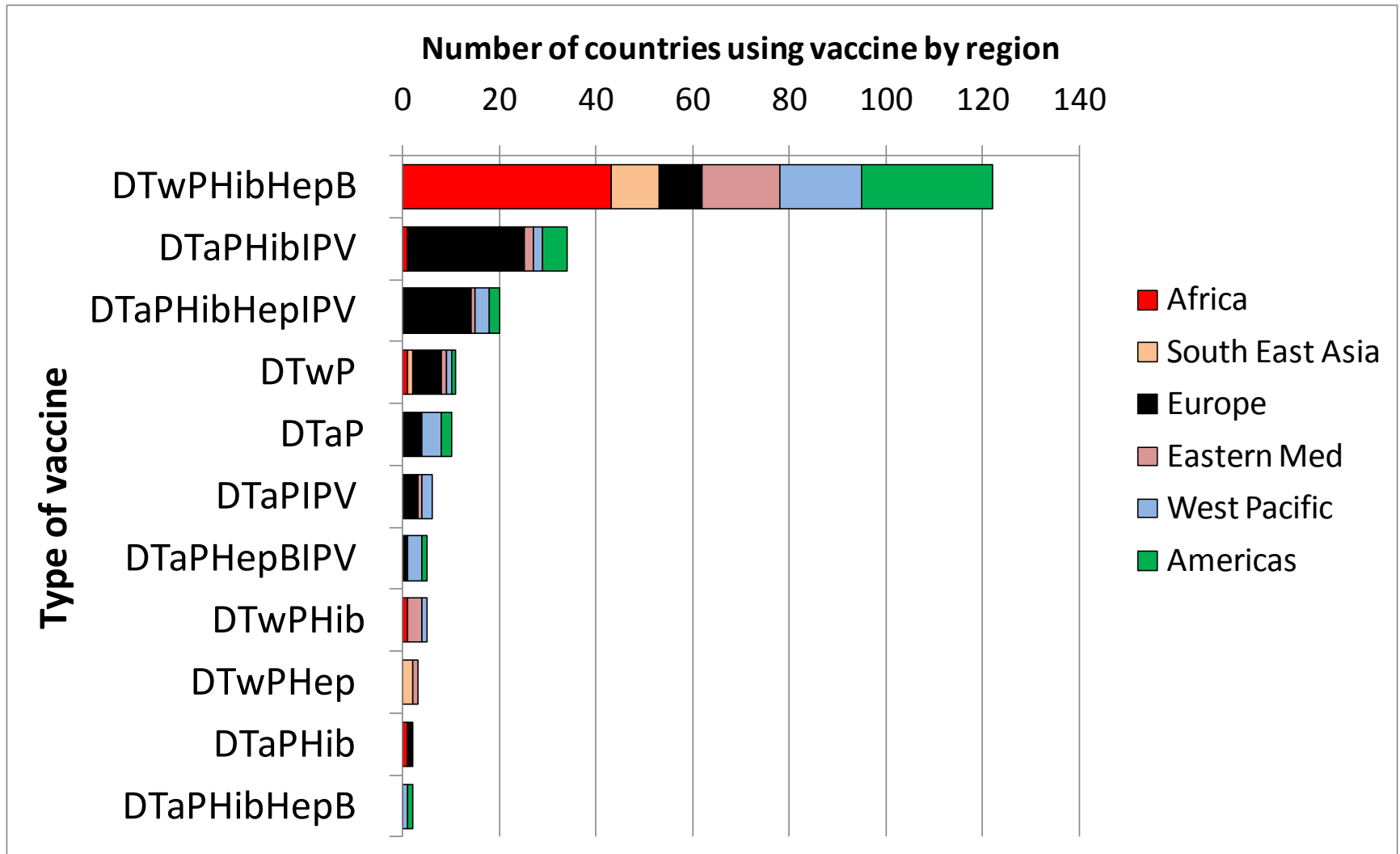


Dose-specific VE of wP: studies reporting on all 3 doses



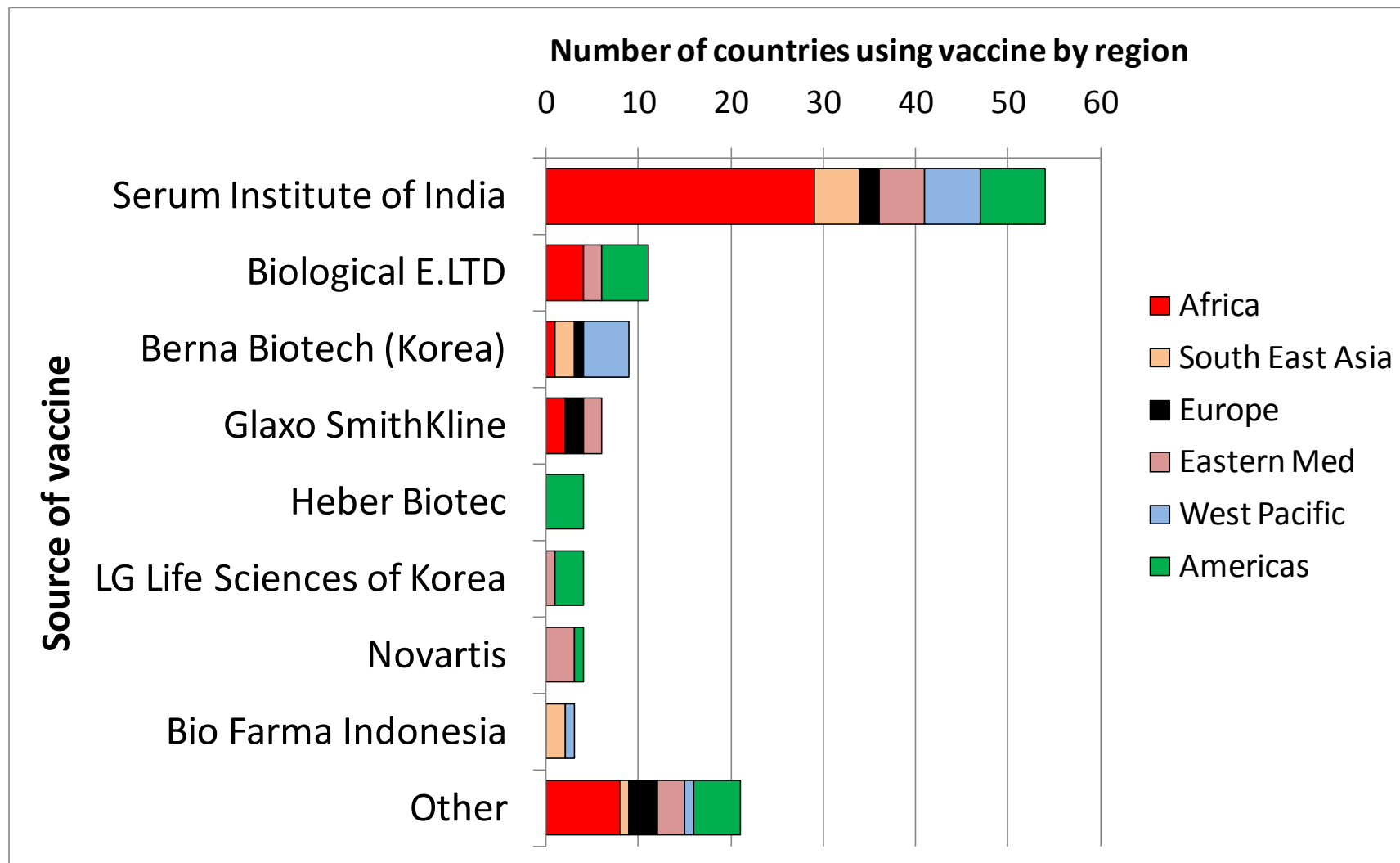
Variation in type of DTP combination used

Number of countries using each type of DTP combination, grouped by region

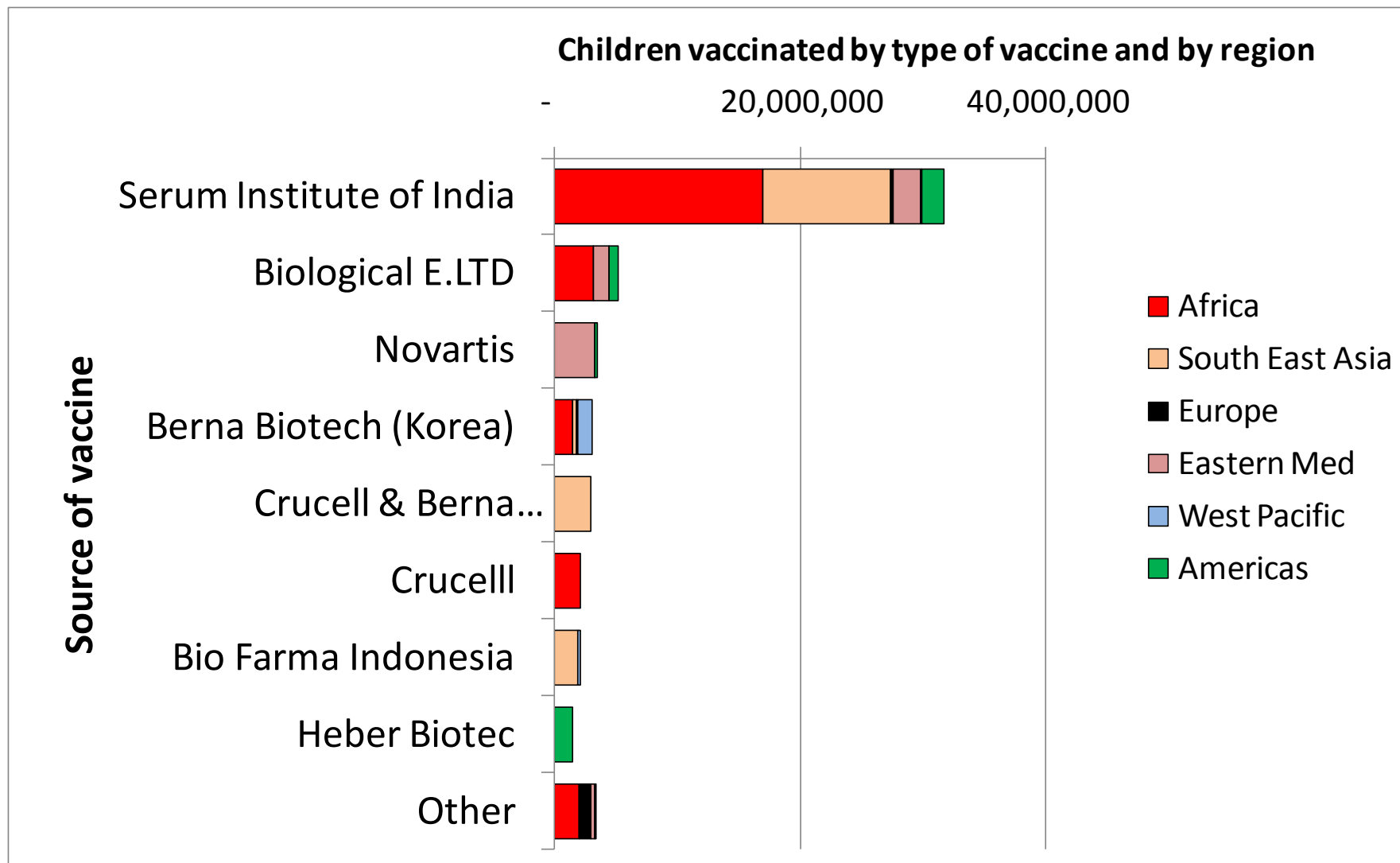


Variation in the source / brand of pentavalent (DTwPHibHepB) vaccine

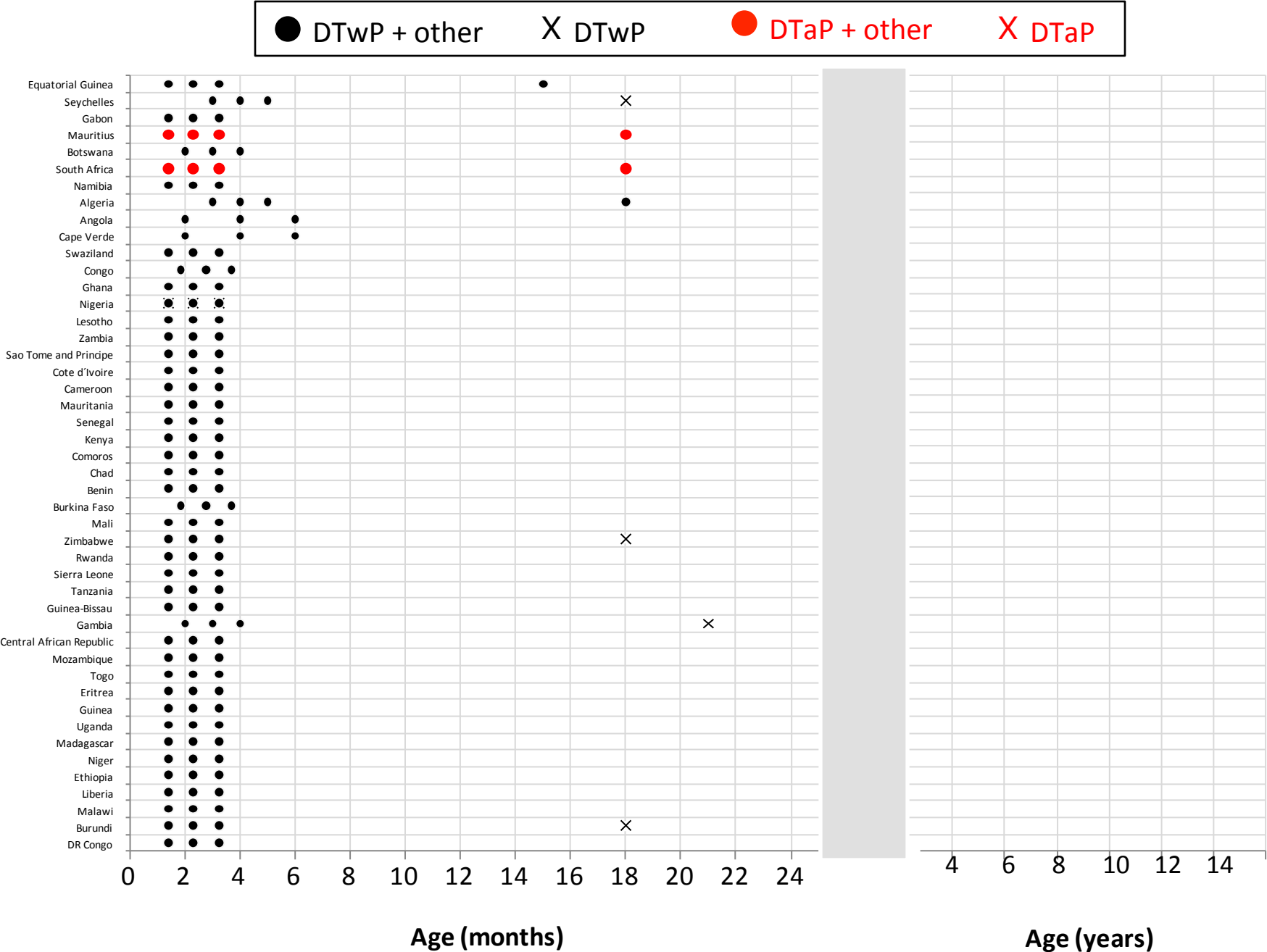
Number of countries using each type of DTwPHibHepB brand, grouped by region



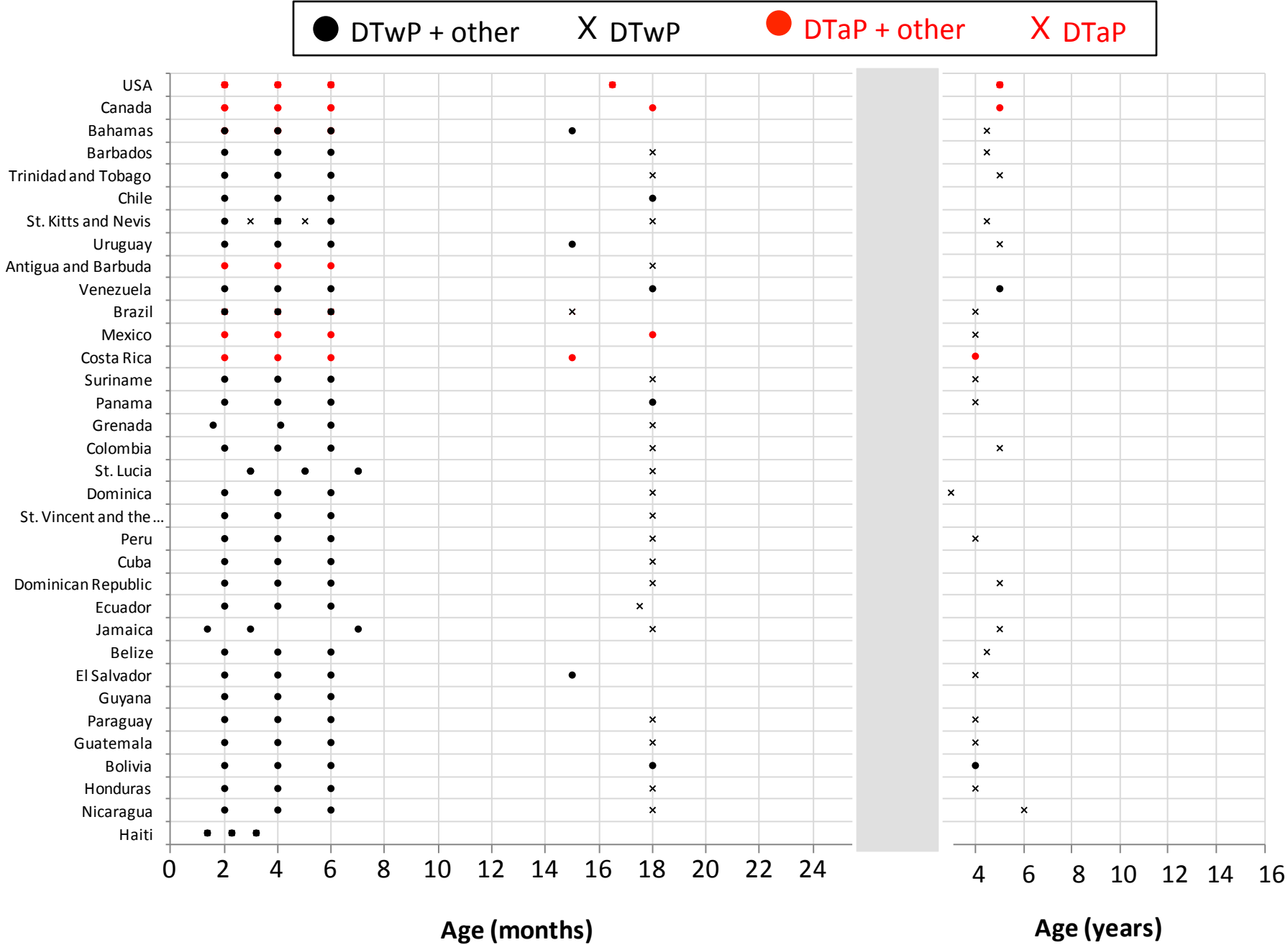
Number of children vaccinated using each type of DTwPHibHepB brand, grouped by region



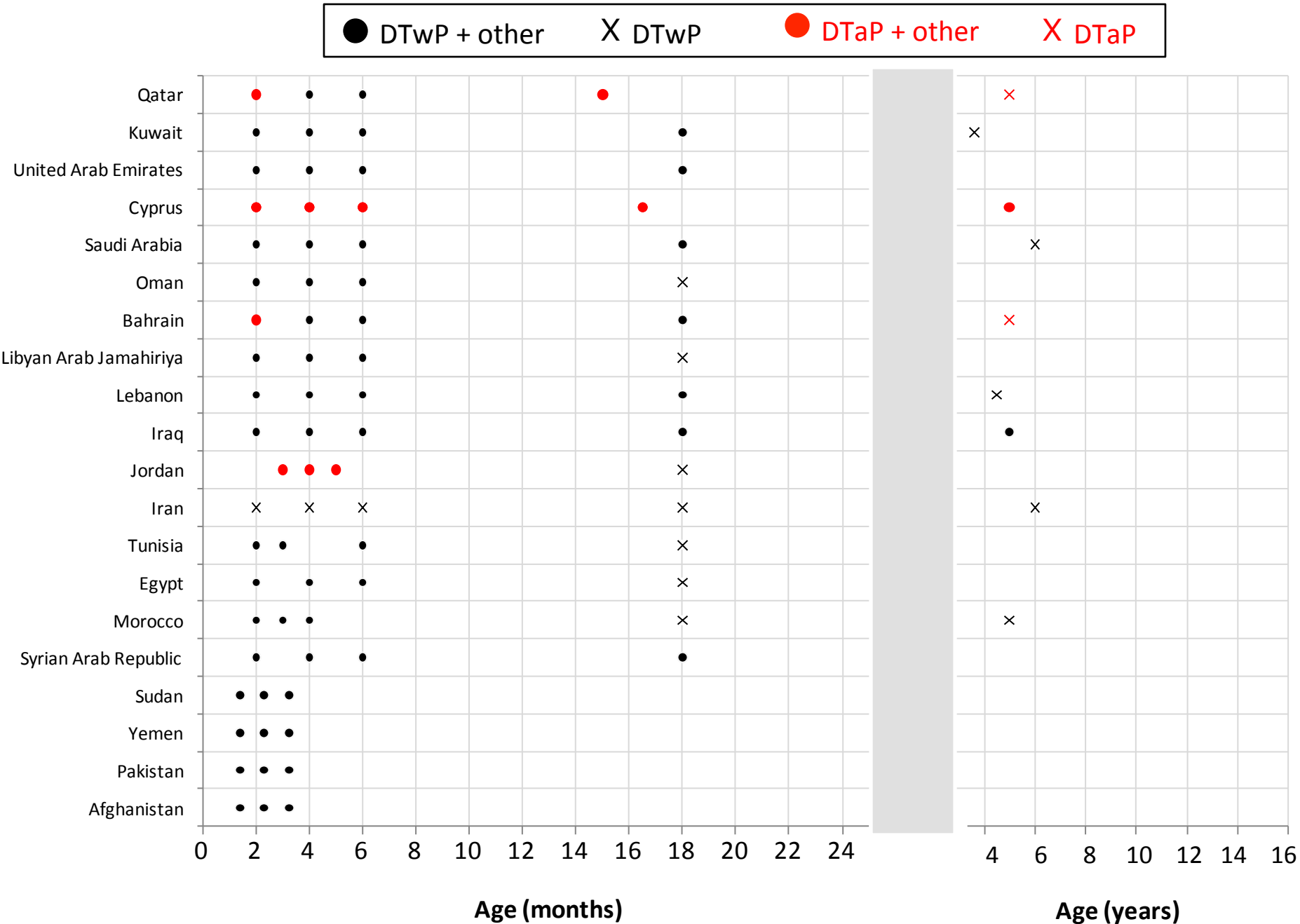
Variation in DTP schedules: Africa



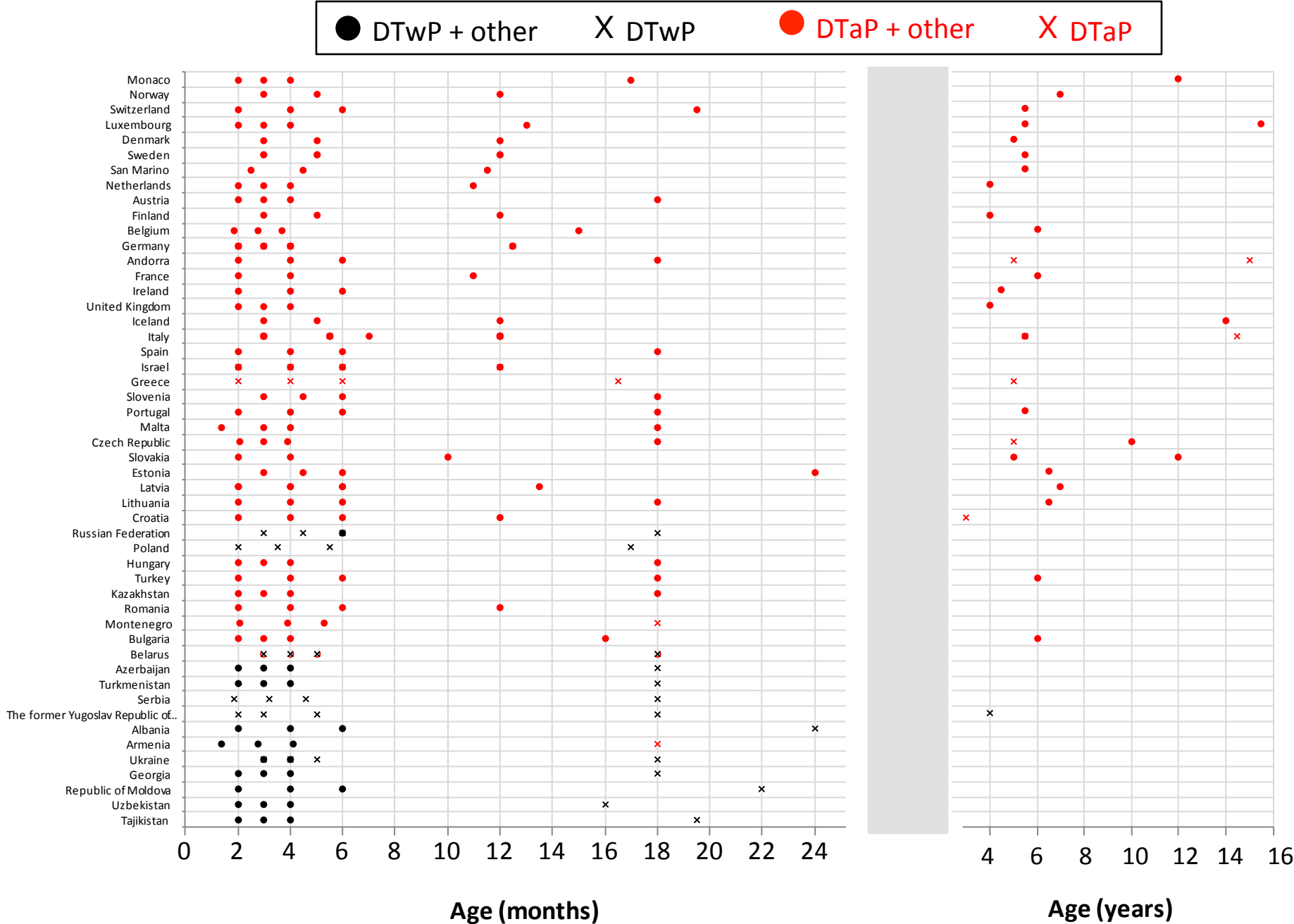
Variation in DTP schedules: **Americas**



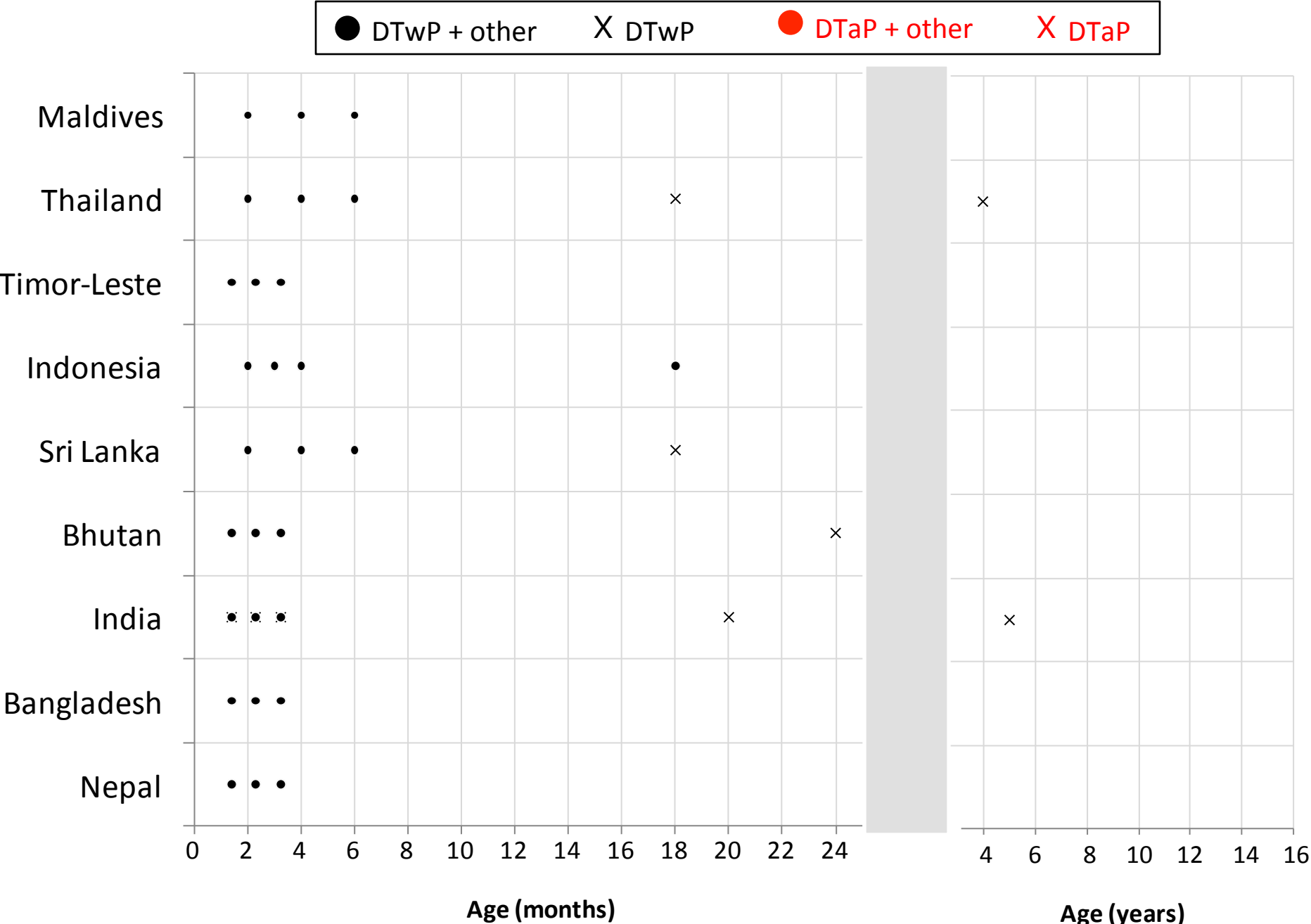
Variation in DTP schedules: Eastern Mediterranean



Variation in DTP schedules: Europe



Variation in DTP schedules: South East Asia



Variation in DTP schedules: Western Pacific

