

THE LANCET

Infectious Diseases

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
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Supplement to: Davis K, Valente Pinto M, Andrews NJ, et al. Immunogenicity of the UK group B meningococcal vaccine (4CMenB) schedule against groups B and C meningococcal strains (Sched3): outcomes of a multicentre, open-label, randomised controlled trial. *Lancet Infect Dis* 2021; published online Jan 8. [https://doi.org/10.1016/S1473-3099\(20\)30600-9](https://doi.org/10.1016/S1473-3099(20)30600-9)

Supplementary Tables and Figures.

Supplementary Figure 1: Grading of local and systemic reactions.

Local reactions:

For redness and swelling “any” severity was recorded if the largest measurement was >0mm and “severe” was recorded if the largest measurement was ≥50mm.

Tenderness: Is there any tenderness at the injection site?

- | | | |
|----------|-----------------|-------------------------------------|
| 0 | None | |
| 1 | Mild | child whimpers when site is touched |
| 2 | Moderate | child cries when site is touched |
| 3 | Severe | child cries when leg is moved |

Systemic reactions:

Fever: “any temperature” was defined as ≥37.5°C and “severe temperature” was ≥39°C.

Has your child been feeding less than usual?

- | | | |
|----------|-----------------|--|
| 0 | None | |
| 1 | Mild | Feeding less than normal for 1-2 feeds |
| 2 | Moderate | Missed 1-2 feeds completely |
| 3 | Severe | Refused most or all feeds |

Has your child been less active than usual?

- | | | |
|----------|-----------------|---|
| 0 | None | |
| 1 | Mild | Less interested in surroundings, toys etc. |
| 2 | Moderate | No interest in above and sleeping through feeds |
| 3 | Severe | Sleeping most of the time |

Has your child been more irritable than usual?

- | | | |
|----------|-----------------|---|
| 0 | None | |
| 1 | Mild | Continuously irritable for less than 1 hour |
| 2 | Moderate | Continuously irritable for 1 to less than 3 hours |
| 3 | Severe | Continuously irritable for 3 or more hours |

Has your child cried persistently?

- | | | |
|----------|-----------------|---|
| 0 | None | |
| 1 | Mild | Cried continuously for less than 1 hour |
| 2 | Moderate | Cried continuously for 1 to less than 3 hours |
| 3 | Severe | Cried continuously for 3 or more hours |

Has your child been sick?

- | | | |
|----------|-----------------|---|
| 0 | None | |
| 1 | Mild | 1-2 episodes without interfering with routine |
| 2 | Moderate | Several episodes & cannot keep any food down |

3 Severe Frequent episodes & taking nothing by mouth

Has your child had diarrhoea?

0 None

1 Mild More loose stools than usual

2 Moderate Frequent runny stools without much solid material

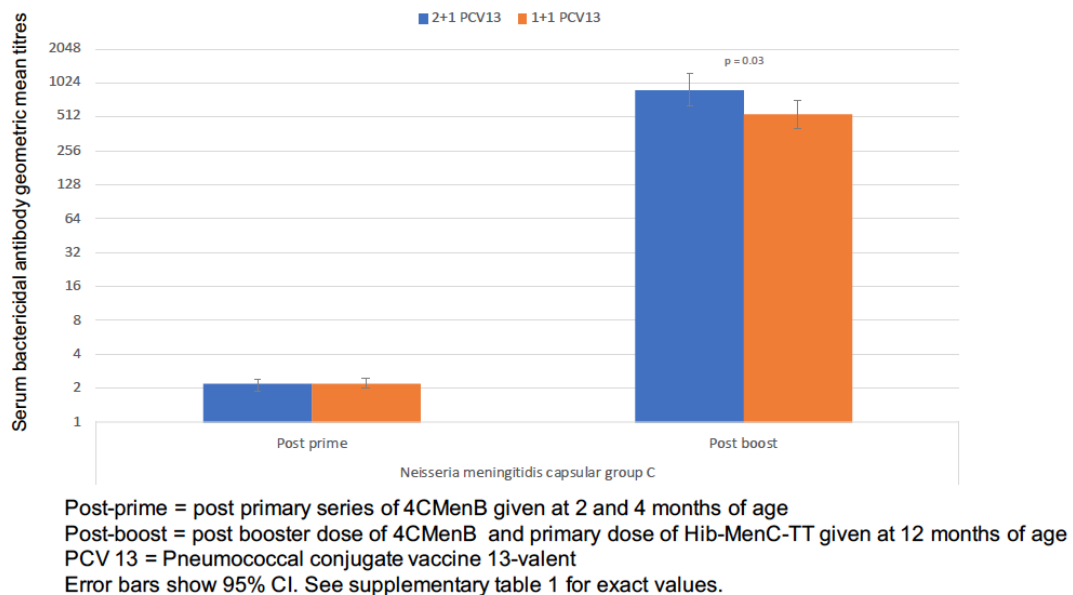
3 Severe Multiple liquid stools without much solid material

Supplementary Table 1: Sched3 immunisation and blood test schedule

	Visit 1 2 months of age	Visit 2 3 months of age	Visit 3 4 months of age	Visit 4 5 months of age	Visit 5 12 months of age	Visit 6 13 months of age
2 + 1 PCV13 doses	DTaP-IPV- Hib 4CMenB PCV13 Rota	DTaP-IPV- Hib Rota	DTaP-IPV- Hib 4CMenB PCV13	Blood test	4CMenB PCV13 ib-MenC- TT	MMR Blood test
1 + 1 PCV13 doses	DTaP-IPV- Hib 4CMenB Rota	DTaP-IPV- Hib PCV13 Rota	DTaP-IPV- Hib 4CMenB

PCV13=Prevenar 13, Pfizer, Sandwich, UK. 4CMenB=Bexsero, GlaxoSmithKline, Rixensart, Belgium. DTaP-IPV-Hib=Infanrix-IPV-Hib, GSK, Rixensart, Belgium. Rota=Rotarix, GSK, Rixensart, Belgium. Hib-MenC-TT=Menitorix, GSK, Rixensart, Belgium. MMR=Priorix, GlaxoSmithKline, Rixensart, Belgium.

Supplementary figure 2: *Neisseria meningitidis* capsular group C reference strain serum bactericidal assay Geometric Mean Titres (SBA GMTs).



Supplementary table 2: Number of participants with SBA titres ≥ 4 against strains 44/76 and/or NZ98/254 post-primary and post-booster vaccine (both groups combined)

		Post-Boost				
Post-Prime		0/2*	1/2	2/2	Missing	Total
	0/2	1	1	0	0	2
	1/2	2	6	13	4	25
	2/2	0	9	101	45	155
	Missing	1	1	18	11	31
	Total	4	17	132	60	213

* 0/2 indicates that that SBA titres ≥ 4 were not seen for either 44/76 or NZ98/254. 1/2 indicates SBA titres ≥ 4 were seen for one of these strains, and 2/2 indicates SBA titres ≥ 4 were observed for both.

Supplementary table 3: Geometric mean concentrations of IgG specific to Diphtheria-toxoid, Tetanus-toxoid and polyribosyl ribitol phosphate (PRP - Hib) and Pertussis antigens (PT, PRN, FHA, FIM 2 and 3) by group, and geometric mean fold ratios (GMFR) with 95% CI.

	Post-Primary				Post-Boost			
	<u>2+1 PCV13 group</u> PCV13: 2,4m MenB: 2,4m (N=69) (Pertussis N=66 to 73)	<u>1+1 PCV13 group</u> PCV13: 3m MenB: 2,4m (N=82) (Pertussis N=82 to 84)	GMFR 1+1 PCV13 group : 2+1 PCV13 group	p-value*	<u>2+1 PCV13 group</u> PCV13: 2,4,12m MenB: 2,4,12m (N=73)	<u>1+1 PCV13 group</u> PCV13: 3,12m MenB: 2,4,12m (N=74)	GMFR 1+1 PCV13 group : 2+1 PCV13 group	p-value*
Anti-diphtheria toxoid IgG IU/ml	0.47 (0.40-0.55)	0.32 (0.27-0.38)	0.69 (0.55-0.88)	0.003	0.68 (0.58-0.81)	0.58 (0.47-0.71)	0.84 (0.65-1.09)	0.20
Anti-tetanus toxoid IgG IU/ml	1.26 (1.08-1.46)	1.38 (1.21-1.57)	1.10 (0.90-1.33)	0.36	4.37 (3.28-5.84)	3.88 (2.97-5.07)	0.89 (0.60-1.31)	0.54
Anti-PRP-Hib IgG µg/mL	1.01 (0.72-1.41)	0.71 (0.54-0.94)	0.70 (0.46-1.07)	0.10	35.77 (26.77-47.8)	28.00 (22.00-35.64)	0.78 (0.54-1.13)	0.19
Anti-PT IgG IU/mL	28.94 (25.43-32.93)	26.32 (22.86-30.31)	0.91 (0.75-1.10)	0.33	3.19 (2.56-3.98)	2.67 (2.16-3.28)	0.83 (0.62-1.12)	0.24
Anti-PRN IgG IU/mL	44.05 (35.72-54.31)	42.08 (34.58-51.21)	0.96 (0.72-1.27)	0.75	5.42 (4.22-6.98)	3.99 (3.22-4.94)	0.74 (0.53-1.02)	0.07
Anti-FHA IgG IU/mL	61.78 (53.75-71)	58.35 (50.57-67.32)	0.94 (0.77-1.15)	0.57	12.94 (9.99-16.76)	10.57 (8.57-13.03)	0.82 (0.59-1.13)	0.23
FIM 2 and 3 IgG U/mL	2.71 (2.15-3.42)	5.17 (3.93-6.80)	1.91 (1.33-2.74)	0.001	1.44 (1.15-1.79)	1.31 (1.10-1.55)	0.91 (0.69-1.20)	0.50

Abbreviations: PRP-Hib: polyribosyl ribitol phosphate-*Haemophilus influenzae* type b; PT: Pertussis toxin; PRN: Pertactin; FHA: Filamentous haemagglutinin; FIM: Fimbriae.

*t-test on logged data

Supplementary table 4: Percentage of participants with IgG to Diphtheria-toxoid, Tetanus-toxoid and polyribosyl ribitol phosphate (PRP - Hib) above correlates of protection (95% CI), difference between groups post-booster adjusting for interval to blood and sex.

	Post-Primary			Post-Boost		
	<u>2+1 PCV13 group</u> PCV13: 2,4m MenB: 2,4m	<u>1+1 PCV13 group</u> PCV13: 3m MenB: 2,4m	p-value*	<u>2+1 PCV13 group</u> PCV13: 2,4,12m MenB: 2,4,12m	<u>1+1 PCV13 group</u> PCV13: 3,12m MenB: 2,4,12m	p-value*
Anti-diphtheria toxoid IgG \geq 0.1 IU/mL	98.5% (92.1-100) [67/68]	95.1% (88-98.7) [78/82]	0.38	100% (95.1-100) [73/73]	94.6% (86.7-98.5) [70/74]	0.12
Anti-diphtheria toxoid IgG \geq 1 IU/mL	13.2% (6.2-23.6) [9/68]	11.0% (5.1-19.8) [9/82]	0.80	34.2% (23.5-46.3) [25/73]	25.7% (16.2-37.2) [19/74]	0.28
Anti-tetanus toxoid IgG \geq 0.1 IU/mL	100% (94.8-100) [69/69]	100% (95.6-100) [82/82]	n/a	100% (95.1-100) [73/73]	100% (95.1-100) [74/74]	n/a
Anti-tetanus toxoid IgG \geq 1 IU/mL	65.2% (52.8-76.3) [45/69]	67.1% (55.8-77.1) [55/82]	0.86	89.0% (79.5-95.1) [65/73]	91.9% (83.2-97) [68/74]	0.59
Anti PRP-Hib IgG \geq 0.15µg/mL	93% (84.3-97.7) [66/71]	100% (95.6-100) [82/82]	0.29	100% (95.1-100) [73/73]	100% (95.1-100) [74/74]	n/a
Anti PRP-Hib IgG \geq 1 µg/mL	49.3% (37.2-61.4) [35/71]	67.1% (55.8-77.1) [55/82]	0.75	98.6% (92.6-100) [72/73]	100% (95.1-100) [74/74]	0.50

*Fisher's exact test

Abbreviations: PRP-Hib: polyribosyl ribitol phosphate-*Haemophilus influenzae* type b; MenB: Meningococcus group B; PCV13: 13 valent pneumococcal conjugate vaccine.