

Supplementary material

Supplementary table 1: Routine vaccines administered to participants in the BEAR Men B study

Vaccine	Product names	Age (months)			
		2	3	4	12
DTaP/IPV/Hib/Hep B	Infanrix Hexa®	✓	✓	✓	
Rotavirus	Rotarix®	✓	✓		
MenB	Bexsero®	✓		✓	✓
PCV13	Prevenar13®	✓		✓	✓
MCC-TT/Hib-TT	Menitorix®				✓
MMR	Priorix®				✓

Supplementary table 2: Comparison of the geometric mean titres between groups for each tested antigen

Time point	Strain	Group One (2+1 schedule)		Group Two (3+1 schedule)		GMR (95% CI)	P value*
		N	GMT (95% CI)	N	GMT (95% CI)		
Post-primary (5 months)	44/76 (fHbp)	56	40.5 (31.0-52.8)	63	27.7 (20.3-37.8)	0.69 (0.46-1.0)	0.13
	5/99 (NadA)	56	481.3 (386.6-599.1)	63	603.9 (509.0- 716.4)	1.25 (0.96-1.64)	0.19
	NZ98/254 (PorA)	56	8.7 (5.8-13.0)	61	11.1 (8.3-14.8)	1.27 (0.79-2.05)	0.4
Pre-booster (12 months)	44/76 (fHbp)	56	2.2 (1.9-2.6)	60	2.3 (1.7-3.0)	1.03 (0.73-1.45)	0.26
	5/99 (NadA)	57	36.1 (22.5-58.0)	60	52.0 (34.5-78.4)	1.44 (0.78-2.65)	0.09
	NZ98/254 (PorA)	57	1.4 (1.2-1.6)	60	2.5 (1.8-3.4)	1.8 (1.3-2.5)	0.002
Post-booster (13 months)	44/76 (fHbp)	57	26.3 (18.5-37.5)	55	34.5 (23.7- 50.4)	1.31 (0.79-2.17)	0.3
	5/99 (NadA)	58	1906.3 (1405.5-2585.5)	57	2124.1 (1655.5-2725.3)	1.11 (0.76-1.64)	0.6
	NZ98/254 (PorA)	58	21.1 (14.2-31.2)	55	27.2 (18.9-39.0)	1.29 (0.76-2.18)	0.5

GMT= geometric mean titre; fHbp= factor H binding protein; NadA= Neisseria adhesin A; PorA= Porin A; GMR= geometric mean ratio; CI= confidence interval. *Kruskall Wallis

Supplementary table 3: Percentage of infants with SBA GMT ≥ 4 only following primary or booster vaccination, at neither time point and at both time points

	44/76 (fHbp)			5/99 (NadA)			NZ98/254 (PorA)		
	Overall (n=106)	Group 1 (n=52)	Group 2 (n=54)	Overall (n=108)	Group 1 (n=52)	Group 2 (n=54)	Overall (n=106)	Group 1 (n=52)	Group 2 (n=54)
Neither time point	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)	9.4% (n=10)	13.4% (n=7)	5.8% (n=3)
Post primary only	3.8% (n=4)	1.9% (n=1)	5.6% (n=3)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)
Post booster only	2.8% (n=3)	1.9% (n=1)	3.7% (n=2)	0% (n=0)	0% (n=0)	0% (n=0)	12.3% (n=14)	19.2% (n=10)	7.4% (n=4)
Both time points	93.4% (n=99)	96.2% (n=50)	90.7% (n=49)	100% (n=108)	100% (n=52)	100% (n=56)	77.4% (n=82)	67.3% (n=35)	87.0% (n=47)

fHbp= factor H binding protein; NadA= Neisserial adhesin A; PorA= Porin A

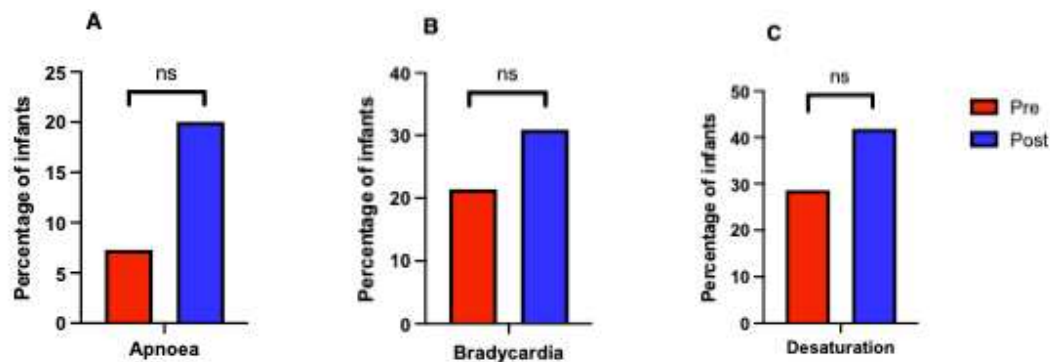
Supplementary table 4: Fold change between post-primary and post-booster sampling points for the three tested strains

Strain	Fold change post-primary to post-booster (95% CI)	
	Group 1 (2+1)	Group 2 (3+1)
44/76 (fHbp)	0.73 (0.5-1.0)	1.2 (0.8-1.8)
5/99 (NadA)	3.9 (2.8-5.3)	3.2 (2.5-4.1)
NZ98/254 (PorA)	2.6 (1.7-3.9)	2.3 (1.6-3.4)

fHbp= factor H binding protein; NadA= Neisserial adhesin A; PorA= Porin A; CI= confidence interval

Supplementary table 5: Baseline characteristics of infants receiving vaccination in hospital or in the community

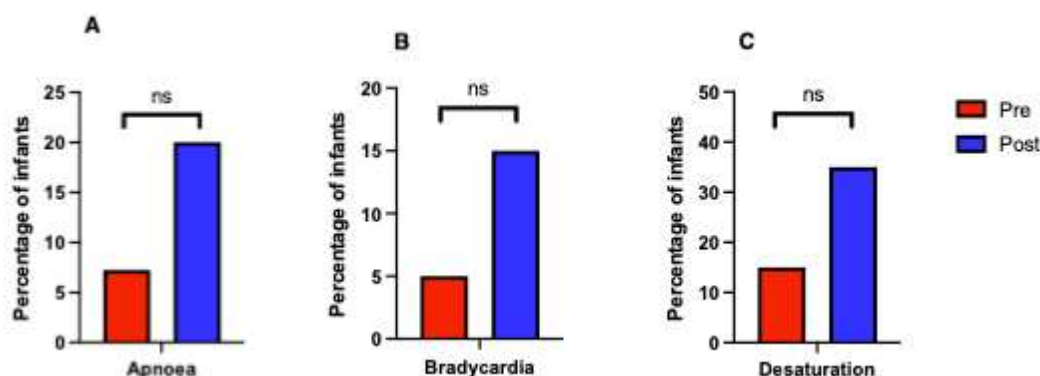
	8 weeks		12 weeks		16 weeks	
	Vaccinated in hospital (n=56)	Vaccinated in community (n=73)	Vaccinated in hospital (n=20)	Vaccinated in community (n=108)	Vaccinated in hospital (n=8)	Vaccinated in community (n=120)
Gestational age category (<30 weeks) % (n)	96.4 (54)	12.3 (9)	95 (19)	39.8 (43)	87.5 (7)	45.8 (55)
Gestational age at birth (weeks) Median (range)	27 ⁺² (23 ⁺⁰ -32 ⁺³)	32 ⁺² (28 ⁺⁰ -34 ⁺³)	25 ⁺⁵ (23 ⁺⁰ -30 ⁺⁶)	31 ⁺² (25 ⁺³ -34 ⁺³)	25 ⁺⁵ (23 ⁺⁰ -30 ⁺⁶)	30 ⁺⁴ (24 ⁺² -34 ⁺³)
Birthweight (g) Median (range)	925 (490-1605)	1700 (930-2790)	754 (490-1170)	1449.5 (672-2610)	669 (490-780)	1372 (580-2610)
Sex (female) % (n)	55.4 (31)	57.5 (42)	50 (10)	58.3 (63)	37.5 (3)	58.3 (70)
CLD % (n)	51.8 (29)	4.1 (3)	70 (14)	15.7 (17)	62.5 (5)	21.7 (26)
Age at vaccination (days) Median (range)	60.5 (52-84)	61 (51-94)	94 (82-138)	93 (80-131)	136 (110-175)	124 (110-164)

Supplementary figure 1: Percentage of infants experiencing apnoea (A), bradycardia (B) and desaturation (C) before and after vaccination at 8 weeks

ns= not significant

Statistical comparison using Fisher's exact test

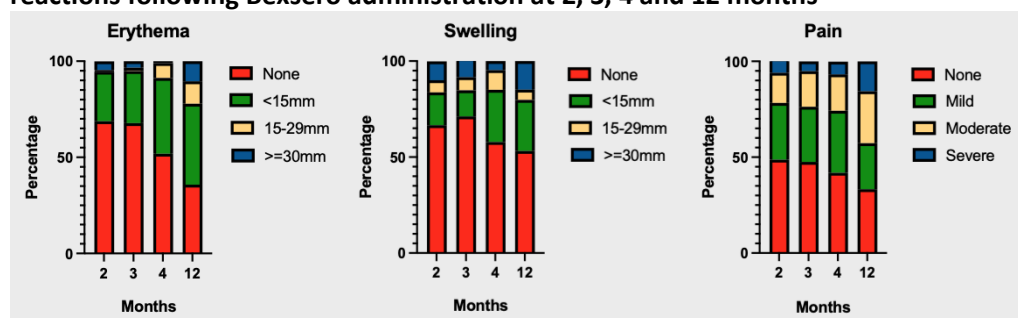
Supplementary figure 2: Percentage of infants experiencing apnoea (A), bradycardia (B) and desaturation (C) before and after vaccination at 12 weeks



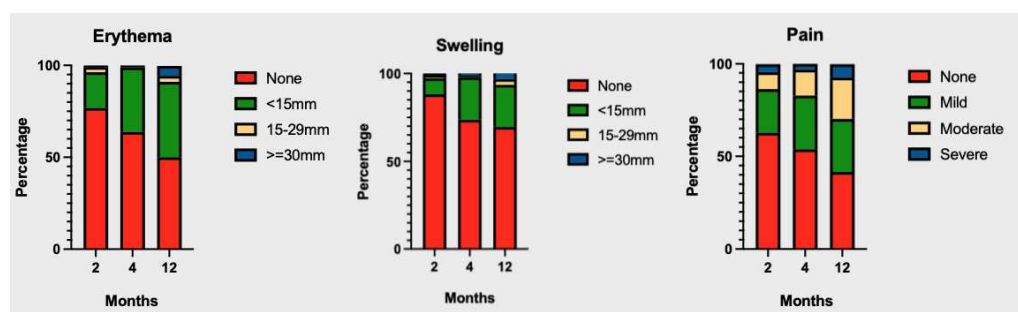
ns=not significant

Statistical comparison using Fisher's exact test

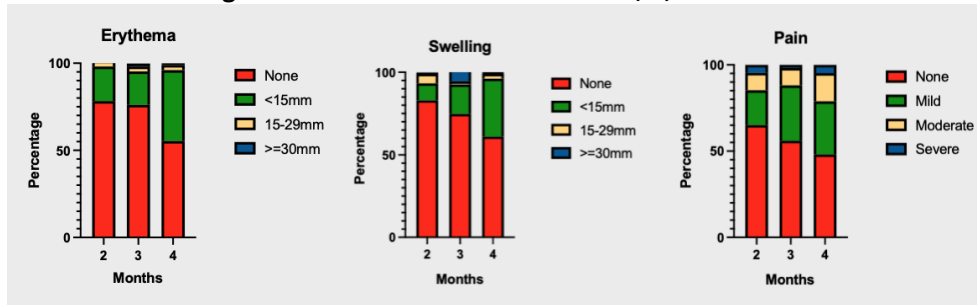
Supplementary figure 3: Graphs showing percentage of infants experiencing local reactions following Bexsero administration at 2, 3, 4 and 12 months



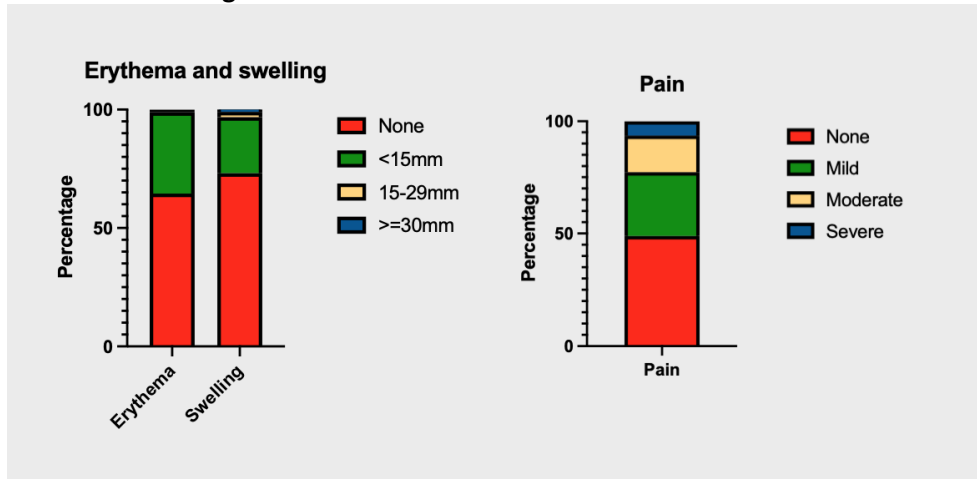
Supplementary figure 4: Graphs showing percentage of infants experiencing local reactions following Prevenar administration at 2, 3, 4 and 12 months



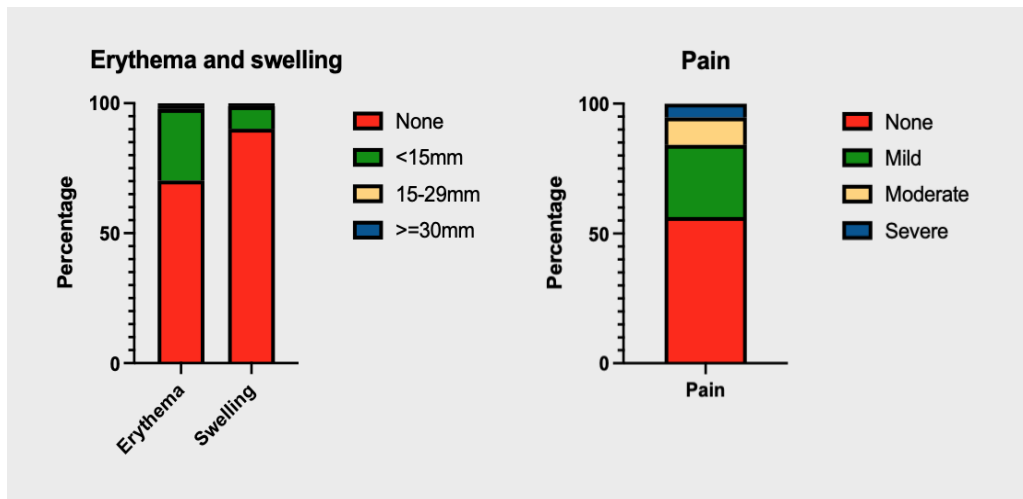
Supplementary figure 5: Graphs showing percentage of infants experiencing local reactions following Infanrix-hexa administration at 2, 3, 4 and 12 months



Supplementary figure 6: Graphs showing percentage of infants experiencing local reactions following Priorix administration at 12 months



Supplementary figure 7: Graphs showing percentage of infants experiencing local reactions following Menitorix administration at 12 months



Supplementary table 6: Percentage of infants experiencing fever or severe fever in the seven days following vaccination

Visit	Group	N	Any		Severe (>=grade 3)		P value*	
			n	Percentage (95% CI)	n	Percentage (95% CI)	Any	Severe
1	Combined	122	7	6 (3-12)	1	0.8 (0.2-4)		
2	Group 1	58	1	2 (0.04-9)	0	0	0.02	1.0
	Group 2	64	9	14 (7-25)	1	2 (1-5)		
3	Group 1	55	11	20 (10-33)	0	0		
	Group 2	57	8	14 (6-26)	0	0		
5	Combined	102	27	26 (19-36)	7	7 (3-14)		

*Fisher's exact test

Supplementary table 7: Participants investigated for sepsis within 7 and 28 days

		N	Investigated for sepsis and commenced on antibiotics within 7 days n (%)	P value*
Visit 1		129	6 (4.7)	
Visit 2	Gp. 1	63	2 (3.2)	1.0
	Gp. 2	65	2 (3.1)	
Visit 3		128	0 (0)	
Visit 5		126	0 (0)	

*Fisher's exact test

Supplementary table 8: Participants who received paracetamol in 24 hours following vaccination

Age (months)		Received at least one dose in 24 hours		Received three doses within 24 hours			
		N	Yes % (n)	No % (n)	N	Yes % (n)	No % (n)
2		114	91.2 (104)	8.8 (10)	97	58.8 (57)	41.2 (40)
3	Gp 1	54	64.8 (35)	35.2 (19)	45	31.1 (14)	68.9 (31)
3	Gp 2	59	94.9 (56)	5.1 (3)	50	66 (33)	34 (17)
4		99	96 (95)	4.0 (4)	85	71.8 (61)	28.2 (24)
12		91	94.5 (86)	5.5 (5)	75	54.7 (41)	45.3 (34)

Supplementary table 9: Recorded SAEs according to group

SAE	Number in group 1	Number in group 2
Stridor		2
Apnoea	3	3
Viral infection	1	
Bronchiolitis	14	5
Respiratory distress	8	7
Anaemia	1	
Gastroesophageal reflux disease	1	2
Cough		2
Cough, fever, reduced feeding	1	
Rash		1
Respiratory failure	1	1
Sudden unexpected collapse	1	
Influenza	1	
Sleepy		1
Screaming		1
Posthaemorrhagic hydrocephalus	1	
Increased ileostomy output		1
Inguinal hernia repair	2	4
Cardiac failure		2
Urinary Tract Infection	2	
Hypertension	1	
Patent ductus arteriosus		1
Altered mental state secondary to hyponatraemia		1
Intestinal prolapse		1
Diarrhoea		1
Constipation	1	1
Elective admission following instability after previous vaccines	1	1
Retinopathy of prematurity	1	1
Static growth	1	
Vomiting	1	
Vaccine reaction causing fever	1	1
Poor feeding		1
Tracheostomy formation		1
Gastroenteritis		2
Upper Respiratory Tract Infection	1	1
Petechial rash		1
Croup and bronchiolitis	1	
Patent ductus arteriosus ligation		2
Infantile spasms		1

Lower respiratory tract infection	1	
Inguinal hernia		1
Cow's milk protein intolerance	1	
Increased oxygen requirement		1
Chronic lung disease and pulmonary hypertension	1	