Early protection against meningococcal disease B in infants

The LION Men B Study

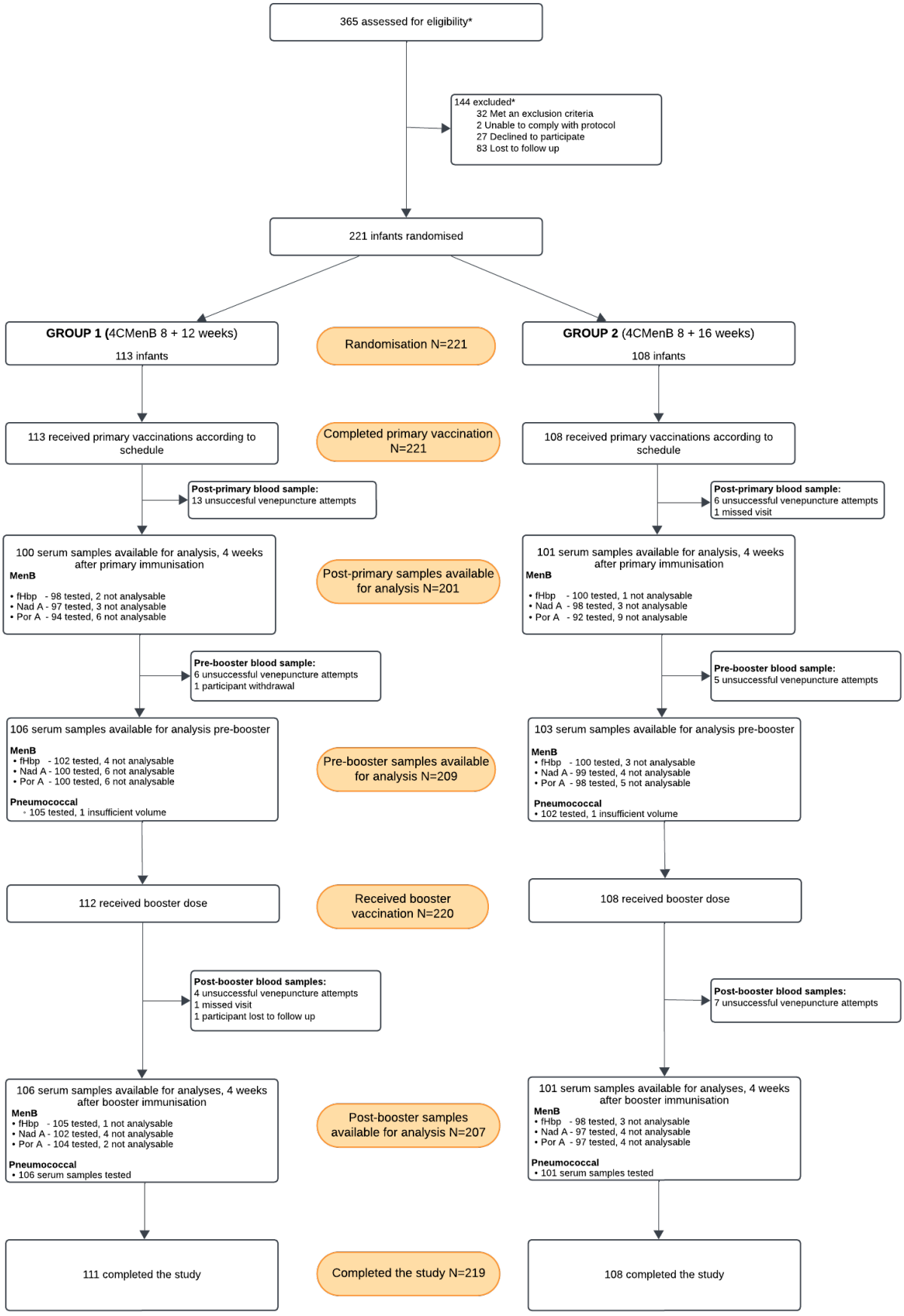
ISRCTN Results Summary

Contains:

- Participant Flow
- Baseline Characteristics Table
- Primary and Secondary Outcome Tables
- Medically Attended Adverse Events Summary
- Serious Adverse Events Summary

Participant Flow: CONSORT Diagram

(Consolidated Standards of Reporting Trials diagram of study participants - see next page)



Screening data available from 5 of 6 sites

Baseline Characteristics of Participants

Variable		Reduced-interval 4CMenB, N=113 n (%)	Standard schedule 4CMenB, N=108 n (%)
Sex	Female	59 (52)	52 (48)
Ethnicity	Asian/Asian British	3 (3)	5 (5)
	Black/Black British	1 (1)	0 (0)
	Mixed or Multiple	10 (9)	11 (10)
	Other/Other not specified	2 (2)	2 (2)
	White	97 (86)	90 (83)
BCG Vaccination	No	102 (90)	97 (90)
	Yes	11 (10)	10 (9)
	Not known	0 (0)	1 (1)
Antenatal pertussis vaccination	Yes	107 (95)	102 (94)
	No	6 (5)	6 (6)
Antenatal influenza vaccination	Yes	92 (81)	84 (78)
	No	20 (18)	23 (21)
	Not known	1 (1)	1 (1)
		Median (IQR)	**Median (IQR)**
Gestation at birth (weeks)		39·5 (39·0-40·5)	39·5 (38·6-40·4)
Birth weight (kg)		3·56 (3·20-3·92)	3·43 (3·15-3·71)
Age at enrolment (days)		61 (58-65)	61 (58-64)
Age at vaccination visits (weeks)	Visit 1	8 (8-9)	8 (8-9)
	Visit 2	13 (12-13)	13(12-13)
	Visit 5	53 (52-53)	53 (52-53)
Vaccination to blood sample intervals*	Post-primary (days)	30 (28-35)	30·5 (28-34)
	Pre-4CMenB booster (weeks)	44 (44-45)	40 (39-41)
	Pre-PCV13 booster (weeks)	40 (39-41)	45 (44-46)
	Post-booster (days)	34 (29-37)	34 (29-40)

**Note vaccination to pre-booster sample interval differs between groups by study design*

Primary and Secondary Outcomes Tables

Immunogenicity Tables

MenB hSBA geometric mean titres

*Geometric mean serum bactericidal antibody assay titres, with human complement (hSBA), against the 3 tested reference strains, at each of the three sampling timepoints, by group. Blood samples were collected at 4 weeks post-primary 4CMenB course, pre-booster at 12 months of age and 4 weeks post-booster. *P-value is by Kruskall-Wallis test, values <0·05 are in bold. N=number of participants with result available. Reference strains are 44/76-SL = factor H binding protein, 5/99 = Neisserial adhesin A, NZ98/254 = Porin A. GMR = Geometric mean ratio, GMT = Geometric mean titre, CI = confidence interval*

Timepoint	Tested strain	Reduced-interval 4CMenB		Standard schedule 4CMenB		GMR (95% CI)	P-value*
		N	hSBA GMT (95% CI)	N	hSBA GMT (95% CI)		
Post-primary	44/76-SL	98	32·7 (25·6-41·7)	100	50·2 (40·0-63·0)	0·65 (0·47-0·90)	**0·02**
	5/99	97	257·8 (212·4-313·0)	98	426·0 (350·5-517·7)	0·61 (0·46-0·79)	**<0·001**
	NZ98/254	94	4·9 (4·0-6·1)	92	6·7 (5·3-8·5)	0·73 (0·53-1·00)	**0·04**
Pre-booster	44/76-SL	102	2·2 (1·9-2·7)	100	2·3 (2·0-2·7)	0·95 (0·76-1·20)	0·25
	5/99	100	27·5 (19·1-39·5)	99	34·8 (25·4-47·7)	0·79 (0·49-1·27)	0·39
	NZ98/254	100	1·1 (1·0-1·3)	98	1·2 (1·1-1·3)	0·95 (0·82-1·10)	0·11
Post-booster	44/76-SL	105	72·6 (57·9-90·9)	98	66·3 (52·5-83·7)	1·09 (0·79-1·51)	0·60
	5/99	102	2,020·4 (1,623·9-2,513·6)	97	1,517·0 (1,124·2-2,047·1)	1·33 (0·93-1·92)	0·31
	NZ98/254	104	36·8 (29·1-46·6)	97	23·7 (18·0-31·3)	1·55 (1·09-2·22)	**0·005**

Proportions with protective MenB hSBA titres

*Proportions of participants achieving serum bactericidal antibody assay titres ⩾4, with 95% confidence intervals. n=number of samples with titre ⩾4, N=number of participants with result available. * P-values are by Fisher's exact test. Reference strains are 44/76-SL = factor H binding protein, 5/99 = Neisserial adhesin A, NZ98/254 = Porin A. hSBA = serum bactericidal antibody assay with human complement, CI = confidence interval*

Timepoint	Tested strain	hSBA titre ≥4 (n/N)		Proportion with hSBA titre ≥4 (95% CI)		P-value*
		Reduced-interval 4CMenB	Standard schedule 4CMenB	Reduced-interval 4CMenB	Standard schedule 4CMenB	
Post-primary	44/76-SL	91/98	97/100	0·93 (0·86-0·97)	0·97 (0·91-0·99)	0·21
	5/99	97/97	98/98	1·00 (0·96-1·00)	1·00 (0·96-1·00)	-
	NZ98/254	60/94	69/92	0·64 (0·53-0·73)	0·75 (0·65-0·83)	0·11
Pre-booster	44/76-SL	27/102	30/100	0·26 (0·18-0·36)	0·30 (0·21-0·40)	0·64
	5/99	82/100	86/99	0·82 (0·73-0·89)	0·87 (0·79-0·93)	0·43
	NZ98/254	5/100	5/98	0·05 (0·02-0·11)	0·05 (0·02-0·12)	1·00
Post-booster	44/76-SL	103/105	96/98	0·98 (0·93-1·00)	0·98 (0·93-1·00)	1·00
	5/99	102/102	95/97	1·00 (0·96-1·00)	0·98 (0·93-1·00)	0·24
	NZ98/254	100/104	90/97	0·96 (0·90-0·99)	0·93 (0·86-0·97)	0·36

Geometric mean pneumococcal antibody concentrations

*Serotype-specific Immunoglobulin G geometric mean concentrations (µg/mL) for the 12 measurable serotypes contained in the PCV13 vaccine. Compared at 12 months of age (pre-booster) and 4 weeks post-booster vaccinations, by group. *P-value is by Kruskall-Wallis test and values <0·05 are in bold. IgG = immunoglobulin G, GMR = Geometric mean ratio, GMC = Geometric mean concentration, CI = confidence interval*

Timepoint	Serotype	Serotype-specific IgG GMC, µg/mL (95% CI)		GMR (95% CI)	P-value*
		Reduced-interval 4CMenB – PCV13 at 16 weeks	Standard schedule 4CMenB – PCV13 at 12 weeks		
Pre-booster	**1**	0·19 (0·16-0·23)	0·12 (0·10-0·14)	1·59 (1·25-2·03)	**<0·001**
	3	0·24 (0·18-0·30)	0·14 (0·12-0·18)	1·64 (1·19-2·27)	**0·001**
	4	0·34 (0·28-0·41)	0·26 (0·21-0·31)	1·31 (1·00-1·71)	**0·048**
	5	0·18 (0·15-0·21)	0·13 (0·11-0·15)	1·41 (1·13-1·76)	**0·003**
	6B	0·06 (0·05-0·07)	0·06 (0·05-0·06)	1·07 (0·95-1·20)	0·38
	7F	0·67 (0·57-0·79)	0·46 (0·38-0·57)	1·44 (1·11-1·86)	**0·013**
	9V	0·14 (0·12-0·17)	0·11 (0·09-0·12)	1·36 (1·09-1·70)	**0·011**
	14	0·44 (0·36-0·54)	0·34 (0·26-0·44)	1·30 (0·93-1·82)	**0·029**
	18C	0·15 (0·13-0·17)	0·12 (0·10-0·14)	1·25 (1·02-1·53)	**0·026**
	19A	0·11 (0·09-0·14)	0·10 (0·08-0·12)	1·17 (0·86-1·59)	0·21
	19F	0·36 (0·28-0·45)	0·23 (0·19-0·29)	1·54 (1·14-2·10)	**0·002**
	23F	0·09 (0·07-0·11)	0·07 (0·06-0·08)	1·27 (0·99-1·62)	**0·017**
Post-booster	**1**	30·30 (24·87-36·91)	26·32 (20·97-33·03)	1·15 (0·86-1·55)	0·36
	3	3·53 (2·91-4·28)	3·54 (2·87-4·37)	1·00 (0·75-1·32)	0·89
	4	35·55 (30·00-42·12)	25·56 (20·31-32·18)	1·39 (1·05-1·84)	0·052
	5	8·09 (6·74-9·72)	7·45 (5·97-9·30)	1·09 (0·82-1·44)	0·79
	6B	2·74 (2·11-3·57)	2·60 (1·96-3·46)	1·05 (0·72-1·55)	0·69
	7F	8·46 (7·30-9·81)	10·83 (9·08-12·93)	0·78 (0·62-0·98)	**0·02**
	9V	10·96 (9·44-12·73)	11·45 (9·25-14·19)	0·96 (0·74-1·24)	0·24
	14	21·83 (17·83-26·72)	23·80 (17·63-32·14)	0·92 (0·64-1·31)	0·15
	18C	9·62 (8·10-11·42)	8·79 (7·28-10·61)	1·09 (0·85-1·41)	0·37
	19A	9·34 (7·46-11·69)	10·22 (8·15-12·82)	0·91 (0·67-1·25)	0·63
	19F	41·86 (34·25-51·17)	39·92 (31·88-50·00)	1·05 (0·78-1·41)	0·78
	23F	5·32 (4·15-6·81)	5·03 (3·90-6·48)	1·06 (0·74-1·50)	0·55

Proportions with protective pneumococcal antibody

*Proportions of participants achieving protective concentrations of serotype-specific Immunoglobulin G (≥0·35µg/mL) for the 12 measurable serotypes contained in the PCV13 vaccine. Compared at 12 months of age (pre-booster) and 4 weeks post-booster vaccinations, by group. n=number of samples with concentration ≥0·35µg/mL, N=number of participants with result available. *P-value is by Fisher's exact test and values <0·05 are in bold. IgG = immunoglobulin G, CI = confidence interval*

Timepoint	Serotype	Serotype-specific IgG concentration ≥0·35µg/mL (n/N)		Proportion with serotype-specific IgG ≥ 0·35µg/mL (95% CI)		P-value*
		Reduced-interval 4CMenB – PCV13 at 16 weeks	Standard schedule 4CMenB – PCV13 at 12 weeks	Reduced-interval 4CMenB – PCV13 at 16 weeks	Standard schedule 4CMenB – PCV13 at 12 weeks	
Pre-booster	**1**	26/105	12/102	0·25 (0·17-0·34)	0·12 (0·06-0·20)	**0·019**
	3	32/105	20/102	0·30 (0·22-0·40)	0·20 (0·12-0·29)	0·079
	4	53/105	40/102	0·50 (0·41-0·60)	0·39 (0·30-0·49)	0·12
	5	25/105	9/102	0·24 (0·16-0·33)	0·09 (0·04-0·16)	**0·005**
	6B	2/105	0/102	0·02 (0·00-0·07)	0·00 (0·00-0·04)	0·50
	7F	82/105	70/102	0·78 (0·69-0·86)	0·69 (0·59-0·77)	0·16
	9V	15/105	9/102	0·14 (0·08-0·22)	0·09 (0·04-0·16)	0·28
	14	72/105	55/102	0·69 (0·59-0·77)	0·54 (0·44-0·64)	**0·033**
	18C	10/105	7/102	0·10 (0·05-0·17)	0·07 (0·03-0·14)	0·61
	19A	14/105	10/102	0·13 (0·07-0·21)	0·10 (0·05-0·17)	0·52
	19F	52/105	29/102	0·50 (0·40-0·59)	0·28 (0·20-0·38)	**0·003**
	23F	9/105	5/102	0·09 (0·04-0·16)	0·05 (0·02-0·11)	0·41
Post-booster	**1**	106/106	100/101	1·00 (0·97-1·00)	0·99 (0·95-1·00)	0·49
	3	104/106	100/101	0·98 (0·93-1·00)	0·99 (0·95-1·00)	1·00
	4	106/106	100/101	1·00 (0·97-1·00)	0·99 (0·95-1·00)	0·49
	5	106/106	100/101	1·00 (0·97-1·00)	0·99 (0·95-1·00)	0·49
	6B	99/106	93/101	0·93 (0·87-0·97)	0·92 (0·85-0·97)	0·79
	7F	106/106	101/101	1·00 (0·97-1·00)	1·00 (0·96-1·00)	-
	9V	106/106	100/101	1·00 (0·97-1·00)	0·99 (0·95-1·00)	0·49
	14	106/106	98/101	1·00 (0·97-1·00)	0·97 (0·92-0·99)	0·11
	18C	106/106	100/101	1·00 (0·97-1·00)	0·99 (0·95-1·00)	0·49
	19A	103/106	100/101	0·97 (0·92-0·99)	0·99 (0·95-1·00)	0·62
	19F	106/106	100/101	1·00 (0·97-1·00)	0·99 (0·95-1·00)	0·49
	23F	99/106	96/101	0·93 (0·87-0·97)	0·95 (0·89-0·98)	0·77

Reactogenicity Tables

Proportions of solicited reactions by group and by vaccination visit

Proportions of participants reporting any grade solicited reaction in the 7 day diary card after vaccinations at 12 and 16 weeks of age and 12 months of age, by group. Followed by proportions of participants reporting grade 3 (severe) solicited reaction in the 7 day diary card after vaccinations at 12 and 16 weeks of age and 12 months of age, by group. Abbreviations: 4CMenB: 4-component meningococcal B vaccine, 6 in 1: Vaccine containing antigens of diphtheria/tetanus/acellular pertussis/inactivated polio vaccine/Haemophilus influenzae Type B and Hepatitis B, (DTaP/IPV/Hib/HepB), PCV13: 13-valent pneumococcal conjugate vaccine, MCCHIB: Meningococcal C and Hib combination vaccine, MMR: Measles, Mumps, Rubella vaccine.

Visit 2 - 12 weeks of age	**Participants reporting symptom of any grade (n/N)**		**Proportion of participants (95% CI)**		
Solicited reaction	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	P-value*
Temperature	11/113	5/107	0·10 (0·05-0·17)	0·05 (0·02-0·11)	0·20
Reduced feeding	50/113	39/104	0·44 (0·35-0·54)	0·38 (0·28-0·48)	0·34
Reduced inactivity	55/113	48/104	0·49 (0·39-0·58)	0·46 (0·36-0·56)	0·79
Irritability	91/113	83/104	0·81 (0·72-0·87)	0·80 (0·71-0·87)	1·00
Crying	61/113	61/104	0·54 (0·44-0·63)	0·59 (0·49-0·68)	0·50
Vomiting	34/113	33/104	0·30 (0·22-0·39)	0·32 (0·23-0·42)	0·88
Diarrhoea	59/113	44/104	0·52 (0·43-0·62)	0·42 (0·33-0·52)	0·17
Erythema (4CMenB)	56/110		0·51 (0·41-0·61)		
Swelling (4CMenB)	38/110		0·35 (0·26-0·44)		
Pain (4CMenB)	47/106		0·44 (0·35-0·54)		
Erythema (6 in 1)	46/110	56/106	0·42 (0·32-0·52)	0·53 (0·43-0·63)	0·13
Swelling (6 in 1)	30/111	34/106	0·27 (0·19-0·36)	0·32 (0·23-0·42)	0·46
Pain (6 in 1)	43/110	51/106	0·39 (0·30-0·49)	0·48 (0·38-0·58)	0·22
Erythema (PCV13)		44/100		0·44 (0·34-0·54)	
Swelling (PCV13)		26/100		0·26 (0·18-0·36)	
Pain (PCV13)		48/100		0·48 (0·38-0·58)	

Visit 2 - 12 weeks of age	Participants reporting Grade 3 symptom (n/N)		Proportion of participants (95% CI)		P-value
Solicited reaction	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	
Temperature	2/113	0/107	0·02 (0·00-0·06)	0·00 (0·00-0·03)	0·50
Reduced feeding	1/113	2/104	0·01 (0·00-0·05)	0·02 (0·00-0·07)	0·61
Reduced inactivity	6/113	6/104	0·05 (0·02-0·11)	0·06 (0·02-0·12)	1·00
Irritability	8/113	7/104	0·07 (0·03-0·13)	0·07 (0·03-0·13)	1·00
Crying	2/113	1/104	0·02 (0·00-0·06)	0·01 (0·00-0·05)	1·00
Vomiting	0/113	0/104	0·00 (0·00-0·03)	0·00 (0·00-0·03)	
Diarrhoea	3/113	5/104	0·03 (0·01-0·08)	0·05 (0·02-0·11)	0·48
Erythema (4CMenB)	1/110		0·01 (0·00-0·05)		
Swelling (4CMenB)	1/110		0·01 (0·00-0·05)		
Pain (4CMenB)	2/106		0·02 (0·00-0·07)		
Erythema (6 in 1)	3/110	1/106	0·03 (0·01-0·08)	0·01 (0·00-0·05)	0·62
Swelling (6 in 1)	2/111	1/106	0·02 (0·00-0·06)	0·01 (0·00-0·05)	1·00
Pain (6 in 1)	2/110	2/106	0·02 (0·00-0·06)	0·02 (0·00-0·07)	1·00
Erythema (PCV13)		1/100		0·01 (0·00-0·05)	
Swelling (PCV13)		1/100		0·01 (0·00-0·05)	
Pain (PCV13)		2/100		0·02 (0·00-0·07)	

Visit 3 – 16 weeks of age	Participants reporting symptom of any grade (n/N)		Proportion of participants (95% CI)		
Solicited reaction	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	P-value
Temperature	6/102	13/107	0·06 (0·02-0·12)	0·12 (0·07-0·20)	0·15
Reduced feeding	28/100	49/105	0·28 (0·19-0·38)	0·47 (0·37-0·57)	**0·006**
Reduced inactivity	32/100	60/105	0·32 (0·23-0·42)	0·57 (0·47-0·67)	**<0·001**
Irritability	69/100	93/105	0·69 (0·59-0·78)	0·89 (0·81-0·94)	**<0·001**
Crying	42/100	70/105	0·42 (0·32-0·52)	0·67 (0·57-0·76)	**<0·001**
Vomiting	17/100	38/105	0·17 (0·10-0·26)	0·36 (0·27-0·46)	**0·003**
Diarrhoea	24/100	35/105	0·24 (0·16-0·34)	0·33 (0·24-0·43)	0·17
Erythema (4CMenB)		60/105		0·57 (0·47-0·67)	
Swelling (4CMenB)		39/105		0·37 (0·28-0·47)	
Pain (4CMenB)		51/96		0·53 (0·43-0·63)	
Erythema (6 in 1)	52/102	60/105	0·51 (0·41-0·61)	0·57 (0·47-0·67)	0·40
Swelling (6 in 1)	30/102	34/105	0·29 (0·21-0·39)	0·32 (0·24-0·42)	0·66
Pain (6 in 1)	38/102	52/103	0·37 (0·28-0·47)	0·50 (0·40-0·60)	0·068

Erythema (PCV13)	46/102		0·45 (0·35-0·55)		
Swelling (PCV13)	26/102		0·25 (0·17-0·35)		
Pain (PCV13)	36/102		0·35 (0·26-0·45)		

Visit 3 – 16 weeks of age	**Participants reporting Grade 3 symptom (n/N)**		**Proportion of participants (95% CI)**		
Solicited reaction	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	P-value
Temperature	1/102	0/107	0·01 (0·00-0·05)	0·00 (0·00-0·03)	0·49
Reduced feeding	0/100	3/105	0·00 (0·00-0·04)	0·03 (0·01-0·08)	0·25
Reduced inactivity	0/100	7/105	0·00 (0·00-0·04)	0·07 (0·03-0·13)	**0·014**
Irritability	4/100	11/105	0·04 (0·01-0·10)	0·10 (0·05-0·18)	0·11
Crying	1/100	4/105	0·01 (0·00-0·05)	0·04 (0·01-0·09)	0·37
Vomiting	0/100	1/105	0·00 (0·00-0·04)	0·01 (0·00-0·05)	1·00
Diarrhoea	0/100	2/105	0·00 (0·00-0·04)	0·02 (0·00-0·07)	0·50
Erythema (4CMenB)		1/105		0·01 (0·00-0·05)	
Swelling (4CMenB)		1/105		0·01 (0·00-0·05)	
Pain (4CMenB)		1/95		0·01 (0·00-0·06)	
Erythema (6 in 1)	3/102	1/105	0·03 (0·01-0·08)	0·01 (0·00-0·05)	0·36
Swelling (6 in 1)	2/102	1/105	0·02 (0·00-0·07)	0·01 (0·00-0·05)	0·62
Pain (6 in 1)	0/102	1/103	0·00 (0·00-0·04)	0·01 (0·00-0·05)	1·00
Erythema (PCV13)	2/102		0·02 (0·00-0·07)		
Swelling (PCV13)	1/102		0·01 (0·00-0·05)		
Pain (PCV13)	0/102		0·00 (0·00-0·04)		

Visit 5 – 12 months of age	**Participants reporting symptom of any grade (n/N)**		**Proportion of participants (95% CI)**		
Solicited reaction	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	**Reduced-interval 4CMenB – PCV13 at 16 weeks**	**Standard schedule 4CMenB – PCV13 at 12 weeks**	p-value
Temperature	27/109	32/104	0·25 (0·17-0·34)	0·31 (0·22-0·41)	0·36
Reduced feeding	52/106	55/100	0·49 (0·39-0·59)	0·55 (0·45-0·65)	0·41
Reduced inactivity	62/106	62/100	0·58 (0·49-0·68)	0·62 (0·52-0·72)	0·67
Irritability	88/106	84/100	0·83 (0·74-0·90)	0·84 (0·75-0·91)	1·00
Crying	52/106	59/100	0·49 (0·39-0·59)	0·59 (0·49-0·69)	0·16
Vomiting	21/106	22/100	0·20 (0·13-0·29)	0·22 (0·14-0·31)	0·73
Diarrhoea	27/106	35/100	0·25 (0·18-0·35)	0·35 (0·26-0·45)	0·17

Erythema (4CMenB)	63/107	63/101	0·59 (0·49-0·68)	0·62 (0·52-0·72)	0·67
Swelling (4CMenB)	57/107	49/100	0·53 (0·43-0·63)	0·49 (0·39-0·59)	0·58
Pain (4CMenB)	58/101	63/96	0·57 (0·47-0·67)	0·66 (0·55-0·75)	0·25
Erythema (MCCHIB)	35/104	45/99	0·34 (0·25-0·44)	0·45 (0·35-0·56)	0·11
Swelling (MCCHIB)	22/105	22/97	0·21 (0·14-0·30)	0·23 (0·15-0·32)	0·86
Pain (MCCHIB)	38/104	44/96	0·37 (0·27-0·47)	0·46 (0·36-0·56)	0·20
Erythema (PCV13)	43/108	51/105	0·40 (0·31-0·50)	0·49 (0·39-0·59)	0·22
Swelling (PCV13)	33/108	38/104	0·31 (0·22-0·40)	0·37 (0·27-0·47)	0·38
Pain (PCV13)	47/108	62/104	0·44 (0·34-0·53)	0·60 (0·50-0·69)	**0·020**
Erythema (MMR)	39/104	45/105	0·38 (0·28-0·48)	0·43 (0·33-0·53)	0·48
Swelling (MMR)	23/104	25/104	0·22 (0·15-0·31)	0·24 (0·16-0·33)	0·87
Pain (MMR)	46/104	55/104	0·44 (0·34-0·54)	0·53 (0·43-0·63)	0·27

Visit 5 – 12 months of age	**Participants reporting Grade 3 symptom (n/N)**		**Proportion of participants (95% CI)**		
Solicited reaction	**Reduced-interval MenB**	**Standard schedule MenB**	**Reduced-interval MenB**	**Standard schedule MenB**	P-value
Temperature	6/109	9/104	0·06 (0·02-0·12)	0·09 (0·04-0·16)	0·43
Reduced feeding	1/106	4/100	0·01 (0·00-0·05)	0·04 (0·01-0·10)	0·20
Reduced inactivity	3/106	5/100	0·03 (0·01-0·08)	0·05 (0·02-0·11)	0·49
Irritability	6/106	10/100	0·06 (0·02-0·12)	0·10 (0·05-0·18)	0·30
Crying	3/106	3/100	0·03 (0·01-0·08)	0·03 (0·01-0·09)	1·00
Vomiting	0/106	1/100	0·00 (0·00-0·03)	0·01 (0·00-0·05)	0·49
Diarrhoea	0/106	2/100	0·00 (0·00-0·03)	0·02 (0·00-0·07)	0·23
Erythema (4CMenB)	10/107	8/101	0·09 (0·05-0·17)	0·08 (0·03-0·15)	0·81
Swelling (4CMenB)	8/107	4/100	0·07 (0·03-0·14)	0·04 (0·01-0·10)	0·38
Pain (4CMenB)	6/101	5/96	0·06 (0·02-0·12)	0·05 (0·02-0·12)	1·00
Erythema (MCCHIB)	0/104	0/99	0·00 (0·00-0·03)	0·00 (0·00-0·04)	
Swelling (MCCHIB)	0/105	0/97	0·00 (0·00-0·03)	0·00 (0·00-0·04)	
Pain (MCCHIB)	1/104	2/96	0·01 (0·00-0·05)	0·02 (0·00-0·07)	0·61
Erythema (PCV13)	1/108	0/105	0·01 (0·00-0·05)	0·00 (0·00-0·03)	1·00
Swelling (PCV13)	0/108	1/104	0·00 (0·00-0·03)	0·01 (0·00-0·05)	0·49
Pain (PCV13)	5/108	5/104	0·05 (0·02-0·10)	0·05 (0·02-0·11)	1·00
Erythema (MMR)	1/104	1/105	0·01 (0·00-0·05)	0·01 (0·00-0·05)	1·00
Swelling (MMR)	1/104	1/104	0·01 (0·00-0·05)	0·01 (0·00-0·05)	1·00
Pain (MMR)	3/104	4/104	0·03 (0·01-0·08)	0·04 (0·01-0·10)	1·00

Combined diary data 12 and 16 weeks of age vaccination visits

*Proportions of participants reporting solicited reactions of any grade at either 12 or 16 weeks of age, highest grade of reaction at either visit captured. N = number of participants with completed diary for both visits, n = number of participants reporting a reaction. *P-values are by Fisher's exact test, significant values <0·05 are bold. Abbreviations as for tables 4a-f.*

12 and 16 weeks of age – combined diary data	**Any grade reaction, n/N**		**Proportion of participants (95% CI)**		**P-value***
Solicited Reaction	**Reduced-interval MenB**	**Standard schedule MenB**	**Reduced-interval MenB**	**Standard schedule MenB**	
Temperature	14/102	16/106	0·14 (0·08-0·22)	0·15 (0·09-0·23)	0·84
Reduced feeding	53/100	62/102	0·53 (0·43-0·63)	0·61 (0·51-0·70)	0·32
Inactivity	58/100	70/102	0·58 (0·48-0·68)	0·69 (0·59-0·77)	0·14
Irritability	87/100	99/102	0·87 (0·79-0·93)	0·97 (0·92-0·99)	**0·009**
Persistent crying	68/100	89/102	0·68 (0·58-0·77)	0·87 (0·79-0·93)	**0·001**
Vomiting	39/100	50/102	0·39 (0·29-0·49)	0·49 (0·39-0·59)	0·16
Diarrhoea	64/100	56/102	0·64 (0·54-0·73)	0·55 (0·45-0·65)	0·20
Erythema (4CMenB)	56/110	60/105	0·51 (0·41-0·61)	0·57 (0·47-0·67)	0·41
Swelling (4CMenB)	38/110	39/105	0·35 (0·26-0·44)	0·37 (0·28-0·47)	0·78
Pain (4CMenB)	47/106	51/96	0·44 (0·35-0·54)	0·53 (0·43-0·63)	0·26
Erythema (PCV13)	46/102	44/100	0·45 (0·35-0·55)	0·44 (0·34-0·54)	0·89
Swelling (PCV13)	26/102	26/100	0·25 (0·17-0·35)	0·26 (0·18-0·36)	1·00
Pain (PCV13)	36/102	48/100	0·35 (0·26-0·45)	0·48 (0·38-0·58)	0·086

*Proportions of participants reporting solicited reactions graded severe only, at either 12 or 16 weeks of age, highest grade of reaction at either visit captured. N = number of participants with completed diary for both visits, n = number of participants reporting a reaction. *P-values are by Fisher's exact test, significant values <0·05 are bold.*

12 and 16 weeks of age – combined diary data	**Severe reactions, n/N**		**Proportion of participants (95% CI)**		P-value *
Solicited Reaction	**Reduced-interval MenB**	**Standard schedule MenB**	**Reduced-interval MenB**	**Standard schedule MenB**	
Temperature	3/102	0/106	0·03 (0·01-0·08)	0·00 (0·00-0·03)	0·12
Reduced feeding	1/100	4/102	0·01 (0·00-0·05)	0·04 (0·01-0·10)	0·37
Inactivity	6/100	11/102	0·06 (0·02-0·13)	0·11 (0·06-0·18)	0·31
Irritability	11/100	14/102	0·11 (0·06-0·19)	0·14 (0·08-0·22)	0·67
Persistent crying	2/100	5/102	0·02 (0·00-0·07)	0·05 (0·02-0·11)	0·45
Vomiting	0/100	1/102	0·00 (0·00-0·04)	0·01 (0·00-0·05)	1·00
Diarrhoea	2/100	6/102	0·02 (0·00-0·07)	0·06 (0·02-0·12)	0·28
Erythema (4CMenB)	1/110	1/105	0·01 (0·00-0·05)	0·01 (0·00-0·05)	1·00
Swelling (4CMenB)	1/110	1/105	0·01 (0·00-0·05)	0·01 (0·00-0·05)	1·00
Pain (4CMenB)	2/106	1/95	0·02 (0·00-0·07)	0·01 (0·00-0·06)	1·00
Erythema (PCV13)	2/102	1/100	0·02 (0·00-0·07)	0·01 (0·00-0·05)	1·00
Swelling (PCV13)	1/102	1/100	0·01 (0·00-0·05)	0·01 (0·00-0·05)	1·00
Pain (PCV13)	0/102	2/100	0·00 (0·00-0·04)	0·02 (0·00-0·07)	0·24

Adverse Events Data

Medically Attended Adverse Events

Medically attended adverse events (MAAE), at any time in the study period from enrolment to final visit, by grade and by group. N = number of participants reporting an MAAE, n = number of events reported

	Reduced-interval MenB Group (N=54)	Standard-schedule MenB group (N=63)
Total number of MAAEs (n)	182	215
Grade 1, n (%)	82 (45)	101 (47)
Grade 2, n (%)	91 (47)	107 (50)
Grade 3, n (%)	9 (5)	7 (3)
Related to study interventions, n	0	1 (Fever, grade 2)

Serious Adverse Events

Serious adverse events (SAE) by category, at any time in the study period from enrolment to final visit, for each group. N = number of participants reporting events, n = number of events reported. None were deemed related to study interventions and none lead to study discontinuation.

SAE CATEGORY	SAE TERM	NUMBER IN REDUCED-INTERVAL MENB GROUP, n (N=6)	NUMBER IN STANDARD-SCHEDULE MENB GROUP, n (N=10)
Hospitalisation or prolongation of hospitalisation	Abnormal movements		1
	Blepharitis		1
	Bronchiolitis	2	3
	Complex febrile seizure*		1
	Cystoscopy	1	
	Fever and poor feeding	1	
	Intussusception		1
	Juvenile idiopathic arthritis*	1	
	Hernia repair		2
	Pneumonia		2
	Preseptal cellulitis		1
	Respiratory deterioration (medication related)	1	
	Sars-Cov-2 infection	1	
	Upper respiratory tract infection	1	
New diagnosis congenital anomaly	Renal anomaly	1	
	Ureteric anomaly	1	
	Heminephrectomy	1	
Total, n		**11**	**12**
Related to study interventions, n		**0**	**0**

**Also an adverse event of special interest (AESI)*