

THE LANCET Infectious Diseases

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Heyderman RS, Madhi SA, French N, et al. Group B streptococcus vaccination in pregnant women with or without HIV in Africa: a non-randomised phase 2, open-label, multicentre trial. *Lancet Infect Dis* 2016; published online Feb 8. [http://dx.doi.org/10.1016/S1473-3099\(15\)00484-3](http://dx.doi.org/10.1016/S1473-3099(15)00484-3).

Supplementary Table 1: Causes of maternal and infant deaths

Vaccine Group	Cause of death	Age at death (days)	Country	Relatedness to study vaccine
Women				
HIV-infected CD4High	<ul style="list-style-type: none"> ▪ Disseminated intravascular coagulation ▪ Hemorrhagic shock ▪ Uterine rupture 	Study Day 72	Malawi	None
Infants				
HIV-uninfected	<ul style="list-style-type: none"> ▪ Neonatal asphyxia 	1	Malawi	None
HIV-uninfected	<ul style="list-style-type: none"> ▪ Hypoxic-ischemic encephalopathy ▪ Neonatal asphyxia ▪ Neonatal aspiration ▪ Neonatal sepsis 	1	Malawi	None
HIV-infected CD4Low	<ul style="list-style-type: none"> ▪ Chromosomal deletion ▪ Neonatal asphyxia ▪ Neonatal aspiration 	1	Malawi	None
HIV-infected CD4Low	<ul style="list-style-type: none"> ▪ Neonatal sepsis 	14	Malawi	None
HIV-infected CD4Low	<ul style="list-style-type: none"> ▪ Neonatal respiratory distress syndrome ▪ Premature baby 	1	Malawi	None
HIV-infected CD4Low	<ul style="list-style-type: none"> ▪ Neonatal respiratory distress syndrome ▪ Premature baby ▪ Petechiae 	1	Malawi	None
HIV-infected CD4High	<ul style="list-style-type: none"> ▪ Stillbirth 	1	Malawi	None
HIV-infected CD4High	<ul style="list-style-type: none"> ▪ Gastroenteritis ▪ Hyponatremia ▪ Metabolic acidosis ▪ Renal impairment ▪ Shock 	4	S. Africa	None

Supplementary Table 2: Number and percentage of women reporting pregnancy events and obstetric outcomes, by HIV status group

	HIV-infected CD4Low <i>n</i>=90	HIV-infected CD4High <i>n</i>=89	HIV- uninfected <i>n</i>=90
<i>Pregnancy events</i>			
Chorioamnionitis	1 (1%)	0	0
Cephalopelvic disproportion	0	0	1 (1%)
(Pre-) eclampsia	0	1 (1%)	1 (1%)
Failed induction	1 (1%)	2 (2%)	0
Fetal distress	1 (1%)	0	0
Gestational diabetes	0	1 (1%)	0
Lacerations/episiotomy	24 (27%)	28 (31%)	28 (31%)
Premature rupture of membranes	0	1 (1%)	0
Prolonged labour	0	1 (1%)	0
Retained placenta and post-partum haemorrhage	0	1 (1%)	0
<i>Delivery Type</i>			
Caesarean	20 (22%)	15 (17%)	16 (18%)
Vaginal	62 (69%)	68 (76%)	66 (73%)
Vacuum	1 (1%)	0	1 (1%)
Forceps or ventouse	0	0	2 (2%)
Not reported	7 (8%)	6 (7%)	5 (6%)
<i>Infants</i>			
	<i>n</i> =91	<i>n</i> =88	<i>n</i> =87
Live birth singletons	85 (93%)	85 (97%)	85 (98%)
Live birth twins	6 (7%)	2 (2%)	2 (2%)
Stillbirth	0	1 (1%)	0

Supplementary Table 3: Geometric mean GBS serotype Ia and III-specific antibody concentrations (GMCs) for HIV positive and HIV negative women, separated by baseline antibody status, relative to lower limit of quantification (LLQ). GMCs are expressed as $\mu\text{g/mL}$ and 95% confidence intervals are given in parenthesis.

	Baseline < LLQ			Baseline \geq LLQ		
	HIV-infected CD4Low	HIV-infected CD4High	HIV- uninfected	HIV-infected CD4Low	HIV-infected CD4High	HIV- uninfected
Serotype Ia						
Day 1 pre- vaccination	0.16 (0.16–0.16) <i>n</i> =72	0.16 (0.16–0.16) <i>n</i> =66	0.16 (0.16–0.16) <i>n</i> =62	0.98 (0.58–1.65) <i>n</i> =18	0.67 (0.41–1.11) <i>n</i> =23	1.81 (1.24–2.64) <i>n</i> =28
Day 15 post- vaccination	1.03 (0.63–1.69) <i>n</i> =65	1.29 (0.77–2.15) <i>n</i> =61	1.83 (1.09–3.08) <i>n</i> =59	41 (19–90) <i>n</i> =17	20 (9.63–41) <i>n</i> =23	105 (61–180) <i>n</i> =28
Day 31 post- vaccination	1.04 (0.63–1.69) <i>n</i> =66	1.40 (0.85–2.32) <i>n</i> =57	2.30 (1.39–3.81) <i>n</i> =56	41 (21–80) <i>n</i> =17	22 (12–41) <i>n</i> =23	105 (66–166) <i>n</i> =28
Delivery	1.0 (0.66–1.51) <i>n</i> =68	1.11 (0.71–1.75) <i>n</i> =58	1.77 (1.12–2.79) <i>n</i> =56	35 (16–77) <i>n</i> =15	18 (9–34) <i>n</i> =23	61 (37–101) <i>n</i> =27
Serotype III						
Day 1 pre- vaccination	0.04 (0.04–0.04) <i>n</i> =22	0.04 (0.04–0.04) <i>n</i> =33	0.04 (0.04–0.04) <i>n</i> =33	0.22 (0.17–0.30) <i>n</i> =43	0.25 (0.19–0.33) <i>n</i> =44	0.28 (0.22–0.37) <i>n</i> =49
Day 15 post- vaccination	0.4 (0.19–0.82) <i>n</i> =21	0.4 (0.22–0.74) <i>n</i> =30	1.66 (0.92–3.02) <i>n</i> =31	2.46 (1.23–4.89) <i>n</i> =39	2.96 (1.49–5.88) <i>n</i> =37	16 (8.7–29) <i>n</i> =48
Day 31 post- vaccination	0.45 (0.22–0.90) <i>n</i> =21	0.39 (0.21–0.70) <i>n</i> =30	1.59 (0.89–2.86) <i>n</i> =30	3.29 (1.66–6.49) <i>n</i> =38	1.97 (1.01–3.83) <i>n</i> =37	14 (7.53–25) <i>n</i> =46
Delivery	0.41 (0.22–0.76) <i>n</i> =21	0.39 (0.23–0.65) <i>n</i> =32	1.12 (0.66–1.90) <i>n</i> =29	1.87 (0.98–3.55) <i>n</i> =40	1.79 (0.88–3.64) <i>n</i> =31	8.84 (4.93–16) <i>n</i> =46

Note: analysis not performed for serotype Ib as too few women had a baseline GMC < LLQ

Supplementary Table 4: Geometric mean antibody concentrations (95% confidence intervals) by HIV status and site.

	HIV-infectedCD4Low		HIV-infectedCD4High		HIV-uninfected	
	S. Africa	Malawi	S. Africa	Malawi	S. Africa	Malawi
Serotype Ia						
Day 1 (pre-vaccination)	0.34 (0.24–0.50) <i>n</i> =45	0.17 (0.15–0.20) <i>n</i> =45	0.37 (0.25–0.54) <i>n</i> =45	0.17 (0.14–0.20) <i>n</i> =44	0.48 (0.33–0.70) <i>n</i> =45	0.26 (0.22–0.31) <i>n</i> =45
Day 15 post-vaccination	5.14 (2.90–9.12) <i>n</i> =45	1.25 (0.65–2.40) <i>n</i> =37	6.13 (3.46–11.0) <i>n</i> =45	1.35 (0.71–2.56) <i>n</i> =39	10 (5.77–18) <i>n</i> =45	1.73 (0.92–3.26) <i>n</i> =42
Day 31 post-vaccination	4.60 (2.75–7.69) <i>n</i> =45	1.44 (0.78–2.66) <i>n</i> =38	6.63 (3.97–11.0) <i>n</i> =45	1.49 (0.79–2.82) <i>n</i> =35	11 (6.68–19) <i>n</i> =45	2.19 (1.17–4.11) <i>n</i> =39
Delivery	4.34 (2.66–7.09) <i>n</i> =43	1.05 (0.61–1.81) <i>n</i> =40	5.02 (3.11–8.11) <i>n</i> =45	1.09 (0.62–1.91) <i>n</i> =36	7.28 (4.43–12) <i>n</i> =42	1.74 (1.01–3.01) <i>n</i> =41
Serotype Ib						
Day 1 (pre-vaccination)	0.52 (0.37–0.74) <i>n</i> =34	0.46 (0.31–0.66) <i>n</i> =29	0.42 (0.30–0.59) <i>n</i> =38	0.31 (0.22–0.43) <i>n</i> =32	0.46 (0.33–0.65) <i>n</i> =35	0.37 (0.27–0.50) <i>n</i> =42
Day 15 post-vaccination	2.51 (1.41–4.48) <i>n</i> =40	2.39 (1.00–5.71) <i>n</i> =30	2.70 (1.57–4.66) <i>n</i> =42	3.45 (1.58–7.55) <i>n</i> =34	5.24 (3.04–9.02) <i>n</i> =44	7.45 (3.95–14) <i>n</i> =40
Day 31 post-vaccination	1.85 (1.11–3.06) <i>n</i> =41	1.70 (0.83–3.50) <i>n</i> =34	2.82 (1.73–4.60) <i>n</i> =43	2.82 (1.39–5.73) <i>n</i> =34	4.20 (2.55–6.90) <i>n</i> =45	5.86 (3.29–10) <i>n</i> =39
Delivery	1.80 (1.09–2.97) <i>n</i> =36	1.87 (0.95–3.70) <i>n</i> =38	2.68 (1.71–4.19) <i>n</i> =43	2.02 (1.06–3.86) <i>n</i> =37	2.97 (1.86–4.75) <i>n</i> =42	5.29 (3.06–9.15) <i>n</i> =40
Serotype III						
Day 1 (pre-vaccination)	0.17 (0.11–0.25) <i>n</i> =40	0.092 (0.061–0.14) <i>n</i> =25	0.11 (0.073–0.16) <i>n</i> =40	0.11 (0.082–0.16) <i>n</i> =37	0.16 (0.11–0.23) <i>n</i> =44	0.11 (0.076–0.15) <i>n</i> =38
Day 15 post-vaccination	1.25 (0.75–2.08) <i>n</i> =42	1.66 (0.74–3.71) <i>n</i> =34	1.93 (1.14–3.28) <i>n</i> =41	0.89 (0.45–1.73) <i>n</i> =36	8.77 (5.41–14) <i>n</i> =45	4.10 (2.21–7.63) <i>n</i> =41
Day 31 post-vaccination	1.35 (0.79–2.28) <i>n</i> =42	2.26 (1.07–4.78) <i>n</i> =36	1.34 (0.78–2.30) <i>n</i> =42	0.77 (0.41–1.44) <i>n</i> =35	6.58 (4.03–11) <i>n</i> =45	4.35 (2.38–7.95) <i>n</i> =37

Delivery	1.10 (0.68–1.77) <i>n</i> =43	1.09 (0.53–2.24) <i>n</i> =40	1.32 (0.80–2.20) <i>n</i> =39	0.72 (0.37–1.37) <i>n</i> =33	4.20 (2.63–6.73) <i>n</i> =42	2.92 (1.64–5.22) <i>n</i> =40
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Supplementary Figure 1: Boxplots of individual maternal antibody concentrations against each serotype at baseline and delivery.

