Supplementary Appendix to Manuscript Entitled

Potential for Maternally Administered Vaccine for Infant Group B Streptococcus

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SUPPLEMENTARY INFORMATION

List of Investigators

The clinical study and seroepidemiology study were a collective group effort across multiple institutions and locations.

Below is a list of sites and principal investigators that significantly contributed to the implementation and conduct of the seroepidemiology study and C1091002 clinical study.

Seroepidemiology study		
Site	Location	Investigators
Chris Hani Baragwanath Academic Hospital	Soweto, South Africa	Prof. S.A. Madhi
Rahima Moosa Mother and Child Hospital	Johannesburg, South Africa	Dr. Renate Strehlau
Charlotte-Maxeke Johannesburg Academic Hospital	Johannesburg, South Africa	Prof. Daynia Ballot
Prince Mshiyeni Memorial Hospital	Durban, South Africa	Dr. Niree Naidoo
Tshwane Academic Laboratory network	Pretoria, South Africa	Dr. Mohamed Said
Mowbray Maternity Hospital in Cape Town	Cape Town, South Africa	Dr. Anika Van Niekerk
C1091002 clinical study		
Site	Location	Principal Investigator
Wits - Vaccines & Infectious Diseases Analytics Research Unit (Wits-VIDA)	Gauteng, South Africa	Prof. S.A. Madhi
Family Centre for Research with Ubuntu (FAMCRU)	Western Cape, South Africa	Dr. S.L. Barnabas
Wits RHI Shandukani Research Centre	Gauteng, South Africa	Dr. L. Fairlie

Seroepidemiology Study Methods

Study Setting and Healthcare Services

The annual birth cohort in Soweto is approximately 28,000, with the majority (99%) of deliveries occurring in health facilities. Healthcare is provided at no cost to all pregnant women and children by the State in South Africa. Three quarters of all births in the public health sector in Soweto occur at Chris Hani Baragwanath Academic Hospital (CHBAH) and the others at one of five midwife operated units (MOUs) or the Bheki Mhlangeni District Hospital (BMDH). Furthermore, there is a low threshold for referrals from the MOUs to the hospital if any sign of imminent obstetric complication is observed before or during labor. Also, there is a low threshold for referring ill neonates from the surrounding primary healthcare clinics to CHBAH for management. As CHBAH was the only public hospital in Soweto that admitted neonates at the time of the study, the majority of invasive Group B streptococcus (GBS) disease (IGbsD) cases diagnosed through standard-of-care practices were likely to have been identified. Rahima Moosa Mother and Child Hospital is a Provincial tertiary-level hospital with an annual birth cohort of approximately 14,000.

The absence of active surveillance and standardization of when to investigate for IGbsD could have resulted in an under-estimate of the burden of IGbsD even for this cohort.

Additional non-cohort invasive GBS cases were enrolled within 72 hours of laboratory confirmation at secondary sites in Johannesburg (Charlotte-Maxeke Johannesburg Academic Hospital), Durban (Prince Mshiyeni Memorial Hospital), Pretoria (Tshwane Academic Laboratory network), Cape Town (Mowbray Maternity Hospital in Cape Town), and Stellenbosch (Tygerberg Hospital).

The final protocol and informed consent document were approved by institutional review boards for each of the investigational centers participating in this study.

Consenting Procedures and Censoring Criteria for Inclusion in Analyses of Cohort Participants

Women were approached for study participation and consenting either at antenatal visits, or during the peripartum period during early stages of labor or immediately post-delivery. Written informed consenting was deferred in women who presented in active phase of labor, however, they were informed about the study and verbally consented for cord blood collection. Written consent was then obtained from the mother for inclusion into the study within 24h of delivery, or once she was comfortable and able to engage in the informed consent process. Cord blood samples collected from newborns whose mothers' refused study participation after delivery were discarded. This strategy was approved by the local Ethics Review committee based on it not being practical to consent women in the midst of labor and the procedures involving the collection of cord blood posed no discomfort or safety concerns to the mother-newborn dyad. All maternal blood samples and recto-vaginal swab samples were collected only after written informed consenting by the women.

The majority of the participants were Black-African (Table S1). The study eligibility criteria for pregnant women included age ≥18 years and delivery of a live birth at CHBAH or RMMCH. The exclusion criteria for study enrolment were refusal to consent, stillbirth delivery, receipt of any blood products in the past 4 weeks and enrolled in GBS vaccine study. The following censoring criteria, that were only assessable after delivery, and which entailed exclusion from analyses were: i. exposure to intrapartum antibiotic prophylaxis for suspected EOD during

delivery precluded the mother-infant dyad being selected as controls; ii. blood transfusion or receipt of any blood products in the women 30 days before delivery or in the infant prior to the onset of IGbsD; iii. infants who died before 90 days of age. Occurrence of invasive GBS disease in potential controls through to 90 days of age was captured by routine surveillance systems.

Collection and Processing of Cord Blood and Maternal Blood

The method for cord blood collection was as follows: after delivery of the baby, the obstetric/neonatal staff completed any procedures required for the care of the mother and newborn, including delayed cord clamping followed by double clamping after which cord blood was extracted, which was the standard operating procedure in the hospital. The placenta was delivered by the hospital staff and then handed, together with the clamped cord, to the study staff in a stainless-steel dish. Universal precautions such as gloves were used. The intended collection area was cleaned with an alcohol-soaked cotton wool swab. A large bore needle (size 18G), attached to a 10ml or 20ml syringe, was inserted directly into the cord blood vessels. The required amount of blood was collected into the syringe. If necessary, a second needle and syringe were inserted into a different vessel to collect the desired volume of blood (minimum 10ml). Maternal blood samples were collected within 24h of delivery using standard procedures. Maternal and cord blood specimens were allowed to stand at room temperature for up to 60 minutes after collection before being refrigerated (2-8°C) if it could not be transferred to the Vaccines and Infectious Diseases Analytical Research Unit (VIDA) laboratory immediately. Blood specimens were transported to the laboratory under refrigerated conditions. Once received by the laboratory, the blood specimens were refrigerated and processed within 24h of blood collection for serum separation. Serum was separated by centrifugation and stored at −70°C until analysis.

Swab Collection for GBS Culture and Serotyping in the Seroepidemiology Study

Enrolment of women for GBS colonization assessment was logistically constrained to sampling no more than 20 women per day, and sampling was done from Sunday to Wednesday. We aimed to obtain the lower vaginal swab prior to the rupture of membranes, failing which it was then collected within 24h of delivery. Swabs, collected by study staff, were taken from women delivering vaginally or by Caesarian section. Separate vaginal and rectal specimens were collected (Vaginal specimens were collected using Copan Liquid Amies Elution Swab [ESwab] Collection and Transport System, catalogue # 480CSR and rectal swabs were collected using rayon-tipped swabs that were placed into Amies transport medium without charcoal [Transwab Amies; Medical Wire, UK]). Swabs were refrigerated and transported to the Vaccines and Infectious Diseases Analytical (VIDA) Research Unit laboratory at 2-8°C, where they were refrigerated at 2-8°C and processed within 24h from the time of collection. For GBS isolation, swabs were inoculated onto CHROMagar StrepB (CA; Media Mage, South Africa).[1] Serotyping was performed by the latex agglutination method with specific antisera (Statens Serum Institut, Sweden) to serotypes Ia to IX capsular polysaccharide antigens.[2] Isolates tested non-typable by latex agglutination were further typed by PCR using primer sequences.[3]

Controls for the Seroepidemiology Study

Women investigated for GBS colonization at delivery were contacted telephonically at 3 months post-partum to ascertain whether their infant had been hospitalized for any suspected infection-related episode (including IGbsD) since birth. Recording of invasive GBS disease among potential controls was also accomplished by routine surveillance systems. Of the GBS vaginally colonized women, only those in whom the infant was deemed to have never been hospitalized for

suspected or confirmed sepsis by direct contact or routine surveillance, were eligible for selection as controls. Potential controls were to be matched to cases by GBS vaginal colonization serotype and infant gestational age (34-<37 weeks vs. ≥37 weeks). Controls for each case were selected at random from the set of all non-cases with exactly matching GBS serotype and infant gestational age, with up to 4 controls selected.

Daily surveillance for isolated GBS from a normally sterile site in infants ≤ 89 days of age was conducted at the National Health Laboratory Service (NHLS), the only laboratories that serves the study centers. Study participants that developed disease would have been identified through this surveillance and all other infants were assumed to not have developed GBS disease within the first 89 days of age.

Eligibility Criteria for the Seroepidemiology Study

The study eligibility criteria for pregnant women included age ≥18 years and delivery of a live birth at CHBAH or RMMCH. The exclusion criteria for study enrolment were refusal to consent or stillbirth delivery, receipt of any blood products in the past 4 weeks and enrolment in a GBS vaccine study. Vaginal and rectal swabs were taken from a random subset of eligible enrolled cohort maternal participants at delivery: subject characteristics of the swabbed subset are compared to the entire cohort population in Table S10.

Statistical Methods for the Seroepidemiology Study

The sample size of the study was based on the power to detect reductions in risk of developing invasive GBS disease for participants with antibody levels above a specified titer compared to below the specified titer. A minimum of 17 cases are required for 80% power to detect a 90% risk reduction, assuming 4 controls per case, 30% of controls exceeding the threshold and a 1-

sided 5% significance level (Table S11): analyses with less than 17 cases were therefore considered insufficient to define an IgG concentration threshold.

The absolute risk of invasive GBS disease conditional on IgG concentration was estimated using a Bayesian model previously described.[4] Briefly, the disease risk may be expressed using Bayes' theorem as

$$Rc(t) = P(Y = 1|t) = \frac{\pi f(t|\theta_1)}{\pi f(t|\theta_1) + (1-\pi) f(t|\theta_0)}$$

where

- Y is the disease event (1: disease; 0: nondisease);
- $f(t|\theta_1)$ is the probability density function of antibody titer (t) values in the disease group assumed to follow a Weibull distribution with scale parameter λ_1 and shape parameter ν_1 ;
- $f(t|\theta_0)$ is the probability density function of antibody titer values in the nondisease group assumed to follow a Weibull distribution with scale parameter λ_0 and shape parameter ν_0; and
- π is the disease prevalence in the population.

In particular, the prior distribution of the scale parameters, λ_1 and λ_0 is assumed to be a very broad lognormal distribution N(0, 10000). The prior distribution on the shape parameters ν_1 and ν_0 is assumed to be an exponential distribution with rate parameter = 0.5. Since the proportion of cases in the case-control study is not the same as the population of interest, we assume that the mixture parameter is very close to 0.001 based on historical data from a large cohort study in South Africa.[5] A strongly informative prior distribution, $Beta(25, 25000)$, is assumed on the mixture parameter, π. Posterior distributions of parameters were obtained from 10,000 Gibbs sampling iterations after discarding 5000 iterations for burn-in. The analysis is implemented using JAGS 4.3.0[6] and R (R2Jags package, Version 0.6-1).

As with any observational study potential confounding variables, measured or unmeasured, may exist. Any confounders which themselves are risk factors for GBS disease may be more prevalent among cases than controls, and therefore failing to account for them could exaggerate differences between cases and controls.

A posterior predictive assessment of the risk-concentration was made to assess goodness of fit of the Bayesian model. We generated 1,000 simulations of the IgG concentration distributions in cases and controls as estimated by models: if the simulated values for a given serotype were less than the LLOQ, a value of 0.5 x LLOQ was substituted to be consistent with how the real data were reported. Figure S1 shows observed summary statistics for IgG concentrations in cases and controls compared to the posterior distributions of those summary statistics as fitted by the models. Observed means and standard deviations were consistent with the posterior distributions, though the model tends to produce somewhat lower standard deviations than observed, for the serotype-specific models.

C1091002 Study Methods

Design

C1091002 is a randomized, placebo-controlled, observer-blinded Phase 1/2 study to assess the safety, tolerability, and immunogenicity of GBS6 in healthy nonpregnant and pregnant women and their infants. Stages 1 and 2 of the study have been conducted across 3 sites in South Africa.

Methods

Written informed consent was obtained from all participants before enrollment. Stage 1 enrolled a cohort of healthy nonpregnant women receiving 20 μg/serotype of GBS6 with or without $AlPO_4$. Following review of Stage 1 safety data, Stage 2 followed a sentinel-cohort design, with

cohort progression (including progression into expanded cohorts) and dose escalation after safety review. The final protocol and informed consent document were approved by institutional review boards for each of the investigational centers participating in this study, and this study was done in compliance with International Council for Harmonisation Good Clinical Practice guidelines and the ethical principles of the Declaration of Helsinki. In addition, study progress reports are submitted to institutional review boards every 6 months throughout the conduct of the study. Signed and dated written informed consent was required from each participant before any study-specific activity was done. The protocol for this study is included in the supplementary appendix.

Safety Assessment

The protocol specified safety stopping rules for Stage 2 GBS6 vaccinated participants enrolled in sentinel cohorts and 1 stopping rule also applied to the expanded cohort. Safety laboratory tests were conducted for Stage 2 sentinel-cohort participants. A toxicity grading scale adapted for use in pregnant women was used to grade laboratory test abnormalities. The Internal Review Committee reviewed the 14-day safety data from each sentinel cohort to determine if expanded cohort enrolment should begin at that dose and if sentinel cohort enrolment for the next higher dose should begin. This study is using an external data monitoring committee that provides regular review of cumulative safety data and ad-hoc review if a stopping rule is met.

Study Procedures

The full schedule of study procedures and study assessments are detailed in the protocol (Appendix). Sera and vaginal/rectal swab samples were collected from maternal participants prior study vaccination and at defined study visits. Cord blood/sera for immunogenicity assessment and oral/rectal swab samples for GBS microbiological culture were collected from infant participants at birth and defined study visits.

Swab Collection for Maternal Participants

Vaginal and rectal swabs were taken at Visit 1 (Vaccination Visit, prior to vaccination) and Visit 4 (at delivery or as early as possible after delivery and up to 72 hours after delivery) by study staff.

Cord Blood Collection

A cord blood sample of approximately 10 mL for immunogenicity assessments was collected in the delivery room. If cord blood was unavailable, a blood sample of approximately 2.5 mL was collected in the infant participants up to 72 hours after delivery.

Swab Collection for Infant Participants

Oral and rectal swabs were taken at delivery by study staff, after the infant had been wiped and prior to the infant being first breastfed. These swabs were taken within 2 hours following birth.

Serological Assay

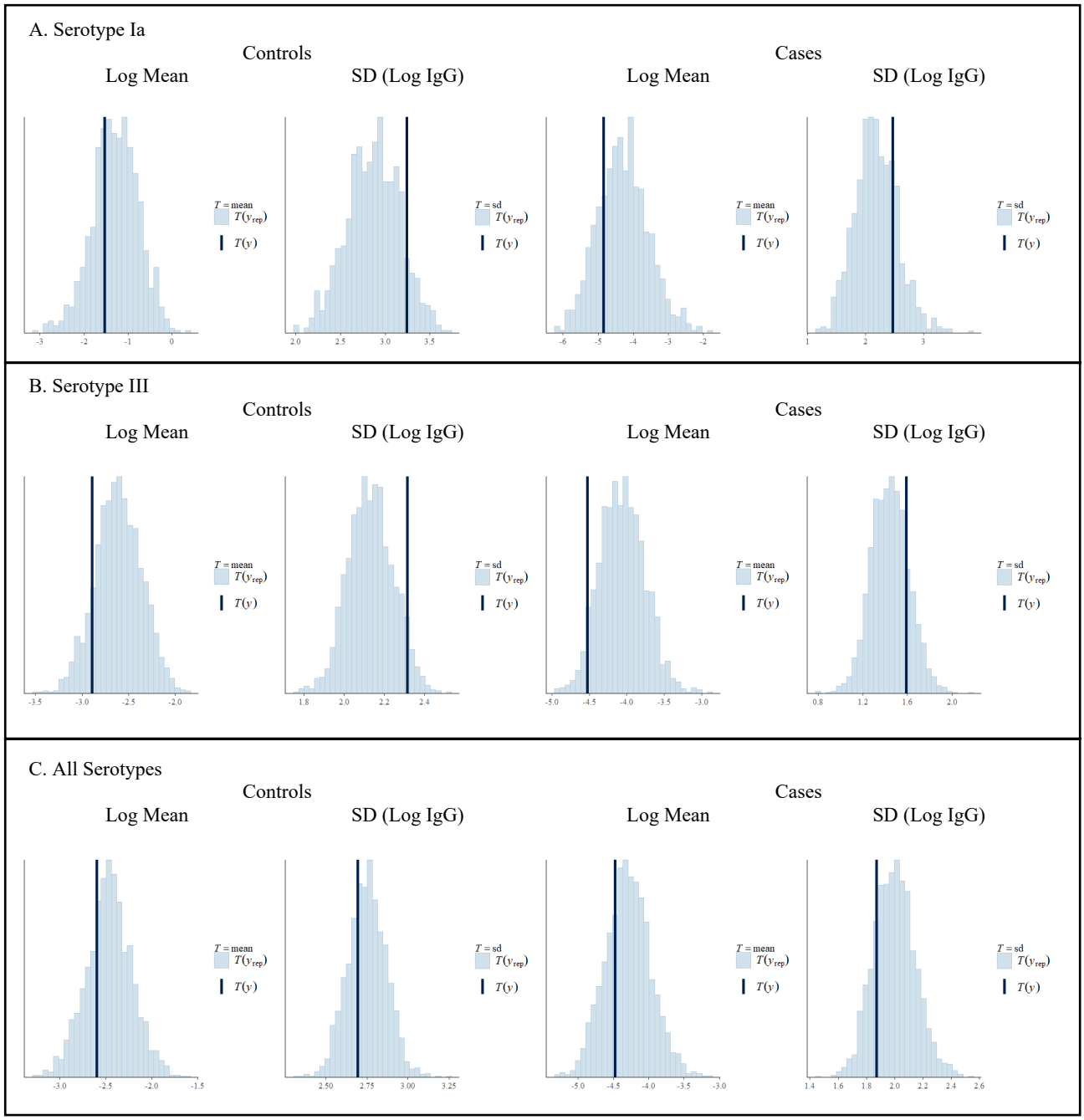
GBS capsular polysaccharides were conjugated to poly-L-Lysine and coupled to the Luminex microsphere beads. An in-house reference standard serum pool of GBS6 immune human sera was used in the assay and was calibrated to permit weight-based comparison of concentrations across the six serotypes (manuscript in preparation). The assay has been validated for specificity, accuracy, precision, and dilutional linearity. For the assay, reference sera, quality control samples, and test serum samples were diluted in assay buffer and incubated with the CPS coated beads overnight at 2-8 ºC with shaking. Following a wash step, bound antibodies were detected with a secondary R-Phycoerythrin-conjugated goat anti-human IgG secondary antibody (Jackson Cat. #109-115-098). Data were recorded as median fluorescence intensities and transformed into weight-based µg/mL concentrations with a log-log linear regression model utilized in the validated Statistical Analysis System (SAS).

Statistical Methods

The immunogenicity endpoints were analyzed based on the evaluable immunogenicity population, which included participants who were eligible, received vaccination as randomized (maternal), had at least one valid and determinate assay result for the 1-month-after-vaccination and delivery/birth visit within a prespecified window and had no potentially important protocol violations. Approximately 3% of maternal participants and 17% of infant participants were excluded from the evaluable population: in most cases due to samples not having been collected for testing. Descriptive summary statistics were provided for all immunogenicity endpoints. There was no imputation of missing serology results.

Supplemental Figures and Tables

Figure S1 Seroepidemiology Study: Posterior Distributions of Summary Statistics for IgG Antibody Concentrations in Cases and Controls Compared to Observed Values



Bold line indicates observed mean or standard deviation (SD) of log IgG concentrations for serotype Ia (Panel A), serotype III (Panel B) and all serotypes combined (Panel C); histograms indicate the distribution of those summary statistics across 1000 simulations of the posterior distributions of IgG concentration from the models

Figure S2 C1091002: GBS Serotype IgG Concentrations at Delivery – Maternal Participants

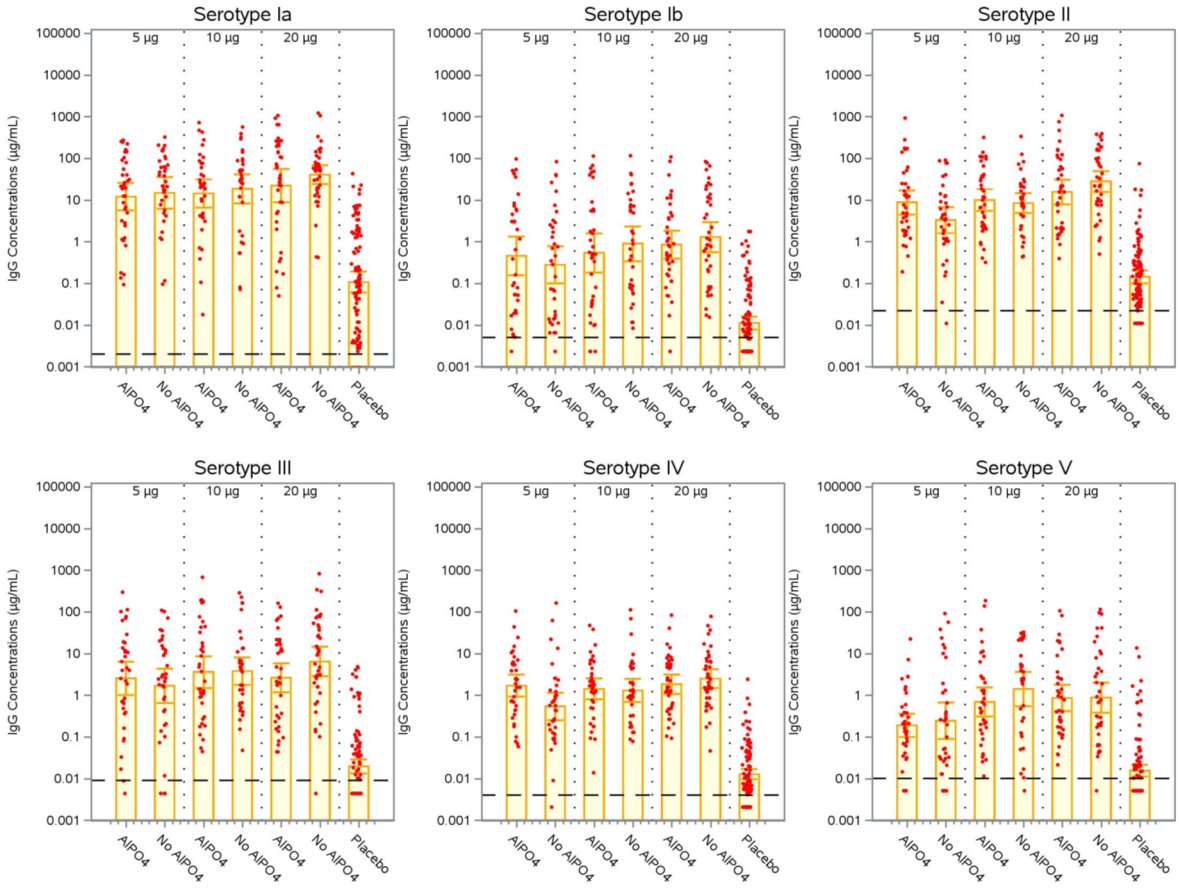


Figure S3 C1091002- GBS Serotype IgG Concentrations at Birth – Infant Participants

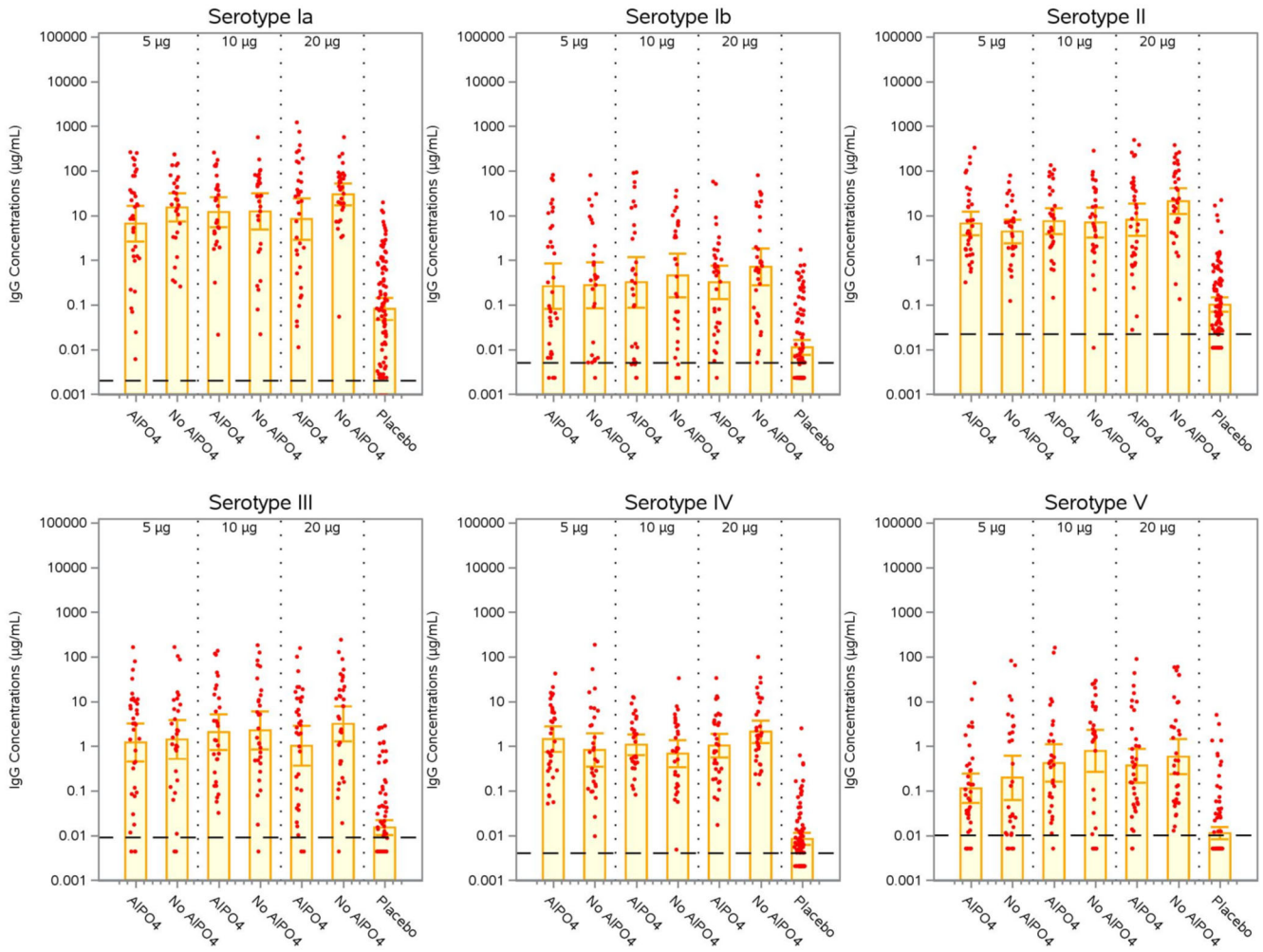


Figure S4 C1091002 – Antibody Response Line Plot of IgG GMCs by Vaccine Group, All Serotypes – Maternal Participants

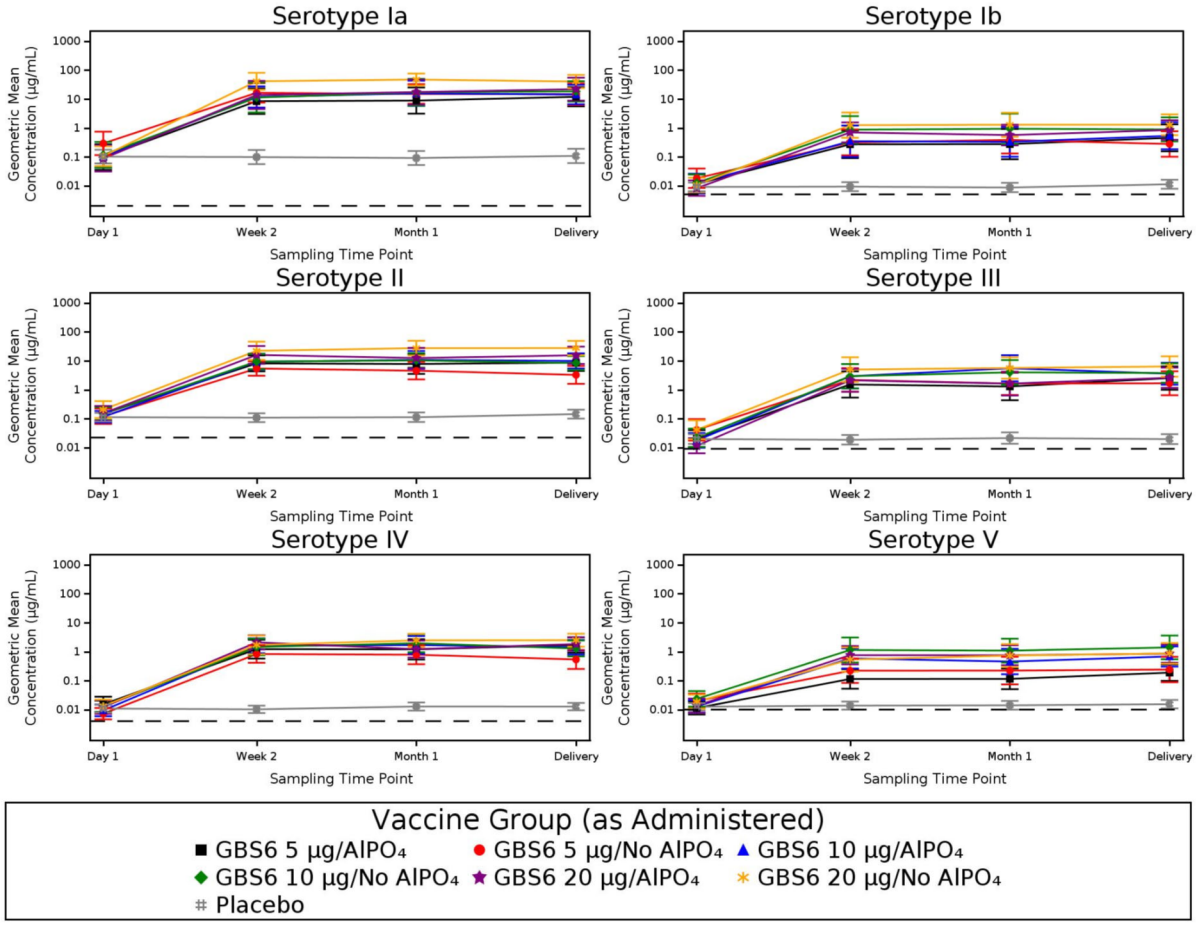


Table S1 Seroepidemiology Study: Demographic and Clinical Characteristics of All Live-Newborns

	Prospective cohort only		All-case and Controls	
Characteristic	**Controls N=67**	**Cases N=20**	**Controls N=250**	**Cases N=77**
Maternal characteristics Median (Interquartile Range)				
Age (y))	29 (24-34) n=66	27 (23-32)	28 (25-34) n=249	27 (23-31) n=73
Gravida	2 (2-3) n=65	2 (1-2) n=18	2 (2-3) n=237	2 (1-3) n=64
Parity)	1 (1-2) n=56	1 (0-2) n=16	1 (1-2) n=209	1 (0-2) n=59
Race				
Black-African	65/66 (98.5)	18 (90.0)	235/246 (95.5)	69/76 (90.8)
Asian	0/66 (0.0)	0 (0.0)	3/246 (1.2)	0/76 (0.0)
Mixed ancestry	0/66 (0.0)	2 (10.0)	6/246 (2.4)	7/76 (9.2)
White	0/66 (0.0)	0 (0.0)	1/246 (0.4)	0/76 (0.0)
Other	1/66 (1.5)	0 (0.0)	1/246 (0.4)	0/76 (0.0)
HIV status				
Negative	44 (65.7)	13 (65.0)	175/248 (70.6)	51/76 (67.1)
Positive	23 (34.3)	7 (35.0)	73/248 (29.4)	25/76 (32.9)
Syphilis status				
Negative	61 (91.0)	19 (95.0)	222 (88.8)	43 (55.8)

Positive	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Unknown	6 (9.0)	1 (5.0)	27 (10.8)	34 (44.2)
Hypertension during pregnancy	7 (10.4)	0 (0.0)	15/248 (6.0)	0/75 (0.0)
Diabetes during pregnancy	0 (0.0)	0 (0.0)	1/248 (0.4)	0/75 (0.0)
Smoking during pregnancy	1/64 (1.6)	1/19 (5.3)	8/229 (3.5)	5/66 (7.6)
Alcohol during pregnancy	0/64 (0.0)	0/19 (0.0)	10/228 (4.4)	0/66 (0.0)
Hemoglobin <9.5 g/dL	18/63 (28.6)	1/16 (6.2)	55/227 (24.2)	9/34 (26.5)
Labor and Delivery				
Rupture of membranes >18h before delivery	8/53 (15.1)	2/15 (13.3)	18/194 (9.3)	4/28 (14.3)
Intrapartum antibiotics	19 (28.4)	2 (10.0)	64 (25.6)	3 (3.9)
Multiple births	3 (4.5)	0/19 (0.0)	7/249 (2.8)	2/70 (2.9)
On ART	19/21 (90.5)	5/7 (71.4)	62/66 (93.9)	20/25 (80.0)
Delivery-related complications				
Antepartum hemorrhage	0 (0.0)	0 (0.0)	2 (0.8)	1 (1.3)
Maternal intrapartum temperature >= 38.0 C (oral)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Maternal tachycardia (>100 bpm) recorded	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
Clinically diagnosed chorioamnionitis	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.6)

Urinary tract infection	0 (0.0)	0 (0.0)	3 (1.2)	0 (0.0)
Meconium-stained liquor	7 (10.4)	1 (5.0)	22 (8.8)	5 (6.5)
Non-stress test (NST)/contraction stress test (CST)	3 (4.5)	0 (0.0)	5 (2.0)	5 (6.5)
Any fetal distress at birth	18 (26.9)	1 (5.0)	57 (22.8)	5 (6.5)
Infant characteristics				
Male sex	38 (56.7)	11 (55.0)	128 (51.2)	38 (49.4)
Race				
Black-African	66/66 (100.0)	18 (90.0)	232/242 (95.9)	66/73 (90.4)
Asian	0/66 (0.0)	0 (0.0)	2/242 (0.8)	2/73 (2.7)
Mixed ancestry	0/66 (0.0)	2 (10.0)	6/242 (2.5)	5/73 (6.8)
White	0/66 (0.0)	0 (0.0)	1/242 (0.4)	0/73 (0.0)
Other	0/66 (0.0)	0 (0.0)	1/242 (0.4)	0/73 (0.0)
Birth weight				
<1500g	0 (0.0)	1 (5.0)	6/247 (2.4)	11/71 (15.5)
1500g-<2500g	9 (13.4)	5 (25.0)	38/247 (15.4)	15/71 (21.1)
≥2500g	58 (86.6)	14 (70.0)	203/247 (82.2)	45/71 (63.4)
Median (Interquartile Range) birth weight (g)	2940 (2705-3282.5)	2885 (2323.8-3458.8)	2975 (2640-3359) n=247	2800 (2006-3160) n=71
Gestational age at Delivery				
<34wk	1 (1.5)	1 (5.0)	19/249 (7.6)	12 (15.6)

>=34 wk	66 (98.5)	19 (95.0)	230/249 (92.4)	65 (84.4)
Mode of delivery				
Cesarian	35 (52.2)	4 (20.0)	109/248 (44.0)	15/72 (20.8)
Elective	4/35 (11.4)	2/4 (50.0)	16/109 (14.7)	3/15 (20.0)
Emergency	31/35 (88.6)	2/4 (50.0)	93/109 (85.3)	12/15 (80.0)
Normal vaginal delivery	32 (47.8)	16 (80.0)	139/248 (56.0)	57/72 (79.2)
Apgar <7 at 1m	4/65 (6.2)	4 (20.0)	13/243 (5.3)	19/59 (32.2)
Apgar <7 at 5m	0/65 (0.0)	0 (0.0)	1/245 (0.4)	4/53 (7.5)

Table S2 Seroepidemiology Study: Summary of Cases Through 90 Days of Life by Serotype and Cohort for Participants in South Africa

Case Type	GBS Serotype	EOD	LOD	All Disease
Prospective	Ia	4	0	4
	Ib	0	0	0
	II	1	0	1
	III	5	10	15
	IV	0	0	0
	V	0	0	0
	Total	10	10	20
Retrospective	Ia	6	8	14
	Ib	3	1	4
	II	1	0	1
	III	16	14	30
	IV	1	2	3
	V	3	2	5
	Total	30	27	57
Total	Ia	10	8	18
	Ib	3	1	4
	II	2	0	2
	III	21	24	45
	IV	1	2	3
	V	3	2	5
	Total	40	37	77

Table S3 Seroepidemiology Study: IgG GMC by Case/Control for Major Serotypes - Infant Blood – by Prospective/Retrospective

			Cases			Controls			Controls/Cases	
Serotype	**Timing[a]**	**Case Type**	**n[b]**	**GMC[c]**	**(95% CI[d])**	**n[b]**	**GMC[c]**	**(95% CI[d])**	**GMR[e]**	**(95% CI[d])**
Ia	All	Prospective	4	0.002	(0.001, 0.006)	13	0.164	(0.021, 1.304)	96.250	(10.888, 850.832)
		Retrospective	14	0.012	(0.003, 0.056)	48	0.232	(0.091, 0.593)	18.976	(3.343, 107.728)
	EOD	Prospective	4	0.002	(0.001, 0.006)	13	0.164	(0.021, 1.304)	96.250	(10.888, 850.832)
		Retrospective	6	0.019	(0.001, 0.478)	24	0.329	(0.090, 1.205)	17.401	(0.668, 453.019)
	LOD	Prospective	0	-	-	0	-	-	-	-
		Retrospective	8	0.009	(0.001, 0.067)	24	0.164	(0.039, 0.689)	18.556	(1.820, 189.226)
III	All	Prospective	15	0.012	(0.005, 0.028)	50	0.056	(0.029, 0.108)	4.717	(1.652, 13.467)
		Retrospective	30	0.010	(0.006, 0.019)	93	0.055	(0.034, 0.089)	5.311	(2.471, 11.415)
	EOD	Prospective	5	0.020	(0.002, 0.242)	16	0.050	(0.014, 0.184)	2.498	(0.205, 30.490)
		Retrospective	16	0.020	(0.007, 0.058)	40	0.062	(0.031, 0.125)	3.108	(0.899, 10.749)
	LOD	Prospective	10	0.009	(0.004, 0.024)	34	0.059	(0.027, 0.131)	6.459	(2.005, 20.805)
		Retrospective	14	0.005	(0.004, 0.006)	53	0.050	(0.025, 0.099)	10.269	(5.039, 20.928)

Note: One serotype Ia prospective case had unknown timing

Abbreviations: CPS = capsular polysaccharide; GMR = geometric mean ratio; GMC = geometric mean concentration; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NE = not estimable; UNK=unknown.

a.Protocol-specified timing for blood sample collection.

b. n = Number of participants with valid and determinate assay results for the specific serotype at the specified time point.

c.GMCs were calculated using all participants with available data at either birth or time of infection.

d.CIs are back transformations of a CI based on the Student t distribution for the mean logarithm of the concentrations.

e.The GMR was calculated as the group mean difference (Control - Case) of logarithmically transformed antibody levels and back transformed to the original units.

Table S4 Seroepidemiology Study: Differences in Infant IgG GMCs Case vs Control

		Case (N[a]=77)			Control (N[a]=250)			Control/Case	
Serotype	**Timing[b]**	**n[c]**	**GMC[d]**	**(95% CI[e])**	**n[c]**	**GMC[d]**	**(95% CI[e])**	**GMR[f]**	**(95% CI[e])**
Ia	All	18	0.008	(0.002, 0.027)	61	0.216	(0.094, 0.495)	27.308	(6.398, 116.545)
	EOD	10	0.007	(0.001, 0.048)	37	0.258	(0.090, 0.743)	35.677	(4.454, 285.756)
	LOD	8	0.009	(0.001, 0.067)	24	0.164	(0.039, 0.689)	18.556	(1.820, 189.226)
Ib	All	4	0.055	(0.001, 2.239)	9	0.047	(0.007, 0.309)	0.841	(0.026, 26.764)
II	All	2	0.218	(0.011, 4.266)	8	0.736	(0.099, 5.486)	3.374	(0.438, 25.969)
III	All	45	0.011	(0.007, 0.017)	143	0.055	(0.038, 0.081)	5.107	(2.785, 9.364)
	EOD	21	0.020	(0.008, 0.049)	56	0.058	(0.032, 0.106)	2.921	(1.021, 8.357)
	LOD	24	0.006	(0.004, 0.009)	87	0.054	(0.032, 0.089)	8.429	(4.481, 15.856)
IV	All	3	0.007	(0.004, 0.011)	9	0.036	(0.006, 0.202)	5.332	(0.946, 30.053)
V	All	5	0.008	(0.002, 0.024)	20	0.016	(0.005, 0.050)	2.108	(0.512, 8.686)

Abbreviations: CPS = capsular polysaccharide; EOD=early-onset disease; GMR = geometric mean ratio; GMC = geometric mean concentration; IgG = immunoglobulin G; LOD=late-onset disease; NE = not estimable.

a.N = number of participants in the group.

b.Timing of invasive disease in cases. Data separated by EOD/LOD only for major serotypes with sufficient data

c.GMCs were calculated using all participants with available data at either birth or time of infection.

d.n = Number of participants with valid and determinate assay results for the specific serotype at the specified time point.

e.CIs are back transformations of a CI based on the Student t distribution for the mean logarithm of the concentrations.

f.The GMR was calculated as the group mean difference (Control - Case) of logarithmically transformed antibody levels and back transformed to the original units.

Table S5 Seroepidemiology Study: Estimated Infant Cord Blood Anti-CPS IgG Thresholds for Selected Risk Reduction All Cases

	Type Ia Only (Case=18;Control=61)	Type III Only (Case=45;Control=143)	All Types (Case=77;Control=250)
IgG Thresholds for Target Risk Reductions[(a)]:			
50%	0.035	0.044	0.049
60%	0.072	0.072	0.083
70%	0.144	0.117	0.14
75%	0.206	0.151	0.184
80%	0.302	0.198	0.246
90%	0.755	0.381	0.494
95%	1.48	0.616	0.827
Parameter Estimates (95% credible interval) of Bayesian Posterior Disease Risk[(b)]			
λ_1	0.039(0.004 0.091)	0.029(0.013 0.048)	0.033(0.017 0.051)
ν_1	0.39(0.264 0.511)	0.504(0.406 0.604)	0.464(0.39 0.535)
λ_0	1.075(0.417 1.843)	0.188(0.116 0.266)	0.301(0.202 0.416)
ν_0	0.388(0.312 0.464)	0.431(0.378 0.48)	0.375(0.344 0.411)
π	0.001(0.001 0.001)	0.001(0.001 0.001)	0.001(0.001 0.001)

(a) Thresholds are derived as the IgG concentration at which the probability of disease is reduced by the stated percentage, relative to the assumed population incidence, for any participants with IgG concentration at or above the threshold.

(b) ν_1 and ν_0 are estimated shape parameter of Weibull distribution in case and control group, respectively; λ_1 and λ_0 are the corresponding scale parameters; π is the GBS disease prevalence in population.

Table S6 C1091002 – Demographics

Demographic Characteristics – Maternal Participants – Stage 2 – Safety Population

	Vaccine Group (as Administered)							
	GBS6 5 µg/ $AlPO_4$ (N^a=40)	**GBS6 5 µg/ No $AlPO_4$ (N^a=40)**	**GBS6 10 µg/ $AlPO_4$ (N^a=40)**	**GBS6 10 µg/ No $AlPO_4$ (N^a=40)**	**GBS6 20 µg/ $AlPO_4$ (N^a=40)**	**GBS6 20 µg/ No $AlPO_4$ (N^a=40)**	**Placebo (N^a=120)**	**Total (N^a=360)**
	n^b (%)	**n^b (%)**	**n^b (%)**	**n^b (%)**	**n^b (%)**	**n^b (%)**	**n^b (%)**	**n^b (%)**
Sex								
Female	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	120 (100.0)	360 (100.0)
Race								
Black or African American	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	120 (100.0)	360 (100.0)
Ethnicity								
Non-Hispanic/non-Latino	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	120 (100.0)	360 (100.0)
Age at vaccination (years)								
Mean (SD)	25.8 (5.16)	27.2 (5.49)	25.7 (5.17)	25.9 (5.43)	25.2 (4.57)	27.2 (5.35)	26.1 (4.67)	26.1 (5.03)
Median	25.0	26.5	25.0	26.0	25.0	26.0	26.0	25.0

Demographic Characteristics – Maternal Participants – Stage 2 – Safety Population

	Vaccine Group (as Administered)							
	GBS6 5 µg/ $AlPO_4$ (N^a=40)	GBS6 5 µg/ No $AlPO_4$ (N^a=40)	GBS6 10 µg/ $AlPO_4$ (N^a=40)	GBS6 10 µg/ No $AlPO_4$ (N^a=40)	GBS6 20 µg/ $AlPO_4$ (N^a=40)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=120)	Total (N^a=360)
	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)
Min, max	18, 37	18, 38	18, 36	18, 38	18, 35	18, 37	18, 37	18, 38
Gestational Age at Vaccination (weeks)								
≥24 to <27 weeks	0	0	1 (2.5)	0	0	0	0	1 (0.3)
≥27 to <30 weeks	17 (42.5)	18 (45.0)	12 (30.0)	12 (30.0)	13 (32.5)	12 (30.0)	53 (44.2)	137 (38.1)
≥30 to <36 weeks	23 (57.5)	22 (55.0)	27 (67.5)	28 (70.0)	27 (67.5)	28 (70.0)	67 (55.8)	222 (61.7)

Abbreviation: CPS = capsular polysaccharide.
Note: Total GBS6 dose: 30 µg (5 µg CPS/serotype/dose); 60 µg (10 µg CPS/serotype/dose); 120 µg (20 µg CPS/serotype/dose).
a. N = number of participants in the vaccine group or total sample. These values are used as the denominators for the percentage calculations.
b. n = Number of participants in the specified category.

Table S7 C1091002: Analysis Populations – Stage 2 Maternal Participants

Analysis Populations – Maternal Participants – Stage 2 – All Randomized Participants

	Vaccine Group (as Randomized)							
	GBS6 5 µg/ $AlPO_4$ (N^a=40)	GBS6 5 µg/ No $AlPO_4$ (N^a=40)	GBS6 10 µg/ $AlPO_4$ (N^a=40)	GBS6 10 µg/ No $AlPO_4$ (N^a=40)	GBS6 20 µg/ $AlPO_4$ (N^a=40)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=120)	Total (N^a=360)
	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)
Safety population	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	120 (100.0)	360 (100.0)
Excluded from safety population								
Not vaccinated	0	0	0	0	0	0	0	0
mITT population	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	120 (100.0)	360 (100.0)
Excluded from mITT population								
No valid and determinate assay results	0	0	0	0	0	0	0	0
Evaluable immunogenicity population	39 (97.5)	40 (100.0)	38 (95.0)	37 (92.5)	39 (97.5)	40 (100.0)	116 (96.7)	349 (96.9)
Excluded from Evaluable immunogenicity population[c]	1 (2.5)	0	2 (5.0)	3 (7.5)	1 (2.5)	0	4 (3.3)	11 (3.1)
Not eligible for the study	0	0	1 (2.5)	0	1 (2.5)	0	0	2 (0.6)
Did not receive the assigned vaccine as randomized	0	0	0	0	0	0	0	0

Analysis Populations – Maternal Participants – Stage 2 – All Randomized Participants

	Vaccine Group (as Randomized)							
	GBS6 5 µg/ $AlPO_4$ (N^a=40)	GBS6 5 µg/ No $AlPO_4$ (N^a=40)	GBS6 10 µg/ $AlPO_4$ (N^a=40)	GBS6 10 µg/ No $AlPO_4$ (N^a=40)	GBS6 20 µg/ $AlPO_4$ (N^a=40)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=120)	Total (N^a=360)
	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)
Visit 3 blood draw collection is not within 27 to 49 days, inclusive, after vaccination	1 (2.5)	0	1 (2.5)	3 (7.5)	1 (2.5)	0	4 (3.3)	10 (2.8)
Did not have at least 1 valid and determinate assay result for 1 month after vaccination (Visit 3) or delivery visit	1 (2.5)	0	1 (2.5)	3 (7.5)	1 (2.5)	0	4 (3.3)	10 (2.8)
Had major protocol violation(s) as determined by the study clinician	0	0	0	0	0	0	0	0

Abbreviation: CPS = capsular polysaccharide.
Note: Total GBS6 dose: 30 µg (5 µg CPS/serotype/dose); 60 µg (10 µg CPS/serotype/dose); 120 µg (20 µg CPS/serotype/dose).
Note: The placebo column combines all participants receiving placebo across all cohorts.
a. N = number of participants in the specified vaccine group or total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants in the specified category.
c. Participants could be excluded for more than 1 reason.

Table S8 C1091002: Analysis Populations – Stage 2 Infant Participants

Analysis Populations – Infant Participants – Stage 2

	Maternal Vaccine Group (as Randomized)							
	GBS6 5 µg/ $AlPO_4$ (N^a=40)	GBS6 5 µg/ No $AlPO_4$ (N^a=39)	GBS6 10 µg/ $AlPO_4$ (N^a=40)	GBS6 10 µg/ No $AlPO_4$ (N^a=40)	GBS6 20 µg/ $AlPO_4$ (N^a=40)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=118)	Total (N^a=357)
	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)
Safety population	40 (100.0)	39 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	40 (100.0)	118 (100.0)	357 (100.0)
Excluded from safety population								
Mother not vaccinated	0	0	0	0	0	0	0	0
mITT population	36 (90.0)	35 (89.7)	35 (87.5)	33 (82.5)	38 (95.0)	37 (92.5)	108 (91.5)	322 (90.2)
Excluded from mITT population								
No valid and determinate assay results	4 (10.0)	4 (10.3)	5 (12.5)	7 (17.5)	2 (5.0)	3 (7.5)	10 (8.5)	35 (9.8)
Evaluable immunogenicity population	36 (90.0)	30 (76.9)	30 (75.0)	30 (75.0)	36 (90.0)	35 (87.5)	100 (84.7)	297 (83.2)
Excluded from Evaluable immunogenicity population[c]	4 (10.0)	9 (23.1)	10 (25.0)	10 (25.0)	4 (10.0)	5 (12.5)	18 (15.3)	60 (16.8)
Not eligible for the study	1 (2.5)	1 (2.6)	1 (2.5)	1 (2.5)	1 (2.5)	0	0	5 (1.4)
Mother did not receive the assigned vaccine as randomized	0	0	0	0	0	0	0	0
Cord blood was not available or Visit 1	4 (10.0)	9 (23.1)	8 (20.0)	8 (20.0)	4 (10.0)	2 (5.0)	16 (13.6)	51 (14.3)

Analysis Populations – Infant Participants – Stage 2

	Maternal Vaccine Group (as Randomized)							
	GBS6 5 µg/ $AlPO_4$ (N^a=40)	GBS6 5 µg/ No $AlPO_4$ (N^a=39)	GBS6 10 µg/ $AlPO_4$ (N^a=40)	GBS6 10 µg/ No $AlPO_4$ (N^a=40)	GBS6 20 µg/ $AlPO_4$ (N^a=40)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=118)	Total (N^a=357)
	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)	n^b (%)
(birth) blood was not drawn for assay testing within 72 hours after birth								
Did not have at least 1 valid and determinate assay result at the birth visit (Visit 1)	4 (10.0)	4 (10.3)	5 (12.5)	7 (17.5)	2 (5.0)	3 (7.5)	10 (8.5)	35 (9.8)
Had major protocol violation(s) as determined by the study clinician	0	0	0	0	0	0	0	0

Abbreviation: CPS = capsular polysaccharide.
Note: Total GBS6 dose: 30 µg (5 µg CPS/serotype/dose); 60 µg (10 µg CPS/serotype/dose); 120 µg (20 µg CPS/serotype/dose).
Note: The placebo column combines all participants receiving placebo across all cohorts.
a. N = number of participants in the specified vaccine group or total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants in the specified category.
c. Participants could be excluded for more than 1 reason.

Table S9 C1091002: IgG GMFRs Maternal Participants

GBS Serotype-Specific IgG GMFRs – Maternal Participants – Stage 2 – Evaluable Immunogenicity Population

		Vaccine Group (as Administered)						
		GBS6 5 µg/ $AlPO_4$ (N^a=39)	GBS6 5 µg/ No $AlPO_4$ (N^a=40)	GBS6 10 µg/ $AlPO_4$ (N^a=38)	GBS6 10 µg/ No $AlPO_4$ (N^a=37)	GBS6 20 µg/ $AlPO_4$ (N^a=39)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=116)
Serotype	Time Point[b]	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])
Ia	Week 2	86.424 (39) (43.724, 170.824)	56.413 (40) (22.926, 138.813)	150.991 (34) (64.253, 354.821)	124.663 (33) (37.254, 417.155)	151.488 (38) (71.963, 318.894)	346.537 (39) (185.359, 647.867)	0.912 (110) (0.741, 1.122)
	Month 1	85.304 (34) (37.251, 195.344)	58.685 (35) (23.726, 145.151)	157.942 (27) (75.014, 332.550)	148.902 (26) (50.456, 439.431)	222.495 (33) (108.516, 456.190)	381.788 (37) (217.254, 670.931)	0.911 (93) (0.688, 1.207)
	Delivery	132.683 (37) (68.265, 257.889)	40.546 (36) (13.222, 124.336)	176.496 (36) (97.803, 318.505)	148.340 (34) (74.772, 294.290)	221.947 (37) (116.902, 421.382)	383.059 (40) (229.454, 639.493)	1.106 (107) (0.875, 1.399)
Ib	Week 2	23.608 (39) (11.442, 48.708)	17.447 (40) (8.001, 38.044)	29.562 (35) (14.604, 59.840)	67.036 (33) (29.129, 154.277)	84.915 (39) (42.201, 170.859)	113.344 (39) (59.146, 217.206)	1.060 (109) (0.889, 1.265)
	Month 1	23.705 (34) (9.509, 59.095)	22.156 (35) (9.789, 50.145)	39.961 (28) (20.743, 76.985)	77.113 (26) (35.076, 169.532)	82.912 (34) (38.512, 178.497)	122.118 (37) (71.044, 209.910)	0.982 (92) (0.840, 1.147)
	Delivery	36.344 (37) (17.694, 74.653)	15.339 (36) (6.508, 36.155)	42.511 (37) (23.159, 78.032)	75.079 (34) (39.804, 141.614)	99.349 (38) (50.027, 197.297)	121.498 (40) (76.340, 193.369)	1.242 (107) (1.052, 1.465)
II	Week 2	55.490 (39) (30.681, 100.360)	44.962 (40) (26.067, 77.553)	83.318 (35) (50.906, 136.368)	59.685 (33) (32.166, 110.748)	105.365 (39) (66.870, 166.021)	101.124 (38) (48.353, 211.486)	0.953 (110) (0.758, 1.197)
	Month 1	60.981 (34) (28.939, 128.501)	40.244 (35) (22.352, 72.457)	93.487 (28) (58.081, 150.476)	59.312 (26) (32.834, 107.145)	83.528 (34) (51.836, 134.595)	121.025 (36) (70.087, 208.983)	1.149 (93) (0.865, 1.526)

GBS Serotype-Specific IgG GMFRs – Maternal Participants – Stage 2 – Evaluable Immunogenicity Population

		Vaccine Group (as Administered)						
		GBS6 5 µg/ $AlPO_4$ (N^a=39)	GBS6 5 µg/ No $AlPO_4$ (N^a=40)	GBS6 10 µg/ $AlPO_4$ (N^a=38)	GBS6 10 µg/ No $AlPO_4$ (N^a=37)	GBS6 20 µg/ $AlPO_4$ (N^a=39)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=116)
Serotype	Time Point[b]	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])
III	Delivery	63.891 (37) (39.241, 104.027)	26.350 (36) (13.299, 52.209)	82.724 (37) (53.601, 127.671)	65.525 (34) (37.862, 113.401)	105.941 (38) (70.097, 160.115)	136.319 (39) (79.116, 234.881)	1.332 (107) (1.084, 1.638)
	Week 2	74.997 (39) (36.230, 155.246)	53.594 (40) (24.353, 117.945)	147.751 (35) (73.649, 296.411)	139.157 (33) (63.268, 306.074)	183.990 (39) (89.014, 380.303)	114.871 (39) (49.160, 268.413)	0.951 (110) (0.760, 1.190)
	Month 1	67.125 (34) (29.343, 153.559)	49.463 (35) (24.148, 101.314)	245.556 (28) (123.697, 487.466)	185.652 (26) (95.013, 362.755)	129.326 (34) (65.188, 256.568)	142.903 (37) (74.861, 272.790)	1.003 (93) (0.774, 1.300)
IV	Delivery	114.543 (37) (59.516, 220.445)	46.471 (36) (20.250, 106.644)	201.940 (37) (119.059, 342.519)	177.239 (34) (112.151, 280.102)	219.467 (38) (115.936, 415.449)	155.788 (40) (87.561, 277.178)	0.998 (108) (0.812, 1.226)
	Week 2	80.221 (39) (36.094, 178.295)	123.854 (39) (74.251, 206.594)	168.202 (34) (108.601, 260.513)	103.885 (33) (57.892, 186.418)	164.613 (36) (88.501, 306.182)	125.746 (39) (65.325, 242.052)	0.917 (106) (0.733, 1.146)
	Month 1	80.362 (34) (40.192, 160.680)	114.304 (34) (70.727, 184.731)	167.648 (28) (97.413, 288.525)	120.655 (26) (60.004, 242.612)	84.881 (31) (44.106, 163.354)	173.897 (37) (117.178, 258.071)	1.146 (89) (0.828, 1.586)
V	Delivery	107.455 (37) (63.200, 182.699)	75.651 (35) (36.846, 155.322)	145.729 (36) (91.777, 231.399)	97.035 (34) (53.982, 174.426)	146.382 (35) (79.113, 270.848)	187.999 (40) (120.991, 292.117)	1.226 (105) (0.985, 1.526)
	Week 2	10.094 (39) (5.572, 18.285)	11.086 (40) (5.669, 21.679)	41.964 (35) (23.794, 74.010)	42.647 (33) (19.021, 95.619)	55.184 (39) (32.108, 94.844)	29.588 (39) (14.773, 59.259)	1.118 (110) (0.941, 1.328)
	Month 1	9.760 (34) (5.048, 18.869)	10.893 (35) (4.637, 25.594)	38.825 (28) (19.011, 79.293)	56.538 (26) (27.979, 114.252)	54.474 (34) (29.683, 99.968)	39.522 (37) (23.109, 67.592)	1.087 (93) (0.892, 1.326)
	Delivery	15.934 (37) (9.600, 26.446)	11.634 (36) (5.624, 24.066)	51.765 (37) (28.813, 93.000)	54.918 (34) (27.574, 109.376)	60.702 (38) (34.558, 106.625)	46.223 (40) (27.790, 76.883)	1.194 (108) (1.019, 1.398)

GBS Serotype-Specific IgG GMFRs – Maternal Participants – Stage 2 – Evaluable Immunogenicity Population

		Vaccine Group (as Administered)						
		GBS6 5 µg/ $AlPO_4$ (N^a=39)	GBS6 5 µg/ No $AlPO_4$ (N^a=40)	GBS6 10 µg/ $AlPO_4$ (N^a=38)	GBS6 10 µg/ No $AlPO_4$ (N^a=37)	GBS6 20 µg/ $AlPO_4$ (N^a=39)	GBS6 20 µg/ No $AlPO_4$ (N^a=40)	Placebo (N^a=116)
Serotype	Time Point[b]	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])	GMFR[c] (n^d) (95% CI[e])

Abbreviations: CPS = capsular polysaccharide; GMFR = geometric mean fold rise; IgG = immunoglobulin G; LLOQ = lower limit of quantitation.
Note: Total GBS6 dose: 30 µg (5 µg CPS/serotype/dose); 60 µg (10 µg CPS/serotype/dose); 120 µg (20 µg CPS/serotype/dose).
Note: The standardized LLOQ values in µg/mL for IgG are Ia, 0.002; Ib, 0.005; II, 0.022; III, 0.009; IV, 0.004; V, 0.01. Assay results below the LLOQ were set to 0.5 x LLOQ.
Note: The placebo column combines all participants receiving placebo across all cohorts.
a. N = number of participants in the vaccine group.
b. Protocol-specified timing for blood sample collection.
c. GMFRs were calculated using all participants with valid and determinant assay results both before vaccination (Day 1) and at the specified time point.
d. n = Number of participants with valid and determinate assay results for the serotype both before vaccination (Day 1) and at the specified time point.
e. CIs are back transformations of a CI based on the Student t distribution for the mean fold rise.

Table S10 Seroepidemiology Study: Demographic and Clinical Characteristics of Participants in the Cohort Study: Maternal Participants Swabbed for GBS Colonization with Consideration as Controls vs. Overall Cohort and Those Not Swabbed

	Prospective cohort		
Characteristic	**Total Cohort N=17752**	**Not Swabbed N= 14798**	**Swabbed N= 2954[a]**
Maternal characteristics **Median (Interquartile Range)**			
Age (y)	28 (24-34) n=17605	28 (24-34) n=14677	28 (24-33) n=2928
Gravida	2 (1-3) n=16465	2 (1-3) n=13823	2 (1-3) n=2642
Parity	1 (1-2) n=14262	1 (1-2) n=11993	1 (0-2) n=2269
Race			
Black-African	16443/17593 (93.5)	13689/14692 (93.2)	2754/2901 (94.9)
Asian	95/17593 (0.5)	80/14692 (0.5)	15/2901 (0.5)
Mixed ancestry	870/17593 (4.9)	764/14692 (5.2)	106/2901 (3.7)
White	100/17593 (0.6)	91/14692 (0.6)	9/2901 (0.3)
Other	85/17593 (0.5)	68/14692 (0.5)	17/2901 (0.6)
HIV status			
Negative	12658/17316 (73.1)	10557/14422 (73.2)	2101/2894 (72.6)
Positive	4658/17316 (26.9)	3865/14422 (26.8)	793/2894 (27.4)
Syphilis status			
Negative	15101/17683 (85.4)	12650/14763 (85.7)	2451/2920 (83.9)
Positive	213/17683 (1.2)	186/14763 (1.3)	27/2920 (0.9)
Unknown	2369/17683 (13.4)	1927/14763 (13.1)	442/2920 (15.1)
Hypertension during pregnancy	1120/17636 (6.4)	906/14728 (6.2)	214/2908 (7.4)
Diabetes during pregnancy	123/17636 (0.7)	111/14728 (0.8)	12/2908 (0.4)

Smoking during pregnancy	709/16288 (4.4)	612/13712 (4.5)	97/2576 (3.8)
Alcohol during pregnancy	871/16269 (5.4)	715/13695 (5.2)	156/2574 (6.1)
Hemoglobin <9.5 g/dL	4150/15784 (26.3)	3481/13251 (26.3)	669/2533 (26.4)
Labor and Delivery			
Rupture of membranes >18h before delivery	1464/12708 (11.5)	1164/10684 (10.9)	300/2024 (14.8)
Intrapartum antibiotics	3872 (21.8)	3111 (21.0)	761 (25.8)
Multiple births	336 (1.9)	274 (1.9)	62 (2.1)
On ART	4092/4310 (94.9)	3389/3575 (94.8)	703/735 (95.6)
Delivery-related complications			
Antepartum hemorrhage	251 (1.4)	213 (1.4)	38 (1.3)
Maternal intrapartum temperature >= 38.0 C (oral)	10 (0.1)	8 (0.1)	2 (0.1)
Maternal tachycardia (>100 bpm)	91 (0.5)	64 (0.4)	27 (0.9)
Urinary tract infection	470 (2.6)	383 (2.6)	87 (2.9)
Clinically diagnosed chorioamnionitis	30 (0.2)	25 (0.2)	5 (0.2)
Meconium-stained liquor	1923 (10.8)	1641 (11.1)	282 (9.5)
Non-stress test (NST)/contraction stress test (CST)	374 (2.1)	276 (1.9)	98 (3.3)
Any fetal distress at birth	2977 (16.8)	2387 (16.1)	590 (20.0)

[a] Includes 4 participants whose infants became prospective GBS cases

Infant characteristics	**Observational N=18144**	**Not Swabbed N= 15116**	**Swabbed N= 3028**
Male sex	9157 (50.5)	7637 (50.5)	1520 (50.2)
Race			

Black-African	16937/17768 (95.3)	14104/14836 (95.1)	2833/2932 (96.6)
Asian	90/17768 (0.5)	77/14836 (0.5)	13/2932 (0.4)
Mixed ancestry	604/17768 (3.4)	535/14836 (3.6)	69/2932 (2.4)
White	82/17768 (0.5)	75/14836 (0.5)	7/2932 (0.2)
Other	55/17768 (0.3)	45/14836 (0.3)	10/2932 (0.3)
Birth weight			
<1500g	492/17948 (2.7)	419/14973 (2.8)	73/2975 (2.5)
1500g-<2500g	2679/17948 (14.9)	2211/14973 (14.8)	468/2975 (15.7)
≥2500g	14777/17948 (82.3)	12343/14973 (82.4)	2434/2975 (81.8)
Median (Interquartile Range) birth weight (g)	3025 (2665-3350) n=17948	3020 (2665-3346) n=14973	3035 (2665-3356.5) n=2975
Gestational age at Delivery			
<34wk	1328/18126 (7.3)	1107/15102 (7.3)	221/3024 (7.3)
>=34 wk	16798/18126 (92.7)	13995/15102 (92.7)	2803/3024 (92.7)
Mode of delivery			
Cesarian	7220/17860 (40.4)	5862/14907 (39.3)	1358/2953 (46.0)
Elective	1819/7220 (25.2)	1571/5862 (26.8)	248/1358 (18.3)
Emergency	5401/7220 (74.8)	4291/5862 (73.2)	1110/1358 (81.7)
Normal vaginal delivery	10640/17860 (59.6)	9045/14907 (60.7)	1595/2953 (54.0)
Apgar <7 at 1m	1015/17601 (5.8)	857/14702 (5.8)	158/2899 (5.5)
Apgar <7 at 5m	239/17591 (1.4)	205/14675 (1.4)	34/2916 (1.2)

Table S11 Seroepidemiology Study: Number of Cases Required for 80% Power to Detect Different Levels of Risk Reduction with Case: Control Ratio of 1:4

Risk Reduction[a]	Number of Cases per Serotype[b]
90%	17
85%	21
80%	25
75%	31
70%	38
65%	47
60%	59

[a] Risk reduction (estimated by odds ratio) associated with a titer above the titer threshold, relative to those below the threshold.
[b] Cases for 80% power using a 1-sided 5% significance level, in a study with 4 controls per case and 30% of control subjects with titers exceeding the threshold.

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