MATISSE Study: Analyses of Infant Safety Outcomes

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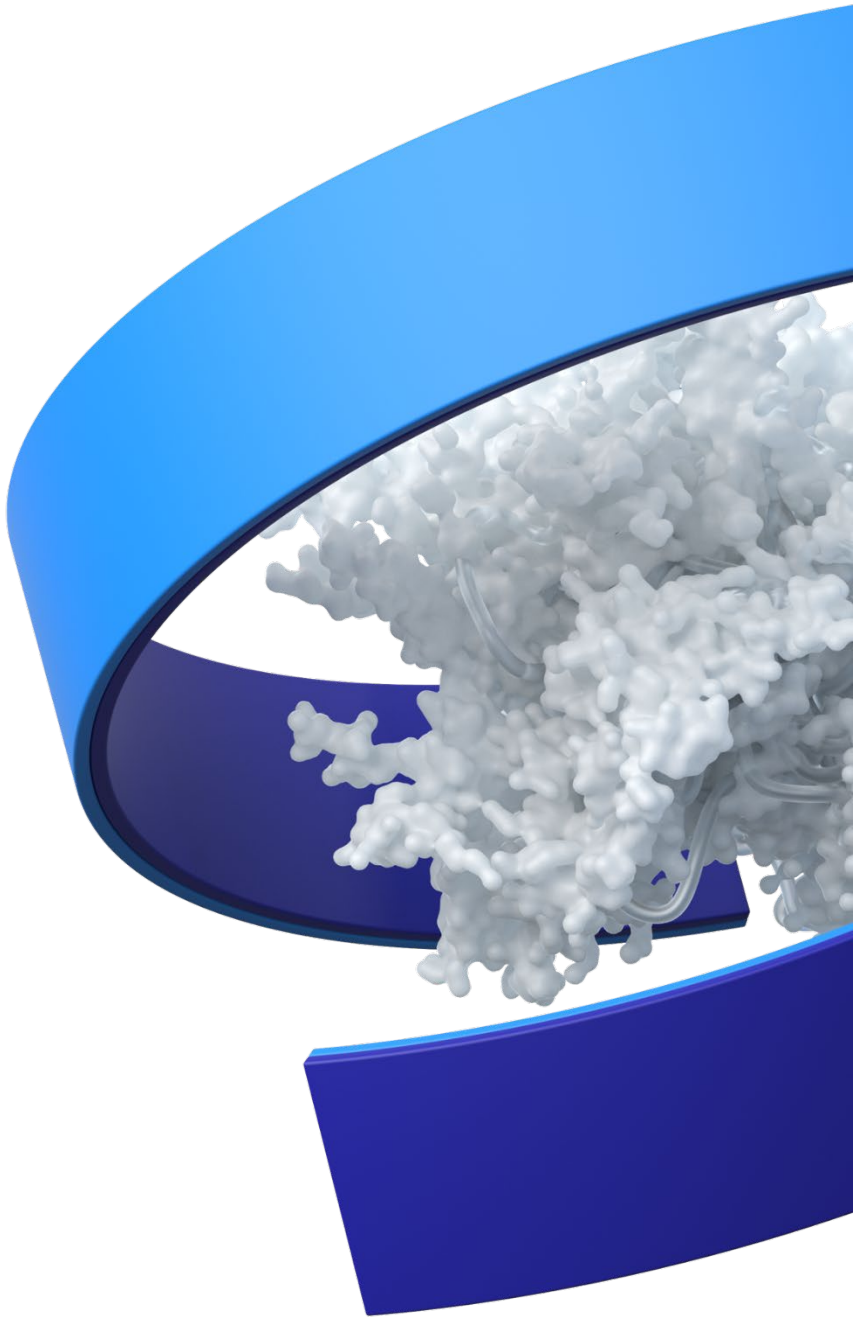
David Radley



MATISSE: Phase 3 Pivotal Maternal Vaccination Trial

Pregnant participants ≤49 years

Between ≥24 and ≤36 weeks gestation

Dose

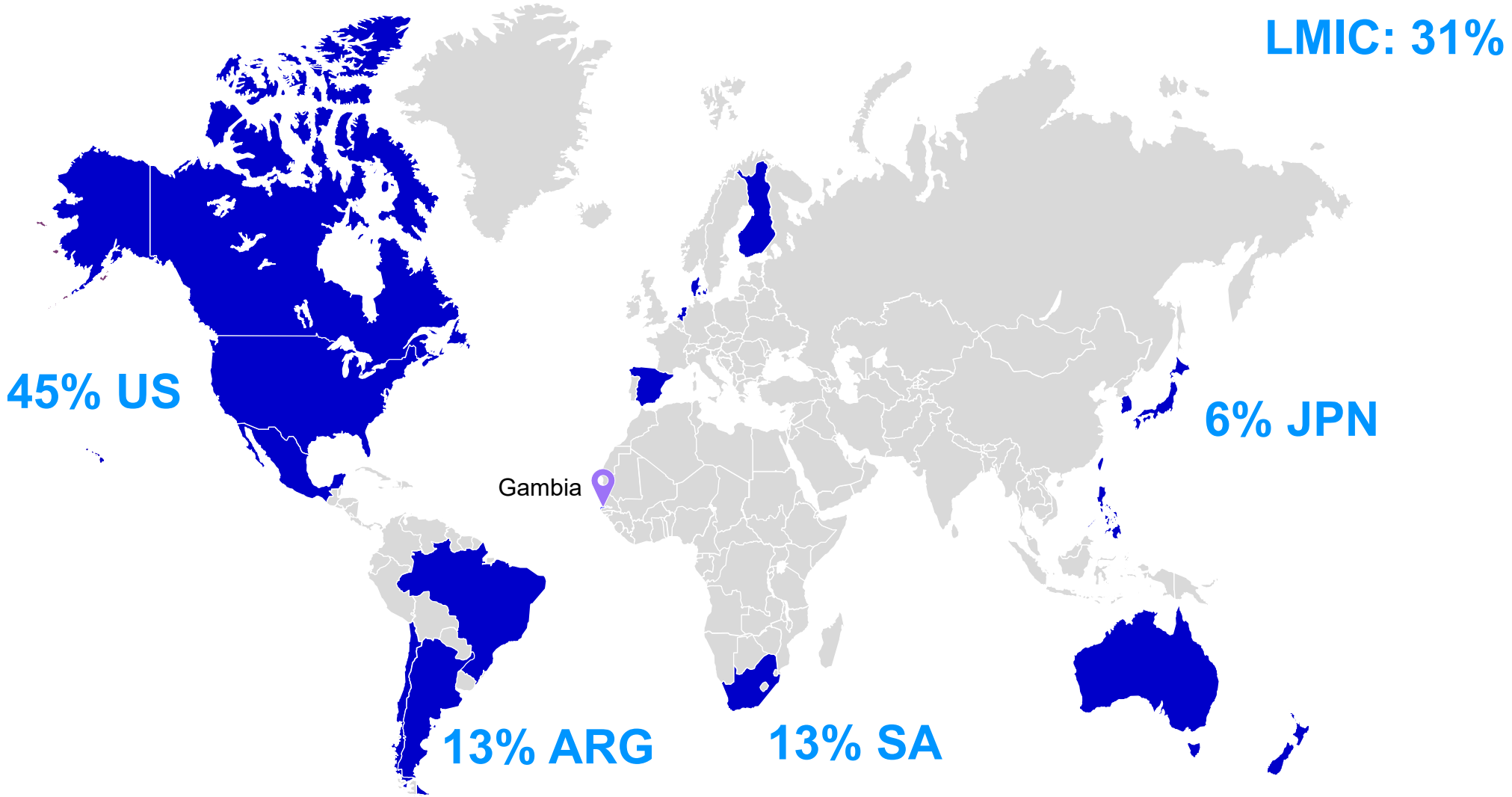
1:1

- **RSVpreF 120 µg**
- **Placebo**

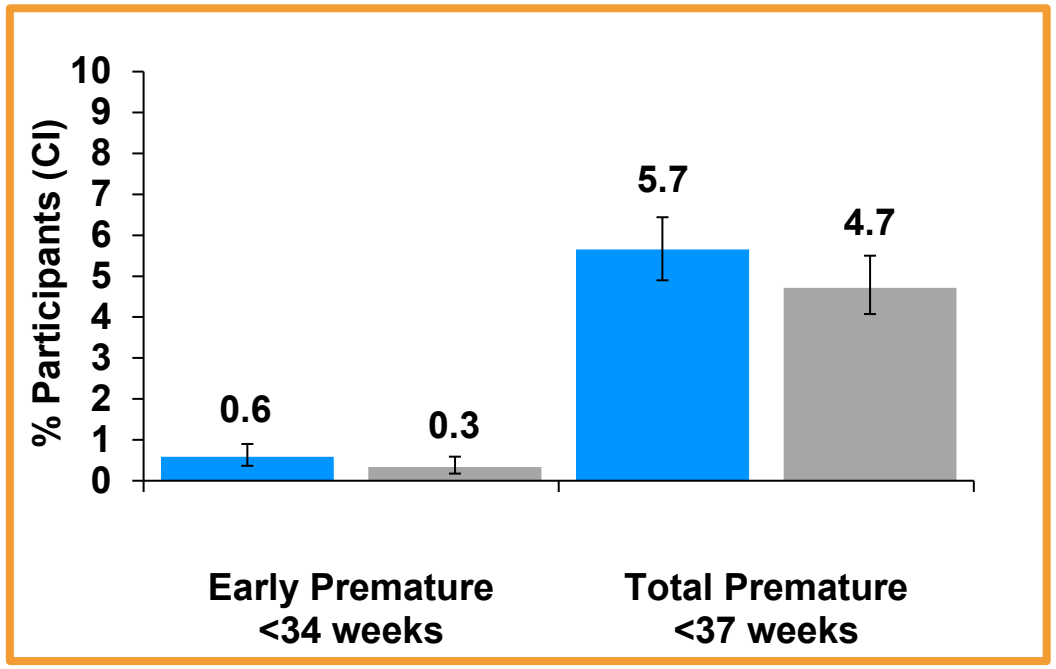
N = 7,386 Maternal Participants; N = 7,307 Infant Participants

Primary Results: Kampmann *et al*, N Engl J Med 2023 Apr 20;388(16):1451-1464
End of Study Results: Simões et al, Obstet Gynecol. 2025 Feb 1;145(2):157-167
Preterm outcomes: Madhi et al, Obstet Gynecol. 2025 Feb 1;145(2):147-156

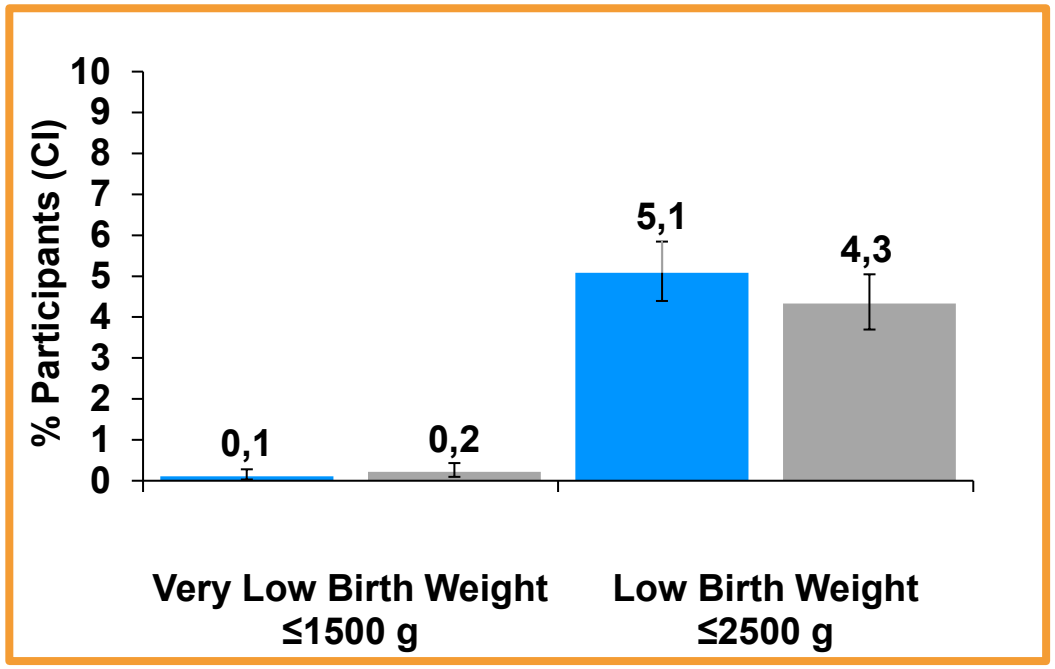
MATISSE: Key Data Provided By Region



Birth Outcomes and Developmental Delay Comparable Between RSVpreF and Placebo



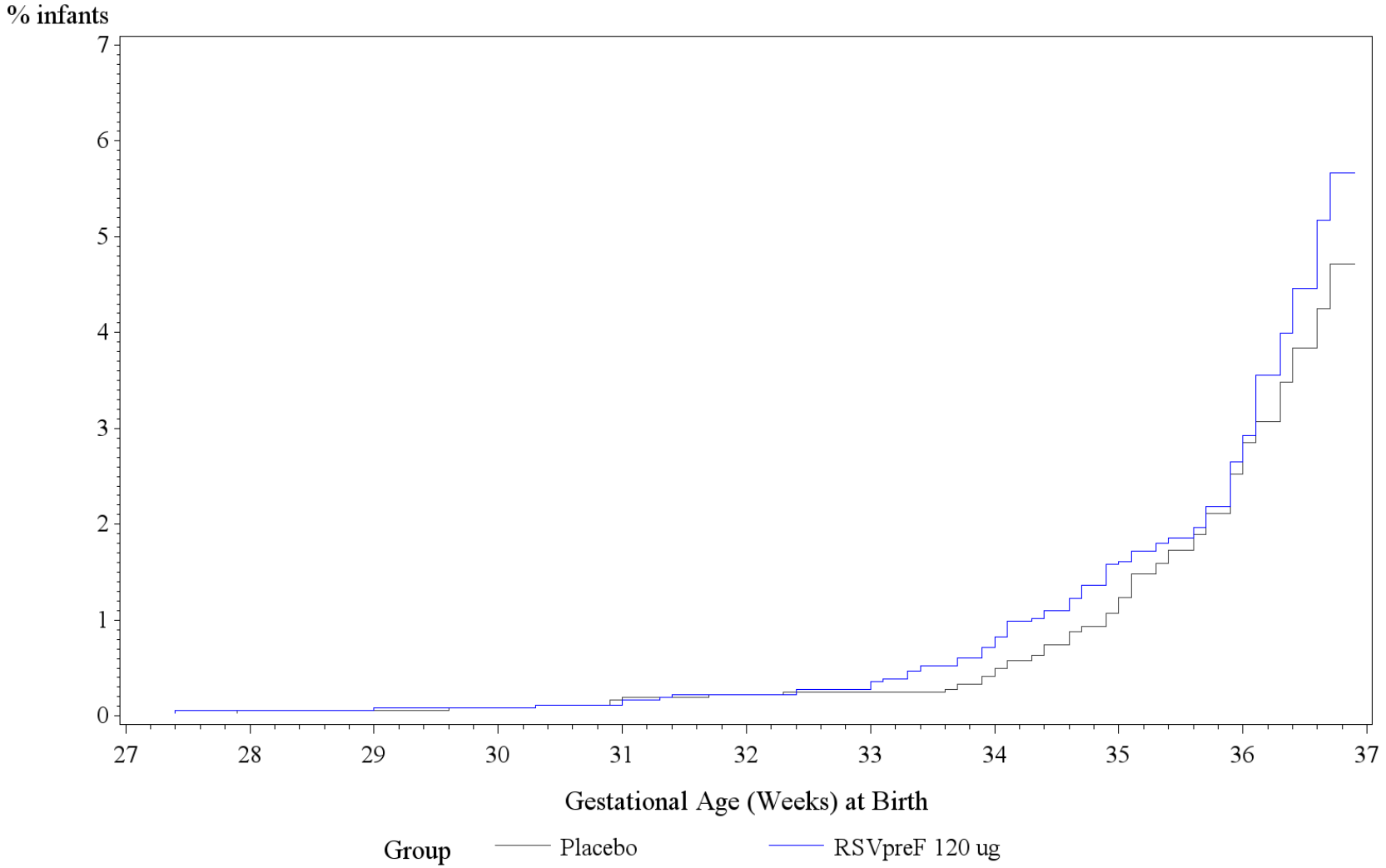
Relative Risk	1.20
95% CI	(0.98, 1.46)



Relative Risk	1.17
95% CI	(0.95, 1.44)

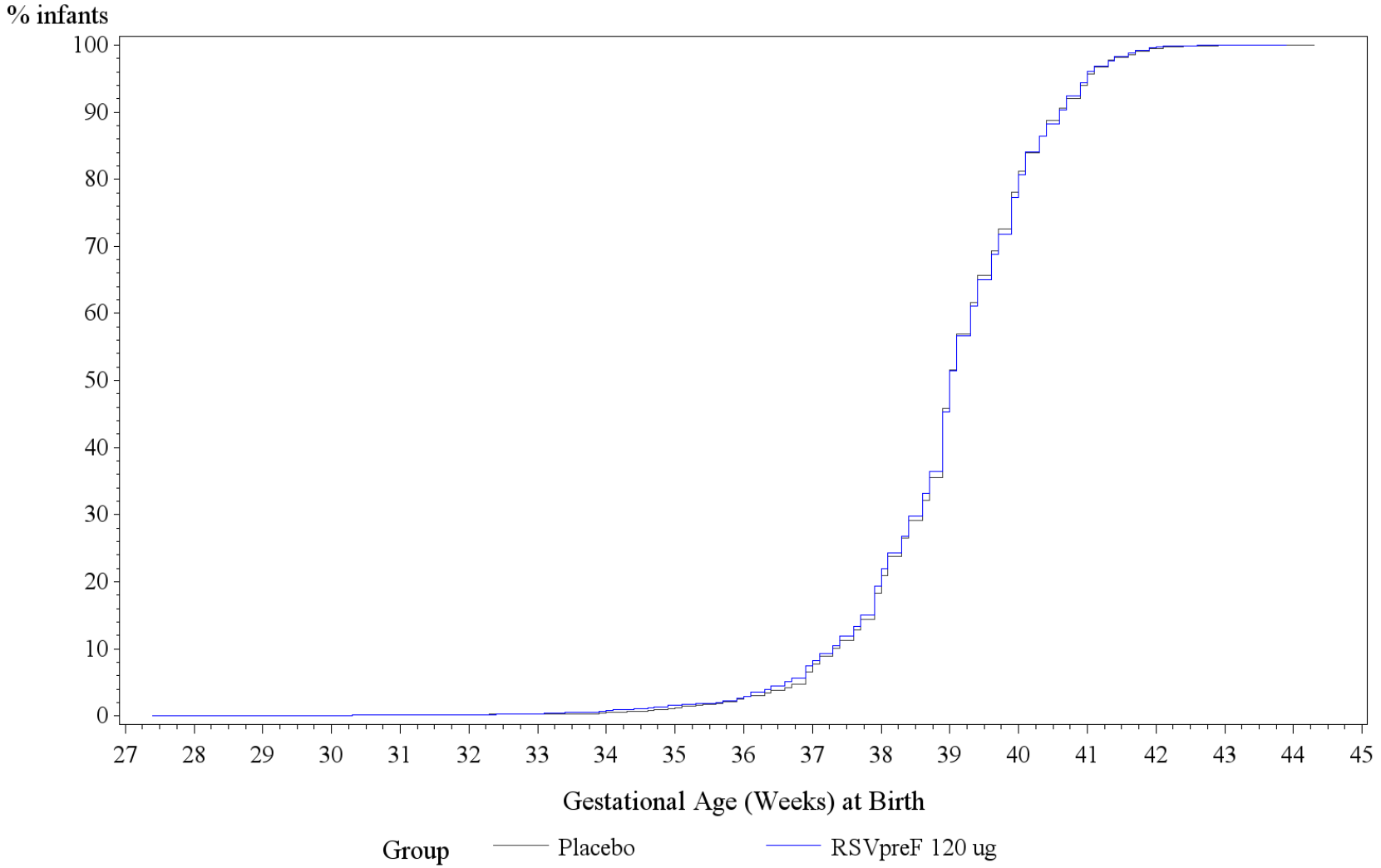
Cumulative Distribution of GA at Birth < 37 weeks

Majority of Preterm Births Were Born Late Preterm and Populations Numerically Diverge after 33 weeks



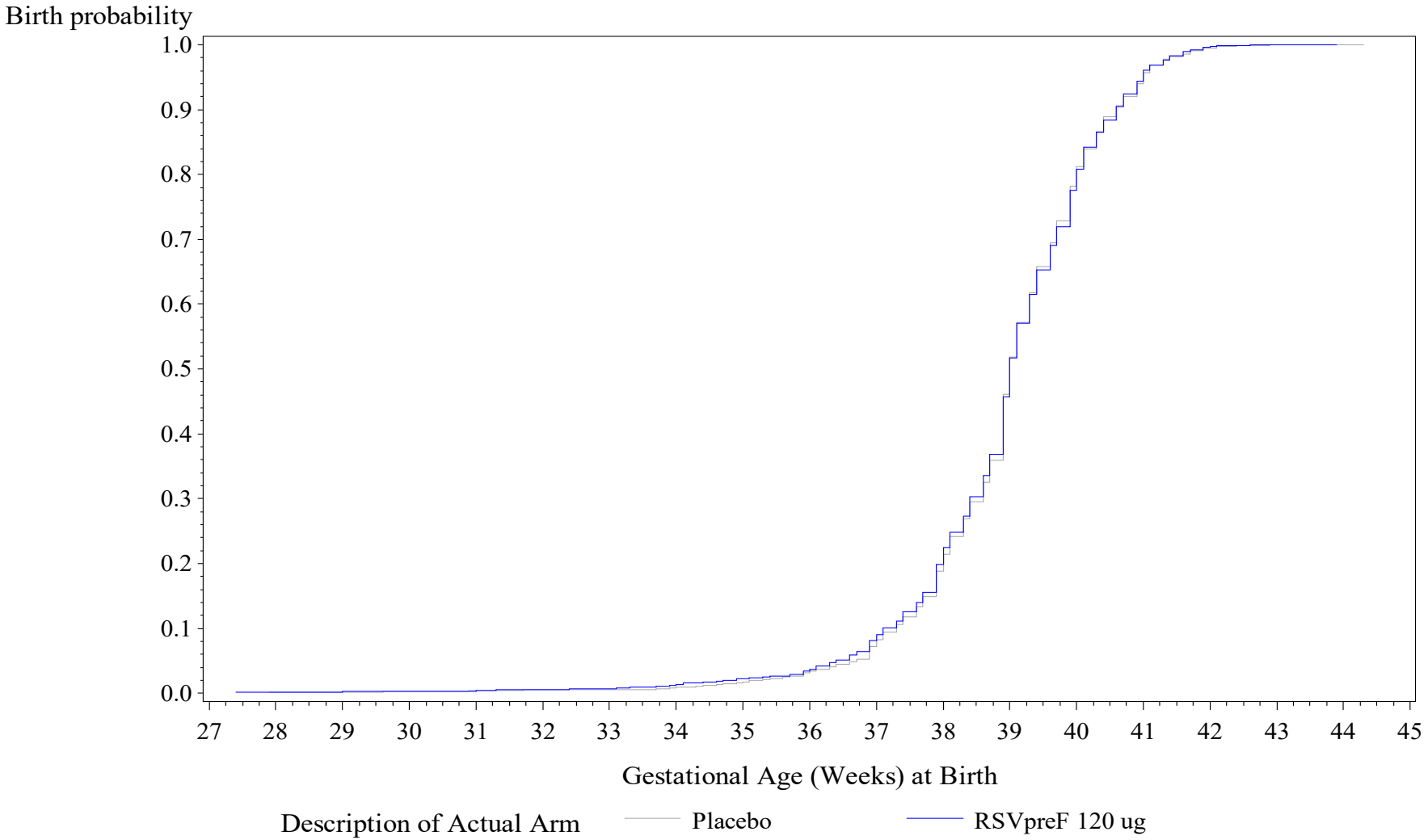
Cumulative Distribution of GA at Birth – All Participants

Very similar distribution of GA overall between groups

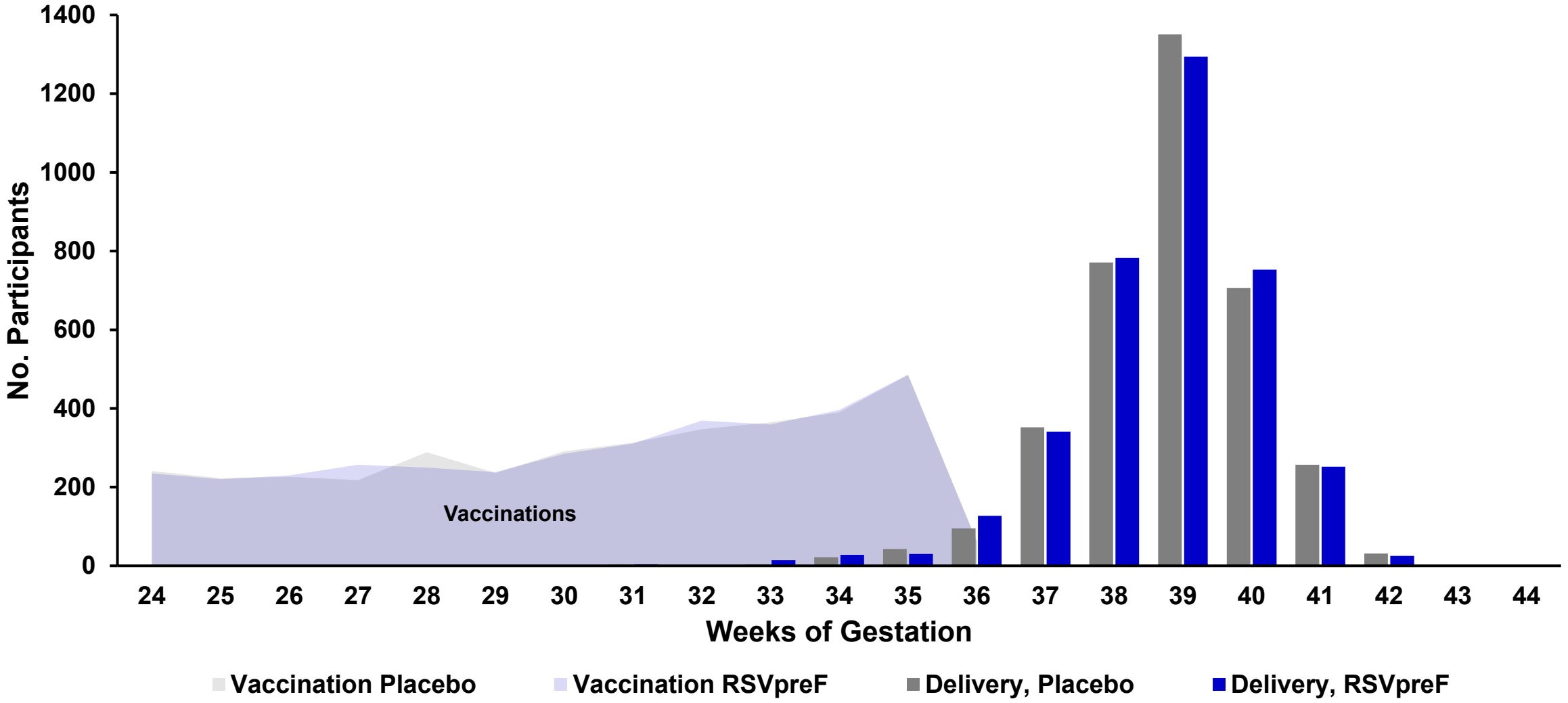


Product-Limit Estimate of Birth Probability by GA

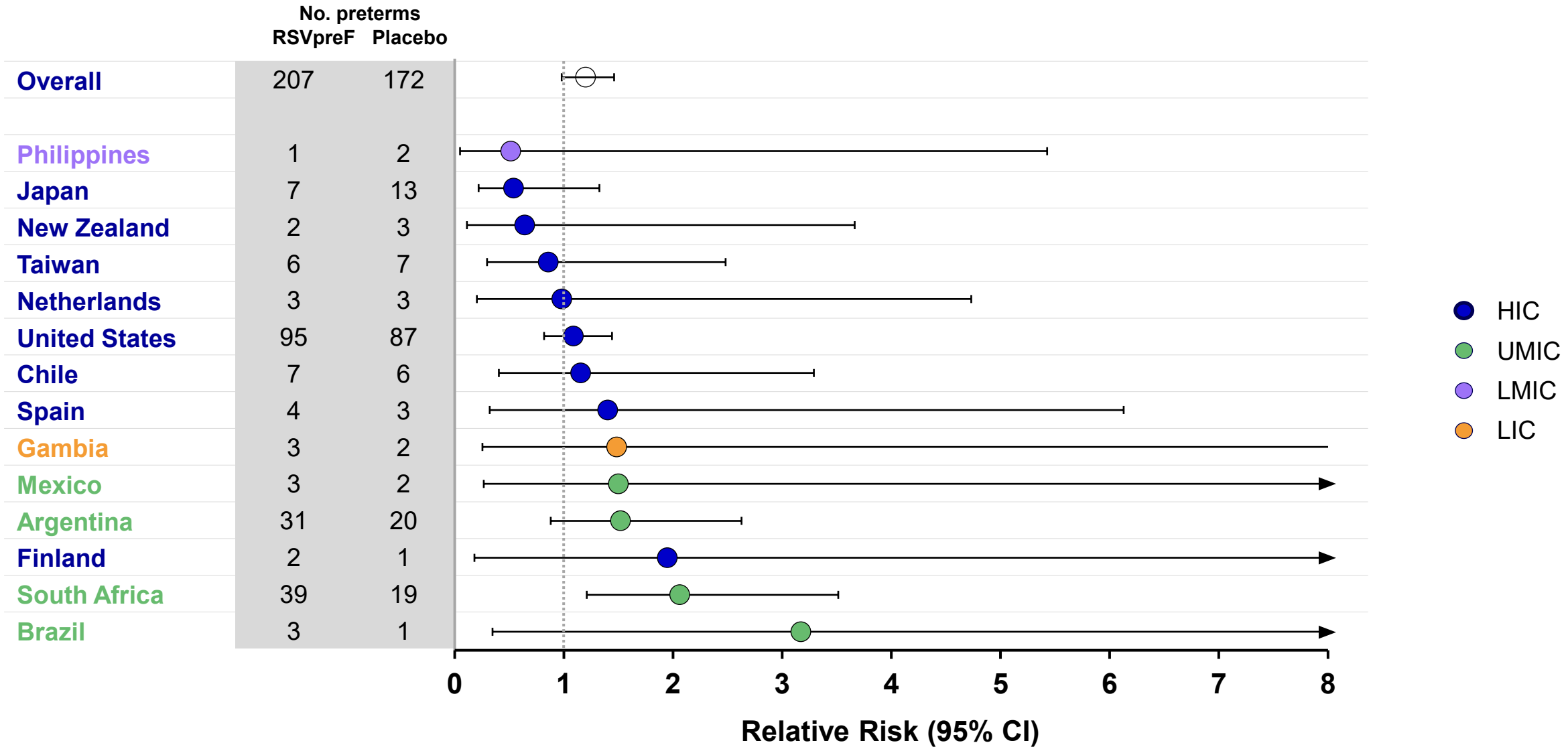
Removes unvaccinated participants from risk set (denominator)



Timing of Participant Vaccination Relative to Births



Preterm Births by Country – Relative Risk / 95% CI



Infant Birth Outcomes Comparable Across Both Groups

Outcome	RSVpreF N=3659 n (%)	Placebo N=3646 n (%)	RR (95% CI)
Preterm Birth < 37 weeks	207 (5.7)	172 (4.7)	1.20 (0.98, 1.46)
Preterm and low birthweight	88 (2.4)	70 (1.9)	1.25 (0.92, 1.71)
Any Infant with Low APGAR Scores*	55 (1.5)	47 (1.3)	1.17 (0.79, 1.72)
Preterm Infants with SAE related Hospitalization in neonatal period	84 (2.3)	81 (2.2)	1.03 (0.76, 1.40)

* First APGAR score < 4 or last APGAR score < 7

Infant Deaths Overall and by Subcategory

Event Type	RSVpreF 120 µg N=3659 n	Placebo N=3646 n	RR (CI)
Total Infant death due to any cause (n=22)	**8**	**14**	**0.57 (0.24, 1.36)**
Infant death due to RSV	0	1	-
Preterm deaths (<37 weeks at birth)	1*	2	0.50 (0.05, 5.49)
Neonatal deaths (<30 days after birth)	3*	5	0.60 (0.14, 2.50)

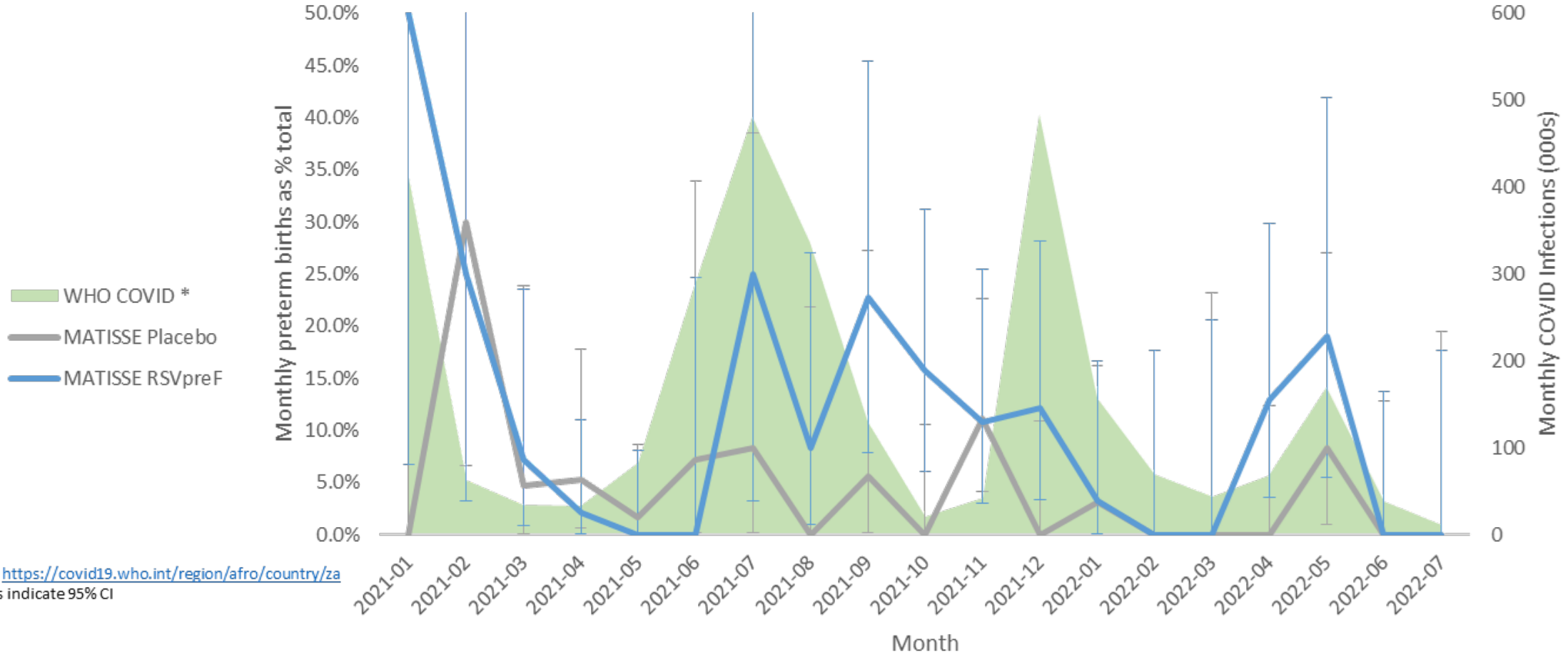
*A single preterm infant died in the neonatal (<30 days) period. The infant was in the RSVpreF group and from South Africa. The infant is represented in both subcategories: preterm and neonatal.

Maternal Factors Across Both Groups

Outcome	RSVpreF N=3697 n (%)	Placebo N=3688 n (%)	RR	RR 95% CI
COVID-19 Detected During Pregnancy*	110	104	1.06	(0.81, 1.37)
• Preterm and COVID-19 Detected During Pregnancy	9	4	2.24	(0.69, 7.28)
Maternal history of other non-study maternal vaccines during pregnancy	2284	2281	1.00	(0.96, 1.04)
• Preterm and non-study vaccines	114	110	1.04	(0.80, 1.34)
• Preterm and no non-study vaccines	92	62	1.47	(1.08, 2.01)

* Systematic testing NOT performed, passive reporting only

Preterm Birth Rates by Calendar Month and Monthly COVID-19 Cases in South Africa



* Source: https://covid19.who.int/region/afro/country/za
Error bars indicate 95% CI

Placebo	Preterm	0	3	1	2	1	1	1	0	1	0	6	0	1	0	0	0	2	0	0
	Total	1	10	21	38	62	14	12	15	18	33	54	32	32	19	14	28	24	27	17
RSVpreF	Preterm	2	2	2	1	0	0	2	2	5	6	4	4	1	0	0	4	4	0	0
	Total	4	8	28	48	44	13	8	24	22	38	37	33	31	19	16	31	21	25	19

Multivariable analyses on Baseline characteristics

- **Logistic regression on binary outcome, preterm <37 weeks / term ≥37 weeks**
- **Restricted to pre-randomization characteristics**

Subject characteristics
- Mother's Age
- GA at vaccination
- Race
- Ethnicity
- Country Income category (HIC/non-HIC)
- Smoking status
- Alcohol use
- Marijuana/illicit drug use

Obstetrical History (≥1 occurrence)
- Previous pregnancy
- Previous live birth
- Previous preterm deliveries
- Previous spontaneous abortions

Vaccine/Placebo

- **Univariable models followed by multivariable model (backwards elimination)**
- **Each univariate factor checked for interaction with Vaccine**

Significant Associations with Preterm Outcome

Univariable Models

- Mother's Age
- GA at vaccination
- Ethnicity
- Smoking status
- Previous pregnancies
- Previous preterm deliveries

NB Vaccine and Country Income Category were **not** significant

Final Multivariable Model

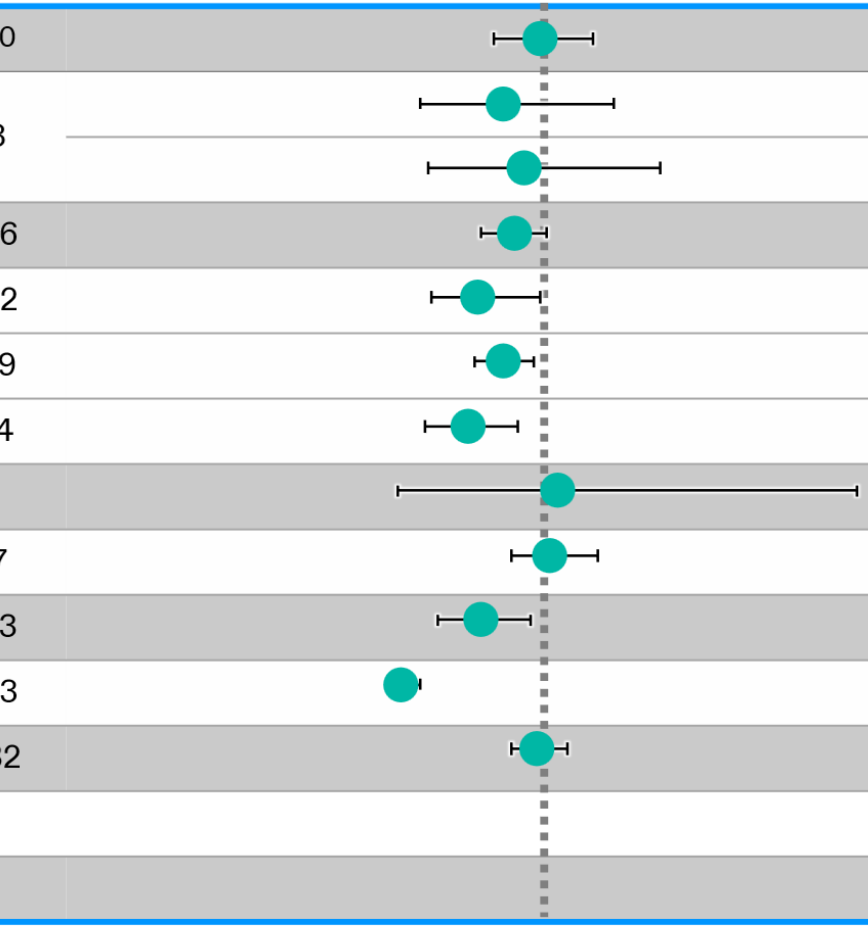
- GA at vaccination
- Ethnicity
- Smoking status
- Pregnancy history (none/term/preterm only)

- Country Income Category*Vaccine
- Pregnancy history*Vaccine

RWE Suggests No Association Between RSV Maternal Vaccination and Preterm Birth

Vaccination window
≥28 weeks of gestation
32–36 weeks of gestation

Country	Study	N	Risk (95% CI)
US	Kitano et al[1]	22,530	OR: **0.98** (0.84–1.14)
	Son et al[2]	2973	aOR: **0.87** (0.62–1.20)
			HR: **0.93** (0.64–1.34)
	CDC[3]	13,966	aRR: **0.90** (0.80–1.00)
	Michnick et al (Apr 26)[4]	13,022	Concurrent aRR: **0.79** (0.65–0.98)
		12,879	Historical aRR: **0.87** (0.78–0.96)
	Michnick et al[5]	13,714	aOR: **0.76** (0.63–0.91)
	Blauvelt et al[6]	647	aOR: **1.03** (0.55–1.93)
	Hsieh et al[7]	6387	RR: **1.01** (0.89–1.15)
	Solsman et al[8]	24,213	aOR: **0.80** (0.67–0.95)
Argentina	Scruzzi et al[9]	21,303	RR: **0.56** (0.51–0.62)
France	Gabet et al[10]	49,782	wIRR: **0.97** (0.89–1.06)
UK	Razai et al[11]	911	*P*=0.980
	UKHSA[12]	NR	**No association**



a, adjusted; CDC, Centers for Disease Control and Prevention; CI, confidence interval; HR, hazard ratio; OR, odds ratio; RR, risk ratio; RSV, respiratory syncytial virus; RWE, real-world evidence; UKHSA, United Kingdom Health Security Agency; wIRR, weighted incidence rate ratio by inverse probability of treatment weighting.

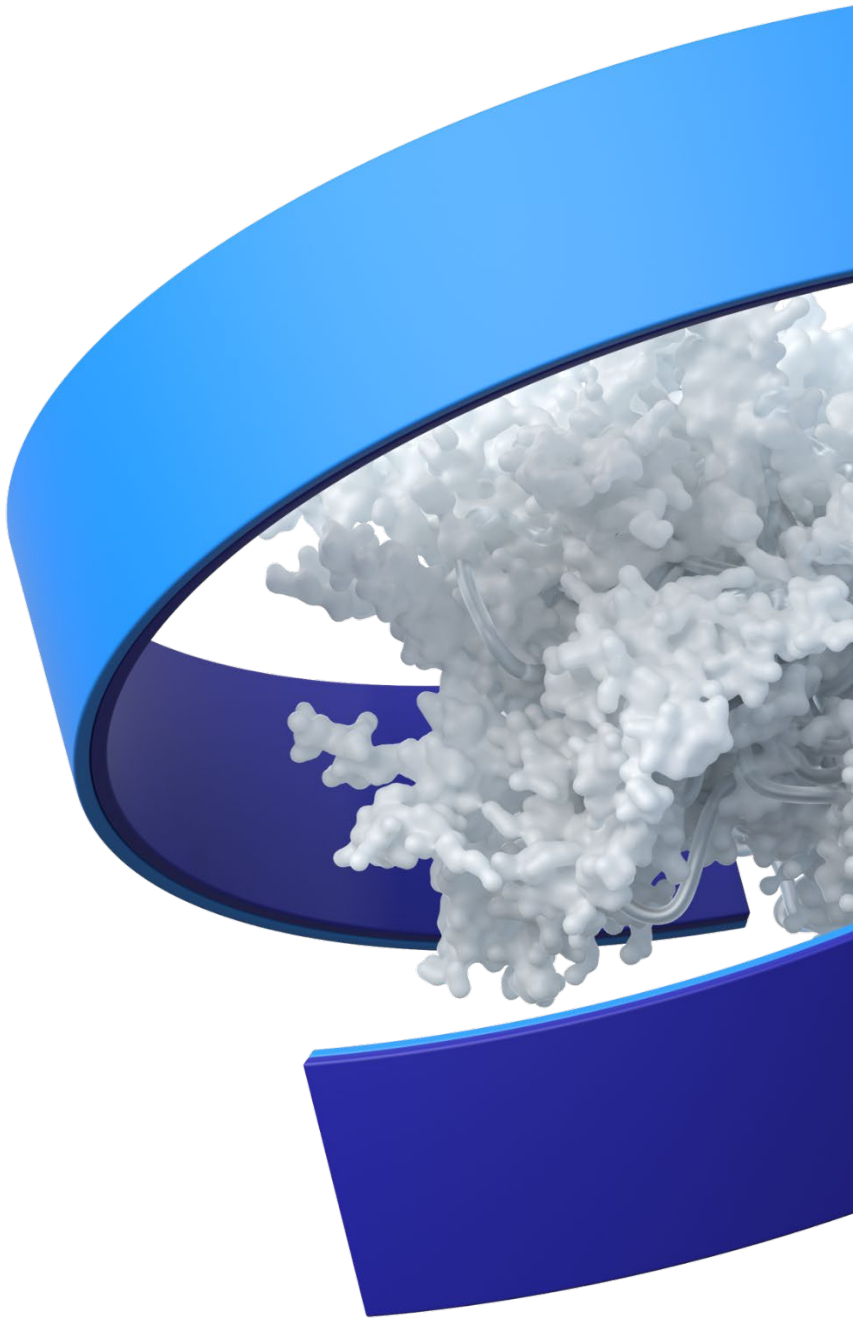
1. Kitano T, et al. *Vaccines*. 2026;11(1):53. 2. Son M, et al. *JAMA Netw Open*. 2024;7(7):e2419268. 3. DeSilva M. Prenatal RSVpreF vaccine safety 2023–2024 respiratory season. The Vaccine Safety Datalink (VSD). ACIP Meeting, June 25, 2025. Accessed May 15, 2026. https://www.cdc.gov/acip/downloads/slides -2025-06-25-26/04a-DeSilva-Mat-Peds-RSV-508.pdf 4. Michnick AI, et al. *JAMA Netw Open*. 2026;9(4):e266190. 5. Michnick AI, et al. *JAMA*. Published Online January 8, 2026. doi:10.1001/jama.2025.23452 6. Blauvelt CA, et al. *JAMA Netw Open*. 2025;8(2):e2460735. 7. Hsieh TYJ, et al. *Am J Obstet Gynecol*. 2025;233(5):e181-e190. 8. Solsman AM, et al. *Obstet Gynecol*. 2026;147(1):127-130. 9. Scruzzi GF, et al. *Medicina (B Aires)*. 2025;85(5):999-1007. 10. Gabet A, et al. *Obstet Gynecol*. 2026;147(1):118-126. 11. Razai MS, et al. *BMJ Open*. 2025;15(9):e101592. 12. Watson C, et al. Oral presentation. Presented at Respiratory Syncytial Virus Vaccines for the World 2026 Conference; February 17-20, 2026.

Pfizer Medical Affairs

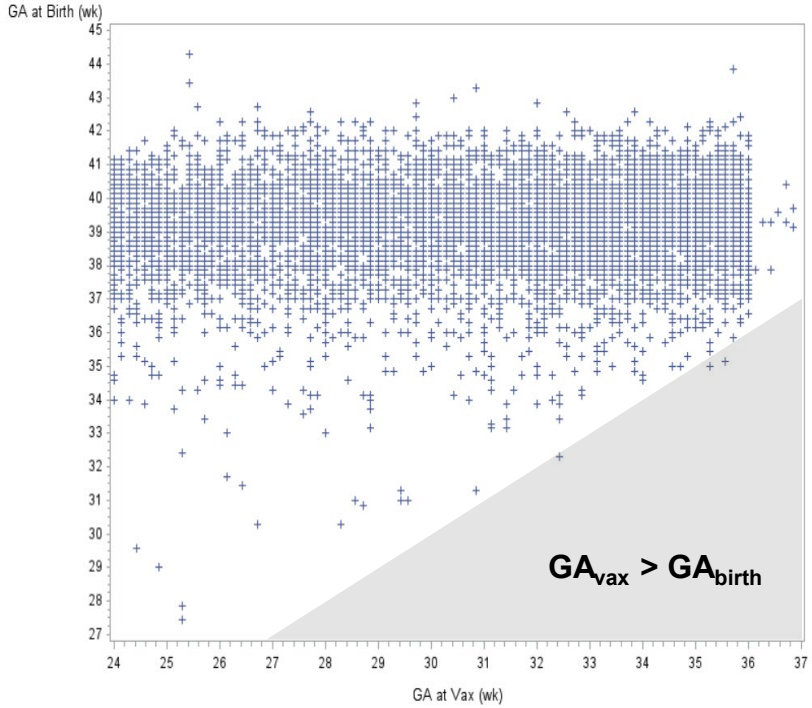
Summary/conclusions

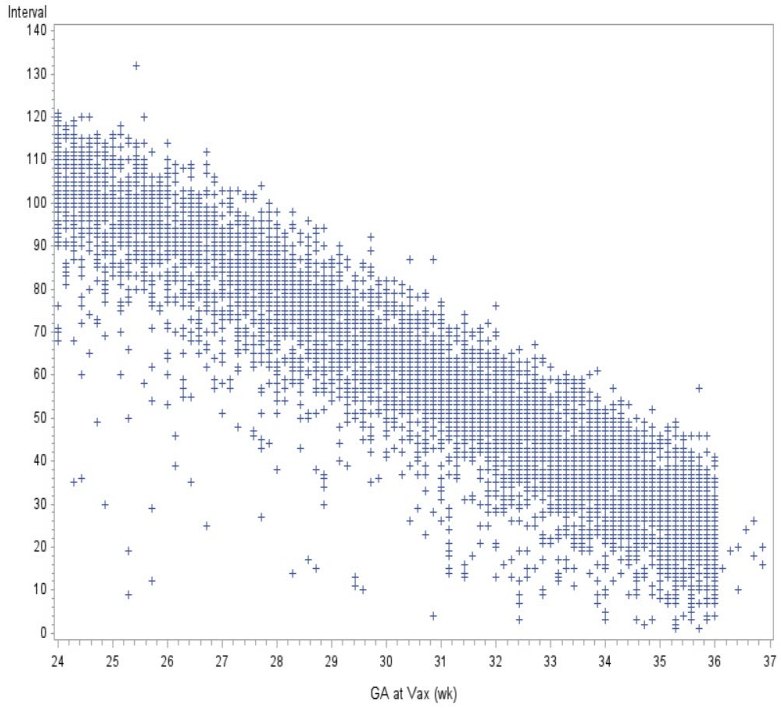
- The numerical imbalance in PTB in the MATISSE trial was concentrated in non-HIC countries
- The imbalance emerges beyond 33 weeks GA. Most PTB occurred 36 weeks or later. Full distribution of GA at birth is similar between groups
- Infant outcomes among PTB were similar. There were no additional hospitalizations or excess infant mortality, in the neonatal period or through end of study (1 year)
- Receipt of other vaccines did not increase risk of PTB; no firm conclusion may be drawn on the impact of the COVID-19 pandemic
- RWE to date suggests vaccination with RSVpreF is not associated with PTB

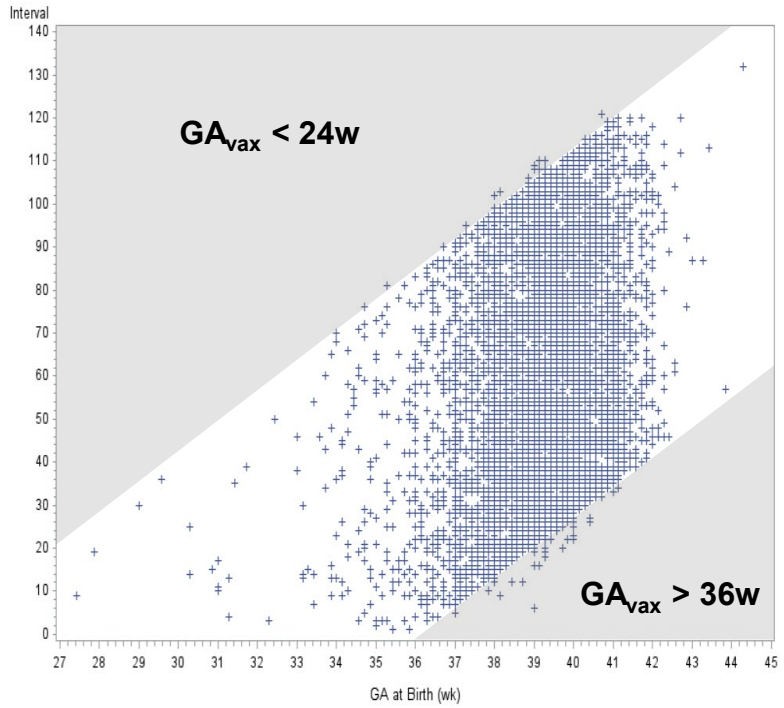
Breakout session – further analyses of MATISSE



Vaccination-Delivery Interval & GA measurements





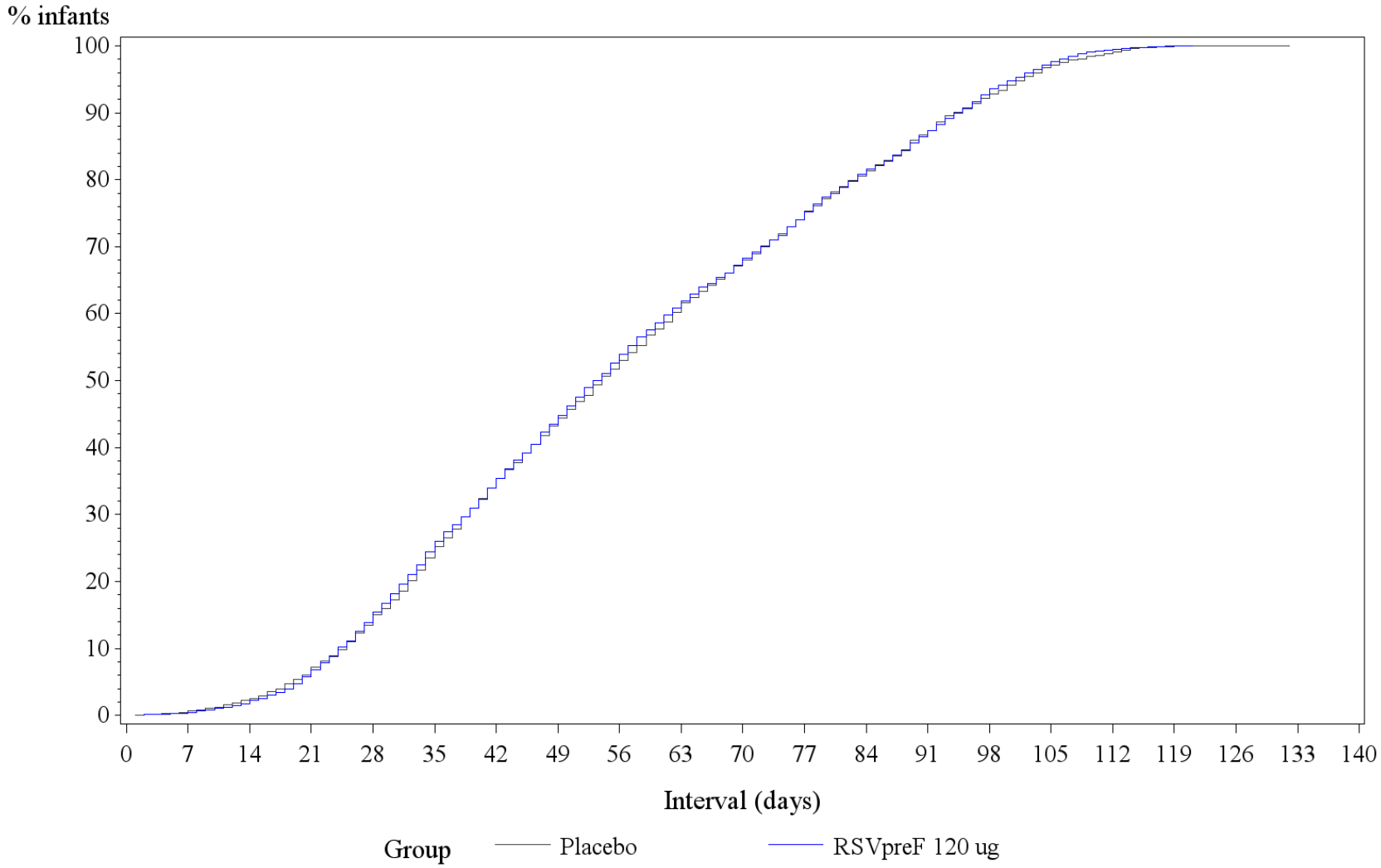


Vaccination-Delivery Interval = GA at birth – GA at vaccination

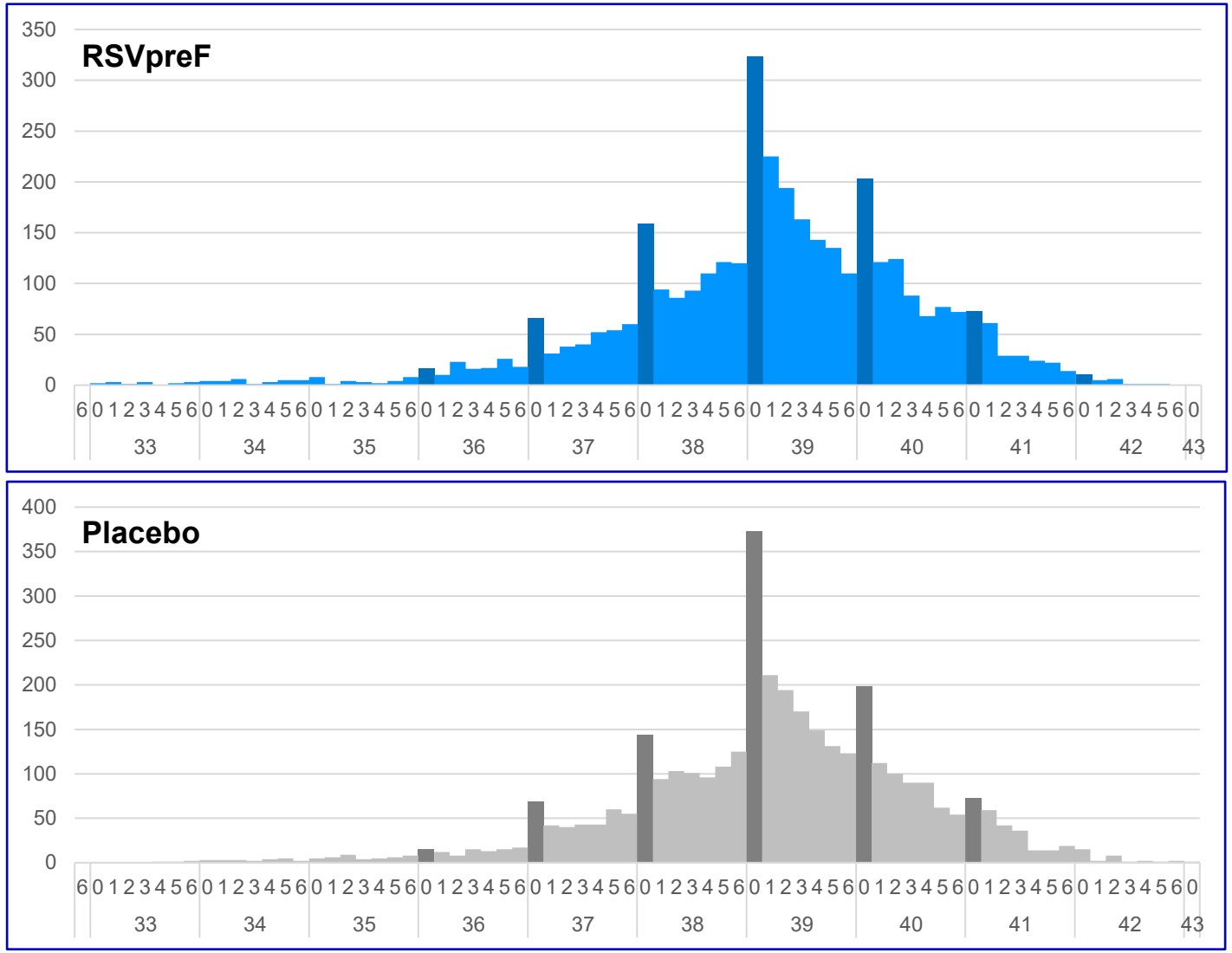
Shaded areas should not be possible with protocol adherence and exact GA measurement

Vaccination-Delivery Interval – Cumulative Distribution

Very similar distribution between groups



GA at birth exhibits rounding to whole weeks



- Preference for recording GA in whole weeks – most obvious at 38, 39, 40 weeks
- Preterm definition = strictly less than 37 weeks. Any rounding up to 37 weeks classifies infant as ‘term’