

Supplementary Table 1 Comparison of assessed and non-assessed surviving infants

	Randomized All (N= 1099)	Randomized Survivors (N=1028)	Survivors Assessed (N=664)	Survivors Not Assessed (N=364)	Risk Difference	95% Confidence Intervals	P value
Perinatal Characteristics							
Multiple births, N (%)	390 (35.5)	371 (36.1)	248 (37.3)	123 (33.8)	3.6	-2.5, 9.7	0.26
Antenatal steroids (any), N (%)	1002 (91.2)	936 (91.1)	610 (91.9)	326 (89.6)	2.3	-1.5, 6.1	0.22
Maternal antibiotics, N (%)	532 (48.4)	496 (48.2)	320 (48.2)	176 (48.4)	-0.2	-6.5, 6.2	0.96
Chorioamnionitis, N (%)	95 (8.6)	86 (8.4)	53 (8.0)	33 (9.1)	-1.1	-4.7, 2.5	0.55
Cesarean section delivery, N (%)	736 (67.0)	693 (67.4)	452 (68.1)	241 (66.2)	1.9	-4.2, 7.9	0.54
Gestational age, mean (SD) weeks	27.9 (2.0)	28.0 (1.9)	27.8 (1.9)	28.4 (1.9)	-0.6	-0.8, -0.3	<0.005
< 28 weeks, N (%)	454 (41.3)	394 (38.3)	276 (41.6)	118 (32.4)	9.1		<0.005
Birth weight, mean (SD) g	1056 (260)	1073 (253)	1059 (257)	1098 (246)	-38.9	-70.8, -6.9	0.02
< 1000g, N (%)	474 (43.1)	416 (40.5)	289 (43.5)	127 (34.9)	8.6	2.5, 14.8	0.01
Birth weight z-score, mean (SD)	-0.4 (1.1)	-0.4 (1.0)	-0.3 (1.1)	-0.5 (1.0)	0.2	0, 0.3	0.02
Male, N (%)	572 (52.0)	528 (51.4)	356 (53.6)	172 (47.3)	-6.4	-12.7, 0.0	0.05
5 min Apgar score, median (IQR): N=1092	8 (7, 9) N=1021	8 (7, 9) N=663	8 (7, 9) N=358			0.0, 0.0	
Age at enrolment, mean (SD) days	2.0 (0.9)	2.0 (0.9)	2.0 (0.9)	2.0 (0.8)	0	-0.1, 0.2	0.45
Age commenced study powder, median (IQR) days N=1071	5.0 (4.0-7.0) N=1018	5.0 (4.0-7.0) N=662	5.0 (4.0-7.0) N=358	4.0 (3.0-6.0) N=358	1.0	0.7, 1.3	<0.005
Neonatal morbidity							
NEC (Bell Stage 2 or more), n (%)	35 (3.2)	17 (1.7)	11 (1.7)	6 (1.6)	0.0	-1.6, 1.6	0.99

IVH Grade 3 or 4 or cystic PVL, n (%)	38 (3.5)	24 (2.3)	13 (2.0)	11 (3.0)	-1.1	-3.0, 1.0	0.28
At least one episode of definite late-onset sepsis, n (%)	161 (14.6)	136 (13.2)	87 (13.1)	49 (13.5)	-0.4	-4.7, 4.0	0.87
BPD at 36 weeks CA, n (%) N=1047	326 (29.7) N=1047	312 (30.4)	213 (32.1)	99 (27.2)	4.9	-0.9, 10.0	0.10
ROP ≥grade 3, n (%)	58 (5.3)	58 (5.6)	35 (5.3)	23 (6.3)	-1.0	-4.1, 2.0	0.49

Abbreviations: N, number; %, percentage; SD, standard deviation; IQR, Interquartile Range (25, 75); g, grams; NEC, necrotizing enterocolitis; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia, BPD, Bronchopulmonary dysplasia; ROP, Retinopathy of prematurity.

Supplemental Table 2: Baseline characteristics of 664 participants assessed at 2-5 years corrected gestational age

	Probiotic group (N=337)	Placebo group (N=327)
Perinatal Characteristics		
Multiple births, N (%)	130 (38.6)	118 (36.1)
Antenatal steroids (any), N (%)	311 (92.3)	299 (91.4)
Maternal antibiotics, N (%)	164 (48.7)	156 (47.7)
Maternal infection (chorioamnionitis), N (%)	25 (7.4)	28 (8.6)
Cesarean section delivery, N (%)	222 (65.9)	230 (70.3)
Gestational age, mean (SD) weeks	27.8 (2.0)	27.8 (1.9)
< 28 weeks, N (%)	133 (39.5)	143 (43.7)
Birth weight, mean (SD) g	1068 (259)	1050 (254)
< 1000g, N (%)	147 (43.6)	142 (43.4)
Birth weight z-score, mean (SD)	-0.3 (1.1)	-0.3 (1.1)
Male, N (%)	173 (51.3)	183 (56.0)
5 min Apgar score, median (IQR): N=335	8 (7-9) N=335	8 (7-9) N=323
Age at enrolment, mean (SD) days	2.0 (0.9)	2.1 (0.9)
Age commenced study powder, median (IQR) days N=335	5.0 (4.0-6.0) N=335	5.0 (4.0-7.0) N=325
Neonatal characteristics		
Any EBM, n (%)	327 (97.0)	324 (99.1)
NEC (Bell Stage 2 or more), n (%)	3 (0.9)	8 (2.4)
IVH Grade 3 or 4 or cystic PVL, n (%)	7 (2.1)	6 (1.8)
At least one episode of definite late-onset sepsis, n (%)	45 (13.4)	42 (12.8)
BPD at 36 weeks, n (%)	110 (32.6)	103 (31.5)
ROP ≥grade 3, n (%)	18 (5.3)	17 (5.2)

Abbreviations: N, number; %, percentage; SD, standard deviation; IQR, Interquartile Range (25, 75); g, grams; NEC, necrotizing enterocolitis; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; BPD, Bronchopulmonary dysplasia; ROP, Retinopathy of prematurity

Supplemental Table 3: Adjusted relative risks, survival without major neurosensory impairment, probiotic vs placebo

Group	Adjustment variables				Relative Risk (95%CI)	P value
	Gender	Gestational age at birth	Birth-weight z-score	(i) IVH Grade 3 or 4 or cystic PVL (ii) BPD at 36 weeks (iii) ROP ≥grade 3 (iv) At least one episode of definite late-onset sepsis and/or NEC (Bell Stage 2 or more)		
Total group					1.01 (0.93 to 1.09)	0.88
	✓	✓	✓		0.99 (0.92 to 1.06)	0.70
	✓	✓	✓	✓	0.99 (0.93 to 1.06)	0.76
Gestation ≥28 wk					1.06 (0.97 to 1.16)	0.19
	✓		✓		1.05 (0.96 to 1.14)	0.31
	✓		✓	✓	1.04 (0.96 to 1.13)	0.34
Gestation <28 wk					0.91 (0.78 to 1.07)	0.25
	✓		✓		0.90 (0.78 to 1.05)	0.18
	✓		✓	✓	0.92 (0.82 to 1.04)	0.18
Birth weight ≥1000g					1.02 (0.94 to 1.12)	0.62
	✓	✓			1.01 (0.92 to 1.10)	0.88
	✓	✓		✓	1.01 (0.93 to 1.09)	0.88
Birth weight <1000g					0.99 (0.85 to 1.15)	0.85
	✓	✓			0.98 (0.85 to 1.13)	0.80
	✓	✓		✓	0.98 (0.87 to 1.10)	0.70

Abbreviations: g, grams; wk, weeks; NEC, necrotizing enterocolitis; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; BPD, Bronchopulmonary dysplasia; ROP, Retinopathy of prematurity