

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

Trial Sites and Study Personnel

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eTable1. Maternal/Neonatal Characteristics for Enrolled vs. Non-Enrolled Follow-Up Participants

Characteristic	Enrolled in Follow-up Study* (N=1,026)	Not Enrolled in Follow-up Study* (N=1,805)
Race/ethnicity [†]		
American Indian / Alaskan Native	2 (0.2%)	5 (0.3%)
Asian	32 (3.1%)	61 (3.4%)
Hispanic	309 (30.1%)	544 (30.1%)
Native Hawaiian / Pacific Islander	3 (0.3%)	6 (0.3%)
Non-Hispanic Black	258 (25.1%)	470 (26.0%)
Non-Hispanic White	417 (40.6%)	691 (38.3%)
More than one self-reported race	2 (0.2%)	5 (0.3%)
Unknown / Not Reported	3 (0.3%)	23 (1.3%)
Age, y	29 (6.2)	28 (6.2)
College degree or higher (maternal)	322/1,005 (32.0%)	406/1,766 (23.0%)
Private insurance [‡]	444 (43.3%)	616 (34.1%)
Employed	445/1,024 (43.5%)	703/1,798 (39.1%)
Number of prior pregnancies >=20 weeks		
No prior pregnancy	417 (40.6%)	720 (39.9%)

1 prior pregnancy	277 (27.0%)	458 (25.4%)
>=2 prior pregnancies	332 (32.4%)	627 (34.7%)
Smoked during pregnancy	108 (10.5%)	282 (15.6%)
Asthma requiring medication during pregnancy	87 (8.5%)	168 (9.3%)
Preeclampsia or gestational hypertension	325 (31.7%)	550 (30.5%)
Gestational diabetes	113 (11.0%)	193 (10.7%)
Indication for trial entry		
Preterm labor with intact membranes	289 (28.2%)	503 (27.9%)
Ruptured membranes	227 (22.1%)	393 (21.8%)
Expected delivery for gestational hypertension or preeclampsia	276 (26.9%)	451 (25.0%)
Expected delivery for fetal growth restriction	30 (2.9%)	60 (3.3%)
Expected delivery for oligohydramnios	25 (2.4%)	65 (3.6%)
Expected delivery for other indication	179 (17.4%)	333 (18.4%)
Treatment Assignment		
Active	522 (50.9%)	907 (50.2%)
Placebo	504 (49.1%)	898 (49.8%)
Cesarean delivery	325/1,026 (31.7%)	560/1,801 (31.1%)
Gestational age at delivery, weeks [§]	36 (35.3,36.7)	36 (35.4,36.7)

Small for gestational age (<10th percentile)	169/1,026 (16.5%)	306/1,801 (17.0%)
Major congenital anomaly [¶]	8/1,026 (0.8%)	24/1,801 (1.3%)
Sex		
Female	470/1,026 (45.8%)	861/1,801 (47.7%)
Male	556/1,026 (54.2%)	940/1,801 (52.1%)
<p>*Data are mean (standard deviation), median (Q1,Q3), or n (%) unless otherwise specified. [†]Maternal race/ethnicity was based on self-report. [‡]Those without private insurance have government-assisted insurance or are self-pay/uninsured. [§]Gestational age at delivery missing in 4. [¶]Although the presence of a major congenital anomaly was an exclusion criterion in the ALPS trial, these disorders were not discovered until birth.</p>		

eTable2. Participants Excluded for Death or Developmental Delay

Exclusion	Betamethasone (N=1,429)	Placebo (N=1,402)	P-value
Infant/Neonatal Death	6 (0.42%)	4 (0.29%)	0.75
Childhood Death	6 (0.42%)	4 (0.29%)	0.75
Maternal Death	6 (0.42%)	4 (0.29%)	0.75
Severe Autism/Developmental Delay	12 (0.84%)	13 (0.93%)	0.80

eTable3. Comparison of Original Cohorts and Cohorts Remaining at ≥ 6 years

Characteristic	Original Cohort (N=2,831)			Unweighted Analysis Cohort (N=1,026)			Weighted Analysis Cohort (N=2,832)*		
	Betamethasone (N=1,429)	Placebo (N=1,402)	Standardized Mean Difference	Betamethasone (N=522)	Placebo (N=504)	Standardized Mean Difference	Betamethasone (N=1,430)	Placebo (N=1,402)	Standardized Mean Difference
Race/ethnicity			0.116			0.250			0.258
American Indian / Alaskan Native	3 (0.2%)	4 (0.3%)		2 (0.4%)	0 (0%)		5 (0.3%)	0 (0%)	
Asian	56 (3.9%)	37 (2.6%)		21 (4.0%)	11 (2.2%)		54 (3.7%)	27 (1.9%)	
Hispanic	405 (28.3%)	448 (32.0%)		147 (28.2%)	162 (32.1%)		411 (28.7%)	470 (33.5%)	
Native Hawaiian / Pacific Islander	3 (0.2%)	4 (0.3%)		0 (0%)	2 (0.4%)		0 (0%)	7 (0.5%)	
Non-Hispanic Black	6 (0.4%)	3 (0.2%)		3 (0.6%)	0 (%)		8 (0.5%)	0 (0%)	
Non-Hispanic White	363 (25.4%)	365 (26.0%)		124 (23.8%)	134 (26.6%)		370 (25.9%)	404 (28.8%)	
More than one self-reported race	580 (40.6%)	528 (37.7%)		222 (42.5%)	195 (38.7%)		575 (40.2%)	496 (35.4%)	
Unknown / Not Reported	13 (0.9%)	13 (0.9%)		3 (0.6%)	0 (0%)		8 (0.5%)	(0%)	
Age, y	29 (6.3)	28 (6.1)	0.127	29 (6.3)	29 (6.1)	0.065	29 (6.3)	28 (6.1)	0.126
College degree or higher (maternal)	381 (27.3%)	347 (25.2%)	0.047	164 (32.0%)	158 (32.1%)	0.003	403 (28.7%)	372 (27.2%)	0.033
Private insurance	558 (39.0%)	502 (35.8%)	0.067	228 (43.7%)	216 (42.9%)	0.017	558 (39.0%)	504 (35.9%)	0.064
Employed	577 (40.5%)	571 (40.8%)	0.005	217 (41.7%)	228 (45.3%)	0.074	564 (39.5%)	581 (41.5%)	0.041
Number of prior pregnancies ≥20 weeks			0.061			0.118			0.130
No prior pregnancy	565 (39.5%)	572 (40.8%)		209 (40.0%)	208 (41.3%)		567 (39.7%)	574 (40.9%)	

1 prior pregnancy	360 (25.2%)	375 (26.7%)		131 (25.1%)	146 (29.0%)		357 (25.0%)	411 (29.3%)	
>=2 prior pregnancies	504 (35.3%)	455 (32.5%)		182 (34.9%)	150 (29.8%)		506 (35.4%)	418 (29.8%)	
Smoked during pregnancy	204 (14.3%)	186 (13.3%)	0.029	55 (10.5%)	53 (10.5%)	0.001	205 (14.3%)	189 (13.4%)	0.026
Asthma requiring medication during pregnancy	129 (9.0%)	126 (9.0%)	0.001	50 (9.6%)	37 (7.3%)	0.080	141 (9.8%)	106 (7.5%)	0.081
Preeclampsia or gestational hypertension	435 (30.4%)	440 (31.4%)	0.020	168 (32.2%)	157 (31.2%)	0.022	463 (32.4%)	422 (30.1%)	0.049
Gestational diabetes	153 (10.7%)	153 (10.9%)	0.007	54 (10.3%)	59 (11.7%)	0.043	149 (10.4%)	160 (11.4%)	0.033
Indication for trial entry			0.041			0.142			0.163
Preterm labor with intact membranes	400 (28.0%)	392 (28.0%)		143 (27.4%)	146 (29.0%)		405 (28.3%)	435 (31.0%)	
Ruptured membranes	316 (22.1%)	304 (21.7%)		119 (22.8%)	108 (21.4%)		319 (22.3%)	291 (20.7%)	
Expected delivery for gestational hypertension or preeclampsia	356 (24.9%)	371 (26.5%)		150 (28.7%)	126 (25.0%)		416 (29.1%)	338 (24.1%)	
Expected delivery for fetal growth restriction	46 (3.2%)	44 (3.1%)		13 (2.5%)	17 (3.4%)		35 (2.4%)	51 (3.6%)	
Expected delivery for oligohydramnios	48 (3.4%)	42 (3.0%)		15 (2.9%)	10 (2.0%)		39 (2.7%)	28 (2.0%)	
Expected delivery for other indication	263 (18.4%)	249 (17.8%)		82 (15.7%)	97 (19.2%)		218 (15.2%)	261 (18.6%)	
Cesarean delivery	454 (31.8%)	431 (30.8%)	0.022	164 (31.4%)	161 (31.9%)	0.011	447 (31.3%)	432 (30.8%)	0.010
Gestational age at delivery, weeks	36.1 (1.1)	36.1 (1.2)	0.006	36.1 (1.1)	36.1 (1.2)	0.015	36.1 (1.1)	36.1 (1.2)	0.001
Small for gestational age (<10th percentile)	255 (17.9%)	220 (15.7%)	0.058	90 (17.2%)	79 (15.7%)	0.042	248 (17.3%)	233 (16.6%)	0.020
Major congenital anomaly†	11 (0.8%)	21 (1.5%)	0.069	1 (0.2%)	7 (1.4%)	0.136	3 (0.2%)	20 (1.4%)	0.134

Sex			0.051			0.048			0.057
Female	690 (48.4%)	641 (45.8%)		233 (44.6%)	237 (47.0%)		632 (44.2%)	660 (47.1%)	
Male	737 (51.6%)	759 (54.2%)		289 (55.4%)	267 (53.0%)		798 (55.8%)	743 (52.9%)	
*Accounts for maternal age, insurance status, and smoking during pregnancy. N's may not total original cohort because of rounding.									
†Although the presence of a major congenital anomaly was an exclusion criterion in the ALPS trial, these disorders were not discovered until birth.									

eTable4. Subgroup Analysis among Preterm and Term Deliveries

Outcome	Betamethasone (N=479)	Placebo (N=470)	Unadjusted*	Adjusted**†
<i>Primary Outcome</i>				
DAS-II General Conceptual Ability < 85‡			<i>Relative Risk</i>	<i>Relative Risk</i>
Preterm	67/398 (16.8%)	67/391 (17.1%)	0.98 (0.72,1.34)	0.98 (0.73,1.30)
Term	15/81 (18.5%)	20/79 (25.3%)	0.73 (0.40,1.33)	0.83 (0.49,1.42)
<i>Secondary Outcomes</i>				
	(N=522)	(N=504)		
Social Responsiveness Scale t-score > 65§			<i>Relative Risk</i>	<i>Relative Risk</i>
Preterm	61/432 (14.1%)	62/421 (14.7%)	0.96 (0.69,1.33)	0.93 (0.67,1.28)
Term	9 (10.5%)	10 (12.1%)	0.87 (0.37,2.03)	0.90 (0.39,2.08)
Gross Motor Function Classification System > Level I¶				
Preterm	1 (0.2%)	1 (0.2%)		
Term	0	0		
<i>Child Behavior Checklist#</i>				
Total problems t-score**			<i>Mean Difference</i>	<i>Mean Difference</i>
Preterm	48.7 (11.2)	48.7 (11.3)	-0.05 (-1.54,1.44)	-0.38 (-1.85,1.09)
Term	47.5 (9.9)	50.8 (10.9)	-3.28 (-6.63,0.06)	-3.25 (-6.54,0.04)

*Data are n (%) or relative risk (95% CI) for categorical outcomes and mean (standard deviation) or mean difference (95% CI) for continuous outcomes.

†Adjusted for maternal age, child age, sex, maternal education, and center.

‡DAS-II denotes Differential Ability Scales 2nd Edition. The DAS-II General Conceptual Ability score has a mean of 100 and a standard deviation of 15; ≥ 85 average and < 85 below average with higher scores indicating greater abilities.

§Social Responsiveness Scale ranges: < 60 normal, 60-65 mild, 66-75 moderate, and ≥ 76 severe with higher scores indicating greater problems.

¶The Gross Motor Function Classification System has 5 levels and increasing level indicates greater functional impairment: walks without limitations, walks with limitations, walks with hand-held mobility device, self-mobility with limitations; may use powered mobility, and transported in a manual wheelchair.

#Child Behavior Checklist total problems t-score ranges: < 60 normal, 60-63 borderline (84th-90th percentile), and ≥ 64 clinical (> 90th percentile) with higher scores indicating greater problems.

**Child Behavior Checklist missing in 3.