

Supplementary data tables

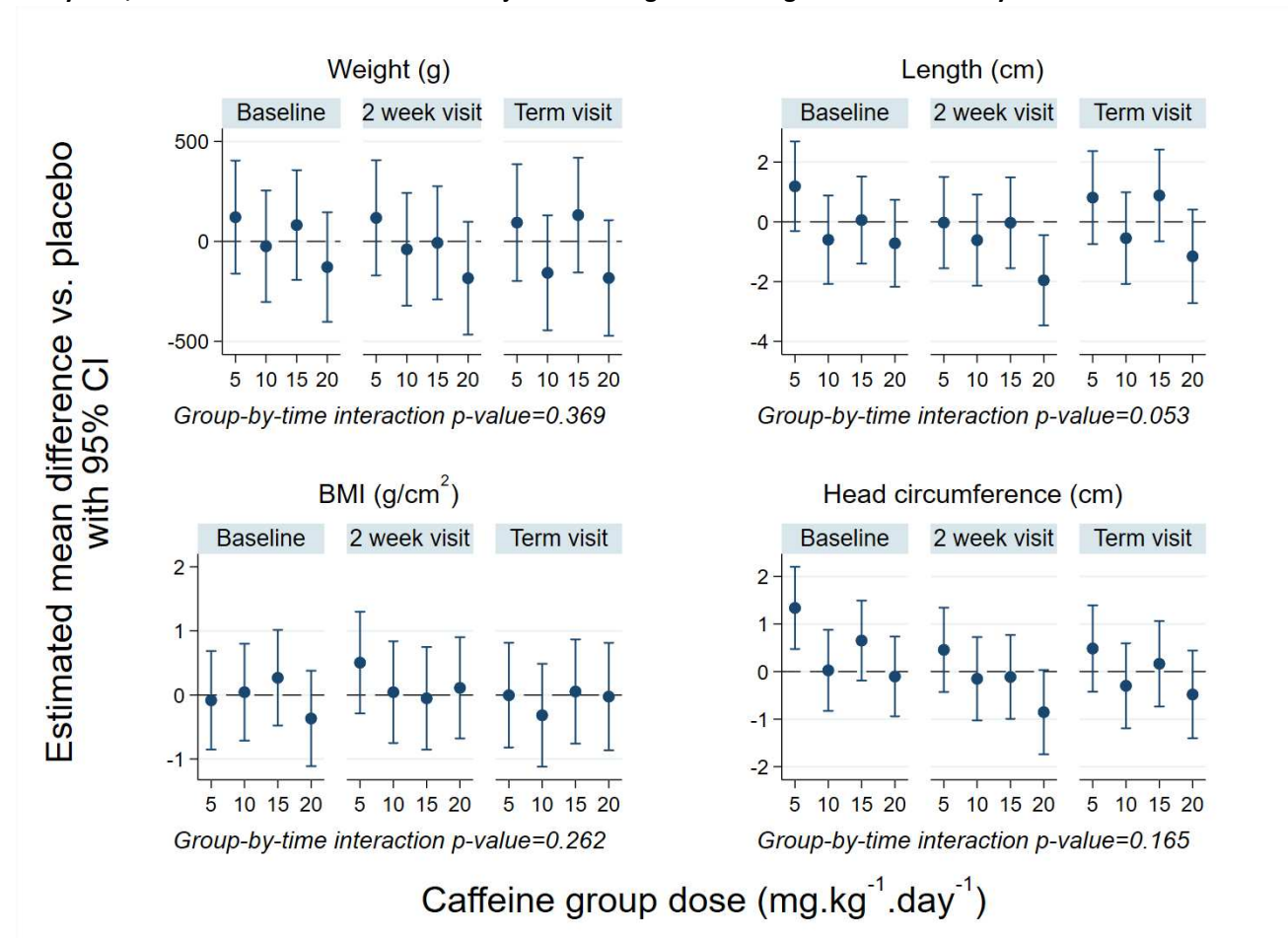
Supplementary Table 1: Anthropometry outcome measures over the study period

	Placebo N = 24 ^a Mean (SD)	Caffeine citrate 5 mg.kg ⁻¹ .day ⁻¹ N = 24 ^a Mean (SD)	Caffeine citrate 10 mg.kg ⁻¹ .day ⁻¹ N = 27 ^a Mean (SD)	Caffeine citrate 15 mg.kg ⁻¹ .day ⁻¹ N = 27 ^a Mean (SD)	Caffeine citrate 20 mg.kg ⁻¹ .day ⁻¹ N = 27 ^a Mean (SD)	Any dose of caffeine N = 105 ^a Mean (SD)
<i>Weight</i>						
Two weeks (g)	2726.4 (352.0)	2826.9 (494.0)	2677.1 (600.7)	2708.1 (412.8)	2480.3 (492.7)	2671.2 (516.5)
Z score	-0.8 (0.7)	-0.6 (1.0)	-1.0 (1.2)	-0.9 (1.0)	-1.4 (1.1)	-1.0 (1.1)
Term (g)	3329.3 (519.4)	3384.7 (526.6)	3210.7 (592.5)	3431.3 (666.7)	3023.8 (594.3)	3264.4 (606.2)
Z score	-0.4 (1.0)	-0.4 (1.1)	-0.7 (1.3)	-0.3 (1.4)	-1.1 (1.3)	-0.6 (1.3)
<i>Length</i>						
Two weeks (cm)	49.1 (2.3)	49.0 (2.4)	48.2 (3.2)	49.0 (2.4)	46.8 (3.7)	48.2 (3.1)
Z score	0.1 (0.9)	0.0 (0.9)	-0.3 (1.2)	0.1 (0.8)	-0.9 (1.5)	-0.3 (1.2)
Term (cm)	50.9 (2.6)	51.5 (2.0)	50.3 (2.9)	51.6 (2.2)	49.2 (2.9)	50.7 (2.7)
Z score	0.0 (1.1)	0.2 (0.9)	-0.3 (1.2)	0.3 (0.9)	-0.8 (1.3)	-0.1 (1.2)
<i>Head Circumference</i>						
Two weeks (cm)	33.6 (1.4)	34.0 (1.7)	33.5 (1.7)	33.4 (1.5)	32.5 (1.8)	33.3 (1.7)
Z score	-0.1 (0.8)	0.2 (1.0)	-0.2 (1.0)	-0.2 (1.0)	-0.8 (1.1)	-0.3 (1.1)
Term (cm)	35.1 (1.5)	35.6 (1.5)	34.9 (1.4)	35.2 (1.5)	34.4 (1.3)	35.0 (1.5)
Z score	0.2 (1.0)	0.4 (1.1)	-0.1 (0.9)	0.1 (1.0)	-0.4 (0.9)	0.0 (1.0)
<i>Body mass index (BMI)</i>						
Two weeks (g/cm ²)	11.3 (0.9)	11.7 (1.3)	11.3 (1.5)	11.1 (1.1)	11.3 (1.5)	11.4 (1.3)
Z score	-1.0 (0.7)	-0.7 (0.8)	-1.0 (1.0)	-1.1 (0.8)	-1.0 (1.0)	-1.0 (0.9)
Term (g/cm ²)	12.8 (1.3)	12.7 (1.4)	12.6 (1.6)	12.8 (1.8)	12.6 (1.5)	12.7 (1.6)
Z score	-0.4 (0.9)	-0.5 (1.1)	-0.6 (1.2)	-0.5 (1.3)	-0.6 (1.1)	-0.5 (1.1)

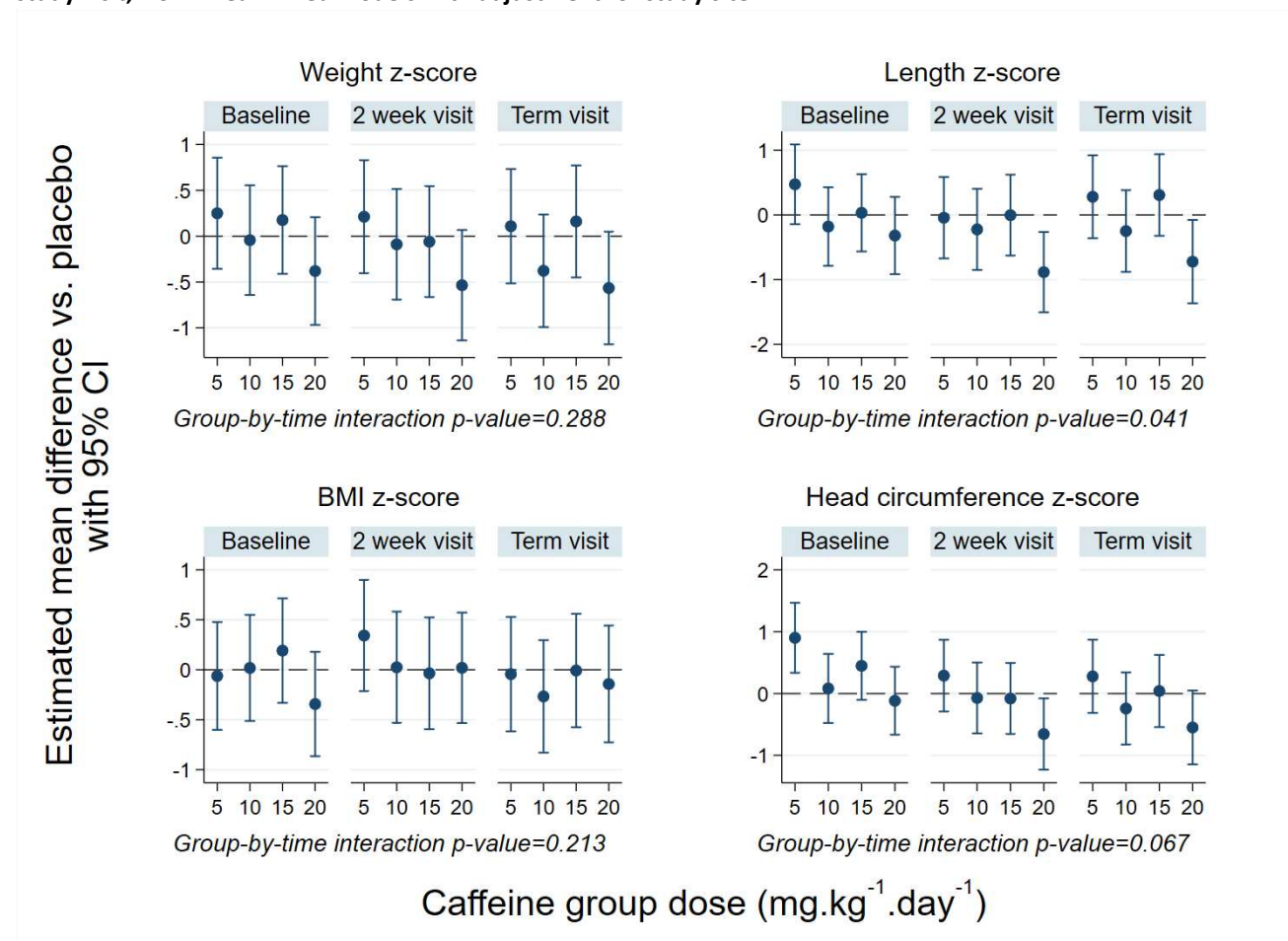
Data presented are mean (SD). Analysis of changes in anthropometric measures over time were performed using linear mixed models with a group-time interaction term.

^a Number of infants with at least one anthropometric measurement at 2 weeks and term, respectively, are: 22 and 20 in placebo group; 21 and 19 in 5 mg.kg⁻¹.day⁻¹ group; 26 and 21 in 10 mg.kg⁻¹.day⁻¹ group; 21 and 19 in 15 mg.kg⁻¹.day⁻¹ group and 22 and 18 in 20 mg.kg⁻¹.day⁻¹ group. ^b Z-scores for weight, length and head circumference were calculated from the revised Fenton growth charts for preterm infants[1], and Z-scores for BMI from the Olsen growth curves for preterm infants[2].

Supplementary Figure 1: Estimated marginal mean differences between caffeine groups and placebo in untransformed anthropometry measures at each study visit, from linear mixed models with adjustment for gestational age at birth and study site



Supplementary Figure 2: Estimated marginal mean differences between caffeine groups and placebo in z-scores for anthropometry measures at each study visit, from linear mixed models with adjustment for study site



Supplementary Table 2: Maternal Edinburgh Postnatal Depression Scores

	Placebo	Caffeine citrate 5 mg/kg/day		Caffeine citrate 10 mg/kg/day		Caffeine citrate 15 mg/kg/day		Caffeine citrate 20 mg/kg/day		Any dose of caffeine	
	Summary data	Summary Data	Ratio of GMs (95% CI), p- value vs placebo	Summary Data	Ratio of GMs (95% CI), p- value vs placebo	Summary Data	Ratio of GMs (95% CI), p- value vs placebo	Summary Data	Ratio of GMs (95% CI), p- value vs placebo	Summary Data	Ratio of GMs (95% CI), p- value vs placebo
Baseline EPDS Score^a											
<i>N</i> (% non-missing, of those with a baseline visit)	22 (91.7%)	22 (95.7%)		23 (95.8%)		25 (100.0%)		26 (100.0%)		96 (98.0%)	
Median (IQR)	6.5 (2.0, 9.0)	4.5 (2.0, 9.0)		5.0 (3.0, 8.0)		5.0 (2.0, 8.0)		5.5 (3.5, 9.0)		5.0 (2.5, 8.0)	
TEA EPDS Score^a											
<i>N</i> (% non-missing, of those with a term visit)	20 (100.0%)	18 (100.0%)		19 (100.0%)		18 (100.0%)		18 (100.0%)		73 (100.0%)	
Median (IQR) [geometric mean; GM]	7.0 (2.0, 9.0) [2.6]	3.0 (1.0, 6.0) [1.6]	0.65 (0.20,2.08) p=0.46	6.0 (4.0, 9.0) [4.0]	1.64 (0.52,5.22) p=0.40	6.0 (2.0, 10.0) [5.6]	1.73 (0.53,5.63) p=0.36	4.0 (3.0, 6.0) [3.0]	1.24 (0.38,4.06) p=0.72	5.0 (3.0, 7.0) [5.6]	1.21 (0.48,3.03) p=0.68
Term score adjusted for baseline			0.78 (0.26,2.34) p=0.65		2.16 (0.74,6.33) p=0.16		2.27 (0.75,6.83) p=0.14		1.30 (0.43,3.94) p=0.63		1.49 (0.62,3.53) p=0.38

^a EPDS data was available in a total of 118 (96.7% of 122) mothers at baseline and 93 (93.9% of 99 mothers remaining) at TEA visit

Supplementary Table 3: Side effects and withdrawals

	Placebo N = 24	Caffeine citrate 5 mg.kg ⁻¹ .day ⁻¹ N = 24	Caffeine citrate 10 mg.kg ⁻¹ .day ⁻¹ N = 27	Caffeine citrate 15 mg.kg ⁻¹ .day ⁻¹ N = 27	Caffeine citrate 20 mg.kg ⁻¹ .day ⁻¹ N = 27	Any dose of caffeine N = 105
Number withdrew (%)	4 (16.7%)	5 (20.8%)	6 (22.2%)	8 (29.6%)	7 (25.9%)	26 (24.7%)
Withdrawal reason; N						
Administration difficulties	0	0	2	3	2	7
Parents changed mind	4	1	1	3	3	8
Side effects or drug not tolerated	0	3	3	1	1	8
Other ^a	0	1	0	1	1	3

^a Including: investigators discretion (n=1), moved outside study follow-up area (n=1), inability to follow up due to the COVID-19 lockdown (n=1)

References

- 1 Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. *BMC Pediatr* 2013;**13**:59. doi:10.1186/1471-2431-13-59
- 2 Olsen IE, Lawson ML, Ferguson AN, *et al.* BMI Curves for Preterm Infants. *Pediatrics* 2015;**135**. doi:10.1542/peds.2014-2777