































	(11.7)	(11.4)	P=0.29
Ethnicity			
– White, n (%)	72 (96)	61 (91)	P=0.32§
– Black, n (%)	1 (1)	1 (1)	
– NE Asia, n (%)	0 (0)	0 (0)	
– SE Asia, n (%)	0 (0)	2 (3)	
– Other/mixed, n (%)	1 (1)	3 (4)	

\*either odds ratio (95% confidence interval [CI]), or mean difference (95% CI), allowing for clustering of multiple births within the same family, unless otherwise stipulated; †born outside a tertiary maternity hospital; ‡Chi-square test over all three categories; §Chi-square test over all five categories

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Table 2. Expiratory flow variables contrasted between caffeine and control groups

Expiratory flow variable	Caffeine n=74	Control n=68	Mean difference (95% CI) P-value*	Mean difference (95% CI) P-value†
zFEV <sub>1</sub> – mean (SD)	-1.00 (1.17)	-1.53 (1.35)	0.54 (0.14, 0.94) P=0.008	0.49 (0.07, 0.91) P=0.023
FEV <sub>1</sub> – % predicted – mean (SD)	88.4 (13.7)	82.0 (15.8)	6.4 (1.7, 11.2) P=0.008	6.0 (1.0, 11.0) P=0.018
zFVC – mean (SD)	-0.51 (1.15)	-0.95 (1.30)	0.44 (0.04, 0.83) P=0.031	0.38 (-0.02, 0.77) P=0.06
FVC – % predicted – mean (SD)	94.2 (13.2)	89.2 (15.0)	5.0 (0.4, 9.5) P=0.032	4.2 (-0.3, 8.7) P=0.07
zFEV <sub>1</sub> /FVC – mean (SD)	-0.73 (1.37)	-0.97 (1.39)	0.24 (-0.21, 0.68) p=0.30	0.23 (-0.24, 0.70) p=0.33
zFEF <sub>25-75%</sub> – mean (SD)	-1.30 (1.14)	-1.75 (1.27)	0.45 (0.05, 0.84) P=0.028	0.42 (0.002, 0.85) P=0.049
FEF <sub>25-75%</sub> – % predicted – mean (SD)	74.0 (22.1)	65.7 (22.7)	8.4 (1.0, 15.7) P=0.026	8.4 (0.4, 16.3) P=0.039
			Odds ratio (95% CI) P-value*	Odds ratio (95% CI) P-value†
zFEV <sub>1</sub> <5 <sup>th</sup> centile – n (%)	17 (23)	25 (37)	0.51 (0.24, 1.08) P=0.08	0.59 (0.25, 1.39) P=0.23
zFVC <5 <sup>th</sup> centile – n (%)	8 (11)	19 (28)	0.31 (0.12, 0.77) P=0.012	0.27 (0.10, 0.74) P=0.011
zFEV <sub>1</sub> /FVC <5 <sup>th</sup> centile – n (%)	17 (23)	21 (31)	0.72 (0.34, 1.53) P=0.40	0.67 (0.29, 1.56) p=0.36
zFEF <sub>25-75%</sub> <5 <sup>th</sup> centile – n (%)	23 (33)	31 (47)	0.57 (0.29, 1.12) P=0.10	0.62 (0.32, 1.28) P=0.20

CI=confidence interval; SD=standard deviation; FEV<sub>1</sub>=forced expired volume in 1 second; FVC=forced vital capacity; FEF<sub>25-75%</sub>= forced expired flow from 25% to 75% of the FVC

\*allowing for clustering of multiple births within the same family

†allowing for clustering of multiple births within the same family and adjusted for baseline variables (outborn status, antenatal corticosteroids, mode of delivery, multiple birth, sex, gestational age, birthweight, surfactant)



**Figure 1.** Plots of z-scores for expiratory flow variables comparing caffeine (C) and placebo (P) groups. Size of circles proportional to sample size. Expected mean value of zero shown as solid line; mean value for each subgroup shown as short solid line. 5<sup>th</sup> centile shown as dotted line; percentages <5<sup>th</sup> centile shown for each subgroup.

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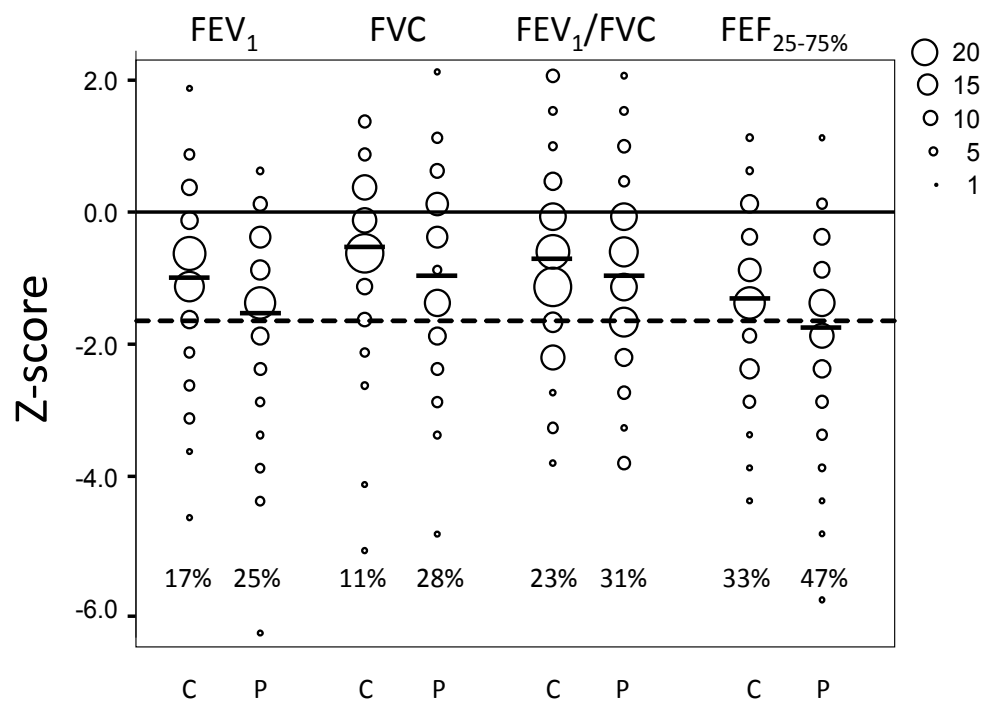
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Figure 1



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Supplementary Table 1. Perinatal and demographic characteristics

Characteristics	Lung function		Statistics*
	yes 142	no 42	
<b><i>Perinatal variable)</i></b>			
Outborn, † n (%)	32 (23)	11 (26)	0.82 (0.37, 1.81) P=0.62
Antenatal corticosteroids, n (%)	134/141 (95)	39 (93)	1.47 (0.36, 6.03) P=0.53
Multiple birth, n (%)	44 (31)	13 (31)	1.00 (0.48, 2.11) p=1.0
Vaginal delivery, n (%)	47 (33)	20 (48)	0.46 (0.22, 0.96) P=0.038
Gestational age at birth - weeks, mean (SD)	27.5 (1.7)	27.8 (1.7)	-0.1 (-0.8, 0.5) P=0.72
Birthweight - grams, mean (SD)	947 (182)	999 (178)	-52 (-114, 10) P=0.10
Male, n (%)	72 (51)	22 (52)	0.83 (0.40, 1.72) P=0.62
Exogenous surfactant, n (%)	90 (63%)	23 (55%)	1.33 (0.64, 2.76) P=0.44
Patent ductus arteriosus, n (%)	46 (32)	16 (38)	0.79 (0.39, 1.59) P=0.50
In oxygen at 36 weeks' postmenstrual age, n (%)	62 (44)	18 (43)	1.03 (0.51, 2.09) P=0.93
<b><i>Primary indication for caffeine</i></b>			
Apnea prophylaxis, n (%)	42 (30)	15 (36)	P=0.68‡
Facilitate extubation, n (%)	58 (41)	17 (40)	
Treat apnea, n (%)	42 (30)	10 (24)	

\*either odds ratio (95% confidence interval [CI]), or mean difference (95% CI); †born outside a tertiary maternity hospital; ‡Chi-square Test

Supplementary Table 2. Expiratory flow z-scores contrasted between caffeine and control groups, before and after adjustment for sex and height at 11 years of age.

Expiratory flow variable	Caffeine n=74	Control n=68	Mean difference (95% CI) P-value*	Mean difference (95% CI) P-value†
zFEV <sub>1</sub> – mean (SD)	-1.00 (1.17)	-1.53 (1.35)	0.54 (0.14, 0.94) P=0.008	0.43 (0.03, 0.83) P=0.034
zFVC – mean (SD)	-0.51 (1.15)	-0.95 (1.30)	0.44 (0.04, 0.83) P=0.031	0.29 (-0.08, 0.66) P=0.12
zFEV <sub>1</sub> /FVC – mean (SD)	-0.73 (1.37)	-0.97 (1.39)	0.24 (-0.21, 0.68) p=0.30	0.23 (-0.23, 0.69) p=0.33
zFEF <sub>25-75%</sub> – mean (SD)	-1.30 (1.14)	-1.75 (1.27)	0.45 (0.05, 0.84) P=0.028	0.38 (-0.01, 0.78) P=0.057

\*allowing for clustering of multiple births within the same family

†allowing for clustering of multiple births within the same family and adjusted for sex and height at 11 years of age

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