The Effect of Breastfeeding on Lung Function at 12 and 18 years – a prospective cohort study

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Online data supplement

**Spirometry** - Biological controls and 3L syringes were used for calibration. Participants were advised to abstain from short acting bronchodilators for four hours and long acting bronchodilators for 12 hours. Height and weight were measured to the nearest 0.1 cm and 0.1 kg respectively. At the 12 year follow up only baseline spirometry was performed (SpiroCard <sup>TM</sup> PC spirometer, QRS Diagnostic, Plymouth, MN, USA). At the 18 year follow up, both pre and post bronchodilator (Salbutamol) parameters were measured with an Easy One<sup>TM</sup> (ndd Medical technologies Inc, Andover MA).

Mediators and confounders- We have previously published a causal diagram [1] to identify confounders and mediators of the relationship between breastfeeding and lung function. Based on this diagram, the following factors were considered as potential mediators: the number of parental reports of lower and upper respiratory tract infections diagnosed by a doctor within the first two years of life; skin prick test reactivity (to one or more allergen) at 6, 12 and 24 months; and the child's height and BMI measured at 12 years and 18 years. A number of factors were considered as potential confounders: maternal and paternal smoking status (at the time of recruitment to the study), maternal and paternal education (higher education or not) and socioeconomic status of the family (ANU3 2 classifications according to the father's occupation at the time of recruitment to the study –see reference [2]. Eczema, defined as either doctor diagnosed eczema, or a rash treated with a topical steroid excluding the nappy and the scalp areas, prior to the cessation of breastfeeding was considered as a potential confounder, as we have previously demonstrated that early onset eczema was associated with prolonged breastfeeding in this cohort [3]. A diagnosis of cough rattle and wheeze prior to cessation of breast feeding was also considered as a potential confounder for similar reasons.

Di Unchounator i	ung function outcome	s at <u>12 years (</u>	<u>n age</u> (n=30 <b>+</b> ).	
Lung function	Exclusive breastfeed	ling	Total breastfeeding	
Pre	Effect per week	P value	Effect per week	P value
bronchodilator	(95%CI)		(95%CI)	
Model 1				
FVC (ml)	-0.5 (-4.9,3.9)	0.836	-0.7(-2.1,0.8)	0.355
$FEV_1$ (ml)	-0.5(-4.4,3.3)	0.782	-0.7(-2.0,0.5)	0.258
MEF (ml/s)	8.9(-1.1,19.0)	0.082	0.2(-3.6,3.1)	0.883
FER %	0.0(-0.1,0.1)	0.875	0.0(-0.1,0.1))	0.767
Model 2*				
FVC (ml)	-0.6(-5.2,3.9)	0.783	-0.9(-2.5,0.6)	0.228
$FEV_1$ (ml)	-0.5(-4.6,3.4)	0.789	-0.9(-2.2,0.5)	0.205
MEF (ml/s)	9.5(-0.7,19.7)	0.069	0.4(-3.5,3.6)	0.978
FER %	0.0(-0.1,0.1)	0.999	0.0(0,0)	0.891
Model 3				
FVC (ml)	-0.6(-5.4,4.1)	0.875	-1.0(-2.6,0.6)	0.226
$FEV_1$ (ml)	-0.4(-4.6,3.7)	0.839	-1.0(-2.5,0.4)	0.151
MEF (ml/s)	11.2(0.5,21.8)	0.040	-0.2(-3.5,3.9)	0.934
FER %	0.0(-0.1,0.1)	0.916	0.0(0,0)	0.809
Model 4				
FVC (ml)	0.3(-4.6,5.1)	0.919	-0.8(-2.5,0.9)	0.335
$FEV_1$ (ml)	-0.1(-4.3,4.2)	0.974	-0.8(-2.2,0.7)	0.316
MEF (ml/s)	8.8(-2.0,19.6)	0.110	0.8(-3.0,4.6)	0.691
FER %	0.0(-1.0,0.1)	0.745	0.0(0,0)	0.908
Model 5				
FVC (ml)	0.2(-5.5,5.8)	0.948	-0.9(-2.8,1.0)	0.347
$FEV_1$ (ml)	0.2(-4.8,5.3)	0.932	-0.9(-2.5,0.9)	0.332
MEF (ml/s)	10.1(-0.5,20.7)	0.061	0.1(-3.6,3.7)	0.977
FER %	-0.1(0.1,0.1)	0.999	0.0(0,0)	0.891

Online repository table S1- Multivariable associations between breastfeeding and pre bronchodilator lung function outcomes at 12 years of age (n=364).

Effects expressed as mean change in lung function associated with each additional week of breastfeeding, for both exclusive and total duration of breastfeeding; CI – Confidence Interval

Model 1- Adjusted for gender, height and age

Model 2\* - results presented in main tables –Adjustments as per model 1, with additional adjustment for maternal and paternal status of education, maternal and paternal status of smoking and socioeconomic status

Model 3 –As per model 2, with additional adjustment for onset of eczema prior to cessation of breastfeeding

Model 4 – As per model 2, with additional adjustment for onset of cough rattle and wheeze prior to cessation of breastfeeding

Model 5-As per model 2, height is removed from the model

Di onchounator	lung lunchon outcon	10 years	$\frac{1}{1} \frac{1}{1} \frac{1}$	
Lung function	Exclusive breastfe	eding	Total breastfeedi	ng
Pre	Effect per week	P value	Effect per week	P value
bronchodilator	(95%CI)		(95%CI)	
Model 1				
FVC (ml)	-3.1(-9.2,3.0)	0.325	-1.1(-3.1,0.9)	0.295
$FEV_1$ (ml)	1.5(-3.9,6.9)	0.591	-0.5(-2.3,1.3)	0.587
MEF (ml/s)	12.7(1.2,24.2)	0.030	-0.7(-4.5,3.1)	0.785
FER %	0.1(0,0.2)	0.021	0(0,0)	0.567
Model 2*				
FVC (ml)	-3.8(-10.1,2.5)	0.233	-1.5(-3.7,0.6)	0.168
$FEV_1$ (ml)	0.2(-5.4,5.8)	0.951	-1.1((-3.0,0.8)	0.242
MEF (ml/s)	10.5(-1.2,22.2)	0.078	-1.8(-5.8,2.2)	0.373
FER %	0.1(0,0.2)	0.061	0(0,0)	0.914
Model 3				
FVC (ml)	-4.2(-10.8,2.4)	0.213	-1.6(-3.9,0.6)	0.154
$FEV_1$ (ml)	-0.6(-6.5,5.3)	0.846	-1.2(-3.3,0.7)	0.208
MEF (ml/s)	9.3(-2.9,21.6)	0.135	-2.1(-6.3,2.1)	0.327
FER %	0.1(0,0.2)	0.103	0(0,0)	0.967
Model 4				
FVC (ml)	-2.7(-9.42,4.1)	0.438	-1.4(-3.7,0.9)	0.251
$FEV_1$ (ml)	0(-5.9,5.9)	0.915	-1.2(-3.2,0.9)	0.267
MEF (ml/s)	7.3(-5.1,19.8)	0.246	-2.2(-6.5,2.1)	0.314
FER %	0.1(0,0.2)	0.280	0(0,0)	0.818
Model 5				
FVC (ml)	-0.1(-1.2,6.9)	0.971	-0.5(-2.9,1.9)	0.703
$FEV_1$ (ml)	3.2(-3.0,9.4)	0.316	-0.1(-2.3,2.0)	0.905
MEF (ml/s)	13.7(1.6,25.5)	0.026	-0.5(-4.6,3.5)	0.793
FER %	0.1(0,0.2)	0.059	0(0,0)	0.751

Online repository table S2- Multivariable associations between breastfeeding and pre bronchodilator lung function outcomes at 18 years of age (n=409).

Effects expressed as mean change in lung function associated with each additional week of breastfeeding, for both exclusive and total duration of breastfeeding; CI – Confidence Interval

Model 1- Adjusted for gender, height and age

Model 2\* - results presented in main tables –Adjustment as per model 1, with additional adjustment for maternal and paternal status of education, maternal and paternal status of smoking and socioeconomic status

Model 3 –As per model 2, with additional adjustment for onset of eczema prior to cessation of breastfeeding

Model 4 – As per model 2, with additional adjustment for onset of cough rattle and wheeze prior to cessation of breastfeeding

Model 5-As per model 2, height removed from the model

Lung function	Exclusive breastfee	eding	Total breastfeeding	
Post	Effect per week	P value	Effect per week	P value
bronchodilator	95%CI		95%CI	
Model 1				
FVC (ml)	-3.6(-9.5,2.2)	0.220	-1.2(-3.1,0.8)	0.239
$FEV_1$ (ml)	-1.2(-6.2,3.8)	0.644	-0.7(-2.3,0.9)	0.426
MEF (ml/s)	5.2(-6.2,16.6)	0.371	-1.4(-5.1,2.3)	0.461
FER %	0.0 (0,0.1)	0.201	0(0,0)	0.412
Model 2*				
FVC (ml)	-4.0(-10.1,2.0)	0.194	-1.4(-3.5,0.7)	0.179
$FEV_1$ (ml)	-2.1(-7.2,3.0)	0.425	-2.8(-6.7,1.1)	0.161
MEF (ml/s)	2.7(-8.9,14.2)	0.652	-1.2(-2.9,0.6)	0.182
FER %	0(0,0.1)	0.425	0(0,0)	0.862
Model 3				
FVC (ml)	-4.5(-10.8,1.9)	0.165	-1.7(-3.8,0.5)	0.132
$FEV_1$ (ml)	-2.6(-8.0,2.8)	0.339	-1.3(-3.2,0.5)	0.150
MEF (ml/s)	3.3(-8.8,15.4)	0.590	-2.8(-6.8,1.3)	0.187
FER %	0(0,0.1)	0.377	0(0,0)	0.738
Model 4				
FVC (ml)	-2.9(-9.3,3.5)	0.376	-1.8(-4.1,0.4)	0.114
$FEV_1$ (ml)	-2.1(-7.6,3.3)	0.441	-1.5(-3.4,0.4)	0.118
MEF (ml/s)	0.1(-12.2,12.4)	0.986	-3.4(-7.7,0.8)	0.113
FER %	0(-0.1,0.1)	0.991	0(0,0)	0.959
Model 5				
FVC (ml)	-0.1(-7.1,6.9)	0.980	-0.4(-2.7,2.0)	0.761
$FEV_1$ (ml)	1.4(-4.6,7.3)	0.650	-0.2(-2.2,1.8)	0.865
MEF (ml/s)	6.6(-5.3,18.3)	0.276	-1.5(-5.6,2.5)	0.460
FER %	0(0,0.1)	0.382	0(0,0)	0.708

Online repository table S3 - Multivariable associations between breastfeeding and post
bronchodilator lung function outcomes at <u>18 years of age</u> .

Effects expressed as mean change in lung function associated with each additional week of breastfeeding, for both exclusive and total duration of breastfeeding

Model 1- Adjusted for gender, height and age

Model 2\* - results presented in main tables –Adjustment as per model 1, with additional adjustment for maternal and paternal status of education, maternal and paternal status of smoking and socioeconomic status

Model 3 –As per model 2, with additional adjustment for onset of eczema prior to cessation of breastfeeding

Model 4 – As per model 2, with additional adjustment for onset of cough rattle and wheeze prior to cessation of breastfeeding

Model 5-As per model 2, height removed from the model

Online repository table S4- The associations between breastfeeding and potential mediators of the relationship between breastfeeding and lung function

	Exclusive breastfeeding (per week)			Total breastfeeding (per week)		
Anthropometry*	Effect	95% CI	P value	Effect	95% CI	Р
	per week			per week		
Height at 12 years (cm)	0.03	-0.05,0.11	0.489	0.01	-0.02,0.035	0.558
Height at 18 years (cm)	0.08	0.01,0.15	0.022	0.03	0.01,0.05	0.029
BMI at 12 years (kg/m <sup>2</sup> )	-0.03	-0.09,0.02	0.192	-0.02	-0.36,-0.01	0.025
BMI at 18 years (kg/m <sup>2</sup> )	-0.39	-0.08,0.01	0.075	-0.13	-0.27,0.01	0.068

Infections	Effect per week	95%CI	P value	Effect per week	95%CI	P value
Number of Upper respiratory tract infections in $1^{st}$ year of life (600/620)	-1.004	-1.01,-1.0	0.132	-1.002	-1.004,1.0	0.044
Inc (000/020)	Odds Ratio	95%CI	P value	Odds Ratio	95%CI	P value
Presence of Lower respiratory tract infection in 1 <sup>st</sup> year of life (617/620)	0.98	0.96,1.00	1.00	0.99	0.98,1.00	0.245

Sensitization to any allergen	Odds Ratio	95% CI	P value	Odds Ratio	95% CI	P value
6 months (551/620)	1.01	0.99,1.04	0.375	1.00	0.99,1.01	0.485
12 months (543/620)	0.99	0.98,1.01	0.806	0.99	0.99,1.00	0.297
24 months (448/620)	1.02	0.99,1.04	0.128	1.00	0.99,1.01	0.149

CI - Confidence Interval:\*Only Height and BMI are adjusted for age and gender

H Upper respiratory tract infections- linear regression models using the log transformed data

¶Lower respiratory tract infections- logistic regression models, a dichotomous variable was

created none vs any lower respiratory tract infections within the first year of life

Online repository table S5-Association between breastfeeding (both total and exclusive duration) and lung function outcomes at 12 and 18 years stratified by maternal asthma status

Lung function	<b>Function</b> Without maternal With maternal asthma		P for interaction
parameter	asthma n=351	n=269	
At 12 years	Effect per week,	Effect per week, 95%CI	
·	95%CI	-	
Exclusive breastfeedi	ng		
FVC ml	-0.8(-7.6,6.0)	-1.2(-7.5,5.1)	0.930
FEV <sub>1</sub> ml	0.1(-5.8,6.1)	-1.7(-7.2,3.8)	0.655
MEF ml/s	12.3(-2.9,27.5)	9.1(-5.1,23.2)	0.758
FER %	0(-0.1,0.1)	0(-0.1,0.1)	0.614
Total breastfeeding			
FVC ml	-1.3(-3.6,1.1)	-0.8(-2.9,1.2)	0.785
FEV <sub>1</sub> ml	-0.7(-2.8,1.3)	-1.1(-2.9,0.7)	0.790
MEF ml/s	-0.8(-6.1,4.4)	0.8(-3.8,5.5)	0.635
FER %	0(0,0.1)	0(-0.1,0)	0.466
At 18 years			
<b>Exclusive breastfeedi</b>	ng		
Pre bronchodilator			
FVC ml	0.5(-8.9,9.8)	-7.8(-16.2,0.6)	0.192
$FEV_1$ ml	0.8(-7.5,9.2)	-0.9(-8.3,6.6)	0.762
MEF ml/s	10.3(-7.1,27.6)	10.2(-5.3,25.6)	0.992
FER %	0(-0.1,0.1)	0.1(0,0.2)	0.339
Post bronchodilator			
FVC ml	0.9(-8.0,9.9)	-8.8(-16.8,-0.8)	0.107
FEV <sub>1</sub> ml	-0.4(-7.9,7.3)	-4.1(10.9,2.8)	0.472
MEF ml/s	5.0(-12.2,22.2)	0.2(-15.2,15.5	0.676
FER %	0(-0.1,0.2)	0.1(0,0.2)	0.271
Total breastfeeding			
Pre bronchodilator			
FVC ml	0(-3.2,3.1)	-3.1(-5.9,-0.3)	0.143
FEV <sub>1</sub> ml	-0.1(-2.8,2.7)	-2.1(-4.5,0.4)	0.256
MEF ml/s	-0.9(-6.8,4.9)	-2.3(-7.6,2.9)	0.713
FER %	0(-0.1,0.1)	0(0,0.1)	0.801
Post bronchodilator			
FVC ml	0.4(-2.6,3.4)	-3.4(-6.1,-0.7)	0.054
$FEV_1$ ml	0.2(-2.4,2.7)	-2.5(-4.8,-0.2)	0.107
MEF ml/s	-1.3(-7.1,4.4)	-3.9(-9.0,1.3)	0.503
FER %	0(0,0.1)	0(0,0.1)	0.682

Effect expressed as per week increase of breastfeeding duration

\*Adjusted for gender, age, height, parents education level, parental smoking status and socioeconomic status

The effect						
	Without	birth weight* (226	<b>5</b> )	With birt	h weight** (226)	
At 12 years	β	(95%CI)	P value	β	(95%CI)	P value
Exclusive breas	stfeeding					
FVC (ml)	4.23	-1.85,10.32	0.171	3.80	-2.43,10.03	0.231
$FEV_1$ (ml)	3.80	-1.44,9.04	0.154	3.03	-2.32,8.39	0.265
MEF (ml/s)	17.62	4.83,30.42	0.007	15.01	1.99,28.04	0.024
FER (%)	00	-0.12,0.18	0.795	00	-0.13,0.12	0.647
Total breastfeed	ling					
FVC (ml)	1.56	-0.48,3.61	0.135	1.45	-0.62,3.52	0.170
$FEV_1$ (ml)	1.38	-0.38,3.15	0.124	1.19	-0.58,2.98	0.187
MEF (ml/s)	2.11	-2.26,6.48	0.343	1.37	-3.01,5.75	0.539
FER (%)	00	-0.04,0.03	0.875	00	-0.04,0.03	0.771
At 18 years						
Pre bronchodila	ator					
Exclusive breas	stfeeding					
FVC (ml)	0.81	-6.74,8.35	0.833	0.50	-7.21,8.21	0.898
$FEV_1$ (ml)	3.57	-3.12,10.26	0.294	3.37	-3.47,10.20	0.333
MEF (ml/s)	10.57	-3.12,24.27	0.130	10.39	-3.61,24.40	0.145
FER (%)	0.06	-0.03,0.16	0.192	0.06	-0.03,0.17	0.197
Total breastfeed	ling					
FVC (ml)	0.85	-1.67,3.36	0.508	0.79	-1.76,3.34	0.542
$FEV_1$ (ml)	1.04	-1.19,3.27	0.359	0.99	-1.27,3.24	0.390
MEF (ml/s)	0.37	-4.21,4.95	0.874	0.25	-4.39,4.88	0.917
FER (%)	0.01	-0.02,0.04	0.719	0.01	-0.03,0.04	0.732
Post bronchodil	lator					
Exclusive breas	stfeeding					
FVC (ml)	-0.19	-7.36,6.98	0.958	-0.66	-7.97,6.65	0.858
$FEV_1$ (ml)	1.04	-4.99,7.07	0.736	1.02	-5.14,7.17	0.745
MEF (ml/s)	3.21	-10.49,16.91	0.645	3.97	-9.99,17.95	0.576
FER (%)	0.03	-0.05,0.11	0.532	0.03	-0.05,0.12	0.410
Total breastfeed	ling					
FVC (ml)	0.45	-1.95,2.85	0.712	0.36	-2.06,2.78	0.771
$FEV_1$ (ml)	0.80	-1.20,2.81	0.430	0.81	-1.21,2.84	0.430
MEF (ml/s)	-0.26	-4.81,4.28	0.909	0.10	-4.69,4.48	0.964
FER (%)	0.01	-0.01.0.04	0.411	0.02	-0.01.0.04	0.334

## Online repository table S6- Effect of additional\* adjustment for birth weight on the associations between breastfeeding and lung function outcomes.

\*All models adjusted for gender, age and height at the time of spirometry

\*\*Also adjusted for birth weight.

\*Excludes a child with reported birth weight of 7 Kg

## References

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