

EXPERT
REVIEWS

The impact of breastfeeding on lung development and function: a systematic review

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With the global trend of increasing asthma and allergic disorders there is strong interest regarding early life nutrition as a potentially modifiable risk factor for lung disease. This systematic review includes 10 studies that assessed the effect of breastfeeding on lung growth and function. The review found breastfeeding to be beneficial for lung function, with the most consistent effect on increased forced vital capacity. There was no clear evidence that the relationship between breastfeeding and lung function was mediated through other factors. Furthermore, the findings from the few studies that investigated if maternal asthma modified the effect of breastfeeding on lung function were inconsistent. Further research is needed to determine the specific details such as duration and type (exclusive vs partial) of breastfeeding that leads to improved lung function.

KEYWORDS: bioactive substances • breastfeeding • exclusive breastfeeding • forced expiratory volume in one second • forced vital capacity • immune mediation • immunoglobulin A • lung function • lung growth • total duration of breastfeeding

Healthy lung development is a major determinant of longevity [1]. Lung growth and development in early life and childhood influences maximal adult lung function and respiratory reserve. With the global increase of respiratory morbidity and mortality [2], there is a need to identify potentially modifiable exposures for respiratory disease that may then be used to implement preventive strategies. One potentially modifiable factor is breastfeeding. There is substantial interest in the effect of breastfeeding on the development of healthy lungs [3].

Development of the lungs is a complex and continuous process which begins during early intrauterine life and continues after birth. The lungs are in the saccular stage at the end of the antenatal period and continue to grow until an individual becomes a young adult, by microvascular maturation [4]. The number of terminal bronchioles in an individual is established by the first trimester of pregnancy and the number of alveoli is finalized at the end of the second year of life [5]. Thus early life exposures, including breastfeeding, may plausibly impact lung growth.

Breast milk is the first food for most newborns and is generally considered 'the best' because of

its reported beneficial effects on health, including better lung function [6]. However, there remains controversy concerning the beneficial effects of the specific aspects of breastfeeding, including whether it needs to be exclusive or partial and the required duration of exclusive and partial breastfeeding, that may be related to specific health benefits [7]. There are variations in the definitions of exclusive and total duration of breastfeeding, but in this review, we will use the WHO definition, unless otherwise indicated. Thus, exclusive breastfeeding is defined as the baby not receiving any food item other than the breast milk, or prescribed medicines. Total duration of breastfeeding is the duration of breast milk feeding, regardless of if other food items have been introduced to the infants diet [8].

Constituents of breast milk change throughout the first year according to the requirements of the newborn and are influenced by maternal factors such as diet [9]. An important function of human breast milk that is related to this review is immune mediation [10]. The immune components of breast milk comprise a variety of bioactive substances, which enhance the biological processes of the body [10]. These include immune cells, anti-infectious agents, anti-inflammatory

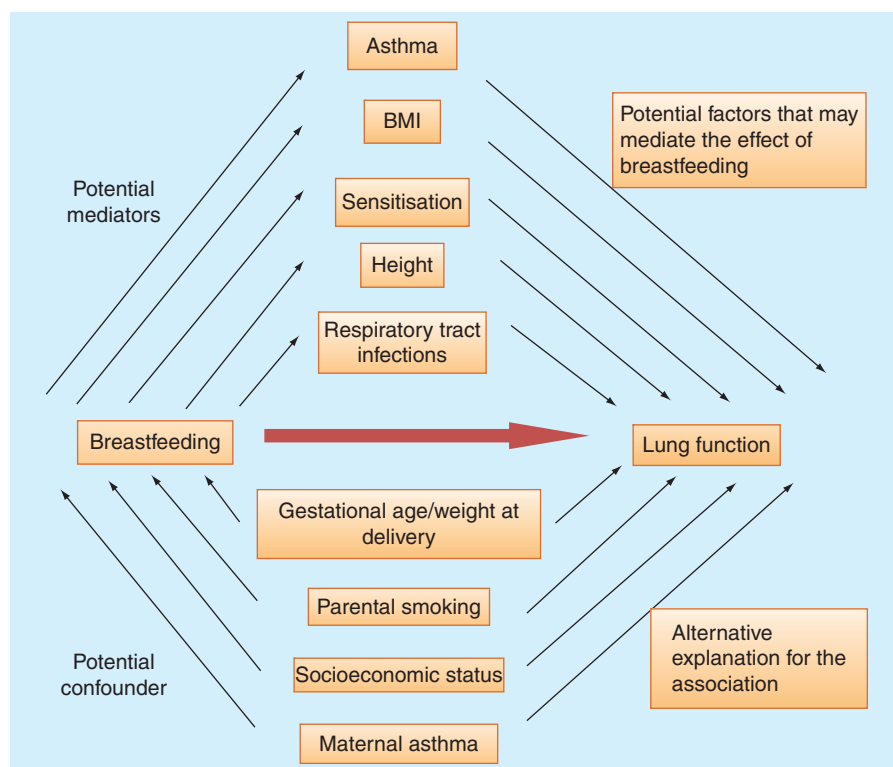


Figure 1. The potential pathway between breastfeeding and lung function.

agents, growth factors and pre-biotics (substances that enhance the quality and diversity of commensal gut micro-biota) [11]. The initial form of breast milk, colostrum, is rich in secretory immunoglobulin (IgA), lactoferrins, leukocytes and growth factors [11].

Possible pathways leading from breastfeeding to improved lung function

Although a number of theories have been proposed, the mechanisms concerning how lung function may be improved by breastfeeding remain unclear (FIGURE 1) [12]. Key among the theories to explain this possible association is via immune-mediated pathways. Innate immunity is the first line of defense in the body and acts within minutes after exposure to a potentially harmful agent [13]. There are many immunogenic factors (including IgA, EGF, TGF, TNF and IL) in breast milk [10]. Immunoglobulin A (IgA), the most common immunoglobulin in breast milk, plays a vital role in first line immunity [10]. Subsequently, T and B lymphocytes are recruited, which not only attack invading pathogens, but also establish an immune memory to attack more rapidly if the body is re-exposed to the same pathogen [13]. These immune mechanisms are protective against respiratory tract infections [14,15], which are known to have a prognostic effect on later lung function and asthma. Reduction of respiratory tract infections [1] by breastfeeding may lead to increased lung growth and function. Furthermore, it is possible that cytokines in breast milk also help to inhibit inflammation and maternally transferred antibodies contribute to reduced airway inflammation [13,16]. Although controversial,

breastfeeding may reduce risk of developing asthma, which is associated with lung function deficits.

There are also potentially non-immune factors which could mediate the association between breastfeeding and lung function. Growth factors, especially TGF- β , that increase the elastin activity in fibroblasts have been demonstrated in animal models [17,18]. EGF and TGF quantities are highest in the colostrum and reduce with the maturation of the milk [10] and both these growth factors may have an effect on the neonatal development of the lungs [4]. Furthermore, it has been found in some studies that children who are breastfed for a longer duration attain a greater height [1], which results in increased lung volumes. In addition, breastfeeding has also been associated with a reduction in obesity [1], and individuals with a BMI above the 85th percentile have a higher risk of asthma and poorer lung function when compared with those with a normal BMI [19]. Also the mechanical pathways, such as suckling and improved diaphragmatic movements with breastfeeding, also

contribute to the increase training of respiratory muscles and improve the coordination between swallowing and breathing [20]. The secretions of the Montgomery glands also help to stimulate the cardiorespiratory response [21].

Although there are plausible biological pathways for breastfeeding to improve lung function, it remains possible that the reported associations between breastfeeding and improved lung function are spurious, and are due to confounding factors. Breastfeeding is a complex exposure, and is influenced by a range of lifestyle and cultural factors, including socio-economic status. Children who are born pre-term have an increased risk of asthma and poor lung function [22] and may have difficulty in establishing breastfeeding. Due to the logistical and ethical issues, it is not possible to randomize individual children to receive breastfeeding, so it is not possible to exclude the possibility of confounding factors.

This systematic review aims to appraise all available data on the possible effect of breastfeeding on lung function. In addition, we examined this evidence to determine the most likely pathway by which breastfeeding influences lung function development.

Methods

Search strategy

MEDLINE (PubMed) was used to search all the English language publications of studies relevant to breastfeeding and lung function. The last search was performed on the 15 June 2013. The keywords used were 'breastfeeding' and 'respiratory physiology' (see online repository TABLE 1 for full details of search strategy).

Table 1. Details of the studies selected for the review with exposure.

Study (year)	Patients' lung function measured in total population (n/N)	Age when lung function measured (years)	Categorization of exposure variable breastfeeding	Study design	Ref.
Birth cohort studies					
Dogaru <i>et al.</i> (2012) Population based Leicestershire cohort study Leicestershire, UK	773/6808	8.5–14 with a mean of 12.2	Total duration of breastfed Not breastfed ≤3 months 4–6 months >6 months	Prospective birth cohort study, children were enrolled at birth. History of breastfeeding was collected at 1 year (n = 979) or between 2 and 4 years (n = 479)	[26]
Soto-Ramirez <i>et al.</i> (2012) & Ogbuanu <i>et al.</i> (2009) Population based Isle of Wight, UK	1121/1456 1033/1456	18 10	Breastfeeding (undefined) <2 months 2–3 months ≥4 months Also measured as continuous exposure	Prospective birth cohort study Breastfeeding details collected at the age 1 and 2 years	[28,30]
Kull <i>et al.</i> (2004) & (2010) Population based BAMSE (Barn (Children), Allergy, Milieu, Stockholm, Epidemiology project) Study Stockholm, Sweden	2965/4089 2564/4089 FEV ₁ 1838 PEF 2564	4 8	Exclusive breastfeeding ≥4 months <4 months	Prospective birth cohort study. Children were enrolled at birth Breastfeeding details were taken at the age of 1 year	[29,31]
Tennant <i>et al.</i> (2008) Population based cohort study Newcastle thousand families cohort, UK	392/1142	49–51	Breastfeeding (undefined) <4 weeks >4 weeks Also measured as continuous exposure	Prospective birth cohort study. Infant feeding details collected prospectively, age not mentioned	[1]
Guilbert <i>et al.</i> (2007) Population based Children's respiratory study, Tucson, AZ, USA	616/1246 479/1246	11 $\dot{C}$ (10.9 ± 0.7) 16 $\dot{C}$ (16.7 ± 0.6)	Total duration of breastfeeding ≤2 months 2 < 4 months ≥4 months	Prospective birth cohort study, children were enrolled at birth followed-up to adolescence Feeding practices were assessed prospectively at the ages of 2, 4, 6 and 9 months	[27]
Cross-sectional studies					
Nagel <i>et al.</i> (2009) ISAAC study International study Population based n = 54,943	4888	8–12	Total duration of breastfeeding Never breastfed <6 months 6–12 months >12 months Exclusive breastfeeding <2 months 2–4 months ≥4 months	Cross-sectional study with breastfeeding history taken retrospectively after recruiting to the study	[32]

Table 1. Details of the studies selected for the review with exposure (cont.).

Study (year)	Patients' lung function measured in total population (n/N)	Age when lung function measured (years)	Categorization of exposure variable breastfeeding	Study design	Ref.
<i>Cross-sectional studies (cont.)</i>					
Lee <i>et al.</i> (2005) Population based n = 58	58 (boys only)	5–7	Breastfeeding (undefined) <6 months >6 months	Cross-sectional study of a selected cohort breastfeeding history taken retrospectively at the time of recruitment	[33]
Shaukat <i>et al.</i> (2005) Population based Erie and Niagara countries, USA n = 6843	2305 (53.2% women)	35–79	Breastfed as an infant yes, no or not sure/don't know	Cross-sectional study breastfeeding history taken retrospectively	[34]

Inclusion/exclusion criteria

Studies were included if there was an association examined between some form of breastfeeding as the exposure variable (either total or exclusive) and at least one lung function parameter measured as the outcome.

Selection of articles

The title and abstract of papers identified by the electronic search were reviewed independently by two reviewers (NW and BC). When inclusion was unclear, the full manuscripts were reviewed, and a third reviewer (AL) was involved in instances of disagreement. Key information was extracted from each publication (author, year of publication, study population, whether a high risk or a population-based cohort, sample size and age group), as was the definition of breastfeeding and which lung function parameters were measured.

Data extraction

The methodology section of each paper was reviewed separately to extract details on the study design, number of participants, age at which the lung function was measured and where applicable, to obtain details of the categorization of breastfeeding. The outcome was extracted from the results section and numerical values were extracted for the review when available. When results were presented from more than one regression model (i.e., models adjusting for different confounders), the estimates from most parsimonious model were extracted. (i.e., the unadjusted models). The overall associations between breastfeeding and lung function did not alter following adjustment for confounders.

Results

The MEDLINE search identified 292 published articles. After reviewing all the abstracts and titles, we found 13 articles matching our selection criteria (FIGURE 2). Of the 13 papers where the full text was retrieved, one was excluded [23] on the basis that lung function parameters were not summarized by breastfeeding, and two studies examining the effect of breastfeeding in children with cystic fibrosis [24,25] were also excluded.

From the 10 studies, 7 studies were birth cohorts (2 studies with two publications on this association [1,26–31] and 3 were cross-sectional studies [32–34]. Most studies assessed outcomes in children and adolescents, but two studies measured outcomes in adults (TABLE 2) [1,34].

Description of the exposures & outcomes

Breastfeeding was described in various ways. Three studies examined total duration of breastfeeding as the exposure variable [26,27,30], two examined exclusive breastfeeding duration [29,31] and five examined duration of breastfeeding without defining if it was exclusive or total [1,28,32–34].

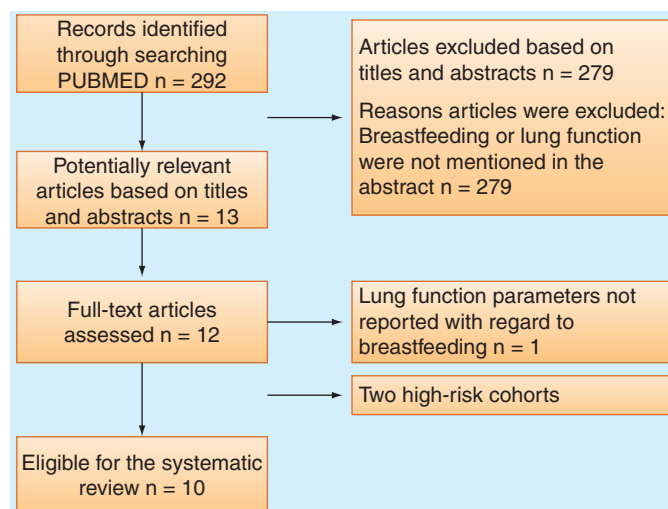
**Figure 2. Flow chart of the search process.**

Table 2. Results for the forced expiratory volume in 1 second.

Study (year)	Patients' lung function measured in total population (n/N) Age at lung function (years)	Breastfeeding exposure ^{†‡§}	Results (FEV ₁ in ml)			Effect	Ref.
			β	95% CI	p-value		
Birth cohort studies							
Tennant <i>et al.</i> (2008)	403/1142 49–51	Continuous (per week) [§] Binary [§] ≥4 weeks <4 weeks	NR Ref -245	NR -416, -74	0.62# <0.01	Not associated Increased FEV ₁	[1]
Ogbuanu <i>et al.</i> (2009)	1033/1456 10	Categorical [†] Not breastfed <2 months 2–4 months >4 months	Ref 14.3 16.8 39.5	 -27.4, 56.0 [¶] -31.2, 64.8 [¶] 0.1, 78.8 [¶]	 0.50 0.49 0.05	Increased FEV ₁	[30]
Soto-Ramirez <i>et al.</i> (2012)	1121/1456 18	Continuous (per week) [§]	1.2	0.1, 2.4 [¶]	0.03	Increased FEV ₁	[28]
Guilbert <i>et al.</i> (2007)	616/1246 11; 479/1246 16	Categorical [†] At 16 years ≤2 months 2 < 4 months ≥4 months	Ref 20 27	 -41, 81 [¶] -42, 96 [¶]	 0.50 0.40	Not associated	[27]
Dogaru <i>et al.</i> (2012)	773/6808 8.5–14	Categorical [†] Not breastfed ≤3 months 4–6 months >6 months	Ref -20 -2 25	 NR NR NR	 0.36 0.95 0.29	Not associated	[26]
Kull <i>et al.</i> (2010)	1838/4089 8	Categorical [†] <4 months ≥4 months	Ref 17.2	 -5.1, 39.4	 NR	Not associated	[29]
Cross-sectional studies							
Shaukat <i>et al.</i> (2005)	2305/6843 35–79	Categorical [§] None Any	Ref 5.5	 -8.7, 20.0	 NR	Not associated	[34]

†Total duration.

‡Exclusive duration.

§Undefined.

¶Original paper presented SE. Review authors estimated CI.

#Parameter estimates and confidence intervals not provided.

FVC₁: Forced vital capacity in one second; NR: Not reported; SE: Standard error.

Table 2. Results for the forced expiratory volume in 1 second (cont.).

Study (year)	Patients' lung function measured in total population (n/N) Age at lung function (years)	Breastfeeding exposure ^{†‡§}	Results (FEV ₁ in ml)			Effect	Ref.
			β	95% CI	p-value		
Cross-sectional studies (cont.)							
Nagel et al. (2009)	4888/54943 8–12	Categorical [§]	FEV ₁ % predicted mean ratio			Increased FEV ₁ , but only in affluent countries	[32]
		Affluent countries	Mean ratio				
		None	Ref				
		Any	1.11	1.02, 1.20	NR		
		Nonaffluent countries					
		None	Ref				
Any	0.89	0.68, 1.17	NR				
Lee et al. (2005)	58/58 5–7 years	Categorical [§]	Mean	SD		Not associated	[33]
		<6 months	1100	200			
					0.30		
		>6 months	1100	300			
[†] Total duration. [‡] Exclusive duration. [§] Undefined. [¶] Original paper presented SE. Review authors estimated CI. [#] Parameter estimates and confidence intervals not provided. FVC ₁ : Forced vital capacity in one second; NR: Not reported; SE: Standard error							

[†]Total duration.[‡]Exclusive duration.[§]Undefined.[¶]Original paper presented SE. Review authors estimated CI.[#]Parameter estimates and confidence intervals not provided.FVC₁: Forced vital capacity in one second; NR: Not reported; SE: Standard error.

Two studies measured lung function repeatedly on two occasions [27,28] while all the others measured lung function at only one time point. The methods used to measure lung function were spirometry [1,25,27,28,30,32,34] and peak expiratory flow meter [26,29,31,33]. A wide range of parameters were assessed among the studies in the review (FVC, FEV₁, FEV₁/FVC, FEF₅₀, FEF_{25–75}). The most common lung function parameter measured was FEV₁ [1,24–30,33,34]. Other common lung function measures were forced vital capacity (FVC – six studies [24,29,31,32], peak expiratory flow rate (five studies [25–27,29,31]) and the FEV₁/FVC ratio (four studies [26–28,30]). From the studies which measured FEF, one study reported FEF₅₀ and the other FEF_{25–75} [26,27] and one FEF_{25–75}/FVC [27].

Associations between breastfeeding & FEV₁ (TABLE 2)

Six of the nine studies that assessed the relationship between FEV₁ and breastfeeding were birth cohort studies [1,26–30] and the others were cross-sectional studies [32–34]. There were five studies [1,26–28,30] that observed an association between breastfeeding (total or undefined) and FEV₁ including two cross-sectional studies [32–34]. A significant increase in FEV₁ was seen among three studies [1,28,30,32]. One study looked at exclusive breastfeeding and FEV₁ but this association was not statistically significant [29].

Associations between breastfeeding & FVC

Of the four studies that assessed FVC, none examined the effect of exclusive breastfeeding, with all either not defining the type of breastfeeding or reporting the associations with total duration (TABLE 3). Of these four studies, two found that longer duration of breastfeeding was significantly associated with a greater FVC [27,28,30]. The only cross-sectional study that addressed this relationship failed to demonstrate an association [32], while the cohort study found a trend toward greater FVC with increasing duration of breastfeeding which did not achieve statistical significance [26].

Associations between breastfeeding & FEV₁/FVC ratio

Of the three studies which assessed the FEV₁/FVC ratio [26–28,30], one study demonstrated a significant decrease [27] in the FEV₁/FVC ratio associated with breastfeeding, while the other two found no association (TABLE 4) [26,28,30].

Associations between breastfeeding & peak flow

Of the studies which looked at the breastfeeding and peak expiratory flow rates [26,29–31,33], one reported the exposure as ever breastfeeding [33], one as exclusive breastfeeding [29,31] and the other two as total breastfeeding [26,30]. Three studies did show a positive effect of breastfeeding on peak expiratory flow

Table 3. Results for the forced vital capacity.

Study (year)	Patients' who underwent lung function in total population (n/N) Age at lung function (years)	Breastfeeding exposure ^{†‡§}	Results (FVC in ml)			Effect	Ref.
			β	95% CI	p-value		
Birth cohort studies							
Ogbuanu <i>et al.</i> (2009)	1033/1456 10	Age 10 years Categorical [†]				Increased FVC	[30]
		Not breastfed	Ref				
		<2 months	9.6	-34.3, 53.5 [¶]	0.67		
		2 <4 months	6.9	-43.5, 57.3 [¶]	0.79		
		>4 months	54.0	12.6, 95.4 [¶]	0.01		
Soto-Ramirez <i>et al.</i> (2012)	1121/1456 18	Age 18 years Continuous (per week) [§]	1.5	0.3, 2.6 [¶]	0.01	Increased FVC	[28]
Guilbert <i>et al.</i> (2007)	616/1246 11; 479/1246 16	Categorical [†]				Increased FVC	[27]
		At 11 years	NR	NR	<0.01*		
		At 16 years					
		≤1 month	Ref				
		2 < 4 months	43	-28, 114 [¶]	0.2		
		≥ 4 months	103	25, 181 [¶]	0.01		
Dogaru <i>et al.</i> (2012)	773/6808 8.5–14	Categorical [†]				Not associated	[26]
		Not breastfed	Ref				
		≤3 months	-39	NR	0.12		
		4–6 months	-10	NR	0.76		
		>6 months	24	NR	0.37		
Cross-sectional studies							
Shaukat <i>et al.</i> (2005)		Catergorical [§]					[34]
	2305/6843	None	Ref				
	35–79	Any	4.9	-8.3, 18.0	NR	Not associated	
[†] Total duration. [‡] Exclusive duration. [§] Undefined. [¶] Original paper presented SE. Review authors estimated CI. *Parameter estimates and confidence intervals not provided. FVC: Forced vital capacity; NR: Not reported; SE: Standard error							

[†]Total duration.

[‡]Exclusive duration.

[§]Undefined.

[¶]Original paper presented SE. Review authors estimated CI.

*Parameter estimates and confidence intervals not provided.

FVC: Forced vital capacity; NR: Not reported; SE: Standard error.

rates [29,30,33]. Interestingly, both studies that examined the association with exclusive breastfeeding observed a beneficial effect on peak expiratory flow (TABLE 5) [29,31].

Associations between breastfeeding & other lung function outcomes

Two studies have measured the midexpiratory flow [26,27] and one found a protective effect ($p = 0.03$) [26]. Furthermore, the ratio between the midexpiratory flow and FVC was

examined in one study that demonstrated a beneficial effect [27].

Mediators between breastfeeding & lung function

It has been proposed that the relationship between breastfeeding and lung function may be mediated by a number of factors (FIGURE 1). Of the studies included, only three assessed the evidence of possible effect of mediators [1,26,28]. From these three studies, one has suggested that weight gain ($\beta = -0.09$ kg

Table 4. Results for the ratio between forced expiratory volume one to forced vital capacity.

Study (year)	Patients' who underwent lung function in total population (n/N) Age at lung function (years)	Breastfeeding exposure ^{†‡§}	Results (the ratio between FEV ₁ /FVC %)			Effect	Ref.
			<i>β</i>	95% <i>CI</i>	<i>p-value</i>		
Birth cohort studies							
Ogbuanu <i>et al.</i> (2009)	1033/1456 10	10 years Categorical [†] Not breastfed	Ref			Not associated	[30]
		<2 months	0.28	-0.56, 1.40 [¶]	0.62		
		2 <4 months	0.57	-0.70, 1.84 [¶]	0.38		
		>4 months	-0.40	-1.44, 0.64 [¶]	0.45		
Soto-Ramirez <i>et al.</i> (2012)	1121/1456 18	Age 18 years Continuous (per week) [§]	<-0.01	-0.02, 0.02 [¶]	0.92	Not associated	[28]
Guilbert <i>et al.</i> (2007)	616/1246 11; 479/1246 16	Categorical [†] At 11 years At 16 years ≤1 months 2 < 4 months ≥4 months	NR NR Ref -0.70 -1.90	NR NR NR -1.88, 0.48 [¶] -3.08, -0.72 [¶]	<0.01* 0.20 <0.01	Decreased ratio	[27]
Dogaru <i>et al.</i> (2012)	773/6808 8.514	Categorical [†] Not breastfed ≤3 months 4–6 months >6 months	Ref 0.70 0.30 0.20	NR NR NR	0.06 0.45 0.56	Not associated	[26]

[†]Total duration.[‡]Exclusive duration.[§]Undefined.[¶]Original paper presented SE. Review authors estimated CI.

*Parameter estimates and confidence intervals not provided.

FEV₁: Forced expiratory volume in one second; FVC: Forced vital capacity; NR: Not reported; SE: Standard error.

association between breastfeeding and weight gain) in the first year of life may mediate the effect of breastfeeding on FVC [28]. Notwithstanding, using a pathway analysis, Tennant *et al.* found no evidence of effect mediation by a range of factors (including birth weight, number of lower respiratory tract infections, smoking pattern and body fat) of the breastfeeding/lung function relationship [1]. The single study that assessed the potential mediating effects of atopy, asthma and lower respiratory tract infections did not find any evidence to support these as proposed mechanisms for the effect of breastfeeding [26].

Assessment of possible effect modification

Of the studies included in this review, five assessed possible effect modification [26–28,30,34] on the breastfeeding and lung function

relationships. From these, three studies examined the interaction between breastfeeding and maternal asthma [26,27,30]. One study suggested that in the presence of maternal asthma, breastfeeding for more than 6 months increased the FVC by 164 ml and FEV₁ by 167 ml compared with the nonbreastfed group [26]. Whereas for the children without maternal asthma, there was no evidence of an association between breastfeeding and lung function (p for interaction for FVC = 0.02 and for FEV₁ = 0.01) [26]. Ogbuanu *et al.* found that the effect of breastfeeding on lung function was not modified by the presence of maternal asthma or maternal atopy [30]. By contrast, Guilbert *et al.* observed that breastfeeding children of mothers with asthma for more than 4 months did not influence FVC (p = 0.70), but FEV₁/FVC ratio (p < 0.01), FEF_{25–75} (p = 0.03) and FEF_{25–75}/FVC (p = 0.01) were significantly

Table 5. Results of the peak expiratory flow rate.

Study (year)	Patients' who underwent lung function in total population (n/N) Age at lung function (years)	Breastfeeding exposure ^{†‡§}	Results (PEFR in ml/s)			Effect	Ref.		
			β	95% CI	p-value				
Birth cohort studies									
Dogaru <i>et al.</i> (2012)	773/6808 8.5–14	Categorical [†]				Not associated	[26]		
		Not breastfed	Ref						
		≤3 months	-10.0	NR	0.87				
		4–6 months	15.0	NR	0.84				
		>6 months	77.0	NR	0.22				
Ogbuanu <i>et al.</i> (2009)	1033/1456 10	Categorical [†]				Increased PEFR	[30]		
		Not breastfed	Ref						
		<2 months	114.7	-22.9, 252.3 [¶]	0.10				
		2 < 4 months	143.4	-14.5, 301.3 [¶]	0.08				
		>4 months	180.8	51.3, 310.3 [¶]	0.01				
Kull <i>et al.</i> (2004)	2965/4089 4	At 4 years (PEFR < median)				Not associated	[31]		
		Categorical [†]	OR						
		0–2 months	1						
		3–4 months	0.98	0.73, 1.01	NR				
		≥4 months	0.94	0.69, 1.30	NR				
Kull <i>et al.</i> (2010)	2564/4089 8	At 8 years				Increased PEFR	[29]		
		Categorical [§]	β						
		<4 months	Ref						
		≥4 months	73.3	12.0, 135.3	NR				
Cross-sectional studies									
Lee <i>et al.</i> (2005)	58/58 5–7	Categorical [§]	Mean	SD		Increased PEFR	[33]		
		<6 months			140			30	0.01
		>6 months			165			40	

[†]Total duration.[‡]Exclusive duration.[§]Undefined.[¶]Original paper presented SE. Review authors estimated CI.[¶]Parameter estimates and confidence intervals not provided.FEV₁: Forced expiratory volume in one second; FVC: Forced vital capacity; NR: Not reported; SE: Standard error.

decreased. Among the children of mothers with neither asthma nor atopy, children who were breastfed had a significantly higher FVC ($p < 0.05$) and a FEF_{25–75}/FVC ratio ($p < 0.05$) compared with those who were not [27].

One study reported on a possible effect modification by height (p for interaction = 0.04) [28]. In taller children there was no apparent effect of breastfeeding on FVC, while in smaller children (<160 cm) breastfeeding for more than 4 months was associated with an increase in the FVC

compared with nonbreastfed children ($p = 0.04$). Finally, a single study which examined the modifying effects of asthma and chronic obstructive lung disease found no evidence for this [34].

Expert commentary

The number of articles published on breastfeeding and lung function has increased during the past decade. None of the studies in this review were published before 2004. The results of the studies reviewed generally suggest that breastfeeding may improve lung

function, particularly the FVC. Despite this apparent beneficial effect, there was some variability in exactly what parameters of lung function were affected by breastfeeding and the optimal age of impact. Strongest evidence of an association between breastfeeding and either FEV₁ or FVC was found when the total duration of breastfeeding was more than 4 months [1,27,28,30]. The magnitude of the effect of breastfeeding was most consistent in improving FVC, with most studies observing a 20–100 ml greater FVC in children who had received more than 4 months of total duration of breastfeeding, compared with children who were not breastfeeding. This seems to be a relatively small increase although this may be quite important, as low FVC is associated with increased mortality risk [35]. To put this into context, a 600 ml (or ~10%) reduction in FVC in adults has been associated with a 15% (95% CI: 10, 20) increased risk for mortality [36]. It was also unclear if the beneficial effects of breastfeeding were more pronounced for exclusive breastfeeding, or total duration, as only one study simultaneously examined the effect of these forms of breastfeeding [31]. Kull *et al.* in their study found exclusive breastfeeding for at least 4 months improved lung function, with continuing partial breastfeeding thereafter conferring additional protection [29]. As few studies performed repeated measurements on individual participants, it was not possible to determine if the effect of breastfeeding on lung function varied at different ages [27].

Many factors could potentially mediate the effect of breastfeeding on lung function outcomes. For example, breastfeeding may reduce the number of respiratory tract infections [15,37], which may plausibly improve growth of the lungs. Also a lower proportion of body fat associated with breastfeeding may have contributed to the improved lung function outcomes [1,37]. Weaning from the breast and the introduction of formula feeds in early life is associated with increased weight gain, but reduced lung growth and function which increased asthma symptoms [38]. Also some researchers have observed an association between increased weight and increased symptoms of asthma [39]. In addition to the body size of the adolescent, many other factors contribute to lung volumes. The elasticity of the lung tissue and the ribcage size has an influence on lung volumes [30]. Somatic growth might override all of the above effects and contribute to lung function [28].

Although many theories had been proposed, the evidence on potential mediators is inadequate to draw firm conclusions. The single study which examined a range of these many potentially mediating factors (birth weight, number of lower respiratory tract infections, smoking behavior and body fat) could not find evidence to support any of these as mediators of the breastfeeding/lung function relationship [1]. Similarly, the single study to examine atopy, asthma or lower respiratory tract infections as possible mediators was unable to demonstrate any such effects [26]. The only variable which was found to be a significant potential mediator was weight gain in the first year of life [28]. In this study, breastfeeding was found to have an inverse association with weight gain during the first year of life and the reduced weight gain in first years of life had a positive association with FVC at the age of 10 years.

Childhood asthma has a significant adverse impact on the adult lung function, [1] but the association between breastfeeding and

asthma remains controversial. While some studies have observed that breastfeeding is associated with reduced risk of asthma and allergic diseases [40,41], others have failed [42] to show such an effect. The available literature also suggests that exclusive breastfeeding was beneficial in the early years of life in protection from asthma, but not during adolescence or adulthood [43,44]. Despite these controversies, it remains plausible that prolonged breastfeeding protects against childhood asthma and atopic wheeze [32] thereby improving lung function. Unfortunately, no clear evidence for this has been demonstrated in the literature to date.

It has been suggested that the effect of breastfeeding on lung function outcomes may be modified by maternal asthma. Breast milk from mothers who suffer from allergies appears to differ from milk of the nonallergic mothers in a number of important ways [43]. For example, CD14 levels are higher breast milk of allergic mothers (mean [standard deviation (sd)]) = 7.6 (2.6) vs 7.0 (2.4) µg/ml, $p = 0.04$), while IL-4 ($p < 0.05$) was found to be higher in colostrum of allergic mothers [44,45]. The maternal immunoglobulin transmitted through breast milk in asthmatic mothers may be different from non-asthmatic mothers [25]. At 3 months, lactation levels of IgA was lower in breast milk of allergic mothers than non-allergic mothers (190 AU (91–315), vs 256 AU (173–397), $p < 0.05$), but was similar in colostrum and 1 month breast milk [46]. Alternatively, some, but not all, studies have found that milk of mother with allergy has a lower content of n-3 long-chain fatty acids (LCP) (1 month breast milk mean [sd] n-3 = 0.96 [1.6] w% vs 1.10 [0.24] w%, $p < 0.05$) and higher n-6/n-3 LCP ratio (2.1 [0.7] w% vs 1.8 [0.42] w%, $p < 0.01$) when compared with milk from mothers with without allergy [46]. These differences in breast milk may generate a differential effect of breastfeeding, between mothers with and without asthma, on allergic disease and lung development outcomes in the child. Of the 12 studies included, only three examined possible effect modification by maternal asthma [26,27,30], and only one showed a positive effect of breastfeeding on FVC and FEV₁ in the presence of maternal asthma, but no effect of breastfeeding in children of non-asthmatic mothers [26]. The other study found breastfeeding in the presence of maternal asthma was related to reduced FEV₁/FVC ratio, but improved FEV₁ and FVC in children of mothers without asthma [27]. The final study could not demonstrate effect modification by maternal asthma [30]. Therefore, the beneficial effects of prolonged breastfeeding in the presence of maternal asthma remain uncertain.

In spite of guidelines and the known benefits of breastfeeding, cultural beliefs and attitudes appear to play an important role in deciding actual breastfeeding behavior [32]. For example, Osman *et al.* found that, in a sample of Lebanese woman, concerns of insufficient breast milk supply and 'bad milk' were relatively common, and were not necessarily expected in this community [45]. For this reasons, breastfeeding programs need to be implemented in a culturally accepted manner [46]. The WHO recommends 6 months of exclusive breastfeeding and to continue breastfeeding thereafter with complementary feeding

according to the individual child's requirements [8]. Adherence to these recommendations is highly variable [47].

This review has a number of limitations. We only included papers published in English, so we may have missed some publications in other languages. All systematic reviews may be subject to the influence of publication bias. All but one [34] of the included studies in this review showed breastfeeding to be associated with improvements in one or more lung function parameters. However, there was a lack of consistency between the studies among the classification of exposure and also in terms of which lung function parameters showed beneficial effects. The studies included in this review all measured lung function at age 4 years and above. Though technically difficult, it is possible to measure the lung functions in very young children [48], and this should be considered in future research, as the effect of breastfeeding may be particularly pronounced in early life. As the categorization of breastfeeding was not consistent, we were unable to perform a meta-analysis of these findings. As such, there may be a relatively small effect of breastfeeding on lung function parameters that individual studies did not have the power to detect, resulting in non-significant outcomes.

As breastfeeding is an area which is highly influenced by social and cultural factors, it remains possible that studies with negative or null effects may not have been published. This may have resulted in an overestimation of the potential benefits of breastfeeding on lung function in this review.

Five-year view

While the existing evidence suggests that breastfeeding may improve lung function, particularly FVC, it remains unclear what the optimal duration and type of breastfeeding is for lung health, or the mechanisms by which breastfeeding has this effect. Despite this lack of clarity, breastfeeding should continue to be promoted and advocated due to the range of benefits. In the next 5 years, the number of studies examining the association between breastfeeding and lung growth and function will expand, including mechanistic studies. The exact mechanism by which breastfeeding improves the lung function and growth will be elucidated during this time. If this association is mediated by immune pathways, this may lead to novel interventions for maximizing infant lung development.

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Key issues

- Breastfeeding is the first dietary exposure and has a range of beneficial effects for both the mother and the child.
- It has been proposed that breastfeeding may improve lung function by a number of mechanisms, including by: reducing the number of respiratory tract infections; protecting against childhood asthma; decreasing sensitization; increasing attained height and reducing risk of obesity.
- It has also been proposed that maternal asthma may modify the effect of breastfeeding on lung function.
- This review, which systematically identified the existing literature on the association between breastfeeding and lung growth and function, found that most studies demonstrate an association of breastfeeding with improved lung function.
- However, studies vary in terms of the lung function parameter that breastfeeding is associated with improvement for, with forced vital capacity showing the most consistent improvement.
- Little evidence exists concerning the factors that mediate the association between breastfeeding and improvement in lung function, and the current literature does not support the proposed indirect effect of breastfeeding on lung function.
- The evidence that maternal asthma modifies the effect of breastfeeding on lung function is conflicting.
- Further research is required to identify the exact type and the duration of breastfeeding that improves lung growth and function.

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