ORIGINAL ARTICLE

Effect of preterm birth on later FEV_1: a systematic review and meta-analysis

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ABSTRACT

Background Increasing evidence suggests that preterm birth affects later lung function. We systematically reviewed the literature to determine whether percentage predicted forced expiratory volume in 1 s (%FEV_1) is lower in later life in preterm-born subjects, with or without bronchopulmonary dysplasia (BPD), compared with term-born controls.

Methods Studies reporting %FEV_1, with or without a term-born control group, in later life for preterm-born subjects (<37 weeks gestation) were extracted from eight databases. Data were analysed using Review Manager and STATA. The quality of the studies was assessed.

Results From 8839 titles, 1124 full articles were screened and 59 were included: 28 studied preterm-born children without BPD, 24 with BPD_{28} (supplemental oxygen dependency at 28 days), 15 with BPD_{36} (supplemental oxygen dependency 36 weeks postmenstrual age) and 34 born preterm. For the preterm-born group without BPD and for the BPD_{28} and BPD_{36} groups the mean differences (and 95% CIs) for %FEV_1 compared with term-born controls were −7.2% (−8.7% to −5.6%), −16.2% (−19.9% to −12.4%) and −18.9% (−21.1% to −16.7%), respectively. Pooling all data on preterm-born subjects whether or not there was a control group gave a pooled %FEV_1 estimate of 91.0% (88.8% to 93.1%) for the preterm-born cohort without BPD, 83.7% (80.2% to 87.2%) for BPD_{28} and 79.1% (76.9% to 81.3%) for BPD_{36}. Interestingly, %FEV_1 for BPD_{28} has improved over the years.

Conclusions %FEV_1 is decreased in preterm-born survivors, even those who do not develop BPD. %FEV_1 of survivors of BPD_{28} has improved over recent years. Long-term respiratory follow-up of preterm-born survivors is required as they may be at risk of developing chronic obstructive pulmonary disease.

Key messages

What is the key question?

- Is percentage forced expiratory volume in 1 s (%FEV_1) lower in later childhood and adulthood in preterm-born subjects (<37 weeks gestation), with or without bronchopulmonary dysplasia (BPD), compared with term-born subjects (≥37 weeks)?

What is the bottom line?

- Preterm-born subjects of <37 weeks who do not develop BPD in infancy have moderate deficits of %FEV_1 of approximately −7.2% compared with term-born controls; infants who develop BPD, defined as supplemental oxygen dependency at 28 days of age or until at least 36 weeks postmenstrual age, have greater deficits in %FEV_1 of −16.2%, and −18.9%, respectively, compared with term-born controls.

Why read on?

- Our findings suggest that all preterm-born survivors are at risk of long-term deficits in %FEV_1; however; there has been an improvement in %FEV_1 over the last three decades for the group with supplemental oxygen dependency at 28 days.

INTRODUCTION

Evidence suggests that being born preterm has adverse effects on later lung function, especially if associated with the development of bronchopulmonary dysplasia (BPD) in infancy.[1 2] BPD, often also called chronic lung disease of prematurity, is a common disease of extremely preterm-born infants characterised by prolonged supplemental oxygen dependency and dysregulated lung growth. While there have been several studies of lung function outcomes in preterm-born subjects, most have focused on those who developed BPD. Some studies have investigated later lung function outcomes of low birth weight infants (<2.5 kg) but do not distinguish between preterm-born and term-born infants with evidence of intrauterine growth restriction.[3] It is clearly important to distinguish between the two as different mechanisms lead to lung function deficits.

Studies reporting respiratory outcomes of preterm birth have produced inconsistent results, which may be explained partly by poorly defined populations, including comparison groups, differences in the gestational ages of the preterm-born subjects and methodological differences. Furthermore, there have been temporal changes in the medical management of preterm-born infants, especially the routine use of antenatal corticosteroids, introduction of surfactant therapy and gentler modes of mechanical ventilation that may have altered the relationship between prematurity, BPD and lung function over time.

Although a systematic review of outcomes in young adults (≥18 years) who had BPD in infancy has recently been published, a formal meta-analysis

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was not possible due to the heterogeneous nature of the studies.[4] To our knowledge, there has not been a systematic review with meta-analyses of all studies reporting later percentage predicted forced expiratory volume in 1 s (%FEV_1) for children or adults born preterm with or without BPD. We therefore conducted a systematic review to determine whether %FEV_1 in later childhood and adulthood is lower in preterm-born subjects (<37 weeks gestation) with or without BPD compared with term-born subjects (≥37 weeks gestation).

METHODS

We developed a search strategy using the keywords and medical subject headings (MeSH) terms given in online supplementary appendix 1 for eight databases: CINAHL, Embase, HMIC Health Management Consortium, Medline, Scopus, OpenSIGLE, Web of Knowledge (Science Citation Index Expanded, Social Science Citation Index, ISI proceedings). The databases were searched in May 2010 and October 2011. Websites of Action Medical Research, SPARKS and the Wellcome Trust were also searched and references in the included studies were also screened for inclusion.

Eligibility criteria

Published studies were eligible for inclusion if they reported %FEV_1 in later life for preterm-born infants, defined as a gestation of <37 weeks, with and without BPD. The comparison with infants born at term, defined as a gestation of ≥37 weeks, was made by comparing with a contemporaneous term-born control group; comparison was also made using historical controls by using the percentage predicted values with the notional 100% representing an average in the population. We included only papers which had already calculated the percentage predicted FEV_1 and did not discriminate on the basis of which reference values were used, assuming the authors would have used the most appropriate reference values for their populations. We included studies that recruited based on the subjects' birth weight, but only included studies which reported the %FEV_1 of preterm-born infants (whether recruited on gestational age or birth weight). BPD was defined as dependence on supplementary oxygen either at 28 days of life or at 36 weeks postmenstrual age (PMA). Childhood was defined as <18 years and adulthood ≥18 years of age. The lung function measure primarily studied was %FEV_1 obtained by spirometry, hence mainly used for children ≥5 years. Studies that reported other measures of lung function were eligible but were not included in the meta-analyses. Studies in all languages and from all countries were included.

Study selection

Two reviewers (SJK and MOE) independently screened each reference title and abstract (if available) using the inclusion criteria. Complete papers were obtained for those that met the inclusion criteria. Abstracts that did not meet the inclusion criteria were excluded. Both reviewers then screened the full paper against the inclusion criteria. For any disagreement, a third reviewer (SK) made a final decision.

Data collection process

A data extraction form (see online supplementary appendices 2 and 3) was initially piloted independently on 10 papers by SJK, WJW, SP, FD, SK and MOE. SJK and MOE extracted data from the remaining articles. The authors of articles were contacted if possible for further details if the information was presented only graphically or if the data were not extractable (eg, if data for term-born and preterm-born children were combined). Multiple articles from the same cohort were reviewed by SK and SJK and the article reporting the most complete data from the highest number of subjects was included in the analysis. Data from included papers were extracted and entered into Review Manager V.5.1 and STATA V.10 (Stata Corporation, Texas, USA) for analysis.

Assessment of study quality and risk of bias

A proforma shown in online supplementary appendix 3 was used to assess study quality based on relevant criteria from the Newcastle Ottawa criteria and the Cochrane risk of bias tool, focusing on the risks of selection, measurement and attrition bias. This was piloted and data extracted as detailed above. Each study was assessed and scored for representativeness of the cohort, appropriate selection of the non-exposed group, exposure ascertainment and demonstration that the outcome of interest was not present at the start of the study, outcome assessment and adequacy of follow-up. The minimum possible score was 6 and the maximum possible score was 20.

Outcome measures

Mean %FEV_1 was the principal outcome.

Statistical analysis

Statistical analyses were performed using Review Manager for studies including a term-born control group and STATA for pooling all the data on preterm-born subjects, with or without a control group. The method of Hozo *et al* was used to convert the medians to means where possible for included articles reporting median values.[5] For graphically presented data, the graphs were read as accurately as possible.

After initial exploration of the data we used random effects meta-analyses to provide a pooled estimate of the mean difference in %FEV_1 between preterm-born subjects and term-born controls to allow for heterogeneity for the following groups:

1. Preterm-born subjects without BPD.
2. BPD_{28} (defined as supplemental oxygen dependency at 28 days of life in preterm-born infants).
3. BPD_{36} (defined as supplemental oxygen dependency at 36 weeks PMA in preterm-born infants).
4. Preterm-born subjects (general populations which may include BPD cases).

Separate analyses were performed for those studies that included term-born controls and those not including term-born controls but reporting %FEV_1 based on historical control (reference value) data. For the latter, separate meta-analyses provided pooled estimates of the mean %FEV_1 for preterm-born subjects; this could be compared with 100% as a notional control mean.

Studies which presented FEV_1 results not expressed as percentage predicted were excluded as insufficient information was available to calculate predicted values. We performed a sensitivity analysis to assess the effect of study quality by including only studies which scored ≥12 in each grouping. A funnel plot was used to assess if there was a risk of publication bias. We also explored if there was an association between year of birth, surfactant use or age at time of FEV_1 testing and later %FEV_1 using linear weighted regression in the BPD groups only. The studies were weighted inversely by the variance of the estimate of the mean. Linearity was checked by examining residuals. In studies which recruited subjects over a number of years, we used the midpoint between the first and last year of birth in the analysis.

RESULTS

Study selection

The search strategy identified 8839 titles and abstracts; 1124 full articles were screened and 206 met the inclusion criteria (figure 1). Of these papers, 59 studies reporting on $\%FEV_1$ for the preterm-born groups were included in the meta-analysis (E1–29, E51–E60, E71, E73–92; online supplementary data). Some were included in more than one analysis. Twenty-eight studies compared a term-born group with a preterm-born group without BPD (E1–E29; online supplementary data); 24 with a BPD_{28} group (E3, E4, E10, E14, E16, E18, E19, E21, E23–E26, E28, E29, E51–E60; online supplementary data); 15 with a BPD_{36} group (E1, E5, E6, E8–E13, E15, E16, E20, E22, E27, E29, E71; online supplementary data); and 34 with a general preterm-born group (including some subjects with BPD) (E1–E4, E6, E7, E9, E14, E15, E17, E20, E22, E24, E26, E73–E92; online supplementary data). Five of the 1124 full articles were excluded as the FEV_1 was not reported as percentage predicted values. Five of 10 articles reporting median $\%FEV_1$ were included as means could be calculated and are included in the 59 included studies.

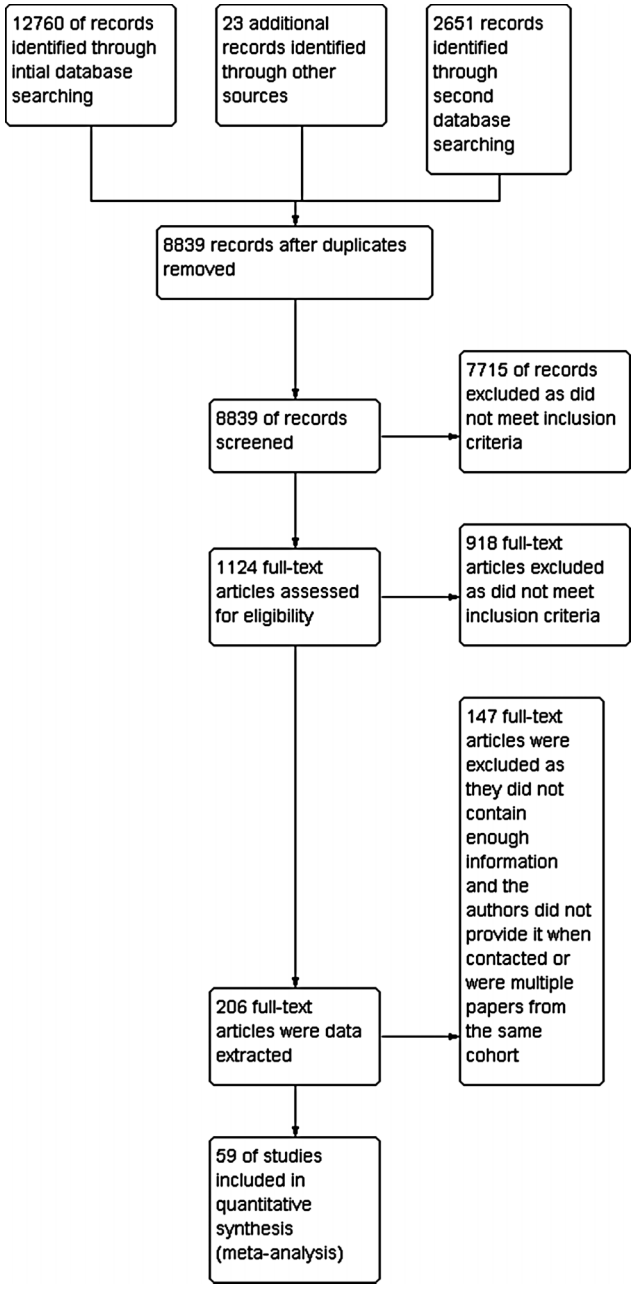

Figure 1 Study selection results.

Study characteristics

The characteristics of the included articles are given in online supplementary tables E1–E4. Studies included subjects born between 1964 and 2000; their ages ranged from 5 to 23 years and the preterm-born subjects were born between 24 and 36 weeks gestation. Term-born control groups in general were of a similar age to the preterm-born children. For the preterm-born subjects, rates of ventilation and surfactant administration varied widely.

Risk of bias across studies

Overall, the studies were of moderate quality with scores ranging from 6 to 19 (median 12). Across the studies there was a moderate risk of selection bias. In 33 studies no information was given about how gestation at birth was measured, so possibly there was a high risk of bias in the domain of exposure ascertainment. In 16 studies data were collected retrospectively so exposure ascertainment would not have been independent of outcome status. In the majority of studies no description was provided about how outcomes were ascertained, so it was not possible to reliably judge the potential for risk of bias in this domain.

Synthesis of results

The primary comparison was between preterm-born and control groups as some of the sources of heterogeneity are removed by this within-study comparison. In the preterm-born group without BPD, the mean difference for $\%FEV_1$ was −7.2% (95% CI −8.7% to −5.6%) compared with term-born controls. The comparisons between the BPD and term-born groups showed larger differences (mean difference for BPD_{28} and BPD_{36} groups −16.2% (95% CI −19.9% to −12.4%) and −18.9% (95% CI −21.1% to −16.7%), respectively). The mean difference for $\%FEV_1$ was −8.7% (95% CI −11.0% to −6.4%) for the preterm-born subjects (including BPD cases) compared with term-born controls (figures 2–5).

Pooling all the data on preterm-born subjects whether or not there was a control group gave a pooled estimate of the mean $\%FEV_1$ of 91.0% (95% CI 88.8% to 93.1%) for the preterm-born cohort without BPD, 83.7% (95% CI 80.2% to 87.2%) for the BPD_{28} group, 79.1% (95% CI 76.9% to 81.3%) for the BPD_{36} group and 89.4% (95% CI 87.0% to 91.7%) for the preterm-born subjects (including BPD cases) (see online supplementary figures E1–E4). These differences using 100% as a notional comparator were slightly larger than when comparing with a control group. Including studies which estimated means from the medians had little impact on the results.

Additional analysis

Funnel plots showed a low risk of publication bias. Including only the higher quality articles made very little difference to the results (see online supplementary data). We examined the effect of year of birth, surfactant use and age at lung spirometry on later $\%FEV_1$ in the BPD groups only. Age at time of FEV_1 testing appeared to have little effect on later $\%FEV_1$ (data not shown). Additional information would be obtained from longitudinal studies, but there were insufficient numbers of these studies to reach a reliable conclusion. There was inadequate data to examine the effect of surfactant. $\%FEV_1$ for the BPD_{28} group may have improved over the years (figure 6).

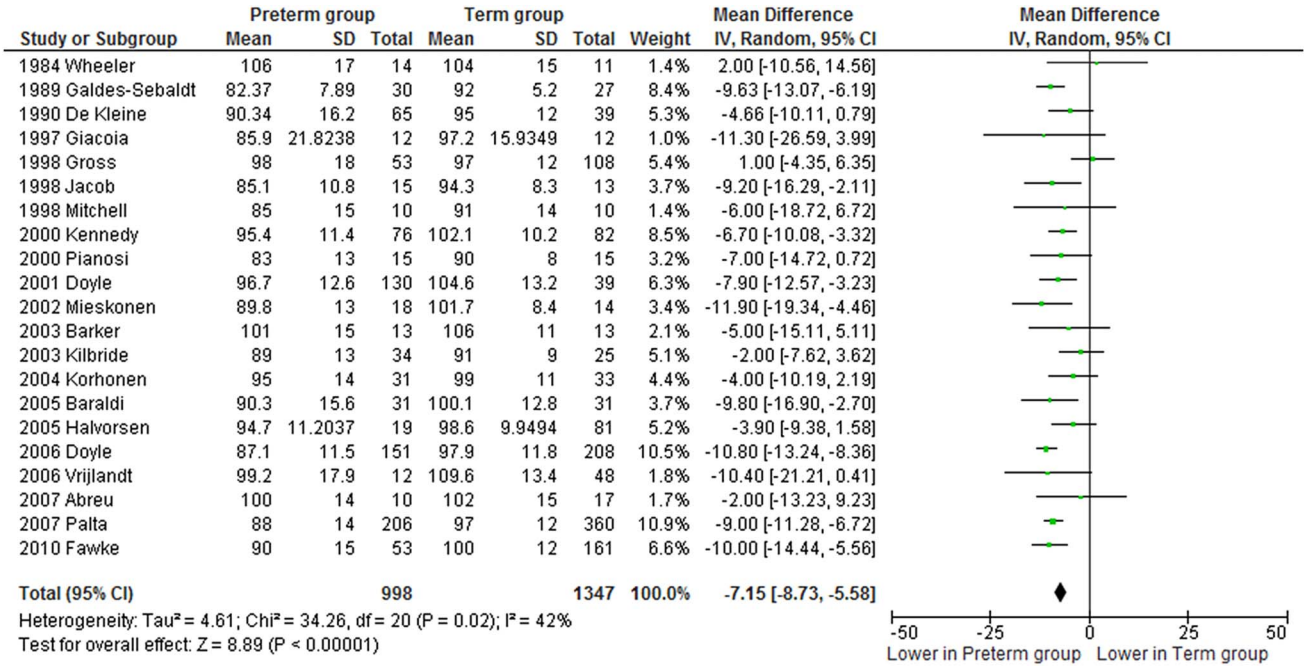

Figure 2 Percentage predicted forced expiratory volume in 1 s (%FEV_1) of the premature group (no bronchopulmonary dysplasia, BPD) compared with term control group.

The estimated change per year of %FEV_1 for the BPD_{28} group was 0.57% and 0.01% for the term-born controls. No such improvement was apparent in the BPD_{36} group, although there were fewer studies reporting this outcome (data not shown).

DISCUSSION

Summary of evidence

To our knowledge, this is the first systematic review and meta-analysis that included all available evidence on later %FEV_1 of preterm-born infants with and without BPD, although a previous descriptive systematic review reported lung function in adult survivors of BPD.[4] With increasing rates of preterm births[6] and improved survival, it is important to investigate the long-term consequences associated with being born during a critical stage of lung development.[7] Our analyses show that preterm-born subjects without BPD had moderate deficits in their %FEV_1 of approximately −7.2%, while the BPD_{28} and the BPD_{36} groups had greater deficits in %FEV_1 of −16.2% and −18.9%, respectively. It is of great interest to note that there was an improvement in %FEV_1 over the three decades in the BPD_{28} group.

Prematurity is associated with delivery at an immature stage of lung development, especially for the very preterm-born infants born at <32 weeks gestation,[7] but even those born at <37 weeks are vulnerable to increased rates of respiratory illness in infancy.[8] The modern management of preterm-born

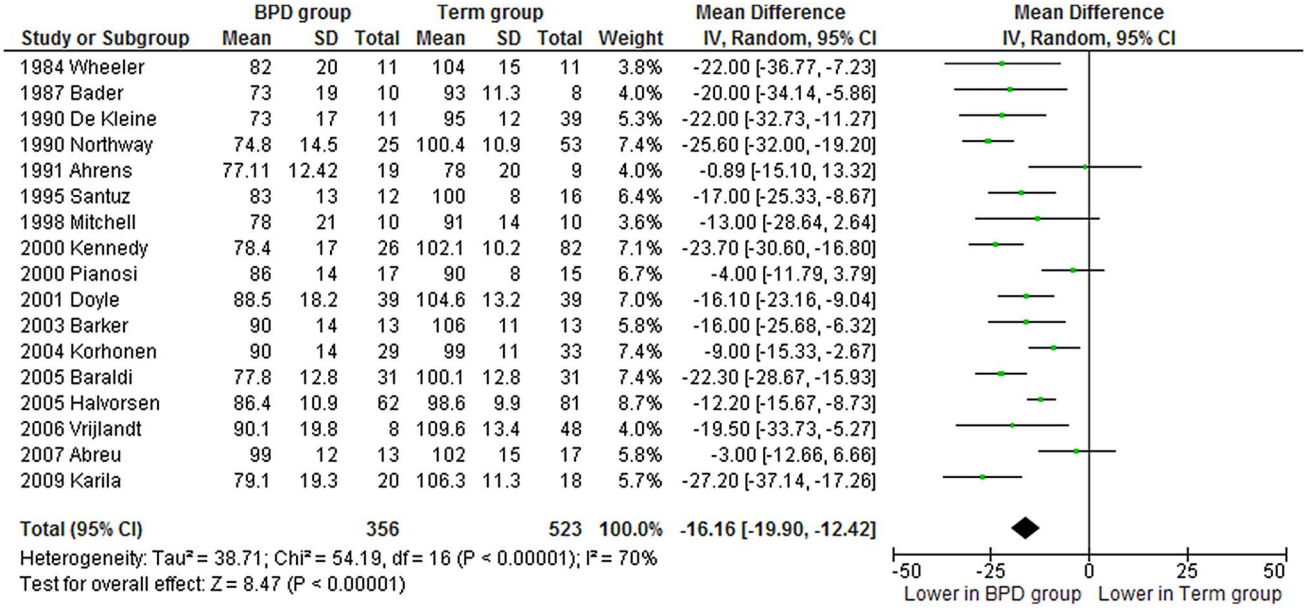

Figure 3 Percentage predicted forced expiratory volume in 1 s (%FEV_1) of the bronchopulmonary dysplasia (BPD) group (supplemental oxygen-dependency at 28 days of life) compared with term control group.

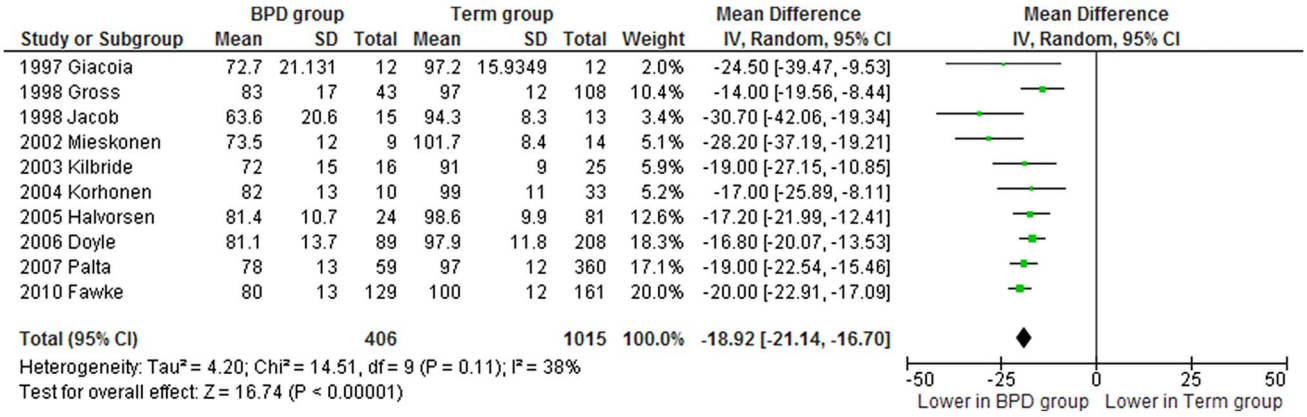

Figure 4 Percentage predicted forced expiratory volume in 1 s (%FEV_1) of the bronchopulmonary dysplasia (BPD) group (supplemental oxygen dependency 36 weeks postmenstrual age) compared with term control group.

infants, including the routine use of antenatal corticosteroids, surfactant treatment and gentle mechanical ventilation, has undoubtedly improved survival, especially of more immature infants, and has possibly led to improved later %FEV_1. Perhaps not surprisingly, preterm-born infants who develop BPD in infancy continue to have respiratory function deficits as has been consistently reported in many studies. However, of particular note is the improvement in %FEV_1 for the BPD_{28} group over the decades despite survival of increasingly preterm-born infants. While our data suggest that %FEV_1 may have improved in the BPD_{28} group over the last few decades, the data need to be interpreted with caution as other factors such as selection bias of the worst survivors of prematurity and small numbers, especially for the early studies, may explain the reported lower %FEV_1 values. Due to a smaller number of studies, confirmation was not possible for the BPD_{36} group. One possible factor for this potential improvement is the introduction of surfactant which improves lung compliance markedly in the neonatal period, but insufficient data were available to perform a meta-regression to assess its role in future lung function.

Barker's hypothesis postulates that low birth weight as a consequence of fetal undernutrition is associated with respiratory, cardiac and metabolic disease in adults.[9–11] However, low birth weight includes both immature infants of appropriate growth for gestation and growth retarded infants who may be physiologically mature at birth. Since the mechanisms that lead to %FEV_1 deficits are likely to be different in these two conditions, it is important to separate these in future studies. In our meta-analyses, preterm-born subjects without BPD had a deficit of −7.2%, which is significantly different from term-born infants. This is an important observation, especially as lung function is thought to track throughout life. Low lung function in early life is likely to lead to failure to attain peak lung function in early adulthood, and we speculate that the natural

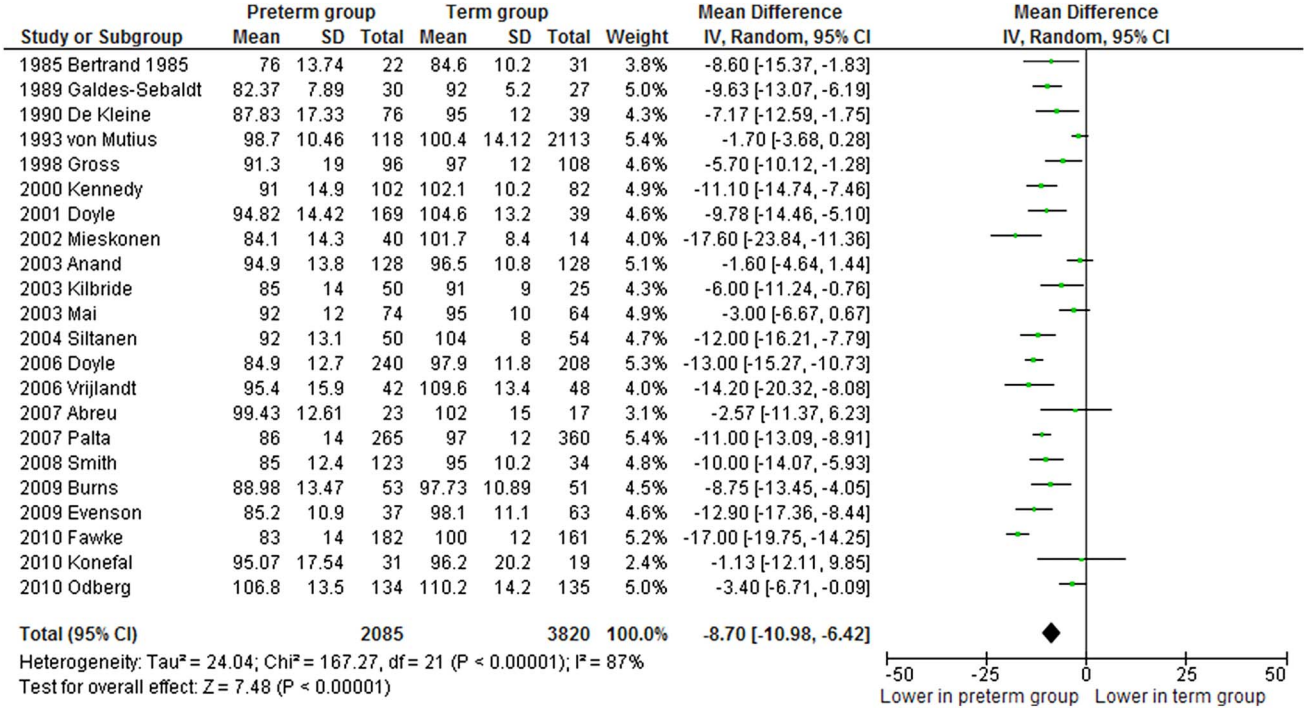

Figure 5 Percentage predicted forced expiratory volume in 1 s (%FEV_1) of the preterm group (including groups with bronchopulmonary dysplasia, BPD) compared with term control group.

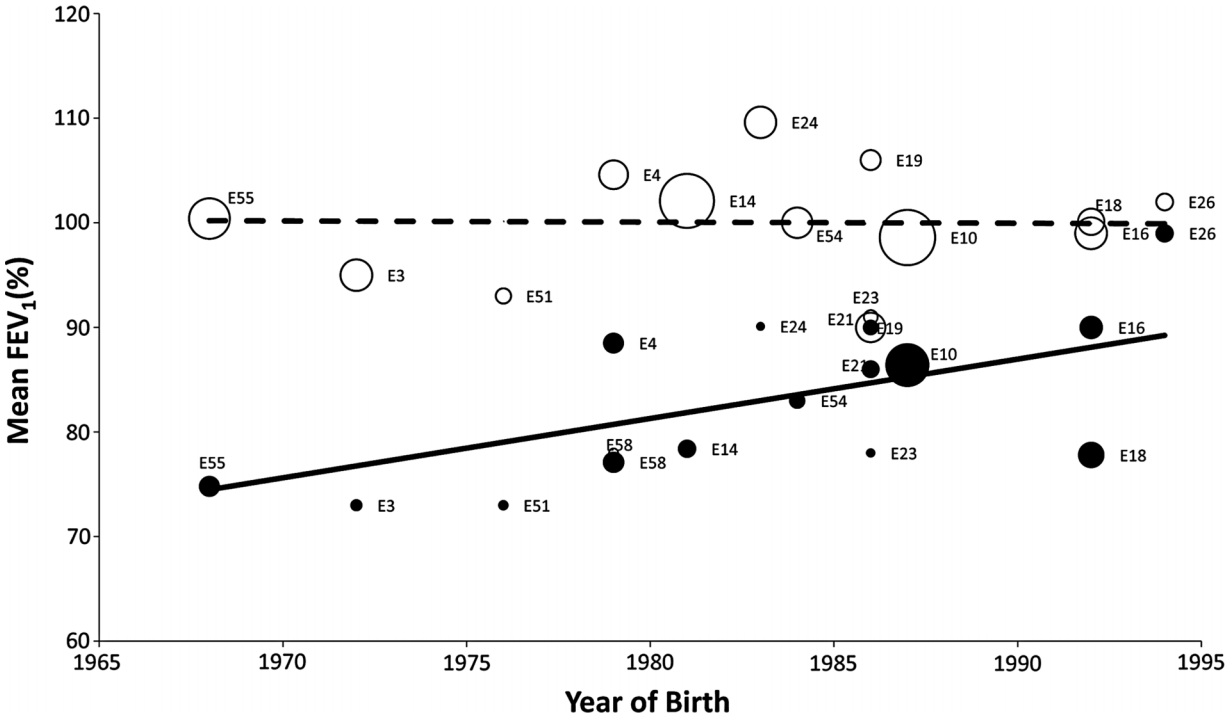

Figure 6 Effect of year of birth on percentage predicted forced expiratory volume in 1 s (%FEV_1) for the bronchopulmonary dysplasia (BPD) group supplemental oxygen dependency at 28 days (closed circles) and the term control group (open circles). Weighting was based on two separate models, one for the BPD_{28} group and one for the term control group. Weighting was defined by variance which differs for the term control and BPD_{28} group. Bubble sizes show relative contributions based on individual weighting of term control and BPD_{28} group. The E-numbers refer to references which are given in the online data supplement.

decline in %FEV_1 from that point onwards will be accelerated by any additional injuries encountered by preterm-born subjects may encounter, for example, tobacco smoking. There is increasing interest in the possibility that chronic obstructive pulmonary disease (COPD) may have its origins in such early life events.[12]

Preterm-born children (with and without BPD) may experience increased respiratory symptoms often reported as asthma and have increased reported bronchodilator use and increased health utilisation including hospitalisation, especially in early childhood.[13] Children who had BPD in infancy may also have increased exercise-induced bronchoconstriction and, importantly, may have reversible bronchoconstriction at rest, as recently reported.[7 14] It is not currently known whether the deficit in %FEV_1 shown for preterm-born subjects without BPD is reversible. We would also have liked to investigate further the influence of gestational age on later %FEV_1, but we were unable to classify the group of preterm-born infants without lung disease into different gestational groups as data were not available. It is likely, as we recently reported, that different gestational groups including the very preterm-born and moderately preterm-born groups (33–34 weeks gestation) have greater deficits of lung function in later life than those born at 35–36 weeks gestation.[15 16] In addition, even infants identified as having BPD will have been exposed to ever-changing interventions and also changing pathology of 'old' versus 'new' BPD. Our data on changes in %FEV_1 over the last 2–3 decades shows an improvement, which may reflect improvements in the management of these infants but may also reflect the changing pathology of the underlying multifactorial disease we recognise as BPD. Identifying the deficits in lung function is important as children born preterm may have life-long consequences including being potential candidates for the development of COPD, especially if they are exposed to noxious substances such as tobacco smoke or increased environmental pollution. Furthermore, it is unclear if the deficits in %FEV_1 that we have reported are translated into increased respiratory symptoms or, indeed, are reversible with bronchodilators. However, it is clear that further studies are required to determine whether these children and young adults would benefit from closer follow-up and treatment in childhood and beyond.

Study limitations

Since some studies did not include a control group but reported %FEV_1 against prevalent reference values at the time of publication, we performed two separate analyses to compare the results obtained when comparisons with a term-born control group or with historical reference values were reported. The pooled effects for the latter were slightly greater and, as expected, there was greater heterogeneity between the studies as systematic differences between populations and methods of calculating predicted values affect this synthesis. In addition, the reference values used may not be contemporaneous, changing only every few decades; and we accepted the reference values used and have not attempted to standardise them which could be another source of heterogeneity. As with all systematic reviews, we were limited by the quality and quantity of information presented in the included articles. This led us to exclude five papers where the results were presented as medians. Further studies which did not report results as percentages of predicted values were also excluded. In a small number of articles we estimated %FEV_1 results from graphically presented data which may have led to small errors, but these are unlikely to have a major effect on the findings. We were only able to contact the authors of the recently published articles, which may be another source of

bias. The articles included were heterogeneous, as expected. This could arise for many reasons. The subjects were of different ages when FEV_1 was measured, although age did not appear to influence $\%FEV_1$ at least for the BPD analyses. An additional factor that may have influenced the results is the age of the child at testing as age is independently associated with FEV_1 (E39). However, since our initial analyses included only papers containing a control group, this influence of age is unlikely to have affected our conclusions. Subjects were born in different decades and treatments have changed over time, which may have led to cohort effects. For example, in some studies a proportion of infants were treated with surfactant to improve their infant lung function, survival and prevent lung injury. The methods for calculating percentage predicted FEV_1 varied between studies. We acknowledge that the preterm-born group containing BPD cases is a very heterogeneous group. The results from this group should be treated with caution, although they were broadly consistent with the results in the tightly defined preterm without BPD population. The other three groups are defined more precisely and included only preterm-born subjects from studies which clearly identified the BPD status. We were therefore able to categorise confidently the preterm-born subjects into groups for analysis.

CONCLUSIONS

This comprehensive systematic review has quantified the deficits in $\%FEV_1$ in later life of a number of different groups of subjects born preterm and has shown that, even in subjects without BPD, later $\%FEV_1$ is lower than in the population born at term. Future research should follow up these cohorts into middle age and beyond to see if these $\%FEV_1$ deficits translate into higher rates of COPD. Efforts should also be made to identify subgroups at higher risk of poorer lung function in later life and to devise interventions to ameliorate the impact of being born preterm.

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Contributors All authors led by SK were involved in the concept and protocol design of the systematic review. SJK and MOE screened the titles and abstracts and data extracted the articles. FD and WJW were primarily responsible for statistical analyses. SP was primarily involved in the interpretation of the quality data. All the authors contributed to interpreting the results. SJK wrote the initial drafts of the paper to which all the authors contributed. SK is the guarantor.

Competing interests None.

Ethics approval Ethics approval was not required as this is a systematic review using previously published studies and no new subjects were studied.

Provenance and review Not commissioned; externally peer reviewed.

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The effect of preterm birth on later forced expiratory volume in one second - a systematic review and meta-analysis

- a systematic review and meta-analysis

Sarah J Kotecha, Martin O Edwards, W John Watkins, John Henderson, Shantini Paranjothy, Frank D Dunstan, Sailesh Kotecha.

ONLINE DATA SUPPLEMENT

Analysis including only the higher quality articles

In the preterm-born group without BPD, the mean difference for $\%FEV_1$ was -6.9% (95%CI -8.7%, -5.1%) compared to term-born controls. The comparisons between the BPD and term-born groups; mean difference for BPD_{28} and BPD_{36} groups were -16.4% (95% CI -20.9%, -11.9%) and -18.9% (95%CI -21.1%, -16.7%). The mean difference for $\%FEV_1$ was -9.0% (95%CI -11.4%, -6.5%) for the preterm-born subjects (including BPD cases) compared to term-born controls.

Table E1a:- Description of the included articles preterm group (no BPD) compared to term control group

STUDY	QUALITY SCORE	OBJECTIVE	STUDY DESIGN	STUDY GROUP	CONTROL GROUP	OUTCOME MEASURES
Fawke[E1]	16	To assess the degree of respiratory morbidity and in extremely premature children in relation to current clinical status and neonatal determinants.	Cohort study	182 EP (≤25 weeks gestation) 53 with no BPD	161 classmate controls excluded classmates who were preterm	Spirometry Post-bronchodilator response Questionnaire
Arad[E2]	8	To compare lung function following neonatal intensive respiratory care on the same children in infancy and childhood	Follow up study	10 PT	X	Spirometry
De Kleine[E3]	18	Examine the effect of lung injury caused by IPPV for HMD on lung function in children	Follow up study	40 PT ventilated for HMD (29 non BPD 27 with LF results) and 38 PT non ventilated with HMD	39 randomly selected pupils of a similar age	Spirometry Respiratory symptoms questionnaire Review of follow up records for PT
Doyle[E4]	19	To determine the respiratory health of children of birthweight <1501g, compared to NBW controls in adolescence	Cohort study	180 VLBW (<1501g) -130 no BPD with spirometry results	42 NBW (>2499g), 39 with spirometry results	Spirometry Assessment of respiratory health
Kulasekaran[E5]	14	To determine the	Cohort	45 PT children	X	Respiratory outcome

		respiratory outcome of children who had BPD compared with a preterm control group of children at school age.		(44 with LF results)		Family History
Doyle[E6]	17	To determine respiratory function at 8 years in ELBW, very PT children born in the 1990s compared with NBW controls	Cohort	298 ELBW (<1000g)/ very preterm (< 28 weeks gestation) 240 with LF results of which 151 with no BPD	208 NBW (>2499g)	Spirometry ISAAC questionnaire
Galdes-Sebaldt[E7]	11	To evaluate the long-term effect of prematurity and/or HMD on pulmonary function and airway reactivity.	Follow up study	30 <1500g children split into 2 groups no HMD and HMD	27 terms	Spirometry Questionnaire Airway reactivity
Giacoia[E8]	12	To investigate the outcome of school-age children with BPD compared to a preterm cohort and term control group	Cohort	12 PT	12 Term Controls	Spirometry Body Composition Dietary intake Intelligence test scores
Gross[E9]	19	To assess long-term pulmonary outcome of a regional cohort of children born <32 weeks' gestation compared with a matched term control group	Cohort	125 PT children born at 24 to 31 weeks gestation. 53 without BPD had spirometry	108 healthy term (38 to 42 weeks gestation) controls	Spirometry Bronchodilator responsiveness Ongoing health problems Rehospitalisation Respiratory symptoms Exercise testing
Halvorsen [E10]	15	To investigate long term	Population-	2 population	81 term	Spirometry

		outcomes in young people after extremely preterm birth and BPD	based long-term follow-up study	based cohorts ≤ 28 weeks gestation or ≤ 1000g birthweight 19 with no BPD	controls birth weight between 3 and 4 kg	ISAAC questionnaire Metacholine provocation test Exercise induced asthma and reversibility to salbutamol Allergy testing
Smith[E11]	9	The aim of the study was to investigate the role of neonatal influences including post-natal corticosteroids and a diagnosis of BPD, on long-term respiratory outcomes in a group of children born very preterm in the 1990s.	Cross-sectional study	102 PT children 65 no BPD	X	Spirometry ISAAC questionnaire
Jacob[E12, E13]	15	To evaluate the long-term pulmonary sequelae of survivors of BPD of sufficient severity to have required oxygen for at least one month after term.	Cohort study	30 PT children 15 no BPD	13 healthy term children	Bronchial symptom questionnaire Spirometry Lung elastic recoil pressure Response to a bronchodilator
Kennedy[E14]	15	To assess the importance of the contributions of birth weight, gestational age, neonatal respiratory illness, and its treatment on subsequent childhood lung function in a cohort of children of birth weight less than 1500g.	Cohort study	VLBW cohort (<1500g) 76 no BPD	82 control children , 1 birth weight <2kg, 2 born at 36 weeks rest at term	Spirometry Respiratory questionnaire
Kilbride[E15]	14	To assess pulmonary function and exercise	Longitudinal follow up study	50 ELBW children <801g	25 age matched NBW children	Medical history and recent Hospitalisations

		capacity of apparently asymptomatic children who were born EP		34 no BPD	>37 weeks gestation and >2500g BW	Spirometry Exercise testing
Korhonen[E16]	16	To assess respiratory outcome and its predictors during the surfactant era in VLBW schoolchildren with and without BPD	Cohort	VLBW cohort (<1500g) 34 no BPD of which 31 had spirometry results	34 term controls of which 33 had spirometry results	Spirometry Mailed questionnaire Atopic tendency testing
Baraldi[E17]	12	To assess the cardio-respiratory and metabolic response to exercise in VLBW children and to compare exercise performance in AGA versus SGA	Area cohort study	15 VLBW children (<1501g)	26 born at term but data not given for spirometry	Spirometry Questionnaire Exercise testing
Baraldi [E18]	11	To measure exhaled nitric oxide and lung function in a group of school-age survivors of BPD.	Cohort study	31 non BPD, PT	31 healthy children born at term matched for sex and age	Spirometry Reversibility to $ß_2$ -Agonists Allergometric study
Barker[E19]	16	To assess the long-term outcome in respiratory morbidity, lung function, submaximal, and peak exercise capacity among a local cohort of school children with a history of treatment in a NICU after preterm birth at VLBW	Area cohort study	13 no BPD, VLBW birth weight < 1500g, and PT birth <37 weeks	13 healthy children born at term matched for age, height and weight	Spirometry Interview on respiratory history and morbidity Exercise testing
Mieskonen[E20]	13	To evaluate the possible inflammatory basis of lung function abnormalities	Cohort study	40 children with a gestational age ≤ 30 weeks or	14 term controls	Spirometry Questionnaires Skin Prick Tests Measurement of exhaled

				birthweight <1500g 18 no BPD		nitric oxide Spirometry before and after Salbutamol
Pianosi[E21]	11	To assess the hypothesis that there would be no significant difference in childhood lung function between patients who were ventilated by conventional or high frequency ventilation.	Cohort study	15 non BPD	15 term born matched controls	Spirometry Bronchodilator responsiveness
Palta[E22]	15	To determine lung function at 10 years in VLBW children and controls	Cohort study	265 VLBW children ≤ 1500g 206 without BPD	360 unselected controls	Spirometry Home spirometry
Mitchell[E23]	11	To test the hypothesis that gas transfer during exercise is reduced in survivors of BPD relative to age-matched control subjects	Cohort study	10 no BPD	10 similar age born full term controls	Spirometry Exercise testing Questionnaire
Vrijlandt[E24]	14	To investigate the long term effects of prematurity on lung function and exercise capacity	Prospective cohort study	12 no BPD (gestational age <32 weeks and/or birthweight under 1500g)	48 healthy term controls	Spirometry Exercise testing
Wheeler[E25]	7	To assess and compare lung function in BPD, RDS, PT and term children	Case control study	14 PT	11 normal term delivery children	Spirometry
Abreu[E26]	14	To investigate cardio respiratory capacity and investigate the presence	Case control study	13 PT children 10 with LF results	20 term children 17 with LF results	Spirometry Exercise testing

		of exercise-induced bronchospasm among children with BPD				
Guimaraes[E27] (Data as Medians in paper)	8	To assess pulmonary function and the prevalence of atopy in school age children who were VLBW and to compare those who had BPD to those who did not.	Cohort study	85 VLBW children 64 with no BPD had LF results	X	Spirometry Questionnaire Allergy skin prick test
Hakulinen[E28] (Data as Medians in paper)	13	To determine the extent to which BPD affects the diffusing properties of lung tissue in childhood.	Cohort study	11 PT children <1250g without BPD	20 healthy term children	Spirometry Questionnaire
Berggren Brostrom[E29] (Data as Medians in paper)	8	To examine the impact of the severity of BPD on pulmonary morbidity at school age	Cohort	60 VLBW children 28 with no BPD	X	Spirometry Oscillometry Thoracic HRCT Allergy skin-prick test Blood sample questionnaire

Table E1b:- Demographics of the included articles preterm group (no BPD) compared to term control group

STUDY COUNTRY	SUBJECTS (GENDER)	GA (WEEKS)	BW (GRAMS)	DURATION ON MECHANICAL	AGE TESTED (YEARS)	YEAR OF	SURFACTANT GIVEN	METHOD OF MEASURING LUNG	METHOD OF STANDARDISING

				VENTILATION (DAYS)		BIRTH		FUNCTION	LUNG FUNCTION MEASUREMENTS
Fawke[E1] **UK and Ireland**	No BPD (20M, 33F), Controls (43% M)	No BPD mean 25.1, SD 0.6 Control X excluded if preterm	No BPD mean 780, SD 120, Controls X	X	Range 10.1 to 12.1. EP No BPD mean 10.9, SD 0.4. Controls mean 10.9 SD 0.55.	1995	No BPD 39/53 Controls X	Portable spirometer (Jaeger Masterscope, Lab Manager, V4.65; CareFusion, Hoechberg, Germany	Spirometry data were expressed as z-scores to adjust for height, age and sex[E30, E31]
Arad[E2] **Israel**	X	PT group mean 30.4, range 28-35	PT 1257g Range 900-1900	8 for between 1 and 11 days, 4 being ventilated for 4 or more days	Mean 6.8 years SD 0.6	1977-1979	X	Pneumotachograph-based system (Hewlett-Packard 47120A Pulmonary Desk System)	Expressed as percentage predicted[E32]
De Kleine[E3] **The Netherlands**	29 non BPD (19M, 10F), 38 non ventilated (24M, 14F), 39 controls (20M, 19F)	Non BPD mean 32.2 SD 1.8, Non ventilated mean 31.8 SD 1.9, Controls X	Non BPD mean 1952 SD 460, Non ventilated mean 1809 SD 419, Controls X	Non BPD 29/29 mean 2.9 days (range 0.8-6.9), non ventilated 0/38, Controls X	Non BPD mean 12.3 SD 2.9, Non ventilated mean 12.8 SD 2.7, Controls mean 13.7 SD 1.6	1967-1977	X	Water sealed spirometer (Lode instruments, Groningen, Netherlands)	Lung function as percentage predicted for sex and height [E32, E33]
Doyle[E4] **Australia**	500-999g group (35M, 43F), 1000-1500g group (55m, 47F)	500-999g group mean 27.5 SD 2.3, 1000-1500g group mean 29.6 SD 1.5, >2499g	500-999g group mean 859 SD 100, 1000-1500g group mean 1259 SD 145, >2499g	X	500-999g group mean 14.1 SD 0.2, 1000-1500g group mean 14.2 SD 0.3, >2499g	1977-1982	Not given	Jaeger Bodyscreen II-Bodybox (Jaeger, Germany)	Lung function as percentage predicted for age, height and gender [E34]

	>2499g group (26M, 16F)	group mean 39.9 SD 1.0	group mean 3420 SD 427		group mean 14.2 SD 0.1				
Kulasekaran[E5] Australia	PT group (22M, 23F)	PT group mean 28.3 SD 1.0	PT group mean 1090 SD 210	PT 30/45, days of mechanical ventilation median 1, IQR 0-3	7-10	1989-1990	0/45	Pulmonary function laboratory system (Sensormedics, Yorba Linda, CA, USA	Spirometry data was expressed as percentage predicted values for height, age and gender[E35]
Doyle[E6] Australia	No BPD X, Control group (98M, 110F)	No BPD group mean 27 .2, SD 2.0 Control group X	No BPD group mean 912, SD 143, Control group Control group >2499	X	8-9	1991-1992	In whole PT cohort 92/240 treated	Jaeger Body-screen II Bodybox (Jaeger, Germany)	Results expressed as percentage predicted for age, height and gender[E34]
Galdes-Sebaldt[E7] USA	<1500g no HMD group (11M, 8F), <1500g HMD group (3M,8F) Controls (14M, 13F)	<1500g no HMD group mean 29.3, SEM 0·4, range 26-32, <1500g HMD group mean 29.5, SEM 0.6, range 26-32, Controls mean 39.9, SEM 0.2, range 38-42	<1500g no HMD group mean 1044, SEM 30, range 900-1290, <1500g HMD group mean 1217, SEM 34, range 964-1361, Controls mean 3429, SEM 64, range 2707-4111	<1500g no HMD 13/19, <1500g HMD 9/11, Controls X	<1500g no HMD group mean 11.1, SEM 0.2, <1500g HMD group mean 11.2, SEM 0.2, Controls mean 11.6 SEM 0.2	1973-1977	X	Automated pulmonary function lab model M100B (SRL Medical Inc, Dayton, OH)	Results as percentage predicted adjusted for height and sex [E35] and ethnicity[E36]

Giacoia[E8] **USA**	PT group (5M, 7F), Controls (5M, 7F)	PT group mean 30.3 SD 1.54, Controls mean 40.07 SD 0.27	PT group mean 1162 SD 216, Controls mean 3663 SD 777	PT group mean 8 days, SD 6.4, Controls mean 0	PT group mean 12.3 SEM 2.6, Controls mean 11.9 SEM 1.6	1978-1986	X	SensorMedics model 2600 pulmonary function monitor (SensorMedics Corp)	Results as percentage predicted [X]
Gross[E9] **USA**	No BPD group (27M, 26F), Control group (62M, 46F)	No BPD group mean 29 SD 2, Control group mean 40.1 SD 1.1	No BPD group mean 1270 SD 306, Control group mean 3565 SD 427	55% of no BPD group median 6	7	1985-1986	0	SensorMedics 2200 Pulmonary Function Equipment (SensorMedics, Anaheim Calif)	Results as percentage predicted for age, height and sex[E37, E38]
Halvorsen[E10] **Norway**	No BPD (12F, 7M) Controls (42F, 39M)	No BPD mean 28.3 SD 1.5 Control group term	No BPD mean 1115.1 SD 158.5 Control group mean 3494 SD 300	No BPD mean 0.5 Range 0-4.8	2 populations assessed 2nd mean 10.6 SD 0.4 1st 17.7 SD 1.2	1982-1985 and 1991-1992	X	Vmax 22 spirometer (SensorMedics Inc., Anaheim, USA)	Expressed as percentage of the predicted values[E39]
Smith[E11] **Australia**	X	For whole preterm group all <32 weeks gestation mean 27 SD 2	For whole preterm group mean 862 SD 161	X	Mean age of BPD and No BPD groups together 10 SD 1	1992-1994	X	Vmax V62J Autobox (Sensormedics Corp, Yorba Linda, CA)	Expressed as percentage predicted[E40, E35, E41]
Jacob[E12, E13] **Canada**	No BPD (6M, 9F), Controls X	No BPD group mean 28.5 SD 2.6 Control group term	No BPD group mean 1044 SD 262.9 Control	No BPD group days of ventilatory assistance median 8.0,	No BPD group mean 11.2 SD 1.5 Control	1981-1987	X	X	Expressed as a percentage predicted for sex and height [E35]. For black subjects 15% was subtracted

			group X	IQR 4.0-32.0 Control group X	group 10.6 SD 2.1				from the predicted values for spirometry[E42]
Kennedy[E14] Australia	No BPD (33M, 43F) Control group (39M, 43F)	No BPD group mean 30.6 SD 2.5, Control mean 40.0 SD 1.6	No BPD group mean 1228.6 SD 204.6, Control group mean 3459.1 SD 509.0	Duration of IPPV No BPD group median 0.7 IQR 0.5, 1.0 Control n/a	No BPD group mean 11.3 SD 0.8, Control 11.4 SD 0.8	1981-1982	X	Pulmonary function testing was performed using the Jaeger Masterlab system	Results were evaluated as percentage predicted for gender and height[E34]
Kilbride[E15] USA	All ELBW (16M, 34F) Control (11M, 14F)	ELBW mean 261 SD 1.6 NBW >37	ELBW mean 701 SD 80 NBW >2500	ELBW mean 33 days SD 20 range 0-78	ELBW group mean 11.3, SD 1.6 NBW mean 11.1 SD 1.3	1983-1989	X	SensorMedics (Yorba Linda, CA), 922 dry, rolling seal spirometer	Expressed as a percentage predicted [X]
Korhonen[E16] Finland	No BPD group (21m 13F) Control group X	No BPD group mean 29 SD 2, range 25-35 Control group term	No BPD group mean 1132 SD 235, range 605-1490	No BPD group 23/34 ventilated duration median 3, range 0-44 days	No BPD group median 7.1 range 6.9-8.1 years Control group median 7.2, range 6.9-8.3	1990-1994	No BPD group 8/34 received	Flow volume spirograms were recorded by mass flow sensor (2200/Vmax 22, SensorMedics BV, Bilthoven, Netherlands)	Finish FVS reference values for children were used [E43].
Baraldi[E17] Italy	VLBW (6M, 9F)	VLBW mean 32.1 SD 3.0 range 28-37	VLBW mean 1287 SD 143 range 1000-1500	7/15 duration 1-8 days	VLBW mean 9.9 SD 1.8 range 7.8-12.2	1976-1979	X	101 water spirometer (Biomedin, Padova, Italy)	Expressed as percentage of reference values[E35]
Baraldi[E18] Italy	No BPD group (14M, 17F)	No BPD group mean 28.9 SEM 0.4	No BPD group mean 965 SEM 40	No BPD group 13/31 mean 2.6 days SEM	No BPD group mean 8.7 SEM 0.3,	1990-1994	No BPD group 7/31 Control group	Flow volume spirometry (Biomedin, Padova, Italy	Lung function as percentage of predicted values for

	Control group (14M, 17F)	Control group term	Control group X	0.7 days Controls X	Controls mean 8.4 SEM 0.4.		X		height and sex[E32]
Barker[E19] Germany	No BPD group (5M, 8F) Control group (8M, 5F)	No BPD group mean 33.5, range 30-36, control group term	No BPD group mean 1264, range 900-1490, Control group X	No BPD group mean 2.1 days, range 0-13, control group X	No BPD group mean 10.4 years (range 8-14), control group mean 10.5 years (8-12)	1983-1989	X	Baseline lung function was measured by standard spirometry and performed additional body plethysmography (Jaeger Body Screen II, Wurzburg, Germany)	Lung function as percentage predicted [X]
Mieskonen[E20] Finland	No BPD group (6M, 12F) Control group X	No BPD group median 27.6, range 25.3-30.9, Controls term	No BPD group median 960, range 727-1575 Controls X	39/40 PT children ventilated, No BPD group median 12 days range 1-39	No BPD group median 8.0 range 7.5-9.2 Controls median 8.9 range 5.3-11.2	1989-1991	X	Spirotrac III, Vitalograph Ltd, Buckingham, UK)	Expressed as percentage predicted [E35]
Pianosi[E21] Canada	Non BPD group (9M, 6F) Controls X	CMV non BPD median 29, IQR 28,30 HFV non BPD median 29.5 IQR 27.5, 31 Control term	CMV non BPD median 1140, IQR 1045, 1280 HFV non BPD median 1400, IQR 1038, 1765 Control X	CMV non BPD median 5.5 days, IQR 5,19 HFV non BPD median 11 days, IQR 6.5, 25 Control X	8-9	1986-1987	X	Spirometry measured in 6200 Autobox, Sensormedics, Yorba Linda CA	Results were expressed as percentage predicted using reference values[E32, E44, E 45]
Palta[E22] USA	No BPD 49% M	No BPD group mean	No BPD group mean	X	All VLBW mean 10.4	1988-1991	Not given for no BPD	Jaeger AM1 portable electronic peak flow	Expressed as percentage predicted

	Controls 56%	30 SD 2.5, Controls X	1178 SD 228 Controls X		SD 0.42, controls mean 9.6 SD 0.72			meter	ratios[E46]
Mitchell[E23] USA	No BPD group (6M, 4F) Control group (4M, 6F)	No BPD group mean 31, SD 3, Control group mean 40, SD 1	No BPD group mean 1421, SD 411 Control group mean 3157, SD 606	no BPD X, Control group X	No BPD group mean 7, SD 1, Term group mean 7, SD 1	1985-1987	X	Spirometry with a calibrated spirometer (SensorMedics 2200)	Results as percentage predicted based on height, gender and race using the standard equation[E41, E42]
Vrijlandt[E24] The Netherlands	No BPD group (12M, 0F) Control group (16M, 32F)	Whole PT group including no BPD group mean 30 SD 2, range 26-36, Control group term range 37-42	Whole PT group including no BPD group mean 1246 SD 232, range 720-1750, Control group X	Whole PT group including no BPD group mean 6.3 days SD 12, range 0-51, Control group X	Whole PT group including no BPD group mean 19 SD 0.3, range 19-20, Control group mean 20.8 SD 1.2, range 18-22	PT group 1983	0/42	Spirometry using a pneumotachograph	Results as percentage predicted based on height[E47]
Wheeler[E25] X	X	X	PT group mean 1506, SD 435,Control group mean 3540, SD 570	X	PT group mean 7.3, SD 0.6, Control group mean 8.3, SD 0.9	X	X	X	Results as percentage predicted [X]
Abreu[E26] Brazil	PT group (8M, 5F) Control	PT group mean 35 SD 2.3 range	PT group mean 1765 SD 621	PT group mean 1 SD 2 range 0-6	PT group mean 8·3 SD 1.11, Control	1993-1996	X	SpiroCard PC Card Flux spirometer (QRS Diagnostic-Plymouth,	Expressed as percentage predicted [E35]

	group (9M, 11F)	28-36 Control group term	range 850-2800 Control group X	Control group X	mean 8.2 SD 1.14			USA)	
Guimaraes [E27] X (Data as Medians in paper)	No BPD group (24M, 40F)	No BPD group median 30 range 26-35, mean 29.9 SD 2.4	No BPD group median 1210 range 655-1500, mean 1162 SD 875	No BPD group 55/64 ventilated median 10 days range 0-72, mean 15.72 SD 16.6	No BPD group median 92 months range 69-105 mean 84.7 SD 13.2	2002-2004	X	Compact Vitalograph, Buckingham, UK	Expressed as percentage predicted [E35]
Hakulinen[E28] Finland (Data as Medians in paper)	Non BPD group (4M,7F) Control group X	Non BPD group mean 28.4 SD 2.4 range 26.7-35.0, Control group term	Non BPD group mean 992 SD 136 range 810-1240, Control group X	Non BPD group duration of ventilator treatment median 9 days, range 0-26, Control group X	Non BPD group mean 9.4 SD 1.2 range 7.5-11.2, Control group mean 8.6 SD 1.1 range 7.1-11.2	1978-1985	X	Flow/volume spirometry with a wedge-bellows-type dynamic spirometer (Vitalograph PS II, Birmingham, UK)	Expressed as percentage predicted[E44, E35, E48, E49, E50]
Berggren Brostrom[E29] Sweden (Data as Medians in paper)	X	Non BPD group median 30, range 28-31	Non BPD group median 1495, range 845-2094	Duration of ventilatory therapy days non BPD group median 0, range 0-5	non BPD group median 91 months, range 78-97	1992-1997	Non BPD group 1/28	Pneumotachograph (Vitalograph)	Expressed as percentage predicted[E35]

Table E1c:- Lung function outcomes of the included articles preterm group (no BPD) compared to term control group

STUDY	FEV_1 PREDICTED	FVC PREDICTED	FEF_{25-75} PREDICTED	RATIOS	TLC	RV	DLCO
Fawke[E1]	No BPD mean 90 SD 15, Controls mean 100 SD 12	No BPD mean 97 SD 13, Controls mean 102 SD 12	No BPD mean 71 SD 25, Controls mean 90 SD 23	FEV_1/FVC No BPD mean 92 SD 11, Controls mean 98 SD 8	X	X	X
Arad[E2]	PT group mean 82.6 SD 10.8	X	X	X	X	X	X
De Kleine[E3]	Non BPD and non ventilated mean 90.34 SD 16.2, Control mean 95 SD 12	X	X	X	X	X	X
Doyle[E4]	No BPD mean 96.7 SD 12.6, NBW mean 104.6 SD 13.2	No BPD mean 101.4 SD 12.0 NBW mean 104.8 SD 12.0	No BPD mean 83.5 SD 23.8 NBW mean 99.1 SD 23.4	FEV_1/FVC No BPD mean 84.2 SD 8.8 NBW mean 87.0 SD 7.0	No BPD mean 99.3 SD 14.2 NBW mean 102.5 SD 13.9	No BPD mean 112.8 SD 37.6 NBW mean 117.4 SD 30.8	X
Kulasekaran[E5]	PT group mean 87.3 SD 12.0	PT group mean 92.1 SD 11.8	PT group mean 81.1 SD 20.5	FEV_1/FVC PT group mean 86.6 SD 5.7	PT group mean 95.0 SD 11.9	PT group mean 100.7 SD 44.3	PT group mean 82.6 SD 11.7
Doyle[E6]	No BPD group mean 87.1 SD 11.5, Control group 97.9 SD 11.8	No BPD group mean 88.0 SD 12.9, Control group 95.2 SD 12.6	No BPD group mean 67.9 SD 22.1, Control group 85.6 SD 20.2	FEV_1/FVC No BPD group mean 88.7 SD 9.0, Control group 91.4 SD 6.6	No BPD group mean 95.1 SD 13.8, Control group 98.5 SD 11.7	No BPD group mean 122.9 SD 43.7, Control group 112.2 SD 34.2	X
Galdes-Sebaldt[E7]	<1500g no HMD	X	<1500g no HMD	X	X	X	<1500g no

	group mean 82 SEM 2, <1500g HMD group mean 83 SEM 2, control group mean 92 SEM 1		group mean 82 SEM 4, <1500g HMD group mean 90 SEM 7, control group mean 104 SEM 3				HMD group mean 87 SEM 3, <1500g HMD group mean 97 SEM 4, control group mean 99 SEM 3
Giacoia[E8]	PT group mean 85.9 SEM 6.3, Control group Mean 97.2, SEM 4.6	X	PT group mean 66.27 SEM 10.3, Control group mean 88.5 SEM 7.1	X	X	X	X
Gross[E9]	No BPD group mean 98 SD 18, Control group mean 97 SD 12	No BPD group mean 104 SD 15, Control group mean 103 SD 11	No BPD group mean 84 SD 27, Control group mean 88 SD 21	X	No BPD group mean 111 SD 16, Control group mean 106 SD 13	No BPD group mean 130 SD 51, Control group mean 112 SD 38	X
Halvorsen [E10]	No BPD mean 94.7 SD 11.2 Control 98.6 SD 9.9	X	X	X	X	X	X
Smith[E11]	No BPD mean 87 SD 12.1	No BPD mean 98	No BPD mean 75	X	X	X	X
Jacob[E12, E13]	No BPD mean 85.1 SD 10.8, Control mean 94.3 SD 8.3	No BPD mean 93.7 SD 8.3, Control mean 99.1 SD 9.4	No BPD mean 78.7 SD 22.7, Control X	FEV_1/FVC No BPD mean 84.1 SD 7.7, Control X	No BPD mean 97.1 SD 7.5, Control X	No BPD mean 114.8 SD 20.2, Control X	No BPD mean 92.4 SD 13.0, Control mean 100.7 SD 17.1
Kennedy[E14]	No BPD group mean 95.4 SD 11.4 Control group mean 102.1	No BPD group mean 101.2 SD 9.5 Control group mean 104.2	No BPD group mean 75.5 SD 22.1 Control group mean 90.7	X	No BPD group mean 100.2 SD 12.7 Control group mean 98.3	X	X

	SD 10.2	SD 9.6	SD 21.8		SD 10.8		
Kilbride[E15]	No BPD mean 89 SD 13 Control group mean 91 SD 9	No BPD mean 94 SD 14 Control group mean 96 SD 11	No BPD mean 92 SD 22 Control group mean 100 SD 17	FEV_1/FVC No BPD mean 89 SD 6 Control group mean 89 SD 5	X	X	X
Korhonen[E16]	No BPD group mean 95 SD 14, range 68-127 Control group mean 99 SD 11, range 72-117	No BPD group mean 100 SD 16, range 72-142 Control group mean 102 SD 8, range 83-117	X	FEV_1/FVC No BPD group mean 91 SD 10, range 69-109 Control group mean 92 SD 7, range 78-104	No BPD group mean 110 SD 14, range 89-145 Control group mean 107 SD 8, range 93-128	No BPD group median 148 range 71-353 Control group median 132 range 60-214	No BPD group mean 91 SD 13, range 68-117 Control group mean 101 SD 15, range 71-138
Baraldi[E17]	VLBW mean 94.2 SD 8.9	VLBW mean 92.8 SD 8.1	VLBW mean 103.4 SD 23.5	X	X	X	X
Baraldi[E18]	No BPD group mean 90.3 SD 15.6 Control group mean 100.1 SD 12.8	No BPD group mean 96.2 SEM 2.2 Control group mean 101.7 SEM 2.5	No BPD group mean 83 SEM 5.6 Control group mean 110.9 SEM 5.1	FEV_1/FVC No BPD group mean 84.3 SEM 5.6 Control group mean 89.4 SEM 1	X	X	X
Barker[E19]	No BPD group mean 101 SD 15 Control group mean 106 SD 11	No BPD group mean 92 SD 14 Control group mean 97 SD 6	X	X	X	X	X
Mieskonen[E20]	No BPD group mean 89.8 SD 13, Control group 101.7 SD 8.4	No BPD group mean 94.0 SD 9.2 Control group 104.5 SD 10.9	X	X	X	X	No BPD group mean 89.0 SD 10.0, Control group 99.5 SD

							11.6
Pianosi[E21]	No BPD group mean 83 SD 13 Control group mean 90 SD 8	No BPD group mean 95 SD 12 Control group mean 96 SD 9	No BPD group mean 68 SD 20 Control group mean 86 SD 12	X	No BPD group mean 103 SD 11 Control group mean 97 SD 10	No BPD group mean 137 SD 50 Control group mean 102 SD 26	No BPD group mean 117 SD 26 Control group mean 109 SD 20
Palta[E22]	No BPD group mean 88 SD 14 Control group mean 97 SD 12	BPD group mean 87 SD 43 Control group mean 99 SD 27	X	X	X	X	X
Mitchell[E23]	No BPD group mean 85 SD 15 Control group mean 91 SD 14	No BPD group mean 95 SD 12 Control group mean 93 SD 15	No BPD group mean 95 SD 12 Control group mean 87 SD 24	FEV_1/FVC No BPD group mean 0.80 SD 0.07 Control group mean 0.88 SD 0.05	X	X	No BPD group mean 80 SE 4, Control group mean 100 SE 3
Vrijlandt[E24]	No BPD group mean 99.2 SD 17.9 Control group mean 109.6 SD 13.4	No BPD group mean 99.2 SD 13.7 Control group mean 106.0 SD 10.8	X	FEV_1/FVC No BPD group mean 82.5 SD 11.1 Control group mean 87.4 SD 6.6	No BPD group mean 102.5 SD 8.3 Control group mean 103.3 SD 9.7	No BPD group mean 111.2 SD 29.1 Control group mean 90.3 SD 25.3	No BPD group mean 94.5 SD 18.0 Control group mean 96.3 SD 9.9
Wheeler[E25]	PT group mean 106 SD 17 Control group mean 104 SD 15	X	BPD group mean 90 SD 21 Control group mean 103 SD 21	X	BPD group mean 101 SD 16 Control group mean 111 SD 34	X	X
Abreu[E26]	PT group mean 100 SD 14, Control group	X	X	X	X	X	X

	mean 102 SD 15						
Guimaraes[E27] (Data as Medians in paper)	No BPD group median 89 extremes 48-124	No BPD group median 91 extremes 56-117	No BPD group median 97 extremes 5-223	FEV_1/FVC No BPD group median 6 extremes 1-43	X	X	X
Hakulinen[E28] (Data as Medians in paper)	Non BPD group median 93, range 47-120 Control group median 99, range 88-119	Non BPD group median 96.6, SE 6.1 range 89-104 Control group median 98.6, SE 2.2 range 93-104	X	FEV_1/FVC Non BPD group median 94.9, SE 2.5 range 90-100 Control group median 102.9, SE 1.5 range 100-106	Non BPD group median 95.7, SE 3.9 range 89-102 Control group median 99.7, SE 2.3 range 95-104	Non BPD group median 82.3, SE 6.0 range 66-101 Control group median 84.0, SE 6.4 range 71-97	Non BPD group median 89.5, SE 3.4 range 82-97 Control group median 100.7, SE 2.2 range 95-106
Berggren Brostrom[E29] (Data as Medians in paper)	Non BPD group median 95·4, min max 75-111	Non BPD group median 98, min max 78-129	Non BPD group median 93, min max 44-123	Given in litres	X	X	X

Table E2a:- Description of the included articles BPD group (supplemental oxygen dependency for at least 28 days from birth) compared to term control group

STUDY	QUALITY SCORE	OBJECTIVE	STUDY DESIGN	STUDY GROUP	CONTROL GROUP	OUTCOME MEASURES
De Kleine[E3]	18	Examine the effect of lung injury caused by IPPV for HMD on lung function in children	Follow up study	40 PT ventilated for HMD (11 BPD)	39 randomly selected pupils of a similar age	Spirometry Respiratory symptoms questionnaire Review of follow up records for

Doyle[E4]	19	To determine the respiratory health of children of birthweight <1501g, compared to NBW controls in adolescence	Cohort study	180 VLBW (<1501g) -39 BPD with spirometry results	42 NBW (>2499g), 39 with spirometry results	Spirometry Assessment of respiratory health
Halvorsen [E10]	15	To investigate long term outcomes in young people after extremely preterm birth and BPD	Population-based long-term follow-up study	2 population based cohorts ≤ 28 weeks gestation or ≤ 1000g birthweight 62 with BPD	81 term controls birth weight between 3 and 4 kg	Spirometry ISAAC questionnaire Metacholine provocation test Exercise induced asthma and reversibility to salbutamol Allergy testing
Bader[E51]	12	To determine the long-term pulmonary sequelae and effect on exercise tolerance of BPD	Area cohort study	10 BPD	8 age matched term children	Spirometry Exercise testing Recent medical history
Karila[E52]	7	To confirm children who have survived BPD display lower ventilation during exercise than healthy children, and to determine whether alveolar hypoventilation associated with exercise induced hypoventilation occurred in these children	Prospective study	20 BPD	18 healthy term matched controls	Spirometry Exercise testing
Kennedy[E14]	15	To assess the importance of the contributions of birth weight, gestational age, neonatal respiratory illness, and its treatment on subsequent childhood	Cohort study	VLBW cohort (<1500g) 26 BPD	82 control children , 1 birth weight <2kg, 2 born at 36 weeks rest at term	Spirometry Respiratory questionnaire

		lung function in a cohort of children of birth weight less than 1500g.				
Korhonen[E16]	16	To assess respiratory outcome and its predictors during the surfactant era in VLBW schoolchildren with and without BPD	Cohort	VLBW cohort (<1500g) 34 BPD of which 29 had spirometry results	34 term controls of which 33 had spirometry results	Spirometry Mailed questionnaire Atopic tendency testing
Koumbourlis[E53]	8	To investigate whether early lung function abnormalities in PT children with BPD improve in late childhood and adolescence	Prospective longitudinal study	17 BPD, PT birth ≤ 32 weeks, birth weight ≤ 1500g	X	Spirometry Histamine challenge Questionnaire
Baraldi [E18]	11	To measure exhaled nitric oxide and lung function in a group of school-age survivors of BPD.	Cohort study	31 BPD, PT <31 weeks, birth weight <2000g	31 healthy children born at term matched for sex and age	Spirometry Reversibility to $ß_2$-Agonists Allergometric study
Barker[E19]	16	To assess the long-term outcome in respiratory morbidity, lung function, submaximal, and peak exercise capacity among a local cohort of school children with a history of treatment in a NICU after preterm birth at VLBW	Area cohort study	13 BPD, VLBW birth weight < 1500g, PT birth <37 weeks	13 healthy children born at term matched for age, height and weight	Spirometry Interview on respiratory history and morbidity Exercise testing
Santuz[E54]	11	To evaluate the lung function of BPD children at school age and to assess the level of	Cohort study	12 BPD	16 healthy controls matched in age, height,	Spirometry Exercise testing Questionnaire

		exercise tolerance of BPD survivors by comparing ventilation and gas exchange during exercise of BPD and healthy children			weight and level of physical activity	
Pianosi[E21]	10	To assess the hypothesis that there would be no significant difference in childhood lung function between patients who were ventilated by conventional or high frequency ventilation.	Cohort study	17 BPD	15 term born matched controls	Spirometry Bronchodilator responsiveness
Northway[E55]	12	To test the hypothesis that the pulmonary function of adolescents and young adults who had BPD in infancy was normal	Retrospective cohort study	26 BPD	53 age matched term subjects	Spirometry Cardiorespiratory history Bronchial hyperreactivity Atopic status
Ng[E56]	7	To assess the prevalence of asthma in children born in the 1990s who had survived BPD	Retrospective cohort study	55 BPD children but only 7 performed spirometry	X	Spirometry Airway hyperresponsiveness Rates of asthma
Mitchel[E23]	11	To test the hypothesis that gas transfer during exercise is reduced in survivors of BPD relative to age-matched control subjects	Cohort study	10 BPD	10 similar age born full term controls	Spirometry Exercise testing Questionnaire
Vrijlandt[E24]	14	To investigate the long term effects of prematurity on lung	Prospective cohort study	8 BPD (gestational age <32 weeks and/or	48 healthy term controls	Spirometry Exercise testing

		function and exercise capacity		birthweight under 1500g)		
Smyth[E57]	7	To assess lung function of children with BPD	Cohort study	9 BPD	X	Spirometry Bronchial hyperreactivity Allergy testing
Wheeler[E25]	7	To assess and compare lung function in BPD, RDS, PT and term children	Case control study	11 BPD	11 normal term delivery children	Spirometry
Ahrens[E58]	Not recorded in translation	To study the long term pulmonary and allergic outcomes of very low birth weight prematures with and without bronchopulmonary dysplasia	Cohort study	19 BPD VLBW <1500g, PT <34 weeks gestation	9 term children	Spirometry Skin Prick Testing Chest X-ray Plethysmography Histamine challenge
Abreu[E26]	14	To investigate cardio respiratory capacity and investigate the presence of exercise-induced bronchospasm among children with BPD	Case control study	13 BPD	20 term children 17 with LF results	Spirometry Exercise testing
Hakulinen[E28] **(Data as Medians in paper)**	13	To determine the extent to which BPD affects the diffusing properties of lung tissue in childhood.	Cohort study	20 PT children <1250g had BPD	20 healthy term children	Spirometry Questionnaire
Blayney[E59] **(Data as Medians in paper)**	7	To evaluate the natural history of BPD	Cohort study	32 children with BPD	X	Spirometry Questionnaire
Aquino[E60] **(Data as Medians in paper)**	9	To correlate high-resolution inspiratory and expiratory CT findings with pulmonary function	Retrospective cohort study	26 children with BPD	X	Spirometry CT

		results in older children and adults who have BPD				
Berggren Brostrom[E29] (Data as Medians in paper)	8	To examine the impact of the severity of BPD on pulmonary morbidity at school age	Cohort	60 VLBW children 28 with mild/moderate BPD	X	Spirometry Oscillometry Thoracic HRCT Allergy skin-prick test Blood sample questionnaire

Table E2b:- Demographics of the included articles BPD group (supplemental oxygen dependency for at least 28 days from birth) compared to term control group

STUDY COUNTRY	SUBJECTS (GENDER)	GA (WEEKS)	BW (GRAMS)	DURATION ON MECHANICAL VENTILATION (DAYS)	AGE TESTED (YEARS)	YEAR OF BIRTH	SURFACTANT GIVEN	METHOD OF MEASURING LUNG FUNCTION	METHOD OF STANDARDISING LUNG FUNCTION MEASUREMENTS
De Kleine[E3] The Netherlands	11 BPD (8M, 3F) 39 controls (20M, 19F)	BPD mean 30.6 SD 2.0 Controls X	BPD mean 1673 SD 340 Controls X	BPD mean 9.0 days (range 1.8-36) Controls X	BPD mean 13.4 SD 3.1 Controls mean 13.7 SD 1.6	1967-1977	X	Water sealed spirometer (Lode instruments, Groningen, Netherlands)	Lung function as percentage predicted for sex and height [E32, E33]
Doyle[E4] Australia	500-999g group (35M, 43F), 1000-1500g group (55m, 47F) >2499g	500-999g group mean 27.5 SD 2.3, 1000-1500g group mean	500-999g group mean 859 SD 100, 1000-1500g group mean 1259 SD 145, >2499g group mean	X	500-999g group mean 14.1 SD 0.2, 1000-1500g group mean 14.2 SD 0.3, >2499g group mean	1977-1982	Not given	Jaeger Bodyscreen II-Bodybox (Jaeger, Germany)	Lung function as percentage predicted for age, height and gender [E34]

	group (26M, 16F)	29.6 SD 1.5, >2499g group mean 39.9 SD 1.0	3420 SD 427		14.2 SD 0.1				
Halvorsen[E10] **Norway**	BPD (30F, 32M) Controls (42F, 39M)	Mild BPD mean 26.8 SD 1.4 M/S BPD mean 26.4 SD 1.4 Control group term	Mild BPD mean 981.0 SD 200.2 M/S BPD mean 868.8 SD 166.0 Control group mean 3494 SD 300	Mild BPD mean 7.2 Range 0-40.0 M/S BPD mean 13.8 Range 0.7-54.5	2 populations assessed 2nd mean 10.6 SD 0.4 1st 17.7 SD 1.2	1982-1985 and 1991-1992	X	Vmax 22 spirometer (SensorMedics Inc., Anaheim, USA)	Expressed as percentage of the predicted values[E39]
Bader[E51] **USA**	10 BPD (6m, 4F) 8 control (4M, 4F)	BPD group mean 29 SEM 0.7, range 26-32, control group mean 40 SEM 0.3, range 39-	BPD group mean 1173 SEM 120, range 765-2000, control group mean 3248 SEM 166, range 2500-3960	BPD group IPPB mean 44 days, SEM 6, range 7-65 Control group 0	BPD group mean 10.4, SEM 0.6, range 7.3-12.2, Control group mean 10.1 SEM 0.9, range 7.5-14	1973-1979	X	Wedge spirometer (model 525, Medscience Electronics Inc., St Louis)	Lung function as percentage predicted X

		41							
Karila[E52] **France**	20 BPD (13M, 7F) 18 controls (8M, 10F)	BPD group mean 31 SD 2.3	BPD group mean 1441 SD 523 Control group X	BPD group mean duration mechanical ventilation 145.1 days SD 130.1 not counting nocturnal home ventilation which was used by 7 children for mean 21.1 months SD 9.3	BPD group mean 10.1 SD 2.3, control 9.9 SD 2.0	X	6 in BPD group received	Conventional spirometry, as recommended by ERS	Lung function as percentage of predicted values for age and sex[E61]
Kennedy[E14] **Australia**	BPD (14M, 12F) Control group (39M, 43F)	BPD group mean 26.8 SD 1.5, Control mean 40.0 SD 1.6	BPD group mean 959.8 SD 163.5, Control group mean 3459.1 SD 509.0	Duration of IPPV BPD groups median 47.0 IQR 24.5, 50.0 Control n/a	BPD group mean 11.3 SD 0.8, Control 11.4 SD 0.8	1981-1982	X	Pulmonary function testing was performed using the Jaeger Masterlab system	Results were evaluated as percentage predicted for gender and height[E34]
Korhonen[E16] **Finland**	BPD group (21m 13F) Control group X	BPD group mean 27 SD 2, range 23-30	BPD group mean 951 SD 207, range 570-1300	BPD group 32/34 ventilated duration median 27, range 0-89	BPD group median 7.1 range 6.7-7.8 Control group median 7.2,	1990-1994	BPD group 14/34 received	Flow volume spirograms were recorded by mass flow sensor (2200/Vmax 22, SensorMedics BV,	Finish FVS reference values for children were used [E43]

		Control group term		days	range 6.9-8.3			Bilthoven, Netherlands)	
Koumbourlis[E53] USA	BPD group (9M, 8F)	BPD group mean 29.1 SD 1.7 Median 29 Range 26-32	BPD group mean 1120 SD 190, median 1110, range 880-1490	BPD group 10/17 ventilated mean 10.8 days SD 8.0, median 9.5, range 3-27	BPD group mean 8.2 SD 1.2	X	X	Lung volumes measured using a 7-liter Collins lung-volume analyzer (Warren E. Collins, Inc., Braintree, MA)MEFV curves were obtained using a 10-liter water-sealed Stead-Wells spirometer (warren E Collins, Inc., Braintree, MA)	Normal predicted values for lung volume etc. were obtained [E62, E63]
Baraldi[E18] Italy	BPD group (14M, 17F) Control group (14M, 17F)	BPD group mean 28.6 SEM 0.3 Control group term	BPD group mean 1081 SEM 57 Control group X	BPD group all ventilated mean 26 days SEM 3.4 days Controls X	BPD group mean 8.6 SEM 0.3, Controls mean 8.4 SEM 0.4.	1990-1994	BPD group 24/31 Control group X	Flow volume spirometry (Biomedin, Padova, Italy	Lung function as percentage of predicted values for height and sex[E32]
Barker[E19] Germany	BPD group (7M, 6F) Control group (8M, 5F)	BPD group mean 30.3, range 28-33, control group term	BPD group mean 1139, range 710-1480, Control group X	BPD group 13/13 mean 30.3 days, range 7-81, control group X	BPD group mean 9.8 (range 8-14), control group mean 10·5 years (8-12)	1983-1989	X	Baseline lung function was measured by standard spirometry and performed additional body plethysmography (Jaeger Body Screen II, Wurzburg, Germany)	Lung function as percentage predicted[X]

Santuz[E54] **Italy**	BPD group (9M, 3F) Control group (11M, 5F)	BPD group mean 30, SD 2, range 27-32, Control group mean 39, SD 1, range 37-40	BPD group mean 1400, SD 335, range 890-1900, Control group mean 3335, SD 418, range 2800-4100	BPD group 12/12 ventilated mean 20 days SD 15, median 17, range 7-60 Control group X	BPD group mean 8.1 SD 1.8, range 6-12, controls mean 8.1 SD 1.5, range 6-12	1981-1987	X	Spirometry by a 10 L bell spirometer connected to a computerized system (Baires; Biomedin, Padova, Italy)	Results were expressed as a percentage of predicted reference values appropriate for height, sex and age [E32]
Pianosi[E21] **Canada**	BPD group (9M, 8F) Controls X	CMV BPD median 27, IQR 26.8,29 HFV BPD median 28, IQR 26, 28.8 Control term	CMV BPD median 1060, IQR 888, 1373 HFV BPD median 1025, IQR 895, 1155 Control X	CMV BPD median 13 days, IQR 8, 44 HFV BPD median 24 days, IQR 9, 33 Control X	8-9	1986-1987	X	Spirometry measured in 6200 Autobox, Sensormedics, Yorba Linda CA	Results were expressed as percentage predicted using reference values[E32, E44, E45]
Northway[E55] **USA**	BPD (18M, 8F) Controls (23M, 30F)	BPD group mean 33.2, SD 3.8, Control group	BPD group mean 1894, SD 703, Control group X	All BPD group ventilated Control group X	BPD group mean 18.3 SD 2.7, controls mean 18.0, SD 3.1	1964-1973	X	Spirometry obtained using Fleisch pneumotachmeter	Results reported as percentages of predicted values according to standardized values for normal children and adults, 15% race-correction factor when

		term							appropriate[E32, E45, E64-E69, E40, E42]
Ng[E56] Hong Kong	BPD group with LF results (5m, 2F)	Whole BPD group mean 28 SD 2.6	Whole BPD group mean 1096 SD 366	55/55 ventilated, mean 29 days SD 17	7 BPD with LF results 7-10	1987-1995	28/55	Spirometry was performed with a portable spriometer (MicroPlus; Micro Medical Ltd, Kent, UK)	Reference values used[E70]
Mitchell[E23] USA	BPD group (7M, 3F) Control group (4M, 6F)	BPD group mean 30, SD 5, Control group mean 40, SD 1	BPD group mean 1359, SD 1041 Control group mean 3157, SD 606	10/10 BPD, Control group X	BPD group mean 7, SD 1, Term group mean 7, SD 1	1985-1987	X	Spirometry with a calibrated spirometer (SensorMedics 2200)	Results as percentage predicted based on height, gender and race using the standard equation[E41, E42]
Vrijlandt[E24] The Netherlands	BPD group (8M, 0F) Control group (16M, 32F)	Whole PT group including BPD group mean 30 SD 2, range 26-36, Control group term range 37-42	Whole PT group including BPD group mean 1246 SD 232, range 720-1750, Control group X	Whole PT group including BPD group mean 6.3 days SD 12, range 0-51, Control group X	Whole PT group including BPD group mean 19 SD 0.3, range 19-20, Control group mean 20.8 SD 1.2, range 18-22	PT group 1983	0/42	Spirometry using a pneumotachograph	Results as percentage predicted based on height [E47]
Smyth[E57]	BPD group	BPD	BPD group	9/9 mean	BPD group	1970-	X	Spirometry with a 9-L	Results as percentage

Canada	(7M, 2F)	group mean 30, range 24-34	mean 1476.5, range 730-2200	duration of IPPV 8 days, range 2-14	mean 8.5, range 7.2-9.6	1972		water spirometer (Warren E. Collins, Inc, Braintree, MA)	predicted [E62]
Wheeler[E25] X	X	X	BPD group mean 1443, SD 463,Control group mean 3540, SD 570	X	BPD group mean 7.2, SD 0.9,Control group mean 8.3, SD 0.9	X	X	X	Results as percentage predicted [X]
Ahrens[E58] Germany	X	BPD group <34, term group term	BPD group <1500g	BPD group 19/19, term group X	Preterm children mean age 7.7, terms 6-7	1977-1981	X	Whole body plethysmography	Results as percentage predicted, given in graphical form so results read of graphs[x]
Abreu[E26] Brazil	BPD group (9M, 4F) Control group (9M, 11F)	BPD group mean 32 SD 1.5 range 30-34 Control group term	BPD group mean 1037 SD 229 range 830-1670 Control group X	BPD group 13/13 mean 11 SD 6.6 range 3-26 Control group X	BPD group mean 8.5 SD 0.97, Control mean 8.2 SD 1.14	1993-1996	X	SpiroCard PC Card Flux spirometer (QRS Diagnostic-Plymouth, USA)	Expressed as percentage predicted[E35]
Hakulinen[E28] Finland (Data as Medians in paper)	BPD group (8M,12F) Control group X	BPD group mean 27.8 SD 1.4 range 25-30.7, Control group	BPD group mean 952 SD 162 range 670-1235, Control group X	BPD group duration of ventilator treatment median 32 days, range 9-88, Control group X	BPD group mean 8.5 SD 1.1 range 7.0-11.2, Control group mean 8.6 SD 1.1 range 7.1-	1978-1985	X	Flow/volume spirometry with a wedge-bellows-type dynamic spirometer (Vitalograph PS II, Birmingham, UK)	Expressed as percentage predicted[E44,E35,E48-E50]

		term			11.2				
Blayney[E59] Canada (Data as Medians in paper)	BPD group 72% M	BPD group mean 29 SD 3.2 range 25-36	BPD group mean 1228 SD 496 range 700-2560	30/32 ventilated Mean days of assisted ventilation 29 SD 22.8, range 0-99	10	1977-1980	X	X	Expressed as percentage predicted[E62]
Aquino[E60] USA (Data as Medians in paper)	BPD group (16M, 10F)	BPD group median 28, range 22-36	BPD group median 900g, range 482-2350g	BPD group median duration of mechanical ventilation 60 days, range 3-135 days	Median 10 range 5-18	X	X	Pneumotachometer (Warren Collins, Braintree, MA)	Expressed as percentage predicted[E35, E42]
Berggren Brostrom [E29] Sweden (Data as Medians in paper)	X	Mild BPD group median 27, range 24-30, Moderate BPD group median 27.5 range 25-30	Mild BPD group median 987.5, range 654-1520, Moderate BPD group median 1133 range 597-1252	Duration of ventilatory therapy days Mild BPD group median 0, range 0-34, Moderate BPD group median 3.5 range 0-38	Mild BPD group median 88.5 months, range 76-99, Moderate BPD group median 87 range 79-95	1992-1997	Mild BPD group 1/20, moderate BPD group 3/8	Pneumotachograph (Vitalograph)	Expressed as percentage predicted[E35]

Table E2c:- Lung function outcomes of the included articles BPD group (supplemental oxygen dependency for at least 28 days from birth) compared to term control group

STUDY	FEV_1 PREDICTED	FVC PREDICTED	FEF_{25-75} PREDICTED	RATIOS	TLC	RV	DLCO
De Kleine[E3]	BPD mean 73 SD 17 Control mean 95 SD 12	X	X	X	X	X	X
Doyle[E4]	BPD mean 88.5 SD 18.2 NBW mean 104.6 SD 13.2	BPD mean 98.2 SD 14.4 NBW mean 104.8 SD 12.0	BPD mean 71.3 SD 30.9 NBW mean 99.1 SD 23.4	FEV_1/FVC BPD mean 78.6 SD 11.1 NBW mean 87.0 SD 7.0	BPD mean 98.9 SD 14.7 NBW mean 102.5 SD 13.9	BPD mean 115.8 SD 53.0 NBW mean 117.4 SD 30.8	X
Halvorsen [E10]	BPD mean 86.4 SD 10.9 Control 98.6 SD 9.9	X	X	X	X	X	X
Bader[E51]	BPD mean 73, SEM 6, range 44-106, Control mean 93, SEM 4, range 75-115	X	BPD mean 55, SEM 9, range 22-105, Control mean 88, SEM 9, range 58-140	X	BPD mean 102, SEM 3, range 92-121, Control mean 103, SEM 3, range 88-119	BPD mean 158, SEM 12, range 104-226, Control mean 110, SEM 11, range 69-160	X
Karila[E52]	BPD group mean 79.1 SD 19.3 Control group mean 106.3 SD 11.3	BPD group mean 89.8 SD 18.8 Control group mean 101.7 SD 10.3	BPD group mean 50.5 SD 26.4 Control group mean 99.8 SD 18.9	FEV_1/VC BPD group mean 73.2 SD 16.3 Control group mean 86.4 SD 4.1	BPD group mean 100.7 SD 15.0 Control group mean 96.8 SD 8.7	X	BPD group mean 97.3 SD 22.2 Control group mean 89.8 SD 9.5
Kennedy[E14]	BPD group mean 78.4 SD 170 Control group mean 102 SD 10	BPD group mean 92.8 SD 11.5 Control group mean 104.2	BPD group mean 54.5 SD 29.2 Control group mean 90.7 SD 21.8	X	BPD group mean 98.1 SD 13.1 Control group mean 98.3	X	X

		SD 9.6			SD 10.8		
Korhonen[E16]	BPD group mean 90 SD 14, range 56-122 Control group mean 99 SD 11, range 72-117	BPD group mean 98 SD 16, range 60-129 Control group mean 102 SD 8, range 83-117	X	FEV_1/FVC BPD group mean 88 SD 9, range 73-108 Control group mean 92 SD 7, range 78-104	BPD group mean 109 SD 14, range 87-139 Control group mean 107 SD 8, range 93-128	BPD group median 159 range 77-327 Control group median 132 range 60-214	BPD group mean 86 SD 16, range 68-130 Control group mean 101 SD 15, range 71-138
Koumbourlis[E53]	BPD group mean 98.6 SD 14.2	X	BPD group mean 73.6 SD 18.7	FEV_1/FVC BPD group mean 92.4 SD 6.5	BPD group mean 98.5 SD 13.1	BPD group mean 125.9 SD 37.7	X
Baraldi [E18]	BPD group mean 77.8 SD 12.8 Control group mean 100.1 SD 12.8	BPD group mean 85.9 SEM 2.5 Control group mean 101.7 SEM 2.5	BPD group mean 63.9 SEM 4 Control group mean 110.9 SEM 5.1	FEV_1/FVC BPD group mean 81.8 SEM 2 Control group mean 89.4 SEM 1	X	X	X
Barker[E19]	BPD group mean 90 SD 14 Control group mean 106 SD 11	BPD group mean 83 SD 12 Control group mean 97 SD 6	X	X	X	X	X
Santuz[E54]	BPD group mean 83 SD 13 Control group mean 100 SD 8	BPD group mean 87 SD 10 Control group mean 96 SD 8	BPD group mean 77 SD 30 Control group mean 110 SD 14	X	X	X	X
Pianosi[E21]	BPD group mean 86 SD 14 Control group mean	BPD group mean 99 SD 11 Control group mean	BPD group mean 72 SD 24 Control group mean	X	BPD group mean 107 SD 8	BPD group mean 141 SD 34	BPD group mean 99 SD 17

	90 SD 8	96 SD 9	86 SD 12		Control group mean 97 SD 10	Control group mean 102 SD 26	Control group mean 109 SD 20
Northway[E55]	BPD group mean 74.8 SE 2.9 Control group mean 100.40 SE 1.5	BPD group mean 96.8 SE 3.2 Control group mean 105.4 SE 1.7	BPD group mean 46.5 SE 3.6 Control group mean 87.8 SE 2.7	X	BPD group mean 108.6 SE 2.9 Control group mean 105.9 SE 1.8	X	BPD group mean 80.2 SE 2.5 Control group mean 87.8 SE 1.7
Ng[E56]	BPD group with LF mean 95 SD 19.4	Results given separately for each of the 7 patients	X	X	X	X	X
Mitchell[E23]	BPD group mean 78 SD 21 Control group mean 91 SD 14	BPD group mean 90 SD 19 Control group mean 93 SD 15	BPD group mean 45 SD 22 Control group mean 87 SD 24	FEV_1/FVC BPD group mean 0.77 SD 0.11 Control group mean 0.88 SD 0.05	X	X	BPD group mean 80 SE 12, control group mean 100 SE 3
Vrijlandt[E24]	BPD group mean 90.1 SD 19.8 Control group mean 109.6 SD 13.4	BPD group mean 96.4 SD 13.1 Control group mean 106.0 SD 10.8	X	FEV_1/FVC BPD group mean 78.8 SD 8.1 Control group mean 87.4 SD 6.6	BPD group mean 102.2 SD 8.9 Control group mean 103.3 SD 9.7	BPD group mean 122.7 SD 25.4 Control group mean 90.3 SD 25.3	BPD group mean 91.4 SD 10.5 Control group mean 96.3 SD 9.9
Smyth[E57]	BPD group mean 67.8	BPD group mean 76	BPD group mean 62	X	X	X	X
Wheeler[E25]	BPD group mean 82 SD 20 Control group mean 104 SD 15	X	BPD group mean 55 SD 23 Control group mean 103 SD 21	X	BPD group mean 116 SD 28 Control group mean 111	X	X

					SD 34		
Ahrens[E58]	BPD group mean 77.11 SD 12.42 Control group mean 78 SD 20	X	X	X	X	X	X
Abreu[E26]	BPD group mean 99 SD 12, Control group mean 102 SD 15	X	X	X	X	X	X
Hakulinen[E28] **(Data as Medians in paper)**	BPD group median 88, range 66-108 Control group median 99, range 88-119	BPD group median 92.1, SE 2.1 range 87-97 Control group median 98.6, SE 2.2 range 93-104	X	FEV_1/FVC BPD group median 95.5, SE 1.7 range 92-99 Control group median 102.9, SE 1.5 range 100-106	BPD group median 94.6, SE 2.0 range 90-99 Control group median 99.7, SE 2.3 range 95-104	BPD group median 91.3, SE 7.7 range 78-105 Control group median 84.0, SE 6.4 range 71-97	BPD group median 91.1, SE 3.4 range 86-97 Control group median 100.7, SE 2.2 range 95-106
Blayney[E59] **(Data as Medians in paper)**	Presented graphically	Given in text	Given in text	Presented graphically	Presented graphically	Presented graphically	X
Aquino[E60] **(Data as Medians in paper)**	BPD group median 64, range 35-96	X	X	X	X	X	X
Berggren Brostrom[E29] **(Data as Medians in paper)**	Mild and moderate BPD group median 81, min max 61-97	Mild and moderate BPD group median 85, min max 66-109	Mild and moderate BPD group median 66, min max 31-107	Given in litres	X	X	X

Table E3a:- Description of the included articles BPD group (supplemental oxygen dependency 36 weeks PMA) compared to term control group

STUDY	QUALITY SCORE	OBJECTIVE	STUDY DESIGN	STUDY GROUP	CONTROL GROUP	OUTCOME MEASURES
Fawke[E1]	16	To assess the degree of respiratory morbidity and in extremely premature children in relation to current clinical status and neonatal determinants.	Cohort study	182 EP (≤25 weeks gestation) 129 with BPD	161 classmate controls excluded classmates who were preterm	Spirometry Post-bronchodilator response Questionnaire
Kulasekaran[E5]	14	To determine the respiratory outcome of children who had BPD compared with a preterm control group of children at school age.	Cohort	47 children with BPD	X	Respiratory outcome Family History
Doyle[E6]	17	To determine respiratory function at 8 years in ELBW, very PT children born in the 1990s compared with NBW controls	Cohort	298 ELBW (<1000g)/ very preterm (< 28 weeks gestation) 240 with LF results of which 89 with BPD	208 NBW (>2499g)	Spirometry ISAAC questionnaire
Giacoia[E8]	12	To investigate the outcome of school-age children with BPD compared to a preterm cohort and term control group	Cohort	12 BPD	12 Term Controls	Spirometry Body Composition Dietary intake Intelligence test scores
Gross[E9]	19	To assess long-term pulmonary outcome of a regional cohort of children born <32 weeks' gestation compared with a matched	Cohort	125 PT children born at 24 to 31 weeks gestation. 43 with BPD had	108 healthy term (38 to 42 weeks gestation) controls	Spirometry Bronchodilator responsiveness Ongoing health problems Rehospitalisation Respiratory symptoms

		term control group		spirometry		Exercise testing
Halvorsen[E10]	15	To investigate long term outcomes in young people after extremely preterm birth and BPD	Population-based long-term follow-up study	2 population based cohorts ≤ 28 weeks gestation or ≤ 1000g birthweight 24 with BPD	81 term controls birth weight between 3 and 4 kg	Spirometry ISAAC questionnaire Metacholine provocation test Exercise induced asthma and reversibility to salbutamol Allergy testing
Smith[E11]	9	The aim of the study was to investigate the role of neonatal influences including post-natal corticosteroids and a diagnosis of BPD, on long-term respiratory outcomes in a group of children born very preterm in the 1990s.	Cross-sectional study	102 PT children 37 with BPD	X	Spirometry ISAAC questionnaire
Jacob[E12,E13]	15	To evaluate the long-term pulmonary sequelae of survivors of BPD of sufficient severity to have required oxygen for at least one month after term.	Cohort study	30 PT children 15 BPD	13 healthy term children	Bronchial symptom questionnaire Spirometry Lung elastic recoil pressure Response to a bronchodilator
Kilbride[E15]	14	To assess pulmonary function and exercise capacity of apparently asymptomatic children who were born EP	Longitudinal follow up study	50 ELBW children <801g 16 with BPD	25 age matched NBW children >37 weeks gestation and >2500g BW	Medical history and recent Hospitalisations Spirometry Exercise testing
Korhonen[E16]	16	To assess respiratory outcome and its predictors	Cohort	VLBW cohort (<1500g) 14	34 term controls of	Spirometry Mailed questionnaire

		during the surfactant era in VLBW schoolchildren with and without BPD		with severe BPD 10 of whom had acceptable spirometry	which 33 had spirometry results	Atopic tendency testing
Mieskonen[E20]	13	To evaluate the possible inflammatory basis of lung function abnormalities	Cohort study	40 children with a gestational age ≤ 30 weeks or birthweight <1500g 9 with BPD	14 term controls	Spirometry Questionnaires Skin Prick Tests Measurement of exhaled nitric oxide Spirometry before and after ol
Palta[E22]	15	To determine lung function at 10 years in VLBW children and controls	Cohort study	265 VLBW children ≤ 1500g 59 with BPD	360 unselected controls	Spirometry Home spirometry
Berman[E71]	6	To provide information about disease evolution and the predictive nature of early studies	Longitudinal study	10 children with BPD	X	Spirometry
Guimaraes[E27] **(Data as Medians in paper)**	8	To assess pulmonary function and the prevalence of atopy in school age children who were VLBW and to compare those who had BPD to those who did not.	Cohort study	85 VLBW children 13 with BPD had LF results	X	Spirometry Questionnaire Allergy skin prick test
Berggren Brostrom[E29] **(Data as Medians in paper)**	8	To examine the impact of the severity of BPD on pulmonary morbidity at school age	Cohort	60 VLBW children 4 with severe BPD	X	Spirometry Oscillometry Thoracic HRCT Allergy skin-prick test Blood sample questionnaire

Table E3b:- Demographics of the included articles BPD group (supplemental oxygen dependency 36 weeks PMA) compared to term control group

STUDY COUNTRY	SUBJECTS (GENDER)	GA (WEEKS)	BW (GRAMS)	DURATION ON MECHANICAL VENTILATION (DAYS)	AGE TESTED (YEARS)	YEAR OF BIRTH	SURFACTANT GIVEN	METHOD OF MEASURING LUNG FUNCTION	METHOD OF STANDARDISING LUNG FUNCTION MEASUREMENTS
Fawke[E1] **UK and Ireland**	BPD (59M, 70F), Controls (43% M)	BPD mean 24.9, SD 0.8 Control X excluded if preterm	BPD mean 740, SD 120, Controls X	X	Range 10.1 to 12.1. EP BPD mean 11.0, SD 0.4. Controls mean 10.9 SD 0.55.	1995	BPD 114/129 Controls X	Portable spirometer (Jaeger Masterscope, Lab Manager, V4.65; CareFusion, Hoechberg, Germany	Spirometry data were expressed as z-scores to adjust for height, age and sex[E30, E31]
Kulasekaran[E5] **Australia**	BPD group (23M, 24F)	BPD group mean 28.5 SD 1.5	BPD group mean 1073 SD 242	BPD 47/47 days of mechanical ventilation median 10, IQR 7-18	7-10	1989-1990	0/47	Pulmonary function laboratory system (Sensormedics, Yorba Linda, CA, USA	Spirometry data was expressed as percentage predicted values for height, age and gender[E35]
Doyle[E6] **Australia**	BPD X, Control group (98M, 110F)	BPD group mean 25.9, SD 1.7 Control group X	BPD group mean 847, SD 183, Control group	X	8-9	1991-1992	In whole PT cohort 92/240 treated	Jaeger Body-screen II Bodybox (Jaeger, Germany)	Results expressed as percentage predicted for age, height and gender[E33]

			Control group >2499						
Giacoia[E8] **USA**	BPD group (5M, 7F), Controls (5M, 7F)	BPD group mean 29 SD 2.5, Controls mean 40.07 SD 0.27	BPD group mean 1015 SD 222, Controls mean 3663 SD 777	BPD group mean 25.8 days, SD 19.3, Controls mean 0	BPD group mean 11.83 SEM 1.74, Controls mean 11.9 SEM 1.6	1978-1986	X	SensorMedics model 2600 pulmonary function monitor (SensorMedics Corp)	Results as percentage predicted[X]
Gross[E9] **USA**	BPD group (23M, 20F), Control group (62M, 46F)	BPD group mean 27 SD 2, Control group mean 40.1 SD 1.1	BPD group mean 1053 SD 356, Control group mean 3565 SD 427	95% of BPD group median 34	7	1985-1986	0	SensorMedics 2200 Pulmonary Function Equipment (SensorMedics, Anaheim Calif)	Results as percentage predicted for age, height and sex[E37, E38]
Halvorsen [E10] **Norway**	BPD (14M, 10F) Controls (42F, 39M)	M/S BPD mean 26.4 SD 1.4 Control group term	M/S BPD mean 868.8 SD 166.0 Control group mean 3494 SD 300	M/S BPD mean 13.8 Range 0.7-54.5	2 populations assessed 2nd mean 10.6 SD 0.4 1st 17.7 SD 1.2	1982-1985 and 1991-1992	X	Vmax 22 spirometer (SensorMedics Inc., Anaheim, USA)	Expressed as percentage of the predicted values[E39]
Smith[E11] **Australia**	X	For whole preterm group all <32 weeks gestation mean 27 SD 2	For whole preterm group mean 862 SD 161	X	Mean age of BPD and No BPD groups together 10 SD 1	1992-1994	X	Vmax V62J Autobox (Sensormedics Corp, Yorba Linda, CA)	Expressed as percentage predicted[E35, E40, E41]
Jacob[E12, E13]	BPD (6M,	BPD group	BPD group	BPD group days	BPD group	1981-	X	X	Expressed as a

Canada	9F), Controls X	mean 28.7 SD 2.1 Control group term	mean 1110 SD 328 Control group X	of ventilatory assistance median 56.0, IQR 21.0-77.0 Control group X	mean 10.6 SD 1.7 Control group 10.6 SD 2.1	1987			percentage predicted for sex and height [E35]. For black subjects 15% was subtracted from the predicted values for spirometry[E42]
Kilbride[E15] USA	All ELBW (16M, 34F) Control (11M, 14F)	ELBW mean 26.1 SD 1.6 NBW >37	ELBW mean 701 SD 80 NBW >2500	ELBW mean 33 days SD 20 range 0-78	ELBW group mean 11.3, SD 1.6 NBW mean 11.1 SD 1.3	1983-1989	X	SensorMedics (Yorba Linda, CA), 922 dry, rolling seal spirometer	Expressed as a percentage predicted[x]
Korhonen[E16] Finland	Severe BPD group (10m 4F) Control group X	Severe BPD group mean 28 SD 2, range 23-30 Control group term	Severe BPD group mean 893 SD 225, range 570-1300	Severe BPD group 13/14 ventilated duration median 45, range 0-89 days	All BPD group median 7.1 range 6.7-7.8 Control group median 7.2, range 6.9-8.3	1990-1994	Severe BPD group 4/14 received	Flow volume spirograms were recorded by mass flow sensor (2200/Vmax 22, SensorMedics BV, Bilthoven, Netherlands)	Finish FVS reference values for children were used [E43].
Mieskonen[E20] Finland	BPD group (5M, 4F) Control group X	BPD group median 26.9, range 24.1-30.7, Controls term	BPD group median 760, range 600-1460 Controls X	39/40 PT children ventilated, BPD group median 42 days range 7-75	BPD group median 8.8 range 8.2-9.6 Controls median 8.9 range 5.3-11.2	1989-1991	X	Spirotrac III, Vitalograph Ltd, Buckingham, UK)	Expressed as percentage predicted [E35]
Palta[E22] USA	BPD 49% M Controls 56%	BPD group mean 28 SD 2.3, Controls X	BPD group mean 930 SD 228 Controls X	X	All VLBW mean 10.4 SD 0.42, controls mean 9.6 SD	1988-1991	Not given for BPD	Jaeger AM1 portable electronic peak flow meter	Expressed as percentage predicted ratios[E46]

					0.72				
Berman[E71] **USA**	X	BPD group mean 29	BPD group mean 1250	X	BPD group mean 5.8 range 4.2-7	X	X	Wedge spirometer (Med Science Electronics St. Louis)	Expressed as percentage predicted[E72]
Guimaraes[E27] **X (Data as Medians in paper)**	BPD group (10M, 3F)	BPD group median 27 range 23-30, mean 27 SD 1.9	BPD group median 850 range 565-1400, mean 900 SD 221	BPD group 13/13 ventilated median 58 days range 7-107, mean 54.5 SD 26.6	BPD group median 84 months range 62-107 mean 91.0 SD 11.3	2002-2004	X	Compact Vitalograph, Buckingham, UK	Expressed as percentage predicted[E35]
Berggren Brostrom[E29] **Sweden (Data as Medians in paper)**	X	Severe BPD group median 28, range 25-29	Severe BPD group median 905, range 775-1210	Duration of ventilatory therapy days Severe BPD group median 23, range 0-33	Severe BPD group median 85.5 months, range 83-90	1992-1997	Severe BPD group 2/4	Pneumotachograph (Vitalograph)	Expressed as percentage predicted[E35]

Table E3c:- Lung function outcomes of the included articles BPD group (supplemental oxygen dependency 36 weeks PMA) compared to term control group

STUDY	FEV_1 PREDICTED	FVC PREDICTED	FEF_{25-75} PREDICTED	RATIOS	TLC	RV	DLCO
Fawke[E1]	BPD mean 80 SD 13, Controls mean 100 SD 12	BPD mean 91 SD 13, Controls mean 102 SD 12	BPD mean 58 SD 21, Controls mean 90 SD 23	FEV_1/FVC BPD mean 88 SD 11, Controls mean 98 SD 8	X	X	X
Kulasekaran[E5]	BPD group mean 82.3	BPD group mean 88.7	BPD group mean 70.1	FEV_1/FVC	BPD group	BPD mean	BPD mean 79.2

	SD 13.9	SD 13.5	SD 24.8	BPD mean 84.0 SD 9.1	mean 94.7 SD 13.0	110.0 SD 48	SD 13.8
Doyle[E6]	BPD group mean 81.1 SD 13.7, Control group 97.9 SD 11.8	BPD group mean 82.9 SD 15.4, Control group 95.2 SD 12.6	BPD group mean 60.4 SD 20.3, Control group 85.6 SD 20.2	FEV_1/FVC BPD group mean 87.9 SD 9.4, Control group 91.4 SD 6.6	BPD group mean 97.5 SD 14.0, Control group 98.5 SD 11.7	BPD group mean 141.0 SD 39.9, Control group 112.2 SD 34.2	X
Giacoia[E8]	BPD group mean 72.7 SEM 6.1, Control group Mean 97.2, SEM 4.6	X	BPD group mean 49.5 SEM 6.0, Control group mean 88.5 SEM 7.1	X	X	X	X
Gross[E9]	BPD group mean 83 SD 17, Control group mean 97 SD 12	BPD group mean 93 SD 16, Control group mean 103 SD 11	BPD group mean 64 SD 24, Control group mean 88 SD 21	X	BPD group mean 104 SD 14, Control group mean 106 SD 13	BPD group mean 133 SD 41, Control group mean 112 SD 38	X
Halvorsen[E10]	BPD mean 81.4 SD 10.7 Control 98.6 SD 9.9	X	X	X	X	X	X
Smith[E11]	BPD mean 83 SD 12	BPD mean 95	BPD mean 67	X	X	X	X
Jacob[E12,E13]	BPD mean 63.6 SD 20.6, Control mean 94.3 SD 8.3	BPD mean 83.1 SD 18.2, Control mean 99.1 SD 9.4	BPD mean 40.3 SD 24.5, Control X	FEV_1/FVC BPD mean 69.2 SD 9.0, Control X	BPD mean 104.7 SD 13.2, Control X	BPD mean 181.8 SD 84.3, Control X	BPD mean 83.4 SD 10.5, Control mean 100.7 SD 17.1
Kilbride[E15]	BPD mean 72 SD 15 Control group mean 91 SD 9	BPD mean 90 SD 16 Control group mean 96 SD 11	BPD mean 67 SD 22 Control group mean 100 SD 17	FEV_1/FVC BPD mean 81 SD 8 Control group mean 89 SD 5	X	X	X
Korhonen[E16]	Severe BPD group mean 82 SD 13,	X	X	X	X	X	X

	Control group mean 99 SD 11, range 72-117						
Mieskonen[E20]	BPD group mean 73.5 SD 12, Control group 101.7 SD 8.4	BPD group mean 84.9 SD 10, Control group 104.5 SD 10.9	X	X	X	X	BPD group mean 82.8 SD 23.2, Control group 99.5 SD 11.6
Palta[E22]	BPD group mean 78 SD 13 Control group mean 97 SD 12	BPD group mean 79 SD 18 Control group mean 99 SD 27	X	X	X	X	X
Berman[E71]	BPD group mean 63 SD 25	BPD group mean 85 SD 21	X	X	X	X	X
Guimaraes[E27] **(Data as Medians in paper)**	BPD group median 79 extremes 58-98	BPD group median 88 extremes 58-111	BPD group median 87 extremes 48-148	FEV_1/FVC BPD group median 8.5 extremes 1-17	X	X	X
Berggren Brostrom[E29] **(Data as Medians in paper)**	Severe BPD group median 68, min max 44-71	Severe BPD group median 74, min max 54-89	Severe BPD group median 42, min max 19-123	Given in litres	X	X	X

Table E4a:- Description of the included articles preterm group (including studies with BPD) compared to term control group

STUDY	QUALITY SCORE	OBJECTIVE	STUDY DESIGN	STUDY GROUP	CONTROL GROUP	OUTCOME MEASURES
Konefal[E73]	15	To evaluate whether mild to moderate infant RDS requiring NCPAP during the neonatal period would	Cross sectional	31 PT children treated with n-CPAP split into 2 groups by	19 children > 36 weeks gestation treated with n-CPAP	Spirometry

		have an impact on pulmonary function		gestation		
Anand[E74]	**16**	To determine if VLBW is associated with reduced lung function and respiratory health in adolescence and if it is whether this impairment is associated with prematurity or IUGR	Cohort	128 VLBW (≤1500g)	128 children assumed to be near to term	Spirometry Questionnaires
Fawke[E1]	16	To assess the degree of respiratory morbidity and in extremely premature children in relation to current clinical status and neonatal determinants.	Cohort study	182 EP (≤25 weeks gestation)	161 classmate controls excluded classmates who were preterm	Spirometry Post-bronchodilator response Questionnaire
Arad[E2]	8	To compare lung function following neonatal intensive respiratory care on the same children in infancy and childhood	Follow up study	10 PT	X	Spirometry
De Kleine[E3]	18	Examine the effect of lung injury caused by IPPV for HMD on lung function in children	Follow up study	40 PT ventilated for HMD (38 with LF results) and 38 PT non ventilated with HMD	39 randomly selected pupils of a similar age	Spirometry Respiratory symptoms questionnaire Review of follow up records for PT
Doyle[E4]	19	To determine the respiratory health of children of birthweight <1501g, compared to NBW controls in adolescence	Cohort study	180 VLBW (<1501g) -169 with spirometry results	42 NBW (>2499g), 39 with spirometry results	Spirometry Assessment of respiratory health
Burns[E75]	16	To investigate he fitness	Case-control	54 ELBW	55 term	Spirometry

		levels and motor competency of non-disabled ELBW children as they were reaching adolescence. It also aimed to determine whether a relationship exists between their motor competence and physical fitness independent of their growth and respiratory status.	study	(<1000g) – 53 with spirometry results	controls – 51 with spirometry results	Movement Assessment Battery for Children Cardio respiratory endurance
Doyle[E6]	17	To determine respiratory function at 8 years in ELBW, very PT children born in the 1990s compared with NBW controls	Cohort	298 ELBW (<1000g)/ very preterm (< 28 weeks gestation) 240 with LF results	208 NBW (>2499g)	Spirometry ISAAC questionnaire
Evenson[E76]	19	To evaluate associations between LBW and body fat, BP, lung and endothelial function, and maximal oxygen uptake in young adults	Longitudinal follow up study	37 PT with VLBW (<1501g)	63 controls with NBW	Spirometry Questionnaire BP Endothelial function Maximal oxygen uptake
Galdes-Sebaldt[E7]	11	To evaluate the long-term effect of prematurity and/or HMD on pulmonary function and airway reactivity.	Follow up study	30 <1500g children split into 2 groups no HMD and HMD	27 terms	Spirometry Questionnaire Airway reactivity
Gappa[E77]	11	To determine long term pulmonary sequelae of surfactant treatment in premature infants with RDS	Follow up study	40 children 25-30 weeks gestation split into 2 groups	X	Spirometry Questionnaire Bronchial hyperreactivity

				29 with LF results		
Grischkan[E78]	19	To assess the role of in utero and perinatal exposures in modifying asthma risk among children born prematurely	Cohort study	251 preterm children (≤36 weeks) split over 2 groups asthma, no asthma groups	X	Spirometry Questionnaire
Gross[E9]	19	To assess long-term pulmonary outcome of a regional cohort of children born <32 weeks' gestation compared with a matched term control group	Cohort	125 PT children born at 24 to 31 weeks gestation - 96 had spirometry results split into 2 groups BPD and no BPD	108 healthy term (38 to 42 weeks gestation) controls	Spirometry Bronchodilator responsiveness Ongoing health problems Rehospitalisation Respiratory symptoms Exercise testing
Kennedy[E14]	15	To assess the importance of the contributions of birth weight, gestational age, neonatal respiratory illness, and its treatment on subsequent childhood lung function in a cohort of children of birth weight less than 1500g.	Cohort study	VLBW cohort (<1500g) 102 children	82 control children , 1 birth weight <2kg, 2 born at 36 weeks rest at term	Spirometry Respiratory questionnaire
Kilbride[E15]	14	To assess pulmonary function and exercise capacity of apparently asymptomatic children who were born EP	Longitudinal follow up study	50 ELBW children <801g	25 age matched NBW children >37 weeks gestation and >2500g BW	Medical history and recent Hospitalisations Spirometry Exercise testing
Baraldi[E17]	12	To assess the cardio-respiratory and metabolic response to exercise in	Area cohort study	15 VLBW children (<1501g)	26 born at term but data not given for	Spirometry Questionnaire Exercise testing

		VLBW children and to compare exercise performance in AGA versus SGA			spirometry	
Wagner[E79]	11	Purpose of the study was to compare the 88% SAT test with spirometry in young children with regard to completion success rate, abnormality, and questionnaire response regarding respiratory health	Follow up study	From 33 PT children with history of RDS 20 had results	X	Spirometry Questionnaire
Mai[E80]	11	To assess the relationship between VLBW and the development of asthma, lung function and atopy	Cohort study	74 VLBW (≤1500g)	64 term born NBW (≥2500g)	Spirometry Questionnaire Skin prick tests Hypertonic saline provocation tests Cell stimulation Cytokine analyses IgE antibody analyses
MacLusky[E81]	10	To identify the incidence and possible factors contributing to the development of long term abnormalities in pulmonary function	Longitudinal cohort study	48 PT children <33 weeks 47 with spirometry	X	Spirometry Metacholine challenge
Mieskonen[E20]	13	To evaluate the possible inflammatory basis of lung function abnormalities	Cohort study	40 children with a gestational age ≤ 30 weeks or birthweight <1500g	14 term controls	Spirometry Questionnaires Skin Prick Tests Measurement of exhaled nitric oxide Spirometry before and after Salbutamol

Odberg[E82]	12	To compare trajectories for growth and somatic health characteristics until adulthood of non-handicapped LBW and NBW children	Population based longitudinal study	134 LBW (<2kg) children	135 term NBW (>3kg) children	Spirometry Questionnaire BP
Rivlin[E83]	9	To study the long term outcomes of children with Wilson-Mikity syndrome	Cohort study	9 PT children with Wilson-Mikity syndrome 8 with spirometry results	X	Spirometry Follow up history Inhalation challenge with metacholine
Wiebicke[E84]	10	To assess outcomes after antenatal versus no antenatal steroid therapy.	RCT follow up	20 PT children given dex or placebo	X	Spirometry
Von Mutius[E85]	12	To investigate the significance of gestational age, birth weight, mechanical ventilation after birth, and a family history of asthma for the development of childhood asthma	Cross sectional study	253 PT children LF results for 118 females given	2113 term girls	Spirometry Questionnaire Cold air challenge Skin prick tests
Palta[E22]	15	To determine lung function at 10 years in VLBW children and controls	Cohort study	265 VLBW children ≤ 1500g	360 unselected controls	Spirometry Home spirometry
Smith[E86]	14	To assess the 10 year lung function and fitness outcomes for children who were born weighing <1000g and before 32 weeks gestation	Cross sectional study	126 children who were born weighing <1000g and before 32 weeks gestation 123 with LF	34 control children born at term	Spirometry Fitness assessment

				results		
Telford[E87]	10	The outcome in late childhood for children entered into a randomised trial of CNEP versus standard respiratory management for the treatment of RDS.	Cohort study	133 PT children split into 2 groups 130 with LF results	X	Spirometry Questionnaire LF pot bronchodilator
Siltanen[E88]	12	To evaluate the association between atopy, wheezing and impaired respiratory function in children born very preterm compared to term controls	Cohort study	72 PT children birth weight <1501g 50 with LF results	65 full term children birth weight >2500g 54 with LF results	Spirometry Questionnaire Skin prick testing Exercise testing
Gross[E89]	11	To study growth, neurodevelopmental, and pulmonary outcomes at adolescence in children who had participated in a double-blind placebo-controlled trial of dexamethasome	RCT follow up	22 PT children (birthweight ≤1250g, gestational age ≤ 30 weeks) 20 with LF results	X	Spirometry Neurodevelopmental outcome
Vrijlandt[E24]	14	To investigate the long term effects of prematurity on lung function and exercise capacity	Prospective cohort study	42 PT (gestational age <32 weeks and/or birthweight under 1500g)	48 healthy term controls	Spirometry Exercise testing
Nikolajev[E90]	7	To quantify the separate effects of prematurity and IUGR on lung volumes and airway flow values.	Cohort study	Authors supplied information on 45 children ≤36 weeks gestation	X	Spirometry Questionnaire

Bertrand[E91]	14	To assess the respective roles of prematurity, RDS and its treatment, and familial airway hyper reactivity in the pathogenesis of long term pulmonary sequelae in children who survive premature birth.	Retrospective case-control study	11 syndrome group, 11 no disease group	11 syndrome group siblings, 11 no disease siblings, 9 control	Spirometry Airway reactivity
Borkenstein[E92]	13	To investigate pulmonary function in long term survivors of artificial ventilation in the neonatal period.	Cohort study	11 children who had ventilation 6 PT children with LF results	X	Spirometry
Abreu[E26]	14	To investigate cardio respiratory capacity and investigate the presence of exercise-induced bronchospasm among children with BPD	Case control study	26 PT children 23 with LF results	20 term children 17 with LF results	Spirometry Exercise testing

Table E4b:- Demographics of the included articles preterm group (including studies with BPD) compared to term control group

STUDY COUNTRY	SUBJECTS (GENDER)	GA (WEEKS)	BW (GRAMS)	DURATION ON MECHANICAL VENTILATION (DAYS)	AGE TESTED (YEARS)	YEAR OF BIRTH	SURFACTANT GIVEN	METHOD OF MEASURING LUNG FUNCTION	METHOD OF STANDARDISING LUNG FUNCTION MEASUREMENTS
Konefal[E73] **Poland**	PT group 28-32 weeks	PT group 28-32 weeks	PT group 28-32	PT group 28-32 weeks	PT group 28-32 weeks	1990-2000	X	Lungtest 500, MES, Cracow Poland	Expressed as percentage

	gestation (4M,3F), PT group 33-36 weeks gestation (10M,14F), Control group (10M,9F)	gestation mean 30.3 SD 1.5, PT group 33-36 weeks mean 35.2 SD 1.05, Control group mean 38.5 SD 1.17	weeks gestation mean 1629 SD 339, range 1300-2100. PT group 33-36 weeks mean 2455 SD 547, range 1500-3680, Control group mean 3235 SD 496, range 2270-4100	gestation mean 4.4 SD 3.1, range 2-10. PT group 33-36 weeks mean 2.4 SD 1.6, range 1-7, Control group mean 2.6 SD 2.3, range 1-10	gestation mean 9.57 SD 3.7, PT group 33-36 weeks mean 10.4 SD 2.8, Control group mean 10.4 SD 2.7				predicted[E93]
Anand[E74] UK	VLBW group (72M,56F) Control group (72M,56F)	VLBW mean 30.7, SD 2.7, range 26-36 Control group assumed to be near to term	VLBW mean 1249, SD 185.2, range 630-1500 Control group mean 3338, SD 507.6, range 2098-4550	VLBW group 83 received respiratory support	15	1980-81	X	Portable spirometer Vitalograph-Alpha-II	Expressed as percentage predicted[E94]

Fawke[E1] **UK and Ireland**	EP (43% M), Controls (43% M)	EP mean 25.0, SD 0.7 Control X excluded if preterm	EP mean 750, SD 120, Controls X	X	Range 10.1 to 12.1. EP mean 10.9, SD 0.38. Controls mean 10.9 SD 0.55.	1995	EP 153/182 Controls X	Portable spirometer (Jaeger Masterscope, Lab Manager, V4.65; CareFusion, Hoechberg, Germany	Spirometry data were expressed as z-scores to adjust for height, age and sex[E30, E31]
Arad[E2] **Israel**	X	PT group mean 30.4, range 28-35	PT 1257g Range 900-1900	8 for between 1 and 11 days, 4 being ventilated for 4 or more days	Mean 6.8 SD 0.6	1977-1979	X	Pneumotachograph-based system (Hewlett-Packard 47120A Pulmonary Desk System)	Expressed as percentage predicted[E32]
De Kleine[E3] **The Netherlands**	11 BPD (8M,3F) 29 non BPD (19M, 10F), 38 non ventilated (24M, 14F), 39 controls (20M, 19F)	BPD mean 30.6 SD 2.0, Non BPD mean 32.2 SD 1.8, Non ventilated mean 31.8 SD 1.9, Controls X	BPD mean 1673 SD 340, Non BPD mean 1952 SD 460, Non ventilated mean 1809 SD 419, Controls X	BPD mean 9.0 days (range 1.8-36), Non BPD 29/29 mean 2.9 days (range 0.8-6.9), non ventilated 0/38, Controls X	BPD mean 13.4 SD 3.1, Non BPD mean 12.3 SD 2.9, Non ventilated mean 12.8 SD 2.7, Controls mean 13.7 SD 1.6	1967-1977	X	Water sealed spirometer (Lode instruments, Groningen, Netherlands)	Lung function as percentage predicted for sex and height [E 32,E33]
Doyle[E4] **Australia**	500-999g group (35M, 43F), 1000-1500g group (55m, 47F) >2499g group	500-999g group mean 27.5 SD 2.3, 1000-1500g group mean 29.6 SD 1.5,	500-999g group mean 859 SD 100, 1000-1500g	X	500-999g group mean 14.1 SD 0.2, 1000-1500g group mean 14.2 SD 0.3,	1977-1982	Not given	Jaeger Bodyscreen II-Bodybox (Jaeger, Germany)	Lung function as percentage predicted for age, height and gender [E34]

	(26M, 16F)	>2499g group mean 39.9 SD 1.0	group mean 1259 SD 145, >2499g group mean 3420 SD 427		>2499g group mean 14.2 SD 0.1				
Burns[E75] **Australia**	ELBW (31M,23F) Controls (28M,27F)	ELBW mean 26.6 SD 2.1 Controls at least 37 weeks	ELBW mean 769g SD 148 Controls X	X	ELBW mean 12 years 6 months SD 8 months, control children 12 years 5 months SD 11 months	1992-1994	X	Spirobank (Medical International Research ISO 9001, EN 46001; Rome, Italy)	Lung function as percentage predicted[x]
Doyle[E6] **Australia**	ELBW (129F,111M), Control group (98M, 110F)	ELBW group mean 26.7, SD 1.9 Control group X	ELBW group mean 885, SD 159, Control group Control group >2499	X	8-9	1991-1992	In whole PT cohort 92/240 treated	Jaeger Body-screen II Bodybox (Jaeger, Germany)	Results expressed as percentage predicted for age, height and gender [E34]
Evenson[E76] **Norway**	VLBW group 37 (20M, 17F), Controls 63 (29M, 34F)	VLBW group median 28, range 24-35, Control median 40, range 37-42	VLBW group median 1245, range 800-1500,	VLBW X, Control 0/63	VLBW group mean 18.2, SE 0.1, Control group mean 18.6 SE 0.1	1986-1988	X	Master screen spirometer (Jaeger, GmbH and Co, KG)	Expressed as percentage predicted adjusted for sex[X]

			Control median 3700, range 2670-5140						
Galdes-Sebaldt[E7] **USA**	<1500g no HMD group (11M, 8F), <1500g HMD group (3M,8F) Controls (14M, 13F)	<1500g no HMD group mean 29.3, SEM 0.4, range 26-32, <1500g HMD group mean 29.5, SEM 0.6, range 26-32, Controls mean 39.9, SEM 0.2, range 38-42	<1500g no HMD group mean 1044, SEM 30, range 900-1290, <1500g HMD group mean 1217, SEM 34, range 964-1361, Controls mean 3429, SEM 64, range 2707-4111	<1500g no HMD 13/19, <1500g HMD 9/11, Controls X	<1500g no HMD group mean 11.1, SEM 0.2, <1500g HMD group mean 11.2, SEM 0.2, Controls mean 11.6 SEM 0.2	1973-1977	X	Automated pulmonary function lab model M100B (SRL Medical Inc, Dayton, OH)	Results as percentage predicted adjusted for height and sex [E35] and ethnicity [E36]
Gappa[E77] **Germany**	Surfactant group (13M,9F), Placebo group (6M, 12F)	Surfactant group mean 28.1 SD 1.5, Placebo group mean 27.2, SD 1.3	Surfactant group mean 1114 SD 271, Placebo group mean 1043, SD 237	X	Surfactant group mean 6.63 SD 0.18, Placebo 6.55 SD 0.23	1987-1988	22/22 Surfactant group, 0/18 placebo group	Ganshorn, Niederluer, Germany in Hannover and Jaeger, Wurzburg, Germany in Ulm and Hamburg	Expressed as percentage predicted reference values appropriate for gender, height and weight [E95]

Grischkan[E78] **USA**	Asthma group 59·8% male, no asthma group 46·1% male	Asthma group mean 30.2 SD 3.1, No asthma mean 31.8 SD 3.0	Asthma group mean 1437.1 SD 572.8, No asthma mean 1620.2 SD 549.4	Asthma group 86.7% ventilated, No asthma group 62.3% ventilated	Asthma group mean 9.4 SD 0.8, No asthma group mean 9.3 SD 0.8	1988-1993	X	Spirometry performed in the sitting position(x)	As percentage predicted adjusted for age, sex and height [E37]. Values for African American children were further adjusted by multiplying the predicted value by 0·85.
Gross[E9] **USA**	No BPD group (27M, 26F), BPD group (23M, 20F) Control group (62M, 46F)	No BPD group mean 29 SD 2, BPD group mean 27 SD 2, Control group mean 40.1 SD 1.1	No BPD group mean 1270 SD 306, BPD group mean 1053 SD 356, Control group mean 3565 SD 427	55% of no BPD group median 6 95% of BPD group median 34	7	1985-1986	0	SensorMedics 2200 Pulmonary Function Equipment (SensorMedics, Anaheim Calif)	Results as percentage predicted for age, height and sex [E37, E38]
Kennedy[E14] **Australia**	VLBW group (47M, 55F) Control group (39M, 43F)	VLBW group mean 29.6 SD 2.8, Control mean 40.0 SD 1.6	VLBW group mean 1160.1 SD 227.1, Control group mean 3459.1 SD 509.0	Duration of IPPV VLBW group median 3.9 IQR 0.2, 14.3 Control n/a	VLBW group mean 11.3 SD 0.8, Control 11.4 SD 0.8	1981-1982	X	Pulmonary function testing was performed using the Jaeger Masterlab system	Results were evaluated as percentage predicted for gender and height [E34]
Kilbride[E15]	All ELBW	ELBW mean	ELBW	ELBW mean 33	ELBW group	1983-	X	SensorMedics (Yorba	Expressed as a

USA	(16M, 34F) Control (11M, 14F)	26.1 SD 1.6 NBW >37	mean 701 SD 80 NBW >2500	days SD 20 range 0-78	mean 11.3, SD 1.6 NBW mean 11.1 SD 1.3	1989		Linda, CA), 922 dry, rolling seal spirometer	percentage predicted[X]
Baraldi[E17] **Italy**	VLBW (6M, 9F)	VLBW mean 32.1 SD 3.0 range 28-37	VLBW mean 1287 SD 143 range 1000-1500	7/15 duration 1-8 days	VLBW mean 9.9 SD 1.8 range 7.8-12.2	1976-1979	X	101 water spirometer (Biomedin, Padova, Italy)	Expressed as percentage of reference values [E35]
Wagner[E79] **USA**	PT group (16M, 17F)	PT group Mean 28.3 SD 2.3 range 25-34	PT group Mean 1055 SD 317	Duration mean 30 days SD 25	5-7 mean 5.9 SD 0.7	X	X	Medical Graphics model 1070	Lung function as percentage predicted [E62, E96,E97]
Mai[E80] **Sweden**	VLBW (44M, 30F), controls (33m, 31F)	VLBW mean 31 SD 2 range 25-36, controls term	VLBW group ≤1500g, controls ≥ 2500g	VLBW group 13/74	VLBW mean 12.6 SD 0.2, Controls mean 12.7 SD 0.3	1987-1988	0	MasterScope spirometer (Jaeger, Wurzburg, Germany)	Expressed as a percentage of the reference values [E61]
MacLusky[E81] **Canada**	PT (22F,26M)	PT mean 29.2 SD 2.1	PT mean 1166 SD 193	30/48 required IPPB mean 109 hours SD 236	Mean 9.1 SD 0.6	1974-1975	X	Systems 80 computerized spirometer, Gould Inc, Dayton, Ohio	Expressed as a percentage of predicted [E62]
Mieskonen[E20] **Finland**	PT group (19M, 21F) Control group X	PT group median 27.9, range 24.1-30.9, Controls term	PT group median 990, range 600-1575 Controls X	39/40 PT children ventilated, median 10 days range 0-75	PT group median 8.3 range 7.5-9.6 Controls median 8.9 range 5.3-11.2	1989-1991	X	Spirotrac III, Vitalograph Ltd, Buckingham, UK)	Expressed as percentage predicted [E35]
Odberg[E82] **Norway**	LBW (61M,73F), NBW	LBW group mean 32.2 SD 33 NBW	LBW group mean 1544g SD	X	Mean age of both groups 18 years and	1986-1988	X	Vmax 22 spirometer (SensorMedics Inc, Anaheim, CA, USA)	Expressed as a percentage predicted [E47]

	(64M,71F)	term	369 NBW >3kg		11 months				
Rivlin[E83] **Canada**	PT (4M,5F)	PT mean 29.1, range 27-32	PT mean 1175.4, range 920-1435	3/9 required mech vent for 5-6 days, and CPAP for 3-8 days, 2/9 required CPAP for 3-7 days	Mean 7.6 SD 0.3	1974-1975	X	Collins 9 liter respirometer	Expressed as percentage predicted [E62]
Wiebicke[E84] **Canada**	PT children (12M, 8F)	Dex group mean 32.8 SEM 0.4, Placebo group mean 32.2 SEM 0.6	X	X	Age of dex group mean 7.5 SEM 0.3, placebo group mean 7.5 SEM 0.3	1976	X	9 liter water-sealed spirometer (Collins, Braintree, MD)	Results expressed as percentage of predicted values [E67, E 97]
Von Mutius[E85] **Germany**	All female	PT <37 weeks, Controls term	Mean not given	40/108 received ventilatory support	Controls mean 10 SEM 0, PT mean 10.1 SEM 0.1	X	X	Pneumoscope II spirometer (Jager, Wurzburg, Germany)	Results as percentage predicted reference population consisted of 2337 German children
Palta[E22] **USA**	VLBW 49% M Controls 56% M	VLBW group mean 29 SD 2.5, Controls X	VLBW group mean 1123 SD 250 Controls X	X	VLBW mean 10.4 SD 0.42, controls mean 9.6 SD 0.72	1988-1991	Varying percentages of children given surfactant across the years	Jaeger AM1 portable electronic peak flow meter	Expressed as percentage predicted ratios [E46]
Smith[E86] **Australia**		PT mean 26.9 SD 1.7, Controls mean 39.4 SD 1.2	PT mean 862.4 SD 160.9, Controls mean	PT 100 required intubation	PT mean 10.1 SD 1.1, Control group mean 11.6 SD 0.8	1992-1994	X	Sensormedics Vmax V62J Autobox (Sensormedics Corp, Yorba Linda, CA)	Expressed as percentage predicted [E40, E35, E41]

			3400.5, SD 512.5						
Telford[E87] **UK**	PT (79M, 54F)	PT median 31 IQR 29-33	PT median 1.59, IQR 1.17-2.04	91/133 intubated at study entry	Median 11.3, 9.6-14.9	X	41/127	Vitalograph Spirometer 2120, Ennis, Ireland)	Expressed as percentage predicted[x]
Siltanen[E88] **Finland**	PT (46M, 26F), Control (34M, 31F)	PT group mean 28.5, SD 2.4, range 23.4-33.7 Control group term	PT mean 1075, control group 3593	X	PT group mean 10.1 SD 0.3 range 9.6-10.8, control group mean 10.1 SD 0.4 range 9.4-10.9	1987-1988	PT 19/72	Vitalograph Compact Spirometer (Vitalograph Ltd, UK)	Expressed as percentage predicted [E37]
Gross[E89] **USA**	All PT (9M, 13F)	42 day dex mean 26 (95% CI 25,27), 18 day dex 26 (95% CI 24,28), control group mean 27 (95% CI 24,29)	42 day dex mean 851 (95% 776,926), 18 day dex 810 (95% CI 620, 1000), control group mean 948 (95% CI 721, 1175)	42 day dex mean 31 days (95% CI 23, 40), 18 day dex mean 114 days (95% CI 39,188), control group mean 75 days (95% CI 44-106)	14.5-15.5	X	X	SensorMedics 2200 (SensorMedics, Anaheim, CA)	Results as percentage predicted on the basis of height, age and gender [E37, E38]
Vrijlandt[E24] **The Netherlands**	PT group (21M, 21F) Control group (16M, 32F)	Whole PT group mean 30 SD 2, range 26-36, Control	Whole PT group mean 1246 SD 232, range 720-	Whole PT group mean 6.3 days SD 12, range 0-51, Control group	Whole PT group mean 19 SD 0.3, range 19-20, Control	PT group 1983	0/42	Spirometry using a pneumotachograph	Results as percentage predicted based on height [E47]

		group term range 37-42	1750, Control group X	X	group mean 20.8 SD 1.2, range 18-22				
Nikolajev[E90] Finland	Not given for 45 PT children	45 children ≤36 weeks	Not given for 45 PT children	Not given for 45 PT children	All children median 10.3 range 7.3-15.3	1979-1986	Not given for 45 PT children	2200 computerized pulmonary function laboratory from Sensor Medics (Yorba Linda, CA)	Results as percentage predicted [E48]
Bertrand[E91] Canada	PT group (9M,13F) Control group (12M,10F) no info on 9 controls	Syndrome group mean 32.5 SD 3.6, No disease group mean 33.4 SD 2.5, Syndrome group siblings mean 39.2 SD 1.5, No disease siblings mean 38.7 SD 1.5 Controls no prematurity	Syndrome group mean 1900 SD 615, No disease group mean 2010 SD 480, Syndrome group siblings mean 3140 SD 400, No disease siblings mean 3040 SD 480 Controls X	X	Syndrome group mean 10.1 SD 1.1, No disease group mean 8.0 SD 1.0, Syndrome group siblings mean 11.4 SD 2.1, No disease siblings mean 9.9 SD 2.1 Controls no prematurity	X	X	SRL Medical	Expressed as percentage predicted [E35]
Borkenstein[E92] Austria	PT group with LF results (3M, 3F)	PT group with LF results range 30-36 mean 33·3	PT group with LF results range 1200-2600 mean 1806·7	PT group with LF results 6/6 IPPV hours range 34-624 mean 189·3	PT group with LF results range 3.5-5.1 mean 4.2	X	X	Pneumotachograph and whole body plethysmograph (Pulmostar, Fenyes & Gut, Basle, Switzerland)	Expressed as a percentage predicted [E35]

Abreu[E26] **Brazil**	PT group (17M, 9F) Control group (9M, 11F)	PT group mean 35 SD 2.3 range 28-36, BPD group mean 32 SD 1.5 range 30-34, Control group term	PT group mean 1765 SD 621 range 850-2800, BPD group mean 1037 SD 229 range 830-1670, Control group X	PT group mean 1 SD 2 range 0-6, BPD group 13/13 mean 11 SD 6.6 range 3-26 Control group X	PT group mean 8.3 SD 1.11, BPD group mean 8.5 SD 0.97, Control mean 8.2 SD 1.14	1993-1996	X	SpiroCard PC Card Flux spirometer (QRS Diagnostic-Plymouth, USA)	Expressed as percentage predicted [E35]

Table E4c:- Lung function outcomes of the included articles preterm group (including studies with BPD) compared to term control group

STUDY	FEV_1 PREDICTED	FVC PREDICTED	FEF_{25-75} PREDICTED	RATIOS	TLC	RV	DLCO
Konefal[E73]	PT group mean 95.07, SD 17.54 Control mean 96.2, SD 20.2	Results given for each group separately	X	X	Results given for each group separately	X	X
Anand[E74]	VLBW group mean 94.9 SD 13.8 Control group mean 96.5 SD 10.8	VLBW group mean 109.5 SD 14.6 Control group mean 106.0 SD 12.2	VLBW group mean 88.1 SD 25.6 Control group mean 100.5 SD 20.0	FEV_1/FVC VLBW group mean 87.0 SD 9.04 Control group mean 90.8 SD 6.4	X	X	X
Fawke[E1]	EP mean 83 SD 14, Controls mean 100 SD 12	EP mean 93 SD 14, Controls mean 102 SD 12	EP mean 61 SD 23, Controls mean 90 SD 23	FEV_1/FVC EP mean 89 SD 11, Controls mean 98 SD 8	X	X	X
Arad[E2]	PT group mean 82.6 SD 10.8	X	X	X	X	X	X

De Kleine[E3]	BPD and Non BPD and non ventilated mean 87.83 SD 17.33, Control mean 95 SD 12	X	X	X	X	X	X
Doyle[E4]	2 LBW groups mean 94.82 SD 14.42 NBW mean 104.6 SD 13.2	Given separately for LBW groups NBW mean 104.8 SD 12.0	Given separately for LBW groups NBW mean 99.1 SD 23.4	FEV_1/FVC Given separately for LBW groups NBW mean 87.0 SD 7.0	Given separately for LBW groups NBW mean 102.5 SD 13.9	Given separately for LBW groups NBW mean 117.4 SD 30.8	X
Burns[E75]	ELBW group mean 88.98 SD 13.47, Control mean 97.73, SD 10.89	ELBW group mean 96.96 SD 12.48, Control mean 98.88, SD 11.02	X	FEV_1/FVC ELBW group mean 93.26 SD 7.84, Control mean 101.55, SD 6.05	X	X	X
Doyle[E6]	ELBW group mean 84.9 SD 12.7, Control group 97.9 SD 11.8	ELBW group mean 86.1 SD 14.1, Control group 95.2 SD 12.6	ELBW group mean 65.2 SD 21.7, Control group 85.6 SD 20.2	FEV_1/FVC ELBW group mean 88.4 SD 9.2, Control group 91.4 SD 6.6	ELBW group mean 96.0 SD 13.9, Control group 98.5 SD 11.7	ELBW group mean 129.9 SD 43.1, Control group 112.2 SD 34.2	X
Evenson[E76]	VLBW group mean 85.2 SE 1.8, Control group mean 98.1 SE 1.4	X	X	X	VLBW group mean 99.2 SE 1.7, Control group mean 100.6 SE 1.3	Given as litres	X
Galdes-Sebaldt[E7]	<1500g no HMD group mean 82 SEM 2, <1500g HMD group mean 83 SEM 2, control group mean	X	<1500g no HMD group mean 82 SEM 4, <1500g HMD group mean 90 SEM 7, control group mean	X	X	X	<1500g no HMD group mean 87 SEM 3, <1500g HMD group mean 97

	92 SEM 1		104 SEM 3				SEM 4, control group mean 99 SEM 3
Gappa[E77]	Premature group combined mean 101.93 SD 14.22	Results given for 2 groups separately	X	X	X	X	X
Grischkan[E78]	2 groups combined mean 90.6 SD 15.76	X	X	Results given separately for 2 groups	X	X	X
Gross[E9]	PT group mean 91.28 SD 19.01, Control group mean 97 SD 12	Results given separately for 2 groups	Results given separately for 2 groups	X	Results given separately for 2 groups	Results given separately for 2 groups	X
Kennedy[E14]	VLBW group mean 91.0 SD 14.9 Control group mean 102.1 SD 10.2	VLBW group mean 99.1 SD 10.6 Control group mean 104.2 SD 9.6	VLBW group mean 70.1 SD 25.7 Control group mean 90.7 SD 21.8	X	VLBW group mean 99.7 SD 12.8 Control group mean 98.3 SD 10.8	X	X
Kilbride[E15]	ELBW mean 85 SD 14 Control group mean 91 SD 9	ELBW mean 93 SD 14 Control group mean 96 SD 11	ELBW mean 84 SD 25 Control group mean 100 SD 17	FEV_1/FVC ELBW mean 86 SD 8 Control group mean 89 SD 5	X	X	X
Baraldi[E17]	VLBW mean 94.2 SD 8.9	VLBW mean 92.8 SD 8.1	VLBW mean 103.4 SD 23.5	X	X	X	X
Wagner[E79]	PT mean 121.2 SD 37.5	Results given individually for each patient	Results given individually for each patient	X	X	X	X
Mai[E80]	VLBW group mean 92 SD 12, Controls mean 95 SD 10	X	MMEF VLBW group mean 85 SD 22, Controls mean 88 SD 20	X	X	X	X
MacLusky[E81]	PT group mean 91.2	PT group mean 86.9	PT group mean 87 SD	X	PT group mean	X	X

	SD 12.7	SD 10.4	24		94 SD 13.9		
Mieskonen[E20]	PT group mean 84.1 SD 14.3, Control group 101.7 SD 8.4	PT group mean 90.2 SD 11.2 Control group 104.5 SD 10.9	X	X	X	X	PT group mean 86.7 SD 12.8, Control group 99.5 SD 11.6
Odberg[E82]	LBW group mean 106.8 SD 13.5, NBW group mean 110.2 SD 14.2	LBW group mean 115.4 SD 13.5, NBW group mean 115.7 SD 14.8	X	FEV_1/FVC LBW group mean 82 SD 10, NBW group mean 85 SD 10	X	X	X
Rivlin[E83]	PT mean 81.3 SD 8.1	Results given individually for each patient	Results given individually for each patient	X	X	X	X
Wiebicke[E84]	PT group mean 86.3 SD 8.9	X	X	Results given for each patient individually	Results given for each patient individually	Results given for each patient individually	X
Von Mutius[E85]	PT group mean 98.7 SD 10.46, Controls 100.4 SD 14.12	Results given for PT in 2 groups	X	X	X	X	X
Palta[E22]	VLBW group mean 86 SD 14 Control group mean 97 SD 12	VLBW group mean 85 SD 26 Control group mean 99 SD 27	X	X	X	X	X
Smith[E86]	PT group mean 85 SD 12.4, control mean 95 SD 10.2	PT group mean 96.3 SD 13.6, control mean 102.1 SD 10.1	PT group mean 82.1 SD 8.3, control mean 86.4 SD 3.7	FEV_1/FVC PT group mean 71.8 SD 22.9, control mean 91.4 SD 15.7	PT group mean 108.7 SD 10.7, control mean 102.8 SD 10.1	PT group mean 140.8 SD 44.4, control mean 98.5 SD 39.8	X
Telford[E87]	PT group mean 85.5 SD 12.54	Results given for PT in 2 groups	X	X	X	X	X
Siltanen[E88]	PT group mean 92 SD 13.1 Control group mean	PT group mean 96 SD 12.6 Control group mean	PT group mean 87 SD 24.0 Control group mean	FEV_1/FVC PT group mean 84 SD 7.8	X	X	X

	104 SD 8.0	102 SD 9.6	114 SD 21.2	Control group mean 88 SD 5.4			
Gross[E89]	PT group mean 79.96 SD 18.3	Results given individually for the 3 groups	Results given individually for the 3 groups	X	Results given individually for the 3 groups	Results given individually for the 3 groups	X
Vrijlandt[E24]	PT group mean 95.4 SD 15.9 Control group mean 109.6 SD 13.4	PT group mean 97.7 SD 13.7 Control group mean 106.0 SD 10.8	X	FEV_1/FVC PT group mean 82.2 SD 8.2 Control group mean 87.4 SD 6.6	PT group mean 100.1 SD 9.9 Control group mean 103.3 SD 9.7	PT group mean 99.4 SD 28.3 Control group mean 90.3 SD 25.3	PT group mean 88.4 SD 13.7 Control group mean 96.3 SD 9.9
Nikolajev[E90]	PT group mean 90.2 SD 9.88	X	Results given separately for 2 PT groups	Results given separately for 2 PT groups	X	X	X
Bertrand[E91]	PT group mean 76 SD 13.4, Term group mean 84.6 SD 10.2,	X	X	X	X	X	X
Borkenstein[E92]	PT children mean 65.4 SD 8.3	Results given for the 6 children individually	X	Results given for the 6 children individually	Results given for the 6 children individually	Results given for the 6 children individually	X
Abreu[E26]	PT group mean 99.43 SD 12.61, Control group mean 102 SD 15	X	X	X	X	X	X

Key to abbreviations in all tables

BW	Birth-weight	**HMD**	Hyaline membrane disease
LBW	Low birth-weight	**RDS**	Respiratory distress syndrome
VLBW	Very low birth-weight	**Dex**	Dexamethasone
ELBW	Extremely low birth-weight	**IPPV**	Intermittent positive pressure ventilation
NBW	Normal birth-weight	**IPPB**	Intermittent Positive Pressure Breathing
PT	Preterm	**HFV**	High frequency ventilation
EP	Extremely preterm	**n-CPAP**	Nasal continuous positive airway pressure
BPD	Bronchopulmonary dysplasia	**CNEP**	Continuous negative

			extrathoracic pressure
M	Male	**ISAAC**	International Study of Asthma and Allergies in Childhood
F	Female	**M/S**	Moderate/severe
X	Missing data	**FEV_1**	Forced expiratory volume in 1 second
SD	Standard deviation	**FVC**	Forced vital capacity
SEM	Standard error mean	**FEF_{25-75}**	Mid-expiratory flow at 75-25% of FVC
IQR	Interquartile range	**TLC**	Total lung capacity
GA	Gestational age	**RV**	Residual volume
RCT	Randomised control trial	**DLCO**	Diffusing capacity of lung for carbon monoxide
NICU	Neonatal intensive care unit	**CT**	Computed tomography

		HRCT	High resolution computed tomography
LF	Lung function	**IUGR**	Intrauterine Growth Retardation
AGA	Appropriate for gestational age	**SGA**	Small for gestational age

Appendix 1

The effect of premature birth compared to term birth on later lung function - a systematic review of the literature.

Review Question

Is lung function in later life poorer in preterm babies compared to babies born at term?

Search strategy

A search strategy was developed for electronic databases using the keywords and MeSH headings below. The search strategy was tested for citations on the OVID Medline database 1950-2010. The Observational Studies search filter used by SIGN (Scottish Intercollegiate Guidelines Network) http://www.sign.ac.uk/methodology/filters.html#obs was adapted to retrieve types of study designs included in the review.

The search strategy will be modified to search rest of the bibliographic databases. In addition, a range of 'snowballing' techniques will be used to increase the sensitivity of the search, including reference list follow up, contact with subject experts and relevant websites/organisations, and table of content scanning for the top three most frequently cited journals.

Keywords/ MeSH headings

Bronchospirometry/
Bronchospirometries
Chronic respiratory questionnaire
FEF 25 75 Percent
Forced Expiratory Volume/
FEVT
Flow Rate, Maximal Expiratory/
Forced Expiratory Flow Rates/
Forced Vital Capacity
ISAAC questionnaire
Lung function test
Lung Volume Measurements/
MEFR
Maximal Midexpiratory Flow Rate/

Maximal Expiratory Flow Rate/
MMFR

Pulmonary Function Test
Respiratory Function Tests/
SGRQ
Spirometry/
Spirometries
St George's respiratory questionnaire
Timed Vital Capacity
Vital Capacity/
Volumes, Forced
Volume, Forced Expiratory/
Birth Weight/
Birth Weight Low/
Fetal Growth Retardation/
Infant, Low Birth Weight/
Infant, Very Low Birth Weight/
Infant, Extremely Low Birth Weight/
Infant, Premature/
IUGR
Intrauterine growth restriction
Low birth weight
Obstetric Labor, Premature/
Premature infant
Preterm labor
Premature labor
Premature birth
Preterm birth

Asthma/
bronchial asthma
Bronchopulmonary Dysplasia/
Chronic lung disease of infancy/
Hyaline Membrane Disease/
Chronic lung disease of prematurity
Respiratory Distress Syndrome, Newborn/
Pulmonary Disease, Chronic Obstructive/

Ovid MEDLINE - Search Strategy

1. exp Bronchospirometry/
2. exp Vital Capacity/

3. exp Forced Expiratory Volume/
4. Respiratory Function Tests/
5. exp Forced Expiratory Flow Rates/
6. exp Maximal Expiratory Flow Rate/
7. exp Maximal Midexpiratory Flow Rate/
8. Spirometry/
9. Lung Volume Measurements/
10. Bronchospirometries.mp.
11. Forced Vital Capacit*.mp.
12. Timed Vital Capacit*.mp.
13. (MEFR or MMFR or FEVt or SGRQ).mp.
14. St George's respiratory questionnaire.mp.
15. Chronic Respiratory Questionnaire.mp.
16. ISAAC questionnaire.mp.
17. Flow Rate, Maximal Expiratory/
18. Volume, Forced Expiratory/
19. Volumes, Forced/
20. Forced volume.mp.
21. ((Maximal or flow rate) adj2 expirator*).mp.
22. FEF 25 75 Percent.mp.
23. ((lung* or respiratory or pulmonary) adj2 (function* or expirator* capacit*)).mp.
24. spirometries.mp.
25. or/1-24
26. ((lung*1 or respiratory or pulmonary) adj2 (disease*1 or disorder*1)).mp.
27. exp Asthma/
28. exp Respiratory Distress Syndrome, Newborn/
29. Bronchial asthma.mp.
30. Chronic lung disease of prematurity.mp.
31. Chronic lung disease of infancy.mp.
32. Hyaline Membrane Disease/
33. Bronchopulmonary Dysplasia/
34. Pulmonary Disease, Chronic Obstructive/
35. or/26-34
36. exp Infant, Low Birth Weight/
37. exp Infant, Very Low Birth Weight/
38. exp Infant, Extremely Low Birth Weight/
39. exp Infant, Premature/
40. Obstetric Labor, Premature/

41. exp Premature Birth/
42. Fetal Growth Retardation/
43. Birth Weight/
44. Low Birth Weight.mp.
45. ((Preterm* or Premature*) adj2 (labo#r* or birth* or born or infant or baby or babies or child or children or girl*1 or boy*1)).mp.
46. Prematurity.mp.
47. IUGR.mp.
48. intrauterine growth restriction.mp.
49. or/36-48
50. 25 or 35
51. 49 and 50
52. Epidemiologic Studies/
53. exp case control studies/
54. exp cohort studies/
55. Case control.tw.
56. (cohort adj (study or studies)).tw.
57. Cohort analy*.tw.
58. (Follow up adj (study or studies)).tw.
59. (observational adj (study or studies)).tw.
60. Longitudinal.tw.
61. Retrospective.tw.
62. Cross sectional.tw.
63. Cross-sectional studies/
64. case-control studies/ or longitudinal/ or follow-up studies/ or prospective studies/
65. or/52-64
66. 51 and 65

The following table is an explanation of the symbols used in the search strategy above.

/	after an index term (MeSH heading) indicates that all subheadings were selected.
*	before an index term indicates that that term was focused - i.e. limited to records where the term was a major MeSH/Emtree term.
"exp"	before an index term indicates that the term was exploded.
.tw.	indicates a search for a term in title/abstract
.mp.	indicates a free text search for a term

#	retrieves records that contain the search term with substituted character(s) in the specified location.
*	at the end of a term indicates that this term has been truncated.
*n	The limited truncation symbol, $n, Retrieves records that contain the search term and all possible suffix variations of a root word with the maximum number of characters that may follow the root word or phrase, specified by n.
?	in the middle of a term indicates the use of a wildcard.
adj	indicates a search for two terms where they appear adjacent to one another

Databases and information sources

Bibliographic databases
CINAHL 1982-
Embase 1980-
HMIC Health Management Information Consortium 1979
Medline 1950-
Medline in Process
Scopus
OpenSIGLE
Web of Knowledge Science Citation Index Expanded 1981- Social Science Citation Index 1981- ISI Proceedings 1990-

Websites
Action Medical Research http://www.action.org.uk/
SPARKS https://www.sparks.org.uk/NetCommunity/SSLPage.aspx?pid=19
Wellcome Trust http://www.wellcome.ac.uk/

Appendix 2

The effect of premature birth compared to term birth on later lung function - a systematic review of the literature

Source	Y/N/not clear/not reported/comment
Study ID number	
Report ID (surname of first author and year study undertaken)	
Title	
Authors names	
Journal	
Language published in	
Reviewed by	
Other comments	
Eligibility	
Confirm eligibility for review	
Gestation ≤ 32 weeks gestation	
Gestation 33-37 weeks gestation	
Other gestation please state	
Age at time of LF testing < 5 years	
Age at time of LF testing ≥ 5 years	
If age less than 5 years method of LF testing	
LF variables collected FEV0.5	
LF variables collected FEV1	
LF variables collected FVC	
LF variables collected FEF25-75/MEF	
LF variables collected Ratios	
LF variables collected TLC	
LF variables collected RV	
LF variables collected DLCO	
LF values reported compared to predicted values or term group comparison	
BPD/CLD group	
Reason for exclusion	
Need to write to authors	
Other comments	
Methods	
Study design	
Age of study groups	

Other comments	
Participants	
Total number	
Total number in CLD/BPD group	
Total number in prem group	
Total number in control group	
Total number excluded	
Reason why excluded	
Setting	
Birthweight	
Social status	
Rate of ventilation	
Personal smoking by the prem subjects	
Age at time of LF testing	
Sex	
Weeks gestation	
Maternal smoking	
Surfactant given and details	
Maternal steroids given and details	
Country	
Co-morbidity	
Ethnicity	
Year of birth of participants	
CLD/BPD and how defined	
Neonatal data information	
Date of study	
Other comments	
Interventions	
Did study consider intervention	
Specific intervention	
Intervention details	
Is baseline data adequate	
Other comments	
Outcomes	

FEV0.5	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			

Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

FEV1	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

FVC	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

FEF25-75/MEF	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of			

standardisation			
Raw values			

ratios	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

TLC	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

RV	Prem	BPD/CLD/	control
Total number in group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

DLCO	Prem	BPD/CLD/	control
Total number in			

group			
Mean			
SD			
Median			
Significance			
Method of measuring LF			
Method of standardisation			
Raw values			

Miscellaneous	
Funding source	
Key conclusions	
Miscellaneous comments from authors	
References to other relevant studies	
Other comments	

Appendix 3

Assessment of study quality

Quality	Scores awarded	
Selection		
1) Representativeness of the exposed cohort		
a) truly representative of the average in the community	4	
b) Somewhat representative of the average in the community	3	
c) Selected group of users eg nurses, volunteers	2	
d) no description of the derivation of the cohort	1	
2) Selection of the non exposed cohort		
a) Drawn from the same community	3	

b) Drawn from a different source	2	
c) no description of the derivation of the non exposed cohort	1	
3) Ascertainment of exposure (weeks gestation)		
a) secure record (scan +/- LMP)	3	
b) Written self report (medical assessment)	2	
c) no description	1	
4) Demonstration that outcome of interest was not present at start of study		
a) yes	2	
b) no	1	
Outcome		
1) Assessment of outcome		
a) independent blind assessment	4	
b) record linkage	3	
c) self report	2	
d) no description	1	
2) Adequacy of follow up of cohorts		
a) complete follow up all subject accounted for	4	
b) subjects lost to follow up unlikely to introduce bias	3	
c) follow up rate low and no description of those lost	2	
d) no statement	1	

Figure E1. Preterm group (no BPD) where the results were reported as percentages of predicted values.

Figure E2. BPD (supplemental oxygen dependency at 28 days of life) results reported as percentages of predicted values.

Figure E3. BPD (supplemental oxygen dependency 36 weeks PMA) where results were reported as percentages of predicted values.

Figure E4. Preterm group (including groups with BPD) where results were reported as percentages of predicted values.

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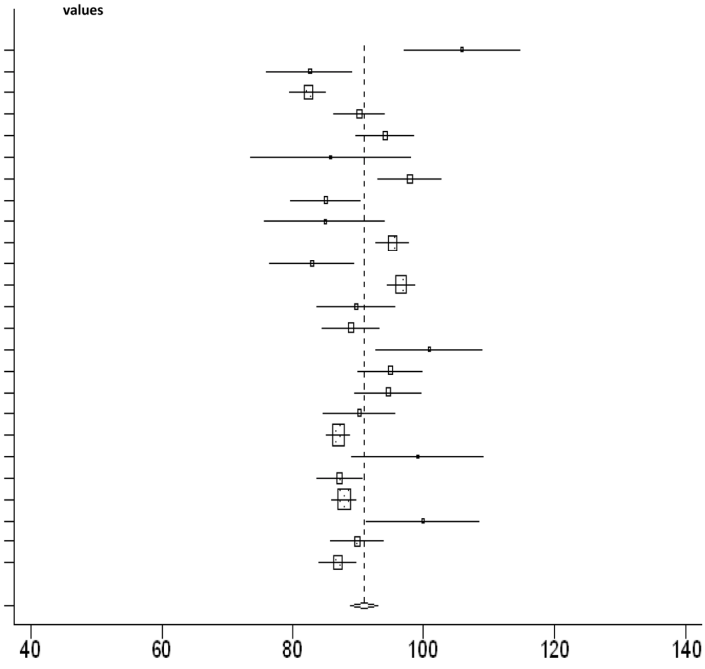
Study	Weight	Study Est	95% CI	
			Lower	Upper
Wheeler 1984	0.02	106	97.1	114.9
Arad 1987	0.03	82.6	75.91	89.29
Galdes-Sebaldt 1989	0.04	82.37	79.55	85.19
De Kleine 1990	0.04	90.34	86.4	94.28
Baraldi 1991	0.04	94.2	89.7	98.7
Giacoia 1997	0.02	85.9	73.55	98.25
Gross 1998	0.04	98	93.15	102.85
Jacob 1998	0.03	85.1	79.63	90.57
Mitchell 1998	0.02	85	75.7	94.3
Kennedy 2000	0.04	95.4	92.84	97.96
Pianosi 2000	0.03	83	76.42	89.58
Doyle 2001	0.04	96.7	94.53	98.87
Mieskonen 2002	0.03	89.8	83.79	95.81
Kilbride 2003	0.04	89	84.63	93.37
Barker 2003	0.03	101	92.85	109.15
Korhonen 2004	0.04	95	90.07	99.93
Halvorsen 2005	0.03	94.7	89.66	99.74
Baraldi 2005	0.03	90.3	84.81	95.79
Doyle 2006	0.04	87.1	85.27	88.93
Vrijlandt 2006	0.02	99.2	89.07	109.33
Kulasekaran 2007	0.04	87.3	83.75	90.85
Palta 2007	0.04	88	86.09	89.91
Abreu 2007	0.02	100	91.32	108.68
Fawke 2010	0.04	90	85.96	94.04
Smith 2011	0.04	87	84.06	89.94

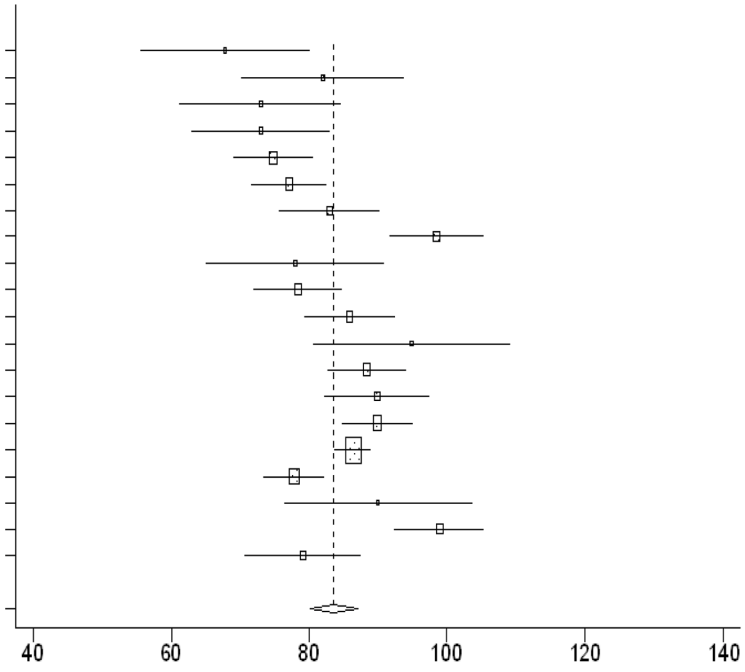
Figure E1 Preterm group (no BPD) where the results were reported as percentages of predicted values



Random pooled est = 90.980 95% CI lower = 88.841, upper = 93.119
Heterogeneity: Q= 164.448 on 24 degrees of freedom (p=0.000)
Moment-based estimate of between studies variance = 22.076

Figure E2 BPD (oxygen dependency at 28 days of life) where the results were reported as percentages of predicted values

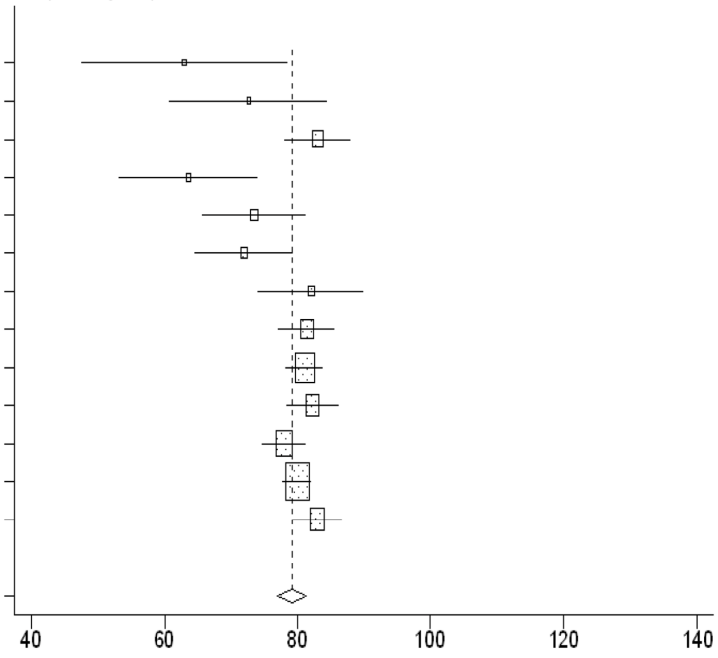
Study	Weight	Study Est	95% CI Lower	95% CI Upper
Smyth 1981	0.01	67.8	55.52	80.08
Wheeler 1984	0.01	82	70.18	93.82
Bader 1987	0.01	73	61.22	84.78
De Kleine 1990	0.01	73	62.95	83.05
Northway 1990	0.02	74.8	69.12	80.48
Ahrens 1991	0.02	77.11	71.53	82.69
Santuz 1995	0.02	83	75.64	90.36
Koumbourlis 1996	0.02	98.6	91.85	105.35
Mitchell 1998	0.01	78	64.98	91.02
Kennedy 2000	0.02	78.4	71.87	84.93
Pianosi 2000	0.02	86	79.34	92.66
Ng 2000	0.01	95	80.63	109.37
Doyle 2001	0.02	88.5	82.79	94.21
Barker 2003	0.02	90	82.39	97.61
Korhonen 2004	0.02	90	84.9	95.1
Halvorsen 2005	0.02	86.4	83.69	89.11
Baraldi 2005	0.02	77.8	73.29	82.31
Vrijlandt 2006	0.01	90.1	76.38	103.82
Abreu 2007	0.02	99	92.48	105.52
Karila 2009	0.02	79.1	70.64	87.56



Random pooled est = 83.666 95% CI lower = 80.187, upper = 87.145
Heterogeneity: Q=97.283 on 19 degrees of freedom (p=0.000)
Moment-based estimate of between studies variance = 45.393

Study	Weight	Study Est	95% CI Lower	Upper
Berman 1986	0.01	63	47.51	78.49
Giacoia 1997	0.02	72.7	60.74	84.66
Gross 1998	0.07	83	77.92	88.08
Jacob 1998	0.03	63.6	53.18	74.02
Mieskonen 2002	0.04	73.5	65.66	81.34
Kilbride 2003	0.05	72	64.65	79.35
Korhonen 2004	0.04	82	73.94	90.06
Halvorsen 2005	0.08	81.4	77.12	85.68
Doyle 2006	0.1	81.1	78.25	83.95
Kulasekaran 2007	0.08	82.3	78.33	86.27
Palta 2007	0.09	78	74.68	81.32
Fawke 2010	0.11	80	77.76	82.24
Smith 2011	0.08	83	79.13	86.87

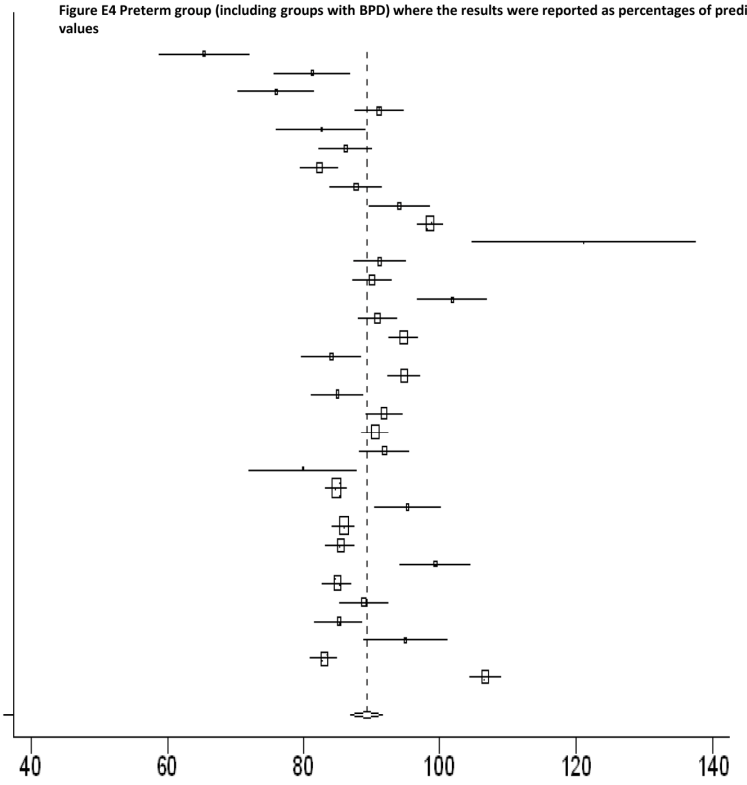
Figure E3 BPD (supplemental oxygen-dependency 36 weeks PMA) where the results were reported as percentages of predicted values



Random pooled est = 79.096 95% CI lower = 76.911, upper = 81.282
Heterogeneity: Q=30.311 on 12 degrees of freedom (p=0.003)
Moment-based estimate of between studies variance = 7.967

Figure E4 Preterm group (including groups with BPD) where the results were reported as percentages of predicted values

Study	Weight	Study Est	95% CI	
			Lower	Upper
Borkenstein 1980	0.02	65.4	58.76	72.04
Rivlin 1985	0.02	81.3	75.69	86.91
Bertrand 1985	0.02	76	70.26	81.74
MacLusky 1986	0.02	91.2	87.57	94.83
Arad 1987	0.02	82.6	75.91	89.29
Wiebicke 1988	0.02	86.3	82.4	90.2
Galdes-Sebaldt 1989	0.02	82.37	79.55	85.19
De Kleine 1990	0.02	87.83	83.93	91.73
Baraldi 1991	0.02	94.2	89.7	98.7
von Mutius 1993	0.02	98.7	96.81	100.59
Wagner 1994	0.01	121.2	104.77	137.63
Gross 1998	0.02	91.3	87.5	95.1
Nikolajev 1998	0.02	90.2	87.31	93.09
Gappa 1999	0.02	101.93	96.75	107.11
Kennedy 2000	0.02	91	88.11	93.89
Doyle 2001	0.02	94.82	92.65	96.99
Mieskonen 2002	0.02	84.1	79.67	88.53
Anand 2003	0.02	94.9	92.51	97.29
Kilbride 2003	0.02	85	81.12	88.88
Mai 2003	0.02	92	89.27	94.73
Grischkan 2004	0.02	90.6	88.65	92.55
Siltanen 2004	0.02	92	88.37	95.63
Gross 2005	0.02	79.96	71.94	87.98
Doyle 2006	0.02	84.9	83.29	86.51
Vrijlandt 2006	0.02	95.4	90.59	100.21
Palta 2007	0.02	86	84.31	87.69
Telford 2007	0.02	85.5	83.34	87.66
Abreu 2007	0.02	99.43	94.28	104.58
Smith 2008	0.02	85	82.81	87.19
Burns 2009	0.02	88.98	85.35	92.61
Evenson 2009	0.02	85.2	81.69	88.71
Konefal 2010	0.02	95.07	88.9	101.24
Fawke 2010	0.02	83	80.97	85.03
Odberg 2010	0.02	106.8	104.51	109.09



Random pooled est = 89.361 95% CI lower = 86.998, upper = 91.725

Heterogeneity: Q=677.081 on 33 degrees of freedom (p=0.000)

Moment-based estimate of between studies variance = 44.464