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(Review)

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[Intervention Review]

Non-pharmaceutical management of respiratory morbidity in children with severe global developmental delay

Naomi R Winfield¹, Nicki J Barker², Esme R Turner³, Gemma L Quin⁴

¹Physiotherapy Department, Milton Keynes Hospital NHS Foundation Trust, Milton Keynes, UK. ²Respiratory Medicine, Sheffield Children's NHS Foundation Trust, Sheffield, UK. ³Hope House Children's Hospices, Shropshire, UK. ⁴School of Health Professions, Plymouth University, Plymouth, UK

Contact address: Naomi R Winfield, naomiwinfield@hotmail.co.uk.

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ABSTRACT

Background

Children with severe global developmental delay (SGDD) have significant intellectual disability and severe motor impairment; they are extremely limited in their functional movement and are dependent upon others for all activities of daily living. SGDD does not directly cause lung dysfunction, but the combination of immobility, weakness, skeletal deformity and parenchymal damage from aspiration can lead to significant prevalence of respiratory illness. Respiratory pathology is a significant cause of morbidity and mortality for children with SGDD; it can result in frequent hospital admissions and impacts upon quality of life. Although many treatment approaches are available, there currently exists no comprehensive review of the literature to inform best practice. A broad range of treatment options exist; to focus the scope of this review and allow in-depth analysis, we have excluded pharmaceutical interventions.

Objectives

To assess the effects of non-pharmaceutical treatment modalities for the management of respiratory morbidity in children with severe global developmental delay.

Search methods

We conducted comprehensive searches of the following databases from inception to November 2013: the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Allied and Complementary Medicine Database (AMED) and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). We searched the Web of Science and clinical trials registries for grey literature and for planned, ongoing and unpublished trials. We checked the reference lists of all primary included studies for additional relevant references.

We updated searches in November 2019 and July 2020 and added six studies to awaiting classification, but these results have not been fully incorporated into the review.

Selection criteria

Randomised controlled trials, controlled trials and cohort studies of children up to 18 years of age with a diagnosis of severe neurological impairment and respiratory morbidity were included. Studies of airways clearance techniques, suction, assisted coughing, non-invasive ventilation, tracheostomy and postural management were eligible for inclusion.

Data collection and analysis

We used standard methodological procedures as expected by The Cochrane Collaboration. As the result of heterogeneity, we could not perform meta-analysis. We have therefore presented our results using a narrative approach.

Main results

Fifteen studies were included in the review. Studies included children with a range of severe neurological impairments in differing settings, for example, home and critical care. Several different treatment modalities were assessed, and a wide range of outcome measures were used. Most studies used a non-randomised design and included small sample groups. Only four randomised controlled trials were identified. Non-randomised design, lack of information about how participants were selected and who completed outcome measures and incomplete reporting led to high or unclear risk of bias in many studies. Results from low-quality studies suggest that use of non-invasive ventilation, mechanically assisted coughing, high-frequency chest wall oscillation (HFCWO), positive expiratory pressure and supportive seating may confer potential benefits. No serious adverse effects were reported for ventilatory support or airway clearance interventions other than one incident in a clinically unstable child following mechanically assisted coughing. Night-time positioning equipment and spinal bracing were shown to have a potentially negative effect for some participants. However, these findings must be considered as tentative and require testing in future randomised trials.

Authors' conclusions

This review found no high-quality evidence for any single intervention for the management of respiratory morbidity in children with severe global developmental delay. Our search yielded data on a wide range of interventions of interest. Significant differences in study design and in outcome measures precluded the possibility of meta-analysis. No conclusions on efficacy or safety of interventions for respiratory morbidity in children with severe global developmental delay can be made based upon the findings of this review.

A co-ordinated approach to future research is vital to ensure that high-quality evidence becomes available to guide treatment for this vulnerable patient group.

PLAIN LANGUAGE SUMMARY

Non-drug management of breathing problems for children with severe physical and intellectual impairment

Background For a variety of reasons, some children live with very severe intellectual and physical problems; they are unable to walk or talk and require a lot of care. In this study we refer to them as children with severe global developmental delay (SGDD); this is not a specific diagnosis but is rather an 'umbrella term' used to describe a group of children with similar problems. These children may have weak or stiff muscles and deformities of their skeleton; often they have problems with swallowing, resulting in food or saliva going into their lungs. Frequently they have a poor cough reflex and lack the strength required to expel secretions when they do cough. When we sleep, our breathing becomes shallower; for some children with SGDD whose breathing is already shallow when awake, falling asleep means that they do not breathe sufficiently deeply to take in enough oxygen and breathe out enough carbon dioxide. The consequence of these problems is that their respiratory system becomes weakened; they are more likely to develop chest infections, and relatively minor infections can make them very unwell. This can result in their spending a lot of time in hospital. This affects the quality of life for these children and families and is very expensive. Many types of treatment could help, but no good summary of studies has been prepared to tell healthcare professionals which treatments are best and when they should be used; this is the reason for this review.

Review question The aim of our review was to discover how effective each type of treatment is for managing breathing problems in children with severe global developmental delay. As so many treatments are available, we decided to look only at treatments that do not involve drugs.

Study characteristics We carried out a wide database search to look for studies of interventions for the management of breathing problems in children with severe neurological impairment. We found 15 studies of interest, which included a number of different types of treatment.

Key results The results showed that several different treatments provided potential benefits, and for most interventions no serious adverse effects were reported. However, the quality of the studies was not good enough to inspire confidence in the findings. Night-time positioning equipment and spinal bracing were shown to have a potentially negative effect in some participants. Although some studies looked at the same type of treatment, they used it in different ways or used different measures to assess effectiveness, so we could not put the results together.

Quality of the evidence Of the 15 studies included here, only four used the 'gold standard' study design for health interventions. The remainder of the studies used less robust study designs, which limits the strength of the results. Further well-designed randomised studies including larger numbers of participants are required to guide healthcare professionals to select the most effective treatments.

This plain-language summary is current to November 2013. We updated searches in November 2019 and July 2020 and added six studies to awaiting classification, but these results have not been fully incorporated into the review.

BACKGROUND

Description of the condition

Improvement in neonatal and paediatric care in recent decades has resulted in the survival of increasing numbers of children with multiple and profound impairments. Babies born early or in frail condition are being successfully treated and are surviving into childhood. Young children suffering serious neurological impairment as a result of infection, illness or trauma are also surviving, as are children with various genetic, neuromuscular and metabolic disorders (Blucker 2011). Although some of these children go on to lead normal lives, others are left with severe impairment in all aspects of functioning. The causes of these impairments are varied; however, these children bear the illness burden of profound and multiple disabilities, and for research purposes may be grouped under the label of severe global developmental delay. SGDD is therefore an umbrella term that broadly captures a population of children with severe intellectual disability and severe motor impairment, most of whom are extremely limited in their functional movement and are dependent upon others for all activities of daily living.

Although SGDD does not directly cause lung dysfunction, the combination of immobility, weakness, skeletal deformity and parenchymal damage from aspiration can lead to a significant incidence of respiratory illness (Toder 2000; McCrea 2013). Respiratory pathology is a major contributory factor to both morbidity and mortality in this patient group (Mestrovic 2006; O'Loughlin 2009). A broad range of treatment options exist; to focus the scope of this review and allow in-depth analysis, we have excluded pharmaceutical interventions.

Description of the intervention

Respiratory problems experienced by this patient group are often multi-faceted and complex, and a myriad of interventions are applied in clinical practice, including chest physiotherapy, suction, mechanical insufflation-exsufflation (MIE), non-invasive ventilation (NIV), postural management and tracheostomy.

How the intervention might work

The rationale by which these interventions may reduce respiratory morbidity broadly includes improved ventilation, enhanced ventilation-perfusion (V/Q) matching and improved mobilisation and expectoration of secretions.

Why it is important to do this review

Patients with SGDD do not share a specific diagnosis, and some have no definitive diagnosis—representative statistics are difficult to obtain. As a result of heterogeneity within this patient group and the breadth of factors impacting upon their respiratory health, no comprehensive review of the literature has been performed.

Current research into paediatric respiratory care tends to focus on very specific groups of patients, such as those with cystic fibrosis, spinal muscular atrophy (SMA) or Duchenne muscular dystrophy (DMD), with consensus guidelines published for the respiratory care of some of these groups (Finder 2004; Wang 2007; Hull 2012). The available literature reflects that respiratory compromise is a major cause of mortality for individuals with cerebral palsy (Sullivan 2006; Somerville 2008; Fitzgerald 2009; Augustine 2010;

Healy 2010; Littleton 2011), neuromuscular disorders (Katz 2004; Simonds 2006; Panitch 2009) and severe developmental disability (Mestrovic 2006; O'Loughlin 2009). It is also a major cause of morbidity (Chatwin 2003; Seddon 2003; Fitzgerald 2009; Healy 2010; Yuan 2010) requiring hospital admissions and impacting upon quality of life.

Children with SGDD often end up in costly acute care for prolonged periods of time. The current economic and political climate has propelled a drive toward community-based care for long-term conditions. Proactive respiratory care, improved access to specialist equipment and the availability of trained staff could allow treatment of subacute and chronic respiratory conditions in the community, while facilitating timely discharge and preventing hospital readmissions, but this would require a change in commissioning driven by clinical evidence. A systematic review that brings together the range of management options in a way that can inform best practice is therefore timely.

An evidence-based approach is necessary to ensure that this growing population of vulnerable children receive equity of care, and that treatment is safe and effective and enhances quality of life for them and for their families.

OBJECTIVES

To assess the effects of non-pharmaceutical treatment modalities for the management of respiratory morbidity in children with severe global developmental delay.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs), controlled trials and cohort studies provided that data from a comparison group were reported (within-participant comparison accepted). Case reports, case series and systematic reviews were not eligible for inclusion.

The rationale for including prospective non-randomised studies (NRSs) was that RCTs are rarely available for this patient group, but other types of studies are available. Lack of RCTs is a challenge for systematic reviews in many population-based studies of child health, for example, child abuse, driving a need to be "creative in our study design and use several sources and study types to inform the evidence base that we draw on in decision making" (Silbert 2007). Thus when a paucity of high-level evidence is found, it is preferable to report other types of studies, whilst remaining aware of the inherent risks of bias in these study designs, to provide a summary of available evidence. In the clinical setting, children with SGDD receive treatment for respiratory morbidity every day. As no published review currently exists, use of these treatments is based upon little more than clinical reasoning and expert opinion. Evidence from non-randomised trials may lack the protection from selection bias that is afforded by randomisation; however, it can provide a starting point for evaluating the safety and efficacy of treatments and can help guide future research.

Types of participants

We included studies of children up to 18 years of age with a diagnosis of severe neurological impairment and respiratory morbidity. Some studies provided both child and adult data. We included studies from which it was possible to extract child data directly from the results. In cases where the data were presented together, we contacted study authors to request separate paediatric data for analysis.

We included studies of children with severe physical neurological impairment but without intellectual impairment, excluding studies only when cognitive impairment would make the intervention studied impracticable in a wider group. Our rationale for this was that severe cognitive impairment makes collecting effort-dependent outcome measures (e.g. many pulmonary function tests) impossible when the actual intervention tested does not require cognitive ability.

We excluded studies of children with a primary respiratory pathology such as cystic fibrosis and those receiving palliative or end of life care.

Types of interventions

Airways clearance techniques, postural drainage, suction, mechanical insufflation-exsufflation, non-invasive ventilation, tracheostomy, postural drainage, sleep systems, postural management.

Types of outcome measures

Primary outcomes

- Respiratory parameters (e.g. tidal volume (V_T), respiratory rate (RR), end-tidal carbon dioxide ($PETCO_2$), peak cough flow (PCF), oxygen saturation (SpO_2), partial pressure of carbon dioxide ($PaCO_2$), partial pressure of oxygen (PaO_2) (as defined by study authors)).
- Number of hospital admissions.
- Number of respiratory infections requiring antibiotics.

Secondary outcomes

- Length of hospital stay.
- Quality of life measures (as defined by study authors).
- Length of survival.
- Mortality.
- Adverse outcomes for each intervention, for example, pain, pneumothorax.

Search methods for identification of studies

Electronic searches

The search strategy was developed in collaboration with an Information Specialist at The Cochrane Collaboration (Elizabeth Stovold) and was designed to capture studies of all design types. We searched the following databases.

- Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 11).
- MEDLINE (Ovid) (1946 to November week 3 2013).
- EMBASE (Ovid) (1980 to week 47 2013).

- Allied and Complementary Medicine Database (AMED) (EBSCOHost) (1985 to November 2013).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOHost) (1982 to November 2013).

See [Appendix 1](#) for the full search strategy. We searched all databases from their inception to the present with no restriction on language of publication. We managed references using EndNote.

We performed further searches in November 2019 and July 2020. Six studies have been added to [Studies awaiting classification](#) and will be incorporated into the review at the next update.

Searching other resources

We searched the Web of Science for grey literature such as conference proceedings, and we searched clinical trials registries for planned, ongoing and unpublished trials. We checked the reference lists of all primary included studies for additional relevant references.

We found evidence from a conference extract of a potentially relevant study that had been completed but had not been published. From the clinical trials registry, we were able to ascertain that this trial was sponsored by the manufacturer of a high-frequency chest wall oscillation (HFCWO) device, whom we contacted for assistance with tracing the study data. This led to the identification of two eligible studies: one pending publication ([Fitzgerald 2013](#)) and one unpublished ([Landon 2013](#)). To avoid risk of bias, we then contacted the main commercial manufacturers that we were able to identify of all included interventions, namely, HFCWO, mechanical insufflation-exsufflation (MIE) and night-time positioning equipment (NTPE), to request information regarding any unpublished data. All replied, but they supplied no new eligible references.

Data collection and analysis

Selection of studies

Two review authors (NW, NB, GQ) independently screened titles and abstracts generated by the electronic and manual searches to ascertain whether studies met the prespecified inclusion criteria ([Appendix 2](#)). We accessed full text for all potentially relevant articles, which two review authors (NW, ET, NB, GQ) reviewed independently to assess eligibility. We resolved disagreements by discussion and reached consensus. It was not necessary to request evaluation by a third independent review author, although this mechanism was available.

Foreign language papers were assessed for eligibility by individuals with appropriate language skills; none of these studies met eligibility criteria, and so further translation was not warranted.

Data extraction and management

Two review authors (NW, ET, NB, GQ) independently extracted data from eligible studies. We resolved disagreements by reaching consensus; the input of a third review author was not required. In a number of cases, we contacted authors of included studies to request important missing data; however only two study authors were able to provide this information.

Two review authors (NW, ET, NB, GQ) extracted all relevant data including demographics of participants, study methodology,

outcome measures and results for each of the included studies; this information was documented on a standardised data extraction form.

Assessment of risk of bias in included studies

Two review authors (NW, ET, NB, GQ) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved disagreements by discussion. Risk of bias was assessed according to the following domains.

- Random sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessment.
- Incomplete outcome data.
- Selective outcome reporting.
- Other sources of bias.

We graded each potential source of bias as having high, low or unclear risk of bias. We present risk of bias tables for each included study within the [Characteristics of included studies](#) tables.

Measures of treatment effect

For continuous variables, we reported mean differences (MDs) with 95% confidence intervals (CIs). We consider a P value less than 0.05 as statistically significant.

We planned to use odds ratios (ORs) for dichotomous data and to present them along with the absolute difference. We planned to calculate risk ratios (RRs) for events presenting 'bad' outcomes, for example, increased exacerbations, development of antibiotic resistance or worsened quality of life.

For ease of communication and for clarity, we planned to calculate the risk difference (RD) and the number needed to treat for an additional beneficial outcome (NNTB).

Unit of analysis issues

For continuous data, we planned to use the mean difference based on change from baseline over mean difference based on absolute. For cross-over trials, we planned to report data when presented with results from a paired t-test, if available. For cluster-randomised trials, we planned to analyse data in consultation with a statistician, using methods recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

We contacted the original investigators to verify study characteristics and to request missing numerical outcome data. We planned to adopt the intention-to-treat principle while analysing the outcomes or to use 'imputation methods' to impute standard deviations. We planned to perform sensitivity analyses to assess the effects of missing data on overall results and conclusions. The potential impact of missing data (if any) on the findings of the review is discussed.

Assessment of heterogeneity

We planned to use the I^2 statistic to measure heterogeneity among the trials in each analysis. An I^2 value greater than 50% would have been considered as providing evidence of heterogeneity.

Heterogeneity in all study characteristics was marked; for this reason results are not combined and are described using a narrative approach.

Assessment of reporting biases

We contacted study authors to request additional information about study methods and missing data when necessary; authors most often failed to respond or were unable to provide the requested information. Risk of bias is discussed further within the narrative text and is presented in tables and figures in the section on [Risk of bias in included studies](#).

Data synthesis

We planned to use fixed-effect models when pooling data. We planned to present the findings of our primary outcomes in a 'Summary of findings' table in accordance with the recommendations provided in the *Cochrane Handbook for Systematic Reviews of Interventions* and using GRADEPro software (Higgins 2011).

When data were not suitable for meta-analysis, we described results for relevant outcomes narratively. We described results from non-randomised studies narratively as well.

As expected in a review covering multiple interventions, heterogeneity among study characteristics was marked. We had planned to perform subgroup analysis for each intervention and to perform meta-analysis when indicated. Even in studies of the same intervention, similarities in population, study protocol and outcome measures were insufficient to allow meta-analysis. For this reason, results are not combined and are described using a narrative approach.

Subgroup analysis and investigation of heterogeneity

For analysis, we grouped studies by type of intervention, namely, ventilatory assistance (VA), postural support (PS) and airways clearance techniques (ACTs).

Sensitivity analysis

We planned to perform sensitivity analyses to examine the effect on results of excluding trials at high risk of bias.

RESULTS

Description of studies

See [Characteristics of included studies](#) and [Characteristics of excluded studies](#).

Results of the search

Our electronic searches identified a total of 1359 unique citations. We identified an additional 20 unique citations from reference lists of included studies. Our title and abstract screening identified 79 citations as potentially eligible for inclusion in this review. We identified a further two studies (one pending publication, one unpublished) following contact with the research department

of the manufacturer of a commercially available HFCWO device after following up a published conference abstract of a potentially eligible study. Full-text screening identified 15 eligible studies (Figure 1). An additional seven studies met eligibility criteria, but adult and child data were combined in the presentation of results.

Correspondence was sent to study authors to request further information, but these authors failed to respond or replied that they were unable to provide the requested data because of time constraints.

Figure 1. Study flow diagram.

We updated searches in November 2019 and July 2020 and added six studies to awaiting classification, but these results have not been fully incorporated into the review. Details of the studies can be found in [Studies awaiting classification](#).

Included studies

Fifteen studies were eligible for inclusion. Studies are grouped by type of intervention for ease of reading; although some studies utilised similar interventions, variability in study protocol, in participant characteristics and in outcome measures precluded meta-analysis.

Four studies assessed effects of ventilatory assistance, four effects of postural support and seven effects of ACTs. Three studies provided data on both children and adults, but results were

presented in such a way that extraction of the data on children was possible ([Vianello 1994](#); [Ayoub 2002](#); [Vianello 2005](#)).

Key features of these studies are summarised in [Table 1](#). [Table 2](#) provides additional information about study design. Four studies were randomised controlled trials ([Nwaobi 1986](#); [Hill 2009](#); [Yuan 2010](#); [Barks 2012](#)), four were prospective controlled non-randomised studies ([Vianello 1994](#); [Klefbeck 2001](#); [Vianello 2005](#); [Falsaperla 2013](#)), three were long-term before and after studies ([Mellies 2004](#); [Fitzgerald 2013](#); [Landon 2013](#)) and four were short-term before and after studies ([Noblejamieson 1986](#); [Ayoub 2002](#); [Lagerkvist 2005](#); [Faroux 2008](#)).

Airways clearance techniques

Seven studies tested effectiveness of airway clearance techniques (ACTs), which included four types of interventions: high-frequency chest wall oscillation (HFCWO) (Yuan 2010; Fitzgerald 2013; Landon 2013), mechanical insufflation-exsufflation (MIE) (Vianello 1994; Faroux 2008), positive expiratory pressure (PEP) (Lagerkvist 2005) and continuous positive airways pressure (CPAP) (Klebeck 2001). Eligible outcome measures included respiratory parameters, length of hospital stay, number of respiratory infections requiring antibiotics, quality of life measures and adverse outcomes.

High-frequency chest wall oscillation

High-frequency chest wall oscillation (HFCWO) (also known as high-frequency chest wall compression therapy, or vest therapy) involves use of an inflatable vest connected by tubes to an air pulse generator, which rapidly inflates and deflates the vest, producing oscillations to the chest wall. The rapid chest movement mimics a cough-like expiratory flow that shears mucus away from the walls of the airways and helps move it along to the central airways (McIlwaine 2012).

Three studies assessed the effectiveness and safety or tolerability of HFCWO (Yuan 2010; Fitzgerald 2013; Landon 2013). All three studies included children with diagnoses consistent with SGDD (e.g. severe cerebral palsy, static encephalopathy) alongside children with neuromuscular disorders (e.g. DMD, SMA). All participants had a history of respiratory morbidity, some of which was severe, requiring use of non-invasive ventilation, tracheostomy or mechanically assisted coughing. All three studies used HFCWO daily in the home setting, with application ranging from twice to three times per day for 10 to 20 minutes at 10 to 15 Hz, over a study period of 5 to 24 months. One study was an RCT (23 participants) that compared HFCWO with 'standard chest physiotherapy' (12 minutes, six positions) (Yuan 2010). The other two studies were long-term before and after studies (22 and 15 participants) that prospectively collected data for the study period during which HFCWO was used, and compared outcomes versus historical data for the same participants over the 12 months before initiation of HFCWO; in one study a standardised chest physiotherapy (CPT) protocol (30 minutes twice per day in 12 positions) guided treatment for all participants over the preceding 12-month period (Landon 2013). Outcome measures tested included number of respiratory infections (Yuan 2010; Fitzgerald 2013; Landon 2013), number of hospital admissions for respiratory exacerbation (Yuan 2010; Fitzgerald 2013; Landon 2013), number of clinic visits (Fitzgerald 2013), reported adverse events (Yuan 2010; Fitzgerald 2013; Landon 2013), length of hospital stay (Yuan 2010; Landon 2013), number of deaths (Yuan 2010), chest x-ray changes (Yuan 2010), use of antibiotics for respiratory infection (Fitzgerald 2013) and overnight polysomnography measures (Yuan 2010).

Mechanical insufflation-exsufflation

As was described earlier, some children with SGDD have an ineffective cough and so are unable to clear their own airway secretions. Mechanical insufflation-exsufflation (MIE, or 'cough assist') utilises a portable device that delivers gradual positive pressure to the airway, assisting inspiration; this is followed by a rapid switch to negative pressure. The rapid change from positive to negative pressure simulates the flow changes that occur during a cough, thereby assisting expectoration of secretions (Chatwin 2003).

Two studies assessed the effectiveness of MIE in children with neuromuscular disorders (Vianello 2005; Faroux 2008). Faroux's short-term before and after study (Faroux 2008) tested MIE at three different pressures in 17 clinically stable children 5 to 18 years of age, previously naive to MIE. In one afternoon, each child performed three MIE sessions consisting of six insufflation-exsufflation cycles (30 seconds of rest between cycles) with an increase in pressure with each session (15, 30 and 40 cm H₂O). MIE was delivered by face mask held firmly to the participant's face. Measurements were taken during two minutes of spontaneous breathing at baseline and for one minute after each application. Outcomes tested included patient comfort on a visual analogue scale (VAS) and physiological effects on vital capacity (VC), peak expiratory flow rate (PEFR), peak cough flow (PCF), sniff nasal inspiratory pressure (SNIP), tidal volume (V_T), minute volume (VE), oxygen saturation (SaO₂) and end-tidal carbon dioxide (PETCO₂).

Vianello's prospective controlled NRS (Vianello 2005) compared short-term outcomes of patients admitted to intensive care with respiratory tract infection who received conventional CPT with the addition of twice-daily MIE versus a historical cohort, which received CPT alone. All study participants received supplemental oxygen and NIV to relieve dyspnoea and to normalise arterial blood gases. On average, CPT was performed twice daily in both groups and MIE was used in the intervention group immediately following conventional CPT. MIE consisted of approximately five cycles interspersed with 20 to 30 seconds of rest. The study included both adults and children, but results were presented in such a way that data on the four included children could be extracted and analysed. Outcome measures included length of hospital stay, time spent receiving NIV, antibiotic use, adverse outcomes and mortality.

Positive expiratory pressure

Positive expiratory pressure (PEP) treatment consists of exhaling against a constant pressure, usually through a mask applied firmly to the face; this increases functional residual capacity and aids mobilisation of secretions through recruitment of collateral ventilation (Elkins 2006; Button 2013).

In a short-term before and after study of 18 severely disabled children (1 to 17 years of age) with 'large quantities of airway [mucus]', transcutaneous partial pressure of oxygen (tcPO₂) and transcutaneous partial pressure of carbon dioxide (tcPCO₂) were measured before and after use of PEP via face mask (Lagerkvist 2005). Baseline values were recorded after 20 minutes seated in the participant's usual wheelchair, then PEP was used for three cycles of two minutes with five-minute rests between cycles; measures were taken during the intervention and for 20 minutes afterward. Manually supported cough was used when required, and the child's respiratory rate and reaction to the intervention were recorded.

Continuous positive airways pressure (CPAP)

A small non-randomised cross-over study of six children 6 to 17 years of age with DMD or SMA type II looked at the effectiveness of short periods of CPAP as a method of airway clearance (Klebeck 2001). Participants were randomly assigned to one of two groups (Group 1 or Group 2). All were naive to positive-pressure treatment, were wheelchair dependent with no bulbar paresis, had no acute or chronic lung disease and had forced vital capacity (FVC) above 40% of predicted value.

Group 1 participants were given a CPAP machine along with instructions to follow a twice-daily treatment protocol for three weeks. After three weeks, participants from both groups inhaled a metered dose of radiolabeled Teflon particles. Profile scanning was performed to measure the distribution of radiolabeled particles and was repeated every 24 hours for three days. Group 1 continued to use CPAP twice daily for these three days. A two-week washout period followed, wherein no participants used CPAP. Following this, Group 2 used CPAP according to the same twice-daily protocol for three weeks. At the end of three weeks, inhalation of particles and scanning were repeated for both groups, with Group 2 continuing to use CPAP over the three-day scanning period. The examiner performing the scanning was blinded to allocation. SaO_2 , PaCO_2 and lung function measures were recorded at the time of particle inhalation.

Non-invasive ventilatory support

Non-invasive ventilation describes mechanically assisted positive-pressure ventilation delivered without the need for an artificial airway; NIV can be delivered via face mask, nasal mask or nasal pillows held in place by straps or a cap. NIV machines are portable, allowing use in the community setting. NIV is commonly used to correct hypercapnia and to relieve dyspnoea.

Four non-randomised studies tested the effectiveness of non-invasive ventilatory support (Vianello 1994; Ayoub 2002; Mellies 2004; Falsaperla 2013). All studies used NIV at night-time. All but one study (Ayoub 2002) tested positive-pressure ventilation with a mask interface. Outcome measures tested were SaO_2 , PaO_2 , PaCO_2 , pH, respiratory rate, heart rate, alveolar-arterial oxygen gradient (A-aDO_2), partial pressure of oxygen/frequency of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) ratio, V_T , inspiratory vital capacity (IVC), forced vital capacity (FVC), forced vital capacity percentage of norm for age- and weight-matched individual (FVC%), mandatory minute ventilation (MMV), peak inspiratory muscle pressure, adverse effects, length of hospital stay, number of respiratory infections, number of hospital admissions, quality of life and polysomnography measures.

Falsaperla's controlled NRS prospectively examined outcomes of children with SGDD admitted in acute respiratory distress (Falsaperla 2013). Families of all children who met eligibility criteria were offered treatment with NIV. Those who consented ($n = 22$) were treated with bilevel positive airways pressure (BiPAP) via full face mask, alongside 'conventional therapies.' Participants in the group that declined were treated with 'conventional therapies' only. Respiratory parameters (PaO_2 , PaCO_2 , pH, respiratory rate (RR), heart rate (HR), $\text{PaO}_2/\text{FiO}_2$ ratio) were compared between groups and within participants at admission and after an hour of therapy. Length of hospital stay was also recorded.

In a short-term before and after study, Mellies 2004 evaluated the efficacy of nocturnal NIV for treating sleep-disordered breathing (SDB) in children with proven SMA I or II and vital capacity $< 60\%$ of predicted or with symptoms of SDB. Twelve children were included in the study, seven of whom had SDB and five who did not and who served as a reference group. On initiation of the study, all participants were in stable condition, free from respiratory infection and with arterial blood gases within normal ranges. Nocturnal NIV (BiPAP) was delivered via face mask by trained caregivers using pressure preset ventilators. Ventilator settings

were selected with the aim of increasing tidal volume, suppressing participant respiratory trigger effort and optimising ventilator synchrony. Settings were adjusted during an initial overnight sleep study with the aim of normalising gas exchange and totally suppressing SDB. Initial setup was done in hospital, and before discharge all participants tolerated NIV for at least six hours during sleep. Four participants used nasal masks and three used face masks; only two used commercial masks, and the remaining five required custom-made silicone masks to prevent pressure areas and ensure an adequate seal. All participants used NIV each night for 7 to 12 hours of sleep, which was corroborated by ventilator data. In the reference group (non-NIV), all but one participant were identified to have ineffective cough, and so caregivers were taught assisted coughing techniques, which they were instructed to perform daily. It is unclear whether the NIV group also used assisted coughing. All participants completed a baseline five-item symptom questionnaire. The NIV group was followed up with polysomnography and a symptom questionnaire at six months, and the reference group at 12 months with pulse oximetry and a symptom questionnaire.

Vianello's controlled NRS prospectively investigated the outcomes of 10 males with DMD and chronic stable daytime hypercapnia. All were advised to commence nocturnal NIV; those who agreed ($n = 5$) used volume-cycled NIV via custom nasal interface for a minimum of seven hours per night (Vianello 1994). Those who declined ($n = 5$) became the control group. Participants from both groups were evaluated at six-month intervals over a period of two years, and pulmonary function measures were repeated. The primary outcome measure for the study was mortality. Investigators also measured number of hospital admissions, spirometry and arterial blood gases. The study included both adults and children, but results were presented in such a way that data on the four included children could be extracted and analysed.

Ayoub's short-term before and after study examined a different method of non-invasive ventilation: the pneumatic abdomino-diaphragmatic belt (PB), a device that inflates and exerts pressure on the abdomen, facilitating active expiration and passive inspiration (Ayoub 2002). Again, the study included both adults and children, but results were presented in such a way that data on the two included children could be extracted and analysed. Participants had DMD with significant respiratory deficits (VC 18% and 27% predicted) but were clinically stable with no evidence of infection. Participants acted as their own controls, and measures with and without PB were compared. Measures were taken after two consecutive nights, first without and then with overnight use of the PB. No information is available on how long the belt was used and who applied it. Tidal volume was measured with spirometric tracing. PaO_2 , PaCO_2 and SaO_2 were measured from an arterial blood sample. In addition, V_T was measured during quiet breathing with participants in supine with a head-up tilt of 0 degrees, 45 degrees and 75 degrees, with and without PB use.

Postural support

Many children with severe physical disability will use devices such as specialist seating, NTPE and/or spinal bracing to assist them to maintain a symmetrical posture. Positioning may have many aims, such as preventing deformities, providing pressure care, allowing access to the environment, feeding and aiding digestion.

Supportive seating

Two small randomised controlled trials assessed the effects of supportive seating on respiratory parameters (airways resistance (R_{AW}), minute volume (MV), V_T , VC, forced expiratory volume in one second (FEV_1), expiratory time (ET)) in non-ambulant children with cerebral palsy (Nwaobi 1986; Barks 2012). In Barks' study, eight children 5 to 10 years of age were seated in a simulator with six different prespecified configurations providing varying degrees of support at the trunk, pelvis and upper limbs, including a control condition with no added support. Measures were taken immediately after seating in each condition. Nwaobi studied eight children 5 to 12 years of age and compared basic sling-type wheelchair seating versus seating in a simulator adjusted to achieve upright midline posture, with hips, knees and ankles at 90-degree angles. Lung function measures were taken after 10 minutes of seating. In both studies, the order of seating was randomly assigned.

Night-time positioning equipment

A small RCT of 10 children with severe cerebral palsy looked at the impact of night-time postural equipment (NTPE) on respiratory function (Hill 2009). Each child underwent two nights of attended polysomnography in a paediatric research laboratory, separated by a minimum of three nights at home. On one night sleep with NTPE was recorded, and on one night sleep without NTPE was recorded. The order of assessment was randomly assigned by the sealed envelope method. Standardised polysomnography of a minimum of two rapid eye movement (REM) cycles was recorded.

Spinal bracing

A short-term before and after study of 40 children with neuromuscular disease investigated the effects of posture and spinal bracing on lung function (Noblejamieson 1986). Children were assigned to one of two groups according to their functional status and the presence of scoliosis. Group 1 consisted of 20 ambulant children without scoliosis, and Group 2 of 20 non-ambulant children with scoliosis, 16 of whom had lightweight polypropylene spinal braces. Lung function tests (LFTs) were performed for all children, and the best of three measures was recorded for each test, with predicted normal values based upon arm span. For Group 1, LFTs were performed in standing, sitting and supine, and for Group 2, in sitting and supine in 15 children, and then in sitting with brace on and off in 16 children. Postural measurements were used as a measure of diaphragmatic function.

Excluded studies

Sixty-one studies were excluded, as assessment of full text revealed that they did not meet the inclusion criteria for eligibility. Individual reasons are given in the [Characteristics of excluded studies](#) tables. Five studies are awaiting classification, as further information was requested but was not received from study authors so eligibility for inclusion could be determined ([Studies awaiting classification](#)).

Risk of bias in included studies

See [Figure 2](#) and [Figure 3](#) for a trial-by-trial risk of bias analysis and summary.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): All outcomes	Incomplete outcome data (attrition bias): All outcomes	Selective reporting (reporting bias)	Other bias
Ayoub 2002	-	-	-	-	+	+	?
Barks 2012	+	-	-	-	-	+	?
Falsaperla 2013	-	-	-	-	+	?	+
Faroux 2008	-	-	?	-	+	+	?
Fitzgerald 2013	-	-	-	-	+	?	?
Hill 2009	+	?	-	-	+	?	?
Klefbeck 2001	+	-	-	+	+	+	?
Lagerkvist 2005	-	-	-	-	+	+	?
Landon 2013	-	-	-	-	+	+	-
Mellies 2004	+	-	?	-	+	+	+
Noblejamieson 1986	-	-	-	-	-	+	-
Nwaobi 1986	?	-	-	-	-	+	-
Vianello 1994	-	-	-	-	+	+	?
Vianello 2005	-	-	-	-	+	+	-
Yuan 2010	+	?	-	?	-	?	?

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Allocation

This review contained only four RCTs. One study used computer-generated randomisation (Yuan 2010), one drew number sequences from a hat (Barks 2012), one did not describe the method used (Nwaobi 1986) and another used the sealed envelope method (Hill 2009). Randomisation gives rise to low risk of bias for sequence generation, but allocation concealment may be unclear, as study authors do not describe how groups were concealed from the investigator at the time of randomisation (Nwaobi 1986; Hill 2009; Yuan 2010), or high (Barks 2012), as once drawn the investigator can see to which group the individual was assigned.

The remainder of the studies were non-randomised. Lack of randomisation in allocation results in an inherently high risk of selection bias; groups are unlikely to be comparable, and researchers, whether consciously or not, may allocate participants to a particular group (Higgins 2011). The studies discussed below presented some additional concerns.

One trial assigned participants to groups on the basis of a functional disability score; detail is lacking regarding how the initial sample was recruited; the groups were split exactly 50:50, raising concerns that a convenience sample could have been selected on the basis of these scores (Noblejamieson 1986).

Another study assigned participants to groups on the basis of participant/parent preference for treatment options but provided no details about how participants and parents were counselled in this decision or by whom, leading to concern about the potential for researchers to influence this choice (Vianello 1994).

Blinding

Because of the nature of the interventions, blinding of participants was largely impractical and hence was not employed in any of the studies. Blinding of assessors would have been impractical in some studies; however few studies described who took the measures or any considerations around blinding, leading to high risk of bias in this domain in most studies. In one study, children were asked to rate 'respiratory comfort' after using MIE at three different pressures (Faroux 2008). Treatment pressures were incrementally increased, and so it is possible that improved comfort at higher pressures may reflect better synchronisation of the children with the device and improved relaxation after repeated

use. Randomisation of order could have prevented this potential for performance bias.

Incomplete outcome data

Four studies were rated as having high risk of bias because outcome data were incomplete. In Noblejamieson 1986, some measures were not taken for all eligible participants with no explanation; Nwaobi 1986 failed to report FEV₁ data for two participants; and Yuan 2010 failed to report polysomnography measures for 15 of 28 participants. In Barks 2012, 12 of 20 children were withdrawn from the study and a reasonable explanation was given for only two of the withdrawals.

Hill 2009 did not report data on one child who was excluded as the did not reach two REM cycles, so we rated this trial as low risk of bias. In the remaining studies, data were available on all participants, including justified reasons for attrition such as death.

Selective reporting

Four studies were rated as having unclear risk of bias in this domain (Falsaperla 2013; Fitzgerald 2013; Hill 2009; Yuan 2010). Falsaperla 2013 was assigned unclear risk in this domain, as two children discontinued the intervention because of discomfort, but it is unclear at what stage and whether their data were analysed in the results. In Fitzgerald 2013 data are not reported for several of the outcomes measured; on contact, the study author stated that only significant data were reported; however this does not allow trends to be examined that did not reach statistical significance but may be clinically relevant. In Hill 2009, a graph reporting outcome data appeared to be missing two lines representing outcome data, though it is possible that the lines were over-lapping. In Yuan 2010 there was no explanation provided for the missing data. The remaining trials we judged to be of low risk of reporting bias.

Other potential sources of bias

Several studies did not adequately describe how the sample group was recruited and provided no justification for sample size, resulting in unclear or high risk of bias (Noblejamieson 1986; Nwaobi 1986; Klefbeck 2001; Ayoub 2002; Lagerkvist 2005; Barks 2012; Fitzgerald 2013; Landon 2013).

Both studies that compared HFCWO versus chest physiotherapy utilised an arduous CPT protocol; this is likely to influence

compliance (Yuan 2010; Landon 2013), the effects of which are impossible to separate from the therapeutic benefits of the intervention. In the Landon 2013 study, one member of the research team was employed by the manufacturers of the oscillating vest. Fitzgerald's study was supported by a grant from the manufacturers of an HFCWO device. Both studies provide insufficient detail on how the sample was recruited.

Effects of interventions

Airways clearance techniques

High-frequency chest wall oscillation

Yuan's study (the only RCT for HFCWO) (Yuan 2010) reported no hospital admissions in the HFCWO group versus four in the standard CPT group. The effect was insufficient to yield statistical significance; in a heterogeneous cohort of children with complex medical presentations, a much larger sample group would be required to afford clinical and statistical significance. Fitzgerald's NRS (Fitzgerald 2013) showed a reduction in the rate of admissions for respiratory exacerbation after HFCWO use, from 45% in the year preceding treatment to 36% after one year of treatment (P value < 0.47) and to 13% after two years of treatment (P value < 0.002). The study authors report a statistically significant reduction in the number of hospital days (P value < 0.003), but further data are not given. Landon's NRS (Landon 2013) reported a reduction in total hospital days from 66 days in the 12 months preceding the study to 21 days in the one-year study period. The data were normalised to average hospital days per participant per month, with reduction from 0.37 to 0.08 (P value < 0.05). ICU days also decreased from 34 to 0. The study author was able to provide data on individuals to demonstrate that results were not skewed by long admissions.

Yuan presented compliance as less than 30%, 30% to 70% and over 70%, indicating that most participants were less than 30% compliant with standard CPT (7/12 participants) and more than 70% were compliant with HFCWO (9/11 participants, P value < 0.004) (Yuan 2010). Only one participant for HFCWO and two for CPT fell into the 30% to 70% compliance group. Landon's study reported that HFCWO was better tolerated than standard CPT in 'medically fragile children' based upon caregiver reports (Landon 2013), and Fitzgerald reported overall compliance as 82% (Fitzgerald 2013). One study showed a trend toward reduced frequency of use of antibiotics for respiratory infections but with no statistical significance (Yuan 2010); another study found no effect (Fitzgerald 2013).

Mechanical insufflation-exsufflation

Faroux's NRS (Faroux 2008) found that use of MIE reduced PETCO₂ at all treatment pressures (P value < 0.0003, reduction from 39.9 mm Hg at baseline to 38.0 mm Hg after application) and improved PCF (P value < 0.02, from 162 to 192 L/min) and respiratory comfort (10-point improvement on 100-point VAS) at 40 cm H₂O. No significant effect on V_T, VE or SaO₂ was reported. In Vianello's NRS (Vianello 2005), data for the whole group suggest effectiveness of MIE in reducing the need for invasive ventilation (P value < 0.047); children in the study did follow this trend, but as only two children were included, these results do not allow for meaningful analysis. Faroux's study of clinically stable children (Faroux 2008) described no adverse effects from MIE, and Vianello's study of patients presenting with acute illness to the intensive care unit (Vianello 2005) reported adverse effects in both of the children

studied. One child experienced stomach distension following MIE, which was complicated by gastro-oesophageal reflux, resulting in recurrent bronchospasm and the need for endotracheal intubation to protect the airways. The other experienced mild nasal bleeding not requiring specific intervention and was successfully treated with NIV. Both were discharged home.

Although both studies were performed on children with NMD rather than SGDD, neither study design required the child to produce a cough during the exsufflation phase of MIE; thus treatment was passive and could reasonably be performed with children with low cognitive function. Neither study included direct measurements of secretion clearance, but the reduction in PETCO₂ seen in Faroux's study (Faroux 2008) is indicative of an improvement in alveolar ventilation; this could be a result of the improved peak cough flow and/or the effect of the intermittent positive pressure that MIE delivers.

Positive expiratory pressure

Lagerkvist's NRS (Lagerkvist 2005) found statistically significant improvement in tcPO₂ after 17 minutes of use (P value < 0.0001, mean increase of 1 kPa from 8.8 to 9.8) but no change in tcPCO₂ or respiratory rate. No adverse effects were described, and all children were reported to accept the mask.

Continuous positive airways pressure

Klebeck's NRS (Klebeck 2001) on effectiveness of CPAP for secretion clearance found that retention of inhaled radiolabeled particles at 72 hours was lower in participants using CPAP. No significant difference was noted between the two groups for lung function tests, SaO₂ or PaCO₂; however as participants were presymptomatic, baseline SaO₂ and PaCO₂ were within normal ranges.

All studies of ACTs were small (four to 23 eligible participants) and included a wide range of diagnoses; all but one used a non-randomised design. Potential benefits were demonstrated for all modalities, with better outcomes than were seen with standard CPT in studies in which this was compared (Vianello 2005; Yuan 2010; Landon 2013). None of the studies were of sufficient quality that changes to practice can be recommended.

Ventilatory support interventions

Only one study assessed use of NIV for acute respiratory distress; the remainder assessed nocturnal NIV.

Four non-randomised studies looked at the effects of NIV on oxygen and carbon dioxide levels (Vianello 1994; Ayoub 2002; Mellies 2004; Falsaperla 2013). Falsaperla's study found statistically significant improvements in PaO₂ (P value < 0.0003, 55.04 mm Hg control, 64.18 mm Hg intervention), PaCO₂ (P value < 0.0001, 51.68 mm Hg control, 42.41 mm Hg intervention), alveolar-arterial oxygen gradient (P value < 0.0001, 381 mm Hg control, 35 mm Hg intervention) and PaO₂/FiO₂ ratio (P value < 0.0001, 78 mm Hg control, 291 mm Hg intervention) one hour after initiation of NIV for acute respiratory distress due to pneumonia (intervention vs control) (Falsaperla 2013). Ayoub's and Vianello's studies (Ayoub 2002; Vianello 1994) reported a trend toward increased PaO₂ (mean 6.6 and 6.8 mm Hg increase) and decreased PaCO₂ (mean 5.6 and 2.8 mm Hg decrease), but the number of paediatric

participants within the cohort was two and four, respectively; therefore participant numbers are too small to suggest significance. Mellies reported improved mean SaO₂ (2% mean increase, P value < 0.05) on polysomnography (Mellies 2004).

One study measured effects of NIV on tidal volume, reporting significant increases in V_T only when the participant was tilted at 45 degrees or 75 degrees (Ayoub 2002). Falsaperla reported significantly reduced heart rate (157 to 101 bpm) and respiratory rate (61 to 43 bpm) one hour after initiation of NIV (P value < 0.0001) (Falsaperla 2013).

One study looking at polysomnography measures reported reduced respiratory disturbance index (reduction in events from 14.1 to 2.7, P value < 0.005), improved mean SaO₂ (2% increase in SaO₂ from 95% to 97%, 5% increase nadir from 87% to 92%, P value < 0.05) and decreased nocturnal pulse rate (100 bpm to 88 bpm, P value < 0.05), bringing the measures in line with the comparison group, which did not suffer from sleep-disordered breathing (SDB) (Mellies 2004).

Only one study used quality of life indicators, reporting significantly reduced SDB symptoms (symptom questionnaire score decreased from 28.7/50 to 14.9; items scored were sleep disturbance, nocturnal sweating, morning headaches, nausea/appetite/feeding problems and daytime sleepiness/fatigue/impaired concentration, P value < 0.005) (Mellies 2004).

Length of hospital stay was measured by Falsaperla 2013, who reported shorter length of stay in the NIV group versus the control group (6.22 vs 11.63 days, P value < 0.0001).

Two studies reported mortality, which was lower in the NIV groups (Vianello 1994—one death in the control group; Falsaperla 2013—one death in the control group), although in the first study the sample group was too small to suggest significance.

All studies of ventilatory support interventions were small (two to 49 eligible participants) and included a wide range of diagnoses and outcome measures. No adverse outcomes were recorded. Overall in these non-randomised studies, potential benefits from NIV were found in reduced length of hospital admission, normalised gas exchange, reduced mortality and improved quality of life, but the strength of the evidence is inadequate to inform changes to clinical practice.

Postural support

Two small RCTs tested the effects of seating on respiratory parameters (Nwaobi 1986; Barks 2012). Nwaobi found a mean increase of 57.7% in VC, 51.6% in FEV₁ and 55% in ET (P value < 0.05) with supportive seating. Barks found no statistically significant results but a trend toward reduced R_{AW} in the condition in which the upper extremities (UEs) were supported and the abdomen offloaded (control R_{AW} 9.84 cm H₂O/L/s, UE supports 6.20 cm H₂O/L/s). No effect on minute volume was noted.

Hill's small RCT of night-time positioning equipment revealed that NTPE had an effect on nocturnal lung function. In some participants, this was a positive effect, with a 1% to 3% increase in mean SaO₂ among three children; however a further six had a 1% to 3% decrease in SaO₂ (Hill 2009). No correlation with sleeping

position was observed. This study was small and was not powered for significance.

Noblejamieson's NRS (Noblejamieson 1986) found that wearing of spinal bracing by children with neuromuscular disorders impaired lung function, with mean FVC and FEV₁ falling by 8% from 36% to 28% (P value < 0.01). Peak expiratory flow rate was not affected by bracing. The study authors report that the two children who showed the greatest impairment in FVC with bracing had severe DMD; the bracing achieved considerable improvement in the Cobb angle (reduction in the degree of spinal curvature) but at the expense of considerable restriction in lung volume.

Although three RCTs were included in this subgroup, all were small and half of the studies did not demonstrate statistical significance. Postural support for children with SGDD can have many goals. The results of these studies are not strong enough to inform best clinical practice, but they do highlight the importance of considering respiratory function when looking at postural support.

DISCUSSION

This review was an ambitious attempt to establish the current evidence base for the treatment of respiratory morbidity in an underrepresented patient group. The broad inclusion criteria and the inclusion of non-randomised study designs have resulted in a narrative overview that we hope will stimulate thought about treatment of these children and will drive future research.

Summary of main results

Our search yielded data on a wide range of interventions of interest, but unfortunately the quality of the evidence is poor. Only four RCTs were included, all of which were limited by small sample size. The remainder of the studies were of a non-randomised design and had intrinsically high risk of bias. This significantly impacts upon our confidence in the outcomes. No studies were identified from which the strength of evidence is sufficient to inform clinical practice.

Ventilatory support and airway clearance techniques largely seemed to be safe, with the only significant adverse incident reported in a clinically unstable child following mechanically assisted coughing (Vianello 2005). Both spinal bracing and night-time positioning equipment had a potentially negative impact on lung function (Noblejamieson 1986; Hill 2009), and supportive seating was shown to have a positive effect (Nwaobi 1986; Barks 2012). In two studies of high-frequency chest wall oscillation (Fitzgerald 2013; Landon 2013) and one of non-invasive ventilation (Falsaperla 2013), a reduction in the overall number of hospital days was reported. Two studies of high-frequency chest wall oscillation did not find an effect on antibiotic use (Yuan 2010; Fitzgerald 2013). Four studies reported improved oxygenation following use of positive expiratory pressure (PEP) (Lagerkvist 2005) or non-invasive ventilation (NIV) (Vianello 1994; Ayoub 2002; Falsaperla 2013), although two studies included a very small number of children, and so their results are not significant (Vianello 1994; Ayoub 2002). Reduced carbon dioxide levels were demonstrated in one study of mechanical insufflation-exsufflation (MIE) (Faroux 2008) and one of NIV (Falsaperla 2013), and a further two studies of NIV demonstrated a trend, but sample size was too small to show significance (Vianello 1994; Ayoub 2002). Improved cough flow was reported in one study of MIE (Faroux 2008). In another study, use of NIV was associated with reduced mortality (Vianello 1994).

Airway suction, standard chest physiotherapy and postural drainage are commonly used secretion clearance modalities, but this review found no studies assessing their benefit.

Children with severe global developmental delay (SGDD) present challenges for researchers, as many outcome measures are effort dependent. Our strategy of including studies of children with low cognitive ability for whom the interventions are possible to use revealed several interventions that may provide benefit for children with SGDD. As discussed, the validity of these results is compromised by poor study design; further caution should be applied, as the quality of evidence is naturally degraded when it is extrapolated to a different, albeit similar, participant group.

Although selection of appropriate outcome measures in a cohort of children with severe cognitive impairment is challenging, development of wearable devices based on principles of respiratory inductive plethysmography (RIP) now enables researchers to non-invasively record volume and timing variables, such as tidal volume, apnoea, hypopnoea, respiratory pattern and respiratory rate (Landon 2009; Wu 2009). Modern RIP-based monitoring systems are designed to allow home use (Landon 2009; Wu 2009) and, more important, use of RIP is non-effort dependent and so lends itself to use in research on children who are too young to co-operate or who lack cognitive ability.

Five studies included in this review (Lagerkvist 2005; Hill 2009; Barks 2012; Falsaperla 2013; Landon 2013) used exclusively non-effort-dependent outcome measures; these included polysomnography, total airways resistance, tidal volume, minute volume, heart rate, respiratory rate, transcutaneous oxygen and carbon dioxide measures, arterial blood gas measures, length of hospital stay, number of hospital admissions or clinic visits, number of respiratory infections, caregiver satisfaction and adverse outcomes.

Children with SGDD often have degenerative or life-limiting conditions; for many, respiratory failure is an inevitable symptom of their decline. The focus of intervention must be prevention of morbidity, symptom control and maximisation of quality of life. "In many circumstances the clinical course can be anticipated so that all options can be explored fully... and decisions made in advance rather than at the time of a respiratory crisis" (Simonds 2006). Although high-quality evidence is lacking, treatment modalities should be selected on the basis of the best available evidence, and selection should be guided by detailed clinical assessment in partnership with realistic long-term goals and a ceiling of escalation appropriate to each individual child and family circumstance.

Overall completeness and applicability of evidence

We used a comprehensive search strategy designed by a research specialist and guided by clinicians with knowledge of this patient group. It is therefore likely that our search captured all available studies.

Only four studies (Lagerkvist 2005; Falsaperla 2013; Fitzgerald 2013; Landon 2013) looked at children with generalised severe multiple disabilities, named in this review as SGDD. The other studies were of children with specific diagnoses such as cerebral palsy or DMD. Patterns of physical disability and respiratory morbidity of participants suggest such similarities in clinical presentation that results may be considered to have some relevance for

children with SGDD; the strength of evidence is naturally degraded by extrapolating to a different patient group, and so results should be applied with caution. One study (Mellies 2004) included children with SMA type I. Children with SMA type I experience a very characteristic and rapid decline in respiratory function characterised by extreme weakness; therefore results of this study are relevant only for children with similar patterns of severe weakness.

Quality of the evidence

The overall quality of evidence is poor. This systematic review found only four small RCTs. Most studies utilised a non-randomised design, which intrinsically causes high risk of bias. Long-term before and after studies relied upon within-participant comparison over prolonged periods of time, rendering it impossible to separate the natural history of the condition from the effects of the intervention. Many of the participants studied had progressive conditions, which may have resulted in an underestimation of the therapeutic effects of interventions tested. Vast heterogeneity was noted among participants, and conditions tested ranged from rapidly degenerative conditions such as SMA I to static conditions such as cerebral palsy. Non-randomised design, lack of information about how participants were selected and who completed outcome measures and incomplete reporting led to high or unclear risk of bias in several studies (see [Risk of bias in included studies](#) and [Characteristics of included studies](#)). Many of the studies were relatively old, and so attempts to contact study authors to clarify such details were largely unsuccessful. One study of HFCWO was supported by a grant from the manufacturers (Fitzgerald 2013), and in another study (Landon 2013), one member of the research team was employed by the manufacturers of the oscillating vests; as with most studies within this review, risk of bias was high because of lack of randomisation; additionally one study offered no justification for the numbers recruited (Landon 2013). All studies were relatively small (2 to 49 participants); two studies had subgroups of only four children (Vianello 1994; Vianello 2005) and one had subgroups of only two children (Ayoub 2002). These factors, combined with lack of consistency between studies in application of interventions and outcome measures used, limits the extent to which results can be generalised.

Potential biases in the review process

We excluded one study (Schwake 2003) on the basis of there not being any relevant outcomes reported. We are unaware of any other potential biases within the review process. We utilised a comprehensive search strategy designed by a research specialist. As with all research, there is a risk of publication bias, by which studies revealing nil effect are not published.

Our electronic searches revealed a conference abstract describing a study that was potentially eligible for inclusion. Our initial attempts to contact the study author directly were unsuccessful; however our search of the clinical trials registry indicated that this study was sponsored by a commercial manufacturer. As was described earlier, we contacted the research department of this manufacturer, which was able to facilitate contact with the author of this study and the author of another unpublished study, both of which were included (Fitzgerald 2013; Landon 2013). To ensure that this direct contact with a manufacturer had not biased our results, we also contacted the research departments of known major commercial manufacturers of other devices eligible for inclusion, for example,

HFCWO and MIE. All replied, but no new, eligible studies were revealed.

The review authors had no conflict of interest, and assessments for inclusion, risk of bias and data extraction were performed independently.

Our research protocol allowed for inclusion only of data on children. Several studies combined data on children with those on adults, and separate data could not be obtained. A further study included a minority of participants who had received diagnoses not eligible for inclusion. In future updates, it may be beneficial for the protocol to allow for inclusion of studies in which most participants (e.g. 80%) met inclusion criteria, provided that only a single characteristic for the minority group was ineligible.

Agreements and disagreements with other studies or reviews

In 2012 the British Thoracic Society (BTS) published 'Guidelines for the Respiratory Management of Children With Neuromuscular Weakness' (Hull 2012). These guideline provide multiple recommendations for practice based upon a review of literature surrounding the respiratory treatment of children with neuromuscular weakness (studies of children with CP or without definitive diagnosis were excluded). This review examined all levels of evidence from RCTs to non-analytical studies such as case reports. A working party comprising numerous experts in the field of paediatric respiratory care and neuromuscular disease reviewed the literature, and so in addition to reporting on available literature, they were able to provide expert consensus opinion on areas in which the evidence base was lacking. In keeping with the results of this review, the working party found that "the evidence for much of current practice is weak" (Hull 2012), and most recommendations were therefore based upon observational studies and expert opinion.

The guideline also established several specific research priorities (Hull 2012). Amongst these are further studies of mechanically assisted cough, comparison of different ACTs during acute respiratory exacerbation and development of quality of life measures. In such examples in which priorities align, researchers of interventions for SGDD should aim to work together with this established group of professionals and, when possible, to use compatible treatment protocols and outcome measures.

Following on from the guideline, the BTS recently published a quality standards document (BTS Quality Standards), which sets out standards of care and measurable good practice markers for the respiratory management of children with neuromuscular weakness to inform National Health Service (NHS) commissioners and planners. The 10 standards proposed are largely compatible with the approach required to drive improvements in care for children with SGDD; commissioners and planners should be urged not to exclude the wider population of children with severe neuro-disability when applying these quality standards.

AUTHORS' CONCLUSIONS

Implications for practice

This review found no high-quality evidence for any single intervention for the management of respiratory morbidity in children with severe global developmental delay (SGDD).

This review found potential benefits associated with use of non-invasive ventilation, mechanically assisted coughing, high-frequency chest wall oscillation, positive expiratory pressure mask use and supportive seating for the management of respiratory morbidity in children with severe neurological impairment. Evidence supporting the use of each intervention was limited, and differing study design and outcome measures precluded the possibility of meta-analysis in studies investigating the same intervention. The results therefore should be regarded as hypothesis generating, rather than suitable for hypothesis testing.

The care burden for families and caregivers of children with SGDD is high. Healthcare professionals should ensure that any additions to this care burden are carefully selected to maximise effectiveness, promote patient dignity and meet individualised treatment goals.

Implications for research

The causes of respiratory morbidity for children with SGDD and the range of available interventions are broad; numerous studies have been undertaken, but as the result of methodological flaws, the quality of existing evidence is poor. Care must be taken to ensure that future studies employ robust designs to produce results that are valid and reliable and inform clinical practice. This review found four small RCTs, demonstrating that RCTs are possible in this patient group. Conducting controlled trials can be ethically challenging when perceived wisdom suggests that a particular treatment is beneficial and that withholding it would be detrimental to the participant. Given the results of this review, this would not apply to any of the interventions described. As SGDD is a broad umbrella term, heterogeneity within the patient group is vast. Large cohorts are required to demonstrate statistical significance and to allow for adjustment of confounding factors; thus a multi-centre approach is essential.

To improve the evidence base, a co-ordinated approach is required. This must be done to bring together experts in the field in a working party to agree on research priorities and develop a set of standardised outcome measures and treatment protocols that will facilitate the multi-centre approach that is essential in ensuring that future studies are adequately powered.

Given the findings of this review, initial priorities include the following.

- When practical, agree that standardised treatment protocols for modalities such as NIV, MIE, PEP and HFCWO, which are widely used in other patient groups, on the basis of limited studies have potential benefits for children with SGDD.
- Disseminate protocol information to healthcare professionals to encourage utilisation in clinical settings.
- Develop standardised outcome measures for studies of comparable interventions, for example, ACTs.
- Initiate pilot studies to be followed by multi-centre studies for agreed upon research priorities.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Ayoub 2002

Study characteristics		
Methods	Short-term before and after study	
Participants	DMD and VC lower than 30% predicted. 7 participants, only 2 met inclusion criteria for age (15 and 18 years old); therefore data extracted for these 2 participants only	
Interventions	Overnight ventilatory assistance by means of pneumatic abdomino-diaphragmatic belt, compared with no assistance overnight. Within-participant comparison. Use of pneumatic abdomino-diaphragmatic belt during quiet breathing with participant in various supine positions (0 degrees, 45 degrees and 75 degrees)	
Outcomes	SaO ₂ , V _T , PaO ₂ , PaCO ₂	
Notes	Each intervention was delivered once. The study also measured other outcomes that were not relevant to this review and therefore were not discussed	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias)	High risk	Study design did not permit

Non-pharmaceutical management of respiratory morbidity in children with severe global developmental delay (Review)

Ayoub 2002 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants entering the study. Missing data when participants could not tolerate the intervention explained
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Unclear risk	No description of how participants were selected or of the setting, and no justification of sample size. Very short intervention period and no long-term follow-up

Barks 2012
Study characteristics

Methods	Randomised controlled trial
Participants	8 children (5 to 10 years of age) with cerebral palsy
Interventions	6 experimental seating conditions using various configurations of 4 wheelchair seating components (upper extremity supports, lateral trunk supports, anterior pelvic belt and posterior seat tilt) were tested consecutively in a single session. These included control condition (no supports, guardian placed hand on participant's thighs for safety), all components, upper extremity supports only, lateral trunk supports only, anterior pelvic belt only and posterior seat tilt only. The order of 4 of the 6 conditions was randomly assigned, with full support followed by no support tested last
Outcomes	R_{AW} , MV, V_T
Notes	Measurements were taken as soon as the child was seated in the wheelchair in each posture; measures were not taken over time

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Numbers drawn from hat to generate sequence
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit. Not practical for the intervention tested
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	High risk	Of 20 initial participants, 8 completed the protocol, 2 did not meet the study criteria (study does not state how/why, as they were originally 'recruited'), 2 withdrew assent by crying or showing aversion during testing, a total of 8 were

Barks 2012 (Continued)

		withdrawn by the investigator for inability to complete the protocol (this is not explained further and is a potential point of bias)
Selective reporting (reporting bias)	Low risk	All outcomes measure reported
Other bias	Unclear risk	Study design did use random order of testing to minimise order effect, but this was later amended to put the control measurement last, as 2 participants who had their control measurement taken first then withdrew from the study, as it was overwhelming for them. Risk of order effect No description of how the sample was obtained and no justification of sample size

Falsaperla 2013

Study characteristics

Methods	Prospective controlled non-randomised study. 2 groups: those accepting NIV (intervention) and those declining (control)
Participants	44 children with 'central nervous system disorders with moderate to severe mental retardation'
Interventions	Intervention group received non-invasive ventilation (BiPAP via face mask) for treatment of acute respiratory distress secondary to pneumonia—applied in accordance with BTS guidelines. Both groups received oxygen therapy to maintain SaO ₂ between 88% and 92%, IV fluids to maintain fluid balance, aerosol therapy with albuterol and IV antibiotics. Outcomes were measured at admission and 1 hour after initiation of treatment for both groups
Outcomes	PaO ₂ , PaCO ₂ , pH, respiratory rate, heart rate, A-aDO ₂ , PaO ₂ /FiO ₂ ratio, adverse effects—measured after 1 hour, compared within and between groups. Length of hospital stay
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	All outcome data reported

Falsaperla 2013 (Continued)

Selective reporting (reporting bias)	Unclear risk	2 children discontinued NIV because of discomfort; it is unclear whether their results are included in the Results section of the study
Other bias	Low risk	No other concerns

Faroux 2008
Study characteristics

Methods	Short-term before and after study
Participants	17 children 5 to 18 years of age with Duchenne muscular dystrophy, spinal muscular atrophy, other myopathies (merosin-deficient MD, spina bifida and unknown myopathy)
Interventions	3 MIE sessions, with each session comprising 6 insufflation-exsufflation cycles. Pressures for the 3 sessions were ± 15 cm H ₂ O, ± 30 cm H ₂ O and ± 40 cm H ₂ O. Timing of a cycle was 2 seconds of insufflation followed by 3 seconds of exsufflation and a 30-second rest. The 3 sessions were performed in the same afternoon, and daily physiotherapy had been received in the morning
Outcomes	VT, RR, VE, SaO ₂ , PETCO ₂ , VC, SNIP, PEF or PCF, respiratory comfort on VAS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It does not state whether participants were aware of the pressures used. This could affect outcomes if participants had an expectation that higher would be better
Blinding of outcome assessment (detection bias) All outcomes	High risk	No information given on who performed what tasks within the study (e.g. carried out the intervention, recorded outcome data, analysed data)
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	Both positive and negative findings reported
Other bias	Unclear risk	It appears that all participants started at low pressure, and pressure then built up. As all were naive to MIE until the time of the study, and it does not appear that they had any 'practise runs,' it may be that measures that improved at higher pressures are simply a reflection of better synchronisation of pressures with the device and improved relaxation, hence increased comfort. Simply

Faroux 2008 (Continued)

randomly assigning the order in which pressures were delivered could have avoided this

Fitzgerald 2013

Study characteristics

Methods	Long-term before and after study
Participants	22 neurologically impaired children with history of frequent pulmonary exacerbations. Initial data collection period of 1 year, extended to 2 years (1-year follow-up, n = 22; 2-year follow-up, n = 15)
Interventions	All participants were instructed to use the vest for 20 minutes twice daily, increasing to up to 4 times daily during lower respiratory tract infection with increased oxygen requirements. Standardised settings of 10 Hz for children 18 to 36 months of age and 12 Hz for children older than 36 months were used. The threshold for compliance was 70%, and when participants were non-compliant, the vest was collected and participants were withdrawn from the study (n = 4). All participants continued with their 'routine care,' for example, use of cough assist, suction and medical therapies
Outcomes	Number of hospital admissions, use of antibiotics, clinic visits, adverse events
Notes	6-Month wash-in period

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	All attrition accounted for
Selective reporting (reporting bias)	Unclear risk	Data for antibiotic use, clinic visits and adverse events not reported—author stated that only significant data reported, but this does not allow trends to be examined that did not reach statistical significance
Other bias	Unclear risk	Study was funded by manufacturers of HFCWO machine. Enrolment was based upon a convenience sample. Description of how the sample was obtained or justification of sample size is inadequate

Hill 2009

Study characteristics

Methods	Randomised controlled trial
Participants	10 children 6.5 to 16.7 years of age with diagnosis of cerebral palsy GMFCS level V or IV
Interventions	Use of night-time postural equipment (NTPE) to assess effects of positioning on sleep quality and respiratory function in children with severe CP. All participants were already established users of NTPE and were supported in positions dependent upon their needs (supine n = 8, side-lying n = 1, prone n = 1). Each child had 2 nights of attended polysomnography in a paediatric research laboratory, separated by a minimum of 3 nights at home. 1 night recorded sleep with NTPE and 1 night without. Order of assessment was randomly assigned by the sealed envelope method
Outcomes	Polysomnography for a minimum of 2 REM cycles; minimum SaO ₂ , mean SaO ₂ , central apnoea index, obstructive apnoea index, respiratory arousal indices, % total sleep time with SaO ₂ > 95%
Notes	This paper also compared sleep quality between children with and without CP; these outcomes are not relevant to this review and so are not discussed here

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned with sealed envelope method for first night sleeping condition
Allocation concealment (selection bias)	Unclear risk	No information on method
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant not included, as did not reach 2 REM cycles
Selective reporting (reporting bias)	Unclear risk	Figure 1 is missing 2 participants; it is possible that 2 followed identical lines
Other bias	Unclear risk	It is not clear how children were initially recruited; however there is no indication of bias in the results and discussion sections

Klefbeck 2001

Study characteristics

Methods	Prospective controlled non-randomised study, cross-over design
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Klefbeck 2001 (Continued)

Participants	6 children with DMD (5) or SMA II (1), 8 to 17 years of age
Interventions	<p>Inhaled radioactive particles for assessment of lung clearance</p> <p>Group 1 used CPAP 10 minutes twice per day for 3 weeks, then inhaled the particles and used it for a further 72 hours until test measurements were taken. Group 2 just inhaled the particles and received no intervention until they had test measurements taken</p> <p>A 2-week break followed, during which neither group used CPAP, then group 2 and group 1 switched protocols</p> <p>Immediately after inhalation and 24, 48 and 72 hours after radioactivity was measured</p>
Outcomes	<p>Deposition of radioactive particles as a representation of sputum</p> <p>Lung function testing and transcutaneous blood gases after 3 weeks of twice-daily CPAP vs control</p>
Notes	Assumes that deposition of radioactive particles is a suitable representation of the behaviour of airway secretions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Cross-over design
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The examiner performing the measurements did not know about the CPAP treatment of the children"
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant refused CPAP, but this is stated and his data for the control phase are included
Selective reporting (reporting bias)	Low risk	All measurements described are reported, and individual data are presented
Other bias	Unclear risk	Method for selection is a little unclear: On what basis were children referred to participate in the study? How did their physicians know about the study, and how can we be sure that they were not selective about whom they referred? Also the discussion makes a lot of presumptions about how radioactive particles and sputum behave

Lagerkvist 2005
Study characteristics

Lagerkvist 2005 (Continued)

Methods	Short-term before and after study
Participants	18 children 1.7 to 17.8 years of age with severe multiple disabilities
Interventions	Participants' baseline tcPO ₂ and tcPCO ₂ were recorded after 20 minutes of sitting in the usual wheel-chair. A PEP mask was then placed over the child's nose and mouth for 2 minutes, followed by 5 minutes of normal breathing, and this was repeated 3 times in total with continuous tcPO ₂ and tcPCO ₂ recording during and for 20 minutes afterward. Manually supported cough was given 'when needed'
Outcomes	tcPO ₂ , tcPCO ₂ , respiratory rate, adverse reactions
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	No information given on whether the person who administered the PEP also collected the outcome measures data and carried the analysis
Incomplete outcome data (attrition bias) All outcomes	Low risk	All outcome data appear to have been reported
Selective reporting (reporting bias)	Low risk	RR data were not discussed but were very neutral and would not have changed study conclusions (i.e. as they did not go significantly up or down, no argument for or against could be made)
Other bias	Unclear risk	It is not clear how sample participants were selected, and it was not stated whether they were naive to PEP, so sample could potentially include children already successfully using PEP

Landon 2013
Study characteristics

Methods	Long-term before and after study
Participants	15 'medically fragile' children (mental retardation with CP 11, SMA 2, MD 1, neonatal anoxia 1), 2 to 17 years of age
Interventions	Use of HFCWO for 10 to 15 minutes at a standard setting of 10 to 15 Hz, pressure setting 5 to 6, twice daily for 16 months, compared with historical intervention of CPT according to standard protocol

Landon 2013 (Continued)

Outcomes	Number of respiratory infections, number of hospital admissions, length of stay, caregiver satisfaction, adverse outcomes	
Notes	Information from direct contact with study author	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all 15 participants are reported
Selective reporting (reporting bias)	Low risk	All variables tested are reported
Other bias	High risk	<p>The chest physiotherapy protocol was very arduous with 12 different positions. This was historic and was not designed by the research team; however this is likely to influence the results as a result of poor compliance</p> <p>1 member of the research team was employed by vest manufacturers</p> <p>Description of how the sample was obtained or justification of sample size was inadequate</p>

Mellies 2004

Study characteristics	
Methods	Long-term before and after study
Participants	12 with SMA type I and II, 1.5 to 11 years of age, intervention group 7 participants with SDB, reference group 5 participants without SDB
Interventions	For the intervention group, nocturnal NIV (BiPAP) was delivered via face mask by trained caregivers using pressure preset ventilators. Ventilator settings were selected with the aim of increasing tidal volume, suppressing participant respiratory trigger effort and optimising ventilator synchrony. Settings were adjusted during an initial overnight sleep study with the aim of normalising gas exchange and totally suppressing SDB. NIV was used each night for 7 to 12 hours of sleep

Mellies 2004 (Continued)

In the reference group (non-NIV), all but 1 participant were identified to have ineffective cough, and so caregivers were taught assisted coughing techniques, which they were instructed to perform daily. It is unclear whether the NIV group also used assisted coughing

Outcomes	Polysomnography, respiratory function (IVC and PIP), number of respiratory infections, number of hospital admissions, length of stay, quality of life (symptom questionnaire)
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Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were not randomly assigned but were allocated according to confirmation of SDB of polysomnography—it would be unethical to use participants with confirmed SDB as a comparison group
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It is unclear who did the testing
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented, no incomplete data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No other concerns

Noblejamieson 1986
Study characteristics

Methods	Short-term before and after study
Participants	40 children with neuromuscular weakness (DMD, limb girdle dystrophy, congenital muscular dystrophy, SMA, 'other'). Participants were assigned to 1 of 2 groups according to their functional status (Vignos score) and presence of scoliosis. Group 1 consisted of 20 ambulant children without scoliosis, and Group 2 of 20 non-ambulant children with scoliosis, 16 of whom had lightweight polypropylene spinal braces
Interventions	Lung function tests were performed, and the best of 3 measures was recorded for each test, with predicted normal values based upon arm span. For Group 1, LFTs were performed in standing, sitting and supine, and for Group 2, in sitting and supine in 15 participants, and then in sitting with brace on and off in 16 participants. Degree of scoliosis (Cobb angle) was measured using sitting radiographs both with and without spinal bracing

Noblejamieson 1986 (Continued)

Outcomes	FEV ₁ , FVC, peak expiratory flow rate
Notes	Posture measurements are not eligible for inclusion in this review; therefore the data for Group 1 are not relevant

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Assigned to groups according to Vignos score; however it seems very convenient that exactly 20 participants were included in each group. If participants were recruited according to their score in the first place—potential for bias here
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	High risk	Table 3 states 20 non-ambulant children with scoliosis, Table 1 suggests that only 15 took part in postural measurements—no explanation is provided for this
Selective reporting (reporting bias)	Low risk	Results for individuals that did not follow the trends are reported
Other bias	High risk	In the results section, the figures quoted do not match the data tables, and each time the percentage change is overstated. How the sample was obtained or justification of sample size is not described

Nwaobi 1986
Study characteristics

Methods	Randomised controlled trial; compared FEV ₁ , VC and ET in unsupported and adapted seating after 10 minutes seated
Participants	8 children with cerebral palsy, 5 to 12 years of age
Interventions	Study compared seating in a non-adapted sling-type wheelchair with seating in a simulator adjusted to achieve upright midline posture, with hips, knees and ankles at 90-degree angles. Spirometry was performed (best of 4 tries) after 10 minutes of sitting in each seat, with the order of seating randomly assigned
Outcomes	FEV ₁ , VC and ET
Notes	

Nwaobi 1986 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method used
Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	High risk	FEV ₁ data not provided for 2 participants, and no explanation given
Selective reporting (reporting bias)	Low risk	All measures taken are reported
Other bias	High risk	No inclusion and exclusion criteria are provided, and how participants were selected for the study is not described

Vianello 1994

Study characteristics

Methods	Prospective controlled non-randomised study
Participants	10 participants including 4 children 15, 13, 16 and 16 years of age, DMD and chronic hypercapnia. 5 declined NIV, so became the control group
Interventions	NIV by volume-cycled portable ventilator and custom-made nasal interface, used for at least 7 hours each night and titrated to normalise gas exchange vs control (no NIV). 2-Year study period
Outcomes	FVC, FVC%, MMV, PaCO ₂
Notes	Child data were extracted from a study including adults

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants recruited into the trial with a new diagnosis of chronic hypercapnia and DMD Groups were based on whether participants accepted NIPPV as a treatment option, no information is provided on how they were counselled in this decision or by whom

Vianello 1994 (Continued)

Allocation concealment (selection bias)	High risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data missing at measures for which participants had passed away—unavoidable
Selective reporting (reporting bias)	Low risk	All measures collected are reported in the results tables and figures except PaO ₂ and PaCO ₂ at two 6 month intervals. Little change in PCO ₂ and PaO ₂ from the beginning to end so reporting these interim figures would not have changed the outcome of the data.
Other bias	Unclear risk	Despite the small sample size and the lack of statistical analysis, study authors made strong statements about the efficacy of NIV It is unclear how a sample of 10 came to be selected—it seems rather too convenient that exactly half of a sample of 10 opted for each group, so one would suspect an element of selection

Vianello 2005
Study characteristics

Methods	Prospective controlled non-randomised study
Participants	27 participants, of whom 4 (2 intervention, 2 control) were children—only child data analysed. 16, 16, 14 and 11 years of age. DMD (2), SMA (1), congenital myopathy (1)
Interventions	Group A: addition of MIE on average twice daily (5 cycles followed by 20 to 30 seconds of normal breathing), co-ordinated with participant breathing, given PRN by trained respiratory therapist and on weekends by a trained caregiver Standard CPT both groups twice per day Group B: CPT only
Outcomes	Length of hospital stay, adverse outcomes, mortality
Notes	Child data were extracted from a study including adults

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study design did not permit

Vianello 2005 (Continued)

Allocation concealment (selection bias)	High risk	Study design did not permit
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study design did not permit
Incomplete outcome data (attrition bias) All outcomes	Low risk	No indication of incomplete data
Selective reporting (reporting bias)	Low risk	No indication of this
Other bias	High risk	Historical control—unclear whether controls were picked to be matched for age/diagnosis or if consecutive or for any other reason—large potential for bias here Unclear why 16 controls and 11 intervention Groups are not well matched, but when the subgroup of only 4 children is analysed, this is not significant

Yuan 2010
Study characteristics

Methods	Randomised controlled trial
Participants	28 children aged 13.6 ± 3.5 and 12.8 ± 3.9 years with CP/ NMD's. Eligible patients were recruited consecutively over a one year period from clinic presentation and computer randomised to receive either 'standard chest physiotherapy' or high frequency chest wall oscillation.
Interventions	Standardised protocols were used for chest physiotherapy and HFCWO; the children's usual caregivers were taught to perform the assigned treatment protocol. Both treatment types lasted 12 minutes and were performed three times per day over a mean five month period.
Outcomes	Overnight polysomnography measures, CXR, number of respiratory infections, number of hospital admissions, length of stay, adverse outcomes, mortality
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was conducted using a computer generated randomisation programme"
Allocation concealment (selection bias)	Unclear risk	No detail on how allocation was concealed from the investigator

Yuan 2010 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Study design did not permit
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor of chest x-Rays was blinded; blinding of other assessors is not mentioned
Incomplete outcome data (attrition bias) All outcomes	High risk	Sleep polysomnography results displayed for only 13 participants, no explanation for missing data
Selective reporting (reporting bias)	Unclear risk	See above
Other bias	Unclear risk	Study protocol for CPT used 6 positions for 2 minutes each, making it a very arduous protocol to follow, which is likely to reduce compliance and so potential efficacy

A-aDO₂: alveolar-arterial oxygen gradient; BiPAP: bilevel positive airways pressure; BTS: British Thoracic Society; CMD: congenital muscular dystrophy; CP: cerebral palsy; CPAP: continuous positive airways pressure; CPT: chest physiotherapy; CXR: chest x-ray; DMD: Duchenne muscular dystrophy; ET: expiratory time; FEV₁: forced expiratory volume in 1 second; FiO₂: fraction of inspired oxygen; FVC: forced vital capacity; GMFCS: gross motor function classification system; HFCWO: high-frequency chest wall oscillation; HMSN: hereditary motor sensory neuropathy; IPPB: intermittent positive-pressure breathing; IV: intravenous; IVC: inspiratory vital capacity; LFTs: lung function tests; MD: muscular dystrophy; MIE: mechanical insufflation-exsufflation; MMV: mandatory minute ventilation; MV: minute ventilation; NIPPV: non-invasive positive-pressure ventilation; NIV: non-invasive ventilation; NMD: neuromuscular disease; NTPE: night-time positioning equipment; PaO₂: partial pressure of oxygen; PaCO₂: partial pressure of carbon dioxide; PCF: peak cough flow; PEF: peak expiratory flow; PEP: positive expiratory pressure; PETCO₂: end-tidal carbon dioxide; PIP: peak inspiratory muscle pressure; R_{AW}: airways resistance; REM: rapid eye movement; RR: respiratory rate; SaO₂: oxygen saturation; SDB: sleep-disordered breathing; SNIP: sniff nasal inspiratory pressure; SMA: spinal muscular atrophy; tPCO₂: transcutaneous carbon dioxide; tPO₂: transcutaneous oxygen; VAS: visual analogue scale; VC: vital capacity; VE: minute volume; V_T: tidal volume.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ashworth 1971	Case series, pharmaceutical intervention
Bach 1995	Case series
Bach 1996	Adult participants
Bach 1997	Adult participants
Bach 2000	Case series
Bach 2002	Case series
Bach 2007	Case series
Bach 2011	Adult participants
Bateman 2001	Not a primary study—a commentary paper

Study	Reason for exclusion
Brooke 1989	Case series
Chatwin 2002	Not a primary study—a letter
Chatwin 2003	Outcome measures do not meet inclusion criteria - measures cough strength, part of intervention requires cognitive ability.
Chatwin 2009	Intervention does not meet inclusion criteria; requires cognitive ability
Chatwin 2011	Case series
Detroyer 1981	Study design, intervention and outcomes all fail to meet inclusion criteria
Dohna-Schwake 2006	Intervention does not meet inclusion criteria; requires cognitive ability
Donna-Schwake 2008	Case series
Ellis 1987	All participants were adults
Fanfulla 1998	Case series
Fitzgerald 2010	Conference extract led to identification of full study—see Fitzgerald 2013
Gisel 2003	Includes a pharmaceutical intervention
Gomez-Merino 2002	Case series and adult participants
Goncalves 2005	Not a primary study—a commentary paper
Hutzler 1998	Intervention does not meet inclusion criteria; requires cognitive ability
Kang 2000	Intervention does not meet inclusion criteria; requires cognitive ability
Kang 2005	Intervention does not meet inclusion criteria; requires cognitive ability
Kang 2006	Intervention does not meet inclusion criteria; requires cognitive ability
Katz 2012	Case series
Khan 1996	No relevant outcome measures, case series
Lemoine 2012	Case series
McCool 1986	No relevant outcome measures, the children in the study have spinal cord injury not SGDD.
Meinesz 2007	Case series
Mellies 2003	Case series
Mellies 2003b	Screened by translator—study design does not meet inclusion criteria
Miske 2004	Case series
Mullerpawlowski 1995	Case series

Study	Reason for exclusion
Niranjan 1998	Intervention does not meet inclusion criteria; requires cognitive ability
Padman 1994	Case series
Padman 1998	Case series
Plioplys 2002	Child and adult data presented together—study author contacted, responded that he would not be able to provide separate child data because of time constraints
Raphael 1992	This study is an interim report for Raphael 1994
Reardon 2005	Intervention does not meet inclusion criteria; requires cognitive ability
Reid 1991	Study participants did not meet inclusion criteria; insufficient physical handicap
Rideau 1993	Case series
Rideau 1995	Case series
Schwake 2003	No relevant outcome measure
Siegel 1975	Intervention does not meet inclusion criteria; requires cognitive ability
Simonds 2000	Case series
Soudon 1995	Adult participants
Tirosch 1995	Participants do not meet inclusion criteria, as they do not have severe neurological impairment
Toussaint 2003	Child and adult data presented together—study author contacted, responded that he would not be able to provide separate child data because of time constraints
Toussaint 2008	Child and adult data presented together—study author contacted, responded that he would not be able to provide separate child data because of time constraints
Tran 2011	Conference abstract, so insufficient detail to assess study design; no full paper published
Trebbia 2005	Adult participants
Tzeng 2000	Intervention does not meet inclusion criteria; requires cognitive ability
Vasconcelos 2005	Case series
Vianello 2011	Case series
Walker 1989	Intervention does not meet inclusion criteria; requires cognitive ability
Whitney 2002	Not a primary study—a commentary paper
Yuan 2007	Pilot study—full study reported in Yuan 2010
Yuan 2010a	Not a study—correspondence about Yuan 2010

Characteristics of studies awaiting classification *[ordered by study ID]*

Andreoli 2019

Methods	Retrospective review
Participants	15 medically complex patients undergoing treatment for dysphagia, aged 2.7 +/- 3 years
Interventions	Neuromuscular electrical stimulation (NMES) therapy to the head and neck
Outcomes	Functional oral intake scale (FOIS), modified barium swallow (MBS)
Notes	Comparison is with pre-treatment period - no direct control group

Bilan 2013

Methods	RCT
Participants	70 intubated patients with neurological weakness, treated following extubation
Interventions	Daily chest physiotherapy ('vibrator' and percussion) vs 'supervision'
Outcomes	Atelectasis on chest radiograph
Notes	Cohort includes 11 children with Guillain-Barré syndrome and 6 with critical illness neuropathy who are not eligible for inclusion. The study author responded to an initial request for information and provided greater detail about the study protocol but has not been able to provide separate data for eligible participants

Chatwin 2008

Methods	RCT
Participants	28 stable neuromuscular and chest wall disease patients with nocturnal hypoventilation, 12 to 73 years of age
Interventions	Home mechanical ventilation (HMV), inpatient initiation vs outpatient, baseline vs follow-up
Outcomes	Blood gas results, compliance, time in hospital, healthcare professional contact
Notes	Includes both child and adult data—separate data requested, no response. Although study primarily compares method of initiating HMV, blood gas and quality of life measures are taken at baseline and at 3, 6 and 12 months, so effect of HMV in these parameters is presented; would be eligible for inclusion

Guo 2019

Methods	Prospective controlled trial
Participants	17 children with spinal muscular atrophy and moderate to severe sleep-disordered breathing, aged 5.1±2.9 years

Guo 2019 (Continued)

Interventions	Night-time non-invasive ventilation
Outcomes	Polysomnography measures, frequency of lower respiratory tract infection, frequency of upper respiratory tract infection, frequency of hospital and intensive care admissions
Notes	Full article is in Chinese language - eligibility for inclusion based upon abstract only

Lechtzin 2016

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Leopando 1999

Methods	Short-term before and after study
Participants	22 non-ambulant participants with quadriplegic cerebral palsy, 5 to 23 years of age
Interventions	Comparison of pulmonary function tests with and without soft Boston orthosis, sitting and supine
Outcomes	Pulmonary resistance, compliance, tidal and minute volume, work of breathing, end-tidal carbon dioxide, oxygen saturation
Notes	Includes both child and adult data—separate data requested, no response

Raphael 1994

Methods	RCT
Participants	70 males with Duchenne muscular dystrophy, free of daytime respiratory failure with FVC 20% to 50% of predicted values, 11 to 33 years of age
Interventions	Nocturnal NIV minimum 6 hours/night with conventional treatment (antibiotics and physiotherapy) vs conventional treatment alone
Outcomes	ABGs and FVC, treatment compliance, survival
Notes	Includes both child and adult data—separate data requested, no response

Siriwat 2018

Methods	RCT
Participants	24 children with quadriplegic spastic cerebral palsy, age 6 months to 18 years, who were admitted to a single acute hospital with acute respiratory tract infection
Interventions	mechanical insufflation exsufflation performed three times per day versus once per day conventional chest physiotherapy (percussion, vibration, postural drainage, manually assisted cough, Ez-PAP for patients with atelectasis).
Outcomes	Length of hospital stay, days of treatment, days of oxygen usage, chest radiograph changes
Notes	

Takano 2015

Methods	Retrospective before and after study
Participants	40 patients with severe motor and intellectual disability and history of intractable aspiration pneumonia, aged 11 months to 29 years, mean age 9 years 1 month (7 patients aged over 18)
Interventions	tracheoesophageal diversion and laryngotracheal separation
Outcomes	Post-operative complications, frequency of secretion suctioning by parents and caregivers, number of hospitalizations due to aspiration pneumonia
Notes	

Ward 2005

Methods	RCT
Participants	48 patients with congenital neuromuscular or chest wall disease, 7 to 51 years of age, VC < 50% predicted
Interventions	Nocturnal NIV vs control (no ventilatory support)
Outcomes	Peak tcCO_2 (transcutaneous carbon dioxide tension) both groups; changes in pulmonary function, respiratory function and QoL in control group
Notes	Includes both child and adult data—separate data requested, no response

ABGs: arterial blood gases; FVC: forced vital capacity; HMV: home mechanical ventilation; NIV: non-invasive ventilation; QoL: quality of life; RCT: randomised controlled trial; tcCO_2 : transcutaneous carbon dioxide tension; VC: vital capacity.

ADDITIONAL TABLES

Table 1. Key features of studies

Refer- ence	CP/ NMD/ other	Num- ber of parti- cants	Inter- vention VA/ACT/ PS	Respiratory parameters	Num- ber of hospital admis- sions	Number of res- pirato- ry infec- tions re- quiring antibi- otics	Length of hos- pital stay	Quality of life mea- sures	Length of sur- vival	Mortali- ty	Adverse out- comes
Ayoub 2002	NMD	2 chil- dren, 5 adults	VA (pneu- mat- ic belt (PB))	✓ Use of PB increased tidal volume, with the greatest increase seen with bed tilted to 45 and 75 de- grees. After overnight use of PB, a small but not clinically significant in- crease in SaO ₂ , a small increase in PaO ₂ and a small reduction in Pa- CO ₂	#	#	#	#	#	#	#
Barks 2012	CP	8	PS (seating)	✓ RAW improved from control with 2 of 5 seating conditions, both of which offloaded weight from the abdomen —not statistically signifi- cant	#	#	#	#	#	#	#
Fal- saperla 2013	'Cen- tral ner- vous sys- tem dis- orders with mod- erate to severe mental retarda- tion'	44	VS (NIV) for acute respira- tory dis- tress due to pneu- monia	✓ 1 hour after therapy; improved in- tervention vs control in PaO ₂ (64.18 vs 55.04) P value < 0.0003, PaCO ₂ (42.41 vs 51.68) P value < 0.0001, RR 43 vs 57) P value < 0.0001, HR (101 vs 132) P value < 0.0001, PaO ₂ / FiO ₂ ratio (291 vs 78) P value < 0.0001, A-aDO ₂ (35 vs 381) P value < 0.0001	#	#	✓ Mean stay shorter in inter- vention group (6.22 vs 11.63) P value < 0.0001	#	#	✓ 1 partic- ipant in control group	✓ Prob- lems with mask fit- ting—all resolved after chang- ing mask size

Table 1. Key features of studies (Continued)

				Statistically but not clinically significant changes in pH							
Faroux 2008	NMD	17	ACT (MIE)	✓	#	#	#	#	#	#	#
				MIE had no significant effect on VT, rr, VE or SaO ₂							
				PETCO ₂ decreased significantly at all treatment pressures, P value < 0.0003							
				PEF/PCF, SNIP and respiratory comfort all improved significantly with the +40 to -40 cycle, P value < 0.02, P value < 0.046							
Fitzgerald 2013	CP and NMD	22 (15 at 2-year follow-up)	ACT (HFCWO)	x	✓	✓	✓	#	#	#	✓
					At 1-year follow-up, number of participants requiring hospital admission was reduced from 45% to 36% (P value < 0.47) and at 2-year follow-up was reduced to 13% (P value < 0.002)	Data collected but not presented, authors state only that significant findings were presented	No data presented, but results state that a significant reduction in hospital days (P value < 0.03) occurred, and that use of MIE/ tracheostomy did not correlate with number of hospital days				No adverse effects

Table 1. Key features of studies (Continued)

Hill 2009	CP	10	PS (NTPe)	✓ No significant differences in respiratory measures when children were in their NTPe compared with sleeping unsupported in bed when compared as a whole group, but within subject analysis showed that 3/9 children had improved SaO ₂ and 6 had decreased SaO ₂ . From the figure presented in the paper, it appears that this difference was between 1% and 2% for the increases, and between 1% and 3% for the decreases, so although they allowed no statistical analysis, this would reach clinical significance	#	#	#	#	#	#	#
Klefbeck 2001	NMD	6	ACT (CPAP for airways clearance, twice per day for 10 minutes, 3 days)	✓ At 72 hours, particle deposition was significantly lower in the CPAP group P value < 0.02 (deposition of radioactive particles used as a representation for sputum). CPAP had no effect on SaO ₂ , FEV ₁ or FVC	#	#	#	#	#	#	#
Lagerkvist 2005	Severe multiple disabilities	18	ACTs (PEP, 3 cycles of 2 minutes with 5 minutes rest between cycles)	✓ Significant improvement in tcPO ₂ 17 minutes after use of PEP (P value < 0.00001, 95% CI 0.6 to 1.05). No significant change in tcPCO ₂ or RR after PEP	#	#	#	#	#	#	✓ 6 of 18 children initially reacted negatively when the PEP mask was held against their

Table 1. Key features of studies (Continued)

Landon, unpublished	'Medical-ly fragile children'	15	ACT (HFC-WO vs standard CPT)	#	#	#	✓	✓	#	#	✓
							Significantly reduced days of hospitalisation (total hospital days from 66 to 21, hospital days per participant per month from 0.37 to 0.08 P value < 0.05) and ICU days (34 to 0) with HFCWO	Parent survey responses regarding HFCWO indicate the following: Participants were more co-operative and less combative during therapy. Time savings were achieved by delivering nebulised medication and HFC-WO simultaneously. Participants tolerated position-in-dependen-			No problems were reported with HFCWO interfering with gastros-tomy, je-junostomy or increase in seizures

Table 1. Key features of studies (Continued)

									dent air- way clear- ance ther- apy better than tradi- tional CPT.			
									All care- givers found HFCWO easy to learn to use and perform.			
									Nearly all caregivers perceived that par- ticipants were soothed by ther- apy and that treat- ments were well tolerated			
Mellies 2004	NMD	12	VA (noc- turnal NIV vs no interven- tion)	✓	Statistically significant improve- ment in all relevant measures dur- ing NIV; RDI 14.1 to 2.7 P value < 0.005, mean SaO ₂ 95% to 97% P value < 0.05, nocturnal pulse 100.0 to 88.0, P value < 0.05	#	#	#	✓	#	#	#
Noble- jamieson 1986	NMD	40	PS (spinal bracing, differ- ent posi- tions— supine,	✓	Wearing a spinal brace in sitting re- duced both FEV ₁ and FVC by 8%, P value < 0.01). PEFR unaffected by bracing	#	#	#	#	#	#	#

Table 1. Key features of studies (Continued)
sitting,
stand-
ing)

Nwaobi 1986	CP	8	PS (adap- tive seating, standard chair vs adapted chair)	✓ Significant improvement in all pa- rameters in the adaptive seating. VC MD 57.7% P value < 0.05, FEV ₁ % VC MD 51.6% P value < 0.05, ET MD 55.0% P value < 0.05	#	#	#	#	#	#	#
Vianello 20055	NMD	4 chil- dren, 23 adults	ACT (MIE along- side CPT, vs CPT only)	✓ Small trend toward reduced PaCO ₂ and increased PaO ₂ in MIE group not seen in CPT only group; howev- er the numbers of paediatric par- ticipants are too small for mean- ingful analysis	#	#	✓	#	#	✓	✓ MIE groups both alive, CPT groups 1 alive, 1 dead 1 partici- pant had nasal bleeding
Vianello 1994	NMD	4 chil- dren, 6 adults	VA (noc- turnal NIV)	Small trend toward reduced PaCO ₂ and increased PaO ₂ in NIV group; however the numbers of paedi- atric participants are too small for meaningful analysis	✓ NIV 1 ad- mission vs 2 non- NIV	#	#	#	#	✓ After 2 years, NIV both alive, non-NIV 1 alive, 1 dead	
Yuan 2010	CP and NMD	23	ACT (HFCWO or CPT 3 times daily)	✓ No significant changes in polysomnography measures from baseline to end of treatment peri- od	✓ Partici- pants re- quiring hospital- isation HFCWO 0/11, CPT 4/12, P	✓ Participants re- quiring POABS HFCWO 3/11, CPT 7/12, not statisti- cally sig- nificant	#	#	#	#	✓ None

Table 1. Key features of studies (Continued)

value <
0.09

A-aDO₂: alveolar-arterial oxygen gradient; ACTs: airways clearance techniques; BiPAP: bilevel positive airways pressure; CMD: congenital muscular dystrophy; CP: cerebral palsy; CPAP: continuous positive airways pressure; CPT: chest physiotherapy; CXR: chest x-ray; DMD: Duchenne muscular dystrophy; ET: expiratory time; FEV₁: forced expiratory volume in 1 second; FiO₂: fraction of inspired oxygen; FVC: forced vital capacity; GMFCS: gross motor function classification system; HFCWO: high-frequency chest wall oscillation; HMSN: hereditary motor sensory neuropathy; HR: heart rate; ICU: intensive care unit; IPPB: intermittent positive-pressure breathing; IVC: inspiratory vital capacity; MD: mean difference; MD: muscular dystrophy; MIE: mechanical insufflation-exsufflation; MMV: mandatory minute ventilation; NIPPV: non-invasive positive-pressure ventilation; NIV: non-invasive ventilation; NMD: neuromuscular disorder; NTPE: night-time positioning equipment; PaO₂: partial pressure of oxygen; PaCO₂: partial pressure of carbon dioxide; PB: pneumatic belt; PCF: peak cough flow; PEF: peak expiratory flow; PEP: positive expiratory pressure; PETCO₂: end-tidal carbon dioxide; PIP: peak inspiratory muscle pressure; POABS: oral antibiotics; PS: postural support; R_{AW}: airways resistance; RDI: respiratory disturbance index; REM: rapid eye movement; RR: respiratory rate; SaO₂: oxygen saturation; SMA: spinal muscular atrophy; SNIP: sniff nasal inspiratory pressure; tcPCO₂: transcutaneous carbon dioxide; tcPO₂: transcutaneous oxygen; VA: ventilatory assistance; VAS: visual analogue scale; VC: vital capacity; VE: minute volume; VS: ventilatory support.

Table 2. Study design

	Reference and intervention	Randomised?	Study design	Method of recruitment and allocation	
				Intervention group	Comparison group
Airways clearance techniques	Yuan 2010 HFCWO vs standard CPT protocol	✓	RCT	<p>"Patients with NMD or CP followed by the... paediatric pulmonary clinic were recruited for the study over a one year period. Recruitment was from consecutive eligible patients presenting to the clinic"</p> <p>Allocated to group following computer-generated randomisation</p>	
	Fitzgerald 2013 HFCWO	#	Long-term before and after study	<p>"Study enrolment was based upon a convenience sample from clinic"</p> <p>Participants were studied prospectively for 24 months (6-month wash-in period for each 12 months of intervention) and outcomes compared with historical data from the same participants over a seasonally matched 6-month period in the 12 months preceding the study</p>	
	Landon HFCWO vs standard CPT protocol	#	Long-term before and after study	<p>"Patients were recruited from the Pediatric Diagnostic Center. The study proceeded as an 'N of 1' with each patient serving as their own historical control". HFCWO was studied prospectively for a mean 16 months and was compared with historical data for the 12-month period preceding the study. All participants had previously been advised to follow a standardised same chest physiotherapy regime in the pre study period</p>	
	Vianello 2005 MIE vs CPT	#	Prospective controlled non-randomised study	<p>"Eleven consecutive NMD patients admitted to our ICU between January 2001 and March 2003 with dyspnoea due to chest infections were recruited"</p>	<p>"The control group consisted of 16 historical controls consecutively admitted to our department between 1996 and 1999; these patients were affected by NMD and had received conventional medical therapy alongside CPT alone." Patients from 2000 were not included, as medical records were unavailable</p>
	Faroux 2008 MIE	#	Short-term before and after study	<p>"Patients were recruited on a consecutive basis from our outpatient clinic"</p> <p>Participants served as their own control; baseline measures were compared with the same measures after application of MIE. All measurements were taken in a single session</p>	
	Lagerkvist 2005 PEP	#	Short-term before and after study	<p>"Seventeen children with severe multiple disabilities and one child with a severe undefined muscle disease participated in the study." No description is provided of how the sample was obtained</p> <p>Participants served as their own control; baseline measures were compared with the same measures after application of PEP. All measurements were taken in a single session</p>	

Table 2. Study design (Continued)

	Klefbeck 2001	#	Prospective controlled non-randomised study, cross-over design	<p>"Children with DMD or SMA II were referred by their physician to participate in the study." No further information about how the sample was obtained or justification of sample size is provided</p> <p>Participants were 'randomly' split into 2 groups (method not described). Half served as the control and half as the intervention; then following a 2-week washout period, the groups crossed over</p>
Ventilatory assistance	Falsaperla 20133	#	Prospective controlled non-randomised study	<p>"We entered into the study children with central nervous system disorders with mental retardation regularly followed up at the unit of paediatric neurology....admitted to the paediatric emergency department between May 2010 and June 2012 for an episode of acute respiratory distress....secondary to very severe pneumonia"</p> <p>On admission to the emergency department, parents were informed of the availability of NIV and of 'traditional objections' to use of NIV in patients with moderate to severe medical retardation. Informed consent was requested for the use of NIV. If accepted, the child entered the intervention group; if they declined, they entered the control group</p>
	Mellies 2004	#	Long-term before and after study	<p>"Between 1999 and 2001 all patients in our neuromuscular clinic (with SMA I or II)....were included in the study when showing symptoms suggestive of SDB or had restrictive lung disease with VC < 60% predicted"</p> <p>All participants underwent polysomnography to assess for SDB. The intervention group consisted of 7 participants with confirmed SDB. Participants served as their own control; baseline measures were compared with the same measures after application of NIV for an average period of months</p> <p>Participants who did not have SDB on polysomnography served as a 'comparison group' for the outcome measures</p>
	Vianello 1994	#	Prospective controlled non-randomised study	<p>10 participants referred to the respiratory pathophysiology department between January 1987 and June 1990 with evidence of stable daytime hypercapnia</p> <p>All were advised to undergo long-term mechanical ventilation via nasal mask. 5 accepted (intervention group), and 5 declined (control group)</p>
	Ayoub 2002	#	Short-term before and after study	<p>"Seven consecutive male patients with DMD...were studied after giving written consent"</p> <p>Participants served as their own control; baseline measures were compared with the same measures after use of PB</p>
Postural support	Barks 2012	✓	RCT	<p>Participants were recruited from the outpatient clinic at a children's orthopaedic hospital. No description of how the sample was obtained or justification of sample size is provided</p> <p>Participants served as their own control; outcome measures were compared after seating in 6 different seating configurations</p>

Table 2. Study design (Continued)

			rations. The order of configurations tested was randomly assigned
Nwaobi 1986	✓	RCT	No description of how participants were recruited, how the sample was obtained or justification for sample size is provided
Supportive seating			Participants served as their own control; outcome measures were compared after seating in 2 different seating configurations The order of configurations tested was randomly assigned
Hill 2009	✓	RCT	"Twenty two established sleep system users...living in the Southampton area were identified." This is the only description of how the sample was obtained
Night-time positioning equipment			Participants served as their own control, with measures taken for 2 nights with and 2 nights without use of NTPE. The order of assessment was randomly assigned by the sealed envelope method
Noble-jamieson 1986	#	Short-term before and after study	No description of how the sample group was recruited is provided
Spinal bracing			2 groups were included: 1 with and 1 without scoliosis. The study looked at spinal bracing in addition to the effects of posture (e.g. sitting, lying down) on pulmonary function—the posture part of the study is not eligible for inclusion, and so Group 1 is not relevant
			In Group 2, 16 participants had spinal braces for scoliosis. Participants served as their own control; baseline measures were compared with the same measures while participants were wearing their spinal braces

CP: cerebral palsy; CPAP: continuous positive airways pressure; CPT: chest physiotherapy; DMD: Duchenne muscular dystrophy; HFCWO: high-frequency chest wall oscillation; ICU: intensive care unit; MIE: mechanical insufflation-exsufflation; NIV: non-invasive ventilation; NMD: neuromuscular disease; NTPE: night-time positioning equipment; PB: pneumatic belt; PEP: positive expiratory pressure; RCT: randomised controlled trial; SDB: sleep-disordered breathing; SMA: spinal muscular atrophy; VC: vital capacity

APPENDICES

Appendix 1. Search strategies

MEDLINE (Ovid)

1. exp Respiratory Therapy/
2. exp Physical Therapy Modalities/
3. Tracheostomy/
4. Patient Positioning/
5. exp Posture/
6. Suction/
7. Mucociliary Clearance/
8. Insufflation/

9. ((chest\$ or respiratory\$) adj3 (physiotherap\$ or physical\$)).tw.
10. (postur\$ adj3 (drain\$ or manage\$)).tw.
11. (CPAP or "continuous positive airway*" or "nasal continuous positive airway pressure" or NCPAP or PPR or "positive pressure respiration" or "Positive end-expiratory pressure OR PEEP" or "inspiratory positive-pressure breathing" or IPB or IPPB).tw.
12. BiPAP.tw.
13. (mechanical\$ adj3 (insufflat\$ or exsufflat\$)).tw.
14. (cough\$ adj3 assist\$).tw.
15. (percussi\$ or oscillat\$ or vibrat\$).tw.
16. suction\$.tw.
17. "sleep system\$".tw.
18. or/1-17
19. Developmental Disabilities/
20. exp Intellectual Disability/
21. exp Child Development Disorders, Pervasive/
22. exp Learning Disorders/
23. Cerebral Palsy/
24. exp Communication Disorders/
25. Disabled Children/
26. (development\$ adj3 (disabiliti\$ or delay\$)).tw.
27. (mental\$ adj3 retard\$).tw.
28. handicap\$.tw.
29. "cerebral palsy".tw.
30. neurodisabilit\$.tw.
31. neurological disabilit\$.tw.
32. (multiple adj3 disabilit\$).tw.
33. exp Neuromuscular Diseases/
34. exp Muscular Diseases/
35. myopath\$.tw.
36. neuromuscular\$.tw.
37. (muscular adj3 dystroph\$).tw.
38. or/19-37
39. exp Respiratory Tract Diseases/
40. Sputum/
41. Mucus/
42. pneumonia.tw.

43. aspiration\$.tw.
44. (secretion\$ or sputum or mucus).tw.
45. bronchiectasis\$.tw.
46. ((respiratory or airway\$ or pulmonary) adj3 (problem\$ or infection\$ or condition\$ or disease\$ or disorder\$)).tw.
47. or/39-46
48. exp Child/
49. exp Pediatrics/
50. exp infant/
51. exp adolescent/
52. (paediatric\$ or paediatric\$ or child\$ or adolescen\$ or infant\$ or young\$ or preschool\$ or pre-school\$ or newborn\$ or new-born\$ or neonat\$ or neo-nat\$).tw.
53. or/48-52
54. 18 and 38 and 47 and 53
55. (clinical trial or controlled clinical trial or randomised controlled trial).pt.
56. (randomised or randomised).ab,ti.
57. placebo.ab,ti.
58. dt.fs.
59. randomly.ab,ti.
60. trial.ab,ti.
61. groups.ab,ti.
62. exp Cohort Studies/
63. cohort\$.ti,ab.
64. (follow-up adj3 (study or studies)).tw.
65. meta analysis.pt.
66. meta-analy\$.tw.
67. metaanaly\$.tw.
68. (systematic\$ adj3 (review\$1 or overview\$1)).tw.
69. Review.pt.
70. or/55-69
71. Animals/
72. Humans/
73. 71 not (71 and 72)
74. 70 not 73
75. 54 and 74

CENTRAL

- #1 MeSH descriptor: [Respiratory Therapy] explode all trees
- #2 MeSH descriptor: [Physical Therapy Modalities] explode all trees
- #3 MeSH descriptor: [Tracheostomy] this term only
- #4 MeSH descriptor: [Patient Positioning] this term only
- #5 MeSH descriptor: [Posture] explode all trees
- #6 MeSH descriptor: [Suction] this term only
- #7 MeSH descriptor: [Mucociliary Clearance] this term only
- #8 MeSH descriptor: [Insufflation] this term only
- #9 ((chest* or respiratory*) near/3 (physiotherap* or physical*)):ti,ab,kw
- #10 ((postur*) near/3 (drain* or manage*)):ti,ab,kw
- #11 (CPAP or NCPAP or PPR or PEEP or IPB or IPPB):ti,ab,kw
- #12 "continuous positive airway*":ti,ab,kw
- #13 "nasal continuous positive airway pressure":ti,ab,kw
- #14 "positive pressure respiration":ti,ab,kw
- #15 "Positive end-expiratory pressure":ti,ab,kw
- #16 "inspiratory positive-pressure breathing"
- #17 BiPAP:ti,ab,kw
- #18 ((mechanical*) near/3 (insufflat* or exsufflat*)):ti,ab,kw
- #19 (cough* near/3 assist*):ti,ab,kw
- #20 (percussi* or oscillat* or vibrat*):ti,ab,kw
- #21 suction*:ti,ab,kw
- #22 "sleep system":ti,ab,kw
- #23 {or #1-#22}
- #24 MeSH descriptor: [Developmental Disabilities] this term only
- #25 MeSH descriptor: [Intellectual Disability] explode all trees
- #26 MeSH descriptor: [Child Development Disorders, Pervasive] explode all trees
- #27 MeSH descriptor: [Learning Disorders] explode all trees
- #28 MeSH descriptor: [Cerebral Palsy] this term only
- #29 MeSH descriptor: [Communication Disorders] explode all trees
- #30 MeSH descriptor: [Disabled Children] this term only
- #31 ((development*) near/3 (disabiliti* or delay*)):ti,ab,kw
- #32 (mental* near/3 retard*):ti,ab,kw
- #33 handicap*:ti,ab,kw
- #34 "cerebral palsy":ti,ab,kw

- #35 neurodisabilit*:ti,ab,kw
- #36 (neurological* near/3 disabilit*):ti,ab,kw
- #37 ("multiple disabilit*"):ti,ab,kw
- #38 MeSH descriptor: [Neuromuscular Diseases] explode all trees
- #39 MeSH descriptor: [Muscular Diseases] explode all trees
- #40 myopath*:ti,ab,kw
- #41 neuromuscular*:ti,ab,kw
- #42 (muscular near/3 dystroph*):ti,ab,kw
- #43 {or #24-#42}
- #44 MeSH descriptor: [Respiratory Tract Diseases] explode all trees
- #45 MeSH descriptor: [Sputum] this term only
- #46 MeSH descriptor: [Mucus] this term only
- #47 (secretion* or sputum or mucus):ti,ab,kw
- #48 pneumonia:ti,ab,kw
- #49 aspiration*:ti,ab,kw
- #50 bronchiectasis*:ti,ab,kw
- #51 ((respiratory or airway* or pulmonary or chest*) near/3 (problem* or infection* or condition* or disease* or disorder*)):ti,ab,kw
- #52 {or #44-#51}
- #53 MeSH descriptor: [Child] explode all trees
- #54 MeSH descriptor: [Pediatrics] explode all trees
- #55 MeSH descriptor: [Infant] explode all trees
- #56 MeSH descriptor: [Adolescent] explode all trees
- #57 (paediatric* or paediatric* or child* or adolescen* or infant* or young* or preschool* or pre-school* or newborn* or new-born* or neonat* or neo-nat*) .ti,ab,kw
- #58 {or #53-#57}
- #59 #23 and #43 and #52 and #58

EMBASE (Ovid)

- 1. exp breathing exercise/
- 2. exp physiotherapy/
- 3. exp tracheostomy/
- 4. exp patient positioning/
- 5. exp body posture/
- 6. suction/
- 7. mucociliary clearance/
- 8. exp aeration/

9. ((chest\$ or respiratory\$) adj3 (physiotherap\$ or physical\$)).tw.
10. (postur\$ adj3 (drain\$ or manage\$)).tw.
11. (CPAP or "continuous positive airway" or "nasal continuous positive airway pressure" or NCPAP or PPR or "positive pressure respiration" or "Positive end-expiratory pressure" or PEEP or "inspiratory positive-pressure breathing" or IPB or IPPB).tw.
12. BiPAP.tw.
13. (mechanical\$ adj3 (insufflat\$ or exsufflat\$)).tw.
14. (cough\$ adj3 assist\$).tw.
15. (percussi\$ or oscillat\$ or vibrat\$).tw.
16. suction\$.tw.
17. "sleep system\$".tw.
18. or/1-17
19. exp developmental disorder/
20. intellectual impairment/
21. exp mental deficiency/
22. exp autism/
23. exp learning disorder/
24. cerebral palsy/
25. exp communication disorder/
26. exp handicapped child/
27. (development\$ adj3 (disabiliti\$ or delay\$)).tw.
28. (mental\$ adj3 retard\$).tw.
29. handicap\$.tw.
30. "cerebral palsy".tw.
31. neurodisabilit\$.tw.
32. neurological disabilit\$.tw.
33. (multiple adj3 disabilit\$).tw.
34. exp neuromuscular disease/
35. exp muscle disease/
36. myopath\$.tw.
37. neuromuscular\$.tw.
38. (muscular adj3 dystroph\$).tw.
39. or/19-38
40. exp respiratory tract disease/
41. sputum/
42. exp mucus/

43. pneumonia.tw.
44. aspiration\$.tw.
45. aspiration/
46. (secretion\$ or sputum or mucus).tw.
47. bronchiectasis\$.tw.
48. ((respiratory or airway\$ or pulmonary or chest\$) adj3 (problem\$ or infection\$ or condition\$ or disease\$ or disorder\$)).tw.
49. or/40-48
50. child/
51. exp pediatrics/
52. infant/
53. adolescent/
54. (paediatric\$ or paediatric\$ or child\$ or adolescen\$ or infant\$ or young\$ or preschool\$ or pre-school\$ or newborn\$ or new-born\$ or neonat\$ or neo-nat\$).tw.
55. or/50-54
56. 18 and 39 and 49 and 55
57. Randomized Controlled Trial/
58. randomisation/
59. Controlled Study/
60. Clinical Trial/
61. controlled clinical trial/
62. Double Blind Procedure/
63. Single Blind Procedure/
64. Crossover Procedure/
65. (clinica\$ adj3 trial\$).mp.
66. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (mask\$ or blind\$ or method\$)).mp.
67. exp Placebo/
68. placebo\$.mp.
69. random\$.mp.
70. ((control\$ or prospectiv\$) adj3 (trial\$ or method\$ or stud\$)).mp.
71. (crossover\$ or cross-over\$).mp.
72. cohort analysis/
73. cohort\$.ti,ab.
74. (follow-up adj3 (study or studies)).tw.
75. meta analysis/
76. "systematic review"/

77. meta-analy\$.tw.
78. metaanaly\$.tw.
79. (systematic\$ adj3 (review\$1 or overview\$1)).tw.
80. Review.pt.
81. or/57-80
82. 56 and 81

CINAHL (EBSCOHost)

- S1 (MH "Respiratory Therapy+")
S2 (MH "Physical Therapy+")
S3 (MH "Tracheostomy")
S4 (MH "Patient Positioning+")
S5 (MH "Posture+")
S6 (MH "Suction+")
S7 (MH "Mucociliary Clearance")
S8 (MH "Insufflation")
S9 (chest* or respiratory*) N3 (physiotherap* or physical*)
S10 postur* N3 (drain* or manage* OR support*)
S11 CPAP
S12 NCPAP
S13 PPR
S14 PEEP
S15 IPB or IPPB
S16 "continuous positive airway*"
S17 "nasal continuous positive airway pressure"
S18 "positive pressure respiration"
S19 "positive end-expiratory pressure"
S20 BiPAP
S21 mechanical* N3 (insufflat* or exsufflat*)
S22 cough* N3 assist*
S23 percussi* or oscillat* or vibrat*
S24 suction*
S25 "sleep system"

S26 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19
OR S20 OR S21 OR S22 OR S23 OR S24 OR S25

S27 (MH "Developmental Disabilities")

S28 (MH "Mental Retardation+")

S29 (MH "Child Development Disorders, Pervasive+")

S30 (MH "Learning Disorders+")

S31 (MH "Communicative Disorders+")

S32 (MH "Cerebral Palsy")

S33 (MH "Disabled+")

S34 development* N3 (disabiliti* or delay*)

S35 mental* N3 retard*

S36 handicap*

S37 "cerebral palsy"

S38 neurodisabilit*

S39 neurological N1 disabilit*

S40 multiple N3 disabilit*

S41 (MH "Neuromuscular Diseases")

S42 (MH "Muscular Diseases")

S43 myopath*

S44 neuromuscular*

S45 muscular N3 dystroph*

S46 S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45

S47 (MH "Respiratory Tract Diseases+")

S48 (MH "Sputum")

S49 (MH "Mucus")

S50 secretion* or sputum or mucus

S51 pneumonia

S52 aspiration*

S53 bronchiectasis*

S54 (respiratory or airway* or pulmonary or chest*) N3 (problem* or infection* or condition* or disease* or disorder*)

S55 S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54

S56 (MH "Child")

S57 (MH "Pediatrics+")

S58 (MH "Adolescence")

S59 paediatric* or paediatric* or child* or adolescen* or infant* or young* or preschool* or pre-school* or newborn* or new-born* or neonat* or neo-nat*

S60 S56 OR S57 OR S58 OR S59

S61 S26 AND S46 AND S55 AND S60

S62 (MH "Clinical Trials+")

S63 randomised or randomised or randomly

S64 placebo*

S65 clinical* N3 (trial* or study or studies)

S66 (single* or double* or triple*) and blind*

S67 (MH "Prospective Studies+")

S68 cohort*

S69 follow-up N3 (study or studies)

S70 (MH "Meta Analysis")

S71 (MH "Systematic Review")

S72 meta-analy* or metaanaly*

S73 systematic* N3 (review* or overview*)

S74 S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73

S75 S61 AND S74

AMED (EBSCOHost)

S1 (DE "RESPIRATORY THERAPY")

S2 (DE "PHYSICAL THERAPY MODALITIES") OR (DE "PHYSICAL THERAPY SPECIALITY") OR (DE "PHYSICAL THERAPY TECHNIQUES") OR (DE "PHYSIOTHERAPISTS") OR (DE "PHYSIOTHERAPY") OR (DE "PHYSIOTHERAPY METHODS")

S3 (DE "TRACHEOTOMY")

S4 (DE "POSTURAL THERAPIES") OR (DE "POSTURE")

S5 (DE "MUCOCILIARY CLEARANCE")

S6 (DE "CHEST PHYSIOTHERAPY")

S7 (chest* or respiratory*) N3 (physiotherap* or physical*)

S8 postur* N3 (drain* or manage* OR support*)

S9 CPAP

S10 NCPAP

S11 PPR

S12 PEEP

S13 IPB or IPPB

S14 "continuous positive airway*"

S15 "nasal continuous positive airway pressure"

S16 "positive pressure respiration"

S17 "positive end-expiratory pressure"

S18 BiPAP

S19 mechanical* N3 (insufflat* or exsufflat*)

S20 cough* N3 assist*

S21 percussi* or oscillat* or vibrat*

S22 suction*

S23 "sleep system"

S24 (DE "POSITIVE PRESSURE RESPIRATION")

S25 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24

S26 (DE "DEVELOPMENTAL DISABILITIES")

S27 (DE "CHILD DEVELOPMENT DISORDERS")

S28 (DE "LEARNING DISORDERS") OR (DE "LEARNINGDISABILITY")

S29 (DE "COMMUNICATIVE DISORDERS")

S30 (DE "CEREBRAL PALSY") OR (DE "CEREBRALPALSY")

S31 (DE "DISABLED") OR (DE "DISABLED CHILDREN")

S32 development* N3 (disabiliti* or delay*)

S33 mental* N3 retard*

S34 (DE "MENTAL RETARDATION") OR (DE "MENTALLY HANDICAPPED")

S35 (DE "HANDICAPPED")

S36 handicap*

S37 "cerebral palsy"

S38 neurodisabilit*

S39 neurological N1 disabilit*

S40 multiple N3 disabilit*

S41 (DE "MUSCULAR DYSTROPHY")

S42 myopath*

S43 neuromuscular*

S44 muscular N3 dystroph*

S45 S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44

S46 (DE "RESPIRATORY SYMPTOMS") OR (DE "RESPIRATORY TRACT DIS") OR (DE "RESPIRATORY TRACT INFECTIONS")

S47 (DE "SPUTUM")

S48 (DE "MUCUS")

S49 secretion* or sputum or mucus

S50 (DE "PNEUMONIA")

S51 pneumonia*

S52 aspiration*

S53 bronchiectasis*

S54 (respiratory or airway* or pulmonary or chest*) N3 (problem* or infection* or condition* or disease* or disorder*)

S55 S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54

S56 S25 AND S45 AND S55

Web of Knowledge

#1 Topic=("respiratory therapy" OR "physical therapy" or physiotherap* or tracheostomy or "patient positioning" or postur* or suction* or "mucociliary clearance" or "airway clearance" or insufflat* or exsufflat* or CPAP or "continuous positive airway" or "nasal continuous positive airway pressure" or NCPAP or PPR or "positive pressure respiration" or "positive end-expiratory pressure" OR PEEP or "inspiratory positive-pressure breathing" or IPB or IPPB or BiPAP or "cough assist" or percussi* or oscillat* or vibrat* or "sleep system")

#2 Topic=("developmental disability" or "developmental disabilities" or "intellectual disability" or "intellectual disabilities" or "development disorder" or "learning disorder" or "cerebral palsy" or "communication disorder" or (development* and delay*) or (mental and retard*) or handicap* or neurodisabilit* or "neurological disability" or "neurological disabilities" or "multiple disabilities" or neuromuscular* or "muscular disease" or myopathy* or "muscular dystrophy")

#3 Topic((((respiratory or airway* or pulmonary or chest*) AND (problem* or infection* or condition* or disease* or disorder*)) OR bronchiectasis* OR secretion* or sputum or mucus OR aspirat* or pneumonia)

#4 #3 AND #2 AND #1

#5 Topic=(paediatric* or paediatric* or child* or adolescen* or infant* or young* or preschool* or pre-school* or newborn* or new-born* or neonat* or neo-nat*)

#6 #5 AND #4

#7 Topic=(randomised or randomised or randomly or placebo* or trial* or study or studies or cohort* or meta-analys* or metaanalys* or "systematic review" or overview)

#8 #7 AND #6

Appendix 2. Inclusion criteria for studies

Inclusion/exclusion criteria

Study design

Included

- RCTs;
- Controlled trials; and
- Cohort studies, provided that data from a comparison group were reported.

Excluded

- Case reports;
- Case series; and
- Systematic reviews.

Participants

Included

- Children from birth to 18 years of age with severe neurological impairment and respiratory morbidity; and
- Children with severe neurological impairment who do not have severe cognitive impairment.

Excluded

- Children with a primary respiratory pathology (e.g. cystic fibrosis); and
- Those receiving palliative/end of life care.

Types of interventions

- Airway clearance techniques.
- Postural drainage.
- Suction.
- MIE.
- NIV.
- Tracheostomy.
- Postural management.

Excluded

- Any intervention for which performance requires cognitive ability (e.g. glossopharyngeal breathing, incentive spirometry).

WHAT'S NEW

Date	Event	Description
7 January 2021	Amended	Four studies added to awaiting classification section

HISTORY

Protocol first published: Issue 2, 2013

Review first published: Issue 10, 2014

Date	Event	Description
26 March 2019	Amended	Two studies added to Studies awaiting classification .

CONTRIBUTIONS OF AUTHORS

Naomi Winfield (NW) conceived, designed and drafted the protocol and co-ordinated the review.

Esme Turner (ET), Nicola Barker (NB) and Gemma Quin (GQ) provided input to the protocol.

NW took the lead role in collecting data, designing search strategies, undertaking searches and organising retrieval of papers.

ET, NB, GQ and NW jointly screened search results, appraised the quality of papers, completed risk of bias assessments and extracted data.

NW took a lead role in writing to the authors of papers to ask for additional information, obtaining additional data on papers and obtaining and screening data from unpublished studies.

NW analysed and interpreted data.

NW, NB and ET provided a clinical perspective.

NW took the lead role in writing the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Cardiff University, UK

Access to dissertation supervisor and support from academic librarians. Library assistance in obtaining references not available online

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We clarified the inclusion criteria for types of studies. We included only studies with a true comparison group and excluded case reports, case series and systematic reviews. We clarified the inclusion of studies of children with no intellectual impairment.

We used the Cochrane risk of bias tool in this review, though it is not recommended for non-RCTs. At the time of writing there was an absence of standardised risk of bias tools for non-randomised studies and the Cochrane tool was selected for its structure and familiarity to Cochrane readers. A new 'Acrobat NRS tool' is due for publication in 2015 and we will apply this tool if the review is updated. Because we did not assess the risk of bias using a NRS tool, we decided not to produce a summary of findings table.

INDEX TERMS

Medical Subject Headings (MeSH)

Chest Wall Oscillation; Developmental Disabilities [*complications]; Positive-Pressure Respiration [methods]; Randomized Controlled Trials as Topic; Respiration Disorders [etiology] [*therapy]; Respiration, Artificial [*methods]

MeSH check words

Child; Humans