

Cerebral palsy in adults

[C2] Identifying and managing respiratory disorders associated with cerebral palsy: assisted ventilation

NICE guideline NG119

Evidence reviews

January 2019

Final

These evidence reviews were developed by National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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Assisted ventilation techniques for adults with cerebral palsy

Review question

C2 Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

Introduction

Conservative treatment for chronic respiratory disorders aims to ensure adequate supply of oxygenation. This is commonly achieved through treatment with bronchodilators, corticosteroids, and controlled oxygen. People who do not respond to such interventions receive ventilation. If ventilation involves any instrument that is inserted in the trachea through the mouth, such as an endotracheal tube, it is referred to as invasive assisted ventilation. This may be associated with adverse events such as tissue damage and infections. In non-invasive ventilation the patient receives air or a mixture of air and oxygen from a flow generator through a full facial or nasal mask which is a less invasive method of supplying sufficient oxygen to the body with potentially fewer adverse events. This evidence review sets out to investigate the effectiveness of assisted ventilation for adults with cerebral palsy who have a chronic respiratory disorder.

PICO Table

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Adults aged 25 and over with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)
Intervention	Assisted ventilation techniques: <ul style="list-style-type: none">• Non-invasive ventilation (NIV)• Ventilation via tracheostomy
Comparison	<ul style="list-style-type: none">• No assisted ventilation• NIV versus standard care• NIV versus ventilation via tracheostomy
Outcome	Critical <ul style="list-style-type: none">• Hospital admissions• Overall survival• Quality of life (carer or self-reported) Important <ul style="list-style-type: none">• Treatment complications• Daytime sleepiness and fatigue

NIV: Non-invasive ventilation

For full details see review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in [developing NICE guidelines: the manual 2014](#). Methods specific to this review question are

described in the review protocol in appendix A and for a full description of the methods see supplementary document C.

Declaration of interests were recorded according to NICE's 2014 conflicts of interest policy from May 2016 until April 2018. From April 2018 onwards they were recorded according to NICE's 2018 [conflicts of interest policy](#). Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Interests Register).

Clinical evidence

Included studies

A systematic review of the clinical literature was conducted but no relevant studies were identified which were applicable to this review question.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies excluded from this systematic review, with reasons for their exclusion, are provided in appendix K.

Summary of clinical studies included in the evidence review

No clinical studies were identified for this review.

Quality assessment of clinical studies included in the evidence review

No clinical studies were identified for this review.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no studies were identified which were applicable to this review question.

Excluded studies

No studies were identified which were applicable to this review question.

Summary of studies included in the economic evidence review

No economic evaluations were included in this review.

Economic model

Whilst this review topic was prioritised for bespoke economic modelling, the failure to identify any clinical evidence meant it would not have been feasible to model clinical and quality of life outcomes in a way which would have assisted in the making of recommendations. A discussion of costs have been presented in the resource impact section.

Resource impact

Table 2: Unit cost for different types of assistive ventilation

Resource	Unit costs†	Source
CPAP Device	£780 (£129-£7,898)	NHS Supply Catalogue 2017
Bi-level CPAP Device	£2,675 (£451-£7168)	NHS Supply Catalogue 2017
Tracheostomy (initial operation)	£2,972 (£175-£4,823)	Department of Health NHS Reference Costs 2016/2017

CPAP: Continuous positive airway pressure; NHS: National Health Service

† Median cost identified with the range of identified costs in parenthesis

Continuous positive airway pressure (CPAP) and Bi-Level CPAP Devices

CPAP and bi-level CPAP devices are full facial or nasal masks which ensure the adequate supply of oxygen to an individual. The main difference between CPAP and bi-level CPAP devices is that a bi-level CPAP device allows for 2 pressure settings for inhalation and exhalation making breathing easier and increasing the volume of air entering and exiting the lungs.

Costs for CPAP devices from NHS Supply Catalogue 2017 ranged from £129 to £7,898 with a median cost of £780. One previous UK economic evaluation was identified, NICE TA139 (2008) which looked at [CPAP for the treatment of obstructive sleep apnoea/hypopnoea syndrome](#). This report estimated a cost of the CPAP device of £280. This cost does not report additional costs such as initial fitting of the mask, replacement parts and batteries for devices, additional equipment such as stands or backpacks and other sundries. Using an annual equivalent cost based on NICE methodology the report estimated the annual costs as £164.64 in the first year and £218.24 per person in subsequent years equivalent to £193.66 and £256.71 in 2017 prices inflated using the hospital & community health services (HCHS) index of the Personal and Social Services Research Unit (PSSRU 2017). These estimates of costs for CPAP devices will likely represent a lower end for the cost of CPAP devices for adults with cerebral palsy. CPAP devices for cerebral palsy are likely to be used more frequently and there may be a need for the devices to be transported. This will increase replacement and maintenance costs and require additional equipment. Adults with cerebral palsy may also be likely to use more expensive CPAP devices with additional features such as breathing monitoring and alarms.

Costs for bi-level CPAP devices ranged from £451 to £7,168 in the NHS Supply Catalogue with a median cost of £2,675. This higher median cost compared to CPAP represents the increased sophistication of the bi-level machines. As above these costs did not include any additional costs although there was no reason to believe that these would differ to that of a CPAP device. One previous UK economic evaluation was identified, NICE NG42 (2016), which looked at non-invasive ventilation for people with [motor neurone disease](#). The report estimated a cost per machine of £4000 which, with the addition of other expenses, almost identical to NICE TA139 described above, and using identical methodology estimated an annual cost of £3,149.39 equivalent to £3440.77 in 2017 prices. It was considered that this would be in line with the cost for adults with cerebral palsy given that both patient groups would be using the devices for extended periods of the day, the need for additional equipment for transportation and relative sophistication of the devices.

Ventilation via tracheostomy

A tracheostomy is an operation where an incision is made in the trachea opening a direct airway. A tracheostomy costs between £175 and £4,823 with a median cost of £2,972 depending on whether it is elective or non-elective or performed on an outpatient, day case or inpatient basis based on Department of Health Reference Costs 2016/2017. No previous

UK costings or economic evaluations were identified which considered ventilation via tracheostomy. Although the real cost drivers of ventilation by tracheostomy is the need for 24 hour access to nursing, medical and technical support. The costs of this can be in the hundreds of thousands of pounds over the life course of the patient. Only a very small number of patients would opt for invasive ventilation over less costly non-invasive ventilation, not only because it is more invasive but also because the majority of patients receiving ventilation in this manner would be unable to receive ventilation by any other means. Therefore invasive and non-invasive ventilation should not be viewed as competing interventions. Patients in this group are also more likely to need treatment for infection (given the open trachea). They are also more likely to need emergency admission although this would be accounted for by this group having greater need for ventilation support rather than because of the intervention given. Both of these would lead to additional costs although they will be small relative to the other costs discussed.

Evidence statements

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The critical outcomes were hospital admissions, overall survival and quality of life, as assisted ventilation techniques are primarily aimed at improving these outcomes. To allow a balance of the benefits and harms of assisted ventilation techniques, treatment complications (for instance mask related difficulties) and daytime sleepiness and fatigue (when assistive ventilation led to sleep disturbance) were included as important outcomes.

The quality of the evidence

No evidence was identified for this review.

Benefits and harms

The committee discussed that people with cerebral palsy may have their own perception about quality of life and what may be considered as good quality of life by one individual, may not be considered acceptable by another. Based on their clinical experience, the committee discussed that some people may want to be put on assisted ventilation following acute deterioration in respiratory function, while others would not consider that as acceptable. The goals of management following acute deterioration in respiratory function may vary from individual to individual. The committee noted that this needs to be considered while managing respiratory conditions. Hence the committee made the recommendation regarding agreeing a plan with person (and family or carers) in the event of infection causing acute deterioration in respiratory function, based on their clinical experience and expertise. The committee recognised that shared decision making will help the people achieve an acceptable level of quality of life. The committee agreed it was important to discuss a management plan with the adult with cerebral palsy who may be at risk to go on to develop respiratory complications. Such a plan would take into account the preferences of the person with cerebral palsy to balance the likely effectiveness of future treatment with its tolerability and impact on independence and family life (for example the impact that home assisted ventilation may have on daily routines).

There was no evidence about home based non-invasive ventilation for adults with cerebral palsy. Based on their knowledge the committee discussed that there is good evidence available regarding the effectiveness of non-invasive ventilation techniques for respiratory failure in progressive neuromuscular conditions (for instance the committee were aware of the recommendations in the NICE guideline on [motor neurone disease](#)). Considering that the

course and symptoms of respiratory failure may be similar in people with cerebral palsy, the committee agreed that non-invasive ventilation could also benefit people with cerebral palsy. Due to the lack of direct evidence the committee decided to make a weak recommendation for this. The committee agreed that the technology and equipment for non-invasive ventilation would need to be checked and its effectiveness monitored. Based on their experience and knowledge they decided that the usual follow-up would be every 3 to 6 months. Having such checks would ensure that equipment failures are identified early and that the treatment is effective.

They noted that good documentation is important for consistency of care and recommended that the preferences for future assistive ventilation should be discussed and recorded in an advance care plan. The objective of an advance care plan is to facilitate people receiving the medical care that is consistent with their values, goals and preferences. The details of how care planning is conducted were outside the remit of this review and guideline. However, the committee stressed that such plans need to take account of the individual's abilities and difficulties. They were aware that there are some examples of plans that have been adapted for people with learning disabilities (such as the hospital [passport](#)) they have also cross referenced to the NICE guideline on [patient experience in adult NHS services](#) in another section of the guideline to highlight how to support people to actively participate in their care and shared decision-making.

The committee discussed that, when non-invasive ventilation techniques fail to meet agreed goals, alternative options like tracheostomy or supportive care should be considered. The committee discussed that, although tracheostomy can be effective in selected cases, it can be helpful when people do not respond to other ventilation techniques. However, it is an invasive ventilation technique and is therefore associated with a risk of adverse events. Respiratory failure is a life limiting condition and people may prefer not to have such invasive treatments when other treatments have not been effective. They may therefore choose to have supportive care (care focused on relieving symptoms caused by serious illnesses) instead. Due to the lack of evidence and an approach that needs to be tailored to each individual's circumstances the committee did not want to be too prescriptive about this and did not make a strong recommendation on tracheostomy or any other alternative treatment option.

Due to the lack of evidence the committee discussed whether a research recommendation should be prioritised. However, they agreed that the treatment with assisted ventilation is individualised and would vary according to needs, preferences and circumstances. They therefore decided that it would be difficult to conduct research in this.

Cost effectiveness and resource use

The committee noted that no relevant published economic evaluations had been identified for this topic.

The committee considered that these recommendations would just reinforce current practice. The committee thought there may be some cost savings from ending assisted ventilation earlier where it is not being effective but that this resource saving would only be small.

Other factors the committee took into account

The committee were aware of NICE Technology appraisal guidance [TA 139] [Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome](#) and cross referred it for further information on assisted ventilation.

Although no evidence exists in the population for cerebral palsy, there is evidence for assisted ventilation in progressive neuromuscular conditions. When they drafted recommendations the committee took some of these recommendations into account in their discussion (for example the NICE guideline NG42 on [motor neuron disease](#)).

References

No studies were included in this review.

Appendices

Appendix A – Review protocols

Review protocol for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

Table 3: Review protocol for assisted ventilation in adults with cerebral palsy with chronic respiratory disorder

Field (based on PRISMA-P)	Content
Review question	Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?
Type of review question	Intervention
Objective of the review	The aim of this review is to determine the effectiveness of the assisted ventilation techniques in adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure) to improve their quality of life.
Eligibility criteria – population/disease/condition/issue/domain	Adults aged 25 and over with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	<ul style="list-style-type: none"> • Assisted ventilation techniques: <ul style="list-style-type: none"> ○ Non-invasive ventilation (NIV) ○ Ventilation via tracheostomy
Eligibility criteria – comparator(s)/control or reference (gold) standard	<ul style="list-style-type: none"> • No assisted ventilation • NIV versus standard care • NIV versus ventilation via tracheostomy
Outcomes and prioritisation	<p>Critical outcomes</p> <ul style="list-style-type: none"> • Hospital admissions • Overall survival • Quality of life (carer or self-reported) <p>Important outcomes</p>

Field (based on <u>PRISMA-P</u>)	Content
	<ul style="list-style-type: none"> • Treatment complications • Daytime sleepiness and fatigue Minimally important differences <ul style="list-style-type: none"> • Any statistically significant improvement in overall survival will be considered clinically important • MID in HrQoL for people with chronic respiratory disease (Wyrwich KW, Tierney WM, Babu AN, Kroenke K, Wolinsky FD. A Comparison of Clinically Important Differences in Health-Related Quality of Life for Patients with Chronic Lung Disease, Asthma, or Heart Disease. Health Services Research. 2005;40(2):577-592). • Other dichotomous outcomes will use default MIDs [RR thresholds of 0.80 and 1.2] • Other continuous outcomes will use default MIDs [0.5 times the SD of the control group]
Eligibility criteria – study design	Only published full text papers – <ul style="list-style-type: none"> • Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) • Cross-sectional studies Consider conference abstract only if related to RCTs.
Other inclusion exclusion criteria	None
Proposed sensitivity/sub-group analysis, or meta-regression	In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: <ul style="list-style-type: none"> • Population subgroups: <ul style="list-style-type: none"> ○ Level of functional disability ○ Severity of chronic respiratory disorder ○ Learning difficulties

Field (based on <u>PRISMA-P</u>)	Content
	<ul style="list-style-type: none"> • Intervention subgroups: <ul style="list-style-type: none"> ○ Type of assisted ventilation ○ Setting (e.g at home, in hospital) ○ Age at initiation of ventilator use ○ Continuous vs night time <p>Severity of chronic respiratory disorder and type of assisted ventilation will be also considered important confounders which ideally should be adjusted for in any included comparative observational studies.</p>
Selection process – duplicate screening/selection/analysis	A random sample of the references identified in the search will be sifted by a second reviewer. This sample size will be 10% of the total, or 100 studies if the search identifies fewer than 1000 studies. All disagreements in study inclusion will be discussed and resolved between the two reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers.
Data management (software)	STAR was used to sift through the references identified by the search
Information sources – databases and dates	Database(s): Embase 1974 to Present, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present;
Identify if an update	Not an update
Author contacts	For details please see the guideline in development web site.
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014 .
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables) of the full guideline.
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).

Field (based on PRISMA-P)	Content
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual 2014 . The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ .
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual 2014 .
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the methods in supplementary document C.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014 .
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014 .
Rationale/context – what is known	For details please see the introduction to the evidence review in the full guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Alliance (NGA) and chaired by Dr Paul Eunson in line with section 3 of Developing NICE guidelines: the manual 2014 . Staff from the NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods in supplementary document C.
Sources of funding/support	NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for those working in the NHS, public health and social care in England.

Field (based on PRISMA-P)	Content
PROSPERO registration number	Not applicable

GRADE: Grading of Recommendations Assessment, Development and Evaluation; HrQoL: Health related quality of life; MID: minimal important difference; NGA: National Guideline Alliance; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; NIV: Non-invasive ventilation; RCT: randomised controlled trial; RoB: risk of bias; RR: risk ratio; SD: standard deviation.

Appendix B – Literature search strategies

Literature search strategy for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

This appendix is a combined search strategy and will be the same for all the evidence reviews for the C review questions as listed below:

C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

C3: Are prophylactic treatments (for example, antibiotics, chest physiotherapy, cough assistance) effective in preventing respiratory infections in adults with cerebral palsy?

Database: Medline & Embase (Multifile)

Database(s): Embase 1974 to 2018 March 22, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

Table 4: Last searched on 22 March 2018

#	Searches
1	exp Cerebral Palsy/ use prmz
2	exp cerebral palsy/ use oemezdz
3	((cerebral or brain or central) adj2 (pal* or paralyz#s or pares#s)).tw.
4	cerebral palsy.ti,ab.
5	little? disease.tw.
6	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) adj5 spastic*).tw.
7	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) adj3 ataxi*).tw.
8	or/1-6
9	limit 8 to english language
10	limit 9 to (adult <18 to 64 years> or aged <65+ years>) use oemezdz [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process; records were retained]
11	limit 9 to "all adult (19 plus years)" [Limit not valid in Embase; records were retained]
12	11 use prmz
13	or/10,12
14	exp Respiration/ or exp Respiration, Artificial/ or exp Respiratory Insufficiency/ or exp Respiration Disorders/ or exp Respiratory Tract Infections/ or exp Respiratory Aspiration/ or exp Pneumonia, Aspiration/ or exp Respiratory System Abnormalities/ or exp Respiratory Therapy/ or exp Respiratory Function Tests/ or exp Respiratory Paralysis/ or exp Respiratory Mechanics /or exp Positive-Pressure Respiration/ or exp Positive-Pressure Respiration, Intrinsic/ or exp Continuous Positive Airway Pressure/ or exp Respiratory Distress Syndrome, Adult/ or exp Respiratory Sounds/ or exp Gastroesophageal Reflux/ or exp Hypoxia/ or exp Sleep Apnea Syndromes/ or exp Sleep Apnea, Obstructive/ or exp Airway Obstruction/ or exp Tracheotomy/ or exp Bronchial Diseases/ or exp Bronchitis/ or exp Bronchiectasis/ or exp Bronchoscopy/ or exp Laryngoscopy/ or exp

#	Searches
	Tracheobronchomalacia/ or exp Tracheal Diseases/ or exp Adenoidectomy/ or exp Tonsillectomy/ or exp Pulmonary Disease, Chronic Obstructive/ or exp Pulmonary Ventilation/ or exp Airway Management/ or exp Suction/ or exp Airway Resistance/ or exp Cough/ or exp Bronchial Spasm/ or exp Ventilator Weaning/ or exp Ventilators, Mechanical/ or exp Ventilators, Negative-Pressure/ or exp Pulmonary Edema/ or exp Oxygen Consumption/ or exp Oxygen Inhalation Therapy/ or exp Administration, Intranasal/ or exp Catheterization/ or exp Intubation, Intratracheal/ or exp Laryngeal Masks/ or exp Masks/ or exp Catheter Ablation/ or exp Pneumonia/ or exp Pneumonia, Ventilator-Associated/ or exp Ventilator-Induced Lung Injury/ or exp Mouth Breathing/ or exp Phrenic Nerve/ or exp Diaphragm/ or exp Hypoventilation/ or exp Oximetry/ or exp Oxyhemoglobins/ or exp Oxygen/ or exp Carbon Dioxide/ or exp Blood Gas Analysis/ or exp Tidal Volume/ or exp Sleep/ or exp Rest/ or exp Fatigue/ or exp Home Care Services/ or exp Self-Help Devices/ or exp Equipment Failure Analysis/ or exp Intensive Care Units/ or exp Dilatation/ or exp Critical Care/ or exp Self Care/ or exp "Quality of Life"/ or exp Ambulatory Care/ or exp Patient Admission/ or exp Hospitalization/ or exp "Length of Stay"/ or exp Institutionalization/ or exp Physical Therapy Modalities/ or exp Pulmonologists/ or exp Breathing Exercises/ or exp Anti-Bacterial Agents/ or exp Drug Resistance, Bacterial/ or exp Albuterol/ or exp "Nebulizers and Vaporizers"/ or exp Bronchodilator Agents/ or exp Administration, Inhalation/ or exp Saline Solution, Hypertonic/ or exp Influenza Vaccines/ or exp Gastrostomy/ or exp Deglutition Disorders/ or exp Deglutition/ or exp Chest Wall Oscillation/ or exp Asthma/ or exp Bronchopulmonary Dysplasia/ or exp Scoliosis/ or exp Amoxicillin/ or exp Penicillins/ or exp Doxycycline/ or exp Clarithromycin/ or exp Bacterial Infections/co [Complications]
15	14 use prmz
16	exp breathing/ or exp artificial ventilation/ or exp respiratory failure/ or exp breathing disorder/ or exp respiratory tract infection/ or exp acid aspiration/ or exp aspiration pneumonia/ or exp respiratory tract malformation/ or exp respiratory care/ or exp oxygen consumption/ or exp diaphragm paralysis/ or exp positive end expiratory pressure/ or exp adult respiratory distress syndrome/ or exp abnormal respiratory sound/ or exp gastroesophageal reflux/ or exp hypoxia/ or exp sleep disordered breathing/ or exp airway obstruction/ or exp dysphagia/ or exp swallowing/ or exp tracheotomy/ or exp lung functioning test/ or exp bronchus disease/ or exp bronchitis/ or exp bronchiectasis/ or exp bronchoscopy/ or exp laryngoscopy/ or exp tracheobronchomalacia/ or exp trachea disease/ or exp adenoidectomy/ or exp apnea monitoring/ or exp tonsillectomy/ or exp chronic obstructive lung disease/ or exp lung ventilation/ or exp breathing mechanics/ or exp respiration control/ or exp suction drainage/ or exp airway suction device/ or exp suction/ or exp tracheal suction catheter/ or exp suction pump/ or exp airway resistance/ or exp coughing/ or exp bronchospasm/ or exp ventilator/ or exp ventilator weaning/ or exp mechanical ventilator/ or exp lung edema/ or exp oxygen therapy/ or exp intranasal drug administration/ or exp catheterization/ or exp endotracheal intubation/ or exp laryngeal mask/ or exp mask/ or exp catheter ablation/ or exp ventilator associated pneumonia/ or exp pneumonia/ or exp ventilator induced lung injury/ or exp mouth breathing/ or exp phrenic nerve/ or exp diaphragm/ or exp hypoventilation/ or exp oximetry/ or exp oxyhemoglobin/ or exp oxygen/ or exp carbon dioxide/ or exp blood gas analysis/ or exp tidal volume/ or exp rest/ or exp sleep/ or exp sleep disordered breathing/ or exp fatigue/ or exp home care/ or exp self help device/ or exp device failure analysis/ or exp intensive care unit/ or exp dilatation/ or exp intensive care/ or exp self care/ or exp "quality of life"/ or exp ambulatory care/ or exp hospital admission/ or exp hospitalization/ or exp "length of stay"/ or exp institutionalization/ or exp physiotherapy/ or exp pulmonologist/ or exp breathing exercise/ or exp antiinfective agent/ or exp bacterial infection/ or exp antibiotic resistance/ or exp antibiotic agent/ or exp salbutamol/ or exp nebulizer/ or exp vaporizer/ or exp bronchodilating agent/ or exp inhalational drug administration/ or exp sodium chloride/ or exp influenza vaccine/ or exp gastrostomy/ or exp asthma/ or exp lung dysplasia/ or exp

#	Searches
	scoliosis/ or exp amoxicillin/ or exp penicillin derivative/ or exp doxycycline/ or exp clarithromycin/
17	16 use oemezdz
18	(respirat* or breath* or ventilat* or tracheo* or trachea* or intratracheal or intubat* or catheter* or airway* or mask* or tent* or sleep apn?ea or tube* or nasotracheal or CNT or obstruct* or mouth* or nose* or nasal or intranasal or nasogastric or failure or distress or pneumon* or lung* or phrenic nerve* or pulmonary* or diaphragm* or tracheo-bronchomalacia or hypoventilat* or positive airway pressure* or negative pressure* or CPAP or negative pressure chamber* or NPC or assist* or manag* or support* or help* or complicat* or leak* or prevent* or prophyla* or monitor* or assistive technology or hypox* or bronch* or bronchopulmonary or laryn* or adenoid* or tonsil* or resistan* or edema* or oxygen* or carbon dioxide or CO2 or inhal* or oximetr* or oxyhemoglobin* or tidal volume* or sleep* or fatigue* or daytime function* or home care or self-help* or self-care* or dilat* or cough* or chest physiotherapy* or antibiot* or critical or quality or hospital admission* or stay or institutional* or thermoplastic patient-ventilator tubing interface* or bedside percutaneous dilatational tracheostomy or PDT or BIPAP or chest infection* or inflammat* or aspiration* or tachypnoea or bronchial spasm* or phlegm* or wheez* or choking or choke* or swallow* or salbutamol or hyperinflation or deglutition* or oscillation* or nebuli?er* or vapor?er* or oral secretion* or saline or oro-pharyngeal suction* or saturation* or vaccine* or pulmonologist* or gastrostom* or bronchitis or percussion* or chest wall vibration* or kyphoscoliosis or amoxicillin or penicillin or doxycycline or clarithromycin).ti,ab.
19	15 or 17 or 18
20	13 and 19
21	conference abstract.pt. use oemezdz
22	letter.pt. or LETTER/ use oemezdz
23	Letter/ use prmz
24	EDITORIAL/ use prmz
25	editorial.pt. use oemezdz
26	NEWS/ use prmz
27	exp HISTORICAL ARTICLE/ use prmz
28	note.pt. use oemezdz
29	ANECDOTES AS TOPIC/ use prmz
30	COMMENT/ use prmz
31	CASE REPORT/ use prmz
32	CASE REPORT/ use oemezdz
33	CASE STUDY/ use oemezdz
34	(letter or comment* or abstracts).ti.
35	or/21-34
36	RANDOMIZED CONTROLLED TRIAL/ use prmz
37	RANDOMIZED CONTROLLED TRIAL/ use oemezdz
38	random*.ti,ab.
39	or/36-38
40	35 not 39
41	ANIMALS/ not HUMANS/ use prmz
42	ANIMAL/ not HUMAN/ use oemezdz

#	Searches
43	exp ANIMALS, LABORATORY/ use prmz
44	exp ANIMAL EXPERIMENTATION/ use prmz
45	exp MODELS, ANIMAL/ use prmz
46	exp RODENTIA/ use prmz
47	NONHUMAN/ use oomezd
48	exp ANIMAL EXPERIMENT/ use oomezd
49	exp EXPERIMENTAL ANIMAL/ use oomezd
50	ANIMAL MODEL/ use oomezd
51	exp RODENT/ use oomezd
52	(rat or rats or mouse or mice).ti.
53	or/40-52
54	20 not 53

Database: Cochrane Library

Table 5: Last searched on 22 March 2018

ID	Search
#1	MeSH descriptor: [Cerebral Palsy] explode all trees
#2	((cerebral or brain or central) N2 (pal* or paraly?s or pare?s))
#3	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) N5 spastic*)
#4	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) N3 ataxi*)
#5	#1 or #2 or #3 or #4
#6	MeSH descriptor: [Respiration] explode all trees
#7	MeSH descriptor: [Respiration, Artificial] explode all trees
#8	MeSH descriptor: [Respiratory Insufficiency] explode all trees
#9	MeSH descriptor: [Respiration Disorders] explode all trees
#10	MeSH descriptor: [Respiratory Tract Infections] explode all trees
#11	MeSH descriptor: [Respiratory Aspiration] explode all trees
#12	MeSH descriptor: [Pneumonia, Aspiration] explode all trees
#13	MeSH descriptor: [Respiratory System Abnormalities] explode all trees
#14	MeSH descriptor: [Respiratory Therapy] explode all trees
#15	MeSH descriptor: [Respiratory Paralysis] explode all trees
#16	MeSH descriptor: [Positive-Pressure Respiration] explode all trees
#17	MeSH descriptor: [Positive-Pressure Respiration, Intrinsic] explode all trees
#18	MeSH descriptor: [Continuous Positive Airway Pressure] explode all trees
#19	MeSH descriptor: [Respiratory Distress Syndrome, Adult] explode all trees
#20	MeSH descriptor: [Respiratory Sounds] explode all trees
#21	MeSH descriptor: [Gastroesophageal Reflux] explode all trees
#22	MeSH descriptor: [Hypoxia] explode all trees
#23	MeSH descriptor: [Sleep Apnea Syndromes] explode all trees
#24	MeSH descriptor: [Sleep Apnea, Obstructive] explode all trees
#25	MeSH descriptor: [Airway Obstruction] explode all trees

ID	Search
#26	MeSH descriptor: [Tracheotomy] explode all trees
#27	MeSH descriptor: [Bronchial Diseases] explode all trees
#28	MeSH descriptor: [Bronchitis] explode all trees
#29	MeSH descriptor: [Bronchiectasis] explode all trees
#30	MeSH descriptor: [Bronchoscopy] explode all trees
#31	MeSH descriptor: [Laryngoscopy] explode all trees
#32	MeSH descriptor: [Tracheobronchomalacia] explode all trees
#33	MeSH descriptor: [Tracheal Diseases] explode all trees
#34	MeSH descriptor: [Adenoidectomy] explode all trees
#35	MeSH descriptor: [Tonsillectomy] explode all trees
#36	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees
#37	MeSH descriptor: [Pulmonary Ventilation] explode all trees
#38	MeSH descriptor: [Pulmonary Ventilation] explode all trees
#39	MeSH descriptor: [Airway Management] explode all trees
#40	MeSH descriptor: [Suction] explode all trees
#41	MeSH descriptor: [Airway Resistance] explode all trees
#42	MeSH descriptor: [Cough] explode all trees
#43	MeSH descriptor: [Bronchial Spasm] explode all trees
#44	MeSH descriptor: [Ventilator Weaning] explode all trees
#45	MeSH descriptor: [Ventilators, Mechanical] explode all trees
#46	MeSH descriptor: [Ventilators, Negative-Pressure] explode all trees
#47	MeSH descriptor: [Pulmonary Edema] explode all trees
#48	MeSH descriptor: [Oxygen Inhalation Therapy] explode all trees
#49	MeSH descriptor: [Administration, Intranasal] explode all trees
#50	MeSH descriptor: [Catheterization] explode all trees
#51	MeSH descriptor: [Intubation, Intratracheal] explode all trees
#52	MeSH descriptor: [Laryngeal Masks] explode all trees
#53	MeSH descriptor: [Masks] explode all trees
#54	MeSH descriptor: [Catheter Ablation] explode all trees
#55	MeSH descriptor: [Pneumonia] explode all trees
#56	MeSH descriptor: [Pneumonia, Ventilator-Associated] explode all trees
#57	MeSH descriptor: [Ventilator-Induced Lung Injury] explode all trees
#58	MeSH descriptor: [Mouth Breathing] explode all trees
#59	MeSH descriptor: [Phrenic Nerve] explode all trees
#60	MeSH descriptor: [Diaphragm] explode all trees
#61	MeSH descriptor: [Hypoventilation] explode all trees
#62	MeSH descriptor: [Oximetry] explode all trees
#63	MeSH descriptor: [Oxyhemoglobins] explode all trees
#64	MeSH descriptor: [Oxygen] explode all trees
#65	MeSH descriptor: [Carbon Dioxide] explode all trees
#66	MeSH descriptor: [Blood Gas Analysis] explode all trees

ID	Search
#67	MeSH descriptor: [Tidal Volume] explode all trees
#68	MeSH descriptor: [Sleep] explode all trees
#69	MeSH descriptor: [Fatigue] explode all trees
#70	MeSH descriptor: [Home Care Services] explode all trees
#71	MeSH descriptor: [Self-Help Devices] explode all trees
#72	MeSH descriptor: [Equipment Failure Analysis] explode all trees
#73	MeSH descriptor: [Intensive Care Units] explode all trees
#74	MeSH descriptor: [Dilatation] explode all trees
#75	MeSH descriptor: [Critical Care] explode all trees
#76	MeSH descriptor: [Self Care] explode all trees
#77	MeSH descriptor: [Quality of Life] explode all trees
#78	MeSH descriptor: [Ambulatory Care] explode all trees
#79	MeSH descriptor: [Patient Admission] explode all trees
#80	MeSH descriptor: [Hospitalization] explode all trees
#81	MeSH descriptor: [Length of Stay] explode all trees
#82	MeSH descriptor: [Institutionalization] explode all trees
#83	MeSH descriptor: [Physical Therapy Modalities] explode all trees
#84	MeSH descriptor: [Pulmonologists] explode all trees
#85	MeSH descriptor: [Breathing Exercises] explode all trees
#86	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#87	MeSH descriptor: [Drug Resistance, Bacterial] explode all trees
#88	MeSH descriptor: [Albuterol] explode all trees
#89	MeSH descriptor: [Nebulizers and Vaporizers] explode all trees
#90	MeSH descriptor: [Bronchodilator Agents] explode all trees
#91	MeSH descriptor: [Administration, Inhalation] explode all trees
#92	MeSH descriptor: [Saline Solution, Hypertonic] explode all trees
#93	MeSH descriptor: [Influenza Vaccines] explode all trees
#94	MeSH descriptor: [Gastrostomy] explode all trees
#95	MeSH descriptor: [Deglutition Disorders] explode all trees
#96	MeSH descriptor: [Deglutition] explode all trees
#97	MeSH descriptor: [Chest Wall Oscillation] explode all trees
#98	MeSH descriptor: [Asthma] explode all trees
#99	MeSH descriptor: [Bronchopulmonary Dysplasia] explode all trees
#100	MeSH descriptor: [Scoliosis] explode all trees
#101	MeSH descriptor: [Amoxicillin] explode all trees
#102	MeSH descriptor: [Penicillins] explode all trees
#103	MeSH descriptor: [Doxycycline] explode all trees
#104	MeSH descriptor: [Clarithromycin] explode all trees
#105	MeSH descriptor: [Bacterial Infections] explode all trees and with qualifier(s): [Complications - CO]
#106	respirat* or breath* or ventilat* or tracheo* or trachea* or intratracheal or intubat* or catheter* or airway* or mask* or tent* or sleep apn?ea or tube* or nasotracheal or CNT or

ID	Search
	obstruct* or mouth* or nose* or nasal or intranasal or nasogastric or failure or distress or pneumon* or lung* or phrenic nerve* or pulmonary* or diaphragm* or tracheo-bronchomalacia or hypoventilat* or positive airway pressure* or negative pressure* or CPAP or negative pressure chamber* or NPC or assist* or manag* or support* or help* or complicat* or leak* or prevent* or prophyla* or monitor* or assistive technology or hypox* or bronch* or bronchopulmonary or laryn* or adenoid* or tonsil* or resistan* or edema* or oxygen* or carbon dioxide or CO2 or inhal* or oximetr* or oxyhemoglobin* or tidal volume* or sleep* or fatigue* or daytime function* or home care or self-help* or self-care* or dilat* or cough* or chest physiotherapy* or antibiot* or critical or quality or hospital admission* or stay or institutional* or thermoplastic patient-ventilator tubing interface* or bedside percutaneous dilatational tracheostomy or PDT or BIPAP or chest infection* or inflammat* or aspiration* or tachypnoea or bronchial spasm* or phlegm* or wheez* or choking or choke* or swallow* or salbutamol or hyperinflation or deglutition* or oscillation* or nebuli?er* or vapor?er* or oral secretion* or saline or oro-pharyngeal suction* or saturation* or vaccine* or pulmonologist* or gastrostom* or bronchitis or percussion* or chest wall vibration* or kyphoscoliosis or amoxicillin or penicillin or doxycycline or clarithromycin
#107	{or #6-#106}
#108	#5 and #107

Database: Web of Science

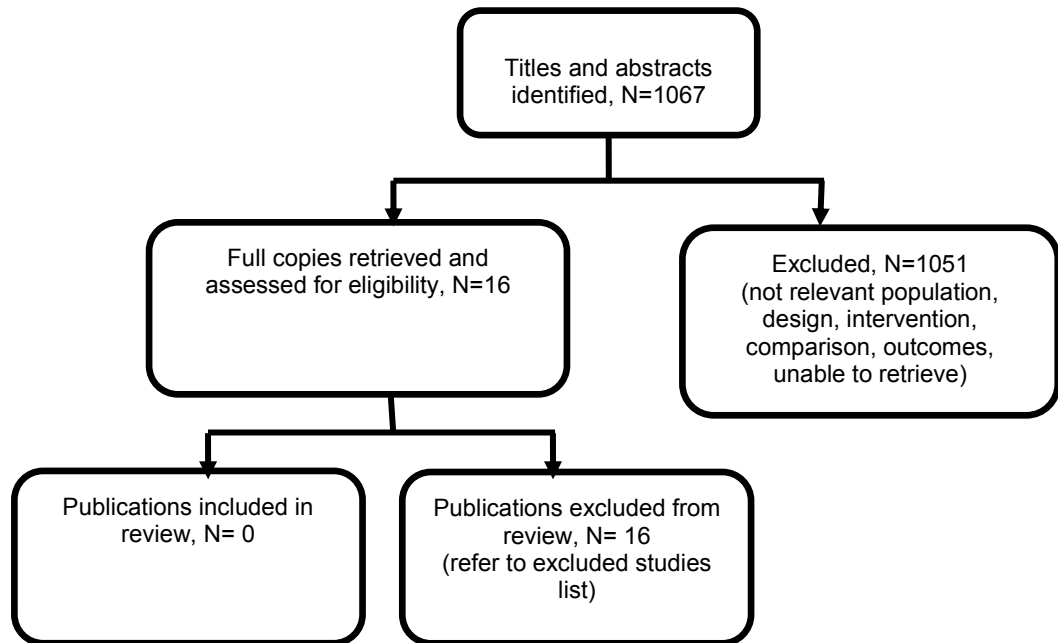
Table 6: Last searched on 22 March 2018

#4	(#3) AND LANGUAGE: (English)
#3	#2 AND #1
#2	ts=Artificial Respiration or ts=Respiratory Tract Infection* or ts=Aspiration or ts=respirat* failure* or ts=Pneumoni* or ts=Respiratory Therapy or ts=Respiratory Distress Syndrome or ts=Airway* Obstruction* or ts=Bronch* Disease* or ts=Pulmonary Ventil* or ts=mechanical ventilation* or ts=Breathing Exercise* or ts=antibiotic* or ts=Vaccine* or ts=Bacterial Infection* or ts=breath* or ts=mask* or ts=tent* or ts=sleep apn?ea or ts=tube* or ts=hypoventilat* or ts=positive airway pressure* or ts=negative pressure* or ts=chest infection* or ts=inflammat* or ts=oxygen* or ts=carbon dioxide or ts=CO2 or ts=bronchial spasm* or ts=phlegm* or ts=wheez* or ts=choking or ts=choke* or ts=swallow* or ts=salbutamol or ts=percussion* or ts=chest wall vibration* or ts=scoliosis or ts=amoxicillin or ts=penicillin or ts=doxycycline or ts=clarithromycin
#1	ts=cerebral palsy

Appendix C – Clinical evidence study selection

Clinical evidence study selection for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

Figure 1: Flow diagram of clinical article selection for this review



Appendix D – Clinical evidence tables

Clinical evidence tables for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No clinical studies were identified for this review.

Appendix E – Forest plots

Forest plots for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No forest plots were included in this review.

Appendix F – GRADE tables

GRADE tables for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No GRADE tables were included in this review.

Appendix G – Economic evidence study selection

Economic evidence study selection for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No economic evidence was identified for this review.

Appendix H – Economic evidence tables

Economic evidence tables for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No economic evidence was identified for this review.

Appendix I – Health economic evidence profiles

Health economic evidence profiles for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No economic evidence was identified for this review.

Appendix J – Health economic analysis

Health economic analysis for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No economic analysis was included in this review.

Appendix K – Excluded studies

Clinical and economic lists of excluded studies for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

Clinical studies

Table 7: Excluded clinical studies for assisted ventilation in adults with cerebral palsy with chronic respiratory disorder

Excluded studies – C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?	
Study	Reason for Exclusion
Bischof, F., Hyperbaric oxygen therapy in cerebral palsy, South African Medical Journal, 91, 182, 2001	Letter to editor about a study on children with cerebral palsy.
Chong, H. S., Alfonso, M. R. P., Kim, J. S., Lee, H. M., Moon, S. H., Suk, K. S., Kim, H. S., Usefulness of noninvasive positive-pressure ventilation during surgery of flaccid neuromuscular scoliosis, Journal of Spinal Disorders and Techniques, 28, 298-300, 2015	Mean age of subjects is less than 18 years. Only two subjects with cerebral palsy included.
Heuser, G., Uszler, J. M., Hyperbaric oxygenation for cerebral palsy, Lancet, 357, 2053-2054, 2001	Reports on a study on children with cerebral palsy.
Holland, L.J., Bhambhani, Y.N., Ferrara, M.S., Steadward, R.D., Reliability of the maximal aerobic power and ventilatory threshold in adults with cerebral palsy, Archives of Physical Medicine and Rehabilitation, 75, 687-691, 1994	Not related to assisted ventilation.
James, P. B., Hyperbaric oxygenation for cerebral palsy, Lancet, 357, 2052-2053, 2001	Related to use of hyperbaric oxygen therapy for children.
Kirby, N. A., Barnerias, M. J., Siebens, A. A., An evaluation of assisted cough in quadriparetic patients, Archives of Physical Medicine & Rehabilitation Arch Phys Med Rehabil, 47, 705-10, 1966	Not related to assisted ventilation technique.
Lampe, R., Blumenstein, T., Turova, V., Alves-Pinto, A., Lung vital capacity and oxygen saturation in adults with cerebral palsy, Patient Preference and Adherence, 8, 1691-1697, 2014	Not related to assisted ventilation techniques.
Ntoumenopoulos, G., Berry, M., Camporota, L., Effects of manually-assisted cough combined with postural drainage, saline instillation and airway suctioning in critically-ill patients during high-frequency oscillatory ventilation: a prospective observational single centre trial, Physiotherapy Theory & Practice Physiother, 30, 306-11, 2014	Does not report on subjects with cerebral palsy.
Pareek, N., Williams, J., Hanna, D., Johnson, W.D., Minocha, A., Abell, T.L., Prokinetic therapy reduces aspiration pneumonia in tube-fed patients with severe developmental disabilities, American Journal of Mental Retardation, 112, 467-471, 2007	Does not report on evaluation of assisted ventilation.
Rashid, A., Raj, B., Stoddart, A., Repeat percutaneous dilatational tracheostomy in an awake and unintubated patient, Acta Anaesthesiologica Scandinavica, 51, 378-379, 2007	Case report of a single patient.
Rose, L., McKim, D., Katz, S., Leasa, D., Nonoyama, M., Pedersen, C., Avendano, M., Goldstein, R., Institutional care for long-term	Data on long term mechanical ventilation cases. Cerebral palsy

mechanical ventilation in Canada: A national survey, Canadian Respiratory Journal, 21, 357-362, 2014	cases included in 'others' category with one included subject.
Rose, Louise, Adhikari, Neill Kj, Leasa, David, Fergusson, Dean A, McKim, Douglas, Cough augmentation techniques for extubation or weaning critically ill patients from mechanical ventilation, Cochrane Database of Systematic Reviews, 2017	Not related to evaluation of assisted ventilation techniques.
Shah, R. K., Lander, L., Berry, J. G., Nussenbaum, B., Merati, A., Roberson, D. W., Tracheotomy outcomes and complications: A national perspective, Laryngoscope, 122, 25-29, 2012	Cerebral palsy adults constitute 0.3% of the sample. Tracheostomy cases included both temporary and permanent tracheostomies, and study population was not restricted to those having chronic respiratory conditions.
Vianello, A., Corrado, A., Arcaro, G., Gallan, F., Ori, C., Minuzzo, M., Bevilacqua, M., Mechanical insufflation-exsufflation improves outcomes for neuromuscular disease patients with respiratory tract infections, American journal of physical medicine & rehabilitation, 84, 83-8; discussion 89-91, 2005	Does not report on subjects with cerebral palsy.
vonScheele, B. H. C., Frojd, J. K., Gahn, E. E., Analysis of breathing behavior in cerebral palsy athletes (CPA): Capnography during deep and "normal" breathing, Biofeedback and Self-Regulation, 21, 385-385, 1996	Does not report on evaluation of assisted ventilation techniques.
Yeow, M. E., Your own sweet time: discontinuing ventilator support at home, Journal of Palliative Medicine, 18, 388-9, 2015	Does not report on evaluation of assisted ventilation techniques.

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

Research recommendations for review question C2: Does assisted ventilation improve quality of life for adults with cerebral palsy who have a chronic respiratory disorder (including respiratory failure)?

No research recommendations were made for this review.