National Institute for Health and Care Excellence

Final

Cerebral palsy in adults

[C1] Identifying and managing respiratory disorders associated with cerebral palsy: protocols for monitoring respiratory health

NICE guideline NG119

Evidence reviews

January 2019

Final

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

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Identifying and managing respiratory disorders

Review question

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

Introduction

Adults with cerebral palsy are at increased risk of respiratory health problems. This may be due to a variety of co-morbidities, including gastro-oesophageal reflux, aspiration of feed or secretions, reduced functional lung volume, muscle tone in the form of respiratory muscle weakness and some side effects of regularly used medication. Identifying adults with these risks and re-appraising risk may help prevent infection, and delay respiratory failure. This review question looks at the evidence of clinical and cost effectiveness for methods of identification and monitoring respiratory disorders.

PICO/PIRO table

Please see Table 1 for a summary of the Population, Intervention/Index test, Comparison/Reference standard and Outcome (PICO/PIRO) characteristics of this review.

Table 1: Summary of the protocol (PICO/PIRO table)

Population	Adults aged 25 years and over with cerebral palsy.
Intervention / Index test	Protocol for monitoring respiratory health defined by: • Setting ○ residential ○ primary care ○ secondary care • Tests used, for example: ○ assessment of vital capacity ○ sleep disordered breathing ○ assessment of fatigue ○ cough peak flow ○ aspiration risk ○ infections ○ oxygen saturation • Who carries out the monitoring, for example ○ GP ○ specialist • Frequency of monitoring
Comparison / Reference standard	• Any other monitoring protocol • No formal monitoring
Outcomes	**Critical** • Respiratory health • Overall survival • Hospital admission

	Important • Secondary conditions (e.g. colds, asthma, sleep apnoea, daytime sleepiness (Epworth Scale), etc.) • Respiratory function • Health related quality of life • Satisfaction *In the absence of test and treat studies[1]:* • Diagnostic accuracy: ○ Sensitivity ○ Specificity ○ Positive/Negative likelihood ratios • Clinimetric properties

GP: General Practitioner
1The review question was framed as an intervention review but in the absence of test and treat studies diagnostic accuracy studies would be included, with the assumption that accurate identification of respiratory health problems is likely to improve outcomes.

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.

As GRADE is designed only for RCTs and observational studies, a modified version of this tool was used in order to appraise the confidence in the included diagnostic test accuracy evidence. The QUADAS-2 checklist risk of bias and applicability items were used for evaluating the risk of bias and indirectness, respectively, of the studies. The quality assessment of inconsistency and imprecision were adapted to take into account the methodological features of diagnostic studies.

GRADE was not used for evidence about clinimetric properties (such as reliability or construct validity), methodological quality was summarised for each publication individually using the consensus-based standards for the selection of health status measurement instruments (COSMIN) checklist for individual studies or the CASP checklist for systematic reviews.

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

Two studies were included. One was a cross-sectional study (Lampe 2014; number of participants in study, N=46), the other was a systematic review including 7 cross-sectional studies (Lennon 2014; N=117).

Lampe 2014 compared chest expansion measured with a tape, lung capacity measured using spirometry and oxygen saturation measured using pulse-oximetry in adults with

cerebral palsy. Lennon 2014 was a systematic review of the clinical usefulness of aerobic or anaerobic fitness measures in adults with cerebral palsy.

Lampe 2014 did not report the sensitivity or specificity of reduced lung capacity for low oxygen saturation, but provided sufficient information for the NGA team to calculate these statistics for a number of threshold values (see appendix E, Figure 3). The threshold value closest to the threshold agreed in the review protocol for high sensitivity (90%; see appendix A) was used in the modified GRADE analysis.

The clinical studies included in this evidence review are summarised in **Table 2 and evidence from these is summarised in the clinical evidence profiles below (** Table 3 and

Table 4).

See also the literature search strategy in appendix B, study selection flow chart in appendix C, sensitivity/specificity plots in appendix E and study evidence tables in appendix D.

Excluded studies

No studies were excluded from this review.

Summary of clinical studies included in the evidence review

Table 2 summarises the characteristics of the included studies

Table 2: Summary of included studies

Study	Design	Participants	Index Test	Reference standard	Outcomes
Lennon 2015	Systematic review of cross-sectional studies	117 teenagers or adults with cerebral palsy (ages ranged from 16 to 67 years), reported in 7 studies. All were ambulatory or self-propelled wheelchair users. GMFCS I (N=45), II (N=25), not reported (N=57) 3 studies (N=42) included only athletes. USA & Netherlands	Lab based aerobic capacity tests: • Bicycle ergometer • Wheelchair ergometer Field based aerobic capacity tests: • 6 minute walk test	Lab based maximal aerobic capacity tests measuring • VO_2 plateau • Heart rate • Respiratory exchange ratio	• Feasibility • Validity • Reliability
Lampe 2014	Cross-sectional study	46 adults with CP, age 22 to 59 years. GMFCS I (N=4), II (N=3), III (N=18) and IV (N=21). 16/46 had scoliosis.	• Lung vital capacity (using spirometer) • Chest expansion	Oxygen saturation (pulse oximeter)	• Sensitivity • Specificity

Study	Design	Participants	Index Test	Reference standard	Outcomes
		Germany			

CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; N: number of participants in study; USA: United States of America; VO_2, oxygen volume

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in

Table 3 and Table 4.

Table 3: Clinical evidence profile for diagnostic accuracy of reduced lung vital capacity (1 litre or more lower than normal) with spirometry for prediction of low oxygen saturation (<96%) in adults with cerebral palsy

Study	N	Risk of bias[1]	Inconsistency	Indirectness[3]	Imprecision[4]	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio[5]	Negative likelihood ratio[5]	Quality
1 observational study	46	Serious[2]	Not applicable	Very serious[7]	Very serious[8]	0.86 (0.42 to 1.00)	0.26 (0.12 to 0.45)	1.16	0.55	Very low

CI: confidence interval; N: number of participants in study
1 Risk of bias evaluated using risk of bias items of QUADAS-2 checklist
2 Unclear risk of bias in patient selection, index test and flow & timing.
3 Indirectness was evaluated using the applicability items of QUADAS-2
4 Judgement of imprecision was based on consideration of the 95% CIs of test sensitivity as this was considered to be the primary measure of interest as a false negative - missing patients with respiratory health problems, was considered more important than a false positive - indicating risks of respiratory health problems when there is none. Studies were considered to be of high sensitivity (and not imprecise) if the 95% CI was above 0.9 or of low sensitivity if it was below 0.75. Studies were assessed as subject to serious imprecision if the 95% CI crossed either 0.75 or 0.9, or subject to very serious imprecision if it crossed both 0.75 and 0.9
5 Positive and negative likelihood ratios calculated from sensitivity and specificity estimates
6 Unclear risk of review bias (lack of blinding in the interpretation both of the index test and reference standard – no details are given in the text) and patient selection; with flow and timing of participants and tests unclear
7 Measurement of oxygen saturation at a single point in the daytime is not a good predictor of early respiratory failure
8 95% CI for sensitivity crosses 0.75 and 0.90

Table 4: Clinimetric properties of bicycle ergometers, wheelchair ergometers and the 6 minute walk test to determine maximal aerobic capacity in adults with cerebral palsy

Test	Criterion validity[4]	Construct validity[5]	Test-retest reliability[6]	Measurement accuracy[7]	Test success rate[1]	Number of participants (studies)	Quality
Lab based maximal aerobic test: bicycle ergometer	Not applicable[3]	Good	Good	Good	64 to 100%	101 (4)	Very low[2]
Lab based sub-maximal aerobic test: bicycle ergometer	Good	Not reported	Not reported	Not reported	Not applicable (not a maximal test)	16 (1)	Very low[2]
Lab based maximal aerobic test:	Not applicable[3]	Not reported	Good	Not reported	100%	22 (3)	Very low[2]

Test	Criterion validity[4]	Construct validity[5]	Test-retest reliability[6]	Measurement accuracy[7]	Test success rate[1]	Number of participants (studies)	Quality
wheelchair ergometer							
Field based 6 minute walk test	Poor	Not reported	Not reported	Not reported	0%[1]	41 (1)	Very low[2]

CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; VO_2: oxygen volume
1 Percentage who reached the maximal aerobic effort criteria
2 Methodological quality was evaluated using the CASP systematic review checklist
3 Maximal laboratory based aerobic tests to determine VO_2max were considered the reference standard
4 Criteria used to confirm or predict maximal aerobic effort, rated good if correlation with reference standard was >0.7
5 Rated good if at least 75% of the test results were in accordance with the hypotheses (e.g. VO_2max is greater for those with GMFCS I compared to GMFCS II)
6 Rated good if correlation between test and re-test results was>0.7
7 Rated good when the minimally clinically important change was greater than the minimum detectable change

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

This question was not prioritised for economic modelling as the committee considered that it was unlikely that any recommendation made would place significant additional costs on NHS or PSS budgets.

Resource impact

No unit costs were presented to the committee as these were not prioritised for decision making purposes.

Evidence statements

Monitoring of respiratory health

No evidence was found about the impact of regular monitoring of respiratory health on outcomes in adults with cerebral palsy.

Lung vital capacity measured using spirometry

Critical outcomes

Respiratory health

No evidence was found for this outcome.

Overall survival

No evidence was found for this outcome.

Hospital admission

No evidence was found for this outcome.

Important outcomes

Secondary conditions

No evidence was found for this outcome.

Respiratory function

No evidence was found for this outcome.

Health related quality of life

No evidence was found for this outcome.

Satisfaction

No evidence was found for this outcome.

Diagnostic accuracy

- Very low quality evidence from one cross-sectional study in 46 adults with cerebral palsy indicates that lung vital capacity (measured using spirometry) is reduced in adults with cerebral palsy compared to people without cerebral palsy, particularly in those with higher GMFCS scores or scoliosis. Reduced lung vital capacity (of at least 1 litre below the predicted normal value), however, is not a good predictor of oxygen saturation with sensitivity of 86% and specificity of 26% for low oxygen saturation. The positive and negative likelihood ratios of 1.16 and 0.55 respectively suggest this test is not useful for ruling low oxygen saturation in or out.

Clinimetric properties

No evidence was found for this outcome.

Tests for maximal aerobic capacity

Critical outcomes

Respiratory health

No evidence was found for this outcome.

Overall survival

No evidence was found for this outcome.

Hospital admission

No evidence was found for this outcome.

Important outcomes

Secondary conditions (e.g. colds, asthma, sleep apnoea, daytime sleepiness)

No evidence was found for this outcome.

Respiratory function

No evidence was found for this outcome.

Health related quality of life

No evidence was found for this outcome.

Satisfaction

No evidence was found for this outcome.

Diagnostic accuracy

No evidence was found for this outcome.

Clinimetric properties

Very low quality evidence from one systematic review including 7 cohort studies in 117 teenagers or adults with cerebral palsy who were ambulatory or self-propelled wheelchair users indicates that lab-based maximal or sub-maximal bicycle and wheelchair ergometer tests are valid tests of aerobic fitness. The 6-minute walk test however is not a valid measure of maximal aerobic capacity.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The critical outcomes were respiratory health, overall survival and hospital admission because poor respiratory function can lead to life threatening illnesses requiring hospital admission. There was a lack of evidence about the impact of regular monitoring of

respiratory function on these critical outcomes so the committee instead considered evidence about the accuracy of tests for respiratory function with the assumption that early diagnosis and treatment of respiratory problems should improve overall health. Important outcomes were secondary conditions (such as colds), respiratory function, health related quality of life and satisfaction

The quality of the evidence

For outcomes from one study a GRADE approach was used that was modified for diagnostic accuracy measures. Outcomes for the other study could only be assessed using the CASP quality checklist. Evidence for all outcomes was rated as very low quality. The included study measured oxygen saturation measured at a single point during the day and the committee agreed this would be less informative about early respiratory failure than a nocturnal monitoring protocol.

The committee considered that evidence about maximal aerobic capacity tests was not relevant to the general population of adults with cerebral palsy, because such tests would be typically used for monitoring the cardiorespiratory fitness of athletes as part of their training programme.

Due to the limitations of the evidence the committee based their recommendations on their expertise and experience.

Benefits and harms

The committee based on their experience and knowledge, agreed that there is a lack of awareness about some of the signs and symptoms that may indicate respiratory impairment. They therefore wanted to describe some of the presentations associated with respiratory impairment to improve recognition and identification of the condition. Timely assessment would also ensure prompt discussion about treatment options.

The committee agreed, based on their experience that respiratory impairment coupled with certain comorbidities could result in respiratory complications. The committee agreed that a referral for a full respiratory assessment was likely to be beneficial in this group as it would afford the chance to prevent or treat respiratory complications. This would also lead to effective management and prevention of further complications. The committee recognised that this recommendation may lead to an increase in the number of referrals, but the resource impact will be balanced by reduced number of complications.

There was also some evidence that oxygen saturation and lung vital capacity measured using spirometry were reduced in those with GMFCS IV to V or with kyphoscoliosis. However, they could not make a strong recommendation for this because the evidence was very limited and of poor quality.

Due to the lack of evidence, the committee made a research recommendation on the methods of detection and management of respiratory impairment in adults with cerebral palsy in the community. Based on their experience, the committee were aware that adults with cerebral palsy are at increased risk of respiratory problems particularly people with some pre-existing respiratory conditions and those with high Gross Motor Function Classification System (GMFCS) and are at a high risk of serious adverse effects. Early detection of respiratory impairment, management and appropriate referral for specialist assessment would enable prevention or treatment of respiratory complications in this high-risk group.

Cost effectiveness and resource use

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

The committee acknowledge that the recommendations would lead to an increase in referrals to a limited number of respiratory specialists with experience in adults with cerebral palsy potentially increasing waiting times or diverting the resource from elsewhere. However, improved outcomes, especially in regards to respiration will lead to a significant increase in quality of life. Some additional resource use will be recouped though a decrease in hospital admissions especially expensive unplanned admissions.

References

Lampe 2014

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

Lennon 2015

Lennon, N., Thorpe, D., Balemans, A. C., Fragala-Pinkham, M., O'Neil, M., Bjornson, K., Boyd, R., Dallmeijer, A. J., The clinimetric properties of aerobic and anaerobic fitness measures in adults with cerebral palsy: A systematic review of the literature, Research in Developmental Disabilities, 45-46, 316-28, 2015

Appendices

Appendix A – Review protocols

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

Table 5: Review protocol for monitoring respiratory health in adults with cerebral palsy

Field (based on PRISMA-P)	Content
Review question	What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?
Type of review question	Intervention (test & treat) / diagnostic test accuracy
Objective of the review	The aim of this review is to assess the impact of formal monitoring protocols on respiratory health outcomes.
Eligibility criteria – population/disease/condition/issue/domain	Adults aged 25 and over with cerebral palsy
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	Protocol for monitoring respiratory health defined by: • Setting (residential, primary care, secondary care) • Tests used (e.g. assessment of vital capacity, sleep disordered breathing, assessment of fatigue, cough peak flow, aspiration risk, infections, oxygen saturation) • Who carries out the monitoring (e.g. GP, specialist) • Frequency of monitoring
Eligibility criteria – comparator(s)/control or reference (gold) standard	Any other monitoring protocol No formal monitoring
Outcomes and prioritisation	Critical outcomes • Respiratory health • Overall survival • Hospital admission Important outcomes

Field (based on PRISMA-P)	Content
	• Secondary conditions (e.g. colds, asthma, sleep apnoea, Daytime sleepiness (Epworth Scale), etc.) • Respiratory function • Health related quality of life • Satisfaction Minimally important differences • Any statistically significant improvement in overall survival will be considered clinically important • 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] • Published MIDs for respiratory function used in COPD: FEV1 100ml, dyspnoea TDI score 1 unit, heath status SGRQ score 4 units. The thresholds for clinical usefulness of tests: Sensitivity and specificity (sensitivity will be prioritised): • High >90% • Moderate 75-90% • Low <75% Positive likelihood ratio: • Very useful test >10 • Moderately useful test 5-10 • Not a useful test <5 Negative likelihood ratio: • Very useful test <0.1 • Moderately useful test 0.1 to 0.2 • Not a useful test>0.2

Field (based on PRISMA-P)	Content
	Reliability, validity, or internal consistency • Poor < 0.4 • Moderate reliability ≥0.4 to 0.6 • Good >0.6 to 0.8 • Excellent > 0.8
Eligibility criteria – study design	This review will look for so-called "test and treat" studies - because an effective monitoring protocol will lead to treatment or management changes that should improve clinical outcomes. Only published full text papers – • Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) Consider conference abstract only if related to RCTs In the absence of test and treat studies diagnostic accuracy studies (cohort studies) will be reviewed – and the committee will consider the likely consequences of the true positives, false positives etc. of respiratory health monitoring on clinical outcomes.
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: • Population subgroups: ○ Level of functional disability

Field (based on PRISMA-P)	Content
	○ Physical issues which may impact respiratory condition (scoliosis, kyphosis, barrel chest etc.) ○ Feeding or swallowing problems ○ Learning disabilities • Intervention subgroups: ○ Setting (residential versus others) ○ Which tests or assessment were used ○ Who carried out the tests and assessments ○ Frequency of assessments Physical issues and level of functional disability will be also considered important confounders which ideally should be adjusted for in any included comparative observational studies.
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, and for data extraction Diagnostic analysis was done using Cochrane Review Manager (RevMan5).
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	This is 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.

Field (based on PRISMA-P)	Content
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).
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).
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/ Please document any deviations/alternative approach when GRADE isn't used or if a modified GRADE approach has been used for non-intervention or non-comparative studies.
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.
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 NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and

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

COPD: Chronic obstructive pulmonary disease; FEV: Forced expiratory volume; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MID: minimally important difference; 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; SGRQ: St. George's respiratory questionnaire; TDI: Transition dyspnoea index;

Appendix B – Literature search strategies

Literature search strategies for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

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 6: Last searched on 22 March 2018

#	Searches
1	exp Cerebral Palsy/ use prmz
2	exp cerebral palsy/ use oemezd
3	((cerebral or brain or central) adj2 (pal* or paralys#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 oemezd [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 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

#	Searches
	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 scoliosis/ or exp amoxicillin/ or exp penicillin derivative/ or exp doxycycline/ or exp clarithromycin/
17	16 use oemezd
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 nasogastic 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

#	Searches
	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 vapori?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 oemezd
22	letter.pt. or LETTER/ use oemezd
23	Letter/ use prmz
24	EDITORIAL/ use prmz
25	editorial.pt. use oemezd
26	NEWS/ use prmz
27	exp HISTORICAL ARTICLE/ use prmz
28	note.pt. use oemezd
29	ANECDOTES AS TOPIC/ use prmz
30	COMMENT/ use prmz
31	CASE REPORT/ use prmz
32	CASE REPORT/ use oemezd
33	CASE STUDY/ use oemezd
34	(letter or comment* or abstracts).ti.
35	or/21-34
36	RANDOMIZED CONTROLLED TRIAL/ use prmz
37	RANDOMIZED CONTROLLED TRIAL/ use oemezd
38	random*.ti,ab.
39	or/36-38
40	35 not 39
41	ANIMALS/ not HUMANS/ use prmz
42	ANIMAL/ not HUMAN/ use oemezd
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 oemezd
48	exp ANIMAL EXPERIMENT/ use oemezd
49	exp EXPERIMENTAL ANIMAL/ use oemezd
50	ANIMAL MODEL/ use oemezd
51	exp RODENT/ use oemezd
52	(rat or rats or mouse or mice).ti.

#	Searches
53	or/40-52
54	20 not 53

Database: Cochrane Library

Table 7: 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 paralys?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
#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

ID	Search
#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
#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

ID	Search
#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 obstruct* or mouth* or nose* or nasal or intranasal or nasogastic 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 vapori?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

ID	Search
#107	{or #6-#106}
#108	#5 and #107

Database: Web of Science

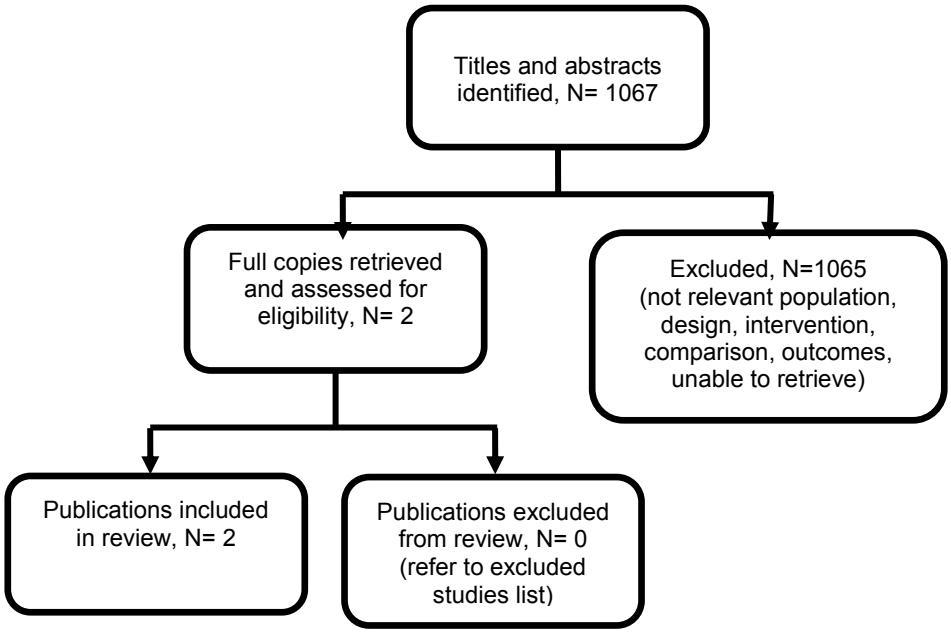
Table 8: Last searched on 22 March 2018

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

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



Appendix D – Clinical evidence tables

Clinical evidence tables for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

Table 9: Studies included in monitoring respiratory health in adults with cerebral palsy

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
Authors Lampe, R., Blumenstein, T., Turova, V., Alves-Pinto, A. **Year of publication** 2014 **Country of publication** Germany **Ref Id** 347233 **Consecutive recruitment** Not reported	**Cohort population** Adults with cerebral palsy (CP) were recruited from a general rehabilitation and training program at a centre for persons with CP. **Inclusion Criteria** Not reported. **Exclusion Criteria** Not reported **Demographics - Total** 46 **Cases** 8 (with OS < 96%) **Statistical method** Vital capacity (VC) was measured with with a spirometer (MiniSpir ®) from MIR (Medical International Research Srl, Rome, Italy). The spirometer was connected to a computer which recorded the measurements. Each participant was asked to completely enclose	**Reference Test** A pulse oximeter (PO80; Beurer GmbH, Ulm, Germany) clamped to the tip of the finger was used to measure the heart rate and OS in the blood. Readings were taken directly from the device or recorded on a computer via a USB connection. Recordings were made over a period of 5 minutes at a sampling rate of 1 Hz. The average value over the measurement period was calculated.	**Raw Data** See table 1 in Lampe (2014)	Using deviation from normal vital capacity (DVC) thresholds to predict abnormally low oxygen saturation (<96%). Calculated from Table 1 in Lampe (2014)[1] **DVC, TP, FP, FN, TN, Sn [95%CI], Sp [95%CI],** -2.0, 7, 31, 0, 0,1.00 [0.59, 1.00], 0.00 [0.00, 0.11] -0.5, 7, 30, 0, 4,1.00 [0.59, 1.00],0.12 [0.03, 0.27] 0.0, 7,28,0,3,1.00 [0.59, 1.00], 0.10 [0.02, 0.26] 0.2, 7,27, 0,4,1.00 [0.59, 1.00], 0.13 [0.04, 0.30] 1.0, 6,23,1,8, 0.86 [0.42, 1.00],0.26 [0.12, 0.45] 1.5,5,16,2,15,0.71 [0.29, 0.96],0.48 [0.30, 0.67] 2.0,3,14,4,17,0.43 [0.10, 0.82],0.55 [0.36, 0.73] 2.5,2,4,5,27,0.29 [0.04, 0.71],0.87 [0.70, 0.96] 3.0,0,1,7,30,0.00 [0.00, 0.41],0.97 [0.83, 1.00] 4.0,0,0,7,31,0.00 [0.00, 0.41],1.00 [0.89, 1.00] There was a significant positive correlation between lung vital capacity and chest expansion (P<0.05). But there was no statistically significant correlation between lung vital capacity and oxygen	**Funding** Not reported (authors report no conflicts of interest). **Quality Items** QUADAS 2 checklist Patient selection Risk of bias: Was a consecutive or random sample of patients enrolled? Unclear Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Unclear Could the selection of participants have introduced bias? Unclear

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
	the turbine with his or her mouth, to inhale up to his or her maximum capacity, and then to exhale with the maximum force possible. Some people could not enclose the turbine completely with their mouths. In these cases, a mouthpiece made of rubber was used. The VC was the difference in the volume between maximal inhalation and maximum exhalation. The measurement was repeated four to five times, and the maximum value used. Chest expansion (CE) was measured with a measuring tape at maximum inspiration and expiration, and during normal breathing. The tape was slightly below the mammillary line. CE was calculated as the difference, in cm, between the perimeter of the chest at maximum inspiration and that at full expiration. The normal values of VC were calculated using the following formulas: VC (male, in l) = 10 -3 × (27.63 - (0.112× age)) × height (cm)			saturation, or between chest expansion and oxygen saturation. As GMFCS level increased the mean lung vital capacity and the chest expansion decreased. Oxygen saturation was typically within the normal range, in spite of reduced lung vital capacity and chest expansion. Although scoliosis was associated with an additional decrease in lung vital capacity, this did not affect blood oxygen supply. So although there was decreased chest expansion and the significantly reduced lung volume in these adults with cerebral palsy, there appeared to be sufficient oxygen supply.	Applicability: Is there concern that the included participants do not match the review question? Unclear Index tests Risk of bias: Were the index tests interpreted without knowledge of the reference standard? Unclear If a threshold was used, was it pre-specified? Not applicable (thresholds were applied by the reviewer) Could the conduct or interpretation of the index test have introduced bias? Unclear Applicability: Is there concern that the index test, its conduct or interpretation differ

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
	VC (female, in l) = 10 -3 × (21.78 - (0.101× age)) × height (cm) This was used to calculate the deviation of VC from the normal value (DVC) **Diagnostic criteria** Normal oxygen saturation (OS) was defined as 96% to 100%.				from the review question? Unclear Reference standard Risk of bias: Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Yes Could the reference standard, its conduct or interpretation have introduced bias? No Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question? No Flow and timing Risk of bias: Was there an appropriate interval

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
					between index tests and reference standard? Not reported Did all participants receive a reference standard? Yes Did participants receive the same reference standard? Yes Were all patients included in the analysis? Yes (some tests were not possible - but these are accounted for) Could the participant flow have introduced bias? No **OVERALL ASSESSMENT:** Very low quality
Authors Lennon, N., Thorpe, D., Balemans, A. C., Fragala-	**Cohort population** 117 teenagers or adults with cerebral palsy (ages ranged from 16 to 67), reported in 7 studies.	**Reference Test** Aerobic capacity: • VO2 plateau • Heart rate		**Results** **Bicycle ergometer** 4 studies (N=101), age (16 to 67), criterion validity not applicable, construct	Funding Grant (Fit Active Habits) from the American Academy of Cerebral Palsy

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
Pinkham, M., O'Neil, M., Bjornson, K., Boyd, R., Dallmeijer, A. J. **Year of publication** 2015 **Country of publication** USA / Netherlands Ref Id 545935 **Consecutive recruitment** Not applicable **Sub-type** Systematic review	All were ambulatory or wheelchair users. GMFCS I (N=45), II (N=25), not reported (N=57) 3 studies (N=42) included only athletes. **Inclusion Criteria** Studies were included if they met the following criteria: • evaluated clinimetric properties of lab or field-based aerobic or anaerobic fitness capacity measures • had a study population who had a diagnosis of CP, • were specific to adolescents (14–18 yrs) and/or adults (>18 yrs) - at least 75% of included participants had to meet the age criteria • published as full reports. **Exclusion Criteria** Studies were excluded if: • they were not published in English, • maximal aerobic exercise test protocols were not	• Respiratory exchange ratio		validity moderate, test-retest reliability moderate, measurement error moderate **Wheelchair ergometer** 3 studies (N=22), age (18 to 33), criterion validity not applicable, construct validity unknown, test-retest reliability limited, measurement error unknown **6 minute walk test** 1 study (N=41), age (16 to 24), criterion validity strong, construct validity not reported, test-retest reliability not applicable, measurement error not applicable	and Developmental Medicine (AACPDM). Quality Items CASP systematic review checklist: Did the review address a clearly focused question? Yes Did the review include the right type of study? Unclear (the included studies do not report clinical outcomes) Did the reviewers try to identify all relevant studies? Yes Did the reviewers do enough to assess the quality of the included studies? Yes If the results of the studies have been combined, was it reasonable to do so? Yes (results

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
	incremental or only measured ability/activity/efficiency, • they used self-report measures • they were review articles, single case studies, or commentaries. **Demographics - Total** 117 **Cases** Not applicable **Statistical method** The overall level of evidence for aerobic fitness tests was derived by combining the results of the methodological quality ranking for the studies with the statistical findings for each clinimetric property (validity & reliability). The Cochrane Back Review Group levels of evidence were used (van Tulder et al., 1997). • strong (consistent findings in multiple studies of good methodological quality or in one study of excellent methodological quality) • moderate (consistent findings in multiple studies of fair methodological quality or in				have been combined for similar tests) How are the results presented and what is the main result? (see results section) How precise are these results? Unclear (there is no pooled effect estimate) Can the results be applied to the local population? Unclear (all ambulatory or self-propelled wheelchair users, high proportion were athletes) Are the benefits worth the harms and costs? Unclear (clinical outcomes not reported) Overall this systematic review provides only indirect evidence about the impact of respiratory

Bibliographic details	Number of Participant & Participant Characteristics	Test/Outcome characteristics	Outcome measures to be used	Results	Reviewer comment
	one study of good methodological quality) • limited (one study of fair methodological quality); • conflicting (conflicting findings); • Unknown (only studies of poor methodological quality). **Diagnostic criteria** Lab based aerobic capacity tests: • Bicycle ergometer • Wheelchair ergometer Field based aerobic capacity tests: • 6 minute walk test				monitoring on patient outcomes - (very low quality) Other information – methodological quality of the individual studies in this review was appraised by the review authors using the COSMIN checklist.

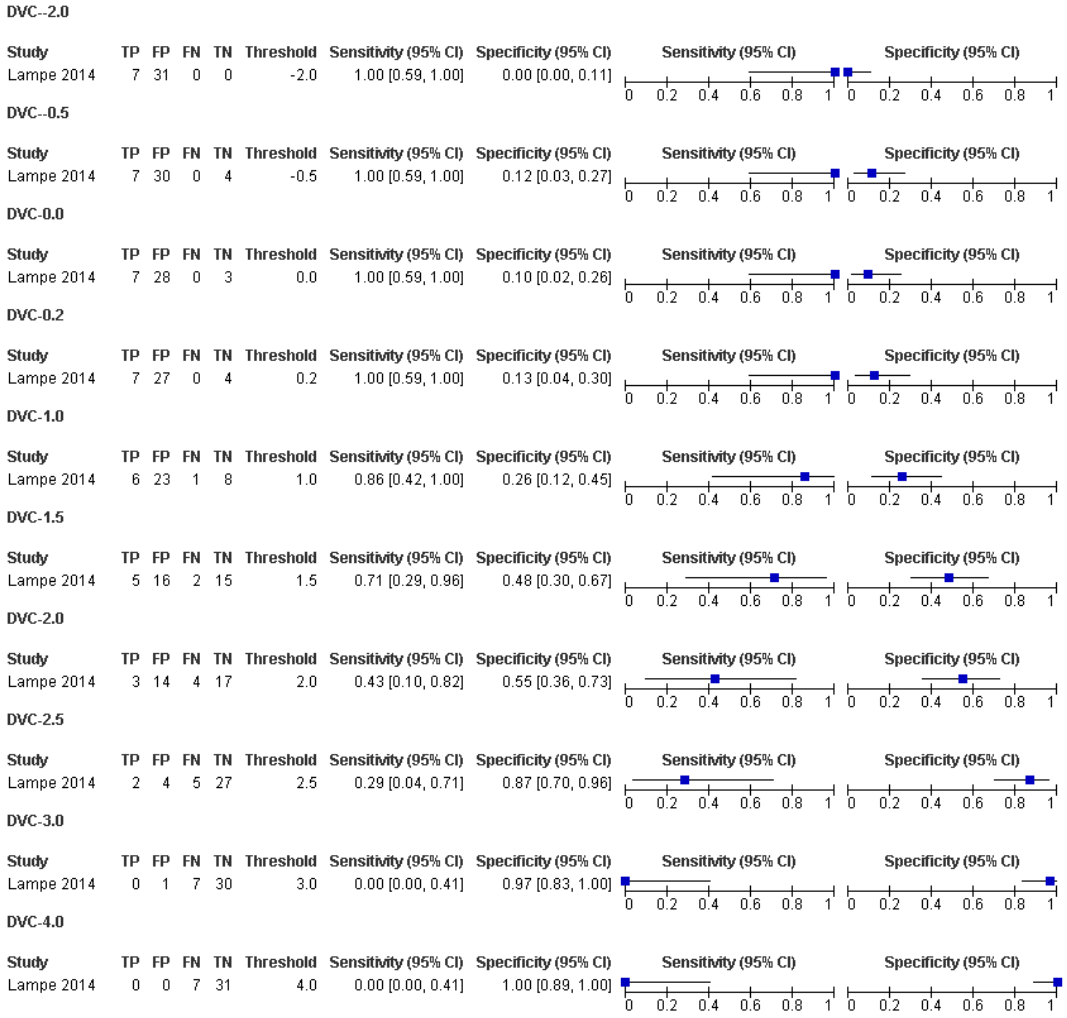
AACPDM: American Academy of Cerebral Palsy and Developmental Medicine; CASP: Critical appraisal skills programme; CE: chest expansion; COSMIN: Consensus-based Standards for the Selection of Health Status Measurement Instruments; CP: cerebral palsy; DVC: Direct vital capacity; GMFCS: Gross motor function classification system; MIR: Medical International Research; NGA: National Guidelines Alliance; OS: Oxygen saturation; QUADAS: Quality Assessment of Diagnostic Accuracy Studies VC: Vital capacity
1. Calculated by the NGA team

Appendix E – Forest plots

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

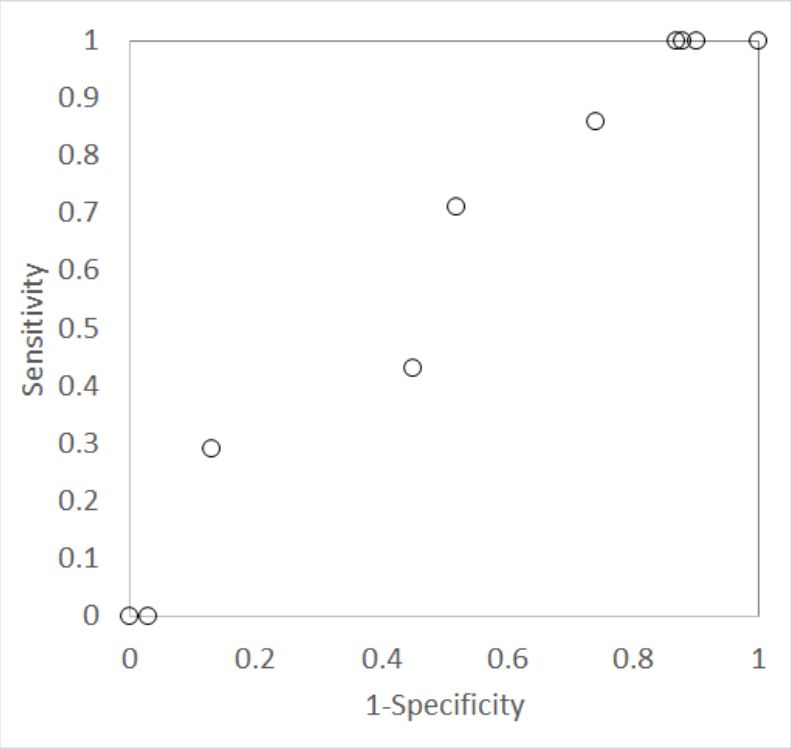
Lung vital capacity measured with spirometry

Figure 2: Diagnostic accuracy of different thresholds for reduced lung vital capacity (measured with spirometry) for prediction of low oxygen saturation (<96%) in adults with cerebral palsy



CI: confidence interval; DVC: deviation of lung capacity (below normal value in litres); FN: false negative; FP: false positive; TN: true negative; TP: true positive

Figure 3: ROC curve of deviation of lung vital capacity from normal to predict low oxygen saturation (<96%) in adults with cerebral palsy



ROC: receiver operating characteristic

Appendix F – GRADE tables

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

Table 10: Clinical evidence profile for diagnostic accuracy of reduced lung vital capacity (1 litre or more lower than normal) with spirometry for prediction of low oxygen saturation (<96%) in adults with cerebral palsy

Study	N	Risk of bias[1]	Inconsistency	Indirectness[3]	Imprecision[4]	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio[5]	Negative likelihood ratio[5]	Quality
1 observational study	46	Serious[2]	Not applicable	Very serious[7]	Very serious[8]	0.86 (0.42 to 1.00)	0.26 (0.12 to 0.45)	1.16	0.55	VERY LOW

CI: confidence interval; N: number of participants in study
1 Risk of bias evaluated using risk of bias items of QUADAS-2 checklist
2 Unclear risk of bias in patient selection, index test and flow & timing.
3 Indirectness was evaluated using the applicability items of QUADAS-2
4 Judgement of imprecision was based on consideration of the 95% CIs of test sensitivity as this was considered to be the primary measure of interest as a false negative - missing patients with respiratory health problems, was considered more important than a false positive - indicating risks of respiratory health problems when there is none. Studies were considered to be of high sensitivity (and not imprecise) if the 95% CI was above 0.9 or of low sensitivity if it was below 0.75. Studies were assessed as subject to serious imprecision if the 95% CI crossed either 0.75 or 0.9, or subject to very serious imprecision if it crossed both 0.75 and 0.9
5 Positive and negative likelihood ratios calculated from sensitivity and specificity estimates
6 Unclear risk of review bias (lack of blinding in the interpretation both of the index test and reference standard – no details are given in the text) and patient selection; with flow and timing of participants and tests unclear
7 Measurement of oxygen saturation at a single point in the daytime is not a good predictor of early respiratory failure
8 95% CI for sensitivity crosses 0.75 and 0.90

Appendix G – Economic evidence study selection

Economic evidence study selection for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

No economic evidence was identified for this review.

Appendix H – Economic evidence tables

Economic evidence tables for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

No economic evidence was identified for this review.

Appendix I – Health economic evidence profiles

Health economic evidence profiles for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

No economic evidence was identified for this review.

Appendix J – Health economic analysis

Health economic analysis for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

No economic analysis was included in this review.

Appendix K – Excluded studies

Clinical and economic lists of excluded studies for review question C1: What is the most effective protocol for monitoring respiratory health in adults with cerebral palsy?

Clinical studies

No studies were excluded from this review.

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

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

Can detection and management of respiratory disorder in adults with cerebral palsy be improved in primary and community care?

Table 11: Research recommendation rationale

Research question	Can detection and management of respiratory disorder in adults with cerebral palsy be improved in primary and community care?
Importance to 'patients' or the population	Improved detection of respiratory impairment Reduce risk of respiratory failure Reduce respiratory symptom burden Reduce hospital admissions Reduce acute antibiotic prescriptions Improve quality of life
Relevance to NICE guidance	Improve future clinical guidelines for monitoring respiratory health in adults with cerebral palsy
Relevance to the NHS	Improve early detection of respiratory impairment Improve management of risk factors causing respiratory impairment Reduce risk of developing respiratory failure and complications Reduced costs related to respiratory failure
National priorities	Reduce variation in treatment
Current evidence base	Current evidence was not clear on respiratory assessment in primary care
Equality	Applies to all adults with cerebral palsy particularly those with underlying risk factors

Table 12: Research recommendation modified PICO table

Criterion	Explanation
Population	Adults (16 or over) with cerebral palsy who are at risk of respiratory complications due to underlying comorbidity such as kyphoscoliosis.
Intervention	Annual respiratory assessment followed by management if necessary
Comparator	Usual care
Outcome	• Accuracy of tests for respiratory function • Hospital admission • Overall survival • Patient satisfaction • Respiratory health
Study design	Multicentre test and treat randomised controlled trial
Timeframe	5 years
Additional information	Need to stratify by: Severity of cerebral palsy according to the Gross Motor Function Classification System (GMFCS Pre-existing co-morbidities (scoliosis, asthma, etc.)