National Institute for Health and Care Excellence

Final

Cerebral palsy in adults

[C3] Identifying and managing respiratory disorders associated with cerebral palsy: prophylactic treatments

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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Prophylactic treatments for respiratory infections

Review question

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

Introduction

Prophylactic or preventative treatments such as posture management, respiratory physiotherapy, cough assist devices, non-invasive ventilation; as well as background medications for gastro-oesophageal reflux, mucolytics and antibiotics can be used to prevent respiratory infections. This question looks at the evidence and cost-effectiveness of these interventions in adults with cerebral palsy.

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 with cerebral palsy, aged 25 and over
Intervention	Any combination of: • Prophylactic antibiotics • Influenza vaccination • Pneumococcal vaccination • Cough assist or stimulation • Breathing exercises • Positioning • Chest physiotherapy • Promotion of safe feeding / eating
Comparison	• Any other combination of prophylactic treatment • No prophylactic treatment
Outcome	**Critical** • Respiratory infections • Hospital admission • Overall survival **Important** • Health related quality of life • Satisfaction

For full details see the 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 not included in this review with reasons for their exclusions 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

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

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Since this question was about prevention of respiratory infections, respiratory infections, hospital admissions and overall survival were the critical outcomes. Other outcomes considered important by the committee were health related quality of life and satisfaction.

The quality of the evidence

No evidence was identified for this review.

Benefits and harms

The committee discussed the government recommendations in the Green book vaccinations. For example it is recommended that people with pre-existing conditions, such as neurological conditions (which would include cerebral palsy) should be offered a flu vaccination. The committee therefore made a strong recommendation that the immunisation programme should be followed to prevent adults with cerebral palsy getting infections that could affect respiratory functions.

Based on their clinical experience and expertise, the committee discussed that prophylactic antibiotics are not helpful in preventing respiratory infections in adults with cerebral palsy. They may also lead to gastrointestinal and cardiac side effects. The committee agreed that the role of antibiotics is limited for prophylaxis of respiratory infections in adults with cerebral palsy. Taking into account potential adverse effects and the antibiotic resistance, the committee agreed that antibiotic prophylaxis should only be used in people at high risk of infection when it is advised by the respiratory specialist. For example, this might be in people with recurrent chest infections and bacterial colonisation identified on sputum culture. The aim in these cases would be to reduce acute antibiotic use and limit symptom burden.

The committee discussed, based on their experience and expertise, that a chest physiotherapy review, including postural management and exercise will be helpful in preventing respiratory infections, in those at high risk. The committee noted that physiotherapists would usually have chest care training which would provide them with the skills to be able to carry out an assessment and suggest treatments. The committee also noted that the effective implementation of these measures will require families and carers to have understanding regarding training and care. Hence, they must be advised on these aspects.

Based on their expertise and experience, the committee agreed that saliva management will benefit in preventing respiratory infections. The committee discussed that adults with cerebral palsy and recurrent chest infections should be referred to a dysphagia-trained speech and language therapist who would be best suited to assess swallowing and saliva control in those with respiratory difficulties. Timely assessment will then help to put into place preventative action against respiratory infections.

Due to the lack of evidence the committee decided to make a research recommendation on the effectiveness of prophylactic antibiotic in the management of respiratory symptoms. The committee agreed that this is important because some individuals with cerebral palsy experience significant respiratory symptomatology as a consequence either of sputum retention and or recurrent respiratory infection, possibly related to aspiration. A smaller proportion of individuals experience chronic pulmonary bacterial colonisation with increased respiratory symptom burden and recurrent infective episodes. No current high quality evidence exists to determine the effectiveness of prophylactic antibiotics in the management

of such patients. Research is recommended to establish the role of prophylactic antibiotics in those with, and without, persistent bacterial airway colonisation with a view to improving quality of life, patient experience and hospital stay.

Cost effectiveness and resource use

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

The recommendation around flu and pneumococcal vaccination reinforces current best practise and is unlikely to have any impact upon resource use.

The recommendations on prophylactic antibiotic use again reinforces best practice. The committee considered that there may be centres in England where antibiotics are given unnecessarily and that the recommendations would lead to a reduction in their use and cost savings.

There will be an increase in resource use, through increased referrals, associated with the recommendations for referral to chest physiotherapy and speech and language therapists although the committee considered that this was likely to be small. Improved outcomes would also likely lead to a reduction in expensive unplanned admissions to hospital.

References

No studies were included in this review.

Appendices

Appendix A – Review protocols

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

Table 2: Review protocol for prophylactic treatments for respiratory disorders

Field (based on PRISMA-P)	Content
Review question	Are prophylactic treatments (for example, antibiotics, chest physiotherapy, cough assistance) effective in preventing respiratory infections in adults with cerebral palsy?
Type of review question	Intervention
Objective of the review	The aim of this review is to compare the effectiveness of prophylactic treatments (for example, antibiotics, chest physiotherapy, cough assistance) in preventing respiratory infections in adults with cerebral palsy.
Eligibility criteria – population/disease/condition/issue/domain	Adults with cerebral palsy, aged 25 and over.
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	Any combination of: • Prophylactic antibiotics • Influenza vaccination • Pneumococcal vaccination • Cough assist or stimulation • Breathing exercises • Positioning • Chest physiotherapy • Promotion of safe feeding / eating
Eligibility criteria – comparator(s)/control or reference (gold) standard	• Any other combination of prophylactic treatment • No prophylactic treatment

Field (based on PRISMA-P)	Content
Outcomes and prioritisation	**Critical outcomes** • Respiratory infections • Hospital admission • Overall survival **Important outcomes** • Health related quality of life • Satisfaction Minimally important differences • Dichotomous outcomes will use default MIDs [RR thresholds of 0.80 and 1.2] • Continuous outcomes will use default MIDs [0.5 times the SD of the control group]
Eligibility criteria – study design	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
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
	  ○ Physical issues which may impact respiratory condition (scoliosis, kyphosis, barrel chest etc.)
	  ○ Feeding or swallowing problems
	  ○ Learning difficulties
	• Intervention subgroups:
	  ○ None

Field (based on PRISMA-P)	Content
	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.
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).
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/
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.

Field (based on PRISMA-P)	Content
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.
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 National Guideline Alliance 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	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The 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

GRADE: Grading of Recommendations Assessment, Development and Evaluation; NGA: National Guideline Alliance; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial;

Appendix B – Literature search strategies

Literature search strategies for review question C3: Are prophylactic treatments (for example, antibiotics, chest physiotherapy, cough assistance) effective in preventing respiratory infections 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 3: 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 Ventilators, Mechanical/ or exp Ventilators, Negative-Pressure/ or exp Pulmonary Edema/ or exp Oxygen

#	Searches
	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

#	Searches
	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).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 4: 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
#37	MeSH descriptor: [Pulmonary Ventilation] explode all trees
#38	MeSH descriptor: [Pulmonary Ventilation] explode all trees

ID	Search
#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
#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

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

Database: Web of Science

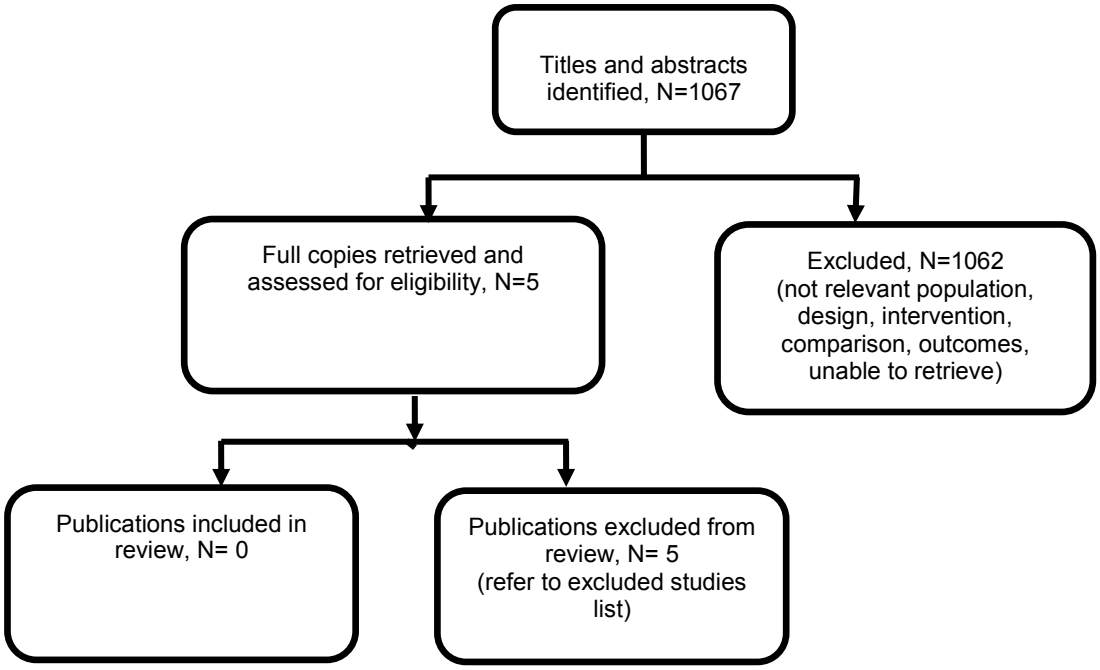
Table 5: Last searched on 22 March 2018

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

No clinical studies were identified for this review.

Appendix E – Forest plots

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

No forest plots were included in this review.

Appendix F – GRADE tables

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

No GRADE tables were included in this review.

Appendix G – Economic evidence study selection

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

No economic evidence was identified for this review.

Appendix H – Economic evidence tables

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

No economic evidence was identified for this review.

Appendix J – Health economic analysis

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

No economic analysis was included in this review.

Appendix K – Excluded studies

Clinical and economic list of excluded studies for review question C3: Are prophylactic treatments (for example, antibiotics, chest physiotherapy, cough assistance) effective in preventing respiratory infections in adults with cerebral palsy?

Clinical studies

Table 6: Excluded clinical studies for prophylactic treatments for respiratory disorders

Excluded studies – C3: Are prophylactic treatments (for example, antibiotics, chest physiotherapy, cough assistance) effective in preventing respiratory infections in adults with cerebral palsy?	
Study	**Reason for Exclusion**
Michaels, M. B., Crytzer, T. M., Commentary on "Effects of Positioning on Respiratory Measures in Individuals With Cerebral Palsy and Severe Scoliosis", Pediatric Physical Therapy, 23, 170-170, 2011	This article is a commentary on a research regarding effect of positioning on respiratory measures. The original research article was also reviewed, but, no outcomes of interest were reported.
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	Exclusion on population and outcomes. Does not report outcomes of interest and does not report on population with cerebral palsy.
Sleigh, G, Brocklehurst, P, Gastrostomy feeding in cerebral palsy: a systematic review (Provisional abstract), Archives of Disease in Childhood, 89, 534-539, 2004	Exclusion by population: This review is for children/paediatric age group.
Torres-Castro, R., Vilaro, J., Vera-Uribe, R., Monge, G., Aviles, P., Suranyi, C., Use of air stacking and abdominal compression for cough assistance in people with complete tetraplegia, Spinal Cord, 52, 354-7, 2014	Mostly patients with spinal cord injury. Outcomes of interest not reported.
Toussaint, M., Boitano, L. J., Gathot, V., Steens, M., Soudon, P., Limits of effective cough-augmentation techniques in patients with neuromuscular disease, Respiratory CareRespir Care, 54, 359-66, 2009	Outcomes of interest not reported

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

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

Are prophylactic antibiotics effective and cost-effective in the management of respiratory symptoms in adults with cerebral palsy with significant respiratory comorbidity?

Table 7: Research recommendation rationale

Research question	Are prophylactic antibiotics effective and cost-effective in the management of respiratory symptoms in adults with cerebral palsy with significant respiratory comorbidity?
Importance to 'patients' or the population	Reduce respiratory symptom burden Reduce hospital admissions Reduce acute antibiotic prescriptions Improve quality of life Monitor for side effects including the development of resistant organisms within airway secretions
Relevance to NICE guidance	Ability to make appropriate, evidenced based, recommendations in future guidance
Relevance to the NHS	Reduce costs related to hospital admissions Reduce costs of acute deteriorations including increased home care, acute antibiotic utilisation and reductions in social interactions due to acute illness
National priorities	Reduce variation in treatment Achieving best possible clinical outcomes, possibly including extending both quality and length of life Limiting overall antibiotic utilisation and reducing development of resistant bacterial strains (good antibiotic husbandry)
Current evidence base	Current evidence was not clear and was graded as very low quality. Evidence was often not patient group specific.
Equality	Applies to all patients with cerebral palsy but especially those with significant and clinically relevant respiratory morbidity

Table 8: Research recommendation modified PICO table

Criterion	Explanation
Population	Adults (18 or over) with cerebral palsy with significant respiratory comorbidity (recurrent infections, persistent bacterial colonisation)
Intervention	Prophylactic antibiotics
Comparator	No intervention Cyclical antibiotics (based on sputum sensitivities) Cyclical antibiotics (broad spectrum) Continuous single agent antibiotics
Outcome	Reduced symptom burden Improved quality of life (HRQoL) Reduced acute antibiotic utilisation Reduced hospital admission Patient satisfaction Overall survival Treatment-related morbidity

Criterion	Explanation
	Cost Rate of antibiotic resistance
Study design	Multicentre large observational cohort study
Timeframe	5 years
Additional information	Need to stratify by: Type of patient (GMFCS level) Additional treatments (ventilation)

HRQoL: health-related quality of life; GMFCS: Gross motor function classification system.