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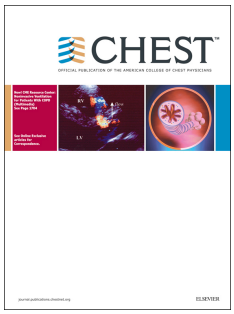

What has been researched in childhood obstructive sleep-disordered breathing: a systematic review

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What has been researched in childhood obstructive sleep-disordered breathing: a systematic review

Short title: Review of childhood sleep-disordered breathing

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Summary conflict of interest statement

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Abbreviation list:

oSDB, obstructive sleep-disordered breathing;

OSA, obstructive sleep apnoea;

AAP, American Academy of Pediatrics;

ENT, ear-, nose- and throat;

RCT, randomised controlled trial;

PSG, polysomnography.

Abstract

Background: Despite recent clinical guideline development, the best pathway of care for children with symptoms of obstructive sleep-disordered breathing (oSDB) is still debated. This systematic review aims to map research in childhood oSDB conducted so far, to support further guideline development, identify evidence gaps and guide future research.

Methods: Systematic search of PubMed, Embase, and Cochrane Library from inception to 26 November 2015. All publications on childhood oSDB were included, irrespective of type and language. The annual number of publications in the field of oSDB was counted over all years; for those published since 1 January 2011 (i.e. date of latest literature search of American Academy of Pediatrics guideline), total and annual numbers of publications across main research themes and methodologies were calculated.

Results: Of the 7637 unique records retrieved, 5871 publications were eligible for inclusion. There is an increase in annual publications since 2000, with 46% published since 2011. Most (61%) publications focused on individual treatment modalities, incidence or prognosis. Few (2.7%) publications focused on health service delivery, outcomes and health economics. 78.5% of publications were observational, 2.4% were randomised controlled trials and 0.4% used a qualitative approach as their main methodology.

Conclusions: A recent surge in research activity in childhood oSDB has improved the knowledge base for this condition; the lack of health services, health economics and outcomes research however impacts on the applicability of evidence informing current guidance and leaves important questions for future research.

Registration: PROSPERO, registration number CRD42015029291.

Introduction

Obstructive sleep disordered-breathing (oSDB) is a condition that encompasses problems with breathing when asleep due to obstruction of the upper airways. It affects both children and adults and ranges in severity from primary snoring with no compromise to nocturnal arterial oxygen saturations, to obstructive sleep apnoea (OSA) syndrome with significant desaturations overnight[1] and potential adverse long-term neurocognitive and cardiovascular outcomes.[2-4]

In children, the prevalence of primary snoring is estimated at 8-27% and that of OSA 1-5%.[1] The most up-to-date and comprehensive guideline on childhood oSDB has been issued by the American Academy of Pediatrics (AAP); it is based on evidence in the field gathered up to 2011 and includes recommendations for further research.[1] Despite this and other clinical guidelines[5,6] providing support, and growing interest in oSDB both clinically and academically, clinicians and parents are faced with many uncertainties about how best to diagnose and manage this very common condition in children (Figure 1). This systematic review maps all research in childhood oSDB undertaken so far, focusing on research activity since the AAP guideline, with the aim to support further guideline development, identify evidence gaps and guide future research.

Materials and Methods

Data sources and searches

Systematic searches of PubMed, Embase and the Cochrane Library were performed from inception to 26 November 2015. A broad search strategy was designed using a combination of any key word relevant to obstructive sleep-disordered breathing and children, with database-specific syntaxes (Appendix Table 1). The first search was performed 12 April 2015; in the updated search 26 November 2015, the original April search was ran and all databases were searched from inception using the additional search term “upper airway obstruction” (Appendix Table 1).

Data management

Duplicate records were removed using Endnotes automatic duplicate identification filter as well as rigorous manual checks to remove any remaining duplicates and errata. Manual checks were facilitated by ordering the data by year, author, title and abstract. Two review authors independently screened titles and abstracts of the unique records to assess potential relevance for inclusion. Any discrepancies were resolved by reviewing the full text followed by discussion with a third review author.

Study selection

All publications relating to childhood oSDB - ranging from primary snoring, upper airway resistance syndrome, obstructive hypoventilation to OSA syndrome - were included, irrespective of article type or language. Publications that solely included adults (16 years and above), animals and central sleep apnoea were excluded.

Data extraction and quality assessment

Year of publication was identified using Endnote's automatic classification system. Since the 2012 AAP guideline was based on a comprehensive assessment of the literature published up to 1 January 2011 (date of their latest search) our assessment of main research themes and methodologies focused on publications since this time. Definitions of research themes and methodologies were adapted from the 'UKCRC Health Research Classification System'[8] and 'A Dictionary of Epidemiology, 6th edition'[9], respectively. To test the feasibility of using these definitions, all review authors independently extracted data from a random sample of 50 publications. The results were discussed and definitions finalised in a consensus meeting with all review authors (Appendix Table 2). From then on two review authors independently extracted these data. Any discrepancies were resolved by discussion in weekly meetings with all review authors.

For publications classified as 'trial', the method of randomisation was verified.[10] For randomised controlled trials (RCTs), publications were linked to the original RCT and type of interventions were extracted.

Data synthesis and analysis

The annual number of publications in the field of oSDB was counted over all years; for those published since 1 January 2011, total and annual numbers of publications across main research themes and methodologies were calculated. For the statistical analyses, Stata version 14.0 SE was used.

Results

Search results

The original search of 12 April 2015 and the updated search of 26 November 2015 yielded a total of 12489 records. Removing duplicates and erratums left 7637 unique records (Figure 2). After screening title and abstract (and full text where necessary), 1766 records were excluded because they were not about oSDB (n=1364), studied solely adults (n=225), central sleep apnoea (n=159) or animals (n=18); this left 5871 publications for inclusion in this review (Figure 2).

Annual number of publications

The annual number of publications in the field of childhood oSDB has increased steadily from 2000 to 2009 and steeply thereafter (Figure 2), with almost half (2708/5871, 46%) published since 1 January 2011 (Figure 2).

Publications since 1 January 2011

Main research theme

As illustrated in Table 1, the focus of research has not changed from 2011 to 2015; the proportion of publications across main research themes has remained similar. 31.1% of the publications focused on individual treatment modalities for childhood oSDB, followed by incidence and prevalence of oSDB in childhood populations (16.7%) and prognosis of the condition (13.5%). Few publications (2.7%) focused on health service delivery, outcomes and health economics in childhood oSDB.

Main research methodology

Table 2 shows that the vast majority (2123, 78.5%) of publications related to observational studies followed by literature reviews (391, 14.6%). Fewer than 1% of all publications used a qualitative approach as their main methodology. Of the 65 publications (2.4%) featured as trials, 18 were classified as non-randomised trials and 47 as RCTs. Seven of the RCT publications were secondary analyses (4 of the 2013 Childhood Adenotonsillectomy Trial[7]), leaving 40 individual RCTs in the field of SDB. Of these, 13 (33%) studied individual perioperative interventions, 11 (28%) surgical, 6 (15%) mechanical, 4 (10%) medical, 3 (8%) diet and exercise interventions, 2 (5%) compared a surgical with a medical intervention and 1 (3%) a surgical with a mechanical intervention.

Discussion

This review provides a comprehensive overview of all research activity in the field of childhood oSDB so far and shows that this activity has increased over the last two decades. There is no doubt that this has improved the knowledge base for this condition[11]; however, the lack of health services, health economics and outcomes research impacts on the applicability of evidence informing current guideline recommendations.

Since publication of the 2012 AAP guideline, the Childhood Adenotonsillectomy Trial[7] has provided key evidence on the benefits of adenotonsillectomy in children aged five to nine years with mild to moderate OSA diagnosed by a polysomnography (PSG). Ongoing RCTs will add to the evidence base by looking at the benefits of adenotonsillectomy in younger children with mild to moderate OSA diagnosed by PSG[12,13], in those with snoring but negative PSG findings[12,14], and in those with snoring and abnormal overnight pulse oximetry findings.[15] In these trials, understandably, confirmation of the clinical diagnosis of OSA is sought by PSG and/or overnight pulse oximetry; this however limits their applicability to daily ear-, nose- and throat (ENT) practice where these diagnostic modalities are not routinely used to select children for surgery.[16,17] As such, some uncertainties around diagnosis and management of childhood oSDB will remain (Figure 1), contributing to ongoing variation in the uptake of sleep studies in the diagnosis of oSDB, indications, rates and techniques for (adeno)tonsillectomies across and within countries.[16-20]

Our review shows that whilst research activity in childhood oSDB has increased rapidly over recent years, key areas of research have received little attention so far. In particular health services and health economics research, exploring how and where health services for children with symptoms of oSDB are best organised and delivered. Recent high quality studies have focused on individual diagnostic and treatment modalities for childhood oSDB: whilst these have produced invaluable evidence to guide clinical decisions, they fail to identify clinical

and cost-effective patient pathways in childhood oSDB.. One way to reconcile practice variation in this field, would be for future research to cross-cut specialties and health care settings and assess outcomes of different patient pathways, thus informing a more streamlined and unified patient care pathway. Such research and subsequent practice recommendations would need to take into account patient preferences as well as availability and access to services such as PSG and should include a thorough health economic evaluation.

Equally important is the need for outcomes research, exploring which outcome measures and instruments best capture the impact of oSDB and its treatments on the child and its family. To ensure future research is of maximum value to both professionals and families of children with oSDB, it is urgent that all stakeholders involved in the care of children with oSDB work together to develop a core set of outcomes[21-23], including those reported by children and their carers, to be used clinically and across future childhood oSDB research.

Recognising that the management of childhood oSDB spans across health care settings and specialties, we established an expert team covering primary care, sleep medicine, ENT surgery and epidemiology to carry out this review and reflect on its results. Using a broad search strategy, wide range of electronic databases, no language restrictions, and rigorous methodology, this review provides a unique and complete overview of the research activity in the field of childhood oSDB. It shows in what areas research is lacking and can be used to guide future work. It also provides a key repository for future clinical guideline development. Our full dataset will be available upon request to those undertaking such work.

Some limitations of our approach deserve further attention. First, unlike previous systematic reviews in childhood oSDB we did not set out to extract data on methodological quality and results of individual publications and therefore are not able to make management recommendations. Second, since some publications had more than one research theme or methodology, some misclassification regarding main research theme and methodology may

have occurred. However, since two review authors extracted these data independently and any disagreements were discussed and resolved by all review authors, it is unlikely that this has had a substantial impact on our findings. Finally, whilst we set out to extract the type of publication, that is full paper versus conference abstract, using Endnote's automatic classification system (see PROSPERO CRD42015029291), this turned out not reliable with over 60% missing classifications for publications up to 2009 and 20% for those published since.

Conclusions and recommendations

A recent surge in research activity in childhood oSDB has improved the knowledge base for this condition. The diagnosis and management of childhood oSDB is, however, complex and requires a 'systems approach' across specialties and health care settings. Research so far has failed to take this perspective and has focused on individual steps and actions in the patient pathway. For future research in oSDB to be of high value to both clinicians, children and their carers, it needs to take wider perspective and collaborative approach with the aim of developing a streamlined and unified patient care pathway.

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Author contributions

RPV planned the study, collected the data, supervised the analyses and interpreted the data. DC, FA, HB collected and interpreted the data. HE collected and analysed the data. IAK supervised the study. AGMS designed and supervised the study. All authors contributed to, reviewed, and approved the final draft.

Guarantor statement

AGMS takes responsibility for (is the guarantor of) the content of the manuscript, including the data and analysis and affirms that the manuscript is a honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned and registered (PROSPERO, registration number CRD4201502929) have been explained.

Conflict of interest statement

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Ethical approval

Not required.

Data sharing

Full dataset available upon request from the corresponding author at a.schilder@ucl.ac.uk.

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Tables and Figures.

Table 1. Research themes in publications on childhood obstructive sleep-disordered breathing published since 1 January 2011

Theme	2011 n (%)	2012 n (%)	2013 n (%)	2014 n (%)	2015 n (%)	Total n (%)
Treatment	146 (31.6%)	177 (32.2%)	195 (30.1%)	169 (28.9%)	154 (33.2%)	**841 (31.1%)**
Incidence/Prevalence	79 (17.1%)	98 (17.9%)	101 (15.6%)	101 (17.3%)	72 (15.5%)	**451 (16.7%)**
Prognosis	61 (13.2%)	90 (16.4%)	81 (12.5%)	74 (12.7%)	59 (12.7%)	**365 (13.5%)**
Aetiology/Risk Factors	54 (11.7%)	59 (10.7%)	87 (13.4%)	68 (11.6%)	54 (11.6%)	**322 (11.9%)**
Diagnosis	34 (7.4%)	47 (8.6%)	78 (12.1%)	78 (13.4%)	63 (13.6%)	**300 (11.1%)**
Underpinning Research	40 (8.7%)	32 (5.8%)	50 (7.7%)	39 (6.7%)	34 (7.3%)	**195 (7.2%)**
Full Spectrum	24 (5.2%)	24 (4.4%)	26 (4%)	27 (4.6%)	10 (2.2%)	**111 (4.1%)**
Service Delivery	9 (1.9%)	8 (1.5%)	15 (2.3%)	10 (1.7%)	7 (1.5%)	**49 (1.8%)**
Outcome Research	3 (.6%)	6 (1.1%)	4 (.6%)	4 (.7%)	3 (.6%)	**20 (.7%)**
Screening	2 (.4%)	2 (.4%)	4 (.6%)	11 (1.9%)	3 (.6%)	**22 (.8%)**
Guidelines	3 (.6%)	4 (.7%)	3 (.5%)	2 (.3%)	3 (.6%)	**15 (.6%)**
Other	6 (1.3%)	1 (.2%)	3 (.5%)	0 (0%)	2 (.4%)	**12 (.4%)**
Economic Analysis	1 (.2%)	1 (.2%)	0 (0%)	1 (.2%)	0 (0%)	**3 (.1%)**
Total	**462 (100%)**	**549* (100%)**	**647* (100%)**	**584 (100%)**	**464^ (100%)**	**2706* (100%)**

* For 1 Chinese and 1 Japanese article neither the abstract nor the full paper could be retrieved; these 2 articles were therefore excluded from further analysis.
^ For 2015, all relevant articles published up to 26 November 2015 (date of updated search) were included.

Table 2. Research methodologies used in publications on childhood obstructive sleep-disordered breathing published since 1 January 2011

Method	2011 n (%)	2012 n (%)	2013 n (%)	2014 n (%)	2015 n (%)	Total n (%)
Cross-sectional	154 (33.8%)	178 (32.7%)	224 (35.1%)	221 (38%)	159 (34.3%)	**936 (34.9%)**
Cohort	117 (25.7%)	157 (28.9%)	181 (28.4%)	143 (24.6%)	125 (26.9%)	**723 (26.9%)**
Review	72 (15.8%)	84 (15.4%)	84 (13.2%)	84 (14.5%)	67 (14.4%)	**391 (14.6%)**
Case control	55 (12.1%)	71 (13.1%)	81 (12.7%)	65 (11.2%)	64 (13.8%)	**336 (12.5%)**
Case report	12 (2.6%)	17 (3.1%)	18 (2.8%)	23 (4%)	14 (3%)	**84 (3.1%)**
Trial	14 (3.1%)	10 (1.8%)	11 (1.7%)	18 (3.1%)	12 (2.6%)	**65 (2.4%)**
E/L/C/S~	13 (2.9%)	10 (1.8%)	18 (2.8%)	10 (1.7%)	12 (2.6%)	**63 (2.3%)**
Case series	9 (2%)	12 (2.2%)	12 (1.9%)	7 (1.2%)	4 (.9%)	**44 (1.6%)**
Research Protocol/Design	4 (.9%)	1 (.2%)	4 (.6%)	3 (.5%)	2 (.4%)	**14 (.5%)**
Guideline Development	3 (.7%)	2 (.4%)	1 (.2%)	2 (.3%)	3 (.6%)	**11 (.4%)**
Qualitative	2 (.4%)	1 (.2%)	3 (.5%)	3 (.5%)	1 (.2%)	**10 (.4%)**
Conference proceeding	4 (.9%)	2 (.4%)	9 (1.4%)	2 (.3%)	0 (0%)	**17 (.6%)**
Educational	2 (.4%)	3 (.5%)	0 (0%)	1 (.2%)	0 (0%)	**6 (.2%)**
Other	1 (.2%)	1 (.2%)	1 (.2%)	2 (.3%)	1 (.2%)	**6 (.2%)**
Total	**462 (100%)**	**549* (100%)**	**647* (100%)**	**584 (100%)**	**464^ (100%)**	**2706* (100%)**

~ E/L/C/S=Editorial/Letter/Commentary/Summary.
* For 1 Chinese and 1 Japanese article neither the abstract nor the full paper could be retrieved; these 2 articles were therefore excluded from further analysis.
^ For 2015, all relevant articles published up to 26 November 2015 (date of updated search) were included.

Appendix Table 1. Search strategy

Search date 12 April 2015		
Pubmed	**Embase**	**The Cochrane Library**
((snoring[Title/Abstract] OR sleep apnoea[Title/Abstract] OR sleep apnea[Title/Abstract] OR obstructive sleep apnoea[Title/Abstract] OR obstructive sleep apnea[Title/Abstract] OR obstructive sleep apnoea syndrome[Title/Abstract] OR obstructive sleep apnea syndrome[Title/Abstract] OR obstructive sleep apnoea hypopnoea syndrome[Title/Abstract] OR obstructive sleep apnea hypopnea syndrome[Title/Abstract] OR sleep disordered breathing[Title/Abstract] OR sleep-disordered breathing[Title/Abstract] OR sleep related breathing disorder[Title/Abstract] OR sleep-related breathing disorder[Title/Abstract] OR upper airway resistance syndrome[Title/Abstract]) AND (infants[Title/Abstract] OR children[Title/Abstract] OR childhood[Title/Abstract] OR pediatric[Title/Abstract] OR paediatric[Title/Abstract]))	((snoring or sleep apnea or sleep apnoea or obstructive sleep apnea or obstructive sleep apnoea or obstructive sleep apnoea syndrome or obstructive sleep apnea syndrome or obstructive sleep apnea hypopnoea syndrome or obstructive sleep apnoea hypopnoea syndrome or sleep disordered breathing or sleep-disordered breathing or sleep-related breathing disorder or sleep related breathing disorder or upper airway resistance syndrome) and (infants or children or childhood or pediatric or paediatric)).ti,ab.	('snoring' OR 'sleep apnoea' OR 'sleep apnea' OR 'obstructive sleep apnoea' OR 'obstructive sleep apnea' OR 'obstructive sleep apnoea syndrome' OR 'obstructive sleep apnea syndrome' OR 'obstructive sleep apnoea hypopnoea syndrome' OR 'obstructive sleep apnea hypopnea syndrome' OR 'sleep disordered breathing' OR 'sleep-disordered breathing' OR 'sleep related breathing disorder' OR 'sleep-related breathing disorder' OR 'upper airway resistance syndrome') AND ('infants' OR 'children' OR 'childhood' OR 'pediatric' OR 'paediatric')
Search date 26 November 2015*		
Pubmed	**Embase**	**The Cochrane Library**
((snoring[Title/Abstract] OR sleep apnoea[Title/Abstract] OR sleep apnea[Title/Abstract] OR obstructive sleep apnoea[Title/Abstract] OR obstructive sleep apnea[Title/Abstract] OR obstructive sleep apnoea syndrome[Title/Abstract] OR obstructive sleep apnea syndrome[Title/Abstract] OR obstructive sleep apnoea hypopnoea syndrome[Title/Abstract] OR obstructive sleep apnea hypopnea syndrome[Title/Abstract] OR sleep disordered breathing[Title/Abstract] OR sleep-disordered breathing[Title/Abstract] OR sleep related breathing disorder[Title/Abstract] OR sleep-related breathing disorder[Title/Abstract] OR upper airway resistance syndrome[Title/Abstract] OR upper airway obstruction[Title/Abstract]) AND (infants[Title/Abstract] OR children[Title/Abstract] OR childhood[Title/Abstract] OR pediatric[Title/Abstract] OR paediatric[Title/Abstract]))	((snoring or sleep apnea or sleep apnoea or obstructive sleep apnea or obstructive sleep apnoea or obstructive sleep apnoea syndrome or obstructive sleep apnea syndrome or obstructive sleep apnea hypopnoea syndrome or obstructive sleep apnoea hypopnoea syndrome or sleep disordered breathing or sleep-disordered breathing or sleep-related breathing disorder or sleep related breathing disorder or upper airway resistance syndrome OR upper airway obstruction) and (infants or children or childhood or pediatric or paediatric)).ti,ab.	('snoring' OR 'sleep apnoea' OR 'sleep apnea' OR 'obstructive sleep apnoea' OR 'obstructive sleep apnea' OR 'obstructive sleep apnoea syndrome' OR 'obstructive sleep apnea syndrome' OR 'obstructive sleep apnoea hypopnoea syndrome' OR 'obstructive sleep apnea hypopnea syndrome' OR 'sleep disordered breathing' OR 'sleep-disordered breathing' OR 'sleep related breathing disorder' OR 'sleep-related breathing disorder' OR 'upper airway resistance syndrome' OR 'upper airway obstruction') AND ('infants' OR 'children' OR 'childhood' OR 'pediatric' OR 'paediatric')

* The first search was performed 12 April 2015; in the updated search 26 November 2015, the original April search was ran and all databases were searched from inception using the additional search term "upper airway obstruction".

Appendix Table 2. Definitions of research themes and methodology as used in this review*

Research themes

Treatment	Testing and evaluation of therapeutic interventions in clinical, community or applied settings. This should involve patients in the testing and evaluation of therapies or be in a clinical or applied setting.
Incidence/prevalence	Studies of the number of new cases or obstructive sleep-disordered breathing related events in a defined population within a specified period of time. It may be measured as a frequency count, a rate, or a proportion OR the total number of individuals who have the condition (e.g., disease, exposure, attribute) at a particular time.
Prognosis	Prognosis research is the investigation of the relations between future outcomes ('endpoints') among people with a given baseline health state ('startpoint') in order to improve health e.g. "What is the prognosis of people with a given disease?" or identification of a prognostic marker associated with an outcome. This category includes studies on the impact of obstructive sleep-disordered breathing on other conditions.
Aetiology/risk factors	Identification and characterization of determinants that are involved in the cause, risk and development of diseases or conditions. If there is no longitudinal time component, cannot be aetiology but can indicate risk factor.
Diagnosis	Discovery, development and evaluation of diagnostic, prognostic and predictive markers and technologies. Includes research where the main aim is to develop diagnostic or prognostic tests for clinical use. Excludes development of lab techniques and tools for basic research. Excludes basic research using imaging or detection techniques in the methodology, where the primary aim of the research is not to develop clinical tests.
Underpinning research	Research that underpins investigations into the cause, development, detection, treatment and management of diseases, conditions and ill health. Research that is concerned with basic sciences.
Full spectrum	Research that investigates or describes the full spectrum of childhood obstructive sleep-disordered breathing, ranging from diagnosis, aetiology, prognosis to treatment.
Service delivery	The study of the organization, functioning, and performance of health services. Health services research is usually concerned with relationships between needs, demand, supply, use, and outcomes of health services.
Outcomes Research	Research on validation of outcome measures of interventions e.g. OSA-22.
Screening	Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment.
Guidelines	Clinical practice guideline publications
Economic analysis	A general term for the economic evaluation of management options. The paper is focused on cost benefit analysis.
Prevention	Research aimed at the primary prevention of disease, conditions or ill health, or promotion of well-being
Other	Research that does not fit into the above categories, these include studies on parental beliefs of obstructive sleep-disordered breathing and educational texts.

Research methodology

Cross-sectional	Population on entry: selected for representative of total population, no prior knowledge of disease status Exposure: measured at one time only per participant Outcome: prevalence Time: not present; all aspects measured at one point (per participant)
Cohort	Population on entry: mostly population with disease but outcome may not yet be known Exposure: measured concurrently but naturally occurring Outcome: RR Time: Measurements occurs at more than one time point
Review	Narrative or systematic review of literature
Case control	Population on entry: selected for having or not having disease, disease status known at the time Exposure: measured retrospectively Outcome: OR Time: not really as all data gathered retrospectively
Case report	Population on entry: selected for having disease (i.e. the case arm of case control) and having 1 case only. Exposure: measured retrospectively Outcome: N/A but needs a full description of case Time: there may be time as the progression of the case may be described
Trial	Population on entry: selected for all having disease Exposure: must be assigned (preferably randomly but not always) Outcome: RR (preferably observed blind for exposure but not always) Time: Measurements occurs at more than one time point
E/L/C/S	Editorial / Letter / Commentary / Summary (of original research article)
Case series	Population on entry: selected for having disease (i.e. the case arm of case control) and having more than one case with a full description of the clinical picture for individual cases Exposure: measured retrospectively Outcome: N/A but needs a full description of cases Time: there may be time as the progression of the cases may be described
Research protocol/Design	Publications describing the protocol and/or design of the original research; this category includes trial registration records
Guideline development	Publications describing the clinical guideline development process
Qualitative research	Publications of qualitative research
Conference proceedings	Proceedings of scientific conference
Educational	Abstract / overview of educational lecture
Other	Research methodology that does not fit into the above categories

* Adapted from the 'UKCRC Health Research Classification System'[8] and 'Dictionary of Epidemiology, 6th edition'[9]

Figure 1. Uncertainties along the patient pathway in childhood obstructive sleep-disordered breathing

oSDB, obstructive sleep-disordered breathing; GP, general practitioner; ENT, ear- nose- and throat; OSA, obstructive sleep apnoea, PSG, polysomnography; CPAP, continuous positive airway pressure; biPAP, bilevel positive airway pressure.

Figure 2. Flow diagram of search results

* The first search was performed 12 April 2015; in the updated search 26 November 2015, the original April search was ran and all databases were searched from inception using the additional search term “upper airway obstruction” (Appendix Table 1).

Figure 3. Annual number of publications in the field of childhood obstructive sleep-disordered breathing

For 2015, all relevant articles published up to 26 November 2015 (date of updated search) were included.

Questions about childhood oSDB								
Setting	**Decision maker**	**History**		**Clinical Examination**	**Investigations**		**Treatment**	
COMMUNITY	Parents	Are there warning signs or symptoms (other than snoring) alerting for OSA? How to educate parents and professionals about oSDB?	When to visit GP?	What symptoms, signs and examination features are suggestive of OSA and can help predict severity?	What is role and interpretation of (overnight) pulse oximetry?	Role of recording child asleep at home or nursery (mobile phone or video recording)?	Role of medical therapy (nasal steroids, leukotriene receptor antagonists) Role of weight management? How to assess improvement?	
	Teacher and/or school nurse		When to alert parents?					
	Health visitor							
PRIMARY CARE	GP		When and who to refer to in secondary or tertiary care?					
SECONDARY CARE	Paediatrician					Role of sleep endoscopy? When to refer for full sleep study? Role and timing of follow-up?		
	ENT surgeon		When to refer to a Sleep specialist?					When to operate? Where to operate? Tonsillectomy or adenoidectomy or both and which technique?
TERTIARY CARE	Sleep specialist	How to evaluate consequences of oSDB?	Role of paediatric sleep questionnaires? Role of OSA biomarkers?			Overnight respiratory polygraphy or full PSG? Role of ambulatory sleep study? Role and timing of sleep team follow-up?		When to refer for ENT surgery? Role of CPAP or BiPAP?
	Oromaxillofacial surgeon and/or Orthodontist							Role of orthodontic management (including myofunctional therapy)? Role of alternative surgical interventions?