

Tracheomalacia and bronchomalacia in children (TF-2016-21)

TOPIC ALLOCATION July 2017. Key question numbers and final section headings

QUESTION AND FINAL TOPIC HEADING	RESPONSIBLE TF MEMBERS
1. What is the definition of tracheal (TM) and major bronchial malacia (BM) and what classifications of severity exist? INTRODUCTION	Deborah Snijders Kostas Douros
2. What are the causes of tracheo-bronchomalacia (TBM)? CONDITIONS ASSOCIATED WITH TBM	Ahmad Kantar Andrew Bush
3. What is the spectrum of clinical presentation, severity and clinical course – to include any studies on the untreated natural history of this condition? CLINICAL SYMPTOMS AND SIGNS	Ernst Eber Rafaella Nenna
4a. In children suspected of having TBM, can pulmonary function tests be used to diagnose TBM 4b. In children with known TBM, what are the pulmonary function abnormalities ROLE OF LUNG FUNCTION	Ann Chang Ahmad Kantar
5. How do we use Imaging to diagnose TM & BM? [To include tracheobronchography] ROLE OF IMAGING	Efthymia Alexopoulou Derek Roebuck
6a. How do we use Bronchoscopy [rigid and flexible] to diagnose TM & BM? 6b. What influence does a general anaesthetic have on the diagnostic testing for TBM ROLE OF BRONCHOSCOPY	Fabio Midulla Kostas Douros
7. Which medical therapies have been suggested for the management of TBM and co-morbidities [e.g. wheezing, endobronchial infection, atelectasis?] MEDICAL THERAPIES	Jayesh Bhatt Andrew Bush
8. What is the role for respiratory physiotherapy? PHYSIOTHERAPY	Anna-Maria Charatsi Julie Depiazzi
9. How and when should we treat TM & BM by internal stenting? SURGERY INCLUDING STENTING	Derek Roebuck Juan Anton-Pacheco
10. What surgical strategies have been suggested for the management of TBM – eg aortopexy, tracheopexy, external splints, tracheal resection, tracheostomy. SURGERY INCLUDING STENTING	Juan Anton-Pacheco
11. What is the indication for long term ventilatory support either by tracheostomy or non-invasive interface and what ventilator strategies have been trialled? VENTILATORY SUPPORT	Mark Everard Ian Brent Masters
12. What is the parent and patient perspective? PARENT AND PATIENT PERSPECTIVE	Courtney Coleman Barbara Johnson

PRISMA for question 1 and 2

Pubmed search (since 1992)

(Tracheomalacia OR Bronchomalacia OR Tracheobronchomalacia) AND (classify OR classification OR define OR definition)

82 articles
identified

screened for
potential
eligibility

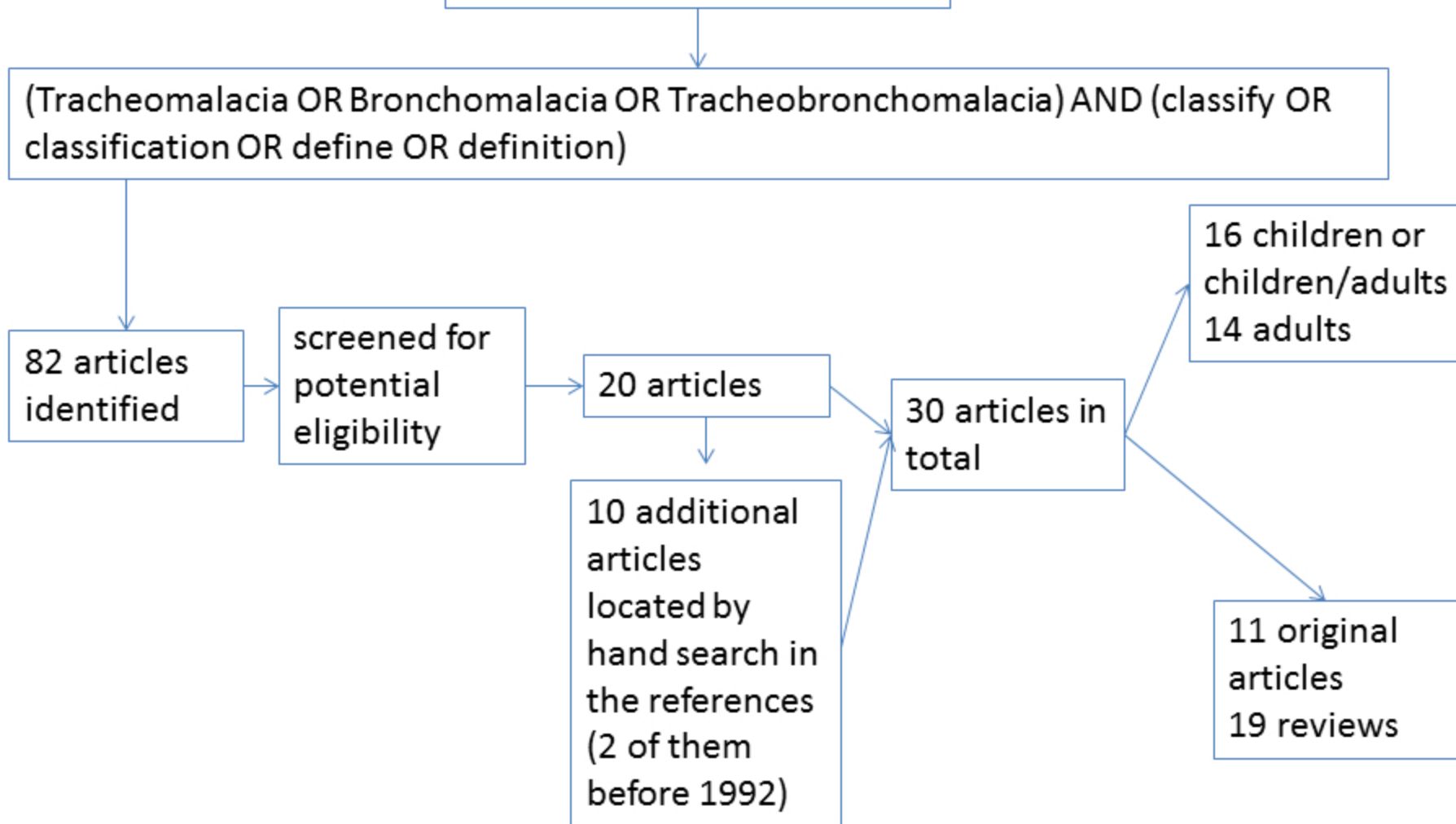
20 articles

10 additional
articles
located by
hand search in
the references
(2 of them
before 1992)

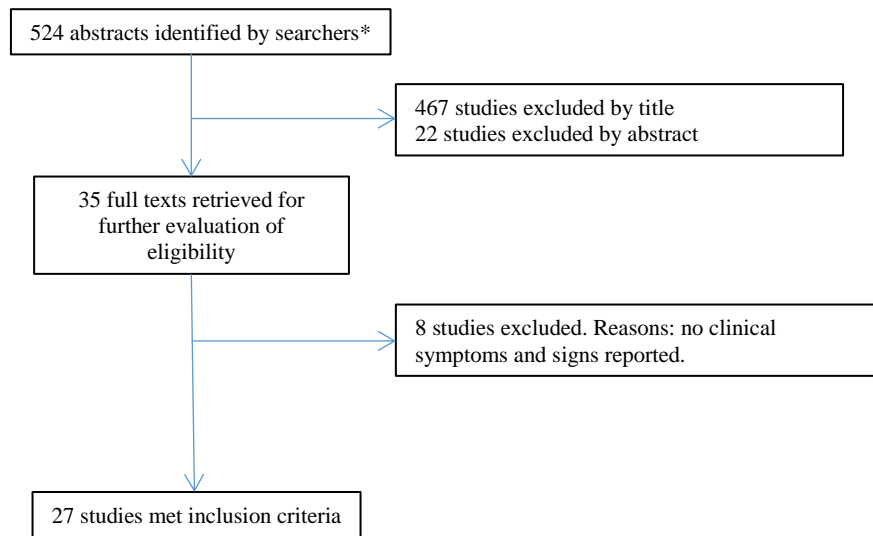
30 articles in
total

16 children or
children/adults
14 adults

11 original
articles
19 reviews



PRISMA: QUESTION 3
Clinical Symptoms and Signs



***Keywords:**

(tracheomalacia or bronchomalacia) and (symptoms or "clinical presentation" or "severity" or "clinical course" or "natural history")

Limited to:

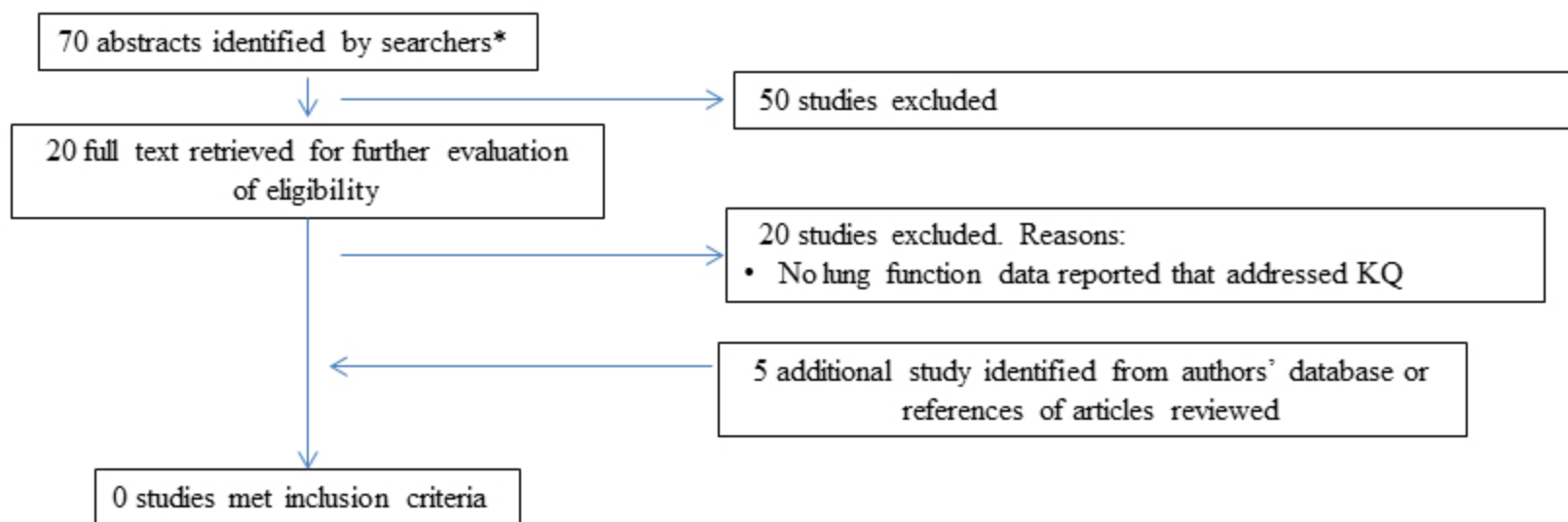
Publication dates: from 01/01/1997 to 01/06/2017

Species: Humans

Languages: English

Figure 4a: Selection of studies that addressed key question (KQ) 4

4a. In children suspected of having TBM, can pulmonary function tests be used to diagnose TBM

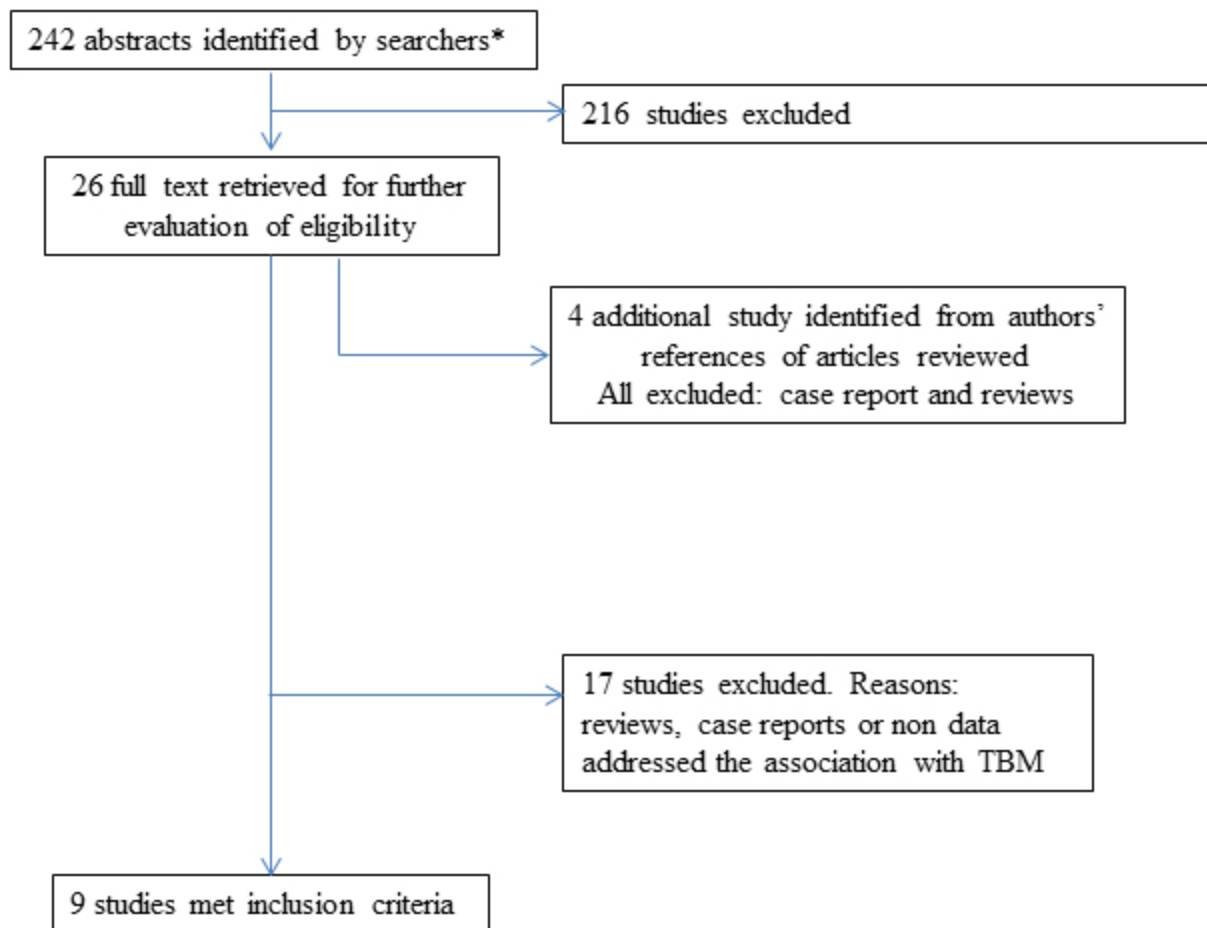


Search on Pubmed (3rd Aug 2017)

("tracheomalacia"[MeSH Terms] OR "tracheomalacia"[All Fields]) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields]) AND ("respiratory physiological phenomena"[MeSH Terms] OR ("respiratory"[All Fields] AND "physiological"[All Fields] AND "phenomena"[All Fields]) OR "respiratory physiological phenomena"[All Fields] OR ("lung"[All Fields] AND "function"[All Fields]) OR "lung function"[All Fields])

PRISMA FOR QUESTION 4B

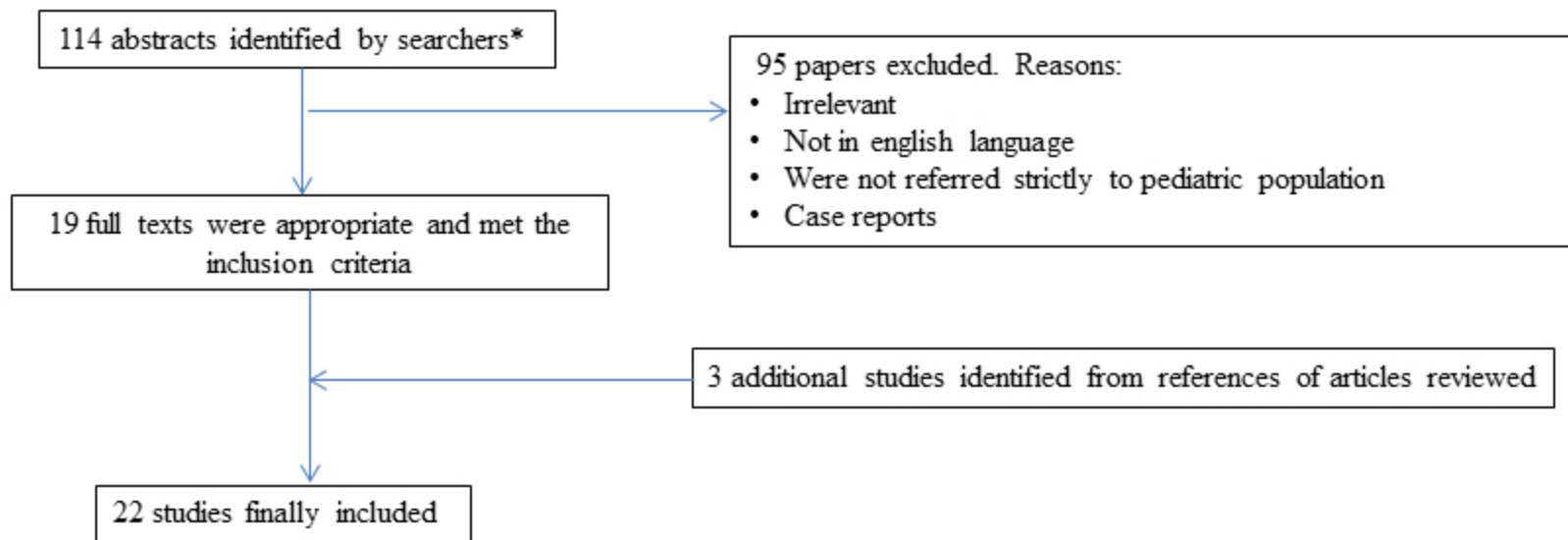
In children with known TBM, what are the pulmonary function abnormalities



Search on Pubmed (3rd Aug 2017)

("tracheomalacia"[MeSH Terms] OR "tracheomalacia"[All Fields]) OR
("bronchomalacia"[MeSH Terms] OR "bronchomalacia"[All Fields]) OR
("tracheobronchomalacia"[MeSH Terms] OR "tracheobronchomalacia"[All Fields]) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields]) AND "infant"[MeSH Terms] OR ("infant"[All Fields])

Selection of studies that addressed key question (KQ) 5
5. How do we use Imaging to diagnose TM & BM? [To include tracheobronchography]



*Search on PubMed (1/1/1997 – 26/8/2017), all the type of articles:

Keywords:

All the possible combinations of: TRACHEOMALACIA, BRONCHOMALACIA, IMAGING, CHILDREN, PEDIATRIC, CT, CT SCAN, MRI, FLUOROSCOPY, RADIOLOGY, BRONCHOGRAPHY

PRISMA QUESTION 7

Which medical therapies have been suggested for the management of TBM and co-morbidities [e.g. wheezing, endobronchial infection, atelectasis?]

64 abstracts identified by searchers*

Excluded 38 citations from abstracts as not relevant or case reports

26 papers retrieved for further evaluation of eligibility

14 papers excluded. Reasons: Not relevant to the KQ

12 additional citations identified from authors' database or references of articles reviewed

24 studies included for this section

Search on Pubmed (10th August 2017)

("tracheomalacia"[MeSH Terms] OR "tracheomalacia"[All Fields]) ("tracheobronchomalacia [MeSH Terms] OR "tracheobronchomalacia"[All Fields])" AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields]) AND ("symptoms"[MeSH Terms] OR ("treatment"[All Fields])

=320 items
Filters activated: Publication date from 1997/01/01 to 2017/12/31, Humans, English.
= 241 items

Excluded:

Diagnosis

Respiratory physiotherapy

Internal stenting

Surgical strategies eg aortopexy, tracheopexy, external splints, tracheal resection, tracheostomy

Long term ventilatory support either by tracheostomy or non-invasive interface

Adults

= 177 excluded

PRISMA QUESTION 8 - PHYSIOTHERAPY

Search terms

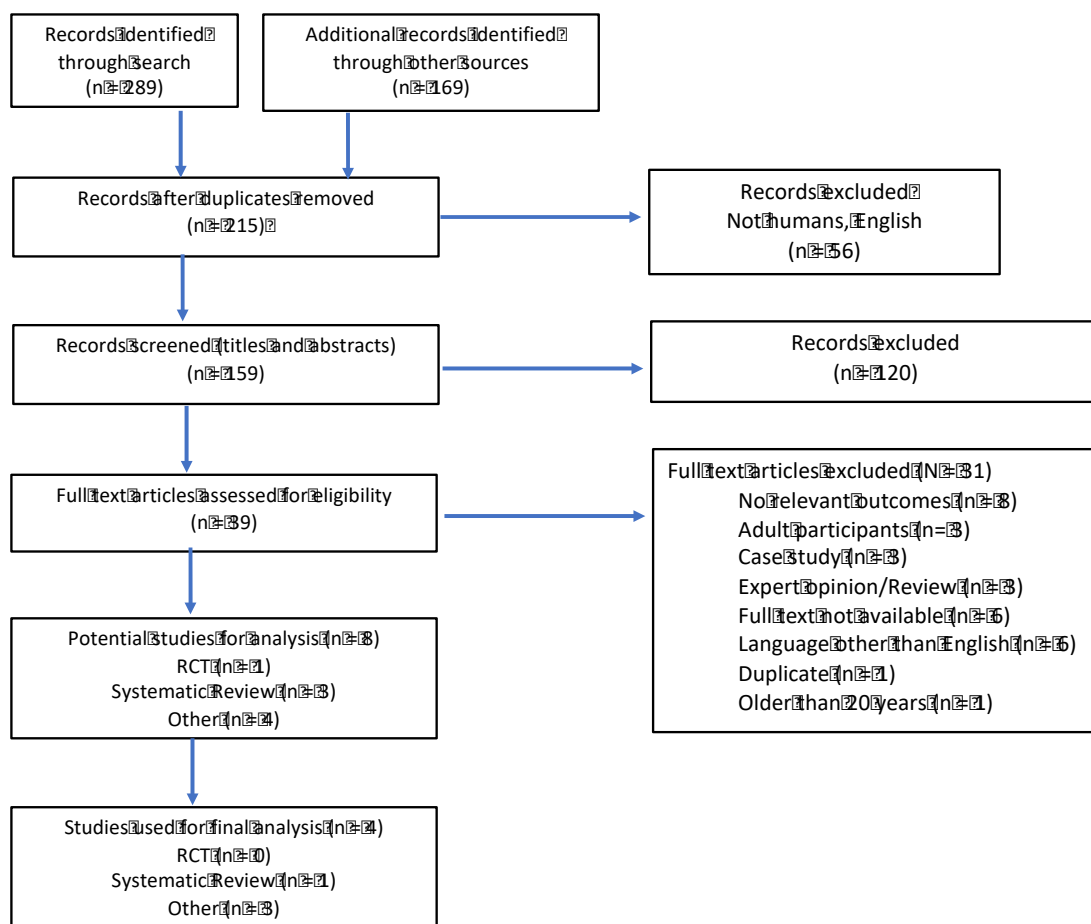
Tracheomalacia OR bronchomalacia OR tracheobronchomalacia OR malacia OR tracheal abnormalities OR tracheal diseases

AND

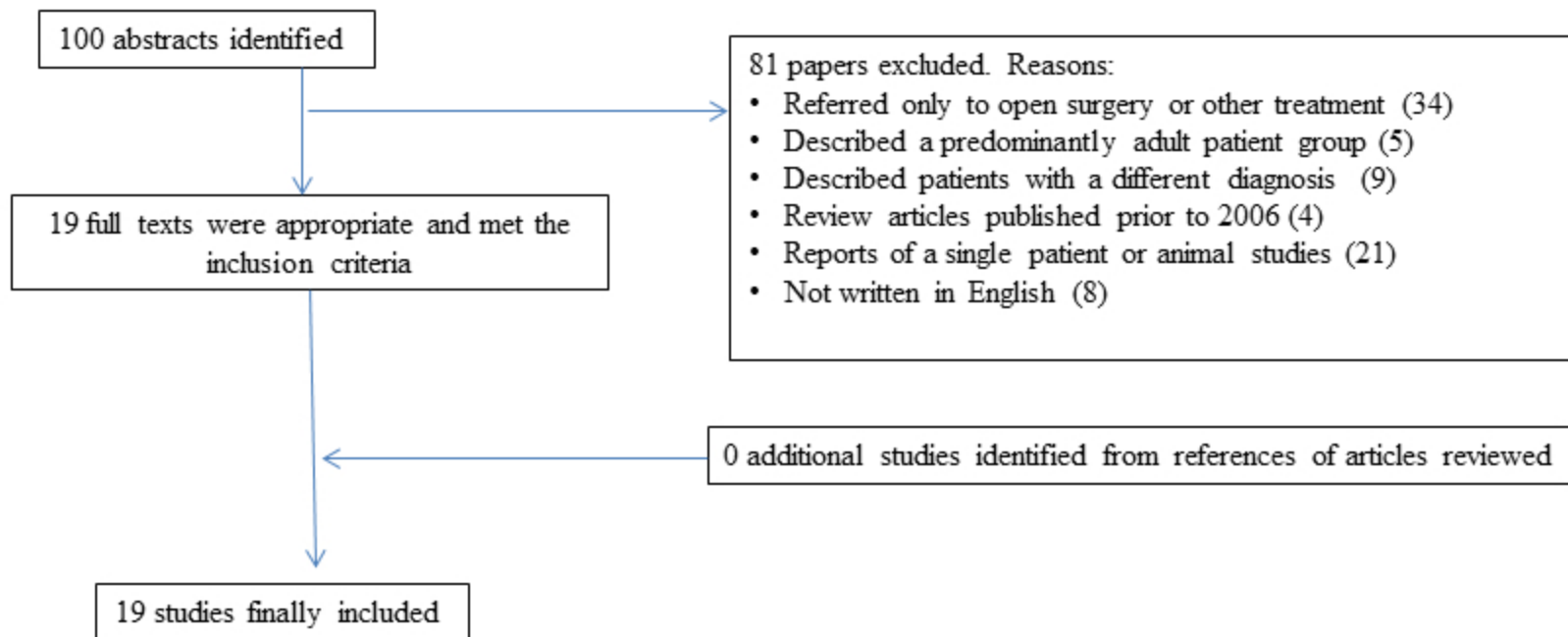
Physiotherapy OR physical therapy OR physical therapy modalities OR airway clearance OR positive pressure and physiotherapy

Exercise tolerance OR exercise therapy

Administration inhalation OR nebulisation OR saline solution hypertonic OR deoxyribonuclease I OR nebulised dornase alfa OR nebulised hypertonic saline



PRISMA. QUESTION 9: STENTS

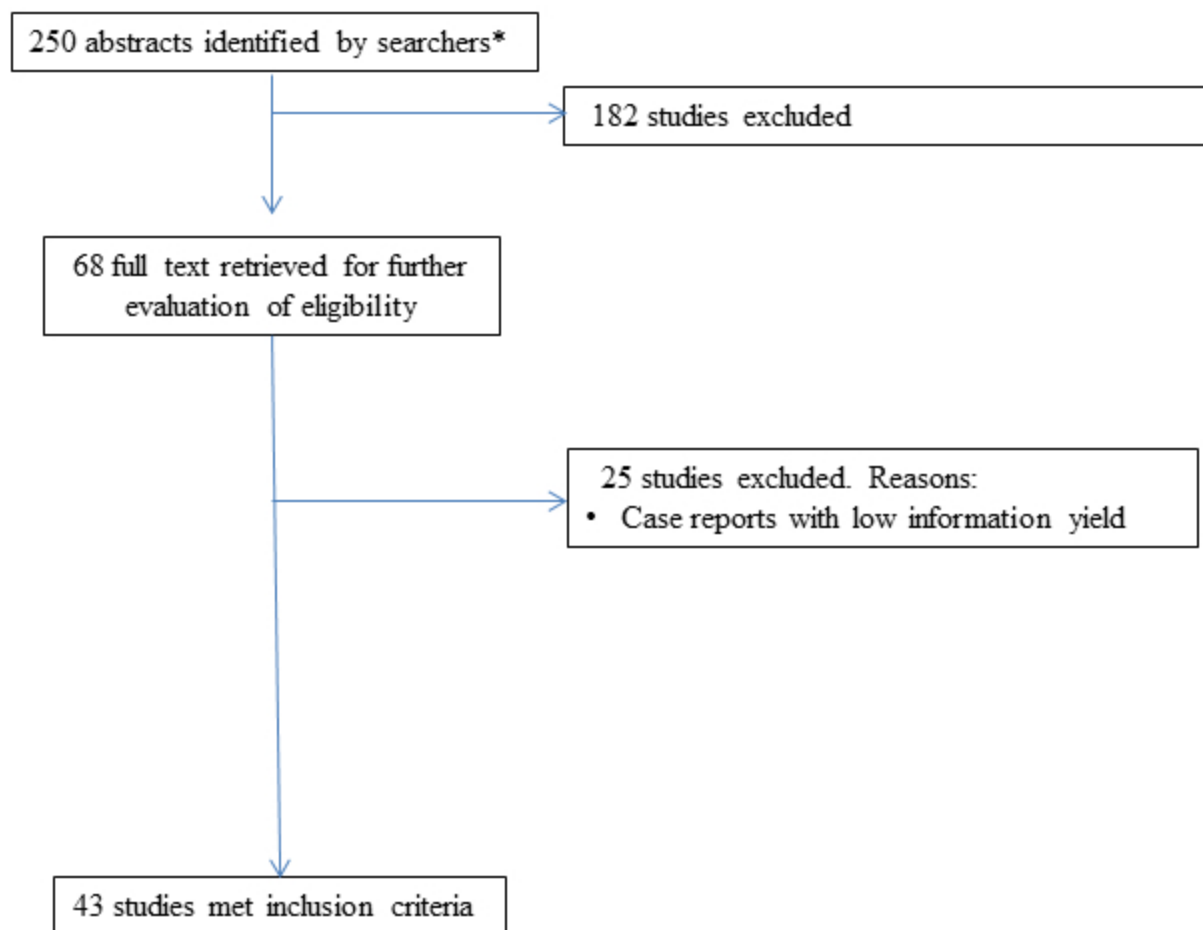


Search on PubMed 30-06-2018

PubMed search: (tracheomalacia OR tracheobronchomalacia OR bronchomalacia) AND stent
limits: age 0-18 years

PRISMA for question 10:

What surgical strategies have been suggested for the management of TBM



Search on Pubmed and Embase (September 2017)

"tracheomalacia/surgery"[MeSH Terms] OR "bronchomalacia/surgery"[MeSH]
AND ("child"[MeSH Terms] OR "infant" (MeSH) OR "adolescent"[MeSH] OR
"children"[All Fields]) AND ("aortopexy OR tracheopexy OR external splint OR
tracheal resection OR Tracheostomy" [MeSH Terms] OR the combination of
the above items.

Question 3: Clinical Symptoms and Signs

1 st author, publication year	Setting; Study design	Inclusion criteria; Exclusion or definitions	Description of cohort	Main aim(s) of study	Primary findings relating to KQ	Main study limitation	Method of confirmation of TBM and type
Adil 2012	Tertiary referral centre; retrospective	130 consecutive preterm and term infants with laryngomalacia, as diagnosed by airway endoscopy between June 2004 and August 2009	TM: 25 infants	1 “to identify the most common area(s) of supraglottic collapse” 2 “to compare airway findings in term and preterm infants” 3 “to evaluate the incidence of secondary airway lesions”	19% of infants with laryngomalacia had TM	Retrospective study; different methods of confirmation of TM	Fluoroscopy and/or direct laryngoscopy and bronchoscopy under general anaesthesia
Boogaard 2005	Tertiary referral centre; retrospective	All flexible bronchoscopies performed between 1997 and 2004 (n=512); malacia defined as collapse of at least 50% of the airway lumen, during expiration, cough or spontaneous breathing, or a ratio of cartilage to membranous wall area of < 3:1.	TM: 63 children; TBM: 49 children; BM: 24 children	1 “to estimate the incidence of primary airway malacia in the general population” 2 “to estimate the predictive value of clinical diagnosis of malacia by paediatric pulmonologists” 3 “to characterise the presenting symptoms and findings in patients diagnosed with primary airway malacia”	Types of symptoms and clinical features	Retrospective study	Flexible bronchoscopy under general anaesthesia; airway malacia was diagnosed by visual inspection of airway shape and dynamics during spontaneous breathing without positive endexpiratory pressure, or during coughing.
Carden 2005	Review	TM and TBM in children and adults	NA	“a comprehensive review of both the adult and paediatric forms of the disease” and “review of the various modalities that are used for diagnosis as well as the state	Types of symptoms, severity, natural history	NA	NA

				of the art of treatment”			
Choo 2013	Review	Tracheomalacia/ Tracheobroncho- malacia and hyperdynamic airway collapse	NA	NA	Types of symptoms, severity, natural history	Adult literature	NA
Dessoffy 2013	Retro- spective	236 children with achondroplasia, who were initially assessed between 1985 and 2012	9 children with TM or TBM	1 “to establish the frequency of airway malacia in a cohort of children with achondroplasia” 2 “to assess its interactions with other known breathing abnormalities in these individuals”	4% of children with achondroplasia had TM or TBM	Retrospective study; different methods of confirmation of TM or TBM	Airway endoscopy or clinical examination
Doshi 2007	Case report	NA	NA	To describe symptoms of TM in an infant	Types of symptoms	Case report	Bronchoscopy
Finder 1996	Retro- spective	Patients with primary BM	17 children (age at diagnosis of BM: 3 months-17 years)	“to determine the natural history of primary BM in infants and children”	Natural history	Retrospective study	Bronchoscopy under light sedation?
Fraga 2016	Review	Primary (congenital) and secondary (acquired) TM and TBM	NA	NA	Time of onset and types of symptoms, severity	NA	NA
Hiebert 2016	Systematic review and meta- analysis	Articles addressing bronchoscopy in children with recurrent croup	11 articles reviewed; 5 articles (455 patients) included in meta-analysis	1. “to identify risk factors that may predict clinically significant findings on bronchoscopy in children with recurrent croup” 2. “to note the frequency of bronchoscopy findings in general”	TBM in 4.6% of children with recurrent croup	Heterogeneity between studies and lack of specificity in patient reporting. Selection bias of the patients.	Bronchoscopy
Hysinger	Review	Focus on TM	NA	1. “to distinguish congenital	Types of symptoms, natural	NA	NA

2015				TM from acquired TM”; 2. “to define respiratory mechanics that affect airway compliance”; 3. “to describe the formation and maturation of the paediatric central airway”; 4. “to describe advantages and disadvantages of the various methods of diagnosing paediatric TM”; 5. “to understand the current available treatment strategies for paediatric TM”	history, associated diseases		
Javia 2016	Review	Congenital/primary and acquired/secondary TM	Neonates	NA	Types of symptoms and clinical features, associated conditions	NA	NA
Keng 2017	Case report	NA	83-year-old woman	NA	Delayed onset of symptoms	Case report, adult patient	NA
Kompare 2012	Retro-spective, specialty clinic	Incl: <60 months of age with cough, wheeze, and/or noisy breathing present for at least 1 month without other diagnoses for whom BAL cultures grew at least 10^4 cfu/mL of a specific organism Excl: asthma, CF, and other chronic diseases TM or BM	70 children	“to examine associated findings and clinical outcome in young children with prolonged cough, wheeze, and/or noisy breathing in whom high colony counts of potentially pathogenic bacteria were cultured from bronchoalveolar lavage (BAL) during diagnostic flexible fiberoptic bronchoscopy”	TM in 20%, BM in 43% and TBM in 11% of patients with protracted bacterial bronchitis	Retrospective study, no control group	Flexible bronchoscopy using topical lidocaine and intravenous procedural sedation

		diagnosed when segmental collapse such that the airway narrowed to a slit during expiration in the absence of suction through the bronchoscope's channel.					
Kugler 2013	Review	TM in children and adults	NA	NA	Types of symptoms	NA	NA
Maeda 2017	Review	TM in children	NA	“to present the technical aspects of diagnosis and treatment of the most common paediatric airway disorders”	Types of symptoms	NA	NA
Masters 2002	Tertiary referral centre; observational study	Children with the endoscopic diagnosis of laryngomalacia, TM or TBM; TM defined as “a membranosa deformity in the trachea” BM defined as “an appearance of deformity in the large right or left main-stem bronchi, and/or their respective divisions at the lobar or segmental	299 children with malacia disorders	1. “to describe an extensive experience of various forms of laryngomalacia, tracheomalacia, and bronchomalacia” 2. “to explore some of the interrelationships that exist between these conditions with respect to their anatomical sites and associations”	Types of symptoms and clinical features, associated conditions	No detailed description of symptoms and signs	Flexible bronchoscopy during spontaneous breathing under gaseous general anaesthesia

		level.					
Masters 2008	Tertiary referral centre; case-control study	Children with chronic respiratory symptoms of cough, stridor, or wheeze present for >3 weeks that underwent bronchoscopy Malacia defined as a deformity of the airway recorded at the end-expiratory point	Cases: 81 children (0.2-12.4 years) Controls: 35 children (0.2-17.3 years)	“to prospectively examine the relationship between site and size of lesions with their respiratory symptoms and illness frequency”	Children with malacia have an increased likelihood of respiratory illness frequency, severity, significant cough, and tendency for delayed recovery. Neither the site nor the severity of malacia exhibited any significant dose effect on respiratory illness profiles.	Sample size	Bronchoscopy with spontaneously breathing oxygen and sevoflurane general anaesthesia
McNamara 2004	Review	Primary and secondary TM	NA	NA	Types of symptoms and clinical features, natural history	NA	NA
Peh 2006	Case report	NA	4-week-old infant	NA	Delayed onset of symptoms	Case report	Bronchoscopy
Peters 2005	Case report and review	NA	20-month-old boy	“to discuss the differential diagnosis and clinical evaluation, and propose a new pathophysiological mechanism by which obstructive sleep apnea causes TM”	Types of symptoms and clinical features	Case report	Bronchoscopy
Rohde 2005	Case report	NA	15-month-old boy	“to stress the importance of considering laryngo-tracheo-bronchomalacia as a cause of death in infancy and early childhood”	Types of symptoms	Case report	Autopsy
Santiago-Burruchaga 2014	Retrospective case-control	Incl: Children with recurrent pneumonia, chronic wet or	Cases: 62 children (12-144 months) Controls: 29	1. “to describe the bronchoscopic changes in children with recurrent lower airways infection”	Airway malacia in 52% of children with recurrent lower airway infection	Retrospective study; control group not normal healthy	Bronchoscopy on spontaneous breathing under sedation-analgesia

	cohorts study	<p>productive cough, persistent atelectasis, or bronchiectasis</p> <p>Excl: Bronchopulmonary dysplasia, prematurity, difficult to control asthma, CF, immunodeficiency, genetic syndromes, neuromuscular, CNS or heart disease, airways or digestive tract malformations, severe scoliosis, protracted endotracheal intubation, tracheotomy or endobronchial aspiration syndrome</p> <p>Airway malacia considered to be present when >50% dynamic collapse of the airways lumen during expiration on spontaneous breathing or during cough,</p>	children (5-168 months)	<p>2. “to investigate the prevalence of lower airway malacia”</p> <p>3. “to assess their prevalence in a control group without recurrent lower airways infection”</p>		children	and local anaesthesia
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		without suctioning					
Snijders 2015	Review	Congenital and acquired TM	NA	“to provide an update on diagnosis of TM in children”	Types of symptoms and clinical features	NA	NA
Vicencio 2006	Short review	TM	NA	NA	Types of symptoms and clinical features	NA	NA
Weinberger 2007	Review	TM	NA	“to increase awareness of common and uncommon entities that have resulted in inappropriate diagnoses of asthma”	Causes of cough in children with TM	NA	NA
Yalcin 2005	Tertiary referral centre; retrospective	Incl: Patients with chronic respiratory symptoms who underwent bronchoscopy between February 1999 and November 2003. Excl: Asthma, cystic fibrosis TM defined as an appearance of deformity and narrowing of the trachea’s cross-sectional area by, at least, more than 25% on expiration; BM defined as an appearance of deformity in the right or left main	34 children with TM and/or BM	1. “to review experience with flexible bronchoscopy for the assessment of TM and BM in children who presented with chronic respiratory problems” 2. “to evaluate their clinical and radiological characteristics and their association with other disorders”	Clinical presentation, associated disorders	Retrospective study	Bronchoscopy under mild sedation and topical anaesthesia

		bronchi, and/or their divisions at the lobar and segmental levels, and narrowing of their cross-sectional areas by, at least, more than 25% on expiration					
Zgherea 2012	Tertiary referral centre; retrospective	<p>Incl: Children with wet cough of more than 4 weeks' duration, unresponsive to therapy, referred for bronchoscopy</p> <p>Excl: Cystic fibrosis, primary ciliary dyskinesia, immunodeficiency syndromes, genetic syndromes, major airway abnormalities, muscle weakness, neurologic disorders, aspiration, asthma</p> <p>TM defined as collapse of at least 50% of the tracheal lumen during expiration</p>	197 children	<p>1. "to determine the frequency of lower respiratory tract bacterial infections in children with wet cough"</p> <p>2. "to analyse the bronchoscopic findings in these children"</p>	9 (14.1%) of children with purulent bronchitis and 6 (13.3%) of children with nonpurulent bronchitis had TM	Retrospective study; no reliable data on the prevalence of certain comorbidities; symptoms of children with TM not provided	Flexible bronchoscopy under light sedation

NA, not applicable;

LITERATURE REVIEW: QUESTION 4B

KQ 4b: In children with known TBM, what are the pulmonary function abnormalities?

1 st author, publication year	Setting; Study design	Inclusion criteria; Exclusion or definitions	Description of cohort	Main aim(s) of study	Primary findings relating to KQ	Main study limitation	Method of confirmation of TBM and type
Abdel 2007	Retro-spective	Incl: children with TM who had aortopexy Excl: aortic arch anomalies; TM not defined	N=20 mean age=29-mo (range 0.25, 11 years)	“Assess the efficacy of aortopexy in the long term, the clinical results and respiratory function...”	Tidal expiratory flow values (TEF25%); median of cohort estimated at 66.5 %pred (range 15, 103)	Data was estimated from the graph provided. No other PFT data provided	Flexible bronchoscopy, spontaneous breathing
Beardsmore 1994	Cohort	Incl; children with esophageal atresia-tracheoesophageal fistula presenting to surgical service; TM not defined	16 children in cohort but only 3 had TM confirmed	1. “Assess the relationship between clinical findings and respiratory function in infants following repairs of esophageal atresia-tracheoesophageal fistula; 2. Determine the value of respiratory function tests in elucidating mechanisms of respiratory disturbances and in predicting clinical outcome”	Increased (>2 z-score) total gas volume in 2 of the 3 children; Increased total airway resistance in 2 of the 3 children	TM undefined	In one child, endoscopic confirmation mentioned; other 2 method not described
Boogaard 2005	Cross section	TM=“collapse of at least 50% of the airway lumen, during expiration, cough or spontaneous breathing, or a ratio of cartilage to membranous wall area of < 3:1”	45 of the 115 children with TM had PFT. Mean age of this group not described	1. Estimate the incidence of primary TBM 2. Estimate the predictive value of a clinical diagnosis of TBM by pediatric pulmonologists 3. Characterize symptoms and findings in patients with primary TBM	Mean % pred (SD) FVC=99.3 (15.9) FEV ₁ =91.5 (19.9) FEV ₁ /FVC=87.7 (14.2) PEF=74.7 (19.4) MEF ₂₅ =62.2 (31.3) Pre and post broncho-dilation undertaken in 35, all values showed increased in mean values but no significant change	Proportion with FVC and FEV ₁ abnormality not provided	Flexible bronchoscopy; primary TM

Davis 1998	Cross section	TM=50% tracheal narrowing at bronchoscopy	6 infants (3- 10 mo old) with moderate to severe TM; Controls: 2- 12 mo old	In children with TM, to determine whether the increase in V'max FRC with CPAP could be explained by the increase in FRC with CPAP (0, 4, 8 cm H ₂ O)	<u>Children with TM</u> Mean FVC=104%pred (SD 10) Mean V'50=56%pred (SD 18) Mean V'75=53%pred (SD 17) <u>Controls</u> Mean FVC=93%pred (SD 21) Mean V'50=112%pred (28) Mean V'75=108%pred (23)		Bronchoscopy (type undefined)
Johnston 1980	Pre, post Sx, Case study	NA; TM undefined	Child with R ligamentum arteriosum, L aortic arch, R descending aorta	To study animal model of tracheomalacia and describe 2 children with symptomatic TM	After stenting- expiratory total pulmonary resistance decreased by 104%; inspiratory equivalent changed by 1% (PFT at ~18 mo)	2 children but only 1 with PFT data. Child also had VSD and tracheostomy decannulated after TM stented	Bronchoscopy (type unspecified); vascular ring divided at 3-mo followed by external rib stent over TM at 12 mo
Moore 2012	Cross section	Incl: Children with TBM (21 of 66 invited participated Excl: laryngomalacia; TM undefined	19 children; median age 9.4 years (range 7.6– 14.3)	To determine “whether children with TBM have persisting respiratory symptoms and/or definable abnormalities of lung function on long-term follow-up”	Mean %pred (95%CI), no abnormal in cohort FEV ₁ =81% (72, 91), 7 FVC=96% (87, 105), 4 FEV ₁ /FVC%=73 (67, 78), 13 FEF ₂₅₋₇₅ =54% (43, 64), 15 PEF=60% (49, 70), 14 Classical TBM flow-volume loop seen in 4 (22%) Mannitol challenge negative in 13 of 15 (93%); 1 of 2 had significant bronchodilator responsiveness		Flexible bronchoscopy
Olbers 2015	Cross section	Inclusion: children born with esophageal atresia who have reached aged 7 years; TM undefined	Group of 13 of 26 children who had TM	1. Assess the prevalence of respiratory morbidity in children born with esophageal atresia 2. Examine the cause this morbidity using pulmonary and esophageal function tests.	Of those with known TM (n=13), 3 had FEV ₁ /FVC below 2 SD, 10 had FEV ₁ /PEF ratio of >8	Other PFTs in TM group not described and TM undefined	Authors stated “diagnosis of TM requires X-ray findings or bronchoscopy”; that was not routinely but done in many

Panitch 1990	Case study	3 children in series but only 1 included as 2 had other concurrent significant lung disease and tracheostomy; TM undefined	Child with repaired laryngo-trachea-esophageal cleft repaired at 1-mo	To study pulmonary mechanics of 3 children with intrinsic TM after bronchoconstrictor and bronchodilator	Reduced (V'maxFRC) c.f. published norms; Methacholine improved V'maxFRC by 14.4%, Albuterol reduced V'maxFRC by 31.6%; saline did not alter VmaxFRC.	Changes described may not be specific to TM{57}	Rigid bronchoscopy
Shell 2001	Case study		Child with TM related to innominate artery compression		Sx to rotate aorta anteriorly and to the left; Pre Sx FEF25-75=28%, post=69%; Pre Sx V'maxFRC=19%, post=57%; Pre Sx FVC 114%, post 116%		Fluoroscopy followed by MRI
Uchida 2009	Case series	NA; TM undefined	3 children with double aortic arch	Description of 3 children mistreated as poorly controlled asthma whereby analysis of flow-volume curve suggested diagnosis	Flow-volume curves #1: plateau of expiratory limb #2: plateau of inspiratory and expiratory limbs #3: plateau of expiratory limb	TM undefined	Chest CT with angiogram showing airway compression (undefined)
Weber 2002	Retro-spective	Children with life-threatening TM who had aortopexy; TM undefined	8 of the 32 in cohort had PFT done (not specifically described)	To report on children with life-threatening TM treated with aortopexy	FEV ₁ pre-aortapexy=52% pred, SD 4% post=82% ± 3% post PFT undertaken 2 weeks to 3-mo post aortopexy		Rigid or flexible bronchoscopy spontaneous breathing

CPAP= continuous positive airway pressure; Excl=exclusion; Incl=inclusion; mo=months; NA=not applicable; PFT=pulmonary function test; pred=predicted; Sx=Surgery; TBM=trachea-broncho-malacia; TM=tracheomalacia; V'maxFRC=maximal flow at functional residual capacity

Summary of data

- Lung function cannot be used to diagnose TBM but provides supportive diagnosis
- Sensitivity and specificity of any PFT cannot be determined
- Although many studies show some have a degree of expiratory airway obstruction; not all have.
- Obstruction pattern defined by reduction in FEV1, V'max FRC, PEF, MEF, TEF, airway resistance, abnormality in flow-volume loops
- FVC not affected or may be elevated, TGV elevated
- AHR present in some children

Limitation of data

- Need PFT related to TBM severity;
- Limited studies- many small number; only 2 cohorts

LITERATURE REVIEW ON QUESTION 5 - RADIOLOGY

How do we use imaging to diagnose TM & BM? [to include tracheobronchography]

1 st author, publication year	Setting; study design	Inclusion criteria; exclusion or definition	Description of cohort	Main aim(s) of study	Primary findings relating to KQ	Main study limitation	Method of confirmation of TBM and type
Austin J, 2003	Review	Do not describe papers search					
Berrocal T, 2004	Review	Do not describe papers search					
Fraga JC, 2016	Review	Do not describe papers search					
Sanchez MO, 2012	Prospective study	Children with a suspected airway abnormality and with clinical symptoms including stridor, chronic cough, recurrent pneumonia, persistent pulmonary infiltrates or atelectasis.	22 children underwent fluoroscopy and Flexible Bronchoscopy (FB). TM was found in 21 children by FB.	To study sensitivity, specificity and predictive ratios of airway fluoroscopy compared with FB.	Fluoroscopy detected TM in 5/21 children. Airway fluoroscopy was poorly sensitive (23.8%) but highly specific (100%) and positive likelihood ratio was 8.6	Small cohort of children	Flexible Bronchoscopy
Berg E, 2008	Retrospective study	Children with stridor who underwent both endoscopy and fluoroscopy within a 5y time period.	39 children, endoscopic findings: 13 with airway stenosis, 11 with laryngomalacia, 7 with airway mass lesion, 5 with tracheomalacia.	To determine the sensitivity and specificity of airway fluoroscopy in the diagnosis of pediatric laryngotracheal abnormalities.	The sensitivity of fluoroscopy in the diagnosis of laryngomalacia, TM, airway stenosis, and an airway mass was 27%, 20%, 69%, and 43%, respectively. The specificity	Small cohort of children. The sample sizes within each diagnostic subgroup were even smaller (eg, there were only 5 patients in the tracheomalacia group).	Endoscopy

					for the same diagnoses was 100%, 94%, 100%, and 100%, respectively. Airway fluoroscopy appeared to have low sensitivity but high specificity in detecting airway abnormalities.		
Lee EY, 2008	Case series (Retrospective review and analysis of radiologic and clinical data)	Infants with mediastinal aortic vascular anomalies referred for paired inspiratory-expiratory MDCT.	5 symptomatic infants underwent paired inspiratory – expiratory MDCT, while 4 underwent bronchoscopy as well.	To assess the feasibility of paired inspiratory – expiratory MDCT for evaluating TM among symptomatic infants with mediastinal aortic vascular anomalies.	TM was confirmed in 3 out of 5 infants at the level of mediastinal aortic vascular anomaly. The CT results were concordant with the results of bronchoscopy in all patients who underwent bronchoscopy.	Limited cohort	Bronchoscopy
Lee EY, 2008	Retrospective study	Pediatric patients with respiratory symptoms who underwent paired inspiratory- expiratory MDCT and were diagnosed with	15 children, underwent paired inspiratory-expiratory MDCT, while 9	To determine the prevalence of TM associated with different types of mediastinal	8 of 15 patients diagnosed with TM, results concordant with Bronchoscopy. Symptomatic	1. Small cohort. 2. Not equal number of cases from each type of vascular	Bronchoscopy and/or paired inspiratory-expiratory MDCT

		mediastinal aortic vascular anomalies.	underwent bronchoscopy as well.	aortic vascular anomalies in symptomatic children using paired inspiratory-expiratory MDCT.	pediatric patients with mediastinal aortic vascular anomalies have a relatively high prevalence of TM. Paired inspiratory-expiratory MDCT should be considered part of the routine preoperative evaluation of TM.	3. Retrospective study.	
Ngerncham M, 2015	Retrospective study	Infants who had esophageal atresia (EA) and underwent MDCT as preoperative evaluation of TBM prior to aortopexy.	18 patients underwent paired inspiratory-expiratory MDCT.	To compare paired inspiratory-expiratory MDCT with intraoperative Diagnostic Laryngoscopy and Bronchoscopy (DLB) in the assessment of TBM in symptomatic pediatric patients with EA.	Overall diagnostic accuracy of dynamic airway MDCT compared to DLB was 91%. MDCT is highly accurate and reliable non-invasive modality for evaluating TBM.	1. Small population size. 2. Retrospective nature of study. 3. No normal control group to be compared.	Intraoperative Diagnostic Laryngoscopy and Bronchoscopy
Lee EY, 2009	Review	Do not describe papers search					
Long FR,	Retrospective	Pediatric patients,	87 children	To describe the	Full inflation	1. Retrospective	Controlled-ventilation

2001	study	who underwent conscious sedation and controlled-ventilation CT (CVCT) of the chest over a 2-year period, because they could not cooperate with breath holding.	underwent conscious sedation and CVCT of the chest.	technique and utility of a non-invasive method called controlled-ventilation CT (CVCT) for obtaining motion-free full-inflation and end-exhalation images of the lung in infants and young children.	CVCT was useful in evaluating tracheal and bronchial stenosis, bronchial wall thickening, early bronchiectasis, bronchial fistula, extend of interstitial fibrosis and lung nodules. End exhalation CVCT was useful in evaluating TM and air trapping.	<ol style="list-style-type: none"> study, which did not compare prospectively the CVCT with the quiet breathing technique. CVCT requires the use of sedation. 	CT
Goo HW, 2013	Retrospective study	Pediatric patients with TM who underwent free-breathing cine-CT.	27 children with bronchoscopic evidence of TM, and a control group (n=320) underwent free breathing cine-CT.	To investigate the accuracy of free breathing cine-CT for diagnosis of TM in young children with bronchoscopy as reference standard.	If a cross sectional area change of the trachea of 31.6% was used as a cut-off value for the diagnosis of TM the sensitivity, specificity and accuracy of cine-CT were 96.3% (26/27), 97.2% (311/320) and 97.1% (337/347), respectively.	<ol style="list-style-type: none"> Bronchoscopy not performed in controls. Only a few slices of the entire trachea were evaluated. A reproducibility study of the measurements was not performed. Sedation might influence tracheal collapse on 	Bronchoscopy

					Free-breathing cine-CT has potential to provide the diagnosis of TM in young children.	cine-CT.	
Tan JZ, 2013	Case series (Retrospective study)	Pediatric patients with complex clinical respiratory presentation who were referred for dynamic assessment of their airways, at a tertiary paediatric centre.	8 infants: 4 with TM, 4 without tracheobronchial abnormalities (proved with bronchoscopy or bronchography). All underwent dynamic volumetric CT (four-dimensional technique).	To evaluate the dynamic volumetric CT (four-dimensional technique) in the assessment of the paediatric airway.	Volumetric CT enables four-dimensional assessment for paediatric TBM without intubation or patient cooperation and at low radiation dose.	Retrospective study with a small sample group.	Bronchoscopy or Bronchography
Greenberg SB, 2014	Retrospective study	Infants with congenital heart disease who underwent Dynamic Pulmonary CTA (DP-CTA) for evaluation of unexplained persistent respiratory distress.	23 infants with congenital heart disease and persistent respiratory distress: 17 with TBM proved by DP-CTA (cine-CT).	To evaluate the efficacy of DP-CTA to provide unique information for patient care in newborns and infants with congenital heart disease and persistent respiratory distress.	DP-CTA is uniquely suited for comprehensive and simultaneous evaluation of airway and vascular abnormalities in infants.	1. Small cohort. 2. Comparative bronchoscopies not performed in enough patients. 3. No long term follow up available.	Dynamic Pulmonary CTA (Cine-CT)
Lee S, 2014	Retrospective study	Infants who underwent both chest CT and bronchoscopy within 1 week.	17 infants who underwent both bronchoscopy and 3D-CT-bronchoscopy:	To evaluate the use of a non-breath held 3D-CT bronchoscopy	In 10 children TM was confirmed. Sensitivity was <75% in	1. 11/17 bronchoscopies were performed after CT and	Flexible Bronchoscopy

				in detecting TBM in infants.	detecting laryngomalacia, TM and BM. Specificity and PPV was 100% in layngomalacia and TM.	<p>the pulmonologist was not blinded.</p> <p>2. Diffuse airway narrowing is difficult to detect in the VR images.</p> <p>3. A selection bias may have occurred from excluding the patients with severe artifacts in the CT scan.</p> <p>4. Small cohort of infants.</p>	
Su SC, 2017	Prospective study	Children aged<18 years scheduled for having both FB (Flexible Bronchoscopy) and MDCT.	53 children evaluated for airway abnormalities: TM was confirmed in 37 at FB.	A Comparison of Virtual Bronchoscopy (VB) versus FB in the Diagnosis of TBM in Children. To determine sensitivity, specificity, PPV and NPV.	VB detected TM in 20patients. Sensitivity of 54.1% (95%CI 37.1–70.2), Specificity 87.5% (95%CI 60.4–97.8), and positive predictive value 90.9% (95%CI 69.4-98.4). VB cannot replace FB as gold standard for detecting TBM in children.	<p>1. Preselection of patients with a diagnosis of TBM.</p> <p>2. Duration of anesthesia was longer by the time FB occurred.</p> <p>3. 7 children who underwent MDCT without sedation received gaseous anesthesia for FB.</p>	Flexible Bronchoscopy

						4. Inability to standardized lung volumes and airway pressure during FB and VB.	
Deacon JWF, 2017	Retrospective study (Data were collected retrospectively by reviewing the medical record files)	Pediatric patients with TM, confirmed by rigid laryngobronchoscopy, over a 3,5-year period.	71 pediatric patients with TM: 28 had chest CTA.	To describe the clinical presentation of children with TM and to analyse the benefits to patient management of investigations used in the diagnosis and imaging of TM.	Rate of TM detection on CTA is 42,9%	Hospital records reviewed was variable and sometimes incomplete.	Rigid laryngobronchoscopy
Lee EY, 2010	Retrospective study (Retrospectively and randomly identify pediatric patients)	All pediatric patients who underwent paired inspiratory and expiratory MDCT studies for the evaluation of clinically suspected TM, on the basis of clinical signs and symptoms.	20 standard-dose and 20 reduced-expiratory dose, paired inspiratory-expiratory MDCT studies performed for the evaluation of suspected TM in paediatric patients (aged <18 years).	To assess the effects of radiation dose reduction on the assessment of the tracheal lumen on expiratory MDCT images of pediatric patients referred for evaluation for TM.	TM was diagnosed by CT in 7 patients who underwent standard-dose and 6 patients who underwent reduced-dose paired inspiratory-expiratory MDCT studies. CT results were concordant with the results of bronchoscopy in all 32 patients who underwent	1. Retrospective study. 2. Subjective grading of the confidence level in measuring the tracheal lumen. 3. Different machines used in the population.	Bronchoscopy

					both procedures. The radiation dose can be reduced by 23% while maintaining similar diagnostic confidence for assessment of the tracheal lumen compared to a standard-dose technique in pediatric patients.		
Javia L, 2016	Review	Do not describe papers search.					
Faust RA, 2001	Prospective, controlled study	Pediatric and adult patients, with respiratory symptoms scheduled for having both Endoscopy and cine-MRI.	A cohort of 10 pediatric patients, 10 adult patients, and 10 normal volunteers: underwent static MRI, as well as cine-MRI.	To investigate the feasibility of using cine-MRI techniques to dynamically image the human airway and to assess laryngeal and tracheal patency and function.	The imaging findings correlated with patient's endoscopy. TM was depicted in 8 pediatric patients. Airway cine-MRI has the potential to provide novel data regarding laryngeal and tracheal patency and function.	Small cohort of children.	Endoscopy
Faust RA,	Case series	Pediatric and adult	2 pediatric + 1	To apply cine-	Both techniques	Very limited	Bronchoscopy

2002		patients in respiratory distress underwent both bronchoscopy and cine-MRI.	adult patients underwent both bronchoscopy and cine-MRI.	MRI to evaluate patients with respiratory distress who exhibited tracheal compression at the level of the innominate artery.	confirmed TM in all cases, mainly at the level of the innominate artery. Cine-MRI provides extremely rapid acquisition for functional imaging of tracheal patency during the respiratory cycle, while it may provide additional insight into innominate artery compression syndrome.	cohort.	
Ciet P, 2014	Retrospective study (Retrospective image analysis)	Children suspected of having TBM underwent cine-MRI.	12 children underwent cine-MRI: TBM was diagnosed in 7.	To evaluate the feasibility of spirometer-controlled cine-MRI as an alternative to cine-CT.	TBM was diagnosed in 7, confirmed with bronchoscopy or chest CT. Spirometer controlled cine-MRI is a promising technique to assess TBM in children and has the potential to replace	1. Retrospective study. 2. Limited cohort.	Flexible Bronchoscopy or chest CT

Rimell FL, 1997					bronchoscopy.		
	Retrospective study (Study was based on a chart review)	Children with various distal airway disorders over a 3-year period, who underwent MRI for the evaluation of the airway.	49 children: 45 underwent both endoscopy and MRI, while 14 underwent fluoroscopy as well.	To determine the role of MRI and how it relates to endoscopy as well as to other imaging modalities in the evaluation of pediatric airway disorders.	Discrepancies between MRI and endoscopy noted in 7, while 2 false negative results noted in fluoroscopy. Magnetic resonance imaging was the most accurate modality in defining extrinsic airway abnormalities. Fluoroscopy combined with barium swallow plays an important role as a screening examination.	1. Retrospective study. 2. No detailed description of TBM patients.	Bronchoscopy

QUESTION 6: LITERATURE REVIEW BRONCHOSCOPY

The role of bronchoscopy to diagnose and grade TB and TB

1 st author, publication year	Setting; Study design	Inclusion criteria; Exclusion or definitions	Description of cohort	Main aim(s) of study	Primary findings relating to KQ	Main study limitation	Method of confirmation of TBM and type
Lee 2007	Case series	Children with MAVA referred for paired inspiratory-expiratory MDCT	N=5 mean age 4.1-mo (range 2 weeks – 6 months)	To assess technical feasibility of paired inspiratory-expiratory MDCT for evaluating TM among infants with MAVA	In patients who underwent bronchoscopy there was concordance between bronchoscopic findings and MDCT findings	1. Small number of patients 2. The technique require cooperation	FB, spontaneous breathing
Sanchez 2012	Case series	Children with a suspected airway abnormality and with clinical symptoms including stridor, chronic cough, recurrent pneumonia, persistent pulmonary infiltrates or atelectasis	22 children median age 33 months range 1-187. (4 with inspiratory, 2 expiratory and 8 biphasic stridor, 13 chronic wheeze, 8 cyanotic episodes)	To study sensitivity, specificity and predictive ratios of airway fluoroscopy compared with FB	TM was found in 21 children, fluoroscopy detected TM in 5 children. Airway fluoroscopy was poorly sensitive (23.8%) but highly specific (100%) and positive likelihood ratio was 8.6	Small cohort of children	FB
Lee 2013	Case series Retrospective study	Infants under 12 months old who underwent both chest CT and bronchoscopy within 1 week	17 patients mean age 2 months, range 1-11 months.	To evaluate the use of a non-breath held 3D-CT-bronchoscopy to detecting TM in infants	In 10 children TM was confirmed. Sensitivity was <75% in detecting laryngomalacia, TM and BM. Specificity and PPV was 100% in	1. 17 bronchoscopies were performed after CT and the pulmonologist was not blinded. 2. Diffuse airway narrowing is difficult to detect in the VR images. 3. A selection bias may	FB

					layngomalacia and TM	have occurred from excluding the patients with severe artifacts in the CT scan	
Su 2016	Case series	Children aged <18 years scheduled for having both FB and MCDT, undertaken 30-min to 7-days of each other.	56 children median age 2.5 years, range 0.8-14.3 years.	To determine sensitivity, specificity, PPV and NPV of VB compared to FB in diagnosis TBM	VB cannot replace FB as gold standard for detecting TBM in children	1.Preselection of patients with a diagnosis of TBM 2. Duration of anesthesia was longer by the time FB occurred. 3. 7 children who underwent MDCT without sedation received gaseous anesthesia for FB 4. Inability to standardized lung volumes and airway pressure during FB and VB	FB
Carden 2005	Review	Do not describe papers search					
Snijders 2015	Review	Do not describe papers search					
Kugler 2014	Review	Do not describe papers search					
Masters 2009	Review	Do not describe papers search					
Wright 2003	Review	Do not describe papers search					
Austin 2003	Review	Do not describe papers search					
Fraga 2016	Review	Do not describe papers search					
Yie Tan 2011	Review	Do not describe papers search					

Nemes 2014	Review	Do not describe papers search					
Masters 2008	Prospective case control study	Children with CRS of cough, stridor or wheeze present for > 3 weeks who underwent FB.	Patients: 116 children (77 male), 81 with TM, median age 2.1 years, range 0.2 -17.3 years. Controls: 31 healthy children	Prospectively examine relationship between TM lesions and their respiratory illness profile	The RR of illness frequency was 2.1 (95% CI 1.3 to 3.4) and of significant cough 7.2 (95% CI 1.01 to 27.22) for the malacia group while the CARIFS day 1 score was 1.66 (95% CI, 1.1 to 2.56) compared to control subjects. Malacia type and severity of lesions were not associated with increased rates of illness or worse clinical profile	<ol style="list-style-type: none"> 1. The tools for the bronchoscopic measurement. 2. Clinical illness outcome scales. 3. Sample size 	FB under sevoflurane general anesthesia. End expiratory airway images were recorded 10 mm from the object and were measured using histogram mode technique.
Majid 2014	Prospective observational pilot study	Adult patients with suspected TM	10 adult patients (median age 65 years, 6 female) with suspected TM	To test inter and intra observer agreement (23 pulmonologist) of dynamic FB data estimating the degree of TB collapse obtained at five different sites during exhalation or excessive dynamic airway collapse.	Inter and intra observer correlation coefficients were: PT 0.85 (0.002) and 0.92 (<0.001); MT 0.68 (0.03) and 0.82 (0.004); DT 0.89 (<0.001) and 0.95 (<0.001); RMSB 0.72 (0.02) and 0.8 (0.02); LMSB 0.92 (<0.001) and 0.96 (<0.001).	<ol style="list-style-type: none"> 1. Video images that are susceptible to distortions 2. Lumen size was estimated by antero-posterior diameter and not quantitatively measured by cross-sectional area. 3. Small number of adult patients 	Dynamic FB
Asai 2001	Case report	A child who presented airway	A 22 month old child with an	Description of a case of airway obstruction with	Obstruction due to TBM during	One case	FB

		obstruction due to TM during emergence from anesthesia.	erythematous lesion on the right arm scheduled for resection of the cutaneous lesion under anesthesia with sevoflurane	hypoxia during emergence from anesthesia due to unexpected TBM	emergence from anesthesia		
Oh 2002	Case report	A child who presented unexpected TM after beginning of the operation	A 12 yr old boy with MS who was scheduled for a spine fusion operation because of scoliosis under general anesthesia	Description of a case of TM in a child with MS who undergo surgery for scoliosis	Obstruction due to TM after beginning operation	1. One case 2. No description of general anesthesia	FB
Okuda 2000	Case report	A child who presented airway obstruction during induction and after anesthesia	A 1 yr old girl with suspected congenital TM scheduled for FB under GA with secifluorane	Description of a case of TM who undergo FB for a suspected congenital TM	Obstruction during induction and after GA	1. One case	FB
Eastwood 2002	Case series	Adult patients recruited from those undergoing minor surgical procedures not involving the head or neck and suitable for GA administered via a face mask	16 adult subjects while supine and spontaneously breathing on nasal positive airway pressure	To measured collapsibility of upper airways in spontaneously breathing during inhalational anesthesia with isoflurane in order to examine the site and mechanism of collapse and the influence on them of anesthetic depth	Isoflurane anesthesia is associated with decreased muscle activity and increased collapsibility of the upper airway	1. Small number of patients 2. Difficulties in the application of the technique	LFT
Eastwood	Case series	Adult patients	12 white adult	1. To determine	Increasing depth of	1. Small number of	LFT

2005		recruited from those undergoing minor surgical procedures not involving the head or neck	volunteers	<p>the effect of varying concentrations of propofol on upper airway collapsibility and the mechanisms responsible for it.</p> <p>2. To identify the effects of anesthesia on central respiratory drive to upper airway dilator muscles</p> <p>3. To determine whether a sufficient dose of propofol could produce complete flaccidity of the upper airways</p>	propofol anesthesia is associated with increase collapsibility of the upper airway	<p>patients</p> <p>2. Difficulties in the application of the technique</p>	
Hillman 2009	Case series	Adult healthy volunteers	9 healthy adult volunteers	To determine how upper collapsibility changes during slow stepwise induction on anesthesia with propofol	The progression of effects during slow stepwise induction of anesthesia with propofol does not occur in smooth continuity but disproportionate changes in upper airway collapsibility in a	<p>1. Small number of patients</p> <p>2. Difficulties in the application of the technique</p>	LFT

					narrow propofol concentrations in each subjects		
Masters 2005	Case series	1. Reliability testing: children who had undergone FB for chronic cough 2. In vivo measurement: children who undergone FB for protracted or chronic cough and or wheeze	1. Reliability testing: 18 children, median age 30 months, range 2-127 months 2. In vivo measurements: 35 children > 3 months of age.	1. To describe a new method to define and measure airway lumen using a FB and a computer software. 2. Describe intra and inter-observer reliability, validation and application of the technique 3. Compare airway size measurements using different methodologies.	1. Validation results showed very high levels of agreement of measurements at all distance 2. Good inter and intra observer reliability 3. The cross sectional area assessed at low light intensity is more likely to be representative of the true cross sectional area than that captured at normal operating light	Factors that govern tissue reflectance and absorption of light during the respiratory cycle while under anesthesia can be compounded by the physical effects of the instruments, the type of light, airway suctioning, and disease processes	FB and computer
Okazaki 2004	Case series	Infants with and without TM	Cases: 8 infants with TM Controls: 4 infants without TM	Static pressure/area relationships of the trachea in infants with TM were obtained and tested if the relationship quantitatively describes collapsibility of the trachea	Tracheal collapsibility of infants with TM can be quantitatively assessed by the static pressure/area relationship of the trachea	1. Insufficient control of tracheal smooth muscle tone that could be influenced by anesthesia 2. Overestimation of the lower airway pressure area because the collapsibility site may have shifted to the endoscope tip with the pressure decrease 3. Difficult to estimate	FB and LFT

						<p>the relative contribution of tracheal stenosis because the method only assesses collapsibility of the trachea</p> <p>4. Deformation of endoscopic image is inevitable for obtain a wide angle view</p> <p>5. Small number of patients</p>	
Loring 2006	Case series	Adult patients referred to FB for suspected TBM	<p>Patients: 80 adult patients (34 men), mean age 63 year, range 29-94 years</p> <p>Controls: 4 adult healthy volunteers (2 men, age range 33-47 years)</p>	To quantify central airway collapsibility and relate it to expiratory flow limitation in patients with TBM	In TBM central airway collapse is not closely related to airflow obstruction and expiratory flow limitation at rest often occurs in peripheral airways without central airway collapse.	<p>1. Small number of patients</p> <p>2. The trachea transmural pressure may have been affected by the presence of the bronchoscope and local anesthetic solution</p> <p>3. The method may overestimates airway size and underestimates airway narrowing</p>	FB and LFT
Negercham (2015)	Case series. Retrospective study	Infants who had esophageal atresia who underwent MDCT as preoperative evaluation of TBM prior to artopexy	18 children (8 male), median age 8 months, range 1month-11 years.	To compare MDCT with intraoperative FB in the assessment of TBM in children who had esophageal atresia	MDCT is highly accurate and reliable non invasive modality for evaluating TBM	<p>1. MDCT depends on patient cooperation.</p> <p>2. Radiation exposure</p>	MDCT and RB
	Review						

MDCT: multidetector CT, MAVA: mediastinal aortic vascular anomalies, TM: tracheomalacia, BM: broncomalacia, VR: volume rendering, TBM: trachea bronchomalacia, CRS: chronic respiratory symptoms, RR: relative risk, TB: tracheobronchial, DAC: dynamic airway collapse, PT: proximal trachea, MT: mild

trachea, DT: distal trachea, RMSB: right main stem bronchus, LMSB: left main stem bronchus, MS: Marfan syndrome, GA: general anesthesia, LFT: lung function testing, RB: rigid bronchoscopy

QUESTION 8

Respiratory physiotherapy systematic search

Search terms

Tracheomalacia OR bronchomalacia OR tracheobronchomalacia OR malacia OR tracheal abnormalities OR tracheal diseases

AND

Physiotherapy OR physical therapy OR physical therapy modalities OR airway clearance OR positive pressure and physiotherapy

Exercise tolerance OR exercise therapy

Administration inhalation OR nebulisation OR saline solution hypertonic OR deoxyribonuclease I OR nebulised dornase alfa OR nebulised hypertonic saline

Tracheomalacia and physiotherapy

Title	Authors	Journal, Date	DOI/PMID	Type	Language	N
Interventions for primary (intrinsic) tracheomalacia in children	Masters IB, Chang AB.	The Cochrane Library 2005, Issue 4	10.1002/14651858.CD005304.pub2	Systematic review	EN	0 studies
Interventions for primary (intrinsic) tracheomalacia in children.	Goyal V, Masters IB, Chang AB.	Cochrane Database Syst Rev. 2012 Oct 17;10:CD005304	10.1002/14651858.CD005304.pub3	Systematic review	EN	1 study
Recombinant human DNase in children with airway malacia and lower respiratory tract infection	Boogaard R, de Jongste JC, Vaessen Verberne AA, Hop WC, Merkus PJ.	Pediatr Pulmonol. 2009 Oct	10.1002/ppul.21073	RCT	EN	40
Positive expiratory pressure to enhance cough effectiveness in tracheomalacia	Sirithangkul S, Ranganathan S, Robinson PJ, Robertson CF.	J Med Assoc Thai. 2010 Nov;93 Suppl 6:S112-8.	21280523	Observational case-control study	EN	40
Effect of continuous positive airway pressure on forced expiratory flows in infants with tracheomalacia	Davis S, Jones M, Kisling J, Angelicchio C, Tepper RS.	Am J Respir Crit Care Med 1998;158:148-152	10.1164/ajrccm.158.1.9711034	Observational prospective study	EN	6
Paediatric chronic suppurative lung disease: clinical characteristics and outcomes	Goyal V, Grimwood K Marchant JM, Masters IB, Chang AB.	Eur J Pediatr. 2016 Aug;175(8):1077-84	10.1007/s00431-016-2743-5	Retrospective study	EN	22 (41% TM)
Tracheomalacia and Tracheobronchomalacia in Children and Adults	Carden KA, Boiselle PM, Waltz DA, Ernst A.	Chest. 2005 Mar;127(3):984-1005.	10.1378/chest.127.3.984	Review	EN	
Primary bronchomalacia in infants and children	Finder JD	J Pediatr. 1997 Jan;130(1):59-66	9003852	Retrospective study	EN	17

LITERATURE REVIEW Tracheomalacia and physiotherapy

1st author, publication year	Setting; Study design	Inclusion criteria; Exclusion or definitions	Description of cohort	Main aim(s) of study	Primary findings related to KQ	Main study limitation	Method of confirmation of TBM
Finder, 1997	Retrospective	not specified	N = 17, mean age = 38 mo (range 3 mo - 17 y) with bronchomalacia	To determine the natural history of primary bronchomalacia	All patients had physiotherapy. All patients aged more than 5 years had exercise limitation	Descriptive study	Bronchoscopy
Goyal, 2012	Systematic review	RCTs related to symptoms associated with primary or intrinsic TM	1 study examined about role of rDNase	To evaluate the efficacy of medical and surgical therapies for children with intrinsic (primary) TM	No RCTs identified about role of physiotherapy	Related to symptoms rather than the impact of physiotherapy	not specified
Davis, 1998	Cross-sectional	TM=50% tracheal narrowing at bronchoscopy	N = 6, mean age 6.8 mo (range 3-10 mo) with moderate to severe TM; Controls: N = 5, mean age 6.4 mo	In infants with TM, to determine whether the increase in V'max FRC with CPAP could be explained by the increase in FRC with CPAP (0, 4, 8 cm H ₂ O)	continuous positive expiratory pressure (CPAP) increases maximal expiratory flow at functional residual capacity secondary to increasing lung volume	Small cohort	Bronchoscopy
Sirithangkul, 2010	Observational case-control study	Incl. children with OA/TOF with corrective surgery; Excl. complex congenital abnormalities (spinal deformity, congenital heart disease or neurological impairment)	N = 40, mean age 12.5 y (range 8 - 18 y); Controls: N = 21, mean age 13.1 y	To determine the effectiveness of increasing levels of PEP during coughing to enhance expiratory flow and improve efficiency of the cough in children with TOF	<u>Children with TOF:</u> PEP=5: +18.8% increase CEF25-75 PEP=10: +11.7% increase CEF25-75 PEP=15: +0.5% increase CEF25-75 PEP=20: -2.4% decrease CEF25-75 <u>Controls:</u> PEP=5: -3.1% decrease CEF25-75 PEP=10: -6.3% decrease CEF25-75 PEP=15: -22.2% decrease CEF25-75 PEP=20: -19% decrease CEF25-75	CEF25-75 were calculated from cough flow-volume curve	History, clinical symptoms

LITERATURE REVIEW QUESTION 9: STENTS

1 st author, publication year	Study design	Number of patients	Type(s) of stent	Outcome (survival at time of report)	Complications	Attempted stent retrieval	Main study limitation
Soong 2018	retrospective	unclear (>21)	BEMS	unclear for TBM patients	tracheal perforation at time of stent removal, granulation tissue, infection, stent fracture	optional	data combined with stenting for other indications
Sztano 2016	retrospective	3	absorbable	2/3, 67%	stent fragmentation, infection, airway obstruction	required for complications	small series presented as review of complications
Anton-Pacheco 2016	retrospective	3	absorbable	3/3, 100%	granulation tissue	no	small series
de Trey 2016	retrospective	15	BEMS, absorbable	11/15 (73%)	stent fracture, infection, airway obstruction	optional (28%)	data combined with stenting for vascular compression
Anton-Pacheco 2008	retrospective	19	BEMS, silicone (Dumon™, Polyflex™)	unclear for TBM patients	stent migration, granulation tissue, infection	optional	data combined with stenting for other indications
Yang 2006	retrospective	3	not stated	1/3 (33%)	not stated	1/3	small series, poor description of patients
Airway Reconstruction team 2005	retrospective	2	BEMS	2/2 (100%)	not stated	unclear	small series
Valerie 2005	retrospective	14	BEMS	13/14 (93%)	death during stent removal	9/14 (64%)	small series
Geller 2004	retrospective	9	BEMS	5/9 (55%)	airway haemorrhage, infection	no	small series
Nicolai 2001	retrospective	4	BEMS, SEMS	1/4 (25%)	pneumomediastinum, difficult stent removal, granulation tissue, stent	yes	small series

					collapse with coughing granulation tissue		
Furman 1999	retrospective	2	BEMS	1/2 (50%)		no	small series
Filler 1998	retrospective	8	BEMS	8/8 (100%)	granulation tissue	6/8 (75%)	small series
Tsugawa 1997	retrospective	2	SEMS	2/2 (100%)	stent too short	1/2 (50%)	small series, experimental device (not available for clinical use)
Santoro 1995	retrospective	3	BEMS	1/3 (33%)		no	small series
Mair 1990	retrospective	2	SEMS, plastic polymer	1/2 (50%)	infection	no	small series, experimental device (not available for clinical use)

TBM = tracheobronchomalacia; BEMS = balloon-expandable metal stent; SEMS = self-expanding metal stent

LITERATURE REVIEW: QUESTION 9 - SURGERY

1 st author, publication year	Setting; Study design	Inclusion criteria	Description of cohort	Main aim(s) of study	Primary findings relating to KQ	Main study limitation	Method of confirmation of TBM and type
Jennings 2014	Retro-spective cohort	children with TM who underwent aortopexy	N=41 median age- 7.5 mo (range 1-136)	To determine the outcomes among three different surgical approaches for performing an aortopexy	The partial sternotomy technique had the most reliable resolution of symptoms and no recurrence requiring reoperation.	Variation in patient populations, ages at operation, surgical teams, use of intraoperative bronchoscopy to assess results.	Flexible bronchoscopy, spontaneous breathing
Briganti 2006	Retro-Spective cohort	children with esophageal atresia-tracheoesophageal fistula presenting segmentary TM	7 children Mean age: 25.2 mo (range 2-103)	Usefulness of preoperative imaging by dynamic fiberoptic bronchoscopy and spiral multilayer computed tomography with 3-dimensional reconstruction	Dynamic fiberoptic bronchoscopy and CT scans allowed us to describe 3 morphological variations of thoracic TM	Short series of cases	Flexible bronchoscopy and CT scan with 3-D reconstruction
Filler 1992	Retro-Spective cohort	children with esophageal atresia tracheoesophageal fistula (EA-TEF) who underwent surgery for severe tracheomalacia	32 children	Surgical outcomes of aortopexy	Aortopexy provides long-term relief of severe symptoms of tracheomalacia associated with EA-TEF in almost all affected children		Chest x-ray, esophagogram, and bronchoscopy.
Morabito 2000	Cohort	children with significant symptoms of TM undergoing aortopexy and/or tracheopexy	16 children	Surgical outcomes of aortopexy and/or tracheopexy	Sustained tracheal improvement and resolution of the life-threatening features of TM		Bronchoscopy (type undefined)
Arnaud	Case study	Children with TM	4 children	To review initial experience	All patients were relieved of	larger and	Bronchoscopy

2014		and EA/TEF undergoing thorascocic aortopexy		with thoracoscopic aortopexy.	their symptoms, and no recurrence was noted.	prospective study with a longer follow-up to confirm these preliminary results, needed	
Shieh 2017	Retro-spective cohort	Children undergoing posterior tracheopexy for tracheomalacia with posterior intrusion	98 patients median age of 15mo (IQR 6-33months)	To review patient outcomes of posterior tracheopexy for tracheomalacia	Tracheomalacia scores on bronchoscopy improved significantly in all regions of the trachea and bronchi (p<0.001). 9.2% had persistent airway intrusion requiring reoperation, usually with aortopexy.		Flexible bronchoscopy with standardized dynamic airway evaluation by anatomical region
Morrison 2015	Case study	3 children with severe TBM treated with a 3D-printed personalized bioresorbable medical device	3 children	Assess the application of 3D printing technology to produce a personalized medical device for treatment of TBM	These infants no longer exhibited life-threatening airway disease and demonstrated resolution of both pulmonary and extra-pulmonary complications of their TBM.	This report was not designed for definitive testing of device safety. Further patient accrument and analysis under a US/ FDA-enabled clinical trial will be necessary.	Bronchoscopy and CT scan with multiplanar reconstruction

PATIENT AND PARENT PERPECTIVE

HTTPS links to internet sources

1. Mumsnet thread: "Anyone's newborn suffered from laryngeal stridor?". 2011. Accessed 5 April 2018. https://www.mumsnet.com/Talk/childrens_health/1123789-Anyones-newborn-suffered-from-laryngeal-stridor
2. Mumsnet thread "floppy windpipe". 2005. Accessed 5 April 2018. https://www.mumsnet.com/Talk/general_health/63818-floppy-windpipe
3. Mumsnet thread "any experts on breathing problems in small babies?". 2009. Accessed 5 April 2018. https://www.mumsnet.com/Talk/childrens_health/694506-any-experts-on-breathing-problems-in-small-babies
4. Baby Center Community thread "Tracheomalacia". 2010. Accessed 6 April 2018. <https://community.babycenter.com/post/a21491171/tracheomalacia>
5. Mumsnet thread "laryngomalacia in newborn; anyone any advice please?". 2006. Accessed 5 April 2018. https://www.mumsnet.com/Talk/general_health/137371-laryngomalacia-in-newborn-anyone-any-advice-please
6. Mumsnet thread "My 4 month old diagnosed with laryngeal or trachea malacia - anyone got any experience?". 2009 - 2011. Accessed 5 April 2018. https://www.mumsnet.com/Talk/childrens_health/714854-My-4-month-old-diagnosed-with-laryngeal-or-trachea-malacia
7. Megan Horwath. I Know You, Tracheomalacia. The Mighty. 2015. Accessed 6 April 2018. <https://themighty.com/2015/03/i-know-you-tracheomalacia/>
8. MedHelp thread "Tracheal-Malaysia". 2011. Accessed 5 April 2018. https://www.medhelp.org/posts/Ear--Nose--Throat/TRACHEAL-MALAYSIA/show/7360#post_7143465
9. Mamapedia thread "How to deal with infant with tracheomalacia?". 2008. Accessed 6 April 2018. <https://www.mamapedia.com/article/how-to-deal-with-infant-with-tracheomalacia>