European Respiratory Society guidelines for the management of children and adolescents with bronchiectasis (Online Supplement - Further description of methods)

Disclosure of potential conflicts of interest (CoI)

All potential CoI according to ERS policy were declared and compliance monitored by the chairs. None declared potential CoI, but it was planned that those with CoI would abstain from question-specific discussions and recommendations.

Professional background of the panel

Name	Speciality
Ahmad Kantar	Respiratory Paediatrics, previous ERS guidelines, Co-chair
Anne Chang	Respiratory Paediatrics, Cochrane, Co-chair
Efthymia Alexopoulou	Paediatric Radiology
Leanne Bell	Parent-Patient Advocate
Jeanette Boyd	European Lung Foundation representative and patient advocate
Andy Bush	Respiratory Paediatrics, links with primary ciliary dyskinesia guidelines
James Chalmers	Respiratory adults, ERS adult bronchiectasis guideline, EMBARC
Rebecca Fortescue	General Practitioner and Joint Co-ordinating Editor, Cochrane Airways Group
Keith Grimwood	Infectious Diseases and General Paediatrics
Adam Hill	Respiratory adults, EMBARC, ERS and British Thoracic Society adult bronchiectasis guidelines
Bulent Karadag	Respiratory Paediatrics, Health in low-middle income countries
Gabrielle McCallum	Registered Nurse, Early Career Researcher
Fabio Midulla	Respiratory Paediatrics
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Deborah Snijders	Respiratory Paediatrics
Woo-Jung Song	Allergy and Clinical Immunology
Thomy Tonia	Senior ERS Methodologist
Christine Wilson	Paediatric Respiratory Physiotherapist
Angela Zacharasiewicz	Respiratory Paediatrics

Additional description of methodology used

For each PICO and narrative question (NQ), at least two people (pairs and/or Fortescue/Chang) screened all the abstracts from the searches. The results were uploaded onto Rayyan (https://rayyan.qcri.org/) and the abstracts selected for retrieving full articles were undertaken. Any disagreements were resolved by consensus among the pairs and/or Fortescue/Chang. We used the specific inclusion and exclusion criteria outlined below for each PICO. Our generic inclusion criteria were children/adolescents aged 0-18 years with bronchiectasis from any cause (other than cystic fibrosis [CF]) and our hierarchy of evidence was RCTs and systematic reviews in children/adolescents. Where there were no RCT data in children/adolescents, we then used systematic reviews in adults with bronchiectasis and finally observational studies in children/adolescents.

We excluded studies published before 1982 (when chest CT-scans became available for diagnosing bronchiectasis). We also excluded systematic reviews where the data within these earlier published reviews were captured in systematic reviews undertaken at later dates. Although our

search strategy (see supplement-search strategy) included all languages, we only included publications in the English language.

The literature search (see Supplement-search strategies for further details) for all questions were based on the a-priori defined criteria outlined below. However, for selected PICOs where there was a lack of evidence, the use of additional search and supportive evidence was discussed. When the panel agreed, we sought supportive evidence from the literature, including the CF literature (as further described where relevant in the PICOs below). These are mentioned in the paragraphs below the relevant tables. A PRISMA diagram was generated for each PICO and NQ (Supplement Figures).

In the EtDs (see Supplement-ETD), for sections where we state there are no data, it refers to data within the included studies.

PICO Question 1:
In children/adolescents suspected of bronchiectasis;
(a) Should multidetector chest computed tomography (MDCT) scans with high-resolution CT (HRCT) be used instead of conventional HRCT alone for diagnosing bronchiectasis?
(b) What CT criteria for broncho-arterial dilatation (BAR) should be used?

Inclusion	Exclude	Intervention	Comparator	Study design	Setting	Publications if no RCTs in children	Timing
Children/ adolescents with BE aged 0-18 yrs investigated for BE	CF or papers before 1982			RCT and obs	Any (hospital, out-patients, home)	Systematic reviews in adults (last 10 years). Exclude non-English articles	Not applicable

CF=cystic fibrosis; BE=bronchiectasis; Obs=observational

For PICO1, only two adult-based studies provided direct data that addressed the PICO. As it was considered important to look at the outcomes chosen for the PICO, we included data that provided indirect evidence for using any CT-scan. These data were summarised in the narrative summary table (Supplement-EtD).

PICO Question 2:
In children/adolescents with bronchiectasis, should asthma-type treatments (inhaled corticosteroids [ICS], short-acting beta$_2$ agonists [SABA], long-acting beta$_2$ agonists [LABA]), compared to no asthma-type treatment, be used routinely? Subgroup analyses for (a) short versus long-term and (b) stable versus exacerbation states.

Inclusion	Exclude	Intervention	Comparator	Study design	Setting	Publications if no RCTs in children	Timing
Children/ adolescents with BE aged 0-18 ys (from all causes)	CF or papers before 1982	Any SABA, LABA, ICS, ICS-LABA	Placebo, no treatment	RCT and obs	Any (hospital, out-patients, home)	Systematic reviews in adults (last 10-years). Exclude non-English articles	Stable: >4-weeks; Exacerbation: ≤4-weeks

For PICO2, the panel considered including large observational studies reporting adverse events of ICS. This is because of the importance of the increasing concerns regarding the adverse events of ICS and the absence of paediatric studies. The evidence table generated from these data was hence developed and presented as part of the evidence tables for this PICO (Supplement-EtD).

PICO Question 3:
In children/adolescents with bronchiectasis, should mucoactive agents (compared to no mucoactive agents) be used routinely? Subgroup analyses for (a) short versus long-term, (b) stable versus exacerbation states, and (c) type of mucoactive agent.

Inclusion	Exclude	Intervention	Comparator	Study design	Setting	Publications if no RCTs in children	Timing
Children/ adolescents with BE aged 0-18 ys (from all causes)	CF or papers before 1982	Any mucoactive agents (oral, nebulised)	Placebo, no treatment	RCT and obs	Any (hospital, out-patients, home)	Systematic reviews in adults (last 10-years). Exclude non-English articles	Stable: >4-weeks; Exacerbation: ≤4-weeks

There were no data in children/adolescents. RCTs in adults were restricted to interventions longer than 2-days (i.e. there were several studies involving single doses of mannitol and hypertonic saline).

PICO Question 4:
In children/adolescents with bronchiectasis, should regular airway clearance techniques (ACT) (compared to no ACT) be undertaken? Subgroup analyses for (a) short versus long-term and (b) stable versus exacerbation states.

Inclusion	Exclud e	Interventio n	Comparato r	Study desig n	Setting	Publication s if no RCTs in children	Timing
Children/ adolescent s with BE aged 0-18 yrs (from all causes)	CF or papers before 1982	Any airway clearance technique (+/- apparatus)	Placebo, sham or no treatment	RCT and obs	Any (hospital , out-patients, home)	Systematic reviews in adults (last 10-years). Exclude non-English articles	Stable: >4-weeks; Exacerbation : ≤4-weeks

After undertaking the searches using the criteria above (see Supplement-search strategy for keywords), the Task Force panel decided to review CF-related data to enhance the narrative evidence, as there were little data in children/adolescents without CF. Thus, in addition to the search undertaken by the external librarian (see Supplement on search strategy), we searched data related to CF for supportive evidence. These searches were limited to PubMed and Cochrane databases and included only systematic reviews in humans aged 0-18 years in the last 5-years. These additional searches were undertaken on 19th July 2019 and 10 April 2020. Of the 77 articles identified, three papers were retrieved [1,2,3] to provide supportive evidence.

PICO Question 5:
In children/adolescents with bronchiectasis, should systemic courses of antibiotics (compared to no antibiotics) be used to treat an acute respiratory exacerbation (type and duration)?

Inclusion	Exclude	Intervention	Comparator	Study design	Setting	Publications if no RCTs in children	Timing
Children/ adolescents with BE aged 0-18 yrs (from all causes)	CF or papers before 1982	Any antibiotics (oral, inhaled, IV)	Placebo, no treatment	RCT and obs	Any (hospital, out-patients, home)	Systematic reviews in adults (last 10-years). Exclude non-English articles	<4-wks

PICO Question 6:
In children/adolescents with bronchiectasis, should eradication treatment be used (irrespective of symptoms) when there is a new isolate of a potentially pathogenic microorganism (compared to no eradication treatment)?

Inclusion	Exclude	Intervention	Comparator	Study design	Setting	Publications if no RCTs in children	Timing
Children/ adolescents with BE aged 0-18 yrs (from all causes)	CF or papers before 1982	Any antibiotics (oral, inhaled, IV)	Placebo, no treatment	RCT and obs	Any (hospital out-patients, home)	Systematic reviews in adults (last 10-years). Exclude non-English articles	Any

For the same rationale as for PICO-4, the taskforce panel decided to review CF-related data to enhance the narrative evidence, given the lack of data in children. Thus, in addition to the search undertaken by the external librarian (see supplement on search), we searched data related to CF for supportive evidence. The same process was undertaken as for PICO-4.

PICO Question 7:
In children/adolescents with bronchiectasis and recurrent exacerbations, should long-term (≥2-months) antibiotics (compared to no antibiotics) be used to reduce exacerbations?

Inclusion	Exclude	Intervention	Comparator	Study design	Setting	Publications if no RCTs in children	Timing
Children/ adolescents with BE aged 0-18 yrs (from all causes)	CF or papers before 1982	Any antibiotics (oral, inhaled, IV)	Placebo, no treatment	RCT and obs	Any (hospital, out-patients, home)	Systematic reviews in adults (last 10-years). Exclude non-English articles	>2-months

References

1 Warnock L, Gates A. Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis. *Cochrane Database Syst Rev* 2015; CD001401.

2 Button BM, Wilson C, Dentice R, et al. Physiotherapy for cystic fibrosis in Australia and New Zealand: A clinical practice guideline. *Respirology* 2016; 21: 656-667.

3 Wilson LM, Morrison L, Robinson KA. Airway clearance techniques for cystic fibrosis: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev* 2019; 1: CD011231.