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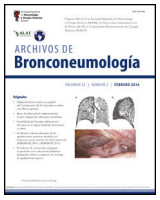

Review Article

The In-between: Time to Talk About Bronchiectasis in Adolescents and Their Transition to Adult Care

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ABSTRACT

Paediatric and adult bronchiectasis patients have been addressed in the literature as two different populations due to several differences, but there is insufficient evidence to understand how and when disease characteristics really change along patients' lifespan. This lack of knowledge is evident in all aspects of the transition: insufficient data is available about radiology, lung function, microbiology and treatment, and only limited information is currently available about changes in clinical presentation and psychosocial aspects. For instance, symptoms seem to improve during the third and fourth decades of life, a period sometimes referred to as the "honeymoon phase". However, adolescents with bronchiectasis have poorer quality of life than healthy peers, suggesting, therefore, potential disease underestimation at this age.

This scarcity of data most likely hinders the design of appropriate evidence-based transition protocols, ultimately limiting our ability to understand the factors driving disease progression and how to prevent it.

Nowadays it is crucial to raise awareness about this neglected aspect of bronchiectasis care, and fill this cultural and scientific gap by joining forces between pediatricians and adult physicians, to understand and stop disease progression and, lastly, to provide the best possible care to our patients in all phases of their lives.

Introduction

Bronchiectasis is a chronic lung disease characterized by productive cough, recurrent exacerbations and abnormal bronchial dilatation at the chest high-resolution computed tomography (HRCT).[1] In contrast to the adult population, paediatric bronchiectasis may be reversible in its first stages if treated promptly.[2,3]

Although clinical guidelines for bronchiectasis are available for paediatric[4] and adult patients,[5] there is limited information on the transitional period between these age groups, and no transition protocols are available. Current paediatric bronchiectasis guidelines[4] aim to guide the management of children and adolescents, but do not specifically address the unique needs of adolescents. As a result, there is no standard, evidence-based transition protocol, so adolescents are treated by either paediatricians or adult physicians, depending on the local healthcare system. However, the literature emphasizes the importance of improving the transition of patients with chronic conditions from paediatric to adult care through evidence-based recommendations.[6]

In clinical practice, the transition of bronchiectasis patients is usually based on models established in other respiratory diseases, especially cystic fibrosis (CF),[7] as well as the experience of paediatricians, physicians, patients and caregivers. Recently, many institutions are implementing internal transition protocols to regulate the passage from paediatric to adult services, but there appears to be limited supporting literature.

To unravel this topic, we conducted a narrative review analysing available literature about adolescence and transition processes in bronchiectasis. We conducted a literature search in PubMed, using the strategy "bronchiectasis AND adolescence" and "bronchiectasis AND transition" (in title/abstract). This search yielded 81 results with the first term and 35 with the second one; 8 results were

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Table 1
Summary of the Literature on Adolescence With Bronchiectasis.

Author, Journal	Year	Country	*n*	Main Topic	Study Design	Study Population	Main Conclusions
Field,[8] Arch. Dis. Child	1969	USA	165	Clinical outcomes	Observational retrospective	Follow-up from childhood to adulthood of 54 medically treated and 111 surgically-treated BE patients.	Prognosis related to the extent of disease and the type of bronchiectasis. Clinical improvement in second decade of life, maintained until the fourth decade. Post-tubercular BE associated with better outcome.
Landau,[9] Thorax	1974	Australia	69	Clinical outcomes	Observational retrospective	Follow-up from childhood to adulthood of 49 medically treated and 20 surgically treated BE patients.	Mild disease in most cases with relatively good lung function, small airway disease being the most common finding. Minimal disability with a marked trend to improvement during adolescence.
Bahali,[10] Gen. Hosp. Psychiatry	2014	Turkey	141	Psycho-social aspects	Observational prospective	Comparison of QoL between 76 BE and 65 healthy controls.	In comparison to healthy controls, adolescents with BE showed poorer QoL but similar anxiety/depression scores. QoL correlated with both clinical and psychological variables.
Kinghorn,[11] Pediatr. Pulmonol.	2018	USA (Alaska)	34	Clinical outcomes	Observational retrospective	Follow up of 14 BE patients in comparison with 20 CSLD.	In comparison with CSLD, 80% of BE patients had persistent symptoms (mostly productive cough and/or wheezing), crackles and lower FEV_1 but a decreasing trend in exacerbations through adolescence.
Moss,[12] J. Paediatr. Child Health	2021	New Zealand	46	Transition	Observational retrospective	Comparison of transition records between 26 BE and 20 CF patients.	Compared with CF patients, less transfer preparation in BE affected health engagement and outcomes. Despite greater severity of disease (lower FEV_1), transfer processes in BE were not standardized, less visits were planned and patients were less likely to attend to scheduled visits.
Sibanda,[13] Int. J. Circumpolar Health	2020	USA (Alaska)	31	Clinical outcomes	Observational retrospective	Follow-up from childhood to adulthood of 31 BE Alaskan native patients.	The main symptom reported in adolescence was wheezing. In adulthood, persistent or intermittent respiratory symptoms were described in half of the patients while 23% were asymptomatic. Severe pulmonary disease was described in 13%. Lack of provider continuity and remote location of patients contributed to worst prognosis.
Blamires,[14] Int. J. Qual. Stud. Health Well-being	2021	New Zealand	15	Psycho-social aspects	Observational prospective	Psycho-social evaluation of BE adolescents (interviews).	Interviewed adolescents describe their life as “pretty normal” compared with peers. The presence of symptoms and need for self-management led patients to find coping strategies.
Schutz,[15] Front. Pediatr.	2023	Australia (Northern Territories)	102	Transition	Observational retrospective	Medical audit of transition processes.	Gap in the documentation of delivery of care. Only 9/102 patients had evidence of transition planning.

BE: bronchiectasis; QoL: quality of life; CSLD: chronic suppurative lung disease; FEV1: forced expiratory volume in the first second.

repeated in both searches. From the 108 results, 103 were excluded because the main topic was not bronchiectasis (cystic fibrosis, HIV, other respiratory diseases), adolescence was not specifically addressed, or focus was not on transition processes. Three more papers, not identified in the first search, were selected from the references' list of other studies, being considered pertinent to the topic.

In this review, we will comment on the eight articles fulfilling our criteria, trying to shed light upon the neglected aspects of bronchiectasis in adolescence and the challenges of transition into adulthood (Table 1).

Evidence on Transition Process in Bronchiectasis Patients

While most authors have addressed various problematic issues surrounding the transition protocol in bronchiectasis, only three have specifically focused on the practical and organizational aspects (Table 2).

The study from New Zealand comparing CF ($n=20$) and bronchiectasis ($n=26$) transfer from paediatric to adult care demonstrated that, despite the greater severity of the disease, the engagement with medical services was poorer in the latter group, with less scheduled visits and poorer attendance, attributed to an insufficient preparation of both patient and healthcare system.[12]

Similar findings were reported in the remaining two papers, which, however, focused on high-risk populations in remote areas. These studies highlighted that the effectiveness of the transition process largely depends on the level of preparedness within the healthcare system.[13,15]

In 2023, an Australian team led by Shutz collected data about transitioning processes in 102 Australian patients with bronchiectasis, focusing especially on First Nation people (indigenous),

Table 2
Main Challenges Identified in Transition Literature and Resolution Proposals.

	Issues Detected	Strategies for Improvement
Moss,[12] Schutz,[15] Sibanda[13]	Lack of transition planning and insufficient communication between paediatric and adult healthcare providers.	Standardize transition process creating formal referral paths between different healthcare providers involved in bronchiectasis care.
Moss,[12] Schutz,[15] Sibanda[13]	Unequal care delivery in disadvantaged socio-economical background, especially in remote areas and high-risk populations.	Guarantee healthcare equity through adaptation of transition and healthcare protocols to local needs.
Kinghorn[11]	Risk of disease severity underestimation due to transient improvement in symptoms during adolescence.	Close clinical follow-up despite mild symptoms.
Blamires[14]	Lack of adherence to follow-up to avoid school interruption.	Adapt follow-up and transition process to logistical needs of the patient and the family.
Blamires[14]	Perception of physiotherapy as a burden possibly threatening compliance.	Improve patient awareness about expected outcomes of physiotherapy. Increase involvement in self-management.
Bahali[10]	Impact of clinical and psychological factors on QoL during growth.	Include QoL questionnaires and mental health workers in multidisciplinary transition team.

QoL: quality of life.

considering the high prevalence of the disease in this ethnic group. They identified a concerning gap in documentation and planning in the transition between paediatric and adult care, emphasizing the need for structured, inclusive and flexible transitioning plans.[15]

In an Alaskan cohort of bronchiectasis patients diagnosed in childhood, paediatric and adult clinical records were compared: in 62% of patients the diagnosis was only documented in the paediatric records. Due to inadequate communication between paediatric and adult services, bronchiectasis was not reported after transition, even though most patients continued to show symptoms.[13]

Bronchiectasis From Childhood to Adulthood: Clinical Management

The literature about practical organization of transition is scarce, yet even less is known about diagnosing and managing bronchiectasis in adolescence, complicating the task of setting evidence-based transition protocols. Also, the lack of a continuum in bronchiectasis follow-up across ages can limit our ability to understand and prevent disease progression.

Only Navaratnam et al. have analysed the tools used for monitoring bronchiectasis in both children and adult, focusing on their peculiarities and contributions in these two age groups.[16] While signs and symptoms, especially changes in expectoration, are helpful variables in both adult and paediatric patients, diagnostic and follow-up methods differ between the two populations.[16]

Diagnostic Workout

HRCT represents the diagnostic gold standard of bronchiectasis; however, its use in the paediatric population requires more caution because of the radiation risk. Low-dose CT could represent a valuable alternative, and recent encouraging data suggest that magnetic resonance imaging (MRI) could be promising, particularly for follow-up. However, high cost, technical difficulties and image quality still limit MRI routine use.[16,17]

The radiological definition of abnormal bronchial dilatation also differs between children and adult: in childhood, bronchiectasis is diagnosed when the broncho-arterial ratio (BAR) is $\geq$0.8, whereas in adults it ranges from $\geq$1 to 1.5, depending on series.[18] However, it remains unclear when the BAR cut-off for diagnosing the disease should be changed.

Aetiology of Bronchiectasis

Regarding bronchiectasis aetiology, there are some differences between paediatric and adult populations. Idiopathic (unknown cause) and post-infectious are common causes in both age groups, while immunodeficiency, ciliary dyskinesia, congenital malformations, and post-infectious *bronchiolitis obliterans* are predominant in children.[19,20] In adulthood, in addition to these aetiologies, bronchiectasis are often also associated with airways diseases[21,22] such as asthma and chronic obstructive pulmonary disease, and other conditions that worsen with ageing, such as autoimmune diseases.

The few data derived from cohorts that include adolescents differ greatly between authors: in a cohort of 8–17-year-old patients, 52.6% of bronchiectasis were classified as idiopathic. Between other aetiologies ciliary dyskinesia was slightly predominant (19.7%), followed by post-infectious disease (15.8%), bronchiolitis obliterans (7.9%) and immunodeficiencies (3.9%).[10]

In contrast, a more recent series including patients from 14 to 20 years old found that most had post-infective bronchiectasis (94.1%), with only a few cases of conditions typical of childhood, such as chronic neonatal lung disease (2%) and foreign body aspiration (2%), and none were classified as idiopathic.[15]

Clinical Manifestations

Between the 1960s and 70s, longitudinal studies from England (n=225) and Australia (n=69) reported improvement in symptoms from childhood to adolescence, which persisted until the fourth decade of age.[8,9] Still, these results are of questionable relevance today: the level of knowledge in bronchiectasis has dramatically improved over the last 20 years, due to the existence of large national and international registries. The availability of national and international guidelines has largely improved bronchiectasis management through the implementation of diagnostic techniques, follow-up methods, treatments, etc. Therefore, the comparison of present data with old ones increases the risk of confusion bias.[1,4,5,23–26] Our search identified only two original studies published in the last 30 years reporting data on bronchiectasis clinical history from childhood to adolescence and adulthood.

Kinghorn and colleagues described in 2018 a decrease in exacerbations from childhood to adolescence, although 80% of adolescents with HRCT-confirmed bronchiectasis remained symptomatic (productive cough and/or wheezing), frequently showing obstructive patterns.[11]

More recently, Sibanda et al. in 2020 reported persistent or intermittent respiratory symptoms in 54% of the 31 adult patients diagnosed in childhood, 13% had severe pulmonary disease, and 23% were asymptomatic. Wheezing was the main symptom reported in adolescence, aligning with Kinghorn's findings.[13]

Both studies were conducted in a Native Alaska population, whose social, logistic, and genetic peculiarities raise concerns about the large-scale applicability of these findings.

Nevertheless, other authors seem to confirm the "honeymoon" state during adolescence: in a Turkish cohort, most patients between 8 and 17 years were in stable state, with only 6 out of 76 (9.2%) experiencing acute exacerbations. Even if the presence and characteristics of chronic symptoms were not specifically assessed, results of quality of life (QoL) questionnaires suggest patients to be minimally symptomatic. Wheezing was the most frequent issue, whose severity directly correlates with QoL.[10]

However, it is possible that coping mechanisms during adolescence may influence symptom's referral: adolescents interviewed by Blamires and colleagues referred to coughing as a frequent symptom, but they did not consider it of great significance outside exacerbation. Also, they considered as "normal" the use of 2–4 antibiotic courses per year.[14] It is possible that the normalization of symptoms delivers an over optimistic clinical picture of patients, masking the presence of progressive worsening. Hence, instrumental follow-up is important to promptly register changes in clinical status and prevent disease progression, even in patients with mild symptoms.

Lung Function

Lung function tests (LFT), especially spirometry, play an essential role in the follow-up of all patients, although there is no specific lung function impairment pattern for bronchiectasis.[27]

In the last decade, the implementation of the universal GLI-2012 and *Z*-scores to interpret LFT has become common in paediatrics,[28] while outdated references are still widely used in adult care. During the transition, the shift from one method to the other could lead to misinterpretation of results and prevent early detection of functional decline. Among the papers included in our review, only three reported on lung function.[10–12]

Moss et al. did not detect any significant trend in lung function over the follow-up period,[12] whereas two other series observed reduced FEV1 and FVC despite normal mean FEV1/FVC ratio. However, these data should be considered with caution due to the small sample size.[10,11] Moreover, none of these papers used *Z*-scores to express lung function.

Microbiology

Unlike CF, the natural history of the microbiology of bronchiectasis during adolescence has not yet been described.

In children, literature reports the dominance of *Haemophilus* spp. (40% of sputum cultures), followed by *Streptococcus pneumoniae* (20%), *Moraxella catarrhalis* (8.5%) and *Pseudomonas aeruginosa* accounting for less than 8% of positive cultures.[29] In adults instead, *P. aeruginosa* plays the prominent role (up to 25%), with *Haemophilus influenzae* shifting to the second place (23%), followed by *Enterobacteriaceae* (15%), *S. pneumoniae* (8%), *S. aureus* (8%) and *M. catarrhalis* (5%), with notable regional variations.[23]

It is unclear what influences this microbiological shift: it could be related to the different distribution of aetiologies, the natural history of the disease with ageing or other unknown factors.

Treatment of Acute and Chronic Symptoms

Another crucial difference emerging from our literary review regards the definition of exacerbation and treatment of acute symptoms. In children and adolescents, the *n* ERS defines a respiratory exacerbation as an increase in respiratory symptoms for at least three days, with or without changes in sputum.[4] On the other hand, Hill's criteria in adults define the increase in sputum volume or consistency for 48 h or more as one of the fundamental symptoms required to diagnose a respiratory exacerbation.[30]

Moreover, the recommendation in children is to treat all acute respiratory exacerbations with 14 days of an appropriate systemic antibiotic,[4] while in adults, not all exacerbations require antibiotic treatment.[30]

Therapeutic adherence and readiness for self-care represents another fundamental aspect of the transition process poorly described in the literature. Transitioning from parental care to self-management is delicate and fraught with risks, as seen in other chronic diseases. Moreover, in respiratory diseases like CF or bronchiectasis, adherence to time-consuming treatments, like physiotherapy, airways clearance techniques (ACT) and inhaled antibiotics, is challenging but crucial to ensure clinical stability and prevent functional decline and exacerbations. These treatments often require the interruption of daily life and reorganization of patients' routine, generating frustration for not being able to attend normal activities such as school, sports, or social events.[14] Physiotherapy has been defined by adolescent patients as "a pain", but the experience of positive results from this self-care helps them in maintaining good adherence and a more conscious and positive attitude to treatment.[14]

Therefore, physiotherapy and ACT must be tailored to the patient's age and lifestyle, whenever possible, to ensure efficacy and adherence, and specific evidence-based protocols should be designed.[31]

Psycho-social Aspects

Psychological preparation and mental health are two of the most critical elements in any transition process. A study published in 2014 observed that depression and anxiety levels in children and adolescents with bronchiectasis were not higher than in the healthy control group. However, bronchiectasis significantly impacted quality of life, correlating with clinical variables and disease severity.[10]

Interestingly, in another study, 15 bronchiectasis adolescents reported perceiving their life as "pretty normal", incorporating symptoms and medical care into their daily life.[14] Not only age and severity but also healthcare organization and resources influence the experience of children and adolescents throughout their development, with differences depending on geographical and socioeconomic context.

Studies on adolescents with chronic diseases observed reduced adherence to treatment and follow-up when their daily routines are disrupted, for example because of frequent visits or hospitalization.[32,33] Transition protocols should take into consideration the need for keeping a normal routine and minimize the impact of treatment and clinical follow-up in school activities.

Conclusions

The current literature on the natural history of bronchiectasis from childhood to adulthood through adolescence is extremely poor, as only a few papers address bronchiectasis as a lifelong chronic disease (Fig. 1).

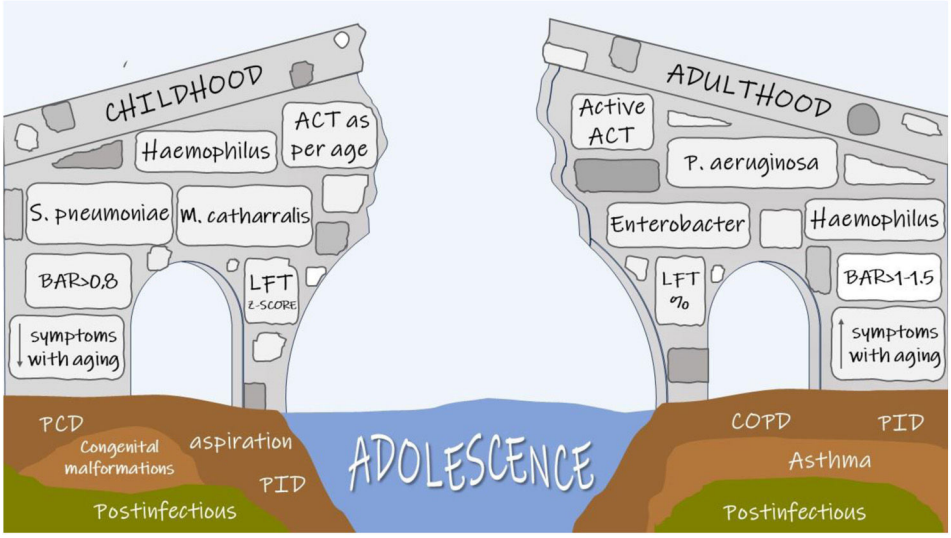

Fig. 1. Adolescence: knowledge gaps between paediatric and adult bronchiectasis. ACT: airways clearance techniques; LFT: lung function test; BAR: broncho-arterial ratio; PCD: primary ciliary dyskinesia; PID: primary immunodeficiencies; COPD: chronic obstructive pulmonary disease.

Collaterally, it is interesting to notice that most of the literature about the transition from paediatric to adult care has been authored by paediatricians, which seems to reflect the insufficient involvement of adult specialists. Indeed, most of these articles were published in paediatric journals, which could lead to reduced diffusion among adult care providers and, to some extent, reinforce the incorrect concept that transition management is exclusively a responsibility of paediatricians.

In conclusion, we identified a lack of data regarding all aspects of bronchiectasis in adolescence, including radiology, microbiology and management of clinical and psychosocial aspects of the disease.

Thus, a stronger collaboration between paediatricians and adult physicians is needed at multiple levels to achieve more evidence about the natural history of the disease across ages and to establish a transition protocol able to overcome the challenges detected so far. Only appropriate and collaborative research between investigators and scientific societies can build bridges to connect the children and adult worlds.

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Conflicts of Interest

The authors declare no conflict of interest.

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Artificial Intelligence Involvement

The authors declare that none of the material has been produced with the help of any artificial intelligence software or tool.

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References

1. Aliberti S, Goeminne PC, O'Donnell AE, Aksamit TR, Al-Jahdali H, Barker AF, et al. Criteria and definitions for the radiological and clinical diagnosis of bronchiectasis in adults for use in clinical trials: international consensus recommendations. Lancet Respir Med. 2021.
2. Gaillard EA, Carty H, Heaf D, Smyth RL. Reversible bronchial dilatation in children: comparison of serial high-resolution computer tomography scans of the lungs. Eur J Radiol. 2003;47:215–20.
3. Chang AB, Kantar A, Redding GJ, Hill AT. Is bronchiectasis a reversible disorder? Arch Bronconeumol. 2023;59:199–200.
4. Chang AB, Fortescue R, Grimwood K, Alexopoulou E, Bell L, Boyd J, et al. European Respiratory Society guidelines for the management of children and adolescents with bronchiectasis. Eur Respir J. 2021;58:2002990.
5. Polverino E, Goeminne PC, McDonnell MJ, Aliberti S, Marshall SE, Loebinger MR, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J. 2017;50.
6. Casseus M, Cheng J. Variations in healthcare transition preparation among youth with chronic conditions. Am J Prev Med. 2022;62:e275–83.
7. Office D, Heeres I. Transition from paediatric to adult care in cystic fibrosis. Breathe. 2022;18:210157.
8. Field CE. Bronchiectasis. Third report on a follow-up study of medical and surgical cases from childhood. Arch Dis Child. 1969;44:551–61.
9. Landau LI, Phelan PD, Williams HE. Ventilatory mechanics in patients with bronchiectasis starting in childhood. Thorax. 1974;29:304–12.
10. Bahali K, Gedik AH, Bilgic A, Cakir E, Ustabas Kahraman F, Keskin Osmanoglu N, et al. The relationship between psychological symptoms, lung function and quality of life in children and adolescents with non-cystic fibrosis bronchiectasis. Gen Hosp Psychiatry. 2014;36:528–32.
11. Kinghorn B, Singleton R, McCallum GB, Bulkow L, Grimwood K, Hermann L, et al. Clinical course of chronic suppurative lung disease and bronchiectasis in Alaska Native children. Pediatr Pulmonol. 2018;53:1662–9.
12. Moss R, Farrant B, Byrnes CA. Transitioning from paediatric to adult services with cystic fibrosis or bronchiectasis: what is the impact on engagement and health outcomes? J Paediatr Child Health. 2021;57:548–53.
13. Sibanda D, Singleton R, Clark J, Desnoyers C, Hodges E, Day G, et al. Adult outcomes of childhood bronchiectasis. Int J Circumpolar Health. 2020;79.
14. Blamires J, Dickinson A, Tautolo ES, Byrnes CA. A “pretty normal” life: a qualitative study exploring young people's experience of life with bronchiectasis. Int J Qual Stud Health Well-Being. 2021;16.
15. Schutz KL, Fancourt N, Chang AB, Morris P, Buckley R, Biancardi E, et al. Transition of pediatric patients with bronchiectasis to adult medical care in the Northern Territory: a retrospective chart audit. Front Pediatr. 2023;11.
16. Navaratnam V, Forrester DL, Eg KP, Chang AB. Paediatric and adult bronchiectasis: monitoring, cross-infection, role of multidisciplinary teams and self-management plans. Respirology. 2019;24:115–26.
17. Lokesh, Jana M, Naranje P, Bhalla AS, Kabra SK, Hadda V, et al. MDCT and MRI in bronchiectasis in older children and young adults – a non-inferiority trial. Indian J Pediatr. 2023.
18. Goyal V, Chang AB. Bronchiectasis in childhood. Clin Chest Med. 2022;43:71–88.
19. Goyal V, Grimwood K, Marchant J, Masters IB, Chang AB. Pediatric bronchiectasis: no longer an orphan disease. Pediatr Pulmonol. 2016;51:450–69.

20. Chang AB, Bush A, Grimwood K. Bronchiectasis in children: diagnosis and treatment. Lancet. 2018;392:866–79.
21. Polverino E, Dimakou K, Traversi L, Bossios A, Haworth CS, Loebinger MR, et al. Bronchiectasis and asthma: data from the European Bronchiectasis Registry (EMBARC). J Allergy Clin Immunol. 2024 [in press].
22. Polverino E, De Soyza A, Dimakou K, Traversi L, Bossios A, Crichton ML, et al. The association between bronchiectasis and chronic obstructive pulmonary disease: data from the European Bronchiectasis Registry (EMBARC). Am J Respir Crit Care Med. 2024 [in press].
23. Chalmers JD, Polverino E, Crichton ML, Ringshausen FC, De Soyza A, Vendrell M, et al. Bronchiectasis in Europe: data on disease characteristics from the European Bronchiectasis registry (EMBARC). Lancet Respir Med. 2023;11:637–49.
24. Martinez-García MA, Villa C, Dobarganes Y, Girón R, Maíz L, García-Clemente M, et al. RIBRON: el registro español informatizado de bronquiectasias. Caracterización de los primeros 1.912 pacientes. Arch Bronconeumol. 2021;57:28–35.
25. Dhar R, Singh S, Talwar D, Mohan M, Tripathi SK, Swarnakar R, et al. Bronchiectasis in India: results from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) and Respiratory Research Network of India Registry. Lancet Glob Heal. 2019;7:e1269–79.
26. Martínez-García MÁ, Máiz L, Olveira C, Girón RM, de la Rosa D, Blanco M, et al. Spanish guidelines on the evaluation and diagnosis of bronchiectasis in adults. Arch Bronconeumol. 2018;54:79–87.
27. Radovanovic D, Santus P, Blasi F, Sotgiu G, D'Arcangelo F, Simonetta E, et al. A comprehensive approach to lung function in bronchiectasis. Respir Med. 2018;145:120–9.
28. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012.
29. Pizzutto SJ, Hare KM, Upham JW. Bronchiectasis in children: current concepts in immunology and microbiology. Front Pediatr. 2017;5.
30. Hill AT, Haworth CS, Aliberti S, Barker A, Blasi F, Boersma W, et al. Pulmonary exacerbation in adults with bronchiectasis: a consensus definition for clinical research. Eur Respir J. 2017;49.
31. Lee AL, Button BM, Tannenbaum E-L. Airway-clearance techniques in children and adolescents with chronic suppurative lung disease and bronchiectasis. Front Pediatr. 2017;5.
32. Chariatte V. Missed appointments in an adolescent outpatient clinic: descriptive analyses of consultations over 8 years. Swiss Med Wkly. 2007.
33. Neal RD, Lawlor DA, Allgar V, Colledge M, Ali S, Hassey A, et al. Missed appointments in general practice: retrospective data analysis from four practices. Br J Gen Pract. 2001;51:830–2.