

Bronchiectasis and Quality of Life; Which is the Best Questionnaire?

David de la Rosa-Carrillo, MD, PhD¹, Annie Navarro-Rolon, MD², and Bruno García-Cabo, MD²

¹Pneumology Department, Hospital de la Santa Creu i Sant Pau, Barcelona; ²Pneumology Department, Hospital Universitario Mutua de Terrassa, Terrassa, Barcelona, Spain

ABSTRACT

In recent years, bronchiectasis has emerged as a heterogeneous syndrome, which can affect individual patients in very different ways. Given the growing interest in precision medicine, multidimensional assessment tools have been developed to assess the severity of this disease, which, however, have so far not included the quality of life assessment. However, there are several quality of life questionnaires that can be used in this condition, some of them adapted from other respiratory diseases, and others specifically designed for use in bronchiectasis. In this article we will review them, describing their main characteristics, advantages and disadvantages. We will also review how quality of life measurement can be applied to future tools to assess the heterogeneity of bronchiectasis, measuring its severity, activity and impact. These tools will allow us to determine precisely how each component of the disease affects each individual patient.

Keywords: Bronchiectasis. Heterogeneity. Individualized medicine. Quality of life.

Correspondence to:

David de la Rosa-Carrillo
Pneumology Department, Hospital de la Santa Creu i Sant Pau
Carrer de Sant Quintí, 89, 08041 Barcelona, Spain
E-mail: david.rosa23@gmail.com

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INTRODUCTION

Bronchiectasis has been classically described as an irreversible dilatation of the airways, associated with chronic respiratory symptoms, recurrent respiratory infections, as well as progressive clinical deterioration leading to increased morbidity and mortality. Today our knowledge of this pathology has experienced great advances, mainly due to the exponential leap in research in this field, in the last 20 years. It is known that bronchiectasis is the final stage of pulmonary involvement that can be caused by hundreds of possible diseases, some of which can influence the clinical course of the disease. Therefore, more than a disease, they actually constitute a “syndrome”, understood as “a set of signs and symptoms that are related to each other without necessarily sharing a single identifiable pathogenesis”¹.

Increased knowledge of the disease and growing interest in precision medicine has led to the appearance of multiple disease proxy scales such as the E-FACED scores - acronym for Exacerbations, forced expiratory volume in the first second (FEV₁), Age, Chronic bronchial infection (Colonization) by *Pseudomonas aeruginosa*, radiological Extension and Dyspnoea - and the Bronchiectasis Severity Index (BSI)². These scores allow us to evaluate through radiological, microbiological, clinical and functional variables, the severity and prognosis of bronchiectasis (Table 1)³. Similar to the trend that has been followed to correctly identify patients with chronic obstructive pulmonary disease (COPD), clinical phenotypes in bronchiectasis have also been recently described, understanding by phenotype “a single or combination of disease attributes

that describe differences between individuals as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death)”⁴. Different phenotypes have been identified in several publications carried out in recent years in Spain, Italy and China⁵. However, there are other possible phenotypes that may be described in the future, taking into account the growing number of publications describing the course of patients with bronchiectasis associated with various entities such as chronic bronchial infection, COPD, asthma, repeated exacerbations or systemic inflammation (Table 2)³. On the other hand, the concept of endotype has recently been described, which refers to the subtype of a disease or syndrome, defined by a different functional or pathophysiological mechanism. Thus, the endotype is a specific biological pathway (defined by a consistent aetiology and/or pathophysiological mechanism) that explains the measurable properties of a phenotype⁶. Potential endotypes in bronchiectasis include immunodeficiency, ciliary dyskinesia, infection (with typical bacteria and non-tuberculous mycobacteria), hypersensitivity to fungi and autoimmunity. Importantly, all of them can potentially become therapeutic targets⁷.

Both prognostic scales and clinical phenotypes and endotypes have been created in an attempt to assess the multidimensionality and heterogeneity of bronchiectasis. However, none of these approaches takes into account the impact of the disease on the patient’s quality of life, despite being one of the main objectives in clinical research today. The impact of the illness and its measurement, regardless of the severity and extent of the disease, is crucial. For this reason, over the last few years,

TABLE 1. BSI, FACED and E-FACED. Quantification variables and description

BSI	Points	E-FACED	Points	FACED	Points
Age (Years)		Age (Years)		Age (Years)	
< 50	0	< 70	0	< 70	0
50-69	2	≥ 70	2	≥ 70	2
70-79	4				
> 80	6				
BMI (Kg/m ²)					
< 18.5	0				
≥ 18.5	2				
FEV ₁ (%pred)		FEV ₁ (% pred)		FEV1 (% pred)	
> 80	0	50%	0	≥ 50%	0
50-80	1	< 50%	2	< 50%	2
30-49	2				
< 30	3				
Hospitalization in the 2 previous years		Hospitalization in the previous year			
No	0	0	0		
SI	5	≥ 1	2		
Exacerbations in the previous year					
0-2	0				
≥ 3	2				
Dyspnoea (MRC)		Dyspnoea (mMRC)		Dyspnoea (mMRC)	
1-3	0	0-II	0	0-II	0
4	2	III-IV	1	III-IV	1
5	3				
Chronic PA infection		Chronic PA infection		Chronic PA infection	
No	0	No	0	No	0
Yes	3	Yes	1	Yes	1
Infection by other PPM					
No	0				
Yes	1				
> 3 lobes involved or cystic bronchiectasis		Lobes involved		Lobes involved	
No	0	1-2	0	1-2	0
Yes	1	≥ 2	1	≥ 2	1
Range (points)	0-26		0-9		0-7
Mild	0-4		0-3		0-2
Moderate	5-8		4-6		3-4
Severe	≥ 9		7-9		5-7

BMI: body mass index; BSI: bronchiectasis severity index; E-facEd: acronym for Exacerbations, FEV₁, Age, chronic *Pseudomonas aeruginosa* bronchial Colonization, radiological Extension, and Dyspnoea; FEV₁: forced expiratory volume in the first second; MRC: Medical Research Council; mMRC: Modified Medical Research Council; PA: *Pseudomonas aeruginosa*; PPM: potentially pathogenic microorganisms.

multiple quality of life questionnaires have been developed. Some have been developed specifically for patients with bronchiectasis while others, developed for other respiratory diseases, have subsequently been adapted to be used in bronchiectasis patients. Their main

characteristics will be described later in this document. These questionnaires allow us to assess the impact on quality of life from different approaches. However, the use of many of them is scarce in routine clinical practice due to multiple factors such as the lack of

TABLE 2. Proposal for possible clinical phenotypes in bronchiectasis and the current scientific evidence. The table shows the different proposals, graded by colour, for possible clinical phenotypes (not confirmed) and the greater or lesser scientific evidence available (more evidence is indicated by a more intense colour)

Potential clinical phenotypes	Clinical symptoms	Pathophysiology	Biomarkers	Outcomes	Treatment	Genomics /Genetics
CBI-PA						
CBI- PPM						
Exacerbator						
Bronchiectasis with few symptoms						
COPD overlap						
Asthma overlap						
Idiopathic						
Rapid lung function decline						
Systemic inflammation						

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CBI: chronic bronchial infection; COPD: chronic obstructive pulmonary disease; PA: *Pseudomonas aeruginosa*; PPM: potentially pathogenic microorganisms.

knowledge of their availability, the time required for the patient to complete it, as well as the time required for its analysis, among others.

According to the above, one of the key points to be taken into account in bronchiectasis syndrome is its heterogeneity and complexity, since they both influence its severity and prognosis as well as the radiological extent of the anatomical pulmonary alterations and/or the respiratory functional involvement. Nowadays, healthcare efforts in the management of diseases are focused on their symptoms and signs, so that in most patients a small number of complementary tests are performed, and a limited range of therapeutic guidelines are contemplated⁸. However, advances in the knowledge of their molecular basis and pathophysiological pathways have revealed that most diseases are very complex entities, in which the interaction between genetics and the environment must also be taken into account.

Thus, the same disease can express itself in very different ways in different subjects. Moreover, there is also the possible synergy with other diseases in the same individual. Exhaustive knowledge and mastery of all these characteristics will bring us into precision medicine, which will allow us in the (hopefully near) future to personalize the treatment of bronchiectasis according to the characteristics of each person.

QUALITY OF LIFE QUESTIONNAIRES

Quality of life questionnaires used in bronchiectasis patients, either in research or in daily clinical practice, are diverse. Some have been developed for other respiratory diseases and subsequently validated in bronchiectasis patients. Only a few questionnaires have been specifically designed for use in bronchiectasis patients. In the following section, we describe the main features of these questionnaires.

Saint George Respiratory Questionnaire (SGRQ)

Originally developed to measure the impact of COPD on the quality of life of patients⁹, it was later translated and validated for other respiratory diseases, being one of the first to be validated for use in patients with bronchiectasis¹⁰.

It is a self-administered questionnaire that evaluates quality of life in three domains: frequency and length of symptoms, limitation of physical activities due to respiratory symptoms, and impact on the social, professional and psychological spheres. It has 50 questions with a total of 76 answers graded from 0 to 100, being 0 the best state in terms of quality of life and 100 the worst. The total score is obtained after adding the items in each domain.

It is a very accurate questionnaire both for the initial prognosis of a patient and for the follow-up of the disease. However, it is very extensive, which implies a substantial amount of time to complete it, it is not specific to the disease, and it cannot be interpreted directly, because it requires the use of a software to determine the score and analyze the results.

Quality Of Life Bronchiectasis Questionnaire (QOL-B)

This is the first disease-specific questionnaire, developed as a measure of quality of life in patients with bronchiectasis¹¹. It is a self-administered questionnaire with 37 questions distributed in eight areas: physical capacity, role limitations, vitality, health awareness, emotional state, social isolation, treatment burden and respiratory symptoms. There is no total score,

but each area is rated from 0-100, the higher the quality of life, the higher the score. It has also been translated and validated in Spanish¹².

As an advantage, it is a self-administered questionnaire and can be completed in about ten minutes by the patient. As a disadvantage, software is required to calculate and analyse the results by areas, and there is no total score that integrates the entire questionnaire, and that can be used to predict exacerbations or to follow-up the disease by integrating all the areas.

Bronchiectasis Health Questionnaire (BHQ)

A questionnaire developed specifically for patients with bronchiectasis¹³. It consists of ten items of which nine are related to the symptoms experienced in the last two weeks, and one of them to the antibiotic treatments received in the previous year.

The answers are rated from one to seven, based on the frequency of symptoms/treatment, with one being the most symptomatic and seven the least, and are scored between 0-100 on a weighted basis. The total score varies between 0 and 100, with 100 being the best possible state. In its first publication, it included versions in 11 different languages. It is a simple, brief, disease-specific questionnaire, from which a single total score is obtained to facilitate its interpretation.

Leicester Cough Questionnaire (LCQ)

This is a self-administered questionnaire developed in 2003 by S.S. Birring¹⁴, which assesses

the effect of chronic cough on quality of life. For this purpose, it has 19 questions with frequency responses, each assigned to a number in a range of one to seven, depending on the frequency with which the patient has experienced the symptoms in the last two weeks, with one being the highest frequency of symptoms and seven being the lowest. The impact of cough is measured in terms of the impact on the physical, psychological and social spheres, obtaining the final result as the average of each of the three spheres and making a final score. A higher total score is interpreted as a better quality of life.

It is a simple questionnaire, with a good correlation with the SGRQ, but its main disadvantage is that it only assesses cough, without considering other important aspects of the disease. It has been validated in Spanish by Muñoz et al¹⁵.

COPD Assessment Test (CAT)

This is a self-administered questionnaire, simpler and easier to complete than the previous ones, which was designed in 2009 for the assessment of quality of life in COPD patients¹⁶. It is widely used in daily clinical practice and its use is considered in the several COPD guidelines to assess the severity of the disease.

Although it has been used for years in the field of bronchiectasis, it was not validated until 2019 in which de la Rosa et al. carried out a prospective study with 96 patients, concluding that there is a good correlation in the assessment of quality of life in patients with bronchiectasis when compared with existing questionnaires (BHQ, QOL-B and BHQ)¹⁷. They

also observed a significant correlation with multidimensional severity scores, with the Charlson comorbidity index, as well as with certain relevant clinical parameters in patients with bronchiectasis, such as FEV₁, dyspnoea, daily amount of expectoration and the value of some peripheral blood inflammatory markers (fibrinogen and C-reactive protein).

The CAT has eight items weighted from zero to five according to the frequency of symptoms (zero best condition and five worst), the result being a sum of the score of all items with a maximum value of 40 (Table 3). In COPD, different clinical research studies have established a cut-off point of ten, where lower values represent a low impact and values above ten, a high impact of the disease on quality of life. In the study by De la Rosa et al.¹⁷, it was evidenced that a CAT above ten points has prognostic capacity to identify patients at risk of presenting more than two or even more than three exacerbations, or patients with at least one hospitalization in the following year (adjusted for severity according to FACED, e-FACED, and BSI). In addition, it was possible to determine that there was a minimal clinically important difference when there was a change of at least three points in the test with respect to the baseline value in a given patient. In daily clinical practice, this could allow early detection of an exacerbation or assessment of the success of a therapeutic intervention (pharmacological or non-pharmacological). It is also essential for the applicability of the CAT to research studies.

Although it was initially developed for application in patients with COPD, nowadays it is one of the best questionnaires available for the evaluation of patients with bronchiectasis, due

TABLE 3. The COPD Assessment Test (CAT) questionnaire

I never cough	0	1	2	3	4	5	I cough all the time	
I have no phlegm (mucus) on my chest at all	0	1	2	3	4	5	My chest is full of phlegm (mucus)	
My chest does not feel tight at all	0	1	2	3	4	5	My chest feels very tight	
When I walk up a hill or a flight of stairs, I am not out of breath	0	1	2	3	4	5	When I walk up a hill or a flight of stairs, I am completely out of breath	
I am not limited to doing any activities at home	0	1	2	3	4	5	I am completely limited to doing all activities at home	
I am confident leaving my home despite my lung condition	0	1	2	3	4	5	I am not confident leaving my home at all because of my lung condition	
I sleep soundly	0	1	2	3	4	5	I do not sleep soundly because of my lung condition	
I have lots of energy	0	1	2	3	4	5	I have no energy at all	
TOTAL SCORE								

COPD: chronic obstructive pulmonary disease.

to the good correlation it has shown with other questionnaires, as well as its simplicity and quickness, both for self-administration by the patient and for interpretation by the physician.

Modified Medical Research Council Scale (mMRC)

It is one of the most widely applied scales to measure dyspnoea in patients with respiratory pathology and in particular with bronchiectasis. The first version was published in 1960 by the Medical Research Council Committee and consisted of five levels. Grade 1 indicated no dyspnoea with activities of moderate intensity compared with persons of the same age, and the highest dyspnoea was grade 5, meaning the appearance of dyspnoea with basic activities of daily living or inability to leave the house due to dyspnoea. The current modified version consists of the same

gradations of zero to four points, with grade 0 being dyspnoea that appears with strenuous activities and grade 4 being dyspnoea with minimal exertion, with inability to leave the house.

It is a simple scale, quick to explain and it can provide a lot of information about the impact of dyspnoea on the daily activities of patients with respiratory diseases in general, and with bronchiectasis in particular¹⁸. Its measurement is essential for adequate clinical follow-up, and it has also a prognostic impact, which is why it is also included in the multidimensional scales described above².

Hospital Anxiety and Depression Scale (HADS)¹⁹

This is a self-administered questionnaire composed of two subscales: one for depression

(seven items) and one for anxiety (seven items). Each item is weighted from zero to three according to the frequency of occurrence of symptoms.

A total score of less than eight correlates with the absence of depressive/anxiety symptoms, between eight and ten are considered mild symptoms, and a score of 11 or higher indicates the presence of clinically significant symptoms of depression and anxiety, the maximum score being 21 points in each of the subscales.

It is a brief scale, which allows screening for the presence or absence of psychiatric disorders related to chronic pathologies in a rapid manner. It has been validated for the bronchiectasis population and has been used in several studies to evaluate the prevalence of psychiatric pathology in this disease²⁰.

HETEROGENEITY OF BRONCHIECTASIS AND QUALITY OF LIFE

As mentioned above, bronchiectasis should be considered as a multidimensional, heterogeneous and complex syndrome³. Unfortunately, our current knowledge of this syndrome is limited, and therefore, both our ability to assess its severity and the treatment offered are often insufficient. The challenge is therefore how to deal more effectively with its heterogeneity and complexity²¹. In recent years, several steps have already been taken to determine the heterogeneity of bronchiectasis, as demonstrated by the creation of multidimensional scales (E-FACED, BSI) or the recognition of the existence of homogeneous groups of patients (or clinical phenotypes). This

has made it possible to differentiate patients with bronchiectasis according to their clinical presentation, prognosis and therapeutic response, making it easier to propose the most appropriate level of care for the management of each patient.

However, this type of multidimensional assessment does not seem to be sufficient to describe the heterogeneity of this disease. For this reason, in a recent article, Martínez-García and colleagues propose the creation of an evaluation tool that allows a more global vision of the bronchiectasis syndrome to be obtained²². The proposal is to create a control panel that encompasses three different dimensions, each comprising a number of variables that are commonly used to define the disease, and which could potentially be treatable. On the one hand, there would be the SEVERITY domain, defined as the functional impairment and its extent to the target organs. Severity would be defined by variables such as FEV₁, radiological extension, comorbidities or aetiology. On the other hand, there would be the ACTIVITY domain, which would be the level of activation of the biological process that drives the progression of the disease or its consequences. This domain would include the presence of purulent sputum, the presence of chronic bronchial infection, the frequency of exacerbations and the body mass index. Finally, the third domain proposed would be the IMPACT of the disease, understood as the patient's perception of the severity and activity of the disease. Data such as the presence of productive cough, the degree of dyspnoea, the presence of depressive symptoms and health-related quality of life should be taken into account here. These last two variables can be quantified with the

questionnaires described above. It is important to note that the questionnaire(s) that should be applied to determine the impact of bronchiectasis should be simple, easy to use in clinical practice and should include psychosocial aspects. For this reason, the ideal questionnaire is probably the CAT, although it could be complemented with the HADS³. From this control panel, we could obtain ways to represent numerically or graphically the degree of affectation of each of the three dimensions assessed in a given patient at a given time²².

This approach would allow moving towards precision and personalized medicine, which brings us to the concept of “treatable traits”. This concept promotes management directed by different biomarkers that would allow carrying out individualized treatments, which may eventually lead to better clinical outcomes. The management of bronchiectasis patients targeting treatable traits would favour a treatment based on the pathophysiology (i.e., endotypes) and clinical phenotypes present in any given patient. We should bear in mind that the beneficial effects observed in the various clinical trials with the treatments usually used in bronchiectasis have so far been scarce or even nil in terms of reducing exacerbations or improving symptoms or quality of life. This is probably because the treatment has only been directed against a single trait (i.e., bronchial infection, bronchial inflammation or airway dehydration), without taking into account the possible presence of multiple other treatable traits that could hinder the effect of that treatment²³. Potentially treatable features in patients with bronchiectasis could fall into four different categories: pulmonary, extrapulmonary, aetiological

and behavioural and lifestyle treatable features. Correct assessment and appropriate treatment of the various features present in a given patient could lead to clinical and quality of life improvement, as can be seen in table 4. For this, once again, it is necessary to have appropriate assessment tools, with quality of life questionnaires being one of the most important.

CONCLUSIONS

In recent years, several quality of life questionnaires have been validated for use in patients with bronchiectasis, and some specific questionnaires have been developed for use in this clinical syndrome. Because of its simplicity and its close relationship with factors related to the severity of bronchiectasis, the authors of this review consider that the CAT is probably the best questionnaire for application in routine clinical practice. In the near future, it should be considered for inclusion among the criteria for determining the severity of bronchiectasis, as is the case in COPD^{24,25}. Bearing in mind that this is a very heterogeneous and complex disease, it is to be hoped that tools will soon be developed and validated to establish the severity of the different aspects that make up its clinical spectrum. These tools should necessarily include the assessment of quality of life by means of specific questionnaires that are easy to apply in clinical practice. This multidimensional evaluation, together with the assessment of the different treatable traits, will allow a personalised treatment to be proposed for each patient, the effectiveness of which will also be possible to monitor on an ongoing basis.

TABLE 4. Proposed treatable traits of bronchiectasis separated in aetiological, pulmonary, non-pulmonary and environment/lifestyle

	Treatable trait	Diagnostic criteria	Treatment	Expected benefits of treatment
Pulmonary	Infection*	Clinical features, Sputum characteristics, Inflammatory markers, Sputum culture	Airway clearance Prompt treatment of exacerbations Long term oral or inhaled antibiotics	Reduce exacerbations, improve QoL
	Chronic Pseudomonas infection	Two or more culture isolates at least 3 months apart in 1 year	Long term inhaled antibiotics Long term macrolides Airway clearance Eradication at first isolation	Reduce exacerbations Improve QoL Slow lung function decline Prevent chronic infection
	Mucus hypersecretion	Volume Colour of sputum	Airway clearance Airway adjunct devices Mucoactive drugs Anti-inflammatories	Reduced sputum volume Reduce viscosity- increased ease of expectoration
	Mucus plugging	Clinical features CT scan	Airway clearance Mucoactive drugs Nebulised Saline Anti-inflammatories	Reduced sputum volume Reduce viscosity/increased ease of expectoration
	Airflow obstruction	FEV ₁ /FVC < LLN Fixed ratio spirometry GLI equations	Bronchodilators Smoking cessation Exercise	Improved exercise capacity and functional status
	Asthma	Bronchodilator reversibility, Peak expiratory flow variability, Elevated sputum or blood eosinophils	ICS Systemic corticosteroids Bronchodilator Leukotriene receptor antagonists Monoclonal antibody anti IL-5, anti-IgE	Reduced exacerbations
	Eosinophilia	Elevated sputum or blood eosinophils Exclude other causes of eosinophilia	ICS Systemic corticosteroids Treatment for underlying cause	Treatment response Improve QoL
	NTM infection ^y	Positive culture and clinical/radiological findings	Long term antibiotic	Achieve remission Improve QoL
	Aspergillus sensitization	Elevated specific IgE/prick test positive	Inhaled corticosteroids, Systemic corticosteroids, Antifungals	Reduced exacerbations Reduced sputum production Improved QoL
	Bronchial hyperreactivity	Challenge tests	ICS	Reduce exacerbations
	Cough hypersensitivity	Clinical features Search other potential extrapulmonary causes Capsaicin cough challenge	Antitussive Chest physiotherapy	Improve QoL
	Respiratory insufficiency	PaO ₂ < 55 mmHg PaCO ₂ > 45 mmHg	Long term oxygen and/or non-invasive ventilation	Improve quality of life, improved survival
Aetiological	Primary Immunodeficiencies	Serum immunoglobulins levels; specific antibody levels	Reference to immunology specialist Immunoglobulin replacement	Improve outcome, QoL and prevent lung damage
	Cystic fibrosis	Clinical features Sweat chloride testing, CFTR genetic analysis +- CFTR physiologic testing	Reference to CF clinic CFTR modulators DNAse	Improve outcome, QoL and prevent lung damage
	Primary ciliary dyskinesia	Clinical features ^e Nasal NO assay Electron microscopy ciliary structure analysis or videorecording ciliary function analysis Genetic testing	Genetic counselling Intensive airway clearance Management of upper airway symptoms	Improve outcome, QoL and prevent lung damage

(continued)

TABLE 4. Proposed treatable traits of bronchiectasis separated in aetiological, pulmonary, non-pulmonary and environment/lifestyle (*continuation*)

	Treatable trait	Diagnostic criteria	Treatment	Expected benefits of treatment
Aetiological (<i>cont.</i>)	ABPA [‡]	Raised specific IgE and/or positive prick skin test to fungi, Raised total IgE Other: eosinophilia, radiological features, raised specific IgG/precipitating antibodies against fungi	Systemic corticosteroids ± Antifungals Monoclonal antibody anti-IgE ICS	Improve outcome, QoL and prevent lung damage
	CTD	Clinical features Serum antibodies	Reference to rheumatologist, Immunosuppressors	Improve outcome, QoL and prevent lung damage
	IBD	Clinical features, Serological markers, Anatomopathological findings on gut biopsy	Reference to gastroenterologist Immunosuppressors Surgery	Improve outcome, QoL and prevent lung damage
Extra-pulmonary (<i>co-morbidities</i>)	Depression/Anxiety	Questionnaires Psychologist/liason psychiatrist assessment	Anxiety management, Breathing retraining, Cognitive behavioural therapy, Pharmacotherapy, Support groups	Improve QoL
	Obesity/underweight	Body mass index	Nutritional evaluation Regular physical activity	Improve QoL and outcome
	GORD	Clinical features Gastric endoscopy pH monitoring	Proton pump inhibitor H2 antagonist Surgery (fundoplication)	Improve QoL
	Cardiovascular disease	Clinical features Electrocardiogram Echocardiogram BNP stress testing	ACE inhibitors Diuretics β-blockers Revascularization Reference to Cardiologist	Improve QoL and outcome
	Rhinosinusitis	Clinical features Imaging	Nasal steroids Leukotriene receptor antagonists Antihistamines Immunotherapy Surgery	Improve QoL
	Iron deficiency anaemia	Full Blood Count Reticulocyte count Serum iron tests Exclude other causes	Oral iron supplements Treatment of underlying cause	Improve QoL, exercise capacity
Environment and lifestyle	Smoking	Patient reported, Exhaled carbon monoxide	Tobacco cessation support Nicotine replacement Antidepressants	Improve QoL, lung function, exercise capacity, response to treatment
	Lack of exercise/ Sedentarism	Cardio-pulmonary exercise testing 6-min walk test	Exercise regularly, Pulmonary rehabilitation, Prescribed exercise programmes	Improve QoL and outcome
	Adherence	Prescription refill rate, Patient feedback	Education, Written instructions Self-management	Improve outcome
	Exposure to air pollution	PM ¹⁰ and NO ₂ concentrations	Reduce exposure	Reduce number of exacerbations

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*The presence of airway infection itself may not be a treatable trait as such since better measures are required to differentiate infection from "colonisation" where the trait is not contributing directly to disease outcome. Additional measures such as bacterial load or microbiota characterisation may be needed to fully operationalize this trait.

[‡]Could be aetiological or complication of disease.

[‡]Recurrent upper and lower tract infections; recurrent otitis in childhood; infertility; laterality disorders.

ABPA: allergic bronchopulmonary Aspergillosis; ACE: angiotensin converting enzyme; BNP: brain natriuretic peptide; CFTR: cystic fibrosis transmembrane regulator; CT: computed tomography; CTD: connective tissue disease; FEV₁: forced expiratory volume in the first second; FVC: forced vital capacity; GLI: Global Lung Function Initiative; GORD: gastro-oesophageal reflux disease; IBD: inflammatory bowel disease; ICS: inhaled corticosteroids; IL: interleukin; LLN: lower limit of normal; NTM: nontuberculous mycobacterial; PaO₂: arterial oxygen tension; PaCO₂: arterial carbon dioxide tension; PM¹⁰: particulate matter with a diameter smaller than 10 µm; QoL: quality of life.

DISCLOSURES

Dr. de la Rosa-Carrillo, Dr. Navarro-Rolon, and Dr. García-Cabo have nothing to disclose.

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