

GOLD Reports on Chronic Obstructive Pulmonary Disease (COPD): Evolutions, Revolutions and Controversies

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ABSTRACT

Twenty years after its start, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) continues to evolve and remains a source of progress and controversy in the area of chronic obstructive pulmonary disease (COPD) management. Major changes in the definition have occurred, influenced by progress in our understanding of the natural history of COPD. Similarly, while few new beneficial pharmacological classes have been developed, the way available medications should be used has significantly evolved. The burden of comorbidities is now well recognised, COPD being most often part of a multi-morbid chronic condition. The role of non-pharmacological approaches has increased with a growing interest in complex interventions such as “integrated care” or “disease management”. Instrumental support/interventions have also been an area of progress with new encouraging data on long-term non-invasive ventilation or endoscopic interventions. Altogether, COPD research is increasingly dynamic, and will most certainly solve future current debates and uncertainties. (BRN Rev. 2019;5(2):104-119)

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INTRODUCTION

The Global Initiative for chronic Obstructive Lung Disease (GOLD) was born in 1997, slightly more than 20 years ago, and produced its first report in 2001¹. A short historical perspective was published in 2017 as an editorial in the *European Respiratory Journal* by Rodriguez-Roisin and colleagues on behalf of all current and past members of GOLD Committees². Initially, GOLD emerged as a reaction against the nihilistic approach that prevailed at that time regarding chronic obstructive pulmonary disease (COPD), which was considered as incurable, self-inflicted and even untreatable, and GOLD provided a stimulus for a fresh, invigorated and proactive approach to reverse the nihilistic attitude regarding care of the COPD patient. This reaction was made possible by progress in the medical communities through newly discovered knowledge of the disease, and by demonstration of the efficacy of several pharmacological and non-pharmacological interventions on symptomatic outcomes.

The GOLD Strategy was built as an international expert panel under the auspices of the World Health Organization (WHO) and the US National Institute of Health (NIH) with the aim of improving the prevention and management of COPD globally. The panel met during several workshops to finally produce the first proposed management strategy, based on existing guidelines and, when controversy was apparent, a regular periodic re-appraisal of newly available literature by the panel¹⁻³. When the level of evidence was insufficient to support a statement, it was labelled “expert opinion”. As such, the GOLD report (which at that time was endorsed by the American Thoracic Society [ATS]) was evidence-based from its

very beginning, although not using the type of methodology that is now required for guidelines (e.g., the GRADE approach)⁴. Although GOLD subsequently became independent from WHO, NIH and ATS, the methods applied remained roughly the same. Therefore, it should now be considered as a strategy rather than a guidelines document, strictly speaking. The document is revised every year, and major changes have occurred every five years (i.e. in 2006, 2011 and 2017)⁵⁻⁷, some leading to large debates, especially following changes in the classification⁸. The recent GOLD 2019 update, although not complying with the timing of a major revision, contains major conceptual modifications regarding the pharmacological management⁹.

During the last 20 years or so, a significant number of studies have focused on COPD clinical care. The main task of the GOLD Science Committee has been to propose the best management strategies based on this literature; each potentially relevant paper identified through a systematic literature search that is appraised by two panel members, to determine whether and how it should lead to a change in the document. When the two experts disagree, the paper is discussed by the entire panel during a workshop (satellite to the European Respiratory Society [ERS] and ATS annual congresses), to reach an agreement. Importantly, the GOLD document intends to be global, i.e. applicable in virtually all areas of the world. This means that the GOLD propositions need to be adaptable to very different healthcare systems and contexts of care, which represents an important challenge.

What are the topics for which major changes have occurred since the first release of a

GOLD report? Not surprisingly, no area is exempt from significant evolutions (i.e. revisions within the same conceptual framework), and many have been subject to revolutions (i.e. conceptual changes). In this review we will follow the contents of the last GOLD report, sequentially focusing on the definition of COPD, the classification of the disease and the role of spirometry, assessment of and care for comorbidities, pharmacological and non-pharmacological strategies, and asthma-COPD overlap (ACO). Within these sections we will more briefly touch on the detection strategy and the development and natural history of the disease. Due to space constraints and the long duration of the GOLD history, we had to make some choices regarding the topics covered. These choices were partly arbitrary, but also guided by the remaining controversies that we hope will be clarified in the next few years.

DEFINITION AND DIAGNOSIS

At first glance, the definition of COPD may be considered of less importance than other priorities of the GOLD committees, focus, but it represents a rather accurate translation of the evolution of some/most of the concepts surrounding the disease. All the changes mentioned below were the result of sometimes intense debates, and most are still areas of controversy.

In 2001, GOLD defined COPD as “a disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases”¹. Since then, several elements have been added

or deleted from this definition: in 2006, the major notion of “preventable and treatable” disease was added to underline the need for action from healthcare providers and deciders⁵. The inflammatory character of the disease was removed in 2017⁷ to prevent the use of inhaled corticosteroids (ICS) from being routinely prescribed to patients with COPD (as found in multiple practice surveys), since many studies suggest that these agents are more useful to prevent some subtypes of exacerbations (those treated with oral corticosteroids), with clearer benefit in some subpopulations of patients (e.g., those with higher blood eosinophil counts)^{10,11}: even if some degree of inflammation can be observed in most patients, it is often poorly sensitive to corticosteroids¹², due to the type of effector inflammatory cells involved (i.e. neutrophils) and to some molecular mechanisms¹³. Other aims of this change were to simplify the definition and to align it to how the diagnosis is made.

The bronchial and parenchymal components of airflow obstruction are specifically highlighted in the definition since 2017, although they were mentioned in all previous GOLD documents^{1,5-7}. At the same time, respiratory symptoms have been added to the definition to prevent physicians from considering that a patient with completely asymptomatic persistent airflow limitation requires COPD therapy. This represents a major difference with the initial GOLD document, which acknowledged that patients with COPD could be asymptomatic but could still require some maintenance therapy¹. Symptoms are also of high importance as triggers of spirometry-based case-finding strategies (Fig. 1)¹⁴, although there is some debate regarding the most effective policy¹⁵. The typical COPD patient has long

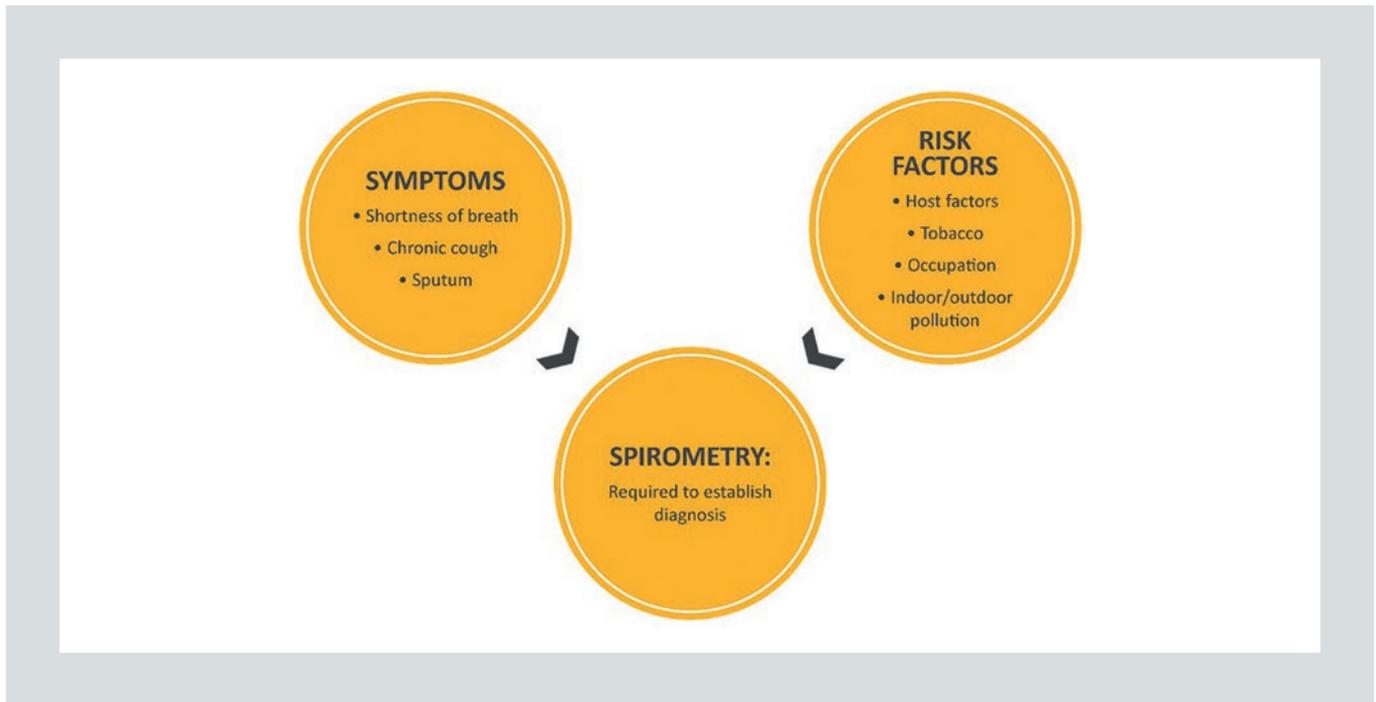


FIGURE 1. Pathways for the diagnosis of chronic obstructive pulmonary disease (reproduced with permission from reference⁹).

been viewed as an elderly man with a history of heavy smoking, chronic dyspnoea and metabolic and/or cardiovascular comorbidities. However, a significant proportion of patients are middle-aged and/or women and/or have no complaints. Moreover, even if they represent only a minority of patients, non-smokers (20% of COPD patients) and non-comorbid patients (about 30% of COPD populations) are not infrequent. Therefore, considering a diagnosis of COPD should not be restricted to subjects exhibiting all the typical features mentioned above.

The high prevalence of COPD worldwide is emphasised since 2011 using the term “common” to qualify the disease. Finally, its “usually progressive” nature has been deleted in 2017 following the publication of long-term cohort studies showing that the disease severity can remain perfectly stable during many

years in a significant proportion of patients⁷. In addition, lung function trajectories leading to COPD are variable, accelerated lung function decline being dominant in some patients while, in others, poor lung development relating to childhood risk factors are involved¹⁶.

Importantly, the only component of the definition to remain constant from the beginning of GOLD history is chronic persistent (= not fully reversible) airflow limitation. This is the source of some complexity regarding COPD management at a global level since it means that COPD cannot be diagnosed without performing spirometry. The unsolved area of debate here is the way to diagnose airflow limitation using the forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) ratio, with a unique 0.7 threshold (easier to operationalise) or using the lower limit of normal (more physiologically correct)^{17,18}.

At the end, are we sure that the current definition is the right one? Certainly not: it could also be that, in some subjects, symptoms in the absence of airflow obstruction indicate early COPD. However, this remains to be formally confirmed. There is even some controversy regarding the very existence of COPD: some top-level experts have suggested that, as advocated by the Dutch hypothesis in the early 1960's¹⁹, asthma and COPD should be considered as a continuum of the same condition²⁰, with variations arising from the types of gene-environment interactions that participated to the development of the condition, leading to identify endotypes (pathophysiological profiles identified through biomarkers), phenotypes (clinical profiles with specific outcomes)²¹ and treatable traits (individual clinical or biological characteristics that represent targets for individual treatments and can be associated differently within individuals)²². This forms the basis of more precise individualisation of treatment approaches, corresponding to precision or personalised medicine, respectively synonymous to or part of Personalised, Preventive, Predictive and Participative (4P)²³.

Another point of discussion is the definition of exacerbations: the GOLD document proposes to define these events as “an increase in symptoms requiring additional therapy”, not mentioning any specific mechanism or aetiology. The document also mentions that COPD exacerbations must be differentiated from other causes of increased respiratory symptoms including cardio-vascular events. The clinical situation is often more complex due to intricated components participating in the increase in symptoms, the challenge being to determine what is the dominant one. We added this point of discussion.

DISEASE CATEGORISATION AND RELATED ASSESSMENT SCHEMES

Purposes of disease categorisation are to establish the prognosis, guide treatment choices, and harmonise communication between healthcare professionals, and with healthcare professionals and patients. Defining categorisation schemes that satisfy all these requirements is highly challenging. As the definition, disease categorisation largely reflects conceptual approaches to disease assessment and therapeutic strategies.

The first GOLD classification of COPD was based only on the level of airflow limitation, and the need for long-term oxygen therapy (LTOT), i.e. the presence of respiratory failure based on resting partial pressure of oxygen (PaO_2) and of clinical signs of right failure (Table 1)¹. Relying only on FEV_1 and arterial blood gases had several advantages: it was simple and based on well-defined prognostic factors and highly robust (i.e. reproducible) variables. Even at that time, however, it was not sufficient to guide treatment choices since other patients' characteristics had to be taken into account to make treatment choices, namely dyspnoea and exacerbations. Thus, the criteria driving therapeutic strategies at that time were very similar to those used now.

The labels of spirometric categories were changed in 2006 (Fig. 2) to qualify patients with FEV_1 between 30% and 50% predicted as severe rather than moderate, and those with FEV_1 below 30% as very severe rather than severe⁵. This new labelling was closer to the clinical impact usually perceived at the considered ranges of FEV_1 impairment.

TABLE 1. GOLD 2001 classification and therapeutic strategy¹

Label	Characteristics	Recommended treatment	
All		<ul style="list-style-type: none"> – Risk avoidance – Influenza vaccination 	
0: At risk	<ul style="list-style-type: none"> – Chronic symptoms – Risk factors – Normal spirometry 		
I: Mild COPD	<ul style="list-style-type: none"> – FEV₁/FVC < 0.7 – FEV₁ ≥ 80% – With or without symptoms 	<ul style="list-style-type: none"> – Short-acting BDs when needed 	
II: Moderate COPD	<ul style="list-style-type: none"> – IIA: FEV₁/FVC < 0.7 – FEV₁ 50%-80% – With or without symptoms 	<ul style="list-style-type: none"> – Regular BDs – Rehabilitation 	<ul style="list-style-type: none"> – ICS if symptoms or lung function response
	<ul style="list-style-type: none"> – IIB: FEV₁/FVC < 0.7 – FEV₁ 30%-50% – With or without symptoms 	<ul style="list-style-type: none"> – Regular BDs – Rehabilitation 	<ul style="list-style-type: none"> – ICS if symptoms or lung function response or repeated exacerbation
III: Severe COPD	<ul style="list-style-type: none"> – FEV₁/FVC < 0.7 – FEV₁ < 30% or respiratory or right heart failure 	<ul style="list-style-type: none"> – Regular BDs – ICS if symptoms or lung function response or repeated exacerbation – Treatment of complications – Rehabilitation – LTOT if respiratory failure – Consider surgery 	

BD: bronchodilators; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; ICS: inhaled corticosteroids; LTOT: long-term oxygen therapy.

Simultaneously, the GOLD 0 stage (chronic bronchitis without airflow limitation, i.e. “at risk of COPD”) disappeared, since the prognostic value and natural history of this “profile” was uncertain, especially regarding the risk of transition to “real” COPD (i.e. with chronic airflow limitation).

At the end of the 2000’s, the large Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) cohort study allowed a thorough analysis of the relations between FEV₁ and clinical features, outlining that FEV₁ cannot exhaustively reflect all of the important clinical components of the disease^{24,25}. The GOLD group thus decided to propose a more individualised categorisation scheme based on both symptoms and exacerbation risk, together with FEV₁

(Fig. 3). This scheme aimed at following more closely the main attainable goals of COPD care identified since the initiation of GOLD, i.e. symptoms relief and improvement of exercise tolerance and health status, and risk (mainly, of exacerbations) prevention⁶.

Dyspnoea predominated as the major target for symptom relief since it is generally more disabling than chronic cough with or without sputum production, and since there is no treatment specifically targeting cough/sputum production²⁶. Interestingly, the “dyspnoea – exercise tolerance – quality of life” sequence found in the “symptoms” group of GOLD-defined treatment goals somehow follows the “impairment – disability/impaired functioning/activity limitation – participation restriction/handicap” sequence described by the

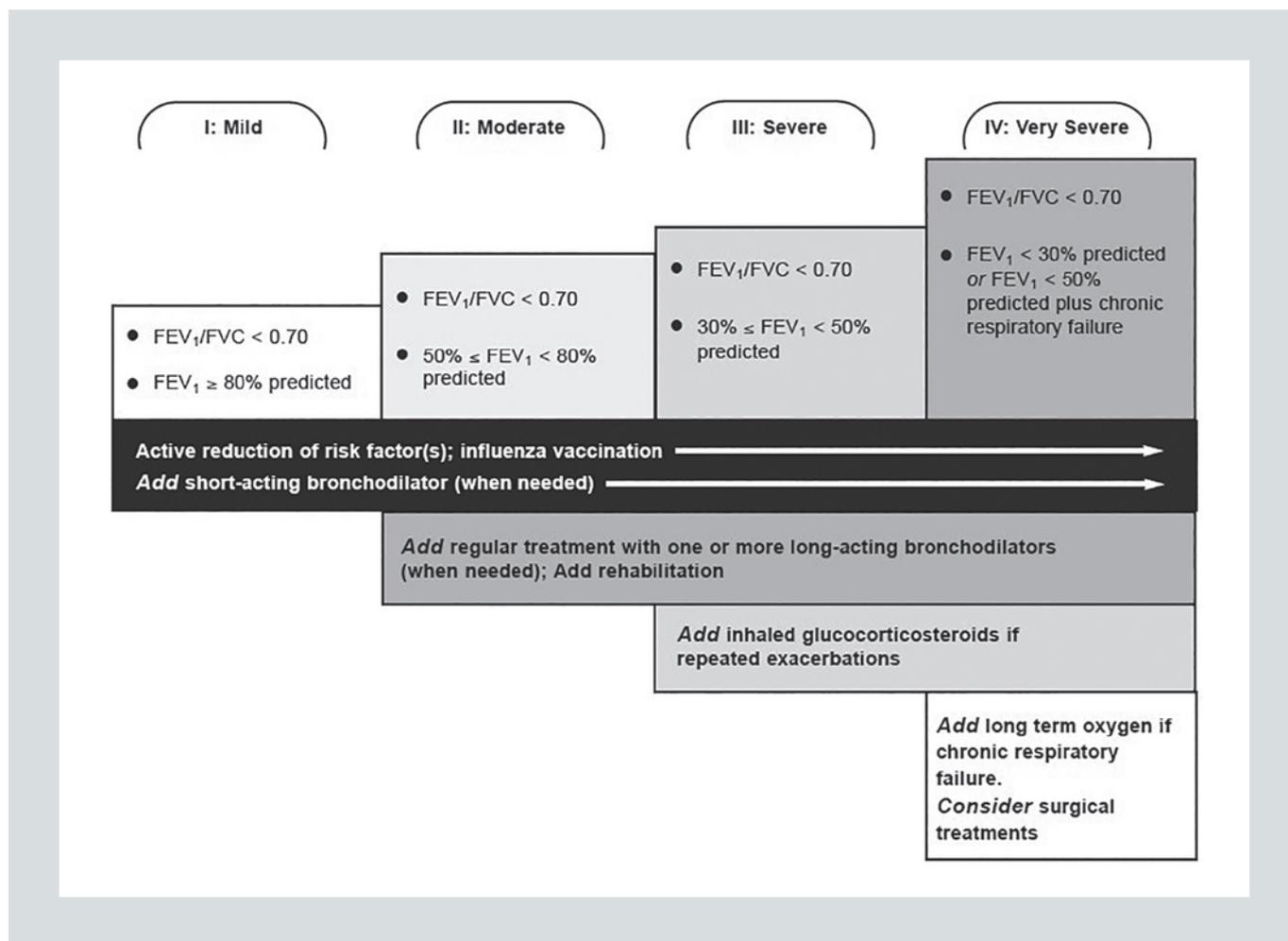


FIGURE 2. GOLD 2006 classification and therapeutic strategy (reproduced with permission from the GOLD 2006 report).

FEV_1 : forced expiratory volume in one second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease.

WHO in its International Classification of Functioning, Disability and Health²⁷.

The GOLD 2012 Revision aimed at emphasising the concept of future risk, including risks of exacerbations, death, disease progression⁶. In terms of exacerbations, several studies including ECLIPSE surmised that the past history of exacerbations is a much stronger predictor of exacerbation risk than FEV_1 , which was subsequently removed from the (2017) GOLD categorisation scheme²⁵. This led to two separate classifications, one for FEV_1 (1-2-3-4) and one for clinical features

(A-B-C-D) based on symptoms/health status and exacerbation history (Fig. 3)⁸. The clinical classification is the only one used to choose between pharmacological treatment options, which led some physicians to fear that spirometry would not be used anymore for COPD management. But, importantly, GOLD emphasises the major roles of spirometry for case-finding, diagnosis and differential diagnosis, prognostic assessment, follow-up of disease evolution and decision of some non-pharmacological treatment interventions. Spirometry keeps a crucial role to guide pharmacological treatment decisions, since the

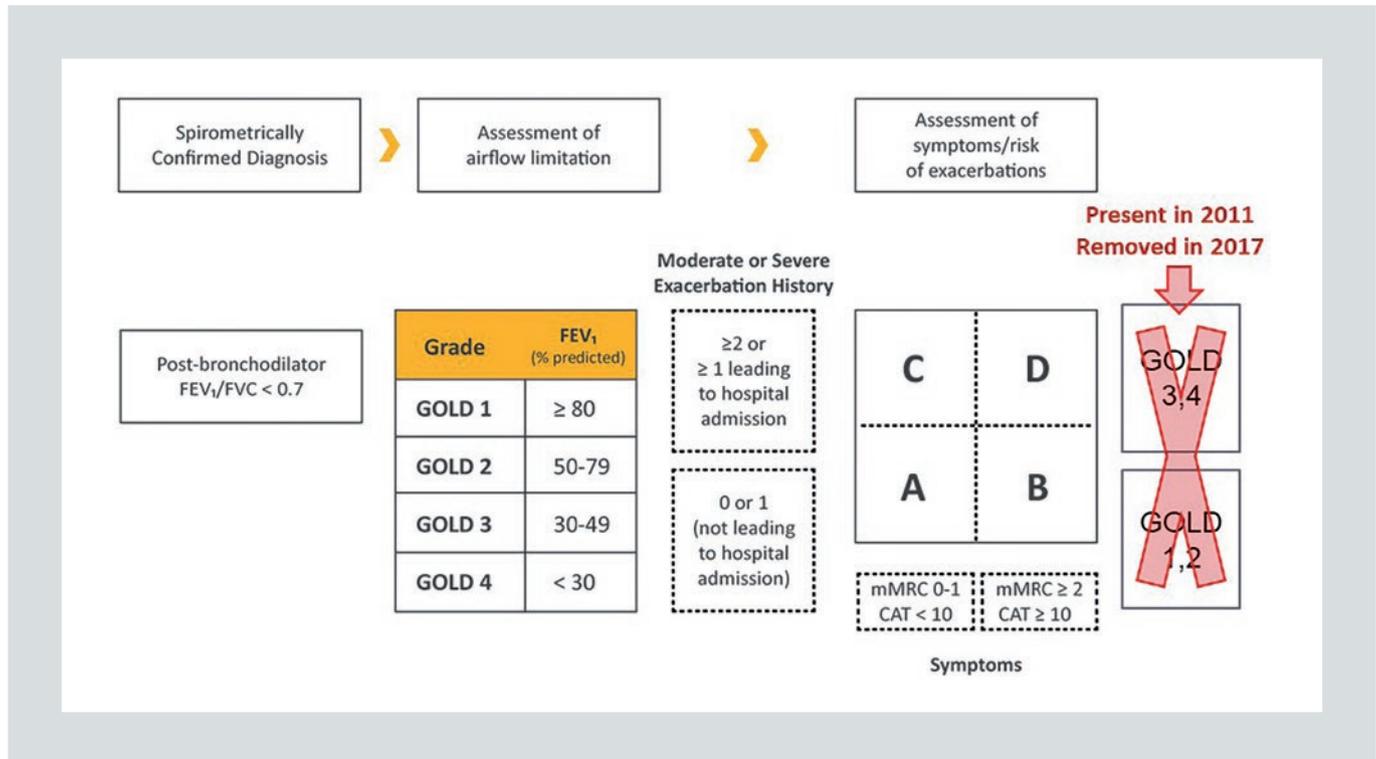


FIGURE 3. GOLD 2011 and 2017 classifications (adapted with permission from reference⁹).

CAT: COPD Assessment Test; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: modified Medical Research Council.

GOLD propositions for medication choices are applicable only to patients with COPD, which implies that spirometric confirmation is always needed.

COMORBIDITIES

Since 2011, a full chapter is dedicated to COPD comorbidities, listed in Table 2⁶. This follows the understanding of the major impact of these conditions on the burden and management of the disease^{28,29}. While this burden is not an area of controversy, the way comorbidities interact with COPD is still debated. At some point COPD has even been considered as being causally linked with other conditions via the systemic inflammation that it induces through uncertain mechanisms, maybe in

part linked to airways inflammation³⁰. Along the same line but with less confidence as to the direction of causality, COPD has been viewed as one component of a systemic inflammatory condition³¹. These concepts have evolved towards a less monolithic association between the type and severity of comorbidity that is associated with COPD. It is now recognised that diverse and complex combinations of multimorbid conditions can be found in patients with COPD^{32,33}.

Most guideline recommendations do not provide clear guidance regarding whether and how patients with COPD should be screened for comorbidities, and vice-versa. The most logical strategy is probably to rely on the same risk-based strategies that are used in the general population, i.e. to screen patients for risk

factors and apply diagnostic procedures based on these factors. In terms of treatment, all guidelines concur in recommending to care for these conditions as in the general population⁹. Importantly, COPD should not be considered as a contraindication to the use of selective beta-blockers when there is a clear cardiovascular indication (ischaemic heart disease, heart failure)³⁴. Some observational studies suggested that drugs used in cardiovascular conditions could improve the prognosis of COPD (exacerbations occurrence, survival), even in the absence of cardiovascular disease or risk^{35,36}. This has not been confirmed in randomised controlled trials (RCTs), so the uncertainty remains³⁷.

PHARMACOLOGICAL THERAPY

The pharmacological classes available for COPD have not changed much over the last 20 years: clinicians still mostly rely on inhaled bronchodilators (beta₂ agonists and anticholinergic agents) and corticosteroids. What has changed is the number of available molecules, their duration of action, the co-administration of various combinations of the molecules, and their mode of administration (the inhaler device).

In parallel, a considerable number of clinical trials has been published⁹, with increasing robustness as illustrated by longer follow-up durations, larger sample sizes, more appropriate type of (active) comparators, etc. These trials allowed to set what can be expected from currently available COPD pharmacotherapy, i.e. symptoms control and exacerbations prevention. Indeed, no clinical trial could reliably establish an effect of any medication on lung

function decline or mortality. Such effects were however suggested in some studies with various molecules, but methodological limitations (e.g., *post hoc* nature of analyses, secondary rather than primary objectives) prevented from deriving firm conclusions³⁸⁻⁴¹. Studies progressively refined the target populations for each type of pharmacological agent (see below), although we are still relatively far away from sophisticated precision medicine. It is indeed interesting to compare the GOLD 2019 document to the 2001 GOLD therapeutic recommendations (Table 1): in 2001 the main driver of therapeutic choices was FEV₁ but clinical features (symptoms, exacerbations) were already clearly taken into account: this is not something that has been “invented” recently^{1,9}. Conversely, one criterium to initiate ICT was lung function reversibility, which has subsequently been completely abandoned, due to its inability to predict long-term outcomes reliably⁴²⁻⁴⁴. Conversely, in 2001 it was already known that a lack of FEV₁ improvement did not preclude bronchodilators from being clinically effective in terms of dyspnoea and exercise tolerance. In the next iteration of the GOLD therapeutic guidance (2006) the therapeutic scheme moved to the “escalator” model (Fig. 2)⁵, which looked mostly FEV₁-based although exacerbations were still present, while dyspnoea was clearly mentioned as the main driver of bronchodilator choice. In 2011 symptoms and exacerbations took a more prominent role as pharmacological treatment drivers (Fig. 4)⁶, and now represent the main criteria to base treatment decisions (Fig. 5)⁷. When considering this description of back and forth movements around how to select and present decision criteria, one could wonder whether we are contemplating significant progresses or running in circles, limited by

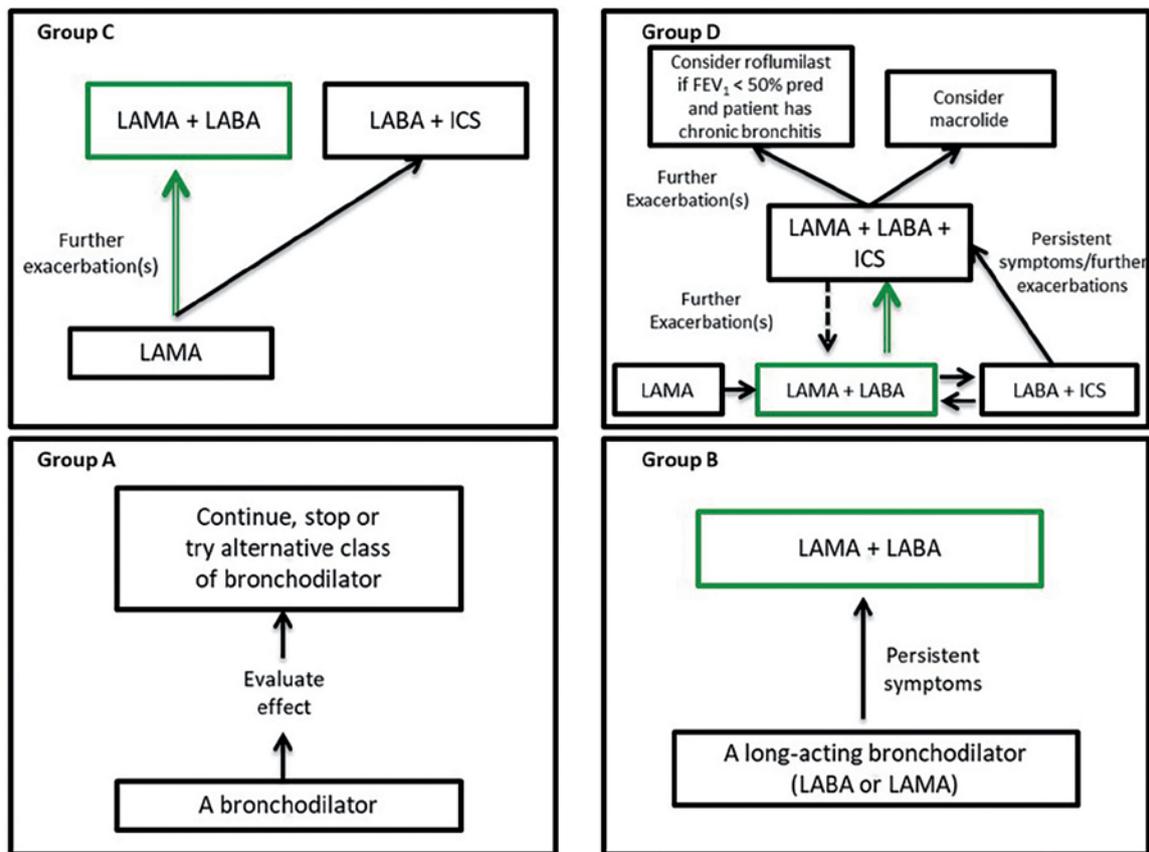


FIGURE 4. GOLD 2017 therapeutic strategy (reproduced with permission from the GOLD 2017 report).

FEV₁ forced expiratory volume in one second; ICS: inhaled corticosteroids; LABA: long-acting β_2 antagonist; LAMA: long-acting muscarinic antagonist.

the lack of new and really effective treatments. What is clear though is that at least concepts have markedly evolved towards more personalised medicine, as discussed earlier and as illustrated by the very recent evidence-based irruption of blood eosinophil counts as guides to help deciding whether or not ICS are indicated⁹. Here the evidence shows that there is a continuous relationship between the preventive effect of ICS added to bronchodilators on exacerbations occurrence, and blood eosinophil counts⁴⁵. Whether the above relates an

effector target of the disease with a clinical treatment response, or is only an indirect reflect of the modulation of other pathways is unknown. Anyway, it may help to select patients who benefit more from a “bronchodilators only” or an “ICS-containing” strategy, given the conflicting results of recent studies as to which of these options provides the greatest prevention of exacerbations. Importantly, the threshold of blood eosinophil count above which an ICS-containing regimen should be preferred (300 or 100/mm³) varies

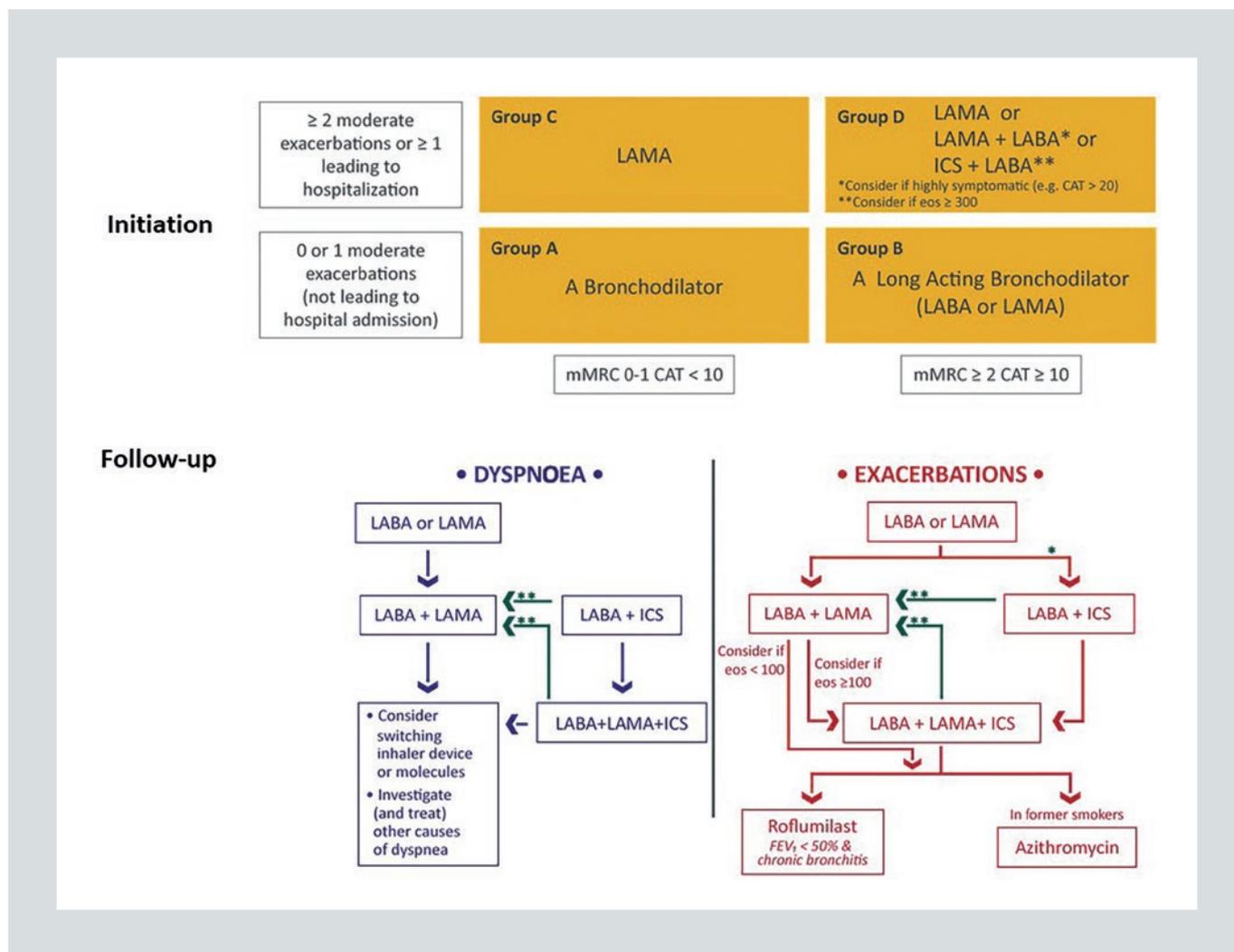


FIGURE 5. GOLD 2019 therapeutic strategy (reproduced with permission from reference⁹).

CAT: COPD Assessment Test; eos: eosinophils; FEV₁: forced expiratory volume in one second; ICS: inhaled corticosteroids; LABA: long-acting β_2 antagonist; LAMA: long-acting muscarinic antagonist; mMRC: modified Medical Research Council.

depending on the risk of exacerbations, as estimated based on the past history of exacerbations⁹.

Another clear application of endotype-driven personalised medicine in COPD is augmentation therapy for alpha1 antitrypsin deficiency. However, randomised trials found that this treatment decreased the rate of decline in lung density but did not affect clinical or lung function variables or survival⁴⁶. The GOLD

strategy proposes to consider this treatment in patients with “progressive disease”, but how this should be defined is unclear.

Over the last few years, other endotypes have been considered: bacterially colonised (or chronically infected) patients also represent an area of interest, especially now we have entered in the microbiome era⁴⁷. Indeed, therapeutic choices for exacerbation treatment and prevention should may differ depending on

the predominant type of exacerbations a patient experiences (inflammatory, especially eosinophilic, leading to prescribe ICS, or bacterial, leading to prefer, e.g., azithromycin)⁴⁸⁻⁵¹.

Besides the question of pharmacological agents per se, the GOLD panel has expressed increasing interest for inhalers: it is now very well demonstrated that poor inhaler technique is associated with poorer outcomes, as in asthma⁵²⁻⁵³. Therefore, GOLD now strongly emphasises the need to provide patient education and to choose inhalers wisely⁵⁴. Poor adherence is also associated with increased mortality, which is not only due to the insufficiency of active treatment since it remains true in patients receiving placebo⁵⁵, suggesting that it is a more global behavioural issue.

A major addition to the most recent GOLD document is the “review – assess – adjust” management cycle, which denotes the need to adapt treatments in a dynamic manner, also illustrated by the decision trees dedicated to follow-up, the ABCD quadrants being used only to decide initial therapy (Fig. 5) while in 2011 there was one decision tree per quadrant (Fig. 4)⁹.

Another area of controversy regarding the assessment of new medications is the level of confidence that we should have in RCTs and observational studies⁵⁶: patients recruited in RCTs are highly selected and, once included, they are cared for in a very controlled environment. Consequently, they differ from what is seen in the real-life, which leads to question the generalisability of their results. On the opposite, RCTs have the highest degree of internal validity. Therefore the

best way to assess a treatment option is probably to combine somehow real-life effectiveness studies and randomised trials. The big issue there is that we do not really know how to do this: the GRADE approach allows to upgrade the level of evidence provided by observational effectiveness studies from low to moderate⁴. But despite all efforts to decrease the risk of bias through matching and adjustments, there is always a risk of hidden residual confounding that prevents from qualifying these studies as “high-level evidence”. Pragmatic RCTs could be a solution to this dilemma and some attempts have been made recently⁵⁷, but progresses remain necessary to improve the reliability and understandability of their results.

NON-PHARMACOLOGICAL APPROACHES

Since the first GOLD document, rehabilitation and education have been strongly promoted. There is no debate regarding the utility of rehabilitation, and the Cochrane collaboration even closed its review on this topic⁵⁸. Conversely, studies are still required to determine the best modalities and settings. In 2014, a rehabilitation program initiated 48 hours after admission for an acute exacerbation of COPD proved ineffective in terms of readmission rate and potentially deleterious in terms of mortality⁵⁹. The data collected during this study could not provide any clear explanation. Similarly and contrary to what has been found in most trials, a self-management program has been unexpectedly shown to be associated with increased mortality⁶⁰. Unwanted behavioural changes such as a lower uptake of further programs or excessive confidence

leading to delayed healthcare contacts in the event of a deterioration have been hypothesised. Complex interventions including self-management interventions, disease management or integrated care programs are being increasingly studied with mitigated results^{61,62}. An important issue there relates to the description of the programs in the related publications, which needs to be sufficiently detailed to be replicated. When the level of detail is insufficient, it makes it difficult to assess these strategies globally. New technologies of information and communication (NTIC) will certainly provide new avenues for patient support^{63,64}. Many connected solutions are currently developed to improve device use, adherence to care and, more globally, health behaviours. Such solutions can also provide education and counselling not only to patients but also to healthcare providers. They will be further reinforced by the development of artificial intelligence, with its predictive potential (regarding, e.g., the real-time risk or detection of exacerbations).

Many new instrumental approaches have been developed and/or tested in the last two decades and some have thus appeared in the GOLD documents. Specifically, there is growing interest in bronchoscopic lung volume reduction interventions using coils, valves, vapor... Some of these techniques are authorised and reimbursed in some countries, based on studies showing benefits, mostly in terms of exercise tolerance in severely hyperinflated patients⁶⁵. These techniques are based on the same concept as lung volume reduction surgery, i.e. that exercise limitation in COPD is mostly related to the imbalance between increased ventilatory constraints and decreased diaphragmatic capacity, both due

to hyperinflation⁶⁶. Lung volume reduction surgery provided one of the first clear illustrations of how care for COPD could and should be individualised, with very different and even opposite results depending on the level of lung function impairment (FEV₁, transfer factor for carbon monoxide [TLCO]), exercise capacity and emphysema heterogeneity and predominance⁶⁷. The results of bronchoscopic techniques seem to be less influenced by these factors, but for some of them (bronchial valves, namely) other factors need to be considered such as the presence of interlobar collateral ventilation.

Whether LTOT can provide some advantage to patients with no “classical” indication but who get hypoxemic during exercise has long been a matter of debate. It now seems that there is no clinical or prognostic benefit to support its use⁶⁸. Finally, while the first studies of long-term non-invasive ventilation in COPD patients were disappointing, two more recent trials found a survival benefit in markedly hypercapnic patients who had been admitted for respiratory failure. What these studies had in common was the relatively high-pressure settings and ambitious targets in terms of partial pressure carbon dioxide (PaCO₂) reduction⁶⁹.

ASTHMA-CHRONIC OBSTRUCTIVE PULMONARY DISEASE OVERLAP

In 2014, the Global Initiative for Asthma (GINA) and GOLD committees (which meet in adjacent rooms before each ATS and ERS annual congress) developed a joint document on the Asthma-COPD overlap syndrome (ACOS), which was subsequently labelled Asthma-COPD

overlap (ACO) since it was agreed that this condition or group of conditions did not meet the definition of a syndrome⁷⁰. The decision to propose a statement on ACO was based on the observation that asthma and COPD can coexist and are sometimes impossible to distinguish when patients exhibit characteristics of both diseases in similar proportions⁷¹. Indeed, the original intent of the GINA-GOLD document on ACOS was to “provide an approach to distinguishing between asthma, COPD and the overlap of asthma and COPD”. In such situations, the logic tells us to treat as a combination of asthma (using ICS) and COPD (using bronchodilators), which also corresponds to the treatment of “pure” asthma with persistent symptoms and airflow limitation, or “pure” COPD with exacerbations and higher blood eosinophils. Following this novel proposal, some controversy arose regarding the definition of ACO, its underlying mechanisms and its relevance as a guide to care⁷². It may be advocated that the most important component of care in this field is to make every possible effort to differentiate asthma from COPD rather than putting them in the same “basket”, which is easier in terms of treatment decisions, but may lead to inadequate strategies, especially in terms of ICS use in COPD. Simultaneously, it is certainly true that, as mentioned above, some patients do present with features of asthma and features of COPD. However, these correspond to several distinct profiles, depending on which features of asthma and which features of COPD are present²¹. These debates get us back to the concepts of phenotypes, endotypes and treatable traits. It may well be that in a few years (or more), asthma and COPD labels will be abandoned, patients being grouped under a “chronic obstructive

airways disease” denomination, treatment choices being guided by their individual traits. Interestingly, this would fit well with the Dutch hypothesis that was formulated half a century ago¹⁹.

CONCLUSIONS

The most important advance contained in GOLD documents is probably the concept that this is a treatable disease. The GOLD strategy faces a great challenge when aiming at being global, i.e. applicable in countries and settings with highly variable economic contexts and access to care: in some countries, spirometry is not widely accessible, and many treatments are not available. Another challenge comes from the limited magnitude of treatment effects that can be expected, given the partly irreversible nature of lung damage, i.e. emphysema and airway remodelling. Treatments targeting these components have not been successful yet⁷³, but active research is ongoing to identify new approaches⁷⁴. Altogether, there have been few new classes of drugs for COPD, although some useful refinements in the way available medications are integrated in the global therapeutic strategies have been suggested. The same is true for non-pharmacological treatments, although in this field novel instrumental approaches are being developed. A crucial issue is to define the role of general practitioners (GPs) in COPD care. This role is central since GPs are in a first line position to identify and follow the patients. In addition, the disease is often associated with comorbidities, making holistic care crucial. Whether and how GPs shall interact with lung specialists is highly dependent on the local organisation of care.

DISCLOSURES

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