GOLD Science Committee recommendations for the use of pre- and post-bronchodilator spirometry for the diagnosis of COPD

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Pre-bronchodilator spirometry can exclude COPD, while post-bronchodilator measurement is needed to diagnose COPD https://bit.ly/4eKAbx8

Cite this article as: Singh D, Stockley R, Anzueto A, *et al*. GOLD Science Committee recommendations for the use of pre- and post-bronchodilator spirometry for the diagnosis of COPD. *Eur Respir J* 2025; 65: 2401603 [DOI: 10.1183/13993003.01603-2024].

Received: 14 Aug 2024
Accepted: 14 Nov 2024

Abstract

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report states that the diagnosis of COPD should be considered in individuals with chronic respiratory symptoms and/or exposure to risk factors. Forced spirometry demonstrating airflow obstruction after bronchodilation is required to confirm the diagnosis using a threshold of forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio <0.7. This GOLD Science Committee review weighs the evidence for using pre- or post-bronchodilator (BD) spirometry to diagnose COPD. Cohort studies have shown that pre- and post-BD spirometry give concordant diagnostic results in most cases, although the prevalence of COPD is up to 36% lower with post-BD values. Discordant results may occur in "volume" or "flow" responders. Volume responders have reduced FVC due to gas trapping causing FEV_1/FVC ⩾0.7 pre-BD, but a volume response occurs post-BD with a greater improvement in FVC relative to FEV_1 decreasing the ratio to <0.7. Flow responders show a greater FEV_1 improvement relative to FVC which may increase FEV_1/FVC from <0.7 pre-BD to ⩾0.7 post-BD; these individuals have an increased likelihood of developing post-BD obstruction during follow-up and require monitoring longitudinally. GOLD 2025 recommends using pre-BD spirometry to rule out COPD and post-BD measurements to confirm the diagnosis. This will reduce clinical workload. Post-BD results close to the threshold should be repeated to ensure a correct diagnosis is made. Post-BD measurements ensure that volume responders are not overlooked and limit COPD overdiagnosis.

Introduction

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report states that the diagnosis of COPD should be considered in individuals with chronic respiratory symptoms and/or exposure to risk factors, such as cigarette or biomass smoke exposure [1]. According to the GOLD report, forced spirometry demonstrating airflow obstruction after bronchodilation is required to confirm the diagnosis of COPD. The combination of clinical evaluation and spirometry reduces the potential for COPD overdiagnosis and overtreatment, which may occur if either step is omitted.

The threshold value which GOLD recommends to define airflow obstruction is a post-bronchodilator (BD) forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio <0.7 [1]. This criterion was established in the first GOLD report in 2001 and, although regularly reconsidered, GOLD has maintained the recommendation [2, 3]. The concept that airflow obstruction in COPD is persistent and cannot be fully reversed provided the rationale for this recommendation, with post-BD FEV_1/FVC <0.7 ensuring that the diagnosis of COPD was confined to individuals with persistent airflow obstruction despite BD treatment [4]. The magnitude of BD responsiveness (BDR) was also believed to enable differentiation of COPD from asthma, although we now know that it has poor discriminative properties [5]. Other reasons why GOLD originally favoured post- over pre-BD measurements included the perception of greater reproducibility (although there is little evidence to support this), that post-BD values provide superior prognostic prediction, and that a pre-BD FEV_1/FVC ⩾0.7 may be observed in COPD patients with significant gas trapping since an increased residual volume (RV) decreases inspiratory capacity (IC) and FVC leading to an increased FEV_1/FVC ratio [6, 7]. In such patients with significant gas trapping, the administration of a BD can reduce gas trapping and increase FVC (a volume response), sometimes to a greater extent than the effect on FEV_1, with the effect of reducing the FEV_1/FVC ratio. The use of post-BD values in clinical trials facilitated widespread acceptance of this measurement for COPD diagnosis.

Spirometry is underutilised to diagnose COPD in clinical practice [8–10], with practical implementation and training issues contributing to low uptake. More widespread use must be encouraged. Studies in England, Wales, Denmark, Sweden, Korea and the USA have shown that spirometry had not been performed in 40–50% of patients diagnosed with COPD [8, 11–15] and post-BD measurements had not been performed in 25–50% of the cases with spirometry [8, 11]. The data from England also show that the proportion of patients who had spirometry at diagnosis has declined in recent years [12]. Even when spirometry has been performed there is evidence of incorrect interpretation resulting in significant misdiagnosis, *e.g.* 25% patients diagnosed with COPD in Wales having incompatible post-BD spirometry [11]. Compared to pre-BD spirometry, the addition of post-BD measurements is more time consuming and complicated to perform. This may impede efficient outpatient operations and contribute to suboptimal uptake in clinical practice.

Given these issues, it is important to ensure that the current recommendations for diagnostic spirometry are both supported by evidence and are as practical as possible. The GOLD Science Committee has conducted a re-evaluation of the evidence and rationale for using pre- or post-BD spirometry for the diagnosis of COPD. Here we discuss the evidence and describe changes to the GOLD 2025 report arising from the review. Of note, the Global Lung Function Initiative (GLI) has established reference ranges using pre-BD values in non-smokers, with age-corrected lower limit of normal (LLN) values used to define abnormal lung function [16]. There has been considerable debate concerning the merits of using a fixed ratio (0.7) *versus* LLN for the diagnosis of COPD [16, 17]. This GOLD Science Committee review focused on the use of pre- or post-BD measurements in the diagnostic process and the issues concerning fixed ratio *versus* LLN or the use of appropriate reference values were not within the current scope.

Effects of bronchodilators on lung physiology in COPD

The hallmark pathophysiological features of COPD include small airway luminal narrowing, caused by inflammation and remodelling, and small airway collapse due to the loss of supporting alveolar attachments [18, 19]. There is also destruction of peripheral airways and parenchyma, with the latter reducing the elastic recoil of the lungs during expiration [6]. Collectively, these features cause increased small airway resistance, reduced expiratory flow and gas trapping on expiration (figure 1) [6]. Expiratory flow limitation with small airway collapse during tidal breathing is common in COPD [20–23]. Increased airway resistance coupled with reduced elastic recoil prevents effort-related increases in expiratory flow rate. Therefore, gas trapping worsens when exercising as there is a hyperventilation-related reduction in expiratory time, causing an increase in operational lung volumes (dynamic lung hyperinflation) and work of breathing which is responsible for dyspnoea on exertion [24].

FEV_1 reflects the expiratory flow rate, while, in contrast, FVC is not time constrained and represents the total volume expired. Lung destruction and gas trapping in COPD both reduce FVC, although there is a

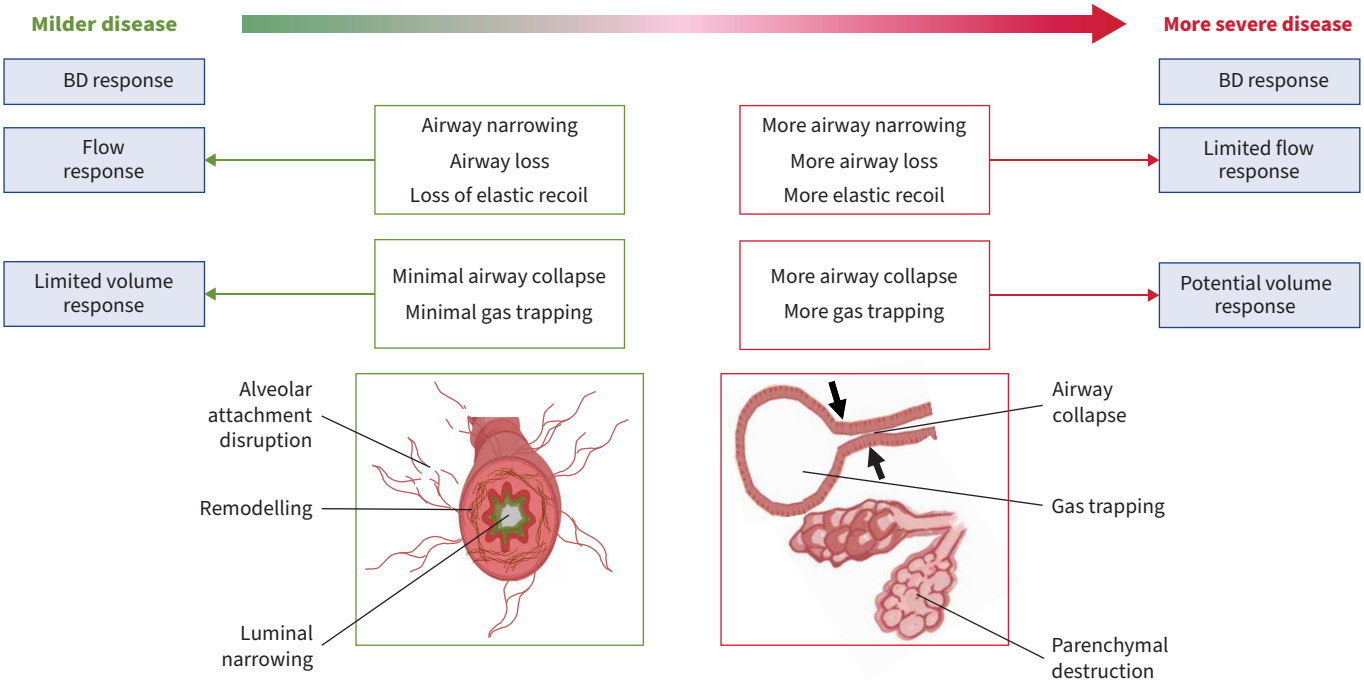


FIGURE 1 Pathological changes in COPD which may cause flow or volume responses to a bronchodilator (BD).

greater relative impairment of FEV_1 as this flow measurement is highly dependent on increased airway resistance caused by airway narrowing. BDs act by relaxing airway smooth muscle in the proximal and distal airways, which increases the airway luminal diameter leading to a reduction in airway resistance [25, 26]. Increases in FEV_1 or FVC after administration of an inhaled BD are often referred to as flow (rate) or volume responses, respectively (figure 1).

The change in FEV_1 after administration of a BD varies considerably between COPD patients and even within the same patient from test to test [27, 28]. In the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study (n=1831), the mean±SD FEV_1 increase in response to salbutamol was lower in more severe COPD patients: 160±170, 100±130 and 50±80 mL in GOLD grade 2, 3 and 4 patients, respectively [29]. A smaller FEV_1 response in COPD patients with lower pre-BD FEV_1 has also been observed when reported as percentage change [28], indicating that the smaller flow responses are not simply explained by lower lung volumes. Both the ECLIPSE study and the National Emphysema Treatment Trial (NETT) showed a smaller FEV_1 increase after BD in COPD patients with more severe emphysema [27, 29]. The presence of expiratory flow limitation due to small airway collapse can explain these observations, as this limits improvements in flow responses after administration of a BD [30].

BDs can improve airway physiology and symptoms even when there is little or no flow response measured by FEV_1 [7]. BDs reduce end-expiratory lung volumes by allowing more volume to be exhaled, thereby improving IC [7]. These shifts in lung volumes can arise from small improvements in flow enabling larger and clinically relevant improvements in volumes, and reduced end-expiratory lung volumes improve the mechanical efficiency of diaphragm contraction thereby decreasing the work of breathing [31]. This leads to downstream effects on exercise tolerance particularly in patients reaching the limits of the ventilatory system during exercise [32]. BDs also improve the mechanical functioning of the small airways, reducing heterogeneity and preventing or delaying closure thus facilitating volumetric responses [33].

Clinical studies have demonstrated considerable interindividual variation in flow and volume responses in COPD patients, with volume responses being associated with greater gas trapping measured pre-BD. WALKER and CALVERLEY [34] reported that flow and volume responses alone (using thresholds of 160 and 330 mL, respectively) were present in 12% and 23% of COPD patients, respectively, after administration of salbutamol (n=266), with 24% displaying both flow and volume responses and 41% displaying neither. Volume responders were characterised by lower FEV_1 and FVC and higher RV. Volume responders also had greater dynamic airway collapse, defined as higher ratio of peak expiratory flow/forced expiratory flow

at 50% of FVC. Newton *et al.* [35] retrospectively analysed the lung function results of 957 individuals (aged >55 years) with hyperinflation defined as total lung capacity (TLC) >115% predicted. The administration of salbutamol caused greater changes in FVC and RV in individuals with severe compared to moderate hyperinflation (TLC >133% predicted and 115–133% predicted, respectively). Furthermore, there was no association between volume and flow (FEV_1) changes.

Collectively, the evidence shows that flow responses decrease in more severe COPD patients, and that volume responses may occur in the absence of flow responses [7, 29, 33, 35, 36]. The relative magnitude of the flow and volume response to a BD can change the FEV_1/FVC ratio; in the ECLIPSE study, GOLD grade 2 patients showed a post-BD increase in this ratio, due to the greater flow responses, while grade 4 patients showed a decrease due to greater volume responses [29].

Forced or slow vital capacity

GOLD and the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines on COPD both defined airflow obstruction by relating the FEV_1 to the FVC [2, 37]. In contrast, the 2005 ATS/ERS Task Force on Standardisation of Lung Function Testing recommended that FEV_1 should be related to vital capacity (VC) rather than just FVC [38]. They recommended that the largest available VC was used, whether obtained on inspiration (IVC), slow expiration (SVC) or forced expiration (FVC). FVC may underestimate the VC (*i.e.* be lower than IVC or SVC) in the presence of increased collapsibility of the small airways [39, 40] and in these circumstances the FEV_1/FVC ratio may underestimate or fail to detect airflow obstruction. One study has shown that 20% of patients referred for hospital pulmonary function tests had a preserved FEV_1/FVC ratio but low FEV_1/SVC ratio [41]. These patients had lower mid-expiratory flows, higher airway resistance, worse gas trapping and many had been diagnosed with an obstructive airway disease by a pulmonologist. Discordant results were more common in patients aged <60 years and those with a body mass index >30 $kg \cdot m^{-2}$. It has been suggested that a slow manoeuvre should be routinely performed in symptomatic subjects with preserved FEV_1/FVC ratio who are <60 years old and obese to identify mild and more peripheral airflow obstruction. Performing additional SVC manoeuvres adds time to the test and the GOLD 2025 report stands by its recommendation that airflow obstruction should be identified using the FEV_1/FVC ratio. However, if there is a strong clinical suspicion of COPD and the FEV_1/FVC ratio is normal, GOLD 2025 recommends further follow-up and investigations, which could include assessment of the FEV_1/SVC ratio. This recommendation is in line with the 2022 ATS/ERS technical standard on interpretation of routine lung function tests which acknowledges that the use of SVC is more sensitive but less specific and adds complexity to lung function testing [16].

Variability in FEV_1/FVC results can arise due to variable expiratory times influencing the FVC values obtained. Using forced expiratory volume in 6 s (FEV_6) rather than FVC has been suggested as a means of overcoming variability in the VC. Measurement of FEV_1/FEV_6 has lower sensitivity for detecting airflow obstruction than FEV_1/FVC but similar specificity [42], and its test–retest intraclass correlation coefficient is not significantly better [43].

Bronchodilator responsiveness

A positive acute BDR test was historically advocated to differentiate asthma from COPD, with a positive response favouring the former. However, many COPD patients demonstrate excellent flow and/or volume responses signalling the poor discriminative properties of BDR testing [5]. The usefulness of BDR testing in clinical practice is hampered by practical issues such as non-standardisation of which BD should be used and at what doses, as well as variable criteria to define a positive response. In patients with an established diagnosis of COPD, there is no consistent evidence that BDR is associated with clinical characteristics or prognosis. In fact, the evidence suggests it is the post-BD value achieved that is of relevance rather than the magnitude of change in response to the BD [7, 44].

The Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS) reported outcomes over 4 years in 1481 smokers who did not meet spirometric criteria for the diagnosis of COPD [45]. BDR was defined using a threshold of 12% and 200 mL (compared to baseline pre-BD value) to define flow (FEV_1) or volume (FVC) responders. Individuals with consistent BDR (at every visit) had the lowest pre-BD FEV_1 (61% predicted) and FEV_1/FVC ratio, while these lung function parameters were also lower in individuals with inconsistent BDR responses *versus* those never showing a BDR response. Computed tomography (CT) scanning showed that BDR was associated with gas trapping and hence greater small airway dysfunction after adjusting for the post-BD FEV_1, irrespective of whether FEV_1 or FVC was used to define BDR. BDR defined using either FEV_1 or FVC was associated with greater progression to a diagnosis of COPD after adjusting for the post-BD FEV_1. In the context of diagnostic testing for COPD, these findings suggest that the magnitude of BDR might offer clinically useful

information in smokers with post-BD $FEV_1/FVC \geqslant 0.7$, as those individuals with greater and more consistent BDR are more likely to progress to COPD. Additionally, some of these smokers would be labelled as preserved ratio impaired spirometry (PRISm), which is defined as low FEV_1 values but normal FEV_1/FVC ratio post-BD; individuals with PRISm sometimes (but not always) progress to develop COPD [46, 47], particularly in individuals who continue smoking or have FEV_1/FVC values close to 0.7.

Pre- *versus* post-bronchodilator: COPD prevalence and clinical outcomes

Studies have consistently shown that the prevalence of COPD is lower when using post-BD spirometry (table 1). The Lung Health Study enrolled current smokers with FEV_1/FVC <0.7 and FEV_1 55–90% predicted [48]. The lung function results after 1 year (n=5307) showed a prevalence of airflow obstruction (FEV_1/FVC <0.7) that was 16.1% lower using post- *versus* pre-BD spirometry (77.7% and 91.4%, respectively). The National Health and Nutrition Examination Survey (NHANES) 2007–2010 conducted spirometry in a US adult population (n=5477), with approximately half being never-smokers [49]. The prevalence of obstructed spirometry (FEV_1/FVC <0.7) was ~33% lower when post-BD values were used compared to pre-BD values. In the Latin American PLATINO study (n=5183), the prevalence of airflow obstruction was 35% lower using post-BD values compared to pre-BD values, decreasing from 21.7% to 14% [50]. In high-risk individuals, defined as having either respiratory symptoms and/or significant environmental exposure, the prevalence was 33.6% lower when using post-BD values (17.4% *versus* 26.2%). A Norwegian study (n=2235) showed 27.1% lower prevalence in a population of smokers and never-smokers, and 31% lower in current smokers with a post-BD prevalence of 8.5% [51]. These large studies recruited diverse populations with different smoking histories, but all showed a consistent pattern of lower rates of obstructed spirometry post- compared to pre-BD, with the reduction up to 33.6% in current and ex-smokers.

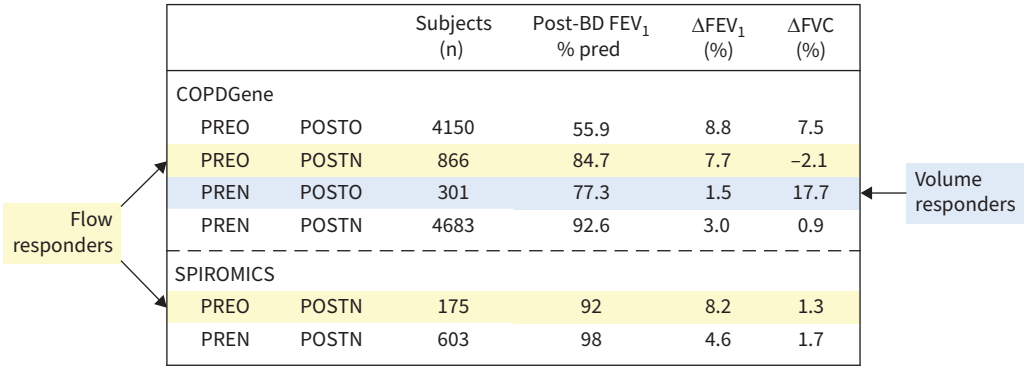
The COPDGene study was conducted in the USA, enrolling individuals with a smoking history >10 pack-years [52]. Pre- and post-BD obstruction defined by FEV_1/FVC <0.7 were termed PREO and POSTO, respectively, while no obstruction (hence normal) was termed PREN and POSTN, respectively. Figure 2 shows that concordant results were obtained in the majority of the cohort (n=10 000), either PREO–POSTO (n=4150) or PREN–POSTN (n=4683). The discordant groups comprised 11.7% of the cohort, PREO–POSTN (n=866) or PREN–POSTO (n=301), with lower post-BD FEV_1 in both groups compared to PREN–POSTN. PREO–POSTN was characterised by greater flow (FEV_1; 7.7%) than volume (FVC; −2.1%) responses, while the opposite occurred in PREN–POSTO (1.5% and 17.7%, respectively). PREN–POSTO individuals (volume responders) had greater dyspnoea and reduced exercise capacity compared to PREO–POSTN, although this finding disappeared in modelling analysis which adjusted for FEV_1. These findings confirm that using post-BD spirometry results in fewer diagnosed COPD cases, while also ensuring that the discordant PREN–POSTO individuals characterised by greater volume responses with more severe disease characteristics are not overlooked.

In COPDGene, both PREO and POSTO measurements were associated with clinical characteristics and outcomes including dyspnoea, exercise capacity, CT measurements of emphysema and gas trapping,

TABLE 1 Prevalence of COPD using pre- or post-bronchodilator (BD) spirometry in cohort studies

First author, year [ref.]	Sample size (n)	Age (years)	Smoking criteria	Smokers[#] (%)	Prevalence (%)[¶]		Reduction pre- *versus* post-BD (%)[+]	Smokers only: reduction pre- *versus* post-BD (%)[+]
					Pre-BD	Post-BD		
Mannino, 2011 [48] Lung Health Study	5307	35–65	Current smokers[§]	100	91.4	77.7	16.1	16.1
Tilert, 2013 [49] NHANES	5477[f]	40–79		50.6	20.9	14.0	33.0	NC
Pérez-Padilla, 2007 [50] PLATINO	5183	>40		63.5[##]	21.7	14	35.5	33.6
Johannessen, 2005 [51]	2225	15–70		61	9.6	7	27.1	20.3
Fortis, 2017 [52] COPDGene	10 000	45–80	>10 pack-years	100	50.2	44.5	11.3	11.3

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; NC: not calculated (data not available). [#]: includes current and former smokers; [¶]: prevalence of FEV_1/FVC <0.7; [+]: reduction (%) pre- *versus* post-BD calculated by 100×(pre-BD−post-BD)/pre-BD; [§]: also required to have post-BD FEV_1/FVC <0.7 at study visit 1 year before; [f]: post-BD conducted in 564 individuals; [##]: includes significant exposure history (to cigarette smoke, biomass or occupational dusts) or respiratory symptoms.



		Subjects (n)	Post-BD FEV_1 % pred	ΔFEV_1 (%)	ΔFVC (%)
COPDGene					
PREO	POSTO	4150	55.9	8.8	7.5
PREO	POSTN	866	84.7	7.7	−2.1
PREN	POSTO	301	77.3	1.5	17.7
PREN	POSTN	4683	92.6	3.0	0.9
SPIROMICS					
PREO	POSTN	175	92	8.2	1.3
PREN	POSTN	603	98	4.6	1.7

FIGURE 2 Discordant diagnostic spirometry in COPDGene [52] and SPIROMICS [53] cohorts. COPDGene participants had >10 pack-year smoking history, while SPIROMICS participants had ⩾20 pack-year smoking history. Change calculated using pre-bronchodilator (BD) value. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; PREO: pre-BD obstruction; PREN: pre-BD no obstruction; POSTO: post-BD obstruction; POSTN: post-BD no obstruction.

exacerbations and mortality, although post-BD measurements performed marginally better in some models including mortality. Similar numbers of PREN–POSTO and PREO–POSTN developed PREO–POSTO after 5 years of follow-up (nearly 50% in both groups).

A similar analysis was performed in the SPIROMICS study (figure 2); 603 smokers were identified without pre- or post-BD airflow obstruction (PREN–POSTN) and 175 smokers with pre-BD obstruction which resolved post-BD and was equivalent to the PREO–POSTN group in COPDGene [53]. PREO–POSTN had lower FEV_1 predicted compared to PREN–POSTN and increased flow but not volume response to BD. The PREO–POSTN group was also characterised by greater small airway dysfunction and emphysema quantified by CT scan. During longitudinal follow-up (mean 7 years) there was a 6.2-fold increased risk of developing COPD (defined by POSTO) in the PREO–POSTN *versus* PREN–POSTN group (61% *versus* 14%, respectively). Overall, these results mirror COPDGene for the PREO–POSTN group with regard to increased flow responses and increased future risk of post-BD obstruction.

The COPDGene analysis showed no or only minor differences between pre- and post-BD measurements in terms of prognosis. The Lung Health Study showed that both measurements offered similar prediction for mortality [48], while a smaller study of COPD patients in China (n=300) favoured post-BD measurements [54].

GOLD recommendations

Figure 3 shows the GOLD 2025 recommendations for the use of spirometry in the diagnosis of COPD. A single normal pre-BD measurement can be used to exclude COPD, but post-BD measurements are required to confirm the diagnosis of COPD and demonstrate without doubt that the individual has persistent airflow obstruction.

A recommendation to use a diagnostic test should be based primarily on sensitivity and specificity, but also consider issues such as data complexity, practicality and cost. For the diagnosis of COPD, pre-BD spirometry detects more people with airflow obstruction so can be viewed as more sensitive overall. However, a significant proportion of patients with pre-BD airflow obstruction are not obstructed using post-BD values (17% of the patients in COPDGene). In parallel, pre-BD measurements miss a small number of cases (~3% of the screened population in the COPDGene study [52]). These missed cases had gas trapping and were volume responders requiring post-BD measurements to reveal an obstructed ratio. The discordant groups in the COPDGene study, ~11% of the screened population, represent individuals who would change diagnosis if one measurement was used rather than another. Mirroring this figure, almost 90% of measurements were concordant, showing that both measurements give similar diagnostic outcomes in most cases.

Large cohort studies have shown no or only minor differences between pre- and post-BD measurements in terms of prognosis [48, 52]. The main reason to favour post- over pre-BD measurements is to ensure that volume responders are not overlooked in the diagnostic process and to limit COPD overdiagnosis, which is

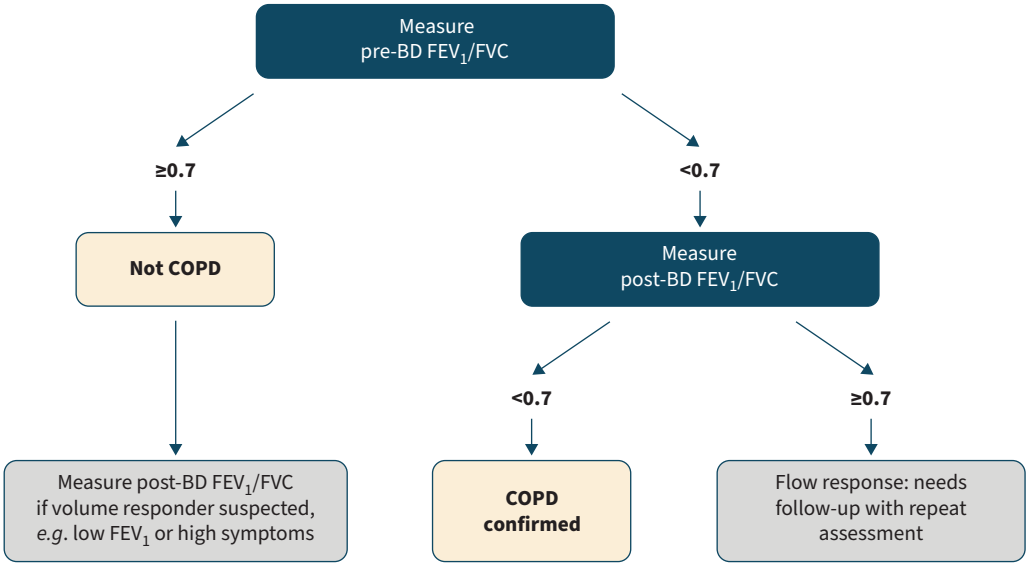


FIGURE 3 Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnostic pathway for spirometry using forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio. BD: bronchodilator.

estimated at ~11–35% from various studies in smokers (table 1) [29, 48, 49, 51, 52]. COPD overdiagnosis inappropriately increases the overall COPD population and burden on health resources.

While there are concerns that using FEV_1/FVC <0.7 may overdiagnose airflow obstruction in older individuals in comparison to the use of LLN [16], this is limited by the requirement to only consider COPD diagnosis in individuals with exposure risk factors and symptoms. The use of post-BD testing for COPD diagnosis further reduces the potential for overdiagnosis.

Most GOLD stage 1 individuals have post-BD FEV_1/FVC values close to the diagnostic threshold with 80% within the range 0.6–0.7, falling to <10% within this range for GOLD stage 3 and 4 [55]. The PREO–POSTN group in the COPDGene study demonstrated that relatively modest flow responses (FEV_1 change 7.7% after BD) changed the diagnostic conclusion in these potentially GOLD stage 1 individuals (post-BD FEV_1 84.7% predicted). As nearly 50% of this PREO–POSTN group progressed to PREO–POSTO during follow-up, GOLD 2025 recommends these individuals (with PREO–POSTN) should be closely followed up, including repeat testing as clinically indicated with a suggested time frame of 3–6 months, given the high likelihood of the development of post-BD obstruction over time (figure 3) particularly in individuals who continue smoking or have FEV_1/FVC values close to 0.7 [47]. A larger BD response, in either FEV_1 or FVC, is also an indicator of greater risk for subsequent COPD development in individuals with post-BD FEV_1/FVC ⩾0.7 [45].

It has been commented upon that removing a COPD diagnosis after a positive treatment response in flow responders (PREO–POSTN) is illogical [56]. The counter-argument (for using post-BD values for diagnostic purposes) is that volume responders (PREN–POSTO) with more severe disease characteristics are diagnosed [35, 52]. Also, the current GOLD 2025 recommendation to closely follow-up individuals with PREO–POSTN ensures that individuals with progressive airflow obstruction are not missed in the diagnostic process.

The GOLD 2025 report recommends that the presence or absence of airflow obstruction should be confirmed by repeat spirometry on a separate occasion if the post-BD FEV_1/FVC ratio is between 0.60 and 0.80 as in some cases the ratio may change as a result of biological variation when measured at a later interval [57, 58]. If the initial post-BD FEV_1/FVC ratio is <0.60 it is very unlikely to rise spontaneously above 0.7 [57]. Repeat spirometry should be guided by clinical status, with a suggested time frame of 3–6 months.

ECLIPSE and other studies have demonstrated that flow responses decrease in more severe COPD, where volume responses can drive a fall in post-BD FEV_1/FVC ratio [29]. This indicates that the potential importance of conducting post-BD spirometry is greater in individuals with lower baseline FEV_1, *e.g.*

TABLE 2 Take-home messages

Pre-BD FEV_1/FVC
⩾0.7 rules out COPD in most cases; no further testing needed
Post-BD FEV_1/FVC
Perform post-BD spirometry to confirm diagnosis if pre-BD FEV_1/FVC <0.7
Volume responders
Gas trapping can reduce FVC; BD can increase FVC
Volume responders can have discordant pre- (⩾0.7) and post- (<0.7) BD ratios
Flow responders
Flow responses can increase FEV_1/FVC ratio from <0.7 (pre-BD) to ⩾0.7 (post-BD)
Increased chance of developing COPD
Follow-up with repeat testing

BD: bronchodilator; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

<80% predicted. The GOLD 2025 report states that pre-BD spirometry provides useful information as an initial test to investigate airflow obstruction in symptomatic patients. If pre-BD spirometry does not show obstruction, then performing post-BD spirometry is not required in the majority of cases. The exception to this is when the clinical suspicion of COPD is high. Importantly, the pre-BD FEV_1 can be used as a guide to the probability that the individual may be a volume responder, as this is more likely with lower FEV_1 measurements, *e.g.* <80% predicted.

The ATS/ERS technical statement on the standardisation of spirometry contains a grading system for the quality of the test session to provide a level of confidence that the results represent the best performance of the individual [59]. Ideally, grade A results which require at least three acceptable measurements within repeatability criteria would be obtained. The guidance states that "some maneuvers may be usable at grading levels lower than A", which includes grade E where only one acceptable test is achieved or even grade U with at least one usable but not acceptable measurement. We agree with the ATS/ERS recommendation that even grade E or U readings can be used for diagnostic purposes when carefully considered alongside clinical information, particularly when used to rule out the diagnosis of COPD. In such circumstances, it is preferable to repeat spirometry to confirm initial findings.

The increasing use of CT scanning, for lung cancer screening and for assessment of respiratory symptoms or abnormal spirometry findings, can provide information relevant to the diagnosis of COPD such as the presence of emphysema. However, the availability and cost of CT scanning currently preclude this from being routinely used to diagnose COPD. Finally, most of the studies that inform current management recommendations have used post-BD values as inclusion criteria. The results of these studies cannot be assumed to apply in a population defined by pre-BD values.

Conclusion

Spirometry remains essential to confirm the presence of airflow obstruction and, therefore, to diagnose COPD. The GOLD Science Committee concludes that using pre-BD values alone would lead to a significant increase in the number of patients labelled as having COPD, putting additional pressures on health services and payors. Post-BD measurements remain the optimum diagnostic methodology for the reasons discussed above. The GOLD 2025 report recognises that measuring post-BD values is more time consuming, so GOLD advocates the use of pre-BD spirometry to rule out COPD and post-BD measurements to confirm the diagnosis. This will reduce workload in practice.

Key take-home messages regarding pre- and post-BD spirometry are shown in table 2. There are clinical situations where the exposure history, burden of symptoms and information from other tests (such as CT scans) raise a high suspicion of COPD but the diagnostic strategy outlined here fails to diagnose COPD. The GOLD 2025 report recommends further follow-up and investigations including repeating the spirometry after an interval in these individuals.

Acknowledgements: The authors thank Augusta Beech (University of Manchester, Manchester, UK) for the original drawing of figure 1.

Conflict of interest: D. Singh reports consulting fees from Adovate, Aerogen, Almirall, Apogee, Arrowhead, AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Cipla, CONNECT Biopharm, Covis, CSL Behring, DevPro Biopharma

LCC, Elpen, Empirico, EpiEndo, Genentech, Generate Biomedicines, GlaxoSmithKline, Glenmark, Kamada, Kinaset Therapeutics, Kymera, Menarini, MicroA, OM Pharma, Orion, Pieris Pharmaceuticals, Pulmatrix, Revolo, Roivant Sciences, Sanofi, Synairgen, Tetherex, Teva, Theravance Biopharma, Upstream and Verona Pharma. R. Stockley reports consultancy fees from Mereo BioPharma, CSL Behring, Vertex and Grifols, payment or honoraria for lectures, presentations, manuscript writing or educational events from GlaxoSmithKline, and participation on a data safety monitoring board or advisory board with Kamada and Arimata. A. Anzueto reports consulting fees from GlaxoSmithKline, AstraZeneca, Sanofi/Regeneron and Pfizer, and payment or honoraria for lectures, presentations or educational events from GlaxoSmithKline, AstraZeneca and Viatris Pharma. A. Agusti reports grants from GlaxoSmithKline, AstraZeneca and Menarini, payment or honoraria for lectures, presentations or educational events from GlaxoSmithKline, AstraZeneca, Chiesi, Menarini, Zambon, MSD and Sanofi, and a leadership role with GOLD as Chairman of the Board of Directors (unpaid). J. Bourbeau reports grants from the Canadian Institute of Health Research (CIHR), Réseau en Santé Respiratoire du FRQS, McGill University, McGill University Health Centre Foundation, AstraZeneca Canada Ltd, Boehringer Ingelheim Canada Ltd, GlaxoSmithKline Canada Ltd, Grifols, Novartis, Sanofi and Trudell Canada Ltd (all paid to their institution), and payment or honoraria for lectures, presentations or educational events from AstraZeneca Canada Ltd, Boehringer Ingelheim Canada Ltd, GlaxoSmithKline Canada Ltd, Trudell Canada Ltd, Pfizer Canada Ltd and Covis Pharma Canada Ltd. B.R. Celli reports support for the present manuscript from Chiesi Farmaceutici, grants from GlaxoSmithKline, AstraZeneca, Menarini, Sanofi Aventis and Axios, consulting fees from GlaxoSmithKline, AstraZeneca and Sanofi Aventis, payment or honoraria for lectures, presentations or educational events from GlaxoSmithKline, AstraZeneca, Menarini, Chiesi and Regeneron, support for attending meetings from GlaxoSmithKline and Sanofi Aventis, and participation on a data safety monitoring board or advisory board with AstraZeneca Therapeutics, Sanofi Aventis and Vertx. G.J. Criner reports grants from ALung Technologies Inc., American College of Radiology, American Lung Associations, AstraZeneca, BioScale Inc., Boehringer Ingelheim, BREATH Therapeutics Inc., COPD Foundation, Coridea/ZIDAN, Corvus, Dr Karen Burns of St Michael's Hospital, Fisher & Paykel Healthcare Ltd, Galapagos NV, GlaxoSmithKline, Kinevent, Lungpacer Medical Inc., NHLBI, Nurvaira Inc., Patient-Centered Outcomes Research Institute, Pulmonary Fibrosis Foundation, PulmonX, Respironics Inc., Respivant Sciences, Spiration Inc., Steward St Elizabeth's Medical Center of Boston Inc. and Veracyte Inc., participation on a data safety monitoring board or advisory board for Chiesi, Pliant and Sanofi, and personal fees from Amgen, AstraZeneca, Boehringer Ingelheim, Broncus Medical, CSA Medical, EOLO Medical, Gala Therapeutics, GlaxoSmithKline, Helios Medical, Ion, Merck, Medtronic, Mereo BioPharma, NGM Biopharmaceuticals, Novartis, Olympus, PulmonX, Respironics Inc., Respivant Sciences, The Implementation Group and Verona Pharma. M.K. Han reports grants from NIH, Sanofi, Novartis, Nuvaira, Sunovion, Gala Therapeutics, COPD Foundation, AstraZeneca, American Lung Association, Boehringer Ingelheim and Biodesix, royalties or licences from UpToDate, Norton Publishing and Penguin Random House, consulting fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pulmonx, Teva, Verona, Merck, Mylan, Sanofi, DevPro, Aerogen, Polarian, Regeneron, Altesa BioPharma, Amgen, Roche, RS Biotherapeutics, Apreo Health and Genentech, payment or honoraria for lectures, presentations, manuscript writing or educational events from Cipla, Chiesi, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Medscape, Integrity, NACE and Medwiz, participation on a data safety monitoring board or advisory board with Novartis and Medtronic (funds paid to institution), leadership or fiduciary roles with the COPD Foundation Board, COPD Foundation Scientific Advisory Committee, ALA advisory committee, American Thoracic Society (journal editor), ALA (volunteer spokesperson), GOLD scientific committee and Emerson School Board, Ann Arbor, MI, stock or stock options with Meissa Vaccines and Altesa BioPharma, and receipt of medical writing support from GlaxoSmithKline, Boehringer Ingelheim, AstraZeneca and Novartis. F.J. Martinez reports grants from AstraZeneca, Chiesi, GlaxoSmithKline, Sanofi/Regeneron and NHLBI, with payments made to the COPD Foundation for partnership in SPIROMICS and/or CAPTURE, consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GlaxoSmithKline, Novartis, Polarean, Pulmonx, Roche, Sanofi/Regeneron, Sunovion, Teva and Theravance/Viatris, payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline and Roche, participation on a data safety monitoring board or advisory board with MedTronic and GlaxoSmithKline, and payment from UpToDate for COPD CME. M. Montes de Oca reports payment or honoraria for lectures, presentations, manuscript writing or educational events from GlaxoSmithKline and Boehringer Ingelheim. O.B. Ozoh reports payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca and Gertz Pharma. A. Papi reports grants from Chiesi, AstraZeneca, GlaxoSmithKline and Sanofi, consultancy fees from Chiesi, AstraZeneca, GlaxoSmithKline, Sanofi, Avillion, Moderna and Roche, payment or honoraria for lectures, presentations, manuscript writing or educational events from Chiesi, AstraZeneca, GlaxoSmithKline, Menarini, Zambon, Mundipharma, Sanofi, Iqvia, Avillion, Regeneron and Zambon, and participation on a data safety monitoring board or advisory board with Chiesi, AstraZeneca, GlaxoSmithKline, Sanofi, Iqvia, Avillion and Moderna. I. Pavord reports consulting fees, payment or honoraria for lectures, presentations or educational events and support for attending meetings from GlaxoSmithKline, Sanofi/Regeneron and AstraZeneca. N. Roche reports grants from Boehringer Ingelheim, Novartis, GlaxoSmithKline and Pfizer, consultancy fees from Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Sanofi, Chiesi, Pfizer, Novartis, Teva, Bayer, Austral and Biosency, payment or honoraria for lectures, presentations, manuscript writing or

educational events from Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Sanofi, Chiesi, Pfizer, Novartis, Teva, Zambon, MSD and Menarini, support for attending meetings from Chiesi, AstraZeneca and GlaxoSmithKline, and is European Respiratory Society Science Council Chair. S. Salvi reports leadership roles with Global Initiative for Chronic Obstructive Lung Disease (unpaid member) and Indian Chest Society (president, unpaid). D.D. Sin reports support for the present manuscript from Chiesi Farmaceutici SpA, grants from Nextone, payment or honoraria for lectures, presentations, manuscript writing or educational events from AstraZeneca, GlaxoSmithKline and Boehringer Ingelheim, participation on a data safety monitoring board for NHLBI, and a leadership role with the European Respiratory Society as Deputy Chief Editor of the *European Respiratory Journal*. T. Troosters has no potential conflicts of interest to disclose. J. Wedzicha reports grants from AstraZeneca, Boehringer, Chiesi, GlaxoSmithKline, Novartis, Genentech and 37Clinical, consulting fees from AstraZeneca, Epiendo, GlaxoSmithKline, Gilead, Novartis, Pieris, Pulmatrix and Empirico, payment or honoraria for lectures, presentations or educational events from AstraZeneca, GlaxoSmithKline, Boehringer, Recipharm and Novartis, participation as data safety monitoring board chair for Virtus, and a leadership role as Editor in Chief of the *American Journal of Respiratory and Critical Care Medicine* until March 2022. J. Zheng reports payment or honoraria for lectures, presentations, speakers bureaus or manuscript writing and support for attending meetings from GlaxoSmithKline, AstraZeneca, Chiesi and Sanofi. C. Vogelmeier reports grants from the German Ministry of Education and Science (BMBF), AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GlaxoSmithKline, Grifols and Novartis, consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GlaxoSmithKline, Insmed, Menarini, Novartis, Nuvaira, Roche and Sanofi, and payment or honoraria for lectures, presentations, manuscript writing or educational events from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GlaxoSmithKline, Insmed, Menarini, Novartis, Roche and Sanofi. D. Halpin reports payment or honoraria for lectures, presentations or educational events from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Inogen, Novartis, Pfizer, Sanofi and Menarini, support for attending meetings from Menarini, and participation on a data safety monitoring board or advisory board with Chiesi.

Support statement: D. Singh is supported by the National Institute for Health Research (NIHR) Manchester Biomedical Research Centre (BRC).

References

1 Agusti A, Celli BR, Criner GJ, *et al.* Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Eur Respir J* 2023; 61: 2300239.
2 Pauwels RA, Buist AS, Calverley PM, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001; 163: 1256–1276.
3 Rodriguez-Roisin R, Rabe KF, Vestbo J, *et al.* Global Initiative for Chronic Obstructive Lung Disease (GOLD) 20th anniversary: a brief history of time. *Eur Respir J* 2017; 50: 1700671.
4 Sterk PJ. Let's not forget: the GOLD criteria for COPD are based on post-bronchodilator FEV_1. *Eur Respir J* 2004; 23: 497–498.
5 Halpin DMG. Bronchodilator responsiveness in asthma and COPD: time to stop chasing shadows. *Am J Respir Crit Care Med* 2024; 209: 349–351.
6 Calverley PM, Koulouris NG. Flow limitation and dynamic hyperinflation: key concepts in modern respiratory physiology. *Eur Respir J* 2005; 25: 186–199.
7 Calverley PM, Albert P, Walker PP. Bronchodilator reversibility in chronic obstructive pulmonary disease: use and limitations. *Lancet Respir Med* 2013; 1: 564–573.
8 Arne M, Lisspers K, Stallberg B, *et al.* How often is diagnosis of COPD confirmed with spirometry? *Respir Med* 2010; 104: 550–556.
9 Halpin DMG. Clinical management of COPD in the real world: can studies reveal errors in management and pathways to improve patient care? *Pragmat Obs Res* 2023; 14: 51–61.
10 Han MK, Kim MG, Mardon R, *et al.* Spirometry utilization for COPD: how do we measure up? *Chest* 2007; 132: 403–409.
11 Fisk M, McMillan V, Brown J, *et al.* Inaccurate diagnosis of COPD: the Welsh National COPD Audit. *Br J Gen Pract* 2019; 69: e1–e7.
12 Halpin DMG, Dickens AP, Skinner D, *et al.* Identification of key opportunities for optimising the management of high-risk COPD patients in the UK using the CONQUEST quality standards: an observational longitudinal study. *Lancet Reg Health Eur* 2023; 29: 100619.
13 Kim KY, Yoo KH, Choi HS, *et al.* Nationwide quality assessment of treatment for chronic obstructive pulmonary disease. *J Thorac Dis* 2020; 12: 7174–7181.
14 Koefoed MM, dePont Christensen R, Sondergaard J, *et al.* Lack of spirometry use in Danish patients initiating medication targeting obstructive lung disease. *Respir Med* 2012; 106: 1743–1748.
15 Nishi SP, Wang Y, Kuo YF, *et al.* Spirometry use among older adults with chronic obstructive pulmonary disease: 1999–2008. *Ann Am Thorac Soc* 2013; 10: 565–573.

16 Stanojevic S, Kaminsky DA, Miller MR, *et al.* ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J* 2022; 60: 2101499.
17 Johannessen A, Lehmann S, Omenaas ER, *et al.* Post-bronchodilator spirometry reference values in adults and implications for disease management. *Am J Respir Crit Care Med* 2006; 173: 1316–1325.
18 Higham A, Quinn AM, Cancado JED, *et al.* The pathology of small airways disease in COPD: historical aspects and future directions. *Respir Res* 2019; 20: 49.
19 Hogg JC, Macklem PT, Thurlbeck WM. Site and nature of airway obstruction in chronic obstructive lung disease. *N Engl J Med* 1968; 278: 1355–1360.
20 Beech A, Jackson N, Dean J, *et al.* Expiratory flow limitation in a cohort of highly symptomatic COPD patients. *ERJ Open Res* 2022; 8: 00680-2021.
21 Dean J, Kolsum U, Hitchen P, *et al.* Clinical characteristics of COPD patients with tidal expiratory flow limitation. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 1503–1506.
22 Dellaca RL, Santus P, Aliverti A, *et al.* Detection of expiratory flow limitation in COPD using the forced oscillation technique. *Eur Respir J* 2004; 23: 232–240.
23 Aarli BB, Calverley PM, Jensen RL, *et al.* The association of tidal EFL with exercise performance, exacerbations, and death in COPD. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2179–2188.
24 Parshall MB, Schwartzstein RM, Adams L, *et al.* An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med* 2012; 185: 435–452.
25 Dean J, Panainte C, Khan N, *et al.* The TRIFLOW study: a randomised, cross-over study evaluating the effects of extrafine beclometasone/formoterol/glycopyrronium on gas trapping in COPD. *Respir Res* 2020; 21: 323.
26 Borrill ZL, Houghton CM, Tal-Singer R, *et al.* The use of plethysmography and oscillometry to compare long-acting bronchodilators in patients with COPD. *Br J Clin Pharmacol* 2008; 65: 244–252.
27 Han MK, Wise R, Mumford J, *et al.* Prevalence and clinical correlates of bronchoreversibility in severe emphysema. *Eur Respir J* 2010; 35: 1048–1056.
28 Tashkin DP, Celli B, Decramer M, *et al.* Bronchodilator responsiveness in patients with COPD. *Eur Respir J* 2008; 31: 742–750.
29 Albert P, Agusti A, Edwards L, *et al.* Bronchodilator responsiveness as a phenotypic characteristic of established chronic obstructive pulmonary disease. *Thorax* 2012; 67: 701–708.
30 Tantucci C, Duguet A, Similowski T, *et al.* Effect of salbutamol on dynamic hyperinflation in chronic obstructive pulmonary disease patients. *Eur Respir J* 1998; 12: 799–804.
31 Hatipoglu U, Laghi F, Tobin MJ. Does inhaled albuterol improve diaphragmatic contractility in patients with chronic obstructive pulmonary disease? *Am J Respir Crit Care Med* 1999; 160: 1916–1921.
32 Saey D, Debigare R, LeBlanc P, *et al.* Contractile leg fatigue after cycle exercise: a factor limiting exercise in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2003; 168: 425–430.
33 Pecchiari M, Santus P, Radovanovic D, *et al.* Acute effects of long-acting bronchodilators on small airways detected in COPD patients by single-breath N_2 test and lung P-V curve. *J Appl Physiol* 2017; 123: 1266–1275.
34 Walker PP, Calverley PM. The volumetric response to bronchodilators in stable chronic obstructive pulmonary disease. *COPD* 2008; 5: 147–152.
35 Newton MF, O'Donnell DE, Forkert L. Response of lung volumes to inhaled salbutamol in a large population of patients with severe hyperinflation. *Chest* 2002; 121: 1042–1050.
36 Ben Saad H, Prefaut C, Tabka Z, *et al.* The forgotten message from GOLD: FVC is a primary clinical outcome measure of bronchodilator reversibility in COPD. *Pulm Pharmacol Ther* 2008; 21: 767–773.
37 Celli BR, MacNee W, Agusti A, *et al.* Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 2004; 23: 932–946.
38 Pellegrino R, Viegi G, Brusasco V, *et al.* Interpretative strategies for lung function tests. *Eur Respir J* 2005; 26: 948–968.
39 Brusasco V, Pellegrino R, Rodarte JR. Vital capacities in acute and chronic airway obstruction: dependence on flow and volume histories. *Eur Respir J* 1997; 10: 1316–1320.
40 Stanescu D. Small airways obstruction syndrome. *Chest* 1999; 116: 231–233.
41 Saint-Pierre M, Ladha J, Berton DC, *et al.* Is the slow vital capacity clinically useful to uncover airflow limitation in subjects with preserved FEV_1/FVC ratio? *Chest* 2019; 156: 497–506.
42 Vandevoorde J, Verbanck S, Schuermans D, *et al.* FEV_1/FEV_6 and FEV_6 as an alternative for FEV_1/FVC and FVC in the spirometric detection of airway obstruction and restriction. *Chest* 2005; 127: 1560–1564.
43 Giraldo AMM, Cadavid LFG, Rosas DB, *et al.* Comparison of new spirometry measures to diagnose COPD. *Respir Care* 2023; 68: 366–373.
44 Hansen EF, Phanareth K, Laursen LC, *et al.* Reversible and irreversible airflow obstruction as predictor of overall mortality in asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999; 159: 1267–1271.
45 Fortis S, Quibrera PM, Comellas AP, *et al.* Bronchodilator responsiveness in tobacco-exposed people with or without COPD. *Chest* 2023; 163: 502–514.

46 Wan ES, Fortis S, Regan EA, *et al.* Longitudinal phenotypes and mortality in preserved ratio impaired spirometry in the COPDGene study. *Am J Respir Crit Care Med* 2018; 198: 1397–1405.

47 Perez-Padilla R, Montes de Oca M, Thirion-Romero I, *et al.* Trajectories of spirometric patterns, obstructive and PRISm, in a population-based cohort in Latin America. *Int J Chron Obstruct Pulmon Dis* 2023; 18: 1277–1285.

48 Mannino DM, Diaz-Guzman E, Buist S. Pre- and post-bronchodilator lung function as predictors of mortality in the Lung Health Study. *Respir Res* 2011; 12: 136.

49 Tilert T, Dillon C, Paulose-Ram R, *et al.* Estimating the U.S. prevalence of chronic obstructive pulmonary disease using pre- and post-bronchodilator spirometry: the National Health and Nutrition Examination Survey (NHANES) 2007–2010. *Respir Res* 2013; 14: 103.

50 Pérez-Padilla R, Hallal PC, Vázquez-García JC, *et al.* Impact of bronchodilator use on the prevalence of COPD in population-based samples. *COPD* 2007; 4: 113–120.

51 Johannessen A, Omenaas ER, Bakke PS, *et al.* Implications of reversibility testing on prevalence and risk factors for chronic obstructive pulmonary disease: a community study. *Thorax* 2005; 60: 842–847.

52 Fortis S, Eberlein M, Georgopoulos D, *et al.* Predictive value of prebronchodilator and postbronchodilator spirometry for COPD features and outcomes. *BMJ Open Respir Res* 2017; 4: e000213.

53 Buhr RG, Barjaktarevic IZ, Quibrera PM, *et al.* Reversible airflow obstruction predicts future chronic obstructive pulmonary disease development in the SPIROMICS cohort: an observational cohort study. *Am J Respir Crit Care Med* 2022; 206: 554–562.

54 Chen CZ, Ou CY, Wang WL, *et al.* Using post-bronchodilator FEV_1 is better than pre-bronchodilator FEV_1 in evaluation of COPD severity. *COPD* 2012; 9: 276–280.

55 Bhatt SP, Nakhmani A, Fortis S, *et al.* FEV_1/FVC severity stages for chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2023; 208: 676–684.

56 Keaney N, Kay A, Taylor I. Guidelines and the diagnosis of COPD. *Am J Respir Crit Care Med* 2009; 179: 734.

57 Aaron SD, Tan WC, Bourbeau J, *et al.* Diagnostic instability and reversals of chronic obstructive pulmonary disease diagnosis in individuals with mild to moderate airflow obstruction. *Am J Respir Crit Care Med* 2017; 196: 306–314.

58 Schermer TR, Robberts B, Crockett AJ, *et al.* Should the diagnosis of COPD be based on a single spirometry test? *NPJ Prim Care Respir Med* 2016; 26: 16059.

59 Graham BL, Steenbruggen I, Miller MR, *et al.* Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *Am J Respir Crit Care Med* 2019; 200: e70–e88.