

The Practitioner®

Improving outcomes in COPD

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Your name:

Today's date:


COPD Assessment Test

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy (0) (1) (2) (3) (4) (5) I am very sad

				SCORE
I never cough	(0) (1) (2) (3) (4) (5)	I cough all the time		
I have no phlegm (mucus) in my chest at all	(0) (1) (2) (3) (4) (5)	My chest is completely 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 one flight of stairs I am not breathless	(0) (1) (2) (3) (4) (5)	When I walk up a hill or one flight of stairs I am very breathless		
I am not limited doing any activities at home	(0) (1) (2) (3) (4) (5)	I am very limited doing activities at home		
I am confident leaving my home despite my lung condition	(0) (1) (2) (3) (4) (5)	I am not at all confident leaving my home because of my lung condition		
I sleep soundly	(0) (1) (2) (3) (4) (5)	I don't 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	

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BOX 1
 COPD Assessment
 Test questionnaire



CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) HAS A MAJOR IMPACT ON HEALTHCARE

services. *The battle for breath* report produced by the British Lung Foundation highlighted the fact that more than 1.2 million people in the UK are living with COPD which equates to 4.5% of those aged 40 years or older. COPD is responsible for more than 140,000 hospital admissions and more than a million bed days per annum placing huge pressure on hospital services.¹

Almost all healthcare professionals will encounter patients with COPD on a regular basis and for many a working knowledge of diagnosis and management is essential.

RISK FACTORS

Cigarette smoking is overwhelmingly the most important risk factor for COPD. In some cases, other factors such as occupation, passive exposure to inhalants and fetal nutrition/low birthweight are also important.

The development of COPD involves a complex interaction between genetic

How should COPD be diagnosed?

How should disease severity be assessed?

What are the evidence-based treatment options?

and environmental factors with fewer than 50% of heavy smokers ever developing COPD. Alpha-1-antitrypsin deficiency is uncommon but, in smokers, leads to early onset COPD and smokers of heroin and crack cocaine appear susceptible to early onset COPD with predominant emphysema.²

DIAGNOSIS

In clinical practice patients with COPD will usually present with breathlessness, cough with/without sputum production, and sometimes more acutely with symptoms of a lower respiratory tract >>

infection. The diagnosis should be suspected in symptomatic patients with risk factors, usually cigarette smoking, and typically aged 40 years or older, albeit the majority of people with COPD present when considerably older.

Physiological confirmation of airflow obstruction with spirometry is essential. Where the test is performed for diagnostic rather than monitoring purposes, use of post-bronchodilator measurements is important.

As with any physiological test it is vital that a diagnostic test is quality assured and carried out by someone who has had the requisite training, who performs the test regularly, and who has appropriate supervision and support.

COPD is defined by the presence of post-bronchodilator airflow obstruction with a FEV₁/FVC ratio < 0.7 required to make the diagnosis.³ If reversibility testing is performed, a modest degree of bronchodilator reversibility is common in COPD⁴ but a FEV₁ improvement > 400 ml is uncommon and strongly suggestive of asthma.

While this makes the results typically straightforward to interpret there are pitfalls, in particular where the results are only modestly abnormal.

The most common pitfall relates to the loss of natural lung elasticity with age which means that it can be easy to overdiagnose milder COPD in older people, particularly men, and, less commonly, underdiagnose COPD in younger people, particularly women. This can be overcome by using standardised residual values which use the lower limit of normal rather than < 0.7 and reduce false-positive results. This approach is supported by the Global Lung Initiative 2012 programme.⁵ However, this does make interpretation of results more complex and for this reason current guidelines continue to recommend use of < 0.7.

It is important to recognise these challenges, to be cautious diagnosing

COPD in someone without symptoms and to consider use of standardised residuals where airflow obstruction is minimal.

The presence of airflow obstruction is far from specific and is also seen in asthma and bronchiectasis. Hence, interpretation of spirometry should always be made in the context of clinical features and risk factors. Therapies and treatment goals differ between the conditions making accurate diagnosis very important.

There has been considerable recent focus on asthma-COPD overlap syndrome, examined in a recent review.⁶

DISEASE SEVERITY AND SYMPTOM MANAGEMENT

One of the biggest changes in COPD management is the focus on symptoms and risk highlighted in the GOLD (Global Initiative for Obstructive Lung Disease) guideline.³

‘One of the biggest changes in COPD management is the focus on symptoms and risk’

The degree of impairment of FEV₁ is no longer used to guide treatment, something which many local guidelines have been slow to adopt. There can be a large discrepancy between level of breathlessness and degree of FEV₁ impairment but this should prompt the clinician to consider other causes of breathlessness.

As shown in figure 1, opposite, management is focused first on relieving symptoms of breathlessness (assessed using the MRC dyspnoea scale) and improving quality of life (assessed using the COPD Assessment Test), see box 1, p13.⁷ The latter is a validated and

‘The degree of impairment of FEV₁ is no longer used to guide treatment’

responsive questionnaire that is freely available, takes less than 5 minutes to complete and provides a score of 0-40 with a score ≥ 10 representing significant quality of life impairment.

Management is also focused on risk reduction assessed by the number of exacerbations and hospitalisations during the previous year. Low risk is defined as 0-1 exacerbation(s) and no episodes of hospitalisation. Patients with COPD are then classified by GOLD as:

- **Group A:** Low symptom score and low risk
- **Group B:** High symptom score but low risk
- **Group C:** Low symptom score but high risk
- **Group D:** High symptom score and high risk

This grouping is used to direct certain pharmacological treatments. Notwithstanding, many COPD treatments have an impact on both symptoms and exacerbations while many patients with COPD have both.

TAILORING TREATMENT

Over time and with additional research greater evidence has accumulated as to which sub-group of patients is likely to derive benefit from a specific treatment such as inhaled corticosteroids (ICS), prophylactic azithromycin and roflumilast. This is incorporated into the GOLD guidance.³ As trials using new agents such as mepolizumab⁸ are published it is highly likely such treatments will be appropriate only for certain individuals and in the UK likely to be accessible via clinical networks.

Lung volume reduction procedures, including surgery, are an early example of a treatment only beneficial to a small proportion of patients with a particular distribution of emphysema whose ability to exercise is limited despite other therapy and who meet specific physiological criteria, see table 1, left. Decisions about suitability for volume reduction procedures are increasingly made via regional emphysema multidisciplinary team meetings.

Social deprivation can have a significant impact on outcomes, for example completion of pulmonary rehabilitation⁹ and local solutions will be important to these challenges.

Table 1

Relative physiological criteria for consideration of lung volume reduction surgery/procedures. Of the many clinical trials each uses different criteria and each centre will typically have their own criteria

FEV ₁ (litres)	20-45% predicted
DLCO (% of predicted value)	> 20% predicted
Plethysmographic residual volume (% of predicted value)	> 180% predicted
Total lung capacity (% of predicted value)	> 100% predicted
Pattern of emphysema	Heterogeneous

SMOKING CESSATION

Cessation of smoking is still the most important intervention in COPD management and has been shown to reduce mortality in patients with milder degrees of COPD. A variety of aids are available to assist quitting and smoking cessation services are available in most areas.

The use of e-cigarettes as an aid to smoking cessation is supported by many professional bodies and Public Health England.¹⁰ However, the impact of long-term e-cigarette use as an alternative source of nicotine rather than as an aid to overcome nicotine addiction is less clear.

TREATMENTS TO RELIEVE BREATHLESSNESS

Pulmonary rehabilitation is a highly effective treatment to relieve breathlessness in patients with COPD, as well as many other cardiorespiratory conditions. The 2015 England and Wales pulmonary rehabilitation audit demonstrated that nearly 80% of patients who completed rehabilitation gained a clinically significant improvement in walking distance, breathlessness, quality of life or a combination of these outcomes.¹¹

It is recognised that post-exacerbation rehabilitation is particularly useful but the audit also highlighted that uptake of rehabilitation in general, and in particular post-exacerbation enrolment, is poor.

Short-acting bronchodilators alone may be appropriate treatment for the small number of patients with COPD who have minimal symptoms and infrequent exacerbations (GOLD group A). However, many more patients with COPD will suffer breathlessness which limits exercise and activity and reduces quality of life (GOLD group B). These individuals appear to benefit from the use of long-acting bronchodilators. Evidence exists that a long-acting antimuscarinic inhaler (LAMA) is an appropriate first choice though many clinicians will opt to prescribe a LAMA combined with a long-acting beta-agonist inhaler (LABA).

The current combinations available are shown in table 2, p16, and the evidence for these agents has been reviewed recently.¹² Not only do these combination inhalers provide better bronchodilation than the single agents but there is also evidence that they have a positive impact on exacerbation rate.¹³

A small number of patients with severe COPD characterised by severe airflow obstruction, marked resting hyperinflation due to emphysema, a

Figure 1a

GOLD guideline criteria for the assessment of symptoms and the risk of exacerbation³

Risk of exacerbation	Symptoms	
	MRC dyspnoea scale score 1-2 CAT score < 10	MRC dyspnoea scale score 3-5 CAT score 10 or more
2 or more annual exacerbations or 1 or more hospitalisation	GOLD C	GOLD D
0 or 1 annual exacerbation with no hospitalisation	GOLD A	GOLD B

CAT = COPD Assessment Test

Figure 1b

Pharmacological treatment algorithms by GOLD grade³

<p>GOLD C</p> <p>LAMA</p> <p>If further exacerbations:</p> <p>Preferred: LABA + LAMA Alternative: LABA + ICS</p>	<p>GOLD D</p> <p>LAMA</p> <p>If further exacerbations:</p> <p>LABA + LAMA</p> <p>If persistent symptoms or further exacerbations:</p> <p>Preferred: LABA/ICS + LAMA Alternative: LABA + ICS</p> <p>If further exacerbations:</p> <ul style="list-style-type: none"> ● Consider azithromycin in former smokers ● Consider roflumilast if FEV₁ < 50% predicted and patient has chronic bronchitis
<p>GOLD A</p> <p>A bronchodilator</p> <p>then evaluate effect</p> <p>Continue, stop or try alternative class of bronchodilator</p>	<p>GOLD B</p> <p>A long-acting bronchodilator (LABA or LAMA)</p> <p>If symptoms persist:</p> <p>LABA + LAMA</p>

LABA = long-acting beta-agonist
LAMA = long-acting antimuscarinic
ICS = inhaled corticosteroid

key points

SELECTED BY

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More than 1.2 million people in the UK are living with COPD which equates to 4.5% of those aged 40 years or older. COPD is responsible for more than 140,000 hospital admissions and more than a million bed days per annum, placing huge pressure on hospital services. Cigarette smoking is overwhelmingly the most important risk factor for COPD. In some cases, other factors such as occupation, passive exposure to inhalants and fetal nutrition/low birthweight are also important.

Patients with COPD usually present with breathlessness, cough with or without sputum production, and sometimes more acutely with symptoms of a lower respiratory tract infection. The diagnosis should be suspected in symptomatic patients with risk factors, usually cigarette smoking, who are aged 40 years or above, albeit a majority of people with COPD present when considerably older.

COPD is defined by the presence of post-bronchodilator airflow obstruction with a FEV₁/FVC ratio below 0.7 required to make the diagnosis. However, it can be easy to overdiagnose milder COPD in older people, particularly men, and, less commonly, underdiagnose COPD in younger people, particularly women. This can be overcome by using standardised residual values which use the lower limit of normal rather than < 0.7 and reduce false-positive results, an approach supported by the Global Lung Initiative.

The 2017 GOLD guideline recommends that management should be focused on two objectives. First, to relieve symptoms of breathlessness (assessed using the MRC dyspnoea scale) and improve quality of life (assessed by the COPD Assessment Test). Second, to reduce risk assessed by the number of exacerbations and hospitalisations in the previous year.

Cessation of smoking is still the most important intervention in COPD management and has been shown to reduce mortality in people with milder degrees of COPD. Pulmonary rehabilitation is a highly effective treatment to relieve breathlessness in COPD as well as in many other cardiorespiratory conditions. Short-acting bronchodilators alone may suffice for COPD patients with minimal symptoms and infrequent exacerbations. However, most patients suffer from breathlessness which limits exercise and activity and reduces quality of life. These individuals appear to benefit from the use of long-acting bronchodilators and evidence suggests that a long-acting antimuscarinic inhaler (LAMA) is an appropriate first choice.

A long-acting antimuscarinic combined with a long-acting beta-agonist inhaler (LAMA/LABA) provides better bronchodilation than the single agents and there is also evidence that combination inhalers have a positive impact on exacerbation rates.

Table 2

Currently available long-acting beta-agonist/long-acting anti-muscarinic combination inhalers

Drug combination and dose	Trial evidence
Indacaterol/glycopyrronium 85/43 mcg one puff daily	<ul style="list-style-type: none"> ● Improves annual exacerbation rate vs salmeterol/fluticasone ● Improves FEV₁ vs salmeterol/fluticasone ● Improves quality of life vs salmeterol/fluticasone ● Improves moderate/severe exacerbation rate vs glycopyrronium ● Improves FEV₁ vs tiotropium and glycopyrronium
Acclidinium/formoterol 340/12 mcg one puff twice daily	<ul style="list-style-type: none"> ● Improves FEV₁ vs formoterol and placebo ● Improves quality of life vs placebo ● Improves breathlessness vs placebo, formoterol and acclidinium
Olodaterol/tiotropium 2.5/2.5 mcg two puffs daily	<ul style="list-style-type: none"> ● Improves FEV₁ vs olodaterol and tiotropium ● Improves quality of life vs olodaterol and tiotropium
Umeclidinium/vilanterol 55/22 mcg one puff daily	<ul style="list-style-type: none"> ● Improves FEV₁ vs vilanterol and tiotropium

heterogeneous pattern of emphysema (predominant upper lobe emphysema) and exercise impairment may derive benefit from lung volume reduction surgery or bronchoscopic procedures (endobronchial valves, coils or glue). As described earlier, selection of appropriate individuals is complex and likely to be best performed by a regional multidisciplinary team.

TREATMENTS THAT REDUCE EXACERBATIONS

Influenza vaccination is arguably the most cost-effective treatment for patients with COPD¹⁴ and has been shown to reduce exacerbation and hospitalisation rates.¹⁵ Despite this many patients still do not receive annual vaccination.

Many long-acting bronchodilators have been shown to reduce exacerbation rate so are also appropriate for patients classified as GOLD groups C and D.

The primary indication for prescription of ICS, in the form of a combined ICS/LABA inhaler, is to reduce exacerbation rate (GOLD groups C and D). There is increasing evidence that individuals with higher serum eosinophil counts are more likely to benefit and although the cut-off value

'Flu vaccination in COPD patients has been shown to reduce exacerbation and hospitalisation rates'

for use has yet to be established in prospective research studies their utility has been seen in people with eosinophil counts > 2% of total white cell count and 0.2 x10⁹ cells/L.

Although, in large randomised controlled trials, ICS/LABA inhalers have also been shown to improve breathlessness and health status it is clear that all ICS increase the risk of pneumonia in patients with COPD and the rate of pneumonia appears to be worse with higher ICS doses.¹⁶ It is important not to use ICS where there is no clear indication and one trial has demonstrated that they can be withdrawn safely.¹⁷

The decision to use or withdraw ICS requires careful discussion with the patient balancing the reduction in exacerbation rate with the small

increased risk of pneumonia. Randomised controlled trials comparing LABA/LAMA with LABA/LAMA/ICS are due to be published in the near future.

Exacerbation rates can be reduced in certain individuals by using low-dose macrolides, in particular azithromycin. However, azithromycin can prolong the QTc interval so care needs to be taken to check for interacting therapies. Any initial gastrointestinal upset tends to settle quickly and the individual should be aware of the, albeit rare, potential effect on hearing. Azithromycin should not be prescribed to smokers as the initial trial showed no efficacy in this sub-group.⁵

Roflumilast is a PDE-4 inhibitor that has been shown to reduce exacerbation rates in those with severe COPD (FEV₁ < 50% predicted) who have chronic bronchitis and at least three exacerbations per year.¹⁸ It has significant side-effects in particular gastrointestinal disturbance, weight loss and sleep and mood disturbance. It is not recommended for patients with a low BMI and those with a history of depression.

OXYGEN THERAPY

Long-term oxygen therapy prescribed for patients who are chronically hypoxaemic (resting PaO₂ < 7.3 kPa when stable) improves mortality. This was established more than 40 years ago. There exists a wealth of evidence that short-burst oxygen therapy does not improve or speed up recovery from breathlessness but there is a role for ambulatory oxygen in people who significantly desaturate on exercise and who walk further when using oxygen.

A recent US trial showed no benefit from prescription of long-term oxygen in patients with COPD and lesser degrees of hypoxaemia and/or exercise-induced desaturation.¹⁹

INHALER DEVICES

In the past few years there has been a huge expansion in the number of inhaler devices available for prescription and while the choice of different therapies is welcome this creates specific challenges. It is vital that inhaler utilisation is not only checked at each review but in particular when there is a change in device. Common sense dictates limiting the number of devices that an individual uses to maximise device consistency.

COMORBIDITIES

Patients with COPD commonly have one or more comorbidities and the most

important recommendation for the clinician is to consider this when assessing any individual. Heart disease is a frequent comorbidity but consideration of osteoporosis, in particular in patients prescribed multiple courses of oral corticosteroids per year, and anxiety and depression is important and often not recognised early. Both pulmonary rehabilitation and cognitive behavioural therapy have been shown to help symptoms of anxiety and depression.

SELF-MANAGEMENT

Self-management is important and when used effectively can reduce hospitalisation rate. There is a wealth of written material available and increasingly self-management material delivered through smart devices. It should be recognised that not all patients will self-manage successfully²⁰ but this does not preclude encouragement of self-management strategies. However, there may be circumstances when prescription of rescue packs requires review if they are being used inappropriately.

CONCLUSIONS

Spirometry is still vital to diagnose COPD but has to be interpreted in the context of clinical features and risk factors. Treatment is now focused around reduction in symptoms and reduction of risk and the 2017 GOLD guidelines³ provide an evidence-based platform to deliver this, in particular tailoring treatment to the individual, which will become increasingly important.

Competing interests: In the past three years Paul Walker has received honoraria for speaking at educational meetings sponsored by Chiesi and AstraZeneca.

REFERENCES

- 1 British Lung Foundation. The battle for breath - the impact of lung disease in the UK. Available from: www.blf.org.uk/what-we-do/our-research/the-battle-for-breath-2016. Last accessed: 31 October 2017.
- 2 Walker PP, Thwaite E, Amin S et al. The association between heroin inhalation and early onset emphysema. *Chest* 2015;148(5):1156-63
- 3 Global Strategy for Diagnosis, Management, and Prevention of COPD (2017). <https://www.goldcopd.org> Last accessed 31 October 2017
- 4 Calverley PM, Albert P, Walker PP. Bronchodilator reversibility in chronic obstructive pulmonary disease: use and limitations. *Lancet Respir Med* 2013;1(7):564-73
- 5 Quanjer PH, Stanojevic S, Cole TJ et al. ERS Global Lung Function Initiative. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012;40(6):1324-43
- 6 Leung JM, Sin DD. Asthma-COPD overlap syndrome: pathogenesis, clinical features, and therapeutic targets. *BMJ* 2017;358:j3772
- 7 Jones PW, Harding G, Berry P et al. Development and first validation of the COPD assessment test. *Eur Respir J* 2009;34:648-54
- 8 Pavord ID, Chanez P, Criner GJ et al. Mepolizumab for

eosinophilic chronic obstructive pulmonary disease. *N Engl J Med* 2017;377(17):1613-29

9 Steiner MC, Lowe D, Beckford K et al. Socioeconomic deprivation and the outcome of pulmonary rehabilitation in England and Wales. *Thorax* 2017;72(6):530-37

10 Public Health England. E-cigarettes: an evidence update (2015). <https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update>. Last accessed: 31 October 2017

11 National Pulmonary Rehabilitation Programme: Pulmonary Rehabilitation Workstream. Steps to Breathe Better (2016). www.rcplondon.ac.uk/projects/outputs/pulmonary-rehabilitation-steps-breathe-better. Last accessed: 31 October 2017

12 Calverley P, Vlies B. A rational approach to single, dual and triple therapy in COPD. *Respirology* 2016;21(4):581-89

13 Wedzicha JA, Banerji D, Chapman KR et al. FLAME Investigators. Indacaterol-glycopyrronium versus salmeterol-fluticasone for COPD. *N Engl J Med* 2016;374(23):2222-34

14 Williams S, Restrick L, Baxter N et al on behalf of London Respiratory Network. COPD value pyramid (2015). <http://www.respiratoryfutures.org.uk/knowledge-portal/london-respiratory-network/copd-value-pyramid-thorax-publication>. Last accessed: 31 October 2017

15 Bekkat-Berkani R, Wilkinson T, Buchy P et al. Seasonal influenza vaccination in patients with COPD: a systematic literature review. *BMC Pulm Med* 2017;7(1):79. doi: 10.1186/s12890-017-0420-8

16 Dransfield MT, Bourbeau J, Jones PW et al. Once-daily inhaled fluticasone furoate and vilanterol versus vilanterol only for prevention of exacerbations of COPD: two replicate double-blind, parallel-group, randomised controlled trials. *Lancet Respir Med* 2013;1(3):210-23

17 Magnussen H, Disse B, Rodriguez-Roisin R et al. WISDOM Investigators. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. *N Engl J Med* 2014;371(14):1285-94

18 Martinez FJ, Calverley PM, Goehring UM et al. Effect of roflumilast on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (REACT): a multicentre randomised controlled trial. *Lancet* 2015;385(9971):857-66

19 Long-term oxygen treatment trial research group, Albert RK, Au DH, Blackford A et al. A randomized trial of long-term oxygen for COPD with moderate desaturation. *N Engl J Med* 2016;375(17):1617-27

20 Bucknall CE, Miller G, Lloyd SM et al. Glasgow supported self-management trial (GSuST) for patients with moderate to severe COPD: randomised controlled trial. *BMJ* 2012;344:e1060

Useful information

British Thoracic Society
www.brit-thoracic.org.uk

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<https://www.blf.org.uk>

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