

All that glitters is not GOLD, nor is it even NICE



Treatment guidelines for 'All that glitters is not GOLD, nor is it even NICE' is a consensus-based article that sets out a simple treatment pathway based on the predominant characteristics of COPD for an individual – whether symptoms or exacerbations – distilled from current guidelines. The article has been developed by a group of clinicians working with and in primary care, facilitated by integrated care consultant Vince Mak; GPs Duncan Keeley, Noel Baxter and Kevin Gruffydd Jones; practice nurse Carol Stonham; and pharmacist Anna Murphy.



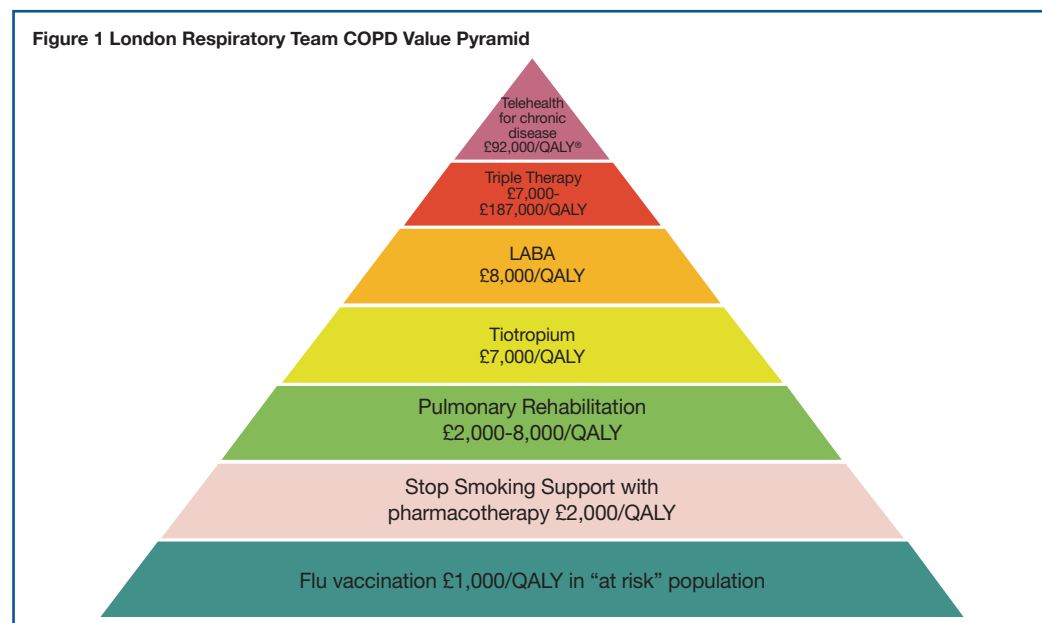
Background

The NICE COPD guideline was first developed in 2004 and partially updated in 2010. Since then, the absence of up-to-date guidance from NICE in a condition which has generated much interest and research in recent years has meant the GOLD COPD strategy (updated every 18–24 months) has gained some traction in the UK. The most recent 2019 GOLD revision was published in November 2018.¹



NICE finally published an updated guideline in December 2018.² At consultation stage in mid 2018, two issues not being covered in the update were identified as omissions, and NICE has decided to add these as a 2019 update for publication in July

2019.³ A draft guideline covering these two areas was put out to consultation in February. The NICE guideline has had to catch up on 8 years of developments, mainly in pharmacological treatment. Since 2010, the management of COPD has changed dramatically from treatment based on severity of FEV1 impairment to treatment based on clinical characteristics of the patient (so-called 'treatable traits' or phenotypes). In addition, the role of inhaled corticosteroids (ICS) in COPD has been more clearly defined and there has been a decline over recent years in the use of ICS – especially high-dose ICS – in England. This may have been driven more by the London Respiratory Team COPD Value Pyramid and highlighting concerns around the use of high-dose ICS in COPD than any specific guideline (Figure 1).⁴



The PCRS published our consensus view on how COPD could be managed in primary care⁵ based on both the GOLD 2017 and NICE 2010 guidelines, attempting to distil the best elements relevant to a primary care setting. Now that we have two up-to-date sets of guidance, we need to consider if our PCRS consensus view needs modifying.

This consensus article will only focus on pharmacotherapy in both GOLD and NICE to highlight similarities and differences. There is very little controversy in any of the other sections of the guidelines; indeed, there is broad agreement.

Treatment algorithms

GOLD 2019

The latest iteration of the GOLD treatment algorithms has changed dramatically from 2017. GOLD still uses the Refined Assessment Tool that was introduced in 2017 to categorise COPD into four groups (A, B, C and D) based on symptoms and risk of exacerbations (Figure 2). Although it continues to use FEV1 to grade severity, this is not part of the assessment tool.

Now there are two separate algorithms, one for initiation of therapy (Figure 3) and another for follow-up treatment (Figure 4). Initial treatment is based upon which of the four groups the patient falls into at diagnosis.

The treatment options in each group have been greatly simplified since 2017. The groupings can be interpreted as Groups A+B (breathless patients) and Groups C+D (exacerbating patients). Reducing to predominantly breathless and predominantly exacerbating patients, this model can be further simplified to:

Breathlessness: SABA → LABA or LAMA

Exacerbations: SABA → LAMA or LAMA/LABA or ICS/LABA (if eosinophils >300)

Following the initiation, the effect of management should be reviewed to see if they have achieved their treatment goals. Inhaler tech-

Figure 2 GOLD Refined ABCD Assessment Tool

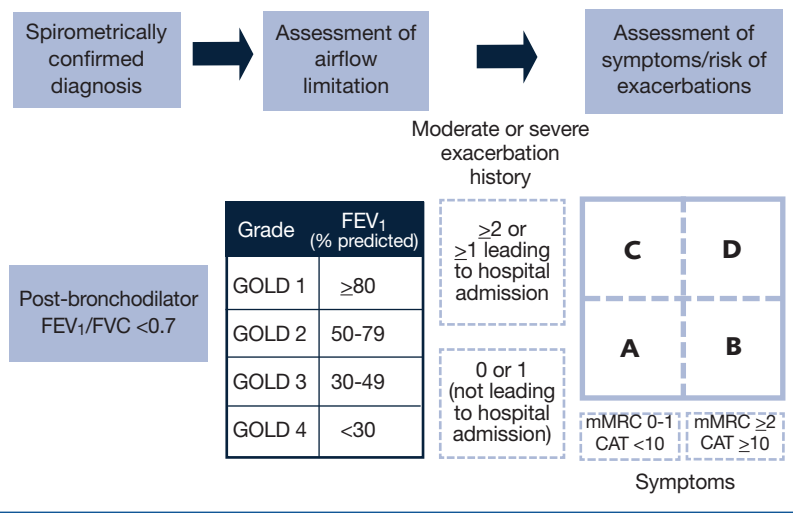


Figure 3 GOLD model for initiation of pharmacological management of COPD

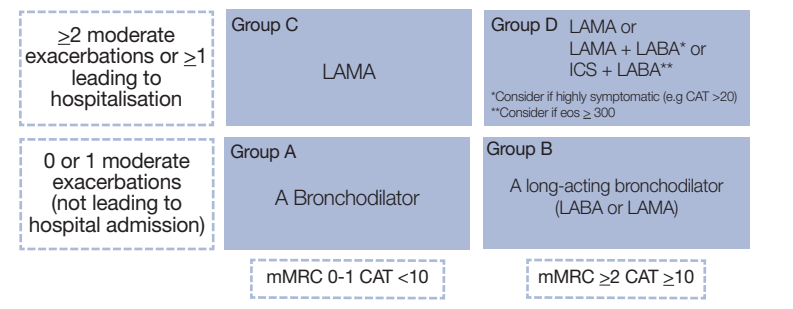
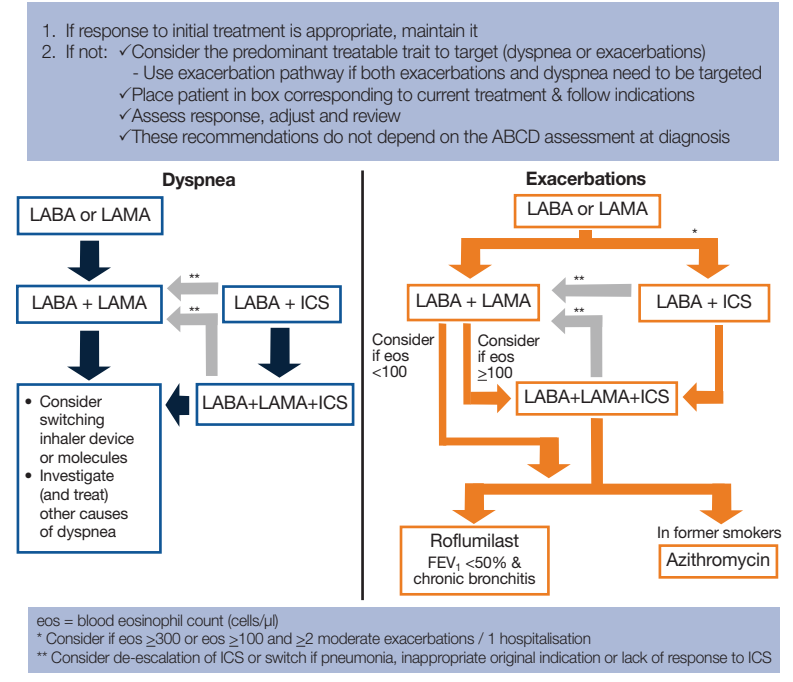


Figure 4 GOLD follow-up pharmacological treatment



nique and adherence should also be assessed along with non-pharmacological interventions. Treatment can then be adjusted, either escalated or de-escalated or a change in inhaler device or molecule as part of a management cycle.

Follow-up treatment is now based on whether the patient has continued breathlessness or frequent exacerbations but not on the patient's GOLD group at diagnosis (even though we can see that GOLD grouping is actually based on symptoms and exacerbations). The new algorithm, even though it is just split into only two treatable patient types, looks very busy as it displays both escalation and de-escalation of treatment within one diagram for both groups. GOLD recommends de-escalation in patients 'who have resolution of symptoms and may require less therapy'. This seems rather odd in a chronic progressive disease, but it seems to be an attempt to withdraw ICS in patients who are not exacerbating. There is no progression to triple therapy for breathless patients, only for those with frequent exacerbations. GOLD does stress that evidence from trials of de-escalation of ICS are limited. The PCRS also provides guidance on stepping down and withdrawal of inhaled steroids in appropriate patients (www.pcrs-uk.org/resource/stepping-down-inhaled-corticosteroids-copd).

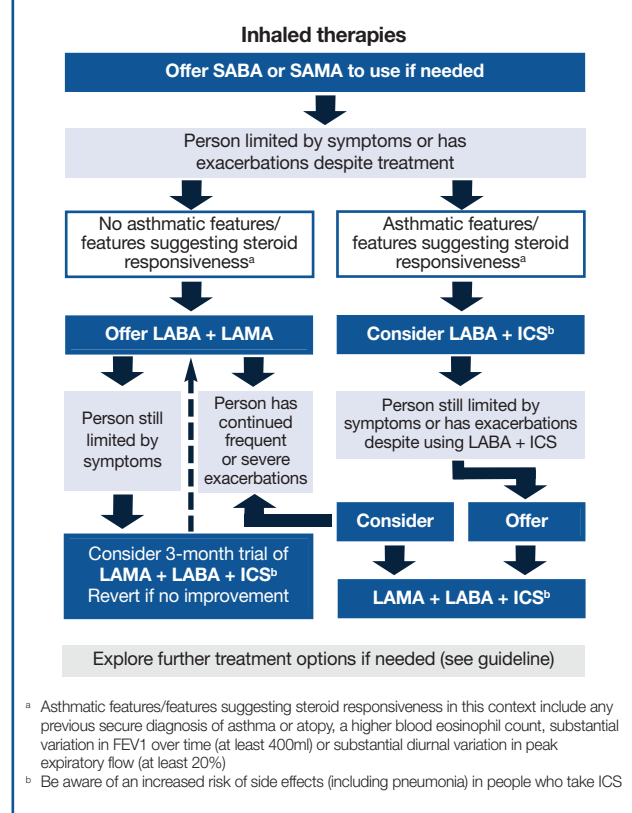
Combining escalation and de-escalation in the one diagram makes it look extremely complicated as it is not immediately obvious what the different coloured arrows represent and they seem to go round in circles (those who are red-green colour blind may also have difficulty). So what started off as a simplified process has become quite confusing to the eye and may limit its application in a primary care audience – especially a non-specialist one.

NICE 2019

NICE published a fairly comprehensive guideline update in December 2018. However, it became clear at consultation of the draft in the summer of 2018 that there were two significant areas not covered in the update – the role of triple therapy (whether in a single inhaler or multiple) and duration of oral corticosteroid treatment. NICE has therefore taken the unusual step of adding these two areas after publication of the 2018 guideline update, and will refer to the version to be published in July 2019, which will include these two new areas, as the 2019 update.

Like GOLD, NICE has abandoned treatment based on severity of FEV1 impairment that was central to the 2010 guidance. Like other guidance, NICE has opted to group COPD into treatable traits, but instead of breathlessness and exacerbations, has opted for the presence or absence of asthma-like features that would suggest steroid responsiveness, and then grouping breathless and exacerbating patients together (Figure 5). These asthmatic features include a previous secure diagnosis of asthma or atopy, high blood eosinophil count (although they do not quan-

Figure 5 NICE inhaled therapies algorithm

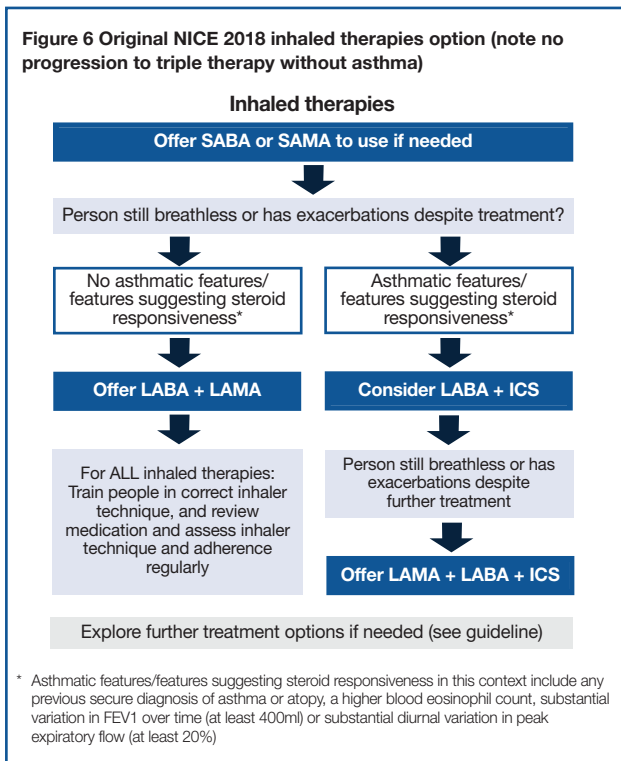


tify what high is), or substantial variation in FEV1 over time (at least 400 mL) or diurnal variation in peak expiratory flow (20%). This group may represent COPD-asthma overlap.

A major difference between NICE and GOLD is that, following SABA alone, whether the patient has breathlessness or frequent exacerbations, the first treatment is combined LABA+LAMA as opposed to long-acting bronchodilator monotherapy. The rationale given for this is that, in some studies, LABA+LAMA has additional benefits over monotherapy in terms of symptoms and exacerbations, and combined treatment may be more cost effective than monotherapy in the long run. Thus, there may be an overall cost saving in terms of consultations for exacerbations and hospitalisations. However, the evidence suggests that LABA+LAMA combinations offer limited improvements over monotherapy and we know that many patients are happy on monotherapy.

A disappointing change following the consultation in September 2018 is that, if there are continuing symptoms or frequent exacerbations, then a step up to triple therapy can be considered. For breathless patients, this should be for a 3-month trial, although if the patient is chronically breathless, it may be unrealistic to think that they will step down from this. Basically, this is the NICE 2010 recommendations all over again in a different guise. Regardless of severity, as long as you have breathlessness or exacerbations,

Figure 6 Original NICE 2018 inhaled therapies option (note no progression to triple therapy without asthma)



you end up on triple therapy which is the same as in 2010. If a person with COPD has asthma and COPD, they are likely to progress to triple therapy. In the original 2018 version there was no triple therapy option for those without asthmatic features (Figure 6) (which is also wrong as frequent exacerbators will benefit from ICS but may not have asthma). NICE do acknowledge the increased risk of pneumonia in those taking ICS but feel that the benefits outweigh the risks.

The role of eosinophils in determining the use of ICS in COPD

GOLD 2019

GOLD has a whole section on blood eosinophil count predicting the effect of ICS in preventing future exacerbations. GOLD describes a continuous relation between eosinophil count and the effect of ICS starting at 100 cells/ μ L and plateauing at 300 cell/ μ L, suggesting that the higher level can be used to identify patients who are most likely to benefit from ICS. But they suggest that ICS are used as an addition to regular bronchodilator treatment in this group rather than as a starting treatment.

NICE 2019

NICE only briefly mentions eosinophils in the context that this might identify patients who have asthmatic features as a guide to who may benefit from ICS. However, they do not address

those who may not have asthmatic features but who have frequent exacerbations despite regular bronchodilator therapy, which is the group that GOLD has highlighted. A 'higher blood eosinophil count' is mentioned in the algorithm but there is no guide as to what 'higher' means.

PCRS

The PCRS acknowledges that there is still some debate on the use of eosinophils to determine the use of ICS in COPD and we have published our own second opinion on this topic (www.pcrs-uk.org/resource/second-opinion-use-blood-eosinophil-count-criteria-ics-use).

GOLD or NICE?

We now have two new sets of guidance which still do not have a consensus. The NICE 2019 (draft version in consultation in February) seems to be NICE 2010 in a different guise, with all roads – once again – leading to triple therapy. The consensus view on the role of ICS in COPD is in the reduction of exacerbations and not in the treatment of breathlessness. NICE does recommend that, when using triple therapy for breathlessness, there should be a review after 3 months to check efficacy, but in reality many patients may remain on triple therapy.

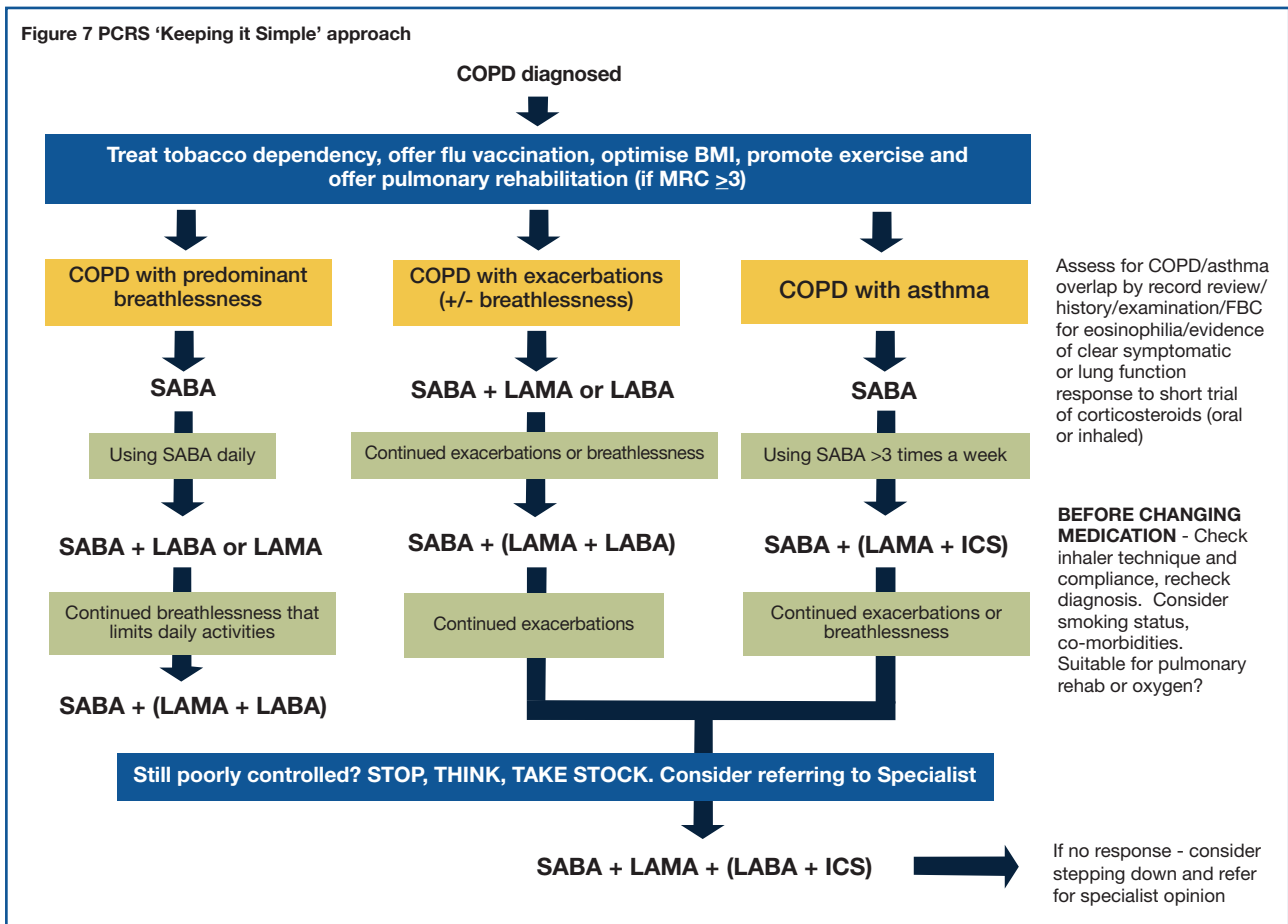
Some may argue that the jump straight to LABA+LAMA is a good thing, to go for maximal treatment right from the start, albeit at a cost disadvantage. However, diagnosing patients earlier (which is in the NHS Long Term Plan) will mean that they may not be very symptomatic and may not require combination treatment as there are patients who are managing very well on monotherapy at present. So not having this as an option to initiate and then progress treatment when more symptomatic will seem strange to some.

GOLD seems to be a bit more logical in its division into treatable characteristics (whereas NICE just differentiates between people with asthma with fixed obstruction and non-asthmatics). GOLD also has progression of treatment which follows what we generally currently practise, but does not recommend (and in fact discourages) triple therapy in patients with just breathlessness. However, to arrive at this point, you have to interpret the rather confusing follow-up algorithms.

Thus both guidelines lead to an element of confusion, so what should primary care practitioners do?

The solution?

A viable solution (without too much bias) is actually still the PCRS treatment algorithm published in 2017 in the 'Going for GOLD' PCRU article (Figure 7).



The 'Keeping it Simple' approach embraces all three of the treatable traits addressed in GOLD and NICE: breathless patients, patients who have frequent exacerbations, and those who have asthmatic features. There is a common-sense progression of treatment that follows the evidence and at reduced cost compared with NICE. The treatment pathways for all three are a distillation of both GOLD and NICE. The breathless and exacerbator pathways agree with GOLD, and the asthmatic features pathway agrees with NICE. There is no progression of all traits to triple therapy, and there is overarching emphasis on non-pharmacological interventions (smoking cessation, vaccination and pulmonary rehabilitation) and review of diagnosis, inhaler technique, adherence and co-morbidities throughout. The only item missing perhaps is a clear cut-off for eosinophil count, but that is another debate.

Figure 7 combines the good elements of both GOLD and NICE in a single, clear, simple to follow treatment algorithm. Thus, in 2017, the PCRS were able to presage the 2019 guidelines of both GOLD and NICE. Would be it too cheeky to suggest that they saw the light and followed PCRS?

Major differences in the advice on how to manage COPD from reputable guideline providers are a problem for primary care. They reflect limitations in the available evidence and difficulties in its

interpretation. This article has outlined what we, as a group of professionals experienced in the management of COPD, consider to be a practical way forward in reconciling this conflicting advice and one that is consistent with the evidence base.

In summary, our view is that the PCRS 'Keeping it Simple' approach may be the most suitable and the easiest one to adopt in a primary care setting.

Acknowledgement

GOLD figures reproduced with permission 2019. Global Initiative for Chronic Obstructive Lung Disease

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