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GOLD 2024: a brief overview of key changes

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Since 2001 (more than twenty years ago) the Global Initiative for Obstructive Lung Disease (GOLD) publishes and updates every year a document that recommends how to best diagnose and manage chronic obstructive pulmonary disease (COPD).[1] This is an enormous and continued team effort, so we want to start by acknowledging the dedication and hard work of all GOLD members through the years (www.goldcopd.org). The GOLD 2024 document has just been released and is available for free download in the GOLD website, together with a pocket guide and a teaching slide set.[2] Here we present a brief overview of what we think are the most relevant changes (or lack of) introduced in this 2024 edition of the GOLD recommendations.

To begin with, it is worth mentioning that, to avoid potential duplications and improve readability of the document, Chapter 3 (Evidence supporting prevention and maintenance therapy) and Chapter 4 (Management of stable COPD) in the GOLD 2023 document have now been merged into a single chapter (new Chapter 3 in GOLD 2024: Prevention and Management of COPD). Besides, the GOLD Science Committee identified a number of topics that, although already discussed in GOLD 2023, required and deserved further discussion. Accordingly, the following aspects about the diagnosis or management of COPD have been expanded and updated in GOLD 2024.

DIAGNOSIS

Spirometry

GOLD 2024 continues to propose that *a post-bronchodilator $FEV_1/FVC<0.7$, in the appropriate clinical context, is mandatory to establish the diagnosis of COPD.*[2] However, we also recognize that there is an ongoing, and not yet resolved, debate on two key aspects of this proposal. First, whether the use of the lower limit of normal (LLN) of the FEV_1/FVC ratio would be better or worse than the use of the currently recommended fixed ratio <0.7.[3] As already discussed in GOLD 2023, and now expanded in GOLD 2024, both options have pros and cons.[2] For instance, subjects classified as normal using LLN criteria but obstructed or restricted using the fixed ratio have a higher risk of mortality.[4] Further, as we know that COPD can occur in young subjects,[5] and that, in them, a fixed ratio may underdiagnose patients who may need treatment.[6,7] Besides, whether the diagnosis of COPD has to be based on pre- or post-bronchodilator spirometric values is also controversial. In this context, it is worth noting the results of a recent analysis in the SPIROMIC cohort that shows that the presence of reversible obstruction is associated with an increased incidence of COPD over time.[8] The GOLD Science Committee will continue discussing these pro- and con- arguments in relation to this key key diagnostic tool for COPD with the goal of providing a more informed proposal in GOLD 2025.

Preserved Ratio Impaired Spirometry (PRISm)

PRISm is a spirometric pattern characterized by $FEV_1/FVC \geq 0.70$ and post-BD $FEV_1 < 80\%$ pred.[9] The pathogenesis of PRISm is still unclear but potential causes may include cardiac disease (i.e., lung edema), initial stages of obstructive or restrictive lung disease, gas trapping and/or incomplete inspiration or expiration (insufficient cooperation).[9,10] Importantly, although PRISm may not be stable over time, it seems associated with an increased cardiovascular risk.[11] Clearly, as discussed in GOLD 2024, PRISm requires research to better understand its pathogenesis and to determine the best management alternatives.[2]

Lung hyperinflation

This is one of the main mechanisms, if not the leading one, of dyspnea in patients with COPD. Hyperinflation can be static (at rest) or dynamic (during exercise) and has prognostic value.[12] Bronchodilator treatment benefits are likely related to pharmacological lung "deflation". This is further discussed in detail in GOLD 2024

Interstitial lung abnormalities (ILA)

ILA are often found in patients with COPD. A new analysis in the COPDGene cohort showed that they are not always detrimental but that those ILAs associated with suspected interstitial lung disease have worse prognosis.[13]

ADDRESSING UNDERDIAGNOSIS: SCREENING AND CASE FINDING

Recent data shows that 57% of 986 individuals screened for lung cancer with low dose CT in whom forced spirometry was also measured had COPD and that, importantly, 67% of them were undiagnosed (hence untreated).

MANAGEMENT OF STABLE PATIENT

Smoking cessation

The section on smoking cessation has been revised, and a new section on pharmacotherapies for smoking cessation has been added. Further, the possibility that e-cigarettes may help as a bridge for smoking cessation was revised and, based on the available evidence and the lack of knowledge about the long-term effects of

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e-cigarettes on respiratory health,[14] GOLD 2024 does not recommend this intervention for smoking cessation in patients with COPD.

Inhaled pharmacologic therapy

Inhaled therapy is the corner stone of pharmacologic treatment in patients with COPD. GOLD 2024 expands the discussion on how to choose the best inhaler device for a particular patient considering her/his ability to use the delivery system correctly. GOLD 2024 also discusses the potential environmental impact of different inhalers and recommend to use, whenever possible, green inhalers.[15]

On the other hand, GOLD 2023 made a practical recommendation to consider *initial* treatment with triple therapy in E patients with more than 300 Eos/mL. Now, a recent retrospective analysis of a large, real-world database (the Clinical Practice Research Datalink) in the UK provides support for this recommendation although it has to be mentioned that this analysis was not based on randomized individuals.[16]

Biologics

Previous studies of mepolizumab[17] and benralizumab[18,19] in COPD yielded inconclusive results. By contrast, the BOREAS study showed clear clinical effects of dupilumab in a selected subgroup of COPD patients (those with more than 300 eosinophils/mL who, despite the use of triple therapy, continue to suffer exacerbations and have symptoms of chronic bronchitis).[20] GOLD 2024 acknowledges these results pending confirmation studies.[2] If confirmed, this would finally open the possibility of using biologic therapy in patients with COPD.[21]

VACCINATION

The term *immunosenescence* refers to the gradual deterioration of the immune system caused by advancing age.[22] It is associated with a reduced ability to respond to infections and develop long-term immune memory.[22] It plays a key role in the development of respiratory infections in the elderly,[22] particularly in patients with COPD.[23] Refraining from smoking, limiting alcohol consumption, regular exercise, appropriate diet and establishing a proper vaccination program can slow down the process of immunosenescence (*immune fitness*).[22] Figure 1 presents the vaccination recommendations for people with COPD, which has been *updated* in line with current guidance by the U.S. Centers for Disease Control (CDC). In particular, GOLD 2024 now recommends the vaccination of COPD patients with the new respiratory syncytial virus (RSV) vaccines, which are highly efficient both in the general population[24] and in older patients with cardio-respiratory comorbidities,[25] on top of those vaccines already recommended in GOLD 2023 (flu, pneumococcus, COVID-19, pertussis and shingles).

EXACERBATIONS

Traditionally the severity of exacerbations has been determined *post-hoc* based on the type and site of treatment received*:* mild if ambulatory with minimal therapeutic changes, moderate if antibiotics and/or systemic steroids were prescribed, and severe if the patient was hospitalized. This classification have been extensively used in many clinical trials as well as to classify *stable* patients in the A, B, or E groups to guide their *initial* pharmacologic treatment.[2] It is useless, however, to guide treatment at the point of care during an actual episode of exacerbation. Because of this, GOLD 2023 adopted the Rome proposal for the definition and assessment of severity of the episodes of exacerbation of COPD at the point of care based on a number of physiological biomarkers independently of the type or site of treatment.[26] GOLD 2024 continues to propose the use of the Rome classification to guide the treatment of the actual exacerbation episode but discusses (and hopefully clarifies) several aspects that

Vaccination for Stable COPD

Figure 3.6

- Influenza vaccination is recommended for people with COPD **(Evidence B)**
- The WHO and CDC recommends SARS-CoV-2 (COVID-19) vaccination for people with COPD **(Evidence B)**
- The CDC recommends one dose of 20-valent pneumococcal conjugate vaccine (PCV20); or one dose of 15-valent pneumococcal conjugate vaccine (PCV15) followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23) for people with COPD **(Evidence B)**
- Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations for people with COPD **(Evidence B)**
- The CDC recommends the new respiratory syncytial virus (RSV) vaccine for individuals over 60 years and/or with chronic heart or lung disease **(Evidence B)**
- The CDC recommends Tdap (dTaP/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD that were not vaccinated in adolescence **(Evidence B)**, and Zoster vaccine to protect against shingles for people with COPD over 50 years **(Evidence B)**

Figure 1. Vaccination for stable COPD. Reproduced from GOLD 2024 with permission.[2]

deserve consideration: 1. it is necessary to separate the physiological classification of exacerbations (Rome proposal), intended to guide treatment at the point of care, from the site of care (outpatient, inpatient), which may be dictated by the clinical severity of the exacerbation but also by the structure of different health systems, availability of resources and/or personal/social conditions (e.g., living alone, comorbidities). In fact, GOLD 2024 now discusses several retrospective studies that confirm the validity of the Rome proposal to predict mortality but also showed that a substantial proportion of hospitalized patients had, according to Rome, mild exacerbations[27,28]; 2. the classification of the stable patient in the A, B or E groups to guide initial pharmacologic treatment must still rely (by necessity) on the history recall of *previous* exacerbations which will have to be classified as moderate or severe by the site and type of treatment received.

CONCLUSIONS

As discussed above, the GOLD 2024 document discusses relevant aspects for the diagnosis, prevention, and management of COPD. Like GOLD has done over the last two decades,[1] it will continue to provide the different stakeholders interested in COPD, including patients, practicing clinicians and other health care professionals, basic science investigators, epidemiologists, pharma industry and payers, with the most updated and critically reviewed evidence on a yearly basis in order to improve the care for COPD patients and the distant goal of eventually eliminate COPD.[29]

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CONFLICTS OF INTEREST

Dr. Alvar Agusti is the Chair of the Board of Directors of GOLD. Dr. Claus Vogelmeier is the Chair of the Scientific Committee of GOLD.

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