Open Respiratory Archives 7 (2025) 100445

Sociedad Española de Neumología y Cirugía Torácica SEPAR

Open Respiratory Archives

www.elsevier.es/ora

Editorial

Challenges of the New Spanish Guideline for Treatment of COPD (GesEPOC 2025)

Retos de la nueva Guía Española para el tratamiento de la EPOC (GesEPOC 2025)

The first edition of the Spanish guideline for the treatment of chronic obstructive pulmonary disease (GesEPOC) was published in 2012.[1] This document was the first to establish recommendations of treatment based on clinical phenotypes of COPD and had a significant impact on subsequent national guidelines in Europe. Since then, two major revisions of GesEPOC have been released, incorporating modifications derived from evolving evidence on the pharmacological treatment of COPD.[2,3]

The first major change was the introduction of a risk classification into low and high risk, replacing the severity classification based on BODE/BODEx indices.[2] This risk classification was subsequently validated prospectively in Spanish cohorts of patients with COPD.[4] The second major update was the simplification of the diagnostic criteria for asthma-COPD overlap (ACO), identifying two main types of patients: those meeting diagnostic criteria for both asthma and COPD, and those with COPD and an eosinophilic (type 2) phenotype.[5]

Finally, due to growing evidence supporting the role of type 2 inflammation in guiding therapy, the previous phenotypic classification—which included ACO, frequent exacerbator, emphysema, or chronic bronchitis—was replaced with a more pragmatic approach: non-exacerbator and exacerbator with or without eosinophilia.[3]

Since the publication of GesEPOC 2021, several advances in COPD management have shed light on unresolved questions and opened new therapeutic possibilities. These developments necessitate periodic updates to the guidelines to incorporate the most recent evidence. The evaluation of evidence in GesEPOC has always followed international standards for clinical practice guideline development, using the GRADE methodology, combined with a pragmatic or narrative review of the evidence, as proposed by the European Respiratory Society guidelines working group.[6] However, this methodology does not provide evidence-based recommendations for all possible treatment alternatives and thus, several relevant challenges remain, including:

1. **Is there still a role for long-acting muscarinic antagonist (LAMA) monotherapy as initial treatment for COPD?** Several studies have shown that the combination of LAMA and long-acting beta-2 agonist (LABA) yields better outcomes than LAMA alone.[7] However, some low-risk patients with mild airflow obstruction may initially be treated with LAMA monotherapy, as the addition of LABA may not provide further benefit due to a ceiling effect.
2. **Does LABA/inhaled corticosteroid (ICS) combination still have a role?** The most recent GOLD guidelines exclude LABA/ICS as an initial treatment option,[8] despite its widespread use in many countries.[9] It is true that eosinophilic exacerbators requiring LABA/ICS may benefit further—both in terms of lung function and exacerbation reduction—from the addition of a LAMA. Nonetheless, some patients with mild lung function impairment and moderate exacerbations may respond well to LABA/ICS alone, with escalation to triple therapy (LABA/LAMA/ICS) as the next step. Therefore, LABA/ICS may still be considered as an initial treatment in a minority of cases, especially when compared with LABA/LAMA or triple therapy.
3. **What is the role of new biologic therapies?** Biologic agents have been extensively studied in asthma, and their safety and efficacy are now being evaluated in COPD, particularly in patients with predominant type 2 (T2) inflammation.[10] This endotype is characterized by biomarkers such as IL-4, IL-5, and IL-13, and by infiltration with Th2 lymphocytes, mast cells, and eosinophils. In clinical practice, this phenotype can be identified by a blood eosinophil count ≥ 300 cells/μL and is found in approximately 25% of COPD patients.[11] Several biologics have been tested for T2-predominant COPD, including mepolizumab and benralizumab, but only dupilumab has so far been approved by the European Medicines Agency (EMA) and is awaiting final authorization for use in Spain.[12] This and future biologics could address an unmet need in patients who, despite triple therapy, continue to suffer frequent or severe exacerbations, which significantly impair quality of life and are the leading cause of death in COPD.[13] These therapies may be highly effective for a select subgroup of patients, and guidelines will be needed for a personalized approach to their treatment.
4. **How should COPD with comorbidities be managed, especially cardiovascular comorbidities?** This remains a key issue, as no randomized clinical trials specifically address treatment in COPD patients with various comorbidities. Consequently, current recommendations rely on expert consensus. It is possible (although quite unlikely) that respiratory medications may influence cardiovascular disease, and some cardiovascular or antidiabetic drugs may also improve respiratory outcomes in COPD. A recent Spanish document has specifically addressed the management

https://doi.org/10.1016/j.opresp.2025.100445

of COPD with cardiovascular comorbidities based on expert opinion.[14]

5. **What is the role of identifying and managing treatable traits (TT)?** This approach is essential for the optimal management of more severe COPD cases. Treatable traits span various domains, some not directly related to the disease itself—such as social, environmental, and behavioral factors.[15] While it is not feasible for a guideline like GesEPOC to address all such traits comprehensively, the 2017 edition already included a list of the most common and clinically relevant traits and corresponding treatments. This list will be updated based on recent evidence.[2]

In summary, the challenge for GesEPOC 2025 is to synthesize the latest evidence on COPD treatment and present it in a way that is accessible and useful to healthcare professionals involved in patient care. This should be done without overcomplicated symbols or codes that might confuse non-expert users, and instead with clear algorithms that support decision-making for individualized treatment in this new era of personalized medicine.

Artificial intelligence involvement

No artificial intelligence involvement in this article

Funding

No funding was received for this article.

Authors' contributions

N/A.

Conflicts of interest

Marc Miravitlles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Glenmark Pharmaceuticals, Menarini, Kamada, Takeda, Zambon, Tabuk Pharmaceuticals, CSL Behring, Zambon, Specialty Therapeutics, Sanofi/Regeneron, Grifols and Novartis, consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim, BEAM Therapeutics, GondolaBio, Chiesi, GlaxoSmithKline, CSL Behring, Ferrer, Korrobio, Menarini, Mereo Biopharma, Spin Therapeutics, Specialty Therapeutics, Palobiofarma SL, Takeda, Novartis, Novo Nordisk, Sanofi/Regeneron, Zambon, Zentiva and Grifols and research grants from Grifols.

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Marc Miravitlles
Center: Pneumology Department, Hospital Universitari Vall d'Hebron/Vall d'Hebron Institut de Recerca (VHIR), Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain
E-mail address: marcm@separ.es