GOLD 2023 Executive Summary: responses from the GOLD Scientific Committee

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Reply from the GOLD Scientific Committee:

We thank the authors of the five letters received in relation to the recent publication of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 Executive Summary in the *European Respiratory Journal* [1] for their interest and insightful comments. We address them below, albeit necessarily briefly, under three categories: a global perspective, diagnostic issues, and management of exacerbations.

1) A global perspective: We thank B.J. Kirenga and co-workers for their look at the 2023 GOLD report [1] through the lens of resource-limited settings in Africa and for recognising the efforts we have made to ensure GOLD is relevant to COPD in low-resource settings [2, 3]. We congratulate them for their work in Uganda defining the epidemiology of chronic respiratory diseases, including COPD, and documenting the challenges around access to affordable diagnostic tests and treatments. We agree with the importance of addressing COPD risk factors beyond cigarette smoking, including the potential role of household air pollution, but note there is a need for high quality research into this and other poverty-related risk factors [4]. While we understand the case for doing so, we would not suggest using questionnaires or peak flow measurements to diagnose COPD, given their poor specificity, and would instead recommend advocating for improved access to affordable spirometry. There are signs that the efforts made by the Pan African Thoracic Society and others on this front are starting to bear fruit [5, 6]. We would take a similar stand in relation to inhaled medications and are actively supporting international efforts to improve the availability and affordability of essential inhaled medicines for everyone with COPD, wherever they live on the globe [7, 8].

Asia, which harbours 59% of the world's population, contributes to 57% of the global COPD burden, but a disproportionate 73% of global COPD deaths and disability-adjusted life years [9]. 46% of the world's smokers come from China, India and Indonesia [10]. Other non-smoking risk factors associated with COPD, such as poor socioeconomic status, indoor use of biomass fuel, high levels of ambient air pollution, post-tuberculosis lung sequelae, bronchiectasis and poorly treated chronic severe asthma are very common in Asia, contributing to a high burden of non-smoking COPD in this region [11]. The economic loss due to COPD in Asia is not very different from, or perhaps even more than, in the western world, yet COPD remains a neglected entity in Asia [12]. F.W.S. Ko and D.S.C. Hui highlight the above facts in their correspondence and emphasise the lack of awareness, underdiagnosis and undertreatment of COPD in Asia. They acknowledge that the GOLD 2023 strategy report offers a scientifically sound and practical knowledge base for diagnosis, treatment and prevention of COPD, but argue that it may be a challenge to follow all the GOLD recommendations due to diverse socioeconomic and cultural reasons. GOLD is aware of the availability, accessibility and affordability of diagnostic tools and therapeutics across 48 countries in Asia and recommends adaptation of the GOLD report to the local culture, for example use of Tai Chi and yoga as part of pulmonary rehabilitation programmes in China and India, respectively. GOLD also recommends conducting clinical studies in Asia that evaluate the cost-effectiveness of various treatment strategies, which should then form the basis of the local COPD management guidelines.

2) Diagnostic issues: We are very pleased that H. Lee and co-workers found that the updated GOLD 2023 report has "made a big step to address an unmet need regarding the challenges of disease definition, pathogenesis and classification". The changes adopted by GOLD were prompted by a recently published in-depth review of how diseases are defined and classified that can be informative for the interested reader [13]. H. Lee and co-workers raise two important questions that need addressing. The first one is whether all chronic airway infections that lead to airflow obstruction can be regarded as COPD-I (COPD due to

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infections). The response is relatively simple, as they elegantly discuss in the third paragraph of their correspondence. If tuberculosis (a bacterial infectious disease) or HIV (a viral one) can cause COPD, it follows that other micro-organisms can indeed end up causing COPD. It is our recommendation that the medical community pay more attention to the different causes of COPD if we are to control this disease worldwide. As far as the second question, which was whether bronchiectasis with airflow obstruction can be regarded as a new etiotype of COPD, the response is a little bit more complex. There is no question that a large proportion of patients with bronchiectasis have airflow obstruction and that a sizable proportion of patients with COPD have bronchiectasis when a computed tomography scan or chest radiograph is obtained [14, 15]. What comes first is not clear and calling bronchiectasis an "etiotype" (in contrast to the infectious agents) is not right, because bronchiectasis itself has several causative agents and constitutes a specific recognised nosological entity. What is clear is that its presence in patients with COPD worsens prognosis and, as such, represents an identifiable important comorbidity of COPD [16]. How they interact over time represents a challenge to be met.

J. Khan and co-workers question the purpose of annual follow-up spirometry for all patients with COPD, as recommended by the GOLD 2023 report [1], similar to what has been recommended in previous reports. J. Khan and co-workers argue that, for a number of reasons that they appropriately discuss, this should be personalised. We could not agree more. COPD is a highly heterogeneous disease, and now we know that not all patients show accelerated lung function decline [17–19]. Yet, enhanced lung function decline is clinically relevant and potentially amenable to treatment, particularly in patients with high circulating eosinophils [1]. Like in many other COPD-related issues, GOLD has to necessarily make general recommendations. In this context, the concept of monitoring lung function periodically by spirometry (as often as the attending physician considers necessary, given the clinical condition and temporal evolution of each patient – *e.g.* in terms of symptoms, smoking status, exacerbations, compliance with treatment, eosinophil counts) seems advisable.

3) Management of exacerbations: We appreciate the correspondence from V. Leung and C. Lee about the appropriate duration of antibiotic therapy for patients with suspected bacterial infection as a cause of their COPD exacerbation (ECOPD). The GOLD 2023 report first indicates in what patients it is appropriate to use antibiotics based on their clinical characteristics [1]. Once clinicians have determined that they would use antibiotics, we suggested the range of 5–7 days [1]. Although the literature has suggested that even less than 5 days of antibiotics for ECOPD will be appropriate for most patients, it is important to highlight that these meta-analyses have evaluated heterogeneous patient populations, from different geographic areas, and as a consequence different patterns of bacterial sensitivity to antibiotics, and using different classes of medications [20, 21]. In most of the studies with shorter duration of therapy patients, received a fluoroquinolone [22]. Furthermore, some of the antibiotics, like gemifloxacin, that showed good efficacy when used for shorter time periods, are no longer available. Thus, we cannot recommend that every patient with a suspected bacterial infection as the cause of ECOPD receives this class of antibiotics, and we do not know if the efficacy would have been found to be similar had the studies been done with other classes of antibiotics. Therefore, we believe that indicating to the reader when to use antibiotics to make their selection based on local patterns of resistance and emphasising shorter duration of therapy are the most appropriate recommendations.

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