Pharmacotherapy for Chronic Obstructive Pulmonary Disease: Molecules and Delivery Are Equally Important

To the Editor:

When prescribing inhaled maintenance therapy for an individual with chronic obstructive pulmonary disease, healthcare professionals (HCPs) should ideally perform three steps: *1*) assess dyspnea/symptoms and future risk of an exacerbation, *2*) select a long-acting inhaled β-agonist and/or a long-acting muscarinic antagonist as well as possibly an inhaled corticosteroid, and *3*) select one of four delivery systems (1). The recent American Thoracic Society Clinical Practice Guideline on Pharmacologic Management of Chronic Obstructive Pulmonary Disease addresses four clinically relevant PICO (Population, Intervention, Comparator, and Outcome) questions related to inhaled therapies (2). The recommendations provide up-to-date and authoritative guidance for HCPs when they consider the first two steps of the decision process noted above.

This guideline (2) as well as the Global Initiative for Chronic Obstructive Lung Disease strategy (1) recommend long-acting inhaled β-agonists, long-acting muscarinic antagonists, and inhaled corticosteroid as groups of medications by necessity rather than as specific molecules with unique delivery systems—pressured metered-dose inhaler, dry powder inhaler, slow/soft mist inhaler, and nebulization. By grouping medications, there are two inherent assumptions: *1*) similar but different molecules are comparable in efficacy and *2*) inhalation of the molecule into the lower respiratory tract using correct technique is comparable regardless of the delivery system. Unfortunately, this overall approach lacks specific guidance for matching individual patient characteristics such as cognitive function, including coordination ability, manual dexterity, and peak inspiratory flow, with the most appropriate delivery system, each of which requires specific instructions for use (3).

Algorithms for selecting the most appropriate inhaler delivery system based on patient characteristics have been proposed (4–6). However, to our knowledge, randomized trials have not been performed to examine whether a particular algorithm makes a difference in patient outcomes. Appropriate guidance for HCPs in inhaler selection appears to be a major unmet need in caring for patients with chronic obstructive pulmonary disease. To fill this gap, we encourage professional organizations such as the American Thoracic Society, patient advocacy groups, and pharmaceutical companies to support prospective studies that examine matching molecule and inhaler according to the abilities and skills of the individual patient (i.e., precision medicine). The inhaler delivery system is equal in importance to the prescribed molecule. ■

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References

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease; 2020 [accessed 2020 Apr 27]. Available from: https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf.
2. Nici L, Mammen MJ, Charbek E, Alexander PE, Au DH, Boyd CM, *et al*. Pharmacologic management of chronic obstructive pulmonary disease: an official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med* 2020;201:e56–e69.
3. Laube BL, Janssens HM, de Jongh FHC, Devadason SG, Dhand R, Diot P, *et al*.; European Respiratory Society; International Society for Aerosols in Medicine. What the pulmonary specialist should know about the new inhalation therapies. *Eur Respir J* 2011;37:1308–1331.
4. Dekhuijzen PNR, Vincken W, Virchow JC, Roche N, Agusti A, Lavorini F, *et al*. Prescription of inhalers in asthma and COPD: towards a rational, rapid and effective approach. *Respir Med* 2013;107:1817–1821.
5. Usmani OS. Choosing the right inhaler for your asthma or COPD patient. *Ther Clin Risk Manag* 2019;15:461–472.
6. Mahler DA. The role of inspiratory flow in selection and use of inhaled therapy for patients with chronic obstructive pulmonary disease. *Respir Med* 2020;161:105857.

Reply to Mahler *et al.*

From the Authors:

We would like to thank Drs. Mahler, Ohar, Ferguson, and Donohue for their interest in the "Pharmacologic Management of Chronic Obstructive Pulmonary Disease: An Official American Thoracic Society Clinical Practice Guideline" (1). We wholly agree with the

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points raised with respect to the need to address medication delivery systems for clinical decision-making. Our Clinical Practice Guideline relied on the available literature to date to perform a rigorous, PICO (Population, Intervention, Comparator, and Outcomes)-driven distillation of scientific evidence to provide recommendations pertaining to key questions regarding the pharmacologic treatment of chronic obstructive pulmonary disease. However, the available evidence did not allow us to address the merits of specific medication delivery devices. As per the committee discussions, we raised the issues of feasibility and acceptability as playing a role in the decision to prescribe various types of inhalers. Though we noted issues such as cost and burden of use of inhalers, we did not specifically identify cognitive ability, dexterity, coordination, and inspiratory flow as additional issues to be addressed. We thank the authors for raising these important considerations in this forum and look forward to future randomized trials that address matching medication delivery devices to specific patient characteristics. ■

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Reference

1. Nici L, Mammen MJ, Charbek E, Alexander PE, Au DH, Boyd CM, *et al*. Pharmacologic management of chronic obstructive pulmonary disease: an official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med* 2020;201:e56–e69.

Treatment Decisions for Unrepresented Patients: American Thoracic Society/American Geriatrics Society Policy Statement Lacks Sufficient Guidance

To the Editor:

The *Journal* recently published a joint statement of the American Thoracic Society and the American Geriatrics Society on medical decision-making for unrepresented patients in the critical care setting (1). This statement is an important contribution, but it neglects at least one significant aspect of the decision-making process for unrepresented patients, as follows: how to identify the point in an unrepresented patient's treatment course at which an alternative decision-making process should be implemented. A comprehensive approach to supporting the decision-making process for these patients requires that this question be answered systematically, and this statement is a missed opportunity in this regard.

There are many ways that this issue can present itself in the clinical setting. For example, in some cases, an unrepresented patient may need a line placement, a blood transfusion, or some other nonemergency but consent-requiring procedure. Should an alternative decision-making process be initiated under such conditions? Is it *really* necessary for the physician to justify the need for a peripherally inserted central catheter line in a hypotensive patient, for example? Some clinical ethicists answer in the affirmative—the procedure requires informed consent, so an alternative process is always required. But this seems a terrible waste of time and resources for all involved, and it can undermine clinician willingness to engage with appropriate processes when more urgently necessary. This sort of challenge is not considered by this statement, except to flag it as something they do not intend to address. Guidance on when to initiate an alternative decision-making process would help clinicians to better navigate these circumstances, and comprehensive guidelines on medical decision-making for unrepresented patients should address this issue.

A lack of implementation guidance also creates the possibility of moving too quickly or too slowly to an alternative decision-making process for unrepresented patients, which may lead to avoidable violations of patient autonomy. For example, a patient with a life-threatening thrombus may benefit from surgical intervention, but this may turn out to be an unwanted intervention once the patient's surrogate decision-maker, perhaps a difficult-to-locate relative, is identified. In this type of case, moving too quickly to an alternative decision-making process can lead to unwanted care. Similarly, an unrepresented patient for whom comfort-focused care is medically and ethically appropriate may end up receiving aggressive care before an alternative decision-making process can be implemented. When the decision-making process is too slow for the developing clinical circumstances, the medical team may feel compelled to provide potentially inappropriate care to unrepresented patients (2).

These are difficult but familiar situations for clinicians to navigate, and a policy statement that declines to offer any guidance about how to address such concerns must ultimately be regarded as incomplete. The issue can be approached conservatively or aggressively or via a nuanced process that considers the many clinical and ethical considerations that might be involved. But neglecting the question altogether is a missed opportunity to provide helpful and much needed guidance for front-line clinicians. ■

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