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Challenges in the Implementation of Chronic Obstructive Pulmonary Disease Guidelines in Low- and Middle-Income Countries An Official American Thoracic Society Workshop Report

Hurst, John R; Buist, A Sonia; Gaga, Mina; Gianella, Gonzalo E; Kirenga, Bruce; Khoo, Ee Ming; Mendes, Renata Gonçalves; Mohan, Anant; Mortimer, Kevin; Rylance, Sarah

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Challenges in the Implementation of Chronic Obstructive Pulmonary Disease Guidelines in Low- and Middle-Income Countries

An Official American Thoracic Society Workshop Report

 John R. Hurst, A. Sonia Buist, Mina Gaga, Gonzalo E. Gianella, Bruce Kirenga, Ee Ming Khoo, Renata Gonçalves Mendes, Anant Mohan, Kevin Mortimer, Sarah Rylance, Trishul Siddharthan, Sally J. Singh, Job F. M. van Boven, Siân Williams, Jing Zhang, and William Checkley; on behalf of the American Thoracic Society Assembly on Clinical Problems


THIS OFFICIAL WORKSHOP REPORT OF THE AMERICAN THORACIC SOCIETY WAS APPROVED FEBRUARY 2021

Abstract

There is a substantial burden of chronic respiratory diseases, including chronic obstructive pulmonary disease (COPD), in low- and middle-income countries (LMICs). LMICs have particular challenges in delivering cost-effective prevention, diagnosis, and management of COPD. Optimal care can be supported by effective implementation of guidelines. This American Thoracic Society workshop considered challenges to implementation of COPD guidelines in LMICs. We make 10 specific recommendations: 1) relevant organizations should provide LMIC-specific COPD management guidance; 2) patient and professional organizations must persuade policy-makers of the importance of lung function testing programs in LMICs; 3) healthcare education and training should emphasize the early-life origins of COPD; 4) urgent action is required by governments to reduce airborne exposures, including exposures to tobacco smoke and indoor and outdoor air pollution; 5) guidance for COPD in LMICs should explicitly link across Essential Medicine Lists and the World Health Organization

package of essential noncommunicable disease interventions for primary health care in low-resource settings and should consider availability, affordability, sustainability, and cost-effective use of medicines; 6) the pharmaceutical industry should work to make effective COPD and tobacco-dependence medicines globally accessible and affordable; 7) implementation of locally adapted, cost-effective pulmonary rehabilitation programs should be an international priority; 8) the World Health Organization Global Action Plan for the Prevention and Control of Noncommunicable Diseases should specify how improvements in respiratory health will be achieved; 9) research funders should increase the proportion of funding allocated to COPD in LMICs; and 10) the respiratory community should leverage the skills and enthusiasm of earlier-career clinicians and researchers to improve global respiratory health.

Keywords: chronic obstructive pulmonary disease; guidelines; implementation; low- and middle-income countries

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Introduction

Abundant data highlight the global burden of chronic respiratory diseases (CRDs). The commonest CRDs in adults, and the two diseases the World Health Organization (WHO) focuses on when using the term “CRD,” are asthma and chronic obstructive pulmonary disease (COPD). Most COPD-related morbidity and mortality occur in low- and middle-income countries (LMICs) (1, 2), and this comes with a consequent socioeconomic burden (3). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) produces an annually updated, evidence-based strategy for the diagnosis, management, and prevention of COPD (4). However, there is limited information tailored to the needs of LMICs (5). Diagnosis, management, and prevention of COPD can be aided by the availability of evidence-based guidance supported by effective dissemination and implementation. This American Thoracic Society (ATS) workshop report considers challenges in the implementation of COPD guidelines in LMICs and is closely aligned with the mission of the ATS “to improve health worldwide by advancing research, clinical care, and public health in respiratory disease, critical illness, and sleep disorders.” We recognize that there is considerable diversity within and between LMICs.

GOLD defines COPD as “a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases” (4). GOLD recommends confirming the diagnosis by demonstrating

poorly reversible airflow obstruction using spirometry (4), with such obstruction being defined as having a fixed forced expiratory volume in 1 second (FEV₁) to forced vital capacity (FVC) ratio of <0.70. The severity of airflow obstruction provides prognostic information (4), and spirometry also informs the differential diagnosis. This particularly applies to asthma, which is also prevalent in LMIC settings, can overlap with COPD, and may be difficult to distinguish from COPD.

The availability of lung function testing including spirometry and interpretation of quality-assured spirometry is limited in many LMICs (6, 7). Even where spirometry is available, differentiating the cause(s) of poorly reversible airflow obstruction in LMICs is challenging because smoking may not be the predominant risk factor in this context (8). Major contributors, alone or in combination with tobacco smoke in LMICs, include poor lung growth and development (9–11) (associated with poverty [12]); inadequately treated respiratory infections (13); indoor (household) (8) and outdoor air pollution, including occupational exposures (14); chronic asthma (15); post-tuberculosis lung disease (14); and bronchiectasis. Respiratory syndromes associated with some of these risk factors are best considered different causes of COPD; others are entirely different conditions. Different lung function trajectories can all result in airflow obstruction that meets spirometric criteria for COPD (16) yet has distinct clinical manifestations likely requiring different interventions. Further complexity is introduced through debate about whether a fixed FEV₁/FVC ratio or, alternatively, criteria based on the lower limit of normal in a reference population is more appropriate for defining COPD (17, 18). Using

the lower limit of normal requires reference values that are often unavailable in LMICs. Using normal values from other populations may result in significant misrepresentations of disease (19, 20).

In summary, and before going on to consider challenges to the implementation of COPD guidelines in LMICs, it is important to appreciate that much of what is labeled as “COPD” in LMICs may represent diverse clinical syndromes and that CRD in LMICs has a broad range of causes and patterns on lung function testing.

Methods

A proposal for this workshop was submitted by the co-chairs (J.R.H., A.S.B., and W.C.) to the ATS in 2019 and, after peer-review, was selected for support. The co-chairs developed the program and invited diverse international speakers and discussants to address the following three objectives:

1. How are COPD guidelines perceived and used in LMICs, and what guidelines are in real-world use?
2. What are the barriers and facilitators to implementation of universal, evidence-based, guideline-driven, cost-effective interventions for COPD in LMICs?
3. How can the respiratory community lead changes resulting in the wider introduction of evidence-based care for COPD in LMICs?

The group included multiprofessional representatives from Brazil, China, India, Malaysia, Peru, and Uganda and members affiliated with the Global Alliance for Chronic

Disease, GOLD, the International Primary Care Respiratory Group, and WHO. All members submitted conflict-of-interest forms.

Speakers provided presentations to the co-chairs in advance. The co-chairs reviewed draft presentations and provided feedback to ensure comprehensive coverage of the subject. The group met virtually for 6 hours over 2 days in September of 2020. Presentations were followed by group discussion. The draft workshop report was prepared by the co-chairs and circulated to all participants. Consensus was achieved through discussion. The agreed final document was submitted to the ATS.

Discussion

Question 1: How Are COPD Guidelines Perceived and Used in LMICs, and What Guidelines Are in Real-World Use?

COPD guidelines have been published by many national and international societies, governmental bodies, and nongovernmental organizations, including the ATS, but none of the major international guidelines provide recommendations of specific relevance to LMIC settings. Where guidance exists, national COPD guidelines are often derived from the GOLD report (4). Through the annual report, together with educational tools and advocacy, GOLD aims to work with healthcare professionals and public health officials to raise awareness of COPD, improving prevention and treatment. GOLD national leaders are appointed in many (but

not all) countries, including many LMICs. These leaders are expected to develop and enact COPD awareness and implementation programs. However, they are not funded to do this, and many national leaders focus their attention on World COPD Day and have limited additional programming. Consequently, acceptance of and adherence to GOLD recommendations by national health programs and healthcare professionals are variable (21), and recognition of GOLD outside specialist practice is low. GOLD does not provide resource-stratified recommendations. Rather, GOLD provides an overarching report based on the best available evidence, but this report requires context-adapted implementation with reference to local resources. This highlights the need for national COPD guidelines in resource-constrained LMIC settings. A 2020 review (22) reported that 1.93 billion people reside in an LMIC without a national COPD guideline (Figure 1).

Even where COPD guidelines in LMICs exist, implementation may be poor, in part because of guideline quality. Fewer than one in four LMIC COPD guidelines contained an implementation or dissemination plan, and LMIC COPD guidelines were often not targeted to or developed with the multiprofessional primary healthcare staff who need them most (23). A 2020 systematic review considering implementation of lung health interventions in LMICs (24) concluded that key factors included understanding needs of local users, ensuring compatibility of interventions with local contexts, identifying influential stakeholders and applying engagement strategies, ensuring adequate

access to knowledge and information, and addressing resource availability. This emphasizes the importance of COPD education and training to primary healthcare staff, including the wider multiprofessional team. Importantly, delivery of education and training requires sufficient resources.

An additional problem is that implementation challenges (25, 26) may differ within individual countries (27). Primary care may experience “guideline overload.” Clinicians must deal with multiple conditions, each with a guideline, in patients presenting with symptoms that may have multiple causes when time with each patient is limited. Once a diagnosis is reached, few guidelines include advice for people in the context of multimorbidity. Guidelines may be particularly challenging to implement in fragmented healthcare systems.

International guidelines for tuberculosis and human immunodeficiency virus (HIV) are widely disseminated and incorporated into national public health programs with good clinician adherence. The ATS has played a central role in the development and dissemination of international tuberculosis guidelines (28), a process that required considerable time and funding. Guidelines for chronic noncommunicable diseases (NCDs) are not perceived with the same urgency or importance as guidelines for infectious diseases, even though the burden may be similar. There are successful examples of guidelines to support respiratory care in LMICs. The Practical Approach to Care Kit program (29) developed in South Africa is a health-system improvement initiative that takes a symptom-based approach and uses evidence to create a decision-support tool by working with local health systems to educate clinicians and determine appropriate task sharing. The original WHO-sponsored program, the Practical Approach to Lung Health program (30), used a diagnostic tree in primary care and public health programs, branching initially to tuberculosis or nontuberculosis.

In summary, although guideline availability and quality are variable in LMICs, the major challenge appears to be effective guideline implementation.

Recommendation 1. *Relevant organizations, including societies, clinicians, and academics, should provide LMIC-specific COPD management guidance spanning from prevention, diagnosis, and management to palliative care. This should be codeveloped with primary healthcare teams and patients. The*

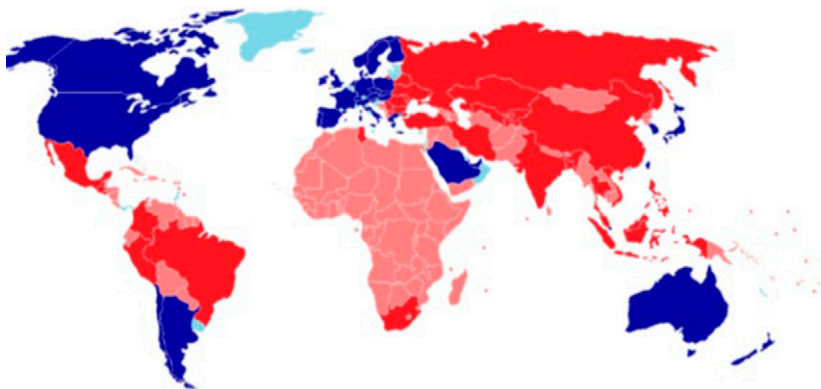


Figure 1. Global national chronic obstructive pulmonary disease guideline coverage (22). Red colors represent low- and middle-income countries, and blue colors represent high-income countries. The darker shades of red and blue represent having a national guideline, and the lighter tints of red and blue represent not having a national guideline. Reprinted by permission from Reference 22.

guidance should include an effective implementation plan that acknowledges clinician education and training, resource availability, and limitation in resources. Guidance should consider the diversity of conditions resulting in poorly reversible airflow obstruction that meet the criteria for COPD in LMIC settings.

Question 2: What Are the Barriers and Facilitators to Implementation of Universal, Evidence-based, Guideline-Driven, Cost-Effective Interventions for COPD in LMICs?

Diagnosis. Spirometry is necessary for the diagnosis of COPD. Spirometry provision can be challenging in high-income countries (HICs) and can be even more challenging in some LMIC settings. There are models for successful spirometry training in LMIC. For example, the Pan African Thoracic Society Methods in Epidemiologic, Clinical and Operations Research Program added spirometry training to training in research methods (6). Students were then offered the opportunity to qualify for the European Respiratory Society Spirometry Driving License, which demonstrates proficiency in administering spirometry and the ability to train others.

In searching for a less costly and simpler alternative to spirometry, there is emerging evidence that a sequential approach using questionnaires and peak expiratory flow (PEF) testing enables identification of people with COPD (31, 32). This pragmatic approach is best used to identify people who will go on to need spirometric confirmation.

Questionnaires are generally simple and cheap to implement but need to be evaluated in LMIC settings. Administering PEF testing requires training and the availability of affordable PEF meters. Microspirometry (using a simple, inexpensive, hand-held spirometer that can give a reasonable assessment of FEV₁) provides an alternative. Use of case-finding questionnaires has yet to be adequately tested in real-world primary care settings in LMICs to demonstrate that the COPD being detected is clinically and economically important (33, 34). When considering implementation of COPD case finding in LMICs, it is also important to consider the potential harm of overdiagnosis, the absence of specialists for continuing care, and the absence of proactive preventative medicine in primary care. Public awareness campaigns around respiratory health,

including the longer-term consequences of not identifying and treating risk factors for respiratory disease, will be important in supporting case finding.

In addition to the diversity of disease meeting the diagnostic criteria for COPD in LMICs, there is poor awareness and understanding of this term, both among affected people and among clinicians (35). This is in contrast to “asthma,” which is widely recognized (with consequent mislabeling of asthma and COPD [36]). Poor recognition of COPD may reflect stigma, and the occurrence of asthma in children may have better motivated policy initiatives. Stigma may be related to the perception that COPD is caused by tobacco smoking and that the individual is therefore at fault. Smoking can be reframed as nicotine addiction (which often starts in childhood), and nicotine addiction can be framed as a treatable condition (37).

Given the diversity of factors causing impaired lung function in LMICs, there is an argument for an approach to the diagnosis of CRD in LMICs that is broader than just COPD and aims to identify all individuals with suboptimal lung function, whatever the cause. LMICs are very diverse, and only in situations in which it is clinically imperative to provide disease-specific treatment is there the need to define specific syndromes, given the universal importance of high-value interventions such as exposure reduction, treatment for nicotine addiction, vaccinations, education, and physical activity.

Recommendation 2. *Patient and professional organizations must persuade policy-makers of the importance of lung function testing programs in LMICs, including adequate provision of spirometry training. In the absence of accessible, high-quality spirometry, the use of micro-spirometry, PEF testing, and questionnaires that assess clinical history can support the diagnosis of COPD.*

COPD prevention and better care for those with a diagnosis of COPD. Support for tobacco control and smoking cessation is critical for prevention of COPD, as has been advocated in the WHO Framework Convention on Tobacco Control (38). Although the precise contribution of biomass smoke exposure to COPD remains controversial, there is evidence that clean cooking stoves reduce indoor pollution (39). Translating this into clinical outcomes requires longer-term prospective studies, but COPD prevalence has been seen to change with such interventions (40). There are implementation challenges around

acceptance of clean cooking stoves. There are also emerging data on the benefits of reducing traffic pollution (41, 42). Interventions to reduce premature births and childhood pneumonia and interventions to promote effective lung growth and development are also all likely to translate into reduced adult cases of poorly reversible airflow obstruction, and a life-course approach to COPD prevention is thus critical (16). It is now recognized that fixed airflow obstruction in adult life can result from different trajectories of lung growth and development, including not only accelerated decline from maximal lung function (the traditional model of COPD) but also “normal” decline from a submaximal level (16). Factors determining submaximal lung growth and development, including prematurity (43), childhood infection (44), and nutrition (45), can therefore be considered targets for the primary prevention of COPD.

Guidelines provide recommendations for nonpharmacological and pharmacological interventions in COPD. Critical for both, especially in LMICs, is the affordability and cost-effectiveness of interventions (46). Cost-effectiveness will vary by context, and willingness-to-pay thresholds are lacking in most LMIC settings. There remains an absence of data on basic interventions such as short-acting bronchodilators, pulmonary rehabilitation (PR), and treatment for COPD exacerbations. WHO considers tobacco control interventions and public awareness about physical activity and diet to be “best buys” (47) and considers smoking cessation and physical activity counseling in primary care, symptom relief with inhaled salbutamol, and treatment of asthma with inhaled beclomethasone to be “effective.” WHO identifies access to improved cooking stoves and cleaner fuels, occupational exposure reduction, and influenza vaccination for people with COPD as potential interventions without cost-effectiveness data (48). There is therefore an urgent need to provide new data on low-cost, effective interventions in LMICs and to consider broader criteria for inclusion, such as the value to society (49, 50). The goal should be to support the delivery of universal health coverage and encourage governments to include a package of noncommunicable respiratory interventions within that coverage (51).

There is a strong evidence base to support PR for CRD (52), and large audit programs have demonstrated the real-world effectiveness of PR in HICs (53). Availability and access to rehabilitation is recognized as

fundamental to achieving WHO Sustainable Development Goal 3. Data are emerging that culturally adapted PR can be successfully implemented for COPD in LMICs (54–58), but cost-effectiveness data are missing and are necessary to help address major challenges around staff training, space, the provision of equipment, the retention rate in programs, and the awareness and support needed to refer people to such programs. Alternative approaches, including digital options, may improve access to PR, but there has been little study of the use of “remote PR” in LMICs.

Regarding pharmacological therapy (59), the majority of effectiveness and cost-effectiveness (60) studies have been conducted in smoking-related COPD in HICs and do not consider the diversity of COPD in LMICs. The need for access to essential medicines and vaccines is stated explicitly within the WHO Sustainable Development Goals (target 3.8) (61) and the Global Action Plan for the Prevention and Control of NCDs (48). WHO produces a biannual essential medicines list (EML) (62) designed to inform country-specific national EMLs. The latest iteration of the WHO EML includes short-acting β -agonists and antimuscarinics, inhaled corticosteroids with and without long-acting β -agonists, and a long-acting antimuscarinic, in addition to influenza vaccines and the oral steroids, antibiotics, and oxygen necessary for exacerbation management. The substance misuse section contains nicotine replacement by using gum and patches but is not cross-referenced to respiratory health. The 2020 version of the WHO Package of Essential NCD Interventions for Primary Health Care in Low-Resource Settings (63) only lists salbutamol, ipratropium, and theophylline and is not aligned with either the EML or the GOLD report. There is variable alignment between the WHO EML and national EMLs (64–66), none of which necessarily consider availability and affordability (64, 67), which vary considerably even within LMICs. There is a circular argument in that pharmacies generally stock what is prescribed but that prescribers only prescribe what is stocked (68). For inhaled drugs, there is little focus on or funding for providing training and incentivization to support effective use (correct inhaler technique and adherence). The universal healthcare package based on *Disease Control Priorities* has little on respiratory disease and COPD (51). Supporting the manufacture of generic medicines, which has been successful for increasing access to antiretroviral therapy in HIV, is more complex for inhalers, for

which both the drug and device must be considered.

Recommendation 3. *The origins of COPD may be in early life, and all clinicians, including those working in maternal and child health, therefore require education and training on basic prevention messages such that smoking in pregnancy is discouraged, premature births are reduced, and childhood respiratory infections are effectively diagnosed and treated.*

Recommendation 4. *Urgent action is required by governments in LMICs to apply successful tobacco control regulations from HICs and to test and extend such approaches to indoor and outdoor air pollution. New creative approaches to tobacco control should be developed and studied.*

Recommendation 5. *Guidance for COPD in LMICs should be set in the framework of universal health coverage and should be explicitly linked across WHO and national EMLs and the WHO Package of Essential NCD Interventions for Primary Health Care in Low-Resource Settings. Guidance should consider the availability, affordability, sustainability (incorporating environmental impact), and cost-effectiveness of medicines and their use and should include supporting patients to use inhalers correctly, which may require adjuncts such as spacers.*

Recommendation 6. *The pharmaceutical industry should work with national governments to make effective COPD and tobacco-dependence medicines globally accessible and affordable to everyone who needs them.*

Recommendation 7. *Implementation of locally adapted, cost-effective PR programs should be an international priority. This will require investment and workforce planning that consider staff training, awareness, referral, and novel approaches to delivery.*

Question 3: How Can the Respiratory Community, through this ATS Workshop, Promote Changes That Result in the Wider Introduction of Evidence-based Care for COPD in LMICs?

COPD is not seen as a public health concern, despite compelling evidence demonstrating a high prevalence and burden in LMICs. Although there is high-quality evidence of cost-effective diagnostic approaches and management strategies in HICs, evidence for successful implementation of such approaches in LMICs is less robust.

COPD often occurs as a component of multimorbidity, and critical interventions for

COPD, including exposure reduction and rehabilitation, have holistic benefits. We will therefore achieve more by building the case for change around existing NCD targets, initiatives, and infrastructure. We must also learn from global initiatives to tackle HIV-AIDS (acquired immunodeficiency syndrome) and tuberculosis and consider ways in which COPD management can be transformed by coordinated approaches at scale.

Advocacy for COPD in LMICs will require clear, simple messaging and engaged, local champions. GOLD and ATS are international organizations and members of the Forum of International Respiratory Societies. Together, they represent a formidable global force of respiratory expertise and offer opportunities to do more by working together. As a respiratory community, we need to shift our own mindset toward prioritizing the needs of the world’s poor. In addition, we need to actively seek out and support earlier-career champions who can continue to work for better global respiratory health in the decades to come. We note the impact that celebrity supporters can bring. A “patient charter” for COPD sets out six principles of COPD care and is relevant to LMICs (69).

There are clear areas for further research on COPD in LMICs (70). As a community, we must lobby for greater research funding for COPD in LMICs where the scale of current investment is not reflective of the disease burden (71).

We are not the only group aiming to address these challenges. GOLD held a 2019 summit on COPD in LMICs (72) that concluded that WHO should coordinate activity in this area, focusing on awareness among the public, healthcare professionals, and governments and ensuring that spirometry and cost-effective pharmacological and nonpharmacological interventions are available and affordable. We also believe that WHO has a critical, central coordinating role. We strongly advocate that specific targets for CRD and COPD should be included in the WHO NCD strategy to monitor progress.

Recommendation 8. *The WHO Global Action Plan for the Prevention and Control of NCDs should specify how the relative reduction of premature mortality from CRD will be achieved and should also focus on morbidity. As interim targets, by 2030,*

- $\geq 50\%$ of people with chronic respiratory symptoms should have access to











	1. Relevant organizations should provide LMIC-specific COPD management guidance.		6. The pharmaceutical industry should work to make effective COPD and tobacco dependence medicines globally accessible and affordable.
	2. Patient and professional organizations must persuade policy-makers of the importance of lung function testing programs in LMICs.		7. Implementation of locally-adapted, cost-effective pulmonary rehabilitation programs should be an international priority.
	3. Health care education and training should emphasize the early-life origins of COPD.		8. The WHO Global Action Plan for the prevention and control of non-communicable diseases should specify how improvements in respiratory health will be achieved.
	4. Urgent action is required by governments to reduce airborne exposures: tobacco smoke, and indoor and outdoor air pollution.		9. Research funders should increase the proportion of funding allocated to COPD in LMICs.
	5. Guidance for COPD in LMICs should explicitly link across Essential Medicine Lists, the WHO PEN, and consider availability, affordability, sustainability and cost-effective use of medicines.		10. The respiratory community should leverage the skills and enthusiasm of earlier-career clinicians and researchers to improve global respiratory health.

Figure 2. Summary of the recommendations. COPD = chronic obstructive pulmonary disease; LMIC = low- and middle-income country; PEN = Package of Essential Noncommunicable Disease Interventions for Primary Health Care in Low-Resource Settings; WHO = World Health Organization.

appropriate assessments, including accurate and timely diagnosis;

- $\geq 60\%$ of those with CRD should have access to effective nonpharmacological and pharmacological treatments; and
- $\geq 70\%$ of those treated for CRD should have well-controlled disease.

Future targets should transition from measurement to monitoring improvement. LMICs are diverse, and in those settings where differentiation among COPD, asthma, and other CRDs is possible (and this must be the aim), specific targets should be developed for COPD.

Recommendation 9. Research funders should increase the proportion of funding allocated to COPD in LMICs to be

commensurate with the burden of disease. Funders should convene a meeting with LMIC researchers and their collaborators to develop a respiratory research roadmap to ensure the best use of limited research funding.

Recommendation 10. The respiratory community should leverage the skills and enthusiasm of earlier-career clinicians and researchers and empower them through investment and global partnerships to take on the challenges of research and clinical care for COPD in LMICs.

Summary and Next Steps

This workshop report is aligned with the ATS mission to improve global lung health by

advancing research, clinical care, and public health in respiratory disease. The report describes the challenges to implementation of COPD guidelines in LMICs. The relative importance of these challenges is context dependent and will vary among and, indeed, within individual LMICs. We have made 10 specific recommendations (Figure 2). These are intended to guide development of strategies and practical tools to assist better implementation of guideline-based COPD care in LMICs. We commit to working from within the ATS to keep these recommendations high on the internal policy agenda. However, the respiratory community must stand together with one voice if we are to deliver better respiratory health in LMICs. Moreover, success will require integration

with international NCD strategies and targets led by WHO, involvement of early-career professionals, and global advocacy. This report must not collect digital dust. We stand ready to take our recommendations forward and to be judged on our results. ■

This official workshop report was prepared by an *ad hoc* subcommittee of the ATS Assembly on Clinical Problems.

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