Challenges in the Implementation of COPD Guidelines in Low- and Middle-Income Countries: an ATS Workshop Report

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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 ten specific recommendations:

1. Relevant organisations should provide LMIC-specific COPD management guidance.

2. Patient and professional organisations must persuade policy-makers of the importance of lung function testing programs in LMICs.

3. Health care education and training should emphasise the early-life origins of COPD.

4. Urgent action is required by governments to reduce airborne exposures: tobacco smoke, and indoor and outdoor air pollution.

5. Guidance for COPD in LMICs should explicitly link across Essential Medicine Lists, the World Health Organisation (WHO) PEN (package of essential non-communicable disease interventions for primary health care in low-resource settings), and 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 programmes should be an international priority.

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.

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

10. The respiratory community should leverage the skills and enthusiasm of earlier-career clinicians and researchers to improve global respiratory health.

Introduction

Abundant data highlight the global burden of chronic respiratory diseases (CRDs). The commonest CRDs in adults, and the two diseases the World Health Organisation (WHO) focuses on when using the term CRD are asthma and chronic obstructive pulmonary disease (COPD). Most COPD-related morbidity and mortality occurs in low- and middle-income countries (LMICs)[1,2], with consequent socio-economic 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 recognise 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], defined as a fixed Forced Expiratory Volume in 1 second (FEV_1) to Forced Vital Capacity (FVC) ratio <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 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 LMIC is challenging as smoking may not be the predominant risk factor here[8]. Major contributors, alone or in combination with tobacco smoke in LMICs include poor lung growth and development[9-11] (associating 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 in association 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 have distinct clinical manifestations likely requiring different interventions. Further complexity is introduced through debate about whether a fixed FEV_1/FVC ratio or, alternatively, criteria based on the lower limit of normal (LLN) in a reference population is more appropriate to define COPD[17,18]. Using LLN requires reference values which are often unavailable in LMICs. Using normal values from other populations may result in significant misrepresentation 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 labelled as 'COPD' in LMICs may represent diverse clinical syndromes, and chronic respiratory disease 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 (SB, WC and JH) to the ATS in 2019 and, following peer-review, was selected for support. The co-chairs developed the programme 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 LMIC?

The group included multi-professional representatives from Brazil, China, India, Malaysia, Peru and Uganda, and members affiliated with the Global Alliance against Chronic Respiratory Disease (GARD), GOLD, the International Primary Care Respiratory Group (IPCRG) and the World Health Organization (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 six hours over two days in September 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

1. How are COPD guidelines perceived and used in LMIC, and what guidelines are in real-world use?

COPD guidelines have been published by many national and international societies, governmental bodies and non-governmental organisations including the American Thoracic Society 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 health care 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 action COPD awareness and implementation programs. However, they are not funded to do this and many National Leaders focus their attention on World COPD Day with limited additional programming. Consequently, acceptance and adherence of GOLD recommendations by national health programmes and health-care professionals is variable[21], and recognition of GOLD outside specialist practice is low. GOLD does not provide resource-stratified recommendations. Rather, GOLD provides an over-arching report based on the best-available evidence, but which 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 a LMIC without a national COPD guideline (Figure 1).

Even where COPD guidelines in LMICs exist, implementation may be poor, in part due to 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 multi-professional primary health-care 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 emphasises the importance of COPD education and training to primary health-care staff, including the wider multi-professional team. Importantly, delivery of education and training requires sufficient resource.

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, and in patients presenting with symptoms that may have multiple causes and where time with each patient is limited. Once a diagnosis is reached, few guidelines include advice for people in the context of multi-morbidity. Guidelines may be particularly challenging to implement in fragmented health-care systems.

International guidelines for tuberculosis and 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 non-communicable disease are not perceived with the same urgency or importance as guidelines for infectious diseases although the burden may be similar. There are successful examples of guidelines to support respiratory care in LMICs: the PACK programme[29] developed in South Africa is a health-systems improvement initiative that takes a symptom-based approach and uses evidence to create a decision support tool working with local health systems to educate clinicians and determine appropriate task sharing. The original WHO sponsored programme, the Practical Approach to Lung Health (PAL)[30] used a diagnostic tree in primary care and public health programs, branching initially to TB or not TB.

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

RECOMMENDATION 1: *Relevant organisations including societies, clinicians and academics should provide LMIC-specific COPD management guidance from prevention, diagnosis and management through to palliative care. This should be co-developed with primary health-care teams and patients. The guidance should include an effective implementation plan which 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.*

2. What are the barriers and facilitators to implementation of universal, evidence based, guideline-driven cost-effective interventions for COPD in LMIC?

►DIAGNOSIS

Spirometry is necessary for the diagnosis of COPD. Spirometry provision can be challenging in high-income countries (HIC) and more so in some LMIC settings. There are models for successful spirometry training in LMIC. For example, the Pan African Thoracic Society MECOR Program added spirometry training to training in research methods[6]. Students were then offered the opportunity to take the ERS Spirometry Drivers' License that 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) is able to identify people with COPD[31,32]. This pragmatic approach is best used to identify people who need to go on and have spirometric confirmation. Questionnaires are generally simple and cheap to implement, but need to be evaluated in LMIC settings. Administering PEF requires training and availability of affordable PEF meters. Micro-spirometry (using a simple, inexpensive hand-held spirometer which can give a reasonable assessment of FEV_1) provides an alternative. Use of case-finding questionnaires has still to be adequately tested in real-world, primary care settings in LMIC 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 over-diagnosis, absence of specialists for onward care, and the absence of pro-active 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 amongst affected people and clinicians[35]. This is in contrast to 'asthma' which is widely recognised (with consequent mislabelling 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 therefore that the individual is at fault. Smoking can be reframed as nicotine addiction (which often starts in childhood), and nicotine addiction 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 LMIC that is broader than just 'COPD' and aims to identify all those with sub-optimal lung function, whatever the cause. LMICs are very diverse and only in situations where 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 organisations 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, micro-spirometry, peak expiratory flow and questionnaires which 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 advocated in the WHO Framework Convention on Tobacco Control[38]. Whilst the precise contribution of biomass smoke exposure to COPD remains controversial, there is evidence that clean cook 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 cook stoves. There are also emerging data on the benefits of reducing traffic pollution[41,42]. Interventions to reduce premature births, childhood pneumonia, and those to promote effective lung growth and development are also all likely to translate into reduced adult cases of poorly-reversible airflow-obstruction and thus a life-course approach to 'COPD' prevention is critical[16]. It is now recognised that fixed-airflow obstruction in adult life can result from different trajectories of lung growth and development including accelerated decline from maximal lung function (the traditional model of COPD), but also 'normal' decline from a sub-maximal level[16]. Factors determining sub-maximal 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 non-pharmacological 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 and treatment for COPD exacerbations. The WHO considers tobacco control interventions and public awareness for physical activity and diet to be 'best buys'[47], and smoking cessation and physical activity counselling in primary care, symptom relief with inhaled salbutamol, and treatment of 'asthma' with inhaled beclomethasone as 'effective'. WHO identifies access to improved cook 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 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 non-communicable respiratory interventions within that coverage[51].

There is a strong evidence base to support pulmonary rehabilitation (PR) for CRD[52], and large audit programmes have demonstrated the real-world effectiveness of PR in HICs[53]. Availability and access to rehabilitation is recognised as fundamental to achieving WHO Sustainable Development Goal (SDG)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 necessary to help address major challenges around staff training, space, provision of equipment, retention rate on programmes and awareness and support to refer people to such programmes. Alternative approaches, including digital options may improve access to PR but the use of 'remote PR' has been little studied 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. Access to essential medicines and vaccines is an explicit statement within the SDGs (Target 3.8)[61], and the Global Action Plan for the Prevention and Control of Non-communicable diseases (GAP)[48]. The WHO produces a bi-annual Essential Medicines List[62] designed to inform country National Essential Medicines Lists (EMLs). The latest iteration of the WHO EML includes short-acting beta-agonists and anti-muscarinics, inhaled corticosteroids with and without long-acting beta-agonists, and a long-acting antimuscarinic, in addition to influenza vaccine and the oral steroids,

antibiotics and oxygen necessary for exacerbation management. The substance misuse section contains nicotine replacement by gum and patch but is not cross-referenced to respiratory health. The 2020 version of the WHO PEN (package of essential non-communicable disease 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 GOLD report. There is variable alignment between the WHO EML and national EMLs[64-66], neither 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 prescribers only prescribe what is stocked[68]. For inhaled drugs, there is little focus or funding on providing training and incentivisation to support effective use (correct inhaler technique and adherence). The Universal Healthcare Package has little on respiratory and COPD[51]. Supporting manufacture of generic medicines which has been successful for access to anti-retroviral therapy in HIV is more complex for inhalers where both the drug and device must be considered.

RECOMMENDATION 3: *The origins of COPD may be in early life and therefore all clinicians, including those working in maternal and child health, require education and training on basic prevention messages such that smoking in pregnancy is discouraged, premature births 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 explicitly link across WHO and National Essential Medicine Lists, the WHO PEN (package of essential non-communicable disease interventions for primary health care in low-resource settings). Guidance should consider the availability, affordability, sustainability (incorporating environmental impact) and cost-effective use of medicines including 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 pulmonary rehabilitation programmes should be an international priority. This will require investment and work-force planning, considering staff training, awareness, referral, and novel approaches to delivery.*

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 LMIC?

COPD is not seen as a public health concern despite compelling evidence demonstrating high prevalence and burden in LMICs. Whilst 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 multi-morbidity, 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 and tuberculosis, and consider ways in which COPD management can be transformed by co-ordinated approaches at scale.

Advocacy for COPD in LMICs will require clear, simple messaging and engaged, local champions. GOLD and ATS are international organisations and members of the Forum of International Respiratory Societies (FIRS). 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 mind-set towards prioritising 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], and global research priorities have recently been produced[71]. As a community we must lobby for greater research funding for COPD in LMICs where the scale of current investment is not reflective of disease burden[72].

We are not the only group aiming to address these challenges. GOLD held a 2019 summit on COPD in LMICs[73] which concluded that the WHO should co-ordinate activity in this area, focusing on awareness among the public, healthcare professionals and governments, and ensuring that spirometry and cost-effective pharmacological and non-pharmacological interventions are available and affordable. We also believe that WHO has a critical, central co-ordinating role. We strongly advocate that specific targets for chronic respiratory disease and COPD should be included in the WHO NCD strategy to monitor progress.

RECOMMENDATION 8: *The WHO NCD global Action Plan for the Prevention and Control of NCDs should specify how the relative reduction of premature mortality from chronic respiratory disease will be achieved, and also focus on morbidity. As interim targets, by 2030:*

- *≥50% of people with chronic respiratory symptoms should have access to appropriate assessments, including accurate and timely diagnosis.*
- *≥60% of those with chronic respiratory disease should have access to effective non-pharmacological and pharmacological treatments.*
- *≥70% of those treated for chronic respiratory disease should have well controlled disease.*

Future targets should transition from measurement to monitoring improvement. LMICs are diverse and in those settings where differentiation between 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, 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 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 LMIC.*

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 between and indeed within individual LMICs. We have made ten 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 the 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.

Figure Legends

FIGURE 1: *Global national COPD guideline coverage[22]. Red colours represent LMICs and blue colours HICs. Darker shading represents a country with a national guideline, lighter colour without. (HICs: high-income countries; LMICs: low and middle income countries).*

FIGURE 2: *Summary of the recommendations.*

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