



## PERSPECTIVE

# Prioritised research agenda for prevention and control of chronic respiratory diseases

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**ABSTRACT:** The 2008–2013 World Health Organization (WHO) action plan on noncommunicable diseases (NCDs) includes chronic respiratory diseases as one of its four priorities. Major chronic respiratory diseases (CRDs) include asthma and rhinitis, chronic obstructive pulmonary disease, occupational lung diseases, sleep-disordered breathing, pulmonary hypertension, bronchiectasis and pulmonary interstitial diseases. A billion people suffer from chronic respiratory diseases, the majority being in developing countries. CRDs have major adverse effects on the life and disability of patients. Effective intervention plans can prevent and control CRDs, thus reducing morbidity and mortality. A prioritised research agenda should encapsulate all of these considerations in the frame of the global fight against NCDs. This requires both CRD-targeted interventions and transverse NCD programmes which include CRDs, with emphasis on health promotion and disease prevention.

**KEYWORDS:** Asthma, chronic obstructive pulmonary disease, chronic respiratory diseases, noncommunicable diseases, prevention, research

**M**ajor chronic respiratory diseases (CRDs) include asthma and rhinitis, chronic obstructive pulmonary disease (COPD), occupational lung diseases, sleep-disordered breathing (SDB), pulmonary hypertension, bronchiectasis and pulmonary interstitial diseases [1].

Over 1 billion people of all ages suffer from CRDs (table 1). Over 500 million of these live in low- and middle-income countries (LMICs). CRDs are increasing in prevalence and severity [1].

CRDs have major adverse effects on the life and disability of patients [1]. It is estimated that 4 million people died prematurely from CRDs in 2005 and it is projected that, globally, the CRD death rate and burden will considerably increase in the future [2].

Everyone in the world is exposed to CRD risk factors, and effective preventive measures are available to reduce the deleterious impact of CRD risk factors: tobacco smoking in all countries, indoor air pollution and particularly biomass fuel combustion in LMICs, outdoor air pollution, unhealthy diet, lack of physical activity and obesity, allergens, and occupational agents [1, 3, 4]. The consequences of these factors start before birth and

continue throughout life [5–7]. Many of them are common to other noncommunicable diseases (NCDs) [2]. Furthermore, in some countries, infectious diseases (including tuberculosis and HIV/AIDS) add to the burden of CRD morbidity. Effective interventions can control CRD and reduce morbidity and mortality.

Most CRDs occur in LMICs, which requires consideration of the following factors. 1) Data on CRD burden and risk factors are scarce and surveillance of CRDs is unavailable in most LMICs. Consequently, the true CRD burden on health services and society is unknown. 2) Infrastructure and programmes for the management of CRDs in many LMICs are not available or poorly developed because of competing priorities. Resources are limited and fragmented. 3) Facilities for diagnosis and monitoring as well as essential medicines for treating CRDs are not available and/or affordable in many LMICs [8, 9]. 4) Strategies for CRD prevention and health promotion are often absent or rudimentary. 5) Programmes for educating healthcare providers (HCPs) in the care and management of patients with CRDs require strengthening. 6) Patient involvement in health promotion programmes is rare or non-existent. A

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**TABLE 1** Estimated prevalence of chronic respiratory diseases (CRDs)

| CRD                         | Prevalence   |
|-----------------------------|--------------|
| Asthma                      | 300 million  |
| COPD                        | 210 million  |
| Rhinitis (excluding asthma) | 400 million  |
| Sleep-disordered breathing  | >100 million |
| Other CRDs                  | >50 million  |

2007 World Health Organization estimates [1]. COPD: chronic obstructive pulmonary disease.

prioritised research agenda should encapsulate all of these considerations in the frame of the global fight against NCDs. This requires both CRD-targeted interventions, and transverse NCD programmes that address CRDs and health promotion to prevent them.

Among the CRDs, there are currently four major topics for which more research is needed: 1) severe/uncontrolled asthma and comorbidities; 2) COPD and comorbidities; 3) SDB, links with obesity and other NCDs; and 4) early determinants of respiratory diseases.

## REVIEW OF SUCCESSFUL INTERVENTIONS

### Asthma

#### *Successful interventions in developed countries*

The implementation of clinical practice guidelines has led to improvements in the quality of care and reductions in the burden of disease [10, 11]. Patient education improves asthma control, reduces urgent care visits and improves quality of life [12, 13]. Environmental control may improve asthma control [14] but single intervention measures are not effective [15].

#### *Successful interventions in LMICs*

Outdoor air pollution may be controlled, thus reducing asthma severity [16]. For LMICs, The International Union Against Tuberculosis and Lung Disease has developed a guide for asthma management focusing on the World Health Organization (WHO) list of essential medicines [17]. A study in a limited number of patients in LMICs has shown benefits [18] and a systematic approach to the organisation of standard case management has been proposed [19].

#### Community-wide programmes

There are limited data on the effectiveness of asthma care in whole populations at the community level. However, there was a considerable cost-effective reduction of hospitalisations and deaths in a study from Finland [20]. In middle-income countries and deprived populations, availability of effective drugs and education reduced hospitalisations and was cost-effective [21–23].

### COPD and comorbidities

#### *Successful interventions in developed countries*

Several guidelines are available for COPD management [24, 25]. However, they should be adapted for LMICs [26]. Environmental control is essential, in particular for tobacco (active and passive smoking, as well as other forms of tobacco) [27–30].

There are several key actions targeting tobacco control such as the WHO Framework Convention on Tobacco Control and the MPOWER package of interventions (monitor tobacco use and prevention policies; protect people from tobacco smoke; offer help to quit tobacco use; warn about the dangers of tobacco; enforce bans on tobacco advertising, promotion and sponsorship, and; raise taxes on tobacco) [31]. Reducing air pollution exposure results in lower CRD morbidity and mortality. Educational interventions have not been fully studied [32]. Pulmonary rehabilitation is effective in COPD [33]. Regular physical activity should be encouraged in these patients. Influenza and pneumococcal vaccinations are recommended for the prevention of COPD exacerbations [25].

#### *Successful interventions in LMICs*

Preventive measures reducing biomass fuel combustion were found to reduce the risk of COPD [3, 34].

#### Community-wide programmes

Community-wide programmes on COPD control have been started in many countries but definitive results are not yet available [35].

### SDB

#### *Successful interventions in developed countries*

Active education programmes on diet and exercise are an important component of SDB management [36]. Continuous positive airway pressure is highly effective in obstructive sleep apnoea syndrome (OSAS) and decreases cardiovascular comorbidities [37, 38].

#### Community-wide programme

A Finnish national programme has been started for the prevention and treatment of sleep apnoea (2002–2012) [39].

### Occupational CRDs

#### *Pneumoconiosis*

Improvement in ventilation and government legislation has dramatically reduced the prevalence of pneumoconiosis in many countries [1] but more data are needed in LMICs.

#### *Occupational asthma in developed countries*

Control of exposure by noxious agent substitution, improvement of ventilation, change in process and enclosure is effective in the primary and secondary prevention of occupational asthma [40, 41].

### Early determinants of chronic respiratory diseases

#### *Successful interventions in developed countries*

In respiratory distress syndrome of premature infants, surfactant and antenatal steroids [42] have dramatically decreased deaths. Primary prevention of allergy and asthma is still a matter of debate, as only multifaceted interventions have shown some efficacy [43, 44]. A Finnish national programme associated with the Global Alliance Against Chronic Respiratory Diseases (GARD) has been started for the prevention and treatment of allergy and asthma (2008–2018) [45].

#### *Successful interventions in LMICs*

Reduction of indoor air pollution exposure from biomass fuel use is a potentially important intervention for the prevention of

acute respiratory infection in children [46, 47] but evidence for its impact is lacking [48].

### **Transverse NCD prevention and control programmes with CRD components**

HCPs face considerable and diverse challenges in LMICs. These include separate, disease-specific interventions fragmenting and duplicating efforts, limiting resources across a range of priorities, as well as competing with programmes against communicable diseases. However, such transverse programmes: 1) may face difficulties in the evaluation of their effectiveness; 2) do not usually provide for adaptation to national, regional, and local needs and resources, resulting in nonfeasibility, nonsustainability or both; 3) do not usually develop a partnership between policy makers and HCPs in the field and, consequently, fail to transform evidence into policies and policies into practice; and 4) do not usually develop and implement affordable educational methods that can be sustained in the resource-poor settings of LMICs.

There are few examples of successful programmes incorporating several NCDs, in some cases with infectious diseases in children and adults [49–51]. Lessons learnt from these initial efforts confirm that such methods may be extended in many LMICs to address priority needs in NCD prevention and management.

### **Models of risk factor effect and avoidance on CRDs**

There is little systematically collected evidence on the overall contribution of environmental risk factors to the global burden of disease. WHO recently completed a comprehensive, systematic and transparent estimate of the disease burden attributable to the environment, and 24% of the global burden of disease was estimated to be due to environmental risk factors [52].

The WHO Comparative Risk Assessment methodology [53] enabled the assessment of global mortality and morbidity resulting from exposures to selected occupational hazards in the year 2000. Occupational risk factors were responsible for 13% of COPD cases, 11% of asthma cases, 9% of lung cancer cases, and 100% of pneumoconioses and mesothelioma cases [54].

Health benefits that environmental interventions could achieve are major considerations when choosing environmental health actions to prevent disease. WHO has released profiles of the environmental burden of disease for 192 countries [55]. 13–37% of the countries' disease burdens could be prevented by environmental improvements, resulting in a reduction of ~13 million deaths per yr [56].

For successful NCD prevention and control strategies, a focus on individuals needs to complement population-wide strategies. Strategies that focus on individuals are cost-effective only when targeted at high-risk groups. Tools predicting an individual's absolute NCD risk are vital for targeting limited resources in high-risk individuals who are likely to benefit the most [57]. The WHO/International Society of Hypertension (ISH) charts, already available, enable the prediction of the future risk of heart attacks and strokes in people living in LMICs [57, 58]. Risk charts are also available for cancer [59].

### **PRIORITISED RESEARCH AGENDA FOR CRDS**

Research opportunities vary between high-income countries, where diagnostic methods and treatments are usually available,

and LMICs. The priorities should be flexible enough to harmonise the specific needs and conditions of the countries. Standardised methods, in particular for epidemiologic studies, should be made available and should be tailored for LMICs. The redefining (phenotyping) of CRDs is ongoing and will influence the programme in coming years as well as the transition of disease burden in different regions and climate changes. Dissemination of the relevant information and training of primary health care should be part of the research programme.

Five topics have been prioritised according to short-, medium- or long-term deliverables (table 2) and depending on burden, perceived need in LMICs, potential impact on health and gaps in knowledge, as well as cost-effectiveness and applicability to LMICs as follows. 1) Severe/uncontrolled asthma is a major health problem and interventions seem to be cost-effective, considerably reducing burden and mortality. They should be tested in various settings and comorbidities should be considered. 2) Modelling for estimates of the impact of interventions for prevention of NCD should be envisaged, and risk charts for COPD and OSAS can be developed. 3) The impact of reduction in obesity on the prevention of SDB should be studied as part of the NCD prevention plan. 4) Assessment of patterns of disease and symptoms in adults presenting to first-level facilities in LMICs should serve as a guide to the development of transverse programmes. 5) Development and evaluation of transverse (integrated) programmes of prevention and care in selected LMICs with different resources and needs employing methods used in the Practical Approach to Lung Health (PAL) [51], Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA Plus) [50, 60] and other similar programmes. A dominant feature of this programme is the strengthening of health systems through education and the optimal use of resources.

Other interventions should be discussed. Research should be conducted to better appreciate definition, risk factors, burden, prevention and control, and a programme should be started when sufficient knowledge becomes available.

### **TOPICS FOR FUTURE RESEARCH**

Some CRDs are known to be of great importance, but further studies are needed to fully define their burden and/or the methods needed to be established/validated for their assessment in population-based surveys in LMICs. There is a need for operational research, better surveillance of vital statistics, standardisation of lung function testing in LMICs and estimation of costs of improving management of CRD. Once these methods are clarified, research should start in areas including SDB, bronchiectasis and pulmonary hypertension.

### **SUPPORT STATEMENT**

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### **STATEMENT OF INTEREST**

Statements of interest for J. Bousquet, G. Joos, M. Humbert and L.M. Fabbri can be found at [www.erj.ersjournals.com/site/misc/statements.xhtml](http://www.erj.ersjournals.com/site/misc/statements.xhtml)

**TABLE 2** Research priorities in chronic respiratory diseases (CRDs) from the public health perspective, proposed to focus on low- and middle-income countries (LMICs) but recommended for all countries

| Topic   | Short term  | Medium term  | Longer term   |
|---|---|--|---|
| <b>1) Severe/uncontrolled asthma and comorbidities</b><br>Gaps in knowledge and gaps in knowledge translation into policies             | To reach consensus on a universal definition of severe/uncontrolled asthma in adults and children with identification of gaps in the knowledge  | To develop and validate, in pilot studies, a protocol to estimate the prevalence, case fatality rate and comorbidities of severe/uncontrolled asthma   | To characterise the phenotypes of patients with severe/uncontrolled asthma and search for specific risk factors and comorbidities   |
|   | To estimate (and monitor annually) the number of countries with access to spirometry, essential medicines for CRDs and adequate care (common to topics 1, 3, 4 and 5)   | To implement studies in LMICs to confirm the impact of access to ICS on morbidity and case fatality of severe/uncontrolled asthma in children and adults   | To investigate genomics<br><br>To redefine severe asthma phenotypes according to latest research  |
| <b>2) Impact of primary and secondary prevention of CRDs</b>  | To develop models to estimate the regional and global attributable fraction of risk of CRD related to tobacco smoke, solid fuel combustion, outdoor air pollution and allergens, and the potential impact of interventions for their reduction<br>To develop models to estimate the impact of healthy diet and physical activity on prevention and control of obesity and its major comorbidities, such as CVDs, type II diabetes and SDB   | To develop risk charts for COPD and OSAS using the methodology of WHO CVD risk charts, and to test its usefulness as a tool to change behaviour of health professionals, users of health services and the community<br>To develop and validate, in pilot studies, simple protocols (including questionnaires and spirometry) to assess the CRD risks | To review risk charts and assess impact of their adoption on tangible health outcomes   |
|   | To develop models to estimate the impact of early detection of occupational CRDs and subsequent intervention on the prevention of disability due to occupational CRDs   |  |   |
| <b>3) Effectiveness of integrated prevention and management of chronic diseases in PHC in low-resource settings</b>                     | To investigate the feasibility, effectiveness and affordability of integrated prevention and management strategies for CRDs, CVDs, diabetes and other priority diseases in PHC in pilot countries. Based on PAL, PALS Plus, IMAI, IMCI and other programmes<br>To investigate the outcomes of a tailored syndromic approach to case management of chronic diseases in PHC by trained nurses with the supervision of physicians in pilot countries using an implementation plan based on PAL, PALS Plus, IMAI, IMCI and other programmes | To assess CRD burden on emergency services and PHC facilities<br><br>To develop methods for measurement of the impact of the interventions (e.g. indicators and outcomes for audit and pragmatic randomised controlled trials)   | To evaluate benefit of large-scale community education campaigns and community participation in the prevention and control of NCDs (including CRDs) in different cultural and economic settings |
|   | To estimate (and monitor annually) the number of countries with access to spirometry, essential medicines for CRDs and adequate care (common to topics 1, 3, 4 and 5)   |  |   |
| <b>4) COPD and comorbidities</b><br>Planning management of a person with COPD and concomitant comorbidities (CVDs, diabetes and others) | To reach consensus on a universal definition of COPD, COPD exacerbations and risk factors for exacerbations, and to address gaps in knowledge to understand mechanisms of exacerbations<br>To propose essential PROs acceptable in all countries<br>To estimate (and monitor annually) the number of countries with access to spirometry, essential medicines for CRDs and adequate care (common to topics 1, 3, 4 and 5)   | Surveys to assess the COPD prevalence, risk factors and comorbidities (CVDs, cancer and diabetes) in population based studies (BOLD initiative)  | Evaluate benefits of treatment on both COPD and all NCDs over treatment of individual diseases, PROs, and specific and general health outcomes, as well as in costs                             |

**TABLE 2** Continued

| Topic   | Short term  | Medium term   | Longer term   |
|---|---|---|---|
| <b>5) Early determinants of CRDs</b>  | To reach consensus on the definition of major CRDs by age groups, risk factors and identify gaps in knowledge   | Surveys using spirometry and other case finding strategies to determine CRD prevalence (including asthma) in children and adolescents, and to identify risk factors in early life | Birth cohort studies and other longitudinal studies to assess genetic and early environmental determinants on CRD causality (especially asthma) |
| Indoor and outdoor air pollution, infections, allergens, lack of awareness and demand to health services, lack of access to proper care | Develop methodology for a survey in LMICs to study prevalence of CRD and high risk patients in children <5 yrs of age   | To develop and validate strategies for the management of acute respiratory diseases and asthma in LMICs for children <5 yrs of age  | Develop and evaluate efficacy of preventive interventions worldwide and in LMICs  |
|   | To estimate (and monitor annually) the number of countries with access to spirometry, essential medicines for CRDs and adequate care (common to topics 1, 3, 4 and 5) |   |   |

A global fund for CRD research in LMICs should be developed. PHC: primary health care; COPD: chronic obstructive pulmonary disease; OSAS: obstructive sleep apnoea syndrome; WHO: World Health Organization; CVD: cardiovascular disease; PAL: Practical Approach to Lung Health; PALSAL Plus: Practical Approach to Lung Health and HIV/AIDS in South Africa; IMAI: Integrated Management of Adolescent and Adult Illnesses; IMCI: Integrated Management of Childhood Illnesses; NCD: noncommunicable disease; PRO: patients' reported outcome; BOLD: Burden of Obstructive Lung Disease; ICS: inhaled corticosteroids; SDB: sleep-disordered breathing.

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