Tackling chronic respiratory disease in low-resource settings

Brakema, E.A.

CHAPTER 14

SUMMARY

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Chapter 1, the introduction, outlines the relevance of this thesis. The global burden of chronic respiratory disease (CRD) is high; the two leading CRDs, COPD and asthma, are responsible for 74.4 and 21.6 million DALYs respectively. COPD has become the third leading cause of death and is killing more people than HIV/AIDS, malaria, and tuberculosis combined. Particularly burdened by CRD are low-resource settings where exposure to risk factors such as tobacco and air pollution is high, while disease awareness and means to combat it are low. Evidence for effective approaches to target CRD is also limited for low-resource settings. However, health programmes are likely to fail when implementation strategies misalign with their local context. Therefore, the aim of this thesis is to generate evidence on how to combat CRD in low-resource settings across the globe. To this end, we first seek to understand the context around CRD in diverse low-resource settings. We then focus on how to implement lung health interventions, aligning their implementation strategy with their local context to facilitate successful implementation.

Of note, many of the studies are part of the Horizon 2020 Free Respiratory Evaluation and Smoke-exposure reduction by primary Health cAre Integrated gRoups (FRESH AIR) research project. FRESH AIR studies the implementation of preventive, diagnostic, and therapeutic interventions targeting CRD in low-resource settings in Africa (Uganda), Asia (Kyrgyzstan and Vietnam), and Europe (rural Greece and a Roma camp).

Part I – Understanding the problem; exploring chronic respiratory disease in its local context

In Part I, the context around CRD is explored in diverse low-resource settings globally, focusing on the direct and indirect burden of disease, on exposure to risk factors, and on how diverse settings approach the risk factor tobacco in their guidelines.

First, the epidemiological study in Kyrgyzstan, **Chapter 2**, compares the prevalence of COPD and its risk factors between a highland (~2050 m above sea level) and a lowland setting (750 m). Earlier studies had reported conflicting results about the relation between altitude and COPD. However, most studies had not accounted for household air pollution. Household air pollution is caused by cooking or heating with solid fuels (such as wood, dung, or coal), as 3 billion people do daily. None of the studies had objectively measured pollution levels. In randomly selected households, we objectively measured both lung function (using spirometry) and personal exposure to household air pollution (particulate matter with an aerodynamic diameter <2.5 μm [$PM_{2.5}$]). We administered a questionnaire on other COPD risk factors like tobacco. COPD was more prevalent among the 199 highlanders than the 193 lowlanders (36.7% *versus* 10.4%; p<0.001). Average $PM_{2.5}$ exposure was also higher in the highlands (290.0 *versus* 72.0 μg·m–3;

p<0.001). High levels of $PM_{2.5}$ exposure (OR 3.174, 95% CI 1.061–9.493), pack-years of smoking (OR 1.037, 95% CI 1.005–1.070) and age (OR 1.058, 95% CI 1.037–1.079) contributed to a higher COPD prevalence among highlanders. In addition, high altitude independently predicted COPD (OR 3.406, 95% CI 1.483–7.825). Findings demonstrate how contexts of neighbouring settings can differ significantly in terms of risk exposure and disease burden. Preventive interventions seem especially warranted in these low-resource, highland settings. Of note, this was among the first spirometry-based prevalence studies in Central Asia.

Chapter 3, an opinion paper, details a then-novel perspective on the origins of COPD in low-resource settings. It explains how risk factors for COPD in these settings typically co-occur and interrelate, leading to a 'false start' in lung function. A complex interplay of disadvantageous factors early in life, such as intra-uterine exposure to household air pollution, malnutrition, or a history of tuberculosis, affect lung development. This increases the likelihood of developing COPD later in life. The trajectory leading to COPD for these patients is not (only) through the 'traditional' accelerated decline of a normal lung function, but through the physiological decline in the function of lungs that never attained their potential maximum value. A low socioeconomic status can further deteriorate lung health, as it is associated with factors like poor access to healthcare, poor nutrition, low birth weight, and poor sanitation. COPD caused by a false start implies that risks should be tackled at much earlier stages, starting before birth, and these approaches should later be combined with 'regular' preventive methods. As risk factors are diverse, the measures should be embedded in a wide, intersectoral approach. Awareness about COPD and its early origins should be raised among communities, health workers, and policymakers, along with awareness on affordable measures to prevent and treat disease. Lastly, a false start also implies a fundamentally different perspective on how to study the effects of interventions targeting household air pollution on lung function. Currently, the effects of interventions are often studied in lungs that have already been irreversibly damaged; effects should also be studied in the yet unborn generation.

Next, the health economics study in **Chapter 4** demonstrates that besides differences in exposure to risk factors, low-resource settings remarkably differ from high-resource settings regarding the socioeconomic burden of CRD. We estimated the work productivity and activity impairment due to CRD across four diverse low-resource settings, and studied modifiable risk factors for impairment. We conducted a cross-sectional, observational study in the four FRESH AIR countries: Uganda, Kyrgyzstan, Vietnam, and Greece. Of the 1040 spirometry confirmed CRD patients, a median [interquartile range] of 40.0% [20.0–60.0] reported impairment in daily activities. The 459 employed patients reported an overall work impairment of 30% [1.8–51.7] and decreased productivity (presenteeism) of 20.0% [0.0–40.0]. Of note, work time missed (absenteeism) was 0.0% [0.0–16.7]. Potentially modifiable risk factors for CRD-related impairment were severity of breathlessness (MRC-scale) (B = 8.92, 95%CI = 7.47–10.36), smoking (B = 5.97,

95%CI = 1.73–10.22), and solid fuel use (B = 3.94, 95%CI = 0.56–7.31). The low absenteeism compared to the substantial presenteeism and activity impairment could be explained by social security systems that are often missing in low-resource settings; patients commonly showed up at work at the expense of lower productivity. This was the first large international study assessing CRD-related work productivity and activity impairment in low-resource settings. Results warrant healthcare workers, policymakers, patients, and employers to increase awareness, take preventive actions, and enhance clinical management of CRD in low-resource settings.

Last, the systematic review in **Chapter 5** focuses on a major risk factor for CRD in different contexts; it compares primary care smoking cessation guidelines across the globe. We identified the guidelines using an online inventory of national guidelines (on treattobacco.net) and by consulting colleagues through the network of the International Primary Care Respiratory Group. Out of 43 identified guidelines from 39 countries, 26 guidelines from 22 countries were relevant for primary care with the guidelines and/or key recommendations (made) available in English. There was almost universal agreement on the need to identify smokers, offer brief advice to quit, assess motivation to quit, and offer assistance with behavioural and pharmacological support. Discrepancies between the guidelines were most prominent for specific recommendations regarding the specific content and delivery format of behavioural support, and the provision of pharmacotherapy. This was likely to be due to different contextual health environments (health infrastructures, risk factor distribution, medication availability, cultures, etc.), or different interpretations of the evidence. Based on these findings, we developed a universal checklist of guideline recommendations for primary care professionals and future guideline developers.

Part II – Towards a solution; facilitating implementation success of lung health programmes by engaging and leveraging their local context

Part II focuses on generating evidence on how to combat CRD in low-resource settings, the development of practical tools and a methodology, and on studying the application of this evidence in practice.

It starts with a systematic literature review and meta-synthesis in **Chapter 6** to identify critical factors to the implementation of interventions targeting CRD in LMICs, and to weigh the level of evidence. After searching eight databases without date or language restrictions in July 2019, we included 37 articles out of 9111 screened. Studies were broadly representative of the population distribution across the world's continents, and conducted in community settings, healthcare settings and schools. Studies regarding cleaner cooking interventions to reduce exposure to household air pollution were so numerous that we decided to separate these from the current review and dedicate a separate review exclusively to this topic (Chapter 9). Many of the 37 (remaining) studies regarded tobacco related interventions, while pulmonary

rehabilitation, patient education, and self-management interventions were underrepresented or even absent. Factors identified with a high level of confidence were 1) Understanding needs of local users; 2) Ensuring compatibility of the intervention with the local context; 3) Identifying influential stakeholders and applying engagement strategies; 4) Ensuring adequate access to knowledge and information; and 5) Addressing resource availability. These real-world findings were consolidated in a hands-on implementation tool for practice. Policymakers, nongovernmental organisations, practitioners, and researchers can use this 'FRESH-AIR Implementation tool' to develop evidence-based implementation strategies for interventions targeting CRD in low-resource settings.

While conducting the literature search above, not only an abundance of evidence was revealed on the implementation of cleaner cooking interventions, but also a lack of the *use* of all the evidence. Therefore, **Chapter 7** concerns a commentary that reflects on decades of substantial discrepancies between the disappointing adoption rates of cleaner cookstoves, and the subsequent failure to adapt implementation strategies accordingly. Several solutions to overcoming this evidence to practice gap are proposed. Above all, the commentary urges all stakeholders to use existing evidence in the design and execution of implementation strategies for improved stoves. First, researchers should consolidate the existing bulge of implementation evidence into a practical tool. Implementors should use this tool, and collaboratively with researchers ensure to continuously update it. They should connect to large network organisations (the World Health Organization, the Clean Cooking Implementation Science Network), which should in turn promote and distribute the tool to make it widely available. In addition, funders, nongovernmental organisations, and development institutions should exclusively grant support for projects with adequate implementation strategies addressing the tool's critical implementation factors. Lastly, carbon credit (offset) projects should not incentivise on the number of stoves distributed, but on the number of stoves adopted. All stakeholders should constantly network to ensure everyone is on the same, up-to-date page. Ultimately, successful implementation would both improve health and benefit the planet, as cleaner combustion requires less fuel use and reduces deforestation.

To practice what we preached, we teamed up with national and international colleagues as a first step. We collaboratively conducted the systematic review dedicated exclusively to cleaner cooking (Chapter 9) to develop this practical implementation tool. An umbrella review, a review of reviews, was considered a more suitable methodology to analyse the evidence of the more than 400 of individual studies we had identified. For full transparency, the updated study protocol in **Chapter 8** details this relatively complex methodology.

Chapter 9, the resulting systematic umbrella review, consolidates evidence from 31 cleaner cooking implementation reviews. Critical factors regarding the implementation of improved

solid fuel cookstoves supported by the highest level of evidence included 'Costs', 'Knowledge & beliefs about the innovation', and 'Compatibility'. Factors for cleaner fuels included 'Costs', 'Knowledge & beliefs about the innovation', and 'External policy & incentives'. The factors were synthesised into the Cleaner Cookstove Implementation Tool (CleanCIT) and the Clean Fuel Implementation Tool (CleanFIT). To bridge the gap from science to practice, we are currently exploring possibilities together with large relevant networks for how to prepare the tools for practical use and disseminate them.

A critical factor identified in both implementation reviews is the compatibility of the intervention with the local context, among which the local beliefs and needs. However, no evidence was available on *how* to map the context to understand it in the first place. Therefore, the methodology paper in **Chapter 10** details the development and prospective validation of a systematic methodology to map local health beliefs and behaviours: the Setting-Exploration-Treasure-Trail-to-Inform-ImplementatioN-strateGies-(SETTING) tool. Together with an expert panel and local end-users we co-created this six-step approach: 1) Co-set study priorities with local stakeholders; 2) Combine a qualitative rapid assessment with a quantitative survey (a mixed-method design); 3) Use context-sensitive materials; 4) Collect data involving community researchers; 5) Analyse pragmatically and/or in-depth to ensure timely communication of findings; and 6) Continuously disseminate findings to relevant stakeholders. We applied the tool in six low-resource settings in the four FRESH AIR countries on three continents; the methodology proved highly feasible, acceptable, and effective in each setting.

Application of the tool is demonstrated in the observational mixed-methods study in **Chapter 11**, aiming to map local beliefs and behaviours regarding CRD across the six diverse low-resource settings in Uganda, Kyrgyzstan, Vietnam and Greece. Qualitative data were collected from 340 informants in more than 200 interviews, focus group discussions, and observations, and findings were triangulated with a quantitative survey among 1037 community members and 204 healthcare professionals. Three key themes were identified that consistently played a key role in CRD-related beliefs and behaviours: 1) Perceived CRD identity (community members in all settings except the rural Greek strongly attributed long-lasting respiratory symptoms to infection, predominantly tuberculosis); 2) Beliefs about causes (65.8% of the community members strongly agreed that tobacco smoking causes symptoms, this was 19.1% for household air pollution; typical perceived causes ranged from witchcraft [Uganda] to a hot–cold disbalance [Vietnam]); and 3) Norms and social structures (such as that 'real men' smoke [Kyrgyzstan and Vietnam]). These key themes should be addressed when designing context-driven implementation strategies for CRD-related interventions across these global settings, each with shared and context-specific beliefs and behaviours. This study also provides an overview of the settings' typical characteristics with their associated prevailing beliefs and behaviours which may serve implementors in settings that share similar characteristics.

Findings of Chapter 11 were then used to design the implementation strategy of a subsequent lung health intervention in an implementation study in **Chapter 12**. We implemented a Ugandan train-the-trainer lung health intervention in Kyrgyzstan and Vietnam, empowering communities to take action against solid fuel- and tobacco smoke. We co-created the design and implementation strategy with local stakeholders, and embedded the programme into existing local health infrastructures. Feasibility and acceptability were considered high; around 15,000 Kyrgyz and 10,000 Vietnamese community members were reached within the budget of around € 11,000 per country. The programme was effective in improving knowledge: scores on lung health awareness questionnaires increased significantly after participation in the programme, to excellent levels in all target groups. Effectiveness was also assessed by behaviour change, namely whether cleaner cooking methods (delivered by a subsequent FRESH AIR intervention study not included in this thesis) were adopted. Adoption was moderately successful in Vietnam, and highly successful in Kyrgyzstan. The current study demonstrates how an implementation strategy for a lung health intervention can be tailored to the context to support implementation success.

The general discussion, **Chapter 13,** reflects on how this thesis navigates from context assessment (epidemiology, health economics, anthropology, comparison of guidelines) to the implementation of context-driven, evidence-based lung health solutions in low-resource settings. Broad, multisectoral interventions are needed that promote lung health even before birth. This thesis demonstrates how exploring, engaging, and leveraging the local context can facilitate implementation success. It also provides an overview of characteristics of the six diverse FRESH AIR study settings in four countries with shared and context-specific themes. These could be considered before implementing a programme targeting CRD in a similar setting. The generalisability of the findings is enhanced as data were collected across the globe. The main challenge that persists is the implementation of this implementation evidence.

CRD in light of the COVID-19 crisis and the climate crisis reinforces the need to take collaborative action globally, using context-driven strategies locally. To "leave no one behind" [UN], we rely on strong global collaborations in which every individual should take a role. Policymakers, healthcare workers, researchers, and others are encouraged to use these findings to effectively implement interventions targeting CRD, thereby optimising the use of resources that are scarce in low-resource settings already, ultimately benefitting health outcomes.