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Implementing lung health interventions in low- and middle-income countries: a FRESH AIR systematic review and meta-synthesis

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This systematic review and meta-synthesis shows why implementation of lung health interventions often fails in low- and middle-income countries, and it provides critical factors to prevent failure with their level of evidence <https://bit.ly/2UYJOSa>

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ABSTRACT The vast majority of patients with chronic respiratory disease live in low- and middle-income countries (LMICs). Paradoxically, relevant interventions often fail to be effective particularly in these settings, as LMICs lack solid evidence on how to implement interventions successfully. Therefore, we aimed to identify factors critical to the implementation of lung health interventions in LMICs, and weigh their level of evidence.

This systematic review followed Cochrane methodology and Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) reporting standards. We searched eight databases without date or language restrictions in July 2019, and included all relevant original, peer-reviewed articles. Two researchers independently selected articles, critically appraised them (using Critical Appraisal Skills Programme (CASP)/ Meta Quality Appraisal Tool (MetaQAT)), extracted data, coded factors (following the Consolidated Framework for Implementation Research (CFIR)), and assigned levels of confidence in the factors (*via* Grading of Recommendations Assessment, Development and Evaluation–Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual)). We meta-synthesised levels of evidence of the factors based on their frequency and the assigned level of confidence (PROSPERO:CRD42018088687).

We included 37 articles out of 9111 screened. Studies were performed across the globe in a broad range of settings. Factors identified with a high level of evidence were: 1) “Understanding needs of local users”; 2) ensuring “Compatibility” of interventions with local contexts (cultures, infrastructures); 3) identifying influential stakeholders and applying “Engagement” strategies; 4) ensuring adequate “Access to knowledge and information”; and 5) addressing “Resource availability”. All implementation factors and their level of evidence were synthesised in an implementation tool.

To conclude, this study identified implementation factors for lung health interventions in LMICs, weighed their level of evidence, and integrated the results into an implementation tool for practice. Policymakers, non-governmental organisations, practitioners, and researchers may use this FRESH AIR (Free Respiratory Evaluation and Smoke-exposure reduction by primary Health cAre Integrated gRoups) Implementation tool to develop evidence-based implementation strategies for related interventions. This could increase interventions’ implementation success, thereby optimising the use of already-scarce resources and improving health outcomes.

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The FRESH AIR study is registered under trial registration number: NTR5759 (<http://www.trialregister.nl/trialreg/admin/rctsearch.asp?Term=23332>). All data and meta-data can be shared upon reasonable request. This includes among others the study protocol and meeting minutes describing considerations for data analysis. Within reasonable time after email request, data will be shared via a secure web-based system.

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Introduction

Chronic respiratory diseases (CRDs) are a silent and growing epidemic in low- and middle-income countries (LMICs). Chronic obstructive pulmonary disease (COPD) is now the third leading cause of death worldwide; over 90% of these deaths and 80% of asthma-related deaths occur in LMICs [1–5]. LMICs are disproportionately burdened by CRDs because of the early and high exposure to risk factors for lung impairment [6–13]. Suboptimal access to diagnostic and treatment options in LMICs additionally exacerbates disease severity [6, 11]. Although promising interventions targeting CRD have existed for decades, many fail to translate into meaningful health outcomes. The disappointing intervention effects are often attributed to implementation failure [14–18]. In some estimates, over 60% of organisations' implementation efforts are unsuccessful [19]. Implementation success of clean cookstove programmes is often reported as strikingly low, with stove adoption rates of 4–10% [20–25].

However, implementation, the act of carrying an intervention into effect [26], is complex. Throughout the entire implementation process, from the dissemination of an intervention to its sustained use [27], numerous factors determine success or failure. These implementation factors are often interacting and influential at multiple levels. To better understand the factors so that they can be adequately addressed in implementation strategies, factors can be pragmatically structured. The Consolidated Framework for Implementation Research (CFIR) integrated 42 implementation factors from existing implementation theories [18], and categorised them in five domains: 1) innovation characteristics (e.g. the adaptability of an intervention); 2) outer setting (e.g. understanding the needs of local users); 3) inner setting (e.g. resource availability); 4) characteristics of individuals (e.g. self-efficacy); and 5) process (e.g. engagement of stakeholder). The importance of each factor depends on the context [28, 29]. Hence, implementation strategies are more successful when context-specific factors are known and addressed.

Therefore, it is essential to understand which specific factors play a role in the context of CRDs in LMICs. Paradoxically, despite the highest burden of CRD in LMICs, precisely in these countries, evidence on what factors determine implementation success is limited, fragmented and of varying methodological quality [30–33]. Extrapolating the evidence from high-income countries to LMICs is inappropriate because of differences in health, economic and cultural contexts. Several calls already highlighted the need for high-quality implementation research in LMICs [25, 34–37]. Therefore, in this study, we aimed to identify factors critical to the successful implementation of interventions targeting CRDs in LMICs, and to weigh their level of evidence.

Methods

This systematic review and meta-synthesis is part of the Horizon2020 FRESH AIR project (Free Respiratory Evaluation and Smoke-exposure reduction by primary Health cAre Integrated gRoups), addressing the implementation of prevention, diagnosis, and treatment of CRD in low-resource settings (trial registration number: NTR5759) [38]. This review is registered at PROSPERO (CRD42018088687) and follows Cochrane methodology [39, 40] and the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) reporting standards [41].

All steps of the review process were performed by two researchers (E.A. Brakema and D. Vermond) independently. Results were compared, and discrepancies solved through discussion. A third researcher (R.M.J.J. van der Kleij) was consulted when consensus could not be reached. We systematically applied validated tools throughout the entire process, to enhance the reproducibility and transparency of our outcomes (figure 1).

Search strategy and selection criteria

We developed the search strategy together with a certified medical librarian; it contained (synonyms of) implementation, LMICs and CRD or specific relevant interventions such as “smoking cessation” (appendix 1). We focussed on asthma and COPD as the most prevalent chronic lung diseases. In PubMed, Embase, Global Health Database, Cochrane, PsycINFO, Emcare, Web of Science and CINAHL, we searched

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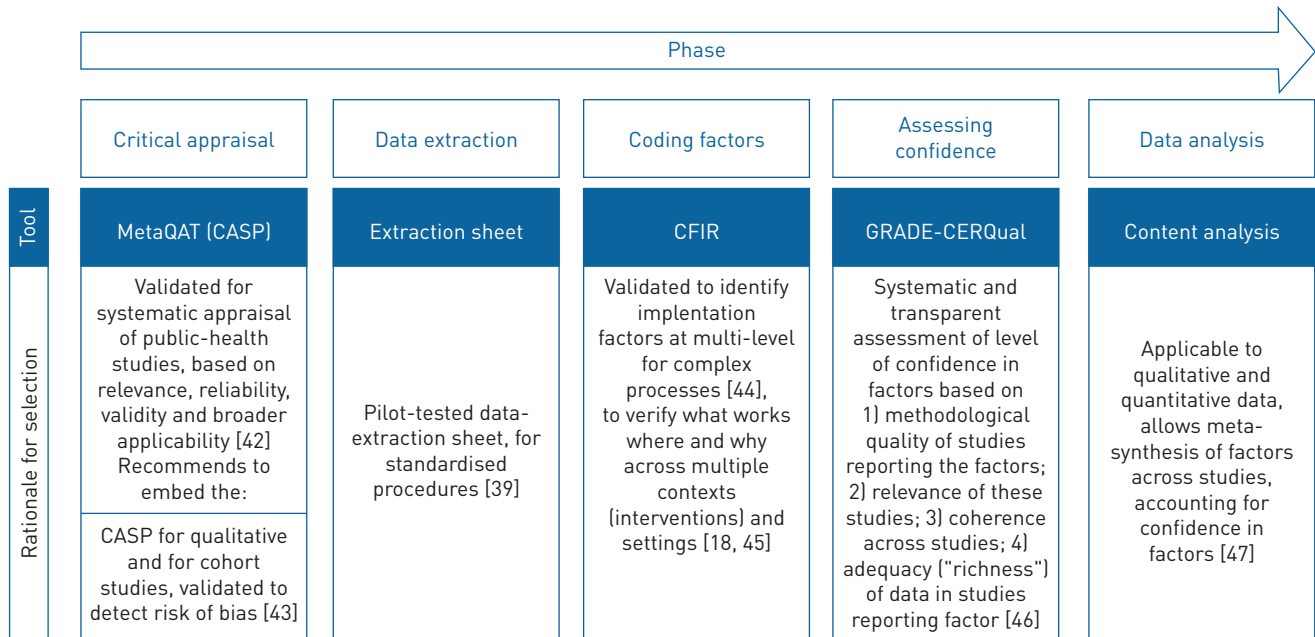


FIGURE 1 Tool used in each phase. Meta-QAT: Meta Quality Appraisal Tool; CASP: Critical Appraisal Skills Programme; CFIR: Consolidated Framework for Implementation Research; GRADE-CERQual: Grading of Recommendations Assessment, Development and Evaluation-Confidence in the Evidence from Reviews of Qualitative research.

without language restriction for articles published by Oct 23, 2017, and updated our search on July 10, 2019. We included all relevant, original, peer-reviewed articles focussing on the implementation of interventions targeting CRD in LMICs (as classified by the World Bank [48]). As recommended for studying implementation, quantitative, qualitative and mixed-method articles were considered relevant [26]. Articles were excluded if they focussed on legislation at a national governmental level (*e.g.* implementation of tobacco taxes) or on hypothetical interventions (*e.g.* theoretical willingness to adopt an intervention), if no factors were reported, or if no full text was available after contacting the authors. Our orienting search resulted in a disproportionate number of articles on the implementation of clean cooking interventions targeting household air pollution. To avoid this specific intervention dominating all review findings, we decided to split our review into two parts. This first review regards the implementation of all but clean cooking interventions, while the second (to be published later) will be exclusively dedicated to those.

Full operationalisation of the search criteria is presented in appendix 1. In addition, we manually searched Google and Google Scholar for the full articles from identified conference abstracts and study protocols, and screened all references from relevant reviews and the included articles.

Critical appraisal

To critically appraise the included articles on relevance, reliability (reporting quality), validity and applicability, we used the validated Meta Quality Appraisal Tool (MetaQAT) [42] (appendix 2) and, as recommended, we embedded the Critical Appraisal Skills Programme (CASP) into it [43]. Results served as input for the assessment of level of evidence of the identified factors (see data analysis).

Data extraction

We extracted descriptive study characteristics (author, year, study design, country, setting/population, intervention, type of outcomes measures used and funding source) and the implementation factors using a pilot-tested, standardised sheet. Speculations (such as "Factor A might have influenced implementation") or repetitions in the reporting of factors within the same article were not extracted. We extracted modifiable factors (*e.g.* factors to address user demographics would be extracted, but demographics on their own would not), to serve the design of future implementation initiatives. Only factors based on original data were extracted. If multiple articles were based on the same study, we compared the article's aim, methods and results in detail. If these were similar, we extracted data from the article that scored highest in our appraisal. If they differed (*e.g.* one was a pilot version and the other the scale-up of the same study), data from both (or more) articles were used.

Data analysis

For our meta-synthesis (weighing of the factors) we used content analysis, in which all data are categorised into themes and the frequencies of the themes are determined. Content analysis is suitable for both qualitative and quantitative evidence [47].

First, we categorised all identified implementation factors by deductive coding using the CFIR [18]. We inductively added several codes to the CFIR (such as “language” or “role model”) when our extracted factors did not match existing codes (appendix 3). Second, we used the Grading of Recommendations Assessment, Development and Evaluation-Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) tool to determine the level of confidence in the importance of the coded factors. The GRADE-CERQual tool has four components (figure 1), and the results of the critical appraisal served as input for scoring those (e.g. a high MetaQAT score for relevance translated into “no to very minor concerns” in the GRADE-CERQual component “relevance”) [46]. Third, each factor was awarded a maximum of four points per component per study in which it appeared (four points for “no to very minor concerns” regarding the component in that specific study, three for “minor concerns”, two for “moderate concerns”, and one for “substantial concerns”). Hence, factors were awarded higher scores when they appeared in more studies (the principle of content analysis), and when the components methodology, relevance and adequacy of the study were appraised as high. The fourth GRADE-CERQual component “coherence” was not rated, because the number of studies in which the factor appeared already accounted for coherence. To conclude, the higher a factor scored, the higher the level of evidence to regard it as an important factor.

Role of the funding source

This study was funded by the European Union Research and Innovation programme Horizon2020 (Health, Medical research and the challenge of ageing) under grant agreement no. 680997. The funders had no role in study design, data collection, data analysis, data interpretation or writing of the report. All authors had full access to all the data and E.A. Brakema, D. Vermond, R.M.J.J. van der Kleij and N.H. Chavannes, the guarantor, had the final responsibility for the decision to submit the study for publication.

Reflexivity

Members of our research team came from diverse backgrounds (researchers and clinicians from psychology and medicine, with work experience in high-income countries, LMICs, or both). In these roles, we had experienced working conditions characterised by many of the factors we identified, such as lack of resources and personnel. We recognised that we were potentially more receptive to factors we had experienced ourselves, so adhered to our standardised extraction procedures.

Results

Search results

Our search resulted in 9111 unique articles. After full-text screening, we included 37 articles derived from 33 different studies (figure 2 and table 1). One article was excluded from the analysis [49], as its factors were based on the exact same study data as another article which scored higher in the critical appraisal [50].

Study characteristics

The studies resulting from our search were conducted in 17 different LMICs across five geographical regions: Latin America (Brazil [51–55], the Dominican Republic [56], Mexico [57], Surinam [58]), Africa (Malawi [59], South Africa [60–62]), the Middle East (Lebanon [63], Syria [64]), Asia (China [65–69], India [49, 50, 70–75], Indonesia [73, 76], Malaysia [77], Nepal [78, 79], Pakistan [80], Russia [81], Thailand [82–83]) and Oceania (Fiji [85]) (table 1 and figure 3). Most studies were based in healthcare settings (n=17; primary care (n=9), secondary care (n=5), primary/secondary care combined (n=3)), followed by schools (n=13), and the community (n=6). The majority of the study interventions focussed on tobacco (n=27; cessation (n=10), prevention (n=8), both (n=2) and control (i.e. smoking-free setting) (n=7)). Three studies focussed on interventions to improve the implementation of guidelines. One study focussed on quality improvement of COPD management, one on delivery of integrated asthma/COPD care, and one on the adaptation of post-partum rituals using biomass smoke to “protect” newborns. Three articles used quantitative methods for determining implementation factors, 31 used qualitative methods, and two used both.

Critical appraisal of the studies

The quality of the articles varied: 19 articles scored high in the MetaQAT on relevance to the research question, 17 scored medium and one scored low (table 1, and for further details appendix 4). Articles scored variably on reliability (15 high, 11 medium, 11 low) and the lower scores were often due to unclear

reporting of methods. Data analyses and researcher reflexivity were particularly poorly reported in many qualitative articles, which affected the reproducibility and transparency (thus validity). 12 articles scored high on validity, 10 scored medium, one scored low and for 14 articles validity was unclear.

Implementation factors

45 implementation factors were identified, with a large variation in factors' levels of evidence (appendix 5). The factors with the highest level of evidence are described in further detail below, these belonged to CFIR domains "Process", "Inner setting" and "Outer setting" (figure 4). A full overview of all weighed factors, their definitions and illustrations of how they occurred in the included studies is detailed in appendix 6.

"Engaging", "attracting and involving appropriate individuals in the implementation and use of the innovation (...)" [18], in the domain "Process" was coded 72 times across 29 articles. Identifying influential stakeholders before and during the implementation process, and developing effective engagement strategies was often reported as "crucial". Moreover, authors stated that the context determined who was considered as influential. The articles addressed relevant deliverers (e.g. teachers, staff, health workers), potential collaborators (e.g. government officials, village leaders or other authorities who could block implementation if not successfully engaged) and recipients of the intervention (e.g. "all villagers at once" versus "initially only highly respected villagers") as important stakeholders to consider. Among a broad range of reported strategies, engagement was frequently established after gaining trust and commitment from the participants, and when a sense of ownership was created (e.g. through participatory approaches). Equally, failure to engage stakeholders was attributed to the lack of engagement activities, e.g. demotivation of intervention recipients due to lack of ongoing communication.

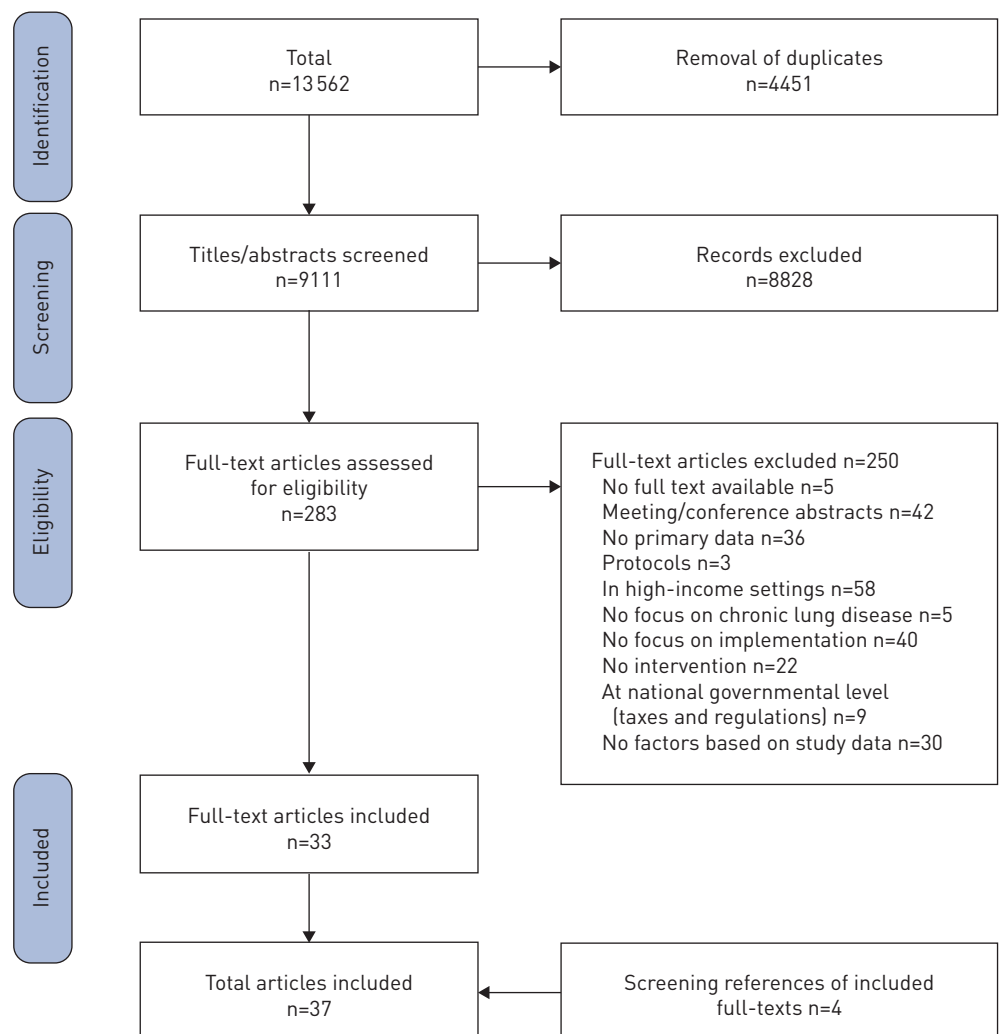


FIGURE 2 Flow diagram of screening process.

TABLE 1 Characteristics of the included studies and critical appraisal, by author

First author [ref.]	Study design	Country	Setting; population	Intervention	Summary of appraisal			
					Rv	R	V	A
AGHI [49] #	Qualitative study within an RCT	India	Public urban and rural schools; health educators, lead teachers and staff	Tobacco cessation	+	-	-	±
ALDINGER [65] [¶]	Qualitative (institutional ethnography)	China	Primary to vocational schools; administrators, staff, teachers, students, and parents	Tobacco prevention within programme of health-promoting schools	± 1	±	±	+
ALDINGER [66] [¶]	Qualitative (institutional ethnography)	China	Primary to vocational schools; administrators, staff, teachers, students and parents	Tobacco prevention within programme of health-promoting schools	-	+	±	+
ASFAR [64]	Qualitative study within an RCT	Syria	Primary healthcare setting; physicians and medical students	Tobacco cessation	+ 1	-	?	±
ASSANANGKORNCHAI [82]	Qualitative (action research)	Thailand	Primary healthcare setting; healthcare workers (nurses, administrators, directors)	Tobacco, alcohol and substance use screening and brief intervention	± 1	±	±	+
BHEEKIE [60]	Qualitative study preparing for an RCT	South Africa	Primary healthcare setting; trained nurses, with a supervisory position as care coordinators	Train-the-trainer programme on implementation of respiratory guidelines on (obstructive) lung diseases	+	+	+	±
BTEDDINI [63]	Mixed-method, with quantitative survey and participatory approach for qualitative data	Lebanon	Seven public and seven private schools throughout the country; trained external facilitators training 10 sessions for 844 students	Waterpipe smoking prevention/delay of starting to smoke	± 1	+	+	+
CASTALDELLI-MAIA [51]	Qualitative	Brazil	Urban psychosocial care units (primary care) across the country; diverse health professionals (e.g. dentist, nurses, physicians, managers)	Tobacco cessation	+ 1	±	?	±
CHATTERJEE [70]	Qualitative	India	Rural villages; community members (programme managers, coordinators, health workers and stakeholders at village level)	Tobacco-free village	+ 1	±	±	+
CRUVINEL [52]	Quantitative, survey design (correlations)	Brazil	Urban, primary healthcare; 149 diverse workers (e.g. community health workers, nurses, physicians)	Training on tobacco, alcohol and drug use screening and brief intervention	±	+	+	±

Continued

TABLE 1 Continued

First author [ref.]	Study design	Country	Setting; population	Intervention	Summary of appraisal			
					Rv	R	V	A
ELSEY [78]	Mixed-method, factors derived from qualitative data (action research)	Nepal	Urban and rural primary healthcare; patients, healthcare providers, managers and policy makers	Tobacco cessation, behaviour support	+ 1	+	+	+
GOENKA [71] ⁺	Mixed-method study within an RCT	India	32 Urban, public and private schools; professionals with a Master's degree in psychology, sociology or nutrition who taught teachers and peer leaders	Tobacco prevention by teachers and peer-leaders	±	+	±	±
GROTH-MARNAT [85]	Qualitative	Fiji	Traditional village; community members	Tobacco cessation	+ 1	±	?	±
ISHAAK [58]	Mixed-method, factors derived from qualitative data	Suriname	Urban junior high school; management and teachers	Tobacco and other drug prevention	±	±	±	±
KHAN [80]	Mixed-method, embedded in RCT, factors derived from qualitative data	Pakistan	30 Primary and secondary level public healthcare facilities; care providers (15 received intervention, interviews in 4 of the centres)	Integrated COPD/ asthma care	+ 1	+	+	+
MALAN [61]	Qualitative	South Africa	Primary care practice; care providers (nurses and physicians)	Brief behaviour change counselling ("5As") for tobacco, diet, physical activity and alcohol abuse	± 1	+	+	+
MARSIGLIA [57]	Qualitative for the factors reported, within a quantitative study	Mexico	Urban public middle schools; teachers	Tobacco and other substance use prevention	±	-	?	-
MASH [62]	Qualitative, prospective (outcome mapping)	South Africa	Urban and rural, primary care to specialised care with a focus on the public sector; doctors, clinical nurse practitioners, pharmacists, National Council for Medical Schemes, the Department of Health, universities and training bodies patients	Asthma-guideline implementation and dissemination	+ 1	±	?	±
McALISTER [81]	Qualitative for the factors reported, within a quantitative study	Russia	Community level; hospital staff, intervention for community smokers	Stop smoking campaign	+	±	?	±
MEDEIROS [53]	Mixed-methods, factors derived from qualitative data	Brazil	Urban schools; teachers, school administrators, coaches, other stakeholders (e.g. municipality) and students	Tobacco prevention within a drug use prevention programme	±	+	+	+

Continued

TABLE 1 Continued

First author [ref.]	Study design	Country	Setting; population	Intervention	Summary of appraisal			
					Rv	R	V	A
MEHANNI [79]	Qualitative	Nepal	Small rural hospital (managed through a public-private partnership)	Quality improvement initiative for management of COPD	+	-	?	±
MELSON [77]	Mixed-methods within pilot RCT; factors derived from qualitative data (quantitative data n.a., regard hypothetic factors prior to implementation). Pro- and retrospective	Malaysia	Secondary school; students	Peer-led anti-smoking intervention (smoke-free class)	+ 1	+	+	+
NAGLER [72] [#]	Qualitative, formative pilot study preparing for an RCT	India	One public urban and one rural school, not included in the RCT; health educators and teachers	Tobacco cessation – school based	±	+	+	±
NICHTER [73]	Qualitative	India & Indonesia	Lead public & private medical schools and outreach to their communities	Training network for tobacco prevention (curricula), outreach and clinic on smoking cessation	+ 1	-	?	±
OSSIP [56]	Qualitative (Rapid Assessment Process)	Dominican Republic	Urban, peri-urban & rural communities with active Community Technology Centers; a multidisciplinary team including specialists of psychology, anthropology, nursing, epidemiology, statistics and public health (from the US) and medicine (DR)	Tobacco cessation – participatory approach	+ 1	±	?	±
PAWAR [50] [#]	Qualitative factors reported within a quantitative study, embedded in an RCT	India	72 Public urban and rural schools; health educators, lead teachers and staff	Tobacco cessation - lay interventionist teaching teachers	±	-	?	-
PEREIRA [54]	Quantitative, population-based cross-sectional survey design	Brazil	Urban public and private schools; 263 school managers (headmasters, pedagogical coordinators, coordinators of the prevention programmes)	Tobacco prevention within a drug use prevention programme	± 1	+	±	±
PERRY [74] ⁺	Qualitative study (translational research) within an RCT following translational research	India	32 urban schools, half were public and half were private; school administration, teachers, and peer-leaders	Tobacco prevention	± 1	-	?	±
PERSAI [75]	Qualitative	India	At district level; senior district officials	Tobacco control	± 1	+	+	+

Continued

TABLE 1 Continued

First author [ref.]	Study design	Country	Setting; population	Intervention	Summary of appraisal			
					Rv	R	V	A
PORTES [55]	Qualitative, retrospective	Brazil	Urban primary healthcare units in a medium-sized municipality; municipal programme coordinator, and senior health professionals trained on smoking cessation or local managers	Tobacco control – training healthcare professionals on facilitating treatment & prevention activities (Furthermore, interventions on governmental level, n.a. to our study)	+ 1	+	+	+
PRASODJO [76]	Mixed-method, factors derived from qualitative data (amongst which participatory action research)	Indonesia	Rural community; local institutions (policy makers, medical staff, community leaders and other stakeholders)	Post-partum smoke ('Sei') traditions – Behavioural change communication campaign targeting household air pollution	+	–	±	±
ROSATI [83]	Mixed-methods, factors derived from qualitative data	Thailand	Urban family setting; health educators towards families	Tobacco, alcohol and other substance abuse prevention, sex education	± 1	±	±	±
SODHI [59]	Mixed-methods, factors derived from qualitative data	Malawi	30 urban and rural, government-funded and non-government funded health centres; primary healthcare workers: clinical officers, medical assistants, and nurses	Train-the-trainer on guideline use for providing integrated primary lung healthcare	± 1	±	±	+
VITAVASIRI [84]	Quantitative questionnaire	Thailand	676 Thai hospitals; personnel	Smoke-free hospitals	+ 1	–	?	–
WANG [67]	Qualitative	China	County-level hospitals; health professionals, hospital president, director of preventive health, representatives of the hospitals	Smoke-free hospitals	+ 1	+	+	+
XIAO [68]	Mixed-method, factors concerned qualitative data	China	41 Hospital across the country, the majority from a tobacco control network; medical doctors and directors	Smoke-free hospitals	± 1	–	?	+
ZIEDONIS [69]	Qualitative	China	Hospital-based mental health centre; personnel and patients	Smoke-free hospitals	+ 1	–	?	±

Studies were prospective unless otherwise indicated. Rv: relevance; R: reliability; V: validity; A: applicability to a wider public health context. RCT= randomised controlled trial. Scored in appraisal as: +: high; ±: medium; –: low; ?: unclear. Relevance '1': Evaluation of implementation was a primary outcome of the article. Articles with matching footnote indicators are from the same study. #: findings from AGHI *et al.* were excluded from the analysis, as PAWAR *et al.* based their findings on the same study data and had higher appraisal scores. NAGLER *et al.* based findings on a different study data (pilot study) and was included. *: findings from both studies were included as these were based on different study data.

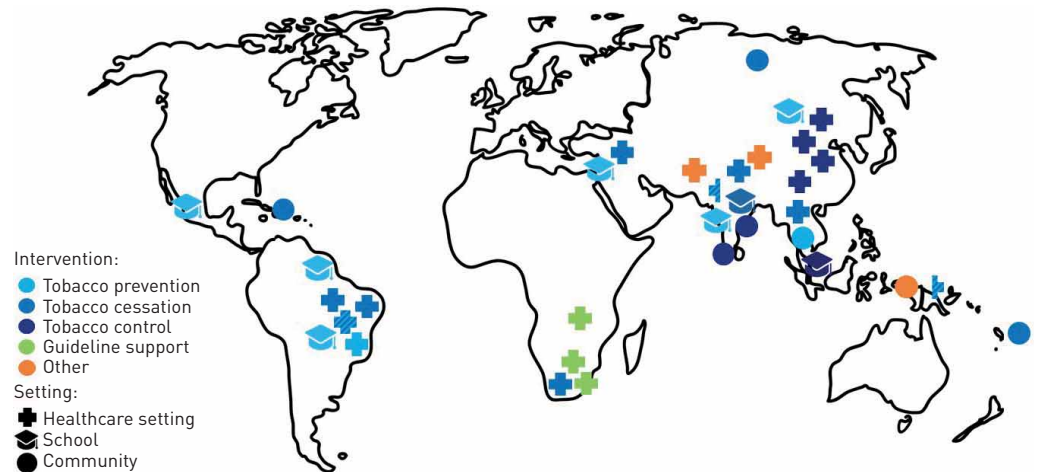


FIGURE 3 Study settings and interventions. Symbols with two colours indicate the study covered both interventions. Half a symbol means half of the study was conducted in this setting and the other half in another setting.

“Compatibility” was another factor with a high level of evidence, coded 48 times across 23 articles. Categorised in the subdomain “Implementation Climate” (domain “Inner setting”), compatibility is defined as the degree of fit between meaning and values attached to the innovation and of the involved individuals, and how the innovation fits with existing workflows and systems [18]. Implementation success was often attributed to embedding interventions into local, existing infrastructures (e.g. the primary care infrastructure), carried out by people in already established networks (e.g. community health workers), and when aligned with local cultural values. This can, for example, be achieved in highly participant-centred interventions. In one study it was stated: “Perhaps the most important lesson was eventually letting go of some of our own techniques and agendas and allowing an indigenous culture to develop their own program.” The local participants developed their own programme and implementation strategy in this study, aligned with their local context and, hence, implementation was highly successful [85].

The second important subdomain in the domain “Inner setting” was “Readiness for implementation” (coded 76 times across 32 articles), of which “Access to knowledge and information” (28 times, 22 articles) and “Available resources” (37 times, 21 articles) were defining factors. Studies generally reported the lack of these factors as implementation barriers. Particularly training in knowledge and skills (e.g. knowledge on risks to lung health or motivational interviewing skills) were reported as insufficient, including lack of access to educational materials. The most commonly lacking resources were time and personnel. Other notable lacking resources were limited physical space (such as crowded consultation rooms), insufficient materials (medication, equipment) or assets (electricity). Funding to overcome these barriers was often not feasible, but authors reported that the (lack of) resources should always be considered in the implementation strategy. Where possible, adaptations can then be made accordingly.

Another notable factor was understanding and accurately prioritising on the “Needs of local users” (“Outer setting”). For example, deliverers in one study realised that Chinese parents did not necessarily feel a need for smoking cessation. They also recognised the parents’ need for connecting with their child (and children had a unique position in the Chinese one-child families). Deliverers then educated the children on smoking and cessation, which eventually helped to motivate their parents to quit [66]. Level of evidence was also high for “Cosmopolitanism” (networks of the organisation with external organisations; “Outer setting”) and “Networks and Communications” (“Inner setting”).

Notably, all factors appeared strongly interrelated; e.g. engaged stakeholders could provide adequate knowledge about the needs of those served by the organisation, which could improve compatibility, which in turn could increase the perceived advantage of the intervention. Also, when comparing the implementation factors and their level of evidence across the geographical regions, findings were highly similar. We compared Latin America, Africa, and Asia (China and India were considered both individually and as part of Asia). The Middle East (n=2) and Oceania (n=1) were not considered because of the small number of studies. Only for China there was a notable difference; factors related to the “Outer setting” (e.g. “External policies and incentives”) were reported less frequently compared with the other regions.

To facilitate future implementors in the translation of the comprehensive overview of all factors to practice, we summarised the factors in a practical, simplified and manageable implementation tool (figure 5

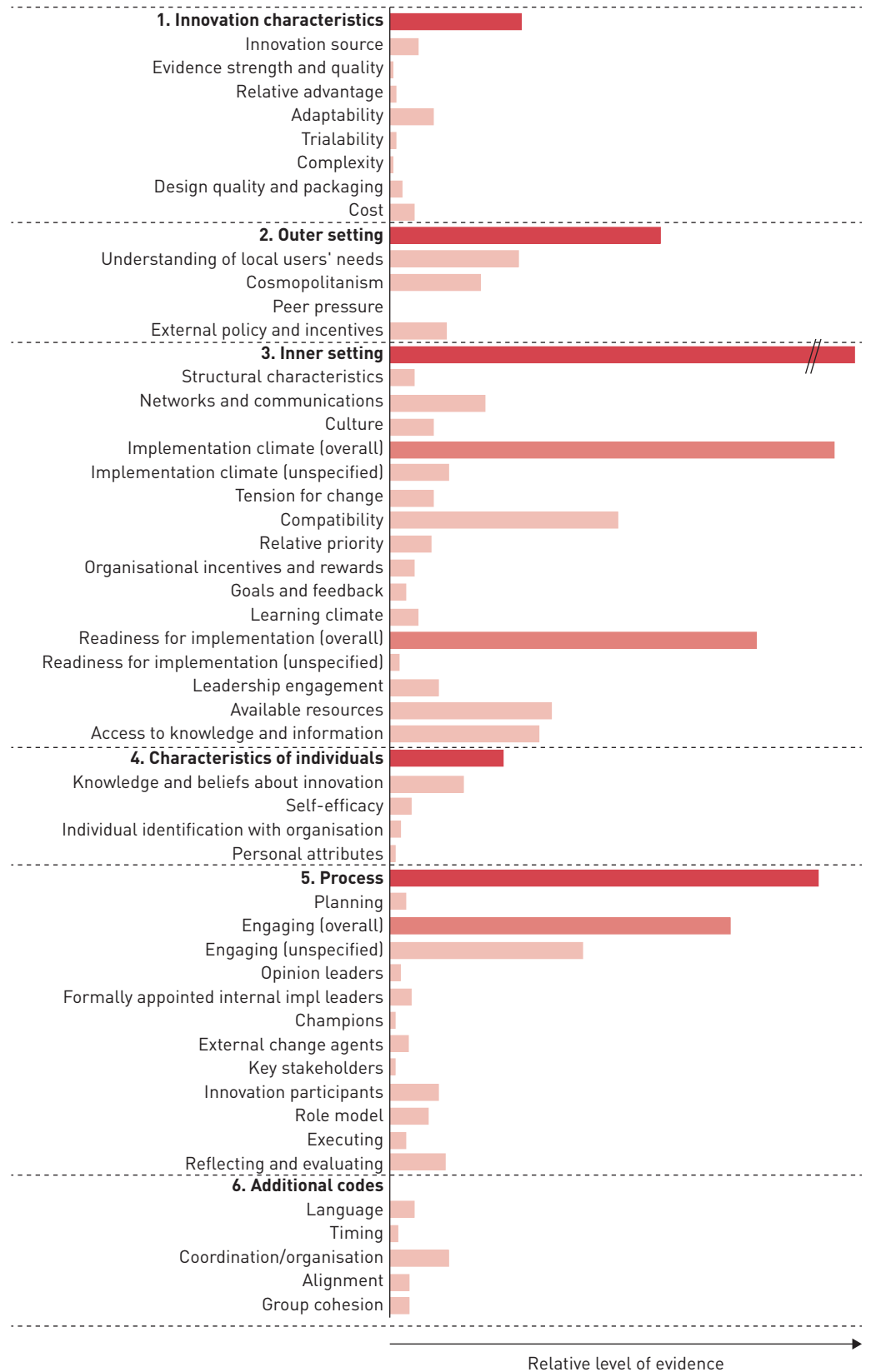







FIGURE 4 Full overview of implementation factors per domain, and the relative level of evidence for the factor.

Key factor	Description	How to address factor# (possible approaches)
 Engage influential stakeholders	Identify the influential stakeholders (e.g. decision makers, community members) and develop an engagement strategy.	Create a sense of ownership for stakeholders using a community-based, participatory approach. Invest in establishing trust.
 Understand local users' needs	Explore and accurately prioritise the needs of intended users; understand barriers and facilitators to meet the needs.	Explore the local context and needs by a team including local members through a rapid appraisal. See also possible approaches for how to address "Engage influential stakeholders"
 Secure necessary resources	Secure sufficient resources for the implementation process and ongoing operations.	If unfeasible, address the lack of resources by adjusting the intervention and/or delivery strategy accordingly. (Ideally, this should go in parallel with investing in strengthening the health system.)
 Facilitate access to knowledge and information	Enable easy access to digestible knowledge and information about the intervention and how to use it.	Organise educational meetings, conduct outreach, facilitate audit- and feedback moments.
 Ensure compatibility	Ensure compatibility between the local (cultural and logistical) context and the intervention and delivery strategy.	Embed intervention in the existing (political, health) infrastructure by co-developing delivery strategy with local users. See "Understanding local users' needs", "Engaging influential stakeholders".


Address and monitor factors throughout entire implementation process: from planning phase to sustained use 

FIGURE 5 Free Respiratory Evaluation and Smoke-exposure reduction by primary Health care Integrated groups (FRESH AIR) Implementation Tool. #: These suggestions are based on the literature specific for interventions targeting chronic respiratory disease in low- and middle-income countries, and on additional, general implementation literature. See Appendix 7 for recommended use of the tool and details on the references.

and appendix 7). The tool contains factors prioritised by their level of evidence and illustrates those factors with examples of how to address them.

Discussion

Main results

In this systematic literature review and meta-synthesis, we identified and weighed factors critical to the implementation of interventions targeting CRD in LMICs. Factors for which the level of evidence was high were: 1) understanding needs of local users; 2) compatibility of the intervention with the local context (such as the political and health infrastructure, or the culture); 3) identification of influential stakeholders and application of engagement strategies; 4) adequate access to knowledge and information (including skills); and 5) sufficient available resources. Additional factors were identified with a lower level of evidence. Most important recommendations for future implementors were compiled in the FRESH AIR Implementation Tool.

Strengths and limitations

To the best of our knowledge, this systematic review is the first to focus on factors critical to the implementation of diverse CRD-interventions. It focussed on LMICs, precisely where the burden of disease is highest, while evidence is fragmented and often poor for these settings. This review had a rigorous design and conduct, following Cochrane methodology and PRISMA reporting standards [39–41]. Every step was standardised and performed independently by two researchers. Validated tools were applied at each stage [18, 42, 43, 46], with a transparent description of their operationalisation. Moreover, we adopted a comprehensive approach with an extensive search in eight databases with no language/date restrictions. We synthesised real-world evidence from highly diverse settings and countries in the included studies, resulting in a high generalisability of the findings to other settings [86]. In fact, the LMICs in this review were broadly representative of the population distribution across the world's continents, among others with many studies conducted in China and India.

However, several relevant types of interventions were underrepresented or even absent in the implementation literature, such as patient education, self-management or pulmonary rehabilitation. Due to the small number of existing studies that focus on such interventions, we were unable to assess whether their implementation factors meaningfully differed from tobacco-related interventions. However, as the desired implementation behaviour is focussed on a similar health goal in similar settings, we assume that there will be at least some overlap in implementation factors. Meanwhile, the high representation of tobacco-related studies in literature remains welcome, with 80% of the world's smokers living in LMICs [87]. As another limitation, we recognise along with other authors that implementation studies are poorly indexed, and we possibly missed relevant studies [88]. Yet, data saturation was still achieved in the identified factors and the hierarchy of their level of evidence. Notably, absence of evidence (factors not

reported) should not be interpreted as evidence of absence (factors not important); [47] we could only determine the level of confidence in the importance of factors, for which we relied on the existing evidence.

Comparison to previous literature

Our findings partly overlap with implementation factors considered important for clean cooking interventions as reported in two reviews [89, 90]. First, our factors “Compatibility” and “Understanding local users’ needs” correspond to “user needs” (e.g. the ability of clean cookstoves to give the food the right taste or save fuel). Second, our factors “Engaging” and “Access to knowledge and information” correspond to “community involvement” and “user training”. The authors of these studies similarly observed that barriers could turn into facilitators when these are adequately addressed and vice versa. They also concluded that factors should be addressed simultaneously because they all interrelate. The overlap between their findings and ours may not be surprising, as clean cooking interventions similarly target CRD in LMICs. Possibly, this supports the assumption mentioned earlier that implementation factors would not differ substantially for those chronic lung health interventions in LMICs that have not yet been studied.

Implementation is a relatively unexplored topic in LMICs, and we predominantly relied on qualitative articles. Qualitative studies allow for a deeper understanding of the how, what and why of implementation processes [91]. As opposed to in quantitative studies, the concept “high level of evidence” cannot be quantified or tested on significance in qualitative studies. Therefore, a combination of qualitative with quantitative (mixed-method) evidence would be highly welcome; such studies are still largely unavailable. The need for more high-quality implementation evidence for LMICs has been highlighted repeatedly [25, 34–37, 92]. Systematic reviews are particularly scarce.

Interpretation and implications for implementation initiatives

Our findings could serve future implementation initiatives, especially those initiatives targeting CRD in LMICs. To facilitate the design of effective implementation strategies for CRD-related interventions, we have developed a comprehensive overview of all implementation factors, their level of evidence and examples of how they played a role in the included studies (appendix 6). In addition, we translated factors from the comprehensive overview into a more pragmatic and hands-on tool for practice (figure 5). Throughout the implementation process, implementors should address these factors in their strategy, and should continuously monitor the effectiveness of their strategy to improve it accordingly [93].

Therefore, awareness of the implementation factors requires additional evidence on how to adequately address them [93, 94]. A suggestion for how to address the two critical factors “Compatibility” and “Understanding local users’ needs”, is developing, testing and disseminating “homegrown” interventions [95]. This was done in another FRESH AIR study by conducting an initial explorative mixed-method rapid assessment of the local context [96]. The results of this assessment informed implementation strategies for improved cookstove interventions in Uganda, Vietnam and Kyrgyzstan [97]. First, the context assessment revealed that communities and their health workers poorly understood the risk of household air pollution and therefore felt no need for change. Hence, the intervention was preceded by an awareness-raising programme. Second, the rapid assessment helped to identify the relevant influential stakeholders in the settings (e.g. village leaders, district health officers). These stakeholders were then involved in the design of the implementation strategy, which ensured high compatibility of the strategy with the local reality and “Engaged the stakeholders” (the third critical factor) for the subsequent delivery [98].

A creative example of addressing the fourth critical factor, “Access to knowledge and information and skilled staff”, could be introducing task-sharing between physician and non-physician health workers. This proved to be effective in lowering blood pressure in LMICs [99]. The fifth critical factor, “Resource availability”, can be particularly challenging to address. One included study reported that workshop facilitators overcame the barrier of transportation costs by ride sharing and delivering several sessions per visit to reduce the number of visits [63]. Reducing the impact of the lack of resources generally requires innovative system strengthening [16].

Overall, opinions on how to address implementation factors most effectively turned out to be highly heterogeneous among experts [100]; additional how-to evidence is required.

Implications for implementation research

Studies that systematically evaluate approaches of how to address implementation factors are needed to provide solid and detailed evidence for future initiatives. We are currently working on part two of this review, which focuses on the implementation of clean cooking interventions. However, we argue that future studies should also focus on topics beyond tobacco and clean cooking, such as personalised asthma

action plans or pulmonary rehabilitation [87]. The studies included in this review consistently missed economic evaluations, so we recommend future studies to also include those [101]. Furthermore, results from the critical appraisal of the studies showed that research quality could generally benefit from more standardised methods and more structured reporting of, for example, context characteristics, implementation strategies and their conduct. These and additional recommendations are further outlined in an article on improving health-care provider practices for LMICs [93], and in the STandards for Reporting Implementation Studies [88].

Implications for practice

Guiding implementation processes by evidence-informed implementation strategies could enhance implementation success. Successful implementation can substantially increase interventions' effectiveness [17]. This could, in turn, optimise the use of already limited resources and decrease the high direct and indirect costs associated with CRD in LMICs [102, 103]. Above all, implementation success could improve health outcomes.

Conclusion

In this study, we systematically searched the literature for factors critical to the successful implementation of lung health interventions. We meta-synthesised the factors' level of evidence and developed an implementation tool for practice. Priority for future implementors should be to understand needs of local users, ensure compatibility of the intervention with the local context, engage influential stakeholders, facilitate adequate access to knowledge and information, and secure sufficient resources. Use of the FRESH AIR Implementation Tool could facilitate policymakers, non-governmental organisations, practitioners, researchers and community members to design evidence-based, tailored implementation strategies to enhance implementation success. This could hence optimise the use of already scarce resources and, ultimately, improve health outcomes.

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