Title

Air pollution interventions and respiratory health: a systematic review

Journal

The International Journal of Tuberculosis and Lung Disease, 24(2)

ISSN

1027-3719

Authors

Saleh, S
Shepherd, W
Jewell, C
et al.

Publication Date

2020-02-01

DOI

10.5588/ijtld.19.0417

Peer reviewed

INT J TUBERC LUNG DIS 24(2):150–164

http://dx.doi.org/10.5588/ijtld.19.0417

STATE OF THE ART SERIES
OCCUPATIONAL LUNG DISEASES
Series editors: T. Driscoll, M. Sim
NUMBER 2 IN THE SERIES

Air pollution interventions and respiratory health: a systematic review

S. Saleh,[1,2] W. Shepherd,[1] C. Jewell,[3] N. L. Lam,[4] J. Balmes,[5,6] M. N. Bates,[6] P. S. Lai,[7] C. A. Ochieng,[8,9] M. Chinouya,[1] K. Mortimer[1]

[1]Liverpool School of Tropical Medicine, London, UK; [2]Malawi-Liverpool-Wellcome Trust Programme, Lilongwe, Malawi; [3]Lancaster University, Lancaster, UK; [4]Schatz Energy Research Center, Humboldt State University, Arcata, CA, [5]University of California, San Francisco, San Francisco, CA, [6]University of California, Berkeley, CA, [7]Harvard Medical School, Boston, MA, USA; [8]National University of Ireland Galway, Galway, Ireland; [9]Stockholm Environment Institute, Stockholm, Sweden

SUMMARY

BACKGROUND: Indoor and ambient air pollution exposure is a major risk to respiratory health worldwide, particularly in low- and middle-income countries (LMICs). Interventional trials have mainly focused on alternatives to cooking stoves, with mixed results. Beyond cooking, additional sources of particulate matter also contribute to the burden of air pollution exposure. This review explores evidence from current randomised controlled trials (RCTs) on the clinical effectiveness of interventions to reduce particulate matter in LMICs.

METHODS: Twelve databases and the grey literature (e.g., Government reports and policy papers) were searched. Eligible studies were RCTs conducted in LMICs aiming to reduce particulate exposure from any source and reporting on at least one clinical respiratory outcome (respiratory symptoms, lung function or clinical diagnoses). Data from relevant studies were systematically extracted, the risk of bias assessed and narrative synthesis provided.

RESULTS: Of the 14 included studies, 12 tested 'improved' cookstoves, most using biomass, but solar and bioethanol cookers were also included. One trial used solar lamps and another was an integrated intervention incorporating behavioural and environmental components for the treatment and prevention of chronic obstructive pulmonary disease. Of the six studies reporting child pneumonia outcomes, none demonstrated significant benefit in intention-to-treat analysis. Ten studies reported respiratory symptom outcomes with some improvements seen, but self-reporting made these outcomes highly vulnerable to bias. Substantial inter-study clinical and methodological heterogeneity precluded calculation of pooled effect estimates.

CONCLUSION: Evidence from the RCTs performed to date suggests that individual household-level interventions for air pollution exposure reduction have limited benefits for respiratory health. More comprehensive approaches to air pollution exposure reduction must be developed so their potential health benefits can be assessed.

KEY WORDS: particulate matter; cookstove; pneumonia; lung function; respiratory symptoms

AIR POLLUTION IS A major environmental risk factor for a range of respiratory and other diseases.[1–3] Airborne particulate matter (PM) plays an important part in the pathophysiology of the development of non-communicable lung disease,[3,4] and has a proposed role in the mechanisms behind susceptibility to acute lower respiratory tract infection (ALRI), a leading cause of mortality worldwide in children under 5 years).[5–7] The great majority of these disease burdens fall on low- and middle-income country (LMIC) populations,[8] exacerbating existing health

Previous articles in the series Editorial: Driscoll T, Sim M. R. Occupational lung disease—scope of the problem, the role of the SDGs and a framework for prevention. Int J Tuberc Lung Dis 2020; 24: 5. **Articles: No 1:** Cormier M, Lemiére C. Occupational asthma. Int J Tuberc Lung Dis 2020; 24: 8–21.

Correspondence to: Sepeedeh Saleh, Malawi-Liverpool-Wellcome Trust Programme, Queen Elizabeth Central Hospital, College of Medicine, PO Box 30096, Chichiri, Blantyre 3, Malawi. email: sepeedeh.saleh@lstmed.ac.uk
Article submitted 25 June 2019. Final version accepted 15 December 2019.

and socio-economic inequalities. Household air pollution from inefficient burning of biomass fuels and kerosene for cooking, heating and lighting is widespread in LMIC settings, and reinforces gendered inequality, as women and children tend to spend the most time engaged in household tasks.

Systematic reviews of air pollution interventions and health to date have largely focused on household air pollution from cooking with biomass, predominantly confined to trials of improved cookstove interventions.[9-11] Cooking sources, however, do not constitute the entirety of PM exposure in LMIC settings: other sources of airborne PM including the burning of waste, motor vehicle and engine exhaust, and burning of solid or liquid fuels for heating or lighting can also contribute to exposure.

One possible explanation for the limited clinical benefits seen in improved cookstove studies is that the particulate and other emission exposure reductions in PM brought about by these specific interventions alone are insufficient to have a substantial impact on the severity or incidence of clinical outcomes. Two recent systematic reviews have reported the effects of such interventions on airborne PM and carbon monoxide (CO) exposures.[9,12] While various cooking interventions, including improved solid fuel stoves and cleaner fuels, were found to achieve reductions in levels of particulate matter <2.5 μm (PM2.5) and CO, both reviews reported that most interventions resulted in post-intervention PM2.5 levels that still greatly exceeded WHO air quality guideline (AQG) limit values.[13] Given recent evidence on elevated morbidity and mortality risks even at PM levels below these limits, it is plausible that the reductions in exposure associated with cookstove interventions may not be sufficient for clinically significant health effects.[14]

Alternative or additional explanations include the continuing impact on health of PM exposures occurring outside the trial households, either in other households or from outdoor sources. A further possibility is that the postulated pathogenic links between air pollution and the clinical outcomes in question (pneumonia, for example) are not as strong as previously thought.[15]

This systematic review assesses the available evidence based on randomised controlled trials (RCTs) for efficacy of interventions aimed at reducing respiratory morbidity and/or mortality in adults and children living in LMICs through reduction in exposure to air pollution.

In limiting this review to RCTs, we aim to constrain methodological heterogeneity, improving the potential for clarity and validity of the overall outcome assessment. We recognise, however, the potential shortcomings of RCTs,[16] particularly for complex air pollution interventions embedded in a wide range of social contexts. Acknowledging this, we present this review as a starting point from which to propose new studies to improve respiratory health outcomes through air pollution reduction.

METHODS

Search strategy

The systematic review protocol was developed collaboratively and registered on Prospero (CRD42019129482).* The review is reported in accordance with PRISMA (Preferred reporting items for systematic reviews and meta-analyses) guidelines.[17]

The following 10 databases were searched, from inception until March 2019: MEDLINE, EMBASE, CINAHL, Web of Science, GlobalHealth, PsycINFO, TRIP database, PubMed, WHO International Clinical Trials Registry Platform and Cochrane Central Register of Controlled Trials (CENTRAL). Google Scholar was also searched from inception, and the first 40 pages reviewed for relevant content.[18] ClinicalTrials.gov was searched for additional relevant trials, with authors of ongoing trials contacted to improve coverage of recent trial results. In addition to the formal database searches and protocol identification, reference lists of key articles and related reviews were searched for additional relevant trials.

Provided they met inclusion criteria, trials evaluating results of LMIC-based RCTs with aims which included improvement in one or more clinical respiratory measures to be achieved through reduced air pollution exposure were included.

In terms of search limits, the validated filter, "Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2008 revision)" was used as appropriate (in an adapted form as necessary for different databases) to identify randomised interventional trials with optimum sensitivity.[19] Another published filter from Cochrane was used,[20] adapted to 2019 World Bank country classifications, and in relevant variations for different databases, to identify trials taking place in LMICs as defined by the World Bank for the fiscal period 2019 (i.e., those with gross national income per capita of $\leq$12,055 US dollars, as calculated by the World Bank Atlas method from 2018).[21]

An example of the full electronic search strategy (for the OVID MEDLINE search) is available as Supplementary Information. Adapted versions of this were used to search other databases, with appropriate alterations to account for differences in search syntax and controlled vocabularies.

* Available at: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019129482

Table 1 PICO search criteria

Population
Adults and children living in low- and middle-income countries (as defined by the World Bank, 2019[1]
Intervention(s)
Any household-level intervention with the primary aim of reducing respiratory morbidity or mortality through reduction in exposure to air pollution, as determined by particulate matter exposure of any size classification. These may include interventions aimed at altering technology, behaviour, educational or other intervention types, or multi-component interventions. Interventions which aimed to mitigate the effects of existing exposure were not considered
Control(s)
No air pollution intervention or respiratory-related intervention (either no intervention or an intervention unrelated to air pollution or lung health)
Main outcome(s)
The main outcomes of interest are clinical respiratory outcomes including, but not restricted to, clinical diagnoses (such as asthma, pneumonia, tuberculosis, obstructive lung disease, and lung cancer), clinical respiratory symptoms and lung function
Study design
Randomised controlled trials only: participants randomly allocated to contemporaneous intervention or control groups

* PICO = Problem/Patient/Population, Intervention/Indicator, Comparison, Outcome, and (optional) Time element or Type of Study.

Study selection

Studies were selected in accordance with the eligibility criteria (Table 1). There were no limitations on the basis of length of follow-up, language, or publication status. In terms of participants, eligible studies included adults and/or children living in LMICs.

Eligible interventions were those aiming to improve respiratory health through reduction in air pollution exposure. Interventions aimed at altering technology, behaviour, educational or other types of intervention, as well as multi-component interventions, were all eligible. Interventions (e.g., masks) aiming to mitigate effects of existing exposure were not included. Control groups included any in which participants had no exposure to an air pollution- or respiratory-related intervention, either with no intervention or with 'control' interventions unrelated to air pollution or respiratory health.

Eligible outcomes were clinical respiratory measures, including clinical diagnoses such as pneumonia, symptoms of respiratory illness and lung function (measured by spirometry). In contrast to recent reviews which considered intermediate outcomes, such as airborne PM levels, the aim of this review is to elucidate whether any PM exposure interventions can bring about measurable improvements in respiratory health. All RCT designs, including individually randomised, cluster randomised, stepped-wedge and cross-over trials, were eligible.

Titles, and abstracts where necessary, of search results were screened for relevance in accordance with the PICOS criteria outlined above. Full texts of the resulting potentially relevant papers were assessed independently by two reviewers (SS and WS) against the same criteria. Those clearly not meeting the inclusion criteria were excluded at this stage. Where there was uncertainty or disagreement, these were resolved independently by a third reviewer (KM).

Table 2 Main variables for which data were collected

Citation information
Study design
Setting
Information on aspects of study duration and follow up
Participant information
Details of intervention(s) and their implementation
Details of comparator (control group)
Outcomes: definitions, measurement, and classification by study authors (primary/secondary/other)
Type of analysis
Data on study power and statistical considerations
Risk of bias assessment outcome

Data extraction and quality assessment

A specifically designed and piloted data extraction tool was developed for the review. Two reviewers independently extracted data using the tool. Results were cross-checked in detail and any areas of discrepancy discussed. The third reviewer was consulted in the case of unresolved issues. Authors of original research were contacted where there were important outstanding data points. The key areas in which data were extracted are outlined in Table 2; the data extraction tool is provided in the Supplementary Information.

A hierarchy of outcomes was constructed by the review authors on the basis of clinical importance and potential for objective assessment. Individual outcome-level quality assessments, primarily considering the highest included outcome from the developed hierarchy, were then carried out for all included studies.

Quality assessment involved two authors (SS and WS) independently assessing risk of bias for each study using the Cochrane Risk of Bias 2 (RoB2) tool,[22] with any points of discrepancy addressed through discussion. The RoB2 Excel tool[22] (MicroSoft, Redmond, WA, USA) was used to collate and process the scores for each study and to tabulate the final results (Figure 1). Elements of review-level risk of bias were considered separately.

Summary measures and statistical analysis

Estimates of relative risks or odds ratios were the principal summary measures extracted from papers (where available) to compare outcomes in the intervention and control groups. These were used for the following main outcomes: incidence of ALRI in children; symptom prevalence (including cough and wheeze) in adults; and difference in mean percentage changes in forced expiratory volume in 1 sec (FEV_1) and FEV_1/FVC (forced vital capacity). These were presented with 95% confidence intervals or *P* values as available. Unadjusted estimates were

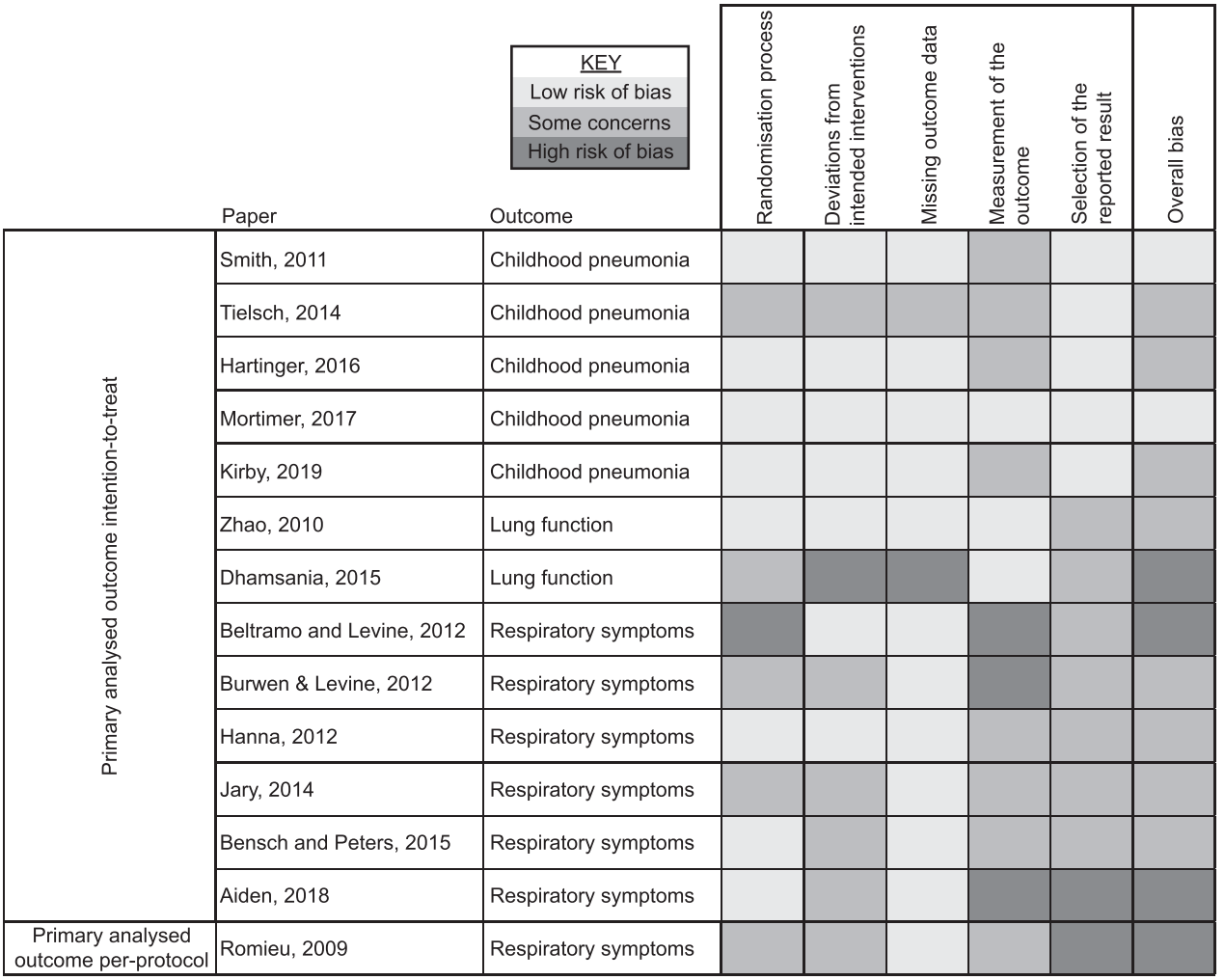

Figure 1 Risk of bias outcomes for included studies based on the Cochrane RoB2 tool.

reported where available to optimise comparability. Where these were not available, we reported the least adjusted estimates. To reflect levels of baseline comparability between the studies, details of settings and populations are provided in Table 3, using the primary study paper for reference. Results for individual outcomes were pooled where appropriate. The online software 'DistillerSR Forest Plot Generator' was used to generate the forest plot.[23] For each outcome, a summary measure, confidence interval and study weighting were presented on a forest plot. Aspects of clinical and methodological heterogeneity between the studies were discussed qualitatively.

RESULTS

We found 7956 papers through our database searches and an additional four papers were identified through other sources. After screening the titles and abstracts, 250 papers remained for more detailed review of the full texts. Fifteen studies met our a priori inclusion criteria and were included in the final review. The main reasons for study exclusion were 1) air pollution studies which had no clinical respiratory outcome (e.g., studies which used PM exposure endpoints, or studies which examined the effects of air pollution on other systems); 2) studies which did not use random allocation, or which had no control group for comparison; and 3) protocols or preliminary reports of studies which were still incomplete or which had not yet reported on clinical respiratory outcomes.

Of the 14 trials included, five were cluster RCTs (including one stepped-wedge design)[24] and the others used individual randomisation. Most of these 14 overarching studies had results available in multiple formats, including working papers and reports, peer-reviewed papers and presentations available online. While the nominated 'key study paper' for each study is used for reference in Table 3, other sources are cited for different outcomes, populations groups and timepoints as discussed throughout the paper, and cross-referenced in subsequent summary tables. Twelve studies tested improved cookstoves (e.g., with more efficient combustion, or chimneys for ventilation, etc.). Of the remaining two studies, one trialled a solar lamp

Table 3 Key features of studies included in analysis

Study	Setting	Population	Intervention	Comparison	Respiratory outcomes	Follow up
Romieu, 2009	Rural highland Mexico	552 women (with child <5 years) throughout follow-up, analysis of ALRI outcome in children under 4 years	Patsari wood cookstove	Traditional open fire	ALRI in past 15 days, in children <4 years, and respiratory symptoms in women (including cough, wheeze)—all results by stove use (intention-to-treat not reported)	10 months
Zhou, 2010	Guangzhou City, China	1 062 adults aged ≥40 years ± COPD (allocated): 872 received; 819 at 4-year follow-up	Integrated intervention (including health education, smoking cessation, participatory clean air project to relocate factory) and COPD management advice	Usual care	Annual rate of FEV_1/FVC ratio decline (adjusted)	4 years
Smith, 2011	Guatemala	534 households (pregnant women/children <4 m)	Locally developed chimney stove	Open wood fires	Pneumonia, severe pneumonia, and numerous other subcategories of pneumonia in children under 18 months. Lung function in children and adult women, respiratory symptoms (including cough, wheeze) in women	26 months
Burwen & Levine, 2012	Sissala West District, (rural) Ghana	768 women (1 from each household)	Self-constructed (guided) improved cookstove with chimney and ventilation hole	Primary traditional stove	Prevalence of respiratory symptoms including 'bad cough outside cooking' in previous week (self-reported)—average across group, where 0 is no and 1 is yes, and number of symptoms (of 5) in previous week in household members	3–5 weeks
Beltramo & Levine, 2013	Senegal	790 women	'HotPot' panel solar cooker	Existing cooking methods (wood)	Self-reported: number of respiratory symptoms (of seven) in last 7 days	6 months
Hanna, 2016	Orissa, India	2 575 households in total 1 679 initial FEV_1/FVC 2 511 cough symptoms	Improved stove (enclosed flame and chimney)	Existing wood stove	Self-reported 'cough or cold', 'any illness' in last 30 days in primary cooks, lung function (including FEV_1, FEV_1/FVC) in primary cooks. Cough, fever, 'any illness' in children aged ≤13 years	4 years
Jary, 2014	Ntcheu District, Malawi	51 women	'Chitetezo' stove (locally produced, more efficient burning)	Traditional open wood fire	Self-reported respiratory symptoms (cough, wheeze) in women	7 days
Bensch & Peters, 2015	Senegal	253 households, women cooks	'Jambaar' improved cookstove—more efficient woodstove	Open fire (bag of rice also given)	Any respiratory symptoms in household cook in last 6 months—group mean, where 0 is no and 1 is yes	12 months
Dhamsania, 2015	Ibadan, Nigeria	303 pregnant women (97 Follow-up spirometry)	'CleanCook' bioethanol stove	Continued use of kerosene/firewood stove	Lung function (spirometry, including FVC, FEV_1, FEV_1/FVC)	6.5 months
Hartinger, 2016	Peru	534 children under 3 (50 communities)	Improved ventilated solid fuel stove (part of integrated programme of interventions)	Unventilated stoves/ open fires + early child development intervention	Episodes of acute respiratory infection, acute lower respiratory infection, prevalence of cough or difficulty breathing, and of cough or difficulty breathing and fever	11 months

Table 3 (*continued*)

Study	Setting	Population	Intervention	Comparison	Respiratory outcomes	Follow up
Tielsch, 2016	Rural district, Southern Nepal	5 254 children from 3 376 households with women (15–30 years) or child <3 years; stepped-wedge design	Two burner biomass stove with chimney for ventilation	Traditional open burning cookstoves	Pneumonia incidence in children (maternal report of 2 or more days of fast/difficult breathing and fever'), incidence of respiratory symptoms including cough, wheeze	6 months run in: 12 months rollout; 6 months follow-up
Mortimer, 2017	2 sites, rural Malawi	10 750 children under 5 (8 626 households)	Biomass force-draft cookstove	Open fire	Incidence of IMCI pneumonia in under 5s (and other pneumonia outcomes: all pneumonia, severe pneumonia, O_2 saturations <90%, death), lung function (spirometry)	24 months
Aiden, 2018	Uganda	230 people (50 households)	Solar LED lamp	Kerosene lamps	Self-reported respiratory symptoms including cough, wheeze	3 months
Kirby, 2019	Western Province, Rwanda	2 440 children (1582 households)	Portable high-efficiency biomass-burning "rocket" cookstove (and advanced water filter—combined intervention)	Traditional biomass-burning stoves (no program activities)	ARIs in the preceding 7 days (carer-reported), healthcare visits for ARI, current IMCI pneumonia, severe pneumonia	12 months

ALRI = acute lower respiratory tract infection; COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 sec; FVC = forced vital capacity; IMCI = Integrated Management of Childhood Illness; LED = light-emitting diode; ARI = acute respiratory infection.

for reducing use of kerosene and the other used an integrated chronic obstructive pulmonary disease (COPD) management/prevention intervention (in seniors with and without COPD). The complex multimodal intervention used in the latter study differed in a few ways from the other studies included in this review. The constituent components of this intervention are described explicitly in the "Lung function" section, and the nature of its effects analysed accordingly.[25] To note, none of the interventions involved gaseous fuels, and the only intervention to involve electricity was a trial of solar-LED lamps.

Follow-up periods ranged from 7 days (for a cookstove pilot) to 4 years in the case of a large improved stove trial and the integrated COPD intervention. The trials were set in countries across Africa, Latin and South America, and Asia. Six trials included estimates of impact on pneumonia incidence in children (of various ages), 10 evaluated estimates of impact on cough and wheeze in adults, and the other key clinical respiratory outcome group was lung function, as assessed using spirometry.

Twelve of the trials had results of clinical respiratory outcomes published in at least one peer-reviewed journal. One trial of a solar lantern intervention in Uganda was only published as a preprint on the 'BioRxiv' platform[26] and the remaining two, both improved stove trials, had associated peer-reviewed publications of other outcomes but reported clinical respiratory outcomes only in abstract.[24,27] Many of the trials were incompletely reported, and often had missing key steps from the CONSORT (Consolidated Standards of Reporting Trials) reporting guidelines,[28] such as participant eligibility criteria, data on sample size calculation, and participant flow.

There were no cases of serious divergence between the RoB2 scores awarded by the two assessors, although in a few selected instances the domain outcomes automatically generated by the RoB2 Excel tool did not match the reviewers' individual judgements. Where this was the case, the reviewer's judgement superseded RoB2. Two studies were judged using the Cochrane RoB2 tool to be at "low risk" of bias. A further four scored as "high risk" of bias, and the remaining eight studies were categorised as having "some concerns" (Figure 1). Common features of papers with moderate to high risk of bias included failure to report details of randomisation or blinding, lack of clarity around primary and secondary outcomes, and a related selectivity around outcomes reported in final papers, with incomplete reporting commonly occurring.

CHILD PNEUMONIA OUTCOMES

Six papers included pneumonia outcomes in children (Table 4).[24,29–33] None of these studies showed a

Table 4 Comparison of childhood pneumonia outcomes across the relevant studies

Study	Upper age limit	Outcome definition	Assessor	Intention-to-treat?	Effect estimate† (95% CI)	*P* value
Smith, 2011	18 months	Incidence IMCI-defined* pneumonia episodes (on weekly visits)	Physician	Yes	RR 0.84 (95% CI 0.63–1.13)	0.257
Tielsch, 2014	3 years	Incidence ALRI (fast or difficult breathing and fever, for ≥2 days)	Mother	Yes	Adjusted OR 0.87 (0.67–1.13)	
Schilmann, 2015; further data from[34]	4 years	'Fast breathing + difficult breathing/ cough' episode in past 15 days, per child-year	Mother + fieldworker	No	RR 0.78 (95% CI 0.59–1.06)	
Hartinger, 2016	3 years	ALRI (cough or difficulty breathing, with raised respiratory rate) on 2 consecutive measurements (7 days without symptoms required between separate episodes)	Mother + fieldworker (with referral to physician as necessary)	Yes	RR 2.45 (95% CI 0.82–7.39)	0.11
Mortimer, 2017	5 years	Incidence IMCI-defined* pneumonia episodes reporting to health facility	Physician (fieldworker referral)	Yes	Incidence rate ratio 1.01 (95% CI 0.91–1.13)	0.80
Kirby, 2019	5 years (infants <2 months excluded)	'Current' IMCI-defined* pneumonia	Enumerators	Yes	Prevalence ratio 0.87 (95% CI 0.58–1.30)	0.491

* World Health Organization's ICMI pneumonia in children is defined as the presence of cough or difficulty breathing and fast breathing.[47]
† Unadjusted unless otherwise specified.
CI = confidence interval; IMCI = Integrated Management of Childhood Illness; RR = relative risk; ALRI = acute lower respiratory tract infection; OR = odds ratio.

statistically significant reduction in child pneumonia incidence in the intention-to-treat analysis, although other significant results were separately reported. These included a reduction in ALRI-prevalent days in the stepped-wedge trial of improved biomass cookstoves in Nepal,[24] reduction in caregiver-reported acute respiratory infection in a combined cookstove and water filtration intervention trial,[33] and significant reductions in three severe pneumonia outcomes in a chimney cookstove trial.[30]

One of the six studies that reported on childhood pneumonia outcomes (a trial of Patsari cookstoves), presented results by reported stove use (a per-protocol analysis), rather than by allocation group (intention-to-treat analysis).[34] This was the only study of the six with high risk of bias, as judged by the Cochrane RoB2 tool. While no protective effect was found on child pneumonia incidence in either analysis, some benefits associated with intervention use were reported for children, including reduction in duration of respiratory infections.[31] Uptake and use of the intervention stoves was variable in this study population, with approximately half of the intervention households reporting continued use of their original stoves during the study period.

Regarding risk of bias, two of the remaining five of the studies were found to have low risk of bias.[30,32] These were large studies, the first an RCT testing locally developed chimney stoves, and the second, a cluster RCT of force-draft biomass cookstoves using solar-powered fans. Although the first of these found non-significant reductions in pneumonia rates in the intervention group, neither evidenced significant benefits in terms of childhood pneumonia outcomes.

As can be seen in Table 4, there was methodological heterogeneity across the studies, with clinical heterogeneity encompassing differences in participant inclusion criteria (in particular, relating to age limits), and outcomes, among other factors. Outcome heterogeneity included differences in diagnostic criteria for pneumonia, and complications around clinical assessment. In one study, for example,[29] where respiratory rate was part of the diagnostic criteria, respiratory rate assessments were only made in respectively 68% and 63% of intervention and control group participants, with medical treatment given prior to respiratory rate assessment in the remaining cases. In a further study,[31] authors cited physician-diagnosed pneumonia rates as an outcome, but only 71% and 65% of fieldworker-diagnosed pneumonia cases in intervention and control groups respectively were subsequently seen by physicians, with the physician-diagnosis data for the other cases estimated using multiple imputation techniques.

Methodological heterogeneity stemmed from the presence of cluster RCTs[29,32,33] and a stepped-wedge trial,[24] as well as individually randomised trials; variability in study implementation and differing

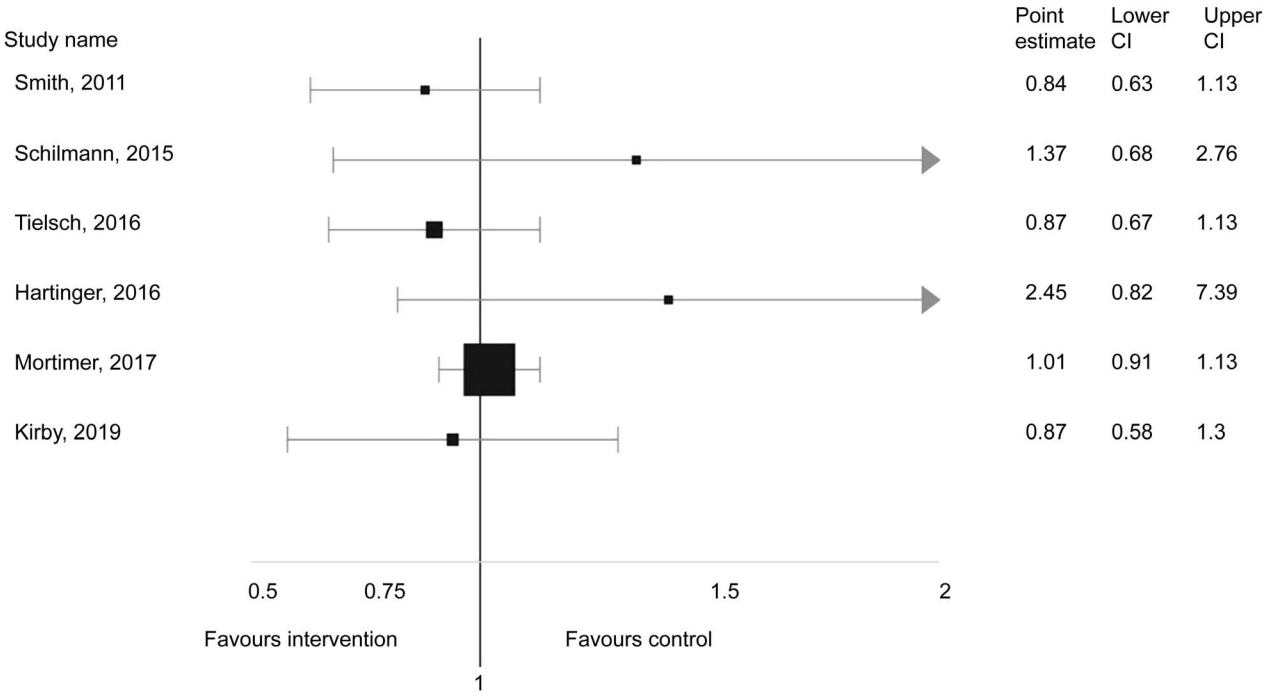

Figure 2 Forest plot depicting child ALRI incidence. CI = confidence interval; ALRI = acute lower respiratory tract infection.

risks of bias (Figure 1). Finally, there were differences in measure of association estimates reported. While most of the studies reported relative risks or equivalent, there were alternatives. Prevalence ratio was the reported outcome in a paper which measured the pneumonia outcome as 'current pneumonia' at the time of the assessor's weekly visit,[33] and the stepped-wedge study by Tielsch et al. used odds ratios.[24] Furthermore, although all studies reported pneumonia incidence, only one reported 'per child-year' data,[35] with the others providing data based on individual children. These differences precluded the intended pooling of outcomes. Instead, we present the child pneumonia results in a forest plot (Figure 2) accompanied by a qualitative commentary.

The forest plot shows relative risk estimates with upper and lower confidence intervals from a total of six randomised controlled trials; their relative weights are indicated by box sizes. For the cluster RCTs, the estimates used were adjusted for clustering to maximise the comparability of the results.[29,32,33] Because of heterogeneity, particularly in terms of clinical diversity, no summary estimate was included.

The confidence intervals of all studies cross one, indicating no statistically significant benefits for any of the interventions, and while some of the confidence intervals are quite wide, effect estimates do not predominantly favour either intervention or control. One study (a large cluster RCT of improved cookstoves) dominated in terms of study size (10 750 children enrolled).[32] The second largest of the studies was a stepped-wedge trial of chimney stoves in Nepal which enrolled 5254 children but encompassed a shorter follow-up period.[24]

In terms of exposure to airborne PM—an important intermediate endpoint on the causal pathway to clinical benefit—closer interrogation of the data provided by study authors goes some way to clarifying the picture. Perhaps the clearest evidence of improvement in exposures was seen in the RESPIRE trial, which reported significant reductions of approximately 50% in personal CO exposures in children (with greater reductions in maternal exposures and kitchen measurements).[36] Even this improvement was insufficient, however, to produce a reduction in the main clinical outcome—child pneumonia—perhaps due to a plateau effect described by the authors, whereby decreases in exposure at high levels are associated with little reduction in outcome.[30]

The failure of interventions to achieve exposure reductions sufficient to impact key clinical respiratory outcomes is a hypothesis supported by available data from the remaining five studies. Evidence from three studies indicated no significant reduction in measured exposure,[33,37,38] one of which found reductions of respectively 27% and 45% in personal CO and PM2.5 measurements among females; however, these were statistically non-significant.[37] Schilmann et al. quoted reductions of almost 80% in kitchen PM2.5 levels in a subset of participants when using patsari intervention stoves, but gave no indication of statistical significance or intention to treat data .[31] Finally, preliminary data from a stepped-wedge study of biomass chimney stoves indicated reductions in kitchen levels of PM2.5 and CO, although data on

statistical significance was again lacking.[24] It is worth noting that, even for studies which demonstrated reductions in exposure, PM2.5 levels remained well above the lower limit suggested in air quality guidelines.[24,37–39]

Respiratory symptoms

Ten papers provided data on respiratory symptoms, with the most frequently cited being cough and wheeze.[24,26,29,34,39–44] All but one of these studies tested cleaner cookstoves of various types, the exception being a study using solar-powered lamps to replace kerosene lamps.[26] This increases the methodological heterogeneity in the study set but the paper remains within the stated inclusion criteria of the current review, since the authors aimed to reduce respiratory morbidity through the reduction of airborne PM levels. This solar lamp intervention was in fact one of six studies reporting improvements in symptoms of respiratory disease (in this case, cough). Authors of this paper also described a significantly greater reduction in the average levels of elemental carbon (soot) in intervention homes compared with control homes, although no differences in organic carbon or PM2.5 were reported.

While six of the 10 studies were able to evidence some form of improvement in respiratory symptoms,[24,26,34,39,40,43] the nature of the outcomes varied. Five of the six studies describing the protective effects of interventions referred to cough and/or wheeze symptoms (an effect which, in one case, was restricted to the intention-to-treat analysis[34]). The fifth of these described the effects on symptoms of a respiratory system disease in the last 6 months.[39] Other studies, none of which evidenced significant differences between control and intervention group symptoms, used endpoints including respiratory symptoms in the last 30 days and counts of symptoms from pre-defined lists. This and other forms of heterogeneity made pooling of these results impossible, and the multiple differing outcomes measured and reported by individual studies raises the question of outcome reporting bias.

With regard to the populations in which outcomes were measured, there was considerable heterogeneity again: papers describing combinations of self-reported symptoms in women (or "primary household cook"), symptoms in children, and in "household members".

Nine of the 10 papers which reported respiratory symptoms included results from intention-to-treat analyses, although one of these reported a combination of intention-to-treat and 'average treatment effect on the treated' results for different outcomes.[39] Incomplete reporting of data was seen in many of the studies with data from selected outcomes reported, in particular for outcomes reaching statistical significance. Key features of the relevant papers and results are presented in Table 5.

LUNG FUNCTION OUTCOMES

FEV_1 and FEV_1/FVC were the most frequently cited outcomes for lung function, reported by six papers. This included five papers describing improved cookstove interventions,[27,38,42,45,46] two of which reported results from different subsets of the same intervention (see Table 6) and a 4-year study (one of the longest timescales among the trials included in this analysis), examining the impact of a complex COPD management/prevention programme.[25]

Of these studies, only the integrated COPD management/prevention programme demonstrated statistically significant lung function benefits (in terms of an annual rate of decline in FEV_1 and FEV_1/FVC) between control and intervention groups.[25] This difference was maintained in the subgroup of participants without COPD.

Interventions in this study included health education relating to COPD, smoking, other unspecified health-related 'habits and behaviours', and improvements in air quality. A subset of participants with COPD, and those deemed to be at "high risk", received additional intensive interventions, including COPD treatment optimisation and support with smoking cessation. This resulted in a doubling of smoking cessation rates in the intervention group compared with that of the control group (21% vs. 8%, $P < 0.004$), and reports of reduced exposure to environmental tobacco in this group alone, which are likely to have contributed substantially to the differences in lung function decline.

There was also a wider environmental aspect of the intervention which incorporated advice on environmental factors (with stoves, kitchen ventilation and living and working environment given as examples), and a successful campaign to relocate and upgrade a local cement factory. Among other differences, this achieved statistically significant improvements in sulphur dioxide and dust concentrations in the intervention group compared with the controls.

In terms of the remaining five studies addressing lung function as an outcome—although length of follow-up was a variable, only one study had a follow-up period in excess of 2 years.[45] These periods are arguably insufficient for improvements in lung function to become apparent. The lung function results often came from subsets of larger trials, not adequately powered to detect substantial changes in these outcomes. There was great variation in reported outcome measures and in the quality of reporting in these outcomes, particularly in papers reporting continued follow-up of participant subsets after initial trials had ended, further hampering assessment of the impacts of exposure reductions on this outcome.

Table 5 Comparison of papers reporting respiratory symptom outcomes

Study	Population for which respiratory symptoms reported	Reported symptom(s) and definition	Follow-up	Intention-to-treat?	Effect estimate* (95% CI)	*P* value
Romieu, 2009	552 women cooks	Respiratory symptoms in last 15 days (survey) symptoms including cough, wheeze, breathing difficulty, phlegm, chest tightness	12 months	No ('no difference' in intention-to-treat analysis)	For cough: age-adjusted RR 0.74 (95% CI 0.59–0.92) in 'mainly Patsari' users For wheeze: age-adjusted RR 0.28 (95% CI 0.11–0.76) in 'mainly Patsari' users	
Smith-Sivertsen, 2009	504 women (subset of total RESPIRE households)[30]	Range of symptoms (cough, phlegm, wheeze or chest tightness) in past 6 months, assessed by survey (standardised tools) and interview at 6, 12, 18 months	Multiple follow-up points including 6, 12 and 18 months	Yes	Reduction in RR across all symptoms, but only statistically significant reduction for wheeze: RR 0.42 (95% CI 0.25–0.70)	
Burwen & Levine, 2012	498 participants followed up; inclusion criteria for respiratory outcomes outside of cooking unclear	Prevalence of named symptoms outside of cooking (and count out of 5): sore throat, bad cough, difficulty breathing excessive mucus, chest pain	8 weeks	Yes	Mean difference for 'cough': 0.11	<0.01
Hanna, 2016	3569 'primary cooks' (for wheeze and tight chest outcomes)	Respiratory symptoms in the last 30 days (wheeze, tight chest, phlegm)	48 months	Yes	For wheeze, reduced form effect (RFE) of stove = –0.001 (RFE approx. 0 for all variables)	
Beltramo & Levine, 2013	744 women at follow up (also data for men and children available)	Number of respiratory symptoms (of predefined list of 7) reported in the last 7 days	6 months	Yes	Difference: treatment minus control group as a percentage of control mean = 3%, SE = –0.12	
Jary, 2014	50 women analysed	Women reporting cough or wheeze at follow up	7 days	Yes	No significant difference between two groups for either symptom	1.000 for both
Bensch & Peters, 2015	Household cooks: 229 analysed (household level analysis also carried out)	Symptoms of a respiratory system disease in the last 6 months in household cook	12 months	Yes	Difference in means between two groups: 7.1	0.01
Hartinger, 2016	499 children under 3 years analysed	Prevalence of cough or difficulty breathing	11 months	Yes	OR 0.97 (95% CI 0.79–1.19)	0.80
Tielsch, 2016	5254 children enrolled	Incidence of reported respiratory symptoms in children including persistent cough, wheeze	Complex (stepped-wedge design), 6 months run in, 12 months rollout, 6 months follow-up	Yes	Adjusted OR for persistent cough, 0.91 (95% CI 0.85–0.97) For wheeze, 0.87 (95% CI 0.78–0.97)	
Aiden, 2018	230 people randomised	Reduction in rates of respiratory symptoms including cough, wheezing, difficulty breathing	3 months	Yes	Significant reduction in cough symptom only: RR 7.1 (95% CI 0.57–0.90)	0.026

* Unadjusted unless otherwise specified.
CI = confidence interval; RR = relative risk; OR = odds ratio.

Table 6 Comparison of papers reporting lung function outcomes

Study	Population for which lung function reported	Follow-up period	Intention-to-treat?	Effect estimate† (95% CI*)	*P* value
Zhou, 2010	872 adults with and without COPD aged 40–89 years	48 months	Yes	Adjusted difference in annual rate of decline FEV_1: 19 ml/year (95% CI 3–36)	0.023
				Adjusted difference in annual rate of decline FEV_1/FVC ratio: 0.6% (95% CI 0.1–1.2)	0.029
Hanna, 2012	Women who regularly cook in household	48 months	Yes	For FEV_1, reduced form effect (RFE) of stove = 0.003	Not statistically significant
				For FEV_1/FVC x100, reduced form effect (RFE) of stove = –0.005	
Dhamsania, 2015	303 pregnant women at baseline, 206, and 96 women at subsequent follow up periods	6.5 months (follow-up timepoints: 26 weeks gestational age, 6 weeks postpartum)	Yes	"No significant differences in pulmonary function between the two control groups at the two follow-up time points". No further data available	
Guarnieri, 2015	Subset of 265 women involved in previous study[30]	Variable, following original RCT, mean follow-up 5.6 years	Yes	β-Co-efficient FEV_1 adjusted annual change in control group (stove after 18 months) compared with intervention group (stove from start): –44 ml/year (95% CI –91 to 4)	0.07
				β-Co-efficient FEV_1/FVC adjusted annual change in control group compared with intervention: –39 ml/year (95% CI –93 to 16)	0.16
Heinzerling, 2016	Subset of 355 children involved in previous study[30]	Variable, following original RCT, mean follow-up 1.3 years	Yes	β-Co-efficient† (adjusted) FEV_1 between two groups: –13.0 ml (95% CI −41.1 to 15.4)	
				β-Co-efficient† (adjusted) FEV_1/FVC between two groups: −0.058% –13.0 (95% CI −0.74 to 0.62)	
Nightingale, 2019	Subset of 424 adults (male and female) involved in the previous cookstove RCT[32]	Undefined period of time following 24-month follow-up period of original study	Yes	Intervention vs. control coefficient estimate for median FEV_1: 0.08 (IQR −0.06 to 0.22)	0.26
				Intervention vs. control coefficient estimate for median FVC: 0.04 (IQR −0.13 to 0.21)	0.62

* Or IQR, where specified.
† Change in lung function for each 1-unit increase in ln-transformed CO (1 ppm).
CI = confidence interval; COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 sec; FVC = forced vital capacity; RCT = randomised controlled trial; IQR = interquartile range; ppm = parts per million.

DISCUSSION

This review identified 14 RCTs testing air pollution reduction interventions and reporting clinical respiratory outcomes. Of these, 12 were trials of improved cookstoves and one was a trial of solar lamps. The remaining study, set in China, tested an integrated COPD prevention/management intervention.[25] Although pooling of the results was not possible due to heterogeneity in study populations and in outcome measures of association, the outcomes for the most commonly assessed primary clinical respiratory diagnosis—childhood pneumonia—consistently indicated no statistically significant associations across the six studies which included this endpoint (Figure 2).

Childhood pneumonia is an important outcome, as its diagnosis is more objective than self-reported symptoms and is less vulnerable to bias, particularly if the diagnosis is made by trained staff who are blinded to intervention status. The lack of evidence of improvement in this outcome across the RCTs to date is therefore an important finding.

One specific qualification relating to this outcome measure is the fact that the existing criteria used to define pneumonia may be said to lack specificity.[47] In terms of alternative outcome definitions, three of the above studies also considered WHO-defined severe pneumonia, but none found significant evidence of intervention benefit.[24,32,33] One chimney stove intervention, however, was associated with significant reductions in the outcome of physician-diagnosed severe pneumonia with hypoxaemia, arguably a more clinically relevant finding.[30]

A number of explanations have been proposed for the apparent resistance of respiratory outcomes to improvement through improved cookstove interventions. First, the degree of exposure reduction required for children to achieve meaningful health improvements may be greater than that achievable through improved cookstoves alone.[30,38] The available evidence on exposure assessment within the childhood pneumonia studies included in the current review went some way to supporting this hypothesis, with post-intervention exposure levels generally remaining well above international standards. In terms of the clinical impact specifically (in this case, reduction in cases of childhood pneumonia), the plateau effect seen in the exposure-response data from the RESPIRE study emphasises this need for further reduction in exposure.[36] Exposure reduction as an outcome in itself was not explored in detail because of the recent systematic reviews on the subject.[9,10,12] These reviews describe findings of variably reduced PM2.5 and CO exposures across studies (with numbers of studies using each intervention type being too small for firm conclusions to be drawn on differences between intervention stove types). All three reviews included conclusions supporting the hypothesis of insufficient exposure reduction for clinical impact.

In view of these findings, additional considerations for further reducing PM exposure, and/or by addressing additional exposure sources may be useful. Examples could include behavioural interventions relating to the drying of fuels (drier fuels cause less smoke), improving the combustion efficiency of stoves, improving ventilation in cooking areas and mitigating other household sources of PM exposure.[48] Ideally, greater accessibility to electricity and electric cookstoves, particularly induction stoves, would form a permanent solution for many.

A second explanation relating to the lack of intervention impacts on respiratory health is that of the credibility of the proposed causal relationship between household air pollution and respiratory diagnoses, which has recently been questioned.[49,50] Furthermore, any such relationship between exposure and pathology is likely to be complex, with adverse effects of exposure possibly starting in the antenatal period.[51] This could help explain the comparative lack of impact of the relatively short-term interventions as those considered in this review. A possible exception is the 4-year integrated COPD management/prevention intervention, which was associated with spirometric improvements in the intervention group.[25] Even this intervention did not lead to significant reductions in cumulative COPD incidence or mortality rates, suggesting that even longer timescales may be required to detect the impact on such long-term clinical outcomes.

Another factor impacting on real-world effectiveness, while less important in the context of RCTs, is the extent of intervention uptake and sustained use.[42] Poor uptake was not commonly seen within the studies in this review, partly perhaps due to the nature of the studies: all RCTs tend to reflect experimental rather than real-world conditions. In the large chimney stove trial in Guatemala, for example, a weekly check and repair service was in place for the intervention stoves, and the recent cluster RCT in Malawi reported their repair and replacement service to be "heavily used".[30,32] Many of the trials involved regular visits by study teams throughout—for example, weekly 'spot check' visits in a combined community study in Peru[29]—potentially affecting intervention use in ways that would not be seen in real life.

One trial which did report poor uptake and use of the interventions reported improvements in the per-protocol analysis which were not seen under the intention-to-treat model.[34] These implementation factors are complex and context-informed, for example, results in one study suggested that participants spent more time in their less-smoky kitchens post-intervention.[29] Further analysis of these factors

requires broader research methods, and qualitative as well as quantitative approaches.

Results of some studies indicated improvement in respiratory symptoms, but substantial heterogeneity in outcomes reported precluded pooling of these results.[24,26,34,39,40,43] The nature of these outcomes—especially where self-reported—has implications for their validity as health indicators.

In a context where participants are given (or asked to buy) a technology to improve their health, factors such as courtesy bias and demand effect are likely to play a role in symptom reporting patterns. This was explicitly discussed by authors of an improved cookstove trial,[43] who noted that there were no associations between either self-reported intervention use or measured CO levels and self-reported health.

Another salient issue relating to self-reported outcomes is that questionnaires, surveys and interviews almost always relied on translation, which is complex, incorporating temporal, regional, cultural and other contextual elements that may subtly change meaning. The use of validated questionnaires can be useful in navigating some of these difficulties, but such tools are not currently available for all settings and languages.[52] Authors of one large study discussed difficulties in developing terminology for symptoms such as 'wheeze' and described a need for different questions at baseline and follow-up time points to clarify timescales for participants.[40,53]

While six studies reported spirometric outcomes, these outcomes were again reported with so much heterogeneity that we judged calculation of a pooled effect estimate to be inappropriate. Only one of these studies reported significant intervention-related improvement in lung function,[25] although data from the RESPIRE study indicated a statistically significant association between exhaled CO and FEV_1.[54] The one study with evidence of spirometric benefits in the intervention group included both COPD patients and those without COPD, and involved numerous intervention components.[25] Interestingly, this intervention bundle was associated with a significantly reduced all-cause mortality rate compared with controls, although there was no significant difference in cumulative COPD incidence or mortality rate between the two groups.[25] The authors of this paper note that their results point to the value of integrated interventions targeting multiple factors in managing and preventing such pathogenically complex diseases. This is a case made also by researchers involved in a recent integrated water filter—the cookstove intervention in Rwanda, who cite movement of cooking from indoors to outside, and even reductions in diarrhoea, as potential contributors to the respiratory improvements seen.[33]

The main limitations in this review concern the amount of between-study heterogeneity—clinical, methodological and statistical—as well as the small sizes of most of the studies. It is interesting to note that these were present even within the subgroup of studies using similar intervention types (improved cookstoves) and similar outcomes (pneumonia in children). This is to some extent unavoidable in such a diverse and applied area of research, although the introduction of standardised criteria for the reporting of results from these studies could help to clarify study methodologies and findings and facilitate future cross-study comparisons.[55] We used unadjusted effect estimates to overcome differences in reporting; however, this introduces the potential limitation of uncontrolled confounding. In spite of the heterogeneity, we were able to recognise relative consistency in a clinically important respiratory outcome in the field—child pneumonia—in the sense that there was little evidence of benefit across the relevant RCTs.

In limiting its scope to RCTs only, this review excluded potential assessments of wider interventional types which may take different approaches to the reduction of air pollution from various sources. Such wide-ranging studies—analysed in a recent Cochrane review[56]—will be important in reflecting on the next steps for the field. While none were identified in this review, trials of interventions using alternative (non-biomass) fuel types in settings where this is feasible also offer potential benefits.[57,58]

CONCLUSION

Evidence from the RCTs performed to date suggests that cleaner-burning, biomass-fuelled cookstoves and other household-level interventions have limited benefits in terms of clinical respiratory outcomes. Given that post-intervention exposure levels generally remained well above international standards, we suggest that more comprehensive approaches to air pollution are required. Alternative means of reducing exposure need to be developed and evaluated in large RCTs for the potential health benefits to be assessed. Greater consistency in measured outcomes for these studies would also help to build the evidence base in this important field.

Supplementary Information

OVID Medline search strategy, data extraction tool and PRISMA checklist available on Harvard Dataverse: https://doi.org/10.7910/DVN/UICCPB.

Acknowledgements

The authors thank the National Institute for Health Research (NIHR; London, UK) Global Health Research Unit on Lung Health and TB in Africa at the Liverpool School of Tropical Medicine, "IMPALA" for helping to make this work possible. In relation to IMPALA (grant number 16/136/35), specifically, IMPALA was commissioned by the NIHR Global Health Research (GHR) using UK aid from the UK Government.

SS is sponsored by a Wellcome Trust Clinical PhD Fellowship (University of Liverpool, Liverpool, UK, block award [203919/Z/16/Z]).

The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care, UK Government.

Conflicts of interest: none declared.

References

1 Prüss-Üstün A, Corvalán C. How much disease burden can be prevented by environmental interventions? Epidemiology 2007; 18(1): 167–178.
2 Lim S S, Vos T, Flaxman A D, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380(9859): 2224–2260.
3 Schraufnagel D E, Balmes J R, Cowl C T, et al. Air Pollution and noncommunicable diseases: a review by the forum of international respiratory societies' environmental committee, Part 2: Air pollution and organ systems: A review by the Forum of International Respiratory Societies' Environmental Committee, Part 2: Air pollution and organ systems. Chest 2019; 155(2): 417–426.
4 Health Effects Institute Household Air Pollution Working Group. Household air pollution and noncommunicable disease. Boston, MA, USA: HEI, 2018.
5 Sonego M, Pellegrin M C, Becker G, Lazzerini M. Risk factors for mortality from acute lower respiratory infections (ALRI) in children under five years of age in low and middle-income countries: a systematic review and meta-analysis of observational studies. PLoS ONE 2015; 10(1): e0116380-e.
6 Rylance J, Chimpini C, Semple S, et al. Chronic Household Air Pollution Exposure Is Associated with Impaired Alveolar Macrophage Function in Malawian Non-Smokers: e0138762. PLoS ONE. 2015; 10(9).
7 Rylance J, Fullerton D G, Scriven J, et al. Household air pollution causes dose-dependent inflammation and altered phagocytosis in human macrophages. Am J Respir Cell Mol Biol 2015; 52(5): 584-93.
8 World Health Organization. Burden of disease from the joint effects of household and ambient air pollution for 2016. Geneva, Switzerland: WHO; 2018.
9 Quansah R, Semple S, Ochieng C A, et al. Effectiveness of interventions to reduce household air pollution and/or improve health in homes using solid fuel in low-and-middle income countries: a systematic review and meta-analysis. Environ Int. 2017; 103: 73-90.
10 Thomas E, Wickramasinghe K, Mendis S, Roberts N, Foster C. Improved stove interventions to reduce household air pollution in low and middle income countries: a descriptive systematic review. BMC Public Health 2015; 15: 650.
11 Thakur M, Nuyts P A W, Boudewijns E A, et al. Impact of improved cookstoves on women's and child health in low and middle income countries: a systematic review and meta-analysis. Thorax 2018; 73(11): 1026.
12 Pope D, Bruce N, Dherani M, Jagoe K, Rehfuess E. Real-life effectiveness of 'improved' stoves and clean fuels in reducing PM2.5 and CO: systematic review and meta-analysis. Environ Int 2017; 101: 7–18.
13 World Health Organization. WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide: global update 2005. Geneva, Switzerland: WHO, 2006.
14 World Health Organization Europe. Review of evidence on health aspects of air pollution—REVIHAAP Project, Technical Report. Copenhagen, Denmark: WHO, 2013.
15 Mortimer K, Balmes J R. Cookstove trials and tribulations: what is needed to decrease the burden of household air pollution? Ann Am Thorac Soc 2018; 15(5): 539–541.
16 Deaton A, Cartwright N. The limitations of randomised controlled trials. VOX CEPR Policy Portal, 9 November 2016. https://voxeu.org/article/limitations-randomised-controlled-trials. Accessed January 2020.
17 Moher D, Liberati A, Tetzlaff J, Altman D G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009; 151(4): 264–269.
18 Gehanno J-F, Rollin L, Darmoni S. Is the coverage of google scholar enough to be used alone for systematic reviews. BMC Med Inform Decis Mak 2013; 13(1): 7.
19 Cochrane handbook for systematic reviews of interventions. Higgins J P T, Green S, eds. Chichester, UK: Wiley-Blackwell, 2008.
20 Cochrane. LMIC Filters 2019. London, UK: Cochrane, 2019. https://epoc.cochrane.org/lmic-filters. Accessed January 2020.
21 The World Bank. World Bank country and lending groups, 2019. Washington, DC, USA: World Bank, 2019. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519. Accessed January 2020.
22 Cochrane. RoB 2: a revised Cochrane risk-of-bias tool for randomized trials. London, UK: Cochrane, 2019. https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials.
23 Evidence Partners. DistillerSR Forest Plot Generator. 2019. https://www.evidencepartners.com/resources/forest-plot-generator/. Accessed January 2020.
24 Tielsch J M, Katz J, Khatry S K, et al. Effect of an improved biomass stove on acute lower respiratory infections in young children in rural Nepal: a cluster-randomised, step-wedge trial. Lancet Global Health 2016; 4(S1): S19-S.
25 Zhou Y, Hu G, Wang D, et al. Community based integrated intervention for prevention and management of chronic obstructive pulmonary disease (COPD) in Guangdong, China: cluster randomised controlled trial. BMJ 2010;34:c6387.
26 Nyakato V N, Mwine N, Aiden E L, Aiden A P. Clean lighting leads to decreased indoor air pollution and improved respiratory health in rural Uganda. bioRxiv. 2018: 455097.
27 Dhamsania V, Alexander D, Ibigbami T, et al. Impact of an ethanol stove intervention on pulmonary function in pregnant women exposed to household air pollution. Chest 2015; 148(4): 765A-A.
28 Schulz K F, Altman D G, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol 2010; 63(8): 834–840.
29 Hartinger S M, Lanata C F, Hattendorf J, et al. Improving household air, drinking water and hygiene in rural Peru: a community-randomized-controlled trial of an integrated environmental home-based intervention package to improve child health. Int J Epidemiol 2016; 45(6): 2089–2099.
30 Smith K R, McCracken J P, Weber M W, et al. Effect of reduction in household air pollution on childhood pneumonia in Guatemala (RESPIRE): a randomised controlled trial. Lancet. 2011; 378(9804): 1717-26.
31 Schilmann A, Riojas-Rodríguez H, Ramírez-Sedeño K, Berrueta V, Pérez-Padilla R, Romieu I. Children's respiratory health after an efficient biomass stove (patsari) intervention. EcoHealth 2015; 12(1): 68–76.
32 Mortimer K, Ndamala C B, Naunje A W, et al. A cleaner burning biomass-fuelled cookstove intervention to prevent pneumonia in children under 5 years old in rural Malawi (the Cooking and Pneumonia Study): a cluster randomised controlled trial. Lancet 2017; 389(10065): 167–175.
33 Kirby M A, Nagel C L, Rosa G, et al. Effects of a large-scale distribution of water filters and natural draft rocket-style cookstoves on diarrhea and acute respiratory infection: a cluster-randomized controlled trial in Western Province, Rwanda. PLoS Med 2019; 16(6): e1002812.
34 Romieu I, Riojas-Rodríguez H, Marrón-Mares A T, Schilmann A, Perez-Padilla R, Masera O. Improved biomass stove intervention in rural Mexico: impact on the respiratory health of women. Am J Respir Crit Care Med 2009; 180(7): 649.

35 Perez-Padilla R, Schilmann A, Riojas-Rodriguez H. Respiratory health effects of indoor air pollution. Int J Tuberc Lung Dis 2010; 14(9): 1079–1086.
36 Smith K R, McCracken J P, Thompson L, et al. Personal child and mother carbon monoxide exposures and kitchen levels: methods and results from a randomized trial of woodfired chimney cookstoves in Guatemala (RESPIRE). J Expo Sci Environ Epidemiol 2010; 20(5): 406–416.
37 Hartinger S M, Commodore A A, Hattendorf J, et al. Chimney stoves modestly improved indoor air quality measurements compared with traditional open fire stoves: results from a small-scale intervention study in rural Peru. Indoor Air 2013; 23(4): 342–352.
38 Nightingale R, Lesosky M, Flitz G, et al. Non-communicable respiratory disease and air pollution exposure in Malawi (CAPS): a cross-sectional study. Am J Respir Crit Care Med 2019;199(5):613-621.
39 Bensch G, Peters J. The intensive margin of technology adoption – Experimental evidence on improved cooking stoves in rural Senegal. J Health Econ 2015; 42: 44–63.
40 Smith-Sivertsen T, Díaz E, Pope D, et al. Effect of reducing indoor air pollution on women's respiratory symptoms and lung function: the RESPIRE Randomized Trial, Guatemala. Am J Epidemiol 2009; 170(2): 211–220.
41 Beltramo T, Levine D I. The effect of solar ovens on fuel use, emissions and health: results from a randomised controlled trial. J Dev Eff 2013; 5(2): 178–207.
42 Hanna R, Duflo E, Greenstone M. Up in smoke: the influence of household behavior on the long-run impact of improved cooking stoves. Am Econ J Econ Policy 2016; 8(1): 80–114.
43 Burwen J, Levine D I. A rapid assessment randomized-controlled trial of improved cookstoves in rural Ghana. Energy Sustain Dev 2012; 16(3): 328–338.
44 Jary H R, Kachidiku J, Banda H, et al. Feasibility of conducting a randomised controlled trial of a cookstove intervention in rural Malawi. Int J Tuberc Lung Dis 2014; 18(2): 240–247.
45 Guarnieri M, Diaz E, Pope D, et al. Lung function in rural Guatemalan women before and after a chimney stove intervention to reduce wood smoke exposure: results from the randomized exposure study of pollution indoors and respiratory effects and chronic respiratory effects of early childhood exposure to respirable particulate matter study. Chest 2015; 148(5): 1184–1192.
46 Heinzerling A P, Guarnieri M J, Mann J K, et al. Lung function in woodsmoke-exposed Guatemalan children following a chimney stove intervention. Thorax 2016; 71(5): 421–428.
47 World Health Organization. Integrated management of childhood illness. Geneva, Switzerland: WHO, 2014. https://apps.who.int/iris/bitstream/handle/10665/104772/9789241506823_Chartbook_eng.pdf?sequence=16. Accessed January 2020.
48 Barnes B R. Behavioural change, indoor air pollution and child respiratory health in developing countries: a review. Int J Environ Res Public Health 2014; 11(5): 4607–4618.
49 Amaral A F S, Patel J, Kato B S, et al. Airflow obstruction and use of solid fuels for cooking or heating: BOLD results. New York, NY, USA: American Thoracic Society, 2018.
50 Balmes J R, Eisen E A. Household air pollution and chronic obstructive pulmonary disease."A riddle, wrapped in a mystery, inside an enigma". Am J Respir Crit Care Med. 2018; 197: 547–549.
51 Balmes J R. When the fetus is exposed to smoke, the developing lung is burned. Am J Respir Crit Care Med 2019; 199(6): 684–685.
52 Saleh S, van Zyl-Smit R, Allwood B, et al. Questionnaires for Lung Health in Africa across the Life Course. Int J Environ Res Public Health 2018; 15(8): 1615.
53 Díaz E, Bruce N, Pope D, et al. Lung function and symptoms among indigenous Mayan women exposed to high levels of indoor air pollution. Int J Tuberc Lung Dis 2007; 11(12): 1372–1379.
54 Pope D, Diaz E, Smith-Sivertsen T, et al. Exposure to household air pollution from wood combustion and association with respiratory symptoms and lung function in nonsmoking women: results from the RESPIRE trial, Guatemala. Environ Health Persp 2015; 123(4): 285–292.
55 Williamson P R, Altman D G, Bagley H, et al. The COMET Handbook: version 1.0. Trials 2017; 18(3): 280.
56 Burns J, Boogaard H, Polus S, et al. Interventions to reduce ambient particulate matter air pollution and their effect on health. Cochrane Database Syst Rev 2019; 5: CD010919.
57 ClinicalTrials.gov. National Library of Medicine (US). Household air pollution and health: a multi-country LPG intervention trial. Identifier: NCT02944682 2000- https://ClinicalTrials.gov/show/NCT02944682. Accessed January 2020.
58 Fandino-Del-Rio M, Goodman D, Kephart J L, et al. Effects of a liquefied petroleum gas stove intervention on pollutant exposure and adult cardiopulmonary outcomes (CHAP): study protocol for a randomized controlled trial. Trials 2017; 18(1):518.

RÉSUMÉ

CADRE : L'exposition à la pollution de l'air intérieur et extérieur est un risque majeur pour la santé respiratoire dans le monde, particulièrement dans les pays à revenu faible et moyen (LMIC). Les essais d'intervention se sont surtout concentrés sur des fourneaux améliorés avec des résultats variables. Au-delà de la cuisine, d'autres sources de particules contribuent également à l'exposition à la pollution de l'air. Cette revue explore les preuves d'efficacité clinique des essais randomisés contrôlés actuels (RCT) en matière d'intervention de réduction des particules dans les LMIC.

MÉTHODE : Douze bases de données et la documentation parallèle ont été explorées. Les études éligibles ont été des RCT réalisés dans un LMIC qui voulait réduire l'exposition aux particules de toutes sources et rapporter au moins un résultat en matière de santé respiratoire (symptômes respiratoires, fonction pulmonaire, diagnostics cliniques). Les données des études pertinentes ont été systématiquement extraites, le risque de biais évalué et une synthèse narrative fournie.

RÉSULTATS : Sur 14 études, 12 ont testé des fourneaux améliorés, la majorité utilisant la biomasse, mais également des fours solaires et du bioéthanol. Une étude a essayé des lampes solaires et la dernière, une intervention intégrée comprenant des éléments comportementaux et environnementaux pour la prévention et le traitement des bronchopneumopathie chronique obstructive. Sur les six études rapportant les pneumonies de l'enfant, aucune n'a démontré de bénéfice significatif en analyse d'intention de traiter. Dix études ont rapporté des évolutions de symptômes respiratoires avec une certaine amélioration: cependant cette évolution étant rapportée par les patients est hautement sujette à des biais. Une considérable hétérogénéité clinique et méthodologique entre études n'a pas permis de calculer des estimations de l'effet combiné.

CONCLUSION : Les résultats des RCT réalisés à ce jour suggèrent que des interventions individuelles au niveau des foyers visant à réduire l'exposition à la pollution de l'air ont des bénéfices limités en termes de santé respiratoire. Des approches plus complètes de réduction de l'exposition à la pollution aérienne doivent être élaborées et évaluées en termes de bénéfices potentiels pour la santé.

RESUMEN

MARCO DE REFERENCIA: La exposición a la contaminación ambiental y del aire en los espacios cerrados representa una amenaza importante a la salud respiratoria mundial, sobre todo en los países de ingresos bajos y medianos (LMIC). Los estudios clínicos de intervención se han centrado en estrategias sobre diferentes opciones de estufas y sus resultados han sido desiguales. Además de la cocción, otras fuentes de partículas también contribuyen a la carga de exposición a la contaminación del aire. En la presente revisión se analiza la evidencia actual proveniente de ensayos clínicos aleatorizados (RCT) sobre la efectividad clínica de las intervenciones de reducción de las partículas en los LMIC.

MÉTODO: Se realizó una búsqueda en 12 bases de datos y la literatura gris. Se consideraron aptos los RCT realizados en un LMIC, encaminados a disminuir la exposición a las partículas de cualquier tipo de fuente y que comunicaban por lo menos un resultado clínico respiratorio (síntomas respiratorios, función pulmonar, diagnósticos clínicos). Se extrajeron sistemáticamente los datos de los estudios pertinentes, se evaluó el riesgo de sesgo y se presenta una síntesis descriptiva de los resultados.

RESULTADOS: De los 14 estudios incluidos, en 12 se evaluaban estufas "mejoradas", la mayoría de las cuales de biomasa, pero también se incluyeron estufas alimentadas por energía solar o bioetanol. En un estudio se ensayaron lámparas que utilizaban energía solar y por último, una intervención integrada que incorporaba componentes comportamentales y medioambientales en la prevención de la enfermedad pulmonar obstructiva crónica y su tratamiento. De los seis estudios que comunicaban resultados sobre la neumonía en niños, ninguno demostró un beneficio significativo en el análisis por intención de tratar. Diez estudios notificaban resultados sobre síntomas respiratorios y referían algunas mejorías, pero estos resultados autorreferidos eran muy propensos al sesgo. La marcada heterogeneidad clínica y metodológica entre los estudios impidió el cálculo de estimaciones de efectos combinados.

CONCLUSIÓN: La evidencia, según los RCT realizados hasta la fecha, indica que las intervenciones en domicilios individuales destinadas a disminuir la contaminación del aire ofrecen beneficios limitados en materia de salud respiratoria. Es imprescindible elaborar estrategias más exhaustivas de disminución de la contaminación del aire y evaluar sus posibles efectos benéficos sobre la salud.