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Evaluation of the effects of clean-burning cookstoves on indoor air pollution and their effects on acute respiratory diseases among children

By

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Doctor of Philosophy

Epidemiology

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An abstract of
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Abstract

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Acute lower respiratory infections (ALRI) contribute to nearly 20% of child mortality globally. Household air pollution (HAP) from burning biomass fuels is a potentially modifiable risk factor of childhood ALRI in developing countries. A large proportion of rural communities in developing countries, where childhood ALRI burden is high, use open fire and biomass fuels for cooking indoors. The three epidemiologic studies in this dissertation aimed to improve our understanding of HAP effects of on childhood ALRI. The first study (**aim 1**) evaluated the effectiveness of improved-combustion biomass stoves in reducing HAP and their acceptability to users in rural Western Kenya. In this pre-/post- intervention study, we compared 48-hour mean personal and kitchen concentrations of particulate matter <2.5μm in diameter ($PM_{2.5,}$ μg/m^3) and carbon monoxide (CO, ppm) during use of six improved combustion cookstoves to those observed with traditional 3-stone fire in 45 households. We assessed improved stove acceptability through interviews and focus groups. Reductions in kitchen $PM_{2.5}$ and CO ranged by stove type from 11.9% to 42.3% and from -5.8% to 34.5%, respectively. Mean kitchen $PM_{2.5}$ (319 to 518μg/m^3) were still considerably higher than WHO indoor air quality guidelines. Women found these stoves acceptable for use but also reported limitations for each. Achieving maximal potential of improved stoves requires adherence to more exclusive use and addressing user reported limitations.

The second study (**aim 2**) evaluated the levels of HAP associated with childhood ALRI through systematic review of literature. We identified 32 studies of household or ambient air pollution, or of second hand smoke effects on ALRI. We conducted meta-analysis and examined the dose-response relationship between PM2.5 and childhood ALRI risk. We found a weak positive association (RR 1.04; 95% CI 1.03, 1.06) and a positive dose-response relationship between the levels of exposure to PM2.5 and ALRI risk. However, due to high level of heterogeneity, the summary estimate should be interpreted with caution. High-quality intervention-based evidence with personal exposure assessment is needed to better quantify exposure-disease relationship.

Lastly, in a prospective cohort study in rural Peru, we evaluated an association between HAP and carriage of *Streptococcus pneumonia* (pneumococcus), one of the major bacterial causes of ALRI in children (**aim 3**). We found no association between kitchen and personal CO levels and density of pneumococcal carriage. More efficient biomass stoves and stoves utilizing clean fuels are needed to achieve measurable health benefits. Results of these studies will help guide policy decisions targeting improvements to indoor air quality to maximize health benefits. The findings of this dissertation should assist organizations working on HAP research and help identify effective stove interventions and potential confounders for further intervention studies of HAP effects on ALRI.

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Introduction and Relevance

Acute lower respiratory infections (ALRI) are the most important cause of death among children less than 5 years of age and contribute to nearly 20% of child mortality globally.[1],[2] A growing body of evidence suggests the link between poor indoor air quality and ALRI in children under age 5 in developing countries.[3-6] Nearly 3 billion people worldwide use solid fuel as their main household fuel source, and household air pollution (HAP) from the burning of biomass fuels was identified as a potentially modifiable risk factor for childhood respiratory infections, including pneumonia. World Health Organization report recently concluded that improved-combustion stoves, improved ventilation, and / or reduced use of solid fuels would help reduce pneumonia morbidity and mortality in children[3].

A large proportion of rural communities in Africa and other parts of the developing world use open fire and biomass fuels for cooking indoors. Given high burden of childhood pneumonia in these populations, we believe that the results of the studies described here can us help understand the burden of pneumonia attributable to HAP from burning of biomass fuel and help guide policy decisions targeting improvements to indoor air quality which would maximize health benefits.

Specifically, results of the first research study (**specific aim 1**) will help identify one or more cookstoves with the potential to reduce indoor pollutants generated from burning biomass fuels to the levels that would benefit health outcomes. These improved stoves can be used as interventions in future clinical trials designed to demonstrate to local policy-makers health benefits of improved stove use, and to promote large-scale uptake of improved biomass stove technologies in populations using open fire for cooking indoors. The second study (**specific aim 2**) will help place the findings of the first study into a broader context needed to understand the levels of HAP associated with health effects. We will estimate the expected impact from improving HAP on childhood pneumonia by developing a dose-response model for the relationship between indoor levels of particulate matter less than 2.5 microns (PM2.5) and the risk of childhood pneumonia. The results of this analysis will allow estimation of the burden of childhood pneumonia attributable to the observed levels of PM2.5. Lastly, to help demonstrate an association between HAP and *Streptococcus pneumonia* (pneumococcus), one of the major bacterial pathogens causing pneumonia in young children, the association between indoor levels of carbon monoxide and density of pneumococcal nasopharyngeal colonization (a risk factor for pneumococcal pneumonia) in young children will be evaluated (**specific aim 3**).

Specific aims

To study the effects of clean burning cookstoves on household air pollution and child health, the following specific aims will be addressed:

1. To evaluate (a) the effectiveness of 6 improved biomass stoves in reducing indoor levels of PM2.5 and CO and personal exposures to household air pollution from biomass fuel, as compared to traditional 3-stone fire and (b) their acceptability in rural Western Kenya
2. To estimate the impact of household air pollution on childhood pneumonia based on measured reductions in levels of PM2.5 through systematic review and meta-analysis
3. To evaluate the association between kitchen levels of CO and density of nasopharyngeal carriage of Streptococcus pneumonia among young children in rural Peru

Literature Review

Household air pollution and acute lower respiratory diseases

Acute lower respiratory infections (ALRI) are the most important cause of death among children less than 5 years of age and contribute to nearly 20% of child mortality globally.[1, 2, 7] According to Global Disease Burden report in 2010, ALRIs are responsible for 5% of disease burden.[7] ALRI are defined in the International Classification of Diseases as infections of the airways below the epiglottis and include laryngitis, tracheitis, bronchitis, bronchiolitis as well as infections of the lung - pneumonia, severe pneumonia and very severe pneumonia, as defined by the World Health Organization.[6] Household air pollution (HAP) resulting from biomass smoke has been identified as a third leading cause of morbidity globally and one of the leading risk factors for childhood respiratory illnesses.[6, 7] A growing body of evidence suggests a link between poor indoor air quality and ALRI in children under age 5 in developing countries.[3-6] The majority of published studies are observational studies and only one is a randomized trial using an intervention to reduce HAP (the RESPIRE study conducted in Guatemala).[4] The overall pooled odds ratio in a recent meta-analysis for risk of developing pneumonia associated with HAP due to use of unprocessed solid fuel was 1.78 (95% confidence interval [95%CI] 1.45-2.18), but there was evidence of publication bias and heterogeneity.[3] The published studies are characterized by methodological weaknesses, mainly due to a wide range of methods of assessing exposure to HAP and a variable and wide range of approaches to detection of childhood pneumonia[8], including parent/care giver recall of a respiratory illness and fast breathing in the prior 2 weeks. A slightly higher odds ratio of 3.53 (95%CI 1.94-6.43) for children developing acute respiratory infection was reported in the metanalaysis by Po and colleagues.[9]

Nearly 3 billion people worldwide use solid fuel as their main household fuel source, and in 1995, HAP from the burning of biomass fuels was identified as a potentially modifiable risk factor for childhood respiratory infections, including pneumonia.[10] WHO guideline level for annual average kitchen $PM_{2.5}$ of $10\mu g/m^3$, and the intermediate target is $35\mu g/m^3$;[11] however, kitchen levels in many households using biomass fuel for cooking exceed these targets by several orders of magnitude.[5] It was recently concluded by the World Health Organization that improved-combustion stoves, improved ventilation, and / or reduced use of solid fuels would help reduce pneumonia morbidity and mortality in children[3]. Traditional cooking areas often involve use of an open fire with fuel such as coal or firewood, either inside or outside the house. Several types of improved stoves have been introduced in areas using biomass as their primary source of fuel, with mixed results.[3, 5] These interventions have ranged from mechanical, such as adding a chimney to an existing stove to using more improved stoves which use a more confined burning area to moderate oxygen access and increase combustion, and / or fuel-based, such as changing from solid biomass fuels (e.g. wood) to liquid fuels (e.g. natural gas or kerosene).

Studies in many regions including Kenya, China, Sudan, Nepal, Guatemala, and Bangladesh have found improved stoves to be beneficial to health and quality of life.[12-16] The relatively low cost of many improved stoves makes these a highly practical intervention for many communities dealing with high levels of HAP from traditional biomass-burning stoves. However, studies integrating evaluation of acceptability to local users with an assessment of impact of improved cookstoves use on indoor air quality are lacking.[17] In addition, few studies measure directly household air pollution in the cooking area along with personal exposure monitoring, qualitative assessment of user perspectives, and can integrate these findings for a number of different makes of improved cookstoves.

Exposure assessment in studies of household air pollution and health effects

Three-stone fire pits used in many parts of developing world for indoor cooking have very low combustion efficiency and, as a result, indoor smoke from biomass burning produces a range of harmful chemicals. Combustion of solid fuels produces a range of harmful substances including inhalable particulate matter (PM), carbon monoxide (CO), oxides of nitrogen and volatile/semi-volatile organic compounds (e.g. polycyclic aromatic hydrocarbons or PAHs, 1,3 butadiene, formaldehyde and benzene).[18] The amounts and relative proportions of air pollutants generated by solid fuels are dependent on several of factors, including fuel type and condition (moisture content), ventilation, and stove technology.[18] In addition to these factors, human behavior, malnourishment, underlying chronic health conditions, weather conditions, and other sources of indoor and outdoor pollution all contribute to variability in assessing human exposure and dose.[19] Seasonality impacts cooking behaviors (e.g. during rainy, cold seasons, more indoor cooking takes place) and, therefore, measurements of HAP may not represent exposures that occur indoors during the year.[20] In addition, it is important to consider duration for measurements of both indoor and personal exposures because daily changes to behaviors can influence the findings.[20] Studies have used 24-hour to several days as the length of exposure monitoring period. The ability to evaluate an effect of exposure on a health outcome depends on the ability to properly assign the magnitude and variation of exposure at an individual or group level. In studies of exposures to HAP from cookstove emissions, accurate exposure assessment is impeded by many factors, including wide variations in emissions between cookstoves and from the same cookstove over time, and variations in human behaviors that affect exposures both between individuals and for the same individual over time. In many cases, precise measurements of ambient concentrations of environmental agents are not possible due either to logistics or costs, and the use of indirect or surrogate measures add to uncertainty and imprecision.

In studies of improved cookstoves, exposures can be measured indirectly through categorical assignments based on type of cookstove (i.e. presence of an improved cookstove determines an exposure status), and through surveys or questionnaires that evaluate cookstove type and use along with behavioral factors, such as cooking practices and fuel preferences. Exposures can also be measured directly through air sampling of a specific area or through air samplers worn by an individual person. Several approaches have been used to assess exposures to HAP from cookstoves including exposure indicators, direct measurements of HAP, and personal exposures to HAP. Most epidemiological studies have used indirect measures of exposure to biomass smoke, such as fuel or housing type, which are less reliable than direct measurements of personal exposure.[5, 15, 19] Exposure indicators are usually obtained via questionnaire, survey, or diary and are typically used to categorize the degree of exposure. This form of exposure assignment may be suggestive of categorical differences in exposure between groups but provides little evidence, if any, concerning temporal variations in exposure or inter-person differences related to behavioral and physiological factors. Data on exposure indicators are relatively easy to collect but yield coarse resolution information (both spatial and temporal) with which to characterize exposure. Measured surrogates for personal exposure, such as area measurements, have also not proven to be reliable.[19]

Direct measurements of HAP (in the kitchen or cooking area) provide a better resolution of pollutant concentrations. Most studies have shown area measurements of HAP are not well correlated with direct measurements of personal exposures.[19, 21] However, personal monitors used in field evaluations come with limitations: traditional personal monitors do not account for variations in breathing volume and inhaled dose, while active personal monitors can be expensive and, therefore, impractical for use in large field studies. Exposure misclassification (e.g. inadequate assessment of personal exposures from surrogate metrics) has been shown to bias the magnitude of effects estimates in epidemiological studies.[22] Field validation studies of individual-level assessment of exposures to biomass combustion products are necessary to reduce exposure errors. Another potential benefit of personal exposure monitoring is the ability for individuals to achieve greater understanding of how their own behaviors influence exposure and risk and modify their behaviors accordingly.

Traditional measurements of PM can be more difficult to conduct in field settings as it often requires use of expensive equipment with a sampling pump and filter. One method of particulate matter measurement involves collection of gravimetric $PM_{2.5}$ sample, a time-integrated sample collected using an active pump (Casella, Buffalo, NY, USA) with a BGI Triplex Cyclone (BGI Incorporated, Waltham, MA, USA), and 37 mm Teflon membranes (Pall, Port Washington, NY, USA). This equipment requires a pre- and post-calibrations in the field using either a rotameter (AALBORG, Orangeburg, NY, USA) or a Dry Cal DC-Lite (Bios International, Butler, NJ, USA). Gravimetric analysis of the filters is conducted after conditioning in temperature- and humidity-controlled environments for 24 hours. Another method involves real-time $PM_{2.5}$ concentrations which can be measured in the kitchen using a portable, battery-operated UCB Particle and Temperature Sensor that can measure $PM_{2.5}$ concentrations between 0.030 mg/m^3 and 25.0 mg/m^3 (UCB-PATS, Berkeley Air Monitoring Group, CA, USA). This type of equipment cannot be used for personal PM monitoring but recently personal PM2.5 monitors have been developed and are starting to be utilized in the field.

Carbon monoxide, a key component of biomass smoke by mass,[23] is easier to measure using relatively inexpensive and lightweight devices to measure both kitchen and personal levels simultaneously. A real-time device for CO measurement (GasBadge Pro, Industrial Scientific, Oakdale, PA, USA) and a passive colorimetric device, Draeger Color Diffusion Tube (Draeger, Pittsburgh, PA, USA) that provides a time-weighted average (TWA) concentration with detection limits between 6 and 600 ppm-hours can be employed for both kitchen and personal CO monitoring. Both instruments can be attached to a string and worn around the neck of adults. Passive tube can also be placed in a holder and be attached to back of clothing for children. At the end of the sampling period, the colorimetric reaction in tubes is measured and concentration (parts per million) is calculated using the colorimetric reaction measurement and sampling time. Use of CO as a marker for $PM_{2.5}$ has been suggested in previous studies.[23, 24]

However, even when a relationship between kitchen CO and $PM_{2.5}$ is demonstrated, this relationship may not be extrapolated to other settings with different cooking behaviors, fuel and stove types.

Preliminary studies in rural Kenya

Figure 1. Traditional 3-stone fire pits used in rural Kenya for cooking.

Much of the poor indoor air quality in developing countries is attributed to incomplete combustion of biomass using simple stoves, such as the three-stone fire pits (Figure 1) used in rural Kenya. Although improved stoves that increase combustion and decrease smoke output are relatively simple to construct and can be made with locally available materials, relatively few people in rural Western Kenya utilize these technologies.[25, 26] A pilot study conducted in Nyando Division identified that nearly all (>99%) of survey respondents used three-stone stoves for cooking, almost three-fourths (72%) cooked inside the home, and cooking frequently occurred in a kitchen located in the same room where people lived or slept.[25] Biomass fuel is the predominant source of fuel for this area. This pilot study evaluated whether locally manufactured Jiko Kisasa stoves can improve indoor air quality and reduce lower respiratory infections. Results from this pilot suggest that, although Jiko Kisasa stoves remove visible smoke and are very acceptable to the local population, they were not found to be effective in reducing particles less than 2.5 microns in diameter ($PM_{2.5}$) to levels of exposure that would likely have an impact on childhood pneumonia and health.[26]

Several new stove technologies have been evaluated in the laboratory setting and have been shown to be effective in reducing household air pollution.[27] Several improved stoves outperformed the open fire in the controlled laboratory settings in terms of fuel efficiency, time required to boil water, reductions in particulate matter and carbon monoxide.[27] (USAID Evaluation of Manufactured Wood Stoves in Dadaab Refugee Camps, Kenya)

A review of available stove technologies was conducted to identify candidate stoves with the evidence of low emissions and fuel efficiency based on laboratory testing or controlled field-testing. Six improved stoves have been evaluated through focus groups and controlled cooking test to assess preliminary evidence of acceptability to local women in rural Western Kenya and efficiency. This component included 1) an introduction of the new stoves to the community through open community meetings where the stoves were presented to the community and community reactions noted; 2) an initial cooking trial and focus group discussions with 30 women (5 groups of 6 women) and 6 different stoves (2 different stoves per each cook) to test acceptability and functionality of the stoves for the main study.

Studies evaluating acceptability, sustainability, and impact on indoor air quality and personal exposures of these improved cookstoves in a setting of everyday stove use are lacking. If proven effective in reducing household air pollution and personal exposures to wood smoke in a setting of everyday use, these stoves should be evaluated as primary interventions in experimental studies evaluating the effect of improving indoor air quality on reducing childhood pneumonia.

Case definitions for pneumonia and implications for intervention trials and observational studies

The diagnosis of pneumonia/ALRI is challenging, especially in developing country settings, where burden of ALRI and mortality from childhood pneumonia is highest. There is a gap in our understanding of ALRIs being studied and the impact improved cookstoves and clean fuels can have. Acute lower respiratory infections (ALRI) are defined in the International Classification of Diseases as infections affecting airways below the epiglottis and including acute manifestations of laryngitis, tracheitis, bronchitis, bronchiolitis, lung infections or any combination among them, or with upper respiratory infections, including influenza. The proper diagnosis and classification of cases of ALRI in studies evaluating disease burden or intervention trials is critical to allow for comparisons across studies. Standardized case definitions applied in intervention trials allow for a more accurate estimation of disease burden preventable through the intervention evaluated, and the comparisons can be made across studies and different regions of the world. In addition, understanding of disease burden preventable through intervention is critical when designing new intervention trials to estimate the sample size based on expected size of effect against pre-determined endpoints.

Community health worker diagnosed pneumonia

ALRI studies conducted in developing countries settings often employ regular home surveillance of a cohort of children by field workers. Enumerators can range from community members, trained community health workers, medical professionals (nurses or physicians) or teams composed of combinations of the above.[4, 28] It has been shown that the enumerators with higher training level are generally associated with lower reported ALRI incidence estimates largely due to case definitions applied that have higher specificity for identifying ALRI.[1]

Clinically diagnosed pneumonia or severe pneumonia

Some ALRI studies in addition to identification and diagnosis by field workers require confirmation of any ALRI episode by a facility-based clinician. Trained clinician confirmation of ALRI improves reliability of diagnosis and allows for comparison of disease burden estimates and the magnitude of intervention impact across the studies. The WHO definition for clinical pneumonia for children <5 years old includes cough and difficulty breathing and fast breathing (respiratory rate ≥60 breaths/min in children <2 months; ≥50 breaths/min in children 2–11 months; ≥40 breaths/min in children 1–4 years) or lower chest wall indrawing.[29] The WHO definitions include the presence of lower chest wall indrawing as the main sign of pneumonia severity. Other indicators of pneumonia severity considered in studies include nasal flaring noisy breathing, vomiting, refusal to breastfeed, respiratory rate >70 breaths/min, illness prompting a visit to a health facility, cyanosis. A more objective method of defining severe pneumonia is hypoxemia from pulse oxymetry but these data are often difficult to obtain in field settings in developing countries.[30]

Radiologically confirmed pneumonia

The clinical criteria for the diagnosis of ALRI may vary among studies, and the use of radiological criteria have been proposed for defining ALRI episodes. This definition has been shown to be likely due to bacterial agents such as *Haemophilus influenzae* type b and *Streptococcus pneumoniae*.[31] Chest X-rays are considered more specific than clinical criteria for identification of severe pneumonia often associated with bacterial etiology. When standard procedures for taking and interpreting the chest X-rays are being used, the estimates of disease burden and impact measured through intervention studies can be compared across settings. The WHO Vaccines and Biologicals Program (VAB) developed a computer-based training program to help standardize chest x-ray interpretation.[32] The WHO Pneumonia Vaccine Trialists Group classifies cases of suspected ALRI into the following categories: 1) primary endpoint pneumonia with endpoint consolidation or pleural effusion (definition consistent with bacterial etiologies of pneumonia) [31]; 2) other consolidation/non-end point infiltrate in the absence of a pleural effusion; and 3) no consolidation/infiltrate/effusion.[32] These definitions have been used in pneumococcal and Hib vaccine intervention trials to estimate vaccine preventable fraction of pneumonia by applying efficacy estimates from these trials to local pneumonia burden.[33, 34] Additional studies have demonstrated that the use of C-reactive protein in conjunction with standard chest x-ray reading can optimize sensitivity without jeopardizing the specificity of pneumonia case definition used in trials of pneumococcal conjugate vaccine.[35, 36]

Biological mechanism for the association between household air pollution and pneumonia

Biological mechanism for HAP causing pneumonia is not precisely understood. Exposure to increased levels of PM2.5 may lead to increase in ALRI through several mechanisms, including structural damage, transport of pathogens, and immune dysregulation. The described mechanism likely includes inflammation in the upper airway and lung, providing a potential portal for invasion of bacterial, viral, mycobacterial and other pathogens. Inflammatory process in the lung can increased alveolar permeability and, thus, exposure to PM2.5, particles size capable of penetrating the lung into alveoli, can increase the risk of ALRI or worsen the course of illness. In the mouse model, exposure to gamma interferon aerosol followed by concentrated ambient particles from urban air prior to infection with *S. pneumoniae* resulted in enhanced lung inflammation (increased PMN recruitment to the lung and elevated pro-inflammatory cytokine mRNAs), impaired bacterial clearance and reduced bacterial uptake by alveolar macrophages and PMNs.[37] Similar mechanisms may also apply to exposure to tobacco smoking that was recently associated with childhood pneumonia in a population-based study in Vietnam.[38] In addition, as reviewed by Domagala-Kulawik, smoke from any source can interfere with immune function including alveolar macrophage function which is critical to host defense.[39] Particles can impair alveolar macrophage superoxide production which can reduce their ability to kill respiratory pathogens.[40]

Streptococcus pneumoniae as a major cause of pneumonia in children

Streptococcus pneumoniae (pneumococcus) is a gram-positive bacterium and is a leading cause of serious illness, including bacteremia, meningitis, and pneumonia among children and adults worldwide.[41] Pneumococcus is a most common bacterial cause of pneumonia.[42] Disease rates are highest in children <5 years and in the elderly.[43, 44] Pneumococcal disease is endemic worldwide, but disease incidence varies geographically. Rates of disease and deaths are higher in developing world than in industrialized countries.[42] Risk factors for pneumococcal infection include young age (<2 years), underlying immunodeficiency (such as HIV infection or AIDS), certain other chronic medical conditions, day care attendance, exposure to tobacco smoke, and preceding viral infection (influenza).[45] Invasive pneumococcal infection rates are also higher among indigenous populations of Australia and New Zealand and among the Black, Alaska Native and American Indian populations in the United States relative to the general population.[45-47]

Pneumococcal carriage and risk factors

Several bacterial pathogens, including pneumococcus, normally reside in the nasopharynx. Although nasopharyngeal colonization does not necessarily lead to infection, it is considered to be an important precursor for infection with several respiratory pathogens. *S. pneumoniae* colonizes nasopharyngeal flora of healthy individuals and person-to-person transmission of this bacteria occurs through contact with secretion of colonized individuals.[48] Most children acquire pneumococcus from family members during their first month of life but the rates of acquisition differ greatly among 94 pneumococcal serotypes described to date, by age group, season, and geography. Crowding, close contact with young children, high rates of respiratory infections, and exposure to HAP pollution have been described as risk factors for pneumococcal colonization; however, exact reasons for increased susceptibility are not precisely understood.[48] Length of colonization can also vary by age (younger infants have longer period of colonization) and by immunogenicity of pneumococcal serotypes (serotypes leading to poor immune response tend to be carried longer). Carriage is more common and with longer duration among children than among adults.[49] Carriage rates are higher among certain ethnic groups and acquisition of carriage is noted earlier in life among children in developing countries than in industrialized settings. In South Africa, pneumococcal carriage was 30% among children sampled at age 6 weeks, 44% at 10 weeks, 51% at 14 weeks and 61% at age 9 months.[50] In Alaska, the prevalence of pneumococcal carriage among Alaska Native children living in rural villages was approximately 60%.[51] In contrast, carriage among children of similar age in the general population in Boston was approximately 25%.[52]

Pneumococcal colonization is relatively common among children but the factors leading to development of pneumococcal disease (e.g. otitis media, pneumonia, bacteremia, or meningitis) are poorly understood. It has been described that exposure to high levels of HAP generated by burning biomass fuels in the kitchen can lead to damage of respiratory epithelium and further development of serious respiratory infections.[5, 40] Whether exposure to HAP pollution plays a role in the dynamics of the pneumococcal carriage has yet to be determined

Density of pneumococcal carriage

It has been hypothesized that pneumococcal nasopharyngeal proliferation, leading to higher density of carriage, can result in micro-aspiration of bacteria leading to pneumonia.[53, 54] Quantitative real-time polymerase-chain reaction (rtPCR) targeting the main pneumococcal autolysin *lytA* on nasopharyngeal swab samples demonstrated pneumococci in more than 50% of HIV-infected adults with community acquired pneumonia and demonstrated correlation of pneumococcal colonization density among adults with pneumonia compared to asymptomatic controls.[53] In another study, an increased pneumococcal load in nasopharynx was independently associated with radiologically-confirmed pneumonia in children.[55] The same study observed an association between pneumococcal load and viral coinfection in children (influenza A, rhinovirus, and RSV). In another study, higher density nasopharyngeal colonization was more common in Vietnamese children with pneumonia (49%) than among children with acute bronchitis (29%) or healthy children (17%).[56] A large multi-center pneumonia etiology case-control study among children found a strong association between density of pneumococcal colonization and microbiologically diagnosed pneumonia.[57] Among factors contributing to increased density of pneumococcal carriage, viral co-infection has been described in several studies. As one of the mechanisms explaining the relationship between pneumococcal colonization, viral co-infection, and development of childhood pneumonia, these studies support the hypothesis that presence of viral infection may lead to increased attachment of pneumococci to virus-infected cells in nasopharynx, which will lead to increased bacterial load, invasion, spread into lower respiratory tract, and pneumonia.[55, 58-60] Whether exposure to HAP pollution plays a role in the density of pneumococcal colonization has not been demonstrated.

Effectiveness of six improved cookstoves in reducing household air pollution and their acceptability in rural Western Kenya

Abstract

Background: Household air pollution (HAP) from biomass fuel burning is linked to poor health outcomes. Improved biomass cookstoves (ICS) have the potential to improve HAP.

Objectives: A pre-/post- intervention study assessed the impact of six ICS on indoor air quality and acceptability of ICS to local users in rural Western Kenya.

Methods: We measured mean personal and kitchen level concentrations of particulate matter <2.5µm in diameter ($PM_{2.5}$, µg/m^3) and carbon monoxide (CO, ppm) during the 48-hour period of each ICS use in 45 households. We compared these levels to those observed with traditional 3-stone fire (TSF) use. We assessed ICS acceptability through interviews and focus groups. We evaluated association of stove type, fuel use, and factors related to cooking practices with mean kitchen $PM_{2.5}$ and CO using multivariable regression.

Results: Stove type, exclusive ICS use (vs. concurrent TSF use), and the amount of fuel used were independently associated with kitchen $PM_{2.5}$ and CO levels. Reductions (95%CI) in mean $PM_{2.5}$ compared to TSF, ranged by ICS from 11.9% (-19.3, 35.0) to 42.3% (21.1, 57.8). Reductions in kitchen CO compared to TSF, ranged by ICS from -5.8% (-39.6, 19.9) to 34.5% (10.6, 52.0). Mean kitchen $PM_{2.5}$ ranged from 319µg/m^3 to 518µg/m^3 by ICS. Women thought ICS were easy to use, more efficient, produced less smoke, and cooked faster, compared to TSF. Women also reported limitations for each ICS.

Conclusions: We documented reductions in HAP from ICS compared to TSF. The $PM_{2.5}$ levels with ICS use were still considerably higher than WHO indoor air quality guidelines. Achieving maximal potential of ICS requires adherence to more exclusive use and addressing user reported ICS limitations.

Background

A growing body of evidence suggests a link between household air pollution and poor health outcomes in developing countries.[3, 9, 61] Nearly three billion people worldwide rely on solid fuels (wood, animal dung, crop wastes, and charcoal) as their main household fuel source, and in most cases, this is burned on open fires or simple stoves with inadequate ventilation. The resulting household air pollution from biomass fuel burning is a potentially modifiable risk factor for childhood acute lower respiratory infections (ALRI). Observational studies and one clinical trial have demonstrated that improved-combustion stoves, improved ventilation, and reduced use of solid fuels would help reduce pneumonia morbidity and mortality in children.[3-5, 9] Recently published evidence on the relationships between particulate matter <2.5µm in diameter ($PM_{2.5}$) exposure and risk of a range of diseases [62] suggest that reductions in exposure to $\leq 35 \mu g/m^3$, intermediate target of annual average set by WHO, are needed to prevent the majority of attributable cases.[11]

A range of biomass stoves evaluated in a controlled laboratory setting by the US Environmental Protection Agency (EPA) have outperformed the open fire in terms of fuel efficiency, time required to boil water, and emissions of particulate matter and carbon monoxide (CO).[27] However, studies integrating evaluation of acceptability to local users with an assessment of impact of improved cookstoves (ICS) use on indoor air quality are lacking.[17] In addition, few studies measure directly household air pollution in the cooking area along with personal exposure monitoring, qualitative assessment of user perspectives, and can integrate these findings for a number of different makes of ICS. We conducted a study in a household setting in rural Western Kenya to determine whether everyday use of the six ICS, which in a laboratory setting reduce emissions by at least 50% compared to the open fire, would deliver levels of $PM_{2.5}$ and CO associated with substantially reduced health risks. We sought to determine both the acceptability of these stoves to local users as well as their effectiveness in reducing indoor concentrations and personal exposure.

Methods

Study design:

We conducted a single-arm pre-/post- intervention study to assess acceptability and performance of six ICS in a setting of daily stove use. In order to limit the inter-household variability in household air pollution levels related to individual household practices, size of the household, and ventilation due to house structure, we employed a cross-over design, which allowed for the evaluation of up to six ICS within one household.

Study population:

This study was implemented in two rural villages in Nyando Division, Nyanza Province, Western Kenya. Nyando Division has a population of approximately 80,000 people and 15,000 households.

Households with women of childbearing age (15-49 years old) and one or more children aged <5 years were identified in the two participating villages. To detect a significant (α=0.05) 20% reduction in mean $PM_{2.5}$ with the use of ICS in the household compared to TSF (paired sample), assuming 80% power and 40% coefficient of variation, 30 households needed to be enrolled for each ICS. Assuming each household tested 5-6 ICS and 10% attrition, 43 households were randomly selected from a list of eligible households in the two villages. Women who provided written consent to participate in the study were enrolled. Women 15-18 years old who were pregnant, married, or a parent were considered “mature minors” and were able to consent for their own participation in the study. Home visits were made to the enrolled households to conduct interviews to assess acceptability of ICS and to measure personal and kitchen level exposures to indoor air pollutants during the 48-hour baseline and follow-up monitoring periods.

Data collection:

Household visits:

Each household tested up to six ICS for two weeks per stove with a one-week break in between. We varied the order in which the stoves were tested in each household. Prior to installation of the ICS, the primary cooks in the household completed a brief questionnaire on current stove use, cooking practices, fuel collection and consumption, and socio-demographic information. Women were trained to use each ICS with a standardized training guide. Their traditional stove (TSF) remained in the home but the women were encouraged to use only the ICS for daily cooking. At the end of each 2-week period, we conducted individual interviews to gather information on stove use patterns, ease of use with local cooking pots, perceptions of smoke levels, cleanliness, safety, and taste, acceptability of cooking methods, comfort and ergonomics when preparing local dishes, and general perception of fuel consumption.

Study stoves

The ICS included in this study were EcoZoom, Prakti (chimney stove), Envirofit, Philips and Ecochula (both forced draft with rechargeable battery and solar-PV panel), and a locally-made ceramic stove, colloquially known as the rocket stove, with a thermoelectric insert enhancement (Rocket with TECA) (Appendix 1).[63] All ICS selected for the study performed well at the EPA laboratory ($\geq$50% reduction in $PM_{2.5}$ emissions compared to TSF)[27], were centrally manufactured, required no assembly, could be easily transported, were designed to burn wood, and were considered acceptable by local women during pilot cooking tests conducted prior to study initiation. The traditional TSF was employed as the baseline comparison cooking method.

In-depth interviews and focus groups

Views on stove characteristics, including efficiency, fuel consumption, health effects, cooking behaviors, and user acceptability were assessed through 262 structured interviews and 11 focus groups. Structured interviews conducted after each two-week period of ICS use assessed acceptability. Focus groups carried out after households had tested four stoves (round 4) and again at the end of the study explored participants' views on stove functionality, design and acceptability, as well as reasons for multiple stove use (i.e., concurrent use of TSF along with ICS).[64]

Kitchen Area and Personal Air Sampling

Air pollution monitoring was conducted at baseline (TSF) and for each ICS during the final 48 hours of the two-week intervention period. The air monitoring consisted of kitchen area air sampling and personal area air sampling. Concurrent 48-hour measurements of gravimetric $PM_{2.5}$, and real-time CO were conducted in the kitchen. The instrumentation was placed on the wall at 1.5 meters from the ground (i.e., approximately the height of the breathing zone). A time-integrated gravimetric $PM_{2.5}$ sample was collected using an active pump (Casella, Buffalo, NY, USA) with a BGI

Triplex Cyclone (BGI Incorporated, Waltham, MA, USA), and 37 mm Teflon membranes (Pall, Port Washington, NY, USA) (Appendix 2). Gravimetric analysis of the filters was conducted after conditioning in temperature- and humidity-controlled environments for 24 hours. Concomitant real-time CO measurements over a 48-hour period were conducted using a GasBadge Pro (Industrial Scientific, Oakdale, PA, USA), with detection limits between 0 -1,500 ppm, set at one-minute intervals; the mean of the measurements taken over the 48-hour sampling period was calculated.

Concomitantly with the indoor measurements, personal CO exposure was monitored in real-time. The GasBadge was worn by the woman and positioned near her breathing zone on her upper chest. The participants were instructed to wear the monitors at all times except when sleeping or bathing, when they placed the monitors next to their bed or bathing area. We assessed compliance to personal monitor use through unscheduled daily visits to participating households during the 48-hour monitoring period. We excluded personal samples collected when GasBadge was reported not to be worn. These exclusions represented <5% of all samples.

Improved stove use

We asked women to complete time activity diaries during each 48-hour monitoring period recording the duration of stove use (minutes) for each cooking episode, type of stove used, type of meal prepared, number of people cooked for, and duration of kerosene lamp use (hours). We also employed temperature data loggers to gather objective data on stove use for both the improved stoves and the traditional stove and to complement findings from time activity diaries. The results of stove use monitoring were reported separately.[65] We measured the amount of fuel used during each 48-hour monitoring period. Women participants were asked to collect sufficient fuel to last for 3 days; the collected fuel was weighed at the beginning and at the end of the 48-hour period.

Data analysis:

The cross-over design allows for within household comparisons of the effects of ICS on indoor air quality, and therefore, adjusts for time-independent factors, such as socioeconomic and demographic factors, house structure and ventilation. In addition, we adjusted for the effect of time (rounds of follow up approximately three weeks apart) on CO and $PM_{2.5}$ concentrations.

We estimated geometric mean concentrations for 48-hour gravimetric time-weighted $PM_{2.5}$ concentrations (μg/m3) and kitchen and personal (woman) CO real-time (ppm) obtained within households using each ICS type and for TSF within the corresponding households. We estimated changes in 48-hour mean (and median) kitchen $PM_{2.5}$ and in kitchen and personal (woman) CO for each ICS compared to TSF within each household. The same analysis was repeated, stratifying by multiple stove use (i.e., “stove stacking”) as reported by women using time-activity diaries. The data for $PM_{2.5}$ and CO were not normally distributed; therefore, comparisons employed the paired t-test with log-normal distribution. We also conducted sensitivity analysis using the sign test.

We used linear mixed effect models with log $PM_{2.5}$ or log CO as the dependent variable to evaluate the association of ICS type with kitchen concentrations of $PM_{2.5}$ and CO. The variability due to unexplained “between-household” differences was modeled as a random effect, allowing for “within household” comparisons between follow-up periods with improved stoves and TSF. The analysis was adjusted for time-dependent variables,

such as multiple stove use (i.e., “stove stacking”), average duration of cooking events, number of meals prepared, number of people cooked for, and amount of fuel used. The variables significant at $\alpha=0.05$ were retained in the final model. We evaluated potential confounding by time-dependent and time-independent variables in the final model. Estimated regression coefficients (and 95% confidence intervals) were exponentiated and subtracted from one to calculate adjusted percent reduction in 48-hour $PM_{2.5}$ and CO concentration for each improved stove type compared to TSF, use of improved stove only compared to multiple stove use, and per unit change for continuous variables.
We used SAS 9.3 software for quantitative data analysis and Dedoose software (SocioCultural Research Consultants© 2014) for qualitative data analysis.

Recordings of structured interviews and focus groups were translated by field workers from Luo to English, and subsequently transcribed. A thematic approach to data analysis was taken, drawing on published methods.[66] All interviews were coded and analyzed initially by round to identify any changes to findings over time. Data from each round were coded to the point of saturation for each stove and each theme.[64]

Funding source and ethical considerations:

Funding for the study was provided by the Centers for Disease Control and Prevention and The Morgan Stanley Foundation. The study was approved by the Institutional Review Boards of the Kenya Medical Research Institute (protocol number 2075) and the Centers for Disease Control and Prevention (protocol number 6155). The Institutional Review Board of the Centers for Disease Control and Prevention provided overall ethical oversight and approved the entire study.

Results

We identified 58 households meeting the eligibility criteria out of 181 households (total population 840) in the two participating villages. Forty-three households were randomly selected through initial draw, four were deemed ineligible following the initial visit (two did not have age-eligible children, one was planning to relocate during the study period, and one did not have a designated area for cooking) and were not enrolled. The replacement households were selected by randomly drawing from the remaining pool of eligible households. Three households dropped from the study (one each following the second, third, and fourth rounds). Two additional households were subsequently selected from the remaining pool and baseline assessment was repeated for the newly enrolled households. In total, 45 households participated in the study: 7 households received all 6 of the study stoves, 30 received 5 stoves, and the remaining 8 households received 2-4 stoves. Participating women were 17 to 45 years of age (mean (SD) age 28 years (7)); 38 (88%) were married and the remaining 5 (12%) were single mothers or widowed. The majority of women (93%) were comfortable with reading or writing, and 58% had completed at least primary education. Fifteen women (35%) farmed their own land, 9 (21%) owned their own business, 6 (13%) worked as day laborers, and the remaining 13 (30%) ran the household (Table 1.1).

No changes were noted in the average number of daily meals prepared, number of people cooked for, and duration of kerosene lamp use by follow up period and by stove type. Reductions in the average time spent cooking a meal were observed with all ICS compared to TSF, except for the Prakti (Table 1.2). Significant reductions ($p<0.01$) in average fuel consumed were found for all ICS.

Stove type, multiple stove use, and other factors associated with air quality

Reductions in mean $PM_{2.5}$ ranged from $109\mu g/m^3$ observed with EcoZoom to $357\mu g/m^3$ with Philips, with statistically significant reductions observed for four out of six ICS compared to TSF (Table 1.3). The largest mean reductions in kitchen CO of 3.4 ppm and personal CO (woman) of 1.7 ppm were observed with use of Envirofit and Ecochula, respectively. The largest median reduction in kitchen CO (2.7 ppm) was observed using Philips, with statistically significant reductions in kitchen CO observed only in households using Envirofit, Philips, and Prakti. Using univariate regression analysis, and accounting for correlated response within household by follow up period, stove type and amount of fuel used were significantly associated with mean kitchen $PM_{2.5}$ (Table 1.4). Each additional hour of kerosene lamp use was associated with 5% increase in mean kitchen $PM_{2.5}$. Univariable analysis of stove type, amount of fuel used, kerosene lamp use, average number of people cooked for, and average duration of cooking episode demonstrated significant associations with mean kitchen CO levels (Table 1.5). Although women were discouraged from using TSF during the monitoring period, 27% to 46% of women reported continued use of TSF along with ICS. Among households reporting exclusive use of ICS during the monitoring period (i.e., no stove stacking), overall larger reductions in $PM_{2.5}$ were observed compared to households reporting continued use of a TSF during the monitoring period (Table 1.6). Among households using only ICS, statistically significant reductions in $PM_{2.5}$ were observed for four ICS, while among stove-stacking households, significant reductions were observed only for two ICS. Among households using only ICS, statistically significant reductions in kitchen

CO concentrations were observed for 3 ICS and in personal (woman) CO concentrations for 5 ICS, while among stove-stacking households, significant reductions were observed only for one ICS, although the small sample size limited our ability to assess statistical significance for comparisons among households reporting multiple stove use. The lowest mean $PM_{2.5}$ concentrations (206μg/m^3), mean kitchen CO (2.4 ppm), and mean personal CO (0.7 ppm) concentrations were observed in households using solely Prakti (i.e., no stove stacking reported).

Stove type, use of only an improved stove (vs. stove stacking), and the amount of fuel used were the only independent predictors of 48-hour mean $PM_{2.5}$ (μg/m^3) in multivariable analysis. Percent reductions in mean $PM_{2.5}$ compared to TSF, adjusting for multiple stove use, and amount of fuel used, ranged from 11.9% for households using Ecochula to 42.3% for Philips (Table 1.4). Use of an improved stove only vs. stove stacking was associated with a 29% reduction in mean $PM_{2.5}$, while each additional kilogram of fuel consumed was associated with 3.0% increase in mean $PM_{2.5}$

Stove type, exclusive use of an improved stove (vs. stove stacking), and amount of fuel used were the only independent predictors of 48-hour mean kitchen CO levels in multivariable analysis (Table 1.5). Percent changes in kitchen CO compared to TSF, adjusting for multiple stove use and amount of fuel used, ranged from 5.8% increase for households using EcoZoom to 34.5% reduction for Philips. Use of the improved stove only vs. stove stacking was associated with 28% reduction in mean CO. Each additional kilogram of fuel consumed was associated with 3.1% increase in mean CO, adjusting for multiple stove use and stove type.

Factors associated with multiple stove use

Given that multiple stove use was an important and potentially modifiable predictor of mean kitchen $PM_{2.5}$ concentration, we evaluated factors associated with multiple stove use using a multivariate linear regression model. Number of people cooked for, the average length of each cooking episode, number of meals prepared during the monitoring period, stove type used, age of cook, and socioeconomic status were examined and found not to be associated with multiple stove use.

Qualitative findings

Analysis of information collected through structured interviews and focus groups indicated that the women liked ICS and found the stoves easy to use compared to the traditional TSF. Overall, women viewed ICS as more efficient, easier to light and retain heat, producing less smoke, and cooking faster. However, women did note that some of the ICS were not well-suited for cooking traditional dishes (EcoZoom and Prakti), had small combustion chambers that filled quickly with ash (EcoZoom), were slow to cook local food (Prakti and Rocket with TECA), or were difficult to use or light (Ecochula and EcoZoom).

During the final focus groups, women were asked to rank their first and second choice ICS. Points were allocated per ranking: 2 points for 1st choice and 1 point for 2nd choice. There were clear preferences for specific ICS with Philips fan stove ranked as first and Ecochula as (last) sixth (Table 1.7). The Philips was associated with the largest percent reductions in mean $PM_{2.5}$ and CO, the largest fuel savings (56% less fuel consumed compared to TSF), though this stove was not associated with the least amount of stove stacking (Table 1.2).

Women reported they liked Philips because of its cooking speed (cooks fastest), ease of use, portability, reduction in indoor smoke and fuel consumption. The concerns women expressed about Philips included the need to prepare small pieces of fuel, the need for constant supervision to maintain fire, instability of cooking pots, and the stove durability and availability of parts to maintain functionality (solar charger, battery). The study stove ranked the lowest by users (Ecochula) was associated with the lowest percent reduction in $PM_{2.5}$ and the second to lowest reduction in CO, though it ranked second in fuel savings.

Discussion

Results of our study evaluating six improved biomass stoves in rural Western Kenyan households demonstrated that in a setting of everyday use these stoves reduce indoor air pollutants and are acceptable to local women. To our knowledge, this is the first study to evaluate several improved stoves in the same set of households. We simultaneously measured the impact of short-term stove use on personal and kitchen levels of $PM_{2.5}$ and CO, and assessed the acceptability of these stoves to users through structured interviews and focus group discussions.

The baseline levels of kitchen $PM_{2.5}$ observed in our study households in Kenya are comparable to those reported in studies in Mexico[67] and India[68] but higher than in Guatemala[69], and are more than 20 times higher than WHO guideline values.[11] While modest reductions in levels of $PM_{2.5}$ were observed for all study stoves compared to the traditional TSF, only four of six stoves generated statistically significant reductions. Studies evaluating the effects of improved cookstove introductions in Guatemala[16, 69] and Mexico[67] demonstrated significant reductions in kitchen $PM_{2.5}$ and of larger magnitude compared to reductions observed in our study, while the study in India did not show significant reductions. An earlier study in the villages of the same district in Kenya found that the households using the locally made upesi jiko stove observed 13% lower kitchen $PM_{2.5}$ levels than households using a TSF, however this difference was not statistically significant despite reports by study participants of visible smoke reductions in households using upesi jikos (CDC unpublished data). Despite achieving percent reductions in mean kitchen 48-hour $PM_{2.5}$ levels of a larger magnitude in our study (ranging from 18% to 45%), none of the ICS achieved the WHO guideline level for annual average kitchen $PM_{2.5}$ of $10µg/m^3$, nor the intermediate target of $35µg/m^3$.[11]

Carbon monoxide is simpler to measure in field settings than particulate matter; the use of relatively inexpensive and lightweight devices allowed us to measure kitchen and personal levels simultaneously. The results of kitchen level CO measurements show reductions in mean 48-hour CO associated with the use of ICS, and these findings are consistent with the reductions observed in kitchen $PM_{2.5}$ by stove type and with the use of improved stoves exclusively. Use of CO as a marker for $PM_{2.5}$ has been suggested in previous studies. However, even though a moderately strong relationship between kitchen CO and $PM_{2.5}$ was demonstrated in our study population, this relationship may not be extrapolated to other settings with different cooking behaviors, fuel and stove types. Interpretation of personal CO results is further complicated by women’s behaviors.

Most participating women reported having duties other than cooking for their households which required them to leave the house for extended periods of time. We were not able to assess whether these behaviors changed between the monitoring periods. In addition, assessment of adherence to personal CO monitor use was based on self-report and periodic visits made during the monitoring period by the field officers. Nevertheless, our results show significant reductions in levels of personal CO for women during use of all ICS as compared to the baseline.

All ICS in this study were first evaluated in a controlled laboratory setting by USEPA and demonstrated >50% reduction in $PM_{2.5}$ emissions compared to TSF.[27] Several factors likely limited the reduction observed in kitchen $PM_{2.5}$ and CO during everyday use. Traditional TSF was used during the monitoring period along with the improved stove in 27% to 46% of households, depending on the ICS type evaluated. In our study, the largest reductions in kitchen mean 48-hour $PM_{2.5}$ and CO were observed among households using ICS only and exclusive use of ICS was an independent predictor of and was associated with an almost 30% reduction in mean kitchen levels of both $PM_{2.5}$ and CO. Continued use of traditional stoves alongside an improved stove has been reported in other studies.[67, 69] Among women's explanations for multiple stove use are convenience of having an additional stove, preference of TSF for certain local dishes or for accommodating large pots, or special family/community occasions requiring additional cooking capacity. One of our study stoves (Prakti) had a second burner, and women reported to like this characteristic that allowed them to "*…cook two things at the same time so fast…*" However, women also reported that the two burners on this stove were not functionally equivalent, and households with this stove also reported using the

TSF more often during the monitoring period. While we were not able to identify any modifiable predictors of multiple stove use, qualitative data suggest that addressing stove design limitations, such as having stoves with two functional burners, ability to accommodate large pots, and capacity to simmer food slowly will help meet cooking needs of users. Qualitative data suggest that women may view ICS as an additional household tool used for cooking rather than a replacement stove, and future studies should take this into account when selecting an acceptable intervention.

Kerosene lamps likely contributed to high levels of kitchen $PM_{2.5}$ observed in our study households. Study participants reported using kerosene lamps on average 6 hours per day indoors. The duration of lamp use did not vary by follow up period or by stove type used and was not an independent predictor of kitchen $PM_{2.5}$ or CO level. We were not able to measure the contribution of the kerosene lamp to 48-hour mean kitchen $PM_{2.5}$ directly, nor were we able to adjust the analysis for the type of kerosene lamp used in each household. However, duration of kerosene lamp use was positively associated with kitchen levels of $PM_{2.5}$ and CO. Studies have demonstrated that use of the crudest "simple-wick" kerosene lamps contributes to indoor levels of $PM_{2.5}$ that are an order of magnitude greater than WHO air quality guidelines.[70, 71] Increasing availability of light emitting diode (LED) or solar powered lamps can help reduce contribution from kerosene lamps to indoor pollution.

Our study was not statistically powered to make direct comparisons among the improved stoves in their effectiveness to reduce indoor air pollution. However, during in-depth interviews and focus group discussions, women's stove preferences clearly emerged. We outlined women's ranking of, and views on, the stoves including a number of stove characteristics that the women valued as well as those that made the stoves less popular. Although we are not able to directly link women's preferences toward improved stoves to actual stove use and performance, it may be reasonable to assume that certain stove characteristics viewed by users as favorable are likely to improve the adherence to stove use. Consequently, we could expect that the stoves women ranked the highest overall and in terms of certain characteristics will be used exclusively more often and will achieve the highest $PM_{2.5}$ reductions. While our data supports part of this assumption, given that the stove ranked the highest overall and based on several characteristics (Phillips) was also the one associated with the largest reductions in kitchen $PM_{2.5}$ and CO, the same Phillips stove did not have the highest level of exclusive use. Likewise, while the stove ranked the lowest (Ecochula) was associated with the lowest percent reductions in $PM_{2.5}$, this stove was not associated with the highest proportion of multiple stove use. We should also note that stoves ranked as second or third were also associated with similar reductions in $PM_{2.5}$, and this ranking does not necessarily imply that women disliked the stoves as compared to the TSF but rather demonstrates how they ranked the stoves relative to each other. A number of factors we identified related to stove preferences that may impact on stove use concur with the literature on barriers and facilitators to scaling up of improved cookstoves.[72] Many of these factors could be taken into account and addressed by the stove manufacturers.

Exposure-response analysis from the randomized controlled trial in Guatemala suggests that achieving exposure reduction needed for prevention of child pneumonia may require use of clean fuels or biomass stoves with cleaner combustion. [4] Recently developed integrated exposure-response functions for five disease outcomes suggests that for the

ALRI outcome the shape of the curve is steeper at lower levels of $PM_{2.5}$ and flattens out at levels higher than 300 µg/ml.[62] Therefore, the relatively modest reductions in kitchen $PM_{2.5}$ observed in our study, would translate into small reduction in estimated relative risk for the ICS compared to TSF given high levels of exposure observed at baseline. At lower baseline levels of exposure, a similar magnitude of reduction in $PM_{2.5}$ is expected to result in larger effect on ALRI risk. Based on this model prediction, exposure has to reach the level at or below the WHO intermediate target level of 35µg/m^3 for $PM_{2.5}$ to lead to substantial ALRI risk reduction. These findings demonstrate the need for more effective solid fuel interventions, clean fuels, and more exclusive use of these, to reduce high baseline indoor levels further and lead to lower personal exposures and a larger health impact.

The traditional TSFs are easy to assemble and could have been built and taken apart anytime during the monitoring period. In this analysis, we used time-activity diaries as a source of stove use data, and women may have underreported TSF use which would have underestimated the measured impact of improved stoves. Even though we collected data on stove use using temperature data loggers, in about 25% of the study days these measurements were missing due to the operational constraints or malfunctioning of temperature data loggers.[65] As a result, stove use data collected through temperature data loggers in this analysis would have limited our sample size. In addition, the short-term follow up with each improved stove does not allow for continuous education on stove use over time, which may lead to a greater familiarity with and in turn adherence to stove use. Introduction of improved stoves into households requires a significant behavioral change for women, as it often involves changing the cooking position, chopping wood into smaller pieces, and the need for closer monitoring of the cooking process to ensure continuous combustion. The impact of the stoves on indoor air quality may improve with longer use of acceptable stoves or may worsen if the stoves are no longer used or lose functionality due to required maintenance. Therefore, longer-term impact of improved stoves, for example over a 12 month period, should also be evaluated.

We limited the influence of household level factors that could be related to stove use or household air pollution by conducting measurements at baseline and after installation of each improved stove within the same households. Although changes in daily activities could still have influenced the findings, the behaviors measured during each follow up period (e.g., number of people cooked for, average time spent cooking a meal, number of cooking events) did not differ by follow up period.

The results of this study have implications for future health impact studies seeking to identify an effective and acceptable intervention that can demonstrate health benefits. Evaluation of stove acceptability by local users is essential during the design phase as well as prior to use in intervention trials or large-scale dissemination. All the study stoves performed better in a controlled laboratory setting, and our field evaluation demonstrated that women’s cooking patterns and behaviors clearly influence ICS performance. Unless the stoves meet the needs and priorities of target users, biomass stoves are unlikely to make an impact on household air pollution. When designing ICS to improve household air pollution, the stove manufacturers should take into account the needs and preferences of users. In addition, more rigorous communication on proper stove use and education on health benefits of improved air quality to influence behavior change and promote adherence to stove use can help maximize benefits of ICS. A more thorough evaluation of other potential sources of indoor air pollution in households (e.g., kerosene lamps) is also needed. Future studies should consider a package of interventions, such as multiple improved stoves or improved stoves with multiple burners and clean sources of lighting to improve indoor air quality.

This study documents the reductions of household air pollution from several improved biomass stoves compared to levels observed in a setting of traditional TSF in rural Kenyan homes. Achieving clean biomass requires understanding and influencing a complex mix of factors such as stove design, performance in the field, users' needs and preferences, fuel type used and moisture content, household ventilation, and other sources of household air pollution. We have demonstrated that several biomass stoves have the potential to improve indoor air quality but achieving their maximal potential requires adherence to more exclusive use, as well as elimination of other sources of household air pollution, principally kerosene lamps. The levels observed in a setting of improved stove use in our study, however, are still considerably higher than indoor air quality standards and consequently risk reductions for a range of child and adult health outcomes are limited. We were unable to demonstrate a link between stove acceptability to stove use and performance but have identified stove characteristics women liked and, therefore, likely promoted use of the improved stove. Although the improved stoves were largely acceptable to local women, all six stoves were reported to have some limitations or concerns, and addressing these could lead to more exclusive and sustained use. Further research is needed on stove use patterns and local user preferences to determine whether useful additional benefits to health can be achieved through the better use of biomass stoves and improvements in the technology. Even if further such benefits can be obtained, this study does suggest that clean fuels will be required in order to meet WHO air quality guidelines for $PM_{2.5}$ in homes. In poor rural populations such as this one, it is challenging to ensure affordable and secure supply of clean fuels; policy makers should therefore consider addressing both enhancing solid fuel technology and support for its best use, as well as working to make clean fuels available.

Table 1.1 Characteristics of participating households

Household characteristics (N=45)	
Average number of members (range)	6.0 (3-10)
Average number of children <5 (range)	1.9 (1-3)
Water source	
Pump	16 (37%)
Well	10 (23%)
Communal standpipe	7 (16%)
Collect from river	10 (23%)
Access to drinking water	43 (100%)
Sanitation	
Latrine in the yard	31 (72%)
Shower/bath in house	11 (26%)
Avg. weekly expenditures per household (KSH)	1381.08 (150- 5,000)
Possessions	
Radio	26 (60%)
TV	8 (19%)
CD player	3 (7%)
Bicycle	26 (60%)
Motorbike	4 (9%)
Car or truck	1 (2%)
Cell phone	33 (77%)
Access to electric generator	2 (5%)
Cow (one or more)	23 (53%)
Land purchased	13 (30%)

Table 1.2. Stove use, cooking practices, and fuel consumption during the 48-hour monitoring period by stove type

	Baseline (TSF) N=45	Ecochula N=36	Envirofit N=35	EcoZoom N=37	Philips N=35	Prakti N=39	Rocket with TECA N=35
Fuel consumed, average (range, kg)	12.0 (3.1-28.8)	7.5 (2.4-20.5)	9.3 (1.9- 17.9)	8.5 (2.0-28.9)	5.3 (0.6-11.9)	9.5 (2.1-41.1)	8.2 (3.4-19.9)
Kerosene lamp use, average (range, hours)	6.1 (2-11)	6.2 (2-12)	6.5 (3-16)	6.1 (3-12)	5.9 (2-10)	6.2 (3-15)	5.8 (2-12)
Time spent cooking a meal, average (range, min)	82 (28-180)	66 (35-128)	68 (28-125)	70 (28-125)	61 (21-127)	84 (37-181)	80 (42-187)
Number of cooking events, average (range)	7 (2-14)	6.1 (1-12)	7.5 (4-14)	7.5 (4-13)	6.6 (4-13)	6.6 (4-15)	6.3 (4-11)
Number of people cooked for, average (range)	5.5 (3-10)	5.4 (2-9)	5.4 (3-10)	5.5 (3-10)	5.5 (2-10)	5.4 (2-9)	5.5 (3-9)
Reported using TSF along with the improved cook stove, N (%)	N/A	13 (36)	10 (29)	10 (27)	12 (34)	18 (46)	13 (37)

Table 1.3. Gravimetric PM$_{2.5}$ (μg/m^3) and kitchen and personal (woman) CO real time (ppm) 48-hour concentration by stove type

	Gravimetric kitchen PM$_{2.5}$ (μg/m^3)					CO real-time kitchen (ppm)					CO real-time personal (ppm)				
Stove type	N	Baseline[a]	Follow up[b]	Difference, mean (median)	p-value[c]	N	Baseline[a]	Follow up[b]	Difference, mean (median)	p-value[c]	N	Baseline[a]	Follow up[b]	Difference, mean (median)	p-value[c]
Ecochula	36	621	518	116 (205)	0.2403	34	6.8	5.4	1.7 (1.1)	0.1379	31	2.5	1.0	1.7 (1.2)	**<0.0001**
Envirofit	35	618	398	277 (186)	**0.0044**	34	6.7	4.9	3.4 (2.1)	**0.0041**	30	2.4	1.1	1.3 (1.2)	**0.0001**
EcoZoom	37	609	503	109 (143)	0.1663	37	6.6	6.7	-0.2 (1.0)	0.9136	31	2.2	1.3	0.7 (0.7)	**0.0003**
Philips	35	604	319	357 (294)	**0.0002**	35	6.5	3.8	2.7 (2.7)	**0.0069**	29	2.1	1.1	0.6 (1.0)	**0.0014**
Prakti	39	588	374	118 (280)	**0.0036**	37	6.6	4.5	0.7 (2.3)	**0.0190**	32	2.0	0.9	0.9 (0.8)	**0.0008**
Rocket with TECA	35	571	368	215 (213)	**0.0121**	34	6.0	4.4	2.5 (1.4)	0.0602	31	2.3	1.4	0.8 (0.8)	**0.0289**

[a] Baseline measurements in a setting of 3-stone fire use (geometric mean)

[b] Measurements in a setting of improved stove use (geometric mean)

[c] Paired t-test, assuming lognormal distribution

Table 1.4. Factors associated with 48-hour mean gravimetric $PM_{2.5}$ (µg/m^3) concentration

	Univariable analysis		Multivariable model[2]	
Variable	Percent reduction (95%CI) in mean $PM_{2.5}$	p-value	Percent reduction (95%CI) in mean $PM_{2.5}$	p-value
Stove type[1]				
Ecochula	18.0 (-9.3, 38.5)	0.1768	11.9 (-19.3, 35.0)	0.4122
Envirofit	35.6 (14.7, 51.3)	0.0024	36.1 (15.1, 51.9)	0.0023
EcoZoom	19.7 (-5.8, 39.0)	0.1199	14.9 (-12.9, 35.9)	0.2640
Philips	45.2 (27.1, 58.7)	<0.0001	42.3 (21.1, 57.8)	0.0007
Prakti	38.6 (19.4, 53.2)	0.0005	41.1 (21.8, 55.6)	0.0003
Rocket with TECA	31.9 (9.1, 49.1)	0.0099	32.7 (9.5, 50.1)	0.0107
Use of improved stove only (vs. multiple stove use) during the follow up period	12.8 (-7.3, 29.1)	0.1976	29.0 (12.8, 42.2)	0.0013
Fuel consumed during the 48-hour monitoring period (kg)	-3.4 (-5.3, -1.6)	0.0003	-3.0 (-5.0, -1.1)	0.0023
Kerosene lamp use, average (hours)	-4.9 (-10.3, 0.1)	0.0583	-	-
Average number of people cooked for	-7.1 (-16.3, 1.4)	0.1063	-	-
Average time spent cooking a meal (min)	-0.3 (-0.6, 0.1)	0.0944	-	-
Number of cooking events	-0.5 (-5.2, 3.8)	0.8182	-	-

[1] Reference category: 3-stone fire; overall p-value for stove type p=0.0005

[2] Mixed effects model, accounting for correlated response within household by follow up period

Table 1.5. Factors associated with 48-hour mean real-time kitchen CO (ppm) concentration

	Univariable analysis		Multivariable model[2]	
Variable	Percent reduction (95%CI) in mean CO	p-value	Percent reduction (95%CI) in mean CO	p-value
Stove type[1]				
Ecochula	21.5 (-4.6, 41.1)	0.0995	14.1 (-16.0, 36.3)	0.3240
Envirofit	27.6 (4.4, 45.2)	0.0237	27.9 (4.4, 45.6)	0.0241
EcoZoom	1.9 (-28.5, 25.2)	0.8875	-5.8 (-39.6, 19.9)	0.6935
Philips	38.5 (18.4, 53.6)	0.0009	34.5 (10.6, 52.0)	0.0082
Prakti	32.3 (11.3, 48.3)	0.0051	33.5 (12.1, 49.8)	0.0047
Rocket with TECA	25.1 (0.1, 43.8)	0.0508	24.6 (-1.4, 44.0)	0.0637
Use of improved stove only (vs. multiple stove use) during the follow up period	11.1 (-9.1, 27.6)	0.2621	27.5 (10.8, 41.0)	0.0027
Fuel consumed during the 48-hour monitoring period (kg)	-3.2 (-5.0, -1.4)	0.0006	-3.1 (-5.0, -1.1)	0.0021
Kerosene lamp use, average (hours)	-6.8 (-12.2, -1.6)	0.0099	-	-
Average number of people cooked for	-10.7 (-20.3, -1.9)	0.0175	-	-
Average time spent cooking a meal (min)	-0.4 (-0.7, -0.1)	0.0175	-	-
Number of cooking events	-3.3 (-8.1, 1.3)	0.1682	-	-

[1] Reference category: 3-stone fire; overall p-value for stove type p=0.0051

[2] Mixed effects model, accounting for correlated response within household by follow up period

Table 1.6. Gravimetric $PM_{2.5}$ ($\mu g/m^3$) and kitchen and personal (woman) CO real time (ppm) 48-hour concentration by stove type, stratified by reported multiple stove use

	Households reporting **multiple stove use**					Households reporting use of **only improved stove**				
Stove type	N	Baseline[a]	Follow up[b]	Difference, mean (median, $\mu g/m^3$)	p-value[c]	N	Baseline[a]	Follow up[b]	Difference, mean (median, µg/m3)	p-value[c]
Gravimetric kitchen $PM_{2.5}$ (mg/m^3), geometric mean										
Ecochula	13	605	549	100 (49.0)	0.6248	23	630	502	125 (392)	0.2950
Envirofit	10	709	527	-5.7 (293)	0.2665	25	585	355	391 (180)	**0.0098**
EcoZoom	10	705	861	-316 (50.5)	0.4044	27	577	412	266 (248)	**0.0435**
Philips	12	750	410	514 (349)	**0.0145**	23	541	281	275 (274)	**0.0043**
Prakti	18	865	751	-33.4 (289)	0.4728	21	422	206	249 (242)	**0.0018**
Rocket with TECA	13	870	402	433 (410)	**0.0042[d]**	22	446	349	86 (170)	0.2861[e]
CO real-time kitchen (ppm), geometric mean										
Ecochula	12	6.5	5.7	0.3 (0.5)	0.5612	22	6.9	5.2	2.4 (3.3)	0.1798
Envirofit	10	8.9	6.5	1.6 (2.1)	0.0641	24	6.0	4.3	4.1 (2.1)	**0.0211**
EcoZoom	10	6.9	9.6	-3.2(-1.0)	0.1478	27	6.5	5.8	0.9 (1.7)	0.5280
Philips	12	7.9	4.8	4.0 (3.8)	0.1353	23	5.9	3.3	2.1 (2.4)	**0.0292**
Prakti	18	8.9	9.4	-2.0 (0.1)	0.7730	20	5.0	2.4	3.2 (3.7)	**0.0026**
Rocket with TECA	13	8.9	5.2	5.0 (1.6)	**0.0228**	21	4.7	4.0	1.0 (1.1)	0.4398
CO real-time personal (ppm), geometric mean										
Ecochula	10	2.2	0.7	2.2 (1.5)	**0.0063**	21	2.7	1.1	1.4 (1.1)	**<0.0001**
Envirofit	9	2.0	1.1	1.3 (0.3)	0.0941	21	2.6	1.2	1.4 (1.4)	**0.0005**
EcoZoom	8	2.3	1.0	-0.4 (0.6)	0.0973	23	2.1	1.4	1.1 (0.7)	**0.0003**
Philips	10	2.4	1.5	-1.0 (1,0)	0.4510	19	2.0	0.9	1.5 (1.3)	**0.0009**
Prakti	13	2.4	1.4	0.9 (0.6)	0.1293	19	1.8	0.7	0.9 (0.9)	**0.0031**
Rocket with TECA	11	1.8	0.9	0.7 (0.9)	0.1407	20	2.6	1.9	0.8 (0.8)	0.1265

[a] Baseline measurements in a setting of 3-stone fire use

[b] Measurements in a setting of improved stove use

[c] Paired t-test, assuming lognormal distribution

[d] Sign test, p-value=0.0479

[e] Sign test, p-value=0.0509

Table 1.7. Main qualitative and quantitative findings by stove type

Source of information	Reduction in 48-hr kitchen measurement, difference (% change[1])		Fuel consumption	Time activity diary		Qualitative interviews and FGDs			
Stove type	PM$_{2.5}$ (µg/m^3)	CO (ppm)	Fuel used, kg (% reduction)	ICS use during monitoring N (%)	Multiple stove use (%)	Overall stove rank order (range 1-6)[2]	Stove characteristics (rank order) women liked	Stove characteristic women disliked	Selected quotes illustrating usability/acceptability
TSF	-	-	12.0	-	-	-			
Ecochula	116 (11.9)	1.7 (14.1)[3]	7.5 (38%)[3]	33 (92%)	36	6	Fuel efficiency (2) - Cooking speed (2) - Suitable for cooking traditional foods (3) - Visually appealing (3)	-Requires pulling out of stove to add fuel -Cooks food unevenly -Concerns around durability and maintenance	*"I like it because ...it consumes less fuel, …uses charcoal, …can also use cow dung and …I don't need to adjust the flame and it doesn't give me hard time of adjusting the flame …and it cooks food so well."* *"It is hard because I use a wok when cooking ugali …you were cooking and the fuel gets finished is when you want to pull it out … have served ugali which is not well cooked."*

Source of information	Reduction in 48-hr kitchen measurement, difference (% change[1])		Fuel consumption	Time activity diary		Qualitative interviews and FGDs			
Stove type	$PM_{2.5}$ ($\mu g/m^3$)	CO (ppm)	Fuel used, kg (% reduction)	ICS use during monitoring N (%)	Multiple stove use (%)	Overall stove rank order (range 1-6)[2]	Stove characteristics (rank order) women liked	Stove characteristic women disliked	Selected quotes illustrating usability/acceptability
Envirofit	277 (36.1)[3]	3.4 (27.9) [3]	9.3 (23%)[3]	35 (100%)	29	3	- Suitable for cooking traditional food (2) - Even heat without flare ups (3) -Cooking speed (3) -Cooking pots fit well (3)	-Small burning chamber -Requires constant supervision	"*…is good for me because I put firewood and that stand holds for me the fuel and it burns so well … even if you put a lot of fuel …and it cooks faster then …and I can carry it and cook with it in the compound or in the other house….*" "*The problem I saw …the pot rest was so small and also the combustion chamber so that if you have a big family you cannot cook with it.*" "*I cannot do anything until I am done using it, after I am done…is when I go and do my work outside*"

Source of information	Reduction in 48-hr kitchen measurement, difference (% change[1])		Fuel consumption	Time activity diary		Qualitative interviews and FGDs			
Stove type	PM$_{2.5}$ (µg/m^3)	CO (ppm)	Fuel used, kg (% reduction)	ICS use during monitoring N (%)	Multiple stove use (%)	Overall stove rank order (range 1-6)[2]	Stove characteristics (rank order) women liked	Stove characteristic women disliked	Selected quotes illustrating usability/acceptability
EcoZoom	109 (14.9) [3]	-0.2 (-5.8)	8.5 (29%)[3]	37 (100%)	27	4	-Even heat without flare ups (1) - Fuel efficiency (3)	-Mixed views on cooking speed -Some women note not good for cooking local dishes -Small burning chamber -Difficult to teach others to use -Difficulties with pot stability and heat adjustment	"*…stove was good, I cooked ugali… it was easy to use, the fire was lighting well and it could reach at the bottom of the cooking pan*" "*Cooking with it was difficult, when you place the cooking pot on the top it shakes, when you adjust the fire sometimes it goes off…*"
Philips	357 (42.3) [3]	2.7 (34.5) [3]	5.3 (56%)[3]	33 (92%)	34	1	-Comfortable (1) -Cooking speed (1) - Fuel efficiency (1) -Reduces smoke (2) -Visually appealing (2) -Cooking pots fit well (2)	-Not good for dishes that require slow cooking -Requires small pieces of wood -Requires constant supervision -Small or instable pot rest -Concerns about durability, maintenance, burns	"*I like it because it cooks so well ...lighting it is also easy such that even if you teach a child she can light it. …I can cook very fast …it also consumes less fuel. During harvesting season I can use the maize cob as fuel and I just keep the firewood.*" "*The problem it has is … the charging knob gets spoiled so there is no way you can repair it*

Source of information	Reduction in 48-hr kitchen measurement, difference (% change[1])		Fuel consumption	Time activity diary		Qualitative interviews and FGDs			
Stove type	$PM_{2.5}$ ($\mu g/m^3$)	CO (ppm)	Fuel used, kg (% reduction)	ICS use during monitoring N (%)	Multiple stove use (%)	Overall stove rank order (range 1-6)[2]	Stove characteristics (rank order) women liked	Stove characteristic women disliked	Selected quotes illustrating usability/acceptability
									… and there is no way you can use it when it is not charged. …when the battery get spoiled, there is no way you can get that battery…”
Prakti	118 (41.1) [3]	0.7 (33.5) [3]	9.5 (21%)[3]	39 (100%)	46	5	-Reduces smoke (1) -Visually appealing (1) -Even heat without flare ups (2) -Two burners (can cook and warm food at the same time)	-Slow cooking speed -Hard to cook traditional dishes -Small pot rest -Concerns of burns from chimney	*“I like it because there isn’t smoke produced in the house since its chimney is directed outside and so when I am cooking I put food on this side and on the other side I put another thing and … you can cook two things at the same time so fast and also it doesn’t consume a lot of fuel”* *“…the two pot rests were made …that if you place the bigger pot on one side then the rest cannot fit the other side …but when you use [only] one side the smoke now comes in the house...”*

Source of information	Reduction in 48-hr kitchen measurement, difference (% change^1)		Fuel consumption	Time activity diary		Qualitative interviews and FGDs			
Stove type	$PM_{2.5}$ ($\mu g/m^3$)	CO (ppm)	Fuel used, kg (% reduction)	ICS use during monitoring N (%)	Multiple stove use (%)	Overall stove rank order (range 1-6)^2	Stove characteristics (rank order) women liked	Stove characteristic women disliked	Selected quotes illustrating usability/acceptability
Rocket with TECA	215 (32.7)^3	2.5 (24.6)^3	8.2 (32%)^3	35 (100%)	37	2	-Suitable for cooking traditional food (1) -Cooking pots fit well (1) -Comfortable (2)	-Mixed opinions on ease of use -Slow cooking speed -Concerns about TECA fan (durability, maintenance)	"*…you don't need to hold pot. It is stable and the pot does not move from place to place.*" "*I was told that when you put the firewood then the machine would fan the fire. I waited …but I did not see it fanning the fire. When I pushed the firewood, I also had some fear that it might touch the metals inside the stove. So it was really hard for me to use.*"

[1] Estimated using multivariable mixed effects model, accounting for correlated response within household by follow up period

[2] During six focus groups, 39 women ranked their 1st and 2nd stove choice. Points were allocated per ranking (2 points for 1st choice and 1 point for 2nd choice)

[3] Statistically significant, $p<0.05$

Appendix 1. Seven cookstoves assessed in the study

3 stone fire (TCS)

Eco Chula

EcoZoom

Envirofit

Philips

Pratki

RTI TECA

Appendix 2. Quality Assurance for Exposure Assessment Methods

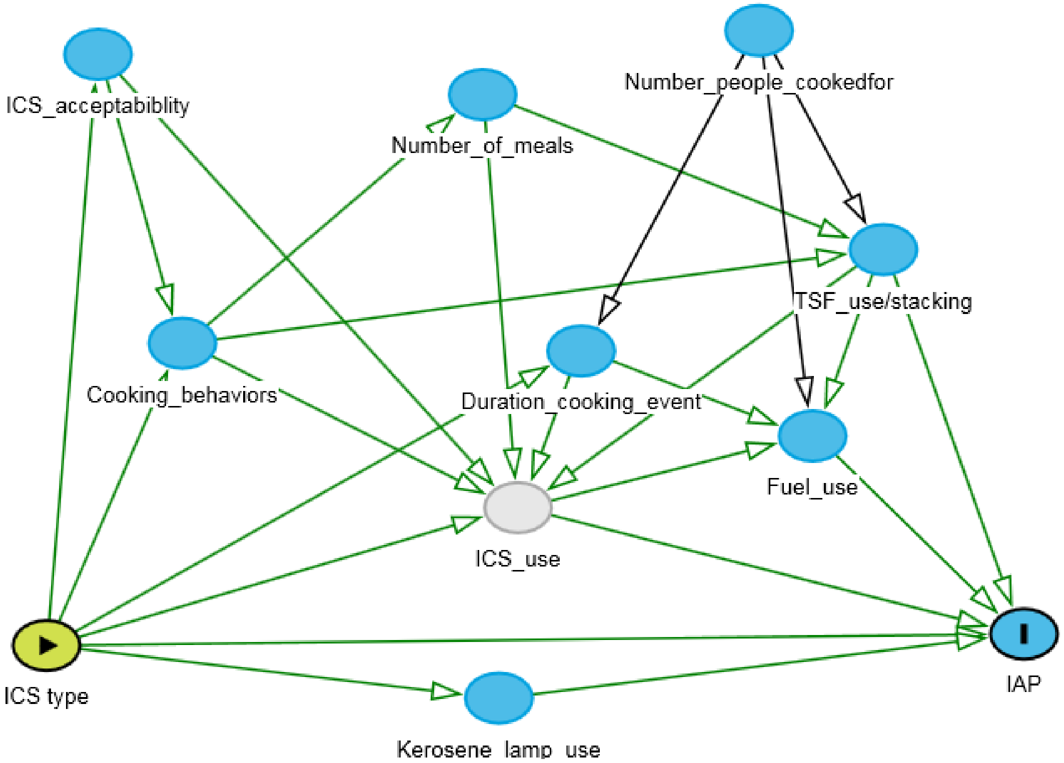
Instrument calibration

For the gravimetric $PM_{2.5}$, the target flow rate was 1.5 L/min. Pre- and post-calibrations were made by either a rotameter (AALBORG, Orangeburg, NY, USA) or a Dry Cal DC-Lite (Bios International, Butler, NJ, USA) in the field. The GasBadge was calibrated in Berkeley Air's laboratory (Berkeley Air Monitoring Group, Berkeley, CA, US) with 20 ppm CO span gas and zeroed in the field prior to each deployment.

Filter weighing

At the beginning of each filter weighing session, a 100 mg calibration weight and three lab blanks were weighed. Zeros were checked after every mass measurement. After every tenth sample, the balance's reproducibility was checked by reweighing the first filter in the previous batch of 10. All filters were weighed twice. If the first and second mass measurements differed by >5 μg (<1% of filters), filters were weighed a third time. At the end of the session, the three lab blanks were re-weighed to assess drift. Field blanks (approximately 5% of the total number of samples) were collected and used for quality assurance.

Appendix 3. Causal Diagram for the Association between Stove Type and IAP



No adjustment is necessary to estimate the total effect of ICS type on IAP

Cooking_behaviors - cooking behaviors assessed during structured interviews

Duration_cooking_event - average duration (minutes) of cooking event

Fuel_use – fuel (kg) used during a 48 hour monitoring

IAP – household air pollutants (PM2.5 and CO) measured during 48 hour cooking episode

ICS_type - main exposure, improved cookstove type

ICS_acceptability - improved cookstove acceptability to users assessed during structured interviews

ICS_use - actual use of improved cookstoves (not measured directly)

Kerosene_lamp_use - duration of kerosene lamp use during 48 hour monitoring

Number_of_meals - average number of daily meals prepared

Number_people_cooked_for - average number of people cooked for

TSF_use/stacking - concurrent use of 3-stone fire (i.e. stove stacking)

Estimating the impact of indoor air pollution on childhood pneumonia using meta-regression

Abstract

Background: Pneumonia contributes to significant morbidity and mortality among children worldwide. Although evidence on the negative effects of indoor air pollution (IAP) from biomass smoke on childhood acute respiratory infections (ARI) is growing, the specific level of reduction in IAP, specifically particulate matter <2.5 μm in diameter (PM2.5), needed to result in reduction in the risk of ARI is not known.

Objectives: The objectives of this study were to 1) systematically evaluate the evidence regarding the dose response relationship between exposures to PM2.5 and risk of ARI and 2) examine the strength of this association for acute lower versus upper respiratory infections (ALRI vs AURI), and at different levels of exposure to PM2.5.

Methods: Through systematic review of literature, we identified 32 studies of indoor or ambient air pollution, or of second hand smoke effects on AURI and ALRI. We abstracted exposure levels, corresponding risks, risk ratios (RR), confidence intervals, and adjusted covariates. For each exposure-response pair, we estimated RR per unit (10 μg/m^3) of exposure to PM2.5 for each disease endpoint (AURI or ALRI). We conducted meta-analysis by fitting random effects model to study-specific dose-response slopes. We also examined the dose-response relationship using models with an exposure level–specific log transformed risk ratio (ln(RR)) for each outcome level (AURI, ALRI, and ARI) as dependent variable and the difference between the highest and the reference PM2.5 category as independent variable.

Results: The overall summary RR from random-effects meta-analysis was 1.04 (95% CI: 1.03, 1.06) but represented a weighted average of highly heterogeneous results (I^2 = 78.7%). Similar results were obtained when analysis included studies with only ALRI or AURI as outcome. The dose response slope was different from the null value (β = 0.00060; 95% CI: 0.00037, 0.00082). Similar results were obtained when the analysis was repeated for studies with AURI or ALRI. Series of sensitivity analysis excluding studies with second hand smoke exposure and restricting to studies with AURI or ALRI produced similar results. When we restricted the analysis to studies with low exposure levels (≤50 µg/ml of PM2.5), relationship between PM2.5 and ln (RR) became stronger (β = 0.00774; 95% CI: 0.00273, 0.01273) and heterogeneity was reduced (I^2=52.8%).

Conclusions

Our systematic review and meta-analysis found a weak positive association and a positive dose-response relationship between the levels of exposure to PM2.5 and risk of acute respiratory infections. However, due to high level of heterogeneity, the summary estimate should be interpreted with caution. There is a need for high-quality intervention-based evidence, including detailed personal exposure assessment, in order to better quantify exposure-disease relationship.

Background

The leading infectious cause of death among children <5 years old is pneumonia, accounting for over one million childhood deaths annually in the world.[73] An estimated 90% of these deaths occur in the developing world, where interventions to reduce burden of pneumonia have the potential to make an enormous public health impact.

A growing body of evidence suggests a link between indoor air pollution (IAP) from biomass fuel burning and risk of childhood acute respiratory infections (ARI).[3, 9, 61] Although the evidence on the negative effects of IAP on childhood pneumonia is growing, this evidence comes almost exclusively from observational studies. The evidence from a recently conducted trial in Guatemala[74] (RESPIRE) suggests non-linear relationships between exposures to IAP and pneumonia, such that large exposure reductions (of around 90% or more, from levels commonly seen in developing country homes) are needed to gain large health benefits.

The specific level of exposure from an intervention to reduce IAP that results in a significant reduction in the risk of pneumonia is not known. It also not known whether interventions leading to improvements in indoor air quality are likely to influence the risk of upper or lower respiratory infections, or both. While the precise mechanism for IAP causing pneumonia is not well understood, the potential mechanisms described to date include inflammation in the upper and lower airway due to exposure to increased levels of particulate matter <2.5 μm in diameter (PM2.5).[39, 40] This inflammation may provide a portal for invasion of bacterial or viral respiratory pathogens.

The association between IAP and acute respiratory illnesses has been examined in previous reviews. The limitation of the previous reviews is that they either did not examine a dose-response relationship between IAP and ARI [3, 75] or did not distinguish between lower or upper respiratory infections as an outcome.[62]

We sought to develop a model using meta-regression to estimate the impact of indoor air pollution on childhood pneumonia. The first objective was to systematically evaluate the evidence regarding the dose response relationship between exposures to PM2.5 and risk of acute respiratory infections. The second objective was to examine whether this association exists and whether the strength of association differs for lower versus upper respiratory infections, and at different levels of exposure to PM2.5.

Methods

We conducted a systematic review of literature for studies evaluating the effects of IAP on childhood pneumonia. To understand the exposure-disease relationship at different levels of PM2.5, we reviewed studies of the effects of IAP, outdoor air pollution, and second hand smoke on childhood ALRI. The review covered the period from 1980 through 2014. We searched the published literature for terms “pneumonia”, “ALRI”, “laryngitis”, “tracheitis”, “bronchitis”, “bronchiolitis”, “lung infections” in combination with “indoor air pollution”, “outdoor air pollution”, “ambient air pollution”, “smoke”, “smoking”. All study designs were eligible but studies were excluded if case definitions for pneumonia were not clearly defined to classify study outcomes into upper and lower respiratory infections. If several estimates for disease risk associated with similar levels of exposure to PM2.5 were obtained, pooled analysis was carried out to obtain a summary measure. From each selected study we abstracted the following measures: sample size, exposure levels, corresponding to each exposure level risks, risk ratios, confidence intervals, and adjusted covariates. For simplicity, all ratio-based measures of association in this analysis will be referred to as “risk ratios”.

The studies were grouped by the following definitions for pneumonia:

- Acute lower respiratory infections/pneumonia (ALRI)
- Upper respiratory infections (e.g. bronchitis, sinusitis) (AURI)
- Upper and lower respiratory infections combined (i.e. unable to stratify or combined data reported) (ARI)

In addition, we recorded information on whether ARI diagnosis was based on:

- Clinician/health care worker diagnosed
- Field worker/community health worker diagnosed or parent reported

Estimates of disease risk associated with high levels of exposure to PM2.5 (>50 µg/m^3) were derived from studies of IAP from solid biomass fuel and pneumonia. Mid- to low level range exposures to PM2.5 and associated risk of pneumonia estimates were obtained from studies of outdoor air pollution (5 to 30 µg/m^3) and second-hand smoke (20 to 50 µg/m^3). IAP and outdoor air pollution studies were excluded if air pollutants measurements were not reported. We assigned a concentration of 50 µg/m^3 for moderate-high exposure, 35 µg/m^3 for moderate exposure, and 25 µg/m^3 for low-moderate exposure to SHS[76]. For each of the exposure-response pair, we estimated the effect size (relative risks) per unit (10 µg/m^3) of exposure to PM2.5 for each pneumonia endpoint. As a comparison, low-level exposure levels for PM2.5 distribution were selected as the levels observed in a setting (i.e. households) of clean fuel use (gas or electricity). In order to derive estimates of personal exposure from kitchen concentrations, we applied a factor of 0.628 to kitchen concentrations. This factor was derived from median ratios between daily average personal exposures (for children) and kitchen concentrations from available published studies to estimate the range of exposures for age and sex-defined population subgroups. These ratios were estimated to at 0.628 for children under 5 years of age[68]. For studies where the authors reported only category cutoffs, we assigned midpoints between cutoff points to each category. For the highest exposure category, we used the lower bound for that category plus the width of the preceding interval. This approach was previously recommended in meta-analyses when the category-specific measures were not available.[77]

We fit random effects model to study-specific dose-response slopes. This model allows for the between study variance and uses an estimated between studies variance component and the within-study variances as the weighting factor. We used Greenland and Longnecker method[78] for meta-analysis of dose response data which adjusts for within study correlations and allows for more accurate variance estimation. We computed study-specific slopes from the correlated natural log of risk ratios across exposure categories and adjusted the standard error of the slope for within study covariance.

We examined the dose-response relationship of PM2.5 exposure with the pneumonia outcome (ARI, AURI, ALRI) across studies using models with an exposure level–specific natural log transformed ratio measure (ln(RR)) of association (i.e., relative risk) between PM2.5 and pneumonia as dependent variable. The independent variable in the analyses was the difference between the highest exposure category and the reference category, and the dependent variable was the corresponding ln (RR). The results of these dose-response analyses are summarized as regression coefficients and the corresponding 95% confidence interval, as well as presented these results graphically. We conducted several sub-analyses to assess the influence of study design, exposure assessment method, outcome definition, and level of exposure on outcome and heterogeneity of summary estimates. We used STATA version 11 for all our analyses.

Results

Characteristics of included studies

In our meta-analysis, we included information from 32 epidemiologic studies in which the associations between air pollution and acute respiratory infections (ARI) in children were assessed (Table 2.1). Figure 1 outlines the process of literature search and selection of studies to be included in this analysis. Of the 32 studies selected for this analysis, 7 studies evaluated the association between ambient air pollution and ARI, 20 studies assessed the relationship between exposure to second hand smoke and ARI, and 5 studies evaluated indoor air pollution and ARI (Table 2.1). With respect to study design, with the exception of one randomized controlled trial, all included studies were observational (case-control or cohort). With respect to exposure measurements, all ambient air pollution studies included in this analysis provided measurements of ambient PM2.5 associated with measures of effect. Among the studies of exposure to second hand smoke, nine studies measured maternal or parental smoking, six studies asked about smoking by any household member, and five studies measured smoking in terms of average number of cigarettes smoked per day in the household. Five indoor air pollution studies measured kitchen levels of particulate matter (PM10 or PM2.5), which we converted to personal PM2.5 as described in methods, and one randomized controlled trial measured personal exposures to carbon monoxide but in a separate publication reported conversions to personal PM2.5 levels.

With respect to outcome definitions and measurements, 14 studies evaluated lower respiratory infections as outcome, including chest x-ray confirmed pneumonia (2), hospitalizations or emergency department visits due to ALRI (4), and clinical WHO criteria-defined severe pneumonia (2). Three of the 14 studies included parental report of clinically attended pneumonia, while 11 out of 14 were based on clinician or health care diagnosis of ALRI. Seventeen studies evaluated upper and lower respiratory infections combined as their outcome (one of which also separated the analysis for ALRI only), and the remaining 2 evaluated only upper respiratory infections as the outcome (AURI). For simplicity, we will refer to this latter group of 17 studies as AURI studies.

Meta-analysis of study-specific regression coefficients

We combined individual measures of association in a random-effects meta-analysis, as shown in Figure 2A, where ln (RR) was the dependent variable and represented a change in risk of ARI per 10 µg/ml of increase in PM2.5. The overall summary estimate was 1.04 with confidence limits excluding null (RR=1.04; 95% CI: 1.03, 1.06; P = 0.000) but this estimate represented a weighted average of highly heterogeneous results (P for heterogeneity= 0.000; I^2 = 78.7%). Similar results were obtained when we repeated the analysis included only studies with ALRI as the outcome (Figure 2B), with summary RR=1.05 (95%CI: 1.03, 1.08; P=0.000) and highly heterogeneous results (P=0.000; I^2=78.6%). When we included studies of only AURI as an outcome or those where ALRI and AURI could not be separated (Figure 2C), the summary measure and heterogeneity did not change (RR=1.03; 95% CI: 1.02, 1.04; P = 0.000; I^2=78.3%, P for heterogeneity 0.000).

Dose-response analysis for the highest versus lowest categories of PM2.5 exposure

The relationship between the maximum difference between PM2.5 levels in the highest versus the lowest exposure category and the corresponding difference in ln (RR) is shown in Figures 3 A-C. The resulting regression slope for all ARI studies was different from the null value (β = 0.00060; 95% CI: 0.00037, 0.00082; P = 0.000) (Figure 3A). Similar results were obtained when the analysis was repeated for studies with AURI-only as an outcome or those where ALRI and AURI could not be separated (Figure 2C). In the analysis limited to studies with ALRI as the outcome (Figure 3B), the confidence limits for the summary regression coefficient included null value (β = 0.00029; 95% CI: −0.00008, 0.00065; P = 0.112).

Examination of reasons for heterogeneity

We further explored the above associations and reasons for heterogeneity by conducting a series of sub-analyses. When the meta-analysis was limited to studies for which the levels of pollutants were measured (i.e. excluding studies with second hand smoking), the summary estimate for all ARI or AURI studies did not change and heterogeneity was not reduced. The corresponding sub-analysis for ALRI studies did not change the summary estimate but slightly reduced heterogeneity (I^2=56.1%, P=0.034).

Results of the sensitivity analysis for dose-response are summarized in Table 2.2. When we excluded studies of second hand smoke exposure, the slope for all ARI studies did not change but heterogeneity was reduced (I^2=59.6%). When we restricted the analysis to studies with low exposure levels ($\leq$50 µg/ml of PM2.5), relationship between PM2.5

levels in the highest versus the lowest exposure category and the corresponding difference in ln (RR) for ARI studies became stronger ($\beta = 0.00774$; 95% CI: 0.00273, 0.01273; $P = 0.004$) and heterogeneity was reduced (I^2=52.8%). The analysis limited to studies with exposures >50 µg/ml of PM2.5 produced the results very similar to the overall model (Table 2.2). For ALRI studies, neither exclusion of second hand smoke studies, nor varying highest levels of exposure reported for the HAP studies changed the results: the summary regression coefficients included null value, although exclusion of second hand smoke studies reduced heterogeneity for all models. For AURI studies, the sub-analyses resulted in similar slope estimates (confidence limits exclude null) and no change in heterogeneity.

Discussion

We conducted a systematic review and meta-analysis to estimate the impact of air pollution on childhood pneumonia. Nearly every study included in our analysis reported an association; however, due to high level of heterogeneity observed, the summary estimate should be interpreted with caution. Our study estimated that with every 10 µg/ml increase in exposure to PM2.5, there is approximately 4% increase in the risk of ARI among children. The strength of association did not differ for studies of lower vs upper respiratory infections. We also identified a positive dose-response relationship between the levels of exposure to PM2.5 and risk of acute respiratory infections overall, with similar dose-response identified for studies evaluating upper respiratory infections. The association was stronger at lower levels of exposure to $PM_{2.5}$ (<50ug/ml) compared to higher levels ($\geq$50ug/ml).

The overall estimate for this study was lower compared to previously published analyses. Our analyses did not include studies without measurement of pollutants, while previous meta-analysis evaluating the impact of cookstove interventions on respiratory infections considered a dichotomous exposure (intervention vs control),[3]did not make adjustments per unit of exposure to PM2.5,[3, 9] or focused on ambient air exposure only with lower levels of PM2.5.[75] Importantly, the studies providing evidence on the exposure–response relationship report that risk falls progressively from higher to lower exposure levels.[62] We conclude that reducing exposure to PM2.5 has the potential to improve morbidity due to acute respiratory disease, and the impact could be greater in developing countries where both household levels of PM2.5 are the highest due to exposure to smoke from biomass fuel levels and burden of pneumonia among children is the highest.

Our study identified positive dose response between exposures to PM2.5 and risk of acute respiratory infections in children; however, these findings represented highly heterogeneous results. Sensitivity analysis did not identify any differences in the strength of association or heterogeneity when limiting the analysis to studies with high or low exposure levels, stratifying by method of exposure measurement, or by outcome (ALRI vs AURI). Various study designs estimating risks and prevalence were combined into a summary measure of effect and could have contributed to observed heterogeneity. Differences in methods of exposure measurement used across various study types could have contributed to heterogeneity. In SHS studies, exposure assignment to three levels based on the amount of smoking in the households and expected exposure to second hand smoke could have led to misclassification. In these studies, second hand exposure for children was reported by parents, and both presence of and levels of exposure could be underreported. Exclusion of SHS studies in our sensitivity analysis did not change the estimate and did not reduce heterogeneity. In AAP studies, PM2.5 were measured using central monitors in metropolitan areas and may not correlate well with personal exposures. Measurement of PM2.5 can be difficult to conduct in field studies as it requires the use of expensive equipment. In addition, personal exposures to PM2.5 are even more challenging to measure because of limited options for the equipment available for use in the field settings, and kitchen levels are being used as a proxy for personal exposures to PM2.5. Restricting analysis to IAP studies with highest exposure levels did not change the results, nor did it reduce heterogeneity.

Various cased definitions ALRI and AURI applied across studies included in our analysis likely contribute to heterogeneity observed in our study. The diagnosis of pneumonia/ALRI is challenging, especially in developing country settings, where burden of ALRI and mortality from childhood pneumonia is highest. At the highest levels of exposure, studies of IAP from biomass stoves are included in our analysis, and these studies are conducted in developing countries where the burden of pneumonia is the highest, while case definitions vary greatly due to challenges in applying standard case definitions in field settings. In our analysis, we adjusted for the study setting by limiting the analysis to IAP studies conducted in developing countries vs SHS and AAP studies conducted in developed countries; this adjustment did not change the association nor reduce the observed heterogeneity. The proper diagnosis and classification of cases of ALRI in studies evaluating disease burden or intervention trials is critical to allow for comparisons across studies. Standardized case definitions applied in intervention trials allow for accurate estimation of disease burden preventable through the intervention evaluated, and the comparisons can be made across different regions of the world. In addition, understanding of disease burden preventable through intervention is critical when designing new intervention trials to estimate the sample size based on expected size of effect against appropriate endpoints.

There is a need to understand what illness or combinations of illness are being studied and what impact improved cookstoves and fuel can have. Biological mechanism for IAP causing pneumonia is not precisely understood. Exposure to increased levels of PM2.5 may lead to increase in ALRI through several mechanisms, including structural damage, transport of pathogens, and immune dysregulation. The described mechanism likely includes inflammation in the upper airway and lung, providing a potential portal for invasion of bacterial, viral, mycobacterial and other pathogens.[39, 40] In the mouse model, exposure to gamma interferon aerosol then concentrated ambient particles from urban air prior to infection with *S. pneumoniae* resulted in enhanced lung inflammation (increased PMN recruitment to the lung and elevated pro-inflammatory cytokine mRNAs), impaired bacterial clearance and reduced bacterial uptake by alveolar macrophages and PMNs.[37] Similar mechanisms may also apply to exposure to tobacco smoking that was recently associated with childhood pneumonia in a population-based study in Vietnam.[38] In addition, as reviewed by Domagala-Kulawik, smoke from any source can interfere with immune function including alveolar macrophage function which is critical to host defense.[39] Particles can impair alveolar macrophage superoxide production which can reduce their ability to kill respiratory pathogens.[40]

This study provides a systematic review and meta-analysis designed to estimate the reduction in the burden of pneumonia among children based on measured reduction in levels of indoor air pollution. The results of this analysis contribute to the process of planning for future health impact studies or intervention trials evaluating the effects of clean burning cookstoves on burden of pneumonia in children. The available biomass stove technologies lead to modest reductions in indoor air pollutants and in personal exposures. Given the observed changes in IAP in field studies evaluating biomass stoves, and the findings from our study, only limited health benefits can be expected using available improved biomass stoves. There remains a need for high-quality intervention-based evidence on effect estimates for childhood pneumonia. These studies should include detailed exposure assessment, specifically, levels of personal exposure, in order to better quantify exposure-response relationships.

Figure 1. Results of literature search to identify studies to be included in meta-analysis

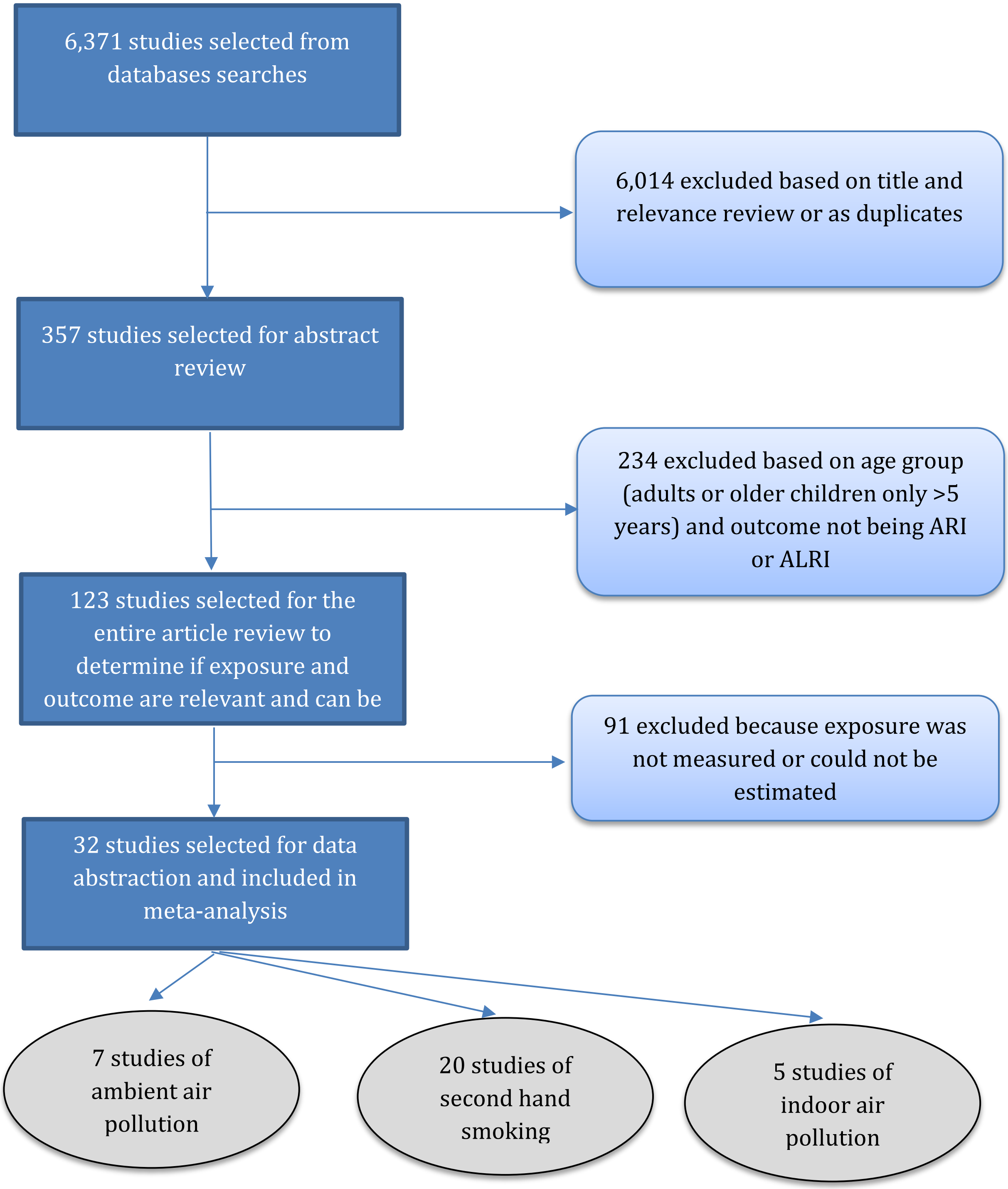


Table 2.1. Summary of studies included in meta-regression analysis

Study Reference	**Exposure assessment**	**ALRI defined**	**Sample, n**	**Risk ratio (RR,95%CI)**	**LnRR per µg/m$_3$**	**Standard Error**	**$PM_{2.5}$ Concentration Used for RR**	**$PM_{2.5}$ Denominator Concentration**
Ambient Air Pollution								
Barnett et al.(2005)[79]	Ambient $PM_{2.5}$	Pneumonia and acute bronchiolitis admissions	Case-crossover in 5 cities	1.06 (1.01, 1.13) [1]	0.016325	0.007842	9.2	-
Brauer et al. (2002)[80]	Ambient $PM_{2.5}$	Doctor diagnosed flu/serious colds	2981	1.12 (1.00-1.27)[2]	0.035415	0.018069	16.9	-
Darrow et al. 2014[81]	Ambient $PM_{2.5}$	ED visits for pneumonia	14,686 ED visits	1.01 (0.99-1.03)[3]	0.001131	0.001137	14.1	-
Darrow et al. 2014[81]	Ambient $PM_{2.5}$	ED visits for URI	124,746 ED visits	1.02 (1.00-1.03)[3]	0.002250	0.000566	14.1	-
Hertz-Picciotto et al. (2007)[82]	Ambient $PM_{2.5}$	Doctor diagnosed bronchitis, bronchiolitis, LRI	1429	1.30 (1.08–1.58)[4]	0.010495	0.003981	22.3	-
Karr et al. (2007)[83]	Ambient $PM_{2.5}$	Hospitalized acute bronchiolitis	18,595 cases 169,472 controls	1.09 (1.04-1.14)[5]	0.008618	0.002288	25	-
Karr et al. (2009)[84]	Ambient $PM_{2.5}$	Hospitalized acute bronchiolitis	2604 cases 23,354 controls	1.04 (0.83-1.29)[5]	0.003922	0.010991	12.1	-
McIntire et al. 2014[85]	Ambient $PM_{2.5}$	Parent reported physician diagnosed pneumonia	10 European birth cohorts	2.58 (0.91, 7.27)[6]	0.189558	0.105711	15	-
Second Hand Smoke								
Blizzard et al. 2003[86]	Second Hand Smoke	Pneumonia, bronchitis, bronchiolitis, pleurisy, influenza with other manifestations	4,500	1.49 (1.04, 2.20)	0.008862	0.004418	50	5
Bonu et al. 2004[87]	Second Hand Smoke	Parent reported ARI episode	33,000	1.15 (1.00, 1.33)	0.003106	0.001649	50	5
Etiler et al. 2002[88]	Second Hand Smoke	Parent reported ARI episode	204	1.07 (0.80-1.43)	0.001504	0.003288	50	5

Study Reference	**Exposure assessment**	**ALRI defined**	**Sample, n**	**Risk ratio (RR,95%CI)**	**LnRR per μg/m^3**	**Standard Error**	**$PM_{2.5}$ Concentration Used for RR**	**$PM_{2.5}$ Denominator Concentration**
Baker et al. 2006[89]	Second Hand Smoke	LRI (98% bronchitis)	452	1.29 (1.01- 1.65)	0.005659	0.002791	50	5
Broor et al. 2001[90]	Second Hand Smoke	Severe LRI (WHO definition)	201 cases 311 controls	1.24 (0.83-1.86)	0.004780	0.004597	50	5
Chen et al. 1994[91]	Second Hand Smoke (#cigarettes/day)	ARI (includes URI and LRI)	3,285	1.40 (0.96-2.03) 1.61 (1.08-2.41)	0.016824 0.010583	0.009479 0.004574	25 50	5
Duijts et al. 2008[92]	Maternal smoking (yes/no)	Parent reported LRI requiring doctors visit	3,418	1.61 (0.99, 2.63)	0.010583	0.005564	50	5
Ekwo et al. 1983[93]	Parents smoking (yes/no)	Hospitalization for respiratory illness	1,355	2.1 (SE 0.666)	0.016381	0.007058	50	5
Ferris et al. 1985[94]	Parents smoking (yes/no)	Doctor diagnosed respiratory illness or LRI index	13, 545	1.85 (p<0.001)	0.020506	0.029232	35	5
Forastiere et al. 1992[95]	Maternal smoking (yes/no)	Pneumonia	3,092	1.3 (0.8, 2.2)	0.008745	0.008947	35	5
Hassan et al. 2001[96]	Smoking in the household (yes/no)	Severe/very severe pneumonia (WHO defined)	148 cases 250 controls	2.16 (1.43-3.28)	0.02567	0.007104	35	5
Islam et al. 2013[97]	Second Hand Smoke	Parent reported ARI episode (includes URI and LRI)	370	1.24 (0.78-1.98)	0.010756	0.011938	25	5
Kock et al. 2003[98]	Smoking in the household (yes/no)	Clinician diagnosed LRI	260	2.13 (1.30- 3.47)	0.016803	0.005522	50	5
Kristensen et al. 2006[99]	Second Hand Smoke	Nurse diagnosed moderate to severe ARI (WHO defined)	571	1.37 (0.95-1.98)	0.006996	0.004176	50	5
Margolis et al. 1997[100]	Smoking in the household (#cigarettes/day)	Parents’ report of LRI symptoms	325	1.5 (1.1- 2.0) 2.2 (1.3- 3.8)	0.020273 0.017521	0.007339 0.006197	25 50	5

Study Reference	Exposure assessment	ALRI defined	Sample, n	Risk ratio (RR,95%CI)	LnRR per µg/m$_3$	Standard Error	PM$_{2.5}$ Concentration Used for RR	PM$_{2.5}$ Denominator Concentration
Ogston et al. 1987[101]	Maternal smoking	Health visit or hospitalization for respiratory illness (URI and LRI)	1,565	-	0.013333	0.004222	50	5
Pedreira et al. 1985[102]	Household member smoking	Doctor's visit for URI or LRI	1,144	-	0.005617	0.003046	50	5
Rylander et al. 1995[103]	Parental smoking status and urine cotinine levels	Hospitalized clinician diagnosed bronchitis with wheezing	199 cases 351 controls	1.8 (1.3-2.6)	0.013062	0.004169	50	5
Suzuki et al. 2009[38]	Parental smoking status (yes/no)	Hospitalization with pneumonia	24,781	1.55 (1.25-1.92)	0.009739	0.002427	50	5
Victora et al. 1994[104]	Household member smoking (#cigarettes/day)	Chest x-ray confirmed pneumonia	500 cases 500 controls	0.99 (0.75-1.31)	-0.00022	0.003158	50	5
Household air pollution								
Collins et al. 1990[105]	Kitchen PM$_{10}$ converted to personal PM$_{2.5}$[7]	Clinician diagnosed ARI (ALRI and AURI)	244 cases 500 controls	2.16 (1.44-3.26)	0.000856	0.000233	1250	345
Ezzati et al. 2001[5]	Kitchen PM$_{10}$ converted to personal PM$_{2.5}$[7]	Trained health care worker assessed ARI	93	2.42 (1.53-3.83) 2.15 (1.30-3.56) 4.30 (2.63-7.04) 4.72 (2.82-7.88) 6.73 (3.75-12.06)	0.009303 0.002251 0.001823 0.000988 0.000939	0.002466 0.000757 0.000314 0.000167 0.000147	215 460 920 1690 3080	120 120 120 120 120
Ezzati et al. 2001[5]	Kitchen PM$_{10}$ converted to personal PM$_{2.5}$[7]	Trained health care worker assessed ALRI	93	1.48 (0.83-2.63) 1.40 (0.74-2.67) 2.33 (1.23-4.38) 1.93 (0.99-3.78) 2.93 (1.34-6.39)	0.004127 0.000990 0.001057 0.000419 0.000530	0.003088 0.000969 0.000403 0.000218 0.000196	215 460 920 1690 3080	120 120 120 120 120
Ram et al. 2014[106]	Kitchen PM$_{2.5}$	Radiographically confirmed pneumonia	97 cases 215 controls	1.00 (0.99-1.03)	0	0.002514	76	70

Study Reference	Exposure assessment	ALRI defined	Sample, n	Risk ratio (RR,95%CI)	LnRR per μg/m$_3$	Standard Error	PM$_{2.5}$ Concentration Used for RR	PM$_{2.5}$ Denominator Concentration
Robin et al. 1996[107]	Kitchen PM$_{10}$ converted to personal PM$_{2.5}$[7]	Hospitalized ALRI	45 cases and 45 controls	7.0 (0.9-56.9)	0.027027	0.014848	98	26
Smith et al. 2011[4, 23]	Personal exposures to CO in children measured[4]; converted to personal PM$_{2.5}$[23]	Physician diagnosed pneumonia	269 intervention and 265 control households	1.3 (0.94,1.69)	0.001975	0.001134	250	125
					0.268264	0.447947	79	49
					0.589684	0.325059	103	49
					0.334639	0.329612	131	49
					0.41961	0.364845	163	49
					0.610787	0.327824	197	49
					0.682406	0.312955	230	49
					0.718465	0.345909	282	49
					0.575364	0.397693	363	49
					0.753269	0.325687	553	49

[1] RR for an interquartile range increase equivalent to 3.8 μg/ml for PM$_{2.5}$

[2] RR for an interquartile range increase equivalent to 3.2 μg/ml for PM$_{2.5}$

[3] RR for an interquartile range increase equivalent to 8.8 μg/ml for PM$_{2.5}$

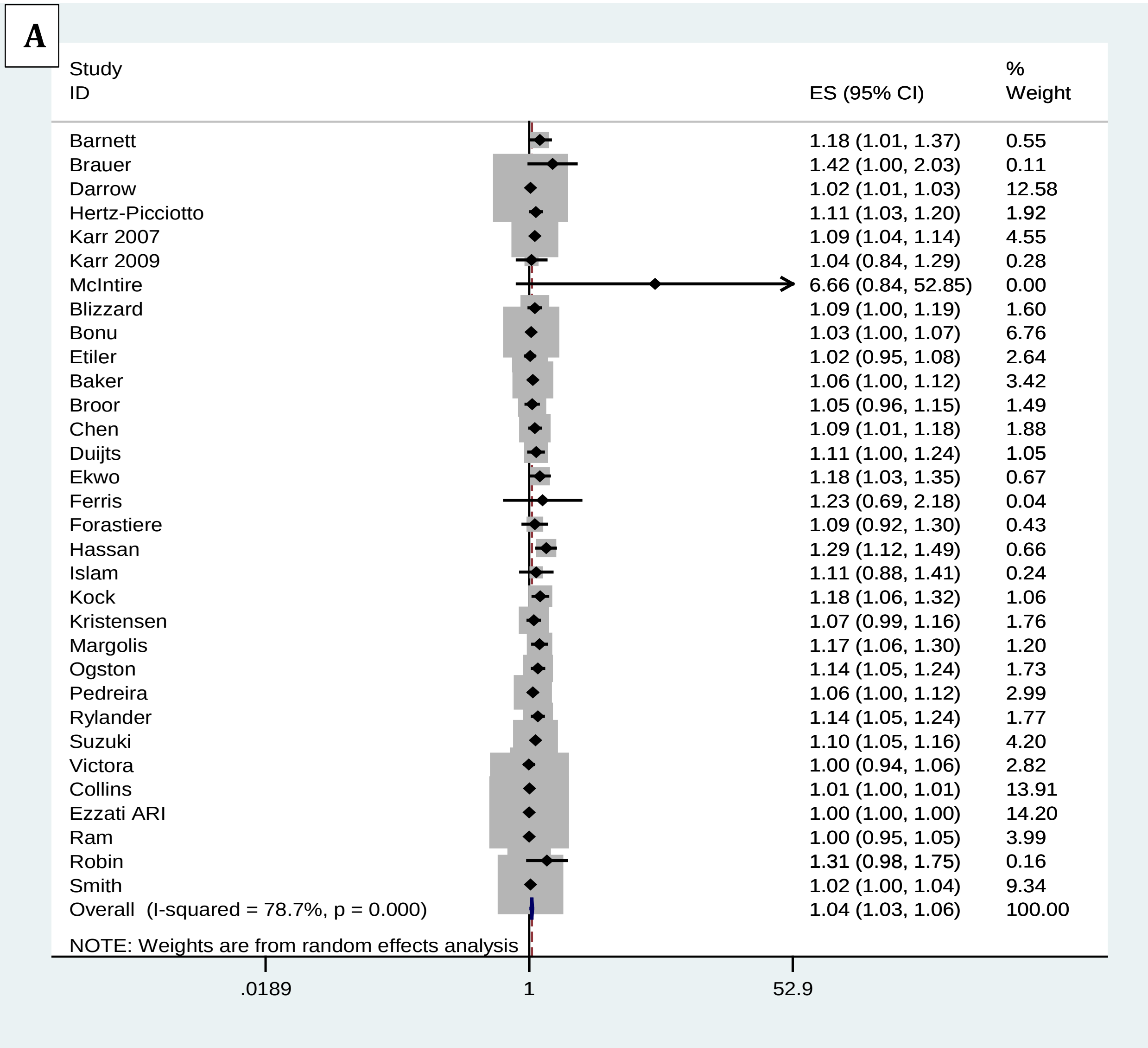
[4] RR per increment of 2 SD increase equivalent to 25 μg/ml for PM$_{2.5}$

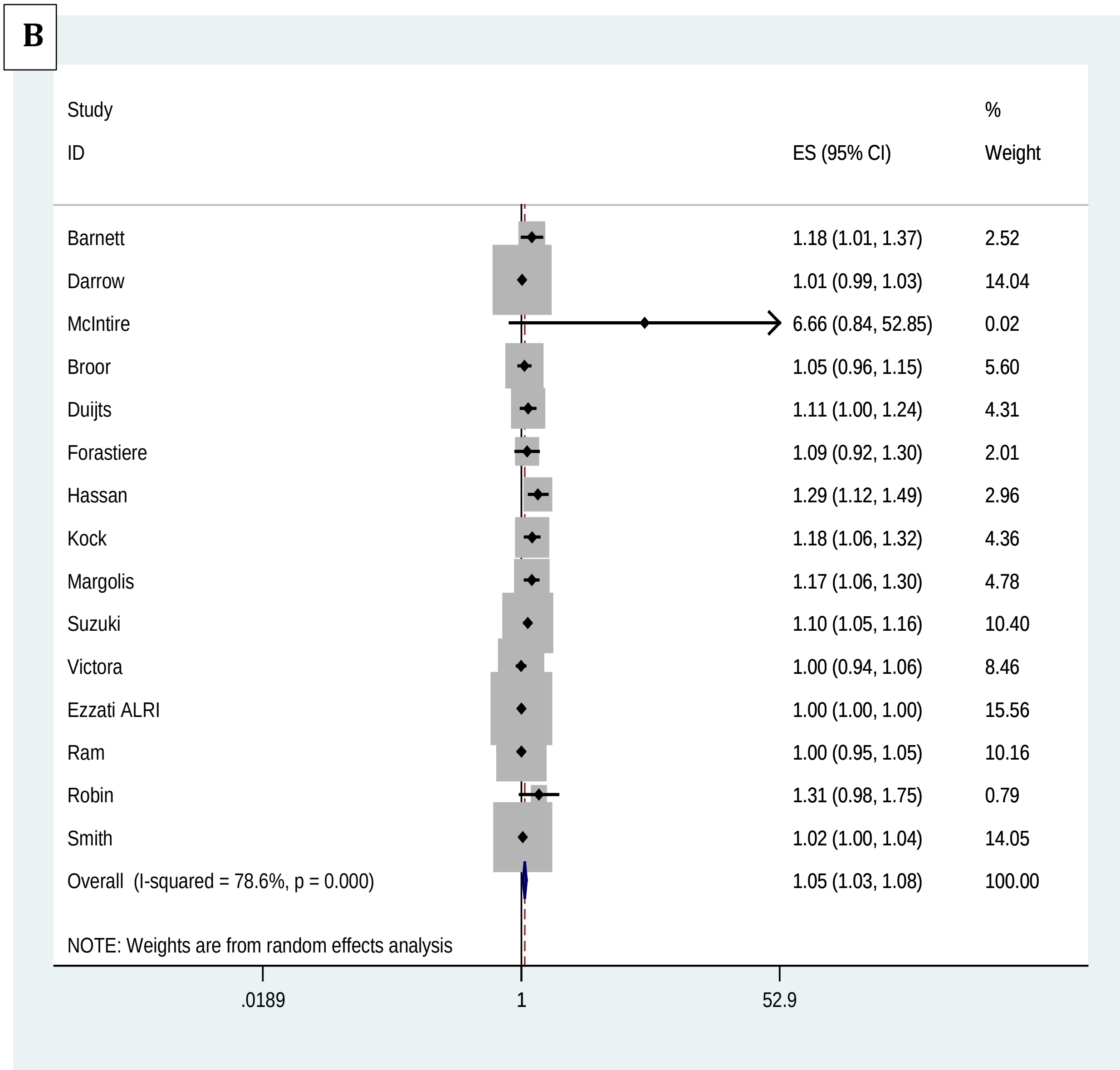
[5] RR per increase equivalent to 10 μg/ml for PM$_{2.5}$

[6] RR per increase equivalent to 5 μg/ml for PM$_{2.5}$

[7] Estimated personal exposure by applying a ratio of 0.628 for children <5 years of age (Balakrishnan K. 2012. Version 2.0. Porur, India; Geneva: Univ. Calif., Berkeley, Sri Ramachandra Univ., WHO)

Figure 2 A-C. Study-specific measures of effect (relative risks and 95% confidence intervals) from a meta-analysis using the natural log-transformed relative risk estimates as the dependent variable. Included studies evaluating ARI (ALRI and/or AURI) in (A), ALRI only studies (B), and AURI studies (C). Each study slope standardized to change in outcome per 10 µg/ml of increase in PM2.5.




B
Study
ID
ES (95% CI)
%
Weight
Barnett 1.18 (1.01, 1.37) 2.52
Darrow 1.01 (0.99, 1.03) 14.04
McIntire 6.66 (0.84, 52.85) 0.02
Broor 1.05 (0.96, 1.15) 5.60
Duijts 1.11 (1.00, 1.24) 4.31
Forastiere 1.09 (0.92, 1.30) 2.01
Hassan 1.29 (1.12, 1.49) 2.96
Kock 1.18 (1.06, 1.32) 4.36
Margolis 1.17 (1.06, 1.30) 4.78
Suzuki 1.10 (1.05, 1.16) 10.40
Victora 1.00 (0.94, 1.06) 8.46
Ezzati ALRI 1.00 (1.00, 1.00) 15.56
Ram 1.00 (0.95, 1.05) 10.16
Robin 1.31 (0.98, 1.75) 0.79
Smith 1.02 (1.00, 1.04) 14.05
Overall (I-squared = 78.6%, p = 0.000) 1.05 (1.03, 1.08) 100.00
NOTE: Weights are from random effects analysis
.0189
1
52.9

C

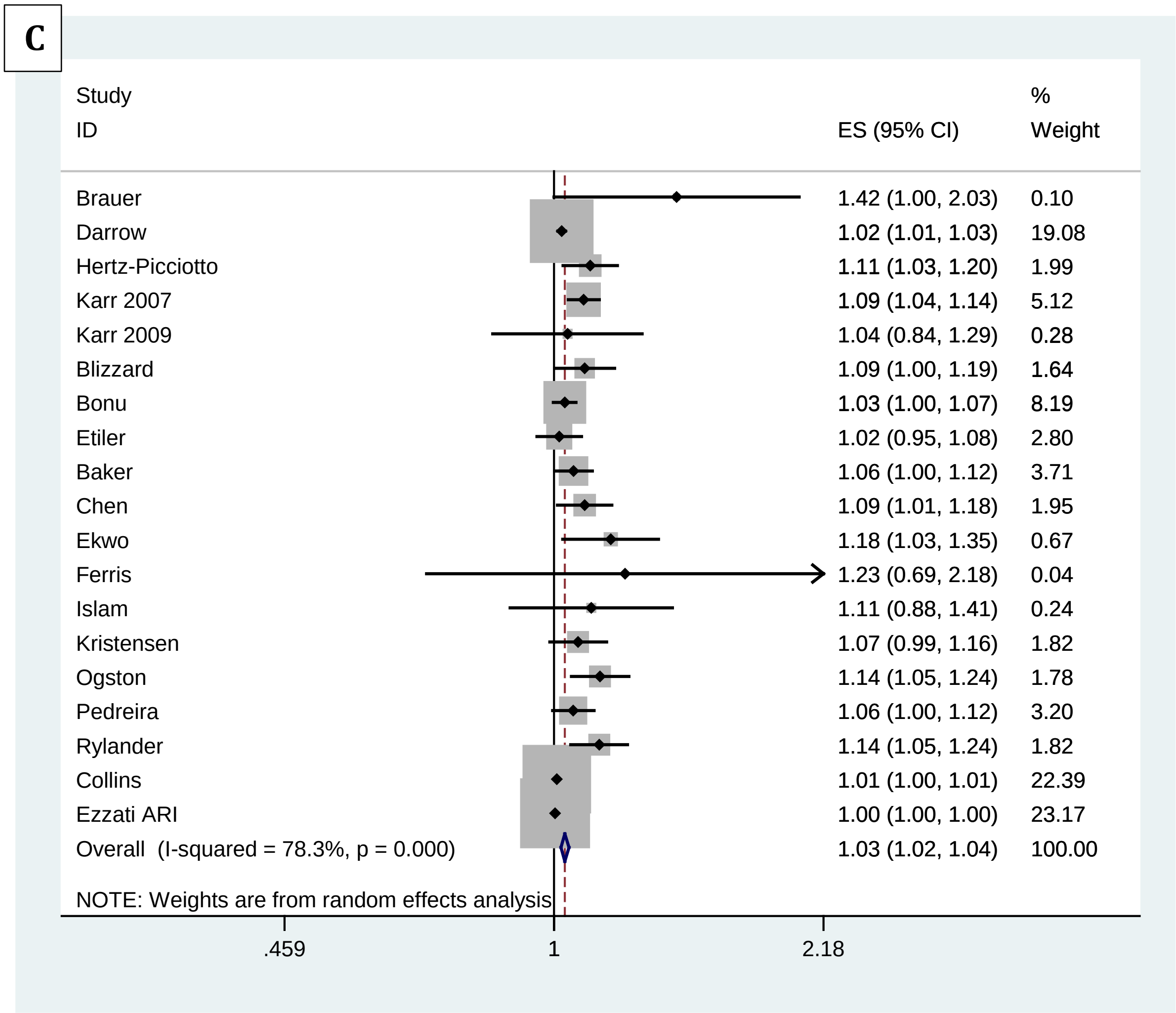
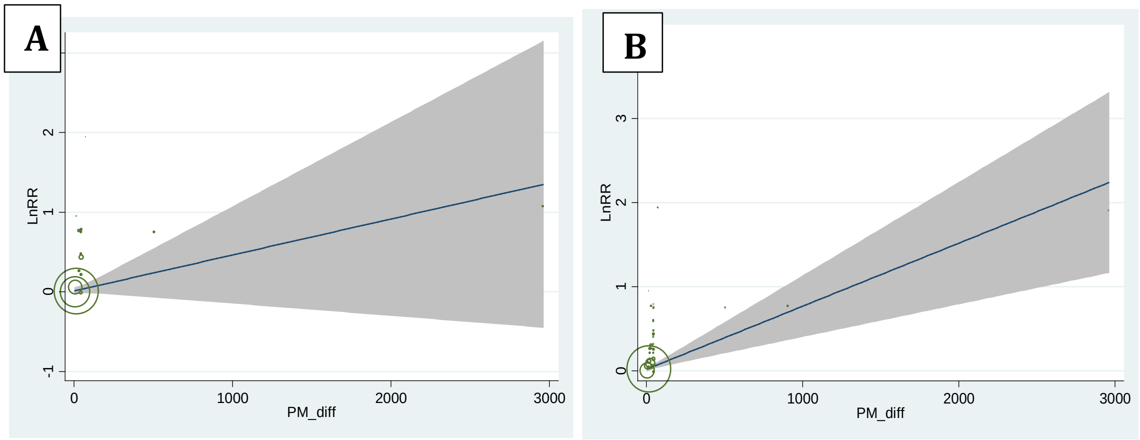
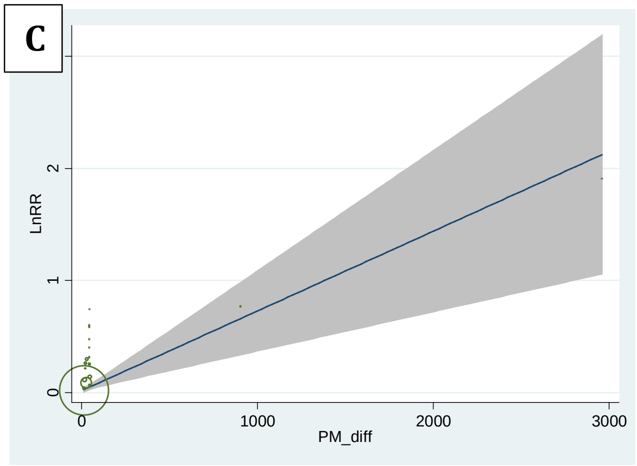

Study
ID
ES (95% CI)
%
Weight
Brauer 1.42 (1.00, 2.03) 0.10
Darrow 1.02 (1.01, 1.03) 19.08
Hertz-Picciotto 1.11 (1.03, 1.20) 1.99
Karr 2007 1.09 (1.04, 1.14) 5.12
Karr 2009 1.04 (0.84, 1.29) 0.28
Blizzard 1.09 (1.00, 1.19) 1.64
Bonu 1.03 (1.00, 1.07) 8.19
Etiler 1.02 (0.95, 1.08) 2.80
Baker 1.06 (1.00, 1.12) 3.71
Chen 1.09 (1.01, 1.18) 1.95
Ekwo 1.18 (1.03, 1.35) 0.67
Ferris 1.23 (0.69, 2.18) 0.04
Islam 1.11 (0.88, 1.41) 0.24
Kristensen 1.07 (0.99, 1.16) 1.82
Ogston 1.14 (1.05, 1.24) 1.78
Pedreira 1.06 (1.00, 1.12) 3.20
Rylander 1.14 (1.05, 1.24) 1.82
Collins 1.01 (1.00, 1.01) 22.39
Ezzati ARI 1.00 (1.00, 1.00) 23.17
Overall (I-squared = 78.3%, p = 0.000) 1.03 (1.02, 1.04) 100.00
NOTE: Weights are from random effects analysis
.459
1
2.18

Figure 3 A-C. Results of a meta-regression for natural log-transformed relative risk estimate (ln(RR)) (y-axis) by maximum difference between the highest and the lowest levels of PM2.5 (x-axis). Included studies evaluating ARI (ALRI or AURI), N=32 (A), ALRI only studies, N=15 (B), and AURI only studies, N=19 (C).



β	95%CI	P value
.00060	.00037, .00082	0.000

β	95%CI	P value
.00029	-.00008, .00065	0.112



β	95%CI	P value
.00060	.00039, .00082	0.000

Table 2.2. Sensitivity analysis for dose-response meta-regression for natural log-transformed relative risk estimate (ln(RR)) by maximum difference between the highest and the lowest levels of PM2.5 to assess the influence of study inclusion decisions on the summary estimates and measures of heterogeneity.

Model	Summary estimate			Test of heterogeneity, I^2
	β	95%CI	P value	
ARI				
Original model (N=32)	0.00060	0.00037, 0.00082	0.000	73.33%
Excluding studies of smoking (N=12)	0.00068	0.00043, 0.00093	0.000	59.59%
Restricting to studies with exposure levels				
PM2.5 ≤50 µg/ml (N=27)	0.00774	0.00273, 0.01276	0.004	52.76%
PM2.5>50 µg/ml (N=5)	0.00064	0.00016, 0.00111	0.024	73.89%
ALRI				
Including varying exposure levels and associated measure of effect for Smith et al and Ezzati et al (N=15)				
Highest level assessed (original model)	0.00029	-0.00008, 0.00065	0.112	78.02%

Model	Summary estimate			Test of heterogeneity, I^2
	β	95%CI	P value	
Mid-level assessed	0.00086	-0.00034, 0.00205	0.146	75.89%
Lowest level assessed	0.00731	-0.00029, 0.01491	0.058	67.59%
Excluding studies of smoking and including varying exposure levels and associated measure of effect for Smith et al and Ezzati et al (N=7)				
Highest level assessed	0.00041	-0.00011, 0.00093	0.099	57.53%
Mid-level assessed	0.00119	-0.00031, 0.00270	0.097	55.00%
Lowest level assessed	0.00424	-0.00458, 0.01307	0.271	48.19%
AURI				
Including varying exposure levels and associated measures of effect for Smith et al and Ezzati et al (N=19)				
Highest level assessed (original model)	0.00060	0.00039, 0.00082	0.000	70.72%
Mid-level assessed	0.00105	0.00055, 0.00154	0.000	70.76%

Model	Summary estimate			Test of heterogeneity, I^2
	β	95%CI	P value	
Lowest level assessed	0.00072	0.00009, 0.00135	0.027	74.03%
Excluding studies of smoking and including varying exposure levels and associated measures of effect for Smith et al and Ezzati et al (N=7)				
Highest level assessed	0.00065	0.00040, 0.00089	0.001	65.27%
Mid-level assessed	0.00114	0.00042, 0.00185	0.009	73.04%
Lowest level assessed	0.00081	-0.00018, 0.00179	0.090	79.54%

Household air pollution and density of nasopharyngeal carriage of *Streptococcus pneumoniae* among young children in rural Peru

Abstract

Background: *Streptococcus pneumoniae* (pneumococcus) is the most common bacterial cause of pneumonia, the leading cause of death among children worldwide. Pneumococcal nasopharyngeal colonization precedes disease and high density of colonization has been associated with increased risk of pneumonia. Household air pollution from burning biomass smoke is an important risk factor for pneumonia.

Objectives: The objective of this study was to evaluate the association between kitchen levels and personal exposures to carbon monoxide (CO) from biomass smoke and density of pneumococcal colonization among young children in rural Peru.

Methods: A cohort study was nested within a randomized community trial evaluating household intervention package which included an improved biomass stove. Pneumococcal colonization evaluated among children 0-36 month old during monthly household visits was confirmed using culture or PCR. Density of colonization (colony forming units per ml, CFU/ml) was measured using quantitative PCR. Kitchen and personal (mother and child) CO levels (parts per million, ppm) were measured using passive diffusion samplers. We used linear mixed effects regression models to assess the association between CO and colonization density.

Results: We included 135 households (children) and 519 nasopharyngeal samples for pneumococcal colonization. Percent changes in mean density of colonization (and 95%CI) associated with each ten-fold increase in CO levels (ppm) were as follows: -11.2% (-83.8,

387) for kitchen, -39.3% (-91.4, 329) for mothers, and -55.0% (-93.5, 210) for children. No differences by household stove type were reported for either kitchen or personal CO levels for mothers. Median child CO levels were slightly higher for households with traditional stove compared to households with improved stoves (p=0.0394).

Conclusions: We found no significant associations between kitchen and personal levels of CO and density of pneumococcal carriage. Our study suggests that larger impact on HAP is needed to observe health benefits. More efficient biomass stoves and stove technologies utilizing clean fuels may be needed to achieve measurable health benefits.

Background

Pneumonia is the leading cause of death in children <5 years old, and accounts for approximately one million childhood annual deaths in the world.[73] Approximately 90% of these deaths occur in the developing world, where interventions that could effectively reduce the burden of pneumonia would have an enormous public health impact. *Streptococcus pneumoniae* (pneumococcus) is the most common bacterial cause of pneumonia, and thus, a leading cause of morbidity and mortality worldwide.[108]

Several bacterial pathogens, including pneumococcus, normally reside in the nasopharynx of children. Although nasopharyngeal colonization does not necessarily lead to disease, it is an important precursor for pneumococcal diseases.[109] Person-to-person transmission of *S. pneumoniae* occurs through contact with secretion of colonized individuals. Most children acquire pneumococcus from family members during their first month of life but the rates of acquisition differ greatly by age group, pneumococcal serotype, season, and geography.[110, 111] Crowding, close contact with young children, high rates of respiratory infections, and exposure to household air pollution have been described as risk factors for pneumococcal colonization.[112] Although immunological responses can in part explain the susceptibility of young children to colonization, this process is not fully understood. Length of colonization can also vary by age (i.e. younger infants have longer a period of colonization) and by immunogenicity of pneumococcal serotypes (i.e. serotypes leading to poor immune response tend to be carried longer). Pneumococcal colonization is relatively common among children but the factors leading to development of pneumococcal disease (e.g. otitis media, pneumonia, bacteremia, or meningitis) are also poorly understood. Nevertheless, high density of nasopharyngeal colonization with *S. pneumoniae* has been associated with an increased risk for developing pneumonia.[53, 55]

Exposure to high levels of household air pollution due to burning biomass fuels for cooking, a common practice in rural areas of developing countries, can lead to damage of respiratory epithelium and further development of serious respiratory infections.[4, 9] There is a surprising lack of data on the interaction between household air pollution and pneumococcal colonization, which is thought to be part of the critical path to pneumococcal pneumonia and its attendant mortality.[113] Whether exposure to household air pollution from biomass burning plays a role in the dynamics of the pneumococcal carriage, specifically density of pneumococcal colonization, has yet to be determined. The objective of this study was to evaluate the association between kitchen levels and personal exposures to carbon monoxide (CO) and density of nasopharyngeal carriage of *Streptococcus pneumoniae* among young children in rural Peru.

Methods

Study design

A prospective cohort study was nested within a community-randomized controlled trial (the parent study)[28, 114, 115] evaluating whether a home-environmental intervention package, including improved biomass stoves, kitchen sinks, household water treatment using solar disinfection of drinking water (SODIS) and food- and personal hygiene promotion, reduces lower respiratory infections, diarrheal disease and improves growth among children <36 months old. For this nested prospective cohort, children 0-36 months of age were enrolled and followed up through weekly household visits. Routine nasopharyngeal specimens were obtained monthly. Exposures to household air pollution were measured during a single visit in a sample of intervention and control households. The current study was restricted to a convenience sample of 135 households that participated in the parent study, had available measurements of air pollution, and had nasopharyngeal samples (described below) collected as part of the prospective cohort study.

The protocol for this study was reviewed by the IRB at Emory University and determined to be exempted from ethical clearance. The prospective cohort study were approved by the Instituto de Investigacion Nutricional and the Vanderbilt IRBs. The parent trial received ethical approval from the Nutritional Research Institute (IIN) Ethical Review Board, the cantonal ethical review board of the University of Basel, Switzerland (EKBB), the Cajamarca Regional Health Authority and the Peruvian National Institute of Health (INS). It was registered at the (INS and in an international trial registry (ISRCTN: ‘ISRCTN28191222’).

Study setting/location

The study was conducted in the Province of San Marcos, Department of Cajamarca, Peru. Cajamarca has a population of about 1.5 million people. San Marcos is a province located in the southeast end of Cajamarca with variable altitude (1500-4000 meters above the sea level), with mainly rural (84%) population and limited access to healthcare services. Ninety three percent of the rural population uses biomass for cooking and heating.

Enrollment (parent study)

The parent study enumerated all the households residing within the catchment area.[28, 114] Field workers visited every household in the area and interviewed family members using a standardized form. Enrollment was based on the following inclusion criteria: households used wood for cooking, had no access to potable water and not connected public sewage system, had at least one child <36 months old, and no plans to relocate out of the study area during the year following the enrollment. Children with chronic medical conditions or congenital defects were excluded from the study. After application of selection criteria, the parent study enrolled 534 households encompassing 51 communities. There were 267 randomized to the intervention and 267 to the control arm. The final study analysis included 248 children from intervention and 251 from the control households.

Intervention

The intervention package included an improved stove, installation of a kitchen sink and drainage, water bottles for solar disinfection of drinking water, and training on the use of interventions, hygiene practices and food safety. The control group received educational materials and toys for each three months age window and parent education on the use of these materials.[115]

The certified improved intervention stove (OPTIMA stove) was built with red-burnt bricks plastered with a mixture of mud, straw, and donkey manure. It has three openings on the stove area designed to hold cooking pots, a closed combustion chamber, metal chimney with a regulatory valve, a hood, and metal rods for support. Kitchen performance tests of the OPTIMA stoves demonstrated a 15% reduction in daily fuel use and a 16% reduction in fuel use per capita compared with the traditional open fire stove. Control households used a wide range of stoves for cooking, including traditional non-vented stove with pot holes for cooking (referred to as traditional or Tulpia) and chimney stoves built with raw material provided by non-governmental organizations or self-improved by households (referred to as hybrid). This randomized trial found no significant difference in the incidence of acute respiratory diseases between the intervention and control arms.[28]

Exposure measurements

Household air pollution (HAP) and personal exposure to HAP assessments were conducted in a convenience sample of intervention (n=161) and control (n=154) households 6 to 8 months following the installation of the improved stoves. Time integrated CO measurements were taken using Drager Diffusion Tubes for Carbon Monoxide, with a range of 6–600 ppm-hour (parts per million-hour). Three CO passive diffusion samplers were set up and left in place for 48 hours in each household to measure exposures to CO. Two tubes were for personal sampling: one worn in the breathing zone of the mother and one worn by a child under the age of 5 years who was enrolled in the parent study. The third tube was set up in the kitchen, at the breathing height (approximately 1.5 m) of the mother and close to where she stands during cooking. This assessment demonstrated only modest differences in measurements of household air pollution between intervention and control arms.[116, 117]

Follow-up

At enrollment, field workers visited each participating household and conducted interviews to collect demographic, socio-economic and other information on risk factors for ARI's and pneumonia. As part of the prospective cohort study, weekly household follow up visits by field workers were conducted to collect information on signs and symptoms of acute respiratory infections (ARI) during the preceding week, recording date of onset, duration of illness, and symptoms reported. Field-workers were trained in the recognition of respiratory signs and symptoms using the Integrated Management of Childhood Illnesses (IMCI) World Health Organization protocol. In addition to the weekly visits, nasopharyngeal (NP) samples were collected on a monthly basis from the enrolled children. For this study, we included samples collected from May through November 2009, the study period more proximal to the exposure measurements.

Outcome

Collected NP samples were placed in skim milk, tryptone, glucose, and glycerine media, transported to the local research laboratory, and stored at −70°C until shipment to Emory University for the identification of *S. pneumoniae* and quantification of nasopharyngeal density. A child was deemed as colonized with pneumococcus if the nasopharyngeal sample was positive for *S. pneumoniae* by either conventional bacteriological culture or polymerase chain reaction (PCR) for *lytA*.[118] Quantitative PCR measured pneumococcal colonization density and results were reported as colony forming units per milliliter (CFU/ml). Further determination of pneumococcal serotype was performed through multiplex PCR using published reactions.[119]

Data analysis

We used multivariable linear mixed effects regression models to assess the association between household air pollution exposure measurements (kitchen levels of CO, ppm) and personal exposures in children and mothers (personal CO, ppm), and the density of pneumococcal colonization. All CO and colonization density data were log transformed for regression analyses. We assigned an arbitrary low density value of 1 CFU/ml to samples with no pneumococcal carriage detected to allow for log transformation of zero density samples. The lowest density detected among samples positive for pneumococcal carriage was 200 CFU/ml. We conducted sensitivity analysis assigning 0.5 CFU/ml to zero density samples (Appendix 2). For each type of exposure (kitchen, mother or child), the analysis took into account potential confounders and the correlation of responses within subjects. The general form of the linear mixed effects model is as follows:

$D_{ij} = \beta_0 + b_{0i} + \beta_1$ (stove type) + β_{2i} (logCO) + γ_{ij} (period) + β_{3ij} (covariates) + β_{4i} (covariates) + ε_{ij}

D_{ij} – log density of colonization for child *i* and measurement *j*

β_0 – overall intercept

b_{0i} – child-specific random effects

β_1 – fixed effects of stove type

β_{2i} (logCO) - natural log of kitchen or personal (child or mother) CO levels

β_{3ij} – time-dependent covariates (child's age at sample collection, month of sample collection, recent ARI episode)

β_{4i} – time-independent covariates (altitude, lighting source in the house, fuel type)

γ_j - time (month of sample collection)

ε_{ij} – vector of residual errors

To account for missing consecutive NP swabs, we conducted sensitivity analyses using spatial covariance matrix, a generalization of autoregressive matrix for unequally spaced non-integer sampling time values, which takes into account absolute difference between sample collection times for errors (Appendix 2).

In addition, we evaluated the association between levels of household air pollution (kitchen levels of CO, ppm) and personal exposures in children (personal CO, ppm) and presence of pneumococcal colonization (sample positive for *S. pneumonia*) using mixed effects logistic regression models. The general form of the model is as follows:

Logit P (D=1|X) = β_0 + b_{0i} + β_1 (stove type) + β_{2i} (logCO) + β_{3ij} (covariates) + β_{4i} (covariates) + γ_j(round)

D –colonization present (Yes/No)

β_0 –intercept

b_{0i} – random effects for child *i*

β_1 – fixed effects of stove type

β_2 (logCO)- natural log of kitchen or personal (child or mother) CO levels

β_{3j} – time-dependent covariates

β_{4i} – time-independent covariates

γ_j - time (month of sample collection)

We used STATA for all our data analysis.

Results

Exposure assessment using time-integrated CO measurement and outcome assessment were available for 135 households (135 children). Fifty-seven of these (42%) were intervention households using OPTIMA stove. The remaining control households included 58 (43%) using traditional Tulpia stove, 17 (13%) using hybrid stoves, and 3 households using other stoves. There were no differences in household characteristics (number of household members, number of rooms in the household, number of smokers in the household, and average time spent cooking) by stove type used. A total of 83 (62%) study children were <2 years of age at enrollment, 72 (53.3%) were male.

A total of 519 nasopharyngeal samples for pneumococcal colonization were included in this study, with an average of 3.8 samples collected (ranging from 1 to 6) per household. Fifty-four (40%) of children missed one consecutive specimen collection, 3 (2%) missed 2 consecutive swab collections. The mean interval between the recorded CO measurement and the first nasopharyngeal sample collection was 5 days (median 28 days). The average number of samples per child with ARI episodes reported within 7 days prior to sample collection was 0.7 (median 1, ranging from 0 to 3).

We found no significant associations between kitchen and personal levels of CO and 1) density of pneumococcal carriage or 2) pneumococcal carriage rates. Results of linear mixed effects model and mixed effects logistic regression model evaluating these associations are presented in Table 1 and 2. The multivariable analysis adjusted for child's age, gender, month of sample collection, altitude, type of lighting in the house, type of stove, and recent ARI. As seen in Tables 1 and 2, percent changes in mean density of colonization (CFU/ml) and percent changes in rates of pneumococcal colonization were not significantly associated with each ten-fold increase in both kitchen and personal CO levels (ppm).

Similar results were obtained when analysis for Tables 1 and 2 were repeated using quantile regression models. No significant associations were found between changes in kitchen and personal CO and pneumococcal carriage (rates or density of carriage), with the following exceptions. Significant reductions in density of pneumococcal carriage were associated with increase in child CO overall (-53% (95%CI -75, -10, p=0.023)) and among households using

OPTIMA stove (-90% (95%CI -98, -48, p=0.007)). Significant increases in density of pneumococcal carriage were associated with increase in kitchen CO overall among households using hybrid stove (>100%, p=0.022).

We compared mean (median) kitchen CO levels and mother and child personal CO levels by stove type in the household (Table 3). No differences by stove type were reported for either kitchen or personal CO levels for mothers. Median child CO levels were slightly higher for households with traditional stove compared to households with hybrid or intervention stoves (p=0.0394). Overall, kitchen CO levels were higher than mean (median) mother and child CO levels.

Comparison of pneumococcal carriage rates or median density of pneumococcal carriage (CFU/ml) by stove type used in households showed no significant differences (Table 4). Carriage rates among children did not differ by quartiles of kitchen CO levels, as well as personal (mother or child) levels of CO. No significant differences in median density of pneumococcal carriage were observed by quartiles of exposure to CO (kitchen and personal levels). In addition, we evaluated both carriage rates and density of carriage by household and child demographic characteristics. There were no significant differences found by child's age or gender, floor material in the household, and source of lighting. Median density of carriage increased during the last 4 months of sample collection, in households living at the lowest and highest quartiles of altitude, and among children reporting recent ARI episode, although there was no difference in geometric mean of density for the same categories (Table 4). We could not assess the influence of fuel used for cooking because the vast majority of study households used wood.

Given the observed differences among kitchen types, altitude, and household lighting type, we conducted secondary analyses stratified by these variables. These analyses used the same model structures as in our primary analysis. Similar results were obtained within each strata, with the following exceptions. Significant reductions in both density of pneumococcal carriage (-97% (95%CI -100, -53, p=0.013), as well as pneumococcal carriage rates (-84% (95%CI -97, -13, p=0.033)) were associated with increase in child CO among households using OPTIMA stove.

Discussion

The study evaluated the association between household air pollution measurements and nasopharyngeal colonization with *Streptococcus pneumoniae*, the most common cause of bacterial pneumonia in children. Our study found no significant associations between indoor levels of CO or personal (mother or child) exposures to CO and rates or density of pneumococcal carriage among young children in rural Peru.

Observational studies and one clinical trial have demonstrated that improved-combustion stoves, improved ventilation, and reduced use of solid fuels could help reduce pneumonia morbidity and mortality in children.[3-5, 9] While it has been hypothesized that exposure to household air pollution can lead to higher density of nasopharyngeal carriage of *S. pneumoniae*, which can in turn facilitate micro-aspiration of bacteria leading to pneumonia, there are few data to support this hypothesis.[53] A nasopharyngeal carriage study among HIV-infected adults identified increased pneumococcal density in more than 50% of participants with community acquired pneumonia.[53] In another study, increased nasopharyngeal pneumococcal density was independently associated with radiologically-confirmed pneumonia in children.[55] Among factors contributing to increased density of pneumococcal carriage, viral co-infection has been described in several studies. As one of the mechanisms explaining the relationship between pneumococcal colonization, viral co-infection, and development of childhood pneumonia, these studies support the hypothesis that presence of viral infection may lead to increased attachment of pneumococci to virus-infected cells in nasopharynx, which will lead to increased bacterial load, invasion, spread into lower respiratory tract, and pneumonia.[55, 58, 59, 120, 121] Exposure to high levels of household air pollution can also lead to damage of respiratory epithelium. While there are no studies evaluating the influence of household air pollution on the dynamics of pneumococcal nasopharyngeal carriage in children, exposure to second-hand smoke has been shown to be associated with pneumococcal carriage.[122, 123]

In our study population, we observed no differences in levels of kitchen CO and personal exposures to CO among households using traditional, hybrid, or intervention stoves. Our findings are consistent with the results of an earlier study which focused on the assessment of the impact of intervention stove on household air pollution and included a larger sample (197 control and 182 intervention households) of households from the parent trial.[116] Commodore et al. found no statistically different measurements in CO across various stove types and attributed this finding to poor stove/chimney maintenance and improper stove use during the study.

In addition, the parent trial study found no impact of the intervention (stove, installation of a kitchen sink, water disinfection, hygiene practices and food safety) on all-cause acute lower respiratory infections among children measured by field workers.[28] In contrast, a large randomized controlled trial conducted in Guatemala demonstrated reductions in CO exposures by 50%, kitchen concentrations by 90%. Nevertheless, these CO exposure changes did not translate into statistically significant differences in childhood pneumonia between intervention and control arms.[4] During the course of that trial, weekly visits were conducted and the maintenance for the stoves was provided as needed to ensure proper functionality of stoves. Accruing evidence from stove intervention studies suggests that exposures to household air pollution related to cookstoves use can be reduced but large and sustained reductions would be needed for several years to lead to greater health benefits.[4, 124] Exposure-response analysis from the same trial suggests that achieving exposure reduction needed for prevention of child pneumonia may require use of clean fuels or biomass stoves with cleaner combustion.[4]

Several previous studies have focused on exposure to particulate matter <2.5 microns (PM2.5) as a proposed mechanisms for the association between HAP and acute lower respiratory infections (ALRI). Exposure to increased levels of PM2.5 may lead to increase in ALRI through: structural damage to respiratory epithelium, inflammation in the upper airway and lung, and subsequently, reduced clearance of bacterial pathogens; transport of pathogens (potential portal for invasion of bacterial or viral pathogens); immune dysregulation through impaired alveolar macrophage function.[39, 40] However, measurements of PM2.5 can be difficult to conduct in field studies as it requires the use of expensive equipment. In addition, personal exposures to PM2.5 are even more challenging to measure because of limited options for the equipment available for use in the field settings. Alternatively, carbon monoxide is also a major component of biomass smoke [23], and it is easier to measure using less expensive and less intrusive equipment such as the passive diffusion tubes utilized in this study. Several studies found good correlation between PM2.5 and CO; however, there are potential limitations to using CO as a proxy for PM2.5.[21, 125] Studies reported differences in the observed correlation between PM2.5 and CO by stove type, limitations of passive CO diffusion tubes to detect low levels (<0.7 ppm) of exposure, and lower PM2.5 emissions for stoves with high temperature combustion.[126, 127] Poor correlation between PM2.5 and CO in households using intervention stove may explain why we observed an inverse relationship between density of carriage and CO measurements among households using this stove.

There are several limitations to this study. First, the sample size for this evaluation was small and restricted to a subset of households where household air pollution was measured. According to studies evaluating impact of HAP on ALRI, the expected magnitude of health effects is relatively small, even in a setting of large impact on HAP observed.[3, 4] We do not know what the expected impact of reducing HAP on density of pneumococcal carriage should be, however, the sample size needed to evaluate effects of small magnitude is likely larger than what we had in our study as can be appreciated in the limited precision of our estimates. Second, the exposure assessment was conducted at one point single 48-hour measurement, and did not always precede the collection of nasopharyngeal specimens. Therefore, we did not assess the effects of temporal and within household variability in exposure. This is an important limitation given the location of the study and seasonal climate changes which influence stove combustion efficiency and cooking practices. Future studies need to consider repeated HAP measurements preceding each carriage sample collection.

Our study findings support the accruing evidence suggesting that larger impact on HAP is needed to observe health benefits. Future studies evaluating the impact of reducing the levels of household air pollution on pneumococcal carriage or the risk of pneumococcal pneumonia should be conducted using more effective biomass stoves or alternate fuels leading to larger magnitude reductions in household air pollution levels. In addition, measurements of PM2.5, both indoor and personal, should be conducted, as the impact of interventions on this indoor pollutant is likely a better predictor of ARI health outcomes. More efficient biomass stoves may have the potential to reduce exposures to household air pollution; however, cleaner fuels (e.g. gas) and stove technologies utilizing clean fuels may be needed to achieve measurable and greater health benefits.

Table 3.1. Result of linear mixed effects model evaluating association between CO (Log_{10}ppm) and density (Log_{10}CFU/ml)

	Univariate			Multivariable[1]		
	Coefficient	%change (95%CI) [2]	p-value	Coefficient	%change (95%CI) [2]	p-value
Kitchen CO	-0.11163	-22.7% (-86.7, 349)	0.775	-0.05136	-11.2% (-83.8, 387)	0.892
Mother CO	-0.23845	-42.3% (-92.1, 322)	0.588	-0.21666	-39.3% (-91.4, 329)	0.617
Child CO	-0.48562	-67.3% (-95.4, 134)	0.265	-0.34708	-55.0% (-93.5, 210)	0.417

[1] Adjusted for age, gender, month of sample collection, altitude, type of lighting in the house, type of stove, and recent ARI

[2] Percent change in mean density of colonization (CFU/ml) per log10 increase in CO

Table 3.2. Result of mixed effects logistic regression model evaluating association between CO (Log_{10}ppm) and rates of pneumococcal carriage (positive for *S. pneumoniae*)

	Univariate			Multivariable[1]		
	Coefficient	%change (95%CI) [2]	p-value	Coefficient	%change (95%CI) [2]	p-value
Kitchen CO	-0.00566	-0.6% (-58.9, 141)	0.990	0.02716[3]	2.8% (-58.6, 155)	0.953
Mother CO	-0.23791	-21.2% (-71.2, 116)	0.643	-0.30950	-26.6% (-74.9, 115)	0.572
Child CO	-0.37309	-31.1% (-73.9, 82.2)	0.452	-0.15280	-14.2% (-68.9, 137)	0.768

[1] Adjusted for age, gender, month of sample collection, altitude, type of lighting in the house, type of stove, and recent ARI

[2] Percent change in rates of pneumococcal colonization per log10 increase in CO

[3] Model did not meet convergence criteria

Table 3.3. Mean (median) CO (ppm) by stove type measured in the households with children <5 years olds assessed for density of pneumococcal carriage

Stove type	Hybrid N=17	Traditional (Tulpia) N=58	OPTIMA (Intervention) N=57	Other N=3	p-value*
Kitchen and personal CO levels, mean (median, ppm)					
Kitchen CO	9.4 (12.1)	9.6 (11.2)	8.7 (9.9)	8.4 (11.5)	0.4641
Mother CO	1.3 (1.0)	1.9 (1.7)	2.0 (1.4)	4.7 (6.6)	0.1863
Child CO	1.3 (0.7)	1.4 (1.3)	1.2 (0.8)	3.2 (3.9)	0.0394

*Kruskal-Wallis equality of population rank test for comparing median for each exposure measurement by stove type; "other" stove category excluded from comparisons

Table 3.4. Comparison of pneumococcal carriage rates (% samples positive) and density of carriage by stove type, exposure level, household, and demographic characteristic

Characteristic	% Samples positive for pneumococcal carriage	Geometric mean (median) density of carriage (CFU/ml x 10^3)[1]
Stove type		
Hybrid	44 (69%)	1.18 (3.05)
Traditional (Tulpia)	170 (74%)	3.15 (4.90)
OPTIMA (Intervention)	172 (80%)	5.26 (8.90)
Other	6 (55%)	0.20 (0.92)
Quartiles of exposure (CO, ppm)		
Kitchen		
1st	102 (76%)	3.59 (5.31)
2nd	94 (74%)	2.93 (4.22)
3rd	101 (76%)	3.29 (6.22)
4th	95 (77%)	3.22 (4.17)
Mother		
1st	104 (78%)	5.11 (5.31)
2nd	94 (71%)	1.96 (4.11)
3rd	97 (76%)	3.48 (5.85)
4th	97 (77%)	3.21 (5.38)
Child		
1st	116 (73%)	2.72 (4.07)
2nd	81 (76%)	4.42 (19.34)
3rd	104 (81%)	5.63 (5.97)
4th	84 (71%)	1.48 (3.74)
Age group		
<2 years	201 (77%)	3.42 (4.25)
≥2 years	191 (74%)	3.09 (5.98)
Gender		
Male	215 (79%)	5.26 (8.08)
Female	177 (71%)	1.92 (3.94)
Month of sampling for carriage		
5	3 (100%)	3.45 (3.79)
6	54 (76%)	0.85 (3.29)
7	61 (85%)	0.97 (2.66)
8	48 (69%)	0.48 (2.44)
9	75 (81%)	3.99 (16.37)
10	78 (73%)	30.31 (415.9)
11	73 (71%)	5.76 (28.18)
Altitude (quartile)		
1st	101 (78%)	4.96 (9.77)
2nd	92 (70%)	1.81 (3.31)
3rd	102 (79%)	3.75 (4.20)
4th	97 (75%)	3.34 (8.81)

Characteristic	% Samples positive for pneumococcal carriage	Geometric mean (median) density of carriage (CFU/ml x 10^3)[1]
Any recent ARI reported within 7 days of sample collection		
Yes	77 (79%)	4.52 (12.33)
No	315 (75%)	3.01 (4.20)
Crowding (household size/number of bedrooms, quartile)		
1st	186 (77%)	4.06 (5.88)
2nd	81 (79%)	4.30 (4.09)
3rd	53 (74%)	2.39 (4.13)
4th	64 (73%)	2.81 (14.66)
Floor material in the home		
Tile	3 (100%)	562 (3687)
Cement	16 (60%)	1.03 (2.57)
Dirt	373 (76%)	3.34 (4.90)
Light source		
Electricity	109 (76%)	3.32 (6.77)
Kerosene	74 (77%)	4.25 (8.61)
Candle	200 (75%)	2.99 (4.21)
Other	9 (75%)	1.88 (4.40)
Fuel source		
Gas	2 (50%)	0.61 (1.43)
Coal	3 (60%)	0.47 (2.94)
Wood	385 (76%)	3.38 (4.90)

[1] Kruskal-Wallis equality of population rank test p-value>0.05 for all, except for months of sampling (p=0.0001)

Appendix 1. Completeness of nasopharyngeal (NP) sample collection

The average number, percentiles of distribution, minimum, and maximum number of NP samples with an ARI reported within 7 days prior to sample collection per child

```
             |      N    mean     p25     p50     p75     min     max
-------------+------------------------------------------------------------------------
             |    135    .719       0       1       1       0       3
```

Number of children who had missed at least one NP by the number with consecutive NPs collected at least 45 days apart (monthly collections were planned)

```
   N missed |      Freq.     Percent        Cum.
------------+-----------------------------------
          0 |         77       57.04       57.04
          1 |         54       40.00       97.04
          2 |          3        2.22       99.26
          3 |          1        0.74      100.00
------------+-----------------------------------
      Total |        135      100.00
```

Appendix 2. Results of sensitivity analyses for mixed effects models

Linear mixed effects model evaluating association between kitchen CO (Log_{10}ppm) and density (Log_{10}CFU/ml) using 1) identity matrix (main analyses) and 2) spatial correlation matrix (sensitivity analyses)

1) Identity matrix

```
------------------------------------------------------------------------------------------------
  Log10CFU/ml |     Coef.        Std. Err.     z            P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------------------------
Log10ppm      | -0.1116        .3897      -0.29          0.775    -0.8755    0.6522
     _cons    |  3.6226        .3671       9.87          0.000     2.9031    4.3422
------------------------------------------------------------------------------------------------
```

2) Spatial correlation matrix

```
------------------------------------------------------------------------------------------------
Log10CFU/ml   |     Coef.        Std. Err.     z            P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------------------------
   Log10ppm   | -0.1221        .3827     -0.32          0.750    -0.8722    0.6279
    _cons     |  3.6150        .3609     10.02          0.000     2.9076    4.3223
------------------------------------------------------------------------------------------------
```

Appendix 2 (cont). Results of sensitivity analyses for mixed effects models

Linear mixed effects model evaluating association between kitchen CO (Log_{10}ppm) and density (Log_{10}CFU/ml) using 1) 1 CFU/ml for samples with no pneumococcal carriage detected (main analyses) and 2) using 0.5 CFU/ml for samples with no pneumococcal carriage detected (sensitivity analyses). The lowest density detected among samples positive for pneumococcal carriage is 200 CFU/ml

1) Assigning value of 1 CFU/ml for samples with no pneumococcal carriage detected to allow for log transformation of zero density samples

```
------------------------------------------------------------------------------------------------------
  Log10CFU/ml |     Coef.       Std. Err.     z             P>|z|    [95% Conf. Interval]
-------------+-----------------------------------------------------------------------------------------
Log10ppm      |  -0.1116       .3897      -0.29           0.775    -0.8755    0.6522
     _cons    |   3.6226       .3671       9.87           0.000     2.9031    4.3422
```

2) Assigning value of 0.5 CFU/ml for samples with no pneumococcal carriage detected to allow for log transformation of zero density samples

```
------------------------------------------------------------------------------------------------------
  Log10CFU/ml      |     Coef.       Std. Err.     z             P>|z|    [95% Conf. Interval]
-------------+-----------------------------------------------------------------------------------------
Log10ppm           |  -0.1113        .4097      -0.27           0.786    -0.9143     0.6918
     _cons         |   3.5485       .3859       9.19           0.000      2.7921     4.3049
------------------------------------------------------------------------------------------------------
```

Conclusions

The first aim of this dissertation sought to identify one or more improved cookstoves with the potential to reduce indoor pollutants generated from burning biomass fuels to the levels that would benefit health outcomes. The study demonstrated that in a setting of everyday use these stoves reduce indoor air pollutants and are acceptable to local women. However, the relatively modest reductions in kitchen $PM_{2.5}$ observed in this study, would likely translate into health benefits of small magnitude given high levels of exposure observed in the study households at baseline. The second study was designed to help place the findings of the first study into a broader context needed to understand the levels of HAP associated with health effects. We conducted a systematic review and meta-analysis to estimate the expected impact from improving HAP on childhood pneumonia by developing a dose-response model for the relationship between the levels of particulate matter less than 2.5 microns (PM2.5) and the risk of childhood pneumonia. Our study identified positive dose response between exposures to PM2.5 and risk of acute respiratory infections in children; however, these findings represented highly heterogeneous results and, therefore, the summary measure of effect should be interpreted with caution. Lastly, to help demonstrate an association between HAP and *Streptococcus pneumonia* (pneumococcus), one of the major bacterial pathogens causing pneumonia in young children, the association between indoor levels of carbon monoxide and density of pneumococcal nasopharyngeal colonization (a risk factor for pneumococcal pneumonia) in young children was evaluated in the third study. Our study found no significant associations between indoor levels of CO or personal (mother or child) exposures to CO and rates or density of pneumococcal carriage among young children in rural Peru. The findings of the three studies highlight limitations with 1) available interventions (improved biomass cookstoves), 2) exposure assessment methods used in field studies evaluating effects of HAP on ALRI, and 3) definitions of ALRI used in HAP studies. Improved biomass stoves available to date have limitations. The accruing evidence, including our studies, suggests that larger impact on HAP than the one achieved with biomass stoves is needed to observe health benefits. Despite reductions in HAP reported in most studies, none of the biomass stoves evaluated as interventions appear to have capacity to achieve the WHO guideline level for annual average kitchen $PM_{2.5}$ of $10\mu g/m^3$, nor the intermediate target of $35\mu g/m^3$. Future studies evaluating the impact of reducing the levels of household air pollution on pneumococcal carriage or the risk of pneumococcal pneumonia should be conducted using more effective biomass stoves or alternate fuels leading to larger magnitude reductions in household air pollution levels. More efficient biomass stoves may have the potential to reduce exposures to household air pollution; however, clean fuels (e.g. gas) and stove technologies utilizing clean fuels are needed to achieve measurable and greater health benefits.

In addition, understanding of user’s perspectives is important: if cookstoves are not acceptable to users in the community, lack of adherence to use will limit the benefits on HAP expected from these stoves. New stove technologies utilizing clean fuels will require significant behavioral change and have the potential of not being utilized if introduced without rigorous communication on proper stove use and education on health benefits of improved air quality. A more thorough evaluation of other potential sources of indoor air pollution in households (e.g., kerosene lamps) is also needed. In addition, our study shows that users may view the intervention stove as an additional household tool used for cooking, heating water, or heating the household. Future studies should consider a package of interventions, such as multiple improved stoves or improved stoves with multiple burners and clean sources of lighting to improve indoor air quality. The relatively short term follow up with after improved stove is introduced in the household does not allow for continuous education on stove use over time, which may lead to a greater familiarity with and in turn adherence to stove use. The impact of the stoves on indoor air quality may improve with longer use of acceptable stoves or may worsen if the stoves are no longer used or lose functionality due to required maintenance. Therefore, longer-term impact of improved stoves on HAP, for example over a 12-month period, should also be evaluated.

Objective exposure measurements are needed in the studies of HAP effects on health. Carbon monoxide, a major component of biomass smoke, is easier to measure using less expensive and less intrusive equipment such as the passive diffusion tubes utilized in two of the research studies of this dissertation. While several studies, including the ones from this dissertation research, found good correlation between PM2.5 and CO, there are limitations to using CO as a proxy for PM2.5. Studies reported differences in the observed correlation between PM2.5 and CO by stove type, limitations of passive CO diffusion tubes to detect low levels (<0.7 ppm) of exposure, and lower PM2.5 emissions for stoves with high temperature combustion. Measurements of PM2.5, both indoor and personal, should be conducted, as the impact of interventions on this indoor pollutant is likely a better predictor of ALRI health outcomes. While many studies report that there are modest correlations between personal and kitchen levels of PM2.5, daily behaviors likely confound the level of personal exposure in the kitchen. While personal PM2.5 levels provide a more objective measurement of PM2.5, use of personal exposure equipment comes with its own set of challenges: adherence to use of this equipment should be monitored to ensure the measurements taken are representative of actual exposures. New compact size technologies for personal PM2.5 measurement, acceptable for personal use have since been developed and are now being utilized in field studies.

There have been several meta-analysis done with the goal to measure the impact of HAP on ALRI. While most studies, including the paper in this dissertation, show weak to moderate association between exposure to HAP and ALRI, there remains a gap in our understanding of the magnitude of expected impact on risk of ALRIs given observed improvements to HAP from interventions being studied. Comparisons across studies are challenging because of a wide range of ALRI definitions applied; many studies do not distinguish between upper and lower respiratory infections and likely include a range of outcomes. Standardized case definitions applied in intervention trials allow for a more accurate estimation of disease burden preventable through the intervention evaluated, and improve our understanding of the ALRIs preventable through HAP improvement.

Multiple etiologies contribute to burden of ALRI, including a range of viral and bacterial pathogens. None of the studies evaluating impact of HAP on ALRI include laboratory diagnosis of pathogens causing ALRI, and in most field settings with limited laboratory capacity etiologic diagnosis will be challenging. Available data from one clinical trial suggest that a severe spectrum of ALRI, likely caused by bacterial pathogens, is preventable through improvements in HAP. Bacterial culture-based diagnoses has low sensitivity; in addition, cultures are not routinely performed in many developing country settings. Pneumococcal density of carriage provides an intermediate endpoint, which is easier to measure, using non-invasive specimen collection. However, measuring this endpoint addresses only a single etiology of ALRI, although the most common bacterial cause of pneumonia. Several multi-pathogen platforms utilizing molecular-based PCR technologies have emerged and provide opportunity to improve etiologic diagnosis of pneumonia. Studies combining etiologic diagnosis with standardized clinical and chest x-ray confirmation of ALRI, can improve our understanding of which ALRIs are preventable through reduction in HAP.

Lastly, given the findings from the three studies, the next steps for research should be highlighted. Given the limitations of available biomass stoves in their effectiveness to reduce HAP in a setting of everyday use, cookstoves utilizing clean fuels should be evaluated in field studies. These studies should include assessment of the long-term impact of stove use on both kitchen levels and personal exposures to PM2.5. Clean fuel stoves will require dramatic change in cooking behaviors and, therefore, these studies should also incorporate the assessment of acceptability to local users.

Assessment of pneumococcal carriage using a clean fuel stove as an intervention will provide a wider range of exposures, to be able to evaluate whether a larger impact on HAP than the one observed in a setting of improved biomass stove has the potential to reduce density of pneumococcal carriage. In future studies, measurement of exposures, ideally personal exposures to PM2.5, should precede collection of nasopharyngeal specimen for each sequential sample obtained.

In order to improve our understanding of the relationship between different levels of exposure to HAP and risk of ALRI, randomized controlled trials using clean fuel stoves as interventions should be conducted in developing countries where exposures to high levels of HAP due to biomass fuel burning occurs and burden of pneumonia is high. Adherence to use of these stoves should be monitored and measured throughout the course of the follow up of the trial, given that field studies demonstrate that even during short-term follow up, the users can revert to the use of traditional stoves. In addition, other sources of HAP, such as tobacco smoke, use of kerosene lamp, and burning of biomass for heating should be identified and eliminated through the use of package of interventions addressing all sources of HAP.

The findings of this dissertation should assist organizations working on household air pollution research and help identify effective stove interventions and potential confounders for further intervention studies of HAP effects on ALRI.

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List of Abbreviations

AAP – Ambient air pollution

ALRI – Acute lower respiratory infections

AURI – Acute upper respiratory infections

ALRI – Acute lower respiratory infections

CDC - Centers for Disease Control and Prevention

CFU – Colony-forming unit

CO – Carbon monoxide

DAG – Directed acyclic graph

EPA – Environmental Protection Agency

GEE - Generalized estimating equation

HAP – Household Air Pollution

IAQ – Indoor Air Quality

OR - Odds Ratio

PCR – Polymerase-chain reaction

PM2.5 – particulate matter sizes less than 2.5 microns in diameter

RR - Risk Ratio

SHS – second hand smoke

WHO-World Health Organization

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