HOUSEHOLD AIR POLLUTION FROM BIOMASS COOKSTOVES AND A LIQUEFIED PETROLEUM GAS INTERVENTION IN RURAL PERU

by

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ABSTRACT

Problem Statement:

Approximately 3 billion people worldwide, mostly from low and middle-income countries, use biomass fuels such as wood and dung for cooking. Household air pollution (HAP) from biomass cookstoves is recognized as one of the largest environmental risk factors for preventable disease. Previous interventions to reduce HAP from biomass cookstoves have shown limited health improvements. As a result, recent efforts are focusing on cleaner fuels such as liquefied petroleum gas (LPG). This dissertation aimed to 1) characterize HAP concentrations from biomass cookstoves, 2) examine the exposure-response relationships between HAP and markers of inflammation, and 3) evaluate the longitudinal impact of an LPG stove intervention on HAP.

Methods:

We conducted a randomized, controlled field trial with 180 female participants that use biomass cookstoves in rural Peru, randomizing half of them to receive free LPG stoves and free fuel delivery for one year. We collected kitchen area concentrations and personal exposures to carbon monoxide (CO), fine particulate matter ($PM_{2.5}$) and black carbon (BC), as well as dried blood samples. In the first manuscript, we determined the associations between household characteristics and HAP at baseline. In the second manuscript, we developed exposure-response models between HAP and markers of inflammation at baseline. In the third manuscript, we assessed the longitudinal impact of the LPG stove intervention on HAP concentrations at baseline and 3-, 6- and 12-months post-intervention.

Results:

In our first study, we observed that roof type has an important impact in kitchen ventilation of households in rural Peru. In our second study, we found statistically significant associations between kitchen area BC concentrations and inflammatory markers that were robust to adjustment for $PM_{2.5}$ concentrations. In our third study, we found that our LPG stove intervention significantly reduced $PM_{2.5}$, BC, and CO concentrations by at least 62%, to levels comparable with health-based guidelines.

Conclusions:

HAP concentrations from biomass cookstoves in rural Peru were well above recommended guidelines. The kitchen area concentrations were associated with inflammation markers. The success of an LPG stove intervention in reducing HAP is encouraging for future LPG programs to potentially improve health in resource-limited settings such as Peru.

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CHAPTER 1:

INTRODUCTION

Household air pollution from biomass cookstoves

Household air pollution (HAP) caused by the combustion of biomass fuels (typically wood, dung, and agricultural crop waste) is a leading contributor to the global burden of disease and it is among the largest environmental risk factors for preventable disease [1–4]. About 3 billion people worldwide, mostly from low and middle-income countries (LMICs), use biomass for their cooking needs [5]. HAP from solid fuels was estimated to be responsible for 2.6 million deaths and 77.2 million disability-adjusted life-years in 2016 [6]. It is recognized as a leading risk factor for bronchitis, chronic obstructive pulmonary disease, lung cancer, childhood pneumonia, acute lower respiratory infections, cardiovascular events, and low birthweight [7–9]. Burning of biomass fuels for cooking is also a major cause of mortality in low and middle-income countries [4]. Women and children have the highest risks of exposure to biomass fuel emissions and were attributed 60% of premature deaths from HAP in 2012 [10].

HAP produces a complex mixture of gases and particulate pollutants. Pollutants of major public health concern that are commonly monitored in resource-limited settings include carbon monoxide (CO) and particulate matter (PM). Ambient CO exposures have been related to cardiopulmonary disease, low birth weight, congenital defects, among others in epidemiological studies [11]. PM is characterized

based on its size and how deeply it can penetrate the respiratory tract. Particles larger than 10 micrometers in aerodynamic diameter are trapped in the nose and pharyngeal region. PM less than 2.5 micrometers in aerodynamic diameter ($PM_{2.5}$), are small enough to deposit in alveoli, initiate inflammatory cascades, and may enter the pulmonary circulation [12]. Extensive epidemiological studies have found strong associations between ambient particulate air pollution and respiratory symptoms, lung cancer, and increased risk of cardiovascular-related morbidity and mortality [8, 13–19, 19–24], yet the drivers of PM composition for these relationships is less clear.

Household air pollution levels and inflammation markers

Based on existing epidemiological literature in humans, as well as animal studies, the positive associations between ambient and traffic-related PM exposure and cardiovascular disease, is potentially related to pulmonary systemic pro-oxidant and pro-inflammatory effects of PM and its constituents [12, 25, 26]. Several studies suggest that inflammatory cytokines induce a systemic response that has an important role in the pathogenesis of the cardiopulmonary adverse health effects associated with ambient or traffic PM exposure [27–29]. There is also evidence that suggests that inflammation might be part of the pathway of disease development when looking at biomass smoke exposure.

There is strong evidence that supports the relationship between systemic inflammation and coronary artery disease [13, 30, 31] and atherosclerosis [26].

Proteins such as C reactive protein (CRP) and fibrinogen have been commonly used as markers of ongoing inflammation [30]. Among the cytokines involved in the synthesis of these acute phase proteins, the most commonly used in air pollution literature include tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-8 (IL-8) and interleukin-6 (IL-6). Dose dependent increases of inflammatory cytokines, including IL-6 and IL-8, have been observed to correlate with wood smoke exposure from human alveolar macrophages from healthy adults exposed to HAP [32].

Markers of inflammation can be obtained from resource limited settings using dried blood spot (DBS) sample collection. DBS are samples of drops of whole blood collected on filter paper from a finger prick. It is a minimally invasive method easier to collect, handle, preserve, and transport that whole blood samples [33]. Several commercially available immunoassay kits are available to analyze cytokines and biomarkers in low volumes of blood such as those collected in a few drops. DBS have been validated as an alternative method to venipuncture assessments [34].

Additionally, determining which PM components are mainly responsible for adverse health effects remains an active area of research in the air pollution literature [35]. It has been suggested that black carbon (BC) may play an important role in cardiovascular disease development [35, 36]. BC is a main component of fine PM resulting from biomass combustion. BC is defined as carbon content as measured by light absorption [37].

Several literature reviews suggest that BC might have stronger association with cardiopulmonary outcomes than with PM mass or than with any other $PM_{2.5}$ species [35, 36, 38–40]. In addition, the associations of cardiovascular and respiratory hospital admissions with ambient and traffic BC concentrations have been shown to be significantly greater than estimated effects of most other single PM elements in several studies involving adult populations [40–46]. It has been suggested that BC elicits cardiovascular endpoints through inflammation pathways [26, 38, 39, 47]. However, the evidence of toxicity of PM and its components has been focused on ambient and traffic air pollution [12, 16, 18, 20, 47]. The toxicity of BC and PM in LMICs and their relationship with markers of inflammation have not been fully explored [48].

Effects of household air pollution on climate and ambient air pollution

HAP is a major contributor to outdoor air pollution [49, 50]. It not only contributes to outdoor PM, but also its emissions of NOx and volatile organic compounds can contribute to ground level formation of ozone, increasing risks of respiratory disease. HAP accounts for 12% of ambient air pollution globally and can contribute to almost 40% of $PM_{2.5}$ in regions such as sub-Saharan Africa [51]. In addition, BC, a major component of PM in HAP [52], is among the most important climate change pollutants after CO_2 and methane [53]. BC impacts climate through different mechanisms including direct solar absorption, influences cloud processes, and alters the melting of snow and ice cover [53, 54]. HAP is estimated to contribute 25% of global emissions of BC. In particular, residential coal and biomass burning can

contribute to more than 60% of BC emissions of Africa and Asia [54]. Biomass combustion also produces methane and N_2O, known greenhouse gases [54].

Biomass cookstove interventions

Previous efforts to reduce exposure related to biomass fuel smoke in LMICs have focused on interventions with improved stoves that use solid fuels [55–59]. Improved cookstoves are stoves designed to reduce HAP through improvements of the combustion efficiency of biomass. Modifications typically include a closed combustion chamber, a chimney, and other similar design improvements that reduce exposures indoors and improve fuel combustion efficiency [9, 60].

Although improved cookstove interventions have achieved important reductions in emissions, concentrations of indoor pollutants still remain significantly higher than the WHO recommended levels [61], and therefore show limited results in improving health [55]. For example, a cross sectional study with Honduran women that evaluated the impact of an improved compared to a traditional cookstove, achieved reductions of 70% on personal exposure to $PM_{2.5}$, nonetheless changes in lung function or CRP concentrations were not observed [62]. Exposure-response studies have found that the greatest risk reductions occur with exposure levels that are unlikely to be achieved with biomass and require interventions with cleaner fuels [2, 59, 63]. Solid fuels such as wood or dung are associated with low combustion efficiencies and, therefore, higher levels of pollution are emitted, as compared to gas based fuels and electricity [64]. It has been observed in studies from Asian cities that

solid fuels can increase emissions per meal nearly two orders of magnitude when compared with to gas fuels for several pollutants including PM [64, 65]. Therefore, recent efforts are moving towards interventions with cleaner fuels such as liquefied petroleum gas (LPG) [57, 58, 66–69].

Laboratory-based testing shows that LPG stove use can reduce HAP enough to meet the WHO recommended guidelines [70]. The WHO estimated that 99% of homes that use biomass cookstoves could meet the WHO annual guideline Interim target-1 of 35 $\mu g/m^3$ for $PM_{2.5}$ with LPG stove use [70]. Nevertheless, estimations based on laboratory data do not incorporate real socio-economic behaviors and typically cannot account for changes in stove efficiency over time, that can impact real performance. Few studies have evaluated HAP from LPG stove use in low-income rural areas that use biomass cookstoves [48, 57, 68, 70–72]. Furthermore, measuring personal exposure directly can reduce bias and increase the precision of estimates when quantifying the relationship between HAP and health risk [48, 73–75].

Cardiopulmonary Outcomes and Household Air Pollution Trial

The proposed work is nested within a study funded by the NIH that is conducting a randomized controlled field intervention trial of LPG stoves and fuel distribution in rural Puno, Peru called Cardiopulmonary Outcomes and Household Air Pollution (CHAP) Trial [76]. This study is evaluating the longitudinal effects of a LPG stove and fuel distribution intervention on adult cardiopulmonary health outcomes, while explicitly investigating longitudinal qualitative factors related to LPG

adoption. LPG stove use is being monitored and compared to standard cooking practices to determine the relative effect of LPG adoption on HAP concentrations and subsequent improvements in cardiopulmonary outcomes over a one-year period. As a secondary objective, this trial includes a second-year of follow-up that is measuring intervention effectiveness by characterizing the sustainability of LPG among participants in the intervention arm and initial adoption of LPG among those in the control arm. This larger study is being implemented in collaboration with Asociación Benéfica PRISMA (A.B. PRISMA), a Peruvian NGO with over 15 years of experience conducting NIH-funded research studies, and Universidad Peruana Cayetano Heredia in Lima, Peru. Both institutions have provided administrative and technical support and have local Institutional Review Board (IRB) oversight over the project. This study was approved by the Institutional Review Boards of Universidad Peruana Cayetano Heredia (Lima, Peru), the Johns Hopkins Bloomberg School of Public Health (Baltimore, USA), and A.B. PRISMA (Lima, Peru).

In this dissertation we characterize kitchen area concentrations and personal exposures to HAP in homes with biomass cookstoves. We also evaluate the exposure-response relationship between $PM_{2.5}$ and BC exposures from biomass cookstoves with markers of inflammation. Finally, we quantify the impact of an LPG stove intervention on HAP in the rural high-altitude settings of rural, Peru.

Dissertation Aims and Structure

The three aims of this dissertation are to:

1) To explore how household characteristics explain variability of kitchen area concentrations and personal exposures to CO, $PM_{2.5}$ and BC from biomass cookstoves among women in rural Peru.

2) To examine the exposure-response relationship between $PM_{2.5}$ and BC, and markers of inflammation among adult women who use biomass cookstoves in rural Peru.

3) To characterize HAP kitchen area concentrations and personal exposures in an LPG stove intervention trial in rural Peru.

The body of this dissertation is comprised of the following: an introduction, three manuscripts (chapters 2-4) corresponding to the three specific aims of this dissertation and a conclusions chapter (chapter 5).

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CHAPTER 2:

HOUSEHOLD AIR POLLUTION EXPOSURE AND ASSOCIATIONS WITH HOUSEHOLD CHARACTERISTICS AMONG BIOMASS COOKSTOVE USERS IN PUNO, PERU

Abstract

Background:

Household air pollution (HAP) from combustion of biomass fuel, such as wood and dung, is among the largest environmental risk factors for preventable disease. Close to half of the world's population relies on biomass cookstoves for their daily cooking needs. Understanding factors that affect HAP can inform measures to maximize the effectiveness of cookstove interventions in a cost-effective manner. In Puno, Peru, the prevalence of biomass cookstove use is high, yet the community has been increasing its participation in ongoing local programs to promote liquefied petroleum gas (LPG) stoves. However, the impact of kitchen and household characteristics, as well as the presence of other types of stoves, on HAP concentrations is poorly understood in this setting.

Objective:

To explore how household characteristics explain variability of kitchen area concentrations and personal exposures to CO, $PM_{2.5}$ and BC from biomass cookstoves among women in rural Peru.

Methods:

Household characteristics and HAP measurements were collected from 180 households in Puno, Peru. Kitchen area concentrations and personal exposures to carbon monoxide (CO), fine particulate matter ($PM_{2.5}$) and black carbon (BC) were sampled for 48 hours. We implemented simple and multiple linear regression models

to determine the associations between household characteristics and both kitchen area concentration and personal exposure to each pollutant.

Results:

Mean daily kitchen area concentrations and personal exposures to HAP were several times above World Health Organization recommendations. We found that having a roof made of natural materials (straw, *totora* or reed) was strongly associated with higher kitchen concentrations and personal exposures for all pollutants when compared to calamine sheet, cement fiber or similar. Personal exposures were, on average, 41%, 36% and 55% higher for $PM_{2.5}$, CO and BC, respectively, in households with natural roof material. Having an LPG stove and having a chimney were associated with reduced personal exposures but were not associated with kitchen area concentrations. Personal exposures were lower by 18% for $PM_{2.5}$, 28% for CO, and 27% for BC concentrations among participants who also had an LPG stove compared to those with only biomass cookstoves.

Conclusions:

Characterizing HAP within different settings can help identify effective and culturally-relevant solutions to reduce HAP exposures. We found that roof type in households has an important impact in kitchen area concentrations and personal exposures to HAP. Although HAP concentrations remained above guidelines for all households, better roof materials, and having LPG stoves may be actionable interventions that can help reduce exposures to HAP in high-altitude rural Peru and similar settings.

Keywords:

Cookstoves, indoor air pollution, household air pollution, personal exposure, biomass fuel, rural Peru.

Introduction

Household air pollution (HAP) from biomass fuel combustion (typically wood, dung, and agricultural crop waste) is among the largest environmental risk factors for preventable disease [1–4]. Close to half of the world's population, mostly from low- and middle-income countries, rely on biomass cookstoves for their daily cooking needs [5]. Exposure to HAP was estimated to be responsible for 2.6 million deaths and 77.2 million disability-adjusted life-years in 2016 [6]. HAP is known to contribute to lower respiratory infections, chronic respiratory disease, cardiovascular disease, and cancer, and is a leading risk factor for childhood pneumonia and low birthweight [7–10]. Exposure to HAP has also been linked to cataracts, adverse pregnancy outcomes, tuberculosis, and upper aero-digestive cancers [7, 11, 12].

The incomplete combustion of biomass fuels produces a wide range of gas and particulate pollutants. The most commonly measured pollutants of HAP are carbon monoxide (CO) and particulate matter (PM) [14–16]. CO has been associated with cardiopulmonary outcomes in epidemiological studies [17]. Fine PM consists of particles smaller than 2.5 micrometers in aerodynamic diameter ($PM_{2.5}$), which are small enough to penetrate deep in the respiratory tract and reach the alveoli. $PM_{2.5}$ from ambient air pollution has been strongly associated with increased risk of

cardiopulmonary-related morbidity and mortality in adults and children [8, 17–29]. Identifying which components of PM are primarily responsible for adverse health outcomes remains one of the biggest knowledge gaps in the air pollution literature [31].

Black carbon (BC), one of the main constituents of $PM_{2.5}$ from the incomplete combustion of carbonaceous materials like biomass fuels, has recently gained attention in air pollution literature due to its potential role in disease development pathways [31, 32] and the ability to be easily measured along with PM [32, 33]. Several literature reviews suggest that BC mass might have stronger associations with cardiopulmonary outcomes than total PM mass or any other $PM_{2.5}$ species [31, 32, 35–37]. However, the literature on exposure to BC from HAP is limited [37, 38].

The most common method for measuring HAP has been placing monitors in microenvironments such as the kitchen or living area and measuring area concentrations. However, area measurements do not consider the movements of individuals and may be poor estimates of true personal exposure [39]. Measuring personal exposure directly can reduce bias and increase the precision of estimates when quantifying the relationship between HAP exposure and health risk [13, 38–40]. However, personal exposure assessment can be challenging due to limitations in monitoring technology. For example, some PM monitors are burdensome when worn by participants. Because of this, some studies have used personal exposure CO measurements as an indicator of HAP personal exposures [42, 43], though this

practice has been shown to have major limitations when compared to measurements of PM exposures [44, 45]. Over the last ten years, smaller $PM_{2.5}$ monitors have been developed to be used as personal samplers, and some incorporate simultaneous integrated gravimetric and continuous nephelometric technology, facilitating more precise and convenient sampling of personal exposure [40, 45, 46].

To reduce HAP exposures, it is important to identify household characteristics that impact indoor concentrations and could be potential actionable interventions. Understanding factors that affect HAP can inform measures to maximize the effectiveness of cookstove interventions in a cost-effective manner. There are several factors that influence combustion of biomass fuels and the resulting HAP concentrations. For example, kitchen design and structure can affect ventilation, while different biomass fuel types can produce different relative concentrations of specific pollutants. According to recent reviews and a WHO database, kitchen area 24-hr average $PM_{2.5}$ concentrations can range from 200 to 3,000 $\mu g/m^3$ [14, 48, 49] in households that use biomass in developing countries. Households that use animal dung as the primary biomass fuel tend to show higher average concentrations compared to households that use wood [49].

The relationship between household characteristics and HAP concentrations can also vary widely across different sites [45, 50, 51]. For example, a study that looked at improved and traditional biomass cookstoves in Honduras found that the presence of windows was most strongly associated with kitchen area HAP [51]. In

contrast, a previous study in Puno, Peru compared urban and rural participants [52], using kitchen area samples for 28 households with chimney and 31 without chimneys. That study, found that the number of windows, presence of chimney, or outdoor concentrations had no influence on indoor HAP concentrations in rural households [52]. However, the authors acknowledged that chimney designs varied considerably across households. Pollard et al. was not able to tease out the impact of different types of fuel on HAP, but their results were suggestive that dung use led to increased PM exposures compared to other biomass fuels [52].

Characterizing HAP from cookstoves in Puno is important due to the high prevalence of biomass cookstoves and the increasing participation of the community in ongoing local programs to promote liquefied petroleum gas (LPG) stoves [53] since the time of the prior study [52]. However, the impact of owning an LPG stove on HAP, accounting for household characteristics, has not yet been evaluated for this area. Investigating a larger sample of households and longer sampling times is warranted to understand the impact of stove ventilation, stove type, fuel type, and household characteristics on HAP in Puno. Furthermore, personal exposures have not been characterized in this community. Characterizing HAP and personal exposures in this area will help us to better understand and potentially maximize the impact of potential interventions.

We performed a detailed exposure assessment of HAP and evaluated household characteristics in Puno, Peru. We collected information on household and

participant characteristics such as number of times participants sleep in the kitchen, frequency of burning trash, use of fuel including LPG stoves as well as stove ventilation, and number of windows or doors and whether they are permanently open. In this paper we explore how household characteristics explain variability of kitchen area concentrations and personal exposures to CO, $PM_{2.5}$ and BC from cookstoves in rural Peruvian households. We attempt to identify kitchen and participant characteristics which are common, culturally relevant, and could be used to maximize the effectiveness of interventions to reduce HAP.

Methods

Study design and settings

The data in this paper was collected as part of the baseline measurements for an ongoing trial [54]. HAP measurements were collected in rural communities surrounding the city of Puno, located at the shore of Lake Titicaca at 3,825 meters above sea level. Enrolled participants traditionally use biomass-burning, open-fire stoves for cooking [52]. We enrolled 180 women aged 25-64 years. Inclusion criteria included: being the primary cook of the household, using biomass fuels daily for cooking, and having the cooking area separate from the sleeping area (which is typical in the region). Each enrolled participant received a set of baseline pre-intervention assessments that included 48-hour HAP measurements. During baseline visits, we also collected basic socio-demographic information, and observed household and kitchen characteristics. Additional information on enrollment and procedures has been previously published [54].

The information we collected on household characteristics was determined *a priori* as potentially relevant to HAP concentrations. We collected information related to kitchen ventilation and cooking practices that impact cooking frequency and duration including: number of windows, number of open windows, number of doors that are permanently open, materials of the roof and walls of the kitchen, the presence of ventilation above the stoves, number of people that lived in the household, trash burning activities, typical cooking durations, and number of dogs and pigs. Previous formative research in the study region showed that these communities cook for their dogs and pigs. We also asked if they owned a secondary stove and if they participated in the local government program that provides LPG fuel (this program is called FISE). This government-sponsored program is aimed at reducing use of solid fuels by increasing access to LPG fuel for cooking to poor Peruvian households [53]. Finally, we collected information about having a chimney or other stove ventilation method. We identified that for those households without a chimney, participants frequently had the stoves located in a recessed area in the kitchen. This structure was previously observed although not included in previous analyses [52]. The recessed area is a small compartment were the stove is located and often has an opening in the ceiling to allow the smoke to go out (Figure 1, shows examples).

We also incorporated basic socioeconomic status indicators including income, education level and a wealth quintile indicator estimated using the Demographic and Health Survey (DHS) wealth quintiles [55] based on a representative sample of

the Peruvian population. Participants in our study were assigned a score based on asset ownership considered by the DHS (for example: windows with curtains, sofa, toilet connected to the sewer, reinforced concrete roof, and brick or cement walls). Participants were grouped into one of the five national wealth quintiles depending on their total score, with one being the lowest and five the highest.

Household air pollution measurements

We enrolled and visited 15 participants every month for a total of 180 participants in one year. Exposure to HAP was assessed by measuring kitchen concentrations and personal exposures over a 48-hour period. Kitchen concentrations were measured using $PM_{2.5}$ and CO monitors located approximately one meter from the combustion zone of the traditional stove, and 1.5 meters of height from the floor (representing the breathing zone), and at least one meter from doors and windows (when possible). Personal exposure was measured by placing a $PM_{2.5}$ and CO monitor near each participant's breathing zone in an adapted apron (commonly used by women in the study site) provided to the participants (Figure 2). Women were encouraged to wear the aprons throughout the duration of the sampling period and to keep the apron close by when sleeping. Direct-reading measures of both $PM_{2.5}$ and CO were logged at 1-minute intervals.

We collected gravimetric and nephelometric $PM_{2.5}$ mass concentration using the ECM, an active, direct-reading aerosol monitor (RTI Inc., Research Triangle Park, NC, USA). The ECM has a light-scattering laser for continuous-time nephelometric

assessment of $PM_{2.5}$, and a pump operating at 0.3 L/minute that collects $PM_{2.5}$ on a filter for gravimetric analysis. We calibrated the ECM pumps daily and measured flow rate before and after sample collection with a TSI 4100 flowmeter (TSI Incorporated 500 Cardigan Road Shoreview, MN, USA). The nephelometric concentration was calibrated using the gravimetric time-weighted average filter samples. Gravimetric $PM_{2.5}$ samples were collected on 15-mm Teflon filters with a 2-μm pore size (Measurement Technology Laboratories LLC, Minneapolis, MN, USA). Filters were pre-weighed and post-weighed at the Johns Hopkins Bloomberg School of Public Health in a humidity and temperature-controlled laboratory using a XP2U microbalance (Mettler Toledo, Columbus, OH, USA). When ECM filters were overloaded and the logged flow rate was imprecise, we used the average of the pre- and post-sampling flow rates measured in lab to estimate the total volume of air sampled, instead of the flow rate logged by the ECMs. We operated ECMs using duty cycles in order to avoid overloading the filters due to the high $PM_{2.5}$ concentrations observed. ECMs used for personal exposure samples operated for 30 consecutive seconds every minute and devices for kitchen samples operated for 20 consecutive seconds every three minutes.

Direct-reading concentrations of CO were measured with the EL-USB-CO data logger (Lascar Electronics, Erie, PA, USA). BC concentrations were determined measuring optical attenuation on the $PM_{2.5}$ gravimetric samples collected on filters (a cumulative measure per sample), using a Magee OT21 Sootscan transmissometer (Magee Scientific, Berkeley, CA).

Kitchen samples of $PM_{2.5}$ and CO included 10% duplicates. In addition, all $PM_{2.5}$ samples included 10% blanks and all reported concentrations were blank-corrected. High correlations were observed for duplicate samples for the baseline measurements (0.94 for CO and 0.95 for BC and $PM_{2.5}$, after excluding one outlier duplicate sample). The limits of detection (LOD) for BC and $PM_{2.5}$ samples were estimated as three times the standard deviation of estimated mass from field blanks. All $PM_{2.5}$ and BC concentration below the LOD were replaced by the LOD divided by the square root of two. During the initial 6 months of the study the pre-weighed filters were loaded into the cassettes of the ECMs in the field site laboratory. For the remainder of the study, the filters were pre-loaded into individual ECM cassettes at the Johns Hopkins Bloomberg School of Public Health laboratory before being sent to the field site. Initially, the $PM_{2.5}$ the LOD was estimated to be 20 μg, after filter handling in the field laboratory was reduced, the LOD decreased to 9.8 μg. The LOD for BC was 1.4 μg throughout the study.

CO measurements were calibrated using correction factors derived by co-locating all CO monitors every 3-4 months in a sealed chamber. The monitors were exposed to clean air (nitrogen gas) and a known gas CO concentration of 100 ppm. Individual slopes and intercepts were estimated for each device and for each co-location timepoint to correct any existing drift on the devices. The LOD for the CO direct-reading instrument was estimated as three times the standard deviation of concentrations logged during the regular clean air calibration checks in the field and was estimated to be 1 ppm. All direct-reading concentrations below the LOD were replaced by the LOD divided by the square root of two.

The Research Electronic Data Capture software (REDCap, Vanderbilt University Medical Center, Nashville, TN) [56] installed on tablets, was used for field forms to record household characteristics and general characteristics of the participants. We also collected information at every exposure measurement visit regarding potential additional exposures such as the use of candles, smoking, or sweeping. The field staff also logged any issues observed with sampling devices that could explain any potential issues with the quality of the samples.

Statistical methods

We estimated 48-hour mean concentrations as the mean of the 2 consecutive daily means. We consider a sample as missing if sample duration was less than 20 hours (4% of CO samples and 1% of $PM_{2.5}$ samples). We estimated 48-hour means by averaging the two 24-hour averages of each consecutive day of sampling. If the second day the sample duration was less than 20 hours (total sample <44-hours), we used the initial 24-hours. For BC, we estimated the integrated time-weighted average concentration from the time-integrated filter-based $PM_{2.5}$ samples at least 20 hours long. Most short duration samples were due to battery issues with the CO and $PM_{2.5}$ devices. Additional missing samples were due to technical issues with the device or the data download process (6% of CO samples and 1% of $PM_{2.5}$ samples).

We implemented simple and multiple linear regression models to determine the association between household characteristics (explanatory variables) and each

pollutant (CO, $PM_{2.5}$, and BC as the outcome variables in each model) from each type of exposure (kitchen area concentrations and personal exposures). We used the natural log-transformed 48-hour average pollutant concentrations to meet linear regression assumptions. Each of the regression model coefficients represents the ratio of the impact on the pollutant compared to the reference category. For example, a ratio of 1.1 translates to a 10% increase and a value of 0.9 translates in a 10% decrease compared to the reference category.

Exploratory data analysis and simple linear regression models (univariate models with one explanatory variable with each pollutant) were developed to make an initial selection of variables that might explain HAP variability. We included rainy season as a binary variable since it might affect dry fuel availability. We included an indicator variable to adjust for samples that had only the initial 24-hours of sample but not the second day of the sample. Collinearity was assessed estimating the variance inflation factors [57] from all the selected variables. Categorical variables were also examined for their potential relationship with other variables. For example, homes with a chimney usually also had a roof, walls and floor made of materials associated with wealth (such as cement or brick). We excluded variables that did not have a consistent or logical association with the pollutants, for example number of windows open was positively associated with HAP in some of the models.

We developed multiple linear regression (multivariable) models for each pollutant (CO, $PM_{2.5}$, BC) and exposure (kitchen area and personal exposures) selecting the

group of household characteristics (explanatory variables) that best explain the variability of each pollutant. We selected the group of variables that were consistently chosen by the following two model selection methods: the backwards, and forward stepwise regression methods [57] (we used a p-value of 0.1 as a criterion for variable inclusion or removal). In addition as part of a sensitivity analysis we estimated the Akaike information criterion (AIC; using it as a criteria to compare models) [58]. All data analyses were conducted with MATLAB (The MathWorks, Inc., Natick, MA) and STATA (StataCorp., College Station, TX).

Results

Household air pollutant concentrations and personal exposures

We collected HAP samples in 180 households, shown as box plots in Figure 3. Mean kitchen area 48-hour CO was 52 ppm (inter quartile range, IQR: 45-59 ppm), about eight times greater than the WHO indoor 24-hour guideline (6 ppm). Average daily kitchen area $PM_{2.5}$ concentrations were 1,205 $\mu g/m^3$ (IQR: 422-1,824 $\mu g/m^3$), 50 times the recommended WHO indoor daily guideline and more than 15 times the most flexible interim WHO guideline of 75 $\mu g/m^3$. The mean time-weighted average BC kitchen area concentration was 171 $\mu g/m^3$ (IQR: 84-282 $\mu g/m^3$), which represents 16% of the estimated $PM_{2.5}$ mass, on average.

Mean 48-hour personal exposure to CO was 6.9 ppm (IQR: 5.6 -8.2 ppm). Daily average personal exposure to $PM_{2.5}$ was 115 $\mu g/m^3$ (IQR: 40-130 $\mu g/m^3$), which is 5

times the recommended WHO daily guideline and almost twice as much as the most flexible interim WHO guideline of 75 μg/m^3. BC personal exposures were estimated to be, on average, 16 μg/m^3 (IQR: 6-29 μg/m^3), which represents 17% of the estimated $PM_{2.5}$ mass for personal exposure.

Household characteristics

Table 1 includes the variables that were initially selected as potentially associated with HAP. All 180 households reported dung as their primary fuel and 42% of homes additionally reported using wood. Most households (73%) reported owning an LPG stove as a secondary stove for cooking (Figure 4 shows examples of different types of LPG stoves observed). Eleven percent (19 households) of participants had rustic chimneys (Figure 5 includes examples of the types of chimneys observed) over their traditional stove and half of participants (91) had the stove in a recessed area with a simple opening in the roof (Figure 1 includes examples). Most of the households reported having electricity in their homes and using it as the primary method used for lighting the home (97%). All households had only one door and 17% reported leaving it permanently open. Most participants (82%) burn trash at home and only 3% reported sleeping in the kitchen.

Household characteristics that influence concentrations and exposures

We found associations between the kitchen area HAP concentrations and the following characteristics: roof material type, rainy season, stove ventilation, wealth quintile and the use of wood fuel in addition to dung. Variables that were associated

with HAP personal exposure included the following: having an LPG stove in addition to the traditional biomass stove, number of bedrooms, roof type, stove ventilation, and sample duration (24-hours versus 48-hours). The final multivariable models explained 15% of $PM_{2.5}$, 26% of CO and 28% of BC kitchen concentration variability (22%, 8%, and 16% variability of personal exposures, respectively)

The kitchen characteristic that was consistently and strongly associated with HAP in the kitchen area and personal exposures was roof material. The associations were robust when controlling for other variables in the multivariable models for all pollutants. The effect of roof type was much larger than the effect of wealth quintile, which incorporates roof type in addition to the possession of other household materials related to higher wealth. Roof material explained the most variability among univariate models for kitchen area $PM_{2.5}$ (12%) and CO (16%). We found that having a roof of natural materials (straw, *totora* or reed) was strongly associated with higher kitchen concentrations and personal exposures for all pollutants compared to calamine sheet, cement fiber or similar. Concentrations in the kitchen were 99%, 139% and 57% higher for $PM_{2.5}$, CO and BC, respectively, for natural fiber roofs (Table 2). Personal exposures were 41%, 36% and 55% higher for $PM_{2.5}$, CO and BC, respectively, in households with natural roof material compared to calamine sheet, cement fiber or similar roof materials (Table 3).

The impact of wealth in kitchen area concentrations was important (showing reductions of 56% and 55% for $PM_{2.5}$ and CO, respectively, for the third quintile

compared to the lowest quintile; Table 2). Wealth was only associated with personal exposures for CO in multivariable models, having a similar impact to that of the kitchen area model (reduction of 49% among those in the third quintile compared to the first quintile indicating the least wealth; Table 3) but not showing significance for other pollutants.

Having an LPG stove in addition to a biomass cookstove did not impact kitchen area concentrations, but it did have an impact in personal exposures. Concentrations were lower by 18% for $PM_{2.5}$, 28% for CO, and 27% BC concentrations when participants reported having an LPG stove. In the kitchen area, the use of wood was generally associated with reduced concentrations in univariate models of all pollutants and was a robust variable explaining variability in the multivariate model for BC. BC concentrations were reduced by 26% in the households where wood fuel was reported to be used, when adjusting for roof type and rainy season (Table 1). Although the use of wood did not explain much of the variability of $PM_{2.5}$ and CO (less than 3%), it was the variable that explained the most variability of BC (9%) kitchen concentrations in univariate models (most other variables explained 2 to 3%).

Better stove ventilation was associated with a reduction of personal exposures particularly for $PM_{2.5}$ and BC in multivariable models. Concentrations were reduced by 36% and 38% for $PM_{2.5}$ and BC, respectively, in households with a chimney compared to households with no stove ventilation. Households with the stove in a

recessed area did not impact any of the pollutants measured. Stove ventilation did not have a significant impact in the multivariable model for CO personal exposures. Although stove ventilation also showed concentrations reductions in univariate models, this variable did not explain variability of HAP in multivariable models of the kitchen area concentrations. The physical structure of the home also influenced personal exposures. Having additional bedrooms reduced personal exposures of $PM_{2.5}$ and BC (-20% and -11% for every additional bedroom, respectively).

Samples taken during the rainy season (December, January, February, March) had lower kitchen area concentrations compared to samples not taken during that season. Having pigs and dogs was associated with a slight increase in kitchen area concentrations although these variables contributed very little (less than 3%) to explaining kitchen area concentration variability.

Variables that did not show significant associations with any of the pollutants included the following: number of windows open, doors reported to be permanently open, the reported time spent cooking, and the number of people that live in the household. Finally, we did not identify any association between the participant's age and kitchen area concentrations or personal exposures. We also didn't identify any relationship between kitchen area concentrations or personal exposures and other socioeconomic status variables (besides wealth quintile) such as income level or years of education.

Discussion

Consistent with previous findings,[52] we identified that roof material had the greatest impact in kitchen area concentrations or personal exposures. We found that the kitchen area concentrations of HAPs can be twice as high in households with natural roofs material as opposed to households with calamine sheet or cement roofs. When visiting participant homes, we observed that the natural straw or *totora* roof materials leave less space between the walls and the roof for smoke to leak out of the home compared to calamine sheet roofs, likely resulting in suppressed ventilation with the straw or totora roofs. In addition, we observed more soot accumulation in the natural roof materials compared to other roof materials, possibly also limiting ventilation. Households that have a roof material that allowed for better ventilation had on average 50% and 60% lower $PM_{2.5}$ and CO concentrations in the kitchen and between 30% to 40% reductions in personal exposures compared to other households. These reductions are even comparable to what has been achieved for some improved stove interventions such as stoves with chimneys [14], although such reductions don't reduce concentrations enough to meet WHO recommendations [14, 15, 39].

Although we didn't find that having an LPG stove as a secondary stove impacted kitchen area concentrations, it did have an impact in personal exposures. We observed reductions of almost 30% in personal exposures among households with an LPG stove compared to no LPG stove. These reductions were consistent for all pollutants ($PM_{2.5}$, CO and BC) after adjusting for other household variables. A

previous paper that evaluated the successes and challenges of the government local program to promote the use of LPG stoves in Puno [53] concluded that less than 5% of beneficiaries reported exclusively using LPG stoves and that the fuel provided by the program is insufficient. That study also suggested a slight reduction in $PM_{2.5}$ personal exposures on a subset of 95 households [53], which is consistent with our results. Rural communities in Puno that have an LPG stove do not show the reductions in HAP concentrations that may be expected from switching from biomass cookstoves to exclusive LPG stove use [48]. It is possible that the reductions of personal exposures are detected because women move away of the traditional stove to use the LPG stove. It is also possible that participants cook some portion of their meals with LPG stove, though not enough to significantly impact HAP in the kitchen area. Interventions that impact personal exposures may have more meaningful impacts on health and should be prioritized.

Personal exposures were also impacted by the number of bedrooms. Having more bedrooms was associated with lower personal exposures (approximately 20% for each additional bedroom). This could be because the participants spend more time in those bedrooms when available and less time in the kitchen. The typical layout of households in this region is that there are generally separate structures for each space or room, and all structures share a common patio area.

Households characteristics and variables that explain HAP vary widely across different settings. Variables that were expected to explain indoor concentrations,

such as the number of windows, were not associated with HAP in any of the models, consistent with the previous findings at this site [52]. However, in other sites, studies have found that windows were important in explaining concentration variability in other locations [51]. Households in rural Puno are at high altitude and in a cold climate, therefore windows are often closed and may not be a major source of ventilation. A recent study that developed a model for rural communities in Paraguay found that garbage burning a was a significant predictor of indoor $PM_{2.5}$, but did not find other household characteristics such as room volume or structure materials to be important [60]. We did not see any impact on burning trash activities, but this might be due to the fact that most participants reported trash burning with few participants as a comparison group.

Compared with previous measurements in rural households in the same area by Pollard et al., the PM concentrations measured in this study were much higher [52]. This difference might be explained by the differences in calibration methods and instrumentation used. Pollard et al. selected a smaller sample of households to measure HAP and collected passive nephelometric measurements on most households. That study used a calibration curve developed with a mixture of urban and rural households included. In contrast, we were able to calibrate every individual sample using simultaneous nephelometric and gravimetric data for all of our samples since our monitors used active sampling (air is sampled using a pump, whereas passive methods do not). Passive sampling has been shown to underestimate concentrations and to have different biases for different types of aerosols mixtures [61].

Contrary to our results, Pollard et al. found that hours spent cooking was related to HAP in Puno. However, Pollard et al. also included urban participants that use cleaner fuels more often compared to rural participants. Rural households in Puno showed little variability in hours cooking (as opposed to urban households in the area). Most of our participants cook for about 3 to 4 hours; compared to urban households that reported a wider range in time spent cooking (from 1 to 6 hours) [52].

Household characteristics that provide ventilation and impact personal exposures can have different impacts on gases compared to particles. The presence of a chimney or having the stove in a recessed area explained variability of personal exposures for $PM_{2.5}$ and BC but not CO. Households structures and air flow in and out the kitchen might remove particles in a different way compared to gases given the mechanism by which they can interact with surfaces after being emitted. Particles have a tendency to impact and get adhered to surfaces much more than gases [60]. We observed thick layers of soot accumulation on kitchen walls and roofs of participants. Gases such as CO are less influenced by kitchen surfaces.

This study has many strengths. We collected household characteristics of all our 180 participants and were able to quantify the impact of household characteristics on HAP. We collected 48-hour samples for most of our participants, which allowed us to estimate typical exposures in this setting. We were able to collect simultaneous

active gravimetric samples and direct-reading continuous measurements for $PM_{2.5}$, which allowed for better precision in calibrating each sample. We were also able to identify the impact of different fuel types on HAP concentrations and personal exposures for the first time in rural Peru. In particular, we quantified the impact of having an LPG stove and the use of wood on HAP concentrations. Being able to incorporate personal exposures in our analysis allowed us to identify associations that had not been previously identified. We developed models for three different pollutants, which was important to identify the consistency of the associations.

We were not able to predict how much would HAP concentrations be reduced if all homes had an improved roof type or chimney. Our goal was not to develop a predictive model because the percent variability explained by the variables included is limited. Our objective was to identify relevant household characteristics that influence HAP the most, and that can be considered as potential points of intervention. Other variables that can have an important impact on emissions such as amount of fuel used by household and details on the characteristics of the fuels were not collected. However, we collected valuable household information that helped us identify the important variables that can be used for future studies or interventions to optimize interventions to reduce HAP exposures.

Conclusions

Characterizing HAP in different settings is important and it can help identify culturally-relevant and effective local solutions to reduce HAP exposures. Every location is different due to the different cultural contexts, building styles, and weather. In Puno, colder weather conditions might explain why the windows might not be related to ventilation. Instead, we found that different roof types had an important impact in HAP and strongly impacted both kitchen area concentrations and personal exposures to HAP. Although chimneys and having an LPG stove didn't have an important impact in kitchen area concentrations, they did reduce personal exposures. Better roof materials, better chimneys and having LPG stoves may be actionable interventions that can help reduce exposures to HAP in high-altitude rural Peru and similar settings.

Table 1. Baseline and household characteristics of study participants

Name	Category	Number (%)
Total number of participants		180 (100%)
Kitchen characteristics		
Number of rooms	1	14 (8%)
	2	74 (41%)
	3	59 (33%)
	4	31 (17%)
	5	2 (1%)
Number of bedrooms	1	66 (37%)
	2	89 (49%)
	3	16 (9%)
	4	9 (5%)
Kitchen roof material	Rustic: Calamine sheet, cement fiber or similar	73 (41%)
	Natural / Light: straw, totora, reed or similar	107 (59%)
Door or entrance in kitchen permanently open		31 (17%)
Kitchen windows permanently open	0	72 (40%)
	1	26 (14%)
	2	7 (4%)
	5	2 (1%)
Burn trash at home		147 (82%)
Ventilation over traditional stove	Stove with no ventilation	70 (39%)
	Stove with chimney	19 (11%)
	Stove in a recessed area	91 (51%)
Fuel used for cooking	Wood	75 (42%)
	Crop residue, grass, straw or bushes	127 (71%)
	Cow dung	179 (99%)
Secondary stove	No other stove	48 (27%)
	LPG stove	132 (73%)
Sleeps in the kitchen		6 (3%)
Number of dogs	0	57 (32%)
	1	92 (51%)
	2	30 (17%)
	3	1 (1%)
Number of pigs	0	74 (41%)
	1 to 2	52 (29%)
	3 to 5	49 (27%)
	6 to 9	5 (3%)
Kitchen separated from main residence	with adjacent walls	105 (58%)
	without adjacent walls	75 (42%)
Participant characteristics		
Average age (SD)*		48.3 SD 10.1
Average years of education (SD)		6.2 SD 3.3
Wealth Quintile	1	101 (56%)
	2	69 (38%)
	3	10 (6%)
	4 and 5	0 (0%)
Time cooking weekly (hours)	0 - 20	31 (17%)
	20 - 30	137 (76%)
	30 - 50	12 (7%)
Number of people in the household	1 - 2	51 (28%)
	3 - 5	105 (58%)
	6 - 9	24 (13%)

*SD: Standard deviation

Figure 1. Examples traditional stoves located in recessed areas in the kitchens of study participants

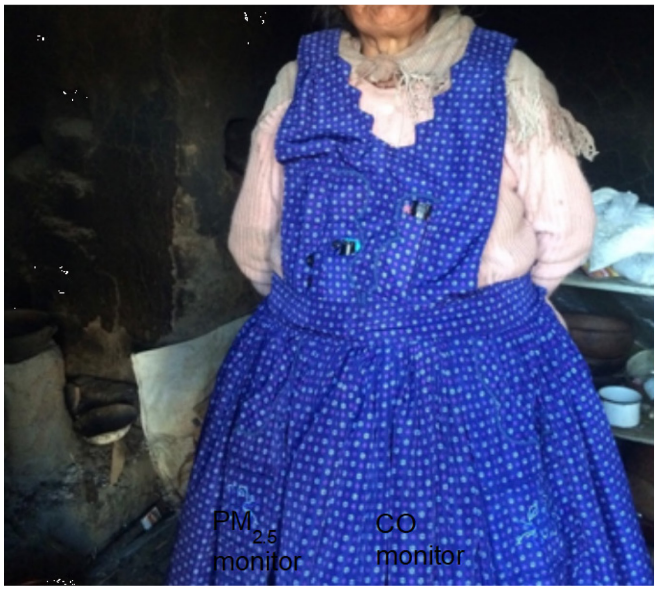

Figure 2. Personal exposure monitor placement on apron for household participants

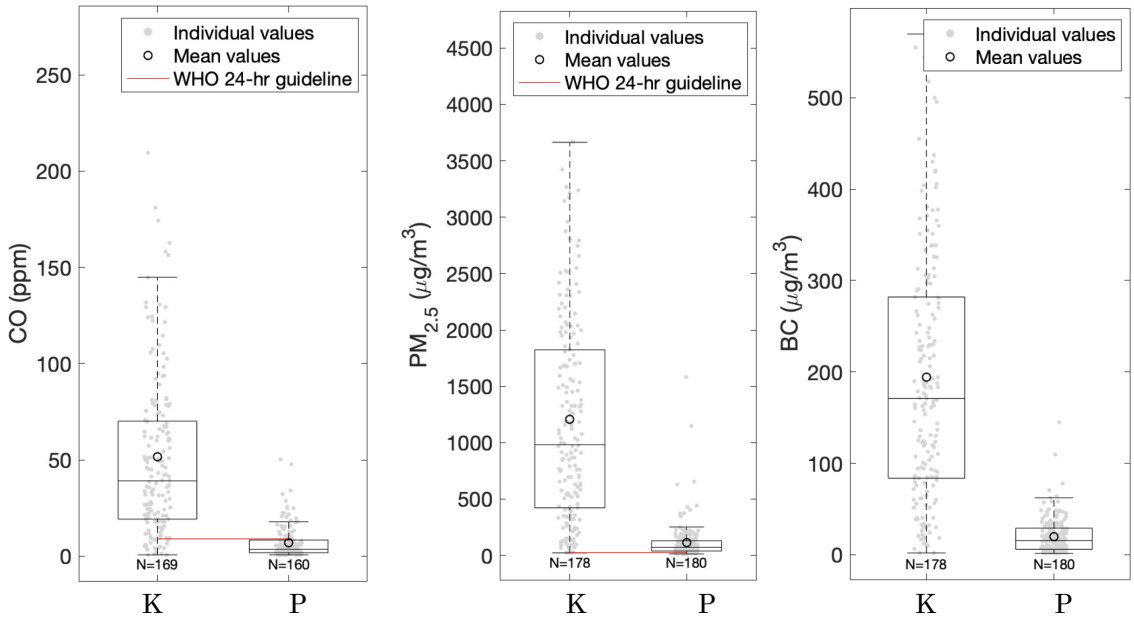

Figure 3. Baseline kitchen area (K) and personal exposure (P) box plots for CO, $PM_{2.5}$, and BC, 48-hour means. Interquartile ranges of the box plots represent the 25th and the 75th percentiles of the 48-hr means for each group; the middle of the box represents the 50th percentile; the circle represents the average of the group; the sample size is indicated under each box plot. The red line represents the World Health Organization recommended guidelines 24-hour averages indoor. Acronyms: BC: black carbon; $PM_{2.5}$: fine particulate matter; CO: carbon monoxide.

Figure 4. Examples of previously owned LPG stoves used in the study area

Figure 5. Examples of chimneys used by study participants with traditional stoves

Table 2. Linear regression coefficient results of household variables in relation to kitchen area concentrations

	Kitchen PM		Kitchen CO		Kitchen BC	
	SLR	MLR	SLR	MLR	SLR	MLR
Variable	Ratio (95% CI)	Ratio (95% CI)	Ratio (95% CI)	Ratio (95% CI)	Ratio (95% CI)	Ratio (95% CI)
N	N = 178		N = 169		N = 178	
Kitchen roof material						
Calamine sheet, cement fiber or similar	Reference					
Natural / Light: straw, totora, reed or similar	**2.18**	**1.99**	**2.48**	**2.39**	**1.55**	**1.57**
(95% CI)	(1.60 -2.96)	(1.45 - 2.72)	(1.80 -3.43)	(1.74 - 3.30)	(1.18 -2.02)	(1.23 - 2.01)
Rainy season	0.86	0.00	**0.59**	**0.59**	**0.48**	0.54
(95% CI)	(0.61 -1.20)	(0.00 - 0.00)	(0.42 -0.84)	(0.42 - 0.81)	(0.37 -0.62)	(0.42 -0.70)
Stove with no ventilation	Reference					
Stove with chimney	**0.47**		0.72		0.85	
(95% CI)	(0.27 -0.82)		(0.40 -1.28)		(0.54 -1.36)	
Stove in a recessed area	0.76		1.27		1.14	
(95% CI)	(0.54 -1.07)		(0.88 -1.83)		(0.85 -1.51)	
Wealth Quintile 1	Reference					
Wealth Quintile 2	**0.66**	**0.75**	**0.62**	0.71	**0.70**	
(95% CI)	(0.48 -0.92)	(0.54 -1.03)	(0.43 -0.89)	(0.51 -0.98)	(0.53 -0.93)	
Wealth Quintile 3	**0.40**	0.56	**0.45**	**0.55**	0.78	
(95% CI)	(0.20 -0.80)	(0.28 -1.11)	(0.22 -0.93)	(0.28 -1.08)	(0.43 -1.41)	
Use of wood	0.77		**0.65**		**0.57**	**0.74**
(95% CI)	(0.55 -1.06)		(0.46 -0.92)		(0.44 -0.74)	(0.57 -0.95)
Number of pigs	1.02		1.09	**1.12**	1.05	
(95% CI)	(0.91 -1.14)		(0.96 -1.23)	(1.01 -1.25)	(0.95 -1.15)	
Having dogs	1.26		1.32		**1.40**	1.26
(95% CI)	(0.89 -1.78)		(0.91 -1.91)		(1.05 -1.86)	(0.98 -1.62)

SLR: simple linear regression results; MLR: multiple linear regression model results selecting the variables that most robustly explained variability of each pollutant. **Bold values**: highlight significant results with p-value<0.05; Each of the regression model coefficient represents the ratio of the impact on the pollutant compared to the reference category. For example, a ratio of 1.1 translates to a 10% increase and a value of 0.9 translates in a 10% decrease compared to the reference category.

Table 3. Linear regression coefficient results of household variables in relation to personal exposure concentrations

	Personal PM		Personal CO		Personal BC	
	SLR	MLR	SLR	MLR	SLR	MLR
Variable	Ratio (SE) (95% CI)	Ratio (SE) (95% CI)	Ratio (SE) (95% CI)	Ratio (SE) (95% CI)	Ratio (SE) (95% CI)	Ratio (SE) (95% CI)
N	N = 180		N = 160		N = 180	
Kitchen roof material						
Calamine sheet, cement fiber or similar	Reference					
Natural / Light: straw, totora, reed or similar	**1.64**	**1.41**	**1.46**	**1.36**	**1.68**	**1.55**
(95% CI)	(1.28 -2.11)	(1.10 -1.81)	(1.06 -2.02)	(0.99 -1.88)	(1.32 -2.14)	(1.21 -1.98)
Stove with no ventilation	Reference					
Stove with chimney	**0.50**	**0.64**	0.66		**0.52**	**0.62**
(95% CI)	(0.32 -0.77)	(0.42 -0.98)	(0.39 -1.13)		(0.34 -0.79)	(0.41 -0.93)
Stove in a recessed area	0.80	0.84	0.90		0.88	0.93
(95% CI)	(0.61 -1.05)	(0.65 -1.07)	(0.64 -1.26)		(0.68 -1.14)	(0.72 -1.19)
Number of bedrooms	**0.75**	**0.80**	**0.82**		**0.82**	0.89
(95% CI)	(0.64 -0.88)	(0.69 -0.94)	(0.67 -1.00)		(0.70 -0.96)	(0.76 -1.04)
Wealth Quintile 1	Reference					
Wealth Quintile 2	**0.76**		0.72	0.78	0.79	
(95% CI)	(0.58 -0.99)		(0.52 -1.01)	(0.56 -1.08)	(0.61 -1.02)	
Wealth Quintile 3	**0.57**		**0.46**	0.49	0.73	
(95% CI)	(0.33 -1.01)		(0.21 -0.99)	(0.23 -1.07)	(0.42 -1.26)	
Secondary stove: LPG gas stove	0.93	**0.82**	0.71	0.72	0.78	**0.73**
(95% CI)	(0.70 -1.24)	(0.63 -1.07)	(0.50 -1.02)	(0.50 -1.02)	(0.59 -1.04)	(0.56 -0.95)
Sample with only initial 24 hrs, not 48hrs	**2.04**	**2.11**	0.99		1.44	1.55
(95% CI)	(1.18 -3.54)	(1.28 -3.50)	(0.54 -1.81)		(0.84 -2.48)	(0.93 -2.57)
Having of dogs (binary)	**1.45**	**1.42**	1.24		1.22	
(95% CI)	(1.11 -1.90)	(1.10 -1.82)	(0.88 -1.75)		(0.93 -1.59)	

SLR: simple linear regression results; MLR: multiple linear regression model results selecting the variables that most robustly explained variability of each pollutant. **Bold values**: highlight significant results with p-value<0.05; Each of the regression model coefficient represents the ratio of the impact on the pollutant compared to the reference category. For example, a ratio of 1.1 translates to a 10% increase and a value of 0.9 translates in a 10% decrease compared to the reference category.

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CHAPTER 3:

BLACK CARBON EXPOSURES FROM HOUSEHOLD AIR POLLUTION AND MARKERS OF INFLAMMATION IN PERU

Abstract

Background:

Approximately 3 billion people worldwide, mostly from low and middle-income countries (LMICs), use biomass fuels such as wood and dung for cooking. Household air pollution (HAP) from biomass cookstoves is recognized as a leading risk factor for several cardiopulmonary outcomes and is among the largest environmental risk factors for preventable disease. The existing literature on the toxicity of particulate matter (PM), an important constituent of HAP, suggests that inflammation is likely to be involved in the pathways of cardiovascular disease development. There is evidence that black carbon (BC) is one of the primary components of PM from biomass combustion and that BC elicits adverse cardiovascular outcomes through inflammatory pathways. However, most of the evidence on BC and inflammation comes from studies of urban, ambient exposures. The relationship between inflammation markers and BC from biomass cookstoves is poorly understood.

Objective:

To examine the exposure-response relationship between $PM_{2.5}$ and BC and markers of inflammation among adult women who use biomass cookstoves in rural Peru.

Methods:

We enrolled 180 women aged 25-64 years from rural communities surrounding the city of Puno, Peru. We measured markers of inflammation, namely CRP, IL-6, IL-10, IL-1β, and TNF-α using dried blood spot samples. We also measured 48-hour kitchen area concentrations and personal exposures to fine PM, BC, and carbon monoxide

for each participant. We used linear regression to develop exposure-response models between these three HAPs and markers of inflammation.

Results:

We found significant associations between kitchen area BC concentrations and the inflammatory markers TNF-α, IL-10 and IL-1β. Kitchen area BC concentrations in the fourth and fifth highest quintiles were associated with 31% and 24% (95% CI: -2 to 73% and -8 to 68%) higher TNF-α concentrations when compared to the lowest quintile (median of 36 $\mu g/m^3$), after adjusting for other HAPs, age, BMI, season (rainy vs. dry), and participant wealth (in quintiles). Kitchen area BC concentrations in the two highest quintiles were also associated with 39% and 35% lower IL-10, an anti-inflammatory marker. However, opposite to what was hypothesized, Kitchen area BC concentrations were negatively associated with IL-1β. These associations were stronger in the multipollutant model when controlling for $PM_{2.5}$. Associations observed were also stronger when restricting the analysis to wood fuel users compared to those who used exclusively dung. No significant associations were identified for IL-6 or CRP or for personal exposures to HAP with any inflammation biomarker.

Conclusions:

In our analysis of women who use biomass cookstoves in rural Peru, the exposure-response association with inflammation markers appears to be stronger with BC than with PM. Further research is needed to understand inflammation responses in people who use biomass cookstoves and interventions that target the reduction of BC to improve public health.

Keywords:

Cookstoves, exposure response, markers of inflammation, TNF-α, IL-10, IL-1β, household air pollution, personal exposure, BC, $PM_{2.5}$, biomass fuel, rural Peru.

Introduction

Approximately 3 billion people worldwide, mostly from low and middle-income countries (LMICs), use biomass fuels such as wood, dung, crop waste and charcoal for their heating and cooking needs [1]. Household air pollution (HAP) from biomass cookstoves was estimated to be responsible for 2.6 million deaths and 77.2 million disability-adjusted life-years in 2016 [2]. HAP from cookstoves is among the largest environmental risk factor for preventable disease [3–6]. It is recognized as a leading risk factor for bronchitis, chronic obstructive pulmonary disease, lung cancer, childhood pneumonia, acute lower respiratory infections, cardiovascular events, and low birthweight [7–9]. In particular, cardiovascular disease accounted for the majority of deaths and disability-adjusted life-years in the Global Burden of Disease study [6]. Burning of biomass fuels for cooking is also a major cause of mortality in low and middle-income countries [6]. Cardiovascular disease is the leading cause of morbidity and mortality worldwide and over 80% of premature CVD deaths occur in LMICs [10].

The incomplete combustion of carbon-containing fuels, such as wood and dung, produces several different types of gases and particulate pollutants. Pollutants of

major public health concern that are commonly monitored in LMICs include carbon monoxide (CO) and particulate matter (PM). Chronic exposure to ambient CO has been associated with congestive heart failure, ischemic heart disease, cardiovascular disease, as well as low birth weight, congenital defects, stroke, asthma in epidemiological studies [11]. Fine particles, smaller than 2.5 micrometers in aerodynamic diameter ($PM_{2.5}$), are small enough to deposit in the alveoli, initiate inflammatory cascades, and may enter the pulmonary circulation [12]. Extensive epidemiological studies have found strong associations between ambient particulate air pollution and respiratory symptoms, lung cancer, and increased risk of cardiopulmonary related morbidity and mortality in adults and children [8, 13–19, 19–24].

The existing literature of PM toxicity suggests that inflammation is likely to be involved in the pathways of cardiovascular disease development [25]. Ambient and traffic-related PM exposure has been associated with pulmonary systemic pro-oxidant and pro-inflammatory effects [12, 26, 27]. In particular, relationships between air pollution and markers of inflammation (including C-reactive protein, CRP, and inflammation cytokines such as TNF-α, IL-1β and IL-6), have been identified in animal models as well as human studies [27–35]. Inflammatory cytokines may induce a systemic response that has an important role in the pathogenesis of the cardiopulmonary adverse health effects associated with ambient or traffic-related PM exposure [36–38].

Identifying which constituents of PM are primarily responsible for adverse health effects remains a large knowledge gap in air pollution literature [33]. The composition of $PM_{2.5}$ varies widely and can include sulfate, nitrate, ammonium, black carbon, and organic carbon in addition to various trace metals [39]. Recent reviews suggest that traffic-related black carbon might play an important role in cardiovascular disease development [33, 40]. Black carbon (BC) is one of the main components of $PM_{2.5}$ resulting from the incomplete combustion of carbonaceous materials. BC, defined as carbon content as measured by light absorption [41], consists of elemental carbon with several organic and inorganic compounds absorbed on to its carbonaceous surface [25, 41, 42].

Several literature reviews suggest that BC mass might have stronger associations with cardiopulmonary outcomes than with total PM mass or than with any other $PM_{2.5}$ species [25, 33, 40, 43, 44]. The effect of BC from traffic-related exposures has been shown to be more robust than the effect of PM mass on mortality, hospital admissions and emergency department visits, both in healthy adults and older, susceptible populations [25, 33, 40, 43]. In addition, the associations of BC concentrations seems to be significantly greater than the estimated effects of most other single PM elements with cardio-respiratory related hospital admissions in adult populations [44–50]. It has been suggested that BC elicits cardiovascular endpoints through inflammation pathways [25, 27] [25, 43, 51]. However, toxicity studies of PM and its components have focused on urban air pollution [12, 16, 18, 20, 51]. Furthermore, most evidence that relates BC with inflammation responses from human studies comes from ambient or diesel exhaust particles [25] or short-term

wildfire events [25, 52]. These relationships with HAP in LMICs have not been fully explored [53].

There is evidence that suggests that inflammation might be part of the pathway of disease development from biomass smoke exposure. A systematic review by Lee et al., concluded that PM from biomass fuel burning seems to alter the innate immune system through alveolar macrophage-driven inflammation, recruitment of neutrophils, and disruption of barrier defenses [36]. Furthermore, acute biomass PM exposure appears to induce different inflammatory profiles depending on the fuel type (dung or wood) and duration of the exposures [36, 38, 54]. In particular, dose dependent increases of inflammatory cytokines, including IL-6 and IL-8, have been observed to correlate with wood smoke exposure from human alveolar macrophages in healthy Malawian adults exposed to HAP [55]. Nevertheless, recent studies show conflicting results. For example, a convenience cross-sectional sample from the RESPIRE trial, which installed a chimney as the intervention, did not identify significant differences in IL-8 levels, fibronectin or myeloperoxidase of participants with chimney compared to those that used an open wood fire stove, despite PM exposure reductions greater than 50% [56].

Few studies have investigated the relationship of HAP with markers of inflammation in the cookstove literature [56–59]. These existing studies have evaluated the impact of different types of cookstoves on markers of inflammation or cardiovascular health, for example comparing biomass cookstoves with clean fuel

use [57–59] or comparing an intervention of stoves with chimney versus without [56]. Furthermore, no cookstove studies have explored the association of BC to inflammation markers. In light of these knowledge gaps, this study aims to examine the exposure-response relationship between BC and markers of inflammation among adult women who use biomass cookstoves in rural Peru.

Methods

Study design and settings

This study was nested within a clean fuel intervention trial among daily users of biomass cookstoves [60]. We used baseline measurements collected from 180 women aged 25-64 years from rural communities surrounding the city of Puno. Puno is located in southeastern Peru, near the shore of Lake Titicaca at 3,825 meters above sea level. We enrolled women who were the primary cook of their household and reported daily use of biomass fuels for cooking. We measured kitchen area concentrations and personal exposures to HAP, collected dried blood spot samples, and recorded basic demographic information. We collected duplicate anthropometric measurements of weight and height and used the mean of the two measurements to estimate BMI for each participant. Socioeconomic status was evaluated through asset ownership, and participants were assigned to a national wealth quintiles using the Demographic and Health Survey (DHS) [61]. Additional information of the trial assessments has been previously published [62].

Exposure assessment

We collected 48-hour samples of kitchen area concentrations and personal exposures to $PM_{2.5}$ and CO among the 180 participants. Kitchen area concentrations were measured by placing CO and $PM_{2.5}$ monitors approximately one meter from the combustion zone and 1.5 meters above the floor (representing the breathing zone), and at least one meter from doors and windows (when possible). Personal exposures were monitored by placing the monitors near each participant's breathing zone in an adapted apron commonly used by women in the study area and provided to the participants [60]. Measures of both $PM_{2.5}$ and CO were logged at 1-minute intervals. Kitchen area samples of $PM_{2.5}$ and CO included 10% duplicates. High correlations were observed for duplicate HAP samples (coefficient of determination using Spearman's correlation coefficient of 0.94 on all HAPs).

The EL-USB-CO data logger was used for CO direct-reading measurements (Lascar Electronics, Erie, PA, USA). Data from the CO monitors was calibrated by co-locating all the monitors in a sealed chamber. The monitors were exposed to clean air (nitrogen gas) and a CO concentration of 100 ppm in the chamber. Individual slopes and intercepts were estimated for each device at each co-location timepoint to correct any drift in the devices. The LOD for the CO monitors was estimated as 1 ppm, which was three times the standard deviation of concentrations logged during the regular clean air calibration checks in the field. Results below the LOD were replaced by the LOD divided by the square root of two.

The ECM aerosol monitor (RTI Inc., Research Triangle Park, NC, USA) was used to measure continuous-time $PM_{2.5}$ concentrations, in addition to an integrated gravimetric sample collected on a filter using a pump at 0.3 L/min flow rate. ECM pumps were calibrated daily with a TSI 4100 flowmeter (TSI Incorporated 500 Cardigan Road Shoreview, MN, USA) and recording the flow rate before and after sample collection. Gravimetric $PM_{2.5}$ samples were collected using 15-mm Teflon filters with a 2-μm pore size (Measurement Technology Laboratories LLC, Minneapolis, MN, USA). Filters were pre- and post-weighed at the Johns Hopkins University in a humidity and temperature-controlled room using a XP2U microbalance (Mettler Toledo, Columbus, OH, USA). Nephelometric concentrations were calibrated using the sample-specific gravimetric time-weighted average filter samples. All $PM_{2.5}$ samples included 10% blanks and all reported concentrations were blank-corrected. The limit of detection (LOD) for $PM_{2.5}$ samples, was estimated as three times the standard deviation of the mass measured from field blanks. For $PM_{2.5}$, the LOD was estimated to be 20 μg for the initial 6 months of the study and 9.8 μg for the subsequent 6 months. This change was due to a reduction of filter handling using pre-loaded filters into individual ECM cassettes before sending the filters to the field site.

BC concentrations were determined from the PM samples measuring optical attenuation using a Magee OT21 Sootscan transmissometer (Magee Scientific, Berkeley, CA). The LOD for BC samples was estimated as three times the standard deviation of the attenuation readings recorded from field blanks. The LOD for BC

was 1.4 μg. For all pollutants, the concentrations below the LOD were replaced by the LOD divided by the square root of two.

Biomarker assessment

Dried blood spot (DBS) samples were collected from participants at the end of the 48-hour HAP sample collection. DBS samples were collected using Guthrie DBS cards from a finger from the non-dominant hand swabbed with a sterile alcohol wipe. A sterile lancet was used to puncture the skin and the initial drop of blood was wiped away with an alcohol swab. The following large drop of blood that appeared on the finger was then applied to an unfilled spot on the collection card. Blood from the finger was allowed to drip onto five standard spots on a Guthrie DBS card. Cards were labeled and dried at room temperature on drying rack for at least 10 hours. Dried cards were placed in individually labeled Ziploc bags with a desiccant pouch and a humidity indicator card. Once dried, all samples were kept at -20°C and were shipped for analysis to Emory University (Atlanta, USA).

Inflammation markers (CRP, IL-10, IL-6, IL-1β, TNF-α) were analyzed in duplicate through immunoassay methods. A 6 mm punch was collected from each DBS card and was eluted with 250 μL phosphate buffered saline (PBS). IL-10, IL-6, IL-1β, and TNF-α samples were analyzed in replicate on a MSD multi-plex Proinflammatory 96-well plate (Meso Scale Discovery Rockville, MD, USA). For CRP, a small aliquot of the initial elute was further diluted 1:10 with PBS, 100 μL of the diluted eluate was placed in replicate on an MSD Multiplex Vascular Injury 96-well plate (Meso

Scale Discovery Rockville, MD, USA). Conjugate solution was added and allowed to react at 23°C for 120 minutes after which read buffer was added (buffer containing tripropylamine as a co-reactant for light generation in electrochemiluminescence immunoassays) [62]. Plates were immediately analyzed using electrochemiluminescence on a MSD Multiplex Immunoassay reader with proprietary wavelengths. Concentrations were calculated based upon the absorbance measurements read using an external standard calibration plot. We assumed a DBS volume of 70 μL to estimate concentrations and 100% extraction efficiency.

For all assays, a 10-point calibration curve, a blank, and 2 quality control materials were analyzed simultaneously with samples. Values of replicates were averaged and relative standard deviations (RSDs) were required to be within 10% for the analysis to be considered valid. Similarly, quality control materials were required to be within 20% of the expected values and the recovery of calibrants were 10% of the expected value. Whenever those quality control parameters were not met, the analysis was repeated. The LODs of the methods were: CRP 13.8 pg/mL; IL-10 0.089 pg/mL; IL-6 0.181 pg/mL; IL-1β 0.135 pg/mL; and 0.081 TNF-α pg/mL. Typical RSDs were less than 10% in QC samples and calibrants. Concentrations below the LOD were replaced by the LOD divided by the square root of 2

Statistical analysis

We developed exposure-response linear regression models for CRP, IL-6, IL-1β, and TNF-α concentrations (outcome variables) with HAPs (explanatory variables). We

used 48-hour means of HAP measurements, estimated by averaging the consecutive individual 24-hour means. A sample was considered missing if the sample had less than 20 hours of measurements. We used the initial 24 hours of the sample if the consecutive second 24-hour sample was missing.

Using the 48-hour averages, we estimated quintiles of personal exposure and kitchen area concentrations of CO, $PM_{2.5}$, and BC to use as our explanatory variables in separate models for each inflammation marker. We controlled for body mass index (BMI), age, and wealth quintiles in all of our models. We also incorporated the following confounders as binary variables: the use of wood as primary fuel and measurements during the rainy season (December to March). All of the participants reported to be non-smokers.

The distribution of our markers of inflammation was right-skewed, so we log-transformed all inflammation marker variables to comply with linear regression model assumptions. Residual plots were assessed to confirm linear regression assumptions were met on every model. All data analyses were conducted with MATLAB (The MathWorks, Inc., Natick, MA) and STATA (StataCorp., College Station, TX).

Associations of HAPs with the markers of inflammation were considered meaningful based on the following: 1) The direction of the association was consistent within pollutant quintiles. 2) The direction of the associations was consistent between

pollutants and exposures (kitchen area and personal exposures), regardless of statistical significance. 3) Statistical significance with a p-value less than 0.1 in models controlling for confounders (BMI, age, and wealth). 4). The association is maintained in multipollutant model (adjusting for levels of other HAPs).

Results

We enrolled 180 female participants, with a mean age of 48 years (standard deviation; SD 10) and an average BMI of 26.8 kg/m^2 (SD 4.2). Most participants were classified to be in the two lowest wealth quintiles (94% in first and second quintile) and none of the participants were in the fourth or fifth (the highest) wealth quintiles. Sixty-three percent of our participants reported having either only primary school or no education at all, and 37% of our participants had secondary level education. All of the participants used dung as their primary fuel and 42% reported the use of wood in addition to dung (Table 4).

We collected a total of 166, 177, and 177 kitchen area samples and 158, 178, and 178 personal exposure samples of CO, $PM_{2.5}$ and BC, respectively. Kitchen area mean daily concentrations were: 50.5 ppm (inter quartile range, IQR: 14-63 ppm) for CO; 1,190 μg/m^3 (IQR: 264-1,674 μg/m^3) for $PM_{2.5}$; and 192 μg/m^3 (IQR: 71-270 μg/m^3) for BC. We were able to obtain concentrations of CRP for 166 participants and TNF-α, IL-1β, IL-10 and IL-6, for 179 participants. Concentrations are summarized in Table 4. CRP concentrations for most participants were below 3 mg/l (95%), which is a

common threshold used for high cardiovascular risk [63]. Most samples were below our limit of detection for IL-6 (76%).

Relationships of household air pollution levels and inflammation markers

We did not identify significant associations in single pollutant models between CO and $PM_{2.5}$ with any markers of inflammation. We found significant associations between BC and TNF-α, IL-1ß, and IL-10. The households with the highest BC concentrations grouped by quintiles were positively associated with the pro-inflammatory marker TNF-α (Figure 6). The kitchen area BC concentrations in the fourth quintile (median of 260 $\mu g/m^3$) was associated with a 19% increase in TNF-α concentrations (95% CI: -2 to 46%; Table 5) compared to the lowest quintile (median of 36 $\mu g/m^3$), after adjusting for age, BMI, rainy season, and wealth quintiles. The kitchen area BC concentrations in the 5^{th} quintile (median of 380 $\mu g/m^3$) was associated with a 13% increased TNF-α although with a wider confidence interval was observed (95% CI: -8 to 39%). BC was also associated with 18%, 29% and 26% reductions in the anti-inflammatory marker IL-10 with the second, third, and fourth quintiles of kitchen area concentrations (median concentrations of: 171 $\mu g/m^3$, 260 $\mu g/m^3$, and 380, respectively) compared to the lowest BC quintile (36 $\mu g/m^3$).

Contrary to what we expected, the highest quintiles of kitchen area BC concentrations were negatively associated with IL-1β (-45% 95% CI: -71 to 4% and -37% 95% CI: -68 to 25%: Figure 7 and Table 5). This association of IL-1β and BC in the kitchen area became stronger in the multipollutant model adjusting for $PM_{2.5}$

and CO (-45% 95% CI: -71 to 4% and -37% 95% CI: -68 to 25%; Table 6). BC concentrations and CRP levels also show an overall negative relationship although the percent changes had wide confidence intervals (Table 5). Despite not being statistically significant, the directions of the associations for CO and $PM_{2.5}$ were consistent with the trends observed for BC and CRP but with p-values between 0.2 and 0.3 (results not shown).

In multi-pollutant models, when further adjusting by CO and $PM_{2.5}$ concentrations, we observed stronger effect estimates and narrower confidence intervals with the association between BC and TNF-α compared with the single pollutant model (Table 6). After controlling for other pollutants, TNF-α concentrations increased 31% and 24% (95% CI: -2 to 73% and -8 to 68%, respectively; Table 6) with the two highest BC kitchen area concentration quintiles (260 $\mu g/m^3$ and 380 $\mu g/m^3$) compared to the lowest quintile (36 $\mu g/m^3$). In the multi-pollutant model, the negative associations of IL-10 (-39% 95% CI: -59 to -9% and -35% 95% CI: -58 to -1%) with BC kitchen area highest quintile levels, was maintained and consistent with the single pollutant model results.

In the multipollutant model, participants that reported the use of wood as fuel in addition to dung had 13% lower TNF-α concentrations (95% CI: -52 to 1%) and 72% greater IL-1β concentrations (95% CI: 24 to 140%), compared to participants that did not report the use of wood (Table 6), regardless of BC quintile level. When restricting the models to only participants that reported the use of wood as a

secondary fuel use and had markers of inflammation detected (N=73), the highest BC kitchen concentration quintiles were strongly and positively associated with TNF-α and negatively associated with IL-1β. Among participants that used wood, the highest quintiles of kitchen area BC concentrations (260 and 380 μg/m^3) had 46% and 32% greater concentrations of TNF-α (95% CI: 14% to 87% and 0.1 to 75%, respectively; Table 7) compared to the lowest quintile (36 μg/m^3). In contrast, in the models excluding wood users (N=104) the results were consistent with null associations (results not shown).

A majority of our samples for IL-6 (77%) were below the limit of detection, we were not able to detect any consistent and significant trends with IL-6 and the different concentrations of HAPs. Sixty seven percent of our IL-10 samples were below the LOD, yet despite this we were able to detect associations. Finally, we did not find significant differences in inflammation markers when considering personal exposures to any of the three monitored pollutants.

Discussion

BC from biomass cookstoves in high altitude rural Puno was related to inflammation markers TNF-α, IL-1β and IL-10. Previous studies that have observed associations of particle mass from biomass with inflammation markers, but limited evidence exists on relationships with BC [64, 65]. We found that BC is more strongly related to these markers of inflammation than $PM_{2.5}$ and that these results were robust to adjustment for $PM_{2.5}$ in multipollutant models. These results are similar to what has

been suggested in the urban air pollution literature [66]; the association between several health outcomes including inflammation and BC is stronger than associations with $PM_{2.5}$. These results add strength to the hypothesis that BC might be one of the components of $PM_{2.5}$ driving inflammation responses that lead to adverse health outcomes [65].

We found positive associations between TNF-α and kitchen area BC concentrations from biomass cookstoves. We found that the highest levels of HAP among biomass cookstoves users in Puno were associated with greater expression of TNF-α compared to lowest quintile. These findings are consistent with previous studies that have reported positive associations with the pro-inflammatory cytokines TNF-α, IL-8, IL-6 among biomass cookstoves users compared to those using stoves burning cleaner fuels or advanced, cleaner-burning biomass stoves in Guatemala [56], India [58, 59] and Nigeria [67]. Although others have reported null associations with markers of inflammation including TNF-α, and HAP reductions in Nicaragua [68] and South Africa [69].

Consistent with an inflammatory response, we also observed a reduction of the anti-inflammatory cytokine IL-10 with increasing levels of HAPs. IL-10 inhibits the production of pro-inflammatory cytokines including IFN-γ, IL-2, IL-3, TNF-α, TNF-ß, and pro-inflammatory responses [70]. Previous studies have shown that PM from woodsmoke promotes the reduction of IL-10, IL-4 and IL-13 while promoting the release of pro-inflammatory cytokines including TNF-α [36]. IL-10 production was

also found to be reduced after biomass PM from wood and PM from cow in the lungs of mice [38].

Contrary to what we expected, BC concentrations were negatively associated with IL-1ß and no associations were identified with IL-6. We also were able to identify that the association with IL-1ß seem to be driven by the participants that reported using wood as fuel. We do not fully understand the reason for the negative association between BC and IL-1ß, but previous studies have shown that the inflammatory profiles shift dramatically between PM from wood or PM from cow dung regarding neutrophilic and eosinophilic responses [36, 38]. A recent cookstove study in Nigeria [67] found that $PM_{2.5}$ was positively associated with TNF-α but not IL-6. However, previous cookstoves studies that have reported associations with TNF-α, also report associations with IL-6 [58, 59]. Most previous cookstove studies do not report measuring IL-1ß [56, 58, 59, 67]. Yet, HAP has been positively related with IL-1ß with wood smoke [12] and urban air pollution [71]. Nonetheless, associations with markers of inflammation and biomass cookstoves are more heterogeneous compared to ambient air pollution [36, 64] and so it is important to further explore the different inflammation pathways in different settings in order to identify differences in the pathways with the different types of biomass fuels.

We did not identify any clear associations with CRP. Although other studies have found positive associations with CRP from HAP [58, 68], a few studies have found null associations [69, 72]. A previous study in Puno was not able to identify CRP

differences among rural participants that used cookstoves compared to urban participants that used cleaner fuels [57]. It is possible that lower concentrations of CRP compared to urban participants might be associated with higher physical activity due to farming [57]. In addition, a chronic continuous exposures to HAP could also lead to compensatory pathways that might reduce CRP levels not observed in other populations with more acute exposure profiles [57]. It is possible that the participants in this community have better cardiovascular health despite of what would be expected due to their HAP exposures [7, 73].

We did not identify associations with personal exposures to HAP. It is possible that given that personal concentrations that were generally lower in magnitude compared to kitchen concentrations, and that personal exposures have greater relative variability, they might require much larger samples sizes to identify meaningful associations. In addition, it is possible that participants were less likely to use the personal devices during the second day of the sampling time. Other cross-sectional studies have detected associations using kitchen area concentrations but not with personal concentrations and markers of cardiovascular health such as blood pressure [74] and markers of inflammation [68]. However, personal exposure measurements, when participants are compliant with wearing the instruments, should reduce exposure misclassification. Efforts should be made to optimize participant compliance for personal exposure monitoring [75].

There are some weaknesses of this study. Validation studies comparing DBS and venous-drawn blood samples have shown strong correlations for some markers such as CRP, although weaker correlations have been observed with other markers including inflammatory cytokines such as those we measured [76–78]. It is possible that DBS might not be a good substitute of serum samples for some of the markers measured in this study. DBS tend to be a faction of typical serum concentrations limiting comparability with results from studies using different methodologies. We also assumed a DBS volume of 70 μL to estimate concentrations and 100% extraction efficiency which can vary from sample to sample [77, 79]. Further research regarding the validity of several inflammation markers from DBS is needed including methods to improve the current protocols [68]. We were not able to measure other cytokines that have been related to biomass cookstoves such as IL-8, or other markers of inflammation. Measuring additional markers might help confirm consistency of results compared to other population studies and to better understand the different profiles elicited with biomass smoke from wood versus dung. Finally, we did not have any information on other potential sources of inflammation responses such as a gastro-intestinal or other temporary illness that might confound the association of HAP and markers of inflammation.

This study is among the first studies to identify exposure-response associations between BC concentrations and inflammation markers, in addition to PM and CO from biomass cookstoves [36, 75]. This evidence suggests a stronger role for BC from biomass cookstoves compared to $PM_{2.5}$ in its relationship with markers of inflammation. Collecting samples using DBS facilitated the logistics of sample

collection and transport. This method also facilitated the participation among this population, who have expressed reluctance to provide venous-drawn blood samples. An additional strength of our study is that, although all of our participants reported the use of dung as their primary fuel, we were able to detect differences in inflammatory markers among the participants who also used wood. These differences in inflammation profiles should be further investigated in population studies that use biomass cookstoves.

Conclusions

HAP from biomass cookstoves was associated with some markers of inflammation (TNF-α, IL-1ß and IL-10). In our analysis of women who use biomass cookstoves in rural Peru, the exposure-response association with inflammation markers appears to be stronger with BC than with $PM_{2.5}$. Our results support previous evidence that biomass smoke from wood and dung induces different profiles of inflammation markers that need to be further investigated in population studies.

Table 4. Basic participant characteristics

Participant characteristics	**Number**	**(%) / SD**
Mean age (years)	48.3	SD 10.1
Mean BMI (kg/m^2)	26.83	SD 4.2
Education level: without education or preschool only	7	(4%)
Education level: primary	106	(59%)
Education level: secondary	67	(37%)
Education level: non-university superior or university	0	(0%)
Wealth Quintile 1 (lowest)	101	(56%)
Wealth Quintile 2	69	(38%)
Wealth Quintile 3	10	(6%)
Wealth Quintile 4 and 5 (highest)	0	(0%)
Fuel used for cooking: Wood & dung	75	(42%)
Fuel used for cooking: Cow dung	179	(99%)
Inflammation markers*	**Median**	**IQR**
CRP (mg/L)	0.29	0.40
IL-10 (pg/mL)	0.04	0.10
IL-1ß (pg/mL)	2.96	4.76
TNF-α (pg/mL)	0.892	0.53

SD: Standard deviation; IQR: inter quartile range. *Inflammation maker assumptions: DBS volume of 70 μL to estimate concentrations and 100% extraction efficiency was assumed.

Table 5. Percent change in markers of inflammation by quintile of BC daily means

		TNFα (N=177)				IL-1β (N=177)				IL-10 (N=177)				CRP (N=164)				
	BC quintile medians	Change (%)	95% CI		p-value	Change (%)	95% CI		p-value	Change (%)	95% CI		p-value	Change (%)	(SE)	95% CI		p-value
	Kitchen BC (μg/m^3)																	
1	36	reference																
2	94	0	-17	21	0.979	-20	-47	22	0.295	-10	-31	16	0.414	-12	23	-48	47	0.623
3	171	-2	-19	19	0.841	-8	-41	42	0.697	**-29**	**-46**	**-7**	**0.014**	-31	19	-60	19	0.179
4	**260**	**19**	**-2**	**46**	**0.084**	**-36**	**-59**	**0.5**	**0.052**	**-26**	**-44**	**-2**	**0.037**	-30	20	-60	22	0.206
5	380	13	-8	39	0.236	-20	-49	26	0.335	-18	-39	8	0.158	-27	21	-59	29	0.274

All models are controlled by age, BMI, wealth quintile, rainy season, use of wood as fuel. Abbreviations are: BC: black carbon; BMI: body mass index; TNF-α and IL-1ß: pro-inflammation markers; IL-10: anti-inflammation marker. BC 48-hour means are grouped into quintiles of pollutants, the median value for each quintile is shown. Results shown from each model correspond to BC as the independent variable and each marker of inflammation as the outcome variable.

Table 6. Percent change in markers of inflammation by BC daily mean quintiles in multipollutant model controlling for $PM_{2.5}$ and CO

		TNFα (N=165)			IL-1β (N=165)			IL-10 (N=165)		
	BC median values	Change (%)	95% CI	p-value	Change (%)	95% CI	p-value	Change (%)	95% CI	p-value
Kitchen BC (μg/m^3)										
1	36	reference								
2	94	2	-19 29	0.863	-28	-57 23	0.234	-20	-43 11	0.181
3	171	2	-22 34	0.886	-21	-57 46	0.453	**-41**	**-60 -13**	**0.008**
4	**260**	**31**	**-2 73**	**0.064**	**-45**	**-71 4**	**0.067**	**-39**	**-59 -9**	**0.015**
5	**380**	**24**	**-8 68**	**0.157**	-37	-68 25	0.185	**-35**	**-58 -1**	**0.047**
Use of wood										
		-13	**-24 1**	**0.070**	**72**	**24 140**	**0.001**	-14	-30 6	0.149

All models are controlled by $PM_{2.5}$, CO, age, body mass index, wealth quintile, rainy season, use of wood as fuel; results shown from each model include all pollutants as the independent variables and each marker of inflammation as the outcome variable. Abbreviations are: BC: black carbon; $PM_{2.5}$: fine particulate matter; CO: carbon monoxide; BMI: body mass index; TNF-α and IL-1ß: pro-inflammation markers; IL-10: anti-inflammation marker.

Table 7. Percent change in markers of inflammation by quintile of BC among wood users

		TNFα (N=73)				IL-1β (N=73)				CRP (N=68)			
	BC quintile medians	Change (%)	95% CI		p-value	Change (%)	95% CI		p-value	Change (%)	95% CI		p-value
Kitchen area BC with use of wood (μg/m^3)													
1	36	reference											
2	94	13	-5	35	0.157	-33	-62	19	0.165	-25	-64	57	0.442
3	**171**	**20**	**-3**	**50**	**0.091**	-32	-67	38	0.282	-50	-81	28	0.147
4	**260**	**46**	**14**	**87**	**0.003**	**-56**	**-81**	**-2**	**0.046**	-45	-80	57	0.263
5	**380**	**32**	**0.1**	**75**	**0.049**	**-54**	**-82**	**15**	**0.096**	-27	-78	146	0.606

All models are controlled by age, body mass index, wealth quintile, rainy season, use of wood as fuel; results shown from each model include BC as the independent variable and each marker of inflammation as the outcome variable. Abbreviations are: BC: black carbon; BMI: body mass index; TNF-α and IL-1ß: pro-inflammation markers; IL-10: anti-inflammation marker.

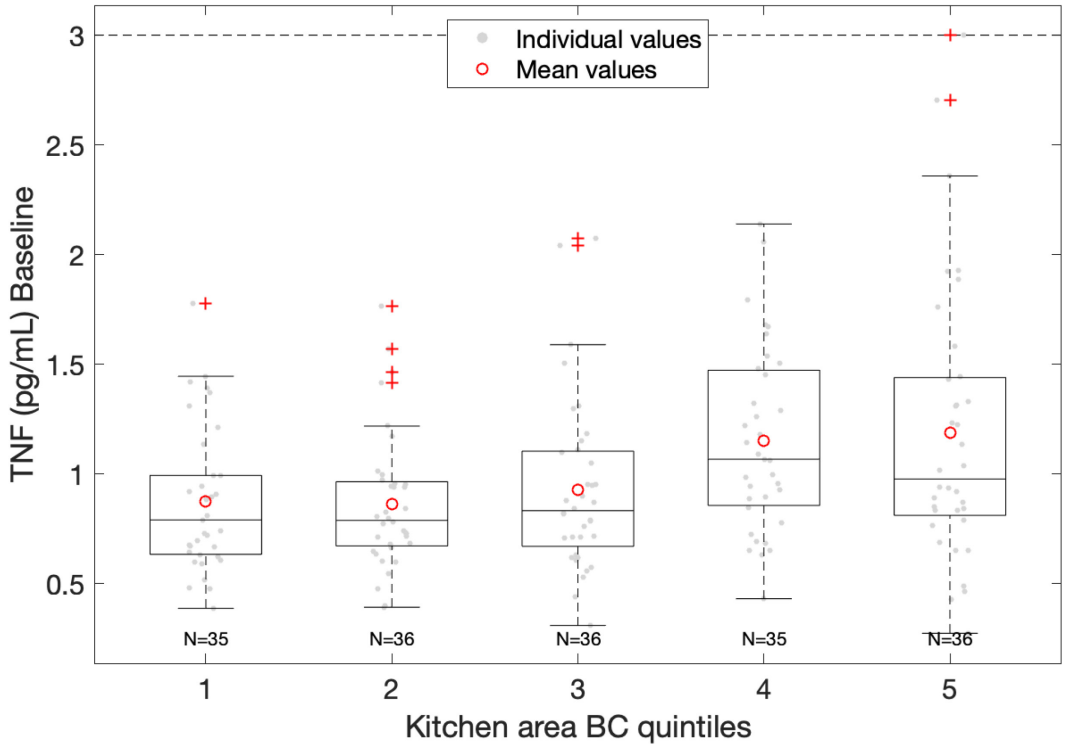

Figure 6. Box plot of TNF-α concentrations grouped by quintile of kitchen area BC concentrations

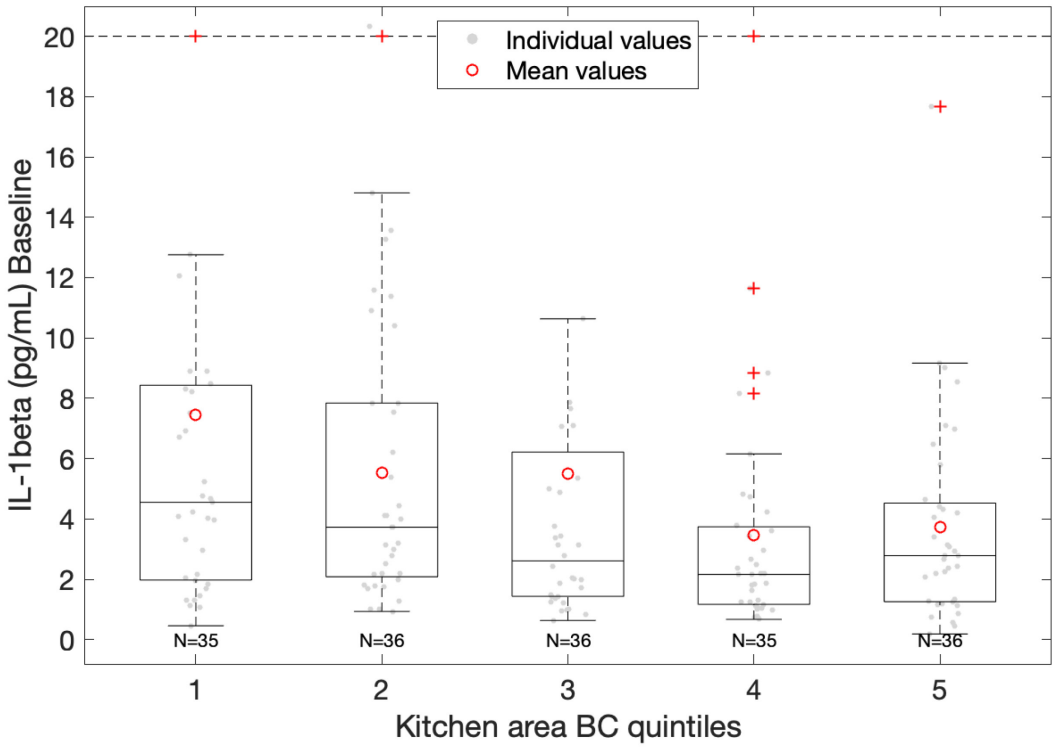

Figure 7. Box plot of IL-1ß concentrations grouped by quintile of kitchen area BC concentrations

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CHAPTER 4:

A LIQUEFIED PETROLEUM GAS STOVE AND FUEL DISTRIBUTION INTERVENTION SIGNIFICANTLY REDUCED HOUSEHOLD AIR POLLUTION CONCENTRATIONS

Abstract

Background:

Household air pollution (HAP) generated from biomass fuel combustion (e.g. wood, dung) is the largest environmental risk factor for preventable disease and a leading contributor to the global burden of disease. Previous interventions with improved designs for biomass cookstoves have shown limited results. As a result, recent efforts are focusing on stoves that use cleaner fuels such as liquefied petroleum gas (LPG).

Objective:

To characterize HAP kitchen area concentrations and personal exposures in an LPG stove intervention trial in rural Peru.-

Methods:

A randomized controlled field trial enrolled 180 female participants and followed them for one year for one year. Ninety participants were randomized to receive free LPG stoves and free fuel delivered to their homes. We collected 48-hour measurements of kitchen area concentrations and personal exposure of fine particulate matter ($PM_{2.5}$), black carbon (BC), and carbon monoxide (CO), at baseline and then at 3-, 6- and 12-months post-intervention.

Results:

After the LPG stove intervention, we observed HAP reductions to levels comparable with health-based guidelines recommended by the World Health Organization (WHO). Twelve months post-intervention $PM_{2.5}$, BC, and CO concentrations in the

kitchen area were reduced by 97% (CI: 96-98%), 98.7% (CI: 98-99%), 87% (CI: 83-91%), respectively. Lower personal exposures were also observed, with reductions of 78%, (CI: 71-82%), 89% (CI: 86-91%) and 62%, (CI: 51-71%), for $PM_{2.5}$, BC, and CO, respectively. Over 76% and 90% of measured personal exposures met WHO recommendations for $PM_{2.5}$, and CO, respectively among participants in the LPG stove intervention group.

Conclusions:

HAP reductions were not only sharp from the initial follow-up visits following intervention, but also sustained throughout a year of follow-up. The success of this intervention is encouraging for future LPG programs to potentially improve health in resource-limited settings such as Peru.

Keywords:

Cookstove, liquefied petroleum gas, indoor air pollution, household air pollution, personal exposure, biomass fuel, particulate matter, black carbon, carbon monoxide

Introduction

Household air pollution (HAP) generated from the combustion of biomass fuels such as wood, and dung, is the largest environmental risk factor for preventable disease [1–4]. Approximately 3 billion people worldwide, mostly from low- and middle-income countries (LMICs), use biomass fuels as their primary energy source for heating and cooking [5]. Exposure to HAP from biomass cookstoves was estimated to be responsible for 2.6 million deaths and 77.2 million disability-adjusted life-years lost in 2016 [6]. HAP morbidity and mortality has been attributed several pulmonary and cardiovascular diseases as well as cancer [7–9]. Women and children comprise 60% of the premature deaths attributed to HAP in 2012, they have the highest risks of biomass fuel exposure [10].

The incomplete combustion of biomass fuels produces a complex mixture of gases and particulate pollutants. Carbon monoxide (CO) and particulate matter (PM) are the most commonly measured for characterizing HAP [11, 12]. The World Health Organization (WHO) has developed indoor air pollution guidelines recognizing the health impact of biomass cookstoves in low-income households [13]. The WHO recommends 24-hour mean $PM_{2.5}$ concentrations to be less than 25 $\mu g/m^3$. Nevertheless, existing evidence suggests that there is no safe level of $PM_{2.5}$ exposure [14, 15]. The same guidelines recommend that hourly mean CO concentrations not exceed 35 mg/m^3, and that 24-hour average should not exceed 7 mg/m^3.

Black carbon (BC), one of the main components of $PM_{2.5}$ resulting from the incomplete combustion of carbonaceous materials, has recently gained attention in the air pollution literature due to its potential role in disease development pathways [16, 17]. It is also becoming more widely measured as its concentrations can be estimated using PM collected on filters [18, 19]. Studies that examine both PM and BC from traffic-related exposures on mortality, hospital admissions and emergency department visits of adults, suggest that the effect of BC can be stronger than the effect of overall PM on those outcomes [16, 17, 20, 21] and stronger than any other single PM constituent [22–28]. However, the literature on BC concentrations from biomass combustion and cookstoves in LMICs is limited [24, 29].

Previous efforts to reduce exposures to HAP have focused on improved cookstoves that still rely on combustion of biomass fuels [11, 12]. Improved cookstoves are designed to reduce HAP through improvements of the combustion efficiency of biomass or by directing smoke outdoors through the incorporation of a chimney, for example [9, 30]. In many studies, improved cookstove interventions have achieved important reductions in emissions, yet the concentrations of indoor pollutants remain substantially higher than the WHO recommended levels [31] and therefore show limited health impacts. Results from a recent review on improved cookstove interventions concluded that self-reported health outcome measures report improvements; however, objective measures have been less conclusive [12]. Limited improvement of health outcomes for previous interventions has been attributed to the continued use of polluting stoves and the inability of the interventions to achieve reductions in personal exposure below indoor air quality recommendations [32–34].

Previous exposure-response analyses have found that the greatest risk reductions occur at much lower exposure levels that are unlikely to be achieved with biomass and require interventions with cleaner fuels [2, 32, 35]. Thus, recent intervention efforts are shifting towards stoves that use cleaner fuels such as liquefied petroleum gas (LPG) [36–41].

Current research has suggested that LPG fuels can significantly reduce HAP when compared to biomass fuels. LPG fuel is a byproduct of natural gas and crude oil production, it is a mixture of propane and butane, generally transported in portable cylinders that are connected to stoves through a hose [42]. As part of the HAP guidelines development, the WHO modeled emission rates and the potential impact of different technologies on HAP. According to this model, 99% of homes could meet the WHO annual guideline Interim Target-1 of 35 $\mu g/m^3$ for $PM_{2.5}$ with LPG stoves [13]. Nevertheless, estimations based on laboratory data do not incorporate social behaviors, cooking patterns, or other variables that affect actual concentrations. According to recent modeled estimates, the potential impact of an LPG stove intervention in rural settings was estimated to result in more modest reductions to concentrations closer to 70 $\mu g/m^3$ for personal exposures of $PM_{2.5}$ since some use of traditional stoves is likely to continue [43]. Evaluating the actual impact of an LPG stove intervention in real-life settings is crucial to understand the potential impact on HAP exposures and health.

To our knowledge, few population-based studies have evaluated HAP from LPG stove use in low-income areas that traditionally use biomass as fuel for cooking [36, 38, 40, 41, 44–46]. A few studies have demonstrated PM reductions with LPG stoves that ranged from 45% to 90%, although these studies were cross-sectional and enrolled a small number of participants (<30 people) [36, 40, 46].

An important additional limitation of existing HAP studies is the lack of personal exposure measurements in most studies [11, 47]. Measuring personal exposure can reduce bias when quantifying the relationship between HAP and health risks. To better understand the impact of an LPG cleaner-cooking intervention of HAP exposures, we quantified HAP reductions from a randomized intervention trial in which half of the participants were randomized to receive LPG stove and gas fuel delivery as needed for one year. We directly measured both kitchen area concentrations and personal exposures to CO, $PM_{2.5}$ and BC for 48-hours at baseline and at three, six, and 12-months after the randomization into an LPG intervention trial.

Methods

Study design and settings

The Cardiopulmonary Outcomes and Household Air Pollution (CHAP) trial [48] is a randomized controlled field trial of an LPG stove and continuous fuel distribution. The CHAP trial was conducted in rural communities surrounding the city of Puno in

southeastern Peru, near the shore of Lake Titicaca, and at 3,825 meters above sea level. Individuals in these rural communities traditionally use biomass-burning with open-fire stoves for cooking. We enrolled 180 women that were the primary cooks in the households and that used biomass fuels daily for cooking. Enrolled participants also had their kitchen area separate from their sleeping area, which is typical in the region. Half of the participants were randomized to receive LPG stoves (Figure 8a) and free fuel for one year (LPG intervention arm) delivered to their homes on a periodic basis. The other half of participants were randomized to a control arm, where they continued to use their traditional cookstoves (Figure 8b) for the first year but received comparable LPG stoves and free fuel in the subsequent year. Additional information on CHAP trial assessments has been previously published [62].

Assessment of Household Air Pollution

HAP was assessed by measuring kitchen area concentrations and personal exposures to $PM_{2.5}$ and CO over 48 hours. Participants were assessed at baseline (pre-intervention), and at three post-intervention follow-up timepoints: 3-, 6-, and 12-months after randomization. During baseline visits, we collected information on kitchen characteristics, such as presence of chimney, roof material, and if participants owned an LPG stove. Wealth status was estimated using the Demographic and Health Survey (DHS) wealth quintiles [49].

Kitchen area concentrations were measured by placing a CO and a $PM_{2.5}$ monitor approximately one meter from the combustion zone and 1.5 meters above the floor

(representing the breathing zone), and at least one meter from doors and windows when possible. Personal exposure was measured by placing a $PM_{2.5}$ and CO monitor near each participant's breathing zone using an adapted apron commonly used by women in the study area and provided to the participants (Figure 2 in Chapter 2). Women were encouraged to wear the aprons throughout the duration of the sampling period and to keep the aprons close by while sleeping.

We used the ECM, an active, direct-reading aerosol monitor (RTI Inc., Research Triangle Park, NC, USA), to measure $PM_{2.5}$ mass concentration via nephelometer and simultaneously collect a filter sample for gravimetric analysis. The ECM has a pump operating at 0.3 L/minute to gravimetrically collect $PM_{2.5}$ on a filter and a light-scattering laser for continuous-time assessment of $PM_{2.5}$. We calibrated the ECM pump flow rate daily before sample collection using a TSI 4100 flowmeter (TSI Incorporated 500 Cardigan Road Shoreview, MN, USA) and recorded ECM flow rate before and after the collection of each sample. The ECMs also logs temperature, relative humidity, and flow rate and reports humidity-corrected nephelometric concentration. Gravimetric $PM_{2.5}$ samples were collected on 15-mm Teflon filters with a 2-μm pore size (Measurement Technology Laboratories LLC, Minneapolis, MN, USA). Filters were pre-weighed and post-weighed at the Exposure Sciences laboratory at the Department of Environmental Health and Engineering at Johns Hopkins University, in a humidity and temperature-controlled room using a XP2U microbalance (Mettler Toledo, Columbus, OH, USA).

Nephelometric concentrations of every sample were calibrated using the sample-specific gravimetric time-weighted average filter samples. Given the high $PM_{2.5}$ concentrations observed in our study, and to avoid overloading of the filters, the ECMs were operated using intermittent duty cycles in households using biomass cookstoves: 30 contiguous seconds every minute for personal exposure samples and 20 contiguous seconds every 3 minutes for kitchen area samples. ECMs used to assess concentrations after randomization in intervention households were set to sample continuously to avoid being below the limit of detection (change was made after the initial 170, 32%, post-intervention samples were collected; 86% of samples from LPG stove intervention arm were below our detection limit prior to the duty cycle change and 33% of filters were below detection limits after this change). When ECMs presented filter overloading issues that affected the logged flow rate, we used the average of the pre- and post-sampling flow rates measured infield laboratory to estimate the total volume of air sampled.

The limit of detection (LOD) for $PM_{2.5}$ samples, was estimated as three times the standard deviation of the mass measured from field blanks. In the initial 6 months of the study pre-weighed filters were loaded into cassettes at the field site laboratory (28% of collected samples). The LOD for $PM_{2.5}$, was estimated to be 20 μg. For the remainder of the study, the filters were pre-loaded to individual ECM cassettes at the Johns Hopkins University laboratory, the LOD was 9.8 μg. All measurements below the LOD were replaced by the LOD divided by the square root of two.

Direct-reading concentrations of CO were measured with the EL-USB-CO data logger (Lascar Electronics, Erie, PA, USA). Data from the CO monitors was calibrated using correction factors estimated every three to four months for each monitor. Calibration factors were derived by co-locating all CO monitors in a sealed chamber in the field laboratory. The monitors were exposed to clean air (nitrogen gas) and a CO concentration of 100 ppm. Individual slopes and intercepts were estimated for each device at each co-location timepoint to correct any drift in the devices. The LOD for the CO monitors was estimated as 1 ppm, which was three times the standard deviation of concentrations logged during the regular clean air calibration checks in the field. Concentrations below the LOD were replaced by the LOD divided by the square root of two.

BC concentrations were determined measuring infrared optical attenuation using a Magee OT21 Sootscan transmissometer (Magee Scientific, Berkeley, CA), on the $PM_{2.5}$ filter samples (a cumulative measure per sample). Attenuation units were converted to mass using the calibration algorithm provided by Magee Scientific (Berkeley, CA) for Teflon filters. The LOD for BC samples was estimated as three times the standard deviation of the attenuation readings recorded from field blanks. The LOD for BC was 1.4 μg. All measurements below the LOD were replaced by the LOD divided by the square root of two.

$PM_{2.5}$ and CO were recorded at 1-minute intervals. Kitchen area samples of $PM_{2.5}$ and CO included 10% duplicates. All $PM_{2.5}$ samples included 10% blanks and all the

reported concentrations were blank-corrected. We rotated monitors monthly to avoid systematic sampling of either biomass or LPG households by specific devices. High correlations were observed for duplicate samples (coefficient of determination using Spearman's correlation coefficient of 0.93, 0.94 and 0.85 for $PM_{2.5}$, BC, and CO, respectively). The difference between the duplicate and the kitchen samples was generally below 10% for PM and BC and below 14% for CO.

Concentrations below the LOD were observed most frequently with the personal measurements from the LPG stove group. For example, CO personal samples from LPG stove intervention arm households had an average of 80% of direct-reading measurements below the LOD; kitchen area BC samples had 70% of the samples below the LOD; kitchen $PM_{2.5}$ concentrations were initially high (close to 70%) but then after duty cycles were adjusted and the filter loading protocol improved the LOD, the percent of samples below the LOD was 30% of the samples.

Kitchen area CO samples in control households had about 35% of the direct-reading measures below the LOD during typical cooking times (between 6:30 to 9:30 am and 6 to 8 pm). Samples in the kitchen from control households had less than 15% of samples below the LOD for $PM_{2.5}$ concentrations, and less than 13% for BC concentrations. Personal samples in the control arm below the LOD ranged between 17% and 30% (in the 3-month to 12-month follow-up visit) for $PM_{2.5}$ and 20 to 30% for BC.

Samples with less than 20 hours of duration were considered missing and were excluded from the analysis. Most short duration samples were due to battery issues with the CO and $PM_{2.5}$ monitoring devices, and on isolated occasions because the participants tampered the devices. When possible, we repeated sample collection when samples were missing (limiting repetition for a household to no more than 2 attempts per follow-up time point). Missing CO samples represented 9% (n=63) and 7% (n=48) of the total number of personal exposure samples and samples in the kitchen, respectively. Personal and kitchen $PM_{2.5}$ samples were missing 0.8% (n=6) and 1.4% (n=10), respectively. For CO samples, about half of the missing samples were missing due to short duration samples and the other half was due to technical issues with the devices or the download process. Whereas for $PM_{2.5}$ samples most of the missing samples were due to technical issues. We didn't identify any consistent patterns of missing samples due to device failures with time or between randomization groups.

Statistical methods

We estimated 24-hour mean concentrations for each day of the 48-hour samples. We calculated maximum hourly mean concentrations using centered 60-minute rolling means. We also calculated the proportion of time that concentrations exceeded the WHO recommended indoor air guidelines for $PM_{2.5}$ and CO. For BC, we estimated the time-weighted average (TWA) concentration for the full sample duration due to the use of the filter samples. We used the first 24-hour averages whenever the full 48-hour averages were not available (6% of samples) for the models and to develop box plots by randomization group and follow-up month. Using the direct-reading

measurements of $PM_{2.5}$ and CO, we estimated the percentage of time the direct-reading concentrations were within different concentration ranges for every minute throughout the sample duration. To assess linear correlations between pollutants, type of exposures (personal or kitchen area), and duplicate samples, we used the coefficient of determination estimated as the squared coefficient of the Spearman's correlation coefficient. To asses similarity between paired consecutive sampling days, we estimated intraclass correlation coefficients using a two-way random-effects model. The intraclass correlation coefficient represents the ratio of the between-participant variance to the total variance of measurements in a two-way random-effects model [50].

Generalized estimating equations were used with linear regression models to account for within-person correlations on subject-specific trajectories of each pollutant ($PM_{2.5}$, BC, and CO). We developed this analysis according to the intention-to-treat randomization allocation. Since the LPG stove intervention was randomized, this model did not include sociodemographic variables as potential confounders. We considered missing data to be missing completely at random.

We log-transformed all pollutant variables to comply with linear regression model assumptions. All data analyses were conducted with MATLAB (The MathWorks, Inc., Natick, MA) and STATA (StataCorp., College Station, TX).

Results

We collected a total of 1,299 CO and 1,424 $PM_{2.5}$ samples from the kitchen area and personal exposures from 180 participants at baseline and three timepoints within one year of follow-up. We performed baseline and follow-up visits on all 180 participants except for one participant who dropped out before their 12-month follow-up visit. Characteristics of the control group and LPG stove intervention group were comparable (Table 8). There were no meaningful or significant differences at baseline when comparing participants from the intervention and control group, including the proportions who already owned an LPG stove (64% and 68%; Table 8). Baseline 48-hour mean CO concentrations from the kitchen area were 52 ppm (inter quartile range, IQR: 45-59 ppm) and the mean personal exposures were 6.9 ppm (IQR: 5.6 -8.2 ppm). For $PM_{2.5}$ the 48-hour average in the kitchen area was 1,205 $\mu g/m^3$ (IQR: 422-1,824 $\mu g/m^3$) with a personal exposure of 115 $\mu g/m^3$ (IQR: 40-130 $\mu g/m^3$; Table 2). BC integrated 48-hour averages were estimated to be 171 $\mu g/m^3$ (IQR: 84-282 $\mu g/m^3$) in the kitchen area, and the personal exposure was 16 $\mu g/m^3$ (IQR: 6-29 $\mu g/m^3$). Baseline 48-hour means, and maximum hourly concentrations were also comparable for both groups (Table 9).

Impact of the intervention on household air pollution

The box plots in Figure 9 summarize daily average concentrations measured in the kitchen comparing intervention and control households at baseline and the different post-intervention follow-up time points. Baseline pre-intervention concentrations, as well as post-intervention concentrations from the control group show high HAP

variability but with most households above the recommended guidelines. For example, the inter-quartile range (the middle 50%) of the 48-hour $PM_{2.5}$ samples range from approximately 420 to 1,800 $\mu g/m^3$. Additionally, most of the 48-hour means were above the WHO guidelines (99% for $PM_{2.5}$ and 90% for CO) at baseline. A dramatic reduction of indoor concentrations in the kitchens was observed at the 3-month post-intervention time point for the intervention group for all pollutants. The observed reductions were sustained at the 6-month and 12-month follow-up measurements. In contrast, the concentrations among the control group were consistent over time and comparable to baseline levels, for all pollutants.

The LPG intervention reduced 48-hour mean personal exposures of $PM_{2.5}$ and CO concentrations to levels close to recommendations by the WHO guidelines (Figure 10). At the 12-month follow up visit, over 76% and 89% of the personal exposure samples met WHO recommendations for $PM_{2.5}$, (25 $\mu g/m^3$), and CO (7 ppm), respectively. When compared with the most flexible interim target recommended by the WHO (75 $\mu g/m^3$), 93% of PM personal exposure samples were below this threshold.

We observed significant reductions (p-values less than 0.001 for all cases) of kitchen area concentrations (between 87% and 99%) and personal exposures (between 70% and 89%) to all pollutants in post-intervention measurements in the LPG stove intervention group (Table 10). The largest reductions were observed for $PM_{2.5}$ and BC concentrations in the kitchen. Reductions of $PM_{2.5}$ kitchen area concentrations

ranged from 92% (CI: 90-94%) at the 3-month follow-up visit to about 97% (CI: 96-98%) at the 12-month follow-up visit. On average, $PM_{2.5}$ kitchen area concentrations were reduced by more than 1,100 μg/m^3. Kitchen area BC concentration reductions were 98.7% at the 12-month follow-up visit (CI: 98-99%), representing reduction magnitudes up to 200 μg/m^3. On average, 48-hour mean CO concentration reductions in the kitchens were between 92% and 87%, more than a 40-ppm reduction for all post-intervention measurements (CI: 89-94% and CI: 83-91%, respectively).

At the 12-month post-intervention visit, personal exposures for $PM_{2.5}$ and CO concentrations were comparable to those recommended by the WHO. $PM_{2.5}$ personal exposures for those in the intervention group had an average daily mean of 26 μg/m^3 (IQR: 8-23 μg/m^3) at 12-months post-intervention (compared to baseline, a reduction of 78%, CI: 71-82%; Table 10). Personal CO daily concentrations was 2.7 ppm (IQR: 0.8-2.1 ppm) at the 12-month post-intervention visit (reduction of 62%, CI: 51-71%, at the 12-month follow-up compared to baseline). The greatest reductions in personal exposures was observed for BC, a decrease of 89% (CI: 86-91%), resulting in a daily mean of 1.9 μg/m^3 (IQR: 1.1-1.3 μg/m^3) at the 12-month post-intervention visit.

There were no significant differences in kitchen area concentrations when comparing the control group at the follow-up post-intervention timepoints to their baseline concentrations (results not shown, p-values between 0.2 to 0.9). Personal

exposures in the control group showed slight reductions compared to baseline, for the 3-month and 6-month follow-up visits of 20% to 30%. However, at the 12-month follow-up period, there were no longer significant differences in the concentrations of control group with its baseline measurements (Table 11).

Kitchen area concentrations and personal exposures show dramatic reductions 3-months post-intervention, but also continued reductions throughout the year of follow-up visits for the intervention group. We observed a negative trend during post-intervention months, showing enhanced exposure reductions over time for both kitchen and personal exposures for $PM_{2.5}$ and BC of the LPG intervention group. Post-intervention concentration reductions in the kitchen area for CO from the intervention group, on the other hand, show a slight linear trend of increasing concentrations with follow-up visits, however mean concentrations for most households still remain below the WHO recommended guidelines.

We also estimated the maximum hourly mean concentration for each household and the average maximum hourly mean for each intervention group. We observed that the maximum hourly mean at baseline for $PM_{2.5}$ concentrations was, on average, 9,700 $\mu g/m^3$ in the kitchen area and 2,000 $\mu g/m^3$ for personal exposures. On average, CO hourly maximums at baseline reached 300 ppm and 73 ppm in the kitchen area and personal exposures, respectively.

Dramatic reductions in the maximum hourly averages are also shown in the right columns of Table 10. The models using the maximum hourly average summary statistic show larger percentage reductions compared to the daily average to those from the models using the daily mean for concentrations in the kitchen Table 10. Reductions of hourly maximum personal exposures range from 80% to 85% for CO and 88% to 90% for $PM_{2.5}$.

Correlations between pollutants, exposures and sampling days

When comparing kitchen area CO with $PM_{2.5}$ concentrations within biomass cookstove users, low correlations were observed (0.23; Table 12); however, concentrations from the kitchens among the LPG stove intervention group show a moderate correlation (0.79). When comparing kitchen area $PM_{2.5}$ with BC, concentrations were moderately correlated (within the control group 0.80; within the LPG stove group 0.59). Most correlations for personal exposures were very low when comparing different pollutants (0.12 to 0.39). Finally, low correlation was observed comparing kitchen area concentrations with personal exposure samples with a coefficient of determination for CO and $PM_{2.5}$ of approximately 0.4 (Table 12). We observed similar results when comparing kitchen area versus personal exposure for CO and $PM_{2.5}$ within each intervention group (LPG stove and control group, results not shown).

We also compared the consecutive days of sampling within pollutants using intraclass correlation coefficients. Interestingly, among the lowest ICCs observed

were personal exposures of $PM_{2.5}$ samples comparing the first and second day of measurements on each visit (ICC=0.34 and 0.52 for $PM_{2.5}$, for control and LPG intervention groups, respectively). In contrast, consecutive day kitchen concentrations were similar for CO (ICC=0.78 and 0.91, for control and LPG intervention groups, respectively) and moderately correlated for $PM_{2.5}$ (ICC= 0.55 and 0.80, for control and LPG intervention groups, respectively).

Direct-reading of household air pollution concentrations by minute of a day

From the direct-reading instruments, we estimated the percentage of samples that fall within different concentration ranges for every minute of all sampling days for CO (Figure 11) and $PM_{2.5}$ (Figure 12). For example, each minute of the day we estimated the percentage of samples whose concentration was greater or equal to 90 ppm, this corresponds to the red color category (Figure 11). We did the same for every minute of the day, estimating the percentage of samples that were in one of five different categories of concentrations; each category was assigned a different color. The lowest concentration corresponding to the lighter blue color (CO between 0-6 ppm; Figure 11).

The top panels of Figure 11 and Figure 12 show baseline samples of the kitchen area concentrations (Panels A1) and personal exposures (Panel B1). Baseline concentrations in the kitchen area for both pollutants showed that at approximately six in the morning only 20% of the households experienced concentrations below the

WHO 24-hr recommended guidelines (7 ppm for CO and 25 μg/m^3 for $PM_{2.5}$). At this time of the day, more than 60% of households had concentrations estimated to be above 1,000 μg/m^3 for $PM_{2.5}$. At six in the morning, about 60% of CO samples were above 90 ppm, which corresponds to the WHO 15-minute guideline. We identified two clear cooking events in each day that are characterized with a morning cooking event with higher concentrations compared to the evening cooking event.

The middle panels of Figure 11 and Figure 12 show post-intervention samples of the kitchen area concentrations (Panels A2) and personal exposures (Panel B2) for the control group. The daily patterns of concentrations throughout the day in the control group are comparable to the baseline behaviors for both pollutants. Finally, panels A3 and B3 of Figures 11 and Figure 12 illustrate the dramatic post-intervention reductions observed on the daily patterns of concentrations for the LPG intervention for both the kitchen concentrations and the personal exposures. Most of the samples in the LPG stove intervention group post-intervention were in the lowest concentration category (CO 6 ppm< and $PM_{2.5}$< 24 μg/m^3) for most of the minutes of the day.

Discussion

This study measured HAP among 180 participants at baseline, and 3-, 6-, and 12-months post-intervention of an LPG stove and free fuel delivery. The LPG stove intervention achieved significant and persistent reductions of CO, $PM_{2.5}$, and BC indoor concentrations throughout the year of the study for the intervention arm. The

sharp reductions observed in this trial achieved concentrations recommended by the indoor air WHO guidelines for many homes. Most kitchen area concentrations and personal exposures to CO after intervention were not only below the 24-hr WHO recommended guidelines, but also the one-hour peaks of personal exposures were comparable to the WHO hourly recommendations (30 ppm). Average kitchen area $PM_{2.5}$ concentrations were reduced to levels comparable with the WHO Interim Target 3 recommended guideline (37.5 $\mu g/m^3$) 12-months post-intervention (only one tier above the most stringent recommended guidelines). After one year of the intervention, most personal exposures were below all of the interim guidelines and close to meeting the 25 $\mu g/m^3$ 24-hour recommended guideline (with IQR from 8 to 23 $\mu g/m^3$).

The concentration reductions observed in this field intervention trial are the largest achieved in any published clean stove intervention trial for users of biomass cookstoves. A recent review and meta-analysis on stove interventions on LMIC estimated pooled $PM_{2.5}$ (CO) kitchen area reductions of 41% (39%) for advanced combustion stoves and of 83% (82%) for ethanol stoves [11], when compared to traditional cookstoves. We observed reductions of 97% (87%). Further, personal exposure reductions in this review were estimated to be 55% for $PM_{2.5}$ and 52% for CO. The LPG stove intervention in our study, resulted in personal exposure reductions of 78% for $PM_{2.5}$ and 62% for CO, after one year of the intervention.

The observed reductions of this study are not only substantial during the first follow-up visits but were also consistent for a year of follow-up. We even observed greater reductions for $PM_{2.5}$ and BC at the end of the year compared to initial follow-up time points, suggesting a trend of enhanced reductions throughout the year within the intervention period. We observed mean $PM_{2.5}$ kitchen concentration reductions starting at 92% at the 3-month follow-up visit and 97% at the 12-month follow-up visit.

Concentrations observed among participants in our LPG stove intervention arm were much lower than what others have reported in previous LPG stoves studies [36, 40, 44–46]. This is probably due to different supportive measures we incorporated to promote exclusive LPG stove use. Our intervention incorporated a steady supply of free, delivered fuel, education on use and maintenance of the stove, and other supportive measures, such as training and cooking demonstrations to promote the use of the LPG stoves [48]. Studies in Guatemala, Bangladesh and India, demonstrated PM indoor area reductions with LPG stove use compared to biomass use which ranged from 45% to 75% [36, 40, 44–46]. All of these studies were cross-sectional, some measured exposures on a small number of participants [36, 40, 46], and in some the LPG stove adoption was mixed with traditional stove use [36, 46]. We also observed reductions greater than what has been estimated through different modeled scenarios with LPG stove interventions. Modeled scenarios estimated that in rural settings, the potential impact of LPG stoves would reduce personal exposures to $PM_{2.5}$ from 270 to 70 $\mu g/m^3$ [43]. In the rural area of Puno,

with low ambient air pollution concentrations [51], personal exposures were less than 37 $\mu g/m^3$.

In addition to the significant personal exposure reductions of the LPG stove arm (70% to 90%), we observed some reductions (20% to 30%) in the concentrations of the control arm during the initial post-intervention follow-up months for $PM_{2.5}$ and BC. These reductions in personal exposures were not comparable to the reductions observed for the LPG stove intervention arm and did not persist through the year. Furthermore, post-intervention average concentrations were not different for the control group in the kitchen area. It has been observed in intervention trials that the control group frequently is observed to show some of the benefit expected for the intervention group, when the intervention is not blinded [52, 53]. For example, an energy package intervention, that included a semi-gasifier cookstove, water heater, chimney, and supply of processed biomass fuel in rural China [54], resulted in reductions in air pollution exposures in both the treatment and control groups. It is possible that some of our control arm participants used their LPG stoves (that they purchased before the start of the study) more after being randomized and learning about the trial.

Baseline HAP in rural homes in high-altitude Peru were comparable with what has been previously reported in the biomass cookstove literature. According to a WHO review and database, households with biomass cookstoves that use animal dung as their primary fuel, were estimated to have a pooled mean $PM_{2.5}$ exposures of about

960 μg/m^3 (95% CI 359, 2520) in the kitchen area, and 390 μg/m^3 (95% CI 148, 1047) for personal exposures, respectively [55]. In CHAP, where all participants reported using dung, baseline concentrations in the kitchen were about 1,204 μg/m^3 (IQR: 422-1,824 μg/m^3) and personal exposures about 115 μg/m^3. (IQR: 40-130 μg/m^3). Similar consistent results were observed when comparing with pooled estimates from previous reviews for CO [11, 56, 57].

When examining correlations between pollutants, CO and $PM_{2.5}$ presented a moderate correlation for samples in the kitchen among the LPG stove group (0.79), but a very low correlation when comparing kitchen area concentrations within the control group (0.23) and when comparing personal exposures (0.12 and 0.19), which highlights the importance of measuring both pollutants and both exposure scenarios in these types of studies. These results are consistent with correlations observed between CO and PM in a recent systematic review which estimated a median correlation of 0.5 for personal exposures and 0.7 for samples in the kitchen, concluding that CO was not a consistent surrogate of $PM_{2.5}$ [58]. Correlations between BC and $PM_{2.5}$ were moderate (0.80 and 0.59) in the kitchen area and low for personal exposures within the control group (0.39), which highlights the importance of measuring BC as a $PM_{2.5}$ constituent because it was not observed to be a constant proportion of the PM mass. Measuring BC separately might provide new information when exploring associations with health outcomes.

Low intra-class correlation coefficients were also observed when comparing the consecutive first and second 24-hour days of sampling of the 48-hour samples particularly for $PM_{2.5}$ personal samples, based on the intraclass correlation coefficients (Table 12). It is possible that participants were less likely to use the personal devices the second day of sampling time, this might explain the low correlations observed. It is also possible that movement patterns, and therefore exposures for participants were different when comparing consecutive days. If this is the case, then one 24-hour sample might not always be sufficient to capture the typical concentrations in these types of settings. Kitchen CO and $PM_{2.5}$ samples were similar when comparing consecutive sampling days except for $PM_{2.5}$ from the control group. This suggests that in rural Puno, a second day of sampling might not be necessary for CO kitchen area concentrations but might be valuable for $PM_{2.5}$.

We faced several challenges during sampling due to the high concentrations observed with traditional stove use that caused some of our filters to overload, draining the battery, and resulting in shorter than intended sample durations. On the other hand, concentrations below our detection limits in the LPG stove intervention were common. However, we were still able to use the nephelometric readings to characterize exposures during cooking events. In contrast to $PM_{2.5}$ and CO, BC samples were only measured on the integrated samples. Thus, it was not possible to identify peaks or daily patterns for this pollutant. Another weakness of our study was the inability to measure LPG stove use for some participants who owned an LPG stove prior to enrollment. Although all participants used biomass

daily at baseline, it is possible some of the controls could have occasionally used some of their previously owned LPG stoves.

Successes of this study were the high retention of participants, with only one follow-up visit lost and the successful reduction of HAP in the intervention group. The ability to use light and small portable sampling devices allowed us to measure personal exposures that are expected to be more relevant to understand the relationship between exposures and health outcomes. The importance of measuring personal exposures is supported by the low correlation observed between kitchen and personal samples in this study. Another important aspect of this study was the ability to collect concentrations for both pollutants at high temporal resolution and that all nephelometric $PM_{2.5}$ samples were gravimetrically corrected providing high data quality. CO samples were also calibrated periodically, ensuring the comparability of devices between samples thought the study.

Conclusions

Significant and sustained HAP reductions were observed with an intervention including an LPG stove and free fuel supply for one year. The intervention resulted in personal exposures to HAP at levels approaching those recommended by the WHO for $PM_{2.5}$ and CO. Significant reductions in BC, a main constituent of $PM_{2.5}$ concentrations were also observed. Low correlations between different pollutants and between kitchen area and personal exposures highlights the importance to measure CO, $PM_{2.5}$ and BC separately as well as the importance of sampling

personal exposures. Results of this trial will inform the feasibility of an LPG stove replacement program to reduce HAP and improve health in resource-limited settings such as Peru.

Table 8. Baseline and household characteristics of study participants

Name	Category	Intervention N(%)		Control N(%)	
Total number of participants		90	(50%)	90	(50%)
Kitchen characteristics					
Presence of second stove	No other stove	26	(14%)	22	(12%)
	LPG gas stove	64	(36%)	68	(38%)
Previously participated in FISE		42	(23%)	46	(26%)
Used FISE in last 3 months		34	(19%)	42	(23%)
Participant characteristics					
Highest level of education achieved	Without education or preschool only	4	(2%)	3	(2%)
	Primary	53	(29%)	53	(29%)
	Secondary	33	(18%)	34	(19%)
	Non-university superior or university	0	(0%)	0	(0%)
Wealth Quintile	1 (lowest)	51	(28%)	50	(28%)
	2	32	(18%)	37	(21%)
	3	7	(4%)	3	(2%)
	4 and 5 (highest)	0	(0%)	0	(0%)
Average years of education (mean / standard deviation)		6	SD 3	6	SD 3

Table 9. Baseline exposure summary statistics comparing control and intervention groups

	Intervention group - LPG stove				Control group - Biomass cookstove				
Variable	N	Median	Mean	IQR	N	Median	Mean	IQR	p-value
Kitchen area 48-hr means									
CO (ppm)	85	42	50	(16 -68)	84	39	53	(13 -64)	0.874
PM (μg/m^3)	89	992	1,187	(304 -1680)	89	973	1,223	(273 -1673)	0.865
BC (μg/m^3)	89	175	207	(53 -297)	89	169	182	(78 -260)	0.604
Kitchen area highest hourly mean									
CO (ppm)	87	306	296	(187 -425)	85	311	306	(202 -420)	0.465
PM (μg/m^3)	89	8924	9411.3	(4520 -13327)	89	9751	10006	(4656 -14845)	0.587
Personal exposure 48-hr means									
CO (ppm)	79	4	7	(1 -8)	81	3	7	(0 -6)	0.526
PM (μg/m^3)	90	77	104	(27 -127)	90	71	126	(30 -113)	0.782
BC (μg/m^3)	90	16	22	(4 -28)	90	15	20	(6 -24)	0.810
Personal exposure highest hourly mean									
CO (ppm)	80	38	85	(6 -71)	81	33	62	(9 -57)	0.104
PM (μg/m^3)	89	1504	1,947	(712 -2296)	90	1387	2,077	(752 -2023)	0.813

Summary statistics for BC do not include the highest hourly means because BC sample were integrated samples throughout the duration of the sampling time. IQR: interquartile range corresponds to the 25th percentile and the 75th percentile

Table 10. Linear model results for pollutant concentration reductions across follow-up visits for the intervention group using 48-hr means and maximum hourly means

		48-hr means				**Maximum hourly means**			
		Reductions in kitchen area		Personal exposure reductions		Reductions in kitchen area		Personal exposure reductions	
	Visit	(%)	95% CI	(%)	95% CI	(%)	95% CI	(%)	95% CI
CO	3	92%	(89% -94%)	61%	(50% -70%)	93%	(90% -95%)	79%	(70% -85%)
	6	90%	(87% -93%)	71%	(62% -78%)	88%	(84% -92%)	85%	(79% -89%)
	12	87%	(83% -91%)	62%	(51% -71%)	85%	(79% -90%)	79%	(70% -86%)
$PM_{2.5}$	3	92%	(90% -94%)	69%	(62% -75%)	93%	(90% -95%)	88%	(84% -91%)
	6	95%	(93% -96%)	70%	(62% -76%)	95%	(93% -96%)	90%	(86% -92%)
	12	97%	(96% -98%)	78%	(71% -82%)	96%	(95% -98%)	91%	(88% -94%)
BC	3	96%	(94% -97%)	85%	(81% -88%)				
	6	97%	(96% -98%)	86%	(83% -89%)				
	12	98.7%	(98% -99%)	89%	(86% -91%)				

Note: All coefficients representing reductions had p-values < 0.0001. Percent reductions using the 24-hour mean as the summary statistic in columns to the left and also the maximum hourly means as the summary statistic in columns to the right.

Table 11. Linear model results for pollutant concentration reductions across follow-up visits for the control group using 48-hr means

Personal exposure changes in 48-hr means of control group					
	Visit	(%)	95% CI		p-value
CO	3	-4%	25%	-26%	0.762
	6	9%	45%	-18%	0.553
	12	6%	35%	-17%	0.630
$PM_{2.5}$	**3**	**-30%**	**-13%**	**-44%**	**0.001**
	6	**-21%**	**-6%**	**-34%**	**0.010**
	12	-14%	4%	-29%	0.123
BC	**3**	**-30%**	**-10%**	**-45%**	**0.006**
	6	**-32%**	**-15%**	**-45%**	**0.001**
	12	-13%	6%	-30%	0.164

Percent reductions in bold have p-values < 0.05. All other reductions are not statistically significant with p-values>0.15.

Table 12. Correlations coefficients for HAP concentrations for different pollutants different exposures and intraclass correlations between consecutive days of sampling

Variables compared	Coefficient of determination	Number of pairs
Comparing pollutants		
Kitchen CO vs PM control group	0.23	360
Kitchen CO vs PM LPG intervention group	0.79	291
Kitchen TWA PM vs BC control group	0.80	400
Kitchen TWA PM vs BC LPG intervention group	0.59	308
Personal CO vs PM control group	0.12	348
Personal CO vs PM LPG intervention group	0.19	275
Personal TWA PM vs BC control group	0.39	402
Personal TWA PM vs BC LPG intervention group	0.60	308
Comparing exposures		
Kitchen PM vs Personal PM day 1	0.45	784
Kitchen CO vs Personal CO day 1	0.35	665
Comparing consecutive days: day 1 vs day 2		
Variables compared	Intraclass correlation coefficient	Number of pairs
Kitchen CO control group	0.78	373
Kitchen CO LPG intervention group	0.91	347
Kitchen PM control group	0.55	377
Kitchen PM LPG intervention group	0.80	379
Personal CO control group	0.70	351
Personal CO LPG intervention group	0.81	339
Personal PM control group	0.34	378
Personal PM LPG intervention group	0.52	383

(a) LPG stove (b) Biomass cookstove with monitoring devices in cage

Figure 8. Kitchens of participants with an intervention LPG stove (a), and a traditional biomass cookstove with HAP monitors in bird cage (b)

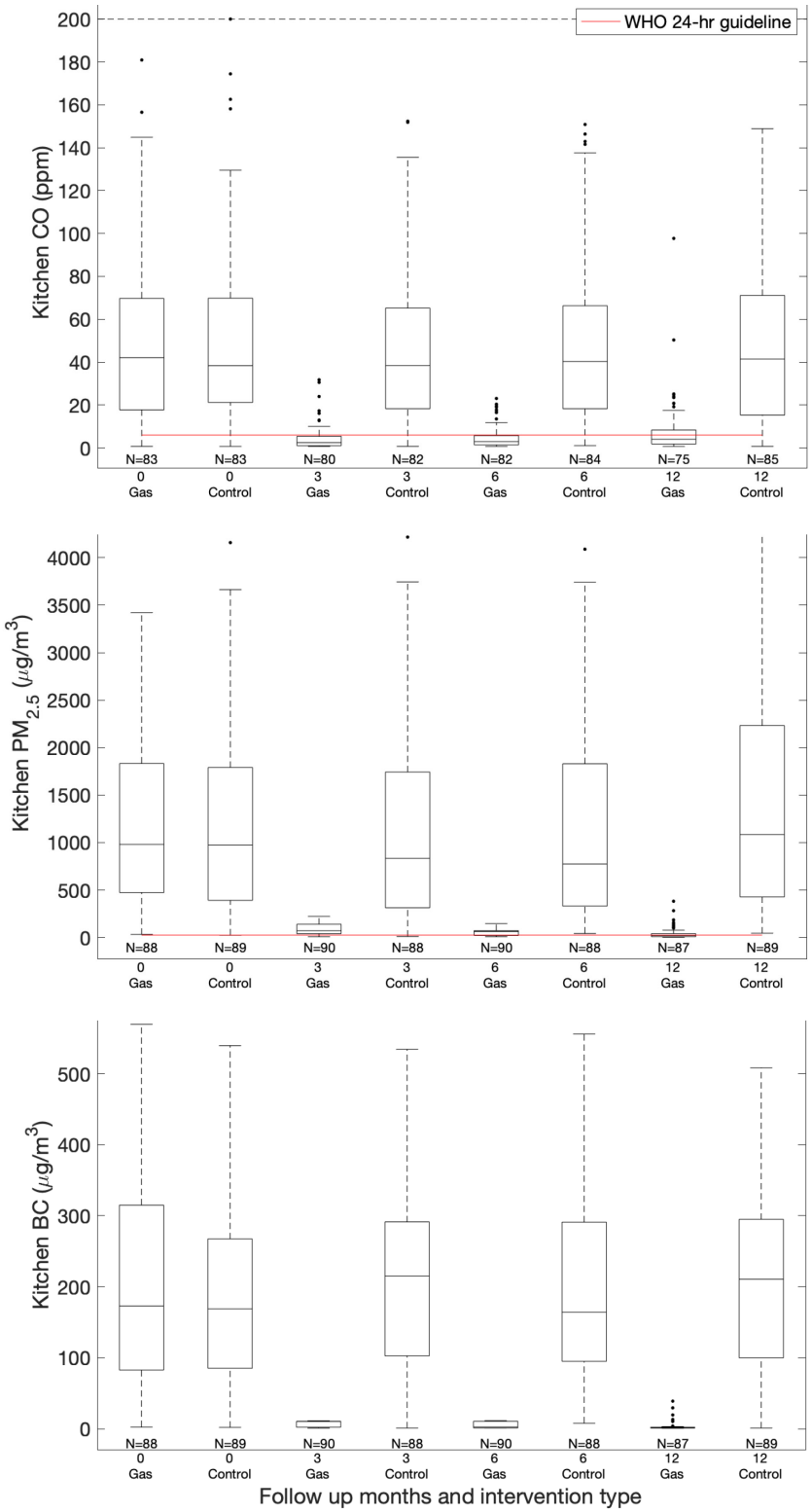

Figure 9. Box plots of 48-hr mean pollutant concentrations at each follow-up visit for LPG stove intervention group (Gas) and control group (Control) in the kitchen area

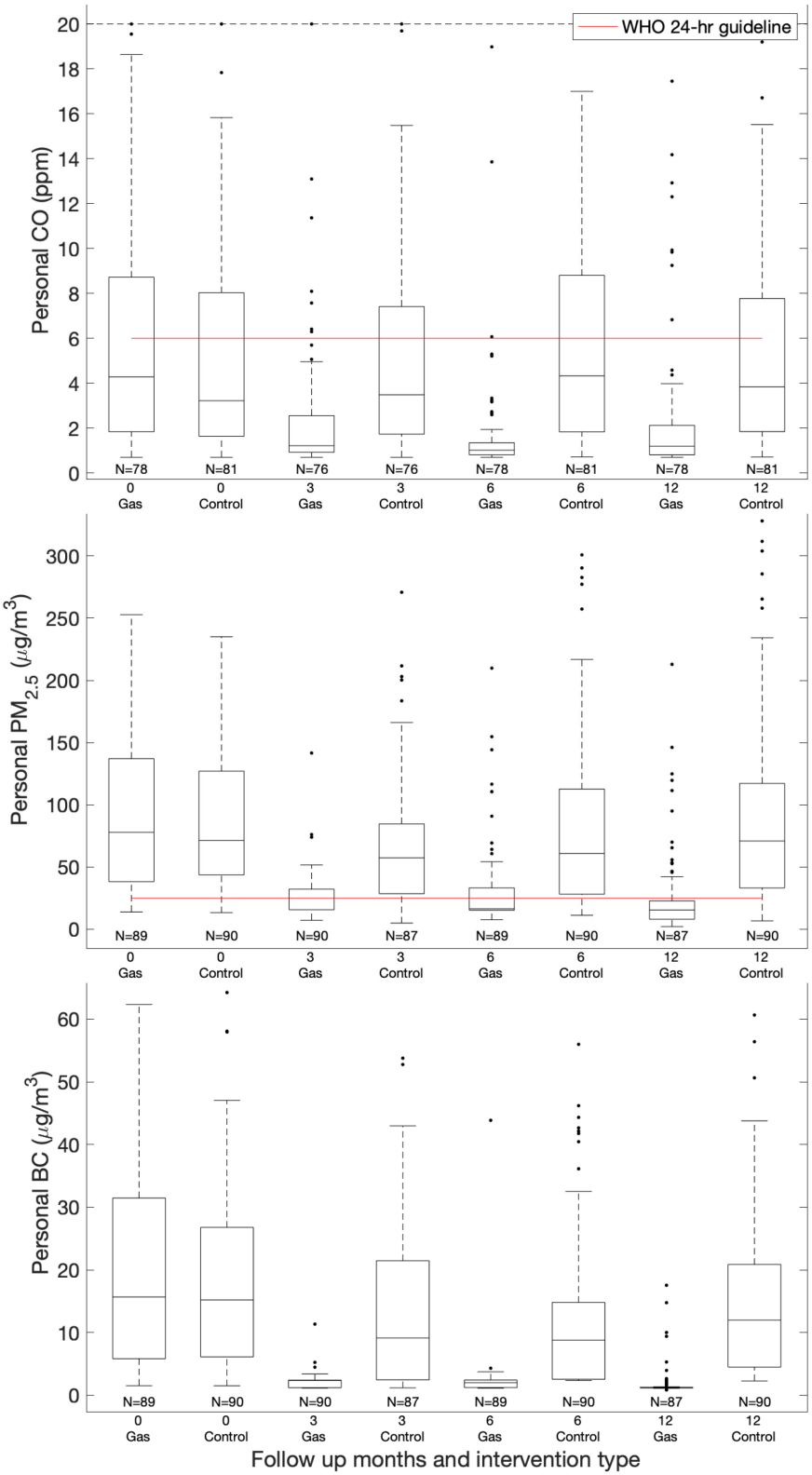

Figure 10. Box plots of 48-hr mean personal exposure concentrations at each follow-up visit for intervention groups (Gas) and control group (Control)

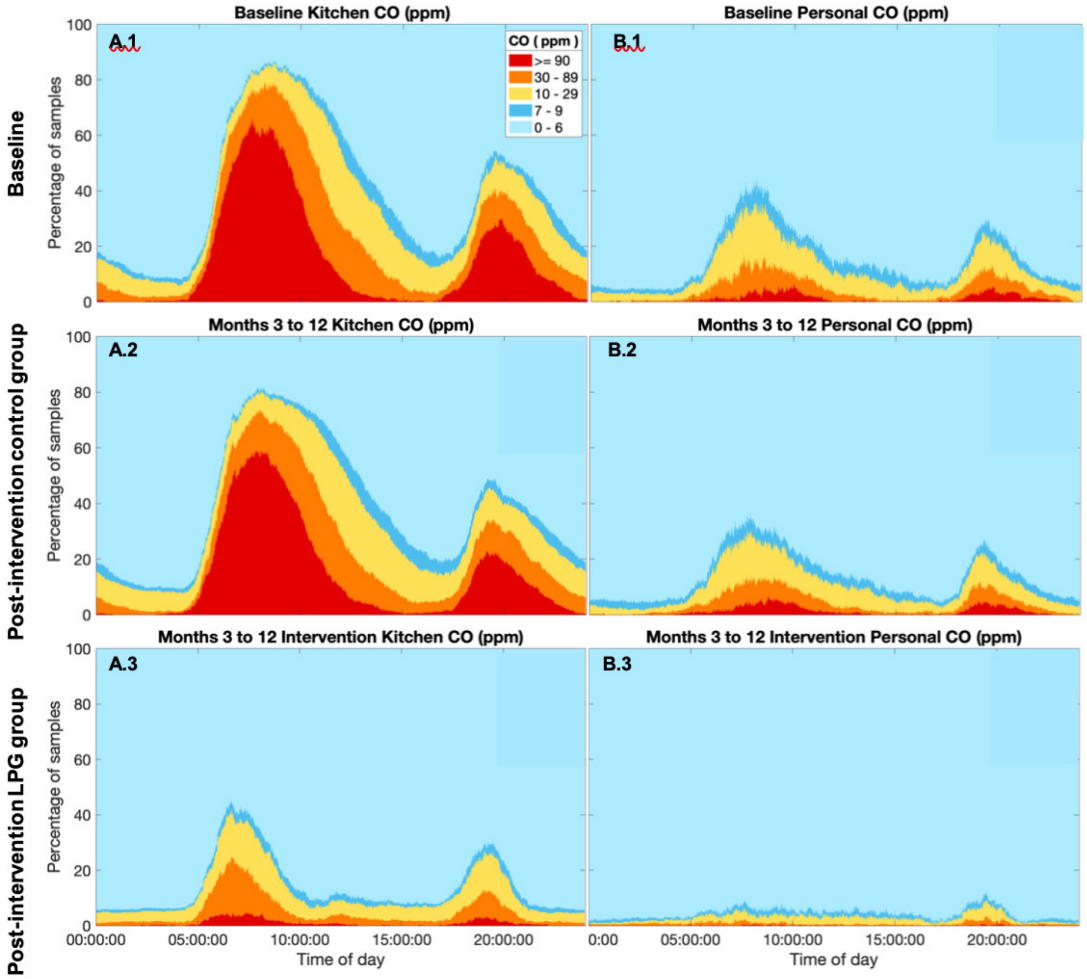

Figure 11. Percent of samples within different concentration ranges of CO concentrations by minute of a day in the kitchen area and personal exposures in rural. Peru at baseline and follow-up months. Panels on the left A1-A3 show the percent of samples within different concentration ranges for kitchen area concentrations, and panels on the right, B1-B3, show personal concentrations. Top figures A1 and B1, represent the percent of samples within different concentration ranges for each minute of the day of all samples obtained at baseline; middle panels A2 and B2 combine the post-intervention follow-up samples taken at the 3-, 6- and 12-month time points for all samples; bottom panels A3 and B3, show the percent of samples within different concentration ranges for the intervention LPG stove group samples for all follow-up timepoint visits, 3-, 6- and 12- months.

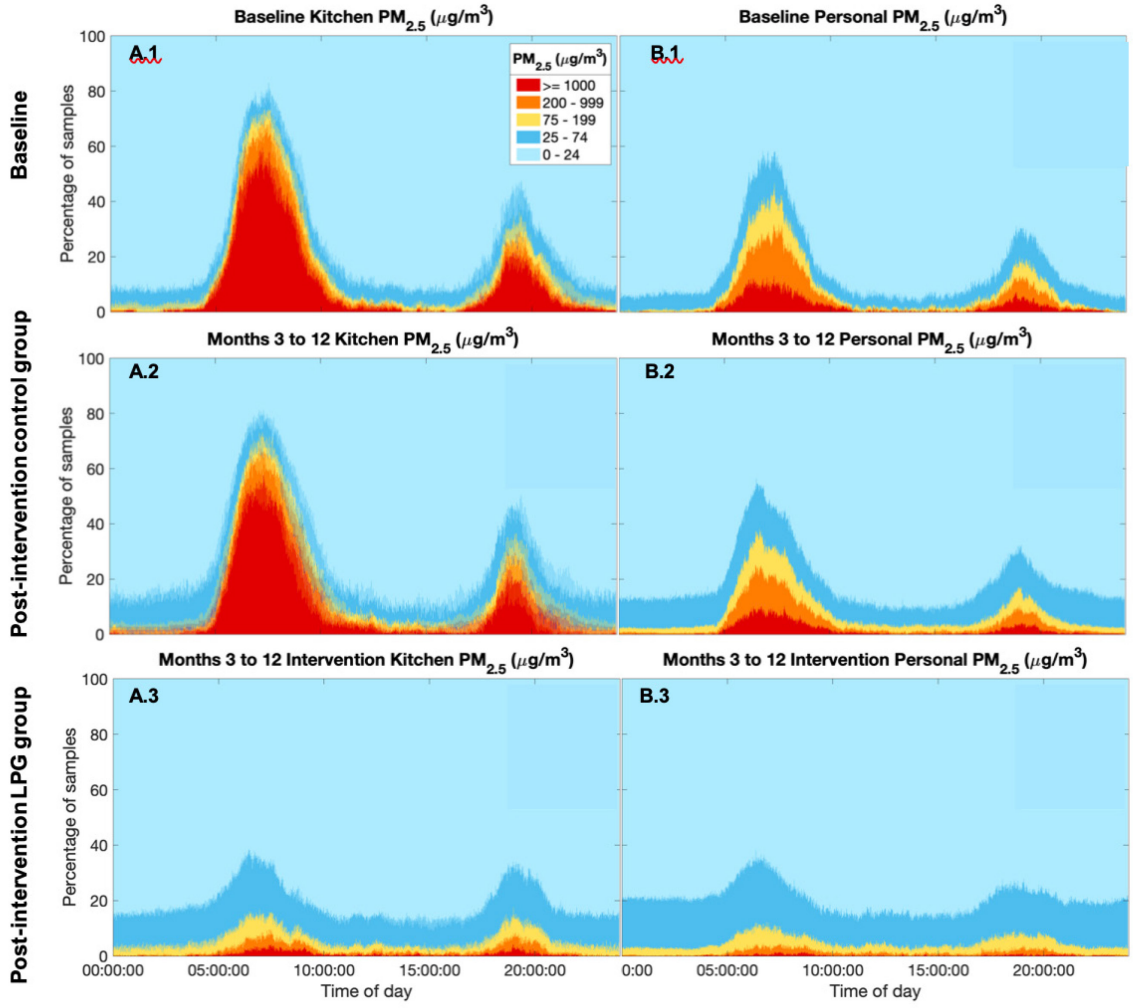

Figure 12. Percent of samples within different concentration ranges of $PM_{2.5}$ concentrations by minute of a day in the kitchen area and personal exposures in rural Peru at baseline and follow-up months. Panels on the left A1-A3 show percent of samples within different concentration ranges for kitchen area concentrations, and panels on the right, B1-B3, show personal concentrations. Top figures A1 and B1, represent the percent of samples within different concentration ranges for each minute of the day of all samples obtained at baseline; middle panels A2 and B2 combine the post-intervention follow-up samples taken at the 3-, 6- and 12-month time points for all samples; bottom panels A3 and B3, show the percent of samples within different concentration ranges for the intervention LPG stove group samples for all follow-up timepoint visits, 3-, 6- and 12- months.

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CHAPTER 5: CONCLUSION

Summary Findings

Aim 1

1) Explore how household characteristics, explain variability of kitchen area concentrations and personal exposures to CO, $PM_{2.5}$ and BC from biomass cookstoves among women in rural Peru.

Mean daily kitchen area concentrations and personal exposures to HAP in rural homes from Aymara communities in Puno, Peru, were several times above World Health Organization (WHO) recommendations. Daily average personal exposure to $PM_{2.5}$ was 122 $\mu g/m^3$ (IQR: 76-167 $\mu g/m^3$) which is 5 times the recommended WHO daily guideline and almost twice as much as the most flexible interim WHO guideline of 75 $\mu g/m^3$. We found that roof type was the household characteristic that explained the most HAP variability. Women with household roofs made of natural materials (straw, *totora* or reed) provide much less ventilation, and had higher kitchen concentrations and personal exposures for all pollutants when compared to calamine sheet, cement fiber or similar. Personal exposures were, on average, 39%, 36% and 57% higher for $PM_{2.5}$, CO and BC, respectively, in households with natural roof material. We also found that women who previously owned an LPG stove and those who had a chimney had lower personal exposures, however these variables did not impact kitchen concentrations. Personal exposures were lower by 24% for $PM_{2.5}$,

28% for CO, and 28% for BC concentrations among participants who also had an LPG stove compared to those with only biomass cookstoves. Characterizing HAP within different settings can help identify effective and culturally relevant solutions that reduce HAP exposures. Although HAP concentrations remained above guidelines for all households, roof materials associated with better wealth (such as calamine sheet) and having LPG stoves may be actionable interventions that can help reduce exposures to HAP in high-altitude rural Peru and similar settings.

Aim 2

2) Examine the exposure-response relationship between $PM_{2.5}$ and BC, and markers of inflammation among adult women who use biomass cookstoves in rural Peru.

We measured markers of inflammation (CRP, IL-6, IL-10, IL-1β, and TNF-α) using dried blood spot samples and measured 48-hour kitchen area concentrations and personal exposures to fine PM, BC, and CO among participants. We used linear regression to develop exposure-response models between quintiles of HAPs and markers of inflammation. We found statistically significant associations between kitchen area BC concentrations and the inflammatory markers TNF-α (positive association), IL-10 (negative association with anti-inflammatory marker) and, IL-1β (unexpected negative association). Associations were stronger in multipollutant models and remained strong when further restricting the analysis to wood fuel users compared to those who used exclusively dung. BC kitchen area concentrations in the fourth and fifth highest quintiles were associated with 31% and 24% (95% CI: -2 to

73% and -8 to 68%) higher TNF-α concentrations when compared to the lowest quintile (median of 36 μg/m^3), after adjusting for $PM_{2.5}$, CO age, BMI, season (rainy vs dry), and wealth quintiles. In our analysis of women who use biomass cookstoves in rural Peru, the evidence suggests a stronger association between inflammation markers and BC than with PM. Further research is needed to understand inflammation responses in people who use biomass cookstoves and interventions that target the reduction of BC to improve public health.

Aim 3

3) Characterize HAP kitchen area concentrations and personal exposures in an LPG stove intervention trial in rural Peru.

We conducted a randomized controlled field trial intervention with 180 participants and followed them for one year. Half of the participants were randomized to receive free LPG stoves and fuel were delivered to their homes. We collected 48-hour measurements of kitchen area concentrations and personal exposure of $PM_{2.5}$, BC, and CO, at baseline and then at 3-, 6- and 12-months post-intervention. After the LPG stove intervention, we observed HAP reductions to levels comparable with health-based guidelines recommended by the WHO. Twelve months post-intervention $PM_{2.5}$, BC, and CO concentrations in the kitchen area where reduced by 97% (CI: 97-98%), 98.7% (CI: 98-99%), 87% (CI: 82-91%), respectively. Lower personal exposures were also observed, with reductions of 78%, (CI: 72-83%), 89% (CI: 86-91%) and 62%, (CI: 51-71%), for $PM_{2.5}$, BC, and CO, respectively. At the 12-

month follow-up timepoint, over 75% and 85% of measured personal exposures among LPG stove intervention participants met WHO recommendations for $PM_{2.5}$, and CO, respectively. Important HAP reductions were observed from the initial follow-up month visits expected from the clean stove adoption and were sustained throughout a year of follow-up. The success of this intervention is encouraging for future LPG programs to potentially improve health in resource-limited settings such as Peru.

Future research and public health implications

Public health implications

HAP from biomass fuels is a leading risk factor for disease that disproportionally affects LMICs. Households characteristics and variables that explain HAP vary widely across settings. Characterizing HAP of different settings is important, and it can help identify culturally relevant and effective local solutions that can help reduce HAP exposures. When trying to understand the mechanisms by which HAP, and particularly PM, can elicit cardiopulmonary outcomes, evidence from urban exposures suggests that BC plays an important role. This dissertation provides evidence that BC may be more important than PM in relation to markers of inflammation within biomass cookstoves exposures. Our results support previous evidence that biomass smoke from wood and dung induces different profiles of inflammation markers that need to be further investigated in population studies.

Recent efforts to address HAP are starting to focus on cookstove interventions that use cleaner fuels such as liquefied petroleum gas (LPG) to reduce the burden of disease. This dissertation provides evidence of the significant reductions that can be achieved with an LPG stove intervention when the stoves and fuel are provided to participants. The concentrations achieved with the intervention are comparable with health-based guidelines recommended by the WHO. HAP reductions were not only sharp from the initial follow-up month visits expected from the clean stove adoption, but also sustained throughout a year of follow-up. The success of this intervention is encouraging for future LPG programs to potentially improve health in resource-limited settings such as Peru.

Future research

Associations with markers of inflammation and biomass cookstoves are more heterogeneous compared to ambient air pollution. It is important to further explore the distinctive inflammation pathways in biomass cookstoves settings in order to identify differences in the pathways with the different types of biomass fuels. Further research is needed to understand inflammation responses in people who use biomass cookstoves and interventions that target the reduction of BC to improve public health.

The economic feasibility of LPG stove replacement programs needs to be further studied to ensure the HAP reductions that were shown to be possible, can be achieved and sustained with exclusive use in this and other similar populations. The

work of this dissertation was nested within a trial that will be exploring several health impacts of and LPG stove intervention. In particular, given the important reductions in BC concentrations, the impact on inflammation markers after the intervention are expected to be significant. Understanding the impact of the intervention on markers of inflammation as well as other health outcomes will inform the effectiveness of LPG stove interventions to impact health outcomes on adult populations from resource-limited settings such as Puno, Peru.

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PUBLICATIONS

- Burrowes VJ, Piedrahita R, Pillarisetti A, Underhill L, Fandiño-Del-Rio M, Johnson M, Kephart JL, Hartinger, S.M., Steenland, K., Naeher, L., Kearns, K., Peel, J.L., Clark, M.L., Checkley, W. Comparison of next-generation portable pollution monitors to measure exposure to PM2.5 from household air pollution in Puno, Peru. Indoor Air. 29 Dec. **2019**.

- Pollard SL, Williams KN, O'Brien CJ, Winiker A, Puzzolo E, Kephart JL, Fandiño-Del-Rio M., Tarazona-Meza, C., Grigsby, M.R., Chiang, M., Checkley, W. An evaluation of the Fondo de Inclusión Social Energético program to promote access to liquefied petroleum gas in Peru. Energy for Sustainable Development. **2018**.

- Fandiño-Del-Rio, M., Goodman, D., Kephart, J.L., Miele, C.H., Williams, K.N., Moazzami, M., Fung, E.C., Koehler, K., Davila-Roman, V.G., Lee, K.A., Nangia, S., Harvey, S.A., Steenland, K., Gonzales, G.F., Checkley, W. "Effects of a Liquefied Petroleum Gas Stove Intervention on Pollutant Exposure and Adult Cardiopulmonary Outcomes (CHAP): Study Protocol for a Randomized Controlled Trial." Trials 18 (2017): 518. PMC. Web. 30 Nov. **2017**.

- Jaller, M., Sanchez, S., Green J., Fandiño, M. Quantifying the impacts of sustainable city logistics measures in the Mexico City Metropolitan Area. Published in Journal Transportation Research Procedia. Volume 12. Page 613 - 626. ISSN: 2352-1465. **2016**.

- Behrentz, E., Fandiño, M. Environmental benefits linked to the public transportation system: case of study of Bogotá. Revista de la Asociación Colombiana de Ingeniería Sanitaria y Ambiental (ACODAL – AIDIS). 224; 19-26 (Article - ISSN: 0120-0798). **2009.**

- Behrentz, E. & Fandiño, M. Environmental rates and taxes. Water and sewer commission (commemorative edition). Pages 58 to 67. **2009**.

- Behrentz, E., Sánchez, N., Fandiño, M., Rodríguez, P.A. Stationary and mobile source emission inventory. Universidad de los Andes and Bogotá Secretariat of the Environment (ISBN: 978-958-695-442-6). **2009**.

- Behrentz, E., Sánchez, N., Bravo, A., Fandiño, M., Gaitán, M., Muñoz, N.E., Rivera, A.J., Rodríguez, P.A., Rodríguez, R.A. Technical guidelines for Bogota's air quality management plan. Bogotá Secretariat of the Environment. Universidad de los Andes. (ISBN: 978-958-695-443-3). **2009**.

- Fandiño M, Kephart JL, Checkley W, Koehler K. Particulate Matter and Black Carbon Personal Exposure Reductions from an LPG Stove Intervention in Rural Households in Puno, Peru: Preliminary Results. Joint Annual Meeting of the International Society of Exposure Science and the International Society for Environmental Epidemiology, Ottawa, Canada. August 2018.

- Kephart JL, Fandiño-del-Rio M, Checkley W, Koehler K. Exposure misclassification from area sampling in epidemiologic studies of cookstove emissions. Poster accepted for presentation at the 31st Annual Meeting of the International Society for Environmental Epidemiology, Utrecht, The Netherlands, August 2019.

- Fandiño, M., Bravo, S., Sánchez, N., Behrentz, E. Updating Bogota´s stationary source emissions inventory. Second Colombian Congress and International Conference on Air Quality and Public Health. Cartagena, Colombia. July, 2009.

- Fandiño, M., Gaitán, M., Rodríguez, R.A., Sánchez, N.P., Behrentz, E. Lessons learned while updating Bogotá air pollutant emissions inventory: stationary sources. South American Emissions, Megacities and Climate Workshop. Inter-American Institute for Global Change Research. Ubatuba (Sao Paulo), Brazil. April, 2008.

- Fandiño, M., Behrentz, E. Methodology to estimate Bogota stationary source emissions inventory. First Colombian Congress and International Conference on Air Quality and Public Health. Manizales, Colombia. March, 2007.

WORK RELATED SKILLS

- I have worked in an environmental engineering laboratory in projects aiming to determine emissions from stack sources as well as ambient air pollutant concentrations.
- I have been responsible for developing protocols to be used during fieldwork campaigns as well as during data analysis and organization.
- I have managed and trained fieldwork personnel.
- I coordinated a public participation workshop aimed at providing stakeholder feedback to the development of an air quality plan.
- I developed workshops in several townships located in northern Colombia with communities to include their needs and priorities in the development of the management plan for the protection of the wetlands of the region. I also coordinated and designed the methodology of such workshops.

OTHER SKILLS

- Spanish: native speaker.
- English (attended a bilingual school): advanced oral and written skills. Toefl score: 108.
- Microsoft Office (Word, Excel, Access, PP), Stata, Matlab, and ArcGIS.

HONORS AND AWARDS

2009 Cum laude – Master of Science in Environmental Engineering. Universidad de los Andes. My master's thesis was awarded the highest score, and I graduated with a GPA among the 3% highest of the last 5 years in the program.

2016 Global Established Multidisciplinary Site Student Award, Johns Hopkins Center for Global Health

2017 David Leslie Swift Fund in Environmental Health Engineering award. - This fund supports exceptional masters, doctoral, or postdoctoral students in the Johns Hopkins Bloomberg School of Public Health.

2017 Global Established Multidisciplinary Site Student Award, Johns Hopkins Center for Global Health

2018 Student Travel Grant to the 2019 37th Aerosol Conference in Portland, Oregon

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