Title

The Feasibility of Implementing Improved Stoves to Mitigate COPD in Communities of the Guatemalan Highlands

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Publication Date

2017-10-01

The Feasibility of Implementing Improved Stoves to Mitigate COPD in Communities of the Guatemalan Highlands

By

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A thesis submitted in partial satisfaction of the

requirements for the degree of

Master of Science

in

Health and Medical Sciences

in the

Graduate Division

of the

University of California, Berkeley

Committee in charge:

Professor John Balmes, Chair
Professor Susan Ivey
Professor Michael Bates

Fall 2017

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Preface

Approximately 40% of the world's population - roughly 2.8 billion people - cooks with biomass fuels, such as wood or other organic matter, on a daily basis.[1] Oftentimes this cooking occurs on open fires indoors creating homes where the particulate matter is often 10 times what is typically found within the ambient air of higher income countries. The resulting household air pollution (HAP) is a major health concern in low- and middle-income countries (LMIC). This has been well-documented with over 200 studies that have assessed the levels of HAP in the past 30+ years.[2]

Part One of this thesis will provide a literature review on the details and extent of this problem with a focus on Chronic Obstructive Pulmonary Disease (COPD) and stove interventions as a way to mitigate HAP.

Part Two of this thesis will document original research on a pilot feasibility study investigating the efficacy of using an improved cookstove intervention to delay the progression of COPD in women exposed to biomass smoke.

Part 1: Literature Review

1: Defining the Household Air Pollution Problem and its Importance

A Brief History of Fire and Fuel Use

The use of cooking fires dates back to the origin of our species.[3] Many have argued that control of wood fires for cooking was, in fact, one of the key factors in the transformation of humans as distinct from other primates, a development on par with the development of tools and blades.[2,4] Since first using fire to harness the energy contained within wood, Hall et al[4] suggest that "the history of human culture can be viewed as the progressive development of new energy sources and their associated conversion technologies." This notion is captured in the concept of a fuel or energy ladder in which rising incomes and increased development lead to the use of cleaner fuels processed and combusted farther from their point of use (*Figure 1)*.[2]

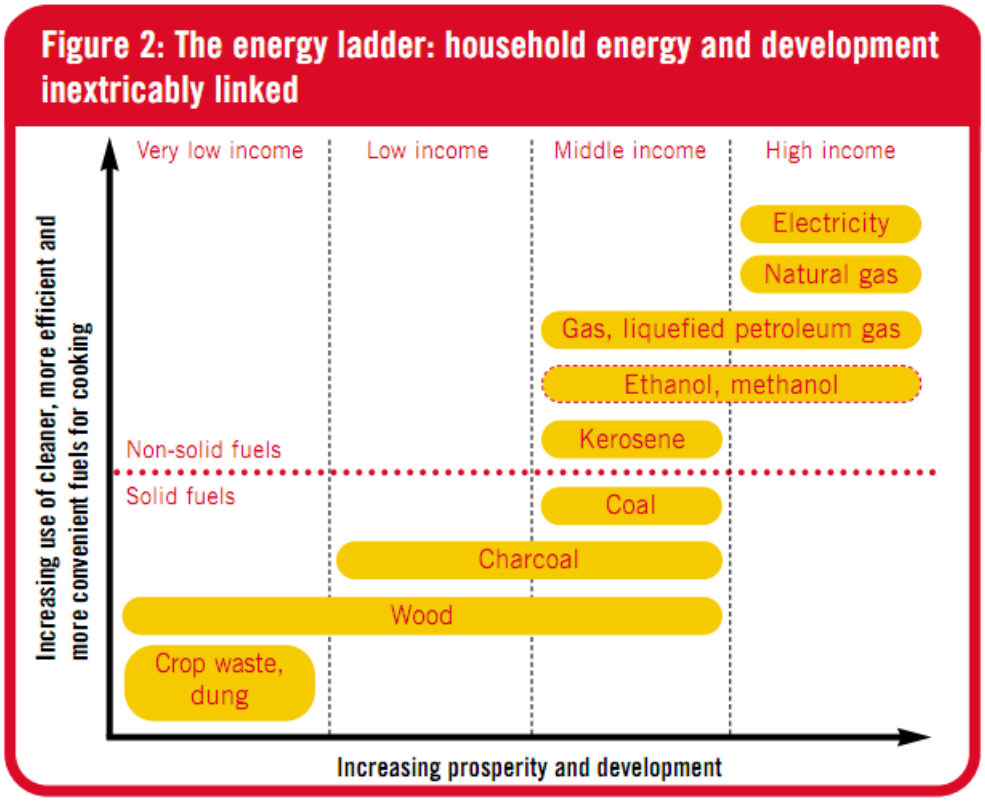


Figure 1 **– The Energy Ladder. From source** [5]

At the bottommost rungs of this ladder are biomass fuel sources, the oldest and most polluting of fuel sources. Biomass fuel refers to organic material derived from living or recently living organisms. Wood, is the earliest used of these biomass fuels, traced back to 500,000 years ago with the Peking man, in what is now China.[6] Traditional biomass usage can also include charcoal, peat, and agricultural wastes

like tree leaves, crop residues, and animal dung.[2,3,7] The term solid fuels or solid biofuels is also used to refer to the same group of fuels but with the addition of coal on top of the traditional biomass sources.[a]

Development of advances in energy sources and conversion has increased the standards of living, lifespan, and population of humans.[4] However, those populations at the bottom rungs of the ladder continue to burn biomass fuels within their own homes producing high levels of household air pollution (HAP), which is the focus of this review. As the reader will come to appreciate, movement up the energy ladder is far more complicated than the premise that rising incomes lead to cleaner fuels in a direct and linear fashion. While a clear trend exists between incomes and access to modern fuels, rising income does not necessarily ensure a progressive transition to cleaner fuels (*Figure 2)*.

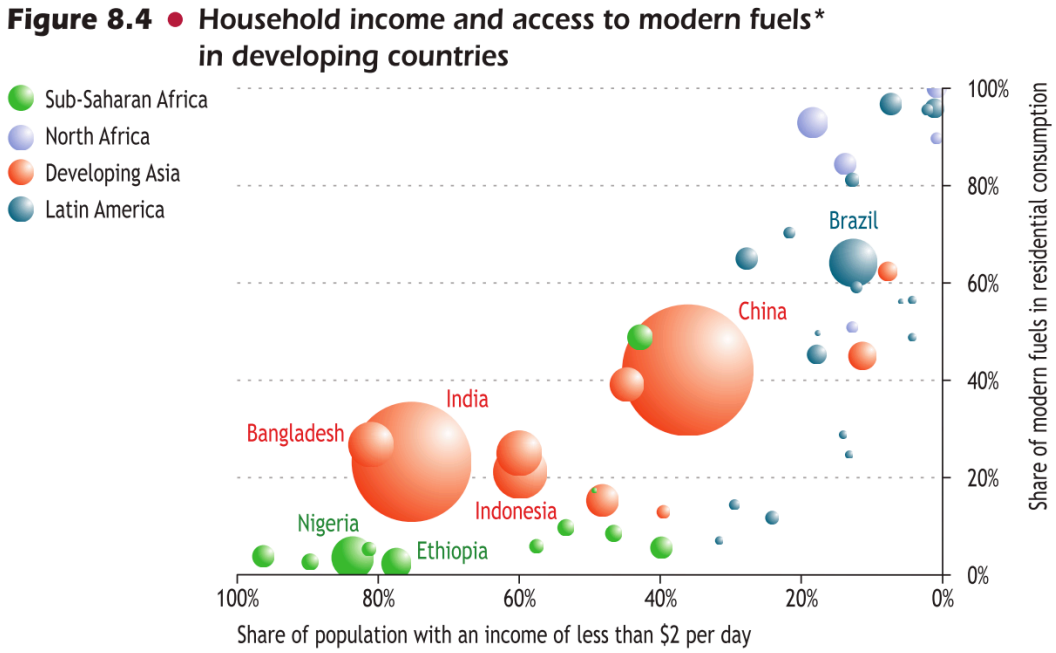


***Figure 2*: The relationship between household income and access to modern fuel sources. From Source [8]**

[a] Traditional biomass is not to be confused with modern biofuels (e.g. biodiesel or ethanol), which have been touted as promising renewable energy sources. In this case, biomass is being converted into liquid biofuels for efficient combustion.

The Spectrum of Fuel Use Today

The range of today's energy sources varies from harvested or scavenged biomass (wood, dung, etc.) to more processed biofuels such as charcoal to the commercial fossil fuels and electricity used in the United States.[2]

As of 2010, the absolute number of people relying on solid fuels has remained around 2.8 billion.[1] While the proportion of the world's households using solid fuels has dropped from 53% in 1990 to 41% in 2010, the International Energy Agency (IEA) projections suggest the absolute number of solid fuel-using households will stay relatively stable through 2030.[8,1]

As *Figure 3* shows below, there is large regional variation in the fraction of populations relying on solid fuels. India and China combined account for over half of this population (27% and 25%, respectively) with sub-Saharan Africa representing an additional 21%.[2] In addition to the global fuel use variation, poverty and rural location predict significant use of solid fuels within a given country.[2] As an example, *Figure 4* below shows the scale of this variation within Guatemala in terms of wood fuel usage across the country. As of 2014, only 36% of Guatemala's population had a primary reliance on clean fuels, a rate that is 2nd only to Haiti in the Western Hemisphere.[9]

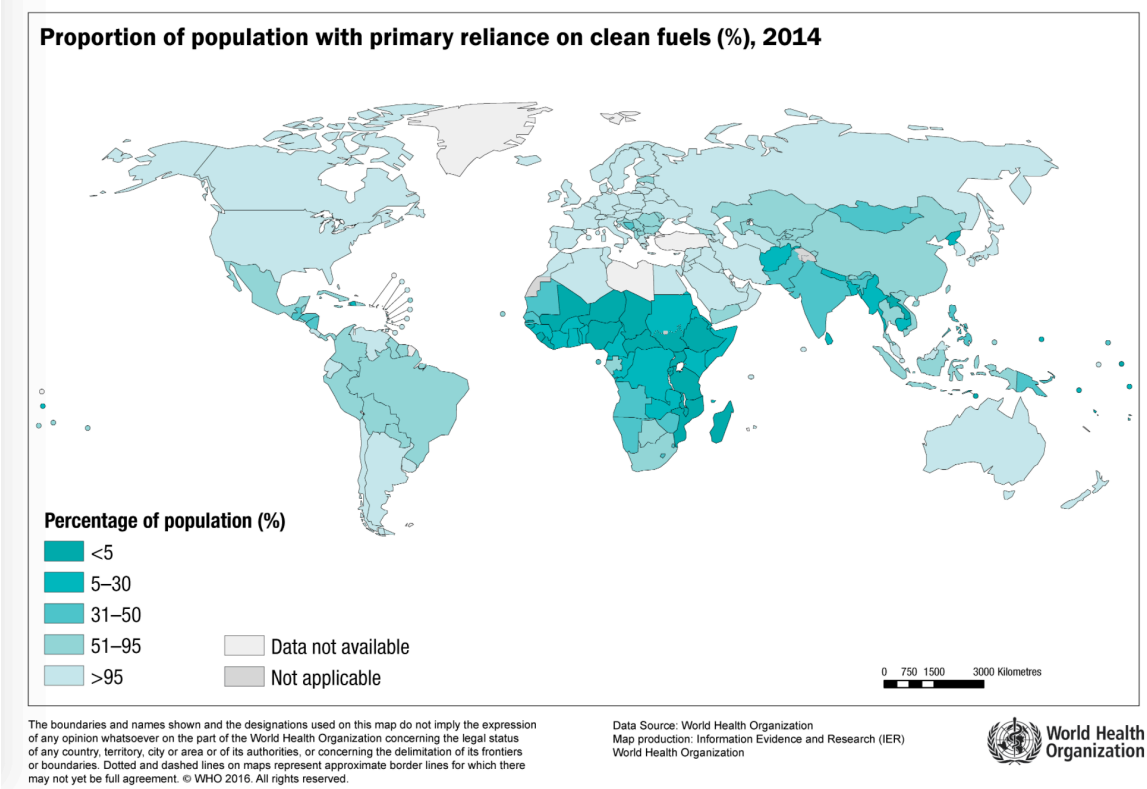


***Figure 3*: Proportion of population with primary reliance on clean fuels. From WHO Data, 2014**

Consumption map (all uses)

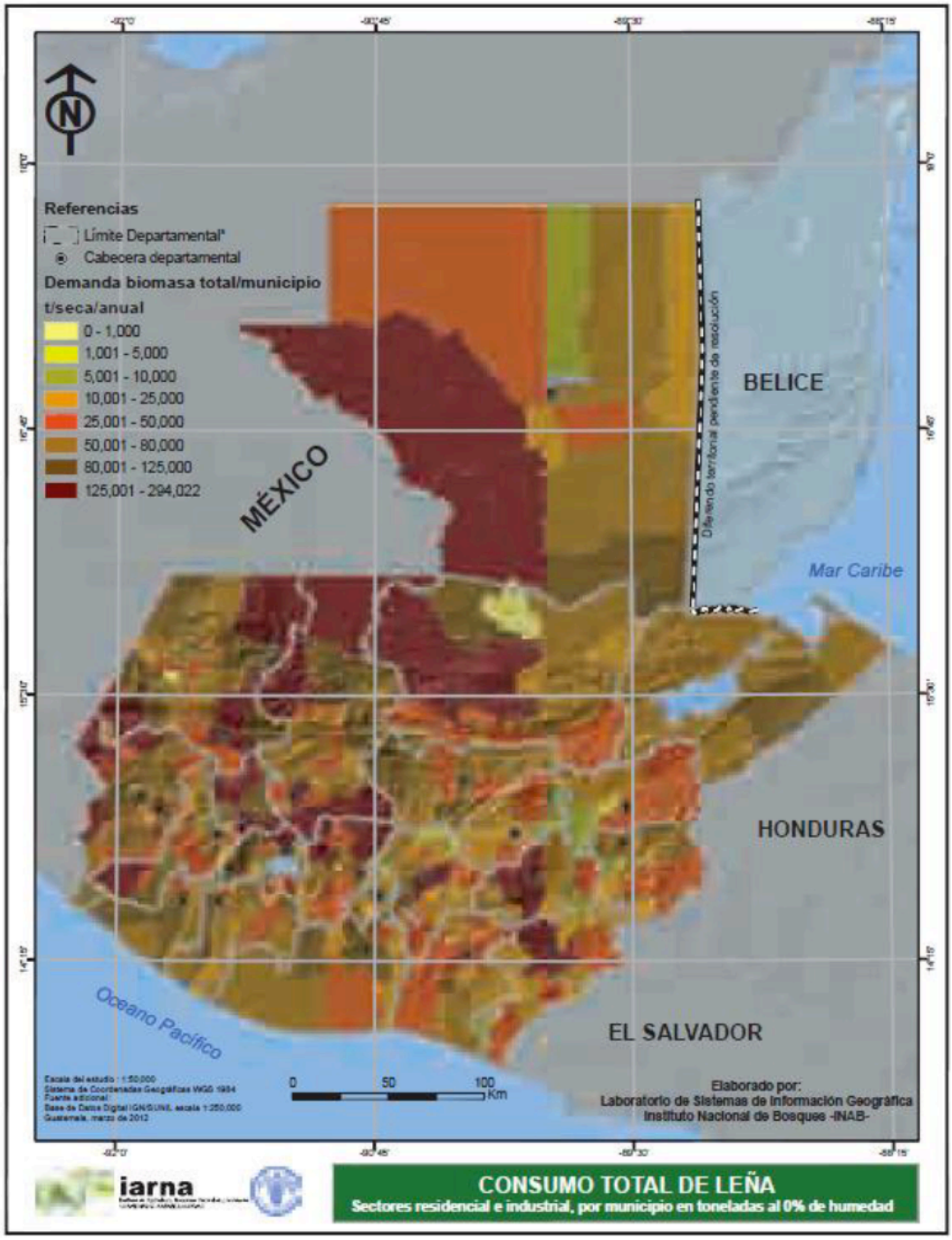


Figure 4: **Countrywide consumption of wood fuel (leña) in Guatemala. From source 10**

All of these facts surrounding polluting household energy sources led to the inclusion of HAP within the United Nation's Sustainable Development Goals (SDGs). Released in September 2015, Goal 7 includes, "Ensure access to affordable, reliable, and modern energy for all" by a target date of 2030.[11] Significant hurdles stand in the way of making this goal happen. *Figure 5* below illustrates the projections of Kuhn et al.[12] through 2025 for the share of households using solid fuel. The hope is for a greater than linear reduction in prevalence of household HAP exposure. Otherwise well over 10% of the world's population will continue to be exposed to HAP by 2030, despite the UN's goals.

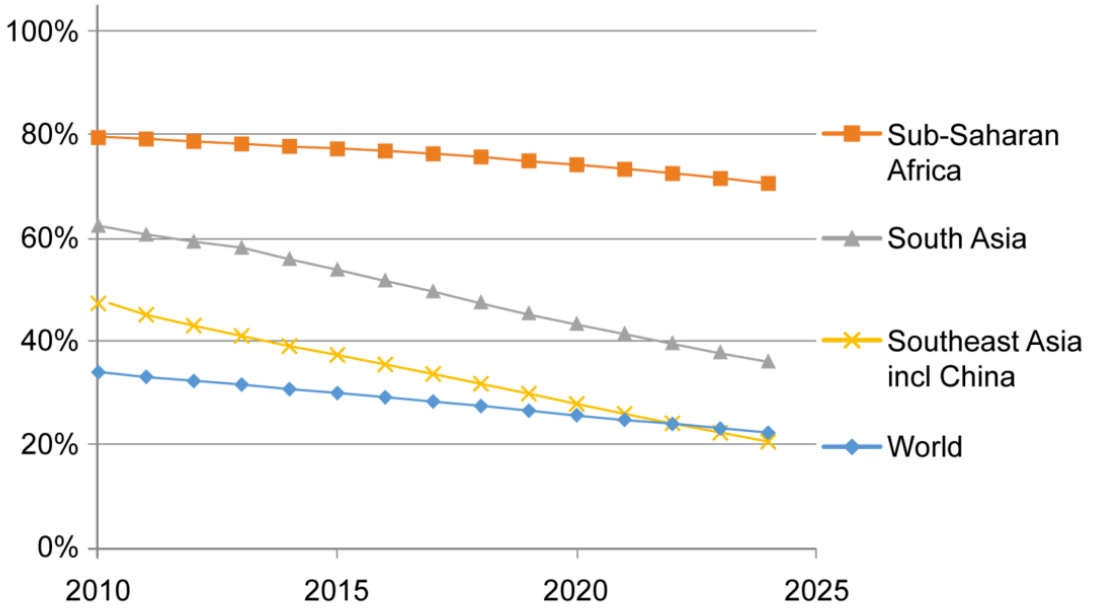


Fig 2. Base case forecast of prevalence of household solid fuel exposure, 2010–2024, World and key GBD super-regions. Source: IFs version 7.01.

doi:10.1371/journal.pone.0149669.g002

Figure 5: Forecast of the prevalence of household sold fuel exposure through 2025. From source 12

A silver lining to the progress towards clean energy for all is that connectedness to electricity has actually grown faster than World Energy Outlook projections over the last 10 to 15 years. The IEA's 2004 World Energy Outlook predicted a 10-year growth for global access to electricity to 78% by 2014 from 73% in 2004.[13] However, most recent estimates showed that 84% of the world's population had access to electricity in 2014.[13] In places, regional growth was even higher. India went from having 44% electricity access in 2002 to more than 80% in 2004, far surpassing projections of 60%. Analysts credit the role of strong policy by the federal and state governments for this success. In Africa, where the policy environment did not change significantly, reality largely matched the pessimistic projections of 2004.[13]

However, as *Figure 6* below reveals, access to clean cooking at a global level actually underperformed the IEA's already tempered projections from 2004. The clean cooking community may be able to learn from the success and failures of policy decisions around electricity access. While access to electricity can be driven by government-level policy decision, ensuring clean cooking can be a far more complicated issue.[7] Movement away from traditional fuels for household heating and cooking (where 90% of biomass fuels are consumed) is a household-level decision. In rural areas –where half of humanity lives – household-level energy use dominates total fuel demand.[7] The predominant factor behind this is that biomass fuels sources such as firewood, crop waste, etc. are often far less expensive – or even free – as compared to electricity, a far more expensive source of energy.

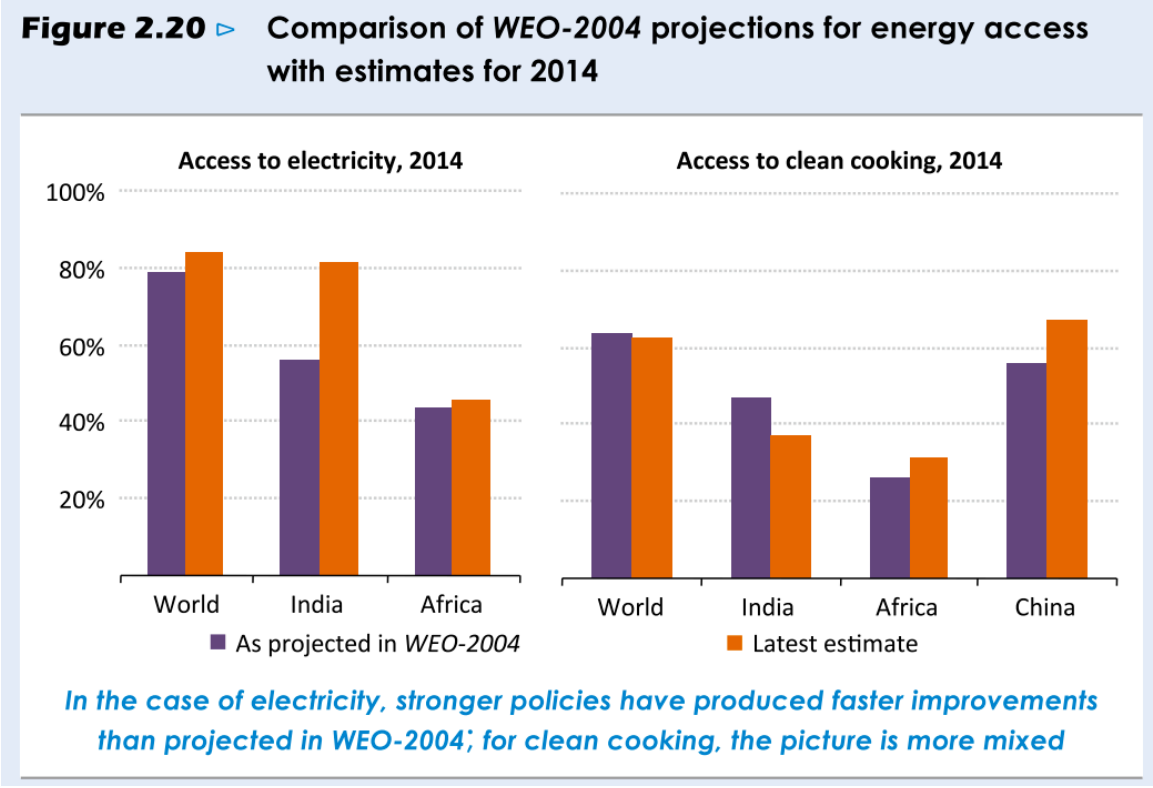


***Figure 6*: Comparisons of 2004 projections and to 2014 estimates for the WEO's 10-year electricity and clean cooking projections. From source 13**

Biomass Cooking & Woodsmoke: What's the Problem?

As this section will begin to explain, household air pollution from the burning of solid fuels within the home is a major health concern in low- and middle-income (LMIC) countries. This has been well-documented with over 200 measurement studies that have assessed the levels of HAP in the past 30+ years.[2]

The tendency to minimize any toxic effects from solid fuel smoke has been a common sentiment because the use of biomass fuels for cooking and warmth has a long and intimate history with human development. The primary reason that solid fuel smoke can be toxic is incomplete combustion, or said another way, poor combustion efficiency.[3,14] This highlights why researchers have reframed the problem as HAP from its original label as indoor air pollution, which implies that simply installing a chimney or venting, can solve the problem completely.[1] However, in many cases ambient pollutants – indoors or not – are at levels sufficient to be damaging in their own right. Harm is not limited to the kitchens of solid fuel-burning homes. The greatest dangers are of course concentrated within homes where high levels of pollution are being released in locations where people are nearly always present. Here the *intake fraction* measuring the portion of pollution released, which is actually inhaled by people, is dramatically higher than outdoor sources.[7,15] When this is combined with the fact that exposures are often for 3 to 7 hours daily for many years, the health effects caused by the cumulative exposures are not particularly surprising.[14]

So what exactly are these pollutants in the case of woodsmoke?

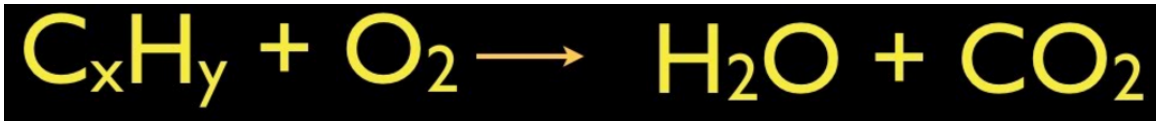


***Figure 7*: Chemical equation for the complete combustion of a generic hydrocarbon**

Wood is primarily composed of the hydrocarbon polymers cellulose and lignin (70 and 30% by weight, respectively). Other biomass fuels also primarily contain these compounds in addition to smaller organic compounds such as resins, waxes, and sugars.[7] The combustion efficiency of biomass compounds is often quite poor (80% compared to 99% for gaseous fuels) meaning the above chemical equation with water and carbon dioxide as sole end products is often incomplete. Hundreds of partially oxidized organic compounds and side products result, and 6 to 20% of fuel may be converted into toxic substances in a typical solid fuel stove.[2,7]

Woodsmoke has been found to contain upwards of 4,000 solid, liquid, and gaseous constituents which varies depending on the specific fuel used and combustion conditions (stove type, temperature, oxygen availability, humidity, etc.) along with other factors.[7] *Figure 8* below summarizes these constituents. The top three most health damaging contents of woodsmoke are: respirable particulate matter, carbon

monoxide (CO), and nitrogen oxides (NO_x). Of these, particulate matter and carbon monoxide are the most easily and commonly measured pollutants.[2]

Table 1 Pollutants from combustion of biomass and fossil fuels. Adapted from References 142 and 196

Pollutant	Known toxicologic characteristics
Particulates (PM_{10}, $PM_{2.5}$)	Bronchial irritation, inflammation, increased reactivity, reduced mucociliary clearance, reduced macrophage response, increased cardiovascular mortality
Carbon monoxide	Reduced oxygen delivery to tissues owing to formation of carboxyhemoglobin; can be acutely fatal
Nitrogen dioxide	Bronchial reactivity, increased susceptibility to bacterial and viral lung infections
Sulfur dioxide	Bronchial reactivity (other toxic end points common to particulate fractions)
Organic air pollutants:	
Formaldehyde	Carcinogenicity
1,3 butadiene	Co-carcinogenicity
Benzene	Mucus coagulation, cilia toxicity
Acetaldehyde	Increased allergic sensitization
Phenols	Increased airway reactivity
Pyrene, Benzopyrene	
Benzo(a)pyrene	
Dibenzopyrenes	
Dibenzocarbazoles	
Cresols	

Figure 8: **Pollutants from the combustion of biomass and fossil fuels. From Source** [2]

The Health Effects of Respirable Particulate Matter in HAP

Respirable particulate matter (PM) is a major health concern and probably the single most damaging constituent of woodsmoke.[7] Since the 1993 "Harvard Six Cities Study", first found the strong association between fine particulate air pollution and mortality, many additional epidemiologic studies have found an association between fine particulate matter and both acute and chronic mortality.[16,17] Specifically, total, cardiovascular, and lung cancer mortality were all positively correlated with ambient PM concentrations while its reduction was associated with decreased mortality risk.[17]

The specific pathogenicity of particles is dependent on their size, composition, origin, solubility and ability to produce reactive oxygen species (*see Figure 10)*. [18] Particles smaller than 10 microns (µm) have been found to be particularly damaging due to their capacity to enter and lodge themselves within the lower respiratory tract of the lung.[3] Air quality standards typically further divide these particles between the fraction, which is smaller than 10 µm, PM_{10}, and those, which are smaller than 2.5 µm ($PM_{2.5}$). $PM_{2.5}$, also commonly referred to as fine PM, is considered to be more damaging as their diameters allow alveolar deposition. Ultra-fine particles (with diameters smaller than 0.1 µm are believed to allow the diffusion of damaging chemicals across the lungs, into the blood, and throughout

body.[18] PM can cause respiratory inflammation that impacts lung function, exacerbates asthma, and promotes lung cancer.[18] However, the damage is not limited to the respiratory system, as increased cardiovascular disease and mortality have also been identified.[19] Potential mechanisms of cardiovascular toxicity include, a) spillover of PM-induced oxidative stress and inflammatory responses in the lungs into the systemic circulation that might induce endothelial dysfunction and atherosclerosis; b) increased risk of thrombosis due to the same responses; and c) lung nosioceptive signals that impair cardiac autonomic function.[19,20]

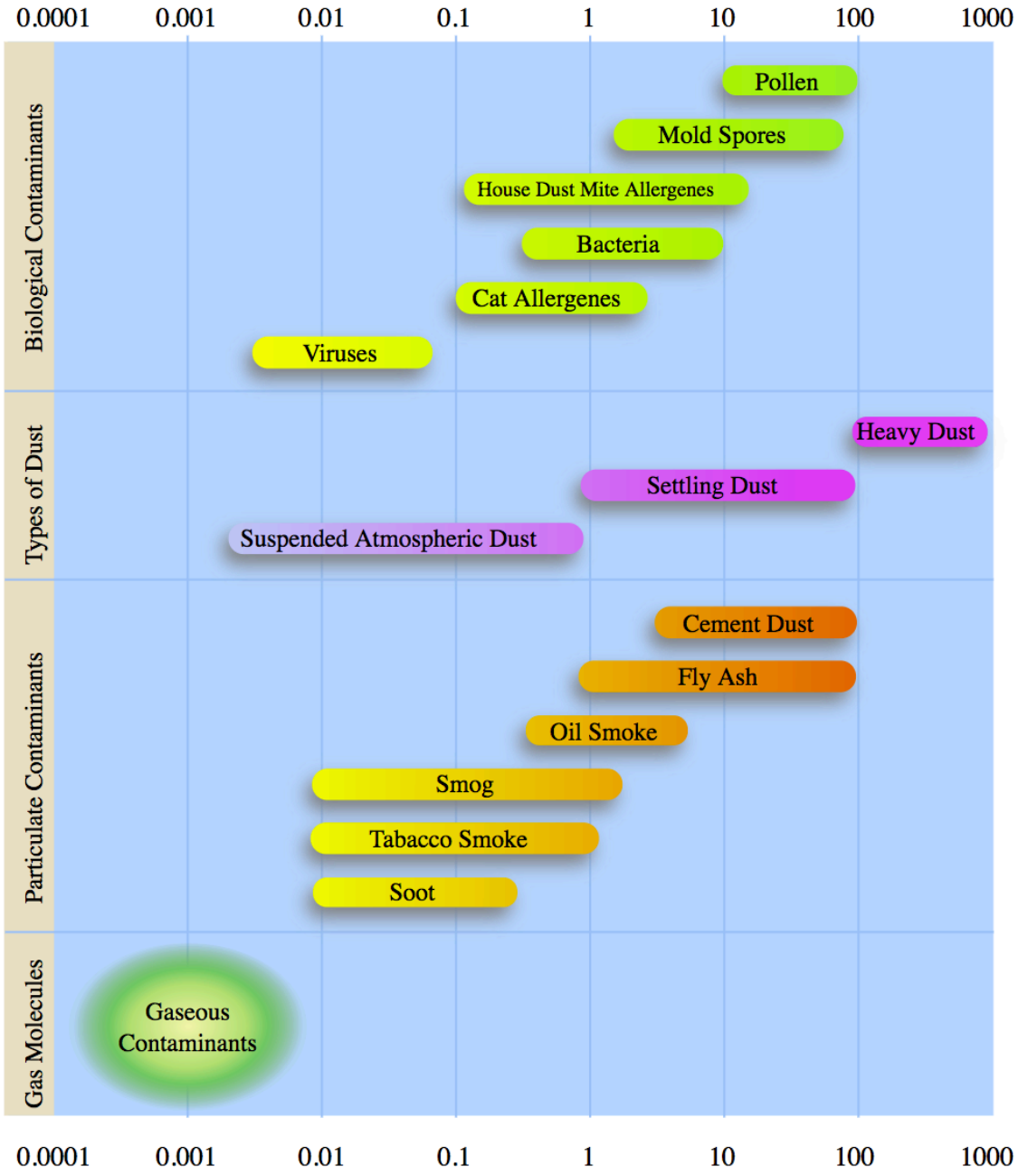


Figure 9: **types, and size distribution in microns (µm), of atmospheric particulate matter. Source Wikipedia (from: GFDL, https://en.wikipedia.org/w/index.php?curid=48987967)**

The US Environmental Protection Agency (EPA) has established regulatory standards for ambient $PM_{2.5}$ and PM_{10} displayed below in *Figure 10* (along with additional pollutants). Regulatory standards are separately specified for 24-h and annual time periods, above which the given PM levels are deemed to be dangerously high.

Pollutant	Averaging Time	Level
Carbon Monoxide (CO)	8-hour	9 ppm
	1-hour	35 ppm
Lead (Pb)	Rolling 3-mo. Average	0.15 $\mu g/m^3$
Nitrogen Dioxide (NO_2)	1-hour	100 ppb
	Annual	53 ppb
Ozone (O_3)	8-hour	0.075 ppm
Particulate Matter ($PM_{2.5}$)	Annual	12 $\mu g/m^3$
	24-hour	35 $\mu g/m^3$
Particulate Matter (PM_{10})	24-hour	150 $\mu g/m^3$
Sulfur Dioxide (SO_2)	1-hour	75 ppb
	3-hour	0.5 ppm

Figure 10: **Air pollutant standards from the US EPA. From Source 21**

In 2000, experts established a 7 $\mu g/m^3$ annual mean for $PM_{2.5}$ concentration as the point where health risks begin.[1] Unsurprisingly the PM levels measured during the use of biomass cooking inside the home are dramatically higher than both this number and EPA standards, at levels of up to 100 times higher and routinely 30 times higher than WHO air quality guidelines.[22–24] The average of particulate exposure with use of indoor cookstoves is in the range of milligrams per cubic meter (note the 100 fold change in units from µg to mg) with peak levels reaching over 10–30 mg/ m^3.[3]

In a 2010 study of the women and children in 63 Guatemalan households using a combination of open wood fires and wood cookstoves with chimneys, Northcross et al.[24] measured $PM_{2.5}$ concentrations of 900 $\mu g/m^3$ over a 48-h averaging time within homes using open fires, a value that is over 128 times the point where health risks are believed to begin. Personal monitoring of the mothers found values of 270 and 220 $\mu g/m^3$ for open fires and chimney stoves, respectively. Concentrations

measured on infants and children were 30 to 40% lower, but still well within the dangerous level.

Figure 11 below shows an example curve for disease (ischemic heart disease) by dose for annual average $PM_{2.5}$ exposure. The shape of this curve, known as an integrated exposure-response function, suggests that amongst those in the solid fuel zone of $PM_{2.5}$ exposure (at the plateaued portion to the far right of the curve) drastic reductions in $PM_{2.5}$ levels would be necessary to meaningfully reduce relative risk.[25] For example, even halving annual average $PM_{2.5}$ from 300 to 150 µg/m^3 would have minimal effects on a reduction of the relative risk of ischemic heart disease.

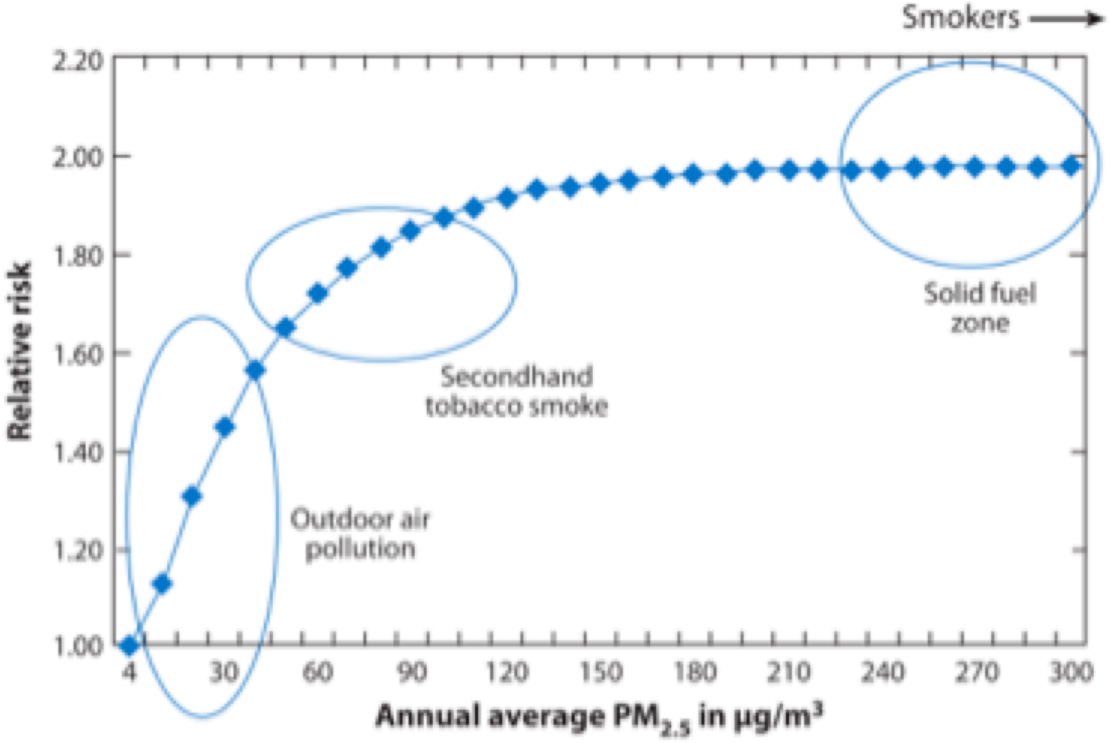


***Figure 11*: Relative risk of ischemic heart disease by average $PM_{2.5}$ concentration. From Source** [2]

While no systematic worldwide measurements for PM levels exist, Smith et al.[2] have posited that data show the following mean values based on fuel type,

- dung: 7,800 ± 11,200 µg/m^3
- charcoal: 3,900 ± 8,400 µg/m^3
- wood: 2,100 ± 3,900µg/m^3

PM values in homes using kerosene are approximately an order of magnitude lower, while those in households using exclusively gas or electricity are even lower.

The Health Effects of Carbon Monoxide in HAP

The toxic effects of carbon monoxide (CO) have been well documented via its interaction with hemoproteins and oxygen binding within the blood.[26] The formation of carboxyhemoglobin (COHb) when CO combines with hemoglobin (Hb) results in a decreased ability to bind oxygen leading to diminished blood oxygen levels and ultimately decreased oxygen delivery to all of the body's tissues. With high enough CO concentrations this will lead to death. The US EPA sets limits for CO concentrations at a maximum of 9 ppm over 8 hours while 35 ppm is the maximum allowable outdoor concentration for a one-hour period in any year (https://www.epa.gov/criteria-air-pollutants/naaqs-table). The US CDC and OSHA define 1,500 ppm as the concentration which is immediately dangerous to life or health (from: https://www.cdc.gov/niosh/idlh/630080.html).

In one of many papers from the seminal RESPIRE study Smith et al.[27] found baseline averages of CO to be 10.2 ppm within Guatemalan kitchens using open fire cooking while personal device monitoring found 48-h levels to be 3.4 ppm for both the mother and children *(see Figure 12)*.

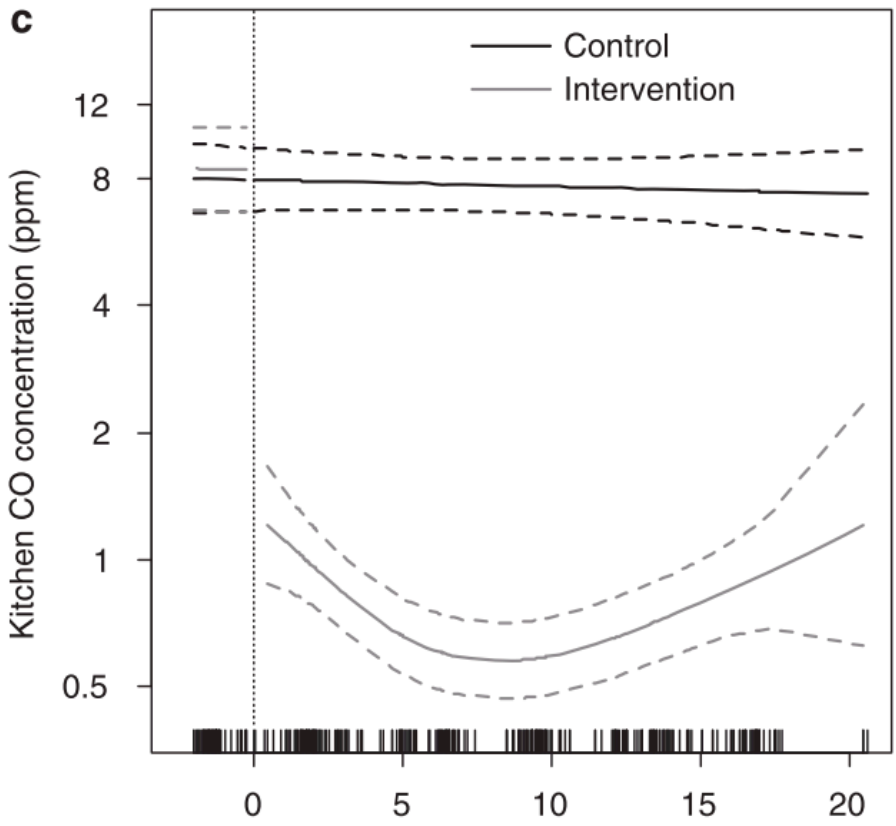


***Figure 12*: From RESPIRE data, showing trends in 48-h CO levels by group assignment over time (months). Dashed lines represent point-wise 95% confidence intervals. Tick marks above x-axis indicate individual measurements at time (months) relative to the intervention. From source 27.**

The Health Effects of Nitrogen Oxides in HAP

Nitrogen oxides (NO_x) is a HAP constituent, though more likely to be produced by the higher temperatures of LPG combustion and motor vehicles.[28] These nitrogen oxides can be a health detriment in and of themselves, as well as being a major component of photochemical smog. By themselves, the damaging effects occur via oxidative damage and free radicalization.[29]

In reviewing the results of challenge studies of healthy subjects and smokers, Bernstein et al. [30] noted that NO_2 exposure (2- 6 ppm) resulted in a mild inflammatory response characterized by increased neutrophils and decreased lymphocytes. Given the relative low intensity of NO2-induced airway inflammation at ambient levels, the primary role of this pollutant may be as a sensitizing agent for inhaled allergens rather than a direct actor.

When nitrogen oxides and volatile organic compounds mix with sunlight and heat in the atmosphere ozone smog results *(Figure 13, below)*.[31] While this is of greater concern in urban centers, HAP is not exclusively a rural issue. Research on the health effects of NO_2 has largely occurred in high-income countries where the robust associations have been between NO_2 exposure and asthma outcomes.[32]

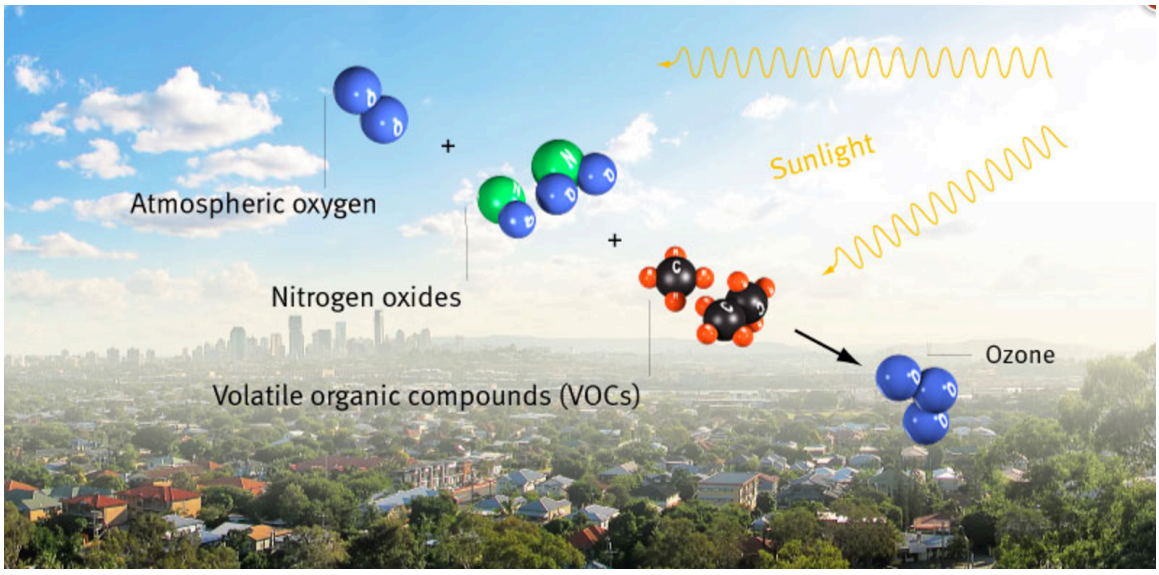


***Figure 13*: The components and reactions resulting in the production of photochemical smog. From source 33**

The Global Health Burden of HAP

The Global Burden of Disease project is an enormous international effort seeking to estimate the death, disease, and injury by age, sex, and disease for 21 world regions, which has occurred in 1990, 2005, 2010, and most recently in 2015. While the most recent GBD results have yet to be fully analyzed, the GBD-2010 was used for the production of a series of Comparative Risk Assessments (CRAs) to estimate the portion of the burden attributable to each of roughly 60 risk factors in the 21 global regions. Lim et al.'s[34] comparative risk assessment for the GBD-2010, attributed 3.5 to 4 million deaths to direct exposure to HAP, identifying it as the 3rd most dangerous risk factor to health, behind only high blood pressure and tobacco smoking, including secondhand smoke (*see Figure 14 below*).[34,35]

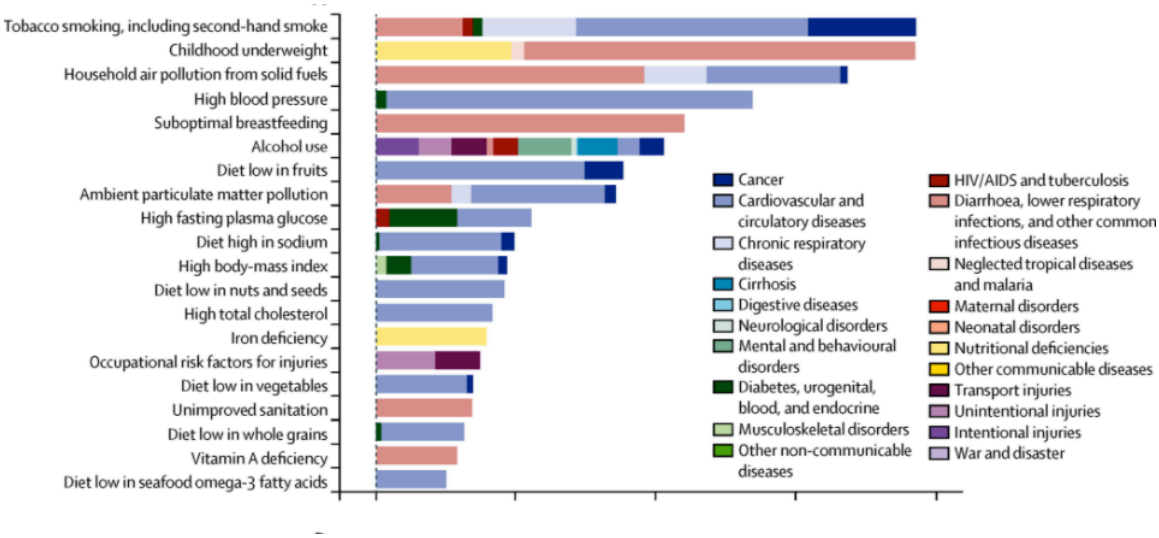


***Figure 14*: Burden of disease attributable to 20 leading risk factors in 2010, expressed as a percentage of global disability-adjusted life-year. From source 34.**

Before I continue, a brief aside should be made regarding the unit of the disability-adjusted life year (DALY) as a measure of disease. Historically, simple mortality data or, where available, prevalence and/or incidence of disease had been used as measures of disease burden.[36] For the first time, in 1993, the world development report utilized DALYs as a measure of disease burden. Its calculation attempts to quantify not only the number of lives lost from disease but also the duration of life lost and length of disability incurred for a given disease to determine those diseases with the greatest burden on the global population. Based on a standardized life expectancy (82.5 for females and 80 for males), DALYs are a metric that quantifies lives lost and/or disability using standardized rates of disability discounting (*see Figure 16)*.[36] In a 1994 *Bulletin of the World Health Organization* Murray justified this decision stating (emphasis my own)[36]:
"[T]he intended use of an indicator of the burden of disease is critical to its design. At least four objectives are important.

- to aid in setting health service (both curative and preventive) priorities;
- to aid in setting health research priorities;
- to aid in identifying disadvantaged groups and targeting of health interventions;
- to provide a comparable measure of output for intervention, programme and sector evaluation and planning.

Not everyone appreciates the ethical dimension of health status indicators… Nevertheless, *the first two objectives listed for measuring the burden of disease could influence the allocation of resources among individuals, clearly establishing an ethical dimension to the construction of an indicator of the burden of disease*.[36]"

While DALYs continue to be widely used as the fundamental unit of disease burden in global health and policy-making decisions, the practice is not without controversy. Chief among the objections is perhaps the use of standardized life expectancies across countries. Implied in this decision is the idea that health interventions alone could erase the difference in life expectancy between high and low-income nations with a disregard for broader social determinants of health and well being. Yet, the alternative of using differing life expectancies across nations is arguably even more problematic for obvious reasons.[37]

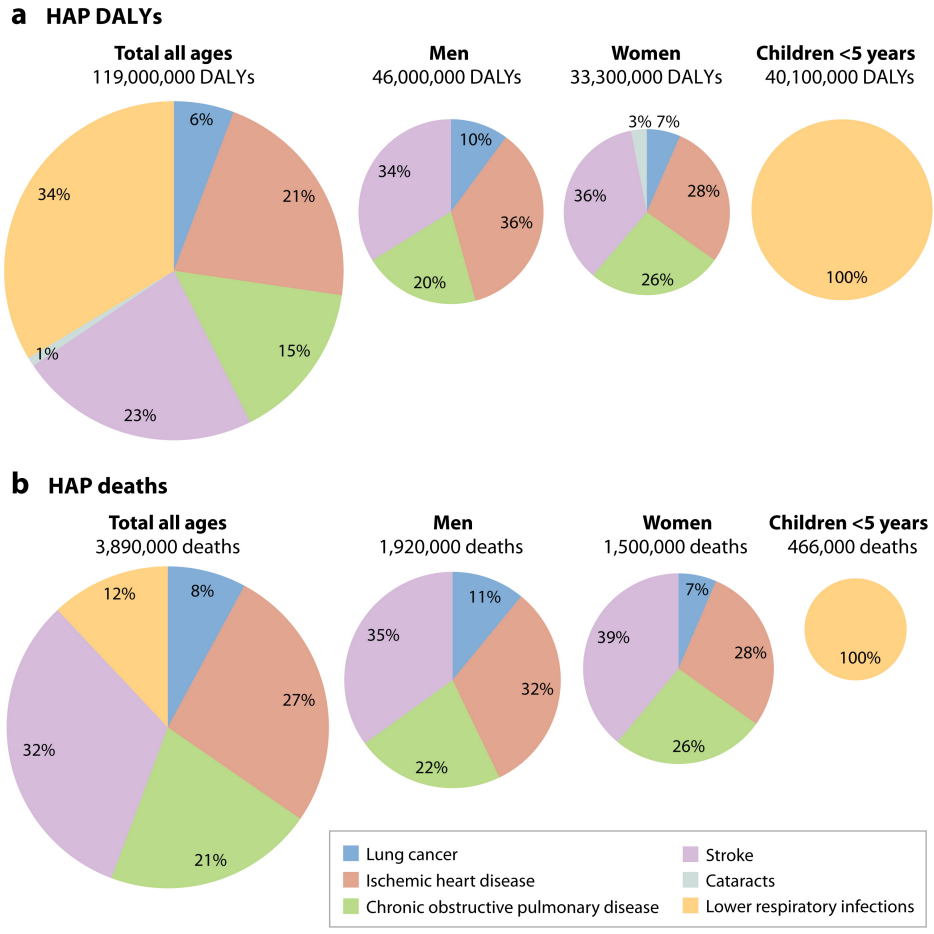
Table 2: **Definitions of disability weighting**

	Description	Weight
Class 1	Limited ability to perform at least one activity in one of the following areas: recreation, education, procreation or occupation.	0.096
Class 2	Limited ability to perform most activities in one of the following areas: recreation, education, procreation or occupation.	0.220
Class 3	Limited ability to perform activities in two or more of the following areas: recreation, education, procreation or occupation	0.400
Class 4	Limited ability to perform most activities in all of the following areas: recreation, education, procreation or occupation	0.600
Class 5	Needs assistance with instrumental activities of daily living such as meal preparation, shopping or housework.	0.810
Class 6	Needs assistance with activities of daily living such as eating, personal hygiene or toilet use.	0.920

Figure 15: **The definitions for disability weighting in the calculation of DALYs. From source 36**

With that said and their various problematic features, DALYs continue to be the de facto unit of measure for disease burden in global public health, and as *Figure 14* above illustrated, HAP is responsible for 4.5% of the total DALYs lost globally.[34] In a 2014 review article Smith et al.[1], elaborated on the comparative risk assessment used in GBD-2010, breaking out the health burden of HAP across age, sex, and region, comparing HAP against other environmental risk factors *(see Figure 16)*.

Based on GBD-2010, HAP was responsible for 119 million DALYs and 3.89 million deaths. Of these DALYs, 38.6% were suffered by men, 28.0% by women, and 33.7% by children under the age of 5. In descending order of impact the top six diseases attributable to HAP are: Lower Respiratory Infections, Stroke, Ischemic Heart Disease, COPD, Lung Cancer, and Cataracts. I will discuss each of these briefly with mention of the role of HAP in the pathogenesis of each disease.



Smith KR, et al. 2014.
Annu. Rev. Public Health. 35:185–206

Figure 16: **Adjusted total HAP burden-of-disease from the analysis of GBD-2010. From source** [1]

Acute Lower Respiratory Infections (ALRI)

Acute Lower Respiratory Infections (ALRI) are the most significant cause of global mortality in children under the age of 5.[1] In terms of mortality and disability, children are the population most affected by HAP-caused ALRI. For a respiratory infection to occur, the cells of the body's innate immune system must first be evaded. When a pathogen is detected, "just right" immune response must occur which is sufficient to kill off the invader but without generating unnecessary and damaging inflammation. The specifics of how HAP interferes with this mechanism are not fully understood, but it is believed that PM in some way interferes with the body's ability to clear potential pathogens.[38]

A 2014 whitepaper review on WHO's Indoor Air Quality guidelines regarding the state of the evidence for the health effects of HAP pooled the results of 26 studies to find a pooled OR of 1.73 (95% CI=1.47, 2.03) for the effect of HAP on ALRI.[39] However, the landmark RESPIRE study in 2011 remains the only RCT showing that reduced exposure to HAP can reduce risk of early childhood ALRI. It found that a 50% reduction in CO exposure was significantly associated with a reduction in physician-diagnosed severe pneumonia (RR 0.82, 0.70–0.98).[40]

Additional reviews include one in 2011 from Po et al.[41] on the effects of solid biomass fuel exposure on the health of rural women and children which found the pooled OR for ALRI to be 3.53 (95% CI 1.94 to 6.43) based on the analysis of 25 studies. More recently in a 2015 pooled analysis assessing the relationship between cooking practices and ALRI in sub-Saharan Africa (n=56,437), Buchner and Rehfuess found significantly increased odds of ALRI in homes using kerosene or solid fuels (OR kerosene: 1.64, CI: 0.99, 2.71; coal and charcoal: 1.54, CI: 1.21, 1.97; wood: 1.20, CI: 0.95, 1.51).[42] Research on HAP and ALRI has generally focused on children, but considering that tobacco smoking is a risk factor for pulmonary tuberculosis, HAP may also increase the risk of tuberculosis.[35]

However, most recently the 2017 Cooking and Pneumonia Study of over 10,000 children in Malawi failed to show a reduced incidence of pneumonia in an intervention group given biomass-fueled improved cookstoves versus a control group using traditional open fires with an incidence rate ratio (IRR) of 1.01 (95% CI 0.91–1.13; p=0·80).[43] The study investigators have not yet reported whether the improved stove actually reduced exposures to biomass smoke.

Cardiovascular Disease

Adverse cardiovascular events (myocardial infarction, stroke, etc.) are a major health concern regarding HAP exposure. Unfortunately, there are little published data on the association between HAP exposure and cardiovascular disease (CVD), largely because HAP exposure tends to occur in low-resource settings. However, analysis has shown that there is a consistent, nonlinear relationship between inhaled dose of $PM_{2.5}$ and cardiovascular disease mortality over several orders of magnitude of dose from cigarette smoking, secondhand smoke tobacco smoke (SHS) exposure, and ambient air pollution (*see Figure 17; note log scale of the x-axis)*.[44,45]

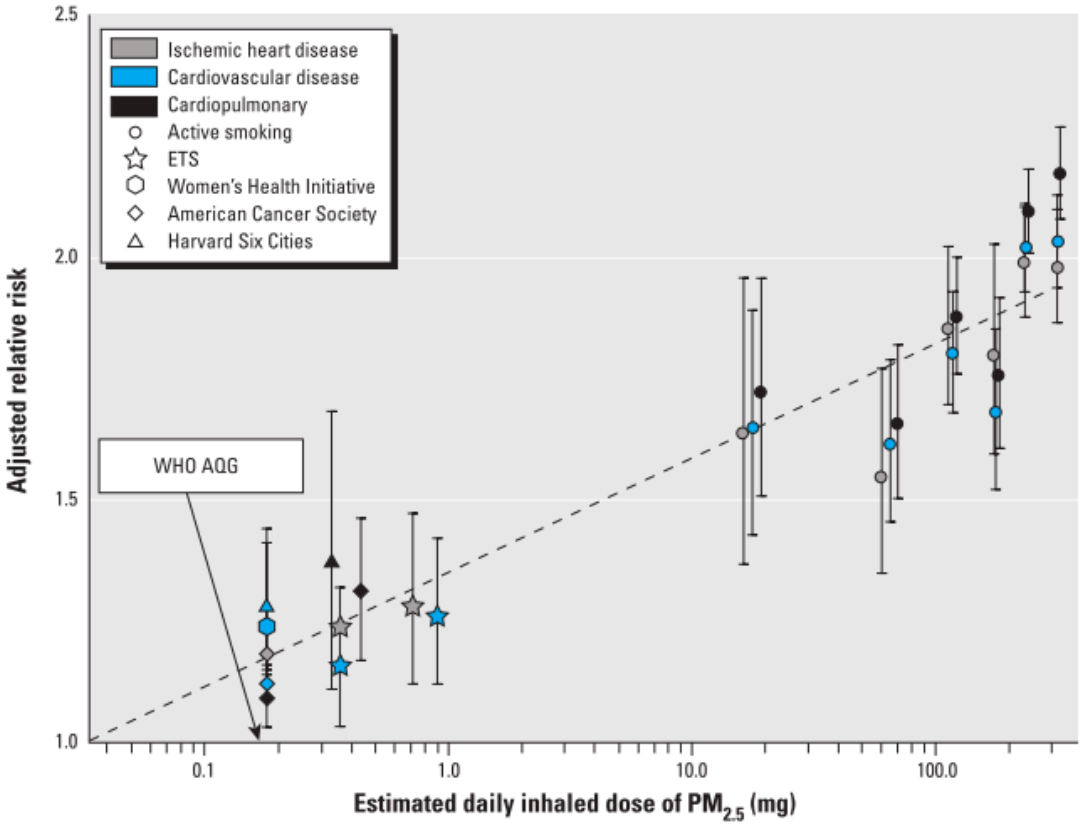


Figure 17: **Adjusted relative risks (95% confidence intervals) of cardiovascular and cardiopulmonary mortality and estimated dose of $PM_{2.5}$ across studies of outdoor air pollution, secondhand smoke (ETS above), and active cigarette smoking. From Source 44,45**

Due to the gap in evidence for the relationship between HAP $PM_{2.5}$ and CVD, the HAP-based CVD disease burden for the GBD-2010[1] relied on interpolation for the levels of $PM_{2.5}$ typically measured in HAP on an integrated exposure-response curve that includes other combustion sources of $PM_{2.5}$. The HAP $PM_{2.5}$ levels fall between the levels of $PM_{2.5}$ known for cigarette smoking and SHS exposure. Based on this and previous observational evidence for outdoor $PM_{2.5}$, a 2010 published statement from the American Heart Association[46] indicated that short-term $PM_{2.5}$ exposure increases the risk of CVD-related mortality while longer-term exposure over the course of a few years increases the risk even more. Proposed mechanisms for how this pathology manifests are shown in *Figure 18* below.

More concretely, in a 2012 study of over 14,000 Chinese adults Lee et al.[47] found that household use of solid fuels was associated with increased risk of self-reported coronary heart disease (odds ratio [OR]: 2.58, 95% confidence interval [CI]: 1.53 to 4.32). Additionally, comparing the highest tertile of duration of solid fuel use with the lowest tertile found a significant association with a history of stroke (OR: 1.87, 95% CI: 1.03, 3.38).

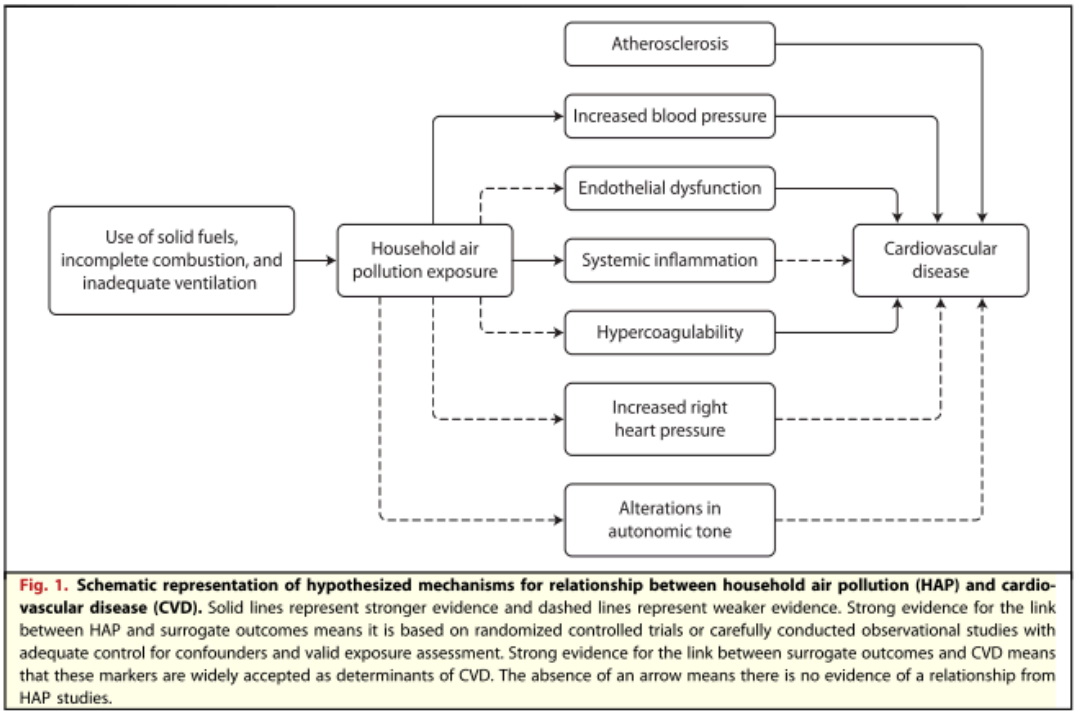


Fig. 1. Schematic representation of hypothesized mechanisms for relationship between household air pollution (HAP) and cardiovascular disease (CVD). Solid lines represent stronger evidence and dashed lines represent weaker evidence. Strong evidence for the link between HAP and surrogate outcomes means it is based on randomized controlled trials or carefully conducted observational studies with adequate control for confounders and valid exposure assessment. Strong evidence for the link between surrogate outcomes and CVD means that these markers are widely accepted as determinants of CVD. The absence of an arrow means there is no evidence of a relationship from HAP studies.

Figure 18: **Proposed mechanisms for the relationship between HAP and CVD. From Source 48**

Lung cancer

The WHO's International Agency for Research on Cancer (IARC) first evaluated the carcinogenicity of HAP in 2006.[49,50] Coal-based HAP was classified as a Group 1 carcinogen indicating definite carcinogenicity. Biomass fuel use meanwhile is Group 2(a) designating it as a probable carcinogen, citing a relative lack of epidemiological evidence.[1] Smith et al.'s review[1], showed an odds ratio of 1.18 (1.03, 1.35) for biomass fuel use leading to lung cancer. In a 2016 study of 606 lung cancer cases amongst never-smokers in Nepal with matched controls, Raspanti et al.[50] found increased risk of lung cancer amongst those exposed to HAP (OR: 1.77, 95% CI: 1.00–3.14).

Cataracts

Cataracts are the leading cause of blindness, globally, with increased rates in those countries with high solid fuel use.[1] A meta-analysis of seven studies reporting on the risk of cataract with exposure to solid biomass fuel in the home showed a pooled OR of 2.46 (1.74, 3.50).[39]

Chronic Obstructive Pulmonary Disease

Chronic Obstructive Pulmonary Disease (COPD) is of significant and growing importance in terms of its share of global mortality and morbidity. Formerly seen as primarily a smoking-related disease in developed countries, by 2020 projections show that COPD will be the 3rd leading cause of global mortality and morbidity. [1,51] The 2005 NHANES III study found that nearly 25% of cases of COPD in the US are in never-smokers, and that number may be in excess of 70% in low-income nations where rates of solid fuel use are high.[14] While smoking remains a major risk factor for the development of COPD, HAP has replaced it as the world's top risk factor globally.[14,52] The greatest share of HAP-related premature deaths comes in the form of nonsmoking women with COPD.[53]

The pathogenesis of COPD is a slow and progressive process due to chronic exposures to damaging particles or gases in a genetically susceptible subset of the population.[51,54] It is a type of obstructive lung disease characterized by chronic respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[55] Exposure to these substances causes chronic inflammation and oxidative stress leading to irreversible damage with two separate but often overlapping phenotypes: emphysema and chronic bronchitis. Chronic bronchitis is characterized by small airways obstruction due to increased mucous production (see *Figure 20).* [55,56] The emphysema phenotype occurs through the destruction of lung parenchyma [55,56] HAP-derived lung disease tends to be less commonly associated with the emphysema phenotype than tobacco smoking.[52]

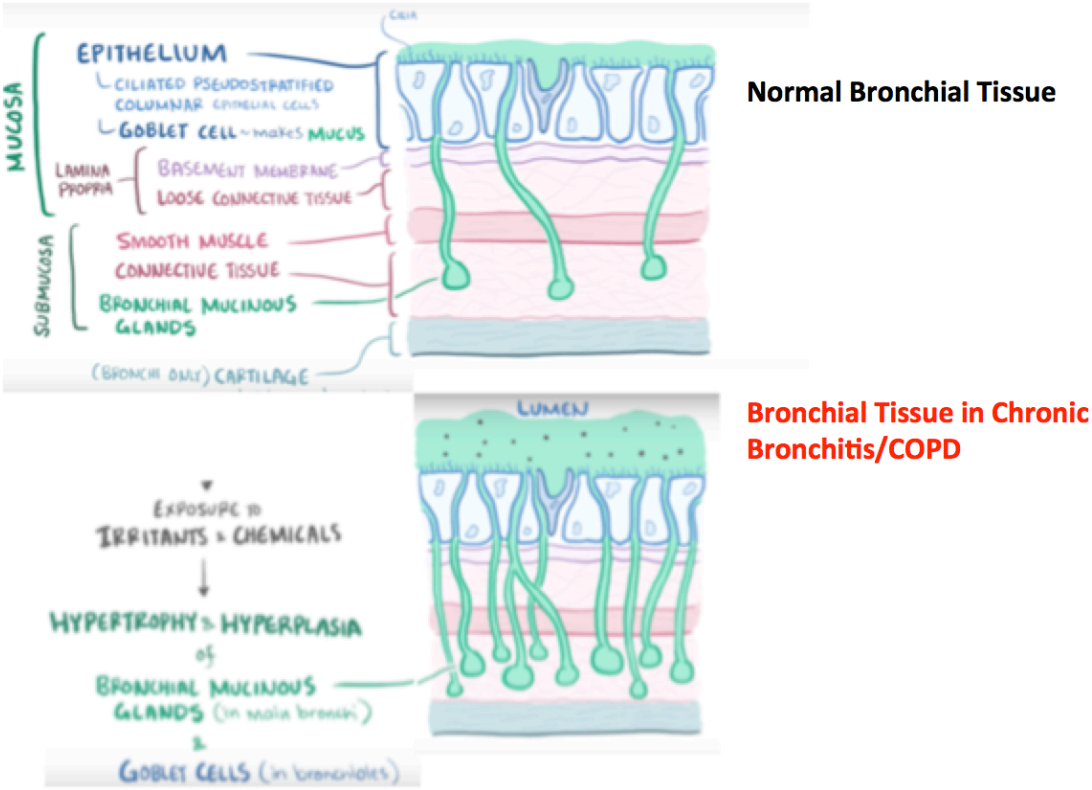


Figure 19: **The pathogenesis of chronic bronchitis preceding the development of COPD. Adapted from Source 57**

While also under the heading of obstructive lung diseases, asthma is distinct from COPD in having reversible bronchospasm after administration of inhaled bronchodilator while typical COPD will be largely non-reversible *(see Figure 20).*

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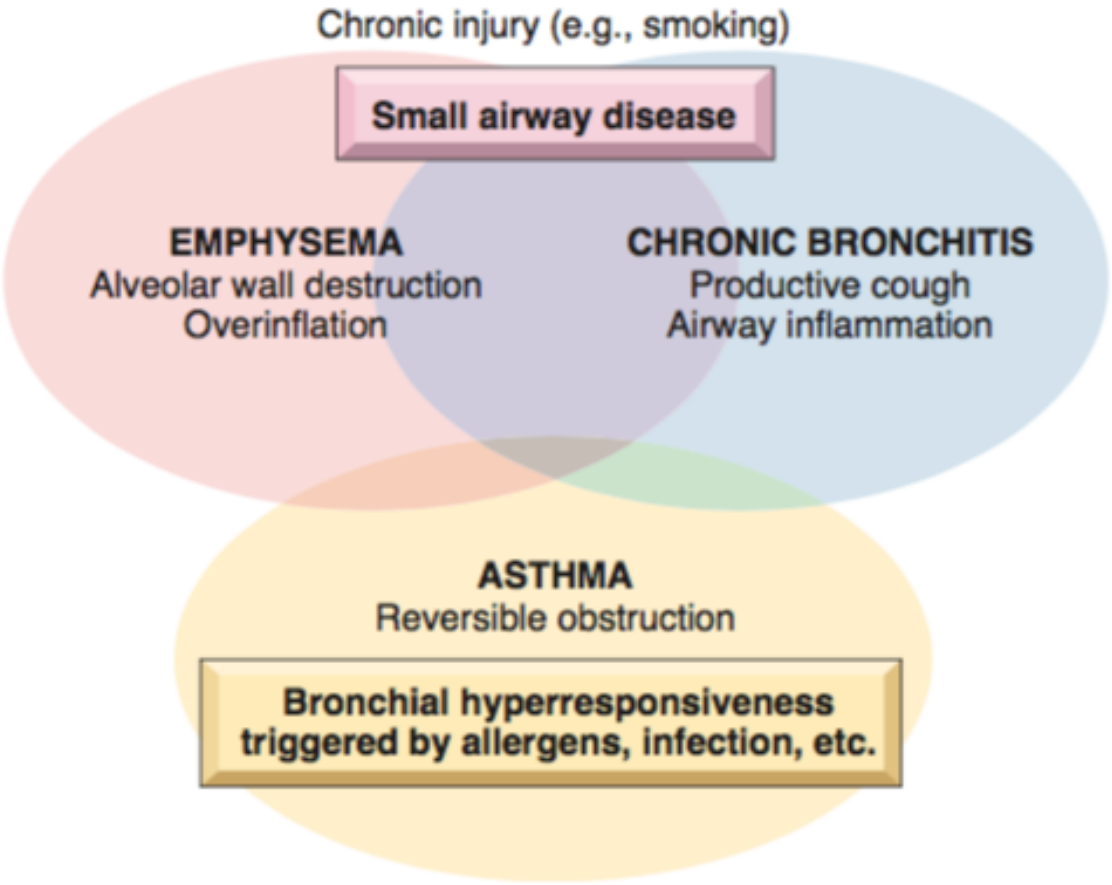

Figure 20: The overlap of chronic obstructive lung diseases. From source 56

While a more detailed discussion of the mechanisms behind the pro-inflammatory mechanisms of biomass smoke leading to the development of COPD is beyond the scope of this review, *Figure 21* below from Silva et al.[54] provides a summary, which may be helpful in showing some of the pro-inflammatory biomarkers involved.

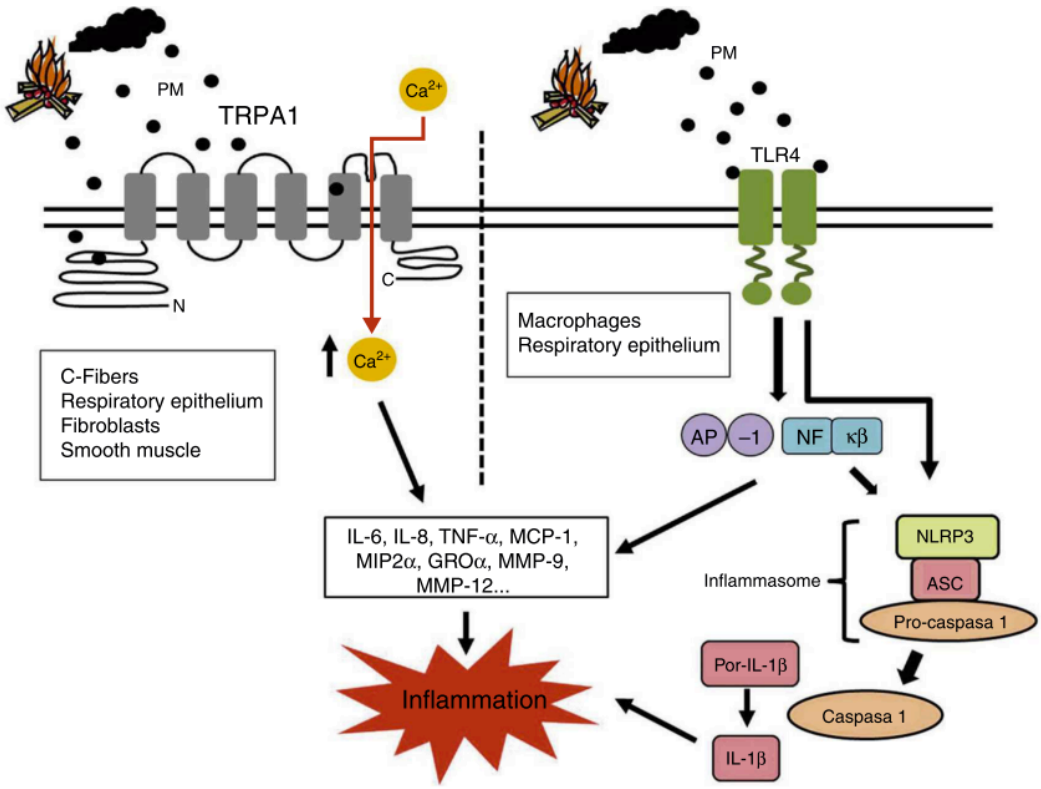

Figure 21: **The pro-inflammatory mechanisms of biomass smoke. From source** [54]

The development of severe COPD is characterized by a rapid decline in the lungs' forced expiratory volume over 1 second (FEV_1) through the destruction of terminal bronchioles and diminished airways.[58] COPD progression often occurs in fits and starts rather than one smooth curve because the rate of decline of FEV1 is dictated by the rate of destruction of terminal bronchioles.[58] Ramirez-Venegas et al[59] showed this in their 2014 study of a cohort of COPD-patients over 15 years.

HAP & COPD, the Strength of Association

A 2010 systematic review by Kurmi et al.[51] sought to quantify the health risk and strength of association between COPD and the use of solid fuels. On the whole, positive associations were found between the use of solid fuels and COPD (OR = 2.80, 95% CI 1.85 to 4.0) and chronic bronchitis (OR = 2.32, 95% CI 1.92 to 2.80). In a 2011 systematic review and meta-analysis Po et al.[41] focused on respiratory disease due to solid biomass fuel exposure in rural women and children. For chronic bronchitis in women they found an OR of 2.52 (95% CI 1.88 to 3.38) while for COPD they found an OR of 2.40 (95% CI 1.47 to 3.93). A 2010 meta-analysis by Hu et al.[60] found that biomass smoke exposure was clearly identified as a risk factor for developing COPD in both women (OR, 2.73; 95% CI, 2.28-3.28) and men (OR, 4.30; 95% CI, 1.85-10.01).

However, a fair bit of heterogeneity was found across the studies included in these systematic reviews and meta-analyses. One reason noted that could have been behind this is a lack of standardization across the definitions of COPD and/or chronic bronchitis.[51] The Global Initiative for Chronic Obstructive Lung Disease (GOLD), American Thoracic Society (ATS) and the European Respiratory Society (ERS) have all tried to resolve this issue with standardized criteria for COPD diagnosis.[55,61] This hinges on the use of spirometry, defining COPD as a post-bronchodilator FEV1/FVC ratio of less than 0.70.[55, 62]

However, this does not change the fact that spirometry, especially when done in the field in low-resource settings, can be a challenging diagnostic test. Alternatively, symptom-based diagnosis of chronic bronchitis is also used based on the Medical Research Council (MRC) standard which defines it as a history of cough with phlegm production for more than three months a year for at least two consecutive years.[63] However, here too issues arise with recall bias and the lack of a simple diagnostic test.

In a 2015, nonsystematic review Assad et al.[52], described COPD outcomes secondary to HAP from the combustion of various types of indoor solid fuel. Clinical evidence of this association has been well documented now for over 30 years, but it was mentioned that more data on exposure–response relationships from longitudinal studies are needed. Furthermore, data from low-income countries remain limited.[52]

The studies on the association between HAP and COPD highlighted by Assad et al.[52] included,

- A 2006 study by Regalado et al.[64] from rural Mexico found that biomass use was associated with a 4% decrease in FEV1/FVC ratio. Additionally, an increase in kitchen particulate concentration of 1,000 mg/m^3 was associated with a 2% reduction in FEV1. [64]
- A 2008 prevalence study of COPD across five cities and 5,500 Colombian adults performed by Caballero et al.[65] found an OR of 1.5 (95% CI, 1.22–1.86) for the association between 10 or more years of biomass stove use and spirometry-diagnosed COPD.
- A more recent 2013 study by Kurmi et al.[66] of 1,600 young adults in Nepal found an OR of 2.1 for the association between GOLD criteria COPD and exposure to (unquantified) biomass smoke.[66]
- A 2011 study of 900 women in India found 1.4 fold increase in COPD prevalence in biomass vs. clean fuel users.[67]
- In Brazil, a cross-sectional study found the prevalence of COPD defined by GOLD criteria in biomass smoke-exposed nonsmokers to be 20%, a rate that was similar to the prevalence in smokers who cook with clean fuel.[68]
- As mentioned, longitudinal studies of the impact of biomass smoke exposure on the development of COPD are lacking, but Ramirez-Venegas et al[69] looked at the association between COPD associated with biomass smoke exposure

and mortality. Their survival analysis over 7 years of follow-up found women with COPD due to biomass smoke had mortality rates similar to men with COPD due to tobacco smoking.

- A 2015 study by Jaganath et al.[70] across a diverse cross-section of Peruvian communities found that daily biomass fuel use for cooking among women in rural communities was associated with COPD with a prevalence ratio of 2.22 (95% CI 1.02–4.81). The population attributable risk (PAR) of COPD due to daily exposure to biomass fuel smoke was 55%.

Returning to the above mentioned 2010 systematic review by Kurmi et al.[51], Figure *22* below shows a forest plot summarizing the effect size of the association between GOLD-standard diagnosed COPD and various biomass fuel exposures. Note the gradient of effects across fuel types with wood smoke being associated with the largest effect.

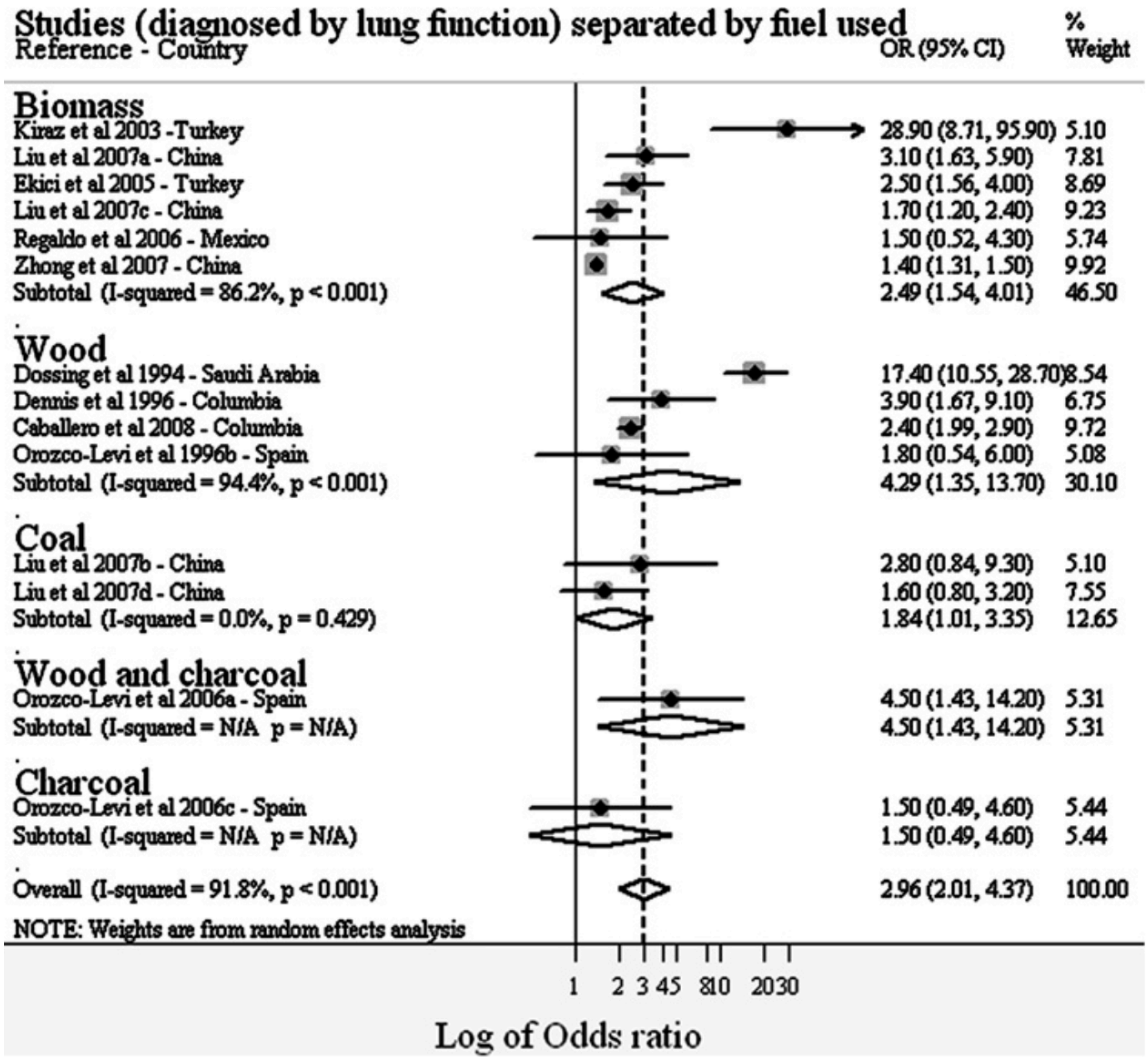

Figure 22: **Forest plot showing the effect size of COPD due to exposure to fuel types (for studies based on lung function diagnosis). N/A = not available. From source 51**

The Exposure-Response Relationship of HAP & COPD

An additional gap in the research regarding HAP and COPD is the characterization of an exposure-response relationship.[52] Such a characterization is vital to determining when and how an intervention could be implemented, and to what extent such an intervention could prevent the progression – or even reverse – the effects of HAP.

When biomass smoke exposure has been quantified by hour-years, a association has been found with FEV1.[68,71] This suggests a greater amount of exposure to biomass smoke is associated with greater respiratory impairment. Another study looked at the individual components of this metric to show that the OR for COPD is greater in subjects with either a greater number of years of exposure or more heavy exposure in the form of hours per day.[72]

Beyond the Traditional Health Impacts

While largely beyond the scope of this review, there are also numerous other impacts of HAP, which may affect health more broadly.

Risk of Physical and Sexual Violence

Girls and women are nearly always responsible for the collection of firewood and several studies have shown this responsibility may expose them to the additional risks of physical and/or sexual violence while walking miles from home.[3,73,74] This can be particularly problematic in refugee crisis situations. Studies have shown increased incidences of violence and rape of women during firewood collection in African refugee camps across Chad, Uganda, and South Sudan.[75]

Time Burden

The time burden of fuel-collection and cooking can be a major source of gender inequality in these communities as girls are more likely to drop out of school at earlier ages than their male peers to help with the labor-intensive cooking process.[73]

Climate Change

The emissions of HAP are known contributors to global warming.[3] In fact, the black carbon emitted from open fires is perhaps the 2nd leading cause of atmospheric carbon.[76] Additionally, the recent recognition of cleaner cooking as a major lever in reducing greenhouse gas emissions from lower income countries has resulted in a renewed effort on the part of development agencies *to scale up clean cooking programs.*[77]

Deforestation

On top of climate change, the consumption of wood leads to deforestation and the associated cascade of social, environmental, and climate consequences to come with it.[3]

2: Cookstoves as an Intervention for Household Air Pollution

The History of Cookstove Programs

As of 2014, there were at least 160 improved cookstove programs globally which has produced a vast and somewhat disorganized body of literature.[6] Even the basic term "improved cookstove" is used nonspecifically in the literature and widely touted by promoters with little consensus on what is the focus of the improvement.[78] This has created, at times, dueling priorities on which factors of improvement should be of focus: fuel-efficiency, HAP, cost-savings, etc. [79] In today's literature improved cookstove (ICS) simply refers to biomass-burning cookstoves which have sought to improve on traditional design to improve cooking efficiency and reduce HAP.[80] Though, it should be noted that ICSs do not necessarily reduce emissions to meet WHO air quality guidelines.[81]

Often seen as the world's leading expert on cookstove programs, researcher Kirk Smith wrote on the "Dialectics of Improved Stoves" in 1989[79] presenting the history of improving stove technology with human development. While humans had always been improving stove technologies Smith cites the 20th century as being unique with the first of "self-conscious" stove improvement movements.

India served as the birthplace of ICS programs with fuel- and cost-savings being the primary driver. Many of these programs origins grew out of the Gandhi era of the early 20th century. HAP was formally identified as a cause of health problems in India as early as the 1950s, and by the 1970s formal scientific research and engineering stove design had turned attention to ICS development.[6] Through this time, an era which Smith has termed the "energy period," the focus on ICS development was driven by "a global interest in appropriate technology, oil shortages, and deforestation.[79]" As mentioned, this created the dueling priorities of fuel-efficiency vs. smokeless stove design. In fact, even up until the turn of the millennium ICS design prioritized energy efficiency over HAP reduction.[78] In addition to India, ICSs were introduced to the Sahel region of Africa in the wake of an extreme drought to the region.[6] Central America also saw its first ICS program in this time after the Guatemalan earthquake of 1976.[82]

Smith called the emerging phase of the 1980s the "Phoenix phase" where experiences from early stove programs could inform the reemergence of successful programs with a focus on HAP. [79] Issues closely associated with traditional stove such as "women-empowerment, enhancement of livelihoods, and natural resource conservation" gained traction for the first time.[6]

The late 1980s into the 1990s ushered in a third phase of cookstove development with government-backed programs in India and China being two of the major events:[6,83]

- From 1982 to 1992 the Chinese National Improved Stove Program (NISP) became the largest and most successful cookstove program in history, introducing approximately 129 million new stoves while focusing on energy efficiency through the use of chimney-based cookstoves. [78,83,84] Even as government funding for the program dried up, private companies emerged, continuing to produce indoor pollution-reducing stoves.[83]

- Following the lead of China, the Indian Ministry for New and Renewable Energy launched an ambitious national cookstove program in 1985 that performed well below expectations.[83] It was concluded that the rural population being targeted had higher priority needs than the government's concern for deforestation. Additionally recognized influence of socio-cultural factors highlighted the need for improved assessment of cookstove programs with surveys and evaluation of cultural barriers.

However, with hindsight, Barnes et al.[85] concluded that the stove programs up to this point were, on the whole, not as successful as they could have been for a number of reasons. A major issue was – and I would argue continues to be – a lack of coordination between the innumerable ICS programs in existence. Additionally it was emphasized that all programs should understand the discrete role of ICS programs in facilitating a clear energy transition. As they said, *"The improved biomass stove should be considered a new stepping stone between the traditional biomass stoves used by rural and urban poor families and the modern fuels and appliances mainly used by urban, better off households."* The unfortunate reality is that a full transition up the energy ladder to complete electrification or clean fuel use such as LPG may be decades away for much of the world's poor (see *Figure 23,* below).[3] ICS programs should aim to alleviate the health burden of HAP while this population continues to rely on biomass fuels.

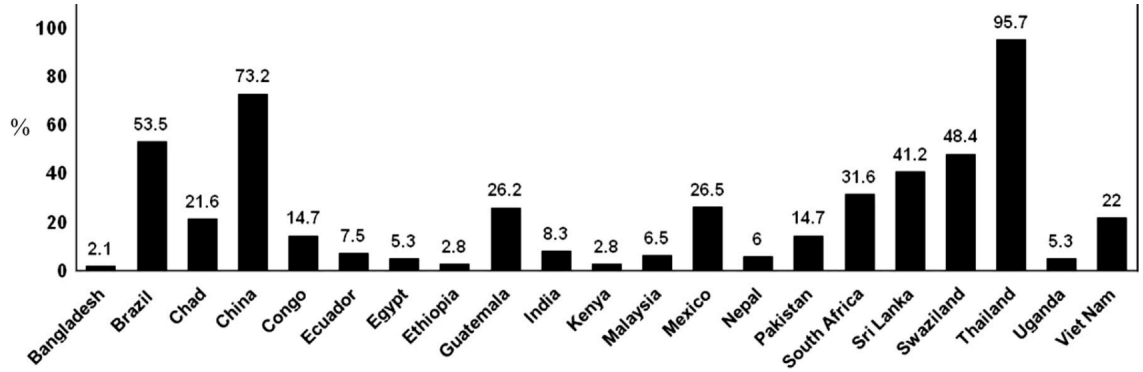

Figure 23: Percentage of people having access to ICS in some low- and middle-income countries as of 2009. From source [6]

In the new millennium, the health impacts of HAP have been more fully recognized as has been thoroughly documented above. This has set the stage for enormous foreign aid involvement on the part of the United States. In 2002, the U.S. EPA

launched the "Partnership for Clean Indoor Air." This was followed by the U.S. Department of State and EPA's co-launch of "The Global Alliance for Clean Cookstoves" in conjunction with the United Nations Foundation in 2010. The Alliance's goal calls for 100 million homes to adopt clean and efficient stoves and fuels by 2020. It has sought to unite more than 12 US governmental agencies and over 600 partners in the creation of global market for cleaner cookstoves.[6]

Types of Improved Stoves

To date countless ICS designs have been produced, a variety of which are pictured below in *Figure 24.*

Figure 24: Cookstoves from around the world. From source 35

Because of the great variety of stove designs, many schemas exist for ways in which to compare and contrast them based on construction material, size, fuel type, combustion, etc.[80] The most recent advances in cookstove technologies makes up a new class of stoves known as advanced biomass cookstoves (ABS).[6,80] Of these ABS stoves there are two primary categories: Rocket and Gasifier stoves.[80]

Gasifier stoves rely on two-stage combustion, meaning the wood (or other fuel material) is first heated to the point of the release of volatile gases.[6,86] These gases are then burned. Gasifier stoves have shown to produce a drastic reduction in emissions as compared to typical single-stage combustion system where the gases may be released up the chimney before being fully combusted. Gasifier stoves are

available with or without the use of a fan system to assist airflow.[6] The two most well-known Gasifier type stoves are currently the "Oorja" of India and the "Philips" stoves (show in *Figure 25 below)*.[6,86]

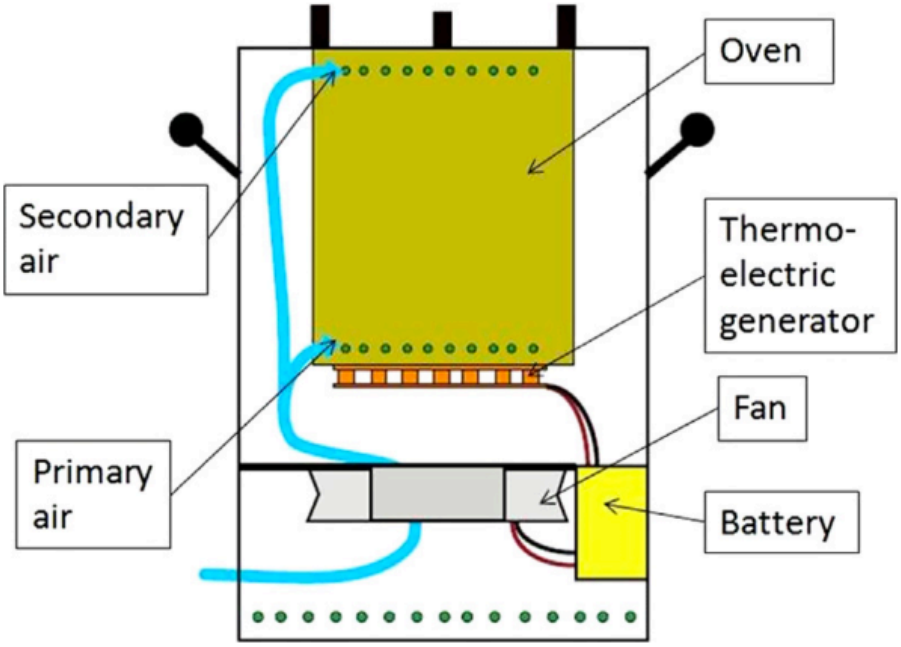

Figure 25: **Schematic of a Philips forced draft type cookstove with a battery-operated fan. From Source 87**

The so-called "Rocket stoves" apply the design principles developed by Dr. Larry Winiarski in 1980 into a characteristic L-shaped design (see *Figure 26* below).[87,88] As a class, Rocket Stoves have proven reliable and at times have performed even better than Gasifier stoves.[6] Still et al.[89] summarized a couple of the key design principles as,

- the use of an insulated and tremendously hot combustion chamber (over 1,100 F) to improve the mixing of fuel and flame resulting in improved combustion efficiency, as well as
- an insulated chimney creating a very strong natural draft

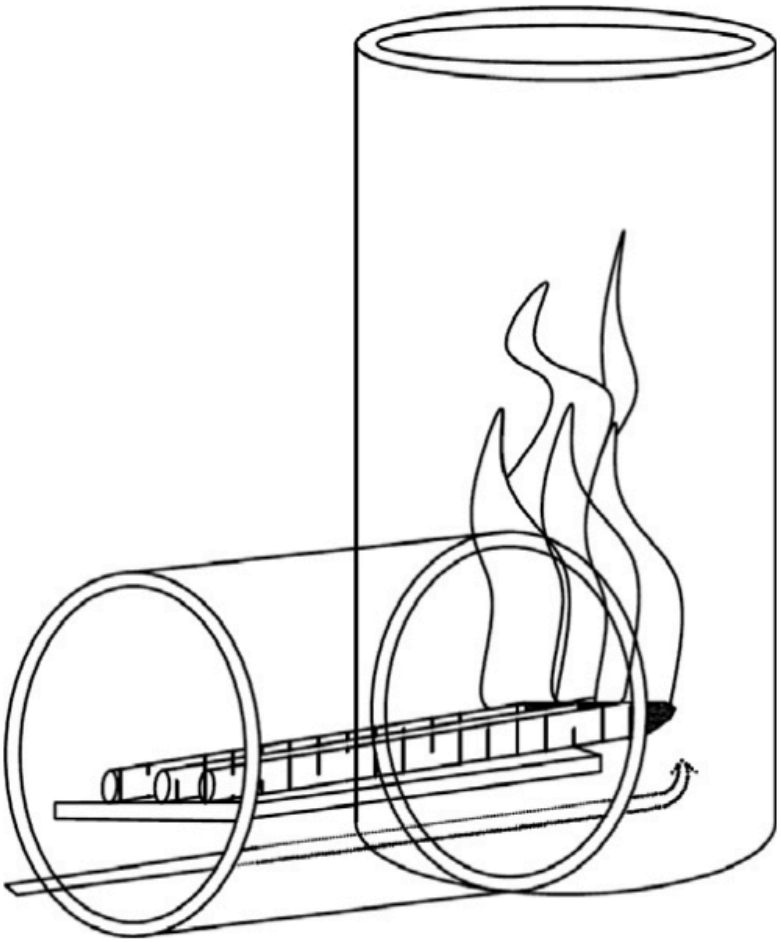

Figure 26: **A Schematic of the Rocket Stove Design. From source 83**

In a 2010 publication by MacCarty et al.[81] the fuel use and emissions performance of 50 different cookstoves were investigated. As a class, the Rocket-type stoves reduced fuel consumption by 33%, CO emissions by 75%, and PM emissions by 46% as compared to the three-stone fire cookstove.

One of the most successfully iterations of the rocket stove design is the ONIL cookstove produce by HELPS International, an international not-for-profit founded to provide medical care for the poor in Central America.[90] The ONIL stove was designed to meet the needs of its users through interviews with 60 women of the Guatemalan highlands (shown in *Figure 27* below).[91] The ONIL cookstoves have now been disseminated in Guatemala, Honduras, and Mexico at a cost of about $125 per stove. [90,92] In their 2014 review of cookstove performances Kshirsagar et al.[6] found the ONIL stove to be high-performing, low-polluting, and very safe to operate.

Figure 27: **Onil Stove. From source 90**

An additional plancha, rocket-stove design is the Ecostufa which is produced in Mexico at a cost of about $200 (see *Figure 28* below).[92,93]. Several thousand Ecostufas have been distributed across several Mexican states.[93]

***Figure 28*: Ecostufa. Source: Author's personal photo**

Liquefied petroleum gas (LPG)

Above improved biomass cookstoves on the energy ladder are the "modern fuels," generally considered to include liquefied petroleum gas (LPG), natural gas, and electricity.[94] Of these, LPG stoves have been most thoroughly investigated as a tool for HAP-reduction in low-income countries. Thus far, of the improved biomass cookstove options, none can reach the cleanliness of LPG. While continued development of fan-assisted gasifier stoves may get close to LPG-like HAP performance, even the best of improved biomass stoves remain at least an order of magnitude more polluting than LPG.[95] In virtually all cases, levels of respirable particulate matter follow the following trend across fuel sources [96]:

Dung > Crop residue > Wood > Charcoal > Kerosene > LPG > Electricity

In a study of more than 400 households, the personal exposure to respirable particulate matter (PM_{10}) was found to be about 70 $\mu g/m^3$ for households using LPG or kerosene compared to 2000 $\mu g/m^3$ for those using biomass as fuel.[96] The evidence is clear that LPG has unrivaled air quality benefits as compared to biomass fuels.[95,97]

In the long term, it is generally thought that modern fuels will be the answer to the HAP problem. The IEA has identified this with its "Universal Modern Energy Access" goal for 2030.[13] However, the current reality seems that LPG is unlikely to be a near-

term fix as it remain unaffordable for the poor of much of the world.[87] Fuel distribution is also a significant hurdle for the rural poor.[95]

Brazil has been a case study of success with the promotion of LPG. A 30-year program there brought significant penetration of LPG and kerosene through subsidies on these modern fuels.[97] However, the appropriate role of fuel subsidies in encouraging fuel switching is a debated topic in developmental economics.[97,98] It has been argued that public subsidies of LPG fuel use in a place like Guatemala would be regressive. By subsidizing current LPG fuel consumption, funds are allocated away from the expansion of modern energy access to those who are the most rural, the most poor, and least likely to have modern energy access.[98]

An additional – and often underestimated aspect – of LPG fuel uptake is the profile of a given household's cooking needs. For example, in Guatemala a major component of food preparation is the cooking of nixtamal (tortilla dough), which requires corn to be slowly cooked in large pots over several hours.[10] Preference and tradition has often made biomass the fuel of choice for this type of cooking, leaving LPG to fill the niche of breakfast and food re-heating fuel.[10]

Cookstove Programs: Barriers to Success

As mentioned above with the discussion of incomplete fuel switching with regards to LPG, so-called "stove stacking" has been a major barrier to success in the ability of ICS and LPG stove programs to reduce HAP as much as hoped. In considering the reality of fuel stacking, the model of an energy ladder with simple linear progression breaks down because a move *up* to a new fuel is not always accompanied by a *move away* from the greater HAP-producing fuels of the lower rungs.[98] Households tend to use every combination of stoves for the tasks that best fulfill their needs (see *Figure 29* below*).*[99]

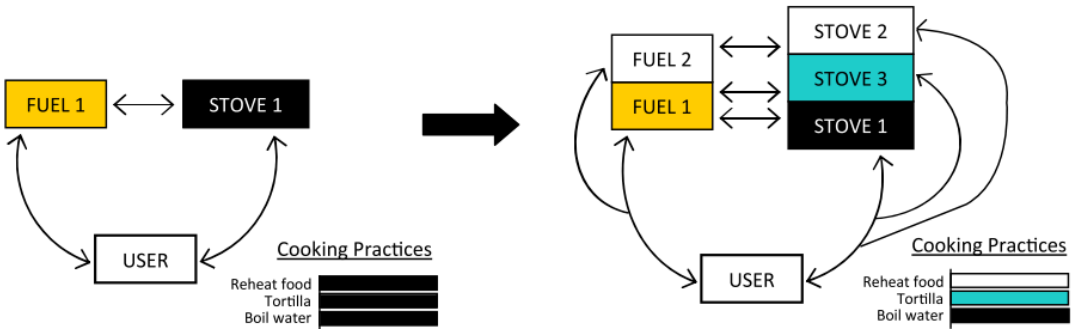

***Figure 29*: A schematic representation of a possible stove-stacking scenario. At left is a household with a single fuel cooking practice. After acquiring new stoves, the original cooking system transforms into a new system of three stoves and two fuels (right). The new stoves find a niche in the cooking practices of making tortillas and reheating food, while the old one is still used to boil water. From source 78**

Heltberg[94,98] has studied this fuel stacking phenomenon throughout the developing world and specifically within Guatemala from a behavioral economics point of view. *Figure 30* below shows that in Guatemala the relationship between the number of different fuels used by a household and welfare is somewhat U-shaped. As income rises, so too does the number of different cooking fuels types used. As income rises further, especially in urban areas, there is a transition back towards a single (modern) fuel. As a result of this phenomenon, firewood and LPG is a common fuel combination in Guatemala where it is used by 26% and 16% of urban and rural households, respectively.[94]

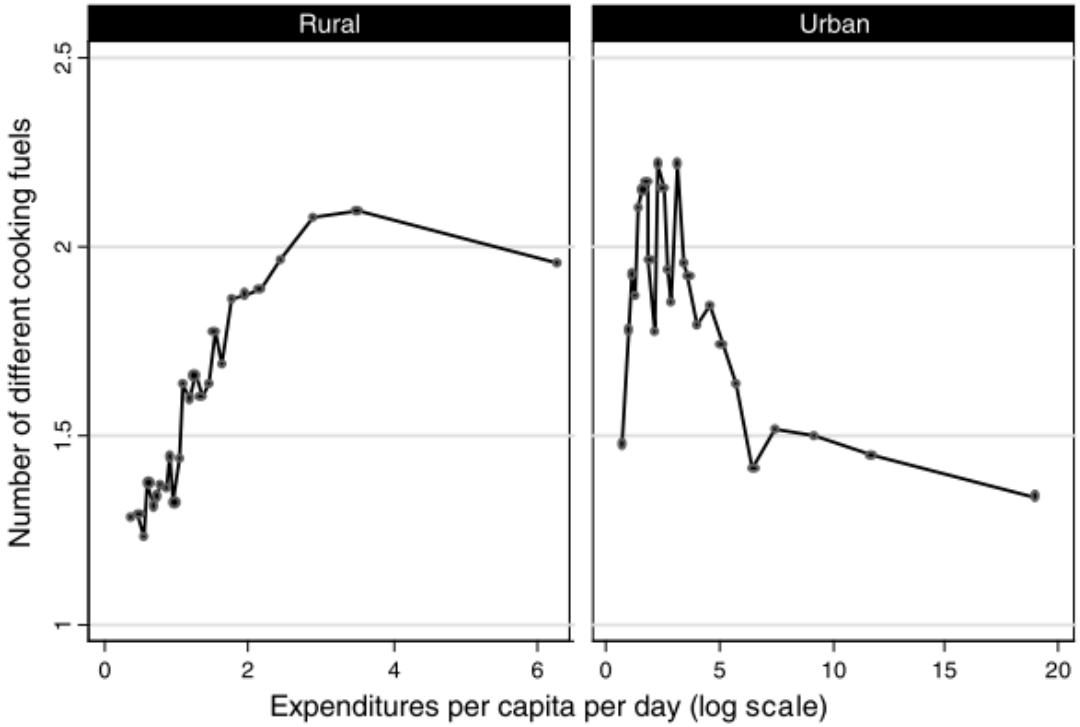

Figure 30: **The relationship between the average number of fuel sources utilized by rural and urban Guatemalan households and per capita, per day fuel expenditures. From Source 98**

A common shortcoming of stove programs is that relatively little effort has been devoted to understanding how well stoves are truly adopted and if their use is sustained over time.[78] However, due to the frequency of the stove-stacking phenomenon, quantitative assessment of stove usage has become a necessity of high quality stove programs. Direct observation of cooking activities has been considered the gold standard but may change participant behavior and is a demanding use of resources.[99] Simple temperature sensors known as Stove Use Monitors (SUMs) have largely replaced questionnaires, diaries, surveys, interviews and observations as a way to easily quantify adoption and fuel stacking.[99]

In addition to the question of whether stoves are being used as expected, there is the question of whether the field performance of an ICS matches laboratory tests of the stove. A 2015 review from Thomas et al.[100] sought to do this and found quite heterogeneous results. Amongst those included in the review, the study with the longest follow-up time (4 years) failed to show HAP reduction beyond one year.

In 2017 the Malawi-based CAPS study became the largest trial of a cookstove intervention on health outcomes in history but failed to find an effect on the primary outcome (childhood pneumonia incidence), an outcome that seems to be attributable to stoves that were not as reliable or effective as laboratory tests suggested, as well as to fairly widespread stacking.[43,101]

A key conclusion of WHO's 2014 indoor air quality guidelines (IAQG) was that while stove programs may produce notable relative reductions of HAP by 50-80%, in many cases the absolute PM levels remain well above the WHO interim target (PM_{10} of 35 $\mu g/m^3$ annual mean) where it is estimated that significant health improvements would result.[102,103] Based on these findings, it has been suggested that perhaps exclusive, community-wide use of clean fuels is the only way to reach the $PM_{2.5}$ guideline and maximize health benefits.[102,104]

Do stoves reduce COPD?

Relatively few studies have investigated the long-term effects of decreased HAP through cookstoves programs on lung function and obstructive lung disease.

In a 2005 study in Xuanwei, China, Chapman et al.[105] compared the incidence of self-reported COPD between people who installed chimneys against those who used only unvented stoves in a retrospective cohort study. The risk of COPD decreased with length of time since installation (see *Figure 31* below).

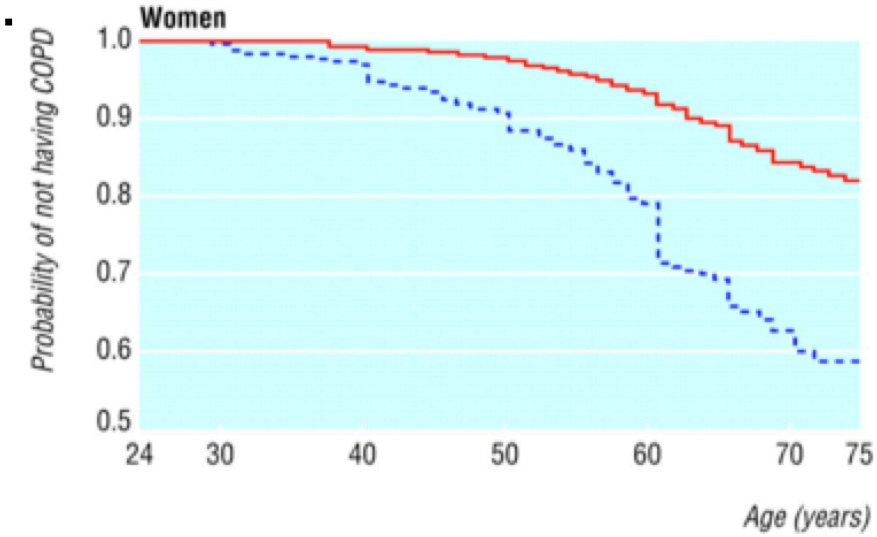

Figure 31: **Product limit survival plots showing probability of not having chronic obstructive pulmonary disease (COPD) by age in years in women according to whether they had a chimney (red solid line) or did not (blue dashed line), Xuanwei, China, 1976-92. From source 105**

Zhou et al.[106] performed a 9-year prospective cohort study on the effects of installing improved biomass stoves and/or exhausts to improve kitchen ventilation. Participants chose for themselves which intervention they wanted to adopt (biogas fuel, a kitchen ventilation fan, both, or neither). The use of the cleaner biogas (methane) fuel was associated with a reduced decline in FEV1 by 12 ml/y (95% CI, 4 to 20 ml/y) compared to those who took up neither intervention.[106] An exposure-response relationship was also seen as the longer duration of clean fuel use was associated with a slower decline in FEV1, as was the combined use of biogas and the kitchen fan .

In a cookstove intervention involving over 500 Mexican women, Romieu et al.[107] (2009) failed to observe a difference in symptoms or lung function between the intervention and control groups attributed to low adherence to use of the improved stove. However, self-reported use of the improved stove was significantly associated with a reduction in both smoke-related symptoms and FEV1 decline over 1 year of follow-up.

As a part of the RESPIRE study, Smith-Sivertsen et al.[108] (2009) also reported that the improved chimney stove was significantly associated with a reduced risk of respiratory symptoms in an intention-to-treat analysis, but no significant effect on lung function was observed. However, in a later exposure-response analysis of the same study participants, reduced exposure to CO was associated with a slower decline in lung function.[109]

3: Conclusions and Research Questions

Ultimately the questions of,

- How clean does a cookstove have to be to reduce and/or eliminate HAP-associated disease?
- And, what household energy technology will get us there?

remain incompletely answered.[110]

Imbedded within the first question is the elucidation of the exposure-response for HAP and obstructive lung disease (chronic bronchitis and COPD). A more complete understanding of this phenomenon is necessary to understand whether the progression of COPD due to HAP may be stopped – or even reversed. These are the beginning steps to understanding how the most effective cookstove intervention should be designed. Perhaps a physician in a low-income country will one day be able to definitively "prescribe" new, cleaner stoves to COPD patients.

Part 2: A Pilot Study for the Intervention of Improved Cook Stoves in the Reduction of COPD in the Highlands of Guatemala

Introduction

Approximately 40% of the world's population - roughly 2.8 billion people - cooks with biomass fuels, such as wood or other organic matter, on a daily basis.[1] Oftentimes this cooking occurs on open fires indoors creating homes where the particulate matter is often 10 times what is typically found within the ambient air of higher income countries. The resulting household air pollution (HAP) is a major health concern in low- and middle-income countries (LMIC). This has been well-documented with over 200 studies that have assessed the levels of HAP in the past 30+ years.[2]

In the Global Burden of Disease's Comparative Risk Assessment, 4.5% of the disability adjusted life-years lost are attributed to HAP due to acute lower respiratory infections in children and chronic obstructive pulmonary disease (COPD), lung cancer, cataracts, and cardiovascular disease in adults. [2,34] COPD, specifically, is of significant and growing importance in terms of its share of global mortality and morbidity. Formerly seen as primarily a smoking-related disease in developed countries, projections show that by 2020 COPD will be the 3rd leading cause of global mortality and morbidity.[1,51]

Women tend to have the highest levels of biomass smoke exposure, and numerous epidemiologic studies of women in developing countries have shown strong associations between the use of biomass cooking fuel and chronic bronchitis and/or COPD.[24,72,111–115] Improved stoves include both designs which use chimney systems to remove smoke from the home and liquid petroleum gas (LPG) stoves, which give off dramatically less particulate matter into the air. Specifically, there have yet to be any longitudinal studies allowing for the quantification of the effect of biomass smoke exposures on the rate of decline in lung function. Nor have there been studies on the efficacy of different improved stove designs to slow the rate of decline in lung function due to biomass smoke.[52,53]

To obtain preliminary data that could serve as a stepping-stone towards a much larger study, we carried out a pilot feasibility study of stove interventions in a cohort of women with chronic obstructive pulmonary disease (COPD) or chronic bronchitis and exposure to HAP from the use of biomass fuels in the rural Guatemalan highlands.

Methods

Ethical Considerations

All research discussed herein was approved by the Research Ethics Committees at the Universities of California-San Francisco, California-Berkeley, and de Guatemala Valle.

Overview

This is a study of a cohort of women with COPD and/or chronic bronchitis and exposure to HAP from the use of biomass fuels followed prospectively for six months. The study was conducted in the Department of Quetzaltenango, Guatemala where 40 participants were randomized into one of four stove intervention strategies intended to reduce HAP exposure: (1) an Ecostufa, improved wood-burning stove with chimney design, (2) a Helps-Onil, improved wood-burning stove with chimney design, (3) a liquefied petroleum gas (LPG) Supercocina stove, and (4) an identical LPG stove with a subsidy for 50% of household propane use (see *Figure 32 below).*

***Figure 32*: The four stove groups**

The goal of this pilot study was to evaluate the feasibility of carrying out a larger stove intervention study to investigate whether an improved stove intervention can slow – or even reverse – the progression of COPD in women exposed to biomass smoke. This goal generates three main research questions:

1. Is it feasible to conduct a large-scale study to test the effectiveness of a stove intervention to delay the progression of COPD in women exposed to biomass smoke?
2. Which of the four interventions evaluated in this pilot study has the greatest effectiveness in reducing exposure to HAP?
3. Which of the four interventions evaluated in this pilot study has the greatest acceptability for use?

The study area includes 10 municipalities around the city of Quetzaltenango in the western highlands of Guatemala (Almolonga, Cantel, Concepción Chiquirichapa, La Esperanza, Olintepeque, Salcajá, San Juan Ostuncalco, San Martín Sacatepequez, San Mateo, Zunil). Illiteracy is common in this region, especially amongst women. Mam is the first language of most people while Spanish is spoken at variable levels of fluency from almost not at all to fully fluent. Prior work here showed both that women spend an average of 5 hours daily in a room with a lit fire and that tobacco smoking levels are very low among Mam women.[116,117]

Timeline

Recruitment and data collection for this study were performed between October 2015 and May 2017. In the manner discussed below, study subjects were recruited and baseline measures were obtained on those who provided consent. Repeat measures were then taken at both 3 and 6 months post-stove installation. Following completion of data collection at approximately 6 months after installation, participants were free to keep the stoves and do with them as they wished (see *Figure 33* below).

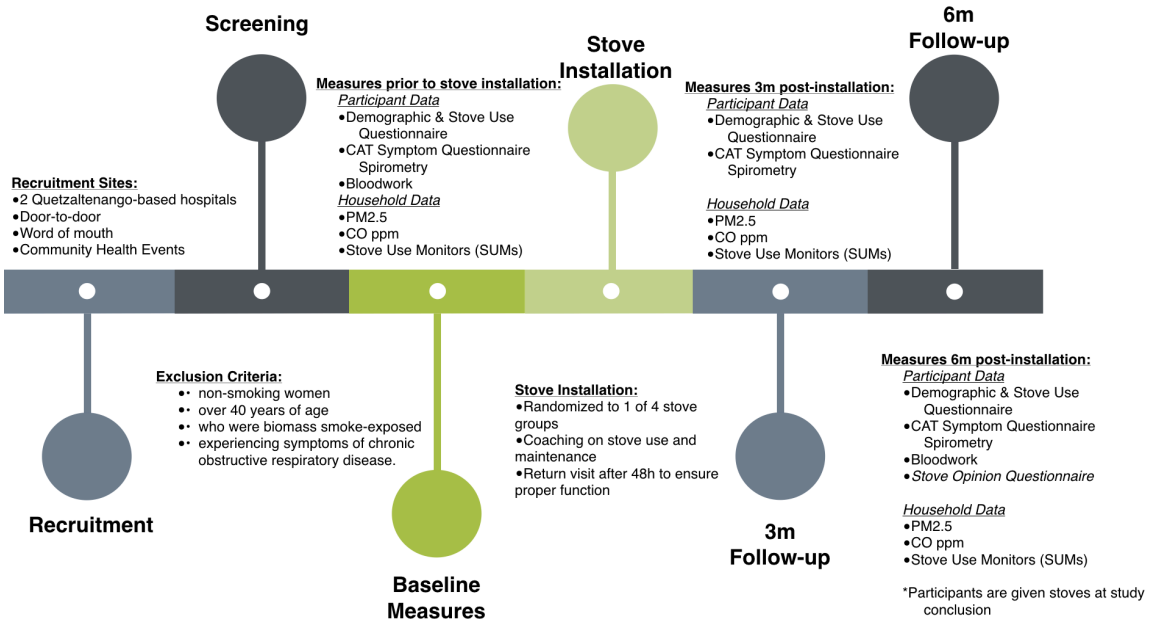

***Figure 33*: Project Timeline**

Participant Inclusion Criteria & Target Number

As originally designed, inclusion criteria for this study were:

- non-smoking women
- over 40 years of age
- who were biomass smoke-exposed,
    - due to either:
        - the use of an open-fire stove without a chimney or
        - the use of a biomass-burning stove with a chimney, which was in poor condition with obvious structural damage and significant smoke leaking into the cooking space
- experiencing symptoms of chronic respiratory disease, including
    - cough,
    - phlegm production, and
    - shortness of breath
- with a spirometry-confirmed diagnosis of COPD according to the ATS-GOLD criteria[55] of an FEV_1/FVC ratio less than 0.70.

After six months of persistent recruitment difficulties, the final criterion of spirometry-confirmed COPD according to GOLD criteria was relaxed to a symptom-based diagnosis of chronic bronchitis according to the Medical Research Council (MRC) standard[63], defined as a history of cough with phlegm production for more than three months a year for at least two consecutive years plus adequate quality spirometry. Due to the expansion of the inclusion criteria, our study population consisted of 20 women with GOLD criteria COPD and 20 women with MRC-standard chronic bronchitis.

As a pilot study, 40 was seen as a practicable and sufficiently large sample size, given limited study resources. Statistical power was not a consideration in sample size decisions, because it was not our objective to determine an association between exposure and outcome.

Recruitment

Recruitment for participation in our study occurred between Fall 2015 and Fall 2016. The initial recruitment plan was that women with chronic respiratory symptoms would be identified among patients hospitalized in or attending the outpatient clinic of the San Juan de Dios Hospital or the Rodolfo Robles Hospital in Quetzaltenango. However, this approach yielded very few participants because

- the majority of patients visiting these hospitals in this urban center were not using open fire stoves, and
- of those who were using such stoves, many arrived at the hospital with severe COPD exacerbations and were too sick to participate in the study.

As a result, additional women with chronic respiratory symptoms were identified through records of health services in each municipality and through home visits in coordination with staff of these health services. To enhance recruitment a combination of door-to-door and word of mouth promotion as well as community health events held at local schools were also utilized in the recruitment process.

Participant Screening

Screening of potential participants for eligibility according to inclusion criteria was performed using a simple questionnaire of demographic variables, exposure, and symptoms associated with COPD. The questionnaire was developed based on screening questionnaire already tested in English and translated into Spanish by a qualified translator. Questionnaires were administered by a bilingual Mam- and Spanish-speaking team of field workers, who carried out all interactions with study participants. If, according to the screening questionnaire, candidates for the study had one of the following:

- cough multiple times a day over the majority of days and nights for the last three months,
- phlegm production the majority of days and nights for the last three months, Or
- shortness of breath during physical activity that they gauged to be worse than others their age

and met the first three elements of the previously defined inclusion criteria (non-smoking women, over 40 years of age, biomass smoke-exposed), they were referred for the spirometry screening described below.

Spirometry

Screening lung function testing by spirometry was carried out on the completion of a positive screening questionnaire. Standing height without footwear was measured

in the field using a stadiometer. Weight was measured in light clothing using an electronic scale. Spirometry was then performed in accordance with European Respiratory Society/American Thoracic Society guidelines using the EasyOne Spirometer (ndd Medical Technologies, Andover, MA, USA). Calibration checks of the spirometer were undertaken at the beginning of each day of use. For spirometry, participants were seated without nose clips. All tests were performed 10 minutes after the administration of 90µg of albuterol using a spacer device. Pre-bronchodilator spirometry was not carried out. Measurements were classified as acceptable if the woman had at least three good exhalations, and if best and second-best values of both FVC and FEV1 did not differ by more than 0.20 L. Two local bilingual (Mam and Spanish) field-workers performed the spirometry testing.

As discussed above, the first 20 participants were women who produced a baseline spirometry with an FEV1/FVC ratio less than 0.70. For the next 20 participants, women who screened positively for MRC-standard symptoms of chronic bronchitis and were able to produce acceptable spirometry were included, even if they did not meet GOLD criteria for COPD.

The women who participated in the study had spirometry testing at three time points: at baseline (prior to new stove installation) as well as 3 months and 6 months post-stove installation.

All spirometry sessions were reviewed by an experienced pulmonologist (Dr. John Balmes) for quality grading, according to modified ATS/ERS performance criteria, as follows:

- 3: All parts of the expiratory flow-volume curve are acceptable and all parameters can be used
- 2: Minor issues may exist (e.g., evidence of cough) but all parameters can be used
- 1: Quality issues exist at the end of test, but the majority of the curve is acceptable. Only the FEV1 value is acceptable
- 0: No portion of the curve is acceptable

Additionally, the EasyOne spirometry software applied a grade of reproducibility for each session where grades are as follows:

- A: >=3 acceptable tests AND the difference between the best 2 FEV1 & FVC is <=100ml
- B: >=3 acceptable tests AND the difference between the best 2 FEV1 & FVC is <=150ml
- C: >=2 acceptable tests AND the difference between the best 2 FEV1 & FVC is <=200ml
- D: >=2 acceptable tests BUT results are not reproducible OR only 1 acceptable test
- F: No acceptable tests

As elaborated below in the statistical methods section, analysis of spirometry data occurred in two rounds:

1. All acceptable FEV1 values (without consideration for reproducibility)
2. Sensitivity analysis using all sessions with reproducibility grades of A, B, or C, where at least two curves were found to be acceptable

Stove Group Randomization and Installation

Women who met the above inclusion criteria and provided informed consent were randomized to one of the four stove groups as indicated above. The field team was kept independent of the randomization of stove types. The Mam- and Spanish-speaking field team was responsible for stove installation. In addition to the installation visit, participant homes were again visited within 48 hours of installation to ensure the stove was working properly and that the participants were familiar with its proper use and maintenance.

Demographic, Respiratory Symptoms, & Cooking Habits Questionnaire

Information on household demographics, current stove use, and fuel types was obtained via an interviewer-administered questionnaire. Questions about chronic respiratory symptoms were from the COPD Assessment Test (CAT), which was translated into Spanish.[118] The CAT consists of scoring eight symptoms of COPD on a scale of 0 (nonexistent) to 5 (very severe). Additional questions regarding health outcomes (e.g., recent illness and exacerbations) were also included in the questionnaire. All interviewers were bilingual in both Mam and Spanish. While the questionnaire was written in Spanish, the interviewer provided Mam clarification as needed.

The demographic, CAT, and cooking habits questionnaire was completed at the same three time points as spirometry: at baseline (prior to new stove installation), 3 months, and 6 months.

Blood Sample Collection

Blood samples were collected by standard phlebotomy at baseline (prior to new stove installation) and six months post-installation. Five mL of whole blood were drawn from participants and divided between two tubes: one for serum and one for whole blood. Once collected from the field, blood samples were transported in coolers to the laboratory at San Juan de Dios Hospital in Quetzaltenango. Lab personnel prepared serum, plasma, buffy coat, and Flinders Technology Associates (FTA) card samples (Whatman, Inc., Clifton, New Jersey). The FTA card samples were kept at room temperature while other samples were maintained at -20°C while in the hospital lab. Biweekly transport of collected samples was made to the University of Guatemala-Valle laboratory in Guatemala City. Here the FTA cards continued to be stored at room temperature while other samples were maintained

at -80°C. Upon collection of all samples, bulk shipment was made to Emory University in Atlanta for analysis. At the date of writing, this analysis has not been completed, but will be included in a future manuscript.

Stove usage measurement

We utilized Thermochron iButtons 1921G (Maxim Integrated Products, Sunnyvale, CA) temperature dataloggers as Stove Use Monitors (SUMs) to determine stove usage and obtain counts of the daily meals from the temperature signals. These button-sized, battery-operated devices did not disrupt cooking activities. Two weeks prior to new stove installation SUMs were placed on the original stove(s) and/or open fires used for cooking in participant homes, for two full weeks of data collection. Additional SUMs data were collected at three and six months post-installation when the SUMs were placed on the intervention stoves as well as the original stoves and/or open fires. Each of the three periods of stove temperature logging lasted two weeks. During periods of SUMs temperature monitoring, return visits were made after one week to ensure the SUMs were functioning correctly.

Spikes in temperature as measured by the SUMs were used to count cooking events and determine the percent of cooking events using the new vs. old stove(s). This analysis will be included in a future manuscript.

Exposure measurement

Kitchen monitoring

For particulate matter (PM) measurements in all participant kitchens, the UCB Particle Monitor and Temperature Sensor (UCB-PATS), a PM monitor based on light scattering, was used with a temperature sensor, which has been validated in the laboratory and in the field and widely used by researchers in India, Nepal, Guatemala, China and elsewhere.[119–122] The UCB-PATS has been widely used in areas in Guatemala around the site of this study. Measurements of PM with a mass median diameter ≤2.5 $\mu m/m^3$ ($PM_{2.5}$) in the kitchens of all participants were carried out using a standard monitor location protocol, placing the UCB-PATS 1.5 meters high on the wall and more than 1 meter away from any door or window.

A sample of one-third of participating households was systematically selected also to have $PM_{2.5}$ concentrations measured in the kitchen using a gravimetric monitor with a TUFF™ Personal Sampling Pump (Casella, Bedford, UK), an SKC impactor (http://www.skcinc.com/pumps.aspz) and pre-weighed 37mm filters. CO measurements were made with a Lascar monitor (EL-USB-CO300). These gravimetric $PM_{2.5}$ and CO monitors were co-located in the area with the UCB-PATS monitors. We took these gravimetric measurements in two 24-hour periods during the study: once before installation of the intervention stove and the second time at three months after installation. These measurements were used for the calibration of the UCB-PATS monitors. Pre- and post- measurement of Casella filter weights

were performed in the same micro-scale (with microgram accuracy) at Harvard University School of Public Health laboratory in a room with environmental control. At the date of writing, analysis of kitchen-based exposure measures has not been completed and will be included in a future manuscript.

Personal monitoring

All participants received personal $PM_{2.5}$ gravimetric monitoring in three 24-hour periods (before installation of the intervention stove, at 3 months and at 6 months) using the same Casella TUFF™ gravimetric measurement devices as above. Flows were set to 1.5 LPM using a rotameter for calibration. A Lascar CO monitor was placed in conjunction with the $PM_{2.5}$ personal monitor and at the same time when CO monitors were placed in the kitchen.

Both devices were set for 24 hours of data collection and fitted within a vest worn outside of the woman's other clothes where each monitor sat in the upper chest area. Willingness to undergo personal monitoring was a condition of participation assessed in our consent procedures. Participants were instructed to go about their days as normally as possible while wearing the vest with the monitors at all times. They were instructed to place the vest with monitors at the head of the bed during sleeping periods. While the Lascar CO data are analyzed here, analysis of the gravimetric $PM_{2.5}$ data will be included in a future manuscript.

Data Management

Initial questionnaire data in the field were recorded on paper. Data were then entered into EpiInfo 2000 software (CDC, Atlanta, USA) before being exported to spreadsheets (Microsoft Excel 2011; Microsoft Corporation, Redmond, WA). Spirometry data were handled in the EasyWare software (ndd Medical Technologies, Andover, MA, USA) before being exported to a database (Microsoft Access 2011; Microsoft Corporation, Redmond, WA).

Statistical analysis

The analysis component of this project was handled in Excel and R (R Development Core Team, 2005). Excel was used to check for data entry consistency, while R was used to execute all data cleaning, statistical analyses**,** and data visualizations.

Baseline Assessment of Normality and Randomization

All baseline variables were examined to check for normality and randomization of their distributions across the stove groups using appropriate statistical tests (chi-squared test for categorical variables and analysis of variance testing for comparison of mean values).

Baseline Analysis

Using measures collected at baseline (prior to stove installation), the following analyses were performed:

1. **Association between symptom burden and mean personal CO level at baseline**

2. **Association between spirometry measures and mean personal CO level at baseline**

Age was considered as a covariate in each of the above analyses and multiple linear regressions were performed.

Longitudinal Analysis

Using changes in measures from baseline to 6 months, the following analyses were performed:

3. **Association between change in mean personal CO level and stove type**

4. **Association between change in symptom burden and stove type**

5. **Association between change in spirometry measures and stove type**

A simple linear regression was used in analyses 3 to 5.

Results

Sociodemographic characteristics and baseline measures

Table 1 shows data on principal background characteristics as well as baseline measures of symptom burden, CO exposure, and spirometry, stratified by stove assignment groups. An indication of differences between stove groups was found only in one instance: weekly use of the temescal.[b] Because the stove groups were assigned randomly, this difference is likely to be a result of chance and would not be likely to occur in a study with a larger sample size. Temescal use is unlikely to have been influenced by the type of stove a participant was assigned, but is a likely source of increased CO exposure.

Approximately 48% of the women cooked using an open fire (n = 19) while the others cooked on a stove determined to be in poor condition with a significantly damaged or non-functional chimney.

[b] A ''temescal'' is a sauna-like structure in which a wood fire is first lit to heat water and rocks. When the fire is out, the people enter the steamy environment to bathe. The interior dimensions are about 1.5 m long by 1 m wide by 1 m high. Bathing in the temescal is typically done once per week and may be a significant source of HAP exposure

Table 1: **Sociodemographic characteristics stratified by stove assignment group.**

† indicates missing data; n = 9 for this measure

	Ecostufa, mean (SD) or n(%)	**Onil,** mean (SD) or n(%)	**Gas,** mean (SD) or n(%)	**Gas Subsidy,** mean (SD) or n(%)	**p**
n	10	10	10	10	
Characteristics of Women					
Age	63.20 (13.44)	59.60 (6.70)	58.50 (9.40)	59.90 (11.44)	0.78
Have Open Fire?	2 (20.0)	5 (50.0)	6 (60.0)	6 (60.0)	0.23
Hours Per Day in Kitchen	4.00 (1.69)	5.80 (1.55)	5.30 (2.06)	4.30 (1.16)	0.081
Years of Education	0.67 (1.32)	0.70 (1.25)	0.70 (1.06)	0.60 (1.26)	1.0
Baseline CAT Burden Score					
Cough	2.90 (1.29)	2.90 (0.88)	2.10 (0.99)	2.60 (1.17)	0.33
Phlegm	2.80 (1.03)	2.90 (0.99)	2.70 (1.25)	3.10 (1.45)	0.89
Chest Pressure	3.30 (0.67)	2.90 (1.20)	2.50 (1.08)	3.20 (0.79)	0.26
Shortness of Breath	3.30 (0.82)	3.20 (0.79)	2.90 (1.20)	3.20 (1.14)	0.83
CAT Burden Sum	23.20 (6.86)	21.89 (5.67)	20.40 (6.60)	23.10† (6.30)	0.74
Household Characteristics					
Smoker in Home?	2 (20.0)	1 (10.0)	1 (10.0)	0 (0.0)	.53
Use a Temescal Weekly?	6 (66.7)	2 (20.0)	5 (50.0)	8 (80.0)	.046*
Electricity in Home	9 (90.0)	10 (100.0)	9 (90.0)	8 (80.0)	.53
People Living in Home	5.00 (3.43)	6.00 (3.71)	6.20 (3.85)	5.10 (2.77)	.82
Baseline Exposure Means					
24h mean personal CO at baseline (ppm)	0.96 (1.08)	1.85 (1.72)	2.08 (2.03)	3.08 (3.66)	0.26

	Ecostufa, mean (SD) or n(%)	**Onil,** mean (SD) or n(%)	**Gas,** mean (SD) or n(%)	**Gas Subsidy,** mean (SD) or n(%)	**p**
Baseline Lung Function Measures					
n	6	8	7	9	
FEV1	1.81 (0.57)	1.95 (0.41)	1.59 (0.45)	1.58 (0.44)	0.33
FVC	2.21 (0.64)	2.65 (0.45)	2.10 (0.53)	2.16 (0.46)	0.16
FEV1/FVC Ratio	.82 (0.04)	.74 (0.10)	.76 (0.11	.73 (0.09)	0.32

*** p < 0.001, ** p < 0.01, * p < 0.05

Baseline Analysis

1. Association between symptom burden and mean personal CO level at baseline

A strong, positive relationship can be seen between age and symptom burden at baseline. The relationship of age to our dependent variable, symptom burden, can be interpreted as a 0.31 point increase every year, or 3.1 points every decade (i.e. worsening symptoms with increasing age) as can be seen below in *Table 2* and *Figure 34*. In the context of the 40-point CAT score, a 2 to 3-point change has been demonstrated to be clinically significant.[123]

While personal $PM_{2.5}$ is considered the gold standard of woodsmoke exposure, it has been shown that personal CO exposure correlates well with exposure to $PM_{2.5}$ in this population of wood-fuel users; some have made the case for its use as a proxy for $PM_{2.5}$ exposure.[24] However, analysis on forthcoming $PM_{2.5}$ data will be performed to validate this assumption.

Carbon monoxide concentrations did not have a significant relationship with the participants' symptom burden (*B = -0.28; p-value = 0.45).* This model's findings support expected health trends with symptom burden increasing with age (and presumed years of HAP exposure) but do not establish a direct link between current CO exposure in the household and respiratory health at baseline.

Table 2: **Regression of CAT symptom burden on age and mean personal CO levels at baseline**

	Coefficient (B)	*SE B*	*t-value*	*P-value*
Intercept	3.98	5.46	0.73	0.47
CO PPM	-0.28	0.37	-0.76	0.45
Age	0.31***	0.08	3.62	<0.01
R^2	0.31			
Num. obvs.	39			
RMSE	5.34			
F-statistic	7.93**			<0.0001

*** p < 0.001, ** p < 0.01, * p < 0.05

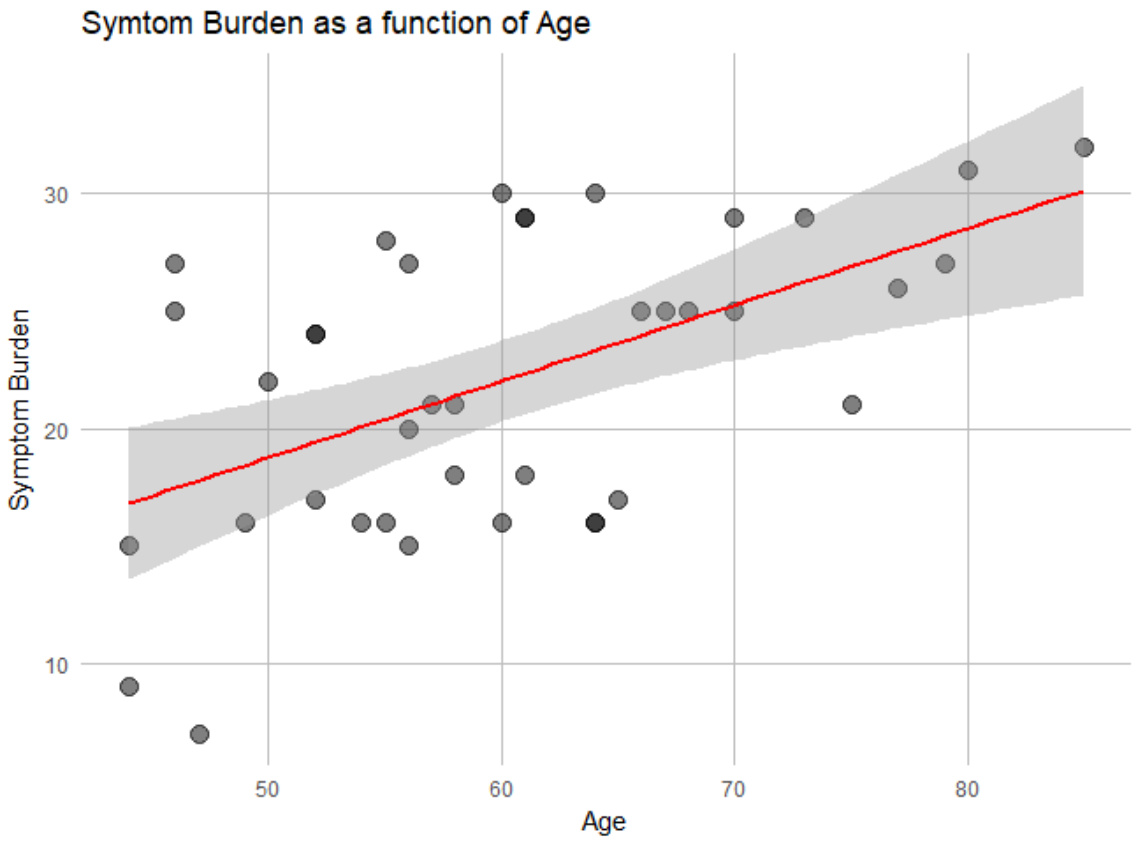

Figure 34: **Linear Regression Plot of Symptom Burden by Age at baseline.**

2. Association between spirometry measures and mean personal CO level at baseline

While the expected decrements in lung function parameters by age were observed, there were no statistically significant associations between mean 24-h personal CO levels at baseline and lung function measures (FEV_1, FVC, or FEV_1/FVC ratio) (*Table 3)*.

Table 3: **Regression output for the association between spirometry measures and mean CO levels and age at baseline**

	Dependent Variable			
	FEV_1	FEV_1 (sens)	FVC	FEV_1/FVC Ratio
Intercept	3.65***	3.97***	3.88***	1.04***
	(0.47)	(0.49)	(0.73)	(0.14)
PPM baseline	0.02	0.02	0.07	0.00

	(0.03)	(0.03)	(0.06)	(0.01)
Age	-0.03***	-0.04***	-0.03*	0.00
	(0.01)	(0.01)	(0.01)	(0.00)
R^2	0.46	0.51	0.30	0.16
Num. obvs.	30	28	26	26
RMSE	0.36	0.35	0.47	0.09
F-Statistic	11.45***	13.05***	4.95*	2.11

*** p < 0.001, ** p < 0.01, * p < 0.05

The f-statistics in the first three models indicate that at least one of the potential predictor variables is associated with the response variables. As expected, the effect estimates show that age has a strong, negative relationship with lung function: Holding CO levels constant,

- FEV1 decreased by 0.03 L for every year increase in age
- FEV1 (sensitivity analysis) decreased by 0.04 L for every year increase in age
- FVC decreased by 0.03 L for every year increase in age

The R^2 value increases when moving from the more inclusive FEV_1 model 1 to sensitivity model with stricter (less inclusive) use of FEV_1 values. Age and CO exposure seemed to have little to no association with the FEV1/FVC ratio. The actual estimate for age was -0.004 with a marginally significant p-value, indicating a weak negative relationship as would be expected.

An outlier in CO concentrations was present in the first three models, but the removal of this outlier did not have much of an effect on the analysis results. Furthermore, the outlier was within reasonable levels for CO levels in the population.

Longitudinal Analysis

3. Association between change in mean personal CO level (baseline to 6 months) and stove type

The outcome variable was the difference in mean 24-h CO level from baseline to six months, and the exposure variable was the type of stove installed in the household.

***Table 4*: A summary of 24h personal CO measures (ppm) across time in the study**

Exposure Means	**Ecostufa,** mean (SD) or n(%)	**Onil,** mean (SD) or n(%)	**Gas,** mean (SD) or n(%)	**Gas Subsidy,** mean (SD) or n(%)	**p**
24h mean personal CO at baseline (ppm)	0.96 (1.08)	1.85 (1.72)	2.08 (2.03)	3.08 (3.66)	0.26
24h mean personal CO at 3 months (ppm)	0.88 (0.48)	1.09 (0.59)	1.12 (0.75)	1.28 (0.89)	0.65
24h mean personal CO at 6 months (ppm)	1.57 (1.17)	2.08 (0.99)	1.74 (1.56)	2.77 (3.61)	0.60
Change in CO from baseline to 6m (ppm)	0.61 (2.00)	0.23 (2.09)	-0.34 (2.92)	-0.31 (5.73)	0.92

The model was:

$$\text{CO difference} \sim \text{stove type} + \text{error}$$

The Ecostufa stove was used as the reference group because it was considered to be the least likely to reduce CO exposure and least popular of the four and, therefore, most similar to the original stoves that were in the homes.

Table 5: **Regression output for the association between change in CO levels and stove groups over 6 months.**

	Delta CO (6 mo-baseline) in PPM			
	Coefficient (B)	*SE B*	*t-value*	*P-value*
Intercept (Ecostufa)	0.61	1.11	0.55	0.59
Onil	-0.37	1.58	-0.24	0.81
Gas	-0.95	1.58	-0.60	0.55
Gas with Subsidy	-0.92	1.58	-0.58	0.56
R^2	0.01			
Num. obvs.	40			
RMSE	3.52			
F-statistic	0.17			0.91

*** p < 0.001, ** p < 0.01, * p < 0.05

The null hypothesis was that there was no change in CO difference across the stove types, and there is insufficient evidence to refute it. An estimate of 0.61 and its associated p-value of 0.59 fail to indicate a non-zero value for the intercept. The estimates for the three other stove types are all slightly negative; however, the standard errors are large enough to create confidence intervals that span 0, and the p-values are well above 0.05. As was anticipated given the small cookstove group sample sizes in this pilot project, the model had difficulty finding anything more than a weak signal in the data.

Two outliers existed with the Gas Subsidy group, as can be seen in the following graph:

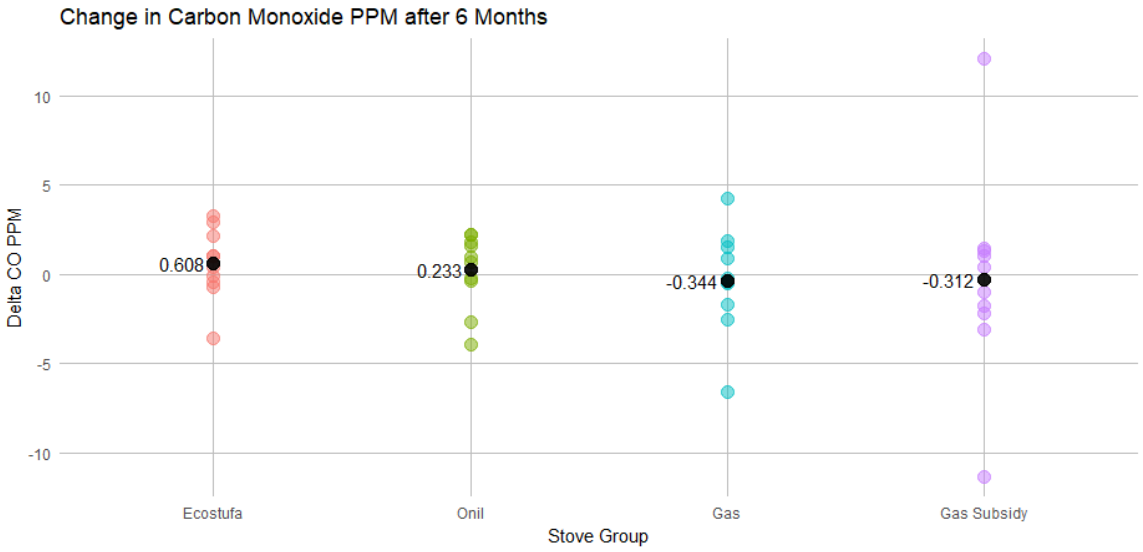

Figure 35: **Dot plot by stove type for the change in CO levels over 6 months.**

While the distribution is evenly dispersed around 0 for the first 3 groups, the fourth has an outlier in either direction, both being well beyond two standard deviations from the mean. Removing the outliers was found to have no substantial change on the descriptive power of the regression model. The presence of two outliers is important to note, but given the sample size only trends are noted, with or without the outliers.

It was discovered that there is a noticeable difference in the change of CO levels at three months compared to baseline and six months (*Table 4* and *Figure 36*). There was a statistically significant reduction at 3 months across all stove types then actually a slight increase over 6 months, with the 6-month change failing to be significant. Removing the extreme values that can be seen in the Gas with Subsidy group reduces the magnitude of this change, but the regression model still supports the significance of this change.

These findings are interesting and could be supplemented by more information on stove use. Perhaps stoves were used initially due to the novelty of them, but old cooking habits returned over time

Table 4: **Regression output of overall change in CO levels over time.**

	CO PPM	CO PPM (outliers removed)
Intercept	1.99***	1.73***
	(0.29)	(0.20)
3 Months	-0.90*	-0.64*
	(0.42)	(0.28)
6 Months	0.05	0.04
	(0.42)	(0.28)
R^2	.05	.06
Num. obvs.	120	118
RMSE	1.86	1.23
F-Statistic	3.33*	3.77*

*** p < 0.001, ** p < 0.01, * p < 0.05

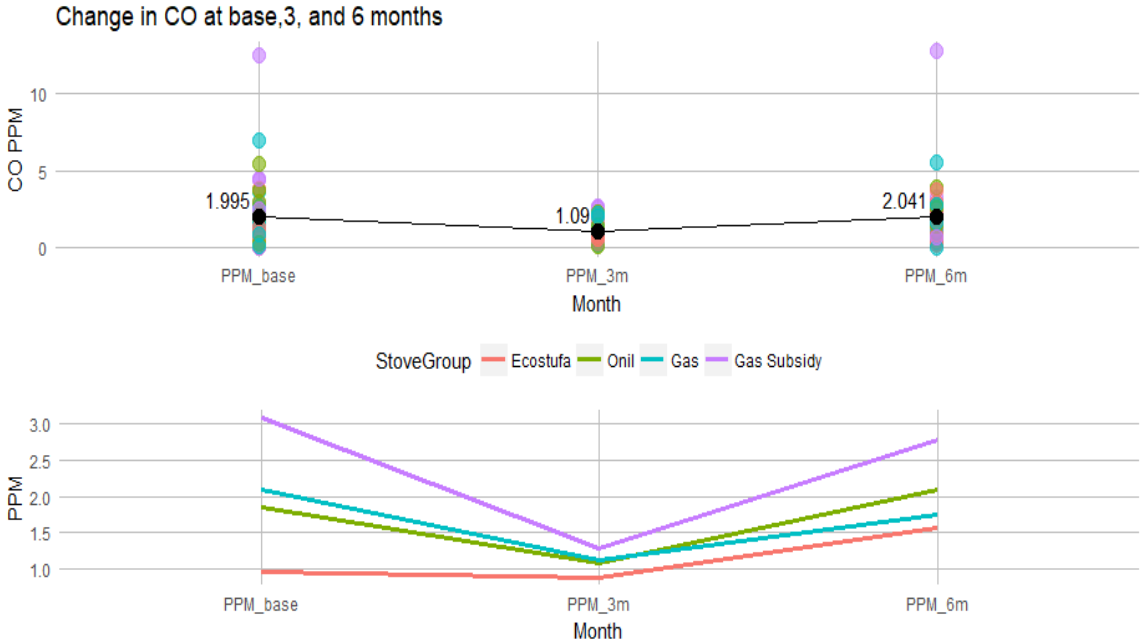

Figure 36: **Change in CO from baseline through 6 months**

4. Association between change in symptom burden (baseline to 6 months) and stove type

Linear regression was used as the model to answer this question. The outcome variable here was the change in CAT symptom score from baseline to 6 months. The model was:

Delta burden sum ~ stove type

Table 5: **Regression output of change in symptom burden by stove type**

	Delta Symptom Burden			
	Coefficient (B)	*SE B*	*t-value*	*P-value*
Intercept (Ecostufa)	-3.30	1.85	-1.78	0.08
Onil	-0.37	2.69	-0.14	0.89
Gas	0.70	2.62	0.27	0.79
Gas with Subsidy	-0.10	2.62	-0.04	0.97
R^2	<0.01			
Num. obvs.	39			
RMSE	5.87			
F-statistic	0.06			

*** p < 0.001, ** p < 0.01, * p < 0.05

The overall model does show a slight decrease in the symptom burden after six months as is indicated by the effect estimate coefficients. The Ecostufa, represented by the intercept, has the coefficient of -3.30 (p-value = 0.08) while the other stove coefficients are in relation to the -3.30-intercept estimate. It is worth noting the decrease shown by the intercept estimate and considering it in the context of our small sample size. Perhaps a clearer signal could be detected in a larger study. The following plot shows the dispersion of the outcome variable across the stove groups:

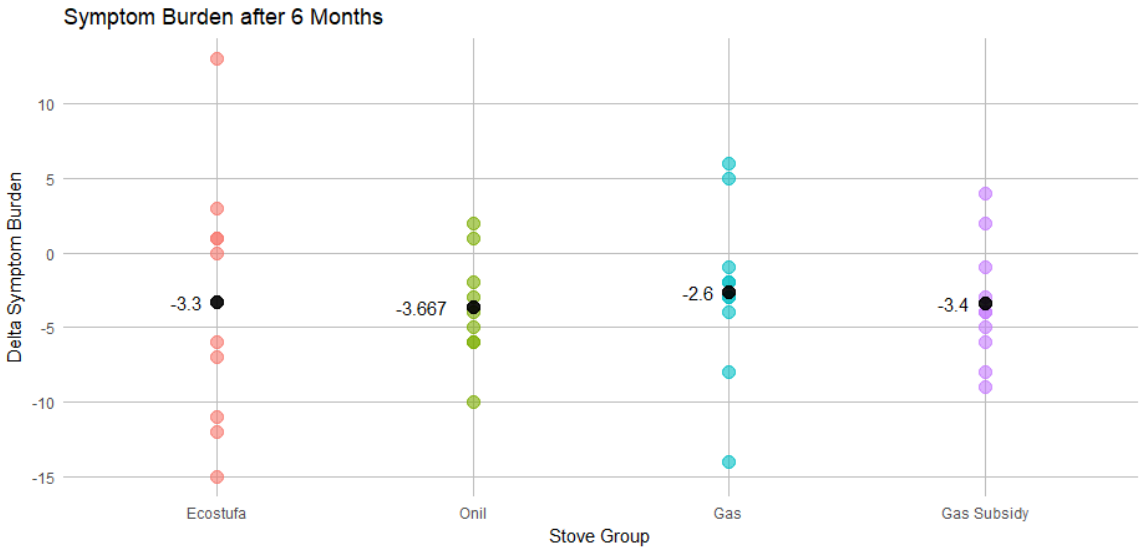

***Figure 37*: Dot plot by stove type for the change in symptom burden over 6 months.**

Clearly, there is a lot of variability in the CAT score outcome variable, but each stove group has a negative score, which reflects a slight drop in symptom burden over six months. A paired t-test was conducted examining the mean score at baseline and six months:

Paired t-test		
t = 3.57	Df = 38	p-value = <.001
95% Confidence Interval		
1.40	5.06	
Mean of Difference		
3.23		

There is evidence to support a 3.23-point decrease (95% confidence interval: 1.40, 5.06) in symptom burden after six months of the improved stoves being installed in the households. While this may not be proof of a causal relationship between the improved stoves and respiratory health, the decline in symptom burden is encouraging.

5. Association between change in spirometry measures (baseline to 6m) and stove type

Although our study was not powered to determine any significant differences between the stove groups regarding their ability to improve pulmonary function after six months of use, we were interested in assessing whether there was any directional change. The four outcome variables of interest were change in FEV1, FVC, and FEV1/FVC Ratio. The regression models were:

Delta FEV1 ~ Stove Group
Delta FEV1 (sensitivity analysis) ~ Stove Group
Delta FVC ~ Stove Group
Delta FEV1/FVC Ratio ~ Stove Group

Which were used to generate *Table 6* below.

Table 6: **Regression output of change in spirometry measures by stove type**

	Dependent Variable			
	Delta FEV1	Delta FEV1 (sens)	Delta FVC	Delta FEV1/FVC Ratio
Intercept (Ecostufa)	0.00	0.00	-0.09	0.04
	(0.12)	(0.13)	(0.18)	(0.04)
Onil	-0.03	-0.03	0.13	-0.08
	(0.17)	(0.17)	(0.24)	(0.05)
Gas	0.02	0.04	0.15	-0.04
	(0.18)	(0.19)	(0.26)	(0.05)
Gas with Subsidy	-0.24	-0.29	-0.26	-0.01
	(0.17)	(0.18)	(0.26)	(0.05)
R^2	0.11	0.15	0.13	0.13
Num. obvs.	30	28	26	26
RMSE	0.33	0.33	0.45	0.09
F-Statistic	1.04	1.38	1.08	1.07

*** p < 0.001, ** p < 0.01, * p < 0.05

No relationships proved strong enough to have statistical significance at the alpha = 0.05 level. One trend is that of the Gas with Subsidy group, which maintained a negative estimate across the four models. Ecostufa is the reference group, so this

negative estimate is relative to the Intercept estimate. This is the opposite of what would be expected if the gas stove was being used properly and frequently, and further examination shows that this may be due to a particular outlier in that group with a large negative value. Removing this outlier did not substantially improve the fit of the model, but did reduce the degree of that negative relationship observed in the regression output table.

The number of observations used decreases from left to right to reflect the increasing stringency with which the spirometry was graded. Both FEV1 tests can be seen below:

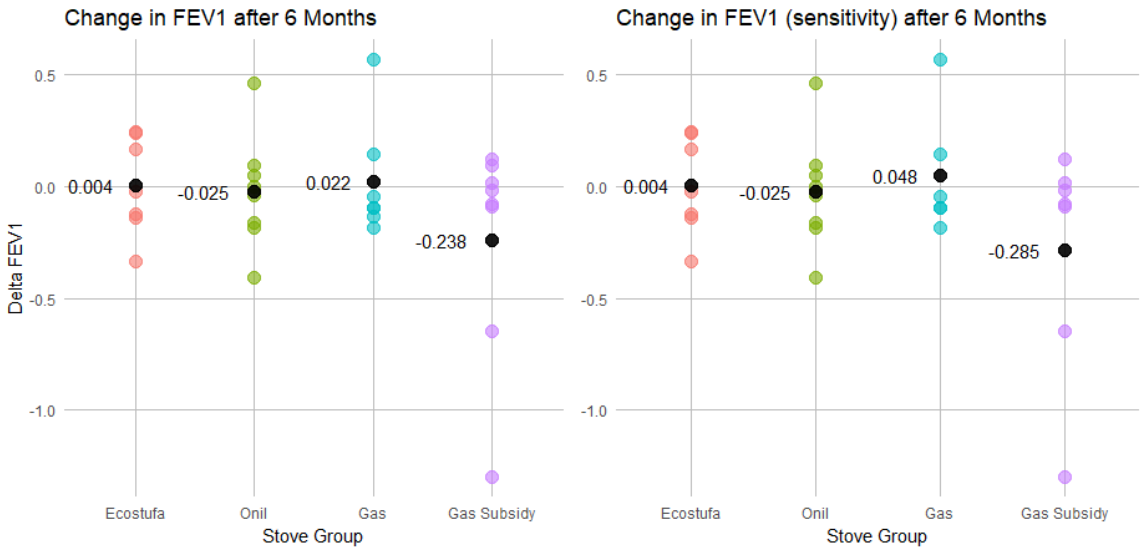

Figure 38: **(Left) Dot plot of overall change in FEV1 after 6 months by stove type. (Right) An identical plot using a sensitivity excluding spirometry trials with poor reproducibility.**

It seems the removal of the two spirometry trials with poor reproducibility in the sensitivity analysis had little effect on the change in FEV1. One point was removed from the Gas group and one from the Gas with Subsidy group, causing slight shifts in their means. In both models, the Gas group performed the best.

The third column in the regression output table denotes the FVC model. Forced vital capacity should have increased if the stoves were having a remedial influence on the participants.

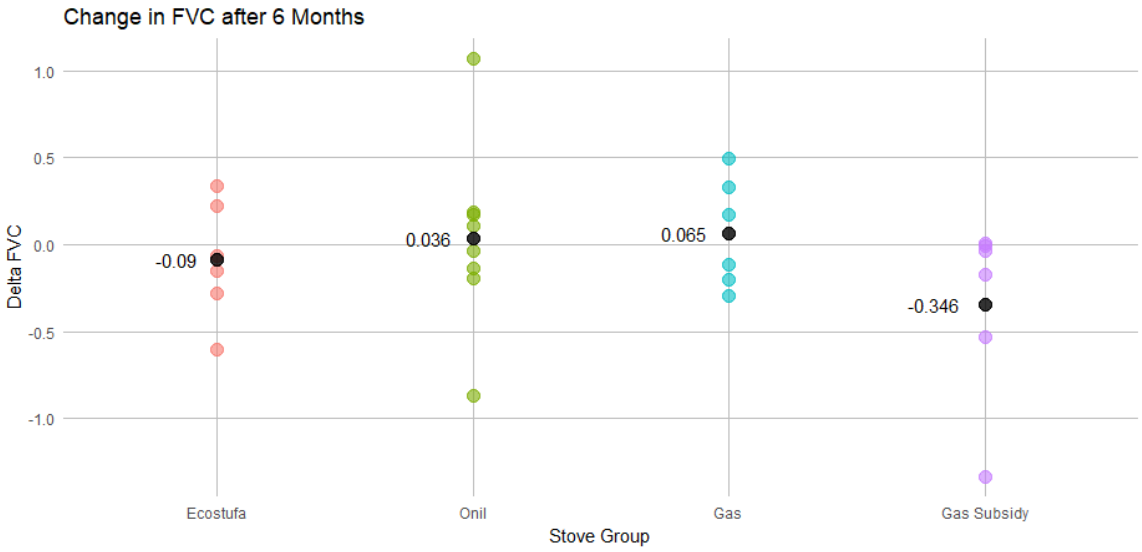

Figure 38: **Dot plot of overall change in FVC after 6 months by stove type**

The Onil and Gas groups improved slightly, while Gas with Subsidy was the lowest group once again. The removal of the outlier does not produce a positive Delta FVC. Ultimately, all values are very close to zero, indicating the stoves did not have a marked effect on FVC.

A similar trend is seen in the final plot, where the values are all close to zero. The distributions are more homogenous in this plot compared to the other three. In contrast to what was seen in the other three tests, the Gas with Subsidy group showed a slight improvement after six months.

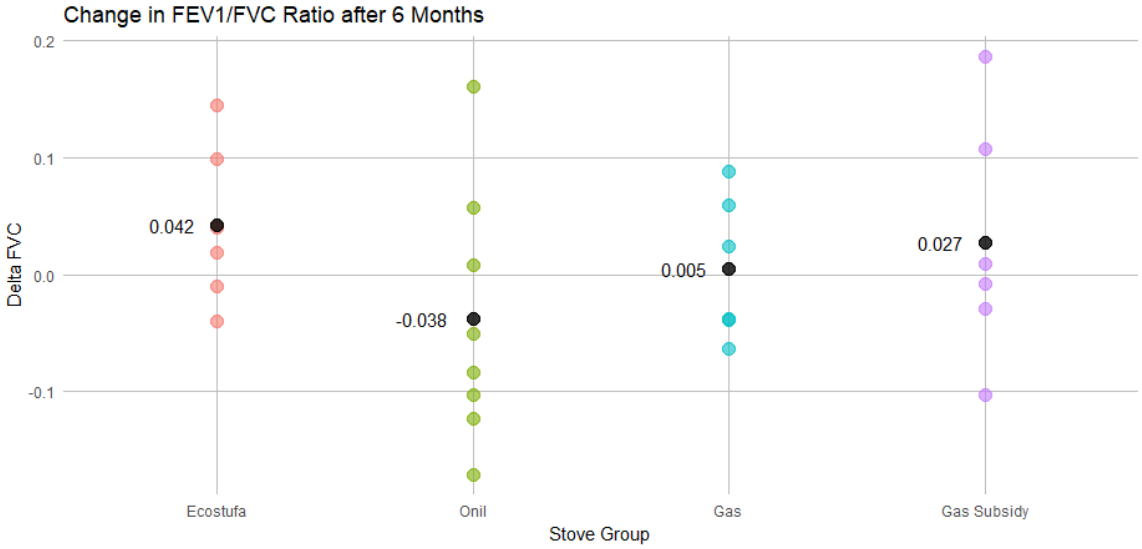

Figure 39: **Dot plot of overall change in FEV1/FVC ratio after 6 months by stove type**

Unfortunately, the data did not have a strong signal to it, and the evidence for a real improvement in lung function in the Gas with Subsidy group is minimal.

An interesting observation from these four plots is that the Gas group demonstrated a slight improvement in every single test. This is the effect expected if the stoves were used properly throughout the six months. More information on stove use frequency may shed light on why the Gas with Subsidy group did so poorly in comparison to the Gas group.

Discussion

This is the first study of its kind to look at four stove interventions in a prospective, randomized fashion with well-measured exposure and outcome data. Despite being a feasibility pilot study without significant statistical power there were notable findings. While 24h-personal CO levels failed to show a reduction in exposure over six months, a statistically significant reduction was seen at three months. Additionally there was a 3.23-point decrease (95% CI: 1.40, 5.06) in CAT symptom burden over six months across all stove types. While no significant changes were seen in spirometry measures, our six-month timeframe was likely too short to observe meaningful changes in spirometry. Forthcoming data on $PM_{2.5.}$ exposure, SUMs stove usage measures, and blood work measures of inflammatory biomarkers should further bolster our results.

What is seen with CO levels dropping then rising again is a notable result that is consistent with evidence in the literature surrounding stove stacking.[99,122,124] It will be necessary to confirm these findings with SUMs data, but several studies including ones in India and Mexico have shown reductions in intervention stove use over time.[124,125] In one of the largest and longest measures of stove usage to date, Pillarisetti et al.[124] found that usage of intervention stoves declined continuously over the first 200 days of the intervention at which point usage stabilized. In a study of Mexican indigenous women the pattern was somewhat different with stove usage increasing until month 4 at which point usage declined before plateauing.[125] Based on CO data it is possible that patterns of use in this study mimicked the latter. Forthcoming SUMs and $PM_{2.5}$ data will be evaluated to further elucidate these patterns.[124,126]

This study was able to detect a small but clinically significant reduction in smoke-related symptoms but as expected given our sample size and timeframe no significant spirometry changes were detected. These finding are consistent with a 2009 cookstove intervention involving over 500 Mexican women.[107] In this study Romieu et al. failed to observe a difference in symptoms or lung function between the intervention and control groups attributed to low adherence to use of the improved stove. However, increased self-reported use of the improved stove was significantly associated with a reduction in both smoke-related symptoms and FEV_1 decline over 1 year of follow-up. The small sample size of our study will likely limit our ability to further investigate symptom and spirometry changes when we analyze stove usage.

This pilot study was novel because it produced a combination of exposure and outcome data across four separate stove intervention in a way that has not previously been achieved in a single project. Strengths of the study include the quantitative nature and breadth of both the exposure and outcome data. While some analysis is yet to occur, the final results will include:

- both personal (24h)- and kitchen- CO and $PM_{2.5}$,
- SUMs stove usage data,
- post-bronchodilator spirometry,
- the well validated COPD Assessment Test (CAT) of respiratory symptoms
- blood biomarkers of inflammation.

Another strength was the collection of field data by a local, multilingual team that was well known in the communities studied.

As has been noted, the small sample size and pilot nature of this study were limitations to producing statistically significant findings beyond the originally desired knowledge regarding future feasibility of a large-scale project. Additionally, there was no true control group of households continuing traditional stove use, which would be important for a future large-scale trial. The question of validity surrounding self-reported symptom scoring is also an important one. Prior work in a similar Guatemalan population suggests "social desirability" bias has a likely but unknowable influence on participant response.[99] All stoves in this study were given fully free of charge. Evidence from India has shown that stoves given free of charge devalue their perceived value and potentially reduce their use over time.[127] While participants in this study were limited to a relatively small geographic area in the department of Quetzaltenango, they were spread across more than five distinct communities. In an aforementioned study in a rural, largely indigenous Mexican population, high levels of heterogeneity was seen in stove adoption across varying communities.[107] Community-level stratification on stove use and exposures is not possible given our data but would be of interest in a future study. This raises the question of neighborhood or village-level pollution levels. This is an important but challenging question about how significantly a single household's exposures can be reduced with an improved cookstove while being surrounded by homes continuing to use traditional stoves. Trying to document the number of immediate neighbors using biomass fuels could be a worthwhile effort in trying to account for a likely confounder.

HAP-associated obstructive lung disease (chronic bronchitis and COPD) is an important and increasing source of global morbidity and morality. A more complete understanding of the exposure-response relationship for HAP and obstructive lung disease is vital to knowing whether the progression of COPD due to HAP may be stopped – or even reversed. This pilot study provided proof of concept for the collection of high-quality data on emissions, stove use, field spirometry, and blood samples in a future large-scale RCT on stove interventions as a treatment for HAP-related chronic lung disease in Guatemala. In conducting this pilot study, we also

showed that improved stoves may produce a clinically significant reduction in the respiratory symptoms over a six-month period. All of our results have pushed forward the question of how the most effective cookstove intervention should be designed in Guatemala. Work remains to be done, but perhaps a Guatemalan physician will one day be able to definitively "prescribe" new, cleaner stoves for the treatment of COPD.

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