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Reductions in urinary metabolites of exposure to household air pollution in pregnant, rural Guatemalan women provided liquefied petroleum gas stoves

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Abstract

Background—Household air pollution from solid fuels is a leading risk factor for morbidity and mortality worldwide. Pregnant women’s exposure to polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs), two components of solid fuel smoke, is associated with adverse birth outcomes. Even with improved solid fuel stoves, exposure to PAHs and VOCs remains high. Therefore, cleaner cooking fuels need to be prioritized.

Objective—We aimed to quantify exposure reduction to PAHs and VOCs among pregnant women in rural Guatemala with a liquefied petroleum gas (LPG) stove intervention.

Materials and Methods—Urine from pregnant women (N=50) was collected twice: at < 20 weeks gestation, when women cooked exclusively with wood, and 6–8 weeks after receiving an LPG stove. Metabolites of 4 PAHs and 8 VOCs were analyzed. Concurrent with urine collection, personal 48-hour PM_{2.5} exposure was measured.

Results—Women cooking exclusively with wood were exposed to high levels of particulate matter (PM_{2.5}), which was reduced by 57% with the LPG stove. Urinary concentrations of total PAH metabolites (–37%), PMA (benzene metabolite; –49%), and CNEMA (acrylonitrile

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metabolite; –51%) were reduced. However, recent use of a wood-fired sauna bath led to large increases in excretion of urinary toxicant metabolites (+66–135%).

Conclusions—This is the first study to report PAH and VOC reductions from an LPG stove intervention introduced during pregnancy. However, other sources of air pollution minimized the gains seen from using an LPG stove. Thus, all sources of air pollution must be addressed in concert to reduce exposures to levels that protect health.

Keywords

solid fuel use; household air pollution; LPG stoves; urinary biomarkers; polycyclic aromatic hydrocarbons; volatile organic compounds

Introduction

Household air pollution (HAP) from solid fuel use is a significant risk factor for morbidity and mortality worldwide. It is the 13th leading cause of death worldwide for women of reproductive age (1). In Guatemala, where 64% of all households and 95% of rural households use wood fuel for cooking (2), HAP is the leading environmental and 6th overall cause of death among women between 15–49 years (1). As a leading risk factor for acute lower respiratory infections, chronic obstructive pulmonary disease, lung cancer, and cerebrovascular and ischemic heart disease (3), it is estimated that annual healthcare expenditures of \$37 billion are related to this exposure (4). Current global burden of disease estimates in children under 5 do not account for any link between HAP exposure and adverse birth outcomes, which if included would increase estimates of the HAP disease burden (5).

Due to low combustion efficiency of even the best performing solid fuel stoves, smoke typically contains high levels of fetotoxic byproducts of incomplete combustion including polycyclic aromatic hydrocarbons (PAHs) (6) and volatile organic compounds (VOCs) (7). Although humans are exposed to PAHs through dermal exposure and food ingestion, inhalation of PAHs is a major pathway when solid fuels are burned for cooking and heating (8). Prenatal exposure to PAHs is associated with adverse birth outcomes such as preterm birth (9,10), congenital defects, including neural tube defects (11,12) and gastroschisis (13), and fetal growth restriction, including small for gestational age (9,14), reduced head circumference (15,16), birth length (17,18), and birthweight (15,17). Additionally, prenatal PAH exposure is associated with impaired neurodevelopment (19) and reduced IQ in offspring (20). Similarly, prenatal VOC exposure is associated with small for gestational age infants (21), reduced birthweight (22), and impaired neurobehavioral performance in young infants (23). Most studies utilized participants who were exposed to low ambient concentrations in the United States (9,10,15,20) or occupational exposures (13,14). Unfortunately, few of these studies included participants who were exposed to burning solid fuels for cooking and heating (11,12).

Clean cookstove interventions have led to reductions in exposure to HAP. Compared to women cooking over open fires in their homes, vented chimney wood stoves have been shown to reduce exposure to particulate matter by over 50% and to PAHs by a lesser degree

(6% increase to 48% reduction) in multiple studies in Latin America (24–27). However, these interventions did not reduce exposure to particulate matter to levels required to protect health, as outlined by the WHO (28). To date, no studies have been conducted that measured reductions in PAHs and VOCs through an intervention using stoves that burn cleaner cooking fuels, such as liquefied petroleum gas (LPG) (8).

We have previously shown that women cooking with solid fuels in the immediate postpartum period are exposed to high levels of PAHs and VOCs, levels comparable to or greater than that from cigarette smoke (29). Given the significant health risk to the developing fetus, it is imperative to reduce these high exposures during pregnancy. Thus, this study aimed to 1) quantify the reduction in exposure to PAHs and VOCs in pregnant rural Guatemalan women who cooked with solid fuels at baseline and after receiving an LPG stove, and 2) correlate PAH and VOC urinary concentrations with personal exposures to particulate matter (PM_{2.5}).

Materials and Methods

Study population and sampling strategy

This sub-study of a cohort study, referred to as NACER II (30), investigated reductions in PAH and VOC exposure among rural women in the Western Highlands of Guatemala between April 2016 and June 2017 using an LPG stove intervention coupled with behavior change reinforcement. The details of the interventions are published elsewhere (30) but, in brief, participants (N=50) received a locally manufactured 3-burner LPG stove specifically chosen to meet the cooking needs of the study population and ten LPG tanks free of charge over the 10-month study. At stove installation, women were trained by study staff on safe LPG stove use and maintenance, reinforced at each LPG tank delivery by field staff. The behavioral intervention component consisted of three interactive classes based on focus groups conducted with pregnant women in the area to discuss barriers and enablers of LPG stove use. Additionally, half of the participants also received a more intensive and targeted behavioral reinforcement visits in the home.

Women were invited to participate in the study if they: had an ultrasound-confirmed singleton pregnancy < 20 weeks; were between 18 and 45 years of age; used an open fire and/or deteriorated chimney stove for cooking; had no plans to migrate in the next year; had access to a cell phone to allow for contact in scheduling study visits (86% of households within the area have a cellphone)(31); and received prenatal care through the Guatemalan Ministry of Health clinic. Women were excluded if they smoked tobacco or already owned an LPG stove. Women exposed to secondhand smoke were included in the study. Women were recruited from a government-run health center by trained, local Mam-speaking fieldworkers. A home visit was scheduled to assess the condition of the wood fuel stove. If the household primarily used a deteriorated chimney stove (e.g. holes in chimney, stove leaking smoke) or used an open fire for cooking and agreed to participate, a written consent was obtained and a follow-up visit was scheduled to take baseline air pollution and urinary biomarker measurements and administer questionnaires.

Urine collection

Study participants provided two urine samples during the prenatal period – after recruitment, while cooking exclusively with wood, and 6 to 8 weeks after receiving an LPG stove. Women were instructed to use the clean-catch method and collected first morning voided urine in sterile polypropylene cups which were immediately stored on ice in small coolers provided to them. Coolers were picked up by study personnel within 6 hours of collection. Samples were processed and stored in a -4°C freezer at the field laboratory and then shipped on dry ice to the United States. To minimize exposure to light, coolers and refrigerators were dark and opened as infrequently as possible. Additionally, samples were transferred to shipping containers as quickly as possible to avoid light exposure and received in the United States within 48 hours of shipment from Guatemala to minimize thawing. Samples were stored at -20°C until laboratory analysis.

PM_{2.5} measurements

Concurrent with urine collection, personal PM_{2.5} exposure was measured gravimetrically over a 48-hour period. This was performed by drawing air through a BGI metal cyclone separator (model SSC1.06 triplex), with a 50% cutpoint at 2.5 μm , onto 37 mm filters with 2 μm pores using battery-operated constant flow SKC air sample pumps at a rate of 1.5 liters/minute. All pumps were calibrated before and after use in the field using a Defender 510 air flow calibrator (MesaLabs, Lakewood, CO). Homes were visited at 24 hours to assess equipment and change filters; thus, the average of two filters represent a 48-hour monitoring period. Filters were pre- and post-weighed by Chester LabNet (Tigard, OR) at a resolution of 1 μg . Participants wore the pump on their back in a specially designed vest with the cyclone affixed to the front of the vest near their right shoulder. They were instructed to wear the vest at all times, and to leave the vest by their beds when they were sleeping. Because the Mam-indigenous communities use the wood-fired sauna bath (referred to as the *temascal* in Spanish) for bathing in this region of Guatemala, we asked participants to not bring the air monitoring vest into the super-saturated sauna bath. Thus, these personal exposures to PM were not quantified.

Study surveys

After consent, fieldworkers verbally administered questionnaires to participants about household demographics, including whether the household burns their trash in or around the home. At each urine collection, participants were asked about the time of the urine sample and recent exposures to PAHs including consumption of high-PAH foods within the prior 24 hours and other sources of smoke exposure, such as secondhand tobacco smoke and personal sauna bath usage. Dietary questions were based on foods commonly eaten in this region of rural Guatemala, such as charred, smoked or fried food, white bread, tomatoes, oranges, eggs, tortillas and tamales, which are known to be high in polycyclic aromatic hydrocarbons (32). Questions on smoke exposure included whether someone recently smoked in the household, the date and time of the participant's most recent sauna bath, and length of time spent in the sauna bath.

Stove use monitoring

To monitor stove usage, iButton (Maxim Integrated) temperature loggers were placed on the LPG stove and any wood stove used for cooking. These sensors measure temperature at 5-minute increments, recording temperature increases and decreases with stove usage. One iButton was placed on each wood stove away from the fire and two were placed on the sides of the LPG stove to allow detection of temperature increase with any burner in use. Additionally, iButtons were placed in the bedroom of two homes made of different building materials to measure ambient air temperature to which stove monitors could be compared. Additionally, all stoves were examined during sensor placement; study staff noted whether solid fuel stoves were destroyed since baseline measurements were taken. Exclusive LPG stove usage was defined as a destroyed or non-existent wood stove since the baseline measurement or LPG stove use greater than 95% of cooking time.

Laboratory procedures for urinary biomarker analysis

The Clinical Pharmacology laboratory at UCSF analyzed urinary metabolites of several PAHs and VOCs (Table 1) by liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS), as previously described (33,34). In brief, hydroxylated PAHs were hydrolyzed by treating urine samples with β -glucuronidase and sulfatase. After extraction and conversion to pentafluorobenzyl ether derivatives, PAH metabolites were analyzed by LC-MS/MS with internal standards. For VOC metabolites, urine with added internal standard was extracted, converted to pentafluorobenzyl ester derivatives and analyzed by LC-MS/MS. Concentrations of all urinary metabolites were normalized to creatinine concentrations. Creatinine concentrations were determined via LC-MS/MS against internal standards.

Statistical analysis

Total PAH concentration was calculated on a molar basis for statistical comparisons. Because urinary biomarker concentrations were right skewed, median concentrations and differences are presented. Median concentrations were compared using the non-parametric Wilcoxon sign rank and rank sum tests. Linear mixed effects models on natural-log transformed concentrations were used for multivariate analyses with subjects as the random effect and season, sauna bath use and time of measure (baseline/follow up) as fixed effects. Exponentiating the intercept yields an adjusted mean concentration and exponentiating coefficients yields a proportional change in the mean concentration for that variable. Spearman rank correlation was used to determine correlations between urinary concentrations and concentrations of $PM_{2.5}$. Because the wood-fired sauna bath is a common, high exposure to smoke in this region of Guatemala (35), we examined these events, defined as sauna use within 48 hours prior to urine collection. Additionally, large seasonal variations in smoke exposure have been seen due to extra stove use for heating, wood-moisture content, and precipitation (36,37). This study took place over two seasons – cold and warm, wet – which could alter stove use and exposure patterns for similar reasons and, thus, was adjusted for in multivariate analyses.

Ethical approval

The study received ethical approval from the Committee for Human Research at UCSF and UVG and was registered on clinicaltrials.gov (ID:). Participants were informed of the study by trained field workers fluent in both Spanish and Mam. Written informed consent was obtained.

Results

Sociodemographic characteristics of participants

The median age of all 50 study participants was 25.4 years (range: 18.4–38.8; Table 1). The majority had an elementary school education or less (n=26; 54%), were Mam-speaking Mayan (n=42; 86%), disposed of garbage by burning in or around the home (n=33; 66%), and used a deteriorated chimney stove for cooking at baseline (n=37; 74%). None of the women actively smoked and few were exposed to secondhand smoke (n=7; 14%, exposed to 1–2 cigarettes smoked a day) or cooked in the same structure as they slept (n=6; 12%). The mean gestational age at the baseline visit with a wood stove was 15.0 weeks (S.D=3.2); mean gestational age was 25.4 weeks (S.D=2.2) at the follow-up visit with LPG stove. The median 48-hour PM_{2.5} exposure was 102 µg/m³ (IQR: 64–211) when cooking with wood exclusively and, after cooking with an LPG stove for a mean of 8.6 weeks, PM_{2.5} dropped to a median of 45 µg/m³ (IQR: 26–67). Two women experienced spontaneous miscarriages so they did not provide urine samples for analysis after LPG stove installation.

Concentrations of urinary metabolites by fuel and reductions with LPG stove

Polycyclic aromatic hydrocarbons—Use of LPG stoves led to large decreases in PAH exposure. The median concentration of total urinary PAH metabolites was reduced by 36% (Table 3). After LPG stove use, among metabolites for individual PAHs, the urinary concentration for 2-naphthol was reduced by 38% and the concentration of hydroxyfluorenes was reduced by 31%. Smaller non-statistical differences were seen for hydroxyphenanthrenes and 1-hydroxypyrene. There were larger reductions in urinary PAH metabolites among those who cooked with LPG exclusively. Among exclusive LPG stove users (N=11; 22% of participants), the median concentration of total urinary PAH metabolites (137.1 pmol/mg creatinine) was 47% lower than those who continued to cook with their biomass fuel stove (256.4 pmol/mg creatinine)(Figure 1). There were, however, marked differences in the concentration of total urinary PAH metabolites in this group based on the use of wood-fired saunas. Exclusive LPG users that used the wood-fired sauna bath (N=2) had a median total PAH urinary metabolite concentration (253.7 pmol/mg creatinine) far higher than exclusive LPG users that did not use the sauna (136.8 pmol/mg creatinine; N=9) and comparable to wood and LPG users who did not use the sauna bath (223.7 pmol/mg creatinine; N=22)(Supplemental Table 1). In mixed-effects models, after adjusting urinary concentrations by recent use of wood-fired sauna baths, as well as seasonal effects, changes in urinary metabolite concentrations were significant for 2-naphthol (40% reduction), total hydroxyfluorenes (48% reduction) and total PAH (37% reduction) (Table 4). Additionally, all PAH metabolites were significantly associated with recent wood-fired sauna bath use (66–135% increase; mean time in sauna bath = 27.5 minutes) (Table 4). Dietary contributions from charred foods, such as toasted tortillas, presence of a smoker in

the household (14% of participants) or reported garbage burning (66% of participants) in or around the home were not associated with PAH metabolites (data not shown).

Volatile organic compounds—LPG stoves led to modest reductions in urinary VOC metabolite concentrations compared to PAHs. However, there were significant reductions in median urinary concentrations in PMA (benzene; 40%), HEMA (ethylene oxide; 12%), and CNEMA (acrylonitrile; 38%) (Table 3). Urinary AAMA (acrylamide) was higher with LPG stove usage, however. After adjusting for seasonal differences in multivariate analyses, there were significant reductions in PMA (benzene; 49%) and CNEMA (acrylonitrile; 51%) with LPG stove use and increases in urinary PMA (benzene; 61%), HEMA (ethylene oxide; 39%), MMA (methylating agents; 86%), and CNEMA (acrylonitrile; 92%) with recent wood-fired sauna bath use. Similar to the results with PAHs, there were no associations of VOC metabolites with diet, second hand smoke in the home or burning garbage close to the home (data not shown).

Correlation of urinary metabolite concentrations with personal exposures

Urinary biomarkers for all PAH and many VOC exposure were associated with particulate matter exposure. All PAH metabolites were moderately correlated with personal particulate matter exposure ($\rho = 0.29 - 0.57$) with stronger correlations among the smaller molecular weight hydroxylated PAHs, 2-naphthol and the hydroxfluorenes (Table 5). In general, the correlations between urinary PAH biomarkers and particulate matter exposure were stronger for measures taken at baseline while women cooked exclusively with wood ($\rho = 0.35-0.69$) and when participants had not recently used a wood-fired sauna ($\rho = 0.41-0.62$). Similarly, PAH metabolites were strongly correlated and were stronger at baseline when women cooked exclusively with wood (Figure 2). Additionally, metabolites of 5 of 9 VOCs were moderately correlated with personal particulate matter exposure: benzene (PMA; $\rho = 0.59$), ethylene oxide (HEMA; $\rho = 0.35$), methylating agents (MMA; $\rho = 0.21$), acrylonitrile (CNEMA; $\rho = 0.57$), and acrolein (3HPMA; $\rho = 0.21$). With the exception of MMA, correlations with these VOC metabolites and particulate matter were stronger when women cooked exclusively with wood at baseline ($\rho = 0.42-0.63$) or had not recently used a wood-fired sauna ($\rho = 0.19-0.61$), though the trend was less consistent. The concentrations of PMA, CNEMA, and AAMA (acrylamide) were all moderate to strongly correlated with PAH metabolite concentrations (Figure 2).

Discussion

Pregnant women cooking with solid fuels in rural Guatemala are exposed to high levels of household air pollution that can be significantly reduced with consistent use of an LPG stove. Women in this study who cooked exclusively with wood had a $PM_{2.5}$ exposure far above the WHO air quality Interim Target-1 of $35 \mu\text{g}/\text{m}^3$ (28) and a total urinary PAH metabolite concentration double that of active smokers who smoke, on average, 18 cigarettes a day (38). These elevated exposures are consistent with other household air pollution studies investigating PAH (24,25,39) and VOC exposure from cooking with solid fuels (29). However, the baseline levels reported here with solid fuel use are particularly alarming given that all participants were pregnant and nearly one-third were measured during the first

trimester when exposure to PAHs is most strongly associated with decreased fetal growth, birthweight and birth length (40). However, when these women adopted the LPG stove, exposures to particulate matter, PAHs and multiple VOCs were significantly reduced from baseline, with personal exposures to particulate matter approaching the WHO air quality Interim Target-1 and even greater reductions with exclusive LPG stove usage.

To our knowledge, this is the first study to examine the effect of an introduced LPG stove on PAH/VOC exposures so direct comparisons to other LPG stove intervention studies cannot be made. There are no other published studies on reductions of VOC urinary metabolite concentrations from a stove intervention (either LPG or an improved solid fuel stove) in the context of household air pollution. However, there have been previous studies investigating the effect of improved solid fuel stoves on urinary PAH metabolites in other Latin American countries that can serve as a benchmark for reducing exposure with new stove technologies (24–27). Absolute reductions of smoke exposure in this study were similar or greater than those of previous intervention studies on household air pollution (Table 6). Compared to stove intervention studies that measured urinary PAH metabolites, we found similar absolute reductions in particulate matter exposure ($57 \mu\text{g}/\text{m}^3$ in our study vs $63 \mu\text{g}/\text{m}^3$ in an intervention study in Peru), although with the LPG stove in our study we were able to reduce personal exposure to $45 \mu\text{g}/\text{m}^3$, well below that with uptake of a solid fuel chimney stove ($70 \mu\text{g}/\text{m}^3$) (24). The magnitude in reduction in urinary 1-hydroxypyrene was similar in our study to other studies that provided an improved chimney wood stove. However, our study showed greater reductions in 2-hydroxynaphthol (89 in our study vs 22–63 pmol/mg creatinine), total hydroxyfluorene (13 in our study vs 1 pmol/mg creatinine) and total hydroxyphenanthrene (10 in our study vs 1 pmol/mg creatinine) than those found in previous solid fuel stove intervention studies (24–27). Of note, the pre-intervention concentrations of PAH metabolites were generally higher than those reported from other studies, potentially due to methodological differences in measuring metabolite concentration or due to the widespread use of sauna baths in our population.

Reductions in PAHs, VOCs and $\text{PM}_{2.5}$ found in this study could have potential positive impacts on fetal health outcomes. Choi et al. (2008) found that every 2.72-fold increase in prenatal personal airborne PAH exposure was associated with a 2.43-fold increase in risk of small for gestational age and a 4.68-fold risk for preterm birth (9). While differences in methodology for measuring PAH exposure prevent direct comparisons, if a similar trend holds for urinary biomarkers, the 37% reduction in our study may significantly reduce the risk for preterm birth and small for gestational age, two birth outcomes measured in the NACER II study. The small sample size of this feasibility study, however, severely limited our statistical power in these analyses.

Despite significant PAH and VOC reductions from LPG stove use in our study, exposure remained high. The total PAH metabolite concentration was reduced from 367 pmol/mg creatinine to 234 pmol/mg creatinine, which remains nearly 100 pmol/mg creatinine greater than that of active cigarette smokers (38). Similarly, concentrations of urinary metabolites of benzene, ethylene oxide, acrylonitrile, acrolein, acrylamide, and crotonaldehyde were comparable to or greater than those exposed to secondhand cigarette smoke for one hour in a controlled experiment (41). In our study, 14% of households had smokers in the home,

which was limited to less than 2 cigarettes a week. Cigarette smoking was not statistically associated with airborne PM_{2.5} or PAH or VOC urinary concentrations in our study. Exposures to other sources of smoke are likely, such as the recent use of wood-fired sauna baths, which produced markedly elevated urinary biomarker concentrations. This was not unexpected; sauna baths used in this region have been shown to greatly increase CO levels, another by-product of incomplete combustion of wood fuel (35,42). This bathing practice, which creates a super-saturated, high heat environment, cannot be measured using typical monitoring methods, such as gravimetric or personal PM_{2.5} monitors, because in our past experience, filters became humid and monitors failed under these conditions. Thus, the inability to account for exposure within the sauna potentially explains the lower correlations between particulate matter and urinary metabolites in our study among women who used the sauna bath prior to urine collection. Additionally, the weaker correlation following adoption of the LPG stove could potentially be attributed to the markedly reduced exposure to PAH from cooking with solid fuels.

Even after accounting for exposure from sauna bath use, concentrations of PAH and VOC metabolites remained significantly elevated, indicating other sources of exposure, possibly from nearby neighbors' kitchens or continued use of the solid fuel stove in the participants' homes. Among households that used LPG exclusively at follow-up, urinary PAH metabolite concentrations were significantly lower than other participants, indicating continued solid fuel use contributed to the levels reported here. However, while approaching the median urinary metabolite concentrations for American men, that with exclusive LPG stove use was still comparable to smokers who smoked an average of 18 cigarettes per day (38). In our area of study, many households burn their trash in open fires away from their home or within their kitchen stoves, which has been shown to produce high levels of PAHs and VOCs (43). While 66% of households in our study reported burning trash, this was not significantly associated with urinary concentrations of PAH and VOC metabolites. Dietary intake is another common source of PAHs (32) and can lead to elevated urinary metabolite concentrations (44). Charred or fried food, eggs, tortillas and tamales are consumed almost daily in this region and are high in PAHs (32). Given low dietary variability and small sample size, though, we were not able to detect a statistically significant association between diet and urinary metabolite concentrations, consistent with prior studies (25,39). Additionally, dermal exposure has been shown to be a contributor to urinary PAH metabolite concentrations (45). Soot from biomass burning contains high levels of PAHs (46) and, thus, dermal exposure to soot or inhalation of volatilized soot PAHs may have contributed to the concentrations seen in this study. While the study was limited in its ability to analyze the effects of soot, cigarette smoke, diet, and trash burning on urinary metabolite levels, they may have potentially contributed to elevated concentrations reported here. Additionally, after participants started using the LPG stove, the proportion of PAH exposure from inhaled PM_{2.5} from the woodstove was reduced in comparison to these other sources, reducing the strength of correlation between PAH and particulate matter at follow-up.

Limitations

This study had a small sample size (N=50) so the results may not be generalizable to a wider population. This small sample size had limited statistical power to determine the effect of

co-variables on urinary metabolite concentrations, as well as direct correlations between LPG stove usage and reductions in urinary metabolite concentrations. Larger, multi-country studies, such as the Household Air Pollution and Health: A Multi-country LPG Intervention Trial (HAPIN) trial ([ClinicalTrials.gov](https://clinicaltrials.gov) Identifier:), are currently being conducted to corroborate the findings reported here.

There were several potential sources of measurement error. While we know that women removed the air pollution monitoring vest when they entered the sauna bath, we do not know if women removed the vest when they visited other homes where cooking may have occurred over solid fuel stoves. This would have reduced the correlation between $PM_{2.5}$ and the urinary biomarkers. However, at 24-hour and 48-hour visits, almost all women had their vests on when fieldworkers arrived (93%, n=169 visits), suggesting that compliance was good. Additionally, we did not measure personal inhalation exposure to PAHs and VOCs nor quantify the concentrations of PAH bound to $PM_{2.5}$. Thus, a direct association between inhaled PAH and urinary biomarkers could not be established. Lastly, PAHs have a short urinary half-life (44) and, thus, values reported here represent acute PAH exposure, which may not be indicative of long-term exposure or increased risk of adverse health outcomes especially given the large daily variation in air pollution measure.

This study has some other potential sources of bias. Participants were surveyed only once at baseline whether they burned garbage and were not asked regarding the frequency of trash burning. Thus, this exposure might not be appropriately accounted for when urine samples were collected, reducing the ability to detect any significant associations with metabolite concentrations. Additionally, there is a potential non-differential misclassification bias for recent sauna bath usage. Women self-reported the times for the urine sample and sauna bath. As such, when this variable was calculated using the difference in these times, women may have been misclassified regarding their recent sauna bath usage. A non-differential misclassification would bias the association of sauna bath usage with PAH concentrations toward null and, thus, estimates presented here may be underestimated.

Conclusions

Household air pollution from solid fuel use is a leading environmental risk factor in Guatemala and worldwide with the health burden primarily falling upon women and young children. PAHs and VOCs, two components of solid fuel smoke, have been shown to be deleterious to fetal development. Even with improved solid-fuel chimney stoves exposure to PAHs and VOCs remains high. This study is the first to determine the reductions in exposure in pregnant women through the use of an LPG stove intervention. Although we found significant reductions in these exposures, other sources of smoke, such as wood-fired sauna baths, continued use of solid-fuel stoves, and smoke from neighbors' homes, prevented reduction to levels needed to minimize health risk. Thus, even with exclusive use of a clean cookstove like LPG, additional exposures to PAHs and VOCs must be addressed to minimize the associated health burden.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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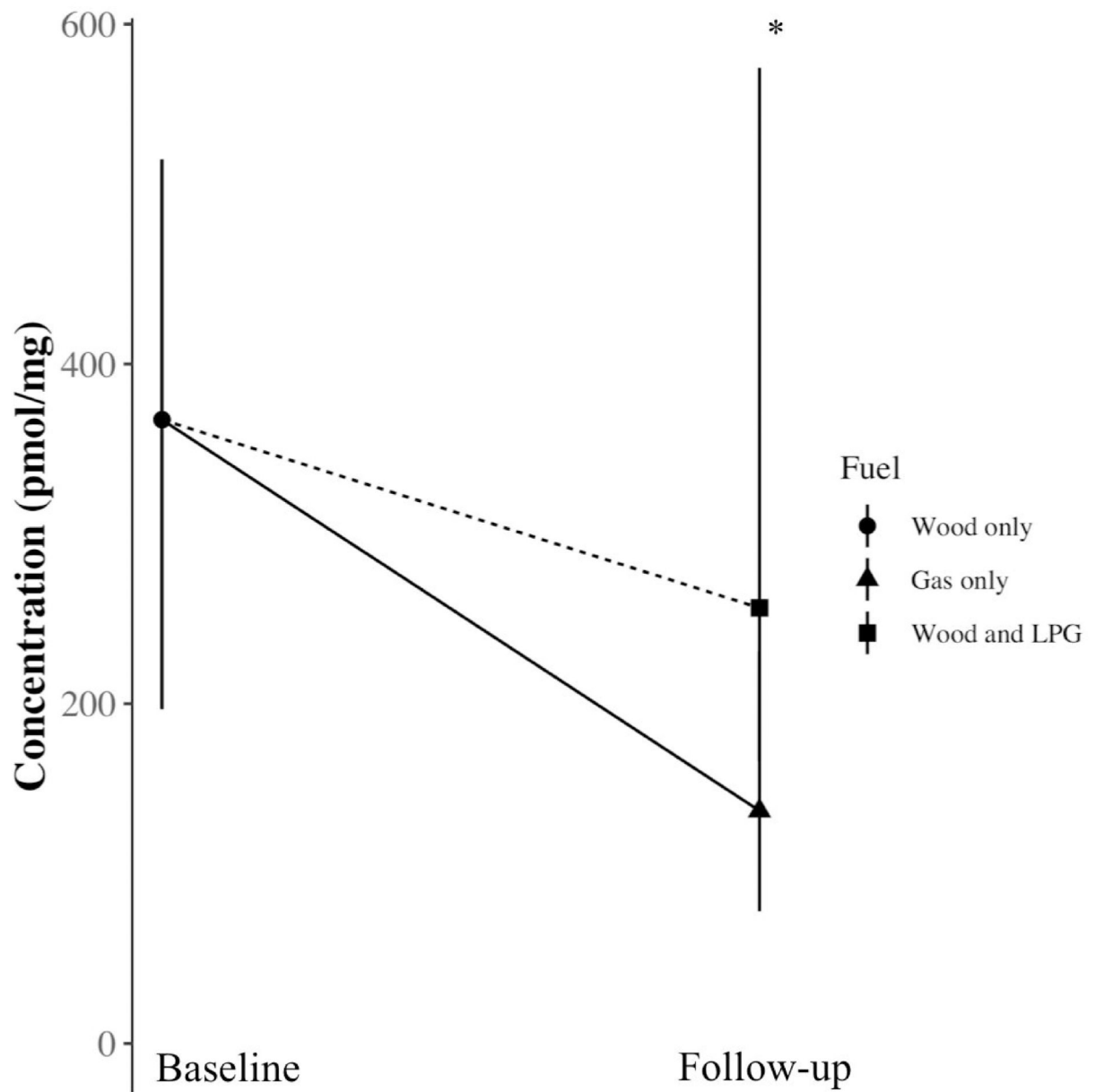


Figure 1.

Median and inter-quartile range of total PAH urinary metabolite concentration by fuel type, at baseline with wood stove (n=50) and at follow-up with exclusive LPG use (n=11) or mixed wood and LPG stove use (n=37).

* Indicates significant difference between median concentrations at follow-up period between those with exclusive LPG use and mixed wood and LPG stove use at follow-up by Wilcoxon rank sum test (* < 0.05; ** < 0.01; *** < 0.005)

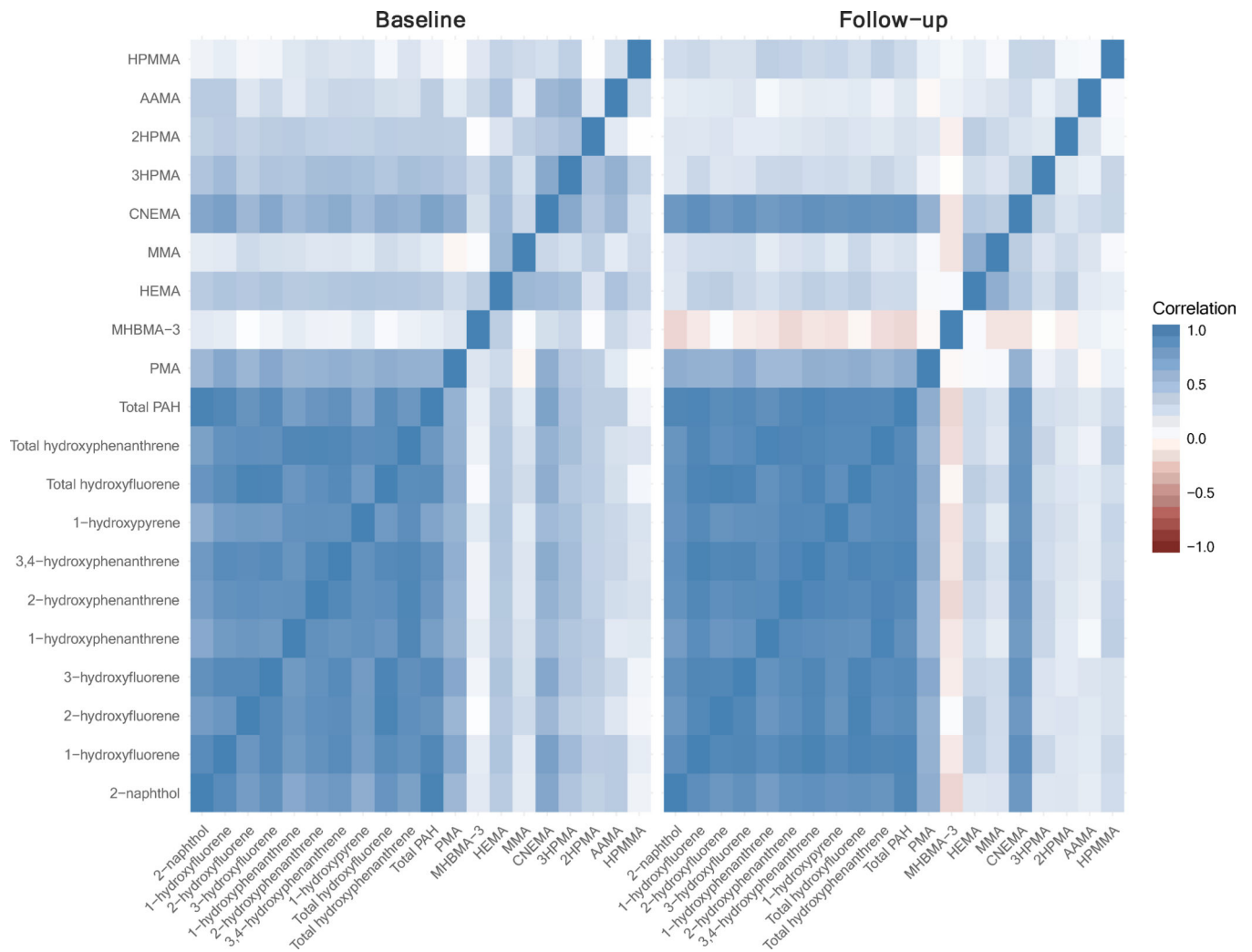


Figure 2. Spearman correlation coefficients of urinary concentrations of PAH and VOC metabolites at baseline and follow-up.

Table 1.

Airborne exposures and the associated urinary metabolite measured by LC-MS/MS.

	Exposure	Metabolite (acronym)
	Naphthalene	2-naphthol
	Fluorene	1-hydroxyfluorene 2-hydroxyfluorene 3-hydroxyfluorene
Polycyclic aromatic hydrocarbons	Phenanthrene	1-hydroxyphenanthrene 2-hydroxyphenanthrene 3,4-hydroxyphenanthrene
	Pyrene	1-hydroxypyrene
	Benzene	phenylmercapturic acid (PMA)
	1,3- butadiene	4-hydroxy-2-buten-1-yl-mercapturic acid (MHBMA-3)
	Ethylene oxide, acrylonitrile, vinyl chloride	2-hydroxyethylmercapturic acid (HEMA)
	Methylating agents	methylmercapturic acid (MMA)
Volatile organic compounds	Acrylonitrile	2-cyanoethylmercapturic acid (CNEMA)
	Acrolein	3-hydroxypropylmercapturic acid (3HPMA)
	Propylene oxide	2-hydroxypropylmercapturic acid (2HPMA)
	Acrylamide	2-carbamoylethylmercapturic acid (AAMA)
	Crotonaldehyde	3-hydroxy-1-methyl-propylmercapturic acid (HPMMA)

Table 2.

Demographic characteristics of study participants (n=50)

Age years, mean (range)	25.4 (18.4–38.8)
Education, n (%)	
None	13 (27)
Elementary school	13 (27)
Middle school	7 (14)
High school	16 (33)
Ethnicity, n (%)	
Indigenous Mam	42 (86)
Spanish-speaking <i>Ladina</i>	3 (6)
Both	4 (8)
Smoker in household, n (%)	7 (14)
Kitchen in separate structure, n (%)	44 (88)
Burns garbage in kitchen or around home, n (%)	33 (66)
Primary stove, n (%)	
Open fire	12 (29)
Stove without chimney	3 (6)
Stove with chimney	37 (74)
Cooking fuel type, n (%)	
Wood only	7 (14)
Wood and crop residue	22 (44)
Wood and plastic	2 (4)
Wood, plastic and crop residue	19 (38)
Weeks between gas stove installation and follow-up, mean (range)	8.6 (2.6–14.9)
48-hour particulate matter 2.5 ($\mu\text{g}/\text{m}^3$), median (IQR)	
At baseline (exclusively wood)	102 (64–211)
At follow-up (gas stove)	45 (26–67)
% change (median (IQR))	–56 (–85, –17)

Table 3.

Urinary concentration of urinary metabolites of PAHs and VOCs.

Biomarker	Median OH-PAH Concentration (IQR) (pmol/mg creatinine)		
	At baseline (n=50)	At follow-up (n=48)	% change
2-naphthol	231.8 (137.8–351.4)	142.7 (77.8–289.6)	–38%
1-hydroxyfluorene	7.3 (3.8–11.0)	4.7 (2.3–10.0)	–36%
2-hydroxyfluorene	24.7 (13.3–33.9)	17.5 (7.6–27.6)	–29%
3-hydroxyfluorene	7.8 (4.1–12.3)	5.3 (2.2–10.3)	–32%
Σ hydroxyfluorenes	42.5 (21.3–55.1)	29.4 (11.7–47.1)	–31%
1-hydroxyphenanthrene	21.7 (11.51–30.22)	19.9 (10.73–42.17)	–8%
2-hydroxyphenanthrene	8.05 (4.4–13.8)	6.9 (3.6–14.5)	–14%
3,4-hydroxyphenanthrene	13.2 (8.0–18.5)	10.2 (4.3–18.1)	–23%
Σ hydroxyphenanthrenes	46.7 (23.8–65.4)	37.0 (18.3–70.7)	–21%
1-hydroxypyrene	19.7 (10.6–27.9)	16.9 (7.2–30.7)	–14%
Total PAH	367.2 (196.8–520.4)	234.5 (137.0–497.0)	–36%
Biomarker	Median VOC Concentration (IQR) (ng/mg creatinine)		
	At baseline (n=50)	At follow-up (n=48)	% change
PMA (benzene)	0.7 (0.3–1.4)	0.4 (0.2–0.9)	–40% *
MHBMA-3 (1,3-butadiene)	0.1 (0.1–0.2)	0.1 (0.1–0.2)	0%
HEMA (ethylene oxide)	3.4 (2.4–5.0)	3.0 (1.7–4.0)	–12% *
MMA (methylating agents)	30.5 (16.8–55.6)	23.3 (15.4–43.1)	–24%
CNEMA (acrylonitrile)	5.0 (2.8–11.0)	3.1 (1.7–7.7)	–37.7% *
3HPMA (acrolein)	264.0 (179.6–398.0)	266.1 (224.3–387.8)	1%
2HPMA (propylene oxide)	19.7 (14.5–24.1)	19.4 (15.5–25.3)	–1%
AAMA (acrylamide)	75.4 (58.9–98.1)	81.5 (62.5–120.9)	8% *
HPMMA (crotonaldehyde)	193.3 (130.3–307.7)	185.8 (155.4–265.4)	–4%

* indicates significant difference between median urinary metabolite concentrations at baseline and follow-up by Wilcoxon sign-rank test (*: p < 0.05, **: p < 0.01, ***: p < 0.005)

Table 4.

Urinary metabolite concentrations (e^{α}) and proportion (e^{β}) with fuel, temascal (wood-fired sauna bath) use and season from mixed-effects model on log-transformed data

	<u>Concentration</u>	<u>Provided gas stove</u>	<u>Recent temascal use</u>	<u>Cold season</u>
2-naphthol	315.2 ^{***}	0.60 ^{***}	1.66 ^{***}	1.38
Σ hydroxyfluorenes	43.9 ^{***}	0.52 ^{***}	2.35 ^{***}	1.61 [*]
Σ hydroxyphenanthrenes	40.8 ^{***}	0.78	2.26 ^{***}	1.42
1-hydroxypyrene	18.1 ^{***}	0.77	2.13 ^{***}	1.31
Total PAH	417.3 ^{***}	0.63 ^{***}	1.85 ^{***}	1.42
PMA (benzene)	1.1	0.51 ^{***}	1.61 [*]	1.73 [*]
MHBMA-3 (1,3-butadiene)	0.2 ^{***}	0.88	1.04	1.04
HEMA (ethylene oxide)	4.0	0.75	1.39 [*]	1.01
MMA (methylating agents)	29.2 ^{***}	0.80	1.86 [*]	0.80
CNEMA (acrylonitrile)	8.9 ^{***}	0.49 ^{***}	1.92 ^{***}	1.74 [*]
3HPMA (acrolein)	305.9 ^{***}	0.96	1.13	1.19
2HPMA (propylene oxide)	16.0 ^{***}	1.14	0.91	0.97
AAMA (acrylamide)	67.5 ^{***}	1.08	1.01	1.37 [*]
HPMMA (crotonaldehyde)	4.9 ^{***}	1.17	1.24	1.00

* indicates significant α or β in the mixed-effects model (*: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.005$)

Table 5.

Spearman correlation of urinary biomarker concentration with personal exposure to PM_{2.5} by fuel type and temascal (wood-fired sauna bath) use

Biomarker	Overall (n=97)	Fuel		Recent temascal use	
		Exclusive wood (n=50)	Provided gas stove (n=47)	Recent (n=31)	No recent (n=65)
2-naphthol	0.57 ^{***}	0.69 ^{***}	0.43 ^{**}	0.50 ^{***}	0.62 ^{***}
1-hydroxyfluorene	0.53 ^{***}	0.68 ^{***}	0.38 ^{**}	0.37 [*]	0.60 ^{***}
2-hydroxyfluorene	0.42 ^{***}	0.48 ^{***}	0.35 [*]	0.25	0.54 ^{***}
3-hydroxyfluorene	0.52 ^{***}	0.64 ^{***}	0.39 ^{**}	0.41 [*]	0.59 ^{***}
Σ hydroxyfluorenes	0.47 ^{***}	0.57 ^{***}	0.38 ^{**}	0.32	0.57 ^{***}
1-hydroxyphenanthrene	0.29 ^{***}	0.37 ^{**}	0.29	0.25	0.32 ^{**}
2-hydroxyphenanthrene	0.37 ^{***}	0.47 ^{***}	0.34 [*]	0.19	0.46 ^{***}
3,4-hydroxyphenanthrene	0.42 ^{***}	0.52 ^{***}	0.37 ^{**}	0.25	0.52 ^{***}
Σ hydroxyphenanthrenes	0.35 ^{***}	0.45 ^{***}	0.33 [*]	0.28	0.41 ^{***}
1-hydroxypyrene	0.37 ^{***}	0.35 [*]	0.40 ^{**}	0.15	0.48 ^{***}
Total PAH	0.52 ^{***}	0.68 ^{***}	0.40 ^{***}	0.43 ^{**}	0.59 ^{***}
PMA	0.59 ^{***}	0.56 ^{***}	0.52 ^{***}	0.44 [*]	0.61 ^{***}
MHBMA-3	0.13	0.23	0.04	0.02	0.16
HEMA	0.35 ^{***}	0.42 ^{***}	0.17	0.31	0.33 ^{**}
MMA	0.21 [*]	0.05	0.33 [*]	0.45 [*]	0.14
CNEMA	0.57 ^{***}	0.63 ^{***}	0.47 ^{***}	0.51 ^{***}	0.60 ^{***}
3HPMA	0.21 [*]	0.44 ^{***}	0.22	0.17	0.19
2HPMA	0.10	0.14	0.19	0.18	0.10
AAMA	0.12	0.44 ^{***}	0.08	0.00	0.19
HPMMA	0.07	-0.11	0.26	0.19	-0.03

* p < 0.05

** p < 0.01

*** p < 0.005

Table 6.

Comparison of reductions in particulate matter and urinary metabolite concentrations among cookstove intervention studies

Intervention, country; comparison	Concentration ^a		Difference ^b	% change ^b	Method	Sample Collection time	Reference
	Pre-intervention/Control	Post-intervention					
<i>PM_{2.5} (µg/m³)</i>							
Chimney wood stove, Peru: before (open fire; n=44) and after (n=44)	133 (med)	70 (med)	-63	-47%	gravimetric	48-hour	Li, 2011
Gas stove, Guatemala: before (wood; n=50) and after (n=48)	102 (med)	45 (med)	-57	-56%	gravimetric	48-hour	Present study
<i>2-hydroxynaphthol (pmol/mg creatinine)</i>							
Chimney wood stove, Peru: control (open fire; n=179) and intervention (n=153)	114.4 (GM)	92.9 (GM)	-21.5	-19%	GC-MS	Fasting	Li, 2016
Chimney wood stove, Peru: before (open fire; n=57) and after (n=57)	132.5 (med)	69.4 (med)	-63.1	-48%	GC-MS	Fasting	Li, 2011
Chimney wood stove, Mexico: before (open fire; n=47) and after (n=47)	110.3 (med)	74.9 (med)	-35.4	-32%	GC-MS	Fasting	Riojas-Rodriguez, 2011
Gas stove, Guatemala: before (wood; n=50) and after (n=48)	231.8 (med)	142.7 (med)	-89.1	-38%	LC-MS	Fasting	Present study
<i>Σ hydroxyfluorene (pmol/mg creatinine)</i>							
Chimney wood stove, Peru: control (open fire; n=179) and intervention (n=153)	34.5 (GM)	33.4 (GM)	-1.2	-3%	GC-MS	Fasting	Li, 2016
Gas stove, Guatemala: before (wood; n=50) and after (n=48)	42.5 (med)	29.4 (med)	-13.1	-31%	LC-MS	Fasting	Present study
<i>Σ hydroxyphenanthrene (pmol/mg creatinine)</i>							
Chimney wood stove, Peru: control (open fire; n=179) and intervention (n=153)	21.7 (GM)	21.0 (GM)	-0.7	-3%	GC-MS	Fasting	Li, 2016
Gas stove, Guatemala: before (wood; n=50) and after (n=48)	46.7 (med)	37.0 (med)	-9.7	-21%	LC-MS	Fasting	Present study
<i>1-hydroxypyrene (pmol/mg creatinine)</i>							
Chimney wood stove, Peru: control (open fire; n=179) and intervention (n=153)	11.5 (GM)	12.2 (GM)	0.7	+6%	GC-MS	Fasting	Li, 2016

Intervention, country: comparison	Concentration ^a		Difference ^b	% change ^b	Method	Sample Collection time	Reference
	Pre-intervention/Control	Post-intervention					
Chimney wood stove, Peru: before (open fire; n=57) and after (n=57)	14.7 (med)	11.5 (med)	-3.2	-22%	GC-MS	Fasting	Li, 2011
Chimney wood stove, Mexico: before (open fire; n=47) and after (n=47)	16.1 (med)	10.9 (med)	-5.2	-32%	GC-MS	Fasting	Riojas-Rodriguez, 2011
Chimney wood stove, Mexico: before (open fire; n=47) and after (n=47)	59.2 (mean)	42.4 (mean)	-16.8	-28%	HPLC	-	Torres-Dosal, 2008
Gas stove, Guatemala: before (wood; n=50) and after (n=48)	19.7 (med)	16.9 (med)	-2.8	-14%	LC-MS	Fasting	Present study

^aMeasures of centrality: GM – geometric mean; med – median.

^bDifference calculated as the arithmetic difference or percent change between measure of centrality in two comparison groups.