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RESEARCH ARTICLE

# Biomass smoke exposures: Health outcomes measures and study design

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**Abstract**
Epidemiological studies of biomass smoke health effects have been conducted in a variety of settings and with a variety of study designs. The Health Effects Workgroup discussed several approaches for the investigation of health effects in communities exposed to wood smoke from nearby wildland fires, intentional agricultural burning, or residential biomass burning devices such as woodstoves or cookstoves. This presentation briefly reviews observational and intervention studies that have been conducted within these exposure settings. The review is followed by a summary of discussion points among the workgroup members with particular emphasis on study design and the use of biomarkers for assessing outcomes in biomass smoke-exposed populations.

**Keywords:** *Biomarkers; biomass; epidemiology; health effects; intervention trials*



## Introduction

Biomass smoke exposure can occur in a variety of settings, ranging from residential exposure to woodstoves or cookstoves to community-wide exposure from nearby wildland fires or agricultural burning. We describe here some of the epidemiological approaches for investigating health effects associated with exposure to biomass smoke. This summary begins with a brief review of selected observational, intervention, and exposure studies conducted in human populations. For a more thorough discussion of these and other biomass smoke studies, refer to the recent review of wood-smoke health effects (Naeher et al., 2007). The background section is followed by a summary of the health effects breakout session, exploring the commonalities and differences that should be considered when conducting health studies in these different settings. Particular attention was paid to the different study approaches for the varying exposure scenarios and to identifying the most relevant outcomes, including subclinical biomarkers of effect.

## Background

### *Observational studies*

Wildland fires, agricultural burning, and biomass burning for domestic heating have provided opportunities to observe health effects associated with biomass smoke-derived elevations in particulate matter (PM). Several cross-sectional studies of wildland firefighters have demonstrated temporary declines in lung-function metrics such as forced expiratory volume in the first second ($FEV_1$) and the ratio of $FEV_1$ to forced vital capacity (FVC) associated with firefighting activities (Betchley et al., 1997; Liu et al., 1992; Rothman et al., 1991). Burning of agricultural residue in areas proximate to rural communities has been shown to exacerbate respiratory symptoms among individuals with preexisting conditions (Golshan et al., 2002; Long et al., 1998). Conversely, elevated levels of $PM_{10}$ due to bushfires near Sydney, Australia, were not associated with adverse effects on peak expiratory flow rates among children with wheeze (Jalaludin et al., 2000).

Studies that have focused on wildfire- or agricultural burning-derived PM and hospital visits for asthma have

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predominantly demonstrated positive associations. Increases in hospital, emergency room, and/or physician visits have been observed among communities temporarily exposed to wildland fire smoke when compared to smoke-free reference periods (Duclos et al., 1990; Emmanuel, 2000; Kunzli et al., 2006; Mott et al., 2005; Mott et al., 2002). Time-series analyses of Sydney bushfires in 1991 also provided weak support for an association between PM and asthma hospital visits (Churches & Corbett, 1991), but analyses of the Sydney bushfires of 1994 demonstrated no such association (Cooper et al., 1994; Smith et al., 1996). More recent time-series studies of both urban and rural Australian communities impacted by smoke from bushfires showed an association between smoke-derived PM and hospital visits for asthma (Chen et al., 2006; Johnston et al., 2002). With a 5-day lag there was a more than doubling in risk for asthma presentations for days with $PM_{10}$ levels greater than 40 μg/$m^3$ compared to days with $PM_{10}$ levels less than 10 μg/$m^3$ (Johnston et al., 2002).

Based on limited data there does not appear to be an increased risk of mortality in communities exposed to smoke from nearby wildfires. At least two studies of wildfire-impacted communities did not observe an increased risk of mortality (Emmanuel, 2000; Vedal & Dutton, 2006). By contrast, elevated mortality was observed in Kuala Lumpur during the 2007 Southeast Asian fires when ambient wildfire-derived PM reached high concentrations (i.e., above 200 μg/$m^3$ $PM_{10}$) (Sastry, 2002).

Health effects among children exposed to biomass smoke in residential indoor environments are most clearly demonstrated in developing countries where biomass cookstoves are commonly used (for review see Naeher et al., 2007). Relatively few studies have been conducted in developed countries to directly assess the health impacts among children due to the more moderately elevated PM from residential woodstove usage. A prospective study of respiratory symptoms among infants observed an association between frequency of cough and woodstove use, but respiratory symptoms were not associated with fireplace use in the home (Triche et al., 2002). Cross-sectional observational studies indicated lung function decrement (Johnson et al., 1990) and higher frequency of symptoms that can be loosely described as asthma related (Butterfield et al., 1989; Honicky et al., 1985) among children living in woodstove homes compared to children living in homes without woodstoves. An ecological study examined respiratory symptoms in a woodstove community compared to a non-woodstove community (Browning et al., 1990). Although there were no differences overall, there was a higher frequency of wheezing among children under five years old in the woodstove community, suggesting that young children may be susceptible to adverse respiratory effects of wood smoke (Browning et al., 1990). Additionally, studies of children living on the Navajo reservation in Arizona demonstrated greater risk of acute lower respiratory illness among children from households with woodstoves (Morris et al., 1990; Robin et al., 1996). A recent evaluation of the panel study of asthmatic children in a woodsmoke-impacted area of Seattle, WA, found inverse associations between pulmonary function measures (i.e., FEV1, midexpiratory flow [MEF], peak expiratory flow [PEF]) and concentrations of the woodsmoke marker levoglucosan outside the homes of subjects (Allen et al., 2008).

### *Intervention studies*

Developing countries have been the focus for several investigations of health outcomes in household-generated biomass smoke exposures, primarily from the use of solid fuels for cooking. It has been estimated that one-half of the world's households continue to cook with solid fuels, approximately 95% of which consists of wood fuel or burning of agricultural residues (Smith et al., 2004). Incomplete combustion and poor ventilation in biomass burning devices used for cooking or heating can result in extremely high PM exposures in these households (Naeher et al., 2007; Smith et al., 2000). Several intervention studies, including RESPIRE/CRECER in Guatemala and PATSARI in Mexico, are currently underway in communities that use biomass cookstoves (Naeher et al., 2000; Zuk et al., 2007). For example, the RESPIRE intervention trial in Guatemala found that compared to women in the intervention arm with the lower PM emission "plancha" stove, women with a traditional biomass burning cookstove had a 3- to 11-fold increased gene expression in sputum for molecules involved in airway inflammation and remodeling (i.e., tumor necrosis factor [TNF]-α, interleukin [IL]-8, matrix metalloproteinase [MMP]-9, and MMP-12) (Balmes, 2007). Importantly, studies in this and similar communities have demonstrated associations between in-home exposures to biomass fuels and chronic obstructive pulmonary disease among adults and acute lower respiratory infection among children (Smith et al., 2004).

Some intervention studies in the United States and other developed countries have focused on the reduction of indoor asthma triggers for the improvement of quality of life among children with asthma. The majority of home-based studies have investigated a variety of interventions aimed at reducing allergen exposures in the home (Bernstein et al., 2006; Carter et al., 2001; Clougherty et al., 2006; Eggleston et al., 2005; Eggleston et al., 1999; Gergen et al., 1999; Gotzsche et al., 2004; Kercsmar et al., 2006; Krieger et al., 2005; Levy et al., 2006; McDonald et al., 2002; Morgan et al., 2004). With few exceptions, these studies have not directly targeted or assessed in-home PM exposures. The multifaceted interventions often included environmental tobacco smoke as a component to be addressed through a combination of education, behavioral alteration strategies, and environmental controls. Two randomized controlled trials have reported on the effectiveness of HEPA filtration units in reducing in-home PM (Eggleston et al., 2005; Reisman et al., 1990). The first study reported a 73% reduction in total suspended particulates due to HEPA usage and found modest improvements in total symptoms among the air filtration treatment group (Reisman et al., 1990). This trial contributed to a 2002 meta-analysis of air filtration unit studies that found significant improvements in total symptoms and sleep disturbance among asthmatics in homes in the air filtration treatment arm (McDonald et al., 2002). A second, more recent randomized controlled trial reporting on PM levels demonstrated a 39% reduction in $PM_{10}$ among homes using HEPA filtration units (Eggleston et al., 2005). This study found overall reductions in symptom reporting among the treatment group, but the multifaceted intervention, which included behavioral and allergen-targeted environmental interventions, makes it difficult to determine the main effect of PM reduction among this treatment group. None of these intervention studies targeted homes at risk for non-tobacco-related PM exposure such as homes using woodstoves as their primary heating source. Currently, communities in Montana and British Columbia with high prevalence of woodstove usage are being investigated to determine the impact of targeted woodstove interventions on the health of susceptible individuals (Allen et al., 2008; Ward & Noonan, 2008).

### *Experimental exposure studies*

A final category of relevant study design is controlled exposure experiments. There are few examples of such studies using biomass smoke exposure chambers for observation in humans. A group in Sweden exposed 13 healthy subjects to 240–280 $\mu g/m^3$ of $PM_{2.5}$ from combustion of birch and spruce. This study evaluated pre- and postexposure blood and urine samples and observed increases in biomarkers of cardiovascular effect as well as increases in a marker of systemic inflammation, 8-isoprostane (Barregard et al., 2006). Another exposure chamber study exposed healthy and asthmatic subjects to rice straw smoke and observed airway inflammation in both healthy and asthmatic subjects (Balmes, 2007).

## Panel discussion

### *Observational studies*

Community-wide exposures from agricultural burning and both prescribed and unintentional wildland fires offer unique and challenging scenarios for study. The overall approach should not be appreciably different from those approaches used in the study of urban-generated ambient particulate matter. The key difference is in the nature of exposure, as agricultural burning and wildland fire exposures are typically episodic exposures of moderate to high intensity for short durations, typically lasting days or weeks.

Limitations of observational epidemiology approaches in these short-duration exposure scenarios were discussed. Hospital-based case-control studies or mortality studies suffer from the difficulties of exposure assessment under these episodic events, which can have wide temporal and spatial variability. Cohort studies were also discussed as an approach for assessing the health effects of community-wide exposure to biomass smoke that would be similar to the Six Cities Study (Dockery et al., 1993). Assembling cohorts of appropriate size would be problematic, however, as most communities exposed to these episodic biomass events are rural and sparsely populated, and the nature of exposure is often unpredictable. Time-series studies have been a common epidemiological approach for investigating health effects of ambient exposure to particulate matter in urban and peri-urban settings. As with cohort studies, the episodic, unpredictable nature of the exposure in small populations offers unique challenges for time series studies of agricultural burning or wildland fire exposures. The challenges are similar when such approaches are applied to studies of communities seasonally exposed to wood smoke for domestic heating. The panel also expressed interest in further investigating the potential for a synergistic effect between cold temperatures and the biomass-associated PM levels on health outcomes.

Some acute or short-term outcomes were discussed as intriguing candidates for future studies in communities at risk for seasonal exposure to biomass smoke. Birth outcomes such as lower birth weight were considered as of potential interest in these exposure settings. The exposure and outcome time window is much shorter than that observed for many of the chronic cardio-respiratory outcomes. The timing of in utero exposure corresponding to these episodic events could be characterized fairly precisely with respect to weeks of gestation or trimester. For cardiovascular effects in adults there was also general agreement that tracking data among patients with implantable cardioverter defibrillators that lived in communities commonly exposed to agricultural burning or wildfires would be useful. For all such studies it was agreed that a reliable biomarker of exposure to biomass smoke would be useful.

### *Intervention studies*

Outcomes evaluated in studies of biomass smoke health effects in developing countries include acute lower respiratory infection in children and chronic obstructive pulmonary disease in adults, primarily women. These were the primary outcomes used to assess biomass smoke-related risk for the World Health Organization's Comparative Risk Assessment Project (Smith et al., 2004). There are limited data available on the effects of biomass smoke on childhood asthma, and asthma was not included in the comparative risk assessment. Further research on this susceptible population is warranted. The working group also agreed that epidemiological studies of biomass smoke should include cardiovascular outcomes as a major focus. As with the observations in the ambient PM literature, cardiovascular outcomes are important from a policy perspective given the potential for a large population attributable risk.

Compliance issues offer an additional challenge for both heating woodstove and cookstove intervention studies. The function and utility of the intervention devices can be affected by human behavior. In the case of cookstoves, residents may alternate between the use of the improved cookstove with a chimney and the traditional open-fire cookstove. In the case of woodstoves, the effective operation of lower emission woodstoves requires some training of the residents. Methods for objectively assessing the proper and consistent usage of these intervention devices should be considered in any health outcomes studies.

***Other considerations for health studies of exposure to biomass smoke***

There were several biomarkers that were discussed as important tools for further investigating the health effects of exposure to biomass smoke. In exposure-chamber studies of secondhand tobacco smoke several markers of acute vascular injury have been observed, including decreased flow-mediated dilation and increases in endothelial progenitor cells. These acute effects would be difficult to observe in field settings, where it may be more realistic to use systemic markers of inflammation such as C-reactive protein in blood and 8-isoprostane or Clara-cell protein in urine. Biomarkers of inflammation or oxidative stress that can be quantified in exhaled breath condensate include pH and 8-isoprostane, but further validation of these biomarkers in PM exposure settings is needed. The Guatemala RESPIRE study observed gene and/or protein expression increases in sputum for molecules involved in airway inflammation and remodeling (i.e., TNF-$\alpha$, IL-8, and MMP-9) among women exposed to high levels of indoor biomass smoke. Finally, exhaled nitric oxide has been effectively used in previous indoor PM studies such as the Seattle panel studies and may be closer to clinically relevant endpoints than other respiratory biomarkers that were discussed.

Effect modifiers were not discussed at length by the group, but it was recognized that attention should be given to some factors that have been recognized as having a potential modifying effect on PM-related health outcomes. These factors include nutritional status such as high-fat diet in developed countries and malnourishment in developing countries, underlying chronic health conditions, and behavioral factors such as exercise and smoking. Genetically determined susceptibilities should also be considered as more information becomes available.

## Conclusion

While it remains to be seen whether or not there are toxicological differences between biomass smoke-generated PM and other sources of PM such as diesel exhaust, the exposure scenarios for biomass smoke offer unique opportunities for epidemiological study. Residents in both developed and developing countries are exposed to moderate to high levels of biomass smoke. These indoor PM sources can be manipulated with relatively simple interventions and offer ideal settings for randomized trial research. Observational epidemiological studies of acute or short-term effects may be more appropriate.in communities with seasonal or episodic elevations in PM from indoor-generated biomass-smoke or exposures from nearby wildland fires or agricultural burning. The development of a reliable biomarker of exposure to biomass smoke PM and the use of biomarkers of effect for these acute or short-term effects will help to advance research in this area.

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