

## Concept Clearance

**Branch:** Population Health Branch

**Council Period:** 201501

**Concept Title:** Household Air Pollutants, Tobacco, and Lung Exposure: Interventions among LMICs

### Introduction

According to the Global Burden of Disease 2010 data, tobacco smoking and household air pollution are the second and third leading risk factors, respectively, after high blood pressure, for global mortality and disability-adjusted life years (DALYs) lost. These exposures disproportionately affect Low and Middle-Income Countries (LMICs), including nonsmoking women and children.

Nearly 3 billion people still cook, heat, and light their homes using open fires and traditional stoves burning solid fuels (i.e. wood, crop wastes, charcoal, coal and dung). Such inefficient cooking fuels and technologies produce high levels of household air pollution with a range of harmful pollutants, including small soot particles that penetrate deep into the lungs. In poorly ventilated dwellings, indoor smoke can be 100 times higher than acceptable levels for small particles. According to WHO estimates, Household Air Pollution (HAP) from solid fuels is responsible for approximately 4.3 million early deaths per year, primarily in LMICs. Approximately 17% of annual lung cancer deaths in adults are attributable to exposure to carcinogens from HAP. Additionally, research has shown that exposure to biomass fuel emissions is associated with low birth weight and higher infant mortality, increased respiratory infections in children, and increased rates of stroke, cardiovascular disease, lung cancer, eye disorders, burn and other injuries in adults. HAP exposures disproportionately affect women and children, as they spend more time inside the home environment.(1)

The World Health Organization has estimated that, globally, smoking is responsible for almost 6 million deaths annually. Among men, lung cancer is the leading cause of cancer death. While tobacco use has been slowly declining in most high income nations, including the US, it is increasing in many LMICs. Indeed, of the 800 million adult men who currently smoke cigarettes, over 80% are in LMICs. Following the Framework Convention on Tobacco Control (FCTC), the first treaty ever negotiated by the World Health Organization, countries are adopting new and innovative tobacco control policies and programs. However, secondhand tobacco smoke exposure in the home environment remains a major challenge for health in many countries. Surveys have shown high levels of secondhand smoke exposure at home among non-smoking women and children in countries with high male smoking prevalence, such as China and Vietnam.(2, 3) 47% of global deaths from second-hand smoke occurred in women, 28% in children, and 26% in men, and over 61% of DALYs were due to exposure in children.(4)

At the same time, a world-wide effort led by the Global Alliance for Clean Cookstoves (GACC) since 2010 has reenergized the agenda to substitute open fires with improved cooking technology devices with a goal of 100 Million improved cookstoves in homes by the year 2020. Several federal agencies including the NIH and USAID, and many other organizations are making significant investments to facilitate this agenda. Hundreds of diverse types of stove and fuel distribution and implementation efforts are already underway around the world.

However, research is lacking on the health impacts from the introduction of modified cookstoves due to a lack of well-designed studies that take into account actual usage and exposures. While progress is tangible and several field trials have demonstrated reductions in environmental emissions with improved cookstoves, a concomitant effect on health outcomes has not always been evident. There is a need for "proof of principle" evidence to support the ongoing and future large scale investments in stove development and rollout programs and for carefully controlled interventional research projects which focus rigorous attention to adoption and use and the cleanest possible fuels/burning methodologies. Moreover, there is a need to frame the research agenda within the complexities tied to the behavioral, cultural and social barriers to cookstove adoption, the socioeconomic determinants of access to cleaner stoves and fuels, and the critical household behaviors behind successful technology adoption.

There is also a need to understand the combined effects of multiple exposures inside the home environment. For example, lung cancer incidence is very high among both men and women in China yet only 2.4% of women smoke, compared with 53% of men. Multiple factors may contribute to lung cancer among non-smoking women in China, including exposure to secondhand smoke and exposure to solid fuel smoke from cooking and heating. However, while several studies have looked at lung cancer among women in China, the relative contributions of these factors are unknown. There is a need to evaluate interventions that combine introduction of improved cookstoves with smoke-free home interventions designed to reduce tobacco smoke exposure in the home.

This concept addresses an issue of high priority for the NIH. At a recent meeting with the Global Alliance for Clean Cookstoves, NIH Director Francis Collins charged an NIH working group with developing a research framework to produce a stronger evidence base linking reduction in HAP exposures to clear health outcomes. To this end the NIH HAP working group led by

NIEHS and FIC has developed a framework for an initiative to facilitate such a study with NHLBI acting as the lead NIH institute.

#### References:

1. WHO. Household air pollution and health. Fact sheet N°292. 2014. Available at: <http://www.who.int/mediacentre/factsheets/fs292/en/>
2. Minh HV, Giang KB, Xuan le TT, Nga PT, Hai PT, Minh NT, Quan NT, Hsia J. Exposure to second-hand smoke at home and its associated factors: findings from the Global Adult Tobacco Use survey in Vietnam, 2010. *Cancer Causes Control*. 2012 Mar;23 Suppl 1:99-107.
3. Yao T, Sung HY, Mao Z, Hu TW, Max W. Secondhand smoke exposure at home in rural China. *Cancer Causes Control*. 2012 Mar;23 Suppl 1:109-15.
4. Oberg M, Jaakkola MS, Woodward A, Peruga A, Prüss-Ustün A. Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. *Lancet*. 2011 Jan 8;377(9760):139-46.

#### Research Goals and Scope

The purpose for an initiative in this area is to support trans-disciplinary teams of researchers to work together within low and middle income countries to develop and/or test improved stove and fuel interventions, along with interventions to reduce tobacco smoke exposure in the home, that may be applicable across diverse community and social and cultural settings. The initiative also aims to leverage existing infrastructure and build upon data already collected around the implementation of household air pollution and secondhand smoke interventions. Field research projects would address both short and long term (4-6 years) health outcomes of interventions by evaluating parameters including, but not limited to, low birth weight and infant mortality, and respiratory infections and, neurocognitive development in children and/or rates of respiratory, stroke, and cardiovascular diseases, lung cancer, and eye disorders, in adults. It is also envisioned that secondary analysis of environmental and behavioral changes before and after an intervention and assessment of the influences that determine preferences for specific practices, motivators and barriers to adoption, and key behaviors associated with use of solid fuels and tobacco smoking inside the home will be an integral addition to the research proposals.

- Successful proposals may incorporate some features of efficacy trials including but not limited to: Use of only the most effective cookstoves, elimination of fuel “stacking”, assurance of complete adherence and adoption of use.
- Test the interventional models that significantly reduce the health impacts of HAP on pregnancy, pregnancy outcomes, low birth weight, co-morbidity in infant and children less than 5 years of age such as acute respiratory illness, growth and cognition in infancy and early childhood.
- For health outcomes with long incubation periods specific biomarkers should be collected at intervals appropriate for the developmental susceptibility of the relevant tissues and may include in-utero and early-life germline, somatic, or tissue-specific epigenetic changes.
- Study design and proposed analyses should account for the possibility that germline or tissue-specific epigenetic changes may be induced by HAP exposure and, therefore, heritable-risk may persist even after exposures are reduced or eliminated.
- Study designs can also incorporate development and validation of novel biomarkers of exposure and effect as a secondary aim
- Interventions must incorporate adequate measures of exposure in the household to HAP and, in any population where relevant, secondhand smoke.

## Mechanism and Justification

This initiative is designed to fill a specific, critical need not met by any other program at the NIH and NIEHS. We propose to issue a Request for Application (RFA) because of the need to foster innovative investigator-initiated research and to provide incentives for more investigators to study a problem with substantial public health importance in a coordinated way. The RFA would encourage multidisciplinary teams of scientists to work together to propose innovative interventions that make use of existing infrastructure and activities of the GACC. The RFA also supports the development of multiple linked projects that follow a similar timeline and which can benefit from exchange and use of common methods and approaches where appropriate. Use of an RFA mechanism will also allow for assembly of a designated review group with the diverse expertise required for this initiative, including reviewers with experience in international research in LMICs.

The U01 cooperative agreement mechanism is proposed since substantial scientific and/or programmatic involvement is required for the efficient and integrated operation of this program. The RFA will support a U01 to a Clinical Coordinating Center (CCC) which will be responsible for daily monitoring of projects, data collection, and coordination of activities. Three to four sub-awards will be awarded to research institutions in LMICs to carry out the field work. The cooperative agreement mechanism supports the development of research collaborations across the initiative, encourages greater involvement of research partners in LMIC institutions, ensures coordination with other partners, including GACC and GACD, and allows for opportunities to address new research questions that emerge during the study period. Additionally, the U01 mechanism facilitates programmatic efforts to encourage more effective translation of research findings into interventions that are effective in practice.

NIEHS is proposing to contribute \$500,000 per year for five years to this initiative. The anticipated total NIH contribution to the initiative is \$15 million over five years. Other IC commitments include \$1 million per year from NHLBI and NCI and \$500,000 per year each from NICHD. Additionally, GACC is expected to provide matching funds of \$1 million per year and \$5 million total over five years.

Oversight and governance of the initiative will be provided by a Steering Committee composed of one NIH project officer from each participating IC, two CCC members, and the PIs of each of the research projects, including representation from both US and foreign institutions. The Steering Committee will identify emerging scientific opportunities or impediments to progress for the network, promote collaboration and communication across study teams, work with other partners, including GACC and GACD, and hold annual meetings of the participating researchers and partners.