



# Indoor air pollution and lower respiratory tract infections in children



World Health  
Organization



# **Indoor air pollution and lower respiratory tract infections in children**

Report of a symposium and a workshop held at the International Society of Environmental Epidemiology, Paris, 4 September 2006, presenting preliminary results of a randomized intervention trial in Guatemala and discussing the implication for policy, advocacy and future research

## WHO Library Cataloguing-in-Publication Data

Indoor air pollution and lower respiratory tract infections in children: report of a symposium held at the International Society of Environmental Epidemiology, Paris, 4 September 2006, presenting preliminary results of a randomized intervention trial in Guatemala and a workshop discussing the implication for policy, advocacy and future research.

1.Air pollution, indoor. 2.Respiratory tract infections. 3.Randomized controlled trials. 4.Health surveys. 5.Intervention studies. 6.Child. 7.Guatemala. I.World Health Organization. II.Title.

ISBN 978 92 4 159572 8 (NLM classification: WA 754)

### © World Health Organization 2007

All rights reserved. Publications of the World Health Organization can be obtained from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857; e-mail: [bookorders@who.int](mailto:bookorders@who.int)). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to WHO Press, at the above address (fax: +41 22 791 4806; e-mail: [permissions@who.int](mailto:permissions@who.int)).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

This publication does not necessarily represent the decisions or the stated policy of the World Health Organization.

Designed by minimum graphics  
Printed in Switzerland

# Contents

<b>Executive summary</b>	<b>1</b>
<b>1 Introduction</b>	<b>2</b>
<b>2 Summary of the abstracts presenting the main findings from the Guatemala Randomized Intervention (RESPIRE) study</b>	<b>3</b>
Background of the study and description of the site	3
Objectives of the trial	3
Study intervention and effect on air pollution	4
Case finding and effect of chimney stoves on childhood pneumonia	4
Conclusion of presentations at the symposium	5
<b>3 Research lessons and future directions from the RESPIRE study</b>	<b>6</b>
Trial findings not reported at the symposium	6
Blood pressure	6
Upper respiratory infections	6
Self-perceived health	7
Non-health outcomes	7
Other similar studies and sources for information	7
Methodological lessons and problems	7
Gaps in knowledge, research needs	9
Additional efficacy trials	9
Effectiveness trials	9
Cohort studies	10
Case-control studies	10
Advanced methods to be considered	10
Additional Guatemala studies (in addition to ongoing CRECER study)	11
Policy and advocacy implications	11
<b>4 What do we tell governments and donors?</b>	<b>12</b>
<b>5 References</b>	<b>14</b>
<b>6 Participants</b>	<b>15</b>

# Acknowledgement

WHO wishes to thank Dr Nigel Bruce, Division of Public Health, University of Liverpool, Liverpool, UK, Dr Byron Arana, Universidad del Valle, Guatemala and Dr Kirk Smith, University of California School of Public Health, Berkeley, CA, USA for convening the symposium “*RESPIRE – the Guatemala Randomized Intervention Trial*” at the International Society for Environmental Epidemiology (ISEE), Annual Meeting, Paris, 4 September 2006; and for the presenters at the symposium for contributing their presentations. It also wishes to thank the participants in the subsequent workshop for their contributions and opinions, and Dr Harry Campbell, Public Health Sciences, University of Edinburgh, for chairing this workshop.

The workshop was supported by the Department of Child and Adolescent Health and Development, WHO, Geneva, Switzerland, with funds made available through the U.S. Agency for International Development (USAID).

# Executive summary

To study the effect of the reduction in air pollution exposures on health outcomes such as pneumonia in young children, a randomized control trial (RCT) using improved woodstoves with chimneys as the intervention was carried out from 2002–2004. The study aimed at improving our understanding of the relationship between pneumonia and indoor air pollution. It was undertaken in the highlands of Guatemala on a population of over 500 Mayan Indian children aged 0–18 months in households that used open wood fires for cooking.

At a symposium at the International Society of Environmental Epidemiology in Paris in September 2006, preliminary results of the trial were presented as 5 papers, – describing the process and methods in conducting the control trial of acute lower respiratory infections and indoor air pollution; – evaluating the performance to optimize case-finding for childhood pneumonia; – examining the impact of a chimney wood stove on the risk of pneumonia in children aged less than 18 months in a rural area; – assessing the impact of a chimney stove on women’s lung health in a rural wood-burning community; and – measuring the impact of social and environmental factors on a vulnerable population by their effects on birth weight, growth, and mortality.

This symposium was followed by a workshop which summarized first some trial findings which were not reported at the symposium, such as effects on blood pressure, upper respiratory tract infections, self perceived health and non-health outcomes (e.g. time and fuel savings). Workshop participants discussed methodological lessons learned and problems encountered, and gaps in knowledge and further research needs.

It was concluded that further trials in different geographical settings are needed. Designs, potential sites and request for such research were considered. Nevertheless, it was considered that there was now a more solid basis for arguing about the effect of air pollution reduction on child health, and that advocacy efforts to donors and governments needed to be scaled up, to address this major risk factor for child mortality.

# 1 Introduction

The deaths every year of nearly 2 million children under the age of 5 years in developing countries from acute lower respiratory infections (ALRI) have not been fully accounted for by well-established risk factors such as malnutrition. Over a dozen observational studies have found consistent associations with indoor air pollution (IAP), including the use of solid fuels in households, but they fall short of fully confirming a causal exposure-response relationship. A randomized control trial (RCT) using improved woodstoves with chimneys as the intervention, originally planned in the mid-1980s but not funded until 2001, was recently carried out to improve our understanding of the relationship between ALRI and IAP. This study, known by the acronym RESPIRE (Randomized Exposure Study of Pollution Indoors and Respiratory Effects), took place from 2002 to 2004 in the highlands of Guatemala on a population of over 500 Mayan Indian children aged 0–18 months in households that used open wood fires for cooking. Primary funding for the trial was provided by the U.S. National Institutes of Health, with additional contribution by WHO.

## 2 Summary of the abstracts presenting the main findings from the Guatemala Randomized Intervention Trial

Five presentations at the symposium on the randomized intervention trial in Guatemala were concerned with:

- describing the process and methods in conducting the control trial of acute lower respiratory infections and indoor air pollution;
- evaluating the performance of methods used to optimize case-finding for childhood pneumonia;
- examining the impact of a chimney wood stove on the risk of pneumonia in children aged less than 18 months;
- assessing the impact of a chimney stove on women’s lung health;
- measuring the impact of social and environmental factors on a vulnerable population by their effects on birth weight, growth, and mortality.

Another symposium presented the findings on biomass smoke exposure among the Guatemalan infants who participated in the trial.

The abstracts are accessible at <http://ehs.sph.berkeley.edu/krsmith/page.asp?id=19>

### Background of the study and description of the site

In 1991 an international committee was established by WHO to locate a suitable site for a randomized control trial based on criteria such as local health situation and logistics, exposure to indoor air pollution (IAP), and institutional conditions. A dozen sites in Asia, Africa, and Latin America were examined, and Guatemala was chosen. Pilot studies were undertaken in the 1990s before launching the trial in 2001.

The population in the selected site are indigenous, primarily agricultural, Mayans living at an altitude of 2200–3000 m in the western highlands of Guatemala. Their local language is Mam, with Spanish as a second language. Nearly all households in the area use only wood for their fuel requirements. Pre-intervention ALRI rates in young children were estimated at 0.5/child-year.

### Objectives of the trial

The main aim of the randomized trial was to determine the impact of using improved wood stoves with chimneys (the intervention group) on ALRI incidence in children aged <18 months, compared with the use of traditional open fires (the control group).

Other objectives were to quantify the difference between the two groups in the children's exposure to indoor air pollution in relation to the risk of ALRI, and to describe the relationship between exposure reduction and health outcomes for the mother and child (e.g. birth weight, growth and mortality among the infants, and respiratory health and lung function among the mothers).

### Study intervention and effect on air pollution

Some 5500 households in the study area were screened for possible recruitment based on the following: use of an open fire for cooking, presence of a pregnant woman or child under 4 months, willingness to participate, and statistical criteria. From a total of 534 households recruited, 518 (97%) contributed to the final dataset. After baseline household and indoor air quality (IAQ) surveys, the households were randomly assigned to receive an improved chimney stove (*plancha*) at the start of the study (intervention group), or at the end of the study when the child reached the age of 18 months – having been the control group during the trial – or when a household dropped out. The *plancha* was popular and capable of substantially improving the air quality in the kitchen; if any structural problems appeared in the *plancha*, it was repaired during the study.

Personal 48-h carbon monoxide (CO) exposures were obtained every 3 months for all the study children and every 6 months for mothers. Intensive monitoring of CO and particulate matter (PM) was conducted in a 13% sub-sample, along with outdoor monitoring and assessment of exposures from use of wood-fired saunas (*temascals*).

At baseline before intervention, the control and intervention groups had similar child CO distributions (mean values  $2.4 \pm 2.4$  ppm and  $2.5 \pm 1.8$  ppm), respectively. In the control group, there was a small reduction to  $2.0 \pm 2.2$  ppm during the trial, which may be attributed to changing time-location patterns associated with age. However, a much more dramatic reduction in exposure to  $1.0 \pm 2.3$  ppm was observed in the intervention group. Adjusting for gender, age, season, and weekday, the mixed model estimated a 44% reduction (95%CI: -48 to -39%) in child CO associated with the improved stove intervention. Younger age, female sex, and the rainy season were associated with slightly higher exposures. The intraclass correlation coefficient (ICC) was 0.28, indicating the limited reliability of a single measure as a surrogate for long-term exposure.

The *plancha* stove provided large reductions in child CO exposure. The low ICC indicates that most of the variability among the data is within-subject rather than between-subject. We will examine this issue in light of the repeated measures on each child and the observed predictors of exposure and consider the implications for child-specific predictions using the BLUP (best linear unbiased predictor) and attenuation of the hazard ratio for the effect of biomass smoke exposure on infant ALRI.

### Case finding and effect of chimney stoves on childhood pneumonia

After stove installation, case finding was carried out through weekly home visits by fieldworkers (FWs) trained to apply IMCI methods to recognize key signs of ALRI (fast breathing, chest wall indrawing, etc.). Cases were referred to a physician (MD) in the community centre; all referrals had their arterial blood oxygen saturation measured by pulse oximetry ( $SpO_2$ ). A RSV (respiratory syncytial virus) direct antigen test was performed on cases diagnosed as ALRI, and chest X-rays were read blind by two radiologists and validated by a WHO panel. Anthropometry was conducted regularly and birth weights were recorded within 48 hours of delivery. Verbal autopsies were conducted on all child deaths.

The outcomes ranged from very sensitive but non-specific (assessed by a field worker), through moderately specific (diagnosed by a physician), to highly specific – defined

according to criteria of a positive RSV, hypoxia measured by pulse oximetry, and chest X-ray (for pneumonia).

Fieldworkers referred >90% of children who met the ALRI criteria, but only about 75% of them were seen by a physician. However, successful referral by the intervention *plancha* group was about 7% higher (significant for some outcome definitions), a trend also seen in compliance with RSV testing and X-ray referral. Consistency between study physicians in recognizing the respiratory signs used for diagnosing ALRI was adequate, with no clear evidence of bias. There was good consistency between clinical diagnosis/severity and oxygen saturation, with substantial differences in mean SpO<sub>2</sub> between children with physician-diagnosed ALRI and acute upper respiratory infections (AURI) ( $p < 0.0005$ ). Chest X-rays were not available in 20% of cases due to parental mistrust of hospital facilities and transportation difficulties. Parental acceptance of hospital referrals increased over time from 70% in the first 6 months to 95% in the second year.

Based on the preliminary analysis presented at the symposium, fieldworkers (FW) identified 735 cases with ALRI signs after 597.6 child-years of follow-up (incidence of 1.23/child/year). There were 265 cases of physician-diagnosed ALRI (incidence 0.44 episodes/child/year). Preliminary intention-to-treat analysis found rate ratio for intervention vs. control of 0.84 (95% CI: 0.73,0.97;  $p = 0.02$ ) for all weeks with FW-defined ALRI; 0.85 (95% CI: 0.67,1.08) for physician-diagnosed ALRI. There was almost 40% reduction between groups over time for RSV-negative cases with hypoxia (SpO<sub>2</sub> <87%: > 2SD below mean for well children at study altitude), with an OR of 0.62 (95% CI: 0.36,1.05;  $p = 0.07$ ), a potentially important finding since these cases are (a) likely to be bacterial and (b) have more severe disease, and hence the highest mortality. In contrast there was no impact on hypoxic RSV-positive cases (OR: 1.01 95%CI: 0.60,1.73). The overall child exposure reduction based on modelling of 48-hour CO measurements was about 44%.<sup>1</sup>

The sample sizes were not expected to provide sufficient power for statistical significance in birth weight and mortality, but the RESPIRE study offered a unique opportunity to monitor the health of children in one of the poorest regions in Guatemala. Intensive surveillance during the study increased the ability to detect low birth weight (LBW), disease incidence, and death and thus may provide more accurate data about this population than national statistics. This population is under high stress as measured by all indicators. Despite active weekly health surveillance and two full-time physicians, 23 deaths occurred, indicating the high vulnerability of these children to common, treatable illnesses, which can proceed from first symptoms to death in a few days.

There were consistent reductions in ALRI between the intervention group (using *planchas* with chimney) and the control group (using open wood fires), as determined by fieldworkers and physicians. If confirmed, the observed 40% reduction in severe RSV-negative cases strongly supports the case for giving high priority to measures to control indoor air pollution.

## Conclusion of presentations at the symposium

The Guatemala randomized intervention trial, 2002–2004, confirms the benefits of reduction of indoor air pollution by the use of *plancha* stoves with chimneys for household cooking. In particular, the benefits include a lower incidence of acute lower respiratory infections among infants up to the age of 18 months.

<sup>1</sup> The odd ratios and CI presented are based on the preliminary analysis at the time of the Symposium, and might change slightly with the definitive analysis.

### 3 Research lessons and future directions from the RESPIRE study

Reported here are the topics discussed at a Workshop following the Symposium in Paris on 4 September 2006 on indoor air pollution (IAP) and acute lower respiratory infections (ALRI) from the Guatemala Randomized Intervention Trial (RESPIRE), which brought together about 20 people including investigators and other participants from the meeting.

#### **Trial findings not reported at the symposium**

##### *Blood pressure*

Both diastolic and systolic blood pressures dropped about 3.5 mmHg in the *plancha* intervention group and again in the control group after echo intervention, an effect stronger than that achieved by salt reduction in most studies. This finding is the first outcome analysed in the sub-study examining the effect of the intervention on indicators of heart disease risk in a subsample of mothers aged  $\geq 38$  years and grandmothers of the children in the main study. A paper has been submitted for publication with these results; the variability in heart rate, which was measured using Holter monitors, is now being evaluated. Similar findings have been found in some, but not all, studies of outdoor air pollution.

The development of heart disease is of major international interest; its importance locally will depend on the background rate, which is determined by a number of risk factors including diet. As blood pressure (BP) is relatively easy to measure and interpret, it is recommended that monitoring of BP be included in future studies, both observational and experimental. Case-control studies are probably needed to elucidate the impact on active heart disease.

##### *Upper respiratory infections*

The usefulness of acute upper respiratory infection (AURI) as an outcome measure was questioned and discussed. It is unlikely that they will be meaningful outcomes in any trial as they are too frequent in a childhood population. It may be that chronic bronchitis cannot be disentangled in the current trial because cough is an entry criterion for assessment. Clearly this is not a significant aspect of the global burden of disease (GBD), but it may be very important to mothers and hence important in promoting the use of improved stoves.

### Self-perceived health

Based on a self-perceived health questionnaire, most women felt that their health had improved with use of the *plancha* stove, but only half felt that it had improved their children's health. A reduction in sore eyes was most frequently mentioned along with improved cooking position, shorter cooking time, and less worry about child burns. The most common complaint about the *plancha* was a longer time needed for cutting wood. Only a small number indicated that it was colder in the kitchen. The reported symptomatic benefits are consistent with analysis of the longitudinal data for the full study sample, which showed that the prevalence of sore eyes and headache over an 18-month period was significantly reduced in the *plancha* group (Díaz E, Smith-Sivertsen T, Pope D, Lie RT, Díaz A, McCracken J, Arana B, Smith KR & Bruce N. Eye discomfort, headache and back pain among Mayan Guatemalan women taking part in a randomised stove intervention. *Journal of Epidemiology and Community Health*, 2006, in press).

### Non-health outcomes

Time was saved during cooking and in collecting firewood. Saving of fuel was not an outcome in Guatemala because the *planchas* used were not significantly more fuel-efficient, at least by measurement. However, it was noted that the women seemed to think they saved fuel, which may indicate that current measurement techniques are inadequate.

While stove developers have produced more efficient stoves, their acceptability is always a problem. The Guatemala *plancha* may not be ideal for fuel consumption, but it was acceptable and used locally. See <http://ehs.sph.berkeley.edu/uat/publications/Maxwell/Granderson-05-1.pdf>

As noted in the surveys, the benefits of the *plancha* type stove include a reduced risk of childhood burns, improved kitchen hygiene, and enhanced ergonomics of cooking due to raising the working surface from the floor and enclosing the fire.

### Other similar studies and sources for information

A related trial is being carried out in Mexico by Isabelle Romieu. With monthly surveillance, however, most outcome assessments rely on the mothers' recall over the previous two weeks. A range of biomarkers, including those in blood, and women's lung function are also being evaluated. Compared to Guatemala, much lower pneumonia rates have been reported, possibly because of better nutritional status and enrolment of older children up to 5 years of age. AURI assessment is still possible but as it is rarely fatal, its importance as an outcome has been questioned.

The findings of the RESPIRE trial will be useful in informing the ongoing analysis of World Health Survey data to investigate links between respiratory symptoms in under-5-year-olds (i.e. cough, rapid breathing) and the use of solid fuels for cooking and heating.

### Methodological lessons and problems

Pulse oximetry, which is easy and cheap to conduct and appeared to work well as an indicator of severe pneumonia, could possibly replace assessment by a physician in larger trials, combined with assessments by fieldworkers using IMCI. There are logistical and ethical problems, however, because of the need to provide care if hypoxemia is found.

Two major assumptions made in sample size calculations before the start of the randomized control trial (RCT) were generally validated:

- The background pneumonia rate, as represented by the rate found in the control group, was nearly the same as that used in the calculations (0.49 instead of 0.5 per child-year).
- The total “drop-out” rate from all causes after surveillance started – because of migration, voluntary withdrawal, or missed weeks of surveillance (it is important to set up a cut-off for consecutive missing weeks especially in communities with a high rate of migration), or stopping before the child reached 18 months, or death – was a little higher than that used in the calculations (23% vs. 20%).
- However, as there was also a significant loss (mainly due to death and miscarriage) between the time of recruitment and the start of surveillance, future studies should expand the number recruited beyond the lower limit indicated by calculations, as was done in this study in which 534 children were recruited but only 518 entered surveillance (97%).

A larger sample size would be important in future trials. This trial was borderline in size (sample size was based on an outcome which is not 100% specific, so there was loss of power; more specific outcomes yielded fewer outcome events; also, there was loss of additional cases due to respiratory syncytial virus (RSV) stratification). Statistical significance was not reached for the main outcome measure (i.e. the number of physician-diagnosed pneumonia cases), although the estimate was in the hypothesized direction. The primary explanation is that one-third of cases were lost as RSV-positive. Assuming a similar pattern of cases and drop-outs, the sample size at the start of surveillance would have had to be about three times larger than the RESPIRE trial (>1500) to reach significance at the OR of 0.86 that was found. A study of that size should give enough power for low birthweight (LBW) also as an outcome.

Future studies should always measure RSV status in both pilot and main studies. Sample sizes can then account for the possibility that little or no effect will be observed in RSV-positive children.

Site selection and exposure assessment protocols in future stove intervention studies should carefully take account of the sources of exposure to combustion pollutants other than the stove. In this trial, two major sources of exposure were not included in the original protocols, which were modified as soon as their importance was realized. These sources – the *dieta* (lying-in of mothers and babies next to an open wood-fire for 25 days after delivery) and the *temascal* (a traditional wood-fired sauna with high levels of air pollution) – did not seem to be appreciably affected by the intervention, but lessened the relative exposure reduction achieved by the intervention. Combustion for cooking of animal food in this area seemed to be less important. Pilot work is needed to determine the importance of these sources and to determine the optimal monitoring techniques.

One of the advantages of this study site was that all significant combustion sources used the same fuel, i.e. wood, making the interpretation of pollution monitoring data less difficult. Future studies may wish to look for similar sites, which are common.

The methods developed for analysis of carbon monoxide (CO) in the breath and CO tube measurement worked reasonably well in Guatemala and should be considered in future studies. Evaluation is still underway, but current analysis indicates that temporal variation (intra-household) is so high that up to ten 48-hour measurements per child would have been needed to pin down individual exposures better than using group averages, instead of the 4–7 measurements per child in the RCT. On the other hand, a few measurements alone may be sufficient to obtain a reasonable estimate of the group average.

There is still a need for personal devices for measuring particulate matter (PM), small, light, and quiet enough to be used in children. The CO–PM correlation, which allows use of CO tubes, will not necessarily hold for mixtures of fuel types or fuel use patterns in other populations.

Analysis of the time-activity sheets is pending, but will be complex and difficult to validate. It should provide useful information for interpreting the exposure data. There are no simple measuring methods that are well validated at this point, although much work is now being done in the exposure field using small electronic devices, such as the UCB Particle Monitor, and UCB Personal Locator developed during the RCT and now being deployed in the second phase of studies at the site (acronym CRECER: Chronic Respiratory Effects of Early Childhood Exposure to Respirable Particulate Matter).

If significantly large sales could be guaranteed, there would be an incentive to develop devices designed specifically for these solid-fuel households by industry as has been the case for vaccines, energy-conserving appliances, and other technologies. Specifications for such devices would need to be worked out, however, with involvement of experts familiar with health-damaging air pollution, engineering, chemistry, and field logistics.

## **Gaps in knowledge, research needs**

### *Additional efficacy trials*

As the Guatemala trial is one whose effects are at the border of significance, more efficacy trials are needed with pneumonia as an endpoint. A characteristic of this study site was the high altitude and high levels of under-nutrition, but it is not known whether and how these might modify the effects of reduced indoor air pollution (IAP) on pneumonia incidence. Given that policy is driven most effectively by locally derived evidence, it would probably be best to choose the next trial sites in Asia and Africa, rather than a repeat in Latin America. The government of India has indicated that it would fund local expenses for such a trial.

Wherever the next trial is to be attempted, however, the experience in Guatemala indicates the extreme importance of good preparatory work to (i) find a suitable site in terms of current pneumonia levels, biomass fuel use, and accessibility, (ii) carry out an intervention that will not only reduce exposures but also be well accepted locally, and (iii) find an excellent and experienced local collaborator.

Whether, after these results, such a trial would be ethically acceptable was discussed at the workshop. If not, it may be desirable to use an entirely different technology as the intervention. Most likely candidates would seem to be the new generation of “gasifier” stoves, which use biomass but burn nearly as cleanly as liquified petroleum gas (LPG) and are coming into use in China, and biogas, which is widely used in several Asian countries.

More research is urgently needed on low birth weight as well as pneumonia. A new trial could start with randomization after delivery of a previous child. There is also little quantitative evidence on how the use of different fuels and stoves is linked to the risk of burns and scalds in children and adults, and on how such risks are affected by different interventions.

### *Effectiveness trials*

Given the large background of observational studies and the relative success in Guatemala, there is probably justification for identifying a location for a large-scale effectiveness trial. The fact that a randomized controlled effectiveness trial (or at least an

individual household randomized study) could be very difficult was discussed, and other designs (including cluster randomized trials), quasi-experimental (comparison group studies), and observational designs may have to be examined.

Electrification in South Africa might provide such an opportunity using a very clean cooking source. The Shell Foundation's and GTZ's rollout of improved stoves and other such large-scale plans like promotions of natural gas in Eastern Europe or of LPG through UNDP and/or WLPGA (World Liquid Petroleum Gas Association) projects potentially offer other opportunities, as would the existing national programmes for clean fuels and biogas in Nepal.

### *Cohort studies*

Although the children in the RESPIRE trial have been turned into a longitudinal cohort (CRECER), with some additional sample enhancement, in order to look for chronic effects including asthma, there is likely to be need for additional efforts along these lines.

Of considerable advantage would be a multi-centre collection of birth cohorts that could be followed for some years to examine a range of endpoints, including, for example, low birthweight, premature birth, stillbirth, neonatal and post-neonatal deaths (depending on sample size), early growth, etc. Such an effort has been proposed as part of UCB's extension of its Fogarty Grant in India in one site, Chennai.

A study approach, like the Tucson respiratory study (Martinez) for developing countries which followed a cohort of children from birth and performed lung function measurements early in life, would be desirable in several sites and give invaluable information on mechanisms.

### *Case-control studies*

Case-control studies are needed for a range of endpoints that are suspected, but not well understood, such as:

- Heart disease
- Lung and other cancers
- Asthma
- Low birthweight and neonatal/infant death
- Case-fatality of respiratory disease (TB, ALRI, COPD, *lung cancer*, etc.)
- Although a 4-site multi-centre study is currently underway in South Asia, there may still be need for additional studies of TB, perhaps in conjunction with HIV status.

### *Advanced methods to be considered*

To enhance their attractiveness in the frontiers of biomedical research and among funders, future studies of any design should seriously consider such advanced methods as:

- Sophisticated biomarkers of exposures, sub-clinical effects and disease, including virology, macrophage viability, oxidative stress, etc.
- Genetic markers
- Interactions with HIV status.

### **Additional Guatemala studies (in addition to ongoing CRECER study)**

- Obtaining birthweights from the RESPIRE/CRECER study area (for example, Comitancillo where 85% of our study population came from) for a case-control study.
- Evaluating cognitive development, which is being considered. (Standardized instruments exist from studies on the effect of lead exposure on cognitive development.)
- Rolling out the intervention in other households or other areas in Guatemala.
- Genetic testing – potential of a “mendelian randomization” type approach if appropriate genetic variants involved in causal pathways can be identified.
- Extension of follow-up of women using *planchas* and open fires (CRECER cohort) to investigate differential rates of decline in lung function, and markers of airway inflammation and remodelling (*Janet Diaz, plan to submit for funding*)
- Investigating the role of oxidative stress as a possible mechanism for PM increasing the vulnerability to bacterial pneumonia (*Plan to submit for funding*).

### **Policy and advocacy implications**

- Kirk R. Smith is involved in redoing comparative risk assessments of household solid fuels in an effort funded by the Health Effects Institute, along with assessing other environmental risks.
- Cost-effectiveness analysis (CEA) and cost-benefit analysis (CBA) have been conducted at global and regional levels; however, given the lack of epidemiological evidence, the impact of improved stoves on childhood ALRI and adult chronic obstructive pulmonary disease (COPD) was based on estimates. The CEA assumption of 75% reduction in childhood ALRI looks far too optimistic in the light of the RESPIRE findings; the CBA assumption of 35% reduction in childhood ALRI (a range of 10% to 60% was tested in the sensitivity analysis) appears more realistic. To improve the relevance of economic analyses to a specific decision-making context, CBA should be repeated at national or sub-national levels in relation to specific, locally available interventions.
- Some work will be done in the context of the Child Health Epidemiology Reference Group (CHERG). The CHERG pneumonia group will undertake the task of estimating the distribution of etiologic agents and of estimating cause-specific trends, splitting age-groups, and reviewing and estimating the impact of interventions.
- WHO is planning for expansion of the UNICEF/WHO advocacy paper on pneumonia published in September 2006. As UNICEF has a renewed focus on child health, they have been contacted and are interested.

## 4 What do we tell governments and donors?

We now have results to promote interventions, such as improved stoves, to reduce the exposure to indoor air pollution, even though more research is needed. As a tool, a global mapping of possible interventions (e.g. stove types) and its acceptability by possible users and donors would be useful. Good and acceptable solutions are better than perfect ones which cannot be financed or are not locally accepted and sustainable. WHO and the University of Liverpool (United Kingdom) are currently undertaking a review of the impacts of past and ongoing projects/programmes to reduce indoor air pollution, which might go some way towards a global mapping of interventions.

Because the cost of the historical next step up the energy ladder (i.e. kerosene and LPG) has increased dramatically, there is now a widened “economic space” above the traditional household use of biomass fuels. Even in those countries where the consumer is insulated from high oil prices by government subsidies of these fuels, the governments are eager to find ways to reduce the enormous cost of the subsidy. This provides opportunities for promoting processed biomass fuels and improved combustion devices which cost substantially less than switching to petroleum-based fuels, but more than many of the so-called improved stoves promoted to date. So-called gasifier stoves and processed biomass fuels such as pellets, ethanol or plant oils are examples of ways to achieve important reductions in actual emissions. These options are important because the RESPIRE trial found that chimney stoves did not reduce women’s and children’s exposures nearly as much as indoor pollution levels, probably mostly due to the exposures from outdoors or neighbouring dwellings that still cook in a traditional way. These findings are confirmed by a number of other studies around the world and lend strong support to the need to actually reduce emissions through cleaner combustion devices rather than simply shifting the smoke outside.

There is a need to persuade industrial partners interested in investing in the development of new technologies to deliver affordable stoves with low emissions. To date, there has been very low investment in this area relative to its importance, although there is some activity now by Phillips, Bosch Siemens and a number of companies in China.

Increasingly, financing opportunities for programmes to promote interventions to reduce indoor air pollution in developing countries are becoming available. The World Bank, through its new investment framework on clean energy for development, has placed some emphasis on access to cleaner fuels and technologies to reduce indoor air pollution and associated health risks. The EU’s Energy Initiative is making available 198 million Euros for household energy provision (electricity and cooking energy) in so-called ACP (Africa, Caribbean, Pacific) countries.

The availability of financing, however, needs to be complemented by increased awareness of governments as well as the lay public in developing and developed countries about the health risks of indoor air pollution and the available solutions. Initiatives to increase such awareness include the engagement of the health sector as well as schools in promoting the message. The media – through radio/TV programmes and advertising, articles in science and women’s magazines and newspapers, as well as the internet – play an essential role. Public visibility can also be increased by involving celebrities and other champions.

## 5 References

The following papers arising from the RESPIRE study have been published by the time of printing of this report.

- Bruce N, Weber M, Arana B, Diaz A, Jenny A, Thompson L, McCracken J, Dherani D, Juarez D, Ordonez S, Klein R, Smith KR, 2007, Pneumonia case-finding in the Guatemala indoor air pollution trial (RESPIRE): standardizing methods for resource-poor settings, *Bull WHO*, 85 (7): 535–544.
- McCracken JM, Smith KR, Mittleman M, Diaz A, Schwartz J, 2007, Chimney stove intervention to reduce long-term woodsmoke exposure lowers blood pressure among Guatemalan women, *Environ Health Perspect.* 115 (7): 996–1001.
- Clark M, Paulson M, Smith KR, Canuz E, Simpson CD, 2007, Urinary methoxyphenol biomarkers and woodsmoke exposure: comparisons in rural Guatemala with personal CO and kitchen CO, levoglucosan, and PM<sub>2.5</sub>. *Environ. Sci & Tech.* 41(10): 3481–3487.
- Díaz E, Smith-Sivertsen T, Pope D, Lie RT, Díaz A, McCracken J, Arana B, Smith KR & Bruce N. 2007, Eye discomfort, headache and back pain among Mayan Guatemalan women taking part in a randomised stove intervention. *J Epidemiology and Community Health*, 61:75–79.
- Smith KR, Bruce NG, Arana B, 2006, RESPIRE: the Guatemala Randomized Intervention Trial (Symposium MS3 at the ISEE/ISEA Annual Conference, Paris), *Epidemiology* 17(6) Suppl November, pp S44–46.

Electronic versions of these and further papers as they are published can be found on the website <http://ehs.sph.berkeley.edu/guat/page.asp?id=32>

# 6 Participants

Harry Campbell (Chair)

Nigel Bruce

Maggie Clark

Mukesh Dherani

Anaite Diaz

Esperanza Diaz

Xaoli Duan

Rufus Edwards

Christine George

Dan Pope

Isabel Romieu

Kirk R. Smith

Michael Johnston

John McCracken

Sumi Mehta

Heidi Mestl

Luke Naeher

Lisa Thompson

Jim Zhang

## WHO

Eva Rehfuss

Martin Weber

ISBN 978 92 4 159572 8



9 789241 595728