ENVIRONMENTAL EXPOSURES, LUNG FUNCTION, AND RESPIRATORY HEALTH IN RURAL LAO PDR

Jaime R Lopez[1], Khamphithoune Somsamouth[2], Boualoy Mounivong[2], Ryan Sinclair[3], Sam Soret[3], Synnove Knutsen[1] and Pramil N Singh[1,4]

[1]Department of Epidemiology and Biostatistics, [3]Department of Environmental Health, [4]Center for Health Research, School of Public Health, Loma Linda University, Loma Linda, California, USA; [2]Center for Information Education for Health, Ministry of Health, Lao PDR

Abstract. Although the individual contributions of smoked tobacco and indoor air pollution have been identified, there are very few studies that have characterized and measured the effects of inhaled particles from a wide range of personal, household, and community practices common in rural Asia. The objective of our study was to examine the association between environmental inhaled exposures and lung function among rural males of Lao PDR. In a sample of 92 males from rural Lao PDR, study subjects completed a survey on household exposures, a physical exam, and the following measures of lung function: FEV1, FVC, and the ratio of FEV1/FVC. Our findings were as follows: a) > 80% of the subjects were exposed to indoor cooking fires (wood fuel), animal handling, dust and dirt; b) 57.6% of subjects were in the impaired range (FEV1/FVC < 0.7); and c) animal handling was negatively associated ($p<0.03$) with FEV1 and FVC. Among males in rural Lao PDR, we found a high prevalence of chronic exposure to inhaled particles (animal handling, dust/dirt, smoke) and a high prevalence of impaired lung function. Findings from this pilot study indicate that associations between exposure to multiple sources of particulate matter common in rural areas and lung function need further investigation.

Keywords: air pollution, lung function, respiratory disease, tobacco use, Lao PDR

INTRODUCTION

In 2004, an estimated 12 million deaths occurred in the Western Pacific Region (WPR), of which approximately one-quarter were attributed to respiratory disease (Jamrozik and Musk, 2011). Within the region, there is emerging community level data implicating specific behavioral and environmental risk factors for respiratory disease (Idolor *et al*, 2011). Existing reports indicate that manufactured cigarettes represent the single most preventable behavioral risk factor for respiratory disease in WPR nations (Zhang and Cai, 2003; Chan-Yeung *et al*, 2004, 2007; Kojima*et al*, 2007; Zhong *et al*, 2007). Recent data from Cambodia (Singh *et al*, 2009), Lao PDR (Lopez *et al*, 2012), Vietnam (Ministry of Health of

Correspondence: Dr Pramil N Singh, Center for Health Research, School of Public Health, Loma Linda University, Loma Linda, California, 92350 USA.
Tel: 909 5581732; Fax: 909 5580326
E-mail: psingh@llu.edu

Vietnam, 2010), China (Lubin *et al*, 1992; Buist *et al*, 1995; Lee and Collin, 2006; Zhong *et al*, 2007; Al-Sadat *et al*, 2010; O'Connor *et al*, 2010; Xiao *et al*, 2010), and Thailand (Centers for Disease Control, 2010) also identify the contribution of other smoked tobacco products such as hand-rolled cigarettes and homemade (bamboo) tobacco waterpipes to the global tobacco epidemic. A recent pilot study in Lao PDR found that cigarette and tobacco waterpipe smoking produced harmful levels of carbon monoxide exhaled by the user (Lopez *et al*, 2012).

In addition to smoked tobacco use, recent reports from the rural WPR have also identified a high prevalence of household, occupational, and community level exposures that may also contribute to poor respiratory health (Anderson, 1979; Dennis *et al*, 1996; Torres-Duque *et al*, 2008; Basu *et al*, 2011). These include (but are not limited to: a) household air pollution (indoor cooking fires, trash fires); b) outdoor air pollution (industrial pollutants, vehicle emissions, crop burning); c) overcrowding and poor building materials; d) occupational dust and dirt; and e) livestock handling. Very few studies have considered the effect of simultaneous exposure to these the inhaled particles from all of these hazards in rural communities.

In the present study of rural men in Lao PDR, the aim of our study was to examine the relation between exposure to inhaled particles from multiple sources (smoked tobacco, household air pollution, dust and dirt, animal handling) and lung function.

MATERIALS AND METHODS

Sample

This population has been described previously (Lopez *et al*, 2012). During March 2010, as part of a study of tobacco use, we worked with the Ministry of Health to select six villages from a rural district of Luang Nam Tha Province that was known to have a high prevalence of tobacco smokers. In each village, we worked with multilingual interviewers to conduct a stratified household sampling (to ensure a sufficient number of non-users and users of smoked tobacco (cigarette, waterpipe).

We selected males aged over 40 years and older. The rationale for this selection criterion was to account for age and gender-related differences in lung function. We also followed the American Thoracic Society criteria to exclude subjects who could bias comparisons: a) observable mental impairment; b) not having muscular coordination in performing the required maneuvers; and c) pre-existing health conditions that could affect lung function testing.

Ethical considerations

Ethics approval was obtained from the Ethics Committee of the Ministry of Health Vientiane Capital (Ref N^{o} 823; 2010 Feb 09) and the Institutional Review Board of Loma Linda University (Confirmation provided: 2013 Nov 20). Informed consent was obtained.

Survey measures

We used the items from Burden of Obstructive Lung Disease (BOLD) questionnaire and key informant interviews to design the survey. Our survey included items on demographics, respiratory symptoms, tobacco use, and other environmental exposures (household air pollution, occupational exposure to livestock, dust, and dirt). Tobacco use measured by the survey was also confirmed by salivary cotinine testing in the field (NicAlert® kit; Nymox Corp, Hasbrouck Heights, NJ).

The tobacco items and pictograms used in this study had been validated regionally (Singh *et al*, 2013). Trained interviewers from the Ministry of Health and local multilingual aids were used to administer the survey.

Lung function and physical exam

Our main measures of lung function (without bronchodilation) included: FEV1 (forced expiratory volume in liters per second), FVC (forced vital capacity in liters), and the ratio of FEV1/FVC. All lung function testing was conducted between 9:00 AM - 12:00 PM local time in each village by one of us (JRL) who was trained in a standardized lung function testing protocol (Miller *et al*, 2005). We used a portable, battery-operated spirometer (EasyOne®; ndd Medizintechnik, Zurich, Switzerland) to measure our lung parameter outcomes. We calibrated our spirometer weekly according to the manufacturer's specifications using a 3-liter syringe and the Easyware® 2010 software package (ndd Medizintechnik, Zurich, Switzerland). Our meter measured expiratory airflow using ultrasonic sensor technology developed to measure maximal flow through a sterile tip modulated with an oral mouthpiece.

With a nose clip attached to obstruct both nares and in a seated position, each subject was instructed to maximally inhale and then forcibly exhale into the meter using the sterile disposal tip. Two health officers "coached" each subject while one of the authors (JRL) visually demonstrated the required maneuver in order to obtain the best test from each subject. Using the EasyOne's "FVC test" protocol, our meter recorded the "best value" of up to eight trials to obtain the best maneuvers. To account for the ethnic anthropometric difference, we used an Asian correction factor of 0.88 in adjusting for differences in thoracic size. Each subject's test score was recorded and saved for subsequent data analysis.

We pilot tested our protocol for the physical exam and spirometry test using a small sample of 15 rural males from villages who were sampled for the larger validity study in Luang Namtha Province. We tested our coaching instructions and a maneuver demonstration with each invited subject to check for any inconsistencies in our testing instructions, coaching, and anthropometric and physiological measurements. Our physical exam included measurements of systolic and diastolic blood pressure, heart rate, oxygen saturation blood level, height, weight, and body mass index (BMI).

Statistical methods

Descriptive analyses were conducted on demographic, environmental, respiratory health, and lung function parameters, and means and proportions were computed. The lung function outcome was assessed by continuous measures (FEV1, FVC, FEV1/FVC) and a categorical measure Global Obstructive Lung Disease Initiative (GOLD) staging criteria (Buist *et al*, 2008).

The relation between tobacco, other environmental exposures, and lung function (FEV1, FVC, and FEV1/FVC) was evaluated in linear regression models with lung function as the outcome variables. Pertinent confounders (age) were also tested. The distribution of the lung function parameters was approximately normal, and transformations did not produce substantially different results. The lung function data (FEV1, FVC) was used analytically to classify subjects based on the 2010 (GOLD) staging criteria by Buist and others (2008).

Briefly, we defined level of impairment with FEV1/FVC less than 0.70. We further defined impairment: FEV1 ≥80% predicted Stage1, ≥50 and <80% FEV1 predicted Stage 2, ≥30 and <50% FEV1 predicted Stage 3, and <30% predicted Stage 4.

For a logistic regression analysis, we defined an outcome variable for impaired lung function (Stages 1-4) based on the GOLD Criteria. We then related impaired lung function to tobacco use and environmental exposures using a similar modeling strategy to the other lung function outcomes. All analyses were conducted using SAS® (version 9.1; SAS Institute, Cary, NC).

To assess the level of type 2 error in our pilot study of 92 subjects, we performed a power analysis for a linear regression model of an FEV1 outcome with four independent variables. We found that in order to have an 80% power and two-tailed alpha of 0.05 to detect small (Cohen's $f^2 = 0.02$), medium (Cohen's $f^2 = 0.15$), and large (Cohen's $f^2 = 0.35$) effect sizes, we needed sample sizes of 602, 85, and 40, respectively. Therefore, with our current sample size we could detect medium and large effect sizes in a linear model. All power analyses were done with G*Power 3 (Dusseldorf University, Dusseldorf, Germany).

RESULTS

We had an overall response rate of 88.5% with a final sample of 92 subjects (37 cigarette, 28 waterpipe, and 27 non-smokers) after exclusion criteria. Our sample from rural Lao PDR (mean age 52 years, SD=9 years) was studied as part of a stratified sampling of male tobacco users and non-users (Table 1). For users of smoked tobacco, we found that most tended to have a long duration habit (mean length of habit=35.7 years). As expected, there was a significant negative association between age and lung function (FEV1, p=0.0068; FVC, p=0.0099). Height (data not shown) was a marginally significant predictor of FEV1 (p=0.08) and a significant predictor in FVC (p=0.005).

Table 1
Anthropometric, health, and environmental exposures in 92 males in rural Lao PDR.

Variable	Value Mean ± SD
Anthropometrics	
Height (cm)	156.9 ± 5.7
Weight (kg)	49.7 ± 8.2
Body mass index	20.2 ± 3.3
Chest size (cm)	84.5 ± 6.3
Abdomen size (cm)	76.3 ± 8.5
Health	
Systolic BP	126.3 ± 21.0
Diastolic BP	85.8 ± 11.7
Pulse	77.9 ± 14.8
Blood oxygen saturation (%)	97.9 ± 2.1
Morning cough when not sick	67.4%
Cough with sputum	75.0%
Chronic cough when not sick	48.9%
Shortness of breath on exertion	31.5%
Smoked tobacco	
Waterpipe	30.4%
Cigarettes	40.2%
Non-smokers	29.4%
Environmental exposures	
Cooking fire inside the home	83.7%
Domesticated animal handling	85.9%
Wood biofuel in any cooking fire	94.6%
Dust-dirt exposure	89.1%

In Table 1, we have characterized the sample based on four domains (anthropometric, health, smoked tobacco, and other environmental exposures). The basic health parameters from a physical exam

Table 2
Spirometric lung parameters of 92 males in rural Lao PDR.

Parameter	Mean ± (SD)
FEV1 (l/s)	1.96 ± 0.70
Predicted FEV_1%	81.2 ± 30.8
FVC (l)	2.96 ± 0.94
Predicted FVC%	94.8 ± 28.6
FEV1/FVC (l/s)	0.65 ± .014
FEF50 (l/s)	2.08 ± 1.30
PEF (l/s)	3.64 ± 1.70
FEF25-75 (l/s)	1.62 ± 1.00
2010 GOLD Staging, *n* (%)	
I: Mild	15 (16.3)
II: Moderate	24 (26.1)
III: Severe	9 (9.8)
IV: Very severe	5 (5.4)

indicate typical anthropometrics of predominantly lean males of rural Southeast Asia (mean BMI=20.2), and additionally, blood pressure, pulse, and oxygen saturation were within the normal range. We found that 67.4% of our sample reported that they currently experience morning cough upon waking, and 75% reported that they are currently coughing with sputum expectorate.

For environmental exposure, we found that more than 80% of subjects handled domesticated animals, were exposed to dust or dirt, and were exposed to cooking fires inside the home. Overall, 94.6% of subjects used wood biofuels in cooking fires in and outside of the home.

In Table 2, we present the mean lung function parameters for the sample and found that values tended to be low relative to cutoff points for impairment (FEV1/FVC<0.7 and predicted FEV1<80%) used in high-income nations. Overall, 57.6% of the subjects had impaired lung function based on FEV1/FVC less than 0.70. GOLD staging indicated most of the impaired were in the mild or moderate categories.

In Table 3, we examined the relation between smoking, environmental exposures, and a COPD screen (FEV1/FVC<0.70). In age-adjusted analyses (Table 3), we found that simultaneous exposure to all daily exposures (dust-dirt, animals, household air pollution, and smoking) produced a two-fold increase in odds of a positive screen for COPD.

In Table 4, we report results concordant with the GOLD staging findings (Table 3) indicating linear regression analyses of a significantly lower FEV1 and FVC for animal handling. Simultaneous exposure to all factors in Table 4 was associated with marginally significant declines in FEV1 and FEV1/FVC ($0.05<p<0.09$).

DISCUSSION

As part of a study of smoked tobacco and health in Lao PDR, we conducted a community-level assessment of tobacco use and environmental exposures with lung function in a sample of males from a northern rural district. Our major findings are as follows. First, more than 80% of the subjects were exposed to indoor cooking fires (wood as the predominant fuel), domesticated animal handling, or inhaled dust and dirt. Second, the prevalence of a positive COPD screen (FEV1/FVC<0.70) was 57.6%. And third, animal handling was associated with a negative linear relation with FVC and FEV1 ($p<0.03$).

Taken together, our findings raise the possibility of an alarming convergence of behavioral (tobacco) and environmental factors in rural Lao PDR that can contribute to poor respiratory health. It is noteworthy, that simultaneous exposure to all measured factors (tobacco, animal

Table 3
Crude and age-adjusted logistic regression on low function relative to normal lung function.

Factors	Crude OR (95%CI)	Age adjusted OR (95%CI)
Daily dust-dirt exposure	1.88 (0.39-8.95)	1.75 (0.37-8.58)
Daily animal handling	1.39 (0.37-5.20)	1.21 (0.31-4.66)
Daily household air pollution	1.11 (0.31-3.95)	1.24 (0.34-4.55)
Daily tobacco smoking (cigarette and waterpipe)	1.27 (0.51-3.09)	1.67 (0.64-4.38)
All daily exposures	1.82 (0.79-4.20)	2.08 (0.87-4.95)

Table 4
Results concordant with the GOLD staging findings.

	Crude		Age-adjusted	
	β	*p*-value	β	*p*-value
FEV1				
Daily dust-dirt exposure	-0.54	0.06	-0.51	0.07
Daily animal handling	-0.59	0.01	-0.52	0.03
Daily household air pollution	0.03	0.89	-0.04	0.85
Daily tobacco smoking (cigarette and waterpipe)	0.04	0.81	-0.08	0.60
All daily exposures	-0.19	0.21	-0.25	0.09
FVC				
Daily dust-dirt exposure	-0.59	0.09	-0.54	0.11
Daily animal handling	-0.71	0.01	-0.63	0.03
Daily household air pollution	0.19	0.52	0.08	0.76
Daily tobacco smoking (cigarette and waterpipe)	0.08	0.70	-0.07	0.74
All daily exposures	-0.12	0.51	-0.19	0.31
FEV1/FVC				
Daily dust-dirt exposure	-0.39	0.50	-0.03	0.53
Daily animal handling	-0.03	0.46	-0.03	0.54
Daily household air pollution	-0.02	0.61	-0.02	0.56
Daily tobacco smoking (cigarette and waterpipe)	-0.02	0.45	-0.03	0.28
All daily exposures	-0.04	0.11	-0.05	0.08

handling, cooking fires, dust/dirt) was associated with a non-significant two-fold increase in odds of a positive COPD screen and a marginal, negative linear association with FEV1/FVC (p=0.08). A possible reason why individual known risk factors did not show a strong association with lung function measures is the extremely high prevalence of multiple inhaled exposures present in a given household.

Our findings concerning rural men from Lao PDR complement recent data from a similar study of women and children in the same communities (Mengersen *et al*, 2011). Specifically, the authors found a positive association between time spent near indoor cooking fires and respiratory symptoms (shortness of breath, cough) and acute respiratory infection among women. Also noteworthy were respiratory symptoms associated with home construction materials (bamboo, wood) and dust-dirt exposure. Similar to the qualitative observations of our study, the authors noted the presence of inadequate ventilation in Laotian domestic households.

A recent report identified several potential respiratory disease risk factors present in rural communities of Lao PDR (Morawski *et al*, 2011). Investigators studied air quality in residential dwellings and found extremely high levels of particulate matter (PM_{10}) emissions from indoor cooking fires, carbon monoxide (CO), and nitric dioxide (NO_2). They attributed exposure to these respiratory risk factors to cooking and smoking within residential homes that lack both chimneys and adequate ventilation. In addition, investigators found that a soil floor and floor dust were significant risk factors.

Other rural areas of the WPR also show similar effects of lifestyle patterns and the environment in rural communities. For example, in the Philippines, a study reported a prevalence of COPD of 20.8% in rural areas as compared to 13.8% in urban areas (Idolor *et al*, 2011). Factors associated with increased odds for COPD in their sample included: >20 pack years of tobacco cigarette use (OR=2.86; 95%CI: 1.78-4.60), >60 years of firewood use (OR= 3.48; 95%CI: 1.57-7.71), and >20 years of farm work (OR=2.48; 95%CI: 1.43-4.30).

Limitations

The small sample size of this pilot study produced important measures of effect that often were non-significant with wide confidence intervals. Our power calculations indicate that medium and large effect sizes could be detected, but a sample size of at least 600 would have been needed to identify small effect sizes. Moreover, to investigate combined exposures (air pollution, tobacco, animal handling), a large sample size would be needed to investigate synergistic effects. We did not measure environmental tobacco smoke exposure at the time of lung function testing. In other samples that were part of our validation studies in the same villages, the prevalence was >60%.

Among males in rural Lao PDR, we found a high prevalence of behavioral and environmental risk factors (tobacco, dust-dirt, animal handling, household air pollution) that could impair lung function and contribute to respiratory disease. The strong association with animal handling was notable. Overall, these findings raise the possibility that public health measures such as tobacco control and environmental health need programmatic linkages to effectively address the cumulative burden of respiratory disease risk factors in Lao PDR.

ACKNOWLEDGEMENTS

The authors are grateful for the assistance of Mr Grant Hillier of the Adventist Development and Relief Agency in Lao PDR. This study was supported by grant R03 TWOO7345-01 from Fogarty/NIH (PI: Pramil N Singh). Mr Lopez conceived the study, collected the data, analyzed the data, and wrote the report. Dr Singh obtained the funding and assisted in report writing and supervising the data collection. Drs Khamphithoune and Mounivong supervised the data collection and assisted in the study design.

Drs Knutsen, Soret, and Sinclair assisted in writing the report.

REFERENCES

Al-Sadat N, Misau AY, Zarihah Z, Maznah D, Tin Tin Su.. Adolescent tobacco use and health in Southeast Asia. *Asia Pac J Public Health* 2010; 22 (suppl): 175-80.

Anderson HR. Chronic lung disease in the Papua New Guinea Highlands. *Thorax* 1979; 34: 647-53.

Basu S, Stuckler D, Bitton A, Glantz SA. Projected effects of tobacco smoking on worldwide tuberculosis control: mathematical modelling analysis. *BMJ* 2011; 343: d5506.

Buist AS, Vollmer WM, McBurnie MA. Worldwide burden of COPD in high- and low-income countries. Part I. The burden of obstructive lung disease (BOLD) initiative *Int J Tuberc Lung* Dis 2008; 12: 703-8.

Buist A, Vollmer WM, Wu Y, *et al*. Effects of cigarette smoking on lung function in four population samples in the People's Republic of China. The PRC-US Cardiovascular and Cardiopulmonary Epidemiology Research Group. *Am J Respir Crit Care Med* 1995; 151: 1393-400.

Centers for Disease Control. Differences by sex in tobacco use and awareness of tobacco marketing – Bangladesh, Thailand, and Uruguay, 2009. *MMWR Morb Mortal Wkly Rep* 2010; 59: 613-8.

Chan-Yeung M, Ait-Khaled N, White N, Ip MS Tan WC. The burden and impact of COPD in Asia and Africa. *Int J Tuberc Lung Dis* 2004; 8: 2-14.

Chan-Yeung M, Ho AS, Cheung AH, *et al*. CSG Hong Kong Thoracic Society. Determinants of chronic obstructive pulmonary disease in Chinese patients in Hong Kong. *Int J Tuberc Lung Dis* 2007; 11: 502-7.

Dennis RJ, Maldonado D, Norman S, Baena E, Martinez G. Woodsmoke exposure and risk for obstructive airways disease among women. *Chest* 1996; 109: 115-9.

Idolor LF, De Guia TS, Francisco NA, *et al*. Burden of obstructive lung disease in a rural setting in the Philippines. *Respirology* 2011; 16: 1111-8.

Jamrozik E, Musk AW. Respiratory health issues in the Asia-Pacific region: an overview. *Respirology* 2011; 16: 3-12.

Kojima S, Sakakibara H, Motani S, *et al.* Incidence of chronic obstructive pulmonary disease, and the relationship between age and smoking in a Japanese population. *J Epidemiol* 2007; 17: 54-60.

Lee K, Collin J. "Key to the future": British American tobacco and cigarette smuggling in China. *PLoS Med* 2006; 3: e228.

Lopez JR, Somsamouth K, Mounivong B, Sinclair R, Singh PN. Carbon monoxide levels in water pipe smokers in rural Lao PDR [Research letter]. *Tob Control* 2012; 21: 517-8.

Lubin JH, Li JY, Xuan XZ, *et al.* Risk of lung cancer among cigarette and pipe smokers in southern China. *Int J Cancer* 1992; 51: 390-5.

Mengersen K, Morawska L, Wang H, *et al.* The effect of housing characteristics and occupant activities on the respiratory health of women and children in Lao PDR. *Sci Total Environ* 2011; 409: 1378-84.

Miller MR, Crapo R, Hankinson J, *et al*. ATS/ERS Task Force. General considerations for lung function testing. *Eur Respir J* 2005; 26: 153-61.

Ministry of Health of Vietnam, Hanoi Medical Univeristy, General Statistics Office, Centers for Disease Control and Prevention, WHO. Global adult tobacco survey (GATS) Vietnam 2010. Geneva: WHO, 2010. [Cited 2013 Sep 12]. Available from: URL: http://www.who.int/tobacco/surveillance/en_tfi_gats_vietnam_report.pdf

Morawski L, Mengersen K, Wang H, Tayphasavanh F, Darasavong K, Holmes NS. Pollutant concentrations within households in Lao PDR and association with housing characteristics and occupants activities. *Environ Sci Technol* 2011; 45: 882-9.

O'Connor RJ, Li Q, Stephens WE, *et al.* Cigarettes sold in China: design, emissions and metals. *Tob Control* 2010; 19 (suppl): i47-53.

Singh PN, Sothy K, Yel D, Nguyen D, Job JS.Validity and reliability of survey items and pictograms for use in a national household survey of tobacco use in Cambodia. *Asia Pacific J Public Health* 2013; Epub 2013 May 21.

Singh PN, Yel D, Sin S, *et al.* Tobacco use among adults in Cambodia: evidence for a tobacco epidemic among women. *Bull World Health Organ* 2009; 87: 905-12.

Torres-Duque C, Maldonado D, Perez-Padilla R, Ezzati R, Viegi G; Forum of International Respiratory Societies Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. *Proc Am Thorac Soc* 2008; 5: 577-90.

Xiao L, Yang Y, Li Q, Wang CX, Yang GH. Population-based survey of secondhand smoke exposure in China. *Biomed Environ Sci* 2010; 23: 430-6.

Zhang H, Cai B. The impact of tobacco on lung health in China. *Respirology* 2003; 8: 17-21.

Zhong N, Wang, Yao W, *et al.* Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. *Am J Respir Crit Care Med* 2007; 176: 753-60.