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Household Fuel Use and Latent Tuberculosis Infection in a Nepali population.

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Abstract

Background—The risk of developing latent tuberculosis infection (LTBI) associated with cooking with solid fuels is unknown. This study examined the relationship between household fuel uses and LTBI in adults living in Nepal, a country with a high incidence of tuberculosis.

Methods—Participants were 1,088 adults aged 18–70 years, members of the control group of a population-based case-control study of pulmonary TB (PTB) in people without previous TB, living in Kaski and neighboring districts of Nepal. Participants were interviewed in their homes with a standardized questionnaire. Blood samples were tested for LTBI using an interferon-gamma release assay. Multivariate unconditional logistic regression was used to examine associations between household fuel sources and LTBI.

Results—The overall prevalence of LTBI in the study population was 36%. Using liquefied petroleum gas (LPG) as the baseline cooking fuel type, the adjusted odds ratio (aOR) for using a primary wood cookstove was 1.13 (95%CI: 0.73,1.77) for all participants and, in women only, 1.14 (0.62, 2.09). Corresponding figures for biogas stoves were 0.64 (0.34,1.20) and 0.59

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(0.24,1.45), respectively. Household sources of air pollution positively associated with LTBI included traditional oil lamps (diyos) used during power outages, for which the aOR in all participants was 2.53 (1.20, 5.31), although the number of users was small. Use of candles for lighting was also associated with increased risk of LTBI among men (aOR = 1.61, 95% CI:1.01, 2.56).

Conclusions—No association was found between use of wood for cooking and LTBI. However, there was some evidence that biogas cookstoves were associated with reduced odds of LTBI. Some exposures at the time of actual infection will have been different than the current exposures used in the analysis, biasing results towards the null. Results are sufficient for the use of diyos to be discouraged for lighting purposes. Overall, results suggest that household cooking fuel use is likely to have more effect on moving from the infected state to PTB than on becoming infected with the *M. tuberculosis* complex. Further research, including longitudinal studies with serial LTBI testing would be useful to more accurately assess the relationships between exposures and infection.

Keywords

biogas; diyos; latent tuberculosis infection; liquefied petroleum gas; wood smoke

INTRODUCTION

Tuberculosis (TB) disease is a major cause of global morbidity and mortality, with 10 million new cases and 1.6 million deaths in 2017 (World Health Organization, 2018). Latent tuberculosis infection (LTBI) is present in approximately one quarter of the global population and will progress to TB disease in approximately 5–15% of infected persons (World Health Organization, 2018). The WHO Southeast Asia region, including Nepal, is estimated to have the highest prevalence of LTBI globally, with more than 30% of the population infected (Houben & Dodd, 2016). Since reducing the risk of infection is important for reducing overall TB incidence, identifying modifiable risk factors for LTBI, particularly in areas of high TB incidence, can play an important role in TB control and elimination.

Well-known risk factors for LTBI include age and close contact with an active TB case (Chen et al., 2015; Gao et al., 2015). Active smoking is associated with increased risk of LTBI (Bates et al., 2007; Lin, Ezzati, & Murray, 2007; Slama et al., 2007), as is male sex (Chen et al., 2015; Gao et al., 2015). An unanswered question is whether or not household fuel use, particularly the burning of biomass for cooking, is a risk factor for LTBI. We identified just two previous studies that had investigated the relationship between household fuel use and LTBI: both used tuberculin skin testing, were in children and had inconclusive results (du Preez et al., 2011; Triasih, Robertson, Duke, & Graham, 2015).

We recently published a case-control study of the relationship between household fuel use and pulmonary TB disease (PTB) in Nepal (Bates et al., 2019). In this paper, we present the results of an analysis involving only the controls of that study, examining whether household sources of smoke are risk factors for LTBI, as measured by an interferon-gamma release assay (IGRA), among individuals who have never had TB disease. Our primary hypothesis was that the use of wood-burning stoves would be a risk factor for LTBI, relative to cooking with liquefied petroleum gas (LPG).

MATERIALS AND METHODS

The parent study from which participants in the present study were drawn was a case-control study of pulmonary tuberculosis (PTB) disease in both men and women, with cases recruited mainly from the Western Regional Tuberculosis Center (WRTC) in Pokhara, Kaski District, Nepal, and controls mainly from the same district. The controls from that study permitted blood samples to be taken for determining LTBI status. Although recruitment and data collection were essentially cross-sectional, for the purposes of the present study we analyze the data as a case-control study—where cases are those who were LTBI-positive and controls those who were LTBI-negative—nested in the parent PTB case-control study.

Prior to commencement of field work, ethical approvals were obtained from the Center for Protection of Human Subjects at the University of California, Berkeley, and the Nepal Health Research Council. Informed consent was obtained from all subjects before they participated in the study.

Eligible for recruitment were males and females, aged 18–70 years. Excluded as participants were:

1. Anyone with known immunosuppressive conditions or taking immunosuppressive drugs (e.g., corticosteroids, cancer chemotherapy). Nepal has a low HIV/AIDS prevalence, but anyone reporting such infection was excluded from the study.
2. Anyone with a history of TB.

Although the original intention of the parent PTB study had been to obtain participants only from Kaski District, where the WRTC is located, towards the end of the field data collection PTB cases were recruited from TB diagnostic centers in districts neighboring Kaski, namely Tanahun, Syanja, and Parbat. This was because recruitment of PTB cases from the WRTC was slower than anticipated. Corresponding controls were additionally obtained from those districts and were used in the present analysis.

Participant recruitment

At the time of the study, rural areas of districts in Nepal were divided into political units called Village Development Committees (VDCs) and metropolitan areas were divided into wards. To achieve a suitable population-based control group for the parent study, we used the geographic distribution of residences of PTB cases in VDCs and wards in Kaski District diagnosed by the WRTC in the previous 3 years. We sought to obtain a geographic distribution of controls (2:1, control to PTB case ratio), aged 18–70 years, which reflected the previous distribution of PTB cases, on the assumption that the distribution of such cases during the period of study data collection would be similar. Recruitment of participants began in May 2013 and concluded in February 2017.

Our goal was to obtain 1,300 controls for the parent PTB study. Houses were randomly selected from the 2008 voter registration list provided by the Nepal Government Electoral Commission in Kathmandu, with each residence in a VDC or ward having a probability of being selected proportionate to the number of registered voters in the household. If more than one person in a household was eligible, a method was used that randomly selected from among those eligible, with a 2:1 ratio of males to females, reflecting the expected ratio among PTB cases in the parent study. We did not obtain historical TB diagnostic data for the VDCs and wards in districts other than Kaski, but for each PTB case two controls were selected from the same VDC/ward using a similar procedure with the voter lists.

The anticipated necessary numbers of controls for the parent PTB study were recruited on a frequency basis, ward by ward and VDC by VDC. Recruitment of controls was made by visits to selected residences. Residences in each ward/VDC were visited in the order of their random selection. If a house contained no person eligible to be a control or a selected potential control was unwilling to participate, then the next household was approached following the random order. All participation refusals were recorded. Blood samples and all study data for participants in the present study were collected during the field visit to the current residences.

The questionnaire

As previously described (Bates et al., 2019), modules in the questionnaire covered means of cooking, heating and lighting in the household, personal history of tobacco use and alcohol consumption, socio-economic factors (education, income, type of work), housing type, health history, household history of TB, food availability, use of mosquito coils and incense, number of people in the household, presence of other household members who were smokers, number of rooms, kitchen configuration, and ventilation features.

LTBI testing:

From each participant a 3 ml blood sample was collected by venipuncture for testing for LTBI using the QuantiFERON-TB Gold test (Cellestis Ltd, Victoria, Australia). This test has the advantage over traditional tuberculin skin testing (TST) in that it does not react to prior BCG vaccination, most non-tuberculosis mycobacterial infections, or prior TST (Pai, Zwerling, & Menzies, 2008).

Blood samples collected were aliquoted in the field into each of the QFT blood collection tubes (TB antigen tube, QuantiFERON mitogen and QuantiFERON nil tube). Tubes were shaken for a minute and incubated at 37°C for 24 hours in a portable, b attery-operated incubator and transported to the research laboratory, Manipal Teaching Hospital, Pokhara for further processing. After the incubation, plasma was harvested and tested for the presence of interferon-gamma (IFN-γ) produced in response to peptide antigens by an ELISA test. Optical density values obtained were analyzed by QFT software (version 2.17) and results were interpreted as per manufacturer instructions.

Diabetes screening test

As previously described (Bates et al., 2019), blood samples were obtained from each participant and tested for Hemoglobin A1c (HbA1c) concentration, as an indicator of Type 2 diabetes.

Conclusion of participation

Each participant received 300 Nepali rupees (about US$3.00) as compensation for their time and effort. Participants were also advised of their HbA1c and LTBI results. If the HbA1c measure was above 6.5%, they were advised to consult a doctor; if they were LTBI-positive they were provided with information on the most common TB symptoms and advised to seek medical care if any of those symptoms arose.

Data analysis

The initial analysis was descriptive, comparing distributions of key variables across cases (LTBI-positive) and controls (LTBI-negative), separately by sex, with calculated bivariate odds ratios and confidence intervals using unconditional logistic regression. Statistical analysis was performed using Stata 14 (StataCorp LP, College Station, TX).

Most households contained more than one stove. Although one of these stoves was designated by the interviewee as the primary stove, we coded all secondary stoves as dichotomous variables denoting presence or absence of each stove type in a household. Any additional stove in a household that was the same type as the primary stove was not coded as present with the secondary stove variables. In households with two kitchens (N=83), a primary stove was identified in each kitchen.

To prioritize the use of a primary stove for the analysis, a main kitchen was first identified using this procedure: (1) if one of the kitchens was used in more seasons than the other, then we selected that kitchen; (2) if seasonal use was equal, we selected the kitchen first in the following sequence: inside the main house, attached to the main house, separate building from the main house. This sequence reflects the descending frequency of main kitchens in single kitchen households. The primary stove used in the main kitchen was designated the primary stove for this analysis.

We asked about ever use of kerosene for lighting, rather than just present use of kerosene lamps. This was because previous research had indicated that kerosene lamp use could be a major risk factor for PTB (Pokhrel et al., 2010), but such lamps were seldom used in Nepal at the time of the study because of the removal of the government subsidy for kerosene.

For diabetes, we coded as diabetic anyone who fell into either of two categories; those who reported a doctor's diagnosis of Type 2 diabetes and those who had HbA1c levels of 7% or greater.

As the PTB study showed substantial differences for males and females and according to where participants lived, we carried out parallel analyses stratified by sex and by urban/rural residential status.

Multivariate analysis was carried out using unconditional logistic regression. For the main models we included all likely sources of household air pollution exposure: cooking, heating and lighting fuels, mosquito coils and incense burning, and having another member of the household who smoked tobacco. Potential confounders were initially identified using a directed acyclic graph (DAG) and then subsequently selected by examining whether covariates were independently associated with the outcome and with the main exposure of interest—primary cookstoves. If potential confounder variables altered any of the main outcomes by 10% or more, they were included in as confounders in the final model, after excluding possible colliders or variables on the causal pathway. Some household fuel uses, such as kerosene stoves and generators used for lighting during power outages, were not considered because of low frequency within the subject households.

RESULTS

Of the 1,222 eligible PTB controls from the parent study, QuantiFERON test results were available for 1,195 individuals (97.8% of total eligible PTB controls). Of these participants, 396 (33.1%) tested positive, 692 (57.9%) tested negative, and 107 (9.0%) had indeterminate test results. Participants with indeterminate results were not re-tested and were excluded from further analysis, resulting in a final study population of 1,088.

Table 1 shows the distributions of cases (LTBI-positive) and controls (LTBI-negative) according to various independent variables, with bivariate odds ratios and confidence intervals. Data are shown for all participants, and for females and males separately. The overall prevalence of LTBI in the study population was 36% (34% in women, 39% in men). As would be expected, there was a nearly monotonic increase in infection prevalence with age, but this was most evident in men, as the prevalence in women showed little increase in the older age categories.

Among household fuel exposures, use of either a primary or secondary wood stove showed no evidence of being a risk factor for infection, relative to use of an LPG stove and not having a secondary wood stove, respectively. Use of a primary biogas stove appeared protective in both sexes. Having a secondary LPG stove appeared protective. Although no participant used a primary kerosene stove, use of a secondary kerosene stove by women was associated with increased odds of LTBI, but only 9 women used such a stove.

With respect to lighting, the use of traditional oil lamps (diyos) during power outages was associated with higher odds of LTBI in both sexes; however, only a small number of participants (n=34) used this type of lighting. The use of candles during power outages also appeared to be a risk factor, but only among men, as did having another household member who smoked. None of the other potential sources of household air pollution—such as the use of other secondary stove types, ever having used kerosene lighting, household heating with fuel, burning of mosquito coils, and burning of incense sticks—had a clear association with LTBI.

Other variables associated with increased odds of LTBI in the bivariate analysis included having had a household member with TB disease, diabetes (women only), smoking (men only), and alcohol use (men only). Belonging to a higher caste and owning buffalo were associated with decreased odds of LTBI.

Table 2 compares the distributions of cases and controls across the same household air pollution variables as shown in Table 1, separately for participants living in urban and rural areas. The other variables shown in Table 1 are not included, as they are not the focus of this paper. Again, there was no evidence that the use of wood as a cooking fuel was a risk factor for LTBI and use of fuel to heat the house did not appear to be a risk factor. Use of a primary biogas stove, as well as the use of a secondary LPG stove, had protective associations in urban, but not in rural, areas. The use of diyos for lighting during a power outage was associated with increased risk among rural participants, but the number using them was small (n=20).

Multivariate analyses for sources of household air pollution for all subjects and stratified by sex and urban/rural residence are shown in Table 3. Among cookstoves, the protective associations with biogas stoves and secondary LPG stoves shown in bivariate analysis (Tables 1 and 2) remained, but most confidence intervals widened to include the null. We had considered whether the protective association with biogas might be confounded by bovine ownership, which also showed evidence of protective associations with LTBI. Possession of one or more cows or water buffaloes, to provide the dung for the digester, is usually necessary for a household biogas stove to be feasible. However, the multivariate models include cow and buffalo ownership variables and the protective associations for biogas stoves remain.

With respect to other sources of household air pollution, the use of traditional oil lamps (diyos) during power outages remained a risk factor, particularly among rural individuals, and the use of candles during a power outage remained a risk factor among men. Having another household member who smoked also remained a risk factor among men. We examined whether this result could have been confounded by active smoking by participants, but that was not the case (results not shown).

DISCUSSION

This study sought to examine associations with LTBI status for a comprehensive range of household sources of air pollution in a large sample of Nepali adults who had not previously been diagnosed with tuberculosis. To our knowledge, it is the first study in any country to do this.

Our primary hypothesis was not confirmed, as wood-burning stoves showed little evidence of being an LTBI risk factor relative to LPG stoves. The study results did, however, suggest that biogas stoves have a protective association with LTBI, relative to LPG stove use. The household fuel exposure most strongly associated with LTBI status was the use of diyos during power outages, particularly among rural-living individuals and there was evidence that use of candles may be a risk factor, particularly among men. In multivariate analysis, there was little evidence that ever-use of kerosene for lighting was a risk factor for LTBI.

As with any epidemiology study, it is necessary to consider the extent to which selection or information biases or confounding could have influenced the results. Considering first selection bias, the participants were selected to reflect the residential geographic distribution of PTB cases in the parent study and 97.3% of those invited to participate agreed to do so (Bates et al., 2019). Selection could not have been influenced by knowledge of LTBI status as this was not known at the time of recruitment. Therefore, we see little opportunity for selection bias to have influenced the results.

In regard to information bias, testing for LTBI status was conducted in a hospital research laboratory according to the manufacturer's instructions. The assay was conducted with no knowledge of participants' characteristics and its reliability is supported by expected patterns in the data, particularly increasing LTBI prevalence with age and increased odds of infection in those who had had a household member diagnosed with TB (Table 1).

All interviews were conducted at participant homes before LTBI status was known and, because the primary focus of the study was on sources of household fuel use, particular attention was paid to confirming and photographing cooking, heating and lighting devices. Therefore, information bias in the form of misclassification of outcome or current exposure status is very unlikely to have influenced results. However, the unavoidable assumption that current exposures represented exposures at the time of infection will almost certainly have resulted in exposure misclassification, since infection may have occurred years or decades earlier. The unknown time elapsed since infection makes true associations with factors that promote infection inherently more difficult to detect than, say, associations with incident TB disease. However, associations with persistent or critical one-time exposures, such as having had a family member with active TB, can be detected. It is likely that for some families household cooking fuel use has remained fairly constant over a long time and current use may reflect cooking fuel use at the time of infection. This is most likely to be so for cooking with wood, since the direction of development is towards gaseous fuels. LPG (and perhaps biogas) use will be relatively recent adoptions for many families. This means the current exposure groups being compared are likely to have been more similar in terms of exposure status at the time of infection than they were at the time of study participation, biasing measures of association towards the null. This problem is difficult to avoid in an essentially cross-sectional study; a large longitudinal study with serial LTBI testing would be necessary to overcome it.

We collected and examined possible confounding by an extensive list of covariates. The final model has been adjusted for a range of confounding factors, including age and socio-economic factors, but the possibility of some presently unknown confounder of the relationships found cannot be excluded.

The strongest and most consistent associations with LTBI were for traditional oil lamps (diyos) used during power outages. Such an association is plausible because diyos give off little light and must be kept close to be useful. However, these lamps were used for lighting by only a small proportion of the study population and could not account for more than a small fraction of the burden of infection in this study. If there are rural areas without electrification where the use of these lamps is more common, their attributable proportion for LTBI may be greater. We did not, however, collect information on the oil type used in these lamps, which are most commonly used for Puja--religious prayers in the household during the morning and evening. During Puja, the oils used are likely to be vegetable oils, such as mustard, sesame and sunflower, but we cannot exclude the possibility that other fuels are used in them for lighting. We did not inquire about use of diyos during Puja in our questionnaire. However, exposure is likely to be less than when they are used for lighting.

Another exposure associated with higher odds of LTBI was use of candles by men for lighting during power outages (Table 3). The corresponding result for women showed no evidence of increased risk. Therefore the result for men could be a consequence of random variation or could reflect a difference in user behaviors between men and women.

Both primary and secondary biogas stoves were associated with reduced odds of infection, relative to LPG stoves or not having a biogas stove, respectively. That biogas stoves were associated with reduced odds of pulmonary TB disease, relative to LPG stoves, in our previous study (Bates et al., 2019), suggests that reduced likelihood of infection accounts at least in part for the reduced odds of PTB. Risk of TB disease conflates the risk of becoming infected and the risk of moving from the infected state to active TB disease. However, given the OR for infection and the OR for TB disease, the OR for moving from the infected state to the disease state can be estimated by dividing the latter OR by the former (Bates et al., 2007). For example, the OR for infection for women who used primary biogas stoves was 0.59 (Table 3) and the corresponding OR for pulmonary TB was 0.21 (Bates et al., 2019). Considering both of these, the OR for moving to PTB from the infected state is 0.36 in our study population. This figure may be further from the null than the true value because the observed association between infection and biogas is probably closer to the null than the true value. However, it suggests that, relative to LPG, biogas has a protective association for infection and, in people who have never had TB, may be less likely to cause activation of the infection. On the other hand, although primary stoves burning wood were less likely to cause active TB than LPG in the parent study (Bates et al., 2019), because the odds of infection are similar in both wood and LPG stove users, all or most of the protective association with using a wood stove rather than an LPG stove appears to be at the stage of moving from infection to active PTB.

It is difficult to conceive of a mechanism that would make biogas actually protective against *M. tuberculosis* complex infection, so it may be the case that, relative to biogas, LPG and (because the ORs are little different to LPG) wood burning are both likely to promote infection. In the absence of some unknown confounder associated with stove type, this property is likely to be a function of the emissions from these two stove types. Complicating this picture is that we found some evidence that secondary LPG stoves had a protective direction of association with LTBI, particularly in people living in urban areas. As this was not clearly confirmed by the results for primary stoves and because the confidence intervals included the null, the most likely explanation at this stage is random variation in the data, or possibly some unknown confounding factor.

In conclusion, we found no clear evidence that use of wood-burning stoves increases the risk of infection with the *M. tuberculosis* complex, but this could be because of exposure misclassification since exposure at the time of infection is unknown. However, we did find that household ownership of a biogas stove was associated with reduced odds of LTBI, relative to LPG stoves. This may go some way towards explaining the protective association of biogas stove ownership with pulmonary TB risk (Bates et al., 2019). Whether this represents an actual protective effect of biogas stove ownership or indicates an increased LTBI risk associated with LPG (and, by implication, wood) stoves is presently unclear. Nonetheless, the apparent protective effect of biogas against infection, relative to other fuels, is worthy of confirmation and mechanistic evaluation, as it may point the way towards a means of reducing the burden of TB disease. Overall, results of this study taken into account with previous findings (Bates et al., 2019) suggest that household cooking fuel use is likely to have more effect on moving from the infected state to PTB than on becoming infected with *M. tuberculosis* complex.

The other important finding of this study is the association of LTBI with use of diyos for lighting during power outages. We could find no evidence that risks associated with diyos had previously been investigated. The use of these devices for lighting during periods of electricity unavailability should now be discouraged as there are plenty of inexpensive, electrical (including solar) lamps now available in Nepal.

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Highlights

- First study of latent TB infection (LTBI) and a range of household smoke sources.
- No evidence that biomass cooking smoke was associated with LTBI relative to LPG.
- Cooking with biogas had a protective association relative to LPG.
- Tobacco smoking was a risk factor for LTBI in both sexes.
- Use of a traditional lamp (diyo) for lighting appeared to be a LTBI risk factor.

Table 1.

Socio-demographic and household fuel use characteristics of study participants and latent tuberculosis infection status, by sex (N = 1,088).

	All (N = 1,088)			Women (N = 578)			Men (N = 510)		
	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% CI)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% CI)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% CI)
TOTAL	396 (36%)	692 (64%)		196 (34%)	382 (66%)		200 (39%)	310 (61%)	
Age (years)									
18–27	53 (13%)	158 (23%)	1.00	34 (17%)	73 (19%)	1.00	19 (10%)	85 (27%)	1.00
28–37	73 (18%)	156 (23%)	1.40 (0.92,2.12)	39 (20%)	101 (26%)	0.83 (0.48,1.44)	34 (17%)	55 (18%)	**2.77 (1.44,5.33)**
38–47	78 (20%)	130 (19%)	**1.79 (1.18,2.72)**	42 (21%)	70 (18%)	1.29 (0.74,2.25)	36 (18%)	60 (19%)	**2.68 (1.41,5.12)**
48–57	92 (23%)	123 (18%)	**2.23 (1.48,3.37)**	42 (21%)	71 (19%)	1.27 (0.73,2.22)	50 (25%)	52 (17%)	**4.30 (2.29,8.08)**
58+	100 (25%)	125 (18%)	**2.38 (1.59,3.58)**	39 (20%)	67 (18%)	1.25 (0.71,2.20)	61 (31%)	58 (19%)	**4.71 (2.55,8.69)**
Sex									
Female	196 (49%)	382 (55%)	1.00						
Male	200 (51%)	310 (45%)	1.26 (0.98,1.61)						
Main Stove									
LPG	245 (62%)	388 (56%)	1.00	114 (58%)	196 (51%)	1.00	131 (66%)	192 (62%)	1.00
Biogas	30 (8%)	87 (13%)	**0.55 (0.35,0.85)**	13 (7%)	49 (13%)	**0.46 (0.24,0.88)**	17 (9%)	38 (12%)	0.66 (0.36,1.21)
Wood	116 (29%)	214 (31%)	0.86 (0.65,1.13)	66 (34%)	135 (35%)	0.84 (0.58,1.22)	50 (25%)	79 (25%)	0.93 (0.61,1.41)
Other	5 (1%)	3 (0%)	2.64 (0.63,11.14)	3 (2%)	2 (1%)	2.58 (0.42,15.66)	2 (1%)	1 (0%)	2.93 (0.26,32.66)
Secondary LPG stove									
No	360 (91%)	600 (87%)	1.00	178 (91%)	329 (86%)	1.00	182 (91%)	271 (87%)	1.00
Yes	36 (9%)	92 (13%)	**0.65 (0.43,0.98)**	18 (9%)	53 (14%)	0.63 (0.36,1.10)	18 (9%)	39 (13%)	0.69 (0.38,1.24)
Secondary Biogas stove									
No	376 (95%)	646 (93%)	1.00	183 (93%)	359 (94%)	1.00	193 (97%)	287 (93%)	1.00
Yes	20 (5%)	46 (7%)	0.75 (0.44,1.28)	13 (7%)	23 (6%)	1.11 (0.55,2.24)	7 (4%)	23 (7%)	0.45 (0.19,1.08)
Secondary Wood stove									
No	345 (87%)	608 (88%)	1.00	172 (88%)	332 (87%)	1.00	173 (87%)	276 (89%)	1.00
Yes	51 (13%)	84 (12%)	1.07 (0.74,1.55)	24 (12%)	50 (13%)	0.93 (0.55,1.56)	27 (14%)	34 (11%)	1.27 (0.74,2.17)
Secondary Kerosene stove									
No	387 (98%)	684 (99%)	1.00	190 (97%)	379 (99%)	1.00	197 (99%)	305 (98%)	1.00

	All (N = 1,088)			Women (N = 578)			Men (N = 510)		
	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% CI)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% CI)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% CI)
Yes	9 (2%)	8 (1%)	1.99 (0.76,5.20)	6 (3%)	3 (1%)	3.99 (0.99,16.13)	3 (2%)	5 (2%)	0.93 (0.22,3.93)
Secondary Electric stove									
No	380 (96%)	662 (96%)	1.00	188 (96%)	369 (97%)	1.00	192 (96%)	293 (95%)	1.00
Yes	16 (4%)	30 (4%)	0.93 (0.50,1.73)	8 (4%)	13 (3%	1.21 (0.49,2.97)	8 (4%)	17 (5%)	0.72 (0.30,1.70)
Secondary Rice Cooker									
No	152 (38%)	285 (41%)	1.00	89 (45%)	178 (47%)	1.00	63 (32%)	107 (35%)	1.00
Yes	244 (62%)	407 (59%)	1.12 (0.87,1.45)	107 (55%)	204 (53%)	1.05 (0.74,1.48)	137 (69%)	203 (65%)	1.15 (0.78,1.67)
Other Secondary stove									
No	373 (94%)	653 (94%)	1.00	182 (93%)	367 (96%)	1.00	191 (96%)	286 (92%)	1.00
Yes	23 (6%	39 (6%)	1.03 (0.61,1.76)	14 (7%	15 (4%	1.88 (0.89,3.98)	9 (5%)	24 (8%)	0.56 (0.26,1.23)
Heat house with fuel									
No	347 (88%)	593 (86%)	1.00	173 (88%)	323 (85%)	1.00	174 (87%)	270 (87%)	1.00
Yes	49 (12%)	99 (14%)	0.85 (0.59,1.22)	23 (12%)	59 (15%)	0.73 (0.43,1.22)	26 (13%)	40 (13%)	1.01 (0.59,1.71)
Ever used kerosene lighting									
No	137 (35%)	263 (38%)	1.00	58 (30%)	140 (37%)	1.00	79 (40%)	123 (40%)	1.00
Yes	259 (65%)	429 (62%)	1.16 (0.90,1.50)	138 (70%)	242 (63%)	1.38 (0.95,1.99)	121 (61%)	187 (60%)	1.01 (0.70,1.45)
Candle use during power outage									
No	286 (72%)	533 (77%)	1.00	147 (75%)	293 (77%)	1.00	139 (70%)	240 (77%)	1.00
Yes	110 (28%)	159 (23%)	1.29 (0.97,1.71)	49 (25%)	89 (23%)	1.10 (0.73,1.64)	61 (31%)	70 (23%)	**1.50 (1.01,2.25)**
Oil lamp use during power outage									
No	377 (95%)	677 (98%)	1.00	183 (93%)	371 (97%)	1.00	194 (97%)	306 (99%)	1.00
Yes	19 (5%)	15 (2%)	**2.27 (1.14,4.53)**	13 (7%)	11 (3%)	**2.40 (1.05,5.45)**	6 (3%)	4 (1%)	2.37 (0.66,8.49)
Burn mosquito coils									
No	286 (72%)	503 (73%)	1.00	143 (73%)	284 (74%)	1.00	143 (72%)	219 (71%)	1.00
Yes	110 (28%)	189 (27%)	1.02 (0.78,1.35)	53 (27%)	98 (26%)	1.07 (0.73,1.59)	57 (29%)	91 (29%)	0.96 (0.65,1.42)
Burn incense inside									
No	104 (26%)	206 (30%)	1.00	58 (30%)	110 (29%)	1.00	46 (23%)	96 (31%)	1.00
Yes	292 (74%)	486 (70%)	1.19 (0.90,1.57)	138 (70%)	272 (71%)	0.96 (0.66,1.40)	154 (77%)	214 (69%)	1.50 (1.00,2.26)
Household Contact with TB diagnosis									

	All (N = 1,088)			Women (N = 578)			Men (N = 510)		
	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% Cl)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% Cl)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% Cl)
No	371 (94%)	668 (97%)	1.00	180 (92%)	368 (96%)	1.00	191 (96%)	300 (97%)	1.00
Yes	25 (6%)	24 (3%)	**1.88 (1.06,3.33)**	16 (8%)	14 (4%)	**2.34 (1.12,4.89)**	9 (5%)	10 (3%)	1.41 (0.56,3.54)
Household Crowding									
≤2 people per room	374 (94%)	637 (92%)	1.00	190 (97%)	352 (92%)	1.00	184 (92%)	285 (92%)	1.00
>2 people per room	22 (6%)	55 (8%)	0.68 (0.41,1.14)	6 (3%)	30 (8%)	**0.37 (0.15,0.91)**	16 (8%)	25 (8%)	0.99 (0.52,1.91)
Smoking Status									
Non-smoker	239 (60%)	490 (71%)	1.00	150 (77%)	303 (79%)	1.00	89 (45%)	187 (60%)	1.00
≤ 8 pack- years	69 (17%)	109 (16%)	1.30 (0.92,1.82)	18 (9%)	40 (10%)	0.91 (0.50,1.64)	51 (26%)	69 (22%)	1.55 (1.00,2.41)
>8 pack- years	88 (22%)	93 (13%)	**1.94 (1.39,2.70)**	28 (14%)	39 (10%)	1.45 (0.86,2.45)	60 (30%)	54 (17%)	**2.33 (1.49,3.65)**
Other Household Smoker(s)									
No	308 (78%)	543 (78%)	1.00	150 (77%)	281 (74%)	1.00	158 (79%)	262 (85%)	1.00
Yes	88 (22%)	149 (22%)	1.04 (0.77,1.40)	46 (23%)	101 (26%)	0.85 (0.57,1.27)	42 (21%)	48 (15%)	1.45 (0.92,2.30)
Education									
None	93 (23%)	171 (25%)	1.00	73 (37%)	144 (38%)	1.00	20 (10%)	27 (9%)	1.00
Primary	82 (21%)	125 (18%)	1.21 (0.83,1.76)	36 (18%)	69 (18%)	1.03 (0.63,1.68)	46 (23%)	56 (18%)	1.11 (0.55,2.23)
Secondary	135 (34%)	210 (30%)	1.18 (0.85,1.65)	54 (28%)	100 (26%)	1.07 (0.69,1.64)	81 (41%)	110 (35%)	0.99 (0.52,1.90)
Post- secondary	86 (22%)	186 (27%)	0.85 (0.59,1.22)	33 (17%)	69 (18%)	0.94 (0.57,1.56)	53 (27%)	117 (38%)	0.61 (0.32,1.19)
Monthly Household Income (Rupees)									
<8K	47 (12%)	86 (12%)	1.00	27 (14%)	54 (14%)	1.00	20 (10%)	32 (10%)	1.00
8–16K	87 (22%)	133 (19%)	1.20 (0.77,1.87)	45 (23%)	76 (20%)	1.18 (0.66,2.14)	42 (21%)	57 (18%)	1.18 (0.59,2.34)
16–32K	114 (29%)	184 (27%)	1.13 (0.74,1.73)	44 (22%)	107 (28%)	0.82 (0.46,1.47)	70 (35%)	77 (25%)	1.45 (0.76,2.77)
>32K	119 (30%)	213 (31%)	1.02 (0.67,1.56)	64 (33%)	93 (24%)	1.38 (0.79,2.41)	55 (28%)	120 (39%)	0.73 (0.39,1.40)
Don't know	29 (7%)	76 (11%)	0.70 (0.40,1.22)	16 (8%)	52 (14%)	0.62 (0.30,1.27)	13 (7%)	24 (8%)	0.87 (0.36,2.08)
Family land ownership									
No	25 (6%)	45 (7%)	1.00	17 (9%)	24 (6%)	1.00	8 (4%)	21 (7%)	1.00
Yes	371 (94%)	641 (93%)	1.04 (0.63,1.73)	179 (91%)	355 (94%)	0.71 (0.37,1.36)	192 (96%)	286 (93%)	1.76(0.76,4.06)
Religion									
Hindu	346 (87%)	610 (88%)	1.00	169 (86%)	346 (91%)	1.00	177 (89%)	264 (85%)	1.00
Buddhist	36 (9%)	56 (8%)	1.13 (0.73,1.76)	17 (9%)	23 (6%)	1.51 (0.79,2.91)	19 (10%)	33 (11%)	0.86 (0.47,1.56)

	All (N = 1,088)			Women (N = 578)			Men (N = 510)		
	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% Cl)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% Cl)	Cases N (%)	Controls N (%)	Bivariate Analysis OR (95% Cl)
Other	14 (4%)	25 (4%)	0.99 (0.51,1.92)	10 (5%)	12 (3%)	1.71 (0.72,4.03)	4 (2%)	13 (4%)	0.46 (0.15,1.43)
Caste									
Dalit	63 (16%)	84 (12%)	1.00	38 (19%)	56 (15%)	1.00	25 (13%)	28 (9%)	1.00
Disadv. Janajati	70 (18%)	113 (16%)	0.83 (0.53,1.29)	39 (20%)	60 (16%)	0.96 (0.54,1.70)	31 (16%)	53 (17%)	0.66 (0.33,1.32)
Disadv. Non-Dalit Terai	3 (1%)	2 (0%)	2.00 (0.32,12.33)	0 (0%)	1 (0%)	1.00	3 (2%)	1 (0%)	3.36 (0.33,34.41)
Religious Minority	8 (2%)	13 (2%)	0.82 (0.32,2.10)	6 (3%)	3 (1%)	2.95 (0.69,12.51)	2 (1%)	10 (3%)	0.22 (0.04,1.12)
Relatively adv. Janajati	111 (28%)	149 (22%)	0.99 (0.66,1.49)	45 (23%)	86 (23%)	0.77 (0.45,1.33)	66 (33%)	63 (20%)	1.17 (0.62,2.23)
Higher Caste	139 (35%)	330 (48%)	**0.56 (0.38,0.82)**	68 (35%)	176 (46%)	**0.57 (0.35,0.94)**	71 (36%)	154 (50%)	**0.52 (0.28,0.95)**
Location of residence									
Rural	238 (60%)	381 (55%)	1.00	115 (59%)	198 (52%)	1.00	123 (62%)	183 (59%)	1.00
Urban	158 (40%)	311 (45%)	0.81 (0.63,1.05)	81 (41%)	184 (48%)	0.76 (0.54,1.07)	77 (39%)	127 (41%)	0.90 (0.63,1.30)
Buffalo ownership									
No	280 (71%)	424 (61%)	1.00	140 (71%)	226 (59%)	1.00	140 (70%)	198 (64%)	1.00
Yes	116 (29%)	268 (39%)	**0.66 (0.50,0.85)**	56 (29%)	156 (41%)	**0.58 (0.40,0.84)**	60 (30%)	112 (36%)	0.76 (0.52,1.11)
Cow ownership									
No	303 (77%)	509 (74%)	1.00	151 (77%)	284 (74%)	1.00	152 (76%)	225 (73%)	1.00
Yes	93 (23%)	183 (26%)	0.85 (0.64,1.14)	45 (23%)	98 (26%)	0.86 (0.58,1.29)	48 (24%)	85 (27%)	0.84 (0.56,1.26)
Alcohol use									
None	157 (40%)	347 (50%)	1.00	130 (66%)	272 (71%)	1.00	27 (14%)	75 (24%)	1.00
Occasional	109 (28%)	180 (26%)	1.34 (0.99,1.81)	43 (22%)	79 (21%)	1.14 (0.74,1.74)	66 (33%)	101 (33%)	**1.82 (1.06,3.11)**
Weekly	130 (33%)	165 (24%)	**1.74 (1.29,2.34)**	23 (12%)	31 (8%)	1.55 (0.87,2.77)	107 (54%)	134 (43%)	**2.22 (1.33,3.69)**
Diabetes									
No	362 (91%)	651 (94%)	1.00	182 (93%)	370 (97%)	1.00	180 (90%)	281 (91%)	1.00
Yes	34 (9%)	41 (6%)	1.49 (0.93,2.39)	14 (7%)	12 (3%)	**2.37 (1.08,5.23)**	20 (10%)	29 (9%)	1.08 (0.59,1.96)

Table 2.

Sources of household air pollution and latent tuberculosis infection status, by rural and urban location of residence (N = 1,088).

	Urban residence (N=619)			Rural residence (N=469)		
	Cases N (%)	**Controls N (%)**	**Bivariate Analysis OR (95% CI)**	**Cases N (%)**	**Controls N (%)**	**Bivariate Analysis OR (95% CI)**
TOTAL	238 (38%)	381 (62%)		158 (34%)	311 (66%)	
Main Stove						
LPG	204 (86%)	311 (82%)	1.00	41 (26%)	77 (25%)	1.00
Biogas	9 (4%)	39 (10%)	**0.35 (0.17,0.74)**	21 (13%)	48 (15%)	0.82 (0.43,1.55)
Wood	23 (10%)	31 (8%)	1.13 (0.64,2.00)	93 (59%)	183 (59%)	0.95 (0.61,1.50)
Other	2 (1%)	0 (0%)	1.00	3 (2%)	3 (1%)	1.88 (0.36,9.73)
Secondary LPG stove						
No	228 (96%)	341 (90%)	1.00	132 (84%)	259 (83%)	1.00
Yes	10 (4%)	40 (10%)	**0.37 (0.18,0.76)**	26 (16%)	52 (17%)	0.98 (0.59,1.64)
Secondary Biogas stove						
No	226 (95%)	364 (96%)	1.00	150 (95%)	282 (91%)	1.00
Yes	12 (5%)	17 (4%)	1.14 (0.53,2.42)	8 (5%)	29 (9%)	0.52 (0.23,1.16)
Secondary Wood stove						
No	209 (88%)	343 (90%)	1.00	136 (86%)	265 (85%)	1.00
Yes	29 (12%)	38 (10%)	1.25 (0.75,2.09)	22 (14%)	46 (15%)	0.93 (0.54,1.61)
Secondary Kerosene stove						
No	229 (96%)	374 (98%)	1.00	158 (100%)	310 (100%)	1.00
Yes	9 (4%)	7 (2%	2.10 (0.77,5.72)	0 (0%)	1 (0%)	1.00
Heat house with fuel						
No	202 (85%)	315 (83%)	1.00	145 (92%)	278 (89%)	1.00
Yes	36 (15%)	66 (17%)	0.85 (0.55,1.32)	13 (8%)	33 (11%)	0.76 (0.39,1.48)
Ever used kerosene lighting						
No	99 (42%)	172 (45%)	1.00	38 (24%)	91 (29%)	1.00
Yes	139 (58%)	209 (55%)	1.16 (0.83,1.60)	120 (76%)	220 (71%)	1.31 (0.84,2.03)
Candle use during power outage						
No	161 (68%)	270 (71%)	1.00	125 (79%)	263 (85%)	1.00

	Urban residence (N=619)			Rural residence (N=469)		
	Cases	**Controls**	**Bivariate Analysis**	**Cases**	**Controls**	**Bivariate Analysis**
	N (%)	**N (%)**	**OR (95% Cl)**	**N (%)**	**N (%)**	**OR (95% Cl)**
Yes	77 (32%)	111 (29%)	1.16 (0.82,1.65)	33 (21%)	48 (15%)	1.45 (0.88,2.37)
Oil lamp use during power outage						
No	230 (97%)	375 (98%)	1.00	147 (93%)	302 (97%)	1.00
Yes	8 (3%)	6 (2%)	2.17 (0.74,6.35)	11 (7%)	9 (3%)	**2.51 (1.02,6.19)**
Burn mosquito coils						
No	167 (70%)	260 (68%)	1.00	119 (75%)	243 (78%)	1.00
Yes	71 (30%)	121 (32%)	0.91 (0.64,1.30)	39 (25%)	68 (22%)	1.17 (0.75,1.84)
Burn incense inside						
No	57 (24%)	94 (25%)	1.00	47 (30%)	112 (36%)	1.00
Yes	181 (76%)	287 (75%)	1.04 (0.71,1.52)	111 (70%)	199 (64%)	1.33 (0.88,2.01)
Other Household Smoker						
No	193 (81%)	307 (81%)	1.00	115 (73%)	236 (76%)	1.00
Yes	45 (19%)	74 (19%)	0.97 (0.64,1.46)	43 (27%)	75 (24%)	1.18 (0.76,1.82)

Table 3.

Multivariate logistic regression analysis of latent tuberculosis infection and sources of household fuel, in and around Kaski district, Nepal, by sex and location of residence.

	All	Women	Men	Urban	Rural
	OR† (95% CI)	OR† (95%CI)	OR† (95% CI)	OR† (95% CI)	OR† (95% CI)
Main Stove					
LPG	1.00	1.00	1.00	1.00	1.00
Biogas	0.64 (0.34,1.20)	0.59 (0.24,1.45)	0.68 (0.26,1.74)	0.74 (0.23,2.40)	0.65 (0.29,1.46)
Wood	1.13 (0.73,1.77)	1.14 (0.62,2.09)	1.25 (0.62,2.50)	1.88 (0.89,3.97)	0.96 (0.52,1.78)
Secondary LPG stove					
No	1.00	1.00	1.00	1.00	1.00
Yes	0.83 (0.49,1.40)	0.90 (0.43,1.88)	0.72 (0.33,1.61)	0.38 (0.12,1.15)	1.02 (0.56,1.88)
Secondary Biogas stove					
No	1.00	1.00	1.00	1.00	1.00
Yes	0.70 (0.39,1.24)	1.06 (0.50,2.26)	**0.38 (0.15,0.96)**	1.01 (0.44,2.30)	0.47 (0.20,1.12)
Secondary Wood stove					
No	1.00	1.00	1.00	1.00	1.00
Yes	1.19 (0.76,1.86)	1.05 (0.56,1.97)	1.50 (0.75,3.00)	1.40 (0.77,2.55)	0.93 (0.46,1.91)
Heat home with fuel					
No	1.00	1.00	1.00	1.00	1.00
Yes	0.79 (0.54,1.17)	0.68 (0.39,1.17)	1.05 (0.58,1.90)	0.92 (0.57,1.48)	0.57 (0.26,1.22)
Ever used kerosene for lighting					
No	1.00	1.00	1.00	1.00	1.00
Yes	1.10 (0.83,1.46)	1.41 (0.93,2.13)	0.82 (0.55,1.24)	0.96 (0.66,1.38)	1.49 (0.91,2.43)
Candle use during power outage					
No	1.00	1.00	1.00	1.00	1.00
Yes	1.27 (0.93,1.74)	0.99 (0.63,1.53)	**1.61 (1.01,2.56)**	1.16 (0.78,1.73)	1.47 (0.86,2.51)
Oil lamp use during power outage					
No	1.00	1.00	1.00	1.00	1.00
Yes	**2.53 (1.20,5.31)**	2.39 (0.97,5.93)	2.61 (0.66,10.34)	1.67 (0.48,5.77)	**3.31 (1.27,8.66)**
Burn mosquito coils					

	All	Women	Men	Urban	Rural
	OR† (95% CI)	OR† (95%CI)	OR† (95% CI)	OR† (95% CI)	OR† (95% CI)
No	1.00	1.00	1.00	1.00	1.00
Yes	0.98 (0.72,1.32)	1.06 (0.69,1.63)	1.00 (0.63,1.57)	0.89 (0.59,1.33)	1.16 (0.70,1.92)
Burn incense inside					
No	1.00	1.00	1.00	1.00	1.00
Yes	1.14 (0.84,1.53)	0.97 (0.65,1.45)	1.40 (0.89,2.20)	1.10 (0.73,1.66)	1.36 (0.87,2.14)
Other Household Smoker					
No	1.00	1.00	1.00	1.00	1.00
Yes	1.22 (0.89,1.69)	0.96 (0.63,1.49)	**1.76 (1.04,2.96)**	1.06 (0.67,1.66)	1.31 (0.81,2.13)

†Adjusted for age (categories as in Table 1), location of residence (urban vs. rural), education, cow ownership, and buffalo ownership.