A report of

Indoor Air Pollution as a Risk Factor for Pulmonary Tuberculosis

A Case Control Study

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Contents

1.0 Background

Approximately half of the world's population and up to 90% of rural households in developing countries still rely on unprocessed solid fuels, such as wood, crop residues or dung cake, for cooking and, sometimes, heating the house[1]. In most of the developing countries, solid fuels are burned in an unvented stove in poorly ventilated kitchens or rooms, throughout the year. As the stoves are not energy efficient, fuels are not burned completely. The incomplete combustion of solid fuel releases a complex mixture of organic and inorganic compounds, such as particulate matter[2, 3], carbon monoxide, polyorganic material, polyaromatic hydrocarbons (PAH), formaldehyde, naphthalene etc[1]. Several studies have suggested that exposure to indoor air pollution (IAP) from household solid fuel use increases the risk for several diseases, particularly in women and children, who receive the highest exposures. For example, based on the strength of evidence from meta-analysis[4], Smith et al (2004) have reported strong evidence of association of IAP with Acute Lower Respiratory Infection (ALRI in children <5 years), Chronic Obstructive Pulmonary Disease (COPD), and lung cancer (from exposure to coal smoke: for women and men ≥ 30 years). Although associations with asthma, cataracts (and other eye conditions), adverse pregnancy outcomes (including low birth weight), other cancers, heart disease, and tuberculosis (TB) have been found, they are not as robust as those for ALRI, COPD and lung cancer. In the case of cataracts or lens opacity and TB, there exist only a few studies of the relationship with indoor air pollution, and they all have important limitations.

1.1 Energy use pattern and incidence and prevalence of TB

1.1.1 Energy use pattern in Nepal

According to 2001 census, Nepal's energy supply is predominantly dominated by solid fuels (biomass based) followed by liquid (kerosene, petrol and diesel) and gaseous (Liquefied petroleum gas and biogas) fuels. In the year 2002/2003, about 87.4% of total energy in the country was supplied by solid fuels, whereas, share of liquid and gaseous fuels were 12.1 and 0.5%, respectively (MOF 2003). In the same year, residential sector consumed about 90.6 % of all energy supplied, which is only slightly lower than a consumption figure of 1994, which was 93.1%. Thus it is highly likely that solid fuels will remain a major source of energy for majority of people for long time.

2.0 Tuberculosis (TB) a major public health problem in Nepal

Tuberculosis (TB) is a highly contagious infection caused by airborne bacteria, *Mycobacterium tuberculosis (MTB).* The TB pathogenesis can be characterized into four stages[5], which can again be separated into two stages: becoming infected and having latent infection turn into an active case. Worldwide Tuberculosis (TB) kills more than 2 million people a year. Despite efforts in the last 20-30 years, TB control achievements are disappointing and TB still remains a serious problem in many developing countries. TB is a multifactorial disorder, a range of social, environmental, and behavioral factor influence exposure and susceptibility to *Mycobacterium tuberculosis* infection. An understanding the individual balance between degree of exposure to the organism, inherited genetic susceptibility to infection, and respective environmental and behavioral factors in development of disease will help develop new avenues by which, TB could be controlled.

The prevalence of TB infection in Nepal has been estimated to be as high as 45% (in adults)[6]. More than 48,000 new active TB cases occur each year along with 11,000 TB deaths[6]. A study comparing active and passive case-finding methods in Nepal have found a female-to-male ratio of 1:1.2 in active tuberculosis case finding and 1:2.6 in self-referred patients[7]. Another study conducted in 45 outreach tuberculosis diagnostic microscopic camps in remote areas have documented significantly higher percentage of females with TB than males (56% vs. 44%); whereas the percentage of females and males attending health posts and clinics with TB were 43% and 57% respectively[8]. These data suggest that there is a gender differences in access to diagnosis and treatment of TB in Nepal and there is a need to identify risk factors leading to TB in women. Identification of risk factors and minimizing such risks could help to control the TB burden in Nepal from further spread.

3.0 Materials and Method

Specific Aim III

Evaluate the association between IAP exposure and tuberculosis (TB) in a case-control study using both a survey-based exposure metric and a long-term exposure index developed from short-term measurements of particle and naphthalene levels and lifetime time-activity information from questionnaires.

As the causal relationship between exposure to indoor smoke and tuberculosis (TB) is biologically plausible, to help understand in more detail the relationship of IAP exposures with TB, a case control study was conducted in the Pokhara municipality of Nepal, where cooking with biomass fuels in unvented indoor stoves is a common practice. Main objectives of this study were to confirm results of earlier studies using clinically confirmed TB case and to investigate possible confounding of the relationship using a validated questionnaire and exposure assessment in the kitchens of a subset of participants' house.

3.1 Hypothesis of TB case-control study

"Cooking with traditional biomass stoves without chimneys increases the risk of tuberculosis among householders, compared with cooking using liquid or gaseous fuels or electricity"

3.2 Research design and methods

This was a hospital based multi center case-control study conducted in collaboration with Manipal Medical College and Regional Tuberculosis Center in Kaski district (Pokhara) of Nepal with the grant assistance from Fogarty International Center and New Aid Foundation.

3.3 Rationale for conducting a hospital based case-control study

In Nepal, population based case ascertainment of TB is not possible because there is no active surveillance program or case registry system. Thus, an incidence-density-based case-control study at the DOTs (Directly Observed Therapy) centers of Manipal Medical College Teaching Hospital (MTH) and Regional TB center in Pokhara was employed to answer the research questions. Together, these DOTs centers see about 150 new cases of confirmed pulmonary TB every year.

3.4 Case definition: selection, exclusion and inclusion criteria

Cases were patients who had been newly diagnosed with active pulmonary TB by chest x-ray, active sputum smear positive test, as routinely conducted at the hospital and private clinics using methods validated through the WHO that involves three consecutive sputum tests. Participants were confined to women between 20-65 years, visiting TB clinics in RTC (90.4%) and MTH (9.6%) and who resided within the Kaski, Lamjung, Parbat, Syangja, Tanahu, Myagdi, Baglung and Gorkha districts, in the mid-western development region of Nepal. All subjects were recruited and interviewed between July 2006 and April 2007. Excluded from case subjects were those who were pregnant, on chemotherapy for cancer, had HIV-AIDS or diabetics, or who had a history of TB.

3.5 Control definition: selection, exclusion and inclusion criteria

Controls between 20-65 years, were recruited from outpatient and inpatient departments (Dental-1.6%, Ear Nose and Thorat-1.6%, Ophthalmology-25.6%, General Medicine-56%, Obstetrics and Gynecology-7.2%, Orthopedics-2.4%, Skin-1.6%, Surgery-3.2%, and Psychiatry-0.8%) at the MTH in the same months when cases were identified. Patients with obstructive rhinitis and otitis media were included. For each case, the control subjects were the first eligible female patients without pulmonary TB, matched to cases on age (five-year frequency bands), who presented at MTH between 9 and 10 AM on the morning after case enrolment. Control subjects were interviewed only after confirmation through medical screening that they did not have tuberculosis. Confirmation procedures included a chest x-ray and an on-the-spot sputum examination. Exclusion criteria for controls were the same as cases, i.e. women with HIV-AIDS, on chemotherapy for any form of cancer, pregnant women and diabetics.

After obtaining an informed oral consent to participate, all cases and controls were interviewed face-to-face by trained interviewers, shortly after diagnosis and while they were still at the hospital. Three interviewers took the interviews of cases and controls. Interviewers were aware of the case or control status but were not aware of the main exposure of interest or hypothesis of the study. All interviewers interviewed a mixture of cases and controls.

3.6 Rationale for controls from hospital

Villages in Nepal do not have population registries or accurate census information that would provide the sampling frame to select community controls. Also, many households in the villages have similar socio-economic characteristics and fuel-use patterns; which may not ensure heterogeneity of exposure. Thus, the study selected controls from the hospital, which generally has patients representing a number of villages from the same districts and geographical proximity as the cases. Thus, it should ensure heterogeneity of exposure. In addition, selecting controls from hospital makes it possible to test that they do not have pulmonary TB.

3.7 Matching

The cases and controls were matched on sex and age (five-year frequency band). The ratio of cases and controls was 1:2.

3.8 Sample Size Consideration

A total of 125 cases and 250 controls were recruited to estimate a minimum relative risk (OR) of 2.00 with 80% power at the 5% significance level.

3.9 Data collection and characterization method

Selection of exposure variables and potential confounders were based on results of several previous epidemiological studies of environmental exposures and TB. However, information on other potential confounders not included in previous studies was also collected. The characterization of exposure information and potential confounders is further discussed below.

3.9.1 Religion

Studies have shown differences in TB rates between racial and religious groups in many countries(Hill et al. 2006; Mishra et al. 1999). In this study, information on the religion of participants was obtained and categorized as "Hindu", "Buddhist", "Christian" and "others".

3.9.2 Area of residence

There is evidence that health inequalities not only exist between developed and developing countries but exist within developing countries and between rural and urban areas. People living in urban areas or cities generally have better medical care access than people living in rural areas. The majority of the population of Nepal lives in rural areas. However, for the last one and half decades Nepal has experienced massive urbanization. Information was obtained on the area of residence of cases and controls, so that the risk of TB by area of residency (urban, peri-urban or rural) could be evaluated. Participants, who reported currently living in municipal areas, were characterized as "urban residents". Those who reported living in Village Development Committees (VDCs), or *Panchayats* were characterized as a "rural residents" and participants from the hinterland were characterized as "peri-urban residents".

3.9.3 Marital status

Studies have shown mixed results for marital status on the risk of TB (Lienhardt et al. 2005; Kaona et al. 2004; Chee et al. 2000). Information was collected on marital status (married, divorced and widowed) and age at marriage.

3.9.4 Level of education

Nepal has a very low women's literacy rate. Only 39.6% of people are literate in Nepal. The literacy rates in rural areas are much worse than in urban areas. Compared to males (54.5% literacy) only 25.1% of females are literate (I Census 2002). Various efforts are undergoing to increase the literacy rate for women in Nepal and one of them is a six months course of non-formal education, where at the end of the course people are able to read and write (Nepali letters). Participants were asked first whether they can read or write, which was followed by the highest level of education they have attained starting from non-formal education to university level.

3.9.5 Occupation

Some occupations can increase the risk of TB. Studies have documented strong relations between employment status and active and passive TB. For example health care workers have been found to be highly susceptible to TB infection (Osiri et al. 2006; Kassim et al. 2006). A large population's based study conducted in the US has found the highest incidence of TB among inhalation therapists' (McKenna M). The risk of TB among health care workers has been found higher in developing countries than in developed countries (Menzies et al. 2007). Exposure to silica dust is another important risk factor for silicosis as well as infection to TB (Rees and Murray 2007; Hnizdo and Murray 1998; Mulenga et al. 2005; Bang et al. 2005). Dust exposure in pottery industry has been found to increase the risk of TB. A large number of adverse respiratory health outcomes have been attributed to agricultural dust exposure (L. Smith et al. 2003; Schenker et al. 1998; Schenker et al. 2005) but not TB.

From the participants, information was obtained about their current (at the time of interview) and past main occupation and secondary occupation, if they had one. Similarly, question was also asked about the duration of each work. This was followed by question whether there is/was any exposure to dust or smoke directly on any of these occupations. The occupation-related question responses included "farming (own land)", "farming on others land-agriculture laborer", "government services", "laborer (non-agriculture)", "laborer (industry)", "house wife" and "other types".

3.9.6 Construction of present and past house

The type or construction of house reflects the economic status of people in Nepal. Participants were asked about their present and previous house constructions. House constructions were categorized as '*pucca'*, 'semi *pucca' and* '*kuchha'* type. Later, *pucca and* semi *pucca* houses were combined and were used as a reference category. The *pucca* houses are houses made with standard materials such as bricks and cement[1] and *kuccha* houses are houses made with brick and mud and thatched or tin roof.

3.9.7 Crowding

Studies conducted in both developed and developing countries have found a significant association of TB disease with various social variables and, importantly with crowding (Hill et al. 2006; Lienhardt et al. 2005; Wanyeki et al. 2006). In crowded houses, a degree of shared airspace increases exposure to MTB bacteria and likelihood of contact between tuberculosis index case and susceptible household members. Children have been found more vulnerable to contract TB in a crowded house. Chapman and Dyerly et al (1964)(Chapman and Dyerly 1964) have shown an association between the risk of tuberculin conversion in children living in the house of an infectious case and the number of cubic feet per person in the house.

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[1] Kuccha: House made from mud, thatch and other low quality materials.
Pucca: House made entirely from high quality materials.
Semipucca: House made from both low and high quality materials

Participants were asked the total number of people currently living in the house and the total number of rooms (except toilet/bathroom) available in both current and previous house. Total number of people living in the house was divided by total number of rooms (except toilet) to get the number of people per room. Houses were considered crowded, when they had more than three people per room. A question about family history of TB was asked separately.

3.9.8 Cooking practices and duration of cooking

In Nepal, women do the majority of the cooking and get more personal exposure to indoor air pollution from fuel combustion. Since personal exposure to indoor air pollution may differ with cooking practices, such that women who cook sporadically will be less exposed to smoke than those who cook regularly. Thus, a series of questions was asked about the present cooking status, age started cooking, and age when cooked last time, if she had stopped cooking. Similarly questions were also asked on number of days per week she spent on cooking and total time she spent cooking.

3.9.9 Kitchen location/ventilation in the kitchen

The characteristics of cooking places are different in the mountainous areas from the plain areas of Nepal. In general, five different cooking locations in or outside the houses can be observed in the mountainous areas. A study conducted in the southern plain areas in India has demonstrated that smoke exposure of cooks varies according to kitchen location (Balakrishnan et al. 2002). This study found persons cooking in kitchens without partitions experienced the highest levels of particulate matter exposure, followed by cooking in kitchens with well-defined partitions, and then persons cooking in outdoor kitchens. Similarly recently conducted TB case-control study in South India have shown not having a separate kitchen as an important risk factor(Shetty et al. 2006). Based on the pilot survey, in this study, kitchen locations were characterized under five categories. This was similar to the South Indian study:

- Open air kitchen out side the house
- Kitchen both inside and outside the house
- Separate kitchen room outside the house
- Separate kitchen room inside the house
- Kitchen inside the house without partition (such as in a corridor or in the room used for sleeping).

3.9.10 Closing doors, opening windows, ceiling and exhaust fan in the kitchen

Windows and other openings in the kitchen play an important role in circulating air in and out of the kitchen (cross ventilation). Participants were asked if they have a window, closing door, and ceiling or exhaust fan in the kitchen. Participants often found it difficult to define windows in the kitchens. Generally, kitchens in *Pucca*[2] houses have conventional or standard glass windows. However, within *pucca* houses, people may cook at the corner of a passage (space between rooms), that may not have windows. Kitchens in the *kuccha* houses may not have conventional windows but may have openings between walls and ceilings. Within *kuccha* houses, people may cook inside the room also used for sleeping. Sometimes within a *kuccha* or *pucca* house, people cook in a semi-enclosed room, such as a gallery or balcony, which has sufficient openings for air exchange. Thus, characterizing a window in the kitchen can be difficult. In this study, the definition of the presence of windows in the kitchen was based on information on the availability of regular/conventional windows, glass windows or an opening in the kitchen that was larger than two A4 size papers. Also, as the presence of a ceiling or exhaust fan in the kitchen helps to dilute the smoke, questions were asked whether there is an exhaust or ceiling fan in their kitchen. The response was documented as 'yes' or 'no'. We did not ask how often ceiling or exhaust fans are used, or whether they are used during cooking time.

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[2] Kuccha: House made from mud, thatch and other low quality materials.
Pucca: House made entirely from high quality materials.
Semipucca: House made from both low and high quality materials

3.9.10.1 Overall ventilation characteristics

Since a cook's personal exposure to indoor air pollutants depends on the overall ventilation character, in which windows, closing doors, ceilings or exhaust fans and kitchen locations play an important role, information on kitchen location and windows was combined to create a composite dichotomous variable for ventilation; "fully/partially ventilated kitchens" and "un-ventilated kitchens". We did not use ceiling fan or exhaust fan and closing door information to create a ventilation characteristics because very few people reported having a ceiling or exhaust fan in the kitchen and we had not asked the frequency of its use. Similarly, we found very difficult to interpret the information on closing doors to characterize the ventilation. Thus, under dichotomized ventilation characteristics, "fully/partially ventilated kitchens" included open-air kitchens, separate kitchens outside the house and partitioned kitchens with windows inside the house and "un-ventilated kitchens" included partitioned kitchens without windows and "non-partitioned kitchens inside the house".

3.9.11 Fuel and stove type

Fuel and stove type are primary exposure variables in this study. Information about the type of fuel and stoves that cases and controls were using at the time of interview or currently in the house, and the duration of use of such fuels and stoves was collected. Information about the types of fuel and stove participants had used during their childhood or before marriage (while at their parents' house) were also collected. Series of questions were asked if they remembered changing fuels or stoves anytime before and after their marriage and types of fuel and stoves they had changed or switched to and duration of their use. This information enabled us to calculate the total durations of exposure to particular stove types, which was used to study the exposure response relationships between duration of cooking with biomass fuel/stoves, kerosene stoves and gaseous stoves and the risk of TB.

Compared with improved biomass stoves, which have flues, solid-fuel stoves without flues emit higher concentration of pollutants inside the house (Smith 1987; Naeher et al. 2000a). Stoves that use gaseous fuel emit less pollution compared to solid fuel stoves (Smith et al. 1993; Ellegard

1997; Naeher et al. 2000b) and kerosene stoves(Balakrishnan et al. 2002; Smith and Staurt 1995). Although kerosene is less polluting in terms of particles than biomass fuels, recent literatures, however, have shown that women using kerosene fuel/stoves could get very high exposure to particles compared with using gaseous fuel stoves (Saksena et al.; Andresen et al. 2005). Thus, for the purpose of this study, fuel such as wood/biomass, cow dung cake and coal/charcoal was characterized as "solid fuel", kerosene fuel as "kerosene fuel" and LPG and biogas as "gaseous fuel".

There is a high correlation between fuel and stove type. For example, gaseous fuel, which is considered to be a cleaner fuel, generally has a clean burning stove, whereas devices that use solid fuel may or may not have a flue. Solid fuel used in a stove with a flue is uncommon compared to unflued solid-fuel stoves. Thus to avoid collinearity, stove type and fuel type were divided into three categories. Stoves that use kerosene (wick or pump) were characterized as "kerosene stoves", LPG and biogas fuel using stoves were characterized as "gaseous stove". Stove with or without a flue (unimproved stoves) that used solid fuel was characterized as "biomass stoves". Along with fuel and stove use, questions were also asked about the type of fuel used to heat the house during winter and frequency of its use.

3.9.12 Source of light

Many villages in Nepal are still not connected to the national power grid. As an alternative source of light, many people in these areas use kerosene wick lamps (*Tuki*), lanterns or petromax. Generally wick lamps, *Tukis*, which are very widely used in the villages are homemade, where glass bottle or tin container is used as the base and a scrap of cloth, dipped in kerosene, as the wick. A study conducted by Smith et al (1995) in India has found Kerosene lamps producing substantial amount of smoke indoors(Smith and Staurt 1995). A question was asked about the main source of light in the house.

3.9.13 Smoking status

The association between smoking and tuberculosis (TB) has been investigated since 1918. Smoking is a well known risk factor for TB (Slam et al. 2007; Chiang et al. 2007) and dose response relation has been observed between tobacco smoking and risk of TB (Leung et al. 2004).

In this study, participants were asked about their past and present smoking habits. Past and present smoking habits were characterized as 'present or regular smoker', 'ex-smoker', 'never smoked in life'. They were also asked the age when they started smoking and the number of years they quit or stopped smoking and age/years when they completely quit or stopped smoking. Participants were also asked their smoke inhalation habit (inhale in to throat, inhale in to throat and chest, and inhale in to chest), type of tobacco product they use regularly such as cigarette, *bidies* (tobacco leaf wrapped in Kendu plant leaf) or *hukkas* (water pipes). These products were further divided into "filtered vs. unfiltered tobacco product". Participants were asked the total number of tobacco products they smoke every day. Later this information was used to calculate the pack-years of smoking. The number of pack-years smoked was calculated as the average number of cigarettes smoked per day multiplied by the duration of smoking divided by 20, assuming that a pack contains 20 cigarettes or *bidis*. The median pack-years were used to access the risk of TB by pack-years. We used a standard questionnaire developed by National Cancer Institute to document tobacco- related information.

3.9.14 Environmental tobacco smoke

Exposure to second hand tobacco smoke (Environmental Tobacco Smoke: ETS) has been linked to a variety of adverse health outcomes. ETS exposure has been found to be causally associated with respiratory illnesses, including lung cancer, childhood asthma and lower respiratory tract infections (Guneser et al. 1994) and TB**.** Epidemiological studies (case-control and cross sectional) have shown close and very close exposure to passive smoking strongly associated with TB in young children and adults (Tipayamongkholgul et al. 2005) (Altet et al. 1996) (Singh et al. 2005)**.** ETS is a complex mixture of chemicals generated during the burning and smoking of tobacco products. Chemicals present in ETS include irritants and systemic toxicants, such as hydrogen cyanide and sulfur dioxide; mutagens and carcinogens, such as benzo[a]pyrene, formaldehyde and 4-

aminobiphenyl; and the reproductive toxicants nicotine, cadmium, and carbon monoxide (Shopland 1997).

Characterization of ETS exposure in air pollution-related epidemiological studies is important, but none of the previously conducted epidemiological studies of exposure to smoke from cooking fuel and the risk of TB has looked at this relationship. In this study, exposure to ETS was defined by other family members smoking inside the house and the number of tobacco products they smoke every day. A question was asked about the types of tobacco products their family members including husband smoked. Smoking status of participants family members were trichotomized as "no family member smoke", "one family member smoke" and "two or more than two family members smoke". Participants, who reported that their spouse did not smoke any of these products but used chewing tobacco, were put under the "not smoking category". There are several limitations in this question. For example, a question was not included on duration of exposure to ETS or ventilation status of the room where ETS exposure occurred.

3.9.15 Exposure to smoke from mosquito coil & incense

Besides smoke from cooking fuel, tobacco products and wick kerosene lamps; mosquito coils (Lee and Wang 2006) (Lin and Shen 2005; Liu et al. 2003; Ibrahim 1992; Saini et al. 1986) and incense(Yang et al. 2007; Lee and Wang 2004; Lofroth et al. 1991; Chen 2005) also contribute smoke indoors. Incense smoke is a complex mixture of gases and particles and has been found to be a significant source of polycyclic aromatic hydrocarbons (PAHs), carbon monoxide, benzene, isoprene and particulate matter (Li and Ro 2000) (Lin et al. 2002) (Fang et al. 2002) (Lung and Hu 2003).

Several studies have linked smoke from mosquito coils and incense to respiratory related illness such as irritation and chronic cough (Ho et al. 2005) and cancer (Friborg et al. 2007; Chiang and Liao 2006), especially among adult and children (Azizi et al. 1995; Yang et al. 1997). However, there do not exist any studies linking exposure to smoke from either mosquito coils or incense with risk of TB. Participants were asked about their practices and frequencies of burning mosquito coils or incense daily or weekly. A question was also asked about the number of incense sticks they burned each day and number of months per year they burn mosquito coils and places where they burned incense mostly, such as in the bedroom or separate room (made for worship).

3.9.16 Age

Age is a well-known risk factor for TB. Information about the participant's age is important in this study because duration of exposure to indoor smoke varies with age. Information was collected on each participant's present age; age at marriage and the number of years she had cooked or not cooked if she reported that she was not directly involved in cooking at the time of interview. This information enabled us to calculate the total duration of cooking (in years) for each subject in her parents' house and after her marriage. Participants were also asked the number of years they cooked on various stove types. This enabled us to calculate the number of years participants spent cooking with various types of fuel and stoves (improved and unimproved stoves).

3.9.17 Alcohol consumption

Alcohol consumption increases host susceptibility to a variety of infections. Studies have shown alcohol consumption associated with respiratory infection and Tuberculosis (Bomalaski and Phair 1982). Alcohol consumption has also been found to effect TB treatment negatively (Albuquerque et al. 2007; Moran et al. 2007). The questionnaire in this study included a question on whether the subject presently consumed alcohol ("yes/no") and the age she started drinking and age she stopped drinking if she was not drinking alcohol currently. A question about quantity of alcohol (in glass) she drinks or used to drink every day or in a week was also asked.

3.9.18 Medicine/Vitamin intake

Information was obtained from each subject about her present intake of any vitamin.

3.9.19 TB in the house

Increased risk of TB has been seen in those who had close contact with index case and family history of TB(Crampin et al. 2004). A question was asked whether any family members have/had TB in the house. If anybody has/had TB then a further question was asked about who had the TB. The relationship was documented.

3.9.20 Vaccination

A question on vaccination was asked to evaluate access to health care and see if vaccination showed any protective association with TB. Most subjects can identify their vaccination status by looking at the scar from BCG on their arm.

3.9.21 Socio-economic status

As measures of socio-economic status, questions on annual income in four categories in Nepali Rupees (NRs); NRs <25,000, <50,000, <100,000 and >100,000 were asked to each participants. Similarly participants were also asked about their land-ownership under ‘yes/no’ response. As personal transportation in the house also reflects socio-economic status (for example people who own a car are generally better off than those who own only a bicycle), participants were asked about the availability of personal transportation in their house.

4.0 Data Analysis

4.1 Statistical method of analysis of TB study

In epidemiological studies, statistical analyses are organized around three different sets of variables: the exposure(s) of interest, other covariate exposures (potential confounders) and the outcome. In this study, the exposures (including covariates) were first analyzed using chi-square tests, followed by univariate calculation of odds ratios for association with the outcome (TB).

Confounding is a type of bias that occurs when an extraneous variable or factor is statistically associated with the exposure and independently affects the outcome. In order to obtain an unbiased estimate of the exposure-outcome relationship, we needed to identify potential confounders, collect information on them and adjust for them. Several authors have emphasized that confounder identification must be grounded on an understanding of the causal network linking the variables under study (Hernan et al. 2002; Weinberg 1993; Rothman and Greenland 1998). To analyze the confounding effect of other variables on the relationship between the primary exposure of interest (exposure to smoke from biomass stoves) and risk of disease (TB), a crude odds ratios (OR) between exposure and outcome was calculated. All statistically significant exposure ORs ($p \le 0.05$) with disease were included in the stepwise unconditional logistic regression model (backward elimination method). A variable selection criterion of $p=0.2$, was applied to all the variables to identify covariates that should be included in the final model. Also included in the final model were variables that are known risk factors for TB. Using the selected covariates, a multivariate unconditional logistic regression model for risk of TB was constructed, and simultaneous effects of multiple variables on the risk of TB were evaluated. From the final model, a female population attributable fractions (PAF) and associated confidence intervals were calculated using the aflogit command of STATA. The calculation assumed that the proportion of controls exposed is a good estimate of the proportion exposed in the target population.

5.0 Results

5.1 Age category

Age is an important risk factor and potential confounders in epidemiological studies. In this study, participants were matched on age. The frequency distributions of age categories are summarized in table 2.

Table 2 Age categories of cases and controls

Subjects Age category	Cases (%)	Controls (%)	Chi-square & P value
20-29 years	54 (43.2)	108 (43.2)	Pearson chi2(4) = 0.00 Pr = 1.00
30-39 years	26 (20.8)	52 (20.8)	
40-49 years	22 (17.6)	44 (17.6)	
50-59 years	3 (2.40)	6 (2.40)	
>60 years	20 (16.0)	40 (16.0)	
Mean age in years	35 (standard deviation: 13)	35 (standard deviation: 13)	

5.2 Religion

Officially, over 86% of people in Nepal are Hindus. After Hindus, the next largest religious groups are Buddhist (8%) and Muslim (4%)(N Census 2002). In this study about 71% of cases and 94% of controls were Hindus; about 25% of cases and 4% of controls were Buddhists; and 3% cases and 2% of controls were Christians and one case was Muslim (0.01%). Since there were very few Christian cases or controls and Muslims, these religion categories were combined. Later the religion was trichotomized as 'Hindus', 'Buddhists' and 'Christians & Muslims'. Religion showed a significant association with TB disease. Buddhists compared with Hindus had a very high risk of TB: OR of 7.09 (95%CI: 3.66-13.74). Table 3 and 4 summarizes the results.

Table 3 Religion of cases and controls

Religion	Cases (%)	Controls (%)	Chi-square & P value
Hindus	89 (71.2)	236 (94.4)	Pearson chi2 (1) = 44.7 Pr = 0.00
Buddhist	31(24.8)	9 (3.60)	
Christian	4 (3.00)	5 (2.00)	
Muslims	1 (0.01)	0 (0.00)	

Table 4 Religion of cases and controls

Religion	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Hindus	89 (71.2)	236 (94.4)	1.00	Pearson chi2 (1) = 40.85 Pr = 0.00
Buddhists	31 (24.8)	9 (3.60)	9.13 (4.18-19.9)	
Christians & Muslims	5 (3.00)	5 (2.00)	2.65 (0.75-9.38)	

5.3 Area of residence

About 30% of cases and 15% of controls in this study were from rural areas (Pearson chi2 (1) = 11.91 Pr = 0.00). Compared with urban residents, rural residents had a two times higher risk of TB (OR: 2.44; 95% CI 1.46-4.08). Tables 5 and 6 summarize the area of residency of cases and controls and the associated odds ratio and 95% confidence intervals.

Table 5 Area of residence of cases and controls

Religion	Cases (%)	Controls (%)	Chi-square & P value
Rural	38 (30.40)	38 (15.2)	Pearson chi2 (1) = 13.39 Pr = 0.00
Urban	81 (64.8)	187 (74.8)	
Peri-urban	6 (4.80)	25 (10.0)	

Table 6 Area of residence of cases and controls

Subjects	Cases (%)	Controls (%)	OR 95% CI	Chi-square & P value
Urban/peri-urban residence	87(69.6)	212 (84.8)	1.00	Pearson chi2 (1) = 11.91 Pr = 0.00
Rural residence	38 (30.4)	38 (15.2)	2.44(1.46-4.08)	

5.4 Marital status

When participants were asked about their marital status, 88% of cases and 83% of controls reported they were married. Only one case reported that she was divorced. This participant was combined with married people. The marital status was then dichotomized as ‘married’ and ‘unmarried’. Compared with unmarried women, married women had higher risk of TB (OR: 1.69; 95% CI 0.89-3.23) but the association was not statistically significant. For married women, a question was asked about the age of their marriage. The mean age of marriage for cases was 19 years (SD: 8) and for controls was 23 years (SD: 21 years). The difference was statistically significant (t =   2.92; p value = 0.00).

Table 7 Marital status of cases and controls

Subjects	Cases (%)	Controls (%)	OR 95% CI	Chi-square & P value
Married	110 (88.0)	206 (82.7)	1.69 (0.89-3.23)	Pearson chi2 (1) =4.28 Pr = 0.12
Unmarried	14 (11.2)	44 (17.3)	1.00	
Divorced	1 (0.80)	0		

5.5 Level of education

Under the series of literacy related questions, participants were asked whether they can read or write Nepali. 49% of cases and 62% of controls reported that they can read and write, whereas 51% of cases and 38% of controls reported they cannot read and write. Compared with those who can read and write, people who cannot read and write had about two times higher risk of TB (OR: 1.68; 95% CI 1.09-2.60). To evaluate whether risk of TB varies by the level of education or years of schooling, participants were further asked about the highest level of education they had attained. Tables 8 and 9 summarize the level of education of cases and controls. To evaluate the association of TB with level of education, some levels of educations were combined. For example, adult education and primary level of education were combined. Similarly, middle and high school level education were combined and college and university level of education were combined. The risk of TB showed a protective effect with higher level of education or years of schooling. The score test of trend p value was 0.05. Table 10 summarizes the results.

Table 8 Literacy of cases and controls

Read and write	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Can read and write	61 (48.8)	154 (61.6)	1.00	Pearson chi2 (1) = 5.58
Cannot read and write	64 (51.2)	96 (38.4)	1.68 (1.09-2.60)	Pr = 0.02

Table 9 Level of education by cases and controls

Participants	Primary	Middle	High	College	University	Adult education	No formal education
Cases	18 (14.4)	17 (13.6)	11 (8.80)	11 (8.80)	2 (1.60)	2 (1.60)	64 (51.2)
Controls	42 (16.8)	26 (10.4)	37 (14.8)	34 (13.6)	1 (0.40)	16 (6.40)	94 (37.6)

Pearson chi2 (1) = 14.15; Pr = 0.03

Table 10 Level of education by cases and controls

Education level	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
No formal education	64 (51.2)	94 (37.60)	1.00	Pearson chi2 (3) = 6.83, Pr = 0.08 Score test for trend of odds
Adult & Primary	20 (16.0)	58 (23.2)	0.51 (0.28-0.93)	chi2(1) = 3.96, Pr>chi2 = 0.05
Middle & High	28 (22.4)	63 (25.2)	0.65 (0.38-1.13)	
College & University	13 (10.4)	35 (14.0)	0.55(0.27-1.12)	

5.6 Occupation

Considering the potential dust exposure to be similar in farming (on own land) and agricultural labor, these two variables were combined as 'farming' under the occupation categories. The government services and commercial jobs were combined as 'government services and commercial'. Since only three people (two cases and one control) reported working in industries as industrial labor, the non-agricultural labor and industrial labor were combined as 'non-agricultural labor'. The category, house-wife was put as 'house wife' and teachers and students were put under 'teacher & student' category considering similar chances of exposure to dust (chalk dust, re-suspension of dust from the ground) and crowding.

More cases than controls were found under the farming occupation (33% vs. 23%) and more controls than cases were found under non-agriculture laborer occupational category (7% vs. 19%). Similarly, more cases than controls were found under the teaching and student occupation (9% vs. 6%). When the risk of TB was analyzed by types of occupation with ‘government services and commerce’ as a reference category, the risk of TB was higher among people engaged in farming, but the result was not statistically significant. Non-agricultural labor was found to be protective. Results of distribution of cases and controls by types of occupations and associated odds ratios are presented in tables 11 and 12.

Table 11 Distribution of occupations of cases and controls

Case/ Control	Farming (own - land)	Farming (agri-labor)	Government services	Commerce & business	Non-agriculture labor	Industrial labor	House wife	Teacher & students
Case	28 (22.4)	13 (10.40)	4 (3.20)	12 (9.60)	7 (5.60)	2 (1.60)	48 (38.4)	11 (8.80)
Control	43 (17.2)	14 (5.60)	21 (8.40)	11 (4.40)	46 (18.4)	1 (0.40)	99 (39.6)	15 (6.00)

Pearson chi2 (7) = 23.04   Pr = 0.002

Table 12 Distribution of occupations of cases and controls (combined categories) and odds ratios

Occupation	Cases	Controls	OR (95%CI)	Pearson Chi 2
Government services & commerce	16 (12.8)	32 (12.8)	1.00	Pearson chi2 (4) = 11.67 Pr = 0.02
Farming	41 (32.8)	57 (22.8)	1.44 (0.70-2.96)	
Non agriculture labor	9 (7.20)	47 (18.8)	0.38 (0.15-0.97)	
House wife	48 (38.4)	99 (39.6)	0.97 (0.49-1.94)	
Teacher & student	11 (8.80)	15 (6.00)	1.47 (0.55-3.92)	

Followed by main occupation related questions, participants were further asked how long they have been working in the present occupation. The duration of work in particular occupation was similar for every category of occupation for cases and controls. Table 13 presents the results.

Table 13 Mean years of employment, standard deviation (SD), confidence interval, and t test and associated p value for duration of present occupations of cases and controls (combined categories)

Occupation	Cases	Controls	t test value	p value (two tail probability)
	Mean (SD) & 95% CI	Mean (SD) & 95% CI		
Government services & commerce	8.4 (8.60) (3.64-13.16)	6.98 (8.15) (4.04-9.92)	t = -0.55	0.59
Farming	21.15(11.8) (17.4-24.9)	25.35(12.86) (21.94- 28.76)	t = 1.65	0.10
Non agriculture labor	8.94(11.35) (0.22-17.67)	5.36(6.79) (3.36-7.35)	t = -1.29	0.20
House wife	17.5(14.58) (13.27-21.73)	20.24(16.30) (17.0-23.5)	t = 0.99	0.32
Teacher & student	17.91(24.1) (1.75-34.07)	14.8(4.52) (12.30-17.34)	t = -0.49	0.63

When participants were asked whether they had experienced dust exposure in their occupation, 79.2 % of cases and 76.8% of controls reported 'yes'. The odds ratio associated with dust exposure on the risk of TB was 1.15 (95%CI: 0.68-1.94).

5.7 Secondary occupation

Participants were asked if they had a secondary occupation and whether they experienced dust exposure in the secondary occupation. About 38% of cases and 41% of controls reported having a secondary occupation. Table 14 presents the results.

Table 14 Secondary occupation of cases and controls

Secondary occupation	Subjects		OR (95 % CI)	Chi-square & P value
	Cases (%)	Controls (%)		
Yes	47(37.6)	102(40.8)	1.00	Pearson chi2 (1) =0.36 Pr = 0.55
No	78(62.4)	148(59.2)	0.87(0.56-1.36)	

The secondary occupation related question was followed by the type of secondary occupation that participants had at the time of interview. Table 15 shows the types of secondary occupation of cases and controls. When asked whether they had experienced dust exposure in their secondary occupation, 89.4% of cases and 97.1% of controls reported yes. The odds ratio associated with dust exposure on the risk of TB was 0.25(95%CI: 0.06-1.11).

Table 15 Types of secondary occupations of cases and controls

Participants	Farming (own land)	Farming (agri-labor)	Government services	Commerce & business	Non-agriculture labor	Industrial labor	House wife	Teacher & students
Case	6 (4.80)	3 (2.40)	0	6 (4.80)	2 (1.60)	0	29 (23.2)	1 (0.80)
Control	11 (4.40)	8 (3.20)	0	3 (1.20)	9 (3.60)	0	71 (28.4)	0

Pearson chi2 (6) = 8.83 Pr = 0.183

A question was also asked if they had ever changed their main occupation. About 5.7% of cases said 'yes' whereas only 4.80% of controls reported that they had ever changed their main occupation. The difference was not statistically significant (Pearson chi2 (1) = 0.12, Pr = 0.73). Similarly, 5.65% of cases and 4.40% of controls reported that they had experienced dust exposure in their previous work [Pearson chi2 (2) = 0.7693 Pr = 0.68].

Table 16 Previous occupations of cases and controls

Case/ Control	Farming (own land)	Farming (agri-labor)	Government services	Commerce & business	Non-agriculture labor	Industrial labor	House wife	No previous work
Case	2 (1.61)	1 (0.81)	0	1 (0.81)	2 (1.61)	0	1 (0.81)	117 (94.35)
Control	5 (2.00)	0	1 (0.40)	0	2 (0.80)	1 (0.40)	3 (1.20)	238 (95.2)

Pearson chi2 (7) = 5.7290 Pr = 0.572

5.8 Present house construction

The type of house reflects the economic status of people in Nepal. In this study, 47% of cases and 32% controls reported living in *Kuccha* house; 42% of controls and 36% cases reported living in a *Pucca* house; and 26% of controls and 17% of cases reported living in a semi-*pucca* house. House type was dichotomized by putting *pucca* and *semi-pucca* under one category and *kuccha* house into a separate category. A higher number of controls than cases reported living in *pucca* and semi-*pucca* houses (better houses). The difference was statistically significant (Pearson chi2 (1) = 8.72 Pr = 0.003). The odds ratio associated with living in a *kuccha* house and TB was 1.93 (95% CI: 1.25-3.00). Table 17 summarizes the results.

Table 17 Present house construction of cases and controls

House type	Case (%)	Controls (%)	OR 95% CI	Chi-square & P values
Pucca	45 (36)	106 (42)		
Semi Pucca	21 (17)	65 (26)		
Pucca + Semi Pucca (Better housing)	66 (53)	171 (68)	1.00	Pearson chi2(1)= 8.72 Pr = 0.003
Kuccha	59 (47)	79 (32)	1.93 (1.25-3.00)	

A question was asked if participants had always lived in the current house. More cases than controls answered 'no'. Table 18 summarizes the result of response of cases and controls and table 19 summarizes the results of total duration of stay in the current house. Similarly graph 1 summarizes odds of risk of TB by duration of living in the present house.

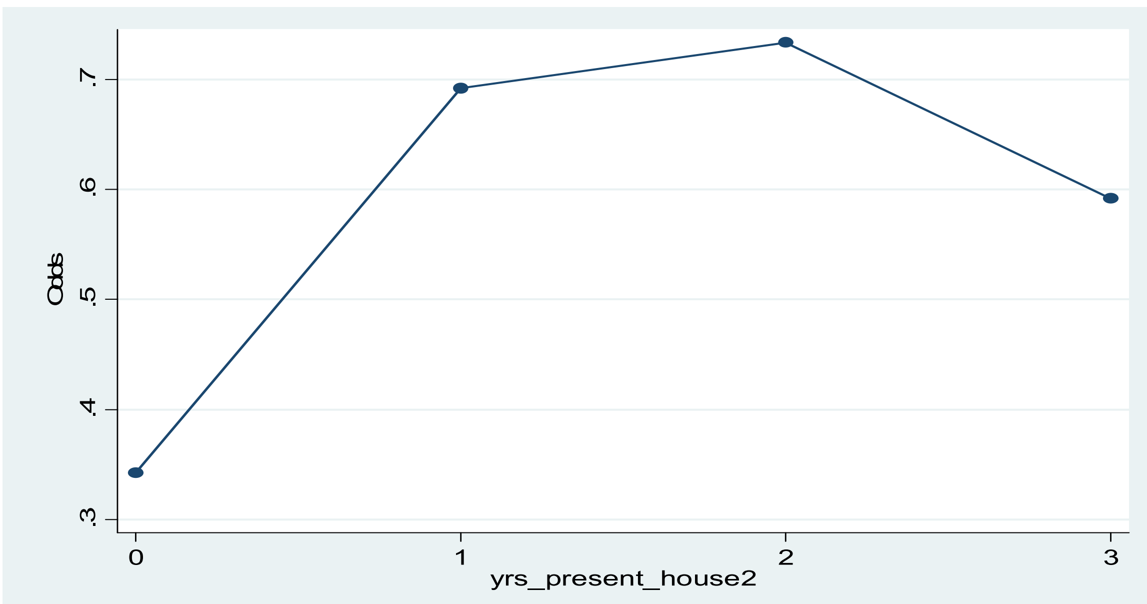
Table 18 always lived in the present house.

Always lived in the present house	Subjects		OR (95 % CI)	Chi-square & P value
	Cases (%)	Controls (%)		
Yes	38(30.4)	111(44.4)	1.00	Pearson chi2 (1) = 6.82 Pr = 0.009
No	87(69.6)	139(55.6)	1.83 (1.16-2.88)	

Table 19 Duration of living in the present house

Duration in years	Subjects		Score test of trend (Chi-square & P value)
	Cases (%)	Controls (%)	
<=1 year	18(13.6)	26(10.4)	Chi-square (2) = 4.31 P value = 0.037
<=2 years	11(8.80)	15(6.00)	
>2 years	58(46.4)	98(39.2)	
Always lived in the present house (0)	38(31.2)	111(44.4)	

Graph 1. Odds of risk of TB by duration of living in present house



5.9 Previous house construction

A question was asked about the construction of previous house of cases and controls. About 45% of cases and 39% of controls reported that the construction of their previous house was *kuccha*. The risk of TB was found to be lower in the cases that had a *kuccha* house previously compared with *pucca* and semi-*pucca* house.

Table 20. Previous house constructions of cases and controls

House type	Cases (%)	Controls (%)	OR 95% CI	Chi-square & P values
Pucca	21 (16.8)	23 (9.20)		
Semi Pucca	9 (7.20)	18 (7.20)		
Pucca + Semi Pucca (Better housing)	30 (24.0)	41 (16.4)	1.00	Pearson chi2(1)= 9.20
Kuccha	56 (44.8)	97 (38.8)	0.79(0.44-1.40)	
Don't know	1 (0.80)	1 (0.40)		Pr = 0.056
Always lived in the same house	38 (30.4)	111 (44.4)		

5.10 Crowding in the present and previous house

The mean number of rooms [case =3 (SD: 3) and controls =3 (SD: 2)] and the mean number of people living in the present house [case =5 (SD: 2) and controls =5 (SD: 3)] were similar for cases and controls. However, the ranges of people living in the present house were different. In the house of cases, the number ranged between one and seventeen where as in the house of controls the number ranged between one and twelve.

Similarly, the mean number of rooms in the previous house of cases and controls was similar [case =3 (SD: 2) and controls =3 (SD: 1)] but the mean numbers of people living in the houses were 6 (SD: 3) for cases and 7 (SD: 4) for controls. The number of people living in the previous house of cases ranged between two and twenty where as in the previous house of controls the ranges were between one and twenty five.

Based on the information about number of rooms and number of people living in the current and previous house, a crowding variable was created and dichotomized as more crowded (>3 people/room) and less crowded (<3 people/room) house. The crowding was not statistically different between the houses of cases and controls in both present and previous houses. Table 21 summarizes the results.

Table 21 Cases and controls present and past crowding status

Crowding in the present house	Subjects		OR (95 % CI)	Chi-square & P value
	Cases (%)	Controls (%)		
Less crowded (<=3 people/room)	104 (83.2)	206 (82.4)	1.00	Pearson chi2 (1) = 0.04 Pr = 0.85
More crowded (>3 people/room)	21 (16.8)	44 (17.6)	0.95 (0.53-1.67)	
Crowding in the previous house	Subjects		OR (95 % CI)	Chi-square & P value
	Cases (%)	Controls (%)		
Less crowded (<=3 people/room)	96 (76.8)	182 (72.8)	1.00	Pearson chi2 (1) = 0.70 Pr = 0.40
More crowded (>3 people/room)	29 (23.2)	68 (27.2)	0.81(0.49-1.33)	

5.11 Kitchen location and ventilation

5.11.1 Cooking/kitchen location and windows in the kitchen

In this study, cases and controls had the following kitchen distributions:

Cooking outside the house in the open air throughout the year (except monsoon): one control and two cases reported that they cooked outside in the open air.

Cooking both inside and outside the house: one control and two cases reported they cooked both inside (in the open air) and outside the house. This means that sometimes they cook outside (for example, the morning meal) and sometimes inside (for example, the evening meal).

Separate kitchen room outside: About 14% of controls and 11.2% of the cases reported they had separate kitchen rooms outside the house.

Kitchen inside the house with partition (or separate kitchen room inside the house): about 53.6% of the controls and 36% of the cases reported that they had a separate kitchen room inside their house.

Kitchen inside the house without separating wall: about 31.6% of the controls and 49.6% of the cases reported that they cooked in the same room as they use for sleeping. Table 22 summarizes the five kitchen locations of cases and controls.

Table 22 Present kitchen locations of cases and controls

Kitchen locations	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Cooking outside the house in open air all the time	2(1.60)	1(0.40)		
Cooking both inside and outside the house	2(1.60)	1(0.40)		
Separate kitchen room outside	14 (11.2)	35(14.0)		
Cook out + Cook out & inside + Separate kitchen outside	18(14.4)	37(14.8)	1.00	Pearson chi2 (3) = 12.60 Pr = 0.002
Kitchen inside the house with partition (or separate kitchen room inside the house)	45(36.0)	134(53.6)	0.69(0.36-1.33)	
Kitchen inside the house without separation	62(49.6)	79(31.6)	1.61(0.84-3.10)	

The risk of TB was analyzed by kitchen locations. For this analysis, the open air cooking, cooking both inside and outside and separate kitchen room outside were combined into one category, which was used as a reference category and the other categories kept the same. A similar proportion of controls and cases were found having separate kitchens outside and cooking outside. However, more controls than cases reported having partitioned kitchens (separated by wall) inside (53.6 vs. 36%). Whereas, more cases than controls had kitchen inside their houses that were not separated by walls (49.6% cases v 31.6% controls). The univariate OR showed a statistically non-significant but apparently protective effect of having a partitioned kitchen inside, whereas kitchen inside the house without separate wall was found to be associated with risk for TB (statistically non-significant association), compared to reference category.

5.11.2 Windows in the kitchen

92.8 % of the controls and 95.12 % of cases reported they had windows or sufficient openings in their kitchens (openings equivalent to two A4 size paper sheets or more). The difference was not statistically significant (Pearson chi2 (1) = 0.75 Pr = 0.385). The OR for the risk of tuberculosis from not having a window in the kitchen compared with having a window was 0.66 (95 % CI 0.25-1.70). Table 23 summarizes this result, where participants who reported cooking mainly outside were excluded.

Table 23 Window/s and sufficient openings in the kitchen of cases and controls

Window/sufficient openings	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Yes	117(95.1)	231(92.8)	1.00	Pearson chi2 (1) =0.75
No	6(4.88)	18(7.23)	0.66(0.25-1.70)	Pr = 0.39

5.11.3 Closing door in the kitchen

96.8 % of the controls and 90.2 % of cases reported they had a closing door in their kitchens. The difference was statistically significant (Pearson chi2 (1) = 6.93 Pr = 0.01). The OR for the risk of tuberculosis from not having a closing door in the kitchen compared with having a closing door was 3.26(95 % CI 1.29-8.19). Table 24 summarizes this result, where participants who reported cooking mainly outside were excluded.

Table 24 Closing door in the kitchen of cases and controls

Closing door in the kitchen	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Yes	111(90.2)	241(96.8)	1.00	Pearson chi2 (1) =6.93
No	12(9.76)	8(3.21)	3.26(1.29-8.19))	Pr = 0.01

Table 25 Closing doors and opening windows by kitchen location of cases and controls

Kitchen location	Kitchen location by cases and controls		Windows in the kitchen				Opening door in the kitchen			
	Cases	Controls	Cases		Controls		Cases		Controls	
			Yes	No	Yes	No	Yes	No	Yes	No
Separate kitchen room outside	14 (11.2)	35(14.0)	12 (86)	2 (14)	34 (97)	1 (3)	12 (86)	2 (14)	33 (94)	2 (6)
Kitchen inside the house with partition (or separate kitchen room inside the house)	45(36.0)	134(53.6)	42 (93)	3 (7)	125 (93)	9 (7)	40 (89)	5 (11)	132 (99)	2 (1)
Kitchen inside the house without separation	62(49.6)	79(31.6)	62 (100)	0 (0)	72 (91)	7 (9)	58 (94)	4 (6)	76 (96)	3 (4)

5.11.4 Ceiling fan in the kitchen

14.4 % of the controls and 10.6 % of cases reported they had a ceiling fan in their kitchen. The difference was not statistically significant (Pearson chi2 (1) =1.09 Pr = 0.30). Having ceiling fan in the kitchen had protective effect on TB. The univariate OR was 0.70(95 % CI 0.36-1.37). Table 26 summarizes this result.

Table 26 Ceiling fan in the kitchen of cases and controls

Ceiling fan in the kitchen	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
No	110(89.4)	213(85.5)	1.00	Pearson chi2 (1) =1.09 Pr = 0.30
Yes	13(10.6)	36(14.4)	0.70 (0.36-1.37)	

5.11.5 Exhaust fan in the kitchen

3.61 % of the controls and 6.50 % of cases reported they had an exhaust fan in their kitchen. The difference was not statistically significant (Pearson chi2 (1) =1.58 Pr = 0.21). The univariate OR for the risk of tuberculosis from having exhaust fan in the kitchen was 1.86 (95 % CI 0.70-4.93). Table 27 summarizes this result.

Table 27 Exhaust fan in the kitchen of cases and controls

Exhaust fan in the kitchen	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
No	115(93.50)	240(96.39)	1.00	Pearson chi2 (1) =1.58 Pr = 0.21
Yes	8(6.50)	9(3.61)	1.86(0.70-4.93)	

Controls who reported having a ceiling fan in the kitchen had mainly the separate kitchen inside the house (72%) followed by kitchen inside the house without separate wall (25%). Among the cases, who reported they had ceiling fan in the kitchen had mainly the separate kitchen inside the house (46%) followed by kitchen inside the house without separate wall (38%). A similar pattern was observed for exhaust fans also. Table 28 summarizes the results.

Besides distribution of ceiling and exhaust fan by kitchen location, a distribution pattern of fans by house construction was also evaluated. Mainly the ceiling fans were found in the kitchens of *pucca* houses (for both cases and controls), followed by semi *pucca* houses. Very few cases and controls living in *kuccha* houses had fans in their kitchen. Table 29 and 30 summarize the results.

Table 28. Ceiling fan and exhaust fan by kitchen location of cases and controls

Kitchen location	Kitchen location by cases and controls		Ceiling fan in the kitchen				Exhaust fan in the kitchen			
	Cases	Controls	Cases		Controls		Cases		Controls	
			Yes	No	Yes	No	Yes	No	Yes	No
Separate kitchen room outside	14 (11.2)	35 (14.0)	2 (14)	12 (86)	1 (3)	34 (97)	1 (7)	13 (93)	0 (0)	35 (100)
Kitchen inside the house with partition (or separate kitchen room inside the house)	45 (36.0)	134 (53.6)	6 (13)	39 (87)	26 (19)	108 (81)	7 (16)	38 (84)	8 (6)	126 (94)
Kitchen inside the house without separation	62 (49.6)	79 (31.6)	5 (8)	57 (92)	9 (11)	70 (89)	0 (0)	62 (100)	1 (1)	78 (99)

Table 29. Ceiling fan in the kitchen of cases and controls according to house type

Participants living in *Pucca* house	Cases (%)	Controls (%)	OR (95% CI)
Ceiling fan : yes	12 (26.7)	28(26.4)	1.01 (0.46-2.23)
Ceiling fan : no	33(73.3)	78(73.6)	1.00
Participants living in Semi-pucca *house*	Cases (%)	Controls (%)	OR 95% CI
Ceiling fan : yes	1(4.7)	4(6.20)	0.76(0.08-7.23)
Ceiling fan: no	20(95.3)	61(93.8)	1.00
Participants living in Kuccha *house*	Cases (%)	Controls (%)	OR (95% CI)
Ceiling fan : yes	0(0.00)	4(5.10)	-
Ceiling fan: no	57(100.0)	14(94.9)	1.00

Table 30. Exhaust fan of cases and controls according to house type

Participants living in *Pucca* house	Cases (%)	Controls (%)	OR (95% CI)
Exhaust fan : yes	6(13.33)	9(8.49)	1.66(0.55-4.97)
Exhaust fan : no	39(86.67)	97(91.51)	1.00
Participants living in Semi-pucca *house*	Cases (%)	Controls (%)	OR 95% CI
Exhaust fan : yes	2(9.5)	0(0.00)	-
Exhaust fan: no	19(90.5)	65(100.0)	1.00
Participants living in Kuccha *house*	Cases (%)	Controls (%)	OR (95% CI)
Exhaust fan : yes	0 (0.00)	0 (0.00)	-
Exhaust fan: no	57(100.0)	78(100.0)	1.00

5.11.6 Overall ventilation characteristics in the kitchens

Since a cook's personal exposure to indoor air pollutants depends on the overall ventilation character, in which kitchen locations and opening windows in the kitchen play an important role, information on kitchen location and opening windows in the kitchen were combined to create a composite dichotomous variable for ventilation. "Fully/partially ventilated kitchens" included Open-air kitchen + kitchen inside & outside + separate kitchen outside with opening window. "Un-ventilated kitchens" included separate kitchen outside without windows and partitioned kitchens inside without windows and non-partitioned kitchen inside the house (in the bedroom).

The risk of TB was evaluated by overall ventilation characteristics of the kitchens. About 64% of controls had fully ventilated kitchens compared with 47% of cases. The difference was statistically significant (Pearson chi2 (1) = 10.17 Pr = 0.001). Compared with persons cooking in fully or partially ventilated kitchens, person cooking in unventilated kitchens had more than two times the risk of TB. This was statistically significant. Table 31 summarizes the results.

Table 31 Ventilation in the kitchen of cases and controls

Subjects	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Fully/partially-ventilated kitchen	59(47.20)	161(64.4)	1.00	Pearson chi2 (1) = 10.17 Pr = 0.00
Unventilated	66(52.8)	89(35.60)	2.02(1.31-3.31)	

5.11.7 Ventilation status by present house type

The ventilation status in the houses of cases and controls were evaluated by their current house construction. Analysis showed that among participants living in *pucca* houses, 68% of controls had fully ventilated kitchen, whereas 67% of cases had such ventilation in their cooking spots (Pearson chi2 (1) = 0.02 Pr = 0.88). In the case of subjects living in semi-*pucca* houses, 77% of controls and 48% of cases had fully-ventilated kitchens (Pearson chi2 (1) = 6.46 Pr = 0.01). In the case of participants living in *kuchha* houses, 49% of controls and 32% of cases cooked in fully ventilated kitchens (Pearson chi2 (1) = 4.08 Pr = 0.04). The univariate OR of unventilated kitchens compared to ventilated kitchens on the risk of TB was 1.06 (95%CI: 0.50-2.22) in the case of *pucca* house construction, 3.67(95%CI: 1.31- 10.3) in semi-*pucca* house construction and 2.05(95%CI: 1.02-4.14) in the case of *kuccha* house construction. Table 32 summarizes the results discussed above.

Table 32 Ventilation characteristics in the kitchens according to house type of cases and controls

Participants living in *Pucca* house	Cases (%)	Controls (%)	OR (95% CI)
Fully & Partially ventilated kitchen	30 (66.7)	72 (67.9)	1.00
Unventilated kitchens	15 (33.3)	34 (32.1)	1.06 (0.50-2.22)
Participants living in Semi-pucca *house*	Cases (%)	Controls (%)	OR 95% CI
Fully & Partially ventilated kitchen	10 (47.6)	50 (77.0)	1.00
Unventilated kitchens	11 (52.4)	15 (23.0)	3.67 (1.31-10.30)
Participants living in Kuccha house	Cases (%)	Controls (%)	OR (95% CI)
Fully & Partially ventilated kitchen	19 (32.2)	39 (49.4)	1.00
Unventilated kitchens	40 (67.8)	40 (50.6)	2.05 (1.02-4.14)

5.12 Participants' current main fuel

In this study, 52% cases of and 40% of controls reported their current main cooking fuel was wood and other biomass. About 15% of cases and 9% of controls reported using kerosene fuel currently; none of the cases (0%) reported biogas but about 3% of controls reported biogas as their current main fuel, and 33% of cases and 48% of controls reported liquefied petroleum gas (LPG) as their current fuel for cooking (Pearson chi2 (3) = 12.99, Pr = 0.005). The difference of solid vs. gaseous fuel between cases and controls was statistically significant (Pearson chi2 (1) = 4.55 Pr = 0.03). The exposure odds ratio for TB was 1.98 (1.24-3.17) for participants cooking with solid fuel and exposure odds ratio was 2.54 (1.26-5.12) for participants cooking with kerosene fuel compared with those cooking with gaseous fuel (LPG & Biogas). Table 33 summarizes the fuel distribution patterns of cases and controls and table 34 provides the associated OR and 95% CI values.

Table 33 Present Fuel distributions of cases and controls

Present fuel at home	Cases (%)	Controls (%)	Chi-square & P value
Wood/Biomass/Dung-cake(solid fuel)	65 (52.0)	101 (40.4)	Pearson chi2 (1) = 12.99 Pr = 0.005
Kerosene (liquid fuel)	19 (15.2)	23 (9.20)	
Biogas (liquid fuel)	0 (0.00)	7 (2.80)	
LPG (liquid fuel)	41 (32.8)	119 (47.6)	

Table 34 Solid fuel and liquid fuel use by cases and controls

Fuel Category	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Biogas & LPG	41 (32.8)	126 (50.4)	1.00	Pearson chi2 (1) =11.0 Pr = 0.004
Wood/Biomass/Dung-cake(solid fuel)	65 (52.0)	101 (40.4)	1.98 (1.24-3.17)	
Kerosene	19 (15.20)	23 (9.20)	2.54 (1.26-5.12)	

5.13 Participants' present stoves

A higher proportion of cases than controls reported that they had unimproved biomass stoves and more controls than cases reported they had gaseous stoves (Pearson chi2 (1) = 13.08 Pr = 0.011). Since very few cases and controls reported they had improved (flued) biomass stove, these stoves were combined with unimproved biomass cook stoves and a variable 'biomass cook stove' was created. Tables 35 and 36 summarize the stove distribution by cases and controls and the associated odds ratios and 95% confidence intervals.

Table 35 Present Stoves distribution of cases and controls

Present Stove at Home	Cases (%)	Controls (%)	Chi-square & P value
Improved Biomass stove	2(1.60)	4 (1.60)	Pearson chi2 (3) = 13.08 Pr = 0.011
Unimproved Biomass stove	63(50.4)	97(38.8)	
Kerosene stove	19 (15.2)	23 (9.20)	
LPG stove	41(32.8)	119 (47.6)	
Biogas stove	0 (0.00)	7 (2.80)	

Table 36 Present Stoves distribution of cases and controls and associated odds ratio and 95% confidence interval.

Stove Category	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Biogas & LPG stove	41 (32.8)	126 (50.4)	1.00	Pearson chi2 (1) =11.0 Pr = 0.004
Biomass cook stove	65 (52.0)	101 (40.4)	1.98 (1.24-3.17)	
Kerosene stove	19 (15.20)	23 (9.20)	2.54 (1.26-5.12)	

5.13.1 Participants present stove type by area of residence

The current stove distributions of cases and controls were evaluated by the area of residency (locality). A higher proportion of cases compared with controls (92% vs.71%) residing in rural areas had biomass stove. The difference was statistically significant. Of the peri-urban residents, all cases (100%) but only 40% of controls had a biomass stove. However, among the participants from urban areas, higher proportion of controls than cases had both biomass stoves and LPG and Biogas stoves. Whereas a higher proportion of cases compared with controls from urban areas had kerosene stoves (23.5 v 8.02%). The distribution of stoves by area of residence of cases and controls are given in tables 37, 38, 39.

Table 37 Present stove distribution of cases and controls residing in rural areas

Case & Controls	Biomass stove	Kerosene stove	LPG stove	Chi-square & P value
Case	27 (92.1)	0 (0.00)	3 (7.9)	Pearson chi2 (1) = 7.53 Pr=0.02
Controls	35 (71.1)	6 (15.8)	5 (13.1)	

Table 38 resent stove distribution of cases and controls residing in peri-urban areas

Case & Controls	Biomass stove	Kerosene stove	LPG stove	Biogas stove	Chi-square & P value
Case	6 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)	Pearson chi2 (1) =6.98 Pr=0.03
Controls	10 (40.0)	2 (8.00)	10 (40.0)	3 (12.0)	

Table 39 Present stove distribution of cases and controls residing in urban areas

Case & Controls	Biomass stove	Kerosene stove	LPG stove	Biogas stove	Chi-square & P value
Case	24 (29.6)	19 (23.5)	38 (46.9)	0 (0.00)	Pearson chi2 (1) = 13.5 Pr=0.004
Controls	64 (34.2)	15 (8.02)	104 (55.6)	4 (2.14)	

5.13.2 Stove change pattern of cases and controls

To evaluate the stove change pattern of cases and controls, a question was asked whether they had ever changed the stove. About 33% cases and 44% controls reported they had changed stove in the past. The difference was statistically significant (Pearson chi2 (1) = 4.65 Pr = 0.031). Table 40 summarize the results

Table 40 Ever changed stoves by cases and controls

Cases and controls	Yes: changed the stove (%)	No: not changed the stove (%)	Chi-square & P value
Cases	41 (32.8)	84 (67.2)	Pearson chi2 (1) = 4.65 Pr = 0.031
Controls	111 (44.4)	139 (55.6)	

5.14 Previous stove type of cases and controls

To evaluate stove switch pattern of cases and controls, a question was asked about their previous stove type. Participants who reported they had different stove previously, about 15.2 % cases reported they had a biomass-unimproved stove, where as 32.8% of controls reported they had biomass-stoves. Similarly, 16.0% of cases and 7.60% controls reported that their previous stove was kerosene stove. Only one control reported switching from electric heater to other stove type.

Table 41 Previous stove type of cases and controls

Cases and Controls	Previous stove type				Number of participants who did not change their stove
	Biomass-unimproved stove	Kerosene stove	LPG stove	Electric heater	
Cases	19 (15.2)	20 (16.0)	2 (1.6)	0 (0.00)	84 (67.20)
Controls	82 (32.8)	19 (7.60)	9 (3.60)	1 (0.40)	139 (55.6)

Pearson chi2 (1) =18.76 Pr = 0.001

5.14. Exposure-response relationship between duration of use of stove type and risk of TB

To evaluate an exposure response pattern, duration of cooking on various stove types was calculated. The total mean duration of active cooking (years participants started active cooking) and total duration of cooking with solid fuel stove by cases and controls was found to be equal. However, the total duration of cooking in kerosene fuel and gaseous fuel stove was different for cases and controls. The mean duration of cooking with current biomass stoves and kerosene stoves by cases was higher than controls. However, in the case of gaseous stoves, more controls than cases were found using gaseous stove for longer duration. Similarly, risk of TB by per year increase in use of current fuel stove type was higher from kerosene stove, followed by solid fuel stove, whereas, per year increase in use of gaseous fuel stove had protective effect on TB. Table 42, 42.1 and 42.2 summarizes the results.

Table 42 Mean duration of cooking with different fuel-stoves during active cooking life of cases and controls

Case & Controls	Mean years of cooking	Years of cooking with current stove type			Years of cooking with previous stove type			Years of cooking with past stove (at parents house)		
		SFS	KFS	GFS	SFS	KFS	GFS	SFS	KFS	GFS
Case	21.02	10.75	1.54	1.53	1.56	1.48	0.14	2.94	0.264	0.08
Controls	20.26	8.13	0.64	3.26	4.73	0.85	0.46	2.68	0	0.28
Difference t-test (p value)	0.76 0.53 0.60	2.61 -1.72 0.09	0.90 -1.73 0.09	1.73 4.23 0.00	3.17 4.25 0.00	0.62 -1.32 0.19	-0.32 1.28 0.20	0.26 -0.63 0.53	0.09 -1.99 0.05	-0.20 1.81 0.07

SFS = Solid fuel stove , * KFS = Kerosene fuel stove , % GFS = Gaseous fuel stove

Table 42.1 Total duration of cooking with different fuel-stoves during active cooking life of cases and controls

Cases & Controls	Total cooking duration	Total years of cooking with SFS	Total years of cooking with KFS	Total years of cooking with GFS
Case	21.02	15.24	3.27	1.74
Controls	20.26	15.52	1.50	3.96
Difference t-test (p value)	0.76 0.53 0.60	-0.28 0.18 0.86	1.77 -2.59 0.01	2.22 4.38 0.00

Table 42.2 Univariate OR of risk of TB by per year increase in duration of cooking with current fuel-stove

Fuel stove type	OR and 95% CI	P value
Solid-fuel stove (SFS)	1.01 (1.00-1.03)	0.08
Kerosene-fuel stove (KFS)	1.06 (1.00-1.13)	0.05
Gaseous-fuel stove (GFS)	0.89 (0.83-0.95)	0.00

The univariate ORs for total duration of cooking with SFS, KFS and GFS were, 1.01 (1.00-1.03), 1.06 (1.00-1.13), 0.89 (0.83-0.95). Similarly, the univariate OR for cooking with SFS, KFS and GFS in five years band is summarized in table 42.3.

Table 42.3 Exposure response relationships based on duration of cooking with biomass and kerosene fuel stove in five years band

Exposure to Solid fuel stove	Cases (%)	Controls (%)	OR (95% CI)
0 years of use of SFS	26 (20.8)	43 (17.2)	1.00
>0 & <=5 years of use of SFS	20 (16.0)	28 (11.2)	1.17 (0.32-4.32)
>5 & <=10 years of use of SFS	18 (14.4)	51 (20.4)	0.64 (0.18-2.20)
>10 years of use of SFS	61 (48.8)	128 (51.2)	0.47 (0.11-2.02)
Exposure to Kerosene fuel stove	Cases (%)	Controls (%)	OR (95% CI)
0 years of use of SFS	86 (68.8)	209 (83.6)	1.00
>0 & <=5 years of use of SFS	12 (9.6)	14 (5.60)	4.96 (1.44-17.1)
>5 & <=10 years of use of SFS	27 (21.6)	27 (10.8)	4.60 (1.34-15.7)

5.15 Heating fuel

Participants' were asked fuel they used for heating in the house. About 68% of cases and 44% controls reported they use wood/log (in biomass-stove) and 1% of cases and controls reported they use electricity. None of the cases reported they use charcoal but one control reported she use coal and another one, case, reported using kerosene. About 30% of cases and 55% of controls reported they do not use heating fuel. Table 43 presents the results.

Table 43 Main heating fuel in the house of cases and controls

Case & Controls	Wood/log	Coal	Kerosene	Electricity	No heating fuel used	Chi-square & P value
Case	85 (68.0)	0 (0.00)	1 (0.40)	1 (0.8)	38 (30.4)	Pearson chi2 (1) = 22.4 Pr=0.00
Controls	109 (43.6)	1 (0.40)	0 (0.00)	3 (1.20)	137 (54.8)	

Table 43.1 Main heating fuel use in the house of cases and controls

Main heating fuel use in the house	Cases (%)	Controls (%)	OR (95% CI)
Electricity	1 (0.8)	3 (1.20)	-
No heating fuel used	38 (30.4)	137 (54.8)	-
Electricity and no heating fuel combined	39 (31.2)	140 (56.0)	1.00
Wood	85 (68.0)	109 (43.6)	-
Coal	0 (0.00)	1 (0.40)	-
Kerosene	1 (0.8)	0 (0.00)	-
Coal and kerosene combined	86 (68.8)	110 (44.0)	2.81 (1.78-4.42)

5.16 Main light source in the house

Compared with controls (1.6%), a higher proportion of cases (14.4%) reported that they use wick lamps or lanterns in house as a source of light. The risk of TB among wick lamp users was about ten times higher than those who had electricity as their main source of light. This was statistically significant (Pearson chi2 (1) = 24.72 Pr = 0.00). Table 44 summarizes the results.

Table 44 Main light source in the houses of cases and controls

Lighting source	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Electricity	107(85.6)	246(98.4)	1.00	Pearson chi2 (1) =24.72 Pr = 0.00
Kerosene lamp	18(14.4)	4(1.6)	10.35 (3.42-31.30)	

5.17 Smoking and risk of TB

Tobacco smoke is a known risk factor for TB. About 20% of controls and 33.6% of cases reported they smoked cigarette/bidis or hukkas regularly. The majority of cases and controls (79% of controls and 76% of cases) reported that they had never smoked in their life. Under the combined dichotomized variable of 'ever v never' smoked category; a significant difference in the smoking status/habits of cases and controls (Pearson chi2 (1) = 8.33 Pr = 0.004) was found. The exposure odds ratio for ever-smokers relative to the never-smokers was 2.02 (95% CI: 1.25-3.28).

Table 45 Smoking habits of cases and controls

Smoking habit	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Never smoked	83(66.4)	200(80.0)	1.00	Pearson chi2 (1) = 8.33 Pr =0.004
Ever smoked	42(33.6)	50(20.0)	2.02 (1.25-3.28)	

5.18 Age started smoking and total duration of smoking by cases and controls

Participants' were asked about the age they started smoking and age they stopped smoking. In addition, they were asked if there was any time (more than six months) they did not smoke or they had quit smoking. Compared with controls, cases were found starting smoking at an earlier age. The mean age of cases when they started smoking was 15 years (SD: 4 years) whereas for controls, it was 19 years (SD: 8 years). The difference was statistically significant (p value 0.003).

A Total duration of smoking was calculated by subtracting age started smoking from age when smokers quit or stopped smoking. The mean duration of smoking by cases and controls were 10 years (SD: 16 years) and 5 years (SD: 12 years) respectively. The difference was statistically significant (p value 0.00). The univariate OR for the risk of TB from a one year increase in duration of smoking was 1.03 (95% CI: 1.01-1.04).

The risk of TB by duration of smoking was further assessed by categorizing smoking as never smoked (0 years of smoking), smoked for <20 years, <40 years and > 40 years categories. Table 46 and 47 summarize the distribution of cases and controls under these categories and score test of trend of odds.

Table 46 Duration of active smoking and risk of TB

Cases/Controls	Never smoked	<20 yrs	<40 yrs	>40 yrs	Chi-square & P value
Cases	83 (66.4)	9(7.20)	25(20.0)	8(6.40)	Pearson chi2 (3) = 10.72 Pr =0.013
Controls	200(80.0)	17(6.80)	27(10.8)	6(2.40)	

Table 47 Risk of TB by duration of smoking by cases and controls

Smoking duration	Odds ratio (95% CI)	Score test of trend of odds
Never smoked (0 years)	1.00	Chi-square = 10.52 P value = 0.001
<20 yrs	1.28 (0.55-2.98)	
<40 yrs	2.23(1.22-4.07)	
>40 yrs	3.21(1.08-9.55)	

5.19 Smoke inhalation method and risk of TB

Participants' were asked about their smoking inhalation practice/habit. Compared with controls more cases reported that they smoke by mouth only and smoke up to chest. A significant difference in the smoke inhalation /habits of cases and controls (Pearson chi2 (3) = 13.91 Pr = 0.003) was found. Table 48 summarizes the results.

Table 48 Smoke inhalation method/practice of cases and controls

Cases/Controls	Non smoker	Smoke by mouth only	Smoke by mouth & throat	Smoke up to chest	Chi-square & P value
Cases	83 (66.4)	10(8.00)	10(8.00)	22(17.6)	Pearson chi2 (3) = 13.91
Controls	200(80.0)	5(2.00)	21(8.40)	24(9.60)	Pr =0.003

The exposure odds ratio for different smoke inhalation methods/habits relative to non-smoker is given in table 49.

Table 49 Exposure odds ratio for smoking inhalation practice

Smoke inhalation	Odds ratio (95% CI)	Score test of trend of odds
Non-smoker	1.00	
Mouth only	4.82(1.60-14.53)	Chi-square = 6.18
Mouth & throat	1.15(0.52-2.54)	P value = 0.013
Inhale up to chest	2.21(1.17-4.16)	

5.20 Risk of TB by smoking filter vs. unfiltered tobacco product

Smoker participants were asked about types of tobacco product they smoke generally. About 17% of cases reported they smoke unfiltered tobacco product and about 10% reported they smoke both filtered and unfiltered tobacco product. Higher proportion of cases than controls reported that they smoke unfiltered and mixed (both filtered and unfiltered tobacco product) tobacco products. The risk of TB was found to be higher in a group who reported they use unfiltered products followed by both filtered and unfiltered products. Tables 50 and 51 summarize the results.

Table 50 Tobacco products mainly used by cases and controls who are current smokers

Cases/Controls	Non smoker	Smoke unfiltered tobacco product	Smoke filtered tobacco product	Smoke both filtered & unfiltered tobacco product	Chi-square & P value
Cases	83 (66.4)	21(16.8)	9(7.20)	12(9.60)	Pearson chi2 (3) = 13.42
Controls	200(80.0)	17(6.80)	21(8.40)	12(4.80)	P value =0.004

Table 51 Exposure odds ratio for the risk of TB by types of tobacco products.

Smoke inhalation	Odds ratio (95% CI)	Score test of trend of odds
Non-smoker	1.00	
Unfiltered tobacco product	2.98(1.50-5.93)	Chi-square = 5.08
Filtered tobacco product	1.03(0.45-2.35)	P value = 0.02
Smoke both filtered and unfiltered tobacco product	2.41(1.04-5.58)	

5.21 Risk of TB by pack years of smoking

The average number of cigarettes smoked per day was recorded for all current smokers. The number of pack-years smoked was calculated as the average number of cigarettes smoked per day multiplied by the duration of smoking divided by 20, assuming that a pack contains 20 cigarettes and *bidis*. The median pack-years of smoking for both cases and controls were 8 pack-years (SD: 13.37 pack-years). To assess the risk of TB by pack-years smoked, this variable was further characterized into three categories, 0 pack-year smoked, <=8 pack-years smoked and >8 pack years smoked. Compared with non-smokers, the risk of TB was three times higher among people who smoked more than eight pack years of tobacco products. Table 52 and 53 summarizes the results.

Table 52 Risk of TB by pack-years of smoking

Cases/Controls	0 pack-years	<8 pack-years	>8 pack-years	Chi-square & P value
Cases	84 (67.20)	16 (12.8)	25 (20.0)	Pearson chi2 (3) = 12.73
Controls	200 (80.0)	31 (12.4)	19 (7.60)	Pr =0.002

Table 53 Exposure odds ratio by pack years of smoking

Smoking pack-years	Odds ratio (95% CI)	Score test of trend of odds
0 pack-years	1.00	Chi-square = 11.35
<8 pack-years	1.23 (0.64-2.37)	P value = 0.00
>8 pack-years	3.13 (1.64-5.99)	

5.22 Risk of TB by number of other members in the house who smoke indoors

Participants were asked if there are other family members who smoke inside the house. About 46% of cases and 66% controls reported no-other family members smoke inside the house. About 38% of cases and 29% of controls reported one family member smoke inside the house and 15% of cases and 5% of controls reported two family members smoke inside the house. Very few cases and controls reported more than three family members smoking inside the house.

Table 54 Number of smokers in the house of cases and controls

Number of smokers in the house	Cases (%)	Controls (%)	Chi-square & P value
No other family member smoke	58 (46.4)	165 (66.0)	Pearson chi2 (1) =19.31
One family member smoke	48 (40.0)	72 (28.8)	Pr = 0.001
Two family members smoke	18 (14.4)	11 (4.40)	
Three family members smoke	0 (0.00)	1 (0.40)	
Four family members smoke	1 (0.80)	1 (0.40)	

Numbers of smokers in the house were categorized in three categories, where more than two members were combined. The trichotomized categories were 'no other family member smoke', 'one family member smoke' and 'more than two family members smoke'. Compared with no members in the family smoke inside the house, the risk of TB was found higher in the houses where one or more than one family members were smokers.

Table 55 Number of family members smoking inside the house and associated exposure odds ratio

Smoking habit/status	Odds ratio (95% CI)	Score test of trend of odds
No other family member smoke	1.00	Chi-square = 17.31
One family member smoke	1.90 (1.18-3.04)	P value = 0.00
Two and more than two family members smoke inside the house	4.16 (1.93-8.95)	

5.23 Mosquito coil use

Mosquito coils are generally burned indoors between March and September months. However, their use is intense during or after the monsoon (rainy season), when the population of mosquitoes peaks. In this study, 39% of cases and 45% of controls reported that they burned mosquito coils in their houses and one control (0.40%) did not specify anything. The practices of burning mosquito coils were similar among cases and controls. The exposure odds ratio for TB with the use of mosquito coil was 0.78 (95% CI: 0.50-1.21). Table 56 presents the results.

Table 56 Mosquito coil use by cases and controls

Using mosquito coil	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
Yes	49 (39.20)	113 (45.2)	0.78 (0.50-1.21)	Pearson chi2 (1) =1.80
No	76 (60.8)	136 (54.4)	1.00	Pr =0.41
Not specified	0 (0.00)	1 (0.40)		

5.24 Duration of use of mosquito coils

Participants' were asked number of months they burn mosquito coils in a year. The mean duration of burning mosquito coil in months was 3.75 for cases and 3.42 for controls, which was statistically different (t = -1.81 Pr = 0.04).

The duration of burning mosquito coils were trichotomized into 0 months, <=3 months and >3 months. Table 57 summarizes the results of distribution of cases and controls burning mosquito coil under three month's categories. The risk of TB increased with duration of burning of mosquito coil and was significant for more than three months use. The results are presented on table 57.

Table 57 Duration of use of mosquito coil by cases and controls

Number of months per year using mosquito coil	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
0	76(60.8)	137(54.8)	1.00	Pearson chi2 (2)= 6.39 P value=0.041
0-3 months	15(12.0)	57(22.8)	0.47(0.25-0.89)	
>3 months	34(27.2)	56(22.4)	1.09(0.66-1.82)	

Participants were further asked number of hours they burn mosquito coils every day. The mean hours of burning of mosquito coils per day for cases and controls were 7 and 6 hours respectively, which was statistically significant (t=-2.71, Pr=0.004). The OR for the risk of TB by burning mosquito coils by one hour/ day was 1.003 (95%CI 0.94-1.07).

Based on the information about duration of use of mosquito coils in months and hours of burning per day and number of days of burning per week, the cumulative hours of exposure to mosquito coil smoke in one year was calculated. The mean hours of mosquito coil burned by cases were 703 hours (SD: 54 hours) and for controls were 558 hours (SD: 25 hours). The difference was not statistically significant. The OR for the unit increase in hours of exposure to mosquito coil was 1.00 (95% CI 0.99-1.00).

5.25 Incense burning

Incense is burned while worshipping in the morning and evening. In Nepal, Hindus and Buddhists use stick incense and Muslims use a special kind of incense called *lobhan.* About 78% of cases and 82% of controls in this study reported they burned incense while worshipping. A non-significant, but protective, association between TB and use of incense was found. Results are shown in table 58

Table 58 Incense burning practices (every day) of cases and controls

Burn incense every day	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
No	28 (22.4)	46 (18.4)	1.00	Pearson chi2 (1) = 0.84
Yes	97 (77.6)	204 (81.6)	0.78 (0.46-1.34)	Pr = 0.36

The incense burning practice of cases and controls by their religion was evaluated. For both Hindus and Buddhist, the risk associated with incense burn was higher but not statistically significant. Results are shown in table 59.

Table 59 Incense-burning practices by cases and controls by religion

Cases & controls	Hindu: burn incense		Buddhist: burn incense		Christian: burn incense	
	Yes	No	Yes	No	Yes	No
Cases	68 (77.3)	20(22.7)	29(87.9)	4(12.1)	0(0.00)	4 (100.0)
Controls	195 (82.6)	41(17.4)	8(88.9)	1(11.1)	1(20.0)	4(80.0)
OR (95% CI)	1.40(0.77-2.55)		1.10(0.11-11.31)		-	

When further asked about the number of incense stick they burn every day, about 74% of cases reported they burn one incense stick and about 3% reported burning more than two incense stick every day, where as 23% of cases reported they do not burn incense. Similarly, 81% of controls reported they burned 1 stick, and 0.4% reported they burn more than one incense sticks, whereas 18% reported they do not burn incense. Participants were asked about number of hours they burn incense everyday. The mean duration of burning of incense every day was higher among controls than cases. The mean duration of incense burning was 0.65 hours (SD: 0.56 hours) for cases and 0.79 hours (SD: 0.73) for controls. The difference was statistically significant (t=1.88, Pr=0.03).

Based on the information about duration of incense burning every day (in hours) and number of sticks of incense burned in one year, a cumulative exposure to incense smoke in one year was calculated for cases and controls. The mean hours of incense burned by cases were 1645 hours (SD: 1447 hours) and by controls were 2005 hours (SD: 1859 hours). The difference was statistically significant (t= 1.89, Pr=0.03), however, the OR for unit increase in hours of exposure to incense smoke was 1.00 (95% CI 0.99-1.00). Similarly, the risk of TB from cumulative exposure to incense smoke was calculated separately by religion. For all religions, the risk was not significant. The ORs were 1.00 (95% CI 0.99-1.00) for both Hindus and Buddhists.

5.25.1 Place of incense burning

To evaluate further the risk of TB from exposure to incense, a question was asked about the place where participants burn incense mostly. 46% of cases and 37% of controls reported that they burn incense in the bedroom, followed the worship room. More controls than cases reported they burn incense in the worship room. The exposure odds ratio showed statistically not significant but positive association between incense burning in the bedroom and TB. Table 60 summarizes the results.

Table 60.Place of incense burning by cases and controls

Place where incense is burned	Cases	Controls	OR (95%CI)	Chi-square & P value
Bedroom	58(46.4)	92(36.8)	1.08(0.61-1.91)	Pearson chi2 (3)= 6.03
Kitchen	15(12.0)	37(14.8)	0.69(0.33-1.49)	P value=0.11
Other place (worship room)	24(19.2)	73(29.2)	0.56(0.29-1.09)	Score test for trend of odds:
Do not burn incense	28(22.4)	48(19.2)	1.00	chi2(1) = 4.80 P value = 0.03

5.27 Alcohol consumption by cases and controls

Historically, TB has been strongly associated with alcohol abuse. About 2.4% of controls and 14% of cases in this study reported they had consumed alcohol regularly. However, the majority of controls and cases (96% of controls and 86% of cases) reported that they had never consumed alcohol.

Participants were asked their age when they started drinking alcohol. Compared with controls, cases had started alcohol consumption earlier. The mean age of cases and controls to start alcohol consumption was 25 (SD: 9.4 years) and 28 years (SD: 13 years) respectively.

Under the combined dichotomized variable of 'ever vs. never' alcohol consumption; a significant difference in the alcohol consumption/habits of cases and controls (Pearson chi2 (2) = 11.8 Pr = 0.001) was found. The exposure odds ratio for ever-alcohol consumption relative to the never-alcohol consumption on the risk of TB was 3.67 (95% CI: 1.68-8.05). Tables 61 and 62 summarize the results.

Table 61 Alcohol consumption by cases and controls

Alcohol Consumption Ever	Cases (%)	Controls (%)	Pearson chi2(2) = 12.01 Pr = 0.002
Yes	18 (14.4)	11 (4.4)	
No	106 (84.8)	238 (95.2)	
Don't know	1 (0.8)	1 (0.4)	

Table 62 Alcohol consumption habit of cases and controls

Ever Alcohol	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P value
Yes	18 (14.5)	11 (4.40)	1.00	Pearson chi2 (1) = 11.8 Pr =0.001
No	106 (85.5)	238 (95.6)	3.67(1.68-8.05)	

5.28 Vitamin intake by cases and controls

The majority cases (86%) and controls (98%) responded that they were not taking any vitamin at the time of interview. Only 2% of cases and 14% of controls reported taking vitamin currently. The associated odds ratio of taking vitamin and TB was 0.15 (95%CI: 0.05-0.51). Table 63 summarizes the results.

Table 63 Vitamin intake by cases and controls

Taking any vitamin at present	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
Yes	3 (2.40)	35 (14.06)	0.15 (0.05-0.51)	Pearson chi2 (1) = 12.3
No	120 (97.6)	214 (85.94)	1.00	Pr = 0.00

Note: one (0.40%) control and two cases (1.60%) said they don't know.

5.29 TB in the house

TB is spread by aerosols from patient with pulmonary TB disease, thus family history of TB (or TB in the house) is a very important risk factor. In this study, about 38% of cases reported that other household members had had TB, where as only 9% of controls reported that other household members had had TB. Relative to having no one in the house with TB, the risk of TB was 6.15 (95% CI: 3.51-10.8) times higher when other household members had TB in the house. Similarly, when analyzed by the index case of TB in the house, compared to no family members with TB in the house, the risk TB was found about seven times higher when husband had TB. Similarly risk of TB was about six and half times higher when parents had TB. For other family members with TB, the risks were similar but still very high, which was four times higher. Tables 64 and 65 present the results.

Table 64 TB among the household members of cases and controls

Any household member had TB	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
Yes	48 (38.4)	23 (9.20)	6.15 (3.51-10.8)	Pearson chi2 (1) = 12.3
No	77 (61.6)	227 (90.8)	1.00	Pr = 0.00

Table 65 Risk of TB by index case in the family/household of cases and controls

Index case	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
None had TB	81 (64.8)	228 (91.2)	1.00	Pearson chi2 (1) = 40.57
Husband had TB	12 (9.60)	5 (2.00)	6.76 (2.31-19.8)	Pr = 0.00
Parent had TB	16 (12.8)	7 (2.80)	6.43 (2.55-16.2)	
Parent-in-law had TB	8 (6.40)	5 (2.00)	4.50 (1.43-14.16)	
Brother/sister had TB	3 (2.40)	2 (0.80	4.22 (0.69-25.72)	
Other family member had TB	5 (4.00)	3 (1.20)	4.69 (1.10-20.07)	

5.30 Socio-Economic status

Studies have linked TB with poverty as it increases the risk of exposure to TB bacilli and risk of infection and disease. A series of questions related to socio-economic conditions of cases and controls was asked. These are discussed in detail below.

5.30.1 Annual income

Participants were asked about their annual family income under four categories. About 7% of participants either refused to answer this question or reported that they don't know their annual family income. A statistically different annual income was observed between cases and controls (Pearson chi2 (1) = 16.83 Pr = 0.01), which is summarized in table 66.

Table 66 Annual incomes of cases and controls

Annual income in NRs	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
< 25,000	26 (20.8)	72 (28.8)	1.00	Pearson chi2 (1) = 16.83
25000-50,000	58 (46.4)	90 (36.0)	1.78 (1.02-3.13)	Pr = 0.01
> 50,000- <100,000	16 (12.8)	51 (20.4)	0.87 (0.42-1.79)	
>100,000	9 (7.20)	25 (10.0)	0.99 (0.41-2.42)	Score test or trend of odds:
Don't know	13 (10.4)	7 (2.80)	--	Chi2(1) = 0.20
Refused to answer	3 (2.40)	5 (2.00)	--	Pr = 0.65

Distribution of stoves by level of income was analyzed. It showed that except for income level <NRs 100 000, in all other income categories, more cases than controls had biomass stove. Similarly, under all income categories more controls than cases had gas burning stoves. Table 67 summarizes the results.

Table 67 Distribution of types of stove of cases and controls by income level

Stove type	<NRs 25000		< NRs 50000		<NRs 100 000		>NRs 100 000	
	Case	Controls	Case	Controls	Case	Controls	Case	Controls
LPG & Biogas	1 (3.80)	12 (16.7)	18 (31.0)	53 (58.9)	9 (56.3)	36 (70.6)	6 (66.7)	22 (88.0)
Biomass stove	21(80.8)	44 (61.1)	28 (48.3)	33 (36.7)	5 (12.5)	13 (25.5)	3 (33.3)	3 (12.0)
Kerosene	4 (15.4)	16 (22.2)	12 (20.7)	4 (4.44)	2 (12.5)	2 (3.92)	0 (0.00)	0 (0.00)
Chi-square & P values	3.92, Pr = 0.14		15.5, Pr = 0.000		2.02, Pr =0.36		2.07, Pr=0.15	

5.30.2 Land ownership

About 74% cases and 67% of controls reported they owned land. A statistical difference in the land ownership status between cases and controls (Pearson chi2 (1) = 2.84 Pr = 0.24) was not observed. The odds ratio between risk of TB and land ownership was 1.47 (95% CI: 0.91-2.38).

Table 68 Land ownership by cases and controls

Land ownership	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
Yes	93 (74.4)	166 (66.4)	1.47 (0.91-2.38)	Pearson chi2 (1) = 2.84 Pr = 0.24
No	32 (25.6)	83 (33.2)	1.00	

One control (0.40%) refused to answer

An analysis was done to investigate whether income level varies by area of residency and landownership of case and controls. The mean income for cases and controls were similar (t = 0.45, p value =0.65), however, when mean income level was analyzed by urban and rural residency and by land ownership then a difference in income levels was observed between cases and controls. For example, the mean income levels of cases and controls living in the urban areas were similar (2.16 v. 2.20) but compared with controls; cases living in rural areas had somewhat higher mean incomes (1.88 vs. 1.70).

5.30.3 Personal transportation in the house of cases and controls

Personal transportation in the house also reflects socio-economic status. Cases and controls were asked questions about forms of personal transportation in their houses. Table 70 shows the highest form of personal transportation in the households of cases and controls. The distribution of forms of transportation was found to be similar for cases and controls (Pearson chi2 (5) = 3.19; Pr =0.36). The personal transportation in the house was further dichotomized as 'any form of personal transportation in the house' and 'no personal transportation in the house'. Having any form of personal transportation in the house showed a protective effect on TB (OR = 0.59; 95% CI: 0.31-1.10) but it was not statistically significant. Tables 71 present the results.

Table 70 Personal transportation in the houses of cases and controls

Personal transport	Cases (%)	Controls (%)	Chi-square & P values
Bicycle	3(2.40)	6 (2.40)	Pearson chi2 (1) = 3.19 Pr = 0.36
Motorcycle	10(8.00)	34 (13.6)	
Motor/car/jeep	2(1.60)	7(2.80)	
Tractor	0	0	
Bullock cart	0	0	
None of these	110(88.0)	203(81.2)	

Table 71 Any personal transport in the house of cases and controls

Any personal transportation in the house	Cases (%)	Controls (%)	OR (95% CI)	Chi-square & P values
Yes	15 (12.0)	47 (18.8)	1.00	Pearson chi2 (1) = 2.79 Pr = 0.10
No	110 (88.0)	203 (81.2)	1.70 (0.91-3.17)	

6. 0 Confounding analysis between exposure and disease relationship

A combination of stepwise backward elimination and prior knowledge of risk factors for TB were considered to identify potential confounders in this study. First, all covariates that showed statistically significant association[3] [ORs (p<= 0.05)] with TB in univariate analysis were included in the stepwise unconditional logistic regression model (backward elimination method). A variable selection criterion of p=0.2, was applied to all the variables to identify covariates that should be included in the final model. The stepwise regression model dropped (*p* value >0.20): solid fuel stove, ventilation, alcohol consumption, <= 8 pack-years of tobacco smoking, one family member smoke inside the house, literacy, present house construction and income in NRs >50,000 - <=100,000 (SES variables). Since these variables are either known risk factors or potential confounders for TB, all variables were included into the final model. In addition an age in 10 years band was included, as it was a matching variable. The result of stepwise logistic regression model is summarized in table 72.

Table 72. Step wise logistic regression model (with cutoff p value >0.20) for TB in women in Nepal with all significant covariates (from table 1) in the model

Variables	OR	95% CI	P values
Kerosene fuel stove	3.05	1.11-8.40	0.031
Biomass, coal or kerosene heating fuel	4.07	1.85-8.99	0.001
Buddhists religion	27.64	9.54-80.09	0.000
Christian & Muslims religions	4.87	1.05-22.06	0.043
Residence other than Kaski district	15.34	4.34-54.18	0.000
Residence locality-rural	0.37	0.12-1.14	0.082
Always living in the present house- (reference: no)	2.72	1.30-5.70	0.008
Kerosene lamp as the main lighting source in the house	8.15	1.38-48.05	0.020
>8 pack years of smoking	4.02	1.19-13.61	0.025
Family history of TB – (reference-no)	8.58	4.00-18.39	0.000
Taking vitamin supplements'- (reference : no)	0.10	0.02-0.58	0.010
Income NRs <25,000 - <=50,000	2.43	1.19-4.95	0.015
Income NRs >100,000	2.75	0.88-8.60	0.081

3 Biomass and kerosene fuel-stove, gas-fuel stove, biomass heating fuel, ventilation, use of kerosene lamp, pack-years of smoking, number of family members smoking indoors, religion, residence district, locality, literacy, present house construction, always lived in the present house, alcohol consumption, family members had TB in the past, taking vitamin supplement, income and age.

6.2 Logistic regression analysis

An unconditional logistic regression model was constructed to evaluate simultaneously the effect of environmental and socio-economic covariates on the risk of TB adjusting potential confounders. In the main logistic regression model, the risk of TB was analyzed by three exposure categories; use of 'gas-fuel stove' (reference category), 'kerosene-fuel stove' and 'solid-fuel unimproved stove or biomass stove' and other predictors as described above. Compared with using a gas-fuel stove (liquefied petroleum gas, biogas), the adjusted odds ratio (OR) for using a biomass-fuel stove was 1.21 [95% confidence interval (CI) 0.48-3.05], whereas use of a kerosene-fuel stove had an OR of 3.36 (95% CI 1.01-11.22). Also particularly strongly associated with TB in the model were use of biomass as a heating fuel (OR 3.45, 95% CI 1.44-8.27), Buddhist religion (OR 31.47, 95% CI 10.3-96.4), kerosene lamps as the main source of lighting in the house (OR 9.43, 95% CI 1.45-61.3), >8 pack-years of tobacco smoking (OR 3.70, 95% CI 0.95-14.4), two or more family members in the house who smoke (OR 2.81 95% CI 0.83-9.52), presently taking vitamin supplements (OR 0.12, 95% CI 0.02-0.67), history of TB in family members (OR 8.66, 95% CI 3.89-19.27), residence district other than Kaski (OR 16.04, 95% CI 4.34-59.4), and not always having lived in the present house (OR 3.21, 95% CI 1.45-7.12). Table 73 summarizes the logistic regression parameters of model 1. The estimated Population Attributable Fractions for exposure to BFS, KFS, biomass as heating fuel, and kerosene lamps in our target population were 9% (95% CI -42% to 41%), 12% (0.1%-22%), 47% (22%-64%) and 12% (0.1%-22%), respectively.

Table 73. Multivariate logistic regression model for TB in women in Pokhara, Nepal[e]
Log likelihood = -118.73, R^2 = 0.44

Variable	Multivariate OR (95% CI)	Univariate OR (95% CI)
Fuel-stove		
Gas	1.00	1.00
Biomass	1.21 (0.48-3.05)	1.98 (1.24-5.12)
Kerosene	3.36 (1.01-11.22)	2.54 (1.26-5.12)
Heating fuel		
No heating fuel use or electricity	1.00	1.00
Biomass, coal or kerosene	3.45 (1.44-8.27)	2.81 (1.78-4.42)
Religion		
Hindu	1.00	1.00
Christian and Muslim	5.95 (1.20-29.59)	2.65 (0.75-9.38)
Buddhist	31.47 (10.28-96.4)	9.13 (4.18-19.9)
Income in Nepalese Rupees (NRs)		
<=25,000	1.00	1.00
>25,000 - <=50,000	3.96 (1.61-9.75)	1.78 (1.02-3.13)
>50,000 - <=100,000	2.89 (0.86-9.69)	0.87 (0.42-1.79)
>100,000	5.89 (1.47-23.58)	0.99 (0.41-2.42)
Residence locality		
Urban	1.00	1.00
Rural	0.36 (0.11-1.16)	2.44 (1.46-4.08)
Residence district		
Kaski	1.00	1.00
Other than Kaski[f]	16.04 (4.34-59.4)	6.56 (3.37-12.8)
Level of literacy		
Literate	1.00	1.00
Illiterate	1.62 (0.65-4.07)	1.68 (1.09-2.60)
Present house construction		
Pucca or semi-pucca	1.00	1.00
Kucha	1.46 (0.66-3.19)	1.93 (1.25-3.00)

[e] Adjusted for age; [f] Tanahu, Syangja, Baglung, Parbat, Myagdi, and Lamjung districts.

Table 73 contd. Multivariate logistic regression model for TB in women in Pokhara, Nepal[e]

Variable	Multivariate OR (95% CI)	Univariate OR (95% CI)
Main light source in the house		
Electricity	1.00	1.00
Kerosene lamp	9.43 (1.45-61.32)	10.35 (3.42-31.3)
Always lived in the present house		
Yes	1.00	1.00
No	3.21 (1.45-7.12)	1.83 (1.16-2.88)
Pack years of smoking		
0 pack-years	1.00	1.00
<=8 pack-yeas	1.29 (0.40-4.21)	1.23 (0.64-2.37)
>8 pack-years	3.70 (0.95-14.36)	3.13 (1.64-5.99)
Number of family members smoking tobacco indoor		
None	1.00	1.00
One	1.48 (0.71-3.10)	1.90 (1.18-3.04)
Two or more	2.81 (0.83-9.52)	4.16 (1.93-8.95)
Alcohol consumption		
Never	1.00	1.00
Ever	0.79 (0.21-3.04)	3.67 (1.68-8.05)
Taking vitamin supplements		
No	1.00	1.00
Yes	0.12 (0.02-0.67)	0.15 (0.05-0.51)
Family history of TB		
No	1.00	1.00
Yes	8.66 (3.89-19.27)	6.15 (3.51-10.8)
Ventilation in the kitchen		
Well ventilated	1.00	1.00
Unventilated	1.05 (0.49-2.25)	2.02 (1.31-3.13)

7.0 Discussion

Approximately 90% of the rural households in the poorest developing countries rely on unprocessed biomass-based solid fuels for cooking and sometimes heating. The majority of households seem to burn solid fuels in un-vented stoves, which emit harmful pollutants. In developing countries, women invariably do most of the cooking and hence have more exposure to smoke. Cigarette smoke and bio-fuel smoke have many similarities. Studies conducted in both developed and developing countries have established an association between cigarette smoking and TB in men and women. Studies have shown that tobacco smoke consumption not only increases the risk of pulmonary TB but it also leads to an extra pulmonary TB. Global burden of TB shows that it is the second leading cause of death world wide, killing about 1.8 million people each year (Frothingham et al. 2005). Despite efforts in the last 20-30 years, the TB situation in many developing countries remains serious, and TB control achievements of the last 2–3 decades are disappointing. In addition to higher prevalence of TB, there has been a coincident rise in the case of multi drug-resistant TB, and the HIV epidemic has made situation more complicated. In 1991, the WHO set up the objectives of treating successfully 85 percent of the TB cases and of detecting at least 70 percent of the smear positive TB cases by introducing the Directly Observed Treatment Short-course Strategy (DOTS). However, DOTS implementation has been slower than anticipated. For example; in 1995, the DOTS strategy was estimated to be accessible to only 23 percent of the world population (Raviglione et al. 1997). Although case findings (TB) still remain largely passive in many developing countries(Raviglione et al. 1997)[4], a global public health effort to fight TB is largely focused on treatment without matching efforts on the prevention side. The continuous rise in TB incidence in developing countries raises the question of whether delivery of treatment programs is sufficient to control this global disease.

The public health history of developed countries suggests that part of the decline of TB was achieved by improving housing and habitat, better nutrition, decreasing crowding, and introducing better hygiene and sanitation (Bloom and Murray 1992, Rieder et al. 1989). While we continue to

[4] The worldwide case-detection rate of new sputum-smear positive cases was 35% in 1995

apply new drug combinations and improved treatment programs in developing countries, therefore, it would seem prudent also to more thoroughly explore the roles of environment and socio-economic factors. In particular, epidemiological methods could help to quantify risk factors for infection/disease that might be addressed to reduce the risk of disease at the individual, family and community levels. Based on recently published exploratory studies in India and Mexico, this study was conducted to investigate in more depth whether household indoor smoke from burning biomass cooking fuels is a significant risk factor for TB in women in Nepal. This study was a part of multi center case-control studies on exposure to biomass smoke and risk of TB in women. Three other study centers were in India (Lucknow, Chandigarh and Chennai). This was a hospital-based case-control study, where participants were all women between 20 and 65 years. The hypothesis of this study was that smoke from solid fuel used in indoor stoves without flues or biomass stove increases the risk of TB in women.

The results of this study suggest that the risk of TB is increased by indoor exposure to smoke from biomass fuel combustion. The risk, however, appears to be mainly associated with use of biomass for heating, rather than cooking. The study also strongly suggests that the risk of TB is increased by exposure to smoke from kerosene fuel combustion, either in stoves or lamps.

In the multivariate model (Table 73), religion, income, residence outside Kaski district, vitamin consumption, a family history of TB, two or more family members in the house who smoke and not always living in the present house also showed statistically significant associations with TB. We suspect that the protective association with vitamin supplement use may be a consequence of TB diagnosis, rather than a truly protective factor. ETS exposure (one or two family members smoking indoors) has been found to be causally associated with respiratory illnesses, including TB. Epidemiological studies have shown close and very close exposure to passive smoking strongly associated with TB in young children and adults (Tipayamongkholgul et al. 2005) Altet et al. 1996) (Singh et al. 2005)**.**

Pack-years of smoking (>8 pack-years) showed a marginally statistically significant association with TB ($p = 0.06$). Smoking is now an established risk factor for TB (Slam et al. 2007; Chiang et al. 2007; Leung et al. 2004; Bates et al. 2007; Yu et al. 1988). The very elevated relative risk estimate for Buddhists relative to Hindus is striking. We considered that this may have been because some Buddhists living around Pokhara are Tibetan and live in refugee camps. Crowded conditions in those camps could facilitate TB transmission, but only 8 of 40 Buddhists in the study (6 cases, 2 controls) were Tibetan refugees-- insufficient to explain the finding. Other studies have also shown differences in TB rates between racial and religious groups, including Tibetan Buddhists (Hill et al. 2006; Mishra et al. 1999; Bhatia et al. 2002; Nelson et al. 2005; Truong et al. 1997).

Before concluding that statistical associations are causal, it is important to consider alternative explanations, particularly whether study results might be a result of selection bias, information bias, or confounding in the study design, data collection or analysis. As with all case-control studies, selection bias in recruitment of controls is a potential concern. In this study, a systematic procedure for recruitment of all controls from inpatient and outpatient departments of MTH was used, and only one potential control refused to participate. Since the majority of cases were recruited from the RTC, and all controls from MTH, the catchment areas for MTH and RTC might have been different. RTC patients came from a broader area, since it is a referral centre for the western development region of Nepal. A higher proportion of cases (28%) than controls (6%) were from five districts other than Kaski. Kaski district includes Pokhara city and, in general, Kaski residents are more likely to live in urban areas and be wealthier. This suggests the possibility of some selection bias. We adjusted for area of residence (Kaski or other districts) in the final model, but this would not necessarily have eliminated such a bias.

Information bias may take the form of outcome misclassification or exposure misclassification. Since all cases were newly diagnosed with active pulmonary TB on the basis of evidence from clinical tests, and controls were also confirmed by chest x-ray and on-the-spot sputum smear testing as not having active pulmonary TB, we consider that disease misclassification is unlikely to have occurred. All the exposure data were obtained by questionnaire. Case-control studies are often considered susceptible to recall bias, in that cases may be more likely than controls to remember past exposures. Since questions asked in this study were about common exposures, however, which both cases and controls experience on a day-to-day basis, we expect recall to have been accurate and any differential recall to have been minimal. The high level of accuracy of reporting of two key exposure variables (stove type and ventilation) was verified by visiting the homes of 28 study participants. Considering this and that there is no prevailing belief that indoor smoke exposure from biomass-burning stoves or kerosene-burning stoves or lamps is related to TB occurrence, we believe exposure misclassification is likely to be minimal. One possible limitation, however, is that we only asked about the main cooking fuel used. This might have led to some misclassification of exposure status.

The third main area of potential bias is confounding. We collected data on a much more comprehensive range of exposures than did previous studies, and investigated their potential to confound the associations with fuel use. Although confounding was present, adjustment with these variables did not eliminate the key associations. There may, of course, be some residual confounding due to mis-specification of the variables, and there is no way to rule out the possibility of unknown confounding factors causing the associations found. To cause the associations, particularly the strong associations with TB of both kerosene lamp use and biomass fuel for heating, however, the unknown confounding factors would have to be even more strongly associated with both TB and with kerosene use, which seems unlikely.

A notable finding in our study was the association with biomass used as a heating fuel. This was unexpected, as the study design had been based on the assumption that it was cooking fuel use that was the likely risk factor. Hence, the study population was limited to women, who generally do the cooking in Nepal. The *a priori* focus on cooking fuel also directed our questionnaire design. Although we collected data on history of stove and cooking fuel use, we did not collect a comparable level of data for heating fuels and so are unable to examine heating fuel use for evidence of an exposure-response relationship.

With hindsight, the findings with biomass as a heating and a cooking fuel make sense. Women may light a cooking fire, set the pot atop it, and leave the room, returning only periodically while cooking takes place. On the other hand, use of heating fuel involves minimization of ventilation and deliberate exposure, as the family sits around the fire. As described earlier, there have been mixed results in other studies of indoor biomass fuel. This may be because there has been something of a focus on use as a cooking fuel, rather than a heating fuel. In fact, in India, Africa and Mexico, where the other studies have been carried out, biomass use as a heating fuel may be rare as the ambient temperatures are generally quite high. The area around Pokhara, however, has a more moderate climate and temperatures can get quite low at times. For example, the average low temperature for January is 4^{o}C (39^{o}F) (http://en.wikipedia.org/wiki/Pokhara), necessitating the use of indoor heating.

Our study also found the OR for TB to be high among both kerosene stove and lamp users, particularly the latter. Kerosene cooking fuel and kerosene lamp users were for the most part mutually exclusive groups. Only one of the 22 kerosene lamp users in the study used a kerosene stove. Kerosene stove users were more likely to use electricity for lighting. With one exception, as far as we are aware, no previous studies have examined a relationship between kerosene and TB (Padilla et al. 2001). This one study, carried out in Mexico, obtained crude ORs for use of kerosene-burning stoves of 1.9 (95% CI 0.8-4.5) for active TB, and 4.4 (95% CI 1.7-11.5) for past TB. No adjusted estimates were presented. We have been unable to find any studies where the relationship between kerosene lighting and TB has been investigated or even incidentally reported.

The question arises why kerosene as a cooking fuel could be a TB risk factor, but not biomass cooking fuel. This could have something to do with the nature of the emissions. Biomass burning produces very obvious smoke, which may irritate the eyes and respiratory tract, encouraging avoidance behavior. Kerosene, on the other hand, has the appearance of burning more cleanly, even if it does produce substantial amounts of fine particulate matter and vapor-phase chemicals, and may not encourage the same avoidance behavior as biomass smoke. Cooks may be more likely to remain in the room while cooking with kerosene fuel. There may also be differences in the toxic effects of the pollutant mixtures from the two fuels.

Kerosene is one of the main sources of cooking fuel in urban areas and lighting fuel in rural areas of developing countries, including Nepal. Therefore, if kerosene burning can be confirmed as a TB risk factor in other studies, the public health implications would be substantial. In rural areas not connected with electric power, kerosene wick lamps are burned at least four to five hours every day. Commonly, these lamps are homemade devices that are highly energy inefficient, with low luminosity. Kerosene lamps emit substantial amounts of smoke and particles (Smith and Staurt 1995). A study conducted in rural Malawi has shown a higher loading of particulates in alveolar macrophages in men from exposure to kerosene in lamps compared with candles, hurricane lamps and electric lamps (Fullerton et al. 2009). Other emissions from kerosene combustion include carbon monoxide, carbon dioxide, sulphur dioxide, nitrogen dioxide, formaldehyde and various VOCs (volatile organic carbons) (Traynor et al. 1983). An indoor air pollution study conducted in Bangladesh slums has shown significantly higher concentrations of benzene, toluene, xylene, hexane and total VOCs emitted from kerosene stoves than from wood-burning stoves (Khalequzzaman et al. 2007).

That kerosene fuel usage is associated with harmful effects has been documented by a few studies. These effects include impairment of ventilatory function and a rise in blood carboxyhaemoglobin in women exposed to kerosene fuel smoke (Behera et al. 1991), and a higher incidence of acute lower respiratory infection in children in homes using kerosene-and biomass fuel stoves (Sharma et al. 1998).

A causal relationship between exposure to biomass fuel smoke and TB is biologically plausible. The smoke could affect either risk of infection or risk of disease in infected people, or both, as has been show to be the case with tobacco smoking (Bates et al. 2007). Without knowledge of the time of infection, however, the present study has no way to distinguish between the two possibilities. Inhalation of respirable particles and chemicals found in smoke from these sources generates an inflammatory response and impairs the normal clearance of secretions on the tracheobronchial mucosal surface and may allow TB bacteria to escape the first level of host defenses, which prevent bacilli from reaching the alveoli (Houtmeyers et al. 1999). Smoke also impairs the function of pulmonary alveolar macrophages, an important early defense mechanism against bacteria (HEI 2002). Alveolar macrophages isolated from the lungs of smokers have reduced phagocytic ability compared to macrophages from non-smokers, and secrete a lower level of proinflammatory cytokines (Sopori 2002). Exposure to wood smoke in rabbits has been shown to negatively affect antibacterial properties of alveolar macrophages, such as their ability to phagocytize bacteria (Fick et al. 1984).

In conclusion, our study provides evidence that the use of biomass fuel for household heating is associated with an increased risk of TB, but adds little evidence that the use of biomass as a cooking fuel is a risk factor in this population. Bias, including potential confounding, does not obviously explain this association, which is biologically plausible and consistent with the results of some other epidemiological studies. Nonetheless, there is some possibility of a selection bias arising from differences in the sources of cases and controls. The study also strongly suggests that kerosene fuel burning, particularly for lighting, is a risk factor for TB. That kerosene lamp burning was more strongly associated with TB than kerosene stove use may be because lamps are likely to be kept burning for longer periods than stoves, which are used only during the period of cooking, and the lamps may be kept closer to people during the evening--increasing the effective intake fraction. Since these kerosene findings are apparently unique, more studies in different settings are needed to confirm them. Should the association with kerosene lamp use be confirmed, replacement of the kerosene lamps with solar lamps or other clean lighting systems would be a solution.

Irrespective of the evidence for associations between indoor biomass use and TB, it is clear that such use produces substantial indoor air pollution with health-damaging chemicals and particulate matter. One, at least partially effective, remedial measure is to replace unflued stoves with chimney stoves. Such stoves, however, require continuing maintenance to maintain good indoor air quality and because they usually just exhaust emission to the near outdoors but not reduce them, even well-operating chimney stoves can only partly reduce total exposures (Smith et al. 2009; McCracken et al. 2009). Ideally, electric stoves or low-emissions biomass stoves, such as semi-gasifier stoves, or those with cleaner burning fuels (biogas or LPG) would be used. It is more difficult to generalize about kerosene stoves and lamps, as emissions vary greatly by type of device and fuel quality, which is not uniform (Smith 1987). Pressurized kerosene stoves and lamps using good-quality fuel may have low particulate emissions if properly maintained, but inexpensive wick-lamps can be dirty, particularly with low-quality fuel. Their replacement with cleaner burning devices may also be justified.

8.0 Conclusion

It is estimated that about half the world's households sometimes heat and regularly cook with biomass fuel, most using unvented stoves, with women, infants and young children experiencing the highest levels of exposure. In several poor and developing countries women commonly suffer social and economic vulnerability, which contributes to inequalities in health and access to health care. Data suggest that there is a gender differences in access to diagnosis and treatment of TB in Nepal. TB is a multifactorial disorder in which environment interacts with host characteristics. Many factors play a role in individual susceptibility to *Mycobacterium tuberculosis* and understanding the individual balance between degree of exposure to the organism, inherited genetic susceptibility to infection, and the role of environmental and behavioral factors in development of tuberculosis disease, would help develop new avenues by which TB could be controlled. TB remains a major public health problem in Nepal today (Paugam and Paugam 1996; Hurtig et al. 2000). The prevalence of tuberculosis infection in Nepal is as high has 45%. More than 48,000 new active cases occur each year, with 11,000 deaths (Editorial 1999). Since Nepal, has quite rugged topography, the Nepal Tuberculosis Center (NTC) has been able to cover only 30% of all TB patients through its 70 under-equipped treatment centers (Editorial 1999). Thus, identification of preventive programs could help control the TB burden in Nepal from further spread. In addition, biomass supplies the bulk of household cooking and space heating needs in Nepal, with some 90% of rural households and approximately 70% of urban household depending on it. In conclusion, this study provides three major findings/evidences:

1. Use of solid fuels for heating indoors increases the risk of TB in women compared with electricity or use of no heating fuel.
2. Use of kerosene stoves increases the risk of TB compared with the use of gas fuel stove.
3. Use of kerosene lamps increases the risk of TB compared with the use of electricity as the main light source in the house.

4. Active tobacco smoking increases the risk of TB.

Bias including potential confounding, is not likely to explain these associations found in this study, which are biologically plausible and consistent with the results of other epidemiological studies. The most effective remedial measure would be to replace unflued stoves with flued stoves, which vent cooking smoke directly to the exterior of the house. Ideally, stoves with cleaner burning fuels, such as gas (Bio gas, LPG) would be used if possible instead of un-flued biomass and kerosene stoves. Since this study provides evidence for the first time that the risk of TB increases with the use of kerosene fuel-stove and kerosene lamps, more study is needed to confirm or refute these findings. As kerosene is one of the main sources of cooking fuel in urban areas and lighting fuel in the rural areas, to minimize the smoke from kerosene combustion, promotion of solar lamps (*Tuki*) or lanterns will be ideal. As this study confirms the risk of from active tobacco smoking, massive tobacco cessation campaign will be needed to reduce the burden of TB from Nepal in men in general and women in particular.

9.0 End Note

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