Tropical Medicine and International Health doi:10.1111/tmi.12013

VOLUME 18 NO 1 PP 101–108 JANUARY 2013

Systematic Review

Systematic review and meta-analysis of the associations between indoor air pollution and tuberculosis

Colin Sumpter and Daniel Chandramohan

London School of Hygiene and Tropical Medicine, London, UK

Abstract OBJECTIVE Half the world's population uses biomass fuel for their daily needs but the resultant emissions and indoor air pollution (IAP) are harmful to health. So far, evidence for a link between IAP and tuberculosis (TB) was insufficient. We report an updated systematic review due to recent increase in the evidence and growing interest in testing interventions.

METHODS Systematic search of PubMed (including Medline), CAB abstracts (through Ovid SP) and Web of Knowledge using the following search terms: 'IAP or biomass or cooking smoke' and 'TB'. 452 abstracts were reviewed, and only 12 articles were deemed to be reporting the effects of IAP on TB and were taken forward to full review, and one study was added through hand search of references. Data on measures of effect of IAP on TB were extracted, and meta-analysis was carried out to estimate pooled measures of effect.

RESULTS Thirteen studies have reported investigating association between IAP and TB since 1996. TB cases are more likely to be exposed to IAP than healthy controls (pooled OR 1.30; 95% CI, 1.04–1.62; $P = 0.02$).

CONCLUSIONS There is increasingly strong evidence for an association between IAP and TB. Further studies are needed to understand the burden of TB attributable to IAP. Interventions such as clean cook stoves to reduce the adverse effects of IAP merit rigorous evaluation, particularly in Africa and India where the prevalence of IAP and TB is high.

keywords air pollution, indoor, tuberculosis

Introduction

Half the world's population, primarily living in low income countries, relies on biomass fuel for heating and cooking. Around 3.4 billion people are burning biomass on open fires for daily cooking. It is also estimated that 1.5 m premature deaths primarily among women and children, and 40.8 million disability adjusted life years (DALYs) are lost each year due to exposure to indoor air pollution (IAP). These estimates are based on IAP effects on pneumonia and other acute lower respiratory infections (ALRI) among children under 5 years of age and chronic obstructive pulmonary disease (COPD) and lung cancer (related to coal use) among adults (WHO 2007). Tuberculosis (TB) is not included in this regularly quoted burden of IAP due to a lack of epidemiological evidence at the time of calculation (Desai *et al.* 2004).

Previous systematic reviews have shown no effect of IAP on TB and have highlighted the limited quality of the available evidence (Lin *et al.* 2007; Slama *et al.* 2010). A review of studies up to 2008, which comprised three case–control and three cross-sectional studies, found no association between IAP and TB (Slama *et al.* 2010). Since 2008, another eight studies of the effects IAP on TB have been published, and thus, it is timely to reconsider the evidence.

Methods

Following the guiding principles laid out in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) document, a systematic search for original research of the effects of IAP on TB was conducted. Studies were considered eligible where they were published in a peer reviewed journal, and written or translated into English. Both observational and experimental studies were eligible as long as they included a TB outcome and provided a measure of effect of IAP.

Reports of previous systematic reviews, policy papers, abstracts to conferences, letters to journals and economic evaluations were excluded.

Two key search concepts were used ('IAP from biomass' and 'TB') along with associated synonyms to account for differences in terminology. Synonyms used for IAP were *biomass* and *cooking smoke*; for tuberculosis, *TB*. These search terms are consistent with previous review approaches (Desai *et al.* 2004; Slama *et al.* 2010). The search was conducted in April 2012 in three online databases: PubMed (including Medline), CAB abstracts (through Ovid SP) and Web of Knowledge. Each previously published systematic review and original study was hand-searched for additional references.

All articles identified were entered into EndNote X3 referencing software (Thompson-Reuters 2009), and duplicates were removed. A title and abstract review was conducted to screen out ineligible articles. Articles which apparently fulfilled the criteria were reviewed in full. After this detailed review a number of papers were excluded. Figure 1 shows the PRISMA chart for this process.

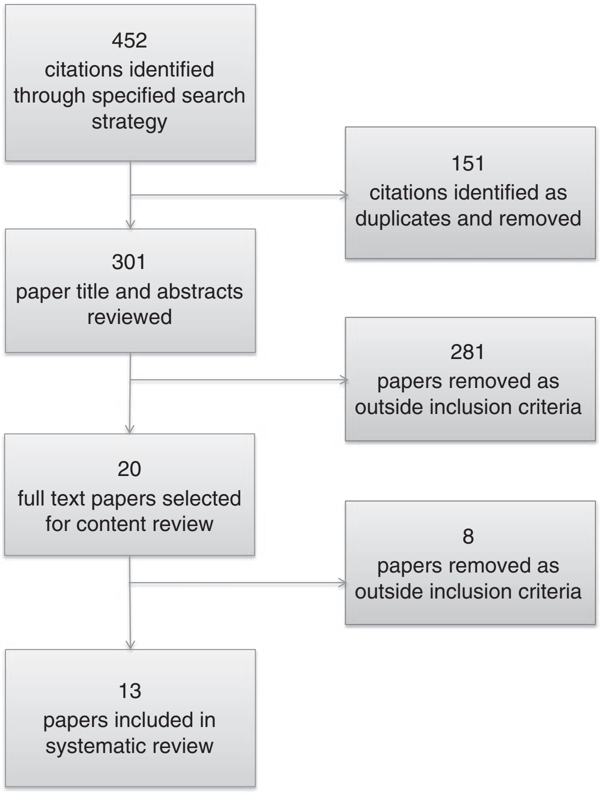

Figure 1 Flow diagram of inclusion/exclusion.

Studies were reviewed for potential bias, methodological rigour and overall quality of the approach. Relevant data were extracted, odds ratios of IAP among TB cases compared with non-TB controls were plotted using forest plots and pooled odds ratio (OR) was calculated. This was repeated for three subgroups of studies – case–control studies only, case–control studies focusing solely on women and cross-sectional studies.

Results

Initially, 452 articles were identified (Figure 1) from Web of Knowledge (188) PubMed (158) and CAB Abstracts (106). After removal of duplicates (151), review of title and abstracts resulted in the exclusion of 281 papers. Reasons for exclusion were a focus on: agriculture or ecology identified through the essential search term 'biomass' (122); microbiology (33); outcomes other than TB (26); efficacy of interventions at reducing exposure rather than health outcomes (12); previous reviews related to IAP (19); policy or economics (19); and mathematical modelling (6). After reviewing full manuscripts, eight were excluded because the data reported were inadequate to calculate a measure of effect of IAP on TB.

Hand search of the bibliographies of reviewed papers identified one further article; thus, a total of 13 articles were included in the systematic review.

We identified 11 case–control studies and two cross-sectional studies investigating the link between TB and IAP. Following a more detailed review, one paper described as a case–control was reclassified as cross-sectional as the reported OR for TB was based on comparison of exposure within a TB-positive control group rather than any comparison between cases and controls. Key study features are summarised in Table 1 for the 10 case–control studies and in Table 2 for three cross-sectional studies. The data presented in these studies were deemed to be of high enough quality to be included in meta-analysis.

The adjusted OR of exposure to IAP among TB cases varied between the studies (Figure 2). Four studies showed that odds of exposure to IAP were slightly lower among TB cases, but none of these observations were statistically significant (Crampin *et al.* 2004; Shetty *et al.* 2006; Behera & Aggarwal 2010; Kan *et al.* 2011). Six studies showed higher exposure to IAP among TB cases, but only three studies showed a statistically significant association (Perez-Padilla *et al.* 2001; Garcia-Sancho *et al.* 2009; Lakshmi *et al.* 2012). The overall fixed effect OR for exposure to biomass amongst those with TB compared with those without TB is 1.30 (95% CI: 1.04–1.62, $P = 0.019$).

Table 1 Case–control studies: characteristics and reported estimates of association between IAP and TB

Study country (period)	Study population	Method of ascertainment of TB	Method of selection of controls	Method of ascertainment of exposure to IAP	Sample size (case:control)	Analytical method	Odds ratio (95% CI)
Urban/rural India (April 2006–March 2007) (Pokhrel *et al.* 2010)	>20-year-old female only	Sputum smear positive for AFB	Clinic recruited non-TB. Matched on age and area of residence	Self-reported biomass fuel use	378 (126:252)	Multivariate logistic regression adjusted for education, kitchen, tobacco smoking and TB in family	3.14 (1.15–8.56)
Urban/rural Nepal (July 2005–April 2007) (Kolappan & Subramani 2009)	>20-year-old female only	Sputum smear positive for AFB	Clinic recruited non-TB. Matched on age and area of residence	Self-reported biomass fuel use Validated by home visit	375 (125:250)	Multivariate logistic regression adjusted for age, religion, income, residence, literacy, house-type, tobacco smoking, family tobacco smoking, alcohol, vitamin supplements, TB family history and ventilation	1.21 (0.48–3.05)
Urban/rural China (September 2008–unknown date) (Lakshmi *et al.* 2012)	>15-year-old 73% men/27% female	Sputum smear positive for AFB	Community recruited non-TB. Matched on age, sex, area	Self-reported biomass fuel use	606 (202:404)	Unadjusted for confounders No adjusted result quoted but stated to be ‘non-significant’	0.75 (0.44–1.27)
Urban Mexico (March 1995–April 2003) (Perez-Padilla *et al.* 1996)	>15-year-old female only	Sputum smear positive for AFB. Community case finding	Community recruited non-TB. Matched on sex, neighbourhood	Self-reported fuel use and length of exposure. Current stove use confirmedby home visit	126 (42:84)	Multivariate analysis adjusted for age, BMI, over-crowding, education and tobacco smoking	3.3 (1.06–10.30)
Urban/rural India (July 2007–March 2008) (Perez-Padilla *et al.* 2001)	>24-year-old female only	Sputum smear positive for AFB	Clinic recruited non-smoking non-TB Unmatched	Self-reported biomass fuel use	204 (94:109)	Multivariate logistic regression adjusted for place of residence, passive smoking, overcrowding, use of separate kitchen and ventilation	0.6 (0.2–1.6)

Table 1 (*Continued*)

Study country (period)	Study population	Method of ascertainment of TB	Method of selection of controls	Method of ascertainment of exposure to IAP	Sample size (case:control)	Analytical method	Odds ratio (95% CI)
Urban India (October 2001–October 2003) (Kan *et al.* 2011)	>15-year-old 58% men/42% female	Sputum smear positive for AFB (82%) and CXR confirmed (18%)	Clinic recruited non-TB. Matched on age and sex	Self-reported biomass fuel use	378(189:189)	Multivariate logistic regression adjusted for education, marital status, religion, household income, overcrowding, separate kitchen, alcohol consumption, smoking and chronic disease	0.9(0.2–1.6)
Urban/rural India (2001–2003) (WHO 2011)	>15-year-old 87% men/13% female	Sputum smear positive for AFB. Community case finding	Community recruited non-TB. Matched on age and sex	Self-reported biomass fuel use	1530 (255:1275)	Adjusted for smoking, alcohol consumption, and socio-economic status	1.7 (1.0–2.9)
Urban Benin (2008) (Gupta *et al.* 1997)	>22-year-old 65% men/35% female	Sputum smear positive for AFB Community case finding	Community recruited non-TB. Matched on age and sex	Self-reported biomass fuel use	600 (200:400)	Multivariate logistic regression adjusted for smoking, sex, alcohol use, family history of TB	1.5 (0.9–2.3)
Urban Mexico (January 1998–April1999) (Garcia-Sancho *et al.* 2009)	>15-year-old female only	Sputum smear positive for AFB	Clinic recruited non-TB. Unmatched	Self-reported current use of a woodstove for cooking	833 (288:545)	Multivariate logistic regression adjusted for age, sex, urban or rural residence, crowding, education, smoking, income	2.2 (1.1–4.2)
Rural Malawi (November 1996–September 2001) (Behera & Aggarwal 2010)	>15-year-old female only	Sputum smear positive for AFB	Community recruited non-TB. Unmatched	Self-reported biomass exposure stratified on placement of fire in wet and dry season	768 (211:557)	Only females included in analysis for cooking smoke exposure Multivariate logistic regression adjusted for age, sex, area and HIV	0.7 (0.3–1.3)

IAP, indoor air pollution; TB, tuberculosis.

Table 2 Cross-sectional studies: characteristics and reported estimates of association between IAP and TB

Study country (period)	Study population	Method of ascertainment of TB	Method of ascertainment of exposure to IAP	Sample size	Analytical method	Odds ratio (95% CI)
Urban Mexico (1996) (Gninafon *et al.* 2011)	>40-years-old female only	Sputum smear positive for AFB	Self-reported biomass exposure stratified on hours exposed (3 levels)	83	Analysis looked at odds of exposure to IAP amongst controls selected as having TB (n = 83) only. Age-adjusted only	2.27 (1.22–4.22)
Rural/urban India (1997) (Gupta *et al.* 1997)	>15-years-old man and female	Sputum smear positive for AFB and CXR confirmed	Self-reported use of wood or cow dung as fuel in the home	707	Multiple logistic regression Age-adjusted only	2.54 (0.5–3.3)
Rural/urban India (1993) (Mishra *et al.* 1999)	>20-years-old man and female	Self-reported active tuberculosis, no confirmation	Use of unprocessed biomass fuel as the primary fuel for cooking in household	260, 162	Multiple logistic regression Adjusted for kitchen type, house type, crowding, age, gender, urban/rural, education, religion, caste and region	2.58 (1.98–3.37)

IAP, indoor air pollution; TB, tuberculosis.

The odds of exposure to IAP among female TB cases were higher (pooled OR 1.7; 95% CI 1.00–2.89) when the studies including men were excluded from the analysis (Figure 3). The pooled estimate from the two cross-sectional studies showed a stronger association between the IAP and TB (pooled OR 2.53; 95% CI 1.99–3.22; $P < 0.001$) though the observation from one study was not statistically significant (Figure 4).

Discussion

The pooled OR from the cross-sectional studies showed a strong effect of IAP. However, adjustment for confounding was limited to age in only two of the three studies, and thus, these observations should be interpreted with caution. At best these cross-sectional studies show that the association is a possibility; this is reflected in the recent shift towards case–control studies.

The quality of case–control studies included in this review was debatable. The ascertainment of the outcome TB was robust as it was sputum-positive TB confirmed by health professionals. However, the ascertainment of exposure to IAP was open to recall bias and misclassification. Two studies verified exposure by home visit (Garcia-Sancho *et al.* 2009; Pokhrel *et al.* 2010) but none measured exposure objectively. It is possible that respondents misclassified themselves or recalled wrongly. Many families use multiple energy sources in their homes, which limits binary classification. Only one study used any gradation (ordered categorical) measure of exposure (Crampin *et al.* 2004), and one study presented a more complex composite measure made up of ventilation, kitchen type, mixed-fuel use and length of exposure, although ultimately this was not used for analysis in this review to ensure consistency with other studies (Behera & Aggarwal 2010). This is a major limitation of the studies included in this meta-analysis. Ideally, the level of IAP needs to be measured using particulate matter readings in dwellings or stove monitors, a costly but possible measure of exposure, after case identification.

All studies made some attempt to adjust for potential confounders. In particular smoking, socioeconomic status and over-crowding are associated with both biomass use and TB. It is possible that these co-linear effects can never be truly removed from observational studies by statistical analysis. Two studies failed to adjust for tobacco smoking but one cited low or zero prevalence of smoking as the rationale for this (Perez-Padilla *et al.* 1996).

Five of the 10 case–control studies employed hospital based controls. This may have led to some selection bias by over-sampling those who seek health service, and it can be seen from sample breakdowns that groups in these

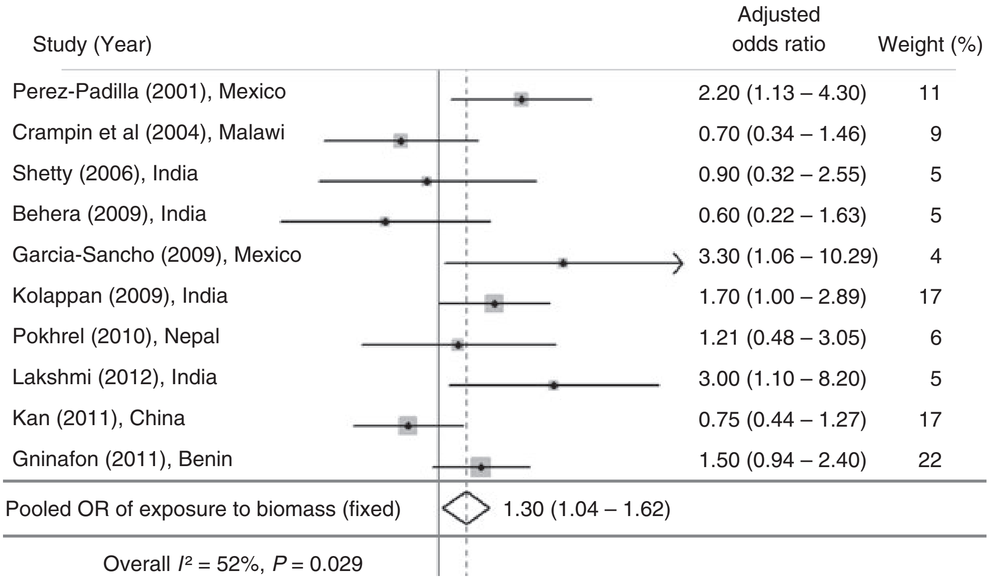

Figure 2 Forest plot of ORs of exposure to biomass among tuberculosis (TB) case *vs*. non-TB controls.

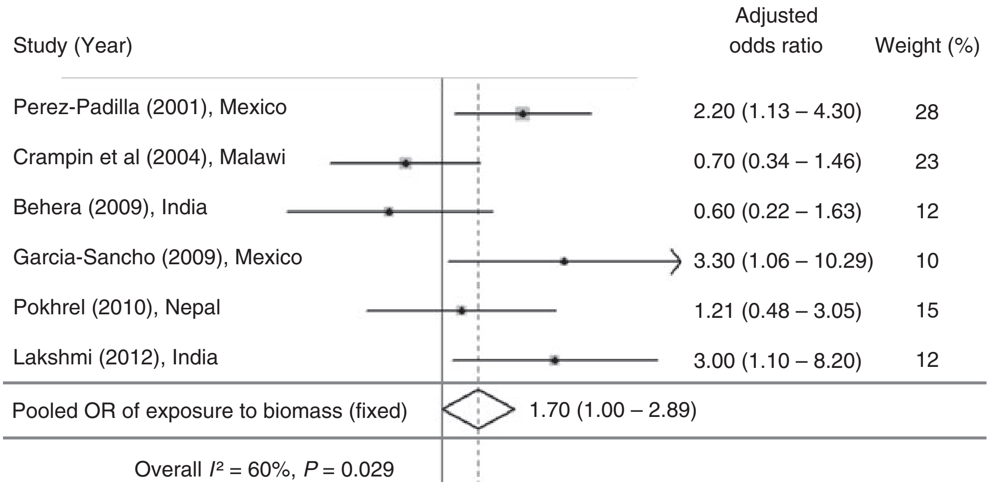

Figure 3 Forest plot of ORs of exposure to biomass among female tuberculosis (TB) case *vs*. non-TB controls.

studies differ, sometimes significantly. The challenge of selecting controls is particularly pronounced, as biomass appears to be pervasive in some areas, and the minority who use cleaner fuels do so apparently because they enjoy a higher socio-economic status. This may lead to overestimates of the effects observed. With three notable exceptions (Garcia-Sancho *et al.* 2009; Kolappan & Subramani 2009; Gninafon *et al.* 2011) studies also used hospital based cases (7/10 studies), which may have led to some selection bias and an underestimate of the effect of the exposure by failing to recruit those at greatest risk of exposure to IAP, people who do not seek treatment for health conditions due to lower socio-economic status.

The study populations are primarily adult women aged >15. However, the four studies that included both men and women tended to have an over representation of men in their sample. These studies are likely to have underestimated the levels of exposure in the population, as many men will be misclassified as exposed due to household ownership of a biomass stove but in reality have little or nothing to do with cooking, where the likely exposure occurs.

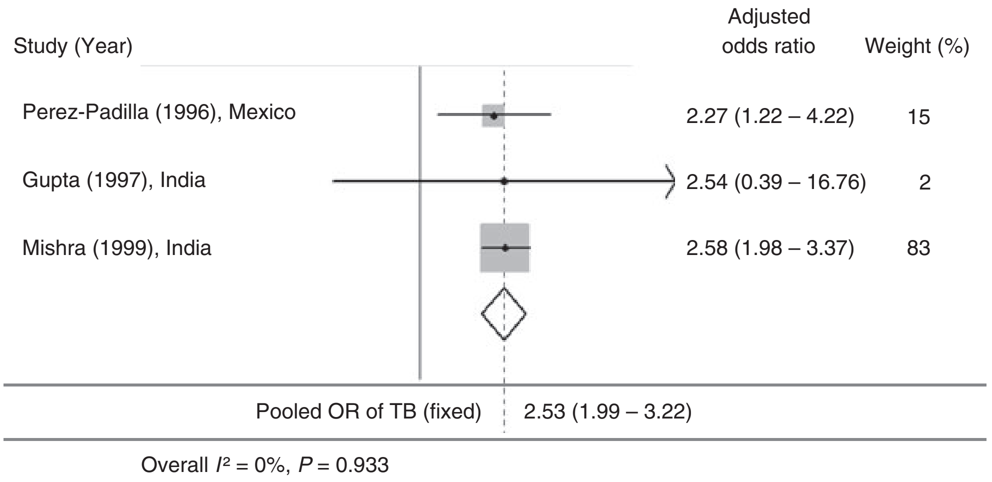

Figure 4 Forest plot of ORs of tuberculosis in those exposed to biomass *vs*. unexposed (cross-sectional).

Although no studies were excluded solely for being in a language other than English, there may be a small risk of English language bias. China has a high burden of IAP and would be a likely source of further detailed research into the health effects, although the focus in Chinese literature is on coal rather than biomass fuel use. There is a noticeable bias in the geographical location for studies into IAP health effects and interventions: The African continent suffers a greater burden than any other region with an average across all African countries of 81% reliant on solid fuel (WHO 2007), but only two of 13 studies were conducted there.

Recently, the body of evidence on associations between IAP and TB has grown significantly. This review found several methodologically robust studies, not included in previous systematic reviews, which, when pooled, provide stronger evidence for an association between TB and IAP. Although there are some limitations in the individual studies, the pooled estimates suggest that there is an association between IAP and TB. The potential impact of any causal relationship between TB and IAP is very large, particularly in Africa and South East Asia, where the prevalence of both IAP exposure and TB is high (WHO 2007, 2011). Further research into this topic should be a high priority.

References

Behera D & Aggarwal G (2010) Domestic cooking fuel exposure and tuberculosis in Indian women. *The Indian Journal of Chest Diseases and Allied Sciences* **52**, 139–143.

Crampin AC, Glynn JR & Floyd S *et al.* (2004) Tuberculosis and gender: exploring the patterns in a case control study in Malawi. *International Journal of Tuberculosis and Lung Disease* **8**, 194–203.

Desai MA, Mehta S & Smith KR (2004) Indoor Smoke from Solid Fuels – Assessing the Environmental Burden of Disease at National and Local Levels. Environmental Burden of Disease Series, No. 4, World Health Organization, Geneva.

Garcia-Sancho C, Garcia-Garcia L & Baez-Saldana R *et al.* (2009) Indoor pollution as an occupational risk factor for tuberculosis among women: a population-based, gender oriented, case-control study in Southern Mexico. *Revista De Investigacion Clinica* **61**, 392–398.

Gninafon M, Ade G, Ait-Khaled N, Enarson DA & Chiang C-Y (2011) Exposure to combustion of solid fuel and tuberculosis: a matched case-control study. *European Respiratory Journal* **38**, 132–138.

Gupta BN, Mathur N, Mahendra PN, Srivastava AK, Swaroop V & Agnihotri MS (1997) A study of household environmental risk factors pertaining to respiratory diseases. *Energy Environment Monitor* **13**, 61–66.

Kan X, Chiang C-Y, Enarson D, Chen W, Yang J & Chen G (2011) Indoor solid fuel use and tuberculosis in China: a matched case-control study. *Bmc Public Health* **11**, Article number: 498.

Kolappan C & Subramani R (2009) Association between biomass fuel and pulmonary tuberculosis: a nested case-control study. *Thorax* **64**, 705–708.

Lakshmi PVM, Virdi NK, Thakur JS, Smith KR, Bates MN & Kumar R (2012) Biomass fuel and risk of tuberculosis: a case-control study from Northern India. *Journal of Epidemiology and Community Health* **66**, 457–461.

Lin HH, Ezzati M & Murray M (2007) Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. *PLoS Medicine* **4**, 173–189.

Mishra VK, Retherford RD & Smith KR (1999) Biomass cooking fuels and prevalence of tuberculosis in India: IJID: official publication of the International Society for Infectious Diseases. *International Journal of Infectious Diseases* **3**, 119–129.

Perez-Padilla R, Regalado J & Vedal S *et al.* (1996) Exposure to biomass smoke and chronic airway disease in Mexican women. A case-control study. *American Journal of Respiratory and Critical Care Medicine* **154** (Pt 1), 701–706.

Perez-Padilla R, Perez-Guzman C, Baez-Saldana R & Torres-Cruz A (2001) Cooking with biomass stoves and tuberculosis: a case control study. *International Journal of Tuberculosis and Lung Disease* **5**, 441–447.

Pokhrel AK, Bates MN, Verma SC, Joshi HS, Sreeramareddy CT & Smith KR (2010) Tuberculosis and indoor biomass and kerosene use in Nepal: a case-control study. *Environmental Health Perspectives* **118**, 558–564.

Shetty N , Shemko M, Vaz M & D'Souza G (2006) An epidemiological evaluation of risk factors for tuberculosis in South India: a matched case control study. *International Journal of Tuberculosis and Lung Disease* **10**, 80–86.

Slama K, Chiang C-Y, Hinderaker SG, Bruce N, Vedal S & Enarson DA (2010) Indoor solid fuel combustion and tuberculosis: is there an association? *International Journal of Tuberculosis and Lung Disease* **14**, 6–14.

Thompson-Reuters (2009) EndNote X3.

WHO (2007) Indoor Air Pollution: National Burden of Disease Estimates. WHO, Geneva, Switzerland.

WHO (2011) Global Tuberculosis Control 2011. WHO, Geneva, Switzerland.

Corresponding Author Colin Sumpter, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. E-mail: colin.sumpter@lshtm.ac.uk