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Household air pollution exposure and risk of tuberculosis: a case–control study of women in Lilongwe, Malawi

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ABSTRACT

Introduction Globally, 3–4 billion people rely on solid fuels for cooking, and 1 billion use kerosene to light their homes. While household air pollution (HAP) emitted from burning these fuels has well-established links to numerous health outcomes, the relationship between active tuberculosis (TB) and HAP exposure remains inconclusive.

Methods We explore the association between HAP exposure and TB among adult women in Lilongwe's high-density suburbs using hospital and community-based health data, objectively measured exposure to HAP, and sociodemographic data controlling for individual, household and community-level confounders. Only one other study combines public health, exposure and sociodemographic data to explore the association between HAP and TB. We report results from a case–control study of 377 primary cooks (76 cases; 301 controls) on the association between risk of developing active TB and HAP exposure. We calculate ORs for developing active TB using indicators of HAP exposure including primary fuel used for cooking, cooking location and frequency of kerosene use for lighting, and in a subset of households, by directly measured cooking area and personal exposure to fine particulate matter ($PM_{2.5}$) and carbon monoxide.

Results We are unable to find an association between self-reported cooking with solid fuels and TB in our sample; we do find that increased frequency of kerosene use for lighting is associated with significantly higher odds of TB. Household area $PM_{2.5}$ concentration is the only direct HAP measure associated with significantly higher odds of TB. We find that 16.8% of the relationship between TB and kerosene use is mediated by increases in area $PM_{2.5}$.

Conclusion Our findings suggest that efforts to reduce the risk of active TB within the home environment should include strategies to reduce or eliminate kerosene, commonly used for lighting and cooking in many low-income country settings.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Evidence on the relationship between air pollution exposure and tuberculosis prevalence is mixed.

WHAT THIS STUDY ADDS

⇒ We find no association between cooking with biomass and tuberculosis (TB); we do find that women in households using kerosene for lighting are at greater risk for TB.

⇒ To study the relationship between air pollution exposure and TB we use direct measures of pollutants; we are the first to do so in a sub-Saharan African context.

⇒ Because of the inclusion of direct measures of pollutants, we more accurately explore the causal pathway between household air pollution (HAP) and TB through mediation analysis.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our results suggest that efforts to combat TB through decreased exposure to area $PM_{2.5}$ include improved ventilation in the home and reduction in use of kerosene for lighting.

⇒ We have improved the quality of data sources and used a novel analysis to study the relationship between air pollution exposure and TB which could be replicated in future studies. Our approach highlights that kerosene lamps and the resultant $PM_{2.5}$ they emit merits focused attention in future research about HAP and TB.

INTRODUCTION

Nearly half the world's population uses solid fuels for heating and cooking and almost 1 billion rely on kerosene lamps to light their homes.[1] In low/middle-income countries (LMICs), exposure to household air pollution (HAP) associated with burning biomass fuels is the fourth largest risk factor for burden of disease causing 2.3 million premature deaths annually.[2 3] Tuberculosis (TB) is one of the top ten causes of death globally and is the second leading cause of death from an infectious agent after SARS-CoV-1.[4] Ninety-five per cent of all TB deaths are in LMICs. People who suffer from other health conditions, (eg, HIV, alcoholism) including some associated with HAP, are at greater risk for contracting TB.[4] While the evidence base for the causal relationship between HAP exposure and a number of other health outcomes is well

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established,[1 5 6] there is no broad consensus on the relationship between HAP exposure and pulmonary TB.[7 8]

Malawi is a critical case for examining the connection between HAP and TB. TB remains a major public health problem in Malawi and is among the top ten mortality causing diseases in the country. Since Malawi began implementing the Directly Observed Therapy strategy, TB case notification increased steadily, most notably from 1995 to 2003 when it reached its peak. After 2003, TB cases have trended downward, decreasing from nearly 50 000 notified cases in 2003 to about 30 000 notified cases in 2010.[9] In 2020, the number of notified cases was 26 000. Incidence of tuberculosis in Malawi fell gradually from 401 cases per 100 000 people in 2002 to 132 cases per 100 000 people in 2021.[10] The rapid scale-up of antiretroviral therapy for HIV/AIDS contributed to the declining case notification, with over 300 000 patients on antiretroviral drugs by 2010 and 800 000 by 2021. Contact tracing occurs in Malawi for household contacts under 5 years of age and for all contacts to multi-drug resistant TB cases. HAP exposure is high in urban Malawi due to limited access to modern lighting and cooking infrastructure. Kerosene (paraffin), a hypothesised risk factor for TB,[11] is widely used for lighting,[1] and there is almost universal reliance on biomass fuels including charcoal and firewood for cooking.[12] The coincidence of these two risk factors makes Malawi an excellent place to study the association between HAP and TB.

From a biomedical perspective, HAP, specifically particulate matter, can be involved in the reactivation of TB through impairing macrophage and respiratory epithelial cell function, as shown in several studies,[13–16] however, evidence on the relationship between HAP and TB is mixed. Two systematic reviews conducted in 2012 found evidence of an association between HAP and TB.[7 8] Sumpter and Chandramohan identified a positive association between HAP and TB (N=13, pooled OR 1.30, 95% CI 1.04 to 1.62) as did Kurmi *et al* (N=10, pooled OR 1.55, 95% CI 1.11 to 2.18). However, a more recent review in 2014[17] critiques previous reviews asserting evidence supporting the association between domestic use of solid fuels and TB risk is weak. Lin *et al* highlight a number of weaknesses in the Sumpter and Chandramohan review including a lack of direct measures of exposure, insufficient consideration of confounding demographic and socioeconomic variables, and reliance on non-population based controls in hospital case–control studies.[17] They find no evidence of an association between HAP and TB in cross-sectional (N=5, pooled OR 1.17, 95% CI 0.83 to 1.65) or case–control (N=10, pooled OR 1.62, 95% CI 0.89 to 2.93) studies. Simkovich *et al* summarise information currently known about the relationship between HAP and TB highlighting only one additional study published since the Lin *et al* review, and also conclude that there is no clear relationship between HAP and TB.[18] Obore *et al* conduct a meta-analysis and find a 68% increase in TB risk among people exposed to HAP (pooled risk ratio 1.68, 95% CI 0.91 to 2.74), but they acknowledge there is considerable heterogeneity in the studies that were included.[19]

While the general relationship between HAP and TB remains unclear, recent studies point specifically to the use of kerosene as a risk factor for TB. Elf *et al* found that wood fuel use in India was not associated with TB but that use of kerosene was.[20] Patel *et al* and Pathak *et al* similarly found a relationship between TB risk and kerosene use in different study sites in India, and Albers *et al* established this relationship in Nepal.[17 21 22]

Even when studies analyse the role of kerosene separately from other fuels it remains uncommon to include measurements of pollutant exposure, which is fundamental to clarifying the causal pathway between HAP and TB. Two recent studies by Jafta *et al* and Elf *et al* were the first to our knowledge to use area concentrations of HAP to study this relationship.[20 23] Jafta *et al* find no significant increase in the risk of childhood TB when exposed to particulate matter smaller than 10 µm in diameter (PM_{10}) and/or nitrogen dioxide (NO_2). Elf *et al* measure indoor concentrations of $PM_{2.5}$.[20] They find a relationship between kerosene use and TB that goes away after controlling for $PM_{2.5}$ suggesting that the increase in $PM_{2.5}$ is perhaps an important pathway between kerosene use and TB. The lack of conclusive evidence of a confirmed association between HAP exposure and risk of TB justifies the need for further studies, particularly those that consider the role of kerosene.

This study aims to fill several gaps identified in the literature by studying the relationship between HAP exposure and TB in adult women in Lilongwe's high-density suburbs. Using a hospital and community-based case–control study design, we combine data on TB status from the Lilongwe District Tuberculosis Control Programme (cases) and community-based testing of TB and HIV status (controls); personal exposure and cooking area concentration measurements for carbon monoxide (CO) and $PM_{2.5}$; and information from a structured sociodemographic and health survey including information on cooking, lighting, and other environmental exposures. This study is one of very few that incorporates direct measures of pollutants, and the first to do so in a sub-Saharan African context.

Our hypothesis is that any causal pathway between household behaviour regarding cooking and lighting, and TB runs through exposure to pollutants resulting from the incomplete combustion of solid fuels and kerosene, specifically $PM_{2.5}$ and CO. We expect that if we find increased TB risk associated with cooking and lighting behaviour, this relationship will be attributable to increases in HAP. Incorporating these direct exposure measurements into the analysis of the relationship between HAP and TB is essential to clarifying the association and confirming the causal mechanism underlying the hypothesised relationship. We know of no other study on the relationship between HAP and TB that combines these diverse data sources to address the question of

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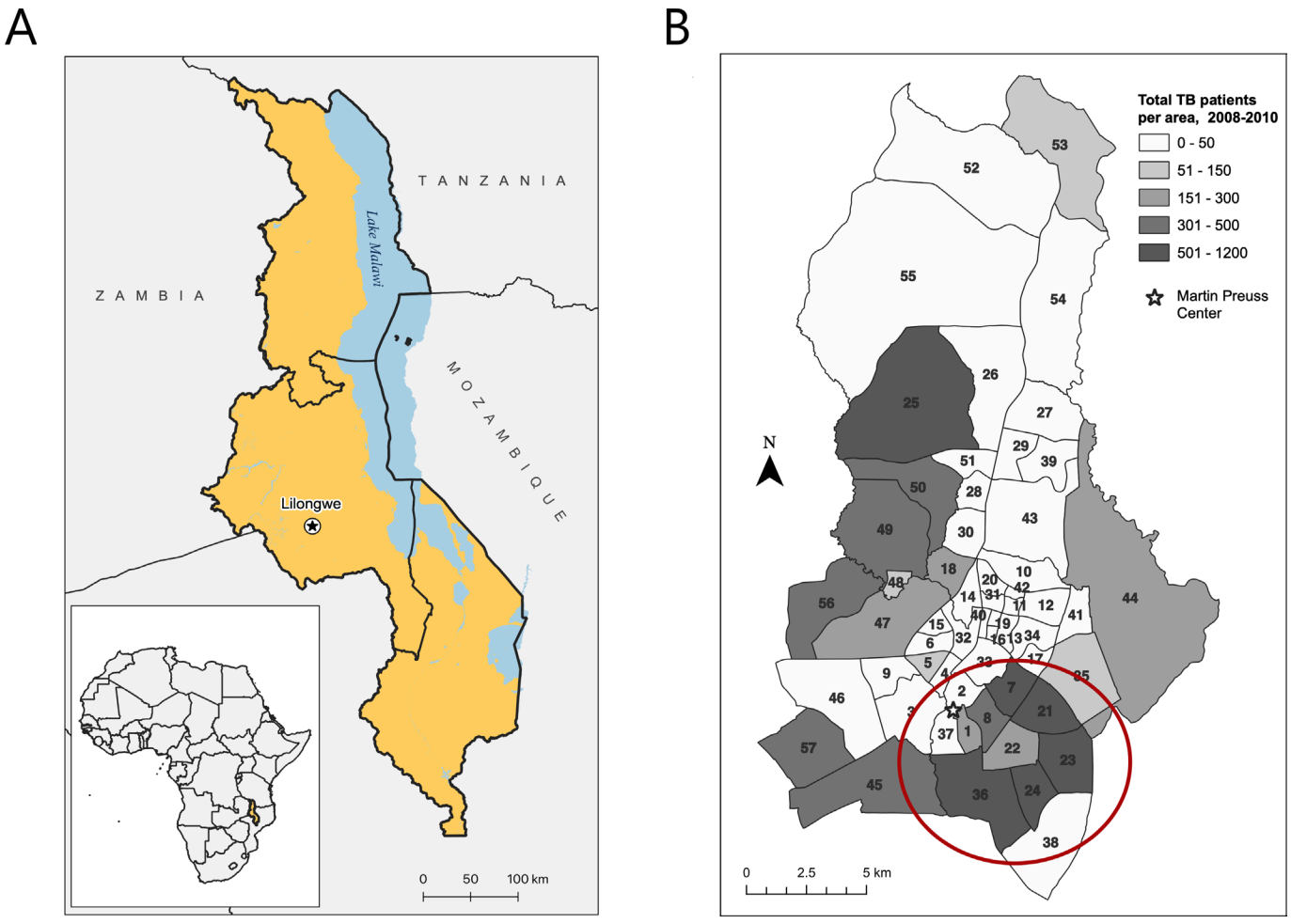

Figure 1 (A) Map of Malawi and location of city of Lilongwe, Malawi. (B) Total number of pulmonary tuberculosis patients by area number 2008–2010, city of Lilongwe, Malawi (study areas in red circle, dark grey shaded neighbourhoods 7, 21, 23, 24, 36).

the mediating role that HAP plays in risk of contracting active TB.

METHODS

Study design

The research design is a hospital and community-based case–control study. We recruited adult female pulmonary TB patients who were no longer infectious but on TB treatment, with high rates of expected HAP exposure living in the high-density suburbs of Lilongwe, Malawi. All participants were primary cooks in their households. We selected four near neighbour controls without active TB for each case recruited into the study.

Study location and population

The study took place in five purposively selected neighbourhoods or 'areas' in low-income high-density suburbs of Lilongwe, Malawi's capital city (figure 1). All five areas fall within the catchment of the Lilongwe District Tuberculosis Control Programme at Bwaila Hospital. Households in these Areas are generally representative of peri-urban Lilongwe. Most people rent their homes. Water and sanitation facilities are limited with most households using communal water tanks to source drinking water and communal pit latrines. People work predominately in daily wage labour and/or jobs in the informal sector. It is common for households to grow crops on small plots in their yards to supplement food purchased at local markets. While the electricity grid runs through these areas, the high cost and poor reliability of electricity severely limits the number of people using electricity for lighting and cooking. Households purchase lighting and cooking fuels in small quantities multiple times a week from ubiquitous local markets that supply charcoal, fuelwood, kerosene and a variety of consumer goods.

Participant recruitment

We recruited women between the ages of 15 and 65 years of age diagnosed with active pulmonary TB by positive sputum smears, culture or chest X-ray 6–12 months prior to being interviewed (cases) from the patient master log book of the Tuberculosis Control Programme at Bwaila Hospital in Lilongwe. All recruited cases were currently on TB treatment, asymptomatic and considered non-infectious. We selected this population because women in this age range typically have high rates of exposure to

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HAP given their role as primary cooks in households. We excluded women who were not the primary cook in their household, were pregnant, were undergoing chemotherapy for cancer, had diabetes, had any respiratory illnesses at the time of the study, had a history of active TB prior to the recent diagnosis, and those who smoked.

Controls were selected from the pool of female primary cooks in a similar age range (eg, ±5 years to control for the cumulative effect of lifetime exposure to HAP) in the four households immediately adjacent in any direction to the recruited cases. Recruited controls with self-reported symptoms suggestive of active TB (ie, weight loss, night sweats, cough lasting more than 2 weeks), a history of active TB or active TB treatment were not enrolled. Selection of controls was confirmed after a sputum sample collected from the prospective female respondent was processed in the microbiology laboratory at Kamuzu Central Hospital to verify the absence of acid-fast bacilli. Any woman with symptoms suggestive of TB or a positive TB sputum test was immediately referred to the TB control programme clinician. All prospective cases and controls were tested for HIV/AIDS. Standard HIV testing and counselling and diagnostic HIV rapid tests were conducted in the home per Malawian standard of care.[24] Women who were uncertain of their pregnancy status were given a rapid urine pregnancy test.

A trained team of enumerators interviewed cases and controls in their households using a structured questionnaire. All respondents were asked a series of questions about disease history, demographics, socioeconomic characteristics of the household, crowding within the household and neighbourhood, environmental exposures, and cooking and lighting practices. We collected health data from respondents including height and weight for calculation of body mass index (BMI), blood pressure and self-reported information about health conditions.

Exposure assessment

We stratified our sample by case and control and randomly selected a subset of approximately 40% of the women in our sample for personal exposure monitoring over 24 hours to assess exposure to CO and $PM_{2.5}$. Carbon monoxide data loggers (Lascar Electronics, model EL-USB-CO) were used to measure and record CO concentrations in 1 min intervals. Before and after the field campaign, the data loggers were placed in a sealed chamber through which a CO calibration gas was passed until the concentrations reached steady state. We applied a correction factor to each data logger based on its response relative to the calibration gas. Fine particulate matter samples were collected using a continuously sampling pump (AirChek XR5000 sample pump, SKC) connected to a single-stage impactor (Personal Environmental Monitor with a 2.5 µm cut-point at 2 L/min, SKC) and a 2 µm polytetrafluoroethylene filter downstream of the impactor. Instruments were affixed to a small backpack with CO and personal exposure monitors positioned with their inlets near the cook's breathing zone.

In personal exposure monitoring households, we also collected CO and $PM_{2.5}$ samples for the same 24-hour period from a fixed location near the cooking area. For area concentration measurements, the instruments were affixed to a tripod positioned 1 m from the primary stove and 1.5 m high. Cooking area $PM_{2.5}$ samples were collected with the pumps operating intermittently (240 cycles of 1 min on and 5 min off) to avoid overloading the filters.

For the $PM_{2.5}$ samples, filters were weighed before and after sampling in a laboratory at the University of North Carolina at Chapel Hill due to lack of access to a microbalance in Malawi. Prior to weighing, filters were placed inside a desiccator containing several dishes of a saturated magnesium chloride solution for at least 24 hours. The saturated solution controlled the relative humidity inside the desiccator to approximately 33%. Each filter was held next to an ionising cartridge (Staticmaster model 2U500; NRD) to minimise static charge, then weighed on a microbalance located on top of a marble table.

Data analysis

We use two samples for our analysis, the full dataset including 76 case households and 301 controls, and an exposure subsample ranging from 32 to 40 case individuals/households and 111–120 controls. While the original sample was the same for all exposure monitoring activities, we ended up with slightly different sample sizes due to variation in the number of complete 24-hour measurements we were able to collect. The analysis was done in Stata/SE V.16.1 (StataCorp, College Station, TX, USA).

First, we executed difference of means and Pearson's χ^2 tests to check for differences in HAP exposure between our case and control households. We then analysed the relationship between cooking/lighting variables and objectively measured exposure through a series of bivariate regression models. We further decomposed the analysis by case and control to see if the relationship between exposure and cooking/lighting differs between case and control households.

We constructed a series of multivariate logistic regression models for risk of TB. The first models (models 1 and 2) use self-reported cooking and lighting as the main explanatory variables and the second set of regressions (models 3 and 4) use exposure measurements. We include results from four models. Models 1 and 3 use just the main explanatory variables (cooking/lighting in model 1; exposure in model 3) and models 2 and 4 add in our control variables. We run the second and fourth models with and without the HIV status variable as a robustness check.

We include individual, household and area-level controls in our analysis. In addition to our main explanatory variables for models 1 and 2 (primary cooking fuel and use of kerosene for lighting), we also include cooking location and household density as suggested in Lin *et al* as a way to reduce bias when

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using primary cooking fuel as a proxy measure for HAP exposure.[18] We also include a log-transformed value of household assets, education, and age of primary cook.

Underlying health problems, in particular HIV, have well-established connections with TB risk.[9 23 25–27] We include BMI and blood pressure in our models and run our models both with and without HIV as a robustness check of our results. Given that systolic and diastolic blood pressure are highly correlated, we combine them into one using a standard formula for calculating mean arterial pressure.[28] Other risk factors for TB include smoking or exposure to secondhand smoke (SHS)[23 29–31] and household crowding.[23 30] We exclude smokers from our study, but control for the presence of other smokers in the household.

Mediation analysis

We bring our causal story together using mediation analysis. Cooking behaviour and lighting are used in analysis of the relationship between HAP and TB risk as a proxy measure for HAP. However, the expectation is that the causal pathway between cooking/lighting and TB risk runs through exposure to air pollutants. As such, personal exposure and area concentration measures of $PM_{2.5}$ and CO act as a mediator in the relationship between cooking/lighting and TB.

We test this hypothesis using the Karlson, Holm and Breen (KHB) model, which requires the confirmation of three independent relationships summarised in figure 2 prior to running the mediation analysis: cooking/lighting behaviour and TB (A); cooking/lighting behaviour and the exposure measurements (B); and exposure measurements and TB risk (C).

If these independent relationships are confirmed, the KHB model decomposes the total effect of cooking/lighting into its direct and indirect effects by parsing the relationship between HAP exposure from cooking and lighting and TB into three models: the reduced form/direct model (A), the full/total effect model (A′) and the difference between the two (M).[32] The coefficient for the reduced model (A) is the relationship between the independent variable (cooking/lighting) and the dependent variable (TB risk) without considering the role of the mediating variable ($CO/PM_{2.5}$). The coefficient from the full model (A′) estimates the relationship between cooking/lighting and TB after accounting for the exposure variables; and the mediation estimate (M) is the difference between A and A′. If the coefficient on the difference (M) is statistically significant, it suggests the relationship between cooking/lighting and TB is partially mediated by exposure to CO or $PM_{2.5}$. All covariates from the regression models are included in the mediation analysis. The coefficients calculated in the model are log odds.

Traditional mediation analysis uses continuous variables[33] and is a challenge for categorical variables since the parameters in the models are often scaled differently.[32] The KHB model includes standardised residuals of the logistic regression of cooking/lighting on TB risk, which allows the coefficients across the different models to be measured on a consistent scale.

Patient statement

Patients and the public were not involved in joint setting of research priorities, defining research questions and outcome measures, providing input into study design and conduct, dissemination of results and evaluation of studies.

RESULTS

Demographic and health variables

The average age of respondents was 31.8 years, with an average of 14 years of experience as the primary cook in the household. Almost all respondents had some formal education (95%). Ninety per cent of households cooked with biomass (eg, fuelwood and charcoal). Thirty-one

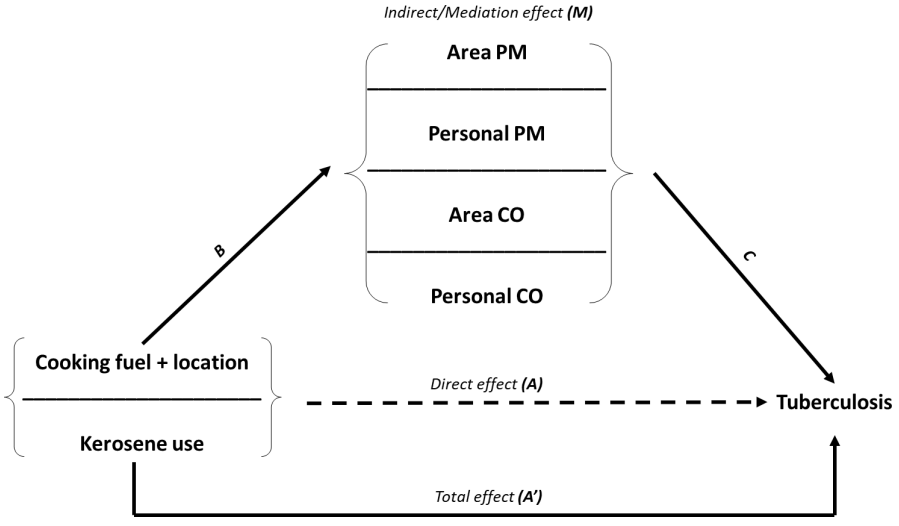

Figure 2 Pathways between household air pollution exposure and tuberculosis.

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per cent cooked exclusively with charcoal and 59% with a mix of charcoal and other biomass sources (primarily fuelwood). The remaining 10% cooked with LPG or electric stoves. Eighty per cent of households reported using kerosene for lighting; 29% used kerosene every day. Descriptive statistics comparing values for case and control respondents and households is in online supplemental table S1.

Differences between case and control groups are common in health status variables, particularly for illnesses such as TB, which have many common comorbidities. Mean arterial pressure and BMI are significantly lower for cases, and rates of testing HIV positive are significantly higher. Seventy per cent of cases were HIV positive compared with only 11.6% of controls. The prevalence of HIV in controls was just slightly below 12.1%, which was the HIV prevalence for women of childbearing age in Malawi at the time data were collected.[30 34]

Exposure variables

A subsample of cooks participated in monitoring to measure personal exposure to $PM_{2.5}$ and CO during a 24-hour period. We additionally measured concentrations of $PM_{2.5}$ and CO in the cooking area of the homes where cooks participated in personal exposure monitoring. There was no significant difference between the exposure measures for case and control households except for area $PM_{2.5}$ (n=32 cases; n=115 controls) (online supplemental table S2). The average concentration of cooking area $PM_{2.5}$ was 690 $\mu g/m^3$ with higher concentrations in the case households (n=40) compared with controls (n=120). The average 24-hour $PM_{2.5}$ exposure was 170 $\mu g/m^3$, which is well above the WHO's 24-hour indoor air quality guideline of 25 $\mu g/m^3$.[35] Personal exposure to CO averaged 7.1 ppm for 144 cooks (n=33 case; n=111 control), which is above the WHO's guideline of 6 ppm.[36] The average concentration of area CO was 14.7 ppm.

Exposure assessment and cooking/lighting

Figure 3A,B presents boxplots, which show the relationship between exposure and cooking and lighting variables for case (orange) and control (green) households figure 2B . A full table of regression results of the effect of cooking and lighting on each exposure measure is in online supplemental table S3. Cooking with charcoal increases concentrations of area CO regardless of cooking location relative to those who cook with other fuels, and those cooking indoors experience the highest concentrations. This is expected given the high levels of CO emitted when burning charcoal. Similarly, cooking with a combination of charcoal and other biomass indoors increases area $PM_{2.5}$ concentrations the most, which is also expected since most of the 'other' biomass combined with charcoal is fuelwood, which emits high levels of $PM_{2.5}$ when burned.

The patterns are not as clear in the personal exposure measurements, which are a continuous measure of the primary cook's exposure throughout their day, not just while cooking. However, the pattern of higher CO exposure in households using charcoal and higher $PM_{2.5}$ exposure in household using a mix of charcoal and fuelwood persists.

We find that increased frequency of kerosene use is associated with an increase in area $PM_{2.5}$ but is not associated with other exposure variables.

Household air pollution

We use a series of multivariate logistic regressions to predict ORs for TB risk based on cooking and lighting variables (arm A from figure 2), and then using direct exposure measures (arm C from figure 2) (table 1).

Model 1 includes just cooking and lighting variables; model 2 includes controls. Positive coefficients provide some indication of a relationship between cooking with biomass and TB risk, but these results are not significant. Kerosene use significantly increases odds of TB in both models after controlling for cooking fuels and location. In model 2, the OR for households that sometimes use kerosene is 3.73 (95% CI 1.97 to 7.07) and for households that use kerosene daily it is slightly lower with an OR of 3.28 (95% CI 1.78 to 6.03), suggesting there is not a dose response to increased frequency of kerosene use in our sample.

Models 3 and 4 include the subsample of households that participated in collection of exposure measures. Model 3 is a naïve model that includes only the exposure variables and model 4 includes the same controls as model 2. We find that area $PM_{2.5}$ significantly increases odds of TB (OR 6.74, 95% CI 2.21 to 20.55). There is a negative relationship between area CO and TB in model 4 that does not show up in the naïve model.

As expected, we find that individual health variables are significantly associated with TB. Lower BMI and higher age are associated with TB. We also see a tight relationship between HIV status and TB (note that HIV status is not displayed in the results in table 1). Interestingly, we do not see a relationship between TB status and having other smokers in the household (a proxy for second hand smoke exposure).

Mediation analysis: kerosene use, area $PM_{2.5}$ and TB

We find from the first stages of our analysis that increased frequency of kerosene use is associated with both $PM_{2.5}$ in the cooking area (B) and TB risk (A), and that area $PM_{2.5}$ is associated with TB risk (C), which provides justification for undertaking a mediation analysis on this set of variables figure 2. Because we do not see a higher increase in odds of TB in the group of people who use kerosene daily (compared with sometimes users), we analyse the mediating relationship for the full group of kerosene users with non-users as the comparison group. The full set of mediation results are available in online supplemental table S4.

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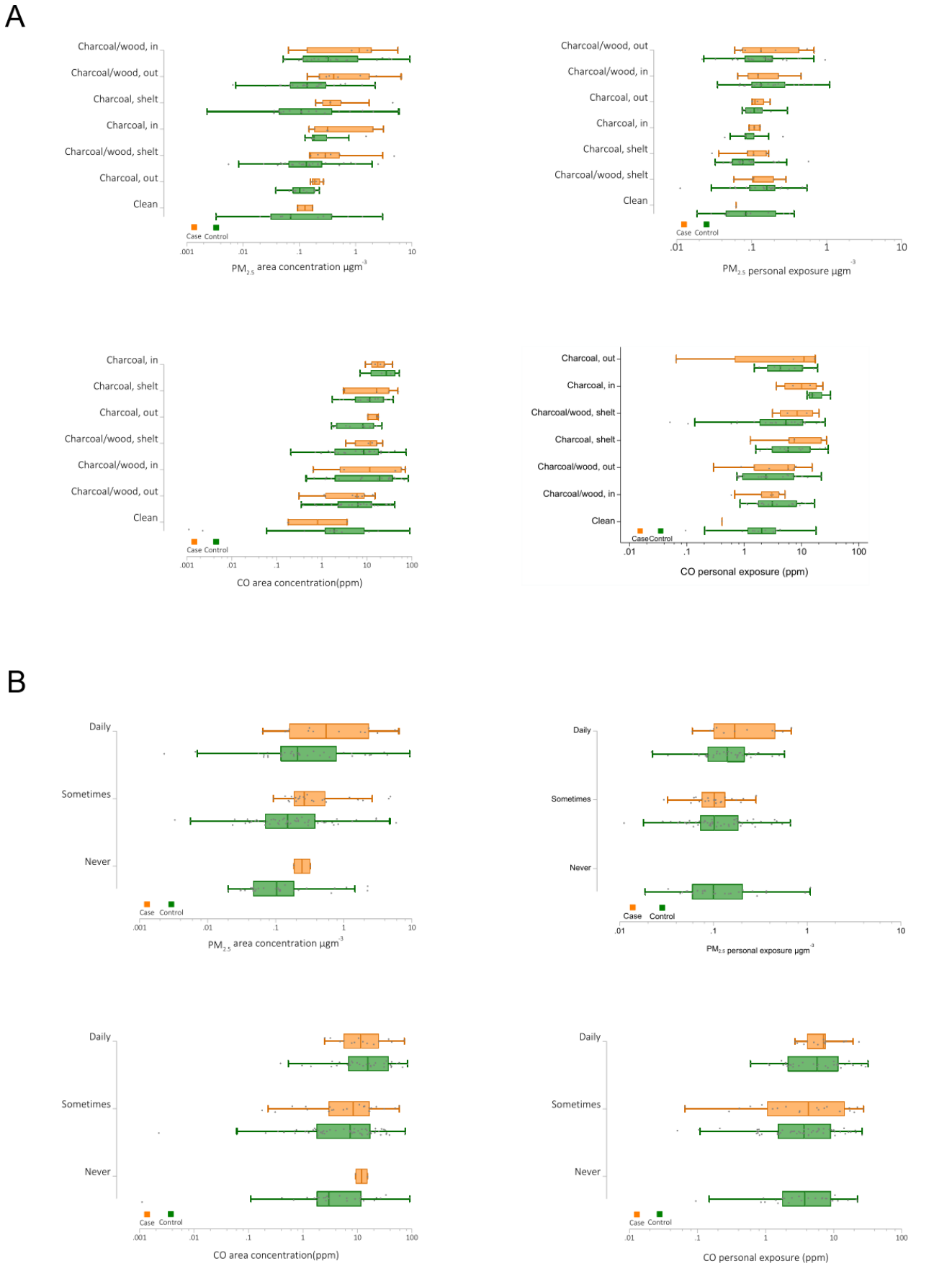

Figure 3 (A) Relationship between exposure and cooking fuel/location in case versus control households (log-values of all household air pollution (HAP) variables used). (B) Relationship between exposure and frequency of kerosene use for lighting in case (orange) versus control (green) households (log-values of all HAP variables used).

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Table 1 Logistic regression results showing ORs of tuberculosis (TB)

	1	2[2]	3	4[2]
	Cooking+lighting (naïve model)	**Cooking+lighting (full model)**	**Exposure (naïve model)**	**Exposure (full model)**
Cooking fuel and location (c.f. clean fuel in any location)				
Charcoal, inside (0/1)	1.83†	2.36*	–	–
	(0.93 to 3.58)	(1.02 to 5.49)		
Charcoal, shelter (0/1)	1.39	2.15*	–	–
	(0.79 to 2.47)	(1.08 to 4.28)		
Charcoal, outside (0/1)	1.80	2.09	–	–
	(0.73 to 4.47)	(0.61 to 7.11)		
Charcoal/wood, inside (0/1)	1.20	1.13	–	–
	(0.58 to 2.49)	(0.43 to 2.97)		
Charcoal/wood, shelter (0/1)	1.28	1.56	–	–
	(0.69 to 2.39)	(0.77 to 5.61)		
Charcoal/wood, outside (0/1)	1.31	2.08	–	–
	(0.60 to 2.87)	(0.77 to 5.61)		
Kerosene use (c.f. never use kerosene)				
Sometimes kerosene use (0/1)	3.36***	3.73***‡	–	–
	(2.28 to 4.96)	(1.97 to 7.07)		
Daily kerosene use (0/1)	3.10***	3.28***‡	–	–
	(1.71 to 5.60)	(1.78 to 6.03)		
Area $PM_{2.5}$ (log mg/m^3)	–	–	4.04***‡	6.74***‡
			(2.19 to 7.45)	(2.21 to 20.55)
Area CO (log ppm)	–	–	0.73	0.44**‡
			(0.41 to 1.30)	(0.21 to 0.92)
Personal $PM_{2.5}$ (log mg/m^3)	–	–	0.39	0.27
			(0.04 to 4.08)	(0.03 to 2.52)
Personal CO (log ppm)	–	–	1.50	2.53
			(0.74 to 3.02)	(0.80 to 8.00)
Age of cook (years)	–	1.05***	–	1.02
		(1.02 to 1.08)		(0.95 to 1.10)
Primary education (c.f. no education)	–	1.69	–	0.30***
		(0.69 to 4.14)		(0.17 to 0.53)
Secondary education or higher (c.f. no education)	–	3.32	–	0.84
		(0.69 to 14.94)		(0.18 to 3.97)
Body mass index (kg/m^2)	–	0.77***‡	–	0.73***‡
		(0.71 to 0.84)		(0.64 to 0.86)
Mean arterial pressure	–	0.98*	–	0.99
		(0.96 to 0.99)		(0.93 to 1.04)

Continued

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Table 1 Continued

	1	2[2]	3	4[2]
	Cooking+lighting (naïve model)	**Cooking+lighting (full model)**	**Exposure (naïve model)**	**Exposure (full model)**
No smokers in household (c.f. smokers in household) (0/1)	–	0.85†	–	0.66
		(0.59 to 1.22)		(0.11 to 3.91)
Household density (residents (n)/rooms for sleeping (n))	–	0.85†	–	0.84
		(0.71 to 1.01)		(0.51 to 1.37)
Assets value (log dollars)	–	1.01	–	1.28**‡
		(0.87 to 1.18)		(1.05 to 1.57)
Observations	378	378	117	117
Pseudo R^2	0.03	0.20	0.09	0.29
AIC	379.57	312.26	127.35	101.14
BIC	395.31	328.01	138.40	112.19

95% CIs in parentheses.
†$p<0.10$, *$p<0.05$, **$p<0.01$, ***$p<0.001$.
‡Results are also significant when models 2 and 4 are run with HIV as a control—it is not included in the original models due to tight correlation with TB status, which inflates the ORs making the estimates imprecise.
AIC, Akaike information criterion; BIC, Bayesian information criterion; CO, carbon monoxide.

The total effect (A′) (figure 4) represents the relationship between kerosene use and TB without accounting for area $PM_{2.5}$. The direct (A) and indirect/mediation (M) effects breakdown the total effect into the amount of the effect of kerosene on TB risk that runs through the pathway of increased area $PM_{2.5}$, and what remains after accounting for the mediating variable. We find that area $PM_{2.5}$ explains 16.8% of the association between kerosene use and TB and this effect is statistically significant. The direct relationship is also significant, which means that area $PM_{2.5}$ is only a partial mediator.

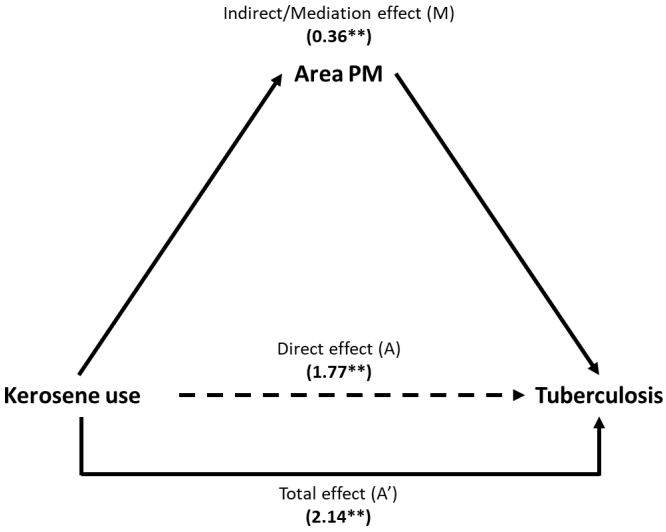

Figure 4 Role of area $PM_{2.5}$ as a mediator in the relationship between kerosene use for lighting and tuberculosis.

DISCUSSION

We analyse the relationship between pollutant concentrations and TB risk specifically considering the role of these pollutants as a mediator of the relationship between cooking and lighting practices and TB. We find increased risk of TB associated with higher household concentrations of $PM_{2.5}$. While we find inconclusive evidence of the relationship between cooking fuel and TB, we have strong evidence to suggest that kerosene lighting increases TB risk, a relationship partially mediated by increases in area $PM_{2.5}$.

Only Jafta *et al* and Elf *et al* also use objective measures of HAP to study the effects on TB.[20 23] Jafta *et al* find no association between childhood TB and increasing levels of PM_{10} and NO_2. However, different mechanisms of disease acquisition and progression between childhood and adult TB make it difficult to compare their findings to our analysis. Childhood TB is usually primary TB, compared with re-activation among adults. Elf *et al* found no relationship between area concentrations of $PM_{2.5}$ and TB risk but they suspect this does not mean there is no relationship, but rather that because ambient $PM_{2.5}$ levels are so high, additional $PM_{2.5}$ from kerosene might not be enough to create a differential effect on TB risk. Their results are like what we find in our analysis in that wood

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fuel use is not strongly associated with TB risk, but use of kerosene is.

Our regression results provide suggestive, but inconclusive evidence of a relationship between cooking with biomass and TB risk, which is in line with two recent review papers on this topic,[18 37] but in contrast with Obore *et al*. Individual studies that do find a relationship between cooking with biomass and TB tend to include people cooking with kerosene in the group of biomass users.[30] When kerosene is not included with other biomass fuels, evidence on the relationship between HAP and TB tends to be less conclusive.[26 38] Our work, along with other recent research that finds a relationship specifically between kerosene and TB,[15 22 38] suggests that kerosene should be analysed separately from other biomass fuels when considering the relationship between HAP and TB.

Our finding that increased use of kerosene for lighting increases odds of TB is robust across models. This relationship is consistent with Pokhrel *et al*, Patel *et al* and Elf *et al* who find increased TB risk for those who use kerosene as a lighting source.[15 17 20] This is true even though the area $PM_{2.5}$ monitors are set up in the cooking area and not designed to exclusively measure the pollution emitted from kerosene lamps. However, we confirm that the relationship between kerosene and area $PM_{2.5}$ concentration only exists when the monitors are set up indoors, which suggests that they are in fact picking up some of the pollution created by kerosene lamps. It is unsurprising that the monitors are detecting some $PM_{2.5}$ from the lamps because houses are small, and it is likely that lamps are being moved into the cooking area (especially in the early morning and evening).

The results of our mediation analysis tell us that the relationship between kerosene use, and TB is partially mediated through area $PM_{2.5}$. It is possible the amount of mediation might increase if the area $PM_{2.5}$ equipment were set up next to the kerosene lamps. Given the importance of this relationship for TB, further studies that include an exposure monitoring component should consider measuring $PM_{2.5}$ concentration wherever kerosene lamps are located and setting up monitors that allow for the parsing of HAP exposures from cooking versus lighting.

We do not find a significant relationship between having other smokers in the household and TB risk. This is in contrast to a number of studies summarised in Obore *et al*'s review.[19] While unexpected, we think it might be due to overall low numbers of households with smokers, especially in control households. We do not think our evidence is sufficient to suggest there is no relationship between SHS and TB risk in this setting.

Limitations

There are several limitations in our study. The data on cooking habits and the exposure monitoring data were collected after TB was diagnosed in our cases. This makes it more difficult for us to know if respondents changed their habits because of a TB diagnosis. We find very few differences between our case and control groups for any variables other than those related to health, which suggests there do not seem to be systematically different habits between cooks diagnosed with TB and those who do not have active TB. We also do not have details on how long respondents have been cooking with biomass or using kerosene for lighting. However, the use of traditional fuels for cooking and lighting is ubiquitous in Malawi so it is unlikely that households have heterogenous histories of cooking and lighting practices.[1 12]

Additionally, there are other known factors associated with both TB and exposure to HAP that we do not have data on in our sample such as diabetes mellitus and other chronic diseases[39] and therefore cannot control for. However, we attempt to at least partially account for overall well-being and health with the inclusion of BMI and blood pressure in our models.

We were also limited by the number of eligible cases in our study area. To ensure we still had an adequate sample size, we increased our case to control ratio to 1:4, considered optimal when the sample size is too small if you use a 1:1 ratio of cases to controls.[40] Additionally, there were very few people in our sample who cooked with clean fuels and/or never used kerosene to light their homes. While representative of the population in Malawi, having larger numbers of clean fuel users intentionally included in future studies would increase the statistical power of the analysis.

Finally, we had hoped to match case and control households by HIV status, but it was difficult to identify control households where the cook was HIV positive. As a result, we had large differences in HIV rates between our case and control groups. To address this, we ran all regressions with and without the HIV status variable as a robustness check of our results.

CONCLUSION

Globally, TB is the second highest cause of death from an infectious agent and air pollution is the fourth highest risk factor for combined death and disability.[2 4] In Malawi, TB is a persistent health problem and reliance on biomass fuels is almost universal. To date, there is no clear consensus on the relationship between HAP and TB risk.

Our findings align with recent review studies[18 37] that find no clear relationship between HAP exposure from cooking with biomass fuels and TB risk. Given the biomedical linkages between pollution, particularly PM and TB incidence[13–16] and the high levels of pollution emitted when combusting biomass cooking fuels, we do not think it is reasonable to conclude that there is no linkage between HAP from cooking with biomass and TB but rather that is not something we detect in our study sample. We do find that lighting with kerosene significantly increases TB risk, even when kerosene lamps are not used every day. Additionally, we find that the relationship between increased frequency of kerosene and

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TB risk is partially mediated by an increase in area $PM_{2.5}$. These results suggest that efforts should be made to decrease exposure to area $PM_{2.5}$ through improved ventilation in the home, and reduction in use of kerosene.

Given that billions of people worldwide are exposed to HAP from cooking and lighting their homes, and that TB is a persistent issue in many countries most affected by HAP, understanding the relationship between HAP and TB is critical. While we do not fully clarify the relationship between the two in this study, we have improved the quality of data sources and used a novel analysis for this relationship. This approach has highlighted that kerosene lamps and the resultant $PM_{2.5}$ they emit merits focused attention in future research about HAP and TB.

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