



Published in final edited form as:

*Int J Tuberc Lung Dis.* 2018 February 01; 22(2): 179–186. doi:10.5588/ijtld.17.0348.

## Socio-economic Statuses and Risk of Tuberculosis – A Case-Control Study of HIV-infected Patients in Asia

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### CONFLICTS OF INTEREST

There are no conflicts of interest.

### AUTHORS CONTRIBUTIONS

AJ performed data collection, data management, statistical analysis, and drafting of the manuscript. ML initiated the study, conceived analysis ideas, and reviewed the manuscript. MPL, KVN, TPM, DDC, RD, EY, SP, FZ, SK, AV, OTN, BLHS, and WW provided data and reviewed the manuscript. JR provided project management and reviewed the manuscript. All authors have reviewed and approved the final version of the manuscript.

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## Abstract

**Setting**—Tuberculosis (TB) is the most common HIV-related opportunistic infection and AIDS-related death. TB often affects those from low socio-economic background.

**Objective**—This matched case-control study was designed to assess socio-economic determinants of TB in HIV-infected patients in Asia.

**Design**—HIV-positive-TB-positive cases were matched to HIV-positive-TB-negative controls according to age, sex and CD4 cell count. A socio-economic questionnaire consisting of 23 questions including education level, employment, housing and substance use, was distributed. Socio-economic risk factors for TB was analysed using conditional logistic regression analysis.

**Results**—A total of 340 patients (170 matched pairs) were recruited, with 262 (77.1%) matched on all three criteria. Pulmonary TB was the predominant type (115, 67.6%). The main risk factor for TB was not having university level education (OR=4.45, 95%CI (1.50-13.17), p=0.007). Burning wood or coal regularly inside the house and living in the same place of origin were weakly associated with TB diagnosis.

**Conclusions**—Our data suggests that lower socio-economic status is associated with increased risk of TB in Asia. Integrating clinical and socio-economic factors into the treatment of HIV may help in the prevention of opportunistic infections and disease progression.

## Keywords

socio-economic; questionnaire; matched; HIV; TB

## INTRODUCTION

There were an estimated 10.4 million new cases of tuberculosis (TB) worldwide in 2015, of which people living with HIV accounted for 1.2 million (11%). Six countries, three of which are in the Asia-Pacific (India, Indonesia and China), accounted for 60% of new TB cases (1). TB is the most common HIV-related opportunistic infection and AIDS-related death (2). The management of HIV and TB co-infection is challenging and often associated with poorer treatment outcomes (3) due to their profound effects on the immune system.

It is recognised that low socio-economic background can contribute to the increased risk of TB and unfavourable TB treatment outcomes (4–6). In sub-Saharan Africa, being single, low education, unemployment, low income, poverty, smoking, and alcohol use were shown to be associated with TB (7, 8). There are currently few data on the effects of socio-economic risk factors for TB in HIV-infected patients in Asia. A Taiwanese study reported HIV-negative patients with lower income levels were at significant risk of having recurrence of TB (9). Furthermore, a Malaysian study found that one fifth of TB patients registered in the national registry in 2012 had unfavourable outcomes. Lower education levels and HIV infection were found to be significant predictors of poor treatment outcomes (10). A study investigating the

risk of TB diagnosis after recruitment into the TREAT Asia HIV Observational Database (TAHOD) reported TB incidence of 1.98 per 100 person-years of follow-up with younger age, lower CD4 cell count, antiretroviral therapy (ART) duration, and living high TB burden countries being significantly associated with the diagnosis of TB (11). Additionally, it was found that delayed ART initiation after TB therapy did not affect mortality rates in TAHOD patients (12).

This matched case-control study consisted of two sub-studies: (i) to conduct a detailed survey and assessment of socio-economic risk factors for TB diagnosis in HIV-infected patients in Asia; and (ii) to determine TB treatment outcomes and the development of multidrug resistant TB. In this particular sub-study, we report results from sub-study (i) with the hypothesis that TB diagnoses would be more common in patients with a range of social and economic pressures that impact health, including education level, employment, housing and substance use.

## METHODS

### Case-control selection

TAHOD is a prospective adult HIV cohort that collects clinical information on patients attending HIV care at urban referral sites across 12 countries in Asia. Patients were recruited into the study between 2012–2014 if they were ART naïve HIV-infected and receiving care at one of the participating TAHOD (13) sites. Consecutive new TB cases were enrolled after a diagnosis (not recurrence) of pulmonary or extra-pulmonary localisation or both, confirmed by either a positive Acid-Fast Bacilli (AFB) smear microscopy of any clinical specimen other than stool, or positive culture and identification of mycobacteria of the tuberculosis-complex specimen, or positive polymerase chain reaction (PCR) -based detection and identification of mycobacteria of the tuberculosis-complex from any clinical specimen. As the World Health Organization (WHO) recommends systematic screening for TB in HIV-positive patients (1), bias due to access to TB testing and treatment would be limited.

TB-negative controls were selected based on medical record information showing a normal chest x-ray within the past six months; the absence of symptoms suggestive of TB, including, cough, fever, unexplained weight loss and night sweats; no prior TB diagnosis; and no prior TB prophylaxis.

### Matching

The control patients were expected to be matched 1:1 to TB cases on sex, age (+/- five years) and CD4 count (by strata: 0–100, 101–200, >200 cells/ $\mu$ L). However, due to difficulty in acquiring appropriate TB-negative controls with the required matching categories, we allowed for mismatches in any of the three criteria.

### Socio-economic questionnaire

All TB cases and control patients were required to complete the study questionnaire, consisting of 23 questions. To ensure that the forms were filled correctly, patients were asked to complete the questionnaire with the study staff.

### Statistical analyses

Due to incomplete case-control matching, socio-economic risk factors for TB, obtained from the questionnaire, were assessed using matched and unmatched logistic regression. The matched (conditional) logistic regression was analysed by including only the pairs that were matched on all three categories (age, sex, and CD4 count). A sensitivity analysis was performed by fitting unmatched logistic regression on all patients, adjusting for age and CD4 count due to incomplete matching on these variables. As this sub-study focused specifically on socio-economic determinants, no other clinical characteristics were included in the analyses. Smoking as a risk factor was not fitted in the multivariate model due to concerns regarding causality relationship with TB. Comparison of proportions was conducted using chi-squared or Fisher's exact test. Regression models were fitted using backward stepwise procedures. Factors significant in univariate analysis at  $p < 0.10$  were included in the multivariate analysis. Factors with  $p < 0.05$  in the final multivariate model were considered statistically significant.

Ethics approvals were obtained from UNSW Sydney Ethics Committee, and respective local ethics committees of all participating sites, the data management and biostatistical centre (UNSW Sydney Ethics Committee), and the coordinating centre (TREAT Asia/amfAR). A written informed consent was obtained from the participants. All data management and statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA) and Stata software version 14.2 (Stata Corp., College Station, TX, USA).

## RESULTS

A total of 340 HIV-infected patients (170 matched pairs) were recruited from China, Hong Kong SAR, Indonesia, Malaysia, the Philippines, Singapore, Taiwan, Thailand and Vietnam. Of 340 patients, 262 (131 matched pairs, 77.7%) were matched on all three criteria (sex, age and CD4 count), 16 (8 matched pairs, 4.7%) were matched on sex and age only, 50 (25 matched pairs, 14.7%) were matched on sex and CD4 only, 2 (1 matched pair, 0.6%) were matched on age and CD4 only, and 10 (5 matched pairs, 2.9%) were matched on sex only. Table 1 shows the demographics of the included patients according to the matching characteristics. Overall, the median age at enrolment was 33 years (interquartile range (IQR): 29–38). There were 284 (83.5%) males, and more than half (58.2%) had a CD4 cell count of  $\geq 50$  cells/ $\mu$ L at enrolment. The median CD4 cell count was 43 cells/ $\mu$ L (IQR: 14–109). Of the TB cases, 115 (67.6%) were diagnosed with pulmonary TB, 25 (14.7%) had extra-pulmonary TB, and 30 (17.6%) had both.

The questionnaire each participant was asked to complete is presented in Table 2. Two patients did not complete the questionnaire. Overall, almost 50% of patients were married. More than half lived in urban areas in a 2–4 persons household, had high-school education

level and were in full time employment at the time of enrolment. Most patients reported having electricity, refrigerator, television and telephone available in their homes. Approximately 70% have ever smoked, 8% drank alcohol every day and 25% have ever injected drugs. Sixty-seven percent have never been vaccinated against TB or did not know their vaccination status.

Table 3 shows socioeconomic risk factors associated with being diagnosed with TB in the patient group who were matched on all three criteria. In univariate analysis, living in rural areas ( $p=0.064$ ), place of origin ( $p=0.021$ ), highest education level ( $p=0.002$ ), occupation ( $p=0.021$ ), wood/coal burning ( $p=0.024$ ) were associated with having TB. Here it can be seen that when unadjusted, those who previously smoked were more likely to have TB compared to those who were current smokers (Odds ratio (OR) = 2.07, 95% confidence interval (CI) 1.02–4.21,  $p=0.045$ ). We believe that these counter-intuitive results may indicate cause-and-effect relationship between smoking and TB. It is plausible that early symptoms of TB prior to diagnosis would lead to smoking cessation. To avoid misinterpretation, we excluded smoking from the multivariate model in both the main and sensitivity analyses.

The final multivariate model in Table 3 were adjusted for place of origin, education level, and wood burning. We have included place of origin and wood burning in the regression model due to its weak association with TB. Our matched analysis shows that patients who did not reach university level education were more likely to have TB (OR=4.45, 95% CI (1.50–13.17),  $p=0.007$ ), compared to those who had attended university. Patients who moved from another province showed almost 50% odds reduction (OR=0.53, 95% CI (0.27–1.02),  $p=0.058$ ) compared to patients who were originally from the same area. Those who did not burn wood or coal regularly inside the home were also less likely to be diagnosed with TB (OR=0.43, 95% CI (0.18–1.07),  $p=0.070$ ), compared to those who did. No other factors were statistically significant.

We performed a sensitivity analysis (Table 4) by including all 340 patients using unmatched logistic regression. We have also included age and CD4 cell count in the regression analysis, as patients were not fully matched on these two criteria. Similar to the matched analysis, living in rural areas ( $p=0.065$ ), place of origin ( $p=0.082$ ), highest education level ( $p=0.001$ ), employment ( $p=0.024$ ), occupation ( $p=0.010$ ), wood/coal burning ( $p=0.007$ ), and smoking status were associated with having TB in the univariate analysis. In the multivariate regression, controlling for age and CD4, not having university level education was associated with TB (OR=2.11, 95% CI (1.24–3.61),  $p=0.006$ ), and not being exposed to regular wood/coal burning at home significantly reduced the chance of being diagnosed with TB (OR=0.34, 95% CI (0.14–0.79),  $p=0.013$ ).

## DISCUSSION

In summary, the study recruited a total of 340 patients with 170 matched case-control pairs. Of these, 77% were successfully matched on all criteria. Among the TB cases, the majority had pulmonary TB. A set of questionnaire was distributed to each participant, with 99% completion rate. The majority were married, living in urban areas and had full-time

employment. In the matched pair analysis, having education below university level significantly increased the chance of having TB, while place of origin and wood/coal burning showed weak associations. In the un-matched analysis, education level and wood/coal burning were significant risk factors for TB.

Socio-economic factors have continued to contribute to TB incidences in both resource-rich and resource-poor settings. In resource-rich settings, social-economic characteristics of TB can differ between those who are migrants and those who are native to the country (14). In Asia, social-determinants of TB often include unemployment, co-habitation with TB infection, poverty, and other risk factors known to be associated with TB (15–18). The results from our main and sensitivity analyses indicate that education level was an important socio-economic risk factor for TB. The majority of our patients were high school educated but did not complete university. Approximately 10% were primary school leavers. The association of low education status and TB has been documented in many settings (19, 20). It was estimated that one third of the population in South-east Asia lived below the poverty line. Families living in poverty usually prefer their children to work for an income rather than attending school (21). Education is not often seen as an urgent priority for these families. In India, it has been reported that the main reason for dropping out of school for boys and girls was due to financial reasons (22). The lack of proper education, in turn, can lead to further poverty. For HIV-infected patients, the prolonged duration of the disease and the associated stigma can lead to job losses and the need to sell family assets (23). Without good education background, HIV-infected patients in resource-limited settings may become stuck in the vicious poverty cycle, which could subsequently increase the risk of contracting TB.

Using biomass fuels (wood, charcoal, etc.) in open fires or stoves exposes the household occupants to extremely high levels of indoor air pollution which could lead to a range of illnesses including stroke, chronic obstructive pulmonary disease and lung cancer (24). There is evidence from various studies suggesting that indoor air pollution, caused by usage of biomass fuels, can increase the risk of TB (25, 26). This increased risk was also evident in our study. Furthermore, our study also shows that there was a weak association between patients who were currently living in their place of origin and TB, compared to patients who have moved from another province. It is known that migrants from high TB-burden countries are at increased risk of TB (27). However, we suspect that the HIV-positive patients in our study group who internally migrated from another province, may have been in better physical health compared to those who have stayed or returned home (28), and therefore were less susceptible to contracting TB.

Smoking is another risk factor widely known to be associated with TB and can ultimately worsen the cure rates compared to non-smokers (29, 30). A case-control study investigating the effects of smoking on TB in HIV-infected patients in South Africa reported increased risks of acquiring TB in current and former smokers compared to those who had never smoked (31). Our unadjusted analysis, however, found that previous smokers who had ceased smoking were more likely to have TB compared to current smokers. We believe this could be explained by the perceived health-risks and the motivation to quit. Patients who experience a smoking-related illness may have a greater risk perception that increases the



awareness of the harmful nature and detrimental effects of smoking on health (32). A intervention study on smoking cessation in rural China reported that more than half of current smokers with TB reported abstinence in cigarette smoking during the study(33). Therefore, the effects of smoking in our study should be interpreted with this in mind.

Over 50% of our patients were enrolled with a pre-ART CD4 cell count of  $< 50$  cells/ $\mu$ L. This indicates that HIV-infected patients in Asia continue to be diagnosed and/or present at advanced stages of HIV disease, despite WHO recommendations for earlier ART initiation. We expect the proportion of patients initiating ART with low CD4 cell count to decrease over time as countries adopt HIV “test and treat” strategies(34). However, more resources should be allocated towards improved HIV case finding and prompt initiation of HIV treatment.

The limitations of the study include the non-strict nature of the matching of the cases and controls. There was unexpected difficulty in obtaining HIV-positive-TB-negative controls with low CD4 cell counts across participating sites. We therefore broadened our search criteria by allowing matching in any of the age, sex and CD4 count category. Another limitation was that we were not able to adjust for other clinical characteristics of the patients, other than age and CD4 cell count in the unmatched analysis. The aim of the protocol was to specifically assess the socio-economic determinants of TB, and therefore other HIV-related measurements were not collected. Lastly, the heterogeneity of our study sites may lead to unobserved confounding. As our patients were matched within the same site, we believe this confounding would be minimised.

## CONCLUSIONS

Our results are broadly consistent with the increased risk of TB in lower socio-economic background. Patients in this group should be closely monitored for early diagnosis and treatment. The interconnected relationship between HIV infection, TB co-infection and socio-economic factors suggests that the integration of socio-economic parameters into the management of HIV infection is crucial in optimising treatment outcomes and prolonging survival.

## Acknowledgments

This study is an initiative of TREAT Asia, a program of amfAR, The Foundation for AIDS Research, with support from the U.S. National Institutes of Health’s National Institute of Allergy and Infectious Diseases, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Cancer Institute, as part of the International Epidemiology Databases to Evaluate AIDS (IeDEA; U01AI069907). The Kirby Institute is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, UNSW Sydney. The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of any of the governments or institutions mentioned above.

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**Table 1**

Patient demographics.

	Total patients (n=340) (%)	Cases (n=170)	Controls (n=170)
<b>Age at enrolment (years)</b>			
30	117 (34.4)	57	60
31-40	157 (46.2)	79	78
41-50	52 (15.3)	26	26
>50	14 (4.1)	8	6
<b>Sex</b>			
Male *	284 (83.5)	142	142
Female	56 (16.5)	28	28
<b>CD4 at enrolment (cells/<math>\mu</math>L)</b>			
50	197 (57.9)	106	91
51-100	56 (16.5)	25	31
101-200	37 (10.8)	18	19
>200	50 (14.7)	21	29
<b>TB Diagnosis Information</b>			
	N/A		N/A
Pulmonary		115	
Extra Pulmonary			
<i>lymph node</i>		10	
<i>pleura</i>		4	
<i>menigitis</i>		3	
<i>other</i>		8	
Both		30	
<b>Country</b>			
China	18 (5.3)	9	9
Hong Kong	8 (2.4)	4	4
Indonesia	96 (28.2)	48	48
Malaysia	26 (7.6)	13	13
Philippines	40 (11.8)	20	20
Singapore	6 (1.8)	3	3
Taiwan	2 (0.6)	1	1
Thailand	22 (6.5)	11	11
Vietnam	122 (35.9)	61	61
<b>Matching Status</b>			
Matched on all criteria (sex, age, CD4)	262 (77.1)	131	131
Matched on sex, age only	16 (4.7)	8	8
Matched on sex, CD4 only	50 (14.7)	25	25
Matched on age, CD4 only *	2 (0.6)	1	1

	Total patients (n=340) (%)	Cases (n=170)	Controls (n=170)
Matched on sex only	10 (2.9)	5	5

\* includes 1 transgender.

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**Table 2**

Responses to socioeconomic risk factor questionnaire

Questions	Total cases n=170 (%)	Total controls n=170 (%)	* p-value
<b>What is your current marital status?</b>			0.657
Married/cohabitating	78 (47)	87 (53)	
Never married/cohabitating	69 (52)	63 (48)	
Divorced/separated	9 (53)	8 (47)	
Widowed and not cohabitating	12 (60)	8 (40)	
No response	2 (50)	2 (50)	
Missing	0 (0)	2 (100)	
<b>Do you live in a rural or urban area?</b>			0.065
Rural	69 (57)	52 (43)	
Urban	101 (47)	116 (53)	
No response	0 (0)	0 (0)	
Missing	0 (0)	2 (100)	
<b>What is your place of origin?</b>			0.078
Where I currently live	118 (53)	103 (47)	
Another province	44 (42)	61 (58)	
Another country	8 (67)	4 (33)	
No response	0 (0)	0 (0)	
Missing	0 (0)	2 (100)	
<b>What is your highest education level?</b>			0.008
No formal education	7 (54)	6 (46)	
Primary school	21 (57)	16 (43)	
High school	111 (56)	87 (44)	
University level	31 (35)	58 (65)	
No response	0 (0)	1 (100)	
Missing	0 (0)	2 (100)	
<b>Are you employed?</b>			0.053
Yes, full-time	100 (48)	110 (52)	
Yes, part-time, or occasionally	17 (40)	25 (60)	
No	51 (61)	33 (39)	
No response	2 (100)	0 (0)	
Missing	0 (0)	2 (100)	
<b>What is your main occupation?</b>			0.070
Farmer	14 (64)	8 (36)	
Construction/industry worker	17 (47)	19 (53)	
Market/street seller	13 (46)	15 (54)	
Civil servant	6 (25)	18 (75)	
Private company employee	31 (41)	44 (59)	
Entertainment worker	2 (50)	2 (50)	
Other	33 (59)	23 (41)	

Questions	Total cases n=170 (%)	Total controls n=170 (%)	*p-value
No response	3 (33)	6 (67)	
Not employed/missing	51 (59)	35 (41)	
<b>How many persons live in your household?</b>			0.724
1, myself	12 (41)	17 (59)	
2-4 persons	95 (51)	91 (49)	
5-7 persons	50 (51)	49 (49)	
>7 persons	13 (57)	10 (43)	
No response	0 (0)	1 (100)	
Missing	0 (0)	2 (100)	
<b>How many rooms (kitchen, living rooms, bedrooms) are there in your house/apartment?</b>			0.865
One	15 (48)	16 (52)	
Two	20 (48)	22 (52)	
Three	43 (56)	34 (44)	
Four	35 (48)	38 (52)	
Over four	57 (50)	57 (50)	
No response	0 (0)	1 (100)	
Missing	0 (0)	2 (100)	
<b>Do you have a house with a tiled or iron sheet roof?</b>			0.470
Tiled	94 (48)	103 (52)	
Iron sheet	23 (51)	22 (49)	
Other	51 (55)	41 (45)	
No response	2 (50)	2 (50)	
Missing	0 (0)	2 (100)	
<b>What type of toilets do you use?</b>			0.732
Flush toilet	107 (49)	111 (51)	
Latrine	60 (51)	57 (49)	
Other	1 (100)	0 (0)	
No response	0 (0)	0 (0)	
Missing	2 (50)	2 (50)	
<b>Are the following facilities available at your home? (Choose all that applies)</b>			~
Electricity (power line)	164 (50)	167 (50)	
Generator	13 (35)	24 (65)	
Refrigerator	133 (48)	145 (52)	
Radio	118 (52)	110 (48)	
Television	166 (50)	165 (50)	
Bicycle	93 (52)	87 (48)	
Motorbike	116 (50)	117 (50)	
Car	35 (42)	48 (58)	
Telephone (fixed or mobile)	159 (49)	165 (51)	
<b>Do you burn wood or coal inside your house?</b>			0.012

Questions	Total cases n=170 (%)	Total controls n=170 (%)	*p-value
Yes, regularly	23 (74)	8 (26)	
Yes, occasionally	26 (48)	28 (52)	
Never	118 (47)	132 (53)	
Used in the past, but stopped	2 (100)	0 (0)	
No response	0 (0)	0 (0)	
Missing	1 (33)	2 (67)	
<b>What is the main source of drinking water you use at home?</b>			0.330
Piped water to your house/plot	75 (50)	74 (50)	
Well/bore water	46 (58)	34 (43)	
Mineral water	41 (43)	54 (57)	
Pond/river	2 (50)	2 (50)	
Other	6 (67)	3 (33)	
No response	0 (0)	1 (100)	
Missing	0 (0)	2 (100)	
<b>Do you eat proteins (meat, seafood, eggs, milk products, soya beans)</b>			0.439
Every day	119 (48)	128 (52)	
2-3 times per week	41 (56)	32 (44)	
1 time per week or less	10 (56)	8 (44)	
No response	0 (0)	0 (0)	
Missing	0 (0)	2 (100)	
<b>Smoking</b>			0.047
Currently smoke	45 (42)	62 (58)	
Ever smoked (previously smoked)	76 (58)	55 (42)	
Never smoked	49 (49)	51 (51)	
No response	0	0	
Missing	0 (0)	2 (100)	
<b>Do you drink alcohol?</b>			0.585
Every day	17 (63)	10 (37)	
Occasionally	73 (49)	76 (51)	
Never	57 (50)	56 (50)	
Used to in the past, but stopped	23 (48)	25 (52)	
No response	0 (0)	1 (100)	
Missing	0 (0)	2 (100)	
<b>Do you use inject drugs such as heroin, opium, others?</b>			0.002
Every day	4 (80)	1 (20)	
>1/week but not every day	11 (100)	0 (0)	
Sometimes, <1/week	12 (63)	7 (37)	
Never	116 (47)	130 (53)	
Used in the past, but stopped	23 (46)	27 (54)	
No response	4 (67)	2 (33)	
Missing	0 (0)	3 (100)	



Questions	Total cases n=170 (%)	Total controls n=170 (%)	*p-value
<b>Have you ever been vaccinated against tuberculosis?</b>			0.280
Yes	54 (50)	55 (50)	
No	72 (55)	59 (45)	
Do not know	43 (44)	54 (56)	
No response	1 (100)	0 (0)	
Missing	0 (0)	2 (100)	
<b>Have you ever been diagnosed with diabetes?</b>			0.641
Yes	1 (33)	2 (67)	
No	144 (50)	146 (50)	
Do not know	25 (56)	20 (44)	
No response	0 (0)	0 (0)	
Missing	0 (0)	2 (100)	
<b>Have you ever been diagnosed with increased lipids levels?</b>			0.933
Yes	5 (45)	6 (55)	
No	132 (51)	129 (49)	
Do not know	32 (49)	33 (51)	
No response	1 (100)	0 (0)	
Missing	0 (0)	2 (100)	
<b>In the last 2 years, has anyone in your immediate family or circle of friends been diagnosed with TB? (Choose all that applies)</b>			~
A household member	13 (48)	14 (52)	
A relative, living elsewhere	16 (50)	16 (50)	
A friend	8 (42)	11 (58)	
A colleague	5 (71)	2 (29)	
No one I know	39 (49)	40 (51)	
Do not know	29 (45)	35 (55)	
<b>Do you do physical exercise?</b>			0.101
Often	37 (43)	49 (57)	
Rarely	87 (50)	88 (50)	
Never	46 (60)	31 (40)	
No response	0 (0)	0 (0)	
Missing	0 (0)	2 (100)	
<b>Do you use public transport?</b>			0.335
Everyday	43 (55)	35 (45)	
Occasionally	75 (46)	87 (54)	
Never	52 (54)	45 (46)	
No response	0 (0)	0 (0)	
Missing	0 (0)	3 (100)	

\* p-value excludes no response/missing values

~ Non-independent observations

**Table 3**  
Factors associated with the diagnosis of TB – matched analysis, n=262 (131 matched pairs)

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>What is your current marital status?</b>						
Married/cohabitating	1		0.375			
Never married/cohabitating	1.58	(0.82, 3.05)	0.174			
Divorced/separated	1.64	(0.50, 5.31)	0.412			
Widowed and not cohabitating	2.23	(0.55, 9.04)	0.263			
No response/missing	0.53	(0.05, 5.56)	0.594			
<b>Do you live in a rural or urban area?</b>						
Rural	1					
Urban	0.60	(0.35, 1.03)	0.064			
No response/missing	N/A					
<b>What is your place of origin?</b>						
Where I currently live	1		0.021			0.043
Another province	0.48	(0.26, 0.89)	0.019	0.53	(0.27, 1.02)	0.058
Another country	2.83	(0.58, 13.92)	0.200	3.27	(0.65, 16.48)	0.151
No response/missing	N/A			N/A		
<b>What is your highest education level?</b>						
Below university level	5.50	(1.90, 15.97)	0.002	<b>4.45</b>	<b>(1.5, 13.17)</b>	<b>0.007</b>
University level	1			<b>1</b>		
No response/missing	N/A			N/A		
<b>Are you employed?</b>						
No	1.59	(0.91, 2.75)	0.102			
Yes	1					
No response/missing	1.26	(0.17, 9.23)	0.821			
<b>What is your main occupation?</b>						
Civil servant or private employee	1					

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
	Other occupation	2.35	(1.13, 4.85)			0.021
	No response/missing	2.42	(1.18, 4.95)			0.016
<b>How many persons live in your household?</b>						
	1, myself	1				0.993
	2-4 persons	0.99	(0.39, 2.50)			0.978
	5-7 persons	1.04	(0.36, 2.99)			0.943
	>7 persons	1.12	(0.31, 4.08)			0.862
	No response/missing					
<b>How many rooms (kitchen, living rooms, bedrooms) are there in your house/apartment?</b>						
	One	1				0.771
	Two	0.93	(0.31, 2.75)			0.889
	Three	1.43	(0.50, 4.06)			0.503
	Four	1.01	(0.35, 2.91)			0.988
	Over four	1.39	(0.55, 3.52)			0.489
	No response/missing					
<b>Do you have a house with a tiled or iron sheet roof?</b>						
	Tiled	1				0.823
	Iron sheet	1.09	(0.47, 2.56)			0.836
	Other	1.22	(0.66, 2.25)			0.532
	No response/missing	N/A				
<b>What type of toilets do you use?</b>						
	Flush toilet	1				
	Latrine	0.93	(0.49, 1.78)			0.826
	Other	N/A				
	No response/missing	0.49	(0.04, 5.44)			0.560
<b>Do you regularly burn wood or coal inside your house?</b>						
	No	0.37	(0.15, 0.88)			0.024
	Yes	1				0.43
						0.070

	Univariate		Multivariate	
	OR	95% CI	OR	95% CI
			p-value	p-value
No response/missing				
<b>What is the main source of drinking water you use at home?</b>				
Piped water to your house/plot	1		0.246	
Well/bore water	1.30	(0.70, 2.42)	0.405	
Mineral water	0.65	(0.31, 1.38)	0.264	
Pond/river	1.00	(0.06, 15.99)	>0.999	
Other	6.18	(0.73, 52.34)	0.095	
No response/missing	N/A			
<b>Do you eat proteins (meat, seafood, eggs, milk products, soya beans)</b>				
Every day	1		0.437	
2-3 times per week	1.29	(0.66, 2.51)	0.455	
1 time per week or less	1.98	(0.64, 6.07)	0.235	
No response/missing	N/A			
<b>Smoking</b>				
Currently smoke	1		0.117	
Previously smoked	2.07	(1.02, 4.21)	0.045	
Never smoked	1.38	(0.59, 3.23)	0.459	
No response/missing	N/A			
<b>Do you drink alcohol?</b>				
Every day	1		0.285	
Occasionally	0.37	(0.11, 1.22)	0.103	
Never	0.44	(0.13, 1.51)	0.191	
Used to in the past, but stopped	0.29	(0.08, 1.04)	0.057	
No response/missing	N/A			
<b>Do you use inject drugs such as heroin, opium, others?</b>				
Every day	N/A		0.842	
>1/week but not every day	N/A			
Sometimes, <1/week	1.42	(0.44, 4.57)	0.558	

		Univariate		Multivariate		
		OR	95% CI	OR	95% CI	p-value
Never		1				
Used in the past, but stopped		1.05	(0.43, 2.58)			0.909
No response/missing		0.67	(0.11, 3.99)			0.657
<b>Have you ever been vaccinated against tuberculosis?</b>						
Yes		1				0.287
No		1.19	(0.62, 2.26)			0.601
Do not know		0.71	(0.34, 1.49)			0.364
No response/missing		N/A				
<b>Have you ever been diagnosed with diabetes?</b>						
Yes		N/A				
No		1				
Do not know		1.17	(0.54, 2.52)			0.695
No response/missing		N/A				
<b>Have you ever been diagnosed with increased lipids levels?</b>						
Yes		1				0.788
No		1.08	(0.21, 5.47)			0.923
Do not know		0.85	(0.16, 4.51)			0.923
No response/missing		0.54	(0.03, 9.8)			0.923
<b>Do you regularly do physical exercise?</b>						
No		1.50	(0.83, 2.72)			0.183
Yes		1				
No response/missing		N/A				
<b>Do you use public transport?</b>						
Everyday		1				0.456
Occasionally		0.70	(0.33, 1.47)			0.346
Never		0.94	(0.41, 2.14)			0.881
No response/missing		N/A				

\* Global p-values are tests for heterogeneity excluding missing cases.

Smoking was not adjusted in the multivariate analysis.

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**Table 4**

Factors associated with the diagnosis of TB – unmatched analysis, n=340

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>Age at enrolment</b>						
30	1		0.947	1		0.910
31-40	1.07	(0.66, 1.72)	0.793	1.08	(0.65, 1.81)	0.759
41-50	1.05	(0.55, 2.02)	0.878	0.83	(0.42, 1.65)	0.597
>50	1.40	(0.46, 4.30)	0.553	1.11	(0.35, 3.52)	0.858
<b>CD4 cell count at enrolment (cells/<math>\mu</math>L)</b>						
50	1		0.380	1		0.624
51-100	0.69	(0.38, 1.26)	0.227	0.73	(0.39, 1.37)	0.333
101-200	0.81	(0.40, 1.64)	0.564	1.10	(0.53, 2.32)	0.793
>200	0.62	(0.33, 1.16)	0.138	0.70	(0.36, 1.38)	0.307
<b>What is your current marital status?</b>						
Married/cohabitating	1		0.659			
Never married/cohabitating	1.22	(0.77, 1.93)	0.392			
Divorced/separated	1.25	(0.46, 3.41)	0.656			
Widowed and not cohabitating	1.67	(0.65, 4.31)	0.286			
No response/missing	0.56	(0.10, 3.13)	0.507			
<b>Do you live in a rural or urban area?</b>						
Rural	1					
Urban	0.66	(0.42, 1.03)	0.065			
No response/missing	N/A					
<b>What is your place of origin?</b>						
Where I currently live	1		0.082			
Another province	0.63	(0.39, 1.01)	0.053			
Another country	1.75	(0.51, 5.97)	0.374			
No response/missing	N/A					

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>What is your highest education level?</b>						
Below university level	2.39	(1.44, 3.95)	0.001	2.11	(1.24, 3.61)	0.006
University level	1			1		
No response/missing	N/A			N/A		
<b>Are you employed?</b>						
No	1.78	(1.08, 2.95)	0.024			
Yes	1					
No response/missing	1.15	(0.16, 8.32)	0.887			
<b>What is your main occupation?</b>						
Civil servant or private employee	1					
Other occupation	1.98	(1.17, 3.33)	0.010			
No response/missing	2.21	(1.24, 3.92)	0.007			
<b>How many persons live in your household?</b>						
1, myself	1		0.727			
2-4 persons	1.48	(0.67, 3.27)	0.333			
5-7 persons	1.45	(0.63, 3.34)	0.388			
>7 persons	1.84	(0.61, 5.57)	0.28			
No response/missing	N/A					
<b>How many rooms (kitchen, living rooms, bedrooms) are there in your house/apartment?</b>						
One	1		0.866			
Two	0.97	(0.38, 2.46)	0.948			
Three	1.35	(0.58, 3.11)	0.483			
Four	0.98	(0.42, 2.28)	0.967			
Over four	1.07	(0.48, 2.36)	0.873			
No response/missing	N/A					
<b>Do you have a house with a tiled or iron sheet roof?</b>						
Tiled	1		0.471			
Iron sheet	1.15	(0.60, 2.19)	0.681			

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>What type of toilets do you use?</b>						
Flush toilet	1					
Latrine	1.09	(0.70, 1.71)	0.701			
Other	N/A					
No response/missing	1.04	(0.14, 7.50)	0.971			
<b>Do you regularly burn wood or coal inside your house?</b>						
No	0.32	(0.14, 0.73)	0.007	<b>0.34</b>	<b>(0.14, 0.79)</b>	<b>0.013</b>
Yes	1			1		
No response/missing	0.17	(0.01, 2.19)	0.176	N/A		
<b>What is the main source of drinking water you use at home?</b>						
Piped water to your house/plot	1					0.343
Well/bore water	1.33	(0.77, 2.31)	0.301			
Mineral water	0.75	(0.45, 1.26)	0.274			
Pond/river	0.99	(0.14, 7.19)	0.989			
Other	1.97	(0.48, 8.19)	0.349			
No response/missing	N/A					
<b>Do you eat proteins (meat, seafood, eggs, milk products, soya beans)</b>						
Every day	1					0.440
2-3 times per week	1.38	(0.81, 2.33)	0.231			
1 time per week or less	1.34	(0.51, 3.52)	0.547			
No response/missing	N/A					
<b>Smoking</b>						
Currently smoke	1					0.049
Previously smoked	1.90	(1.13, 3.19)	0.015			
Never smoked	1.32	(0.76, 2.29)	0.316			
No response/missing	N/A					

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>Do you drink alcohol?</b>						
Every day	1		0.593			
Occasionally	0.57	(0.24, 1.31)	0.185			
Never	0.60	(0.25, 1.42)	0.244			
Used to in the past, but stopped	0.54	(0.21, 1.42)	0.212			
No response/missing	N/A					
<b>Do you use inject drugs such as heroin, opium, others?</b>						
Every day	1		0.314			
>1/week but not every day	N/A					
Sometimes, <1/week	0.43	(0.04, 4.64)	0.486			
Never	0.22	(0.02, 2.02)	0.182			
Used in the past, but stopped	0.21	(0.02, 2.04)	0.180			
No response/missing	0.20	(0.02, 2.58)	0.217			
<b>Have you ever been vaccinated against tuberculosis?</b>						
Yes	1		0.282			
No	1.24	(0.75, 2.07)	0.403			
Do not know	0.81	(0.47, 1.40)	0.455			
No response/missing	0.51	(0.04, 5.78)	0.586			
<b>Have you ever been diagnosed with diabetes?</b>						
Yes	1		0.646			
No	1.97	(0.18, 22.00)	0.581			
Do not know	2.50	(0.21, 29.60)	0.467			
No response/missing	N/A					
<b>Have you ever been diagnosed with increased lipids levels?</b>						
Yes	1		0.934			
No	1.23	(0.37, 4.12)	0.740			
Do not know	1.16	(0.32, 4.20)	0.817			
No response/missing	0.60	(0.04, 8.73)	0.708			

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
<b>Do you regularly do physical exercise?</b>						
No	1.48	(0.90, 2.42)	0.119			
Yes	1					
No response/missing	N/A					
<b>Do you use public transport?</b>						
Everyday	1		0.336			
Occasionally	0.70	(0.41, 1.21)	0.201			
Never	0.94	(0.52, 1.71)	0.841			
No response/missing	N/A					

\* Global p-values are tests for heterogeneity excluding missing cases.  
Smoking was not adjusted in the multivariate analysis.