

Investigating the Risk Factors for Contraction and Diagnosis of Human Tuberculosis in Indonesia using Data from the Fifth Wave of RAND's Indonesian Family Life Survey (IFLS 5)

Nathan Adam^{1*}, Saseendran Pallikadavath¹, Marianna Cerasuolo², and Mark Amos¹

¹*Portsmouth-Brawijaya Centre for Global Health, Population, and Policy, University of Portsmouth, PO1 2UP, Portsmouth, UK,*

²*School of Mathematics and Physics, University of Portsmouth, Portsmouth, UK*

*Corresponding author. Email: nathan.adam@myport.ac.uk

Abstract

Tuberculosis (TB) is a globally widespread disease, with approximately a quarter of the world's population currently infected (WHO, 2018). Some risk factors (e.g., HIV status, nutrition and body mass) have already been thoroughly investigated. However, little attention has been given to behavioural and/or psychological risk factors (e.g., stress and education level). In this study, risk factors were investigated via statistical analyses of publicly available data from the most recent wave (2015) of the Indonesian Family Life survey (IFLS 5). For comparison and completeness, variables were divided into levels: individual, household, and community. The most prominent and interesting variables which influence TB diagnosis (on each level) were investigated, and a logistic regression was subsequently developed to understand the extent to which each risk factor acted as a predictor for being diagnosed with TB. Age, health benefit or insurance, stress at work, and living in a rural area all showed significant association with TB diagnosis. The outcomes of this study suggest that suitable control measures, such as BCG vaccinations, schemes for improving mental health/stress reduction, and improved access to healthcare in rural areas should be implemented to address each of the key factors identified.

Keywords: Risk Factors, Logistic Regression, tuberculosis

Introduction

1 Tuberculosis is an infectious bacterial disease caused primarily (in humans) by *Mycobacterium*
2 *tuberculosis*. TB typically affects the respiratory system (throat and lungs) and is transmitted
3 via the air when a person with active TB coughs, sneezes or speaks. This 'ancient scourge' has
4 plagued humans and their ancestors throughout known history. Despite the existence of a cure
5 for TB since 1949 and vaccination (administered predominantly to high risk infants shortly
6 after birth) since 1921, TB is still a great public health concern, with approximately 1.7 billion
7 people currently (latently) infected worldwide (Daniel, 2006; WHO, 2018). Around 5-10% of
8 these 1.7 billion people will develop active TB during their lifetime, which means that the
9 disease will become symptomatic and transmissible. Instances of active TB are referred to as
10 TB cases. The majority of worldwide TB cases arise in developing countries such as Indonesia
11 (Bock & Cox, 2017). In the Indonesian context, money for procuring (and access to) healthcare
12 is often lacking. Additionally, Indonesia's Impoverished living conditions are said to contribute
13 to TB's high burden. According to the World Health Organisation, there were approximately
14 319 new cases of TB per 100,000 people during 2017 in Indonesia alone. To put this into
15 perspective, the incidence rates per 100,000 people in some other high-burden countries are
16 423 (Central African Republic), 361 (Zambia) and 554 (The Philippines). Two thirds of global
17 TB cases (in 2017) occurred in 8 countries, including Indonesia (and the Philippines) (WHO,
18 2018). TB causes a great economic burden to the Indonesian economy; approximately US\$6.9
19 billion was lost in 2015, with 86.6% of this accounted for by premature death resulting in lost
20 productivity (Collins et al., 2017). Although this disease is curable, multi-drug resistance
21 caused by improper treatment regimens or non-compliance with regimens has made TB difficult
22 to treat effectively. Also, TB was thought to be receding in the past decade, but there is evidence
23 that it has been re-emerging in recent years (Shajahan et al., 2016).

24 The known risk factors regularly associated with TB are: being young, male, living in a
25 developing country, being a health care worker, poor ventilation, exposure to contaminated air,
26 and having a compromised immune system (e.g., due to smoking). HIV infection and
27 (consequently) AIDS are the most prominent risk factors for contracting TB (Dye et al., 1999;
28 Fogel, 2015). In recent years, the importance of extensive interdisciplinary research into TB
29 has been appreciated as TB's various socio-politico-economic risk/exacerbating factors have
30 come to light, and this has prompted the need to delve beyond the purely biomedical model
31 (Mason et al., 2016; Mason et al., 2017). However, risk factors related to stress or education
32 have not (yet) been examined as extensively within the existing literature; they are rarely
33 included in the analysis, but a lack of education may hinder one's ability to take measures to
34 protect themselves from disease (Baker et al., 2011). There are various stigmatic associations
35 pertaining to TB, such as belonging to a low social class, poverty or indecorous behaviour.
36 Contempt towards TB sufferers can manifest as social exclusion, which heightens allostatic
37 load, resulting in worsened ability to perform daily tasks (Simandan, 2017a), thereby delaying
38 recovery. Anticipation of such contempt can even discourage disclosure of TB sufferers'
39 diagnoses to friends and family, thereby generating avertable risks to loved ones and public
40 health (Simandan, 2017b). Additionally, implementations of politico-economic ideologies such
41 as neoliberalism have led to layoffs and uncertainty regarding employment conditions,
42 inducing fear and anxiety coinciding with (and explaining) the increased incidence of TB in
43 affected countries (Simandan, 2017a). The complicated interplay that stress has with anxiety,
44 substance abuse and depression can lead to non-compliance with treatment regimens and
45 aggravate health outcomes (Zvonareva et al., 2019). Worse yet, stress also adversely affects
46 immunity (Morey et al., 2015). Evidently, the detrimental effects that stress, anxiety and
47 allostatic load have on the acquisition, persistence and recrudescence (de Oliveira et al, 2000)
48 of TB warrant further study. Indeed, reciprocity amongst TB researchers from various
49 disciplines is required to understand and ameliorate the burden of this multi-faceted disease
50 (Mason et al., 2016). These causal/exacerbating factors may have various sources or triggers,

51 but this study focuses only on the association between occupational stress (stress at work) and
52 the diagnosis of TB infection.

53

54 The widespread burden of TB in Indonesia and its re-emergence prompt an urgent need to
55 cover the aforementioned research gaps, and form the motivation for this study. The aim is to
56 explore a wide variety of risk factors on a variety of levels (individual, household and
57 community) for comparison and completeness, incorporating both existing understanding of
58 the risk factors for TB as well as expanding the understanding of hitherto neglected factors.
59 Bivariate measures of association and logistic regression will be used to quantify the extent to
60 which they act as predictors for contracting and subsequently being diagnosed with TB. With
61 reference to relevant literature, qualitative meaning will be appended to the results and logical
62 control measures will be suggested. The key contribution is the emphasis on behavioural and
63 psychological risk factors (especially stress) as opposed to more commonly understood ones
64 (e.g., HIV). This research is important because the findings may ultimately lead to a reduced
65 burden of TB in Indonesia as well as improved socioeconomic status for Indonesian citizens.

66

Materials & Methods

67 Publicly available demographic household survey data from the fifth wave of the Indonesian
68 Family Life Survey (IFLS 5) were used. The primary motivation for using IFLS datasets were
69 that they contain TB markers whereas other common datasets (e.g., DHS) do not. While this is
70 a longitudinal survey, only the most recent wave is used to explore the cross-sectional
71 association between the incidence of TB and relevant risk factors. The survey samples from a
72 frame of approximately 83% of the Indonesian population, and each wave of the survey
73 encapsulates responses from over 30,000 respondents who are living in 13 out of the 27
74 Indonesian provinces. The names of the surveyed provinces are: North Sumatra, Yogyakarta,
75 West Sumatra, East Java, South Sumatra, Bali, Lampung, West Nusa Tenggara, Jakarta, South
76 Kalimantan, West Java, South Sulawesi, and Central Java. These data were collected by RAND
77 (Research and Development) Corporation staff from anonymous face-to-face household
78 questionnaires (RAND, 2018). The resultant data sets are very rich, with information on various
79 aspects of socio-economic status and health. The data and documentation are publicly available
80 on request at <https://www.rand.org/labor/FLS/IFLS/>.

81 Prior to analysis, variables were transformed/modified as appropriate, to ensure that the
82 analyses would be meaningful. Bivariate measures of association were used to assess the
83 relationship between having received a TB diagnosis and each selected variable, based on a chi-
84 square test for categorical variables and ANOVAs for continuous variables. Logistic regression
85 was then used to quantify the relationship between TB diagnosis and selected variables
86 simultaneously. Associations were said to be significant at a 5% level in all cases. Data were
87 analysed using SPSS 20 for Windows and R 3.4.4. for Windows.

88 Many variables had a very limited number of respondents' answers corresponding to
89 them (such as distance to and knowledge of medical facility). Therefore, the number of
90 variables that were used in this study was restricted in order to preserve the number of cases
91 available for the logistic regression. The number of variables that were non-significant and/or
92 less prolific in the literature compared to the other variables was also limited in order to retain
93 the power of the logistic regression, especially when there was evidence of collinearity in the
94 model. Since the asthma and other lung condition variables have similar symptoms to TB and
95 are both representative of access to healthcare, they have been omitted from the logistic
96 regression due to their redundancy.

97 Stress and education level are often overshadowed by other, well-known risk factors (e.g.,
98 HIV), so less attention has been given to these risk factors. Due to stress and education level
99 being underexplored in the existing literature, these variables were examined with particular
100 attention. In this study, stress is represented by the responses to the survey question “My job
101 involves a lot of stress”, with 4 different answers pertaining to level of agreement with this
102 statement. In order to compare high and low levels of stress, a category (‘High’) was formed for
103 the 2 highest stress levels. Similarly, a category (‘Low’) was formed for the two lowest stress
104 levels.

Variable Selection

105 The dependent variable, corresponding to the survey question “Has a
106 doctor/paramedic/nurse/midwife ever told you that you had TB?” (TB Diagnosis Status) is
107 used as the indicator of TB cases for the analysis. Due to TB’s non-specific symptoms,
108 misdiagnoses may have occurred, especially in cases where TB infection was not
109 bacteriologically confirmed. Furthermore, TB infection may remain undiagnosed, perhaps due
110 to latent infection (which is asymptomatic), or a lack of access to diagnostic healthcare.
111 Selection of explanatory variables was based on existing literature, which highlights age,
112 smoking, malnutrition, HIV/AIDS, body mass and poverty/impooverished living conditions as
113 the predominant risk factors (Duarte et al., 2018; Keflie et al., 2018). Variables corresponding
114 to age and smoking were readily available, but HIV data were missing. In the absence of clinical
115 nutrition data, a variable pertaining to how satisfied the respondents were with the adequacy
116 of the level of their food consumption was used; this acts as a proxy for both nutrition and body
117 mass. About two thirds of responses for annual salary data were missing, so a variable relating
118 to where the majority of household members went to the toilet was also used — this acts as a
119 proxy for impoverished living conditions/hygiene. Education level was considered because,
120 although it is typically overlooked, there is some evidence that it may have a considerable effect
121 on health (Baker et al., 2011). Stress at work was also used to investigate the apparent
122 association between stress and TB (Morey et al., 2015; Simandan, 2017a). Communicable
123 diseases in general are associated with crowded conditions and urban areas, where people are
124 often in close contact for extended periods of time. Therefore, variables corresponding to the
125 number of people living in each household, and whether the household resides in an urban or
126 a rural area were used. With regards to occupational risk factors, TB is typically associated with
127 working in travel or healthcare industries, so the respondents’ sectors of work were
128 considered. Since asthma and other lung conditions are pulmonary diseases, their relationships
129 to TB (which is typically a pulmonary infection) were investigated. The following remaining
130 variables were chosen to be investigated because they relate to health or disease
131 transmission/diagnosis in general: gender (Nhamoyebonde & Leslie, 2014), knowledge
132 of/distance from medical/health facilities, and health benefit/insurance (O'Donnell, 2007).
133

Results

Cross-tabulation, Chi-Square tests (of association) and ANOVA

134 To assess the relationships between the explanatory variables and TB, Chi-Square tests (for
135 categorical variables) and ANOVA (for numerical variables) were utilised alongside a cross-
136 tabulation. The results are shown in Table 1 overleaf.

137 The categorical variables: age, stress, gender, work sector, asthma, other lung conditions,
138 health benefit or insurance, and rural or urban area were found to be significantly associated
139 with TB Diagnosis ($p < 0.05$ in Chi-Square tests) in this study.

140 The non-significant variables in this study were : cigarette consumption, education level,
141 food consumption satisfaction, health facility location knowledge, annual salary, number of
142 people living at household, toilet used by household occupiers, and distance from medical
143 facility ($p > 0.05$ in Chi-Square tests or ANOVA).

Logistic Regression

144 The results of the logistic regression with 11 variables, 9725 cases, and a Hosmer-Lemeshow
145 p value of 0.679 are shown in Table 2 overleaf. These results should be interpreted with the
146 limitations or assumptions of logistic regression in mind; for example, a uniform relationship
147 between the explanatory variables and the dependent variable is assumed (Ranganathan et al,
148 2017). The Hosmer-Lemeshow p value of 0.679 (> 0.05) suggests that the model fits the data
149 rather well. However, this metric should be interpreted with caution due to its limitations; for
150 example, it tends to have low power (Hosmer et al., 2013).

151 From the logistic regression, the significant predictors of being diagnosed with TB are stress at
152 work, living in a rural area, age, and having health benefit or insurance ($p < 0.05$).

Individual-level Risk Factors

153 The odds ratio (OR) of 2.76 for the 44+ age group suggests that middle-aged or elderly citizens
154 are 276% as likely to have been diagnosed with TB than very young people (14-30). Cigarette
155 consumption has an OR of 1.00 and is not significant, suggesting that, at least according to these
156 results, it is a poor predictor for being diagnosed with TB. Education level is difficult to interpret
157 here due to the various categories and large standard errors which led to large confidence
158 intervals. At a first glance it looks like those with higher levels of education than the reference
159 category have lower chances of contracting and being diagnosed with TB (each OR < 1: 0.67,
160 0.29, 0.40, 0.87). However, when considering the ORs CI, it is clear that the association is not
161 significant here. With regards to food consumption (satisfaction), consuming an 'adequate' or
162 more than adequate amount (rather than a less than adequate amount) of food appears to
163 marginally alter the odds of being diagnosed with TB by factors of 1.13 and 0.98 respectively,
164 implying that those with less than adequate or more than adequate food consumption are at a
165 slightly lower risk of contracting TB. However, the authors expected that increased food
166 consumption would lower the risk of TB, since low body mass is a risk factor for TB. The
167 association is also not significant in this case. The OR for gender is just slightly greater than 1
168 (1.07) and is not significant in this study. Having health benefit or insurance increases the odds
169 of successfully being diagnosed with TB by a factor of 1.53 (1.01, 2.34); this variable probably
170 indicates improved surveillance rather than being a risk factor for contracting TB itself. From
171 this study, there is a clear association between TB diagnosis and (occupational) stress; people
172 with higher levels of stress at work appear to be 2.34 (1.43, 3.83) times as likely to be diagnosed
173 with TB

Household-level Risk Factors

174 The number of household occupiers variable has an OR of 1.05 and was not found to be
175 associated with TB Diagnosis Status in this study. The waste disposal system appears to have
176 some effect on the chance of being diagnosed with TB; those using toilets without a septic tank
177 are 1.30 times as likely to be diagnosed as those using toilets with septic tanks. Using a toilet
178 with a septic tank appears to have little impact on TB diagnosis compared to the use of 'other'
179 facilities (OR=0.97).

Community-level Risk Factors

180 In this study, living in a rural area raised the odds of being diagnosed with TB by a factor of
181 1.80, and this effect is significant. Sector of work appears to have some effect on the chances of

182 being diagnosed with TB, although this effect is not significant according to these results. The
183 odds ratios of 0.74 and 0.63 suggest that those working in agricultural, mining, manufacturing,
184 electrical or construction industries are relatively higher risk occupations compared to the
185 other areas of work considered.

Discussion and Conclusion

186 The purpose of the study was to investigate several potential risk factors for tuberculosis in
187 Indonesia, especially behavioural or psychological risk factors. The publicly available survey
188 data were investigated using statistical methods alongside appropriate software to investigate
189 the relationships between the explanatory variables and the dependent variable (TB Diagnosis
190 Status). Some of the results agreed with contemporary literature, whereas other results were
191 unexpected.

Individual-level Risk Factors

192 The results show a significant association between age and TB Diagnosis Status. The average
193 age of those who had not been diagnosed with TB was roughly 5 years younger than those who
194 had been diagnosed. This is expected; the research conducted by Pawelec (2018) states that
195 older people have a higher risk of contracting diseases due to gradual weakening of the immune
196 system with increasing age. The chances of having been diagnosed with TB appeared to be
197 roughly the same for 14-30 and 31-43s year olds (OR=1.10), which is also to be expected;
198 immune function tends to only begin decreasing substantially at about 50-60 years of age. The
199 44+ age group, predictably, had much higher odds (OR=2.76) of being diagnosed with TB
200 compared to the other age groups.

201 In this study the relationship between cigarette consumption (smoking) and TB Diagnosis
202 Status contradicted the literature (Duarte et al., 2018) — there did not appear to be any
203 significant relationships between the variables, and the values for cigarette consumption
204 between the TB Diagnosis Status categories were very similar (12.35 and 12.23 for those who
205 had or had not been diagnosed with TB, respectively). This result disagrees with the global
206 consensus that smoking significantly influences contraction of TB (WHO, 2007). However,
207 there is some evidence that in the Indonesian context, the effect of smoking on TB is not
208 significant (Sahiratmadja & Nagelkerke, 2016). It has been shown that smoking causes damage
209 to the throat, lungs, and cilia (which help to remove pathogens from the immune system) (Bates
210 et al., 2007); one would therefore have expected that smoking would significantly impact TB
211 Diagnosis Status. Even when comparing smokers to non-smokers (past and present), there was
212 no significant association; this suggests that smoking may not be so influential as a risk factor,
213 at least in Indonesia. However, it's likely that some people reduced their cigarette consumption
214 upon experiencing symptoms of TB or being diagnosed with TB; smoking exacerbates TB
215 symptoms. Furthermore, since, in Indonesia, smoking is legal in both private and government
216 offices, restaurants, and pubs, many people would be affected by passive smoking, which was
217 not accounted for in the survey. Therefore, it's not possible to understand the relationship
218 between smoking and TB without further analysis.

219 Since education can have a prominent impact on health (Baker et al., 2011), the highest
220 education level achieved was investigated as a predictor for TB Diagnosis Status. However, no
221 significant association was found. This may be due to the lack of specificity in the data
222 regarding subjects studied and academic attainment. For example, people who studied health
223 or biological sciences at high school were in the same category, regardless of attainment.
224 Additionally, people studying subjects unrelated to health and disease transmission at the same
225 level (e.g., at university) were in the same category as those studying the aforementioned

226 subjects. Therefore, a lot of relevant information, which may have acted as predictors for TB,
227 was not accounted for.

228 Malnutrition and body mass are said to be prominent risk factors for tuberculosis and
229 diseases in general (Keflie et al., 2018), especially considering the importance of vitamins,
230 minerals, carbohydrates and proteins for maintaining a strong immune system. As a proxy for
231 malnutrition and body mass, a survey question regarding the respondent's satisfaction with
232 their food consumption was used. However, no clear association between this variable and TB
233 Diagnosis Status was found. Data directly relating to nutrition (for example, blood test results
234 for vitamin A and zinc) and body mass (e.g., scale readings) would probably have led to a better
235 investigation into the relationships that nutrition and body mass have with TB.

236 Gender is also an interesting factor, and it could be argued that it is a behavioural risk factor
237 — in patriarchal societies, like Indonesia, men constitute a considerably larger proportion of
238 the workforce than women (Organisation for Economic Co-operation and Development, 2018),
239 who are likely to stay at home to look after children. Therefore, men generally have
240 considerably more exposure to TB. Despite that, no significant association between gender and
241 TB Diagnosis Status was found in this study. These results disagree with numerous studies,
242 even if the 95% confidence interval contains the odds ratio between men and women, 1.61,
243 estimated in the study by Marçôaa (2018).

244 Health benefit or insurance is an excellent indicator for access to healthcare. The OR of 1.53
245 suggests that those with health benefit or insurance are significantly more likely to be
246 successfully diagnosed with TB than those without. It may be noted that the Indonesian
247 government introduced universal health coverage (UHC) in 2014 to improve access to health
248 care.

249 Stress at work has been a variable of great interest in this study, but it has often been
250 overlooked previously. There is minimal consensus and various schools of thought regarding
251 the classification of events as stressful. One perspective of particular note, arising from
252 occupational stress literature is that a stressful event is one where demands exceed resources.
253 However, many researchers define stressful events differently (e.g., as events consensually
254 seen as harmful or threatening) (Cohen et. al, 2019). In this study, the data is from respondents
255 who individually, subjectively appraised their perceived stress levels (psychological stress) at
256 work. This variable should be considered in the context of allostatic load theory, which aims to
257 delineate the physiological mechanisms which lead from stressors experienced to ill health
258 (Simandan, 2010), all the while offering precise terminology free of the inherent ambiguity of
259 the word 'stress'. The substantial evidence that there is an association, and possibly a causal
260 link between stress (especially allostatic load) and TB, both due to weakened immunity, (Morey
261 et al., 2015) and reduced ability to carry out daily duties (Simandan, 2017a) prompted the need
262 for exploration of pertinent data. According to the results of this study, there is indeed a
263 significant association between (occupational) stress and TB Diagnosis Status, and stress at
264 work is a prominent predictor for contracting TB. The high odds ratio (2.34) suggests that
265 appropriate control measures should, quite urgently, be implemented. In the context of
266 occupational stress, there is probably an inverse relationship between chronicity and intensity,
267 which may be important to consider for future research directions, especially when considering
268 the relationship between chronicity of stress and immune function (Dhabir & McEwen, 1999).

269 Despite TB's sobriquet of 'poor man's disease', the results do not reveal a significant
270 relationship between annual salary amongst groups with distinct diagnosis statuses. In fact,
271 dissimilarly to the study undertaken by Bhunu et al.(2012), people diagnosed with TB seemed
272 to be wealthier (they had a higher average annual salary) than those who hadn't been
273 diagnosed. This could potentially be explained by difficult circumstances (e.g., due to having to
274 repay debts, or financially assisting family members) resulting in living conditions remaining

275 or becoming impoverished. Additionally, this variable doesn't provide data on total income
276 (just income from the respondent's main job), and the respondent may have been diagnosed
277 with TB prior to getting a higher-paying job.

278
279

280 According to the Chi-Square tests, other lung conditions and asthma were found to be
281 significantly associated with TB Diagnosis Status. However, this may be due to people with
282 asthma or other (known) lung conditions being closely monitored by healthcare professions,
283 so this association may pertain to surveillance.

Household-level Risk Factors

284 To investigate the effect of overcrowding or population density on TB Diagnosis Status, the
285 number of people living within each household was considered. However, no statistically
286 significant differences between the means for this variable amongst the TB Diagnosis Status
287 categories were found in this study. Additionally, this variable was not a significant predictor
288 in the logistic regression, but logistic regression's assumption of relational uniformity is
289 important to note here — there may have been, for example, more cases of TB at lower values
290 (due to, e.g., struggling single parent families) and at higher values (due to overcrowding), or
291 particular ranges of values with many cases of TB. A lack of ventilation and airflow is also said
292 to contribute to TB transmission in households (Duarte et al., 2018), although there were no
293 data available to investigate this. There may have been more interesting results if there were
294 data on community-level population density.

295 Due to the importance of investigating sanitation and poverty levels, variables relating to
296 where household occupiers went to the toilet were considered. Unlike annual salary, there
297 were considerably fewer missing data for this variable. However, no significant association
298 between these variables and TB Diagnosis Status were found; this, alongside the investigation
299 of annual salary, suggests that poverty may not be as prominent of a risk factor as the existing
300 literature (Fuady et al., 2018) suggests.

Community-level risk factors

301 There is no clear consensus in the literature regarding whether living in an urban or rural
302 area has a significant impact on the likelihood of becoming infected with TB. Living in an urban
303 area has often been associated with crowdedness and pollution (Keller, 2018), whereas living
304 in a rural area is associated with having to pay medical expenses out of pocket and having to
305 travel long distances to arrive at medical facilities. Furthermore, rural areas are considerably
306 more likely to have farms, where bovine TB could spread to humans (Davis, 2000; Amo-Adjei,
307 2016). In principle, either living in an urban area or a rural area could potentially increase one's
308 susceptibility to TB, but from this study, those living in rural areas of Indonesia were
309 significantly more likely to be diagnosed with TB, and this may be due to UHC introduced in
310 2014 in Indonesia.

311 Sectors of work were investigated as risk factors. The literature states that people working in
312 travel or healthcare sectors are at a high risk of acquiring TB due to extensive exposure. From
313 the Chi-Square tests, there is a significant association between work sector and TB Diagnosis
314 Status, which aligns with the studies conducted by Rim & Lim (2014). However, inferences
315 regarding specific sectors of work were not made — the sample sizes would have been too
316 small to make these analyses meaningful.

Summary and Conclusion

317 In summary, several potential risk factors for TB Diagnosis Status were investigated using
318 statistical methods, providing a comprehensive overview of the risk factors for TB diagnosis,
319 expanding on previous analyses by including educational level and stress. Age, stress at work,
320 living in a rural area, and having health benefit or insurance were the most significant
321 predictors of TB Diagnosis Status, and these results are supported by the literature, although
322 stress is rarely explicitly discussed. What's interesting here is that most of these variables relate
323 to immune system deficiencies or vulnerabilities (and surveillance), rather than exposure to
324 the disease itself — this aligns with TB's reputation of being an 'opportunistic' disease (Barnes
325 et al., 1993). People with healthy immune systems will often be able to fight off the infection,
326 even if their exposure to TB is high (Fogel, 2015). Some results were unexpected, with cigarette
327 consumption and annual salary not being significantly different amongst TB Diagnosis Status
328 categories. Although several variables were analysed, it would have been beneficial to have had
329 even more variables to investigate, such as those relating to HIV status and body mass. Survey
330 questions directly related to knowledge of TB would also have been highly desirable.
331 Nonetheless, according to the Hosmer-Lemeshow test, the logistic model fits the data rather
332 well, so the model (as well as some other findings) may potentially be useful in real-world
333 scenarios, especially for investigations regarding the 13 Indonesian provinces in which the IFLS
334 5 survey was carried out.

335 The role of stress in these results is a pertinent one. The results may potentially be of
336 interest in the field of behavioural epidemiology and could prompt further research into stress
337 as a risk factor for TB (or other diseases). This research may also be of great interest to
338 employers and companies; one can see from the findings that stress at work is associated with
339 TB, and from the literature review it's clear that TB is detrimental to productivity and,
340 consequently, the Indonesian economy (Collins et al., 2017). It could therefore be highly
341 beneficial for companies to introduce schemes for alleviating the stress levels of their
342 employees. This work may also be of value to medical practitioners, academics, researchers or
343 centres for disease control for determining comparative TB risk in the absence of HIV data and
344 other data. As expected, age was found to be a prominent risk factor for TB, and these findings
345 may act as a catalyst for the implementation of interventions which prioritize care for elderly
346 citizens. This would also be applicable to those with asthma and other lung conditions. The fact
347 that TB was concentrated in people living in rural areas suggest that there is a great need for
348 additional affordable and accessible healthcare institutions to be established in these areas.
349 Indeed, the high basic reproduction number of TB (estimated to be 4.5 by Blower et al. (1995))
350 suggests that powerful control measure(s) would need to be implemented to eradicate this
351 persistent disease. Further studies should also be conducted to understand the nature of TB
352 risk factors; this could include undertaking multivariate analyses using the IFLS 5 data, or
353 analyses of other variables using alternative data sets, and comparisons of the analyses of
354 similar datasets between different countries or regions. Developing a logistic model tree (or
355 other suitable and sufficiently complex models) would also be an excellent way of expanding
356 upon this work, but this was not within the scope of this study.

Limitations

The questionnaires and resultant secondary data obtained from RAND's IFLS 5 were not tailored specifically to the study, and lacked pertinent information directly relating to HIV, blood pressure, body mass, malnutrition and knowledge of TB. This study was liable to some frame bias; the reliance on household level enumeration excluded traveller or slum dwelling populations which may not have been enumerated and, worse yet, are more likely to be at an

elevated risk of developing active TB. Furthermore, only 0.01% of the Indonesian population was surveyed, from 13 out of the 27 Indonesian provinces. People with extreme cases of TB (especially in the case of TB-HIV co-infection) may have been too unwell (and possibly hospitalised) to answer the survey questions. Furthermore, the survey question relating to TB Diagnosis Status was not restricted to any time period, so the interaction between TB and its predictors could not be fully ascertained.

Acknowledgements

The authors would like to thank RAND Corporation for the open-access survey data, and for assistance with handling the data files.

Ethical Approval

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008

Declaration of Interest

The authors have no conflicts of interest to declare.

Funding

This research received no specific grant from any funding agency, commercial entity or not-for-profit organization.

References

- Amo-Adjei J** (2016) Individual, household and community level factors associated with keeping tuberculosis status secret in Ghana. *BMC public health* **16**(1), 1196.
- Baker DP, Leon J, Smith-Greenaway EG, Collins J and Movit M** (2011) The education effect on population health: a reassessment. *Population and development review* **37**(2), 307–332.
- Barnes PF, Le HQ and Davidson PT** (1993) Tuberculosis in patients with HIV infection. *The Medical clinics of North America* **77**(6), 1369-1390.
- Bates MN, Khalakdina A, Pai M, Chang L, Lessa F and Smith KR** (2007) Risk of tuberculosis from exposure to tobacco smoke: a systematic review and meta-analysis. *Archives of internal medicine* **167**(4), 335–342.
- Bhunu C, Mushayabasa S and Smith R** (2012) Assessing the effects of poverty in tuberculosis transmission dynamics. *Applied Mathematical Modelling* **36**(9), 4173–4185.
- Blower SM, Mclean AR, Porco TC, Small PM, Hopewell PC, Sanchez MA and Moss AR** (1995) The intrinsic transmission dynamics of tuberculosis epidemics. *Nature medicine* **1**(8), 815-821.
- Bock P and Cox H** (2017). Acute care—an important component of the continuum of care for HIV and tuberculosis in developing countries. *Anaesthesia* **72**(2), 147–150.
- Cohen S, Murphy ML and Prather AA** (2019) Ten surprising facts about stressful life events and disease risk. *Annual review of psychology* **70**, 577-597.

Collins D, Hafidz F and Mustikawati D (2017) The economic burden of tuberculosis in indonesia. *The International Journal of Tuberculosis and Lung Disease* **21**(9), 1041–1048.

Daniel TM (2006) The history of tuberculosis. *Respiratory Medicine* **100**(11), 1862 – 1870.

Davis AL (2000) A historical perspective on tuberculosis and its control. In Reichman, LB and Earl, SH (eds) *Tuberculosis: a comprehensive international approach*. CRC Press, pp. 3–54.

de Oliveira HB and Moreira Filho DDC (2000) Tuberculosis recurrence and its risk factors. *Pan American Journal of Public Health* **7**(4), 232-241.

Dhabhar FS and McEwen BS (1999) Enhancing versus suppressive effects of stress hormones on skin immune function. *Proceedings of the National Academy of Sciences*, **96**(3), 1059-1064.

Duarte R, Lönnroth K, Carvalho C, Lima F, Carvalho A, Muñoz-Torrico M and Centis R (2018) Tuberculosis, social determinants and co-morbidities (including HIV). *Pulmonology* **24**(2), 115 – 119.

Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC (1999) Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. *Jama* **282**(7), 677–686.

Fuady A, Houweling TA, Mansyur M and Richardus JH (2018) Catastrophic total costs in tuberculosis-affected households and their determinants since Indonesia's implementation of universal health coverage. *Infectious diseases of poverty* **7**(1), 3.

Fogel N (2015) Tuberculosis: a disease without boundaries. *Tuberculosis* **95**(5), 527–531.

Hosmer Jr DW, Lemeshow S and Sturdivant RX (2013) *Applied logistic regression* (Vol. 398). John Wiley & Sons.

Keflie TS, Samuel A, Woldegiorgis AZ, Mihret A, Abebe M and Biesalski HK (2018) Vitamin A and zinc deficiencies among tuberculosis patients in Ethiopia. *Journal of clinical tuberculosis and other mycobacterial diseases* **12**, 27-33.

Keller PM (2018) Urban transmission of tuberculosis in china. *The Lancet Infectious Diseases*, **18**(7), 706 – 707.

Marçôaa R (2018) Tuberculosis and gender – factors influencing the risk of tuberculosis among men and women by age group. *Pulmonology* **24**(3), 199-202.

Mason PH, Roy A and Singh P (2017) Reciprocity-building and the importance of interdisciplinary collaboration in tuberculosis research. *Journal of biosocial science* **49**(4), 559-562.

Mason PH, Roy A, Spillane J and Singh P (2016) Social, historical and cultural dimensions of tuberculosis. *Journal of biosocial science* **48**(2), 206-232.

Morey JN, Boggero IA, Scott AB and Segerstrom SC (2015) Current directions in stress and human immune function. *Current opinion in psychology* **5**, 13-17.

O'Donnell O (2007) Access to health care in developing countries: breaking down demand side barriers. *Cadernos de saude publica* **23**(12), 2820-2834.

Organisation for Economic Co-operation and Development (2018) Employment: Labour Force Participation, by Sex and Age Group. URL: <https://stats.oecd.org/index.aspx?queryid=54741> (accessed 21st May 2020).

Pawelec G (2018) Age and immunity: what is “immunosenescence”? *Experimental gerontology* **105**, 4-9.

RAND (2018) RAND IFLS-5 Survey Description. URL: <https://www.rand.org/well-being/social-and-behavioral-policy/data/FLS/IFLS/ifls5.html> (accessed 21st May 2020).

Ranganathan P, Pramesh CS and Aggarwal R (2017) Common pitfalls in statistical analysis: Logistic regression. *Perspectives in clinical research* **8**(3), 148.

Rim KT and Lim CH (2014) Biologically hazardous agents at work and efforts to protect workers' health: A review of recent reports. *Safety and Health at Work* **5**(2), 43 – 52.

Sahiratmadja E and Nagelkerke N (2016) Smoking habit as a risk factor in tuberculosis: a case-control study. *Universa Medicina* **30**(3), 189-196

Shajahan R, Navaratnam P, Kasinathan G, Kadirvelu A and Pillai N (2016) Predictors of re-emerging tuberculosis: a review. *Open Access Library Journal* **3**(3), 1-18.

Simandan D (2010) On how much one can take: relocating exploitation and exclusion within the broader framework of allostatic load theory. *Health & Place* **16**(6), 1291-1293.

Simandan D (2017a) Considering neoliberalism, contempt and allostatic load in the social dynamics of tuberculosis. *Journal of biosocial science* **49**(4), 557-558.

Simandan D (2017b) Wisdom and the path-dependent politics of biomedical research. *Journal of biosocial science* **49**(4), 563-565.

Nhamoyebonde S and Leslie A (2014) Biological differences between the sexes and susceptibility to tuberculosis. *The Journal of infectious diseases* **209**(suppl_3), S100-S106.

World Health Organization (WHO) (2007) A WHO/The Union monograph on TB and tobacco control: joining efforts to control two related global epidemics. URL: <https://apps.who.int/iris/handle/10665/43812> (accessed 21st May 2020).

World Health Organization (WHO) (2018) Global tuberculosis report 2018. URL: https://www.who.int/tb/publications/global_report/en/ (accessed 21st May 2020).

Zvonareva O, van Bergen W, Kabanets N, Alliluyev A and Filinyuk O (2019) Experiencing syndemic: disentangling the biosocial complexity of tuberculosis through qualitative research. *Journal of biosocial science* **51**(3), 403-417.

Table 1. A cross-tabulation for each explanatory variable against TB Diagnosis Status.

Explanatory Variables	Categories	Diagnosed with TB, n(%)	Not diagnosed with TB, n(%)	Total, n(%)	P value
Individual-Level Variables:					
Age	14-30	85(0.69)	12229(99.31)	12314(100)	0.000
	31-43	105(0.99)	10525(99.01)	10630(100)	
	44+	138(1.22)	11160(98.78)	11298(100)	
Cigarette Consumption (cigar/ettes per day) ^a		12.35(8.04)	12.23(8.56)	12.23(8.56)	0.876
Diagnosed with Asthma	Yes	45(4.5)	956(95.5)	1001(100)	0.000
	No	283(0.85)	32963(99.15)	33246(100)	
Diagnosed with other lung condition	Yes	43(6.96)	575(93.41)	618(100)	0.000
	No	284(0.84)	33342(99.16)	33626(100)	
Education Level	Elementary/Kindergarten/None	108(1.05)	10148(98.95)	10256(100)	0.108
	High School	149(0.87)	16979(99.13)	17128(100)	
	Adult Education / Pesantren	3(2.33)	126(97.67)	129(100)	
	College/University	6(1.75)	336(98.25)	342(100)	
	Other	49(1.06)	4559(98.94)	4608(100)	
Food Consumption Satisfication	Less than adaqueate	39(0.97)	3965(99.03)	4004(100)	0.586
	Just adaqueate	161(0.87)	18412(99.13)	18573(100)	
	More than adaqueate	87(0.98)	8773(99.02)	8860(100)	
Gender	Male	183(1.12)	16146(98.88)	16329(100)	0.002
	Female	145(0.81)	17769(99.19)	17914(100)	
Health Benefit or Insurance	Yes	202(1.21)	16507(98.79)	16709(100)	0.000
	No	126(0.72)	17348(99.28)	17474(100)	
Health Facility Location Knowledge	Yes	76(1.54)	4860(98.46)	4936(100)	0.407
	No	13(1.71)	746(98.29)	759(100)	
Salary, Annual(rupiah) ^a		25074366.34 (30218003.89)	20473061.51 (30438212.77)	30438024.89 (273838.87)	0.130
Stress at Work	High	29(1.33)	2151(98.67)	2180(100)	0.021
	Low	179(0.87)	20438(99.13)	20617(100)	
Household-Level Variables:					
Number of people at household(#) ^a		4.26(178)	4.24(1.91)	4.24(1.91)	0.862
Toilet used by Householders	Toilet with Septic Tank	245(0.96)	25343(99.04)	25588(100)	0.410
	Toilet without Septic Tank	22(0.77)	2851(99.23)	2873(100)	
	Other	61(1.06)	5677(98.94)	5738(100)	
Community-Level Variables:					
Medical Facility, Distance from(km) ^a		8.11(34.87)	7.32(38.27)	7.33(38.21)	0.858
Urban or Rural area	Urban	223(1.1)	20063(98.9)	20286(100)	0.001
	Rural	105(0.75)	13858(99.25)	13963(100)	
Work Sector	Agriculture/Mining/Manufacture/ Electrical/Construction	80(0.71)	11122(99.29)	11202(100)	0.001
	Wholesale/Transportation/ Finance/Social Services	131(1.02)	12668(98.98)	12799(100)	
	Other	8(2.39)	327(97.61)	335(100)	
^a Mean(SD)					

With p values for the ANOVA or Chi-Square tests.

Table 2. Results from a binary logistic regression (predicting TB) with odds ratios

Explanatory Variables	OR	95% CI for OR		P value
		Lower	Upper	
Individual-Level Variables:				
Age (ref. category = '14-30')				0.01
Age(31-43)	1.10	0.69	1.74	0.69
Age(44+)	2.76	1.44	5.29	0.00
Cigar/ette Consumption	1.00	0.98	1.02	0.93
Education Level (ref. category= 'Elementary School or Kindergarten or None')				0.38
Education Level (High School)	0.67	0.40	1.14	0.14
Education Level (Adult Education or Pesantren)	0.29	0.04	2.21	0.23
Education Level (College or University)	0.40	0.09	1.74	0.22
Education Level (Other)	0.87	0.40	1.88	0.71
Food Consumption (ref.category = 'Less than Adequate')				0.82
Food Consumption (Adequate)	1.13	0.62	2.06	0.69
Food Consumption (More than Adequate)	0.98	0.49	1.98	0.96
Gender (ref.category = 'Female')	1.07	0.33	3.47	0.91
Health Benefit or Insurance (ref.category = 'Yes')	1.53	1.01	2.34	0.05
Stress at Work (ref.category = 'Low')	2.34	1.43	3.83	0.00
Household-Level Variables:				
Number of Household Occupiers	1.05	0.94	1.18	0.41
Toilet used by Householders (ref.category= 'toilet with septic tank')				0.81
Toilet used by Householders (toilet without septic tank)	1.31	0.56	3.04	0.53
Toilet used by Householders (other)	0.97	0.54	1.74	0.93
Community-Level Variables:				
Urban or Rural Area (ref.category = 'Urban')	1.80	1.10	2.95	0.02
Work Sector (ref. category= 'Agriculture/ Mining/Manufacturing/Electrical/ Construction')				0.38
Work Sector (Wholesale/Transportation/ Finance/Social Services)	0.74	0.47	1.15	0.18
Work Sector (other)	0.63	0.15	2.68	0.53
Constant	14.45			0.01