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## Pulmonary tuberculosis risk factors in Almaty, Kazakhstan

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<b>Corresponding Author:</b>	Baurzhan Zhussupov, MS Almaty, KAZAKHSTAN
<b>Corresponding Author Secondary Information:</b>	
<b>Corresponding Author's Institution:</b>	
<b>Corresponding Author's Secondary Institution:</b>	
<b>First Author:</b>	Baurzhan Zhussupov, MS
<b>First Author Secondary Information:</b>	
<b>Order of Authors:</b>	Baurzhan Zhussupov, MS Sabrina Hermosilla Assel Terlikbayeva Angela Aifah Xin Ma Zhaxybay Zhumadilov Tleukhan Abildayev Meruyert Darisheva Kulzhan Berikhanova Sandro Galea Neil Schluger Nabila El-Bassel
<b>Order of Authors Secondary Information:</b>	
<b>Abstract:</b>	<p><b>Objectives</b> This study examines the association between social and behavioral drivers of tuberculosis (TB) incidence in Almaty Oblast, Kazakhstan.</p> <p><b>Methods</b> We used a matched case-control design to estimate the role of factors for acquiring TB among 324 individuals. Participants included 110 TB index cases with newly detected pulmonary TB, 107 household contacts of index cases and 107 community controls.</p> <p><b>Results</b> TB cases were more likely to be younger, recent smokers and have diabetes, when compared to household controls. Between TB cases and community controls, TB is significantly associated with age, non-married family status, living in rented home, recent smoker, and having diabetes. Comparing TB cases and with both control groups, we found that foreign birth was also associated with incident TB case status.</p> <p><b>Conclusions</b> Our findings confirm the role of modifiable risk factors for TB in Kazakhstan; highlighting the importance of developing interventions addressing social determinants and proximate risk factors for high TB burden regions.</p>

<b>Suggested Reviewers:</b>	Gombogaram Tsogt tsogt@who.uz Dr. Tsogt has worked in Central Asia including Kazakhstan in TB-related areas.
	Samantha Huffman shuffman@alum.emory.edu
	Susan van den Hof vandenHofS@kncvtbc.nl

**Title: Pulmonary tuberculosis risk factors in Almaty, Kazakhstan**

B. Zhussupov <sup>1,\*</sup>, §, S. Hermosilla <sup>2,\*</sup>, A. Terlikbayeva <sup>1</sup>, A. Aifah <sup>2</sup>, X. Ma <sup>2</sup>, Z. Zhumadilov <sup>3</sup>, T. Abildayev <sup>4</sup>, M. Darisheva <sup>1</sup>, K. Berikhanova <sup>3</sup>, S. Galea <sup>2</sup>, N. Schluger <sup>2</sup>, N. El-Bassel <sup>2</sup>.

<sup>1</sup> Columbia University Global Health Research Center of Central Asia; 102 Luganskogo Street, Almaty 050051, Kazakhstan

<sup>2</sup> Columbia University in the City of New York; 722 West 168<sup>th</sup> Street, Room 507, Box 13, New York, NY 10032, United States of America

<sup>3</sup>Center for Life Sciences Nazarbayev University; 5 Kabanbay Batyr Street, Astana 010000, Kazakhstan

<sup>4</sup>National Center for Tuberculosis in Kazakhstan; 5 Bekhodjin Street, Almaty 050059, Kazakhstan

**Corresponding Author:** Baurzhan Zhussupov, 102 Luganskogo Street, Almaty 050051, Kazakhstan; baurzhan.zhussupov@gmail.com; tel: +7(727) 2646930; fax: ext. 112

## **Abstract**

### **Objectives**

This study examines the association between social and behavioral drivers of tuberculosis (TB) incidence in Almaty Oblast, Kazakhstan.

### **Methods**

We used a matched case-control design to estimate the role of factors for acquiring TB among 324 individuals. Participants included 110 TB index cases with newly detected pulmonary TB, 107 household contacts of index cases and 107 community controls.

### **Results**

TB cases were more likely to be younger, recent smokers and have diabetes, when compared to household controls. Between TB cases and community controls, TB is significantly associated with age, non-married family status, living in rented home, recent smoker, and having diabetes. Comparing TB cases and with both control groups, we found that foreign birth was also associated with incident TB case status.

### **Conclusions**

Our findings confirm the role of modifiable risk factors for TB in Kazakhstan; highlighting the importance of developing interventions addressing social determinants and proximate risk factors for high TB burden regions.

## Introduction

Tuberculosis (TB) is a leading cause of global morbidity and mortality and remains an acute threat to global public health (Organization 2011). While there has been a recent leveling off of the global TB burden of disease, the increase in TB cases after the dissolution of the Soviet Union has been well documented in the region (Ríos 2009). Multidrug-resistant TB (MDR-TB), a major public health problem that threatens progress made in TB control and care programs, has also been on the rise in Kazakhstan (Ewing 1984). While TB notification rates have declined in Kazakhstan in recent years, there is still a lack of understanding into the specific mechanisms that are driving TB transmission locally (Terlikbayeva et al. 2012). This study explores the drivers of incident TB case notification in Almaty Oblast, Kazakhstan in 2012.

Tuberculosis incidence and prevalence have stabilized in recent years in Kazakhstan, (Falzon et al. 2013; Terlikbayeva et al. 2012) with a reported incidence of 81.7 cases per 100,000 population and a prevalence of 143.5 cases per 100,000 population in 2010 (Terlikbayeva et al. 2012). MDR-TB continues to rise with an incidence of 10.7 cases per 100,000 population and prevalence of 62.5 cases per 100,000 population in 2012 (Ewing 1984). The national tuberculosis program (NTP) oversees the surveillance and care of patients in Kazakhstan. The NTP provides diagnostic and treatment services to all legal residents of Kazakhstan at no cost through a network of microscopy laboratories, primary health care centers and district level TB clinics (Ewing 1984). Despite improvements in laboratory capacities to detect resistance to common anti-tuberculosis drugs, problems remain with diagnosis of incident TB cases (Terlikbayeva et al. 2012). This process has limited the control and treatment efforts in Kazakhstan; TB and MDR-TB are not currently distinguishable in early treatment phases.

Globally, epidemiologic research has identified many known drivers of TB, such as modifiable socio-behavioral factors including confined living conditions such as imprisonment, (Balabanova et al. 2011; Baussano et al. 2010; Editors et al. 2010; Stuckler et al. 2008; Vagenas et al. 2013; van den Hof et al. 2013; Vinkeles Melchers et al. 2013) migrant status, (Huffman et al. 2012; Rhodes et al. 1999; Terlikbayeva et al. 2012) cigarette

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3 smoking, (Altet-Gomez et al. 2005; den Boon et al. 2005; Lin et al. 2009; Maurya et al. 2002; Pednekar and  
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5 Gupta 2007) alcohol consumption, (Bumburidi et al. 2006; Fox and Menzies 2013; Murray et al. 2011;  
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7 Raviglione et al. 2012; Vagenas et al. 2013; Waitt and Squire 2011) and co-morbidity with HIV, (Mor et al.  
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9 2012; Rhodes et al. 1999; Schluger et al. 2013) diabetes, (Baker et al. 2011; Dooley and Chaisson 2009;  
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11 Goldhaber-Fiebert et al. 2011; Lonroth et al. 2009) and some mental health illnesses (Doherty et al. 2013).  
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13 Given limitations in known risk factor documentation among official surveillance channels, (Terlikbayeva et al.  
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15 2012) specific drivers of TB in Kazakhstan are still largely unknown.  
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21 Building on research conducted in many parts of the world on geographic heterogeneity of incident case  
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23 distribution,(Terlikbayeva et al. 2012) this study examines the association between tuberculosis and the social  
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25 and behavioral drivers of tuberculosis incidence in Almaty Oblast, Kazakhstan, an analysis that will inform  
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27 national and regional policy. We specifically investigated whether factors such as age, gender, socio-economic  
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29 status, confined living conditions and increased burden of co-morbidity would be associated with incident  
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31 tuberculosis.  
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## 36 **Methods**

### 37 **Sample**

38  
39 We used a matched case-control design to estimate the role of demographic, social, and behavioral factors of  
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41 acquiring TB by comparing index cases with household controls and randomly selected community controls.  
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43 Presented here are baseline data from Almaty oblast, the first completed region of an ongoing four-region  
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45 longitudinal study on drivers of tuberculosis in Kazakhstan. The sample consists of 324 individuals that were  
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47 divided into three groups: 110 TB index cases with newly detected pulmonary TB; 107 household contacts of  
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49 index participants; and 107 external community controls.  
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57 Index tuberculosis cases were defined as cases of pulmonary tuberculosis initially diagnosed within three  
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59 months from data collection. Other eligibility criteria were universal across all study groups and include that  
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3 participant: was at least 18 years old at study screening; had a permanent address and been residing there for  
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5 more than three months; had at least one other adult household member; had no plans to relocate in the next 12  
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7 months; spoke Russian or Kazakh fluently; did not have any severe psychiatric condition that could impede their  
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9 ability to provide informed consent, assessed by research assistants during screening; and did not have an illness  
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11 that was expected to be terminal within a year of screening, assessed by research assistants during screening.  
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13 Both household and community control participants had no previous diagnosis of pulmonary tuberculosis. The  
14  
15 household contact was matched with the index case by ethnicity. Community control participants were  
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17 randomly selected from households located near the TB index case. The Kish method was used to select a  
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19 household or community contact participant if more than one eligible contact was available in a selected  
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21 household or community contact participant if more than one eligible contact was available in a selected  
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23 household.  
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### 27 **Study sites**

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29 The study was conducted in six administrative regions of Almaty oblast (province) of Kazakhstan including  
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31 Alakolskiy, Balkhashskiy, Enbekshikazakhskiy, Jambyl'skiy, Sarkand'skiy regions and Kapchagay city. All new  
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33 TB cases (n=126) registered from June 2012 to January 2013 in these regions were prescreened, 110 of them  
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35 met the eligibility criteria and all agreed to participate in the study. The response rate for community and  
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37 household control was 97%, 107 controls from 110 indemnified ones agreed to participate in the study in both  
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39 groups.  
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### 45 **Case definitions**

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47 Consistent with World Health Organization (WHO) recommendations,(Organization 2011) individuals were  
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49 classified as TB cases if they were either: culture positive with positive smear examination confirmed by nucleic  
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51 acid amplification testing, or had clinical and radiographic presentation consistent with tuberculosis and  
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53 responded to treatment with anti-tuberculosis drugs. New cases of pulmonary tuberculosis were eligible for  
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55 inclusion to the study if diagnosed within three months of the prescreening date.  
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### 61 **Data collection**

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3 Socio-demographic, occupational, and behavioral information was collected from participants through a 60  
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5 minute audio computer assisted self-interview (ACASI). We used DatStat, a software package providing audio  
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7 and video presentation of questions and response options on a computer in both Kazakh and Russian (DatStat  
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9 2012). All interviews were conducted in private rooms with a research assistant available to assist participants,  
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11 as needed. The data were collected from September 2012 to March 2013.  
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16 Collected socio-demographic variables included age, gender, religion, profession, educational attainment,  
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18 marital status, family composition, and variables on income, food security, and home ownership. Behavioral  
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20 factors such as incarceration history, smoking history and status, alcohol consumption (both absolute and CAGE  
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22 dependency scale(Ewing 1984)), physical activity and body mass index (BMI) were measured to explore  
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24 associations and potential mechanisms of increased tuberculosis risk. Co-morbidity with hypothesized and  
25  
26 known risk factors such as diabetes, HIV, hepatitis C virus (HCV), and common cancerous conditions were also  
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28 assessed through interviews.  
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### 32 33 34 **Data analysis**

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36 We analyzed the data using R version 3.0.1. We used univariate associations to describe the study population  
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38 and assess variable level missingness. Religion had the highest variable level missingness (n=53, 16%), but was  
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40 not imputed or used in further analysis as over 80% of the respondents recorded the same religion and no  
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42 variation across populations was suggested. For categorical variables, we used frequencies and for continuous  
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44 variables we explored mean, median, and standard deviation estimates. We calculated bivariate Mantel-  
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46 Haenszel odds ratios (OR) to examine the associations between TB case status and control group status.  
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48 Conditional logistic regressions produced matched bivariate and multivariable effect estimates. We analyzed  
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50 three datasets for the final analysis, comparing index TB cases to their household matched control; to their  
51  
52 community control; and to both their household and community controls. Variables were considered for  
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54 inclusion into the final multivariable model if the bivariate OR estimate was significant at a 0.10 level or had  
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56 demonstrated epidemiological significance with incident TB diagnosis. Variables included in the final models  
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58 were age, sex, birth country, education, current employment, housing, and marital status, and incarceration,  
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3 smoking, alcohol abuse, diabetes and urinary tract or kidney disease history. The predictive accuracy of  
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5 regression models was evaluated through classification tables.  
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## 9 **Ethics**

10 The institutional review boards of Columbia University and the Ethics Review Board of the Kazakh School of  
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12 Public Health approved protocols of this study.  
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## 19 **Results**

20  
21 Table 1 shows the baseline characteristics of the complete study population. The mean age of participants was  
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23 40 (SD 13.58), slightly more female than male participants, predominantly Kazakh (by birth and ethnicity), and  
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25 Muslim. Twelve (3.7%) participants were ever incarcerated, 100 (30.9%) had smoked tobacco in the past twelve  
26  
27 months, and 298 (92.0%) have a low reported alcohol abuse score based on the CAGE alcohol dependency  
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29 scale. A total of 13 (4.0%) participants had a previous diabetes diagnosis, 8 (2.5%) had a previous HCV  
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31 diagnosis, 2 (0.8%) reported a positive HIV result, and 34 (10.5%) had a previous urinary tract or kidney disease  
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33 diagnosis.  
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39 More than half of incident TB cases interviewed (56%) were male, household and community control groups  
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41 were more likely to be female (34% and 48% respectively). Mean age of TB cases was 35 years; household and  
42  
43 community controls were 43 and 41 years respectively. Most study participants were Kazakh (more than 75%),  
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45 with Russians representing the next highest percentage in the sample (slightly more than 10%). The majority of  
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47 respondents in all groups were Muslims (more than 80%). Around 60% of cases and approximately 80% of  
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49 controls were married. One third of cases were never married.  
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55 Bivariate results are summarized in Table 2. Three models are presented: model 1 has incident TB cases  
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57 compared to household controls; model 2 has incident TB cases compared to community controls; and model 3  
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3 has incident TB cases compared to both control groups. We excluded BMI from the models as weight loss is  
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5 considered both a symptom and potential risk factor for TB diagnosis (Lonnroth et al. 2010).  
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10 Table 3 presents the final multivariable models. Model 1 (TB cases and household controls) results show that  
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12 TB cases were more likely to be younger (OR=11.36, 95% CI=1.67-77.49 for 18-24; OR=7.41, 95% CI=1.29-  
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14 42.52 for 25-34; OR=1.99, 95% CI=0.35-11.47 for 35-44; OR=1.5, 95% CI=0.23-9.6 for 45-54 years old),  
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16 smoked in past 12 months (OR=3.27, 95% CI=1.10-9.68) and had diabetes (OR=48.59, 95% CI=3.05-773.01).  
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18 Model 2 (TB cases and community controls) found that TB is significantly associated with age (18-24 as  
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20 compared to 55 plus, OR=5.13, 95% CI=1.01-26.18), non-married family status (OR=3.21, 95% CI=1.28-8.05),  
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22 living in rented house or flat (OR=5.15, 95% CI=1.39-19.05), smoking in past 12 months (OR=4.07,  
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24 95% CI=1.16-14.32), and having diabetes (OR=23.43, 95% CI=1.86-295.49). In addition to previously identified  
25  
26 associations, Model 3 (TB cases and both control groups) found that foreign birth (OR=3.16, 95% CI=1.08-9.29)  
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28 was also positively associated with incident TB case status. The first, second, and third models correctly predict  
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30 84.4%, 82.2%, and 75.8%, respectively, of participants' TB status.  
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## 37 **Discussion**

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39 Modifiable socio-behavioral risk factors and non-communicable co-morbid states are associated with incident  
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41 TB case status. Consistent with current literature (Lienhardt et al. 2001) our multivariable model showed strong  
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43 positive associations with young age, single marital status, and living in a rented house or apartment. Comparing  
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45 to household and community controls, incident TB cases are younger (less than 35 years old), tend to be single  
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47 and live separately in a rented house or apartment with roommates or friends. These factors are both reflective  
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49 of demographics and socio-economic status (SES). We assessed living conditions as a proxy for income and  
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51 SES as both concepts are relatively difficult to measure. In another study ownership of the house by the TB  
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53 case's family was a constant predictor of the TB case's SES (Lienhardt et al. 2001).  
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3 Smoking in the past 12 months was found as an independent risk factor for TB. We assessed smoking in the past  
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5 12 months as opposed to current smoking to avoid the effect of reduced smoking because of the TB disease  
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7 status. Other studies have also confirmed the association of smoking as a risk factor for TB morbidity and have  
8  
9 even gone further to show that it leads to a more severe progression of TB (Altet-Gomez et al. 2005; Maurya et  
10  
11 al. 2002). We found that a history of diabetes was a risk factor for TB in this population. This finding is  
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13 consistent with reports from other studies linking type 2 diabetes mellitus with TB (Baker et al. 2011; Dooley  
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15 and Chaisson 2009; Goldhaber-Fiebert et al. 2011). Data shows that type 2 diabetes mellitus not only increases  
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17 the risk of treatment failure and death among TB patients but also increases relapse (Baker et al. 2011).  
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23 Foreign-born individuals from a high TB burden country still retain higher risks of the disease development in  
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25 the future as compared to their household and community controls who were born in the host country (Huffman  
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27 et al. 2012). This could be the result of an exogenous re-infection or endogenous reactivation of original latent  
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29 infection (Lienhardt et al. 2001). As the NTP provides free TB care and treatment for all legal residents of  
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31 Kazakhstan, we included only migrants with temporary or permanent legal status as controls as only they would  
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33 be captured in the TB incident case registry used as the sampling frame base. Past migration was evaluated. A  
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35 statistically significant association between TB and immigration was found in Kazakhstan, the country with high  
36  
37 TB burden. Thus, the immigration could also be linked with TB through worsened living conditions. BMI was  
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39 significantly associated with TB in a univariate analysis but excluded from the final multivariable model based  
40  
41 on concerns around temporality in a cross-sectional study. Associations between BMI and TB have been shown  
42  
43 in a few studies (Lonroth et al. 2010). However, a complexity of mechanisms linking BMI and TB, and case-  
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45 control design of this study makes it difficult to determine temporality.  
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52 There are available interventions addressing social determinants and risk factors for TB globally. Innovative  
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54 integrated community and household socioeconomic interventions include food and cash transfers, microcredit,  
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56 microenterprise, vocational training, community mobilization, education, and psychosocial support (Rocha et al.  
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58 2011). Such interventions provided in economically deprived areas of Kazakhstan can address the social and  
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60 economic causes of vulnerability and could increase uptake of TB prevention and services. In Kazakhstan,  
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3 interventions such as food and money transfers, transportation vouchers, hygienic packages, and  
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5 accommodation have been made available for some TB patients. Legal and psychosocial support is currently  
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7 provided. As an effort to address other risk factors, tobacco control interventions, screenings for TB among  
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9 persons with diabetes and migrants are routinely implemented in Kazakhstan. However, availability and  
10  
11 coverage of these services have been unequal and inadequate. The preventive therapy with isoniazid is offered  
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13 only to children and HIV-positive individuals (Health 2011) .  
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18 This study has a number of strengths. It is the first case-control study in Kazakhstan assessing complex risk  
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20 factors for TB consistently and estimating the effects of these factors. All incident cases were approached for  
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22 inclusion into the study, further strengthening the applicability of our findings. Some limitations of our study  
23  
24 include: data was cross-sectional, which precludes us from determining the temporal relationships between risk  
25  
26 factors and TB infection; data collected are all self-reported, thus vulnerable to recall bias; and TB indexes had  
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28 to have a household control, i.e. TB indexes living alone or not having a stable living place were excluded from  
29  
30 the study. We have no reason to believe that these limitations would result in systematic error.  
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## 36 **Conclusions**

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39 This case-control study, for the first time in Kazakhstan, confirmed roles of major risk factors for TB: young  
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41 age, single marital status, living in rented apartment, smoking, diabetes and migration. These findings have  
42  
43 important TB prevention and control implications for the NTP. In addition to medical technologies focused on  
44  
45 stopping TB transmission, it is important to develop and strengthen existing interventions addressing social  
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47 determinants and proximate risk factors for TB. Mapping key population groups with high risk of tuberculosis  
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49 and offering preventive chemotherapy to selected groups at higher risk of converting from latent infection to  
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51 active disease, including diabetes patients and migrants, can be included into the NTP. Health system  
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53 strengthening and collaboration with other public health and social programs, such as tobacco and diabetes  
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55 control as well as migration policies should be part of the national TB prevention and control strategies.  
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## List of abbreviations used

<b>ACASI</b>	audio computer assisted self-interview
<b>BMI</b>	body mass index
<b>HCV</b>	hepatitis C virus
<b>MDR-TB</b>	multidrug-resistant TB
<b>NTP</b>	national tuberculosis program
<b>SES</b>	socio-economic status
<b>TB</b>	tuberculosis
<b>WHO</b>	World Health Organization

## Competing interests

None to declare

## References

- Altet-Gomez MN, Alcaide J, Godoy P, Romero MA, Hernandez del Rey I (2005) Clinical and epidemiological aspects of smoking and tuberculosis: a study of 13,038 cases *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 9:430-436
- Baker MA et al. (2011) The impact of diabetes on tuberculosis treatment outcomes: a systematic review *BMC medicine* 9:81 doi:10.1186/1741-7015-9-81
- Balabanova Y et al. (2011) Survival of civilian and prisoner drug-sensitive, multi-and extensive drug-resistant tuberculosis cohorts prospectively followed in Russia *PLoS one* 6:e20531
- Baussano I, Williams BG, Nunn P, Beggiato M, Fedeli U, Scano F (2010) Tuberculosis incidence in prisons: a systematic review *PLoS medicine* 7:e1000381
- Bumburidi E et al. (2006) Progress toward tuberculosis control and determinants of treatment outcomes--Kazakhstan, 2000-2002 *MMWR Morbidity and mortality weekly report* 55 Suppl 1:11-15
- DatStat (2012) DatStat Inc. vol Illume, 5.1.1 edn., Seattle
- den Boon S et al. (2005) Association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area *Thorax* 60:555-557 doi:10.1136/thx.2004.030924
- Doherty AM, Kelly J, McDonald C, O'Dwyer AM, Keane J, Cooney J (2013) A review of the interplay between tuberculosis and mental health *General hospital psychiatry* 35:398-406 doi:10.1016/j.genhosppsych.2013.03.018
- Dooley KE, Chaisson RE (2009) Tuberculosis and diabetes mellitus: convergence of two epidemics *The Lancet infectious diseases* 9:737-746 doi:10.1016/S1473-3099(09)70282-8
- Editors PLM, Barbour V, Clark J, Jones S, Veitch E (2010) The health crisis of tuberculosis in prisons extends beyond the prison walls *PLoS Med* 7:e1000383 doi:10.1371/journal.pmed.1000383
- Ewing JA (1984) Detecting alcoholism. The CAGE questionnaire *JAMA : the journal of the American Medical Association* 252:1905-1907
- Falzon D, Jaramillo E, Wares F, Zignol M, Floyd K, Raviglione MC (2013) Universal access to care for multidrug-resistant tuberculosis: an analysis of surveillance data *The Lancet infectious diseases* 13:690-697 doi:10.1016/S1473-3099(13)70130-0
- Fox GJ, Menzies D (2013) Epidemiology of tuberculosis immunology *Advances in experimental medicine and biology* 783:1-32 doi:10.1007/978-1-4614-6111-1\_1
- Goldhaber-Fiebert JD, Jeon CY, Cohen T, Murray MB (2011) Diabetes mellitus and tuberculosis in countries with high tuberculosis burdens: individual risks and social determinants *International journal of epidemiology* 40:417-428 doi:10.1093/ije/dyq238
- Health Mo (2011) On some issues to combat tuberculosis. Minister of Health of the Republic of Kazakhstan, Kazakhstan
- Huffman SA, Veen J, Hennink MM, McFarland DA (2012) Exploitation, vulnerability to tuberculosis and access to treatment among Uzbek labor migrants in Kazakhstan *Social science & medicine* 74:864-872 doi:10.1016/j.socscimed.2011.07.019
- Lienhardt C, Rowley J, Manneh K, Lahai G, Needham D, Milligan P, McAdam KP (2001) Factors affecting time delay to treatment in a tuberculosis control programme in a sub-Saharan African country: the experience of The Gambia *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 5:233-239
- Lin HH, Ezzati M, Chang HY, Murray M (2009) Association between tobacco smoking and active tuberculosis in Taiwan: prospective cohort study *American journal of respiratory and critical care medicine* 180:475-480 doi:10.1164/rccm.200904-0549OC
- Lonroth K, Jaramillo E, Williams BG, Dye C, Raviglione M (2009) Drivers of tuberculosis epidemics: the role of risk factors and social determinants *Social science & medicine* 68:2240-2246 doi:10.1016/j.socscimed.2009.03.041

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Lonnoth K, Williams BG, Cegielski P, Dye C (2010) A consistent log-linear relationship between tuberculosis incidence and body mass index *International journal of epidemiology* 39:149-155 doi:10.1093/ije/dyp308

Maurya V, Vijayan VK, Shah A (2002) Smoking and tuberculosis: an association overlooked *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 6:942-951

Mor Z, Pinsker G, Cedar N, Lidji M, Grotto I (2012) Adult tuberculosis in Israel and migration: trends and challenges between 1999 and 2010 *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 16:1613-1618 doi:10.5588/ijtld.12.0296

Murray M, Oxlade O, Lin HH (2011) Modeling social, environmental and biological determinants of tuberculosis *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 15 Suppl 2:S64-70 doi:10.5588/ijtld.10.0535

Organization WH (2011) *Global Tuberculosis 2011* vol ISBN: 9789241564380. World Health Organization, Geneva, Switzerland

Pednekar MS, Gupta PC (2007) Prospective study of smoking and tuberculosis in India *Preventive medicine* 44:496-498 doi:10.1016/j.ypmed.2007.02.017

Raviglione M et al. (2012) Scaling up interventions to achieve global tuberculosis control: progress and new developments *Lancet* 379:1902-1913 doi:10.1016/S0140-6736(12)60727-2

Rhodes T et al. (1999) HIV infection associated with drug injecting in the newly independent states, eastern Europe: the social and economic context of epidemics *Addiction* 94:1323-1336

Ríos M (2009) A graphical study of tuberculosis incidence and trends in the WHO's European region (1980–2006) *European journal of epidemiology* 24:381-387

Rocha C et al. (2011) The Innovative Socio-economic Interventions Against Tuberculosis (ISIAT) project: an operational assessment *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 15 Suppl 2:S50-57 doi:10.5588/ijtld.10.0447

Schluger NW, El-Bassel N, Hermosilla S, Terlikbayeva A, Darisheva M, Aifah A, Galea S (2013) Tuberculosis, drug use and HIV infection in Central Asia: An urgent need for attention *Drug and alcohol dependence* doi:10.1016/j.drugalcdep.2013.07.012

Stuckler D, Basu S, McKee M, King L (2008) Mass incarceration can explain population increases in TB and multidrug-resistant TB in European and central Asian countries *Proceedings of the National Academy of Sciences* 105:13280-13285

Terlikbayeva A et al. (2012) Tuberculosis in Kazakhstan: analysis of risk determinants in national surveillance data *BMC infectious diseases* 12:262 doi:10.1186/1471-2334-12-262

Vagenas P, Azbel L, Polonsky M, Kerimi N, Mamyrov M, Dvoryak S, Altice FL (2013) A review of medical and substance use co-morbidities in Central Asian prisons: Implications for HIV prevention and treatment *Drug and alcohol dependence* doi:10.1016/j.drugalcdep.2013.07.010

van den Hof S, Tursynbayeva A, Abildaev T, Adenov M, Pak S, Bekembayeva G, Ismailov S (2013) Converging risk factors but no association between HIV infection and multidrug-resistant tuberculosis in Kazakhstan *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 17:526-531 doi:10.5588/ijtld.12.0703

Vinkeles Melchers NV, van Elsland SL, Lange JM, Borgdorff MW, van den Hombergh J (2013) State of affairs of tuberculosis in prison facilities: a systematic review of screening practices and recommendations for best TB control *PLoS One* 8:e53644 doi:10.1371/journal.pone.0053644

Waite CJ, Squire SB (2011) A systematic review of risk factors for death in adults during and after tuberculosis treatment *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease* 15:871-885 doi:10.5588/ijtld.10.0352

# Tables

**Table 1. Tuberculosis cases, household, and community control participants in Almaty Region, Kazakhstan**

	<i>n</i> (%)	Total <i>N</i>
Socio-demographic		
Age, years, mean [SD]	39.59 [13.58]	324
Sex		324
Female	175 (54.0)	
Male	149 (46.0)	
BMI, kg/m <sup>2</sup> , median [range]	22.78 [14.53-	324
Ethnicity		324
Kazakh	254 (78.4)	
Russian	38 (11.7)	
Other	32 (9.9)	
Kazakhstan born	269 (83.0)	324
Religion		324
Muslim	271 (83.6)	
Christian	39 (12.0)	
Agnostic	14 (4.3)	
Completed education		324
Less than high school	28 (8.6)	
High school <sup>a</sup>	146 (45.1)	
Vocational education	104 (32.1)	
Some higher education <sup>b</sup>	46 (14.2)	
Current professional status <sup>c</sup>		322
Employee	137 (42.3)	
Pensioner	70 (21.6)	
Business owner	19 (5.9)	
Student	15 (4.6)	
Unemployed, able to work	61 (21.6)	
Unemployed, disable	20 (6.2)	
Monthly income, in USD, mean [SD]	179 [188]	
Currently rent home	44 (13.6)	324
Marital status		324
Single, never married	51 (15.7)	
Married	234 (72.2)	
Previously married <sup>d</sup>	39 (12.0)	
Have children	261 (845.6)	324
Behavioral		
Ever incarcerated	12 (3.7)	324
Recently smoked tobacco <sup>e</sup>	100 (30.9)	324
Alcohol abuse <sup>f</sup>		324
0-1	298 (92.0)	
>2	26 (8.0)	
Physical activity, days <sup>g</sup>		324
0	75 (23.1)	
1-3	41 (12.7)	
4-7	208 (64.2)	
Co-morbidity		



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Diabetes diagnosis <sup>h</sup>	13 (4.0)	324
HCV diagnosis <sup>h</sup>	8 (2.5)	324
Recent HIV+ result <sup>i</sup>	2 (0.8)	253
Urinary tract or kidney disease diagnosis <sup>h</sup>	34 (10.5)	324

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<sup>a</sup> High school includes completed education through grade 11

<sup>b</sup> Started higher education, university or college

<sup>c</sup> Primary professional status for the past twelve months

<sup>d</sup> Category includes divorced, separated, and widowed

<sup>e</sup> Past twelve months

<sup>f</sup> Based on the CAGE scale with a maximum score of 4

<sup>g</sup> Days within the past seven days

<sup>h</sup> Ever diagnosed with disease

<sup>i</sup> Result of most recent HIV test

BMI = body mass index; HCV = hepatitis C virus; SD = standard deviation; USD = United States Dollar conversion of Kazakh tenge \$1USD = 154 tenge; HIV = human immunodeficiency virus

**Table 2. Factors associated with tuberculosis case status in Almaty Region, Kazakhstan**

Variable	Model 1		Model 2		Model 3	
	OR (95%CI)	<i>P</i> value	OR (95%CI)	<i>P</i> value	OR (95%CI)	<i>P</i> value
Socio-demographic						
Age						
18-24 years	7.91 (2.15-29.08)	0.002 <sup>e</sup>	3.05 (1.03-9.02)	0.044 <sup>e</sup>	4.95 (1.91-12.81)	<0.001 <sup>e</sup>
25-34 years	3.31 (1.07-10.26)	0.038 <sup>e</sup>	1.86 (0.73-4.75)	0.196	2.36 (1.03-5.44)	0.043 <sup>e</sup>
35-44 years	1.21 (0.39-3.77)	0.747	0.65 (0.23-1.86)	0.424	0.84 (0.34-2.11)	0.714
45-54 years	1.05 (0.28-3.89)	0.940	1.01 (0.34-3.01)	0.991	1.07 (0.4-2.84)	0.892
>55 years	Reference		Reference		Reference	
Sex						
Male	1.93 (1.21-3.07)	0.006 <sup>e</sup>	1.47 (0.82-2.64)	0.192	1.77 (1.13-2.77)	0.012 <sup>e</sup>
Female	Reference		Reference		Reference	
BMI, kg/m <sup>2</sup>	0.77 (0.69-0.86)	<0.001 <sup>e</sup>	0.87 (0.81-0.93)	<0.001 <sup>e</sup>	0.82 (0.76-0.88)	<0.001 <sup>e</sup>
Birth country						
Born outside Kazakhstan	2.0 (0.60-6.64)	0.258	2.11 (0.96-4.67)	0.065	1.89 (0.91-3.94)	0.089
Born inside Kazakhstan	Reference		Reference		Reference	
Education						
Some higher education	0.75 (0.32-1.78)	0.514	0.90 (0.37-2.21)	0.819	0.83 (0.4-1.74)	0.623
Less than higher education	Reference		Reference		Reference	
Current employment status <sup>a</sup>						
Employed	0.58 (0.34-1.0)	0.050 <sup>e</sup>	0.77 (0.45-1.32)	0.347	0.67 (0.42-1.06)	0.084
Unemployed	Reference		Reference		Reference	
Current housing status						

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	Rent home	2.33 (0.60-9.02)	0.220	2.37 (1.04-5.43)	0.040 <sup>e</sup>	2.36 (1.03-5.41)	0.043 <sup>e</sup>
	Own home	Reference		Reference		Reference	
	Marital status						
	Single, never married	4.57 (2.02-10.36)	<0.001 <sup>e</sup>	2.44 (1.36-4.36)	<0.001 <sup>e</sup>	3.0 (1.76-5.12)	<0.001 <sup>e</sup>
	Ever married	Reference		Reference		Reference	
	Behavioral						
	Incarceration						
	Ever incarcerated	1.0 (0.2-4.95)	1.000	0.33 (0.07-1.65)	0.178	0.62 (0.17-2.32)	0.481
	Never incarcerated	Reference		Reference		Reference	
	Recent tobacco smoking <sup>b</sup>						
	Smoked	1.82 (1.01-3.29)	0.047 <sup>e</sup>	1.32 (0.73-2.39)	0.367	1.58 (0.95-2.63)	0.077
	Did not smoke	Reference		Reference		Reference	
	Alcohol abuse <sup>c</sup>						
	Ever abused	1.0 (0.32-3.10)	1.000	0.30 (0.08-1.09)	0.067	0.57 (0.21-1.55)	0.273
	Never abused	Reference		Reference		Reference	
	Co-morbidity						
	Diabetes diagnosis <sup>d</sup>						
	Yes	11.0 (1.42-85.2)	0.022 <sup>e</sup>	10.8 (1.38-85.2)	0.028 <sup>e</sup>	10.54 (2.33-47.67)	0.002 <sup>e</sup>
	No	Reference		Reference		Reference	
	Urinary tract or kidney disease diagnosis <sup>d</sup>						
	Yes	0.33 (0.11-1.03)	0.057	0.38 (0.14-1.08)	0.069	0.38 (0.15-0.97)	0.043 <sup>e</sup>
	No	Reference		Reference		Reference	

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Model 1 compares household controls to TB cases; model 2 compares community controls to TB cases; model 3 compares both household and community controls to TB cases

<sup>a</sup> Primary employment status within the past 12 months

<sup>b</sup> Past twelve months

<sup>c</sup> CAGE score  $\geq 2$

<sup>d</sup> Ever diagnosed with disease

<sup>e</sup> Statistically significant at a  $p < 0.05$  level

TB = tuberculosis; OR = odds ratio; CI = confidence interval; HIV = human immunodeficiency virus

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**Table 3. Multivariable factor associations with tuberculosis case status in Almaty Region, Kazakhstan**

Variable	Model 1		Model 2		Model 3	
	AOR <sup>a</sup> (95%CI)	<i>P</i> value	AOR <sup>a</sup> (95%CI)	<i>P</i> value	AOR <sup>a</sup> (95%CI)	<i>P</i> value
Age						
18-24 years	11.36 (1.67-77.49)	0.013 <sup>f</sup>	5.13 (1.01-26.18)	0.049 <sup>f</sup>	8.4 (2.16-32.72)	0.002 <sup>f</sup>
25-34 years	7.41 (1.29-42.52)	0.025 <sup>f</sup>	2.77 (0.64-12.01)	0.172	4.78 (1.37-16.69)	0.014 <sup>f</sup>
35-44 years	1.99 (0.35-11.47)	0.440	0.54 (0.1-2.89)	0.471	1.19 (0.31-4.54)	0.798
45-54 years	1.5 (0.23-9.66)	0.672	2.39 (0.46-12.6)	0.303	1.99 (0.5-7.89)	0.326
>55 years	Reference		Reference		Reference	
Sex						
Male	1.24 (0.54-2.84)	0.610	0.87 (0.3-2.49)	0.789	1.3 (0.63-2.69)	0.486
Female	Reference		Reference		Reference	
Birth country						
Born outside Kazakhstan	5.1 (0.72-35.98)	0.102	2.85 (0.9-9.0)	0.074	3.16 (1.08-9.29)	0.036 <sup>f</sup>
Born inside Kazakhstan	Reference		Reference		Reference	
Education						
Some higher education	1.08 (0.31-3.76)	0.898	0.92 (0.23-3.69)	0.909	1.1 (0.38-3.22)	0.855
Less than higher education	Reference		Reference		Reference	
Current employment status <sup>b</sup>						
Employed	0.75 (0.32-1.77)	0.514	0.75 (0.33-1.68)	0.480	0.8 (0.41-1.55)	0.503
Unemployed	Reference		Reference		Reference	

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3 Current housing status

4 Rent home	0.93 (0.14-6.15)	0.942	5.15 (1.39-19.05)	0.014 <sup>f</sup>	2.94 (0.95-9.11)	0.062
6 Own home	Reference		Reference		Reference	

7  
8 Marital status

9 Single, never married	3.49 (0.99-12.23)	0.051	3.21 (1.28-8.05)	0.013 <sup>f</sup>	2.91 (1.4-6.06)	0.004 <sup>f</sup>
11 Ever married	Reference		Reference		Reference	

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13 Incarceration

14 Ever incarcerated	0.63 (0.06-6.54)	0.697	0.66 (0.08-5.24)	0.693	0.92 (0.16-5.4)	0.930
16 Never incarcerated	Reference		Reference		Reference	

17  
18 Recent tobacco smoking <sup>c</sup>

19 Smoked	3.27 (1.1-9.68)	0.032 <sup>f</sup>	4.07 (1.16-14.32)	0.029 <sup>f</sup>	2.87 (1.2-6.89)	0.018 <sup>f</sup>
21 Did not smoke	Reference		Reference		Reference	

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23 Alcohol abuse <sup>d</sup>

24 Ever abused	0.66 (0.1-4.3)	0.668	0.16 (0.02-1.16)	0.069	0.24 (0.05-1.02)	0.053
26 Never abused	Reference		Reference		Reference	

27  
28 Diabetes diagnosis <sup>e</sup>

29 Yes	48.59 (3.05-773.01)	0.006 <sup>f</sup>	23.43 (1.86-295.49)	0.015 <sup>f</sup>	30.73 (4.31-218.99)	0.001 <sup>f</sup>
31 No	Reference		Reference		Reference	

32  
33 Urinary tract or kidney disease  
34 diagnosis <sup>e</sup>

35 Yes	1.39 (0.29-6.59)	0.676	0.29 (0.06-1.38)	0.120	0.61 (0.19-1.98)	0.410
37 No	Reference		Reference		Reference	

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Model 1 compares household controls to TB cases; model 2 compares community controls to TB cases; model 3 compares both household and community controls to TB cases

<sup>a</sup> Adjusted for all other covariates in model

<sup>b</sup> Primarily employed within the past 12 months as compared to unemployed in the past 12 months

<sup>c</sup> Past twelve months

<sup>d</sup> CAGE score  $\geq 2$

<sup>e</sup> Ever diagnosed with disease

<sup>f</sup> Statistically significant at a  $p < 0.05$  level

TB = tuberculosis; AOR = adjusted odds ratio; CI = confidence interval; HIV = human immunodeficiency virus