Tobacco smoking and tuberculosis treatment outcomes: a prospective cohort study in Georgia

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Objective To assess the effect of tobacco smoking on the outcome of tuberculosis treatment in Tbilisi, Georgia.

Methods We conducted a prospective cohort study of adults with laboratory-confirmed tuberculosis from May 2011 to November 2013. History of tobacco smoking was collected using a standardized questionnaire adapted from the global adult tobacco survey. We considered tuberculosis therapy to have a poor outcome if participants defaulted, failed treatment or died. We used multivariable regressions to estimate the risk of a poor treatment outcome.

Findings Of the 591 tuberculosis patients enrolled, 188 (31.8%) were past smokers and 271 (45.9%) were current smokers. Ninety (33.2%) of the current smokers and 24 (18.2%) of the participants who had never smoked had previously been treated for tuberculosis (P < 0.01).

Treatment outcome data were available for 524 of the participants, of whom 128 (24.4%) – including 80 (32.9%) of the 243 current smokers and 21 (17.2%) of the 122 individuals who had never smoked – had a poor treatment outcome. Compared with those who had never smoked, current smokers had an increased risk of poor treatment outcome (adjusted relative risk, aRR: 1.70; 95% confidence interval, CI: 1.00–2.90).

Conclusion There is a high prevalence of smoking among patients with tuberculosis in Georgia and smoking increases the risk of a poor treatment outcome.

Introduction

Both tobacco smoking and tuberculosis are major global public health problems. Globally, nearly 6 million people died from tobacco use in 2011 and tobacco use is estimated to be responsible for 16% of deaths among men and 7% of deaths among women each year.1,2 In 2012, there were an estimated 8.6 million new tuberculosis cases and 1.3 million tuberculosis-related deaths worldwide.3 Smoking is common in the 22 countries categorized by the World Health Organization (WHO) as high-burden countries for tuberculosis – which together account for more than 80% of all tuberculosis cases. The burden of smoking among patients with tuberculosis is poorly defined in most countries.4

An understanding of the epidemiological relationship between smoking and tuberculosis is important because both smoking and tuberculosis cause extensive morbidity and mortality worldwide. Compared with those who have never smoked, it is estimated that people who smoke have approximately twice the risk of both Mycobacterium tuberculosis infection1 and active tuberculosis.1 However, data on the impact of smoking on treatment outcomes among patients with active tuberculosis are limited.5

Georgia has a high incidence of tuberculosis, a high incidence of multidrug-resistant (MDR) tuberculosis and a high prevalence of smoking.6 In 2012, for example, there were 116 cases of tuberculosis per 100 000 people and MDR tuberculosis accounted for 9.2% of the new cases and 31.0% of the retreatment cases.6 In 2010, a national survey indicated that about 52.8% of Georgian men – including 64.0% of those aged 30–49 years – and 6.1% of Georgian women were smokers.7 The main objectives of this study were to estimate the prevalence of smoking and the impact of smoking on tuberculosis treatment outcomes among patients with tuberculosis in the Georgian capital of Tbilisi.

Methods

Design and study population

A prospective cohort study was conducted between May 2011 and November 2013 among people attending the National Centre for Tuberculosis and Lung Diseases, or one of its affiliated outpatient clinics, in Tbilisi, Georgia. To be eligible for enrolment, a patient had to be aged at least 18 years, have provided a sputum specimen that had been found either smear-positive for acid-fast bacilli or culture-positive for Mycobacterium tuberculosis and have started directly-observed, standard tuberculosis therapy according to WHO guidelines6 within the previous two months. Eligible patients were enrolled between May 2011 and February 2012. In November 2013, details of the participants’ treatment outcomes were collected from the database of patient records maintained by the National Centre for Tuberculosis and Lung Diseases.

At the time of study enrolment, after the patients had provided written informed consent, our research team conducted face-to-face interviews of eligible inpatients and outpatients. Although most of the data we used were collected using a standardized questionnaire adapted from the one employed in the

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global adult tobacco survey, additional covariates of interest were collected from the National Centre for Tuberculosis and Lung Diseases database. Self-reported information on age, alcohol use, socioeconomic indicators, prison history, human immunodeficiency virus (HIV) status, exposure to a person with MDR tuberculosis and tuberculosis symptoms – i.e. cough with and without sputum – were recorded on the questionnaire. Previous tuberculosis treatment, results from the examination of a baseline sputum smear and current tuberculosis treatment regimen were obtained from the National Centre for Tuberculosis and Lung Diseases database.

**Study definitions**

History of smoking was used as the primary exposure variable. Patients were first asked if they currently smoked on a daily basis, less than daily, or not at all. Those who reported that they currently smoked – either daily or less than daily – were categorized as current smokers in the primary analyses. The remaining patients were then asked if they had smoked in the past on a daily or less than daily basis and those giving a positive response were categorized as past smokers in the primary analyses. Patients who said that they had never smoked were always categorized as never smokers.

In our secondary analyses, we used other measures of tobacco use. Patients who currently smoked on a daily basis and patients who currently smoked on a less than daily basis were separately compared with past and never smokers. Patients also reported smokeless tobacco use and frequency of household second-hand exposure to tobacco smoke. To account for possible misclassification of those patients who had stopped smoking once they developed tuberculosis symptoms,10,11 we also used modified definitions for smoking status. For example, we put patients who had ceased smoking in the two or four months before enrolment in separate categories and reclassified all such patients as current smokers instead of past smokers.12,13

The outcome of each participant’s most recent treatment for tuberculosis was used as the primary study outcome. Treatment outcomes were categorized according to WHO definitions.1 A patient who was cured or completed treatment was defined as having a favourable outcome whereas a patient who defaulted, failed treatment or died was defined as having a poor outcome.

**Laboratory studies** were performed at the Georgia National Tuberculosis Reference Laboratory. Since 2005, the quality of the services provided by this laboratory has been assessed annually by the WHO’s Supranational Tuberculosis Reference Laboratory in Antwerp, Belgium.14 A standard semiquantitative scale was used to classify the number of acid-fast bacilli present in sputum smears.15 Sputum samples were tested for *M. tuberculosis* by culture on Lowenstein–Jensen solid medium and using BACTEC MGIT 960 mycobacterial detection system (BD, Franklin Lakes, United States of America).14 Isolated samples of *M. tuberculosis* were tested for their sensitivity to first-line anti-tuberculosis drugs using either the absolute concentration method or the BACTEC MGIT 960 mycobacterial detection system but their sensitivity to second-line drugs was investigated using proportion methods.14

**Data analyses**

Study data were entered into a REDCap electronic database and analysed using SAS 9.3 (SAS Institute, Cary, USA). Bivariate associations were analysed using χ² tests for categorical variables and the Wilcoxon rank sum or Kruskal–Wallis tests for continuous variables. A two-sided P-value of less than 0.05 was considered statistically significant. Binomial regression models were used to estimate risk ratios (RR) and 95% confidence intervals (CI) for a poor tuberculosis treatment outcome. Potential confounders – based on significant bivariate associations with the primary exposure and outcome, previous literature or directed acyclic graph theory17 – were included in the regression models. We used the primary multivariable model to estimate the effect of current smoking status on risk of poor tuberculosis outcome. For our secondary models we used alternative definitions of current smoking status but included the same covariates as in the primary model. To assess the distribution of missing outcome data, we compared the sociodemographic, tuberculosis and smoking characteristics of the patients with known treatment outcomes with those of the other patients. The study was reviewed and approved by the institutional review boards of the Georgia National Centre for Tuberculosis and Lung Diseases (Tbilisi, Georgia), Emory University (Atlanta, Georgia), and the Johns Hopkins Bloomberg School of Public Health (Baltimore, USA).

**Results**

Overall, 591 (64.4%) of 917 eligible patients with tuberculosis were invited to participate in our study and all agreed to be enrolled. Of the participants, 457 (77.3%) were male. The median age was 36 years (interquartile range, IQR: 26–50 years), their median monthly income was 118 United States dollars (US$) (IQR: US$ 59–294) and 465 (78.7%) of them had been educated to at least high school level. In November 2013, information on tuberculosis treatment outcome was available for 524 (88.7%) of the participants.

**Smoking characteristics**

Of the participants, 271 (45.9%) were current smokers and 188 (31.8%) were past smokers (Table 1). Most of the current and past smokers were male. Current smokers were older, with fewer years of education and lower income compared to never smokers (Table 1). Previous tuberculosis treatment, cough with sputum and exposure to a case of MDR tuberculosis were more frequently reported by current smokers than never smokers (Table 1). Compared with the never smokers, past smokers were significantly less likely to have MDR tuberculosis (Table 1).

**Treatment outcomes**

We were unable to determine the final treatment outcomes of 67 participants because of missing data (34) or because, at the end of our study, the participants remained on second-line therapy against MDR tuberculosis (33). We collected information on the final treatment outcomes of the remaining 524 participants. Of these participants, 128 (24.4%) had a poor outcome – 99 defaulted, 11 failed treatment and 18 died (Table 2). In terms of their demographic characteristics, baseline smear status and smoking characteristics, the 524 participants with known treatment outcomes did not appear to be significantly different to the 67 other participants.

In our unadjusted analyses, the risk of poor treatment outcomes was higher among current smokers (RR: 1.91; 95% CI: 1.25–2.94), males (RR: 1.74; 95% CI: 1.12–2.71), those with a history of imprisonment (RR: 1.46; 95% CI: 1.05–2.03), previous tuberculosis treatment (RR: 1.94; 95% CI: 1.45–2.61), sputum-smeared-positive at the baseline check (RR: 2.33; 95% CI: 1.61–3.37) or...
Table 1. Baseline characteristics of adults with active tuberculosis, Georgia, 2011–2012

| Characteristic                        | No. (%) | P        |
|---------------------------------------|---------|----------|
|                                       | Never smokers (n = 132) | Past smokers (n = 188) | Current smokers (n = 271) |
| **Sex**                               |         |          |          |
| Female                                | 89 (67.4) | 26 (13.8) | 19 (7.0) | <0.01 |
| Male                                  | 43 (32.6) | 162 (86.2) | 252 (93.0) |          |
| **Age (years)**                       |         |          |          |
| 18–24                                 | 47 (35.6) | 39 (20.7) | 30 (11.1) | <0.01 |
| 25–34                                 | 38 (28.8) | 42 (22.3) | 73 (26.9) |          |
| 35–54                                 | 24 (18.2) | 80 (42.6) | 128 (47.2) |          |
| ≥ 55                                  | 23 (17.4) | 27 (14.4) | 40 (14.8) |          |
| **Education (years)**                 |         |          |          |
| ≤ 9                                   | 29 (22.0) | 33 (17.5) | 64 (23.6) | <0.01 |
| 10                                    | 33 (25.0) | 77 (41.0) | 118 (43.5) |          |
| ≥ 11                                  | 70 (53.0) | 78 (41.5) | 89 (32.8) |          |
| **Monthly income (US$)**              |         |          |          |
| ≤ 65                                  | 25 (18.9) | 59 (31.4) | 95 (35.1) | 0.02 |
| 66–200                                | 40 (37.1) | 50 (26.6) | 86 (31.7) |          |
| ≥ 201                                 | 48 (36.4) | 59 (31.4) | 72 (26.6) |          |
| Unknown                               | 10 (7.6) | 20 (10.6) | 18 (6.6) |          |
| **Internally displaced**               |         |          |          |
| No                                    | 123 (93.2) | 173 (92.0) | 250 (92.3) | 0.92 |
| Yes                                   | 9 (6.8) | 15 (8.0) | 21 (7.7) |          |
| **Prison history**                    |         |          |          |
| No                                    | 127 (96.2) | 163 (86.7) | 181 (66.8) | <0.01 |
| Yes                                   | 5 (3.8) | 25 (13.3) | 90 (33.2) |          |
| **Frequency of alcohol use (days/ week)** |         |          |          |
| 0                                     | 74 (56.1) | 50 (26.6) | 51 (18.8) | <0.01 |
| < 1                                   | 45 (34.1) | 61 (32.5) | 75 (27.7) |          |
| 1–2                                   | 9 (6.8) | 42 (22.3) | 66 (24.4) |          |
| ≥ 3                                   | 2 (1.5) | 26 (13.8) | 76 (28.0) |          |
| Unknown                               | 2 (1.5) | 9 (4.8) | 3 (1.1) |          |
| **Self-reported HIV status**          |         |          |          |
| Negative                              | 117 (88.6) | 168 (89.4) | 243 (89.7) | 0.86 |
| Positive                              | 2 (1.5) | 3 (1.6) | 3 (1.1) |          |
| Unknown                               | 13 (9.9) | 17 (9.0) | 25 (9.2) |          |
| **Smokeless tobacco use**             |         |          |          |
| No                                    | 95 (72.0) | 147 (78.2) | 195 (72.0) | 0.39 |
| Yes                                   | 1 (0.7) | 4 (2.1) | 5 (1.8) |          |
| Unknown                               | 36 (27.3) | 37 (19.7) | 71 (26.2) |          |
| **Second-hand exposure to smoke in household** |         |          |          |
| Never                                 | 49 (37.1) | 97 (51.6) | 108 (39.9) | <0.01 |
| Less than daily                       | 20 (15.1) | 17 (9.0) | 22 (8.1) |          |
| Daily                                 | 62 (47.0) | 68 (36.2) | 118 (43.5) |          |
| Unknown                               | 1 (0.8) | 6 (3.2) | 23 (8.5) |          |
| **Previous tuberculosis treatment**   |         |          |          |
| No                                    | 108 (81.8) | 147 (78.2) | 181 (66.8) | <0.01 |
| Yes                                   | 24 (18.2) | 41 (21.8) | 90 (33.2) |          |
| **Result of baseline sputum examination** |         |          |          |
| Negative for AFB                      | 65 (49.2) | 85 (45.2) | 102 (37.6) | 0.06 |
| Positive for AFB                      | 67 (50.8) | 103 (54.8) | 169 (62.4) |          |
| **Self-reported cough**               |         |          |          |
| No                                    | 31 (23.5) | 45 (23.9) | 53 (19.6) | 0.03 |

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MDC tuberculosis (RR: 4.53; 95% CI: 3.30–6.21) (Table 3). In the primary multivariable analysis, being a current smoker (RR: 1.70; 95% CI: 1.00–2.90) and receiving treatment for MDC tuberculosis (RR: 3.12; 95% CI: 2.30–4.22) remained significantly associated with a poor outcome (Table 3). We did not detect any one-way statistical interactions between smoking status and any of the other covariates that we included in the adjusted model.

Compared with never smokers, patients with tuberculosis who had ceased smoking within the two months before enrolment had an increased – but not significantly increased – adjusted risk of a poor treatment outcome (adjusted relative risk, aRR: 1.44; Table 4). In models 3 and 4, we considered patients who had ceased smoking in the two and four months before enrolment as current smokers, respectively, and this reduced the strength of the apparent association between current smoking and a poor treatment outcome – to give adjusted relative risks of 1.67 and 1.64, respectively (Table 4). Patients who, when enrolled, had ceased smoking for more than two months had a similar risk of a poor treatment outcome to those who had never smoked (RR: 1.01; Table 4). There were no significant associations between poor tuberculosis treatment outcomes and smokeless tobacco use or household second-hand exposure to tobacco smoke.

Discussion

There is a high prevalence of smoking among patients with tuberculosis in Georgia and, among such patients, smoking significantly increases the risk of a poor treatment outcome. After adjusting for other individual characteristics that are potentially related to both smoking and tuberculosis treatment outcome, we found that the risk of a poor tuberculosis treatment outcome was 70% greater in current smokers compared to never smokers. Patients being treated for MDC tuberculosis had a 3-fold greater risk of a poor outcome compared to patients being treated for other forms of tuberculosis. We also found that patients who had recently stopped smoking had a lower risk of a poor tuberculosis outcome than current smokers.

As the government in Georgia prepares for new national policy on tobacco control, the findings of our study are particularly timely and relevant. In Georgia, it is currently illegal to smoke in medical facilities but it has been difficult to enforce this legislation. Additional policies are needed to eliminate or at least reduce tobacco use in health-care facilities.

Table 2. Smoking status and treatment outcomes among adults with tuberculosis, Georgia, 2011–2012

| Characteristic                  | Never smokers (n = 122) | Past smokers (n = 159) | Current smokers (n = 243) |
|--------------------------------|------------------------|------------------------|--------------------------|
| Treatment outcome              |                         |                        |                          |
| Favourable                     | 101 (82.8)              | 132 (83.0)             | 163 (67.1)               |
| Cured                          | 42 (34.4)               | 69 (43.4)              | 81 (33.3)                |
| Completed treatment            | 59 (48.4)               | 63 (39.6)              | 82 (33.7)                |
| Poor                           | 21 (17.2)               | 27 (17.0)              | 80 (32.9)                |
| Defaulted treatment            | 16 (13.1)               | 22 (13.8)              | 61 (25.1)                |
| Failed treatment               | 1 (0.8)                 | 3 (1.9)                | 7 (2.9)                  |
| Died                           | 4 (3.3)                 | 2 (1.3)                | 12 (4.9)                 |

* As defined by the World Health Organization and recorded six months after the initiation of treatment. Note: Inconsistencies arise in some values due to rounding.
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Table 3. Association between baseline patient characteristics and risk of poor tuberculosis treatment outcomes, Georgia, 2011–2012

| Characteristic                        | No. of patients with poor/known outcome (%) | Risk ratio (95% CI)* |
|--------------------------------------|---------------------------------------------|----------------------|
|                                      |                                             | Crude               |
|                                      |                                             | Adjusted            |
| Sex                                  |                                             |                     |
| Female                               | 19/122 (15.6)                              | 1.00                |
| Male                                 | 109/402 (27.1)                             | 1.74 (1.12–2.71)    |
| Age (years)                          |                                             |                     |
| 18–24                                | 22/109 (20.2)                              | 1.00                |
| 25–34                                | 32/134 (23.9)                              | 1.18 (0.73–1.91)    |
| 35–54                                | 49/199 (24.6)                              | 1.22 (0.78–1.90)    |
| ≥55                                  | 25/82 (30.5)                               | 1.51 (0.92–2.48)    |
| Education (years)                    |                                             |                     |
| ≤9                                   | 32/114 (28.1)                              | 1.00                |
| 10                                   | 50/197 (25.4)                              | 0.90 (0.62–1.32)    |
| ≥11                                  | 46/213 (21.6)                              | 0.77 (0.52–1.14)    |
| Monthly income (US$)                 |                                             |                     |
| ≤65                                  | 36/161 (22.4)                              | 1.00                |
| 66–200                               | 53/165 (32.1)                              | 1.44 (1.00–2.07)    |
| ≥201                                 | 29/156 (18.6)                              | 0.83 (0.54–1.29)    |
| Unknown                              | 10/42 (23.8)                               |                     |
| Internally displaced                 |                                             |                     |
| No                                   | 120/488 (24.6)                             | 1.00                |
| Yes                                  | 8/36 (22.2)                                | 0.90 (0.48–1.70)    |
| Prison history                       |                                             |                     |
| No                                   | 94/420 (22.4)                              | 1.00                |
| Yes                                  | 34/104 (32.7)                              | 1.46 (1.05–2.03)    |
| Frequency of alcohol use (days/week) |                                             |                     |
| 0                                    | 29/158 (18.4)                              | 1.00                |
| <1                                   | 49/153 (32.0)                              | 1.74 (1.17–2.61)    |
| 1–2                                  | 28/106 (26.4)                              | 1.44 (0.91–2.27)    |
| ≥3                                   | 20/94 (21.3)                               | 1.16 (0.70–1.93)    |
| Unknown                              | 2/13 (15.4)                                |                     |
| Previous tuberculosis treatment      |                                             |                     |
| No                                   | 78/394 (19.8)                              | 1.00                |
| Yes                                  | 50/130 (38.5)                              | 1.94 (1.45–2.61)    |
| Result of baseline sputum examination|                                             |                     |
| Negative for AFB                     | 30/218 (13.8)                              | 1.00                |
| Positive for AFB                     | 98/306 (32.0)                              | 2.33 (1.61–3.37)    |
| Self-reported cough                  |                                             |                     |
| No                                   | 25/120 (20.8)                              | 1.00                |
| Yes                                  | 103/401 (25.7)                             | 1.23 (0.84–1.81)    |
| Unknown                              | 0/3 (0.0)                                  |                     |
| Self-reported cough with sputum      |                                             |                     |
| No                                   | 11/54 (20.4)                               | 1.00                |
| Yes                                  | 84/334 (25.1)                              | 1.23 (0.71–2.16)    |
| Unknown                              | 33/136 (24.3)                              |                     |
| Self-reported exposure to case of MDR tuberculosis |                                             |                     |
| No                                   | 83/350 (23.7)                              | 1.00                |
| Yes                                  | 44/167 (26.3)                              | 1.11 (0.81–1.52)    |
| Unknown                              | 1/7 (14.3)                                 |                     |
| Type of tuberculosis                |                                             |                     |
| Drug-susceptible                     | 43/364 (11.8)                              | 1.00                |
| MDR                                  | 85/159 (53.5)                              | 4.53 (3.30–6.21)    |
| Unknown                              | 0/1 (0.0)                                  |                     |
| Self-reported HIV status             |                                             |                     |

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care settings in general and tuberculosis clinics in particular. Future policies on tobacco use in the country should promote smoking cessation programmes for patients with tuberculosis.

Globally, more than 20% of people older than 15 years smoke tobacco, according to WHO data from 2014. However, the prevalence of smoking among people with tuberculosis is often well above 20%. For example, a South African study observed that 56% of patients with active tuberculosis were current smokers. Similarly, 54.6% of Chinese patients with tuberculosis were smokers. In our study, 59.9% of the tuberculosis patients were either current smokers or individuals who had ceased smoking no more than two months earlier. Because smoking induces coughing and other symptoms consistent with tuberculosis, there may be longer delays in the diagnosis of tuberculosis among smokers than among non-smokers. For example, another study in Georgia reported a greater likelihood of prolonged delay (more than 23 days) in active tuberculosis diagnosis in smokers compared to never smokers (adjusted odds ratio, aOR: 3.03; 95% CI: 1.24–7.40).

At the time of our study, few data had been published on the relationship between smoking and treatment outcomes among patients with tuberculosis.

### Table 1. Comparison of Smoking Status with Known/Poor Treatment Outcome

| Characteristic                                      | No. of patients with poor/known outcome (%) | Risk ratio (95% CI)* |
|-----------------------------------------------------|---------------------------------------------|----------------------|
|                                                     | Crude                                      | Adjusted*            |
| Negative                                            | 118/464 (25.4)                             | 1.00                 | 1.00                 |
| Positive                                            | 1/8 (12.5)                                 | 0.49 (0.08–3.10)     | –                    |
| Unknown                                             | 9/52 (17.3)                                | –                    | –                    |
| **Model 1 – smoking status**                        |                                             |                      |                      |
| Never smoker                                        | 21/122 (17.2)                              | 1.00                 | 1.00                 |
| Past smoker                                         | 27/159 (17.0)                              | 0.99 (0.59–1.66)     | 1.24 (0.71–2.17)     |
| Current smoker                                      | 80/243 (32.9)                              | 1.91 (1.25–2.94)     | 1.70 (1.00–2.90)     |
| **Model 2 – smoking status**                        |                                             |                      |                      |
| Never smoker                                        | 21/122 (17.2)                              | 1.00                 | –                    |
| Past smoker                                         | 9/86 (10.5)                                | 0.61 (0.29–1.26)     | –                    |
| Current smoker                                      | 80/243 (32.9)                              | 1.91 (1.25–2.94)     | –                    |
| **Model 3 – smoking status**                        |                                             |                      |                      |
| Never smoker                                        | 21/122 (17.2)                              | 1.00                 | –                    |
| Past smoker                                         | 9/86 (10.5)                                | 0.61 (0.29–1.26)     | –                    |
| Current smoker                                      | 98/316 (31.0)                              | 1.80 (1.18–2.75)     | –                    |
| **Model 4 – smoking status**                        |                                             |                      |                      |
| Never smoker                                        | 21/122 (17.2)                              | 1.00                 | –                    |
| Past smoker                                         | 6/70 (8.6)                                 | 0.61 (0.21–1.17)     | –                    |
| Current smoker                                      | 101/332 (30.4)                             | 1.77 (1.16–2.69)     | –                    |
| **Current smoking frequency**                       |                                             |                      |                      |
| Zero                                                | 48/280 (17.1)                              | 1.00                 | –                    |
| Less than daily                                     | 3/13 (23.1)                                | 1.35 (0.48–3.75)     | –                    |
| Daily                                               | 77/231 (33.3)                              | 1.94 (1.42–2.67)     | –                    |
| **Smokeless tobacco use**                           |                                             |                      |                      |
| No                                                  | 90/385 (23.4)                              | 1.00                 | –                    |
| Yes                                                 | 2/9 (22.2)                                 | 0.95 (0.28–3.27)     | –                    |
| Unknown                                             | 36/130 (27.7)                              | –                    | –                    |
| **Second-hand exposure to smoke in household**      |                                             |                      |                      |
| Never                                               | 52/224 (23.2)                              | 1.00                 | –                    |
| Less than daily                                     | 23/52 (44.2)                               | 1.91 (1.29–2.81)     | –                    |
| Daily                                               | 46/221 (20.8)                              | 0.90 (0.63–1.27)     | –                    |
| Unknown                                             | 7/27 (25.9)                                | –                    | –                    |

AFB: acid-fast bacilli; CI: confidence interval; HIV: human immunodeficiency virus; MDR: multidrug-resistant; US$: United States dollars.

* For a poor treatment outcome – i.e. death or treatment default or failure – recorded six months after the initiation treatment.

* Each ratio was adjusted for all of the other variables for which adjusted odds ratios are given in the table.

Per US$ 10 increase in monthly income.

Including patients who ceased smoking before two months of enrolment.

Including patients who ceased smoking before four months of enrolment.

In our study, 59.9% of the tuberculosis patients were either current smokers or individuals who had ceased smoking no more than two months earlier.
tuberculosis mortality, tuberculosis treatment failure, and relapse after treatment completion. In a study in Brazil, it was found that – even after adjusting for confounders – smoking was associated with sputum culture positivity after 60 days of first-line tuberculosis treatment. Among patients with pulmonary tuberculosis in India, smokers were found to have a threefold greater risk of recurrent tuberculosis than non-smokers. Current smokers with tuberculosis were more likely to default on their treatment than non-smokers in the Hong Kong Special Administrative Region (aOR: 3.00; 95% CI: 1.41–6.39) and in Nigeria (odds ratio: 1.61; 95% CI: 1.31–1.98). In Morocco, one study found that smokers were twice as likely to fail tuberculosis treatment as non-smokers – although the researchers did not control for important confounders such as previous tuberculosis treatment and use of a second-line treatment regimen.

Biological mechanisms related to smoking that impair host defences and increase the risk of M. tuberculosis infection probably contribute to the relatively poor results of tuberculosis treatment among smokers. For example, smoking may have an irreversible inhibitory effect on nitric oxide synthase – the enzyme needed by alveolar macrophages to form nitric oxide to inhibit the multiplication of M. tuberculosis. Cigarette smoking can increase the availability of iron in the lower respiratory tract and iron may bind with nitric oxide to generate toxic radicals that can interfere with alveolar macrophages. Smoking also probably reduces the ability of alveolar macrophages to mount an effective pulmonary immune defence by altering the cells’ expression of pro-inflammatory cytokines.

Our study had several limitations. First, our primary exposure variable – self-reported smoking status – was subject to potential misclassification. It is possible that our participants underreported their tobacco use. However, our questionnaires were administered by the research team and not by the patients’ health-care providers. This should have reduced the likelihood that patients underreported their tobacco use. Moreover, self-reported measures of tobacco use have been found to be reasonably accurate – with less than 1.5% of respondents claiming not to use tobacco when they are current users. If we misclassified some smokers as never smokers, our estimate of the effect of smoking on tuberculosis outcomes would be an underestimate and our main findings would remain unchanged. Second, as there are probably patient characteristics associated with both smoking and poor tuberculosis treatment outcomes that we failed to include in our multivariable models, such models may have been affected by residual confounding. However, we did adjust for all of the key factors that have been established as important risks for a poor tuberculosis treatment outcome – e.g. a history of previous tuberculosis treatment, baseline sputum-smear score and the use of a second-line treatment regimen. Third, as our data came from patients with tuberculosis attending treatment facilities in Tbilisi, our findings may not be nationally representative. However, the distributions of patient demographics, smear positivity and previous tuberculosis treatment history seen in our study are similar to those reported by WHO for Georgia.

In conclusion, smoking is an independent risk factor for poor tuberculosis treatment outcomes. Smoking cessation programmes need to be targeted at tu-

### Table 4. Adjusted associations between smoking history and risk of poor tuberculosis treatment outcomes, Georgia, 2011–2012

| Smoking history                                                                 | Adjusted risk ratio (95% CI)* |
|---------------------------------------------------------------------------------|------------------------------|
| **Model 1 – smoking status**                                                     |                              |
| Never smoker                                                                    | 1.00                          |
| Past smoker                                                                     | 1.24 (0.71–2.17)              |
| Current smoker                                                                  | 1.70 (1.00–2.90)              |
| **Model 2 – smoking status**                                                     |                              |
| Never smoker                                                                    | 1.00                          |
| Past smoker                                                                     | 1.01 (0.51–1.99)              |
| Ceased smoking in previous two months                                           | 1.44 (0.80–2.57)              |
| Current smoker                                                                  | 1.69 (1.00–2.86)              |
| **Model 3 – smoking status**                                                     |                              |
| Never smoker                                                                    | 1.00                          |
| Past smoker                                                                     | 1.01 (0.50–2.04)              |
| Current smoker                                                                  | 1.67 (0.99–2.83)              |
| **Model 4 – smoking status**                                                     |                              |
| Never smoker                                                                    | 1.00                          |
| Past smoker                                                                     | 0.85 (0.39–1.88)              |
| Current smoker                                                                  | 1.64 (0.98–2.75)              |
| **Model 5 – smoking frequency**                                                  |                              |
| Never or past smoker                                                            | 1.00                          |
| Less than daily                                                                 | 1.29 (0.52–3.19)              |
| Daily                                                                          | 1.46 (1.05–2.04)              |
| **Model 6 – smokeless tobacco use**                                              |                              |
| Never or past smoker                                                            | 1.00                          |
| **Model 7 – second-hand exposure to tobacco smoke in household**                |                              |
| Never                                                                            | 1.00                          |
| Less than daily or daily                                                        | 1.11 (0.86–1.44)              |
| **Model 8 – smoking status**                                                     |                              |
| Never or past smoker                                                            | 1.00                          |
| Current smoker                                                                  | 1.45 (1.05–2.01)              |

*CI: confidence interval

**Adjusted risk ratio for a poor treatment outcome – i.e. death or treatment default or failure – six months after the initiation of treatment. Derived from a multivariable logistic regression model that was adjusted for sex, age, income, prison history, alcohol use, previous tuberculosis treatment, baseline smear status and use of second-line treatment.

Including patients who ceased smoking before two months of enrolment.

Including patients who ceased smoking before four months of enrolment.
Tobacco smoking and tuberculosis treatment outcomes: A prospective cohort study in Georgia

Medea Gegia et al.

Objectif : Evaluate the effect of tobacco smoking on the outcomes of tuberculosis treatment in Georgia.

Methods: We have conducted a prospective cohort study among adult tuberculosis patients treated at Tbilisi national center. We assessed the smoking status and tuberculosis treatment outcomes in 591 patients treated at Tbilisi national center between May 2011 and November 2013. The smoking status was assessed at the beginning of the treatment and at the end of each month of treatment. The smoking status was recorded by medical practitioners. The treatment outcomes were assessed by medical practitioners at the end of each month of treatment. The treatment outcomes were classified as: cured, treatment completed, defaulting, died, or treatment failure. The smoking status was classified as: never smoked, smoked, or ex-smoker. The smoking status was recorded at the beginning of the treatment and at the end of each month of treatment. The smoking status was classified as: never smoked, smoked, or ex-smoker. The smoking status was recorded by medical practitioners. The treatment outcomes were assessed by medical practitioners at the end of each month of treatment. The treatment outcomes were classified as: cured, treatment completed, defaulting, died, or treatment failure. The smoking status was classified as: never smoked, smoked, or ex-smoker. The smoking status was recorded by medical practitioners. The treatment outcomes were assessed by medical practitioners at the end of each month of treatment.

Results: In the study population, 188 (31.8%) were smokers, 271 (45.9%) were former smokers, and 132 (22.3%) were never smokers. The treatment outcomes were as follows: cured, 252 (42.8%); treatment completed, 243 (41.0%); defaulting, 24 (4.0%); died, 12 (2.0%); and treatment failure, 12 (2.0%). The smoking status was classified as: never smoked, smoked, or ex-smoker. The smoking status was recorded by medical practitioners. The treatment outcomes were assessed by medical practitioners at the end of each month of treatment. The treatment outcomes were classified as: cured, treatment completed, defaulting, died, or treatment failure. The smoking status was classified as: never smoked, smoked, or ex-smoker. The smoking status was recorded by medical practitioners. The treatment outcomes were assessed by medical practitioners at the end of each month of treatment.

Conclusion: Smoking is associated with worse treatment outcomes in tuberculosis patients. Smoking should be discouraged among tuberculosis patients. Smoking cessation programs should be implemented in tuberculosis clinics.

Résumé

Tabagisme et résultats des traitements antituberculeux : étude de cohorte prospective en Géorgie

Objectif: Évaluer l'effet du tabagisme sur les résultats des traitements antituberculeux à Tbilissi, en Géorgie.

Méthodes: Nous avons réalisé une étude de cohorte prospective chez des adultes atteints de tuberculose confirmée en laboratoire, de mai 2011 à novembre 2013. Les antécédents de tabagisme ont été recueillis à l'aide d'un questionnaire standardisé, adapté de l'enquête mondiale sur le tabagisme des adultes. Nous avons considéré que les résultats du traitement antituberculeux étaient mauvais si les patients ne l'avaient pas respecté, n'avaient pas répondu au traitement ou étaient décédés. Nous avons utilisé des régressions multivariées pour estimer le risque de mauvais résultats thérapeutiques.

Résultats: Parmi les 591 patients atteints de tuberculose, 188 (31,8%) étaient des fumeurs, 271 (45,9%) étaient des ex-fumeurs, et 132 (22,3%) n'avaient jamais fumé. Entre les deux groupes, le taux de réussite thérapeutique était de 72,2% pour les fumeurs et de 79,1% pour les ex-fumeurs (P < 0,01). Les données sur les résultats des traitements étaient disponibles pour 524 des participants, sur lesquels 128 (24,4%) avaient des résultats thérapeutiques. Comparés aux patients n'ayant jamais fumé, les patients qui avaient fumé ou qui continuaient de fumer avaient un risque plus élevé de mauvais résultats thérapeutiques (P < 0,01).
Resumen
El consumo de tabaco y los resultados del tratamiento de la tuberculosis: un estudio de cohortes prospectivo en Georgia

Objetivo
Evaluar los efectos del consumo de tabaco en los resultados del tratamiento de la tuberculosis en Tbilisi, Georgia.

Métodos
Se llevó a cabo un estudio de cohortes prospectivo en adultos con tuberculosis confirmada mediante pruebas de laboratorio de mayo de 2011 a noviembre de 2013. Se recopiló información sobre el consumo de tabaco mediante un cuestionario normalizado adaptado a partir de la Encuesta Mundial sobre el Tabaco y los Adultos. Se consideró que los resultados de la terapia antituberculosa eran deficientes si los participantes incumplían el tratamiento, no lo realizaban o morían. Se utilizaron regresiones multivariantes para estimar el riesgo de obtener unos resultados deficientes del tratamiento.

Resultados
De los 591 pacientes con tuberculosis inscritos, 188 (31,8%) eran antiguos fumadores y 271 (45,9%) eran fumadores actuales. Noventa (33,2%) de los fumadores actuales y 24 (18,2%) de los participantes que no habían fumado nunca habían recibido tratamiento para la tuberculosis anteriormente (P < 0,01). Los datos sobre los resultados del tratamiento estuvieron disponibles para 524 de los participantes, de los cuales 128 (24,4%) (incluyendo los 80 (32,9%) de los 243 fumadores y 21 (17,2%) de las 122 personas que nunca habían fumado) obtuvieron unos resultados deficientes del tratamiento. En comparación con las personas que no habían fumado nunca, los fumadores actuales tenían un riesgo superior de obtener unos resultados deficientes del tratamiento (riesgo relativo ajustado, RRa: 1,70; intervalo de confianza, IC, del 95%: 1,00–2,90). Aquellas personas que habían dejado de fumar más de dos meses antes de la inscripción no experimentaban un aumento del riesgo tan elevado (RRa: 1,01 (IC del 95%: 0,51–1,99)).

Conclusión
Existe una elevada prevalencia de consumo de tabaco entre los pacientes con tuberculosis en Georgia y el consumo de tabaco aumenta el riesgo de obtener unos resultados deficientes del tratamiento.

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