High prevalence of multidrug-resistant tuberculosis in Georgia

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High prevalence of multidrug-resistant tuberculosis in Georgia

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KEYWORDS
Tuberculosis; Multidrug-resistance; Prevalence

Summary
Background: Tuberculosis (TB) has emerged as a serious public health problem in the country of Georgia. However, little or no data exist on rates and risk factors for drug-resistant TB, including multidrug-resistant (MDR)-TB, in Georgia.
Objective: To assess the prevalence and risk factors for drug-resistant TB.
Methods: A cross-sectional prospective survey of patients with suspected pulmonary TB was carried out at four sentinel sites (Tbilisi, Zugdidi, Kutaisi, and Batumi) in Georgia between January 1, 2001 and December 31, 2004.
Results: Among 1422 patients with suspected pulmonary TB, 996 (70.0%) were culture positive; 931/996 (93.5%) had drug susceptibility testing performed. Overall, 64.0% of patients (48.3% of new and 85.3% of retreatment cases) had positive cultures for Mycobacterium tuberculosis resistant to ≥1 first-line antituberculosis drugs. The overall prevalence of MDR-TB was 28.1% (10.5% of newly diagnosed patients and 53.1% of retreatment cases). In multivariate analysis, risk factors for MDR-TB included: being a retreatment case (prevalence ratio (PR) = 5.28, 95% CI 3.95—7.07), history of injection drug use (PR = 1.59, 95% CI 1.21—2.09), and female gender (PR = 1.36, 95% CI 1.12—1.65).
Conclusions: MDR-TB has emerged as a serious public health problem in Georgia and will greatly impact TB control strategies.

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Introduction

Tuberculosis (TB) has emerged as an enormous public health problem in the former Soviet republics, due to economic decline and the general failure of tuberculosis control and other health services following the break-up of the Soviet Union.\(^1,2\) The country of Georgia, an independent nation that was previously part of the former Soviet Union (Figure 1), has one of the highest rates of tuberculosis among former Soviet republics.\(^3,4\) In 2005, a total of 6448 TB cases were reported in Georgia; the incidence of TB was 97 cases per 100 000 population and the prevalence 147 cases per 100 000 population.\(^5\) In 2003, the cohort treatment success rate was 67%; an additional 2% died, 4% failed, 15% defaulted, 8% transferred, and 4% had missing data.\(^3\) The situation in Georgia was exacerbated by a civil war in 1992—1993 following independence, which resulted in several hundred thousand internally displaced persons who have been noted to have high rates of tuberculosis.\(^1\)

Despite high rates of TB in Georgia, little or no data exist on the prevalence of or risk factors for drug-resistant tuberculosis. High rates of drug-resistant TB were reported among persons incarcerated in Georgian prisons in the late 1990s,\(^6\) but there are little or no previous data available about rates or risk factors for drug-resistant tuberculosis or multidrug-resistant (MDR) tuberculosis (defined as resistance to at least isoniazid and rifampin) among the Georgian civilian population. Drug-resistant TB, especially MDR-TB, is associated with significantly higher morbidity and mortality than the drug-susceptible disease.\(^7,8,9\) Drug resistance rates also reflect current and prior effectiveness of TB control programs.\(^10\) Drug-resistant TB may threaten TB control efforts by reducing the effectiveness of short-course antituberculosis regimens delivered under the World Health Organization (WHO) recommended directly observed therapy, short course (DOTS) strategy\(^7,11\) and by disproportionately absorbing TB control program resources.

The purpose of our prospective study was to assess rates of and risk factors for drug-resistant TB, including MDR-TB, in Georgia. This information is important for developing effective TB control strategies in Georgia and assessing the need for implementation of the DOTS-Plus strategy for the treatment of MDR-TB.\(^12\)

Methods

Study population

A cross-sectional prospective survey was carried out at four sentinel sites in Georgia. Patients aged 15 years and older, highly suspected of having pulmonary tuberculosis (i.e., patients with clinical symptoms and chest radiograph findings suggestive of TB), presenting to four sentinel sites (inpatient facilities in four Georgian cities — Tbilisi, Zugdidi, Kutaisi, and Batumi) between January 1, 2001 and December 31, 2004 in the country of Georgia were eligible for enrollment into the study. In Georgia, patients are offered hospitalization for the intensive phase of TB treatment. Written informed consent was obtained from all patients prior to enrollment. The study was approved by the Georgian National Center for Tuberculosis and Lung Disease (NCTLD) Ethics Committee, the Georgian National Center for Disease Control Ethics Committee, and the Emory University Institutional Review Board (IRB).

Data collection and definitions

Clinical, demographic, and epidemiologic data were collected through interview of patients and review of medical records. Demographic data included patient age, gender, nationality (Georgian, Armenian, Azeri, Russian, and other), region of residence, status of an internally displaced person (IDP), incarceration history, employment status, and history

Figure 1  Map of the country of Georgia. Red dots show the four sentinel sites where the study was conducted (Tbilisi, Zugdidi, Kutaisi, and Batumi).
of tobacco, alcohol, and injection drug use. In addition, data on comorbid illnesses including hepatitis, HIV infection, diabetes mellitus, gastritis, and peptic ulcer disease were collected. The case status for each patient with TB was recorded (newly diagnosed vs. previously treated) as well as the primary reason for culture examination (initial diagnosis vs. follow-up visit). The study focused primarily on patients with TB who had positive cultures.

New cases were defined as patients who had never had treatment for TB or who had received antituberculosis drugs for less than one month. Retreatment cases were defined as patients who had a prior history of treatment with antituberculosis drugs for more than one month. Retreatment cases included relapses, treatment after failure, treatment after default, and chronic cases (i.e., a patient with TB who is sputum-positive at the end of a standard retreatment regimen). Multidrug-resistance (MDR) was defined as resistance to at least both isoniazid and rifampin. Monoresistance was defined as resistance exclusively to one of the four first-line antituberculosis drugs tested. Polyresistance was defined as resistance to two or more of the five first-line antituberculosis drugs, but not both isoniazid and rifampin.

### Laboratory methods

Three sputum samples for acid-fast bacillus (AFB) smear microscopy and culture were obtained from each patient enrolled into the study. Specimens were obtained at each sentinel site and then transported to the Georgian National Reference Laboratory in Tbilisi where AFB cultures were performed with Lowenstein–Jensen media using standard methodologies. Drug susceptibility testing (DST) to first-line antituberculosis drugs (isoniazid, rifampin, ethambutol, and streptomycin) was performed on *Mycobacterium tuberculosis* isolates using the absolute concentration method. The concentrations of the antituberculosis drugs tested were as follows: isoniazid 0.1 µg/ml, rifampin 40.0 µg/ml, streptomycin 10.0 µg/ml, and ethambutol 2.0 µg/ml.

### Statistical analysis

All statistical analyses were performed using SAS, version 9.0 (SAS Institute Inc., Cary, NC, USA). Trends in the prevalence of drug resistance over time were assessed using the Chi-square test for trends. Risk factors for having any resistance and multidrug-resistance among culture-confirmed TB cases were assessed. Univariate analysis was performed to determine unadjusted association of TB drug resistance with patient clinical and demographic characteristics. For dichotomous variables, prevalence ratios (PR) with 95% confidence intervals (CI) were calculated using PROC GENMOD in SAS. To obtain the adjusted estimates, two multivariate log-binomial regression models were fitted with DST results (any resistance vs. fully susceptible and MDR-TB vs. non-MDR-TB, respectively) as outcome variables. Variables significantly associated with an outcome of interest in the univariate analysis as well as potential confounders and effect-modifiers based on literature review were included in the final multivariate model. Interaction and confounding were assessed. A p-value of ≤0.05 was considered statistically significant.

### Results

A total of 2212 patients underwent culture examination during the four-year period. Patients with tuberculosis who had sputum collected at these sites for reasons other than diagnosis of TB (N = 607; e.g., follow-up specimens for patients undergoing current treatment or unknown reason for sputum examination) were excluded from the analysis. A total of 1605 patients with suspected tuberculosis who had sputum specimens collected for diagnostic purposes as the primary reason for culture examination at four sentinel sites in Georgia were enrolled into the study. Among the 1605 patients with suspected TB enrolled into the study, 1422 (88.6%) had valid culture results (either positive or negative cultures) and constituted the sample for culture confirmation analysis (Figure 2). Of these 1422 patients, 996 (70.0%) had a positive culture for *M. tuberculosis*. Drug susceptibility testing results were available for 931 of 996 patients (93.5%) with positive cultures. AFB smear results were available for 1188 patients with positive or negative culture results; of these 925 (77.9%) were AFB smear positive and 263 (22.1%) were smear negative. A total of 66 patients with a negative smear (5.6% of all with available smear results) had a positive culture.

The mean age of the 1422 patients with culture results was 38 years (range 15–81 years); 73.5% were male, 87.1% had Georgian nationality, and 54.3% resided in Tbilisi (Table 1). The history of previous treatment was known for 1154 of 1422 patients (81.2%), and of those, 682 (59.1%) were newly diagnosed cases and 472 (40.9%) were retreatment cases (Table 1). Having a positive culture for *M. tuberculosis* was significantly associated with male gender and residence outside Tbilisi (Table 1). Patients in age groups 55–64 and >65 years were significantly less likely to have had a positive culture compared to those aged 15–24 years. Patients with unknown treatment history had positive cultures significantly less often than new cases.

### Risk of drug-resistant tuberculosis

Drug susceptibility test (DST) results were available on *M. tuberculosis* isolates recovered from 931 patients (534 newly diagnosed cases, 388 retreatment cases, and nine cases with unknown treatment history). The prevalence of different patterns of resistance is shown in Table 2. Overall, 596 patients (64.0%; 258 (48.3%) new and 331 (85.3%) retreatment cases) had isolates resistant to one or more first-line antituberculosis drugs. Risk factors for resistance to one or more antituberculosis drugs in univariate analysis are shown in Table 3. When nine patients with unknown treatment history were excluded, analysis yielded similar results (data not shown). In multivariate analysis, having any resistance to one or more first-line antituberculosis drugs was independently associated with being a retreatment case (PR = 1.75, 95% CI 1.58–1.94) and being an internally displaced person (PR = 1.10, 95% CI 1.00–1.21).

Two hundred sixty-two of 931 patients (28.1%) were demonstrated to have MDR-TB. The prevalence of MDR-TB was significantly higher among retreatment cases than among newly diagnosed cases (206/388 (53.1%) vs. 56/534...
Figure 2  Study sample of patients with suspected pulmonary tuberculosis at four sentinel sites in the country of Georgia (DST = drug susceptibility testing; TB = tuberculosis).

<table>
<thead>
<tr>
<th>Variable</th>
<th>All suspected TB cases (N = 1422)</th>
<th>Culture positive (N = 996)</th>
<th>Culture negative (N = 426)</th>
<th>PR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>237 (16.7%)</td>
<td>174 (17.5%)</td>
<td>63 (14.8%)</td>
<td>Ref.</td>
</tr>
<tr>
<td>25–34</td>
<td>408 (28.7%)</td>
<td>301 (30.2%)</td>
<td>107 (25.1%)</td>
<td>1.00 (0.91–1.11)</td>
</tr>
<tr>
<td>35–44</td>
<td>376 (26.4%)</td>
<td>285 (28.6%)</td>
<td>91 (21.4%)</td>
<td>1.03 (0.94–1.14)</td>
</tr>
<tr>
<td>45–54</td>
<td>216 (15.2%)</td>
<td>146 (14.7%)</td>
<td>70 (16.4%)</td>
<td>0.92 (0.82–1.04)</td>
</tr>
<tr>
<td>55–64</td>
<td>111 (7.8%)</td>
<td>65 (6.5%)</td>
<td>46 (10.8%)</td>
<td>0.80 (0.67–0.95)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>74 (5.2%)</td>
<td>25 (2.5%)</td>
<td>49 (11.5%)</td>
<td>0.46 (0.33–0.64)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1045 (73.5%)</td>
<td>749 (75.2%)</td>
<td>296 (69.5%)</td>
<td>1.09 (1.01–1.19)</td>
</tr>
<tr>
<td>Female</td>
<td>377 (26.5%)</td>
<td>247 (24.8%)</td>
<td>130 (30.5%)</td>
<td>Ref.</td>
</tr>
<tr>
<td>Case status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New</td>
<td>682 (48.0%)</td>
<td>579 (58.1%)</td>
<td>103 (24.2%)</td>
<td>Ref.</td>
</tr>
<tr>
<td>Retreatment</td>
<td>472 (33.2%)</td>
<td>408 (41.0%)</td>
<td>64 (15.0%)</td>
<td>0.98 (0.94–1.03)</td>
</tr>
<tr>
<td>Unknown</td>
<td>268 (18.8%)</td>
<td>9 (0.9)</td>
<td>259 (60.8)</td>
<td>0.04 (0.02–0.07)</td>
</tr>
<tr>
<td>Residence (9944/417c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tbilisi</td>
<td>766 (54.3%)</td>
<td>513 (51.6%)</td>
<td>253 (60.7%)</td>
<td>0.88 (0.84–0.96)</td>
</tr>
<tr>
<td>Other</td>
<td>645 (45.7%)</td>
<td>481 (48.4%)</td>
<td>164 (39.3%)</td>
<td>Ref.</td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Georgian</td>
<td>1239 (87.1%)</td>
<td>872 (87.6%)</td>
<td>367 (86.2%)</td>
<td>1.04 (0.93–1.16)</td>
</tr>
<tr>
<td>Other</td>
<td>183 (12.9%)</td>
<td>124 (12.4%)</td>
<td>59 (13.8%)</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

* Unadjusted prevalence ratio (PR) for comparison of culture positive to culture negative patients.

b Number of patients with positive cultures for whom data were available.

c Number of patients with negative cultures for whom data were available.
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Table 2  Prevalence of first-line antituberculosis drug resistance at four sentinel sites in Georgia, 2001—2004

<table>
<thead>
<tr>
<th>Resistance profile</th>
<th>All cases</th>
<th>New cases</th>
<th>Retreatment cases</th>
<th>Unknown treatment history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Total number of strains tested</td>
<td>931</td>
<td>100.0</td>
<td>534</td>
<td>100.0</td>
</tr>
<tr>
<td>I. Any drug resistance</td>
<td>596</td>
<td>64.0</td>
<td>258</td>
<td>48.3</td>
</tr>
<tr>
<td>INH</td>
<td>442</td>
<td>47.5</td>
<td>159</td>
<td>29.8</td>
</tr>
<tr>
<td>RIF</td>
<td>287</td>
<td>30.8</td>
<td>66</td>
<td>12.4</td>
</tr>
<tr>
<td>SM</td>
<td>490</td>
<td>52.6</td>
<td>199</td>
<td>37.3</td>
</tr>
<tr>
<td>EMB</td>
<td>210</td>
<td>22.7</td>
<td>56</td>
<td>10.5</td>
</tr>
<tr>
<td>II. Monoresistance</td>
<td>188</td>
<td>20.2</td>
<td>126</td>
<td>23.6</td>
</tr>
<tr>
<td>INH only</td>
<td>59</td>
<td>6.3</td>
<td>39</td>
<td>7.3</td>
</tr>
<tr>
<td>RIF only</td>
<td>7</td>
<td>0.8</td>
<td>3</td>
<td>0.6</td>
</tr>
<tr>
<td>SM only</td>
<td>108</td>
<td>11.6</td>
<td>75</td>
<td>14.0</td>
</tr>
<tr>
<td>EMB only</td>
<td>14</td>
<td>1.5</td>
<td>9</td>
<td>1.7</td>
</tr>
<tr>
<td>III. MDR-TB</td>
<td>262</td>
<td>28.1</td>
<td>56</td>
<td>10.5</td>
</tr>
<tr>
<td>INH + RIF</td>
<td>15</td>
<td>1.6</td>
<td>6</td>
<td>1.1</td>
</tr>
<tr>
<td>INH + RIF + EMB</td>
<td>6</td>
<td>0.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>INH + RIF + SM</td>
<td>98</td>
<td>10.5</td>
<td>26</td>
<td>4.9</td>
</tr>
<tr>
<td>INH + RIF + SM + EMB</td>
<td>143</td>
<td>15.4</td>
<td>24</td>
<td>4.5</td>
</tr>
<tr>
<td>IV. Polyresistance</td>
<td>146</td>
<td>15.7</td>
<td>76</td>
<td>14.2</td>
</tr>
<tr>
<td>INH + EMB</td>
<td>2</td>
<td>0.2</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>INH + SM</td>
<td>86</td>
<td>9.2</td>
<td>48</td>
<td>9.0</td>
</tr>
<tr>
<td>INH + EMB + SM</td>
<td>33</td>
<td>3.5</td>
<td>15</td>
<td>2.8</td>
</tr>
<tr>
<td>RIF + EMB</td>
<td>3</td>
<td>0.3</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>RIF + SM</td>
<td>13</td>
<td>1.4</td>
<td>5</td>
<td>0.9</td>
</tr>
<tr>
<td>EMB + SM</td>
<td>2</td>
<td>0.2</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>EMB only</td>
<td>7</td>
<td>0.8</td>
<td>5</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Number of drugs resistant to:

| Susceptible to 4 drugs     | 335       | 36.0      | 276             | 51.7         | 57        | 14.7      | 2          | 22.2       |
| Resistant to 1 drug        | 188       | 20.2      | 126             | 23.6         | 59        | 15.2      | 3          | 33.3       |
| Resistant to 2 drugs       | 126       | 13.5      | 66              | 12.3         | 56        | 14.4      | 4          | 44.4       |
| Resistant to 3 drugs       | 139       | 14.9      | 42              | 7.9          | 97        | 25.0      | 0          | 0          |
| Resistant to 4 drugs       | 143       | 15.4      | 24              | 4.5          | 119       | 30.7      | 0          | 0          |

INH, isoniazid; RIF, rifampin; EMB, ethambutol; SM, streptomycin; MDR-TB, multidrug-resistant tuberculosis (resistance to at least both isoniazid and rifampin); polyresistance, resistance to two or more drugs but not both isoniazid and rifampin.

a p < 0.001 in Chi-square test for comparison of prevalence of resistance pattern in retreatment cases to that in new cases.
b p = 0.002 in Chi-square test for comparison of prevalence of resistance pattern in retreatment cases to that in new cases.
c p = 0.25 in Chi-square test for comparison of prevalence of resistance pattern in retreatment cases to that in new cases.

More than half of MDR-TB cases (143/262 (54.6%)) were resistant to all four first-line antituberculosis drugs tested (Table 2). Retreatment cases were significantly more likely to have MDR-TB than non-MDR-TB (206/262 patients (78.6%) with MDR-TB were retreatment cases compared to 182/669 (27.2%) non-MDR-TB cases (PR = 5.06, 95% CI 3.88—6.60) (Table 4)). Other significant predictors of MDR-TB in univariate analysis included patient age groups 25—34 and 35—44 years (compared to age group 15—24 years), living outside of Tbilisi, history of incarceration, unemployment, and history of injection drug use (Table 4). When nine patients with unknown treatment history were excluded from analysis, the results were similar (data not shown). In multivariate analysis, independent risk factors for MDR-TB included being a retreatment case (PR = 5.28, 95% CI 3.95—7.07), history of injection drug use (PR = 1.59, 95% CI 1.21—2.09), and female gender (PR = 1.36, 95% CI 1.12—1.65) (Table 5).

Resistance to rifampin was a significant predictor of resistance to isoniazid and streptomycin: 262 of 287 isolates (91.3%) resistant to rifampin were also resistant to isoniazid (PR = 11.59, 95% CI 7.85—17.12), and 256 isolates (89.2%) were also resistant to streptomycin (PR = 7.43, 95% CI 5.24—10.55).

The prevalence of any drug resistance among TB cases significantly decreased during the study period from 83.5% in 2001 to 54.1% in 2004 (p-value for trend <0.001) (Figure 3). The prevalence of MDR-TB decreased from 33.3% in 2001 to 20.0% in 2004 (p-value for trend <0.001) (Figure 3). Similar trends were observed for both new and retreatment cases (data not shown).
Table 3  Univariate analysis of association of having resistance to at least one first-line antituberculosis drug with patient demographic and clinical characteristics (N = 931)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Any drug resistance (N = 596)</th>
<th>Drug susceptible (N = 335)</th>
<th>Prevalence ratio (PR) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>83 (13.9)</td>
<td>78 (23.3)</td>
<td>Ref.</td>
</tr>
<tr>
<td>25–34</td>
<td>197 (33.0)</td>
<td>84 (25.1)</td>
<td>1.36 (1.15—1.61)</td>
</tr>
<tr>
<td>35–44</td>
<td>187 (31.4)</td>
<td>87 (25.9)</td>
<td>1.32 (1.12—1.57)</td>
</tr>
<tr>
<td>45–54</td>
<td>76 (12.8)</td>
<td>58 (17.3)</td>
<td>1.10 (0.89—1.36)</td>
</tr>
<tr>
<td>55–64</td>
<td>41 (6.9)</td>
<td>16 (4.8)</td>
<td>1.40 (1.12—1.74)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>12 (2.0)</td>
<td>12 (3.6)</td>
<td>0.97 (0.63—1.49)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>147 (24.7)</td>
<td>81 (24.2)</td>
<td>1.01 (0.90—1.13)</td>
</tr>
<tr>
<td>Male</td>
<td>449 (75.3)</td>
<td>254 (75.8)</td>
<td>Ref.</td>
</tr>
<tr>
<td>Case status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New</td>
<td>258 (43.3)</td>
<td>276 (82.4)</td>
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<td>285 (47.9)</td>
<td>193 (57.8)</td>
<td>0.87 (0.79—0.96)</td>
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<td>Other</td>
<td>310 (52.1)</td>
<td>141 (42.2)</td>
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<td>500 (93.1)</td>
<td>276 (97.2)</td>
<td>Ref.</td>
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<td>History of incarceration (537a/283b)</td>
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</tr>
<tr>
<td>Yes</td>
<td>87 (16.2)</td>
<td>16 (5.7)</td>
<td>1.35 (1.22—1.49)</td>
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<tr>
<td>No</td>
<td>450 (83.8)</td>
<td>267 (94.3)</td>
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<td>Unemployed (509a/271b)</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>427 (83.9)</td>
<td>206 (76.0)</td>
<td>1.21 (1.04—1.41)</td>
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<tr>
<td>No</td>
<td>82 (16.1)</td>
<td>65 (24.0)</td>
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<td>Tobacco use (538a/284b)</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>268 (49.8)</td>
<td>141 (49.6)</td>
<td>1.00 (0.91—1.11)</td>
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<td>No</td>
<td>270 (50.2)</td>
<td>143 (50.4)</td>
<td>Ref.</td>
</tr>
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<td>Alcohol use (537a/283b)</td>
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<td>76 (26.9)</td>
<td>1.00 (0.90—1.12)</td>
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<td>No</td>
<td>392 (73.0)</td>
<td>207 (73.1)</td>
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<tr>
<td>History of injection drug use (477a/272b)</td>
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<td>Yes</td>
<td>19 (4.0)</td>
<td>3 (1.1)</td>
<td>1.37 (1.15—1.63)</td>
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<tr>
<td>No</td>
<td>458 (96.0)</td>
<td>269 (98.9)</td>
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</tr>
<tr>
<td>Hepatitis (508a/271b)</td>
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<td></td>
</tr>
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<td>40 (7.9)</td>
<td>14 (5.2)</td>
<td>1.15 (0.97—1.36)</td>
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<td>No</td>
<td>468 (92.1)</td>
<td>257 (94.8)</td>
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<td>HIV</td>
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<td></td>
<td></td>
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<td>No</td>
<td>135 (22.7)</td>
<td>92 (27.5)</td>
<td>Ref.</td>
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<td>456 (76.5)</td>
<td>243 (72.5)</td>
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<td>Diabetes mellitus (518a/273b)</td>
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<tr>
<td>Yes</td>
<td>25 (4.8)</td>
<td>11 (4.0)</td>
<td>1.06 (0.88—1.33)</td>
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<td>No</td>
<td>493 (95.2)</td>
<td>262 (96.0)</td>
<td>Ref.</td>
</tr>
<tr>
<td>History of gastritis/peptic ulcer disease (517a/273b)</td>
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<td></td>
<td></td>
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<td>Yes</td>
<td>17 (3.3)</td>
<td>11 (4.0)</td>
<td>0.93 (0.68—1.25)</td>
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<td>No</td>
<td>500 (96.7)</td>
<td>262 (96.0)</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

a Number of patients with any drug resistance for whom data were available.
b Number of patients with drug susceptible cultures for whom data were available.
### Table 4: Univariate analysis of association of having MDR-TB and patient demographic and clinical characteristics (N = 931)

<table>
<thead>
<tr>
<th>Variable</th>
<th>MDR-TB case (N = 262)</th>
<th>Non-MDR-TB case (N = 669)</th>
<th>Prevalence ratios (PR) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
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<tr>
<td>Age group, years</td>
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<td>15—24</td>
<td>33 (12.6)</td>
<td>128 (19.1)</td>
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<tr>
<td>25—34</td>
<td>90 (34.4)</td>
<td>191 (28.6)</td>
<td>1.56 (1.10—2.21)</td>
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<td>35—44</td>
<td>83 (31.7)</td>
<td>191 (28.6)</td>
<td>1.48 (1.04—2.10)</td>
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<td>45—54</td>
<td>36 (13.7)</td>
<td>98 (14.6)</td>
<td>1.31 (0.87—1.98)</td>
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<td>55—64</td>
<td>15 (5.7)</td>
<td>42 (6.3)</td>
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<td>&gt;65</td>
<td>5 (1.9)</td>
<td>19 (2.8)</td>
<td>1.02 (0.44—2.35)</td>
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<td>Gender</td>
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<tr>
<td>Female</td>
<td>70 (26.7)</td>
<td>158 (23.6)</td>
<td>1.12 (0.89—1.41)</td>
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<td>Male</td>
<td>192 (73.3)</td>
<td>511 (76.4)</td>
<td>Ref.</td>
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<td>Case status by history of TB treatment</td>
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<td>478 (71.4)</td>
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<td>9 (1.4)</td>
<td>Undefined</td>
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<td></td>
<td></td>
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<td>Tbilisi</td>
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<td>368 (55.1)</td>
<td>0.69 (0.56—0.85)</td>
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<td>Other</td>
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<td>300 (44.9)</td>
<td>Ref.</td>
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<td>Nationality</td>
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<td>89 (13.3)</td>
<td>Ref.</td>
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<td>Internally displaced person (246&lt;sup&gt;a&lt;/sup&gt;/575&lt;sup&gt;b&lt;/sup&gt;)</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>17 (6.9)</td>
<td>28 (4.9)</td>
<td>1.28 (0.87—1.89)</td>
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<tr>
<td>No</td>
<td>229 (93.1)</td>
<td>547 (95.1)</td>
<td>Ref.</td>
</tr>
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<td>History of incarceration (246&lt;sup&gt;a&lt;/sup&gt;/574&lt;sup&gt;b&lt;/sup&gt;)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>53 (21.5)</td>
<td>50 (8.7)</td>
<td>1.91 (1.53—2.39)</td>
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<tr>
<td>No</td>
<td>193 (78.5)</td>
<td>524 (91.3)</td>
<td>Ref.</td>
</tr>
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<td>Unemployed (235&lt;sup&gt;a&lt;/sup&gt;/545&lt;sup&gt;b&lt;/sup&gt;)</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>203 (86.4)</td>
<td>430 (78.9)</td>
<td>1.47 (1.06—2.04)</td>
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<td>No</td>
<td>32 (13.6)</td>
<td>115 (21.1)</td>
<td>Ref.</td>
</tr>
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<td>125 (50.6)</td>
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<td>Ref.</td>
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<tr>
<td>Yes</td>
<td>65 (26.4)</td>
<td>156 (27.2)</td>
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<td>Ref.</td>
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<td></td>
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<td>15 (6.9)</td>
<td>7 (1.3)</td>
<td>2.47 (1.81—3.36)</td>
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<td>No</td>
<td>201 (93.1)</td>
<td>526 (98.7)</td>
<td>Ref.</td>
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<td>20 (8.4)</td>
<td>34 (6.3)</td>
<td>1.24 (0.86—1.78)</td>
</tr>
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<td>No</td>
<td>217 (91.6)</td>
<td>508 (93.7)</td>
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<td>HIV</td>
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<tr>
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<td>2 (0.8)</td>
<td>3 (0.5)</td>
<td>1.40 (0.47—4.17)</td>
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<td>65 (24.8)</td>
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<td>23 (4.2)</td>
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<tr>
<td>No</td>
<td>230 (94.7)</td>
<td>525 (95.8)</td>
<td>Ref.</td>
</tr>
<tr>
<td>History of gastritis/peptic ulcer disease (243&lt;sup&gt;a&lt;/sup&gt;/547&lt;sup&gt;b&lt;/sup&gt;)</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>11 (4.5)</td>
<td>17 (3.1)</td>
<td>1.29 (0.80—2.07)</td>
</tr>
<tr>
<td>No</td>
<td>232 (95.5)</td>
<td>530 (96.9)</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

<sup>a</sup> Number of patients with positive cultures for whom data were available.

<sup>b</sup> Number of patients with negative cultures for whom data were available.
Our study demonstrated high rates of drug resistance including MDR-TB in Georgia, among both newly diagnosed and retreatment cases in the civilian population. Overall, 64.0% of the TB cases had resistance to \( \geq 1 \) antituberculosis drug (48.3% of new and 85.3% of retreatment cases). The overall prevalence of MDR-TB in Georgia in our study was 28.1%, with very high prevalence both in newly diagnosed patients (10.5%) and in retreatment cases (53.1%). Resistance to any first-line drug was independently associated with being a retreatment case and being an internally displaced person. Independent risk factors for MDR-TB included being a retreatment case, history of injection drug use, and female gender.

To our knowledge, our study is the first to report rates of drug resistance among TB cases in a civilian population in Georgia. High rates of MDR-TB (4—5% in new cases and 19—25% in retreatment cases) have been reported from Abkhazia, an autonomous republic of Georgia, which functions independently from Georgia.\(^{17,18}\) Our findings of high rates of drug-resistant TB including MDR-TB in Georgia are similar to what has been reported from other former Soviet republics. This region has among the highest prevalence of drug-resistant TB in the world.\(^{19}\) In countries of the former Soviet Union, MDR-TB rates have been reported to range from 4% (Dashoguz, Turkmenistan) to 22.7% (Samara, Russia) in new cases,\(^{20,21}\) and from 18% (Dashoguz, Turkmenistan) to 54—60% (Republic of Lithuania and Arkhangelsk, Russia, respectively) in retreatment cases.\(^{20,22,23}\) High rates of MDR-TB have also been reported from Kazakhstan (14.2%), Tomsk, Russian Federation (13.7%), and Estonia (12.2%).\(^{19}\) The median prevalence of resistance to the four first-line drugs among retreatment cases in the countries of the former Soviet Union was as high as 30%, compared to a median of 1.3% in all other settings.\(^{19}\)

In general, high rates of MDR-TB among newly diagnosed patients suggest problems with TB control in the past, while high rates of MDR-TB among retreatment cases is suggestive of existing problems in the TB control program including suboptimal treatment regimens and poor compliance with treatment.\(^{10}\) TB has emerged as a major public health problem in Georgia following the dissolution of the Soviet Union in 1991. Following independence, there was a civil war in 1992—1993, which resulted in a large number of internally displaced persons. Living conditions in Georgia deteriorated for a large proportion of the population, the healthcare infrastructure was destroyed, and there was increased poverty and migration. Inadequate management of TB services, a significant shortage or absence of TB drugs, institutional spread, and poor mechanisms to ensure adherence to treatment\(^{1,2,6}\) are factors that have likely contributed to the high rates of drug-resistant TB found in our study. High default rates, which were reported to be as high as 23—25% among new cases and 39% among retreatment cases in a study in 1995—1996, and 15% among new cases and 23% among retreatment cases in 2003,\(^{2,3}\) have likely contributed to the emergence of MDR-TB as well. While high rates of drug-resistant TB including MDR-TB have been previously reported from correctional facilities in Georgia,\(^{6}\) our study is the first to report the prevalence and risk factors for drug-resistant TB in the civilian population in Georgia.

The Georgian National Tuberculosis Program was established in 1995. After its formation, Georgia started implementing pilot projects based on the WHO-recommended DOTS strategy with WHO support,\(^{2,24}\) and currently Georgia has 100% of DOTS coverage.\(^{4}\) However, implementation of DOTS in Georgia was limited until recent years, when robust DOTS programs in selected regions (including Gori and Tbilisi) were achieved. Temporal trends between 2001 and 2004 in our study demonstrate a significant decrease in the overall prevalence of MDR-TB, any resistance, and polyresistance (resistance to two or more drugs but not both isoniazid and rifampin) during the study period. These decreases likely reflect enhanced TB control efforts in Georgia, including implementation of standardized TB treatment (including the provision of directly observed therapy), improved drug supply system, improved diagnostics and laboratory capacities, implementation of proper recording and reporting, and training of healthcare staff.\(^{2,24}\) Despite these improvements, MDR-TB rates among new and retreatment cases remain high, providing important challenges for TB control in Georgia. In settings with existing high rates of MDR-TB, the current WHO standard treatment policy of administration of first-line drugs to retreatment cases should be revised.\(^{7}\) About one third of the study population would not have responded to

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**Table 5** Multivariate analysis of risk factors for multidrug-resistant tuberculosis (MDR-TB) in Georgia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted prevalence ratios (PR) (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retreatment case</td>
<td>5.28 (3.95—7.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of injection drug use</td>
<td>1.59 (1.21—2.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.36 (1.12—1.65)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

---

**Figure 3** Dynamics of the prevalence of antituberculosis drug resistance over time in the country of Georgia, 2001—2004.
the standard WHO retreatment regimen with first-line drugs (five drugs with the addition of streptomycin), and drug resistance could be amplified by receiving such regimens. Better access to DST results including rapid DST methods at the time of TB diagnosis would facilitate appropriate selection of treatment regimens. Limited resources and laboratory capacity remain limitations to the implementation of this strategy. However, increasing laboratory capacity to deal with MDR-TB as recommend by the Global Plan to Stop TB (e.g., at a regional level) and better referral of specimens from patients living in remote areas to regional/national reference laboratories should be encouraged to meet this challenge. The application of the Georgian National TB Program to the Green Light Committee was approved, and treatment of TB patients with drug-resistant tuberculosis using second-line drugs started in 2007.

The strongest predictor of having both any drug resistance and multidrug resistance in our study was being a retreatment case. Previous treatment is a well-known risk factor for the development of drug resistance. The WHO/IUATLD (International Union Against Tuberculosis and Lung Disease) Global Project on Anti-tuberculosis Drug Resistance Surveillance demonstrated that the proportion of retreatment cases among the total number of cases was significantly associated with both MDR and any drug resistance. Previous treatment was also demonstrated as the strongest determinant of MDR-TB in Europe in a systematic review based on studies from 12 European countries. The likelihood of having MDR-TB increases linearly with increasing total time of prior treatment. The current WHO treatment recommendations for relapses and failures in category II, which includes administration of five already used drugs, may result in monotherapy and lead to further amplification of resistance.

In our study, internally displaced persons (IDP) had an increased risk of having any resistance to first-line antituberculosis drugs. IDPs are ethnic Georgians from the north-west province of Abkhazia who were forced to flee their homes during the civil war of 1992–1993 and reside in other parts of Georgia, often in places such as former hotels or hospitals where overcrowding is common. IDPs have been reported to be at increased risk for TB infection and disease. These conditions may favor transmission of TB including drug-resistant strains. Internally displaced status and risk of drug resistance could be influenced by previous treatment. In some studies, injection drug use has been reported to be a risk factor for MDR-TB in newly diagnosed cases, while other studies have failed to find such an association. The association of injection drug use with MDR-TB could be related to close contacts of drug users and transmission of resistant strains within this group. Also it has been demonstrated that injection drug use is a significant predictor of TB treatment nonadherence, which may impact the development of resistance.

Tuberculosis, including MDR-TB, is more common among men. In a systematic review by Faustini et al., MDR-TB cases were more likely to be male in Western Europe, while in Eastern Europe male gender was not associated with MDR-TB. These authors assumed that male gender could modify the association between previous treatment and MDR-TB since men are believed to be less adherent to treatment than women. Interestingly, we found that female gender was an independent risk factor for MDR-TB in Georgia. Preliminary results of a population-based study in Georgia also found that female gender is independently associated with an increased risk for MDR-TB. Our finding in Georgia that women are at increased risk for MDR-TB if they have TB is similar to that reported in two studies conducted in former Soviet republics (Arkhangelsk, Russia, and Estonia). The reasons for the association between female gender and MDR-TB are unclear and deserve further study. We hypothesize that this association could be related to the fact that women care for men and others with MDR-TB both in households and in healthcare settings in Georgia, where the majority of healthcare workers are female. There has previously been no treatment available in Georgia for MDR-TB and therefore such patients likely remain infectious for long periods of time, increasing the risk of household and institutional transmission of MDR-TB. We found that a higher proportion of women had new cases of MDR-TB compared to men.

Our study is subject to several limitations. One of these is the potential misclassification of new and retreatment cases; some cases registered as new may actually have had TB treatment in the past. Classification was based on patient history of prior treatment for TB and review of medical records (which were not available for all patients enrolled). Some patients with suspected TB had contaminated cultures and were excluded from the analysis, which has the potential for introducing selection bias. In addition, further bias is possible because our study was carried out at selected sites in Georgia and was not population-based. The high rate of missing data among those with a negative AFB culture was due to the fact that the study focused primarily on patients with a positive culture. However, our study provides important initial data on drug resistance in Georgia and enhanced infrastructure development, which has allowed for the subsequent development of a population-based study on drug resistance; this study is ongoing.

In summary, drug-resistant tuberculosis including MDR-TB has emerged as a serious public health problem in Georgia and will greatly impact TB control strategies. The overall prevalence of MDR-TB was found to be 28.1% (10.5% of newly diagnosed patients and 53.1% of retreatment cases). In multivariate analysis, risk factors for MDR-TB included: being a retreatment case (PR = 5.28), history of injection drug use (PR = 1.59), and female gender (PR = 1.36). This study has important implications for TB control in Georgia. It highlights the need to fully implement the Georgia National Tuberculosis Program’s new five-year plan for TB control, which is based on The Global Plan to Stop TB (2006–2015). This includes rapid DOTS expansion so that DOTS is fully implemented throughout Georgia in order to prevent further emergence of drug resistance. Other measures include development of the capacity to treat those with MDR-TB in Georgia through implementation of DOTS-Plus (provision of diagnosis, treatment, and management for all patients with MDR-TB through the DOTS-Plus strategy), implementation of TB infection control measures to prevent institutional spread of tuberculosis, engaging the overall health system in TB-related activities, empowering patients and communities to support TB control and reduce TB-related stigma, and enabling and promoting TB-related research (including research into simplified and easy to use tests to detect drug resistance).
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References