Eliminating the category II retreatment regimen from national tuberculosis programme guidelines: the Georgian experience


**Abstract**

*This experience can serve as a successful model for other countries to make informed decisions about the use of category II therapy.*

**Introduction**

Management of patients who have been previously treated for tuberculosis (TB) has been a cause of much debate. In 1991, the World Health Organization (WHO) recommended the use of the “category II retreatment regimen” for all patients with a prior history of TB treatment. The category II regimen added streptomycin to the first-line agents and extended treatment to 8 months. Multiple observational studies have examined outcomes among individuals receiving category II treatment and shown mixed results. Overall success rates are in the 60–80% range, with notably worse outcomes seen among patients who failed or relapsed after their initial treatment episode.

WHO TB treatment guidelines published in 2010 recommend treatment guided by drug susceptibility testing – using rapid molecular tests where possible – for all previously treated patients. The category II regimen, however, is still recommended for certain patients who return after default or relapse in settings with low risk of multidrug-resistant TB (MDR-TB). There is little documentation concerning implementation of these guidelines and category II remains the standard of care for patients requiring retreatment in most settings in the world. This paper presents the experience of Georgia – a country with a substantial population of previously treated patients and high rates of MDR-TB – in eliminating category II therapy from its National TB Program (NTP) guidelines.

**Local setting**

Georgia is a country of 4.4 million people located in the South Caucasus region. The WHO TB case notification rate is 102 per 100 000 population. All Georgian TB patients receive culture and drug susceptibility testing as a standard part of tuberculosis diagnosis. In 2009, routine surveillance found multidrug-resistant tuberculosis in 10.6% of newly diagnosed patients and 32.5% of previously treated cases.

**Relevant changes**

Category II retreatment regimen is no longer used in Georgia. Treatment is guided by results of drug susceptibility testing – using rapid molecular tests where possible – for all previously treated tuberculosis patients.

**Lessons learnt**

There was little resistance to policy change because the review was initiated and led by the National Tuberculosis Program. This experience can serve as a successful model for other countries to make informed decisions about the use of category II therapy.

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In 1991, the World Health Organization (WHO) recommended the use of the "category II retreatment regimen" for all patients with a prior history of TB treatment. The category II regimen added streptomycin to the first-line agents and extended treatment to 8 months. Multiple observational studies have examined outcomes among individuals receiving category II treatment and shown mixed results. Overall success rates are in the 60–80% range, with notably worse outcomes seen among patients who failed or relapsed after their initial treatment episode.

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Georgia is a country of 4.4 million people located in the South Caucasus region. The WHO TB case notification rate is 102 per 100 000 population. All Georgian TB patients receive culture and drug susceptibility testing as a standard part of tuberculosis diagnosis. In 2009, routine surveillance found multidrug-resistant tuberculosis in 10.6% of newly diagnosed patients and 32.5% of previously treated cases. Programmatic management of drug-resistance TB in Georgia was started in 2006 and in 2009 the country achieved universal access to MDR-TB treatment.

**Approach**

An operational assessment of the utility of category II in Georgia was done in July and August 2010, led by members of the Georgian NTP with a WHO-recruited consultant. The steps taken were: (i) programme review, (ii) consensus building, and (iii) implementation planning (Table 1).

**Programme review**

Outcomes of patients treated with category II were assessed in addition to the local epidemiology and programme resources in Georgia. More than 6500 patients received category II therapy between 2007 and 2009 and their outcomes are shown in Table 2.

Georgia has a high burden of TB, particularly drug-resistant TB. Prevalence of HIV in the country is low (< 1%). Culture of
the Mycobacterium tuberculosis and drug susceptibility testing is done for all patients diagnosed with TB and Georgia has the resources (human and financial) to continue to do this. It also has a national programme for managing drug-resistant TB. Patients with documented resistance are given treatment regimens based on drug susceptibility test results.

Consensus building

Following this review, the NTP decided to no longer recommend category II treatment in Georgia because of: (i) poor outcomes among patients on category II therapy; (ii) high rates of streptomycin resistance among previously treated patients; (iii) lack of evidence to support category II; and (iv) widespread access to both drug susceptibility testing and treatment for drug-resistant TB. The NTP concluded that patients with documented resistance, including those with mono-resistance, would receive a regimen based on drug susceptibility test results. Those with a history of previous treatment who had pan-susceptible disease would receive HREZ (first-line drugs).

Consensus building was initiated and led by the Georgian NTP; as such, there was strong political will. It held a series of meetings with TB care providers to review and discuss the decision openly. Most of the NTP staff in Georgia are actively involved in TB patient care, and ongoing provider relationships allowed for rapid consensus building. The NTP also used an evidence-based analysis to support its decision. There were some concerns that previously treated patients with pan-susceptible disease still needed a “stronger” regimen but, upon further review, there was little evidence to support this claim. There was little resistance to this policy change so, once internal consensus was reached, the NTP applied for regulatory changes and category II was removed from recommendations for TB treatment.

Implementation

Following the elimination of category II treatment, the programme has committed time and resources to expanding access to rapid, molecular-based drug susceptibility testing. Georgia will also continue its commitment to universal management of all forms of drug-resistant TB and monitor resistance and patient outcomes. Operational research on the discontinuation of category II treatment – including cost implications and provider and patient experiences – will be carried out as funding permits.

Lessons learnt

The experience from Georgia is an important example of how category II treatment can be successfully removed from NTP guidelines in settings where it is of limited utility. Georgia used an operational assessment of its national data to reach consensus on the use of category II within its specific context. There was little resistance to policy change in the country because the review was initiated and led by the NTP. Although it may not be possible to generalize this experience to all settings, the review was done retrospectively and outcome data are pending, the Georgian experience may serve as a roadmap for other countries.

The operational assessment concluded that there were no patients in Georgia for whom category II treatment was appropriate. Patients with a history of previous treatment who have pan-susceptible disease are now treated with first-line drugs. Patients with mono- or poly-resistance are treated with appropriate regimens. Patients with MDR-TB are treated with second-line therapy.

Georgia is a unique setting but other countries with different profiles may be able to use this model to determine

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Table 1. Key steps in review of category II retreatment regimen in Georgia

<table>
<thead>
<tr>
<th>Step</th>
<th>Data</th>
<th>Conclusion/recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Programme review</td>
<td>Outcomes poor</td>
<td>Category II is inadequate therapy for the management of retreatment TB patients in Georgia</td>
</tr>
<tr>
<td></td>
<td>Drug susceptibility testing done on all patients; MDR-TB programme exists</td>
<td>Georgia has sufficient resources to implement other strategies for patients</td>
</tr>
<tr>
<td>Consensus building</td>
<td>Project led by National TB Program and thus consensus built rapidly</td>
<td>Category II not relevant for any persons in Georgia; recommendation endorsed by providers</td>
</tr>
<tr>
<td></td>
<td>Evidence-based review with frank discussion</td>
<td></td>
</tr>
<tr>
<td>Implementation</td>
<td>Improved diagnostics, ongoing treatment and monitoring</td>
<td>Ongoing operational research</td>
</tr>
</tbody>
</table>

MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

Table 2. Treatment outcomes among patients on category II retreatment regimen in Georgia, 2007–2009

<table>
<thead>
<tr>
<th>Outcome</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Successa</td>
<td>1311</td>
<td>59</td>
<td>1178</td>
</tr>
<tr>
<td>Failed</td>
<td>231</td>
<td>10</td>
<td>531</td>
</tr>
<tr>
<td>Defaulted</td>
<td>307</td>
<td>14</td>
<td>147</td>
</tr>
<tr>
<td>Died</td>
<td>164</td>
<td>7</td>
<td>118</td>
</tr>
<tr>
<td>Transferred out</td>
<td>103</td>
<td>5</td>
<td>102</td>
</tr>
<tr>
<td>Unknown</td>
<td>109</td>
<td>5</td>
<td>178</td>
</tr>
<tr>
<td>Total</td>
<td>2225</td>
<td></td>
<td>2254</td>
</tr>
</tbody>
</table>

a Combined cure and completion.

Box 1. Summary of main lessons learnt

- The National Tuberculosis Program initiated and led the policy decision and worked closely with health-care providers to build consensus.
- Evidence-based analysis was used to support the decision.
- Time and resources were committed to expand access to rapid, molecular-based drug susceptibility testing and management of drug-resistance.
Lessons from the field
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whether they should use category II. Each country will need to do its own programme review of category II outcomes. They can then use these data to prioritize whether they will continue to use category II or invest in improved diagnostics and drug-resistant TB treatment or both. This paper presents an important example of putting WHO recommendations into action. It is hoped the experience from Georgia can inspire other TB programmes to assess the utility of category II regimens – and other programmatic TB recommendations – in their settings (Box 1). ■

Competing interests: None declared.

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Резюме

Устранение режима лечения больных с диагностической категорией II из методических рекомендаций Национальной программы по борьбе с туберкулезом: грузинский опыт

Проблема Режим лечения больных с диагностической категорией II предназначен для лечения туберкулеза у пациентов, уже проходивших лечение. Этот режим, который начали применять в начале 90-х гг., включает в себя 8 месяцев общей терапии с добавлением стрептомицина к стандартным лекарственным препаратам первой линии. Анализ данных 6500 пациентов, проходивших в Грузии лечение для больных с диагностической категорией II, выявил низкую эффективность лечения и высокий уровень невосприимчивости к стрептомицину.

Подход В рамках Национальной программы по борьбе с туберкулезом был применен научно-основанный анализ данных, полученных в национальном масштабе. Полученные результаты были представлены директивным органам в качестве обоснования для устранения лечения больных с диагностической категорией II из национальных методических рекомендаций Грузии.

Местные условия Показатель Всемирной Организации Здравоохранения по регистрации случаев заболевания туберкулезом в Грузии составляет 102 случая на 100 000 человек. В рамках стандартной процедуры диагностики туберкулеза всем пациентам проводится тестирование на восприимчивость к лекарственным средствам и осуществляется посев. В процессе проведения планового наблюдения в 2009 г., у 10,6% впервые диагностированных пациентов и у 32,5% пациентов, проходивших лечение ранее, выявлен туберкулез с широкой лекарственной устойчивостью.

Осуществленные перемены Режим лечения больных с диагностической категорией II в Грузии более не используется. Лечение всех пациентов, уже проходивших лечение от туберкулеза, проводится по результатам тестирования на восприимчивость к лекарственным средствам, которое, по возможности, проводится с использованием молекулярных экспресс-тестов.

Выводы Данное изменение в проводимой политике не встретило значительного сопротивления, поскольку исследование было инициировано и проводилось под руководством Национальной программы по борьбе с туберкулезом. Полученный опыт может служить в качестве успешной модели для других стран для того, чтобы принимать обоснованные решения в отношении применения режима лечения больных с диагностической категорией II.

References