OUT OF STEP in EECA:

TB Policies in 8 Countries in Eastern Europe and Central Asia

A survey of prevention, testing and treatment policies and practices

November 2017
MSF is an international, independent medical humanitarian organisation that delivers medical care to people affected by armed conflicts, epidemics, natural disasters and exclusion from health care. Founded in 1971, MSF has operations in over 60 countries today.

MSF has been involved in TB care for 30 years, often working alongside national health authorities to treat patients in a wide variety of settings, including chronic conflict zones, urban slums, prisons, refugee camps and rural areas. MSF’s first programmes to treat multidrug-resistant TB (MDR-TB) opened in 1999. MSF has TB treatment projects in 28 countries; it is one of the largest non-governmental providers of treatment for drug-resistant TB. In 2016, MSF supported more than 20,000 TB patients on treatment, including 2,700 patients with drug-resistant forms of TB.

In 2015, MSF, Partners in Health and Interactive Research & Development launched the endTB project. Expand new drug markets for TB (endTB) seeks to improve treatment outcomes for people with MDR-TB.

Stop TB Partnership

The Stop TB Partnership is leading the way to a world without TB—a disease that is curable but still kills three people every minute. Founded in 2001, the Partnership’s mission is to serve every person who is vulnerable to TB and to ensure that high-quality treatment is available to all who need it.

The Stop TB Partnership’s programmes include the Global Drug Facility, which provides quality-assured and affordable TB medicines and diagnostics to countries around the world, and TB REACH, which has helped diagnose and treat over 2 million people with TB by providing small grants to identify and scale up innovative approaches to TB.

The Stop TB Partnership and its 1,600 partners are a collective force that is transforming the fight against TB in more than 110 countries. They include international and technical organisations, government programmes, research and funding agencies, foundations, NGOs, civil society and community groups, and the private sector.

The Stop TB Partnership operates through a secretariat hosted by UNOPS in Geneva, Switzerland, and is governed by a Coordinating Board that sets strategic direction for the global fight against TB.

*Out of Step in EECA* is dedicated to people affected by TB around the world who are fighting for the treatment they need, many of whom are still unable to access the latest diagnostics and medicines. No one should die of a curable disease for reasons of geography or economic status.

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*Out of Step in EECA: TB Policies in 8 Countries in Eastern Europe and Central Asia*

A survey of prevention, testing and treatment policies and practices

November 2017

To access the report online:
MSF: msfaccess.org/outofstep2017
Stop TB Partnership: stoptb.org/outofstep
#StepUpforTB Campaign: stepupfortb.org

Front cover photo: Lana Abramova/MSF
*Out of Step in EECA* is a regional adaption of *Out of Step 2017.*
OUT OF STEP in EECA: TB Policies in 8 Countries in Eastern Europe and Central Asia

A survey of prevention, testing and treatment policies and practices

November 2017
The TB hospital in Mykolaiv, Ukraine. About 530 people with TB are being treated here – many with drug-resistant TB.
EXECUTIVE SUMMARY

Although it can be prevented and successfully treated, tuberculosis (TB) is the world’s deadliest infectious disease. In Eastern Europe and Central Asia (EECA), conditions are ripe for TB proliferation, with suboptimal TB diagnosis and treatment, poor treatment adherence rates, limited health care in prisons, and high rates of HIV infection and injection drug use, all against a backdrop of weak health care systems. In 2015, most of the 323,000 new TB cases and the 32,000 deaths due to TB in the WHO European Region occurred in EECA. In 2015, an estimated one in five MDR-TB cases globally occurred in the European Region. While there have been substantial and important innovations in the fight against TB, including faster, more accurate diagnostic tests and the first new medicines in nearly 50 years, deadly gaps remain in implementing and providing access to these advances, especially for vulnerable and underserved populations, such as prisoners, people living with HIV, internal and external migrants and drug users.

Out of Step in EECA considers current TB diagnosis and treatment challenges in 12 EECA countries, and presents the results of an eight-country survey of national TB policies and practices conducted to identify where countries need to focus their efforts in order to reduce needless transmission, illness and death.*

*Aisara Goboeva, who has DR-TB, at home in Kysyl-Ordo, Kyrgyzstan.

Twelve countries in the EECA region are covered in this report: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan. Eight of these countries were included in the Out of Step in EECA survey: Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan and Ukraine.
World Health Organization (WHO) guidelines and policies that are proven to reduce TB incidence and death must be both adopted and fully implemented; however, this report reveals that some countries are lagging far behind. Outdated policies, practices and tools for diagnosing and treating TB, conservatism and inaction in registering and using newer TB medicines, and failure to reach key populations are barriers to turning around the TB epidemic and are fuelling a DR-TB crisis. The crisis cannot be brought under control unless governments in the region work harder to close these gaps.

Diagnosing TB quickly and accurately, so that people receive appropriate treatment, is an imperative first step. While many countries have adopted WHO guidelines and policies for diagnosis, the glacial pace of implementation is costing both lives and livelihoods. In 2015, more than 4 million people with TB went undiagnosed worldwide and less than 25% of people estimated to have DR-TB were diagnosed and treated. More than 46,000 people with TB went undiagnosed and less than 47% of people estimated to have DR-TB were diagnosed and treated in the 12 EECA countries considered in this report: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan.

The first step to closing the deadly diagnosis gap is initial testing for all with Xpert MTB/RIF, a rapid molecular test that can diagnose TB and detect rifampicin resistance in two hours. For people with rifampicin-resistant (RR) TB, additional drug-susceptibility testing (DST) should be available so that they can be treated with medicines most likely to be effective. Of the eight EECA countries surveyed, 75% (6) have adopted a policy of ‘Xpert for all’, but only 50% (3/6) have implemented the test widely. All eight countries provide initial testing with Xpert MTB/RIF for high-risk groups (people living with HIV and people at risk for drug-resistant forms of TB), but only 63% (5) have implemented this policy widely. Also, countries must ensure that universal DST moves from policy to practice; while all EECA countries surveyed recommend it, only 63% (5) have implemented it widely.

Once a person with TB has been properly diagnosed and started on treatment, ongoing care must be patient-centred and easily accessible to all who need it. It has been more than 50 years since WHO recognised that limited resources were best used for ambulatory TB care instead of hospital beds. In 2011, WHO recommended that “patients with multidrug-resistant tuberculosis should be treated using ambulatory care.” Decentralising TB treatment relieves the deadly bottleneck delaying treatment initiation, lowers the cost of treating TB, is preferred by patients and appears to be as effective as hospital-based approaches. Moreover, decentralised treatment for MDR-TB could increase the risk of MDR-TB transmission and has been associated with poorer retention in care. Community-based health workers can improve DR-TB treatment adherence by providing education, support and counselling and by facilitating decentralisation of DR-TB treatment. People with TB must have full access to social support as part of a package of care. However, the shift from compulsory hospitalisation to ambulatory care at the primary health care (PHC) level has been stalled by the slow pace of much-needed health reform.

The lag in policy adoption is reflected in the Out of Step in EECA findings; drug-susceptible (DS) TB treatment is started at the PHC level in only 37% (3) of EECA countries (in some countries exceptions are made for people who are smear-negative and on a case by case basis), and only Kazakhstan has implemented this policy widely. Of the 63% (5) of countries surveyed where treatment for DR-TB is initiated at the district level, only 60% (3/5) have implemented the policy widely. Although hospitalisation should be reserved only for the sickest DR-TB patients, 75% (6) of countries still require it for nearly all patients. These results indicate that the decentralisation of treatment must significantly accelerate if countries are to seriously improve treatment outcomes for people diagnosed with TB.

TB is the leading cause of death among HIV-positive people; HIV increases vulnerability to TB by up to 31-fold. In EECA – the only region in the world where the epidemic continues to grow rapidly – there was a 57% increase in annual new HIV infections between 2010 and 2015. In the WHO European region, HIV co-infection among TB cases increased by 40% between 2011 and 2015. However, in 2015 only two-thirds of the estimated 27,000 TB/HIV co-infected patients were diagnosed and 5,800 started antiretroviral (ARV) treatment; around 40% were successfully treated. In 2015, 4,408 HIV-positive people died of TB in EECA. In each country the public health system must clearly do more to ensure that the new paediatric formulations are reaching patients.

Children are especially vulnerable to TB. In 2015, an estimated 1 million children fell ill with TB globally and approximately 18,000 children under 15 years of age developed TB in the EECA region. The lack of child-friendly drug formulations has complicated paediatric TB treatment, but child- and caregiver-friendly paediatric fixed-dose combinations (FDCs) for DS-TB are now available and recommended by WHO. However, the new paediatric FDCs for DS-TB are the standard of care in only 25% (2) of surveyed countries, and only Tajikistan has implemented this policy widely. Children have long been neglected in TB care due to the difficulty of diagnosing and treating the disease. Nevertheless, governments must clearly do more to ensure that the new paediatric formulations are reaching patients.

Treatment for DR-TB can be shortened to nine months under certain circumstances; for people who are eligible, shorter treatment is equally effective and spares them
from months of terrible side effects. However, only 25% (2) of surveyed countries recommend it and neither has implemented it widely for eligible patients. Bedaquiline and delamanid – newer TB medicines recommended for people with difficult-to-treat forms of MDR-TB and those who suffer adverse events or risk of poor outcomes with conventional treatment – are included in 75% (6) and 62% (5) of national guidelines, respectively. Out of Step in EECA reveals that countries are too conservative in implementing new treatment regimens that could significantly improve cure rates for DR-TB, have proved successful in pilot projects in the region10 and could help curb the spread of drug-resistant strains. Although an estimated 119,700 people could have benefited from DR-TB treatment, only 55,900 were treated.4 As of July 2017, only 2,441 people in the eight countries surveyed in this report had been treated with bedaquiline and 333 people with delamanid.11

Access to new treatments must be accelerated. This requires governments to take bold steps to improve how medicines are regulated and made available in their countries. Only 57% (4/7) of countries surveyed have accelerated registration mechanisms in place, while 86% (6/7) allow access to unregistered TB medicines through compassionate use programmes, import waivers, or by other means. Furthermore, 50% (4) of countries are enrolled in the WHO Collaborative Registration Procedure, which accelerates approval of and access to quality-assured originator and generic medicines, including TB medicines, for public health needs in developing countries.12 None of the eight countries surveyed list all of the anti-TB medicines recommended by WHO for the treatment of DR-TB in the TB medicines section of their national Essential Medicines List (EML), and only 38% (3) include bedaquiline or delamanid in their national EML.

TB can be prevented. Preventive therapy can stop people with latent TB infection (LTBI) from developing active TB disease, but access is not universal. While all of the countries surveyed provide preventive therapy to the most vulnerable groups (child contacts and HIV-positive people), 25% (2) have not implemented it widely. None of the countries provide preventive therapy to other high-risk groups; only the Russian Federation and Belarus provide it to adult contacts. Countries must pay more attention to TB prevention if they are to make serious inroads in stopping the spread of this debilitating and deadly disease.

We are still out of step in preventing and diagnosing TB, providing patient-centred care, accelerating research, and expanding access to new, lifesaving medicines. Although we have modern tools to fight this ancient disease, we are not using them effectively where they are needed the most. Out of Step in EECA’s findings clearly show that governments, global health actors and donors urgently need to step up to stop the world’s poorest and most vulnerable people from needlessly falling ill, suffering and dying from TB.


- **Programmatic management of DR-TB (Guidelines)**
- **Contact tracing of people with infectious TB (Recommendations)**
- **Collaborative TB/HIV activities (Guidelines)**
- **Delamanid for DR-TB treatment (Interim policy guidance)**
- **Management of TB in children (Guidance)**
- **Chest radiography for TB detection (Guidance)**
- **Molecular line-probe assays (LPAs) for detection of second-line resistance (Policy guidance)**
- **Delamanid for children/adolescent MDR-TB treatment (Interim policy guidance)**
- **Treatment of DS-TB and patient care (Guidelines)**

- **Interferon-Gamma Release Assays (IGRAs) for TB infection (Policy statement)**
- **Xpert MTB/RIF for rapid TB detection and RIF resistance (Policy statement)**
- **Care and control of TB and diabetes (Framework)**
- **Systematic screening for active TB (Principles and recommendations)**
- **Bedaquiline for DR-TB treatment (Interim policy guidance)**
- **TB prevention: 36 months IPT for HIV+ adults/adolescents (Recommendation)**
- **Management of latent TB infection (Guidelines)**
- **Surveillance of drug resistance (Guidelines)**
- **The use of lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis and screening of active tuberculosis in people living with HIV (Policy guidance)**
PERCENTAGE OF PEOPLE WITH TB DIAGNOSED AND NOTIFIED TO WHO IN OUT OF STEP COUNTRIES (2015)*

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–74%</td>
<td>Armenia, Azerbaijan, Georgia,</td>
</tr>
<tr>
<td></td>
<td>Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Russian Federation, Belarus, Republic of Moldova, Ukraine, Uzbekistan</td>
</tr>
<tr>
<td>75–90%</td>
<td>Armenia</td>
</tr>
</tbody>
</table>

* Diagnosed and notified to WHO for 2015. The case detection rate was calculated as the number of cases notified divided by the number of cases estimated for that year, expressed as a percentage.

#STEPUPFORTB CAMPAIGN
Every 18 seconds a person dies from TB, but this can change if governments implement the current policies and practices recommended by WHO. The #StepUpforTB campaign, a collaboration between MSF and the Stop TB Partnership, aims to increase awareness about how the gaps in TB policies and practices lead to unnecessary TB deaths around the world. The goal of the #StepUpforTB campaign is to encourage governments to adopt and implement up-to-date TB policies and guidelines. Join the #StepUpforTB campaign at: http://stepupfortb.org
METHODOLOGY

Out of Step in EECA covers five key areas: diagnostics, models of care, treatment for drug-susceptible (DS) and drug-resistant (DR) TB, drug regulation, and prevention.

Eight countries were surveyed in this report: Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan and Ukraine. Countries were selected based on the presence of a Stop TB Partner or MSF project. With the exception of Armenia and Georgia, countries surveyed have a high burden of TB and/or TB/HIV and/or multidrug-resistant (MDR) TB according to WHO criteria (2016).³

Out of Step in EECA is a regional adaption of the Out of Step 2017 report, which surveyed 29 countries. Findings presented in this report are based on the data from EECA countries gathered and validated for Out of Step 2017. No additional data were collected. Findings are reported as both percentages and numbers. Unless otherwise noted, the denominator is 8, for all countries included in the survey.

The complete methodology for the 29-country survey is presented below

Out of Step reports

The Out of Step reports were created to identify gaps and monitor progress in adoption of international standards into national TB policies and practices. Countries can use Out of Step to measure or compare their progress, and TB advocates can use it to inform their efforts. The first edition, published in 2014, monitored progress in eight countries, including those with a high burden of TB. The second edition, published in 2015, covered 24 countries. The 2017 edition of Out of Step covers five key areas: diagnostics, models of care, treatment for drug-sensitive (DS) and drug-resistant (DR) TB, drug regulation, and prevention. Out of Step 2017 covers 23 of the 24 countries from the 2015 edition plus six additional countries where there is a Stop TB Partner or MSF project and the country has a high burden of TB and/or TB/HIV and/or multidrug-resistant (MDR)-TB according to WHO criteria. 1 All but three countries (Afghanistan, Armenia and Georgia) are included in at least one of these high-burden categories, as defined by WHO.1 The 29 countries surveyed for this edition of Out of Step are home to 82% of the global TB burden.1 These are: Armenia, Afghanistan, Bangladesh,
Belarus, Brazil, Cambodia, Central African Republic (CAR), China, Democratic Republic of Congo (DRC), Ethiopia, Georgia, India, Indonesia, Kazakhstan, Kenya, Kyrgyzstan, Mozambique, Myanmar, Nigeria, Pakistan, Papua New Guinea (PNG), Philippines, Russian Federation, South Africa, Swaziland, Tajikistan, Viet Nam, Ukraine and Zimbabwe.

Development and content of the questionnaire

MSF and Stop TB Partnership developed a semi-structured questionnaire to assess the national adoption and implementation of TB diagnostics, models of care, treatment for DS- and DR-TB, the regulatory environment for TB medicines, and TB prevention. The questionnaire was developed between September and November 2016 by experts from MSF and Stop TB Partnership.

Process for data collection, analysis and validation

From October to mid-November 2016, MSF and Stop TB Partnership conducted a desktop review of current TB and HIV policy documents and guidelines from each country. In November 2016, each national TB programme (NTP) manager received a list of country-level documents and a request for additional information (national Ministry of Health [MoH]-approved policy documents and guidelines covering the five key areas of Out of Step), as needed. They were given 3 weeks to review the information that was provided and share updates about the status of their national policies and guidelines, including whether the policies and guidelines were in the process of being updated or if new versions had been drafted. Of the 29 NTPs, 21 responded and approved the existing documents or provided additional documents. Countries that did not share their guidelines were sent requests and reminders via email and phone calls.

MSF followed up in the 18 countries where it has TB projects (Armenia, Belarus, Brazil, CAR, DRC, Georgia, India, Kenya, Kyrgyzstan, Mozambique, Myanmar, PNG, Russian Federation, South Africa, Swaziland, Tajikistan, Ukraine and Zimbabwe), and Stop TB Partnership followed up in the remaining countries (Afghanistan, Bangladesh, Cambodia, China, Ethiopia, Indonesia, Kazakhstan, Nigeria, Pakistan, Philippines and Viet Nam). In some cases, MSF and Stop TB Partnership worked together to collect data from NTPs.

Stop TB Partnership used the information from the NTPs and the desktop review to pre-fill the questionnaires for 11 countries. These were sent to the NTPs to ensure that the answers reflected the national TB policies and guidelines, and that the level of implementation for each was accurately characterised. If there were discrepancies in the answers, clarification or additional documents were sought from respondents. In some cases, the questionnaire was shared multiple times until any doubts or concerns about the questions were resolved. Once completed, each questionnaire was reviewed by an independent, professional fact checker and TB experts from MSF and Stop TB Partnership. This validation process began in February 2017 and was completed in mid-May 2017.

Phone calls to collect and validate information were made between February and May 2017. Stop TB Partnership and MSF country teams exchanged numerous phone calls and emails with NTPs.

MSF shared the questionnaire with country teams on 1 December 2016 for completion by 20 January 2017. In eight countries, MSF teams worked closely with the NTPs to complete the questionnaire. If the NTP did not share any documents, MSF country teams obtained national documents to fact-check the NTP’s responses. The full list of references is included in the online version of the report, available at: stepupfortb.org. After MSF teams completed the questionnaires, they were checked by a Stop TB staff member. The questionnaires were then returned to the MSF country teams to clarify responses over multiple rounds of phone calls. Once questions were resolved, each questionnaire was reviewed by a fact checker and a team of MSF pharmacists and diagnostic and treatment experts. The validation process was completed in the third week of May 2017.

Challenges

For the eight countries where there was no response from NTPs, MSF country teams provided the necessary documents to complete the survey. Source documents were often available only in the local language; these were translated from Russian, Portuguese and Armenian by a professional, UN-approved translation services company.

The questionnaire consisted of two main parts. The first part asked whether national policies were aligned with current WHO guidelines, calling for yes or no answers; in cases where there was no response, the answer was recorded as ‘unknown’. The second part included questions about the implementation of policies, asking whether and how widely they had been implemented. One limitation of the data on implementation was that there were only three possible responses (‘yes’, ‘yes, but not widely’, or ‘no’). In some cases, the level of implementation may have been over-reported, as ‘yes but not widely’ may have been interpreted differently by each country. If the answer about an existing policy was ‘no’, responses about implementation were not included in this report.
In a few cases, there was confusion over the responses*. In such instances, we tried to clarify these responses with the NTPs and country teams via phone and email exchanges. If responses could not be clarified, the answer was considered to be ‘unknown’. In countries where MSF does not have TB operations, Stop TB Partnership contacted the NTPs to validate information. There was no response to our numerous phone and email attempts from the NTP of Indonesia, hence the questionnaire for Indonesia could not be validated.

If information was not provided by countries and could not be found by reviewing source documents and country guidelines, the response was recorded as ‘unknown’.

Data were collected until mid-May 2017.** Since there is a lag between the release of WHO guidelines and their adoption by countries, some countries were in the process of updating their guidelines during the survey period. If guidelines were being updated at the time of the survey and the NTP or country office provided information about their content, the status of the document was noted.

**Interpretation of answers/results**

Key findings are provided for each area, reported as both percentages and numbers. Unless noted, the denominator is 29, for all countries included in the survey. If a country did not answer a question, both the numerator and denominator were adjusted.

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* One question in the survey asked countries if chest x-ray should be carried out to identify people who need to be tested with Xpert MTB/RIF. Most respondents did not understand the question; the majority actually answered ‘Yes’ if chest x-ray was a part of the overall diagnostic package, regardless of whether or not chest x-ray was used as a screening tool to identify Xpert-eligible patients. For this reason, it was not possible to interpret national x-ray policies.

** Questions about policies and implementation of TB-LAMP (loop-mediated isothermal amplification; a test that WHO recommends to replace microscopy for diagnosing pulmonary TB in adults with signs and symptoms of TB) were not included in the survey, since the guidance was very new when the data collection began.
**KEY POLICIES DASHBOARD**

### DIAGNOSIS

<table>
<thead>
<tr>
<th>Policy</th>
<th>Armenia</th>
<th>Belarus</th>
<th>Georgia</th>
<th>Kazakhstan</th>
<th>Kyrgyzstan</th>
<th>Russian Fd.</th>
<th>Tajikistan</th>
<th>Ukraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>First-line DST (rifampicin and isoniazid) is done for all RR-TB cases or for people at risk of DR-TB</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Second-line DST (fluoroquinolones &amp; second-line injectable agents) is done for all DR-TB cases</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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### MODELS OF CARE

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</thead>
<tbody>
<tr>
<td>DS-TB treatment is started at the primary health care level*</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>DR-TB treatment is started at the district level*</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hospitalisation is NOT required for DS-TB treatment**</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hospitalisation is NOT required for DR-TB treatment**</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>ARV treatment is offered to all people living with HIV/AIDS (<em>test and start</em>)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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### TB AND DR-TB TREATMENT

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<tr>
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<tbody>
<tr>
<td>New paediatric TB FDCs are the standard of care</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>National policy reflects WHO guidance on bedaquiline use for adults</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>National policy reflects WHO guidance on delamanid use for adults and children</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>National policy includes the WHO recommended, nine-month (shorter) MDR-TB treatment regimen</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</table>

### MEDICINE REGULATORY ENVIRONMENT

<table>
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<th>Georgia</th>
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<th>Russian Fd.</th>
<th>Tajikistan</th>
<th>Ukraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR-TB medicines can receive accelerated registration</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Unregistered TB medicines are available through CU/other legal mechanisms**</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Country is enrolled in WHO Collaborative Registration Procedure</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tr>
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</table>

### LEGEND

- **Yes**
- **No**
- **Unknown**

(*) Including smear-positive individuals. In some countries exceptions are made for people who are smear-negative and on a case by case basis. (**) The implementation of the policy was not assessed for the hospitalisation questions. (**) Compassionate use, expanded access programmes, import waivers or other legal mechanisms. (a) The initial diagnostic test is microscopy, but regardless of microscopy result, every person to be evaluated for TB is tested with Xpert. (b) Part of an initial diagnostic package of tests. (c) At facilities that offer DR-TB regimens with BDQ or DLM. (d) Xpert is part of a package of diagnostic tools; other diagnostic tests can be used, including other rapid molecular methods. (e) Except for people who are smear-negative and on a case by case basis. (f) Patient receives a prescription at TB facilities. (g) DR-TB treatment can be started and dispensed from the district level, but only after decision and prescription from the regional TB committee. (h) Implementation in pilot sites. (i) Only if already approved by an SDRA.
OUT OF STEP in EECA

CLOSING THE GAPS IN TB AND DR-TB TESTING AND TREATMENT

KEY INDICATORS IN 29 COUNTRIES SURVEYED IN ‘OUT OF STEP 2017’

LEGEND

<table>
<thead>
<tr>
<th>Estimated TB incidence rate per 100,000 population</th>
<th>Number of GeneXpert MTB/RIF modules for rapid molecular testing procured (2010–2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–19</td>
<td>1–16</td>
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<tr>
<td>20–49</td>
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<td>50–124</td>
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<td>125–299</td>
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</tr>
<tr>
<td>300–499</td>
<td></td>
</tr>
<tr>
<td>≥500</td>
<td></td>
</tr>
</tbody>
</table>

MDR-TB TREATMENT COVERAGE
(percentage of people who started MDR-TB treatment relative to estimated incidence of MDR-TB)

TB/HIV CO-INFECTION RATE
(percentage of people with TB who are estimated to be HIV-positive)

GAP BETWEEN ESTIMATED AND DETECTED CASES
(percentage of people estimated to have TB that are missing in the country’s case detection rates)

WHO HIGH TB OR HIGH TB/HIV OR HIGH MDR-TB BURDEN COUNTRIES

OTHER

EECA COUNTRIES


Data on procurement of GeneXpert MTB/RIF modules were obtained from its manufacturer Cepheid

DISCLAIMER: Boundaries used on this map do not imply the expression of any opinion whatsoever on the part of the Stop TB Partnership or MSF concerning the legal status of any country or territory or of its authorities, or concerning the delimitation of its frontiers or boundaries.
The director of the TB hospital in Mykolaiv, Ukraine has helped to modernise the facility with tools such as GeneXpert MTB/RIF.
Xpert MTB/RIF is recommended as the initial test for all by 75% (6) of countries, but only 50% (3/6) have implemented the policy widely.

Rifampicin resistance testing for all people with bacteriologically confirmed TB is recommended in the guidelines in all eight countries.

Universal drug-susceptibility testing (DST; rifampicin resistance testing for all people with bacteriologically confirmed TB, followed by second-line DST for fluoroquinolones [FLQs] and second-line injectable drugs [SLIDs] for all people with rifampicin-resistant [RR]/multidrug-resistant [MDR] TB) is recommended in the guidelines in all eight countries, but only 63% (5) have implemented the policy widely.

Second-line DST (DST for at least SLIDs and FLQs) for all RR- and MDR-TB cases is recommended in the guidelines in all eight countries.
BACKGROUND

The first step towards reducing sickness and the spread of TB is diagnosing it quickly and accurately so that people can receive appropriate treatment. Yet, millions of people with TB have died, many before they were diagnosed, without the chance to be cured. In 2015, an estimated 46,000 people in EECA with DR-TB went undiagnosed and less than 47% of people estimated to have DR-TB were diagnosed and treated.4

To close the diagnosis gap, the End TB Strategy endorsed by all WHO member states, calls for countries to implement initial diagnostic testing with a WHO-recommended rapid diagnostic test (RDT) that can also detect resistance to rifampicin by 2020, and by 2018 in countries with high burdens of TB, MDR-TB and TB/HIV co-infection.5 By 2025, at least 90% of people should be diagnosed with a WHO-recommended RDT, and 100% of those diagnosed should receive DST.5

Xpert MTB/RIF and the next-generation version, Xpert MTB/RIF Ultra,6 are WHO-recommended RDTs that can diagnose TB and detect rifampicin resistance in two hours.7 Xpert MTB/RIF is more accurate and faster than conventional diagnostics, such as sputum smear microscopy and culture.8

In 2015, Out of Step reported that only four of eight EECA countries surveyed* were using Xpert MTB/RIF as the initial diagnostic test for all.9 This report found that 75% (6) of countries have guidelines recommending the use of rapid molecular tests as the initial diagnostic, but still only 50% (3/6) have implemented this policy widely.

Although Xpert MTB/RIF has many advantages, financial, logistical and operational challenges must be overcome to facilitate greater scale-up.

TB drug-resistance testing and effective treatment are essential to halting illness and death from, and the onward transmission of, DR-TB. Although rapid molecular tests such as Xpert MTB/RIF can detect RR-TB, people with RR-TB also need DST for SLIDs and FLQs in order to determine which medicines will be effective, and to tailor their treatment accordingly.

The global TB community applauds the development of new diagnostic tools, but these must be accompanied by programmes to implement them. A number of studies and programmatic evaluations have found that Xpert MTB/RIF testing alone does not increase the number of people who start on treatment.10

* Armenia, Belarus, Georgia, Kyrgyzstan, Russian Federation, Tajikistan, Uzbekistan and Ukraine.
* 6.1 million new TB cases were notified to national authorities and reported to WHO in 2015.
KEY DIAGNOSIS POLICIES

<table>
<thead>
<tr>
<th>Country</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Belarus</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Georgia</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Tajikistan</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
<tr>
<td>Ukraine</td>
<td>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</td>
</tr>
</tbody>
</table>

LEGEND

- Yes
- No
- Unknown

(a) The initial diagnostic test is microscopy, but regardless of microscopy result, every person to be evaluated for TB is tested with Xpert. (b) Part of an initial diagnostic package of tests. (c) At facilities that offer DR-TB regimens with BDQ or DLM. (d) Xpert is part of a package of diagnostic tools; other diagnostic tests can be used, including other rapid molecular methods.

RAPID MOLECULAR TESTING

In 2010, the Xpert MTB/RIF test was hailed as a revolutionary advance in public health. It can diagnose TB and detect resistance to rifampicin (a powerful first-line drug) in less than two hours. This rapid turnaround time makes it possible to start TB treatment right away, thereby lowering the risks of loss to follow-up and ongoing transmission.

In 2010, WHO endorsed Xpert MTB/RIF, and in 2011, WHO issued a policy statement recommending it as the initial diagnostic test for presumptive MDR-TB or HIV-associated TB in adults. In 2013, WHO expanded its recommendation to include children, adding that Xpert MTB/RIF may be used as an initial diagnostic test for adults and children with signs and symptoms of TB (instead of smear microscopy and culture). In March 2017, WHO recommended a next-generation assay, Xpert MTB/RIF Ultra, which uses the same equipment as Xpert MTB/RIF and will gradually replace it. The Ultra assay is more sensitive than Xpert MTB/RIF for diagnosing smear-negative, culture-positive TB, paediatric and extrapulmonary TB, and HIV-associated TB. However, the specificity of Xpert Ultra is somewhat lower than that of the previous Xpert MTB/RIF, which could lead to overtreatment, particularly in patients with a history of TB.

The Global Laboratory Initiative (GLI), a working group of the Stop TB Partnership, has developed practical guidance for an easy transition to Xpert Ultra, and WHO is planning to release policy recommendations for Xpert Ultra in 2018.

Cepheid is also developing a new system, Xpert Omni, a small, portable, battery-operated instrument that can be used in remote rural settings. The Omni will be able to initially run Xpert MTB/RIF and Ultra cartridges, and other Xpert disease-specific cartridges. However, the Omni cartridges will differ from the current Xpert cartridges, as they will be equipped with a near field communication (NFC) chip that will be required for the Omni instrument to function. The NFC chip will be required for wireless connectivity to transmit real-time data via a smartphone. The launch of the one-module Omni model will be around US$ 5,315 versus the US$ 17,000 reduced price for the current four-module GeneXpert model. With the purchase of a set of two Omnis, the price per instrument will be US$ 4,655. It is expected that by 2020 the price will fall to US$ 3,895 per instrument. The Omni is expected to be available by the middle of 2018.

The 2017 GLI recommends Xpert MTB/RIF as the preferred initial diagnostic in its model TB diagnostic algorithm. However, some high-burden countries still use smear microscopy as the initial diagnostic test, even though it is less sensitive for people living with HIV/AIDS, children and people with extrapulmonary TB - and it cannot detect drug resistance.

Rolling out Xpert MTB/RIF requires more than simply purchasing the device and securing a sustainable source for supplies. Sites need a stable, uninterrupted power supply and may require air-conditioning, as well as room to store equipment. The devices must be checked, calibrated and repaired, staff must be trained to use them and quality assurance measures must be in place to monitor and evaluate the system.
FINDINGS:

Xpert MTB/RIF is recommended as the initial diagnostic test for all people in 75% (6) of countries (see Table 1), but only 50% (3/6) have implemented the policy widely (see Table 2).

Xpert MTB/RIF is recommended as the initial diagnostic test for high-risk groups (adults and children at risk for DR-TB and HIV-associated TB) in all eight countries (see Table 1), but only 63% (5) have implemented the policy widely (see Table 2).

<table>
<thead>
<tr>
<th>TABLE 1: XPERT MTB/RIF POLICIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xpert as the initial diagnostic test for all people to be evaluated for TB</td>
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<tr>
<td>Xpert as the initial diagnostic test only for high-risk groups</td>
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<tr>
<td>Armenia, Belarus, Georgia, Kyrgyzstan, Russian Federation, Tajikistan</td>
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<td>Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan, Ukraine</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 2: IMPLEMENTATION OF XPERT MTB/RIF POLICIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation of “Xpert for all”</td>
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<tr>
<td>Implementation of ‘Xpert for high-risk groups’</td>
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<td>Armenia, Belarus, Georgia</td>
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<td>Kyrgyzstan, Russian Federation, Tajikistan, Ukraine</td>
</tr>
</tbody>
</table>

LEGEND

- Yes
- Yes, but not widely

COSTS ASSOCIATED WITH XPERT MTB/RIF

In 2012, the price of Xpert MTB/RIF cartridges was reduced from US$ 16.86 to US$ 9.98 in 145 high TB burden and developing countries for use in public facilities.26,27 The concessional price for the device itself (a standard four-module GeneXpert instrument with a desktop) is US$ 17,000 and includes a two-year warranty.

Cartridge prices represent a large expense, and there are additional costs for salaries, training, equipment, repairs, module calibration and maintenance, and general laboratory operation. For example, detailed costing analyses for India and South Africa suggested that the overall costs per Xpert MTB/RIF test were US$ 11.60 and US$ 14.90, respectively.28,29 In the Russian Federation, the cost of Xpert MTB/RIF cartridges is over US$ 50 per cartridge. Although Xpert MTB/RIF implementation is cost-effective,20 additional funding is required to make it available to all people. According to WHO, changing from current diagnostic tests to “Xpert for all” will create a 38% increase in annual costs for the 30 high TB burden countries;30,31 this figure does not include additional costs for distribution, customs and equipment maintenance. TB funding often strongly depends on international donors.

Governments and global health actors are exploring strategies to further reduce the price of Xpert MTB/RIF through (i) renting and leasing equipment instead of purchasing it, (ii) integrating maintenance and service costs into the test price instead of using standalone services and maintenance contracts, and (iii) negotiating volume-based pricing, including across countries and pathologies (e.g. cartridges for HIV, hepatitis C virus [HCV] and human papillomavirus [HPV]).
Yury, 38 years old, was diagnosed with TB after experiencing symptoms of fever, fatigue and loss of appetite. Yury and his doctors were fighting the disease for two years, facing a form of XDR-TB, using all the medicines available at the time. “When they poured more than 20 [pills] before me, everything went dark before my eyes,” he says, explaining that the high dose of drugs made him feel permanently sick and weak. On top of the physical impacts of the disease, Yury was concerned about the reaction of others. “I thought everything had ended, that everybody would turn away from me,” he says. He informed his family so they could get themselves checked but did not tell anyone else, even when he had been in hospital for a long time.

Several times, it seemed that the disease had abated and the tests would come back clear. But in a few months’ time, they would be positive for TB again. Just when he had begun to lose hope, the doctors told Yury about a new treatment programme with MSF in Minsk where he would have access to newer TB medicines. Yury agreed to join the programme. “My doctors told me: ‘This is the only chance’,” he recalls.

Within two days, he was fitted with a port – an implanted system that allows continuous intravenous infusions. The treatment with imipenem, bedaquiline and several other medicines began. “I started to improve immediately,” says Yury. “I didn’t feel better – I had no appetite. But the tests, the x-rays – everybody was surprised!”

Yury is now the first patient to complete treatment and be cured as part of the programme in Belarus.

MSF is supporting the Ministry of Health in Belarus in four TB facilities in the country, providing access to the newer, improved TB medicines supplied through the endTB project. So far MSF has provided treatment to nearly 60 patients.
A doctor from the Ministry of Health speaks with a person with TB during the inauguration ceremony of the new TB facilities in TB Cabinet 1, built by MSF in Kyrgyzstan.
DRUG-SUSCEPTIBILITY TESTING

Drug-resistant forms of TB can be directly transmitted\textsuperscript{22} and will continue to spread unless people are treated and cured. By 2040, DR-TB is more likely to be directly transmitted than a consequence of unsuccessful treatment.\textsuperscript{33} DST is essential for stopping TB, since people who are not properly diagnosed cannot be effectively treated.

Drug resistance evaluation methods include genotypic diagnostics such as Xpert MTB/RIF, Xpert MTB/RIF Ultra, line probe assay and phenotypic diagnostics via culture-based methods for TB detection and first and second line drug susceptibility testing. Both LPA and culture are labour-intensive and require substantial lab infrastructure; results from phenotypic testing methods can take up to several weeks.

DST is also key to implementing the 2016 WHO recommendation for a shorter treatment regimen (9 to 12 months) for RR- and MDR-TB under certain circumstances. Eligibility is based on a person’s TB treatment history and results from DST for resistance to FLQs and SLIDs, when available (or, in the absence of DST, use of surveillance data on prevalence and types of resistance in the area).\textsuperscript{34}

Implementing the shorter regimen can spare people being treated for DR-TB from months of toxic treatment, ease financial and other hardships, and save money for TB programmes. Second-line DST using LPA is ideal before starting the shorter treatment regimen for MDR-TB, as the results are available quickly compared to phenotypic tests; however, WHO guidance also allows for culture-based DST and starting the shorter treatment without DST if it is unavailable.\textsuperscript{35}

The 2016 GLI framework of indicators and targets for laboratory strengthening under the End TB Strategy helps to pave the way for widely accessible drug-resistance testing and shorter treatment by calling on countries to adopt universal rifampicin resistance testing for all people with bacteriologically confirmed TB and, subsequently, DST for at least FLQs and SLIDs for all people with RR-TB.\textsuperscript{13} Countries with a high burden of MDR-TB should implement this strategy by 2018, while all other countries should adopt it by 2020.\textsuperscript{13}

FINDINGS:

Rifampicin resistance testing for all people with bacteriologically confirmed TB is recommended in the guidelines in all eight countries, but only 75% (6) have implemented the policy widely (see Table 3).

Second-line DST (at least for SLIDs and FLQs) at least for all RR-TB cases is recommended in the guidelines in all eight countries, but only 63% (5) have implemented the policy widely (see Table 3).

TABLE 3: DRUG-SUSCEPTIBILITY TESTING (FOR ALL PEOPLE WITH BACTERIOLOGICALLY CONFIRMED TB)

<table>
<thead>
<tr>
<th>COUNTRIES THAT HAVE THE POLICY IN PLACE</th>
<th>IMPLEMENTATION LEVEL</th>
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</thead>
<tbody>
<tr>
<td>Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan, Ukraine</td>
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</tr>
<tr>
<td>Kyrgyzstan, Tajikistan</td>
<td>Kyrgyzstan, Russian Federation, Tajikistan</td>
</tr>
</tbody>
</table>

**LEGEND**

- Yes
- Yes, but not widely
ELDAR’S STORY:  
AFTER 10 LONG YEARS, FINALLY CURED

Eldar is 29 and has been battling TB since 2006. In 2016, 10 years after his original diagnosis, Eldar was still sick, and continued to test positive for the disease. He was referred to the MSF-supported NTP near Senaki, a town in western Georgia, where he was enrolled in the new treatment programme using bedaquiline and delamanid, the first new TB medicines developed in nearly 50 years.

After almost two more years of treatment that included bedaquiline, Eldar recently received the news that he had finally tested negative for TB. He was cured. Eldar has experienced some hearing loss due to his earlier treatment with older TB medicines and still suffers from terrible chest pain. However, even though Eldar’s x-ray still reveals heavy scarring inside his lungs – damage left by years of infection – his tests remain negative and his condition is now steadily improving.

Although the incidence of TB is lower in Georgia than in some other countries in the region, Georgia is grappling with a particularly high burden of DR-TB. Within the framework of the endTB project, MSF set up a TB treatment support programme with the newer medicines in partnership with the Georgian Ministry of Health, Labour and Social Affairs and the National Center for TB and Lung Diseases. Georgia is adding the newer medicines to treatment regimens with endTB and MSF assistance, and is running both an observational study on their safety and efficacy and a clinical trial.

MSF currently provides and studies the effects of the newer medicines in four TB hospitals in Zugdidi, Batumi, Abastumani and Tbilisi. MSF teams also regularly visit several smaller health centres across Georgia, like the ambulatory point in Senaki where Eldar received treatment. By the end of 2016, some 300 people with TB across Georgia were started on the newer treatments. Although studies are still underway, initial outcomes are promising. Of the patients started on the newer medicines from April 2015 to December 2016, 86.8% tested negative for TB after six months of treatment.36
TB Policies in 8 Countries

TB-LAM FOR DIAGNOSING TB IN PEOPLE LIVING WITH HIV

There was a 57% increase in annual new HIV infections in the EECA region between 2010 and 2015; it is the only region in the world where the epidemic continues to grow rapidly. HIV increases vulnerability to TB, and increases TB morbidity and mortality. Consequently, HIV co-infection among people with TB increased by 40% between 2011 and 2015 in the WHO European region. HIV-positive people with latent TB infection (LTBI) are 26 times more likely to develop active TB than HIV-negative people. TB is the leading cause of death among people living with HIV. In 2015, 4,408 people living with HIV died from TB co-infection in EECA.

Given the prevalence and severity of TB co-infection among people living with HIV, WHO recommends that HIV-positive people be screened for active TB at each visit to a health care facility. But TB can be difficult to diagnose in people living with HIV. More than 50% of people with TB/HIV co-infection are smear-negative due to their inability to produce sputum, low sputum bacillary loads or because they have extrapulmonary TB. In 2015, only two-thirds of the estimated 27,000 TB/HIV co-infected patients in the WHO European Region were diagnosed and 5,800 started antiretroviral (ARV) treatment (around 40% successfully treated).

Simple, more accurate tests are needed to diagnose TB co-infection in people living with HIV. Although it is not recommended as a standalone test – or for HIV-negative people – TB-LAM is a rapid, point-of-care urine test that detects lipoarabinomannan (LAM), a marker of active TB disease and increased mortality risk during TB treatment in HIV-positive people. TB-LAM is most sensitive in HIV-positive people who are seriously ill and/or have low CD4 cell counts. Therefore, WHO recommends TB-LAM specifically for helping to diagnose active TB in HIV-positive adults with TB signs and symptoms and a CD4 cell count of ≤100 cells/μL, or those who are very sick, at any CD4 cell count. Since it delivers results in less than 30 minutes and is priced between US$ 2.66 and US$ 3.50 per test, TB-LAM can be a valuable tool for identifying people with the most urgent need for TB treatment.

FINDINGS:

- None of the eight countries surveyed have a guideline on the use of TB-LAM for diagnosing TB in people living with HIV/AIDS.
- The Russian Federation uses TB-LAM in selected facilities.
MODELS OF CARE

Safar Naimov explaining the importance of Tajikistan’s mHealth TB tool for communities.
Routine hospitalisation for the treatment of DS-TB is required in 75% (6) of countries.

Initiation of DS-TB treatment at the primary health care (PHC) level is recommended in the guidelines in only 38% (3) of countries. In Armenia, the majority of people start DS-TB treatment at a central-level hospital or at regional DS-TB units.

The HIV ‘test and start’ ARV treatment policy (providing ARV treatment to all HIV-positive people) has only been adopted in Georgia, which has implemented the policy widely.

Initiation of DR-TB treatment at the district level is recommended in the guidelines in 63% (5) of countries.

Routine hospitalisation for the treatment of DR-TB is required in 75% (6) of countries.
A patient-centred approach is one of the important underlying principles of the End TB Strategy. Such an approach promotes adherence, improves quality of life and relieves suffering (see TB-REP Blueprint); moreover, it demands respect for people with TB and ensures that they are treated as individuals and partners in their own TB care.44

Keeping people with TB at the centre of their TB and DR-TB treatment is essential to successful treatment. Over 50 years ago, WHO recognised that resources were best used for ambulatory TB care instead of for hospital beds.45 A WHO strategy recognised that TB treatment must be expanded to the “poorest urban and rural settings involving providers who practice close to where patients live.”46 Patient-centred care should match services to the needs of patients and their families, take into account social determinants of health, adapt services to different settings, recognise the need for flexibility in responding to patients’ needs, ensure well-functioning referral systems, implement a robust data-reporting system, and protect patients and their families from catastrophic financial costs.47

However, most EECA countries continue to use outmoded models of care. Common myths include that hospitalisation is necessary to ensure adherence in people with TB and that all people with TB are infectious. In fact, most people with TB are no longer infectious within a month of starting treatment. Moreover, ambulatory MDR-TB care is as effective as – and significantly less expensive than – hospitalisation. A single day in the hospital can cost up to 15 times more than an outpatient visit.48 A recent systematic review including eight studies in six countries assessed decentralised versus centralised care for MDR-TB (1994–2013), finding that decentralised care was more likely to lead to treatment success than centralised care. Influencing factors include greater retention in care and reduced loss to follow-up. Decentralised care is also likely to remove certain barriers to treatment adherence, such as unaffordable hospital costs or the inability to access family support.5

Compulsory hospitalisation can facilitate the spread of TB and DR-TB because of lengthy delays prior to treatment initiation and poor infection control in hospitals.49,50 Decentralising TB and MDR-TB treatment relieves a deadly bottleneck by expediting time to treatment initiation; moreover, patients prefer it.51 The models of care in EECA countries must be updated to reflect the advancements in TB medicines and the rise of MDR-TB.

TB services should be integrated into broader health and social systems, for example service integration with HIV/AIDS, diabetes and other non-communicable diseases, maternal and child health, and addiction services. TB services must reach vulnerable groups, including homeless people, people who inject drugs, people co-infected with TB and HIV, migrants, displaced populations and refugees. Finally, TB services must close the gap between national services and TB services in the penitentiary system to ensure that people in prisons receive continuity of care and TB services in line with national standards.47

For example, the deadly link between TB and HIV can be broken through a ‘one-stop shop’ that facilitates testing, care and treatment for HIV and TB in one place, and makes it faster and easier for patients to access lifesaving treatment for both. ARV treatment, which is now recommended for all HIV-positive people of any age regardless of CD4 cell count,9 and TB preventive therapy, which is also recommended for HIV-positive people in high-prevalence and resource-limited settings,52 are protective against TB, especially in combination.53
**TB REGIONAL EASTERN EUROPE AND CENTRAL ASIA PROJECT (TB-REP)**

The overall goal of TB-REP is to reduce the burden of TB and to halt the spread of drug resistance by increasing political commitment and translating evidence into implementation of a people-centred model of TB care. The project is being implemented from 2016 to 2018 by the Moldovan Centre for Health Policies and Studies, with technical support from the WHO Regional Office for Europe and financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria. Other partners include the European Respiratory Society, Alliance for Public Health, Stop TB Partnership, TB Europe Coalition, the London School of Hygiene and Tropical Medicine, and the London School of Economics and Political Science. The focus countries are Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Republic of Moldova, Tajikistan, Turkmenistan, Ukraine and Uzbekistan.


**TB treatment initiation**

The decentralisation of HIV treatment initiation and task-shifting to nurses and community health care workers has increased ARV treatment access and uptake, improving adherence and treatment outcomes. The same is true for TB: Decentralising treatment is preferable for people with TB who wish to remain in their communities, and has improved treatment outcomes and lowered costs per patient.

**FINDINGS:**

- **Initiation of DS-TB treatment at the PHC level is recommended in the guidelines in only 38% (3) of countries, and only Kazakhstan has implemented the policy widely.**
- **According to national guidelines, nurses and health care workers other than doctors can start adults on DS-TB treatment in 25% (2) of countries: Georgia and Kazakhstan – both of which have implemented the policy widely.**
KEY MODELS OF CARE POLICIES

<table>
<thead>
<tr>
<th>Country</th>
<th>Armenia</th>
<th>Belarus</th>
<th>Georgia</th>
<th>Kazakhstan</th>
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<th>Russian Fed.</th>
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<tbody>
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<tr>
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<td>□</td>
</tr>
<tr>
<td>Hospitalisation is NOT required for DR-TB treatment**</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>ARV treatment is offered to all people living with HIV/AIDS (‘test and start’)</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

**LEGEND**

- *Yes*
- *No*
- *Unknown*

(*) Including smear-positive individuals. In some countries exceptions are made for people who are smear-negative and on a case by case basis. (a) The implementation of the policy was not assessed for the hospitalisation questions. (b) Except for people who are smear-negative and on a case by case basis. (c) DR-TB treatment can be started and dispensed from the district level, but only after decision and prescription from the regional TB committee.

DR-TB TREATMENT INITIATION

In 2015, only one in five people estimated to have MDR-TB worldwide made it through the diagnostic and treatment pathway. Lengthy travel to specialised facilities, stigma, and bureaucratic health care systems cause delays in treatment initiation and high rates of loss to follow-up.

FINDINGS:

DR-TB treatment is started at the district level in 63% (5) of countries, but only 60% (3/5) have implemented the policy widely: Kazakhstan, Kyrgyzstan and Russian Federation.
Makka, a former teacher, lives in Avtury, Shali district in Chechnya, Russian Federation. She was diagnosed with XDR-TB in April 2016 and was started on treatment two weeks after she was hospitalised. Her treatment included the newer TB medicine, bedaquiline. Beginning in May 2016, she was allowed to continue treatment at home with visits from MSF staff to help her and monitor her treatment. After five months of treatment, Makka’s sputum tested negative. She has now been on treatment for a year and three months.

“Treatment is going well for me,” says Makka. “In the beginning it was certainly hard, and I do not always tolerate the pills well now. Sometimes I throw up.”

Makka’s circumstances at home are not easy. Her father was taken away during the war 17 years ago and never came back. She now lives with her mother, brother and sister-in-law, who offer her their support. “My family also helps me, they support me in everything,” Makka says. “My mother asks me several times a day: ‘Have you taken your medicines? Have you eaten well?’”

Makka is positive about her treatment but recognises that it is a tough journey for many people: “I’m young, at least, but there are elderly patients – grandmothers, grandfathers, 70 or 80 years old,” she says. “You look at them and you feel sorry. It’s so difficult for them to endure. I wish there were no side effects of the treatment. When I saw elderly patients in the hospital, I thought: ‘God forbid that my mother gets sick because of me and ends up here.’”
AMBULATORY CARE

WHO recommends expanded services and ambulatory care for people with DR-TB, reserving hospitalisation only for people who are very ill. In the past, people with DR-TB faced up to eight months of mandatory hospitalisation. At the time, this approach was thought to limit transmission, ensure that patients were taking their medication, and allow for management of adverse events. However, limited space delayed hospital-based treatment initiation; a study in 2007 found that, in some settings, newly diagnosed DR-TB patients had to wait up to 120 days to start treatment.60 Furthermore, poor infection control in hospitals can actually facilitate the spread of DR-TB to other patients and health care workers.48,49 In addition, the high cost of hospitalisation is not feasible for resource-limited countries, where a day in the hospital costs 2 to 15 times more than an outpatient visit.50 The first proof that home-based TB care was effective came from a study among people with DS-TB conducted over 50 years ago. The study found that people treated at home had similar outcomes to hospitalised patients,45 despite poorer nutrition, overcrowding and more advanced TB.61 Home-based treatment was not found to increase transmission to close contacts.62 These findings led to a 1964 WHO recommendation that “all financial resources and manpower available for tuberculosis control in developing countries be confined to organizing efficient ambulatory care and not to constructing new beds.”63 Since then, numerous studies have found that hospital-based DR-TB treatment does not result in better outcomes than community-based treatment.50,64 Hospitalisation isolates people from their families, who often cannot afford to travel long distances for visits. Decentralised, ambulatory care allows people to stay among their family and friends, and rely on their encouragement; their families prefer it because they can provide emotional support.65 Patients, along with their families and communities, believe that psychosocial support associated with home-based care is more conducive to recovery than hospitalisation.66 Decentralised and ambulatory DR-TB treatment increases case notification rates, speeds up treatment initiation, improves survival and is cost-effective.67,68,69

FINDINGS:
Routine hospitalisation for the treatment of DS-TB and the treatment of DR-TB is required in 75% (6) of countries (see Table 4).

TABLE 4: DS-TB AND DR-TB TREATMENT INITIATION POLICIES

<table>
<thead>
<tr>
<th>DS-TB treatment started at primary health care level</th>
<th>DR-TB treatment started at district level</th>
<th>Hospitalisation required for DS-TB treatment</th>
<th>Hospitalisation required for DR-TB treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kazakhstan, Kyrgyzstan, Tajikistan</td>
<td>Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan, Ukraine</td>
<td>Armenia, Belarus*, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation*</td>
<td>Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation</td>
</tr>
</tbody>
</table>

* Preferably as opposed to required.
* There are TB facilities at the primary health care level, but these facilities are separate from general primary health care facilities.

SERVICES FOR PEOPLE LIVING WITH HIV

The HIV and TB epidemics fuel one another; each infection worsens the other. HIV increases vulnerability to TB infection by up to 31-fold.64 Recognising the deadly nature of these co-epidemics, in 2004, WHO released an interim policy on TB/HIV collaborative activities and, in 2012, issued an evidence-based update, emphasising the need to deliver TB and HIV services at the same location and time: a ‘one-stop shop’.70 WHO now recommends ARV treatment for all HIV-positive adults, adolescents, children and infants, at any CD4 cell count;71 it has recommended TB preventive therapy for all people living with HIV (without signs and symptoms of active TB) since 1998.72 On their own, both ARV treatment and TB preventive therapy lower the risk for TB; combining them increases protection against TB.54,73 DR-TB treatment is just as effective for HIV-positive people, provided they are receiving ARV treatment and have a CD4 cell count of at least 100 cells/μL.54 See Table 5 for information on the level of integration of TB and HIV services.
FINDINGS:

The HIV ‘test and start’ ARV treatment policy (providing ARV treatment to all HIV-positive people) has only been adopted by Georgia, which has implemented the policy widely.

TABLE 5: POLICIES FOR INTEGRATION OF TB AND HIV SERVICES

<table>
<thead>
<tr>
<th>TB treatment can be started in health facilities providing HIV care</th>
<th>HIV treatment can be started in health facilities providing TB care</th>
<th>The same health worker can provide TB and HIV treatment at the primary health care level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia, Kyrgyzstan</td>
<td>Armenia*, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Ukraine</td>
<td>Kazakhstan, Tajikistan</td>
</tr>
</tbody>
</table>

* Applicable for inpatient TB care facilities and not outpatient TB care facilities

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**Tajikistan’s mHealth TB tool for communities**

The TB Community mHealth Platform was developed in 2017 by the Stop TB Partnership, Dure Technologies and civil society partners. The platform is the first digital tool of its kind for people with TB and community organisations supporting people with TB; it includes smartphone applications to collect, analyse and communicate key information about the availability and quality of TB services. In May 2017, partners including the Republican Centre of Population Protection from Tuberculosis Tajikistan and STOP TB Partnership Tajikistan worked to adapt the Stop TB Community Platform to the local context. The following Tajik language modules are now available:

- A ‘Knowledge’ module, which provides information about MDR-TB treatment and possible drug side effects, and includes encouraging messages from people who have survived MDR-TB in Tajikistan;
- An ‘Access’ module, which informs people about MDR-TB services available in their area; and
- A ‘Report Challenges’ module, which enables people with TB to record key information about the availability and quality of TB care services and any challenges they face in accessing those services.

An initial pilot of the mHealth Platform is underway, involving 100 people affected by MDR-TB and 13 patient support group volunteers in 10 districts. A total of 677 issues have been reported to date: side effects (314), access to health care and support (162), poor quality services at the facility (92), and stigma (109).

“This is a major step forward to have information coming straight from people who have direct experience with TB,” said Dr Lucica Ditiu, Executive Director of the Stop TB Partnership. “This platform can bring the voice of communities directly into the TB response.” Throughout 2017 and 2018, the Stop TB Partnership will support a number of community and civil society organisations in leveraging mobile technologies to put people at the centre of the TB response.
Kale Mantkava, a DR-TB patient, in his hospital room in Abastumani, Georgia.
KEY FINDINGS

- **Age- and weight-appropriate doses of first-line medicines for children largely reflect the latest WHO guidance in 75% (6) of countries.**

- **The WHO-recommended nine-month (shorter) MDR-TB treatment regimen is included in the guidelines of Kyrgyzstan and Tajikistan only; neither has implemented it widely.**

- **The new paediatric TB fixed-dose combinations (FDCs) are the standard of care in only Kyrgyzstan and Tajikistan; only Tajikistan has implemented the policy widely.**

- **Bedaquiline is included in the national guidelines for DR-TB treatment in 75% (6) of countries.**

- **Delamanid is included in the national guidelines for DR-TB treatment in 63% (5) of countries.**

- **All countries have national treatment guidelines that reflect WHO DR-TB treatment guidelines.**
BACKGROUND

TB is the world’s deadliest infectious disease. In 2015, it claimed 1.8 million lives, despite being preventable and curable.

TB treatment has evolved from a time when clean air, rest and a good diet offered the best hope for a cure, to today’s six-month regimen for DS-TB (isoniazid, rifampicin, ethambutol and pyrazinamide). According to WHO, this regimen cures more than 80% of people who complete it. However, there is still ample room for improvement. To achieve the Stop TB Partnership’s Global Plan to End TB’s 90-(90)-90 targets, 90% of all people diagnosed with TB must be cured. This calls for the development of shorter, more tolerable, affordable treatments for all forms of TB – and making them universally accessible and delivered with community-based treatment support.

Drug-resistant forms of TB continue to spread and kill. In 2015, WHO estimated that there were 580,000 people with drug-resistant forms of TB; 40% of them (250,000 people) died from DR-TB. Only 132,120 people with DR-TB (less than 25%) were diagnosed, and only 124,990 of them began DR-TB treatment. MDR-TB is more difficult to treat than DS-TB; globally, MDR-TB treatment is successful for only 52% of people who complete it. To meet the 2035 goals of the End TB Strategy (i.e. to reduce the number of new cases of and deaths from TB by 90% and 95%, respectively, from 2015 levels), safe, effective, tolerable and affordable treatment for drug-resistant forms of TB is urgently needed.
The first pillar of the End TB Strategy is: "Integrated, patient-centred care and prevention." A crucial component of the Strategy is to ensure access to treatment for people with all forms of TB.

Treatment for DS-TB is usually effective if it is completed without interruption. But side effects, such as vision loss, fever, weakness, nausea, vomiting and peripheral neuropathy (numbness, tingling or burning sensations in the hands and feet) make adherence challenging, underscoring the need for improved treatment. According to WHO, in 2014, the overall treatment success rate for DS-TB treatment was 83%.

TB TREATMENT IN ADULTS AND CHILDREN

The first pillar of the End TB Strategy is: "Integrated, patient-centred care and prevention." A crucial component of the Strategy is to ensure access to treatment for people with all forms of TB.

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**FIXED-DOSE COMBINATIONS (FDCs)**

TB treatment guidelines from WHO recommend the use of FDCs. FDCs have many advantages: They simplify treatment delivery, improve adherence and reduce the risk of single-drug stockouts (which can lead to drug resistance and treatment failure); furthermore, because dosing is more straightforward, prescription errors are likely to be less frequent, and weight-based dosing is easier than with multiple pills.

**CATEGORY II TREATMENT**

In the past, a combination of medicines known as the 'category II retreatment regimen' was recommended for people with a history of TB treatment. As of May 2017, WHO recommends that ‘the category II regimen should no longer be prescribed and drug-susceptibility testing should be conducted to inform the choice of treatment regimen.’ WHO also recommends that the empirical MDR-TB regimen be used if DST is not available to guide the choice of regimen.
OUT OF STEP in EECA

TB TREATMENT IN CHILDREN

Children are especially vulnerable to TB, particularly if they are malnourished and/or HIV-positive. In 2015, 1 million children worldwide fell ill with TB, and approximately 210,000 children under the age of 15 died from it. The new FDCs replaced older FDCs that had to be crushed to assure weight-based dosing. With the new FDCs, the number of tablets is adjusted based on weight to ensure that children get the right amount of medication. Child-friendly FDCs in the new dosage formulations are available from the Global Drug Facility (GDF) of the Stop TB Partnership.

FINDINGS:

National treatment guidelines for children reflect the 2014 WHO guidance in 88% (7) of countries, and 86% (6/7) have implemented the policy widely (see Table 6).

The new paediatric TB FDCs are the standard of care in Kyrgyzstan and Tajikistan; only Tajikistan has implemented the policy widely.

First-line medicines and regimens for children largely reflect the latest WHO guidance in 75% (6) of countries.

TABLE 6: IMPLEMENTATION LEVEL OF PAEDIATRIC TB TREATMENT POLICY

<table>
<thead>
<tr>
<th>POLICY IMPLEMENTATION LEVEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>According to national guidelines, increased doses of first-line drugs for children are in line with 2014 WHO guidance</td>
</tr>
<tr>
<td>isoniazid (H) 10 mg/kg (range 7–15 mg/kg); maximum dose 300 mg/day</td>
</tr>
<tr>
<td>rifampicin (R) 15 mg/kg (range 10–20 mg/kg); maximum dose 600 mg/day</td>
</tr>
<tr>
<td>pyrazinamide (Z) 35 mg/kg (range 30–40 mg/kg)</td>
</tr>
<tr>
<td>ethambutol (E) 20 mg/kg (range 15–25 mg/kg)</td>
</tr>
</tbody>
</table>

| Armenia, Belarus, Georgia, Kazakhstan, Tajikistan |
| Kyrgyzstan |

LEGEND

- Yes
- Unknown
HCV co-infection is common among people with TB. For people with DR-TB, HCV is particularly challenging because it damages the liver, which can exacerbate the often severe side effects people experience with DR-TB treatment. Before new direct-acting antiviral medicines (DAAs) to treat HCV became available, standard HCV treatment was contraindicated in patients co-infected with TB. Now, with the use of these DAAs, treatment of both diseases has become possible.

MSF has been supporting the National Centre for Tuberculosis Control in Armenia since 2015. In 2017, MSF supported a programme to begin providing DAAs to patients with DR-TB who are also co-infected with HCV. So far, 21 co-infected patients have received this treatment, either in combination with their TB treatment or after having completed it. Andranik Hakobyan received treatment for DR-TB – including one of the newer medicines, delamanid – and also treatment for HCV with a DAA.

“I’m 58 years old and I live here in Gyumri, in northwest Armenia; it’s where I was born,” says Andranik. “I have drug-resistant TB, which is why I’m given intravenous infusions of imipenem every morning and evening. I’ve been on treatment for 16 months now.

When you’re on TB treatment, they monitor your heart, your liver and other parts of your body. That’s how they found out that I also have hepatitis C. I took the pills [for hepatitis C] at 9am every day. They told me the treatment would take 90 days. I take all these drugs but continue to work. As you see for yourself, I can’t stay idle. And given that my house is run down, there’s always something to do. I’m active all day long. I hope to live longer. If I am cured, I will be able to live longer.”

When Andranik was tested after three months of the new treatment, HCV was no longer detected. A second test will confirm he is cured. Meanwhile, he continues his battle against TB.
OUT OF STEP in EECA

DR-TB TREATMENT IN ADULTS

Drug-resistant forms of TB can be acquired or directly transmitted. Several factors drive the development of TB drug resistance, including misdiagnosis leading to ineffective treatment; prescribing, dispensing or dosing errors; substandard medicines; treatment interruptions or poor adherence; medicine stockouts; insufficient medicine levels in the body; and the inability of medicines to penetrate into TB lesions. According to epidemiological modelling, without changes to current TB prevention and treatment, both direct transmission and rates of MDR- and XDR-TB will continue to increase in high-burden countries.

Drug-resistant forms of TB are more difficult to treat than DS-TB. Until 2016, when WHO released updated guidelines for shorter MDR-TB treatment, treatment could last for up to 24 months and involved eight months of painful daily injections and nearly 15,000 pills, many of which have severe side effects. Undergoing DR-TB treatment is an ordeal for patients, their families and governments. People with DR-TB face the risk of permanent deafness and organ damage from their treatment, as well as catastrophic costs, unemployment, and separation from their families and communities. Worse, they may not survive treatment, as treatment success rates are suboptimal: 52% for MDR-TB and 28% for XDR-TB. The price per treatment course ranges from US$ 2,000 to US$ 20,000. DR-TB treatment is becoming shorter, less toxic and more effective. Newer TB medicines and treatment strategies can drastically improve the outcome of DR-TB treatment. Combinations of repurposed medicines that were originally approved for different conditions, companion drugs (that protect against resistance to the main TB medicines), and newer TB medicines bring hope to people with all forms of DR-TB.

FINDINGS:

All countries have national treatment guidelines that reflect WHO DR-TB treatment guidelines. However, as illustrated in the following sections, countries still must do much more to reduce death and suffering from DR-TB.

BEDAQUILINE AND DELAMANID

Newer, highly effective medicines for MDR-TB have received accelerated approval from the US Food and Drug Administration (USFDA) and conditional marketing authorisation from the European Medicines Agency (EMA); however, few people are benefiting from the medicines today. Globally, only 5% of those who could have benefited from bedaquiline and delamanid were treated with the newer medicines in 2016. WHO guidelines recommend that MDR-TB be treated with at least four effective medicines. Bedaquiline and delamanid are recommended as ‘add-on’ agents for people with MDR-TB who do not have other treatment options, and for people at high risk for poor treatment outcomes (people with extensive TB disease and/or TB/HIV co-infection, and people who cannot tolerate other TB medicines). However, the uptake of bedaquiline and delamanid has been far lower than the actual need for these medicines.

In the eight countries surveyed in this report, 119,700 people are in need of DR-TB treatment, but access to the newer medicines is limited. According to data from the DR-TB Scale-Up Treatment Action Team (DR-TB STAT), as of July 2017, the newer medicines were available in six of the countries surveyed in this report and dispensed to less than 3% of the people who could benefit from them, as shown in Table 7.
TABLE 7: CUMULATIVE NUMBER OF PEOPLE TREATED WITH BEDAQUILINE OR DELAMANID

<table>
<thead>
<tr>
<th></th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>RUSSIAN FED</th>
<th>TAJIKISTAN</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedaquiline</td>
<td>115</td>
<td>389</td>
<td>262</td>
<td>196</td>
<td>1444</td>
<td>35</td>
<td>2441</td>
</tr>
<tr>
<td>Delamanid</td>
<td>54</td>
<td>65</td>
<td>87</td>
<td>103</td>
<td>108</td>
<td>6</td>
<td>333</td>
</tr>
</tbody>
</table>

FINDINGS:

- Bedaquiline is included in the national guidelines for DR-TB treatment in 75% (6) of countries (see Table 8).
- Delamanid is included in the national guidelines for DR-TB treatment in 63% (5) of countries (see Table 8).

TABLE 8: NATIONAL GUIDELINES INCLUDE BEDAQUILINE AND DELAMANID

<table>
<thead>
<tr>
<th>Bedaquiline included in national guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Russian Federation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delamanid included in national guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan</td>
</tr>
</tbody>
</table>

In countries eligible for Global Fund grants, bedaquiline and delamanid are available from the GDF of the Stop TB Partnership. According to cumulative reports from GDF, as of August 2017, bedaquiline was delivered to seven of eight countries surveyed in this report (Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan and Ukraine); delamanid was delivered to five countries (Armenia, Belarus, Georgia, Kazakhstan and Tajikistan).
One reason for the low uptake of the new medicines has been knowledge gaps on how best to use these newer TB medicines in treatment regimens. Notably, there has been a lack of data on the combination of bedaquiline and delamanid; their interactions with other standard TB medicines and ARVs; and their safety and effectiveness in specific populations (such as pregnant women, children, and people living with HIV/AIDS). Now, there is new evidence on optimal regimens and treatment duration.

While delamanid has had limited use outside of clinical trials, MSF results from a multi-centric retrospective analysis of patients receiving delamanid under programmatic conditions show good tolerability and treatment response with 68% culture conversion at six months.83

On the use of bedaquiline in children, preliminary results show that bedaquiline can be used safely in children over 12 years of age with appropriate monitoring and could be considered for younger children under select circumstances, when no other options are available and benefits are likely to outweigh risks.84

Yet to be published data from MSF (presented at the Union World Conference on Lung Health in October 2017) demonstrate the early safety and efficacy of bedaquiline and delamanid combination for DR-TB in Armenia, India and South Africa.

Ongoing trials will yield more information on the best combinations and treatment duration for bedaquiline and delamanid. In the interim, MSF is working with national programmes to offer people optimal treatment (including bedaquiline and/or delamanid) adapted to their individual needs, with support from the endTB Medical Committee.

MSF is working with national treatment programmes in Armenia, Belarus, Georgia, Kyrgyzstan, Russian Federation, Tajikistan, Ukraine and Uzbekistan to give people with MDR-TB and limited treatment options the best hope for a cure.

Results from cohorts of extremely difficult-to-treat patients without other treatment options have been impressive. In Armenia and Georgia, 82 people with MDR-TB received bedaquiline through compassionate use between April 2013 and April 2015. Most (84.2%) were resistant to FLQs, of which 48.8% were extensively drug-resistant. All had been treated with second-line medicines, while 39% had received clofazimine. Among the 64 people who were culture-positive at initiation, 54/64 (84.4%) achieved six-month culture conversion (a sign that treatment is working). However, 10/54 (18.9%) reverted back to positive later in the treatment. Treatment outcomes were: 54.8% successful, 12.2% death, 7.3% failure and 21.9% lost to follow-up.

These results show a very high rate of culture conversion for very resistant strains of MDR-TB. However, the high proportion of relapses after six months of treatment is alarming, calling into question WHO’s previous recommendation of limiting bedaquiline to 24 weeks. In addition, the high proportion lost to follow-up – likely due to the long duration of treatment – remains a concern. Similar results were seen in a cohort of patients treated in Chechnya; a study comparing treatment with bedaquiline, linezolid and clofazimine to regimens without these medicines showed better culture conversion at six months.85
SHORT-COURSE DR-TB REGIMEN

In 2016, WHO issued a recommendation supporting a shorter RR- or MDR-TB treatment regimen (9 to 12 months versus up to 24 months) under specific circumstances. The shorter regimen of existing medicines is only recommended for people with RR- or MDR-TB who have never received second-line TB medicines and who are not – or are highly unlikely to be – resistant to FLQs and SLIDs (based on second-line DST or, if unavailable, surveillance data on prevalence and types of drug resistance). In addition, WHO regrouped the medicines used for RR- and MDR-TB (see Table 9). This recommendation was based on evidence from operational research studies, which found the shortened regimen to be more effective for eligible patients and the price dropped to less than US$ 1,000 per treatment course.

Modelling the impact of shorter treatment on MDR-TB incidence found that shorter treatment has the potential to markedly reduce the incidence of MDR-TB if access to shorter and more effective treatment is expanded, and in the absence of additional drug resistance.

FINDINGS:

The WHO-recommended nine-month (shorter) MDR-TB treatment regimen is included in the guidelines in Kyrgyzstan and Tajikistan only.

According to national guidelines, Kyrgyzstan and Tajikistan require a second-line DST by LPA before starting the short-term regimen.

DR-TB TREATMENT IN CHILDREN

Unfortunately, there are no child-friendly formulations to treat drug-resistant forms of TB. Data on the safety and effectiveness of bedaquiline and delamanid in paediatrics are limited. Based on data from an ongoing study in children, WHO has recommended that delamanid could be added to treatment for DR-TB in children and adolescents (6–17 years of age) under specific circumstances (e.g. ineligibility for shorter treatment because of treatment history or resistance profile, or contraindications).

Currently, bedaquiline is approved for adults over 18 years of age; an ongoing phase II study is exploring the dosing, safety and efficacy of bedaquiline-containing TB treatment in ages 0–18, and another study in HIV-negative and HIV-positive infants, children and adolescents up to 18 years of age is planned.

TABLE 9: WHO: REGROUPED MEDICINES RECOMMENDED FOR RR- AND MDR-TB

<table>
<thead>
<tr>
<th>GROUP A: Fluoroquinolones, in order of preference for use</th>
<th>levofloxacin, moxifloxacin, gatifloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP B: Second-line injectables</td>
<td>amikacin, capreomycin, kanamycin, streptomycin (in some cases)</td>
</tr>
<tr>
<td>GROUP C: Other core second-line agents, in order of preference for use</td>
<td>ethionamide/prothionamide, cycloserine/terizidone, linezolid, clofazimine</td>
</tr>
<tr>
<td>GROUP D: Add-on agents</td>
<td>D1: pyrazinamide, ethambutol, high-dose isoniazid</td>
</tr>
<tr>
<td></td>
<td>D2: bedaquiline, delamanid</td>
</tr>
<tr>
<td></td>
<td>D3: p-aminosalicylic acid, imipenem-cilastatin, (complementary) meropenem, amoxicillin-clavulanate, thioacetazone (only if HIV-negative)</td>
</tr>
</tbody>
</table>
Tajikistan is a high MDR-TB burden country. In 2015, 546 children were diagnosed with DR-TB, 21 with MDR-TB. Use of the newer medicines, bedaquiline and delamanid, has been included in national policy and proved successful in pilot sites.

Dr Zulfiya Dusmatova, an MSF medical doctor working with the Ministry of Health, describes the experience of using bedaquiline and/or delamanid with other medicines to treat children with DR-TB in Tajikistan.

"Paediatric fixed-dose combinations (FDCs) of DS-TB medicines have definitely made treatment easier for small children, since they don’t have to swallow such a large number of pills every day. But there are currently no FDCs available for children with DR-TB, so in Tajikistan, MSF has supported the Ministry of Health with the introduction of drug-compounding techniques (in this case, the preparation of a syrup formulation) for some DR-TB drugs. The syrup formulation has certainly helped the youngest patients, who have difficulty swallowing tablets, and greatly improved treatment tolerability and adherence among children with DR-TB.

Currently, MSF uses bedaquiline and delamanid through a humanitarian import waiver as agreed by the Ministry of Health of Tajikistan. As of July 2017, MSF’s first cohort of five patients with pre-XDR and XDR-TB – who started treatment with bedaquiline between April and June 2015 – are confirmed cured with a success rate of 100%. All five patients finished 24 months of treatment. Tajikistan must now build upon this success story by scaling up programmatic use of the newer medicines."
**MANAGEMENT OF CO-INFECTIONS**

Collaborative TB and HIV activities are a key component of the End TB Strategy’s Pillar 1. Prevention, testing, care and treatment services for HIV and TB must be integrated and easily accessible to people living with, or at risk for, both infections.

TB and HIV are a deadly – and common – combination. People with weakened immune systems due to HIV or other causes, such as diabetes and malnutrition, are especially vulnerable to falling ill with and dying from TB.

ARV treatment reduces the risk for and rate of TB among HIV-positive people, and lowers TB-associated mortality among people living with HIV. WHO now recommends ARV treatment for all HIV-positive people, initiated within two to eight weeks of starting TB treatment (depending on CD4 cell count).

People with diabetes are more susceptible to developing active TB; diabetes triples a person’s risk of developing TB. People with TB should be systematically screened for diabetes and vice versa (especially in settings with a high TB prevalence).

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**TB REGIMEN DEVELOPMENT**

Since TB must be treated with combinations of medicines, the most effective research focuses on entire regimens and strategies to optimise them, instead of developing medicines one by one. The ultimate goal is to develop an affordable, short-course, oral ‘pan-TB’ regimen with few side effects.

The Life Prize is dedicated to initiating a better, faster way to develop a short-course pan-TB regimen, instead of developing single medicines. The Project builds affordability into drug development, ensuring development costs are covered up front; Prize money goes towards early-stage development, grants pay for trials that combine new medicines, an open collaborative platform ensures access for developers, and the pooling of data, intellectual property and products ensures accelerated and affordable access.

Several studies (including NC-005, NIX, TB PRACTECAL and endTB) are looking to increase effectiveness and shorten treatment duration by combining old, new and repurposed medicines with some promising TB medicines that are in the development pipeline, such as pretomanid – a medicine from the same family as delamanid – and sutezolid, which may be more tolerable than linezolid.

**MEDICINES: ACCESS AND AFFORDABILITY**

Medicines need to be available and affordable to be effective. A conventional, WHO-recommended, standard 24-month treatment course for MDR-TB can cost between US$ 1,600 and US$ 4,000; this does not include clinical management, laboratory tests and hospitalisation, which can be up to 14 times higher than the price of the regimen. Currently, the price of delamanid in countries eligible for Global Fund support is US$ 1,700 for a six-month course.

Current pricing for a six-month course of bedaquiline is US$ 900 in low- and middle-income countries (LMICs), US$ 3,000 in middle-income countries (MICs), US$ 30,000 in high-income countries (HICs), and US$ 1,970 in the Russian Federation; bedaquiline is also available through a donation programme for Global Fund-eligible countries outside of the Commonwealth of Independent States (CIS). More needs to be done, by governments and pharmaceutical companies, to ensure access to affordable medicines.
A nurse lays out antibiotic drugs used to treat MDR-TB at the National Center for Tuberculosis and Lung Disease in Georgia’s capital, Tbilisi. They include delamanid and bedaquiline.
25% (2) of countries have either bedaquiline or delamanid listed on their national Essential Medicines List (EML).

75% (6) of countries have more than 50% of the WHO-recommended medicines (Groups A, B, C, D1, D2 and D3) listed specifically in the anti-TB medicines category of their national EML.

50% (4) of countries are enrolled in the WHO Collaborative Registration Procedure.

50% (4) of countries have accelerated registration mechanisms in place that could potentially be applied to new and repurposed DR-TB medicines.

88% (7) of countries have a policy in place that requires a prescription for TB medicines.

Unregistered TB medicines are available through compassionate use or other national-level legal mechanisms in 75% (6) of countries.

Bedaquiline is registered in only the Russian Federation and Armenia; delamanid is not registered in any of the countries surveyed in this report.
BACKGROUND

TB medicines should be quality-assured and WHO-pre-qualified (or approved by a stringent drug regulatory authority [SDRA]) to avoid substandard and falsified products.

Many important TB medicines have not been registered in high-burden countries, including TB medicines listed in the WHO Model List of Essential Medicines. Furthermore, some of the necessary set of medicines for TB may not be registered for this use. Drug registration can be a lengthy process, given that national drug regulatory authorities (NDRAs) have their own procedures, timelines and capacities, and originator companies prioritise registering their drugs in the most profitable markets, instead of where they are needed the most. The WHO Collaborative Registration Procedure accelerates approval of and access to originator and generic medicines, including TB medicines, for public health needs in developing countries. Using this procedure ensures that medicines can get to the people who need them faster.

Other mechanisms, such as import waivers or compassionate use programmes, can provide access to lifesaving TB treatment in countries where the medicines are not registered.

Of the countries surveyed in this report, access to bedaquiline and delamanid in Ukraine has been significantly delayed due to the lack of local registration. Under Ukrainian law, unregistered medicines can only be accessed through research projects. Other countries in the EECA region have allowed access to bedaquiline and delamanid either through import waivers, compassionate use programmes, or local registrations. While import waivers and compassionate use can be useful supply channels in the short term, only local registration can guarantee a secure, long-term supply. So far, bedaquiline is registered only in Armenia and the Russian Federation. Dossiers have been rejected due to a lack of phase III data in Georgia, Kazakhstan and Kyrgyzstan, which do not grant conditional approval for medicines that have not completed clinical development. A dossier has been submitted to regulatory authorities in Belarus and is currently under assessment. Dossiers have not been submitted by Janssen in Ukraine or by Pharmstandard in Tajikistan. Delamanid is not yet registered in any of the surveyed countries. R-Pharm, Otsuka’s partner in the EECA region, is urged to submit dossiers to NDRAs as soon as possible.
NATIONAL ESSENTIAL MEDICINES LIST (EML)

The WHO EML identifies medicines that are prioritised based on their safety, efficacy, cost-effectiveness and importance in meeting people’s health needs. When a medicine is included in the WHO EML, it sends a powerful signal to countries for their own national EML; this, in turn, can ease importation of the listed medicines.

The 20th edition of the EML includes most WHO-recommended TB medicines with a TB indication. Clofazimine, a key medicine of the MDR-TB shorter treatment regimen, has been added to the latest WHO EML as an anti-TB medicine.

All TB medicines recommended in WHO guidelines should be included in WHO and national EMLs.

FINDINGS:

- 75% (6) of the countries surveyed have more than 50% of the medicines (Groups A, B, C, D1, D2 and D3) listed specifically in the anti-TB medicines category of their national EML.
- No country has the full set of WHO-recommended DR-TB medicines listed in the TB section of their EML.
- In Georgia, no valid national EML currently exists, but one is in the process of being finalised and approved. In the interim, the WHO EML is being used as a reference. In Kyrgyzstan, the new national EML is awaiting approval.

KEY REGULATORY POLICIES

<table>
<thead>
<tr>
<th></th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
<th>TAJIKISTAN</th>
<th>UKRAINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR-TB medicines can receive accelerated registration</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Unregistered TB medicines are available through CU/other legal mechanisms*</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Country is enrolled in WHO Collaborative Registration Procedure</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Compassionate use, expanded access programmes, import waivers or other legal mechanisms. (a) Only if already approved by an SDRA.
QUALITY ASSURANCE

TB medicines should be quality-assured – either WHO-prequalified or approved by an SDRA – to avoid substandard or falsified products. In 2011, WHO reported that 11% of certain first- and second-line TB medicines gathered from public TB treatment centres and private pharmacies in Armenia, Azerbaijan, Belarus, Kazakhstan and Ukraine failed quality standards, including 28% of rifampicin capsules. A recent study of anti-TB medicines from private-sector pharmacies in 19 cities reported that nearly 4% of all tested medicines were substandard in five countries, including the Russian Federation.

Many NTPs use the GDF – a pooled procurement mechanism – to procure quality-assured TB medicines, particularly DR-TB medicines financed through grants from the Global Fund. However, the Global Fund has been changing its co-financing and allocation policies to fully or partially move out of MICs, including those with high burdens of TB and DR-TB. The Global Fund’s policies led to a 15% funding cut in the 2014–2016 allocation period in the region; additional and significantly larger cuts are anticipated in the next allocation period (2017–2019). As EECA governments are rapidly forced to pay for a larger share of their TB medicines and diagnostics, they may transition from pooled procurement to national-led procurement. This could result in a lower quality of medicines being procured and also split the market for TB medicines and diagnostics between pooled procurement mechanisms and national procurement, which may have an impact on the pricing and quality of these commodities.

EARLY ACCESS PROVISIONS

Lack of registration can be a primary barrier to accessing medicines in high-burden countries, since some countries do not have mechanisms in place to provide access to unregistered medicines. Manufacturers may be reluctant to register their medicines in LMICs, even though these countries bear the brunt of the global TB epidemic. Some medicines that are used to treat DR-TB are registered for a different purpose (such as linezolid, clofazimine and imipenem/cilastatin) and may also be unavailable.

Bedaquiline and delamanid have not been registered in many countries, and delamanid has not been registered in any high MDR-TB burden country. For example, neither drug has been registered in Kyrgyzstan, which has a high burden of MDR-TB. Due to the absence of phase III trial data, bedaquiline was rejected by Kyrgyzstan because it does not grant conditional approval for medicines that have not completed clinical development. Furthermore, importation of clofazimine is limited because it has not been registered with a TB indication. MSF worked to provide access to these lifesaving medicines in Kyrgyzstan by applying to the Ministry of Health for import waivers, which are granted under certain conditions for medicines that are not on the national EML or not included in national treatment guidelines or protocols for first-line treatment.

FINDINGS:

According to national guidelines, 75% (6) of countries can procure unregistered TB medicines through compassionate use or other legal mechanisms. In Ukraine, these mechanisms are not in place. See Table 10 for mechanisms in two countries.

<table>
<thead>
<tr>
<th>Country name</th>
<th>Mechanism being utilised</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEORGIA</td>
<td>Compassionate use, regular import procedure, exemption mechanisms, importation for unregistered medicines, under programmatic use</td>
</tr>
<tr>
<td>TAJIKISTAN</td>
<td>Humanitarian access channel</td>
</tr>
</tbody>
</table>

TABLE 10: EXAMPLES OF MECHANISMS BEING UTILISED IN THE COUNTRIES SURVEYED
ACCELERATED APPROVAL

Marketing authorisation procedures can delay access to lifesaving TB medicines, especially in countries where they are needed most. The pathways, requirements, local processes, timelines and capacities of NDRAs vary. A few countries lack alternative approval mechanisms, while others do not always favour mutual recognition agreements or do not recognise the technical assessments of SDRAs such as the EMA or USFDA.

In 2015, WHO launched the WHO Collaborative Registration Procedure to facilitate access to generic or originator medicines, including TB medicines, for public health needs in developing countries. Participating NDRAs have 90 days to review the dossiers of SDRA-approved or WHO-prequalified products, under confidentiality, in a globally harmonised format aligned with the same system used for WHO prequalification. Through this process, NDRAs can follow their national legislation and responsibilities, collect fees, and develop risk-management and pharmacovigilance plans with applicants.100

FINDINGS:

50% (4) of countries are enrolled in the WHO Collaborative Registration Procedure.

The following countries have no legal mechanism in place to allow for the accelerated registration of medicines, including DR-TB medicines: Belarus, Russian Federation and Tajikistan.

Bedaquiline is registered in only the Russian Federation and Armenia; delamanid is not registered in any of the countries surveyed for this report (see Table 11).

PRESCRIPTION REQUIREMENTS

Too often, TB medicines are dispensed in the private sector without linkage to NTPs; people may seek treatment directly from a pharmacy, where staff are untrained, and necessary medicines may be unavailable or of poor quality.101,102 Over-the-counter sales facilitate drug resistance, since people may not receive recommended, quality-assured medicines and/or regimens for their TB.103 In 2014, WHO called for a ban on over-the-counter sales of TB medicines, and recommended a mixed public–private approach to ensure that providers who are not affiliated with NTPs are following international standards and national treatment guidelines.103

Although many countries have regulations prohibiting over-the-counter sales of TB medicines, these are difficult to enforce. WHO recommends making TB a notifiable disease, including tracking how all forms of TB are diagnosed and managed.103

FINDINGS:

88% (7) of countries have a policy in place that requires a prescription for TB medicines.

TABLE 11: REGISTRATION OF BEDAQUILINE AND DELAMANID

<table>
<thead>
<tr>
<th>Status</th>
<th>Registered</th>
<th>Bedaquiline</th>
<th>Armenia, Russian Federation</th>
<th>Delamanid</th>
</tr>
</thead>
<tbody>
<tr>
<td>None of the surveyed countries have registered delamanid</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Marta Askalyan had XDR-TB and spent 16 months in hospital. She is pictured here in Yerevan, Armenia, in early 2014 after starting treatment that included bedaquiline the previous year.
Treatment for latent TB infection (LTBI), also known as preventive therapy, is provided and implemented widely for adult contacts, child contacts and people living with HIV in the Russian Federation and Belarus.

Treatment for LTBI is provided to child contacts under five years of age and people living with HIV in all countries surveyed; 75% (6) have implemented the policy widely. No country provides LTBI treatment to other WHO-recommended at-risk populations (prisoners, miners, people with silicosis, people with diabetes, and organ and transfusion recipients).

A tuberculin skin test (TST) must be carried out prior to starting treatment for LTBI in all countries surveyed; 63% (5) have implemented the policy widely.

Six-month isoniazid (INH) is provided as the preventive therapy regimen in all of the countries.

Three- to four-month isoniazid plus rifampicin and a three-month course of weekly rifapentine plus isoniazid (known as the 3HP regimen) is provided in Georgia and the Russian Federation.

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BACKGROUND

All people exposed to TB are at risk of becoming sick. Globally, 30% of the population has LTBI. Although they are infected with TB, they are not ill or infectious unless they develop active TB disease. Over a lifetime, people with LTBI have a 5–10% risk of TB reactivation; this usually occurs within five years of infection. Preventive treatment reduces the risk of people with LTBI developing active TB by up to 90%.

Prevention is essential to achieving the goals and targets of the End TB Strategy. The End TB Strategy and the Global Plan to End TB call for at least 90% coverage of two key initiatives as early as possible but no later than 2025: (i) systematic screening for high-risk groups and those who have had close contact with people with infectious TB and (ii) preventive therapy that protects people with LTBI from developing active TB disease.

Treatment is more complex for people who have been exposed to drug-resistant forms of TB. Clinical assessments are required to look for active disease for prompt initiation of treatment. For those without active disease, there are currently two commonly used strategies that may be followed: ongoing screening and monitoring for a minimum of two years, or provision of FLQ-based treatment of infection based on recent findings of a 90% reduction in TB incidence. More clinical trials are under way.
SCREENING OF HOUSEHOLD CONTACTS AND PEOPLE LIVING WITH HIV

Since TB is airborne, it can be easily transmitted in crowded places: households, prisons, hospitals, homeless shelters, cramped living quarters and workplaces, and even between minibus commuters. Nearly 5% of those who have close contact with people with infectious TB have active TB disease, and over 50% of them have LTBI. However, many people with early-stage TB do not exhibit the usual symptoms and are unaware that they have TB.

Instead of relying on passive case finding (i.e. testing only those who seek health care for TB signs and symptoms), WHO recommends systematic screening of high-risk groups, with priority given to close contacts of people with TB, HIV-positive people, and workers exposed to silica. Screening of other risk groups should be based on local epidemiology, resources, capacity and other factors.

FINDINGS:

All countries have policies in place to carry out active case finding for children under five years of age who have been living in the same household as a confirmed TB patient; 88% (7) have implemented this policy widely.

All countries have policies in place to carry out active case finding for all household contacts regardless of age, but only 50% (4) have implemented this policy widely.

All countries have policies in place to conduct active case finding among people living with HIV, but only 63% (5) have implemented this policy widely.

PREVENTIVE TREATMENT IN CHILDREN AND PEOPLE LIVING WITH HIV/AIDS

WHO recommends prioritising those most vulnerable to developing severe and disseminated forms of TB, including children under five years of age and people living with HIV/AIDS.

CHILD HOUSEHOLD CONTACTS

In EECA, an estimated 17,991 children under 15 years of age developed TB in 2015; it is estimated that half of them were under five. TB is especially serious for children in this age group. Children are more vulnerable; TB is harder to diagnose in them; they are more likely to have serious forms of the disease, such as TB meningitis or disseminated TB; and the disease usually progresses rapidly.

In 2015, globally 1.2 million children under five years of age were estimated to be household contacts of infectious TB patients and therefore eligible for preventive therapy; yet only 7.1% (or 87,000) of them received it.

PEOPLE LIVING WITH HIV

The risk for TB reactivation is much higher for people living with HIV, who face an annual reactivation risk of 5% to 15%, and TB is likely to be deadlier. Since 1998, WHO has recommended preventive therapy for all people living with HIV (without signs and symptoms of active TB). Preventive therapy protects HIV-positive people from TB, even at high CD4 cell counts (>500 cells/μL), and especially when used in combination with ARV treatment. However, countries have been slow to roll out preventive therapy. In EECA, an estimated 330,900 people were living with HIV/AIDS in 2015, and 27,994 of them were newly enrolled in care in 2015. Only 10,023 (35.8%) started on preventive therapy.
PREVENTING MDR-TB

Treating household contacts of MDR-TB patients could help to prevent the spread of MDR-TB. By the time a person with MDR-TB is diagnosed, 5% to 10% of their household contacts have active TB and nearly 50% of them have LTBI.\textsuperscript{107}

Preventive therapy for latent MDR-TB is challenging and relies on medicines that are likely to be ineffective, as DST can only be performed in people with active TB and their contacts do not always have the same form of TB. Nonetheless, given the toxicity, limited effectiveness and expense of DR-TB treatment, it is critical to prevent progression of drug-resistant LTBI. Treatment of people who have been exposed to drug-resistant forms of TB is complicated and relies on a detailed exposure history. All people exposed to DR-TB should have urgent clinical assessments to look for active disease, so they can promptly be started on therapy based on the drug-susceptibility pattern of the known source case.

In people without active TB disease, two approaches may be followed: The first involves ongoing screening and monitoring for signs and symptoms of active TB for a minimum of two years, with prompt initiation of empirical MDR-TB treatment based on the resistance pattern of the known contact for those with likely TB;\textsuperscript{102} the second involves the provision of FLQ-based treatment of infection. A recent meta-analysis of the efficacy of FLQ-based treatment found a 90% reduction in TB incidence in people exposed to DR-TB who received six months of FLQ-based therapy.\textsuperscript{105} A trio of clinical trials are currently exploring optimal preventive regimens for MDR-TB contacts, using levofloxacin versus delamanid or placebo, but results are not expected until 2020.

FINDINGS:

- Treatment for LTBI is provided to children and people living with HIV/AIDS in all countries, and 75% (6) have implemented the policy widely.
- Treatment for LTBI is provided and implemented widely for adult contacts, child contacts and people living with HIV in the Russian Federation and Belarus.
- In all countries, it is compulsory to carry out a test for LTBI, such as a TST or interferon-gamma release assay (IGRA), prior to prescribing preventive therapy. Kyrgyzstan requests compulsory TSTs to select people eligible for preventive therapy, but when there are TST shortages – which occurs often – it prescribes preventive therapy based on a clinical evaluation.
- In all countries, the guidelines recommend six-month INH treatment to treat LTBI upon exclusion of active TB.
- Six months of daily INH is the preferred regimen in all countries. Some of the surveyed countries use different preventive therapies, as highlighted in Table 12.

### TABLE 12: EXAMPLES OF PREVENTIVE THERAPY REGIMENS IN TWO COUNTRIES THAT USE REGIMENS OTHER THAN INH ALONE

<table>
<thead>
<tr>
<th>Country</th>
<th>Medicines used in preventive therapy and duration of treatment (including RPT, RIF and Rfb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEORGIA</td>
<td>6 months INH (preferred)</td>
</tr>
<tr>
<td>RUSSIAN FEDERATION</td>
<td>6 months INH</td>
</tr>
</tbody>
</table>

INH = isoniazid, RIF = rifampicin, RPT = rifapentine, Rfb = rifabutin
Jayna was diagnosed in 2013 with XDR-TB. In June 2015, she started a new treatment regimen with the newer TB drug, bedaquiline, in Grozny, Chechnya.

There is excitement at home for Jayna, a mother of three young children who has just completed XDR-TB treatment provided by MSF in Grozny, Chechnya in the Russian Federation. Jayna’s six-year-old daughter, Khadija, is about to start school. “We are already studying with her,” says Jayna. “I’m teaching her; we have already finished the primer in two months, and she’s already learned to read!”

It is a happy time for Jayna because she was not sure she would live to see this day. “When I came here two years ago, I thought that I would not see my children again,” she remembers. “My husband tells me now: ‘I thought that you would die.’”

Jayna was first diagnosed with TB in 2008 and had several relapses in the years that followed. In 2013, she was diagnosed with XDR-TB in Saratov in the Russian Federation, where she lives. In June 2015, she started a new treatment regimen with the newer TB medicine, bedaquiline, in Grozny. She felt immediate improvement after just a week and remained very optimistic and positive throughout her treatment. Jayna supported other patients in the ward to motivate them to adhere to treatment. “My husband supported me a lot,” she says. “And now, thank God, I’m walking, everything is fine, and there are no problems.” Now Jayna looks forward to a brighter future with her family, including her two sons – 10-year-old Ali and 8-year-old Hamza. “They missed me very much when I was getting treatment,” Jayna remembers. “Thank God, we are now together, alive and healthy. Inshallah, life will be even better.”
Governments and treatment providers in EECA must act urgently to prevent vulnerable people from needlessly falling ill, suffering and dying from TB. There is no time for delay. In the WHO European Region, the majority of the 323,000 new TB cases and 32,000 deaths occur in EECA, and DR-TB is increasing by more than 20% each year in Eastern Europe. With the advent of improved TB diagnostic tests and medicines – and evidence of their efficacy in hand – we already have the means to conquer TB. It is up to governments and treatment providers to seize the moment and do all they can to reduce TB deaths.

The evidence cited in this report shows that many of the 32,000 annual TB deaths in EECA could be averted if countries in the region fully implement existing recommended policies and practices for TB prevention, diagnosis and treatment. To accomplish this, countries must pull TB at the top of their national health agendas and join forces with neighbours facing similar challenges.

Ending TB in EECA requires the implementation of broad-based public health measures, thoughtful design of patient-centred models of care and decentralised health services that can be provided on an ambulatory basis. Once diagnosed, people need access to the best treatments available, along with education, counselling and support to help them successfully complete their treatment. Development of new TB treatments must be centred on meeting people’s health needs and must prioritise affordability and access early in the research process. Treatments that can cure all forms of TB disease and are easy for patients to tolerate and complete must be prioritised.

Governments must explore all opportunities to improve TB care in their own countries, such as revamping drug regulatory pathways, adjusting procurement processes and ensuring health budgets are matched to health needs. At the same time, countries must continue to advocate for additional funding, research and political attention on a global scale. A multi-sector approach at the national and international level is required.

None of this will be easy, but we cannot afford the alternative: Failure to fully scale up each step towards successful TB treatment will hasten the spread of drug-resistant forms of the disease and prolong the dismal trends in missed diagnoses, long-term morbidity and avoidable TB deaths.

We have the means to end the global TB epidemic. We have the strategies, tools, plans and targets to guide our way. What we need now is political will, adequate resources, accelerated research, and full implementation of the policies and practices that we know will reduce TB suffering and death.
WHAT NEEDS TO HAPPEN

DIAGNOSIS

**Rapid diagnostic testing:** Countries need to be bold by accelerating access and increasing their capacity to universally provide Xpert MTB/RIF testing for all instead of microscopy, with urgent prioritisation of key populations (people at risk for DR-TB, people living with HIV, and children).

MODELS OF CARE

**Patient-centred:** People receiving TB treatment must be at the centre of their care, and be supported and encouraged as such.

**Decentralisation:** TB services need to be decentralised to improve access and decrease out-of-pocket costs.

**Ambulatory care:** Compulsory hospitalisation should be replaced with ambulatory care, including for DR-TB. The resulting cost savings could be used to provide support services and community systems that enable communities to provide patient support during ambulatory care.

**Integrated care:** TB/HIV care and treatment should be closely linked in order to support adherence and successful treatment outcomes (e.g. one treatment facility and one medical team).

**Treatment as prevention:** Given the benefits of ARV treatment in reducing TB incidence, morbidity, mortality and transmission, it is imperative – and urgent – for countries with high rates of TB/HIV co-infection to implement ARV ‘test and start’.

TREATMENT

**Treatment gap:** More effort is needed to close the deadly gap between adults and children who need treatment and those who are actually receiving it, for all forms of TB.

**Co-infections:** Co-infections should be managed effectively, especially TB/HIV co-infection.

**Paediatric TB:** Countries should introduce the dose-optimised paediatric FDCs as the standard of care for DS-TB.

**R&D:** Governments should support the launch of innovative research to develop new, affordable all-oral regimens that are shorter, have fewer side effects and have a lower pill burden. This includes the Life Prize, an initiative designed to use innovative funding and pooling mechanisms to develop a short-course pan-TB regimen, instead of developing single medicines.

REGULATORY ENVIRONMENT FOR TB MEDICINES

**Quality:** Countries should ensure the procurement and use of quality-assured (including WHO-prequalified and SDRA-approved) TB medicines.

**Registration:** Drug companies must do better to prioritise the registration of medicines in countries with large numbers of people with TB, so that the medicines can be readily used.

**TB indication:** Repurposed medicines, such as clofazimine, should have a TB indication and be registered with a TB indication in high-burden TB countries as a priority.

**National mechanisms:** For their part, countries should provide mechanisms for the rapid entry of new medicines, including expedited registration through enrolment in the WHO Collaborative Registration Procedure or another mechanism, and the use of import waivers and other legal mechanisms until local registration is granted.

PREVENTION

**Reach key populations:** Countries need to develop programmes to reach vulnerable and key populations, including children, HIV-positive people and prisoners, among other groups.

**Ensure that tests for TB infection are not mandatory for HIV-positive people, child contacts or people with high-risk household exposures prior to the initiation of LTBI treatment:** HIV-positive people with negative symptom-based screening should be offered treatment for LTBI.

**Ensure that all people exposed to DR-TB receive urgent assessments to rule out active disease and are followed routinely over a period of two years.**

**Optimise treatment for LTBI by making affordable FDCs and increasing the use of the 3HP regimen (three months of weekly RPT + INH) for populations where effectiveness is clear.**
NEEDED: EIGHT COMMITMENTS FOR TB

Governments should commit to a set of time-bound targets at the Global TB Ministerial Conference in Moscow in November 2017 and UN High-Level Meeting on TB in 2018, as well as taking other opportunities to do so. These should include commitments to:

- Implement the latest WHO TB prevention, testing and treatment guidelines by World TB Day 2018.
- Ensure that Xpert MTB/RIF is the initial diagnostic test for adults and children being investigated for TB by 2020.
- Find and treat all children with TB, including children exposed to TB.
- Integrate TB and HIV services at every level, including social support. All people living with HIV should be provided immediate ARV treatment through the ‘test and start’ approach.

- Provide TB services that are patient-centred, free (including treatment allowances for costs outside of treatment such as social support and treatment for adverse side effects) and decentralised, with hospitalisation reserved for only the sickest DR-TB patients.
- Use newer medicines, including bedaquiline and delamanid, to treat people with DR-TB who could benefit.
- Eliminate catastrophic costs associated with TB, and provide adequate and appropriate services to key populations, including prisoners, refugees, detainees, health care workers, people who use drugs and alcohol and people with co-morbidities including HIV.
- Ensure donor support (including from donors such as the Global Fund) for countries in the EECA region to improve TB outcomes across the cascade of care; from prevention to diagnosis, care and cure.
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ARV</td>
<td>Antiretroviral</td>
</tr>
<tr>
<td>CIS</td>
<td>Commonwealth of Independent States</td>
</tr>
<tr>
<td>DAA</td>
<td>Direct-acting antiviral medicine</td>
</tr>
<tr>
<td>DR-TB</td>
<td>Drug-resistant tuberculosis</td>
</tr>
<tr>
<td>DS-TB</td>
<td>Drug-susceptible tuberculosis</td>
</tr>
<tr>
<td>DST</td>
<td>Drug-susceptibility testing</td>
</tr>
<tr>
<td>EECA</td>
<td>Eastern Europe and Central Asia</td>
</tr>
<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>EML</td>
<td>Essential Medicines List</td>
</tr>
<tr>
<td>FDC</td>
<td>Fixed-dose combination</td>
</tr>
<tr>
<td>FLQ</td>
<td>Fluoroquinolone</td>
</tr>
<tr>
<td>GDF</td>
<td>Global Drug Facility</td>
</tr>
<tr>
<td>GLI</td>
<td>Global Laboratory Initiative</td>
</tr>
<tr>
<td>HCV</td>
<td>Hepatitis C virus</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papillomavirus</td>
</tr>
<tr>
<td>HIC</td>
<td>High-income country</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>IGRA</td>
<td>Interferon-gamma release assay</td>
</tr>
<tr>
<td>INH</td>
<td>Isoniazid</td>
</tr>
<tr>
<td>LAM</td>
<td>Lateral flow urine lipoarabinomannan</td>
</tr>
<tr>
<td>LIC</td>
<td>Low-income country</td>
</tr>
<tr>
<td>LMIC</td>
<td>Low- and middle-income country</td>
</tr>
<tr>
<td>LPA</td>
<td>Line probe assay</td>
</tr>
<tr>
<td>LTBI</td>
<td>Latent TB infection</td>
</tr>
<tr>
<td>MDR-TB</td>
<td>Multidrug-resistant tuberculosis</td>
</tr>
<tr>
<td>MIC</td>
<td>Middle-income country</td>
</tr>
<tr>
<td>MSF</td>
<td>Médecins Sans Frontières</td>
</tr>
<tr>
<td>MTB</td>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>NDRA</td>
<td>National drug regulatory authority</td>
</tr>
<tr>
<td>NFC</td>
<td>Near field communication</td>
</tr>
<tr>
<td>NGO</td>
<td>Non-governmental organisation</td>
</tr>
<tr>
<td>NTP</td>
<td>National TB programme</td>
</tr>
<tr>
<td>PHC</td>
<td>Primary health care</td>
</tr>
<tr>
<td>PQ</td>
<td>Prequalification</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research and development</td>
</tr>
<tr>
<td>RDT</td>
<td>Rapid diagnostic test</td>
</tr>
<tr>
<td>RR-TB</td>
<td>Rifampicin-resistant tuberculosis</td>
</tr>
<tr>
<td>SDRA</td>
<td>Stringent drug regulatory authority</td>
</tr>
<tr>
<td>SLID</td>
<td>Second-line injectable drug</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TST</td>
<td>Tuberculin skin test</td>
</tr>
<tr>
<td>USFDA</td>
<td>US Food and Drug Administration</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>XDR-TB</td>
<td>Extensively drug-resistant tuberculosis</td>
</tr>
</tbody>
</table>
Glossary

Active case finding: Strategy of actively screening and diagnosing individuals at high risk for TB (e.g. people living with HIV, miners, etc.). Risk groups vary, depending on national TB epidemiology.

Antiretroviral (ARV) treatment: Medicines used to treat HIV. The standard of care is a combination of medicines that target different steps in the virus lifecycle to prevent it from replicating and to prevent the development of drug resistance. ARV treatment dramatically reduces mortality and morbidity rates among HIV-positive people, and improves their quality of life.

Category II (Category 2) treatment: A TB treatment strategy that is no longer recommended.

CD4 count: Testing done in people who are HIV-positive to measure the number of CD4 T-cells in a sample of blood; this number indicates the status of a person’s immune system.

Clinical trials: Studies looking at medical strategies, treatments and devices to see if they are safe and effective in people.

Compassionate use: The terms “compassionate use,” “expanded access” or “special access” refer to programmes that are intended to provide potentially lifesaving experimental treatments to patients suffering from a disease for which no satisfactory authorised therapy exists and/or to patients who cannot enter a clinical trial. Compassionate use refers to programmes that make medicinal products available either on a named patient basis or to cohorts of patients. Compassionate use needs to be framed within a national legislation that establishes the conditions under which the medicine is made available. Refer to Annex 5 (Use of experimental drugs outside of clinical trials “compassionate use”) of the “WHO guidelines for the programmatic management of drug-resistant tuberculosis: Emergency update 2008.”

Culture: Bacterial culture is a laboratory method that multiplies bacteria to see if they are present in a sample from a patient. Culturing lets bacteria grow in a pre-determined culture medium under controlled laboratory conditions outside of the natural environment where the bacteria usually grow (e.g. for TB, the human body).

Culture-converted: A person whose last two clinical samples no longer show growing M. tuberculosis, implying that the bacteria are no longer present – a sign that TB treatment is working.

Drug resistance: When a drug used to treat an illness, including TB, is ineffective; it does not kill viruses or bacteria, or prevent them from growing. When a drug is not effective against a strain of M. tuberculosis, the bacteria are said to be drug-resistant. Bacteria can be resistant to one or more drugs.

Drug-susceptible/drug-sensitive TB: When a given drug is effective (meaning it kills bacteria or prevents it from reproducing) against a type of virus or bacteria. This means that the drug can help to clear infections (although TB and many other infections need to be treated with more than one drug). TB strains that are susceptible to all first-line drugs are called drug-susceptible or drug-sensitive.

Drug-resistant TB (DR-TB): A broad term to encompass all forms of drug-resistant TB, including multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Essential Medicines List: A list of the minimum medicines needed for a basic health care system. The EML includes the most effective, safe and cost-effective medicines for priority conditions. WHO updates its EML every two years. The WHO EML serves as a model for national EMLs.

Extensively drug-resistant TB: see XDR-TB.
Extrapulmonary TB: A form of TB in which *M. tuberculosis* infects parts of the body other than the lungs, most commonly the lymph nodes, bones, central nervous system, and cardiovascular and gastrointestinal systems.

First-line drugs: The first drugs used to treat a disease. In the case of TB, the following four drugs are usually chosen: isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z). These drugs are highly effective in treating drug-susceptible TB.

Fixed-dose combination (FDC): A combination of more than one medicine in a single tablet.

Global Fund: The Global Fund to Fight AIDS, Tuberculosis and Malaria is an international financing institution that invests the world’s money to save lives. It invests in 150 countries to support the large-scale prevention of these three diseases through treatment and care programmes. It channels 82% of the international financing for TB.

Group 5 TB medicines: Anti-TB medicines with unclear efficacy or an unclear role in MDR-TB treatment as per WHO MDR-TB guidelines.

High TB burden countries: As defined by WHO, the 30 high TB burden countries are the 20 countries with the highest estimated numbers of incident TB cases plus the top 10 countries with the highest estimated TB incidence rates that are not in the top 20, by absolute number (threshold: >10,000 estimated incident TB cases per year).

High MDR-TB burden countries: As defined by WHO, the 30 high MDR-TB burden countries are the 20 countries with the highest estimated numbers of incident MDR-TB cases plus the top 10 countries with the highest estimated MDR-TB incidence rates that are not in the top 20, by absolute number (threshold: >1,000 estimated incident MDR-TB cases per year).

Microscopy: Currently the most commonly used TB diagnostic test, using two or three samples per person. The sample is stained and later read under the microscope. If TB bacilli are present, they are visible in the form of small red rods.

Multidrug-resistant TB (MDR-TB): MDR-TB is resistant to at least two TB medicines, including isoniazid and rifampicin, the two most powerful first-line antibiotics used for TB treatment.

Mycobacteria: Types of bacteria of the genus *Mycobacterium* that cause disease, including TB and leprosy.

*M. tuberculosis*: *Mycobacterium tuberculosis* is a pathogenic bacterial species of the genus *Mycobacterium* and the causative agent of most cases of TB; it was first discovered in 1882 by Robert Koch.

Preventive therapy: Preventive treatment, also known as chemoprophylaxis, to reduce the risk of (i) a first episode of TB occurring in people exposed to infection or with latent infection and (ii) a recurrent episode of TB.

Pulmonary TB: Form of TB where *M. tuberculosis* bacteria infect the lungs.

Repurposed drugs: Drugs that were not developed for use against TB, but are effective and used to treat some forms of DR-TB.

Second-line drugs: Second-line drugs are used in people who have forms of TB that are resistant to first-line drugs. Second-line TB drugs are less effective than first-line drugs and have more side effects.

Second-line DST: Testing for resistance to second-line injectable TB drugs and fluoroquinolones.

Smear-positive pulmonary TB: An individual whose sputum is positive for acid-fast bacilli (AFB) by smear microscopy.

Smear-negative pulmonary TB: An individual whose sputum is negative for AFB by smear microscopy, but is diagnosed as TB based on other methods such as culture.

Stringent drug regulatory authority (SDRA): An SDRA is defined as an International Committee on Harmonization (ICH) member country, an ICH observer or any country whose regulatory authority is associated with an ICH member through a legally binding mutual recognition agreement, or is approved or subject to a positive opinion under the Canada S.C. 2004, c. 23 (Bill C-9) procedure, or Art. 58 of European Union Regulation (EC) No. 726/2004 or United States FDA tentative approval.

Task-shifting: The rational redistribution of tasks among teams of health care workers. Specific tasks are moved, where appropriate, from highly qualified health care workers to health care workers with less training and fewer qualifications in order to increase efficiency.

Universal DST: Providing drug-susceptibility testing (DST) for at least rifampicin in all patients with bacteriologically confirmed TB, and providing additional DST for at least fluoroquinolones and second-line injectable agents for all people who have rifampicin-resistant TB.

WHO Prequalification (PQ) Programme: The Prequalification Programme, set up in 2001, is a service provided by WHO to facilitate access to medicines that meet the unified standards of quality, safety and efficacy for HIV/AIDS, malaria and TB. Please consult http://apps.who.int/prequal/.

WHO ‘test and start’ recommendation: A recommendation that all HIV-positive people receive ARV treatment, regardless of CD4 cell count.

XDR-TB (extensively drug-resistant TB): Patients are described as suffering from XDR-TB when they have MDR-TB and also show resistance to second-line drugs, including at least one from the class known as fluoroquinolones and one of the injectable drugs.
ANNEXES
## I. DIAGNOSIS

### DIAGNOSIS: ACCORDING TO NATIONAL POLICY

<table>
<thead>
<tr>
<th>Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
<th>TAJIKISTAN</th>
<th>UKRAINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Xpert MTB/RIF is the initial TB diagnostic test for high-risk groups*</th>
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<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
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<th>RUSSIAN FED.</th>
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<td>Yes</td>
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</table>

<table>
<thead>
<tr>
<th>TB-LAM is used to diagnose TB in people living with HIV/AIDS with CD4 ≤100 cells/µL or seriously ill</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
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<table>
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<th>Rifampicin resistance testing is done for all bacteriologically confirmed TB cases</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
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<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
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<tr>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>First-line DST (rifampicin and isoniazid) is done for all RR-TB cases or for people at risk of DR-TB</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
<th>TAJIKISTAN</th>
<th>UKRAINE</th>
</tr>
</thead>
<tbody>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second-line DST (fluoroquinolones and second-line injectable agents) is done for at least all RR-TB cases</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
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<th>UKRAINE</th>
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<tbody>
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<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>LPA is the initial test for second-line DST**</th>
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<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
<th>TAJIKISTAN</th>
<th>UKRAINE</th>
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<tbody>
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<td>Yes</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Active case finding for TB is carried out among people living with HIV/AIDS</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
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<th>UKRAINE</th>
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<tr>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Active case finding for TB is carried out for household contacts under the age of five</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
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<tr>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Active case finding for TB is carried out for all household contacts</th>
<th>ARMENIA</th>
<th>BELARUS</th>
<th>GEORGIA</th>
<th>KAZAKHSTAN</th>
<th>KYRGYZSTAN</th>
<th>RUSSIAN FED.</th>
<th>TAJIKISTAN</th>
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<tbody>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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### LEGEND

<table>
<thead>
<tr>
<th>Is this policy in place at the national level?</th>
<th>If Yes, is the policy being implemented?</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="icon.png" alt="Yes" /></td>
<td><img src="icon.png" alt="Yes" /></td>
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<tr>
<td><img src="icon.png" alt="No" /></td>
<td><img src="icon.png" alt="Yes, but not widely" /></td>
</tr>
<tr>
<td><img src="icon.png" alt="Unknown" /></td>
<td><img src="icon.png" alt="Unknown" /></td>
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</tbody>
</table>

(*) High-risk groups include adults and children at risk for drug-resistant TB and HIV-associated TB. (**) Drug-sensitivity testing to fluoroquinolones and second-line injectable agents for patients with confirmed RR- or MDR-TB. (a) The initial diagnostic test is microscopy, but regardless of microscopy result, every person to be evaluated for TB is tested with Xpert. (b) Part of an initial diagnostic package of tests. (c) At facilities that offer DR-TB regimens with BDQ or DLM. (d) Xpert is part of a package of diagnostic tests; other diagnostic tests can be used, including other rapid molecular methods.
### II. MODELS OF CARE

#### MODELS OF CARE: ACCORDING TO NATIONAL POLICY

<table>
<thead>
<tr>
<th>DS-TB treatment is started at the primary health care level*</th>
<th>Armenia</th>
<th>Belarus</th>
<th>Georgia</th>
<th>Kazakhstan</th>
<th>Kyrgyzstan</th>
<th>Russia</th>
<th>Tajikistan</th>
<th>Ukraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR-TB treatment is started at the district level*</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
</tr>
<tr>
<td>Nurses and health workers other than doctors can start adults on DS-TB treatment</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
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</tr>
<tr>
<td>Hospitalisation is NOT required for DS-TB treatment**</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
</tr>
<tr>
<td>Hospitalisation is NOT required for DR-TB treatment**</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
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<tr>
<td>TB treatment is started in facilities providing HIV care</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
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<tr>
<td>HIV treatment is started in facilities providing TB care</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
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<tr>
<td>The same health workers provide TB and HIV treatment at primary health care level</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
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<tr>
<td>ARV treatment is offered to all people living with HIV/AIDS (<em>test and start</em>)</td>
<td>◆</td>
<td>◆</td>
<td>◆</td>
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If NO, the CD4 count (cells/μL) threshold for ART initiation is...  

<table>
<thead>
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<th>≤ 500</th>
<th>≤ 350</th>
<th>≤ 350</th>
<th>≤ 500</th>
<th>≤ 500</th>
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<th>≤ 500</th>
</tr>
</thead>
</table>

#### LEGEND

- **Yes**
- **No**
- **Unknown**
- **Not applicable**

(*) Including smear-positive individuals. In some countries exceptions are made for people who are smear-negative and on a case by case basis. (◆) The implementation of the policy was not assessed for the hospitalisation questions. (a) Except for people who are smear-negative and on a case by case basis. (b) Patient receives a prescription at TB facilities. (c) DR-TB treatment can be started and dispensed from the district level, but only after decision and prescription from the regional TB committee.
### III. TB & DR-TB TREATMENT

#### TB & DR-TB TREATMENT: ACCORDING TO NATIONAL POLICY

<table>
<thead>
<tr>
<th></th>
<th>Armenia</th>
<th>Belarus</th>
<th>Georgia</th>
<th>Kazakhstan</th>
<th>Kyrgyzstan</th>
<th>Russian Fed.</th>
<th>Tajikistan</th>
<th>Ukraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guidelines for children reflect the latest WHO guidance</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<td>✔️</td>
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<tr>
<td>Increased doses of first-line medicines for children are in line with latest WHO guidance**</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>New paediatric TB FDCs are the standard of care</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<tr>
<td>DR-TB treatment reflects the latest WHO guidelines</td>
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<td>✔️</td>
<td>✔️</td>
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<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Reflect WHO guidance on bedaquiline use for adults</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<tr>
<td>Reflect WHO guidance on delamanid use for adults and children</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<tr>
<td>Includes the WHO-recommended, nine-month (shorter) MDR-TB treatment regimen</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<tr>
<td>Details of nine-month (shorter) treatment regimen</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<td>✔️</td>
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<tr>
<td>Second-line DST by LPA (e.g. Hain) should be performed before starting nine-month treatment course</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<td>✔️</td>
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<td>✔️</td>
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</tbody>
</table>

#### LEGEND

- **Yes**: Is this policy in place at the national level?
- **No**: Is this policy being implemented?
- **Unknown**: Data not available
- **Not applicable**: Not applicable

*The data could not be verified. (***) Isoniazid (H) 10 mg/kg (range 7–15 mg/kg); maximum dose 300 mg/day; rifampicin (R) 15 mg/kg (range 10–20 mg/kg); maximum dose 600 mg/day; pyrazinamide (Z) 35 mg/kg (range 30–40 mg/kg), ethambutol (E) 20 mg/kg (range 15–25 mg/kg). (a) Implementation in pilot sites. (b) Guidelines need to be updated to reflect the latest groupings, including the specific mention of new and repurposed medicines.
## IV. REGULATORY ENVIRONMENT FOR TB MEDICINES

### REGULATORY ENVIRONMENT FOR TB MEDICINES: ACCORDING TO NATIONAL POLICY

<table>
<thead>
<tr>
<th>Regulator</th>
<th>DR-TB medicines can receive accelerated registration</th>
<th>Group A medicines are registered*</th>
<th>Group B medicines are registered*</th>
<th>Group C medicines are registered*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
<td>✅ Yes, except for Gfx</td>
<td>✅</td>
<td>✅</td>
<td>✅ Yes, except for Eto and Pto, Cfx</td>
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<td>Georgia</td>
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</tr>
<tr>
<td>Ukraine</td>
<td>✅ Yes, except for Gfx</td>
<td>✅</td>
<td>✅</td>
<td>✅ Yes, except for Cfx</td>
</tr>
</tbody>
</table>

*Group A medicines are registered*  
*Group B medicines are registered*  
*Group C medicines are registered*

<table>
<thead>
<tr>
<th>Regulator</th>
<th>Group D1 medicines are registered*</th>
<th>Group D2 medicines are registered*</th>
<th>Group D3 medicines are registered*</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>Ukraine</td>
<td>☐</td>
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</tbody>
</table>

*Group D1 medicines are registered*  
*Group D2 medicines are registered*  
*Group D3 medicines are registered*

### Unregistered TB medicines are available through compassionate use/other legal mechanisms**

<table>
<thead>
<tr>
<th>Regulator</th>
<th>Unregistered TB medicines are available through compassionate use/other legal mechanisms**</th>
<th>If YES, which of these mechanisms is in place?</th>
<th>National Essential Medicines List (nEML) reflects WHO recommendations***</th>
<th>Group A medicines are on the nEML***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
<td>✅</td>
<td>☐</td>
<td>☐</td>
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<td>Belarus</td>
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<tr>
<td>Russian F.</td>
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<tr>
<td>Ukraine</td>
<td>☐</td>
<td>☐</td>
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</tr>
</tbody>
</table>

*Unregistered TB medicines are available through compassionate use/other legal mechanisms**  
*If YES, which of these mechanisms is in place?*  
*National Essential Medicines List (nEML) reflects WHO recommendations***  
*Group A medicines are on the nEML***

### LEGEND

Is this policy in place at the national level?  
✅ Yes  ☐ No  ☐ Unknown  ☐ Not applicable
### REGULATORY ENVIRONMENT FOR TB MEDICINES: ACCORDING TO NATIONAL POLICY

<table>
<thead>
<tr>
<th>Country</th>
<th>Group B medicines are on the nEML***</th>
<th>Group C medicines are on the nEML***</th>
<th>Group D1 medicines are on the nEML***</th>
<th>Group D2 medicines are on the nEML***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
<td>Yes, except for Lzd, Cfz</td>
<td>Yes, except for Lzd, Cfz</td>
<td>Yes, except for Lzd, Cfz</td>
<td>Yes, except for Lzd, Cfz</td>
</tr>
<tr>
<td>Belarus</td>
<td>Yes, except for Am</td>
<td>Yes, except for Lzd, Cfz</td>
<td>Yes, except for Lzd, Cfz</td>
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<tr>
<td>Georgia</td>
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<td>Yes, except for Eto, Pto, Lzd, Cfz</td>
<td>Yes, except for Lzd, Cfz</td>
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<tr>
<td>Kazakhstan</td>
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<td>Yes, except for Lzd, Cfz</td>
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<td>Kyrgyzstan</td>
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<td>Yes, except for Lzd, Cfz</td>
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<td>Russian FED.</td>
<td>Yes, except for Am, Km, S</td>
<td>Yes, except for Lzd, Cfz</td>
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<td>Yes, except for Dlm</td>
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<tr>
<td>Ukraine</td>
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<td></td>
<td></td>
<td>Yes, except for Bdq</td>
</tr>
</tbody>
</table>

### LEGEND

- **(*)** Group A: levofloxacin (Lfx), moxifloxacin (Mfx), gatifloxacin (Gfx) / Group B: amikacin (Am), capreomycin (Cm), kanamycin (Km), (streptomycin, S) / Group C: ethionamide (Eto) (or prothionamide, Pto), cycloserine (Cs) (or terizidone, Trd), linezolid (Lzd), clofazimine (Cfz) / Group D1: pyrazinamide (Z), ethambutol (E), high-dose isoniazid (Hh) / Group D2: bedaquiline (Bdq), delamanid (Dlm) / Group D3: p-aminosalicylic acid (PAS), imipenem-cilastatin (Ipm/Cln), meropenem (Mpm), amoxicillin-clavulanic acid (Amx-Clv), (thioacetazone, T). (Notes: streptomycin is part of the category II retreatment regimen, which should no longer be prescribed according to WHO’s latest recommendations (May 2017); registration of isoniazid in regulatory databases was taken into account since it covers regulatory approval of high-dose isoniazid).

- **(**)** Compassionate use, expanded access programmes, import waivers or other legal mechanisms.

- **(*****)** Group A: levofloxacin (Lfx), moxifloxacin (Mfx), gatifloxacin (Gfx) / Group B: amikacin (Am), capreomycin (Cm), kanamycin (Km), (streptomycin, S) / Group C: ethionamide (Eto) (or prothionamide, Pto), cycloserine (Cs) (or terizidone, Trd), linezolid (Lzd), clofazimine (Cfz) / Group D1: pyrazinamide (Z), ethambutol (E), high-dose isoniazid (Hh) / Group D2: bedaquiline (Bdq), delamanid (Dlm) / Group D3: p-aminosalicylic acid (PAS), imipenem-cilastatin (Ipm/Cln), meropenem (Mpm), amoxicillin-clavulanic acid (Amx-Clv), (thioacetazone, T). (Notes: streptomycin is part of the category II retreatment regimen, which should no longer be prescribed according to WHO’s latest recommendations (May 2017); only medicines listed in anti-TB sections of nEMLs are listed as YES.

- **(a)** Only if already approved by an SDRA.

- **(i)** Answers could not be confirmed. **(ii)** The national EML is currently being updated. **(iii)** No valid Georgian National EML exists. It is in the process of being finalised and approved. Meanwhile, WHO EML is used as a reference. **(iv)** The new national EML is currently being approved. **(v)** Updated in October 2017.
## V. PREVENTION

### PREVENTION: ACCORDING TO NATIONAL POLICY

<table>
<thead>
<tr>
<th>Country</th>
<th>TB preventive therapy is provided for adult contacts, child contacts and people living with HIV/AIDS</th>
<th>People living with HIV/AIDS</th>
<th>Child contacts</th>
<th>Adult contacts of people living with HIV/AIDS</th>
<th>TB preventive therapy is provided for at-risk populations: prisoners, miners, people with silicosis/diabetes, organ/transfusion recipients</th>
<th>Tuberculin skin or IGRA test must be carried out prior to starting preventive therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
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<td><img src="#" alt="Yes" /> <img src="#" alt="No" /> <img src="#" alt="Yes" /> <img src="#" alt="No" /> <img src="#" alt="Yes" /> <img src="#" alt="No" /> <img src="#" alt="Yes" /> <img src="#" alt="No" /> <img src="#" alt="Yes" /> <img src="#" alt="No" /></td>
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**LEGEND**

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<th>If Yes, is the policy being implemented?</th>
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</table>

(a) For children only. (b) When there is a stockout of TST, IPT can be prescribed without carrying out the test. (c) TST done for people living with HIV/AIDS, not known for children.

*INH* = isoniazid, *RPT* = rifapentine, *RIF* = rifampicin
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ТАДЖИКИстан

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**Map design**: Missing Element, Czech Republic

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