World Health Organization
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Compendium of good practices in the implementation of the Tuberculosis Action Plan for the WHO European Region 2016–2020

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ABSTRACT

Tuberculosis (TB), especially drug-resistant TB, is a public health challenge in both civilian and penitentiary sectors worldwide. The global End TB Strategy envisages specific measures to be taken by WHO Member States globally to tackle the problem and address the challenge. The WHO Regional Office for Europe has developed the Tuberculosis Action Plan for the WHO European Region 2016–2020 to achieve the milestones and objectives set by the global End TB Strategy. This first Compendium of good practices in the implementation of the Tuberculosis Action Plan for the WHO European Region is an essential publication for implementation of the Strategy, providing examples of treatment and care following the recommendations proposed for WHO and its partners.

Keywords
TUBERCULOSIS – prevention and control
TUBERCULOSIS, MULTIDRUG-RESISTANT – prevention and control
EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS – prevention and control
COMMUNICABLE DISEASE CONTROL
DELIVERY OF HEALTH CARE
PRACTICE GUIDELINES AS TOPIC

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ABBREVIATIONS

AFB	acid-fast bacilli
ART	antiretroviral therapy
Bdq	bedaquiline
Dlm	delamanid
DOT	directly observed treatment
DR-TB	drug-resistant tuberculosis
DS-TB	drug-susceptible tuberculosis
DST	drug-susceptibility testing
FLD	first-line antituberculosis drug
LJ	Löwenstein–Jensen
LTBI	latent tuberculosis infection
M&E	monitoring and evaluation
MDR-TB	multidrug-resistant tuberculosis
MGIT	mycobacteria growth indicator tube
MSF	Médecins Sans Frontières
M/XDR-TB	multidrug- and extensively drug-resistant tuberculosis
NGO	nongovernmental organization
NRL	National Reference Laboratory
NTP	national tuberculosis programme
PCR	polymerase chain reaction
RR-TB	rifampicin-resistant tuberculosis
SLD	second-line antituberculosis drug
TB	tuberculosis
TST	tuberculin skin test
USAID	United States Agency for International Development
VOT	video-observed treatment
XDR-TB	extensively drug-resistant tuberculosis

FOREWORD

The United Nations 2030 Agenda for Sustainable Development calls for leaving no one behind. Tuberculosis (TB), and especially multidrug-resistant TB (MDR-TB), is a major global public health concern, which continually ranks among the top 10 causes of death worldwide. Although the WHO European Region has seen one of the sharpest declines in TB globally, one fifth of all MDR-TB patients in the world are from the Region, while TB/HIV coinfection has risen exponentially over the last decade.

To accelerate efforts to end TB, the Tuberculosis Action Plan for the WHO European Region 2016–2020, endorsed by the 65th session of the WHO Regional Committee for Europe, sets regional goals, targets and actionable areas for the response to TB and MDR-TB. It defines strategic directions and suggested activities to be carried out by all relevant stakeholders to ensure no one is left behind using a whole-of-society and whole-of-government approach and following the principles of universal health coverage.

To document and disseminate successful interventions aligned with the Action Plan, I am pleased to present this ***Compendium of good practices in the implementation of the Tuberculosis Action Plan for the WHO European Region 2016–2020****. These practices are examples of effective and efficient interventions in line with the three pillars of the End TB Strategy: (i) integrated, people-centred care and prevention; (ii) bold policies and supportive systems; and (iii) intensified research and innovation. I encourage Member States and partners to sustain, replicate and scale up these and other similar good practices to ensure implementation of the End TB Strategy as an integral part of Health 2020 and to eliminate TB in the Region.*

Dr Zsuzsanna Jakab
WHO Regional Director for Europe

PREFACE

Two years following the launch of the new Tuberculosis Action Plan for the WHO European Region 2016–2020 and the WHO End TB Strategy, it is important to take stock of good practices in the response to tuberculosis (TB) in the Region. Therefore, we are pleased to issue this ***Compendium of good practices in the implementation of the Tuberculosis Action Plan for the WHO European Region 2016–2020***. The document had been developed through the joint work of the WHO Regional Office for Europe and in collaboration with all main stakeholders and this collection of good practices has been designed to share them and promote the continued implementation of the End TB Strategy in our Region and beyond.

As a result of impressive political commitment by Member States, support by WHO and partners, and essential work of civil society organizations, TB-related mortality has continued its sharp decline with average annual decline of 10.6 %, starting from 2012, in comparison with annual decline of 8.6% annual decline for the period from 2007. We expect that 1.4 million TB patients to be cured and 3.1 million lives to be saved with full implementation of the *Regional TB Action Plan*. In addition, health systems have been strengthened in the Region to effectively introduce people-centred and comprehensive TB care following the principles of a public health approach and universal health coverage. Despite positive declines, TB, and especially M/XDR-TB, seriously burdens patients and their families, as treatment lasts up to two years and carries serious side-effects; thereby affecting capacities for improved health and livelihoods. Satisfactory treatment outcomes for all forms of TB and for all those affected, without discrimination and stigma, is still an urgent need in the Region.

This compendium of good practices was created to share knowledge gained in the management of TB. Scaling up these and related good practices is crucial to end the TB epidemic. Through intersectoral collaboration, stronger health systems, the assurance of universal access to care without financial hardship and a focus on leaving no one behind, the goal of ending TB can be achieved.

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EXECUTIVE SUMMARY

In 2015, in consultation with Member States and both national and international stakeholders, the WHO Regional Office for Europe prepared the Tuberculosis Action Plan for the WHO European Region 2016–2020.

We are currently midway through implementing the TB Action Plan, which aims to operationalize the global End TB Strategy in the regional context. This plan and its accompanying resolution EUR/RC65/17 (endorsed by all 53 Member States at the 65th session of the WHO Regional Committee for Europe in 2015) sets a regional goal and targets for the care and control of tuberculosis (TB) and drug-resistant TB (DR-TB) from 2016 to 2020.

In order to facilitate the transfer of knowledge and experience among countries and improve the health system approach in the Region, the Regional Office has been collecting and disseminating good examples of the prevention, control and care of TB and multidrug-resistant TB (MDR-TB) and extensively drug-resistant (XDR-TB; together known as M/XDR-TB) in the Region. With examples from nearly half the Region, a Compendium of best practices in prevention, control and care for drug-resistant tuberculosis was presented at the 63rd session of the WHO Regional Committee for Europe in 2013.

Since the ultimate success of the TB Action Plan and the global End TB Strategy depends on the commitment of all stakeholders to address the challenges in ending the TB epidemic, the Regional Office on 1 December 2017 launched a special call for Member States, partners and communities to share their good practices in implementation of the TB Action Plan. Examples of good practice were collected over the six-month period from December 2018 to June 2018, and were compiled and evaluated against predefined selection criteria by the panel of experts and multistakeholder representatives.

With 59 examples from nearly half of the countries and almost all of the high-priority countries for MDR-TB in the WHO European Region, this Compendium of good practices highlights the pioneers in adapting and accomplishing the objectives of the TB Action Plan at national level according to country specificities, and supports the work ahead by sharing experience and lessons learned. One of the Compendium's goals is to recognize the efforts of countries, stakeholders and partners in combating TB, as well as encouraging further input. It is not meant to be an exhaustive list of instructions, but is rather supposed to present ideas for consideration on what options might be available in a given context. The examples presented are the sole work of the authors listed.

The WHO Regional Office for Europe encourages the continued submission of good practices to its TB programme[1] for possible inclusion in an open access database of good practices and future compendiums.

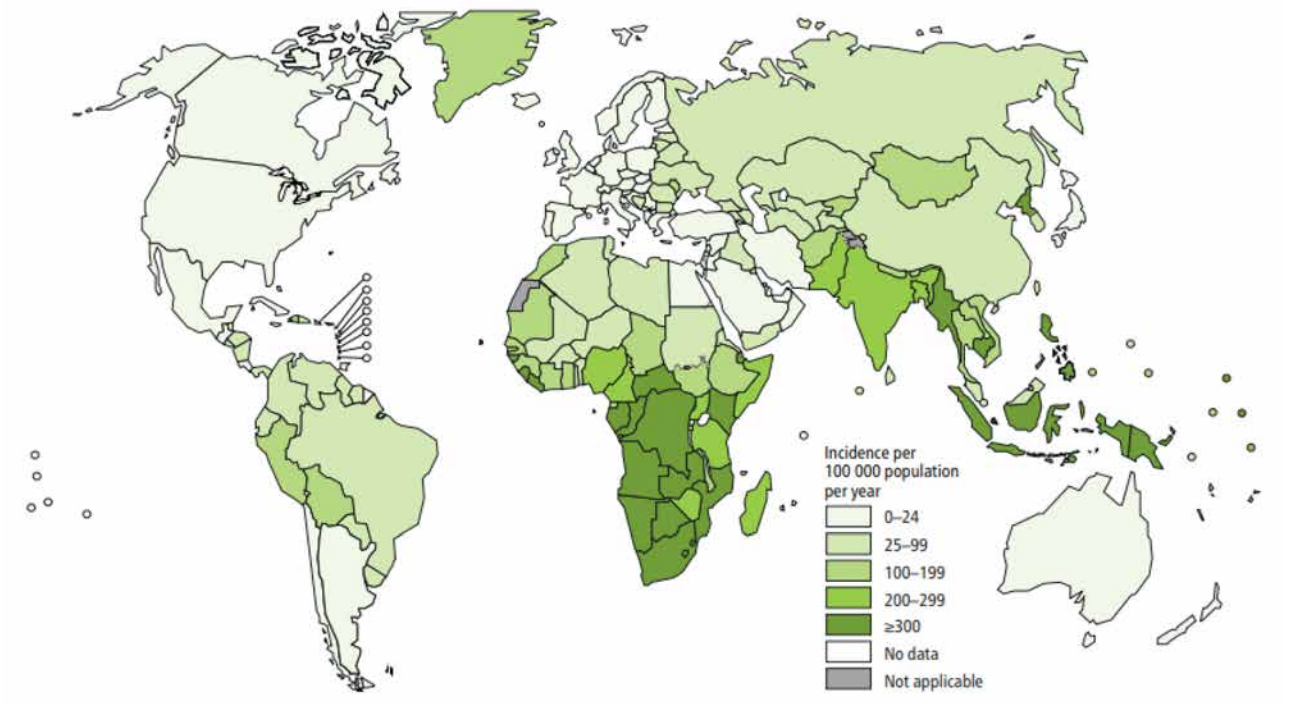
[1] Email address: eurotb@who.int.

INTRODUCTION AND BACKGROUND

The global and regional burden of TB

TB remains a leading cause of death and life-threatening illness which disproportionately affects low and middle-income countries. It is also the main cause of deaths related to antimicrobial resistance and the leading killer of the people living with HIV. In 2016, there were an estimated 10.4 million new cases of TB worldwide and 1.7 million people died from the disease (Fig. 1) *(1)*.

Fig. 1. Estimated TB incidence rates per 100 000 population, 2016



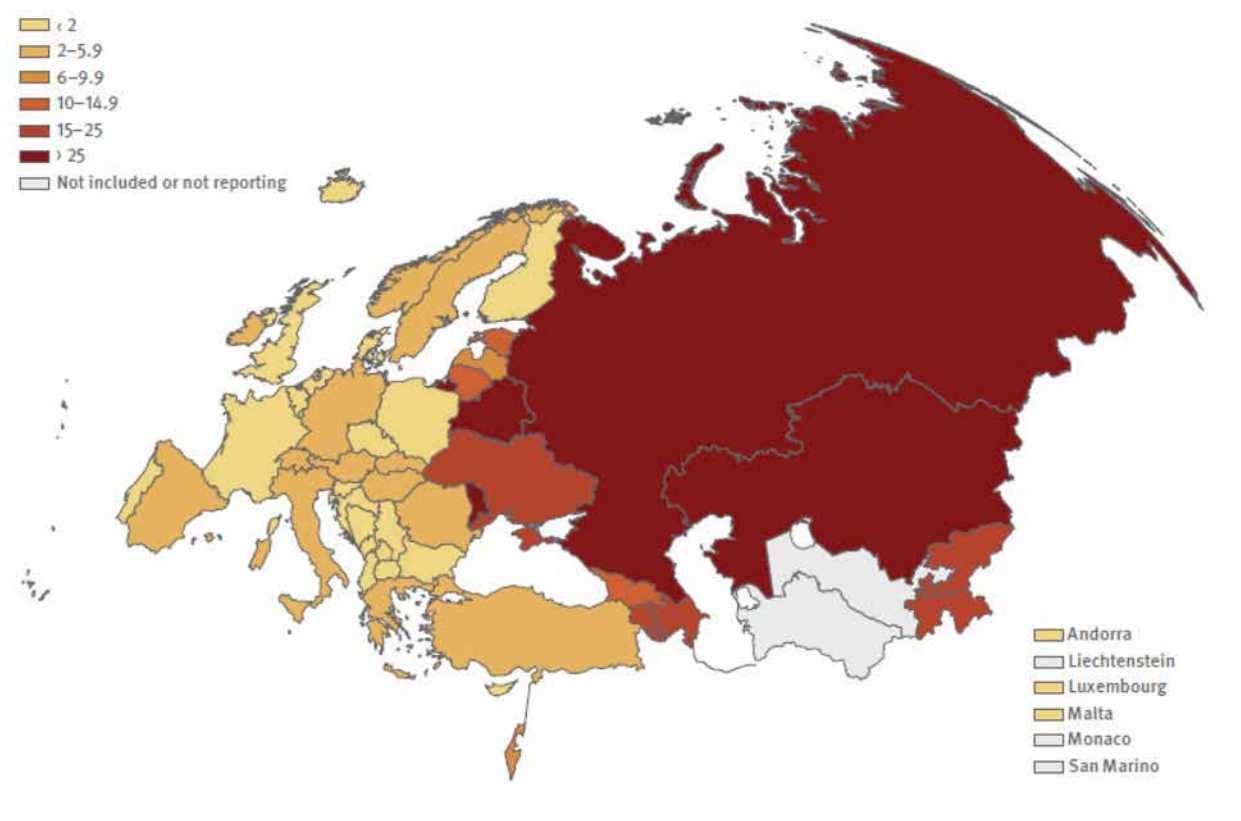
In 2016, the TB incidence in countries of the European Region was an estimated 290 000 cases, equivalent to an average incidence of 32 cases per 100 000 population. Since 2000, the TB incidence in the Region has been consistently decreasing. The average annual decline in TB incidence rate was 4.3% during the 2007–2016 period *(2)*. However, despite being the fastest decline of all WHO regions, it is not fast enough to achieve the target set by the Sustainable Development Goals of ending the TB epidemic by 2030 *(3)* and the End TB Strategy *(4)*.

At the regional level, the TB mortality rate fell by 57% between 2007 and 2016, dropping from 6.5 to 2.8 deaths per 100 000 population, with an average annual decline of 8.6%. Between 2012 and 2015 the annual decline in TB mortality accelerated to 10.6%, notably higher than the global average (3.2%).

Although the WHO European Region carries only 3% of the global TB burden, it has one of the highest rates of MDR-TB. Despite a steady decline in new TB cases, the disease remains a major public health threat in the Region (Fig. 2). The MDR-TB rate rose by an average of 5% per year during the 2012–2016 period, rising from 4.6 to 5.7 cases per 100 000 population. The MDR-TB case detection rate increased significantly with improved diagnosis, from 33% in 2011 to 73% in 2016. At well above the global average of 44%, it is now the highest in the world.

The distribution of age- and sex-specific TB rates varies widely across countries. Twice as many male TB cases as female cases are reported. This gender difference in TB case notification reflects the prevalence of men in TB risk groups, notably the homeless, prisoners, seasonal migrant workers, people living with HIV and people who inject drugs. The European Region is

Fig. 2. Percentage of notified TB cases with multidrug resistance among new pulmonary laboratory-confirmed TB cases, WHO European Region, 2016



the only WHO region with an increasing rate of new HIV infections; the incidence of TB/HIV coinfection continues to rise by an annual average of 13%. People with TB/HIV coinfection in the Region are seven times more likely to fail treatment and three times more likely to die compared with HIV-negative TB patients. In 2016, 12% of incident TB cases were estimated to be people coinfected with HIV.

Despite almost universal treatment coverage for rifampicin-resistant TB (RR-TB) and MDR-TB patients (96%), the treatment success rate for DR-TB in the Region is still below the regional target of 75% (but improved from 48% in 2016 to 55% in 2018). Several countries with a high MDR-TB burden (such as Kazakhstan and Latvia) have managed to achieve remarkable success in curing more than 70% of MDR-TB patients.

The regional average TB notification rate in prisons is 862 cases per 100 000 population. In 2016, 12 298 (6%) of the new and relapsed TB cases in the Region were reported from prisons, with 11 863 (97%) of these in the high-priority countries.

Global End TB Strategy

Following the Global Plan to End TB 2006–2015 *(5)*, WHO developed an ambitious post-2015 global End TB Strategy *(4)*, which was endorsed by the World Health Assembly in 2014 through resolution WHA67.1 *(6)*. The Strategy comprises three main pillars and several milestones for 2020 and 2025, as well as targets for 2030 and 2035, with the goal of ending the TB epidemic. The Strategy's ultimate success depends on the commitment of Member States and partners. With this in mind, the resolution urges all Member States to adapt their use of the Strategy to their national priorities and specificities, and invites regional partners to support implementation of the Strategy. The WHO Regional Office for Europe has responded to this call by developing an ambitious Action Plan and Roadmap to implement the tuberculosis action plan for the WHO European Region 2016–2020: towards ending tuberculosis and multidrug-resistant tuberculosis (Table 1) *(7,8)*.

Table 1. Outline of the Tuberculosis Action Plan for the WHO European Region 2016–2020

Vision	An end to the TB epidemic, with zero affected families facing catastrophic costs due to the disease
Goal	To end the spread of DS-TB and DR-TB by achieving universal access to prevention, diagnosis and treatment in all Member States in the WHO European Region, thereby contributing to the global End TB Strategy goal of ending the TB epidemic
Targets (to be achieved by 2020)	35% reduction in deaths due to TB
	25% reduction in TB incidence
	75% treatment success rate among MDR-TB patients
Strategic directions	
1. Work towards elimination of TB by strengthening the response of health systems to the prevention, control and care of TB and DR-TB	
2. Facilitate intersectoral collaboration to address the social determinants of and underlying risk factors for TB	
3. Work in national, regional and international multistakeholder partnerships, including civil society and communities	
4. Foster collaboration for the development and use of new diagnostic tools, medicines, vaccines and other treatment and preventive approaches	
5. Promote the rational use of existing resources, identify gaps and mobilize additional resources to ensure sustainability	
6. Ensure that the promotion of sound ethics, human rights and equity is embedded in all areas of the strategic interventions against TB	
Areas of intervention	
1. Integrated, people-centred care and prevention	
a. Systematic screening of contacts and high-risk groups	
b. Early diagnosis of all forms of TB and universal access to drug-susceptibility testing, including with rapid tests	
c. Equitable access to high-quality treatment and a continuum of care for all people with TB, including DR-TB, and support to facilitate adherence to treatment	
d. Collaborative TB/HIV activities and management of comorbid conditions	
e. Management of latent TB infection, preventive treatment of people at high risk and vaccination against TB	
2. Bold policies and supportive systems	
a. Political commitment with adequate resources, including a universal health coverage policy	
b. Strengthening of all functions of health systems, including well-aligned financing mechanisms for TB and human resources	
c. Regulatory frameworks for case-based surveillance, and strengthening of vital registration and of the quality and rational use of medicines and pharmacovigilance	
d. Airborne infection control, including regulated administrative, engineering and personal protection measures in all relevant health-care facilities and congregate settings	
e. Community systems and civil society engagement	
f. Social protection, poverty alleviation and action on other determinants of TB, such as migration and imprisonment	
3. Intensified research and innovation	
a. Discovery, development and rapid uptake of new tools, interventions and strategies	
b. Research to optimize implementation and impact and promote innovation	

DS-TB: drug-susceptible TB.

Compendium of good practices in the implementation of the Tuberculosis Action Plan for the WHO European Region 2016–2020

The Compendium provides examples from Member States of the WHO European Region with high and low incidences of TB and MDR-TB and in which TB is being addressed. The case studies are categorized according to the sections of the global End TB Strategy *(4)*.

The examples are the joint work of the authors and WHO, as listed for each good practice. The Compendium is not intended to be a comprehensive collection of all the excellent, indispensable work being carried out by national TB programmes (NTPs) for the prevention and care of TB and M/XDR-TB in the Region. Rather, it represents good practices compiled during the period up to April 2017. None of the submitted good practices was rejected and a WHO selection committee has worked with countries to ensure the quality and content of the shared practices (Table 2). As time constraints or other logistic difficulties may have prevented other programmes, partners and organizations from making submissions, the WHO Regional Office for Europe encourages the continued submission of good practices to the its Joint Tuberculosis, HIV and Viral Hepatitis programme.[2]

Good practices could include: national health strategies that have clearly outlined targets or visions for managing TB and M/XDR-TB; initiatives and activities to address any of the determinants of TB and M/XDR-TB; the introduction of services in non-traditional locations to ensure better access to care; financial incentives to promote certain models of service delivery; intersectoral alignment of funds to promote people-centred service delivery; training of health professionals in the civilian and penitentiary sectors in the prevention or management of TB and M/XDR-TB; re-/profiling of health workers' skills to better serve patient needs; financing schemes that provide coverage for medications; investments in public research and the development of medicines for care and prevention; and mobilizing mhealth (the practice of medicine and public health supported by mobile devices) and/or e-Health (the practice of medicine and public health provided via electronic platforms) or innovative technologies to improve the prevention and care of TB and M/XDR-TB.

National health authorities, including NTPs, ministries of health, ministries of internal affairs, ministries of justice or any other relevant responsible governmental, partner or nongovernmental (NGO) organization working to combat TB and M/XDR-TB in the Region were invited to submit examples of good practices by an open call and submission form available online in English and Russian. The call for good practices was launched on 1 December 2017 and further disseminated in the WHO newsletter, on the Regional Office website and in social media. The call was open to all stakeholders, individuals, stakeholders and partners. Examples were collected over the six-month period from December 2017 to June 2018. At the end of the collection period, all reported practices were compiled and evaluated against the selection criteria listed in Table 2.

[2] Email address: eutb@who.int.

Table 2. Selection criteria for good practices on implementation of the Tuberculosis Action Plan for the WHO European Region 2016–2020

Criterion	Description
Relevant[a]	Must address one of the targets or areas of intervention of the Tuberculosis Action Plan for the WHO European Region 2016–2020
Sustainable[a]	Can be implemented and sustained over a long period of time (including policy decisions) without a massive injection of additional resources
Efficient[a]	Must produce results with a reasonable level of resources over a reasonable period of time
Ethically appropriate[a]	Must respect the current ethical rules for treating human populations
Equity/gender	Addresses the needs of vulnerable populations and/or gender in an equitable manner
Effective	Must work and has achieved results that have been measured
Possibility for scale-up	Can be scaled up to a larger population
Partnership	Involves satisfactory collaboration between several stakeholders
Community involvement	Involves participation of the affected communities
Political commitment	Has support from the relevant national or local authorities

[a] Required.

PART 1. INTEGRATED, PEOPLE-CENTRED CARE AND PREVENTION

1A. Systematic screening for TB

Portugal. Menos Tuberculose Pedreiras 2018–2020: TB screening in stone quarries

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Background

The Tâmega subregion, part of the northern region of Portugal and of the district of Porto, has an increased incidence of TB compared with the other parts of the region (22 cases per 100 000 population in 2016) and the country (18 cases per 100 000 population in 2016). In the municipalities of Penafiel and Marco de Canaveses, the annual incidence reached 76 and 59 cases per 100 000 population, respectively, during the 2012–2016 period. An estimated 30% of people with TB were or had been working in stone quarries. Such TB cases are frequently identified as the index cases in lower risk communities. Stone quarry workers are at increased risk of TB mainly because of previous lung disease (silicosis) *(9)*), increased alcohol intake *(10)* and smoking *(11)*, poor housing and transportation conditions, and job precariousness. Transmission between colleagues seems to occur when they share transportation to the workplace (which can be far from their place of residence), accommodation (some workers only return home at the weekend) and venues such as restaurants or canteens. When a new TB case is diagnosed, close contacts at work are screened for active TB and latent TB infection (LTBI) at TB outpatient centres (primary care, part of the National Health Care Services). Nevertheless, new TB cases among previously screened individuals are still occurring among stone quarry workers, probably because of decreased adherence to TB screening and a refusal to undergo preventive treatment. This specific population has some features that make intervention more difficult, such as low literacy, high alcohol intake, frequent job switching and illegal/precarious jobs. Several opportunities have also been identified, such as occupational health service cooperation, political commitment to the problem, the involvement of the National Industry Association and raised awareness of TB and silicosis among employers.

Description of the good practice

The Menos Tuberculose Pedreiras 2018–2020 project consists of annual screening for active TB and LTBI in workers in the stone quarries in the municipalities of Penafiel and Marco de Canaveses, in which at least two cases of TB were reported during the 2012–2017 period. Screening activities are performed by the occupational health services in collaboration with public health units, TB outpatient centres and the laboratory. Screening consists of a symptom questionnaire and chest X-ray, as well as sputum examination (smear microscopy and culture) for diagnosing active TB and the interferon-gamma release assay for diagnosing LTBI. Screening tests are performed at the stone quarries by occupational health professionals (from or contracted by the company that runs the quarry) and blood and sputum specimens are transported by these services to a public TB laboratory. The laboratory does not charge the companies nor the occupational health services for this additional work: the costs are covered by the Northern Regional Health Administration. Chest X-ray is done at the quarry (if a mobile X-ray device available) or in nearby clinics as part of the workers' health surveillance (for workers at increased risk of silicosis), with costs covered by the employers.

The project promotes the systematic screening of a population at increased risk of TB, with a focus on identifying and treating LTBI. To achieve this objective, occupational health professionals were trained in TB screening and communication was strengthened between the different health-care services and sectors. Employers and stone quarry workers were systematically informed about the project through information sessions. Municipalities and national industry associations were involved as partners: their roles included launching the project and related public events.

Evidence of impact

During the first three months of the implementation phase, 430 individuals were screened for active TB and LTBI) in seven stone quarries of the Tâmega subregion. Most were male (94%) and the median age was 45 years (interquartile range, 37–52 years). The overall adherence to screening was 83%.

Thanks to the Menos Tuberculose Pedreiras project, a better understanding of the stone quarry workers health profile was achieved. In all, 5% of screened workers (*n* = 23) had a previous TB diagnosis, but only 2% (*n* = 9) reported a previous LTBI diagnosis. A history of contact with a person with active TB was reported by 64% of workers (*n* = 274), and 18% reported having a cough (*n* = 79).

None of the 430 workers screened so far was diagnosed with active TB, but 15% (61 out of 398 individuals eligible for LTBI screening) were diagnosed with LTBI and preventive treatment was proposed. Through treating LTBI we expect to decrease the TB incidence among stone quarry workers to the same level as in the general population of the Tâmega subregion.

In all, 24% of screened workers had a radiological diagnosis of silicosis (84 out of 355 individuals who had undergone a chest X-ray examination). Of these, 38 (45%) were unaware of their condition and were referred to their work physician.

According to the information available, occupational health professionals did not administer routine chest X-rays to stone quarry workers, but this practice was changed during implementation of the Menos Tuberculose Pedreiras project. The good practice of arranging periodic chest X-rays for these high-risk workers for silicosis screening was enhanced. Finally, communication between health services (including occupational health services) was improved by establishing new communication channels and awareness of was raised in health-care professionals through training in TB screening.

Sustainability of the good practice

TB screening among stone quarry workers will remain in place after 2020 as occupational health professionals are trained to screen for active TB and LTBI and are committed to continuing regular screening for TB and silicosis in their workers as part of health vigilance. Increasing TB-related skills in occupational health professionals may contribute to increasing the health literacy of stone quarry workers.

Results so far have been communicated to stakeholders and to regional and national health authorities in order to promote TB and silicosis prevention at different levels (from primordial to quaternary care). Our main recommendations were to:

1. reinforce the use of personal and collective protective equipment in all sectors involving employers and workers;

2. promote the early diagnosis of silicosis (and TB) through periodic chest X-ray examination by occupational health professionals;

3. ensure that primary care services (including TB outpatient centres) and occupational health services have the resources and knowledge needed to prevent, diagnose and treat TB and silicosis; and

4. facilitate communication between all heath service levels (public health, primary care services, occupational health services and hospitals).

Republic of Moldova. Joint effort of state and civil society actors in the early detection of active TB among contacts and high-risk groups

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Background

The Republic of Moldova has a high incidence of TB and DR-TB. The national TB notification rate (new and relapsed) was 83.3 cases per 100 000 population, at 3358 cases in 2017 (according to the National TB Surveillance and Monitoring System). According to the report, Tuberculosis Surveillance and Monitoring in Europe 2018 (developed by WHO and the European Centre for Disease Control) *(2)*, the Republic of Moldova is among the 18 countries with the highest TB burden in the European Region and among the 30 countries worldwide with the highest burden of DR-TB; the country has more than three times the average number of TB cases registered in the WHO European Region. The estimated TB incidence (all forms) is 101.0 cases per 100 000 population.

In 2017, of the 2368 newly detected cases of pulmonary TB, 36.8% (872 cases) were of destructive TB. People who are not diagnosed until they have severe forms of TB are at an increased risk of serious complications and worse outcomes, thus contributing to the spread of infection in society.

Despite all of the interventions in TB control, including the application of new and rapid diagnostic methods for TB, late diagnosis remains one of the major challenges in the Republic of Moldova and is an obstacle to effective disease control. Some of the factors contributing to late TB diagnosis are a shortage of human resources in the health sector and the reluctance of groups with a high risk of TB to actively to seek health-care. To address this, in May 2017 the Ministry of Health, Labour and Social Protection reviewed and adjusted the ministerial order on the systematic screening of high-risk groups and updated the list of at-risk groups (to include people living with HIV, people living with diabetes and chronic lung diseases, people without shelter, ex-offenders, people who use drugs, people with alcohol use disorders and other people who are vulnerable or in a vulnerable situation). The ministerial order takes into account the WHO principles and recommendations on systematic screening for active TB.

Description of the good practice

The active involvement of Moldovan civil society organizations in TB control activities was made possible by a Memorandum of cooperation, signed by NGO members of the National TB Platform, with funding from the NTP Coordination Unit and the Global Fund to Fight AIDS, Tuberculosis and Malaria through Soros Foundation Moldova's small grants programme.

Together, The Soros Foundation Moldova, the NTP Coordination Unit and NGOs coordinators developed the algorithm for activities implementation, taking into account previous experience, specific local needs, available community resources and the current context as follows.

- The NGO team, in partnership with the NTP Coordination Unit, will organize an initial meeting at rayon (local) level, with the participation of key stakeholders, to establish a working schedule for carrying out the activities.
- The NGO team will visit selected localities and mobilize primary health-care and local social assistance for the compilation/update of lists of persons from high-risk groups.
- All persons included in the lists will undergo clinical examination by family doctors with documentation/ notes added to their personal medical records and referral to chest X-ray examination.
- The NGO will raise the awareness of local public authority representatives of the TB context in the country and lobby authorities to ensure transportation of people for chest X-ray examination and advocate for identification of financial resources from local budgets to cover transportation and/or investigation costs.
- The NGO in collaboration with local public authorities and primary health-care and social services will organize, accompany and ensure transportation for identified persons to attend chest X-ray examination.

- At the end of the project, the NGO, in collaboration with the rayon TB programme coordinator, will hold a meeting at rayon level to present the results and share information and experiences.

NGO members of the National TB Platform were awarded seven small grants to catalyse, with the support of the NTP Coordination Unit, effective cooperation among all involved and responsible service providers from the health and social sectors, local public authorities, education sector and civil society organizations to ensure early TB diagnosis among high-risk groups. The activities were implemented over five months (August to December 2017) in eight rayons of the country (representing about a quarter of the population of the Republic of Moldova) as follows:

1. Anenii Noi rayon: TB detection among vulnerable groups in Anenii Noi project, Act for Involvement Anenii Noi NGO;

2. Cantemir rayon: Improving TB detection among risk groups and groups requiring vigilance in Cantemir rayon project, Step by Step Cahul NGO;

3. Cimişlia rayon: Motivating community for an early TB detection in Cimişlia project, Association of Psychologists Tighina;

4. Comrat rayon, Facilitating access of people from risk groups/groups requiring high vigilance for early TB detection project, Comrat Regional Social Centre for People Living with HIV Together for Life;

5. Floreşti rayon: TB examination of risk groups in Floreşti rayon, National Moldovan Association of TB Patients, Bălți;

6. Rîşcani and Făleşti rayons: Improving TB detection among risk groups in Rîşcani and Făleşti rayons project, Speranta Terrei NGO Bălți; and

7. Soroca rayon: TB detection among risk groups and groups requiring vigilance in the Soroca rayon project, House of Hope Social Assistance Centre.

Evidence of impact

TB-related results include:

- increased population awareness of TB in 191 villages from eight rayons (Anenii Noi, Cantemir, Cimişlia, Comrat, Făleşti, Floreşti, Rîşcani, Soroca);

- family doctors in 191 villages are mobilized and determined to update or develop the lists of high-risk groups in the communities covered by project activities;

- a total of 4502 persons from the updated/developed lists have been examined/screened by family doctors, of which 4289 have been referred for further TB investigation;

- 4289 persons (100%) from high-risk and most vulnerable populations have been referred, transported and accompanied by NGO project team members for chest X-ray investigation;

- 89 persons (2.1%) have been detected with presumptive TB; and

- 81 persons (1.9%) have been diagnosed with TB.

Non-TB-related results include:

- 281 persons (6.6%) have been detected with TB sequelae; and

- 324 persons (7.6%) have been diagnosed with bronchitis, pneumonia, oncological or cardiovascular diseases.

In summary, from August to December 2017, 4502 persons from high-risk groups were screened for TB, with 81 TB cases detected. Outcomes of the implemented activities have shown how commitment, engagement and good collaboration between state and civil society organizations can increase the access of high-risk groups to health services to ensure their systematic screening for TB and early detection of the disease.

While primary health-care and local public authorities are key players in TB control and their engagement is critical in identifying high-risk groups in their communities, the involvement of civil society organizations in TB detection activities among these groups is essential

in ensuring access to hard-to-reach populations, thus bringing health-care services closer to the beneficiaries and/or facilitating greater access to these services.

Project activities were implemented in the last quarter of the year. Although this is not the optimal time to raise funds from local public authorities, effective advocacy and communication by NGOs made it possible to identify and allocate financial resources to co-fund project activities.

In conclusion, advocacy, mobilization and support have stimulated motivation for TB engagement; support in planning helped to avoid overcrowded rooms and problems in scheduling examinations for high-risk groups; behavioural and health issues of these populations, such as lack of a permanent residence, substance abuse and comorbidities, were successfully tackled by civil society through community and peer supporters; and increased interaction and communication between key actors improved coordination between local public authorities, health-care, social and community services, and civil society, resulting in a qualitative list of high-risk groups that need attention.

Sustainability of the good practice

During the 2018–2020 period, NGO activities for early TB detection will be supported from the new Global Fund grant. However, in the context of external donor withdrawal, social contracting from domestic funding for NGOs to provide specific TB-related activities is an emerging issue that must be addressed during the 2018–2020 period to ensure the sustainability of activities by civil society to support the health sector in the national TB response.

Spain. Study of Contacts: a pilot programme through the coordination of the different assistance levels in the Avilés health area, Asturias, Spain

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Background

Asturias is a region in northern Spain with about 1 million inhabitants; it is divided into eight health areas, including the Avilés health area (Fig. 3). Before the start of the study, the number of TB cases had decreased from 84 in 2000 to 32 in 2007 (with only sporadic MDR-TB cases), corresponding to incidence rates of 53 and 20 cases per 100 000 population, respectively. A study of TB contacts was performed before 2008 by primary care services; however, this was done on an individual basis without recording the study procedures and results.

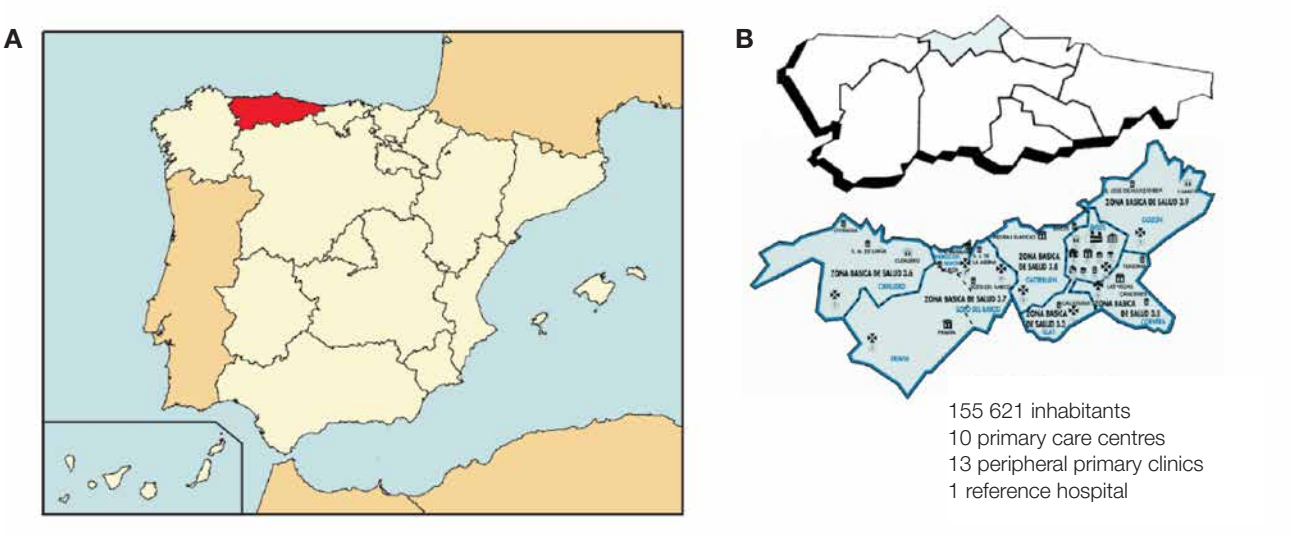
The aim of this study was to organize the investigation of TB patient contacts in a health area and to assess the difficulties in implementation and development of the Study of Contacts programme.

Description of the good practice

We assembled a Working Group on Tuberculosis from staff members of various services: the Public Health Service was responsible for collecting epidemiological data, the Specialized Care Service was responsible for most treatments for TB patients (including respiratory, internal medicine and paediatric services), the Microbiology Service was responsible for diagnostic and genetic studies, and the Primary Care Service was in charge of the contact tracing study and treatment. An initial period was included for recruiting appropriate health personnel and establishing consensus on the study protocol. We then collected data on previous BCG (Bacillus Calmette–Guérin) vaccination, previous TB and TB treatment, previous tuberculin skin test (TST) and prophylaxis, contact characteristics, symptoms, chest X-ray and diagnosis of TB infection (TST and QuantiFERON). We created a website (accessible via a username and password) to present data and therapeutic decisions. Weekly conferences between members of the programme enable decisions to be made on what care should be offered to the different patients (Fig. 4).

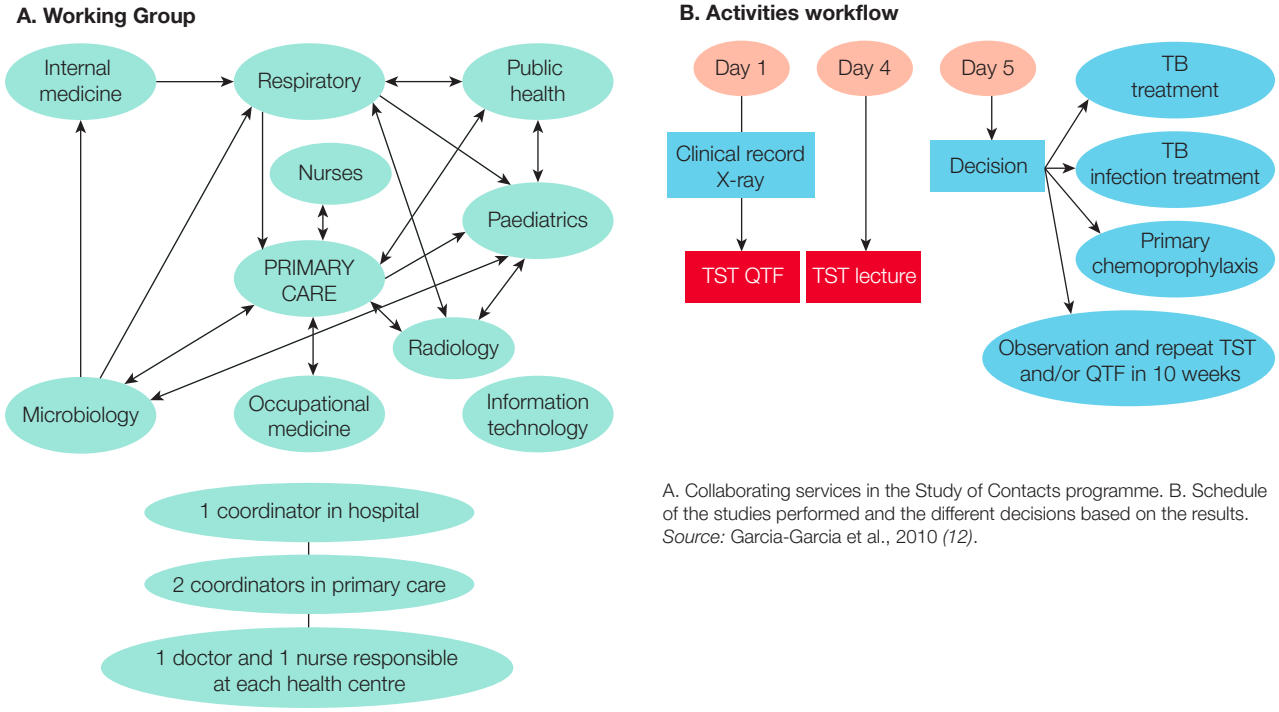
The Avilés health area covers a population of 160 000. From 1 April 2008 to 2010, we studied 254 contacts of

Fig. 3. The Avilés health area



A. Map of Spain with the Asturias region shown in red. B. Upper, all eight health areas in Asturias, with the Avilés health area shown in blue. Lower, map of the Avilés health area, indicating its population and health resources.
Source: AsturSalud health map of Asturias.[3]

Fig. 4. Descriptions of the Working Group and activities workflow



A. Collaborating services in the Study of Contacts programme. B. Schedule of the studies performed and the different decisions based on the results.
Source: Garcia-Garcia et al., 2010 *(12)*.

[3] AsturSalud health map of Asturias. Oviedo: Government of the Principality of Asturias; 2018 (https://www.astursalud.es/noticias/-/noticias/mapa-sanitario-de-asturi-1, accessed 21 September 2018).

50 TB patients. A total of 110 contacts (43.3%) were infected, with 73 started on treatment. A total of 117 contacts (52.8%) were not infected. Three contacts had active pulmonary TB (Table 3).

Table 3. Outcomes of the participants in the Study of Contacts programme

Outcomes	*n*	%
TB infection – treatment	73	28.7
TB infection – without treatment	37	14.6
TB disease	3	1.2
Exposed without infection	117	46.1
In follow-up	15	5.9
Missed follow-up	9	3.5
Total	254	100

Source: Garcia-Garcia et al., 2010 *(12)*.

The secondary aim of the study was to evaluate the level of agreement between the TST and QuantiFERON-TB Gold (QTF) test in LTBI diagnosis in the Study of Contacts programme. Every patient underwent interferon-gamma release assays, a technique we are experienced in using. Each close contact of a TB patient underwent a QTF test (according to the manufacturer's instructions; Cellestis, Australia) followed by a TST (using 2 IU of purified protein derivate RT23; Mantoux test) on the same day. Overall 252 close contacts were tested by both tests. If the results of the initial tests (QTF1 and TST1) were negative, we repeated the both tests (TST2 and QTF2) after 10 weeks. We defined TST positivity as induration of less than 5 mm and QTF positivity as a result greater than 0.35 IU/mL. We defined conversion as a change from a negative to a positive result and reversion as a change from a positive to a negative result. TST1 was positive for 82 out of 252contacts (32.5%) and QTF1 was positive for 64 out of 244 contacts (24.2%). TST2 was positive for 34 out of 148 contacts (23.3%) and QTF2 was positive for 20 out of 160 contacts (12.5%). Results were concordant between TST1 and QTF1 (both tests positive or negative) for 197 contacts out of 243 contacts (81.1%) and discordant for 46 out of 243 (19.4%). Results were concordant between TST2 and QTF2 for 110 out of 141 contacts (78.01%) and discordant for 31 out of 141 contacts (21.9%). The overall level of concordance was 79.99%. We had 31 conversions and three reversion with TST criteria and 12 conversions and four reversions with QTF criteria. In six patients, the results of both tests changed from negative to positive (conversion in TST and QTF). 19 patients had TST conversion without QTF conversion and two patients had QTF conversion without TST conversion. 95 patients had negative results for all four tests (both TST and QTF).

In a prospective study of TB patient contacts, we found overall concordance between the TST and QTF test in 80% of contacts. Conversions with both tests were seen (true conversions), although differences in conversion were seen between tests. Both TST and QTF test negativity support exposure without infection. Although results differed between tests, both are useful in LTBI diagnosis.

Evidence of impact

The number of TB cases decreased from 2000 to 2017 (shown in Fig. 5). The number of sputum smear-positive cases also decreased over the period. For example, in 2008 a total of 30 TB cases was recorded, of which 15 were sputum smear positive.

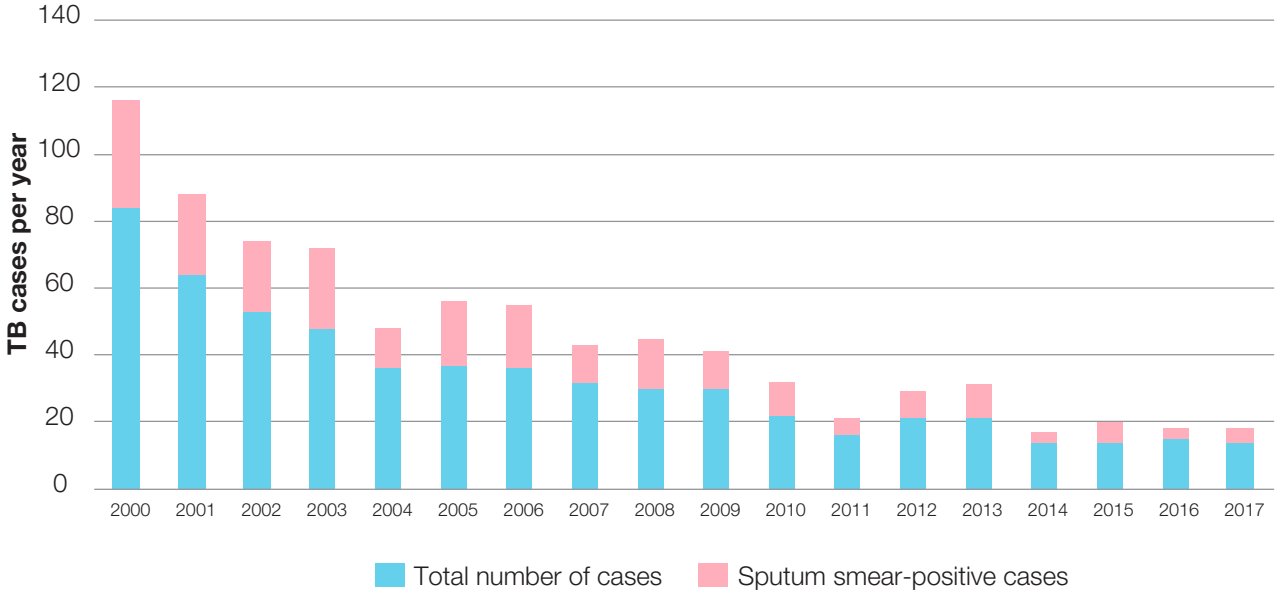
Sustainability of the good practice

The Study of Contacts programme promotes coordination between health personnel and the various services involved in the study and has proven very useful in the study of TB patient contacts.

The programme started in 2008 and is continuing to systematically study all contacts of TB patients in the Avilés health area. We were able to maintain the programme without additional resources.

Acknowledgements. The study was funded by a grant from Instituto Carlos III (PI07/90456).

Fig. 5. TB incidence, Avilés health area, 2000–2017



Source: García-García et al., 2010 *(13)*.

Tajikistan. Household contact tracing of children exposed to DR-TB in Tajikistan

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Background

In 2016, there were an estimated 10.4 million incident TB cases globally, of which 9.4 million were adults and 1.04 million were children. While children are known to be particularly vulnerable to severe disease and death (16% of deaths in 2016 occurred among children), paediatric TB still remains neglected and underdiagnosed: the many challenges contributing to these figures include limitations in active case-finding, lack of appropriate diagnostic tools and limited treatment formulations *(1)*.

In the WHO Global Tuberculosis Report 2107, Tajikistan was named one of the 30 countries with a high MDR-TB burden *(1)*. The TB incidence is 85 cases per 100 000 population, with MDR-TB accounting for 22% of new cases and 45% of re-treatment cases. According to national statistics, and in keeping with globally reported figures, children represented 10.8% of all new TB cases in 2017. However, only 6.5% of all MDR-TB cases were detected in children, revealing a significant discrepancy. This incidence is also reflected in globally reported data (children aged under 15 years accounted for 6.9% of the new and relapse TB cases notified in the world in 2016). Paediatric MDR-TB is generally believed to be largely unknown and definitely underreported *(14)*. Differences in epidemiology, access to the health-care services or reporting practices contribute to these figures; however, the main factor seem to be the difficulty in diagnosing children, who mainly have paucibacillary disease.

Description of the good practice

In 2011, Médecins Sans Frontières (MSF; Doctors without Borders) in Tajikistan, in collaboration with the NTP and Ministry of Health and Social Protection started providing comprehensive TB care for the paediatric population and adult contacts in Dushanbe and the surrounding areas. Since then, various approaches have been applied to improve case detection and MDR-TB diagnosis among children, enabling the timely initiation of effective treatment (including the use of new drugs, bedaquiline (Bdq) and delamanid (Dlm)), thus reducing morbidity and mortality in this vulnerable population.

The comprehensive approach towards paediatric MDR-TB in Tajikistan can be divided into several

activities: (i) **find**, case-finding; (ii) **diagnose/confirm**, using various methods suitable for the paediatric population; (iii) treat, timely effective treatment initiation in appropriate formulations and with correct doses; (iv) **record**, proper data collection and recording; and (v) **adopt the guidelines**.

1. **Find.** Historically, passive case-finding, relying on the screening of symptomatic patients attending health-care facilities, was the main entry point for patients. This approach relies heavily on the health-care-seeking behaviour of individual patients and families (and thus their social and financial situation), as well as the clinical skills of individual primary health-care practitioners. Focusing on training and coaching of primary health-care practitioners strengthens this very important pillar of passive case-finding. In response to a remaining diagnostic gap, additional attention was paid to active case-finding activities in Dushanbe. An understanding that families face multiple barriers in accessing health care, and based on the fact that approximately 30–50% of all household contacts (especially children or immunosuppressed individuals) *(14)* will become infected within two years of index case diagnosis and 2–25% of them will develop active TB *(15,16)* lead to greater cooperation between MSF and the Ministry of Health and Social Protection in household contact tracing in Dushanbe. To ensure its sustainability, this activity was included in the daily routine schedule of health-care providers: while mornings are occupied with monitoring TB patients who are already on treatment, afternoons are dedicated to planned visits to households affected by TB. These targeted household visits are conducted by a Ministry-appointed nurse who is accompanied by the MSF nurse with verbal consent from the family. During the visit all family members are screened for the signs and symptoms of TB and receive health education on disease transmission and infection control. Individuals exhibiting one or more signs of TB are referred to the local health-care facility for the further investigation including, but not limited to, chest X-ray, Mantoux test (TST) and GeneXpert sputum investigation.

2. **Diagnose/confirm.** TB diagnosis in children is complicated by several factors. First, TB has different immunological and pathophysiological characteristics in this vulnerable population compared with adults. Obtaining a biological sample for resistance testing can be difficult, especially in children aged under 5 years. Careful history taking and consideration of the drug-susceptibility pattern of the index case remain crucial to differential diagnosis. In order to improve diagnostic accuracy in children, sputum induction was introduced in Tajikistan in 2013. While this activity was initially centralized (at the beginning it was conducted only in the pilot project in Dushanbe), it provided better conditions for training and ensured a high quality of diagnosis. This simple, inexpensive method allows the collection of sample material for further testing, thus enabling a tailored treatment regimen.

3. **Treat.** With the help of active case-finding, knowledge on the drug-susceptibility pattern of the index case and sputum induction, health-care workers have been able to identify cases earlier, gain valuable information on drug-susceptibility testing (DST) and adjust treatment regimens accordingly. However, while DR-TB detection in children has improved, challenges remain in providing effective treatment. To address the lack of child-friendly formulations of second-line anti-TB drugs (SLDs), drug compounding was piloted by the MSF and Ministry of Health and Social Protection for eligible children. Drug compounding is the preparation of SLDs against DR-TB in paediatric formulations through the use of commercially available syrup. In addition, for children with advanced drug resistance, Bdq and Dlm (alongside other repurposed anti-TB drugs such as clofazimine, imipenem and linezolid) have been used successfully. A comprehensive approach to each child's care includes the monitoring and management of adverse events, psychosocial care (including schooling) and nutritional support according to the individual needs of each family.

4. **Adopt the guidelines.** the Tajikistan health ministry and NTP have recently published the revised third edition of the Guidelines for the diagnosis and treatment of TB in children of the Republic of Tajikistan. This guideline reflects on the activities mentioned above, including the use of the sputum induction and new drugs, and adopts them into nationwide practice.

Evidence of impact

The paediatric case detection rate in the MSF/Ministry of Health and Social Protection Dushanbe project improved significantly after the introduction of

household active case-finding. Since late 2015, 1184 families consisting of 5747 individuals and including 3648 children have been screened for TB. In all, 472 people have been referred for further investigation, with 46 new TB cases diagnosed including 36 in children (Table 4). According to our data, 115–124 people need to be screened to find one new TB case. TB diagnosis among children with suspected disease was improved by sputum induction combined with GeneXpert testing of the induced sputum.

Table 4. Active case-finding among contacts of TB patients, Tajikistan, 2015–2017

Contact	2015	2016	2017	Total
Families screened *(n)*	78	427	679	1184
Family members screened *(n)*	508	1960	3279	5747
Children *(n)*	230	1252	2166	3648
Suspected individuals sent for further investigation *(n)*	230	198	251	472
Total TB diagnoses *(n)*	1 (child)	17 (15 children, 2 adults)	28 (20 children, 8 adults)	46 (36 children, 10 adults)
Individuals screened for one patient identified *(n)*	–	115	121	124

Source: MSF internal Koch6 database of contact tracing activity.

As a result of active case-finding combined the sputum induction, the number of newly enrolled paediatric MDR-TB cases in the Dushanbe pilot project doubled compared with previous years: from 23 in 2014 and 13 in 2015 to 24 in 2016 (10 of these through contact tracing) and 41 in 2017 (20 of these through contact tracing; Figs 6 and 7). Among these cases, drug-susceptible TB (DS-TB) was confirmed in five children, MDR-TB in 14 children, pre-XDR-TB in six children and XDR-TB in 11 children (Table 5). Of paediatric cases identified from both passive and active case-finding, 12 children were started on Bdq-containing treatment regimens and 15 children were started on a Dlm-containing treatment regimen.

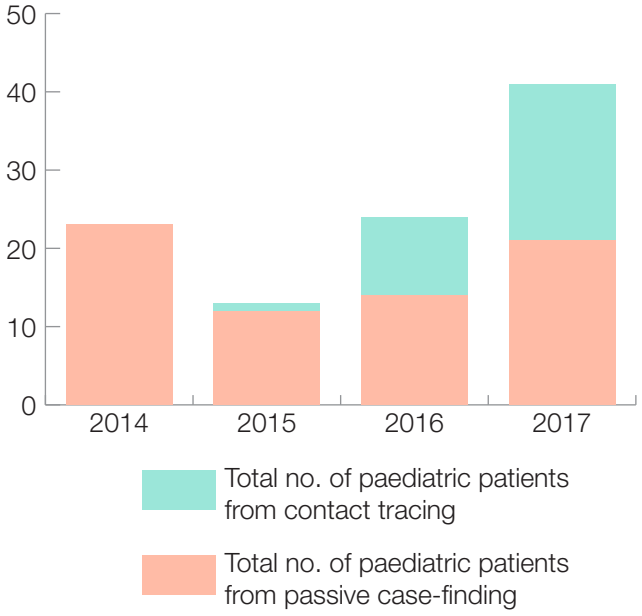
These activities, some of which were implemented in Tajikistan for the first time, are now regular components of the programme in MSF-supported Ministry of Health and Social Protection facilities and have been incorporated into routine daily work.

Table 5. Cases found during contract-tracing activities, stratified by drug-resistance pattern

Type of TB	2015		2016		2017		2018	
	<18 years	>18 years	<18 years	>18 years	<18 years	>18 years	<18 years	>18 years
DS-TB	0	0	5	0	0	1	5	1
MDR-TB	1	0	7	1	6	1	14	2
XDR-TB	0	0	3	1	8	5	11	6
Pre-XDR-TB	0	0	0	0	6	1	6	1
Total	1	0	15	2	20	8	36	10

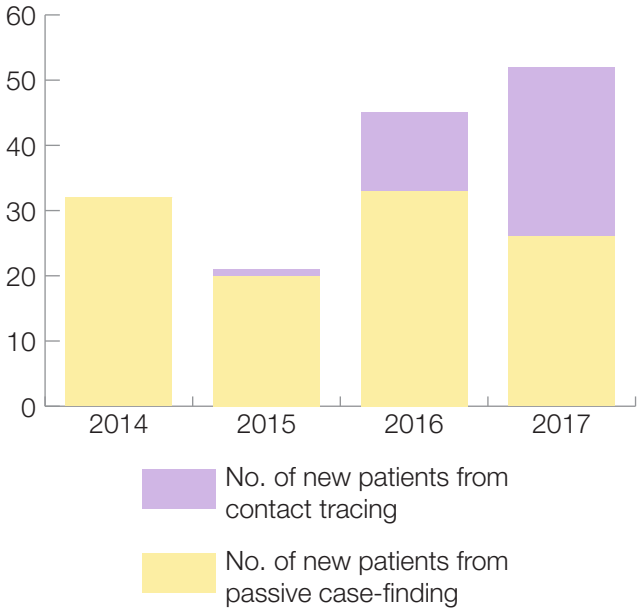
Source: MSF internal Koch6 database of contact tracing activity.

Fig. 6. Proportion of children found during contact tracing among new paediatric patients in the cohort



Source: MSF internal Koch6 database of contact tracing activity.

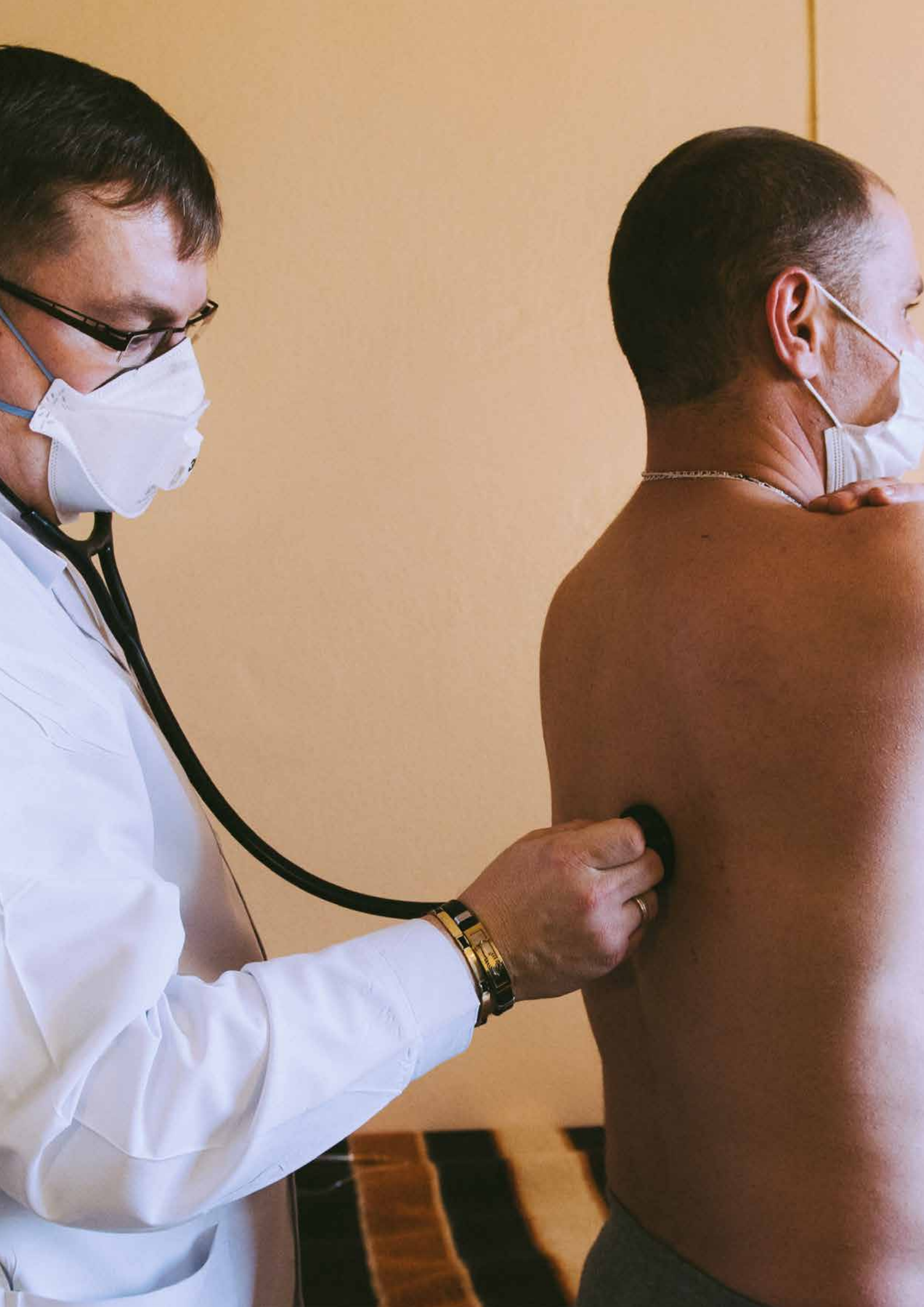
Fig. 7. Proportion of new patients found during contact tracing of the total new patients in the cohort



Source: MSF internal Koch6 database of contact tracing activity.

Sustainability of the good practice

All of the above-mentioned activities were incorporated into the National paediatric guidelines of Tajikistan. The whole programme is conducted through existing Ministry of Health and Social Protection resources and organization.



1B. Early diagnosis of all forms of TB and universal access to drug-susceptibility testing, including with rapid tests

Azerbaijan. TB laboratory network in Azerbaijan

Submitted by: Kadyrova Agigat Abdul kyzy | Abuzarov Rafig Mahmud ogly | Sayfuddinova Mehriban Nadir kysy | Akhundova Irada Mirsaab kyzy

Research Institute of Lung Diseases, Ministry of Health, Baku

Background

The laboratory component is one of the priorities of the National Strategic TB Control Plan. The NTP laboratory network of Azerbaijan includes the National Reference Laboratory (NRL), five level II regional laboratories and the reference laboratory in the penitentiary sector. The NRL and the laboratory in the prison sector perform microscopy examinations, phenotypic culture on solid Löwenstein–Jensen (LJ) medium and mycobacteria growth indicator tube (MGIT) medium, DST for first-line anti-TB drugs (FLDs) and SLDs, as well as rapid tests (such as the GeneXpert MTB/RIF and Hain assays) to FLDs and SLDs.

The regional laboratories use the following methods:

1. Gäncä – GeneXpert MTB/RIF assay, smear microscopy, Hain tests, culture on solid and liquid media (LJ medium and MGIT) for DST to FLDs;
2. Guba – GeneXpert MTB/RIF assay, smear microscopy and culture on LJ medium;
3. Masalli – GeneXpert MTB/RIF assay, smear microscopy and culture on LJ medium;
4. Nakhichevan Autonomous Republic – GeneXpert MTB/RIF assay, smear microscopy, culture on solid and liquid media (LJ medium and MGIT) for the DST to FLDs; and
5. Zaqatala – GeneXpert MTB/RIF assay, smear microscopy and culture on LJ medium.

Description of the good practice

Following a thorough needs assessment, some extra laboratory equipment was procured for the NRL and regional laboratories. In addition, the ventilation systems at the NRL and regional laboratories were repaired to ensure proper infection control.

Development of a sustainable sputum transportation system that ensures timely delivery of the laboratory specimens is one of the key goals specified in the National TB Control Strategy. Sputum specimens collected daily are being delivered to the NRL and regional laboratories within the framework of the NTP for TB diagnosis in individuals with presumed TB and for TB treatment monitoring. All laboratories are fitted with modern equipment and reagents and have the infection control measures in place.

Laboratory staff receive training in sputum testing from NRL experts (Figs 8 and 9).

Fig. 8. NRL training for level I and II laboratory staff

Through e-Health (Ministry of Health), all tests results are being reported by email.[4] This helps improve communication between the laboratories and TB facilities and significantly reduces the time to obtain test results.

[4] Email address: title of facility@esehiyye.gov.az.

Since 2017, the country's entire laboratory service has completely switched to the laboratory diagnostic algorithm recommended in 2017 by WHO and the European Laboratory TB Initiative (ELI). A new diagnostic algorithm is reflected in the new (2017) Protocol for pulmonary TB management, which was developed by the Research Institute of Pulmonary Diseases based on the WHO guidelines.

The delivery mechanism for DST results from the NRL to TB facilities was improved after the procurement of computers for the regions and training for operators on the e-TB management system. In addition, the NTP plans to introduce the GxAlert system which:

1. ensures real-time delivery of the patient's laboratory test results to the existing electronic patient registration system;
2. keeps track of cartridge usage (GeneXpert MTB/RIF assay) to generate proper future orders; and
3. sends reports in text message format to the email addresses of the health policy-makers.

Quality control of the regional laboratories by the NRL experts revealed a need for training on standard operating procedures and innovative diagnostic methods. For this purpose, the laboratory doctors from all regional laboratories were trained by the NRL specialists.

It is currently planned to decentralize DST to SLDs and introduce LJ medium and MGIT culture for DST to SLDs into practice in the Nakhichevan and Gäncä regional laboratories.

Evidence of impact

Implementation of a diagnostic algorithm in accordance with the WHO/ELI recommendations has led to increased bacteriological confirmation among notified TB cases. According to national statistics, over the last two years (2016–2017) the bacteriological confirmation rate for TB increased significantly from 61% among incident pulmonary TB cases in 2016 *(1)* to 74% in 2017, respectively. A further increase is anticipated in 2018.

Sustainability of the good practice

The Ministry of Health of Azerbaijan is committed to support the current practice. At the moment, the partial costs of laboratory diagnostics tests, including smear, culture and DST to FLDs and SLDs on solid medium, are ensured by state funding. The government is committed to taking over procurement of all necessary diagnostics, including rapid tests, by 2021.

Georgia. Use of GeneXpert MTB/RIF as the primary test for TB diagnosis among presumptive TB cases

Submitted by: Rusudan Aspindzelashvili | Inga Kinkladze | Zaza Avaliani

National Centre for Tuberculosis and Lung Diseases, Tbilisi

Background

Despite a significant decrease in TB incidence from 103 cases per 100 000 population in 2013–2014 to 92 cases per 100 000 population in 2016, TB remains a major public health problem in Georgia. In 2016, the proportion of TB cases with MDR-TB was 10.2% for new cases and 38.0% for previously treated cases *(2)*.

Description of the good practice

A main target for eliminating TB is the timely diagnosis of TB patients and their prompt inclusion in appropriate treatment regimens. For a long time, the TB control programme has focused on identifying pulmonary, contagious TB patients. However, since fast diagnostic testing (GeneXpert MTB/RIF assay for TB and RR-TB) has become available, recommendations and an algorithm for primary diagnosis with the GeneXpert MTB/RIF assay were proposed by European Laboratory Initiative. After this, the GeneXpert MTB/RIF assay became routinely available for all presumptive TB cases in Georgia.

Evidence of impact

Use of GeneXpert MTB/RIF as the primary diagnostic test for TB presumptive cases increased the rates of early detection and prompt inclusion into an appropriate treatment regimen. Moreover, implementation of GeneXpert MTB/RIF testing decreased the number of pulmonary, contagious cases: more specifically, bacteriologically positive TB cases are mostly acid-fast bacilli (AFB) negative. In 2013, of the bacteriologically confirmed patients, 54.6% were AFB positive and

44.2% were AFB negative; however, in 2017 42% bacteriologically confirmed patients were AFB positive and 56% were AFB negative. This indicates an increased rate of early detection of TB cases (i.e. before patients become AFB positive and contagious), highlighting the importance of this methodology for epidemiological purposes. In addition, identifying rifampicin resistance at an early stage made it possible to link relevant patients to adequate treatment more rapidly than before the intervention. On average, the time to initiation of adequate treatment, especially for AFB-negative patients, has decreased from a mean of 32 days to a mean of five days.

Sustainability of the good practice

Early detection and timely initiation of the treatment regimen is an indicator of the effectiveness of GeneXpert MTB/RIF as the primary test for detecting *Mycobacterium tuberculosis* infection and rifampicin resistance. Therefore, to increase the number of early detected cases, the GeneXpert MTB/RIF assay has been included in the national TB management guidelines *(17)*. We also aim to implement the test more broadly in general hospitals within the FAST strategy.[5]

[5] FAST stands for Finding TB cases Actively, Separating safely, and Treating effectively.

Kazakhstan. Strengthening medicines quality control laboratories to ensure the quality of TB medicines

Submitted by: Archil Salakaya | Aubrey Clark

Promoting the Quality of Medicines (PQM) Program, United States Pharmacopeia, Rockville, Maryland, United States of America

Background

The TB incidence in Kazakhstan has fallen steadily since 2004 *(18)*. However, the persistent challenges of MDR-TB and RR-TB increasingly threaten these gains. Together, MDR-TB and RR-TB make up 26% of new TB cases and 44% of previously treated cases in the country, which has one of the highest MDR-TB burdens globally *(1)*.

Encouragingly, Kazakhstan has prioritized treatment coverage for TB patients, ensuring universal treatment coverage *(18)*. Ensuring that all individuals who require treatment are able to receive it is vital to curb the spread of TB, MDR-TB and RR-TB. It is important, however, that these efforts are accompanied by commensurate efforts to ensure that the medicines used in TB treatment programmes are of assured quality and used rationally.

Health system challenge: availability of poor-quality medicines hinders progress against TB

Kazakhstan procures most of its TB medicines locally with domestic funding. For the most part, these medicines are from sources that have not been WHO prequalified and therefore may not be quality assured. In fact, studies conducted to assess the quality of TB medicines in Kazakhstan have found that non-quality-assured medicines are available on the local market. A WHO study conducted in 2009, for example, found that 23.3% of TB medicines sampled were of substandard quality, the highest proportion detected among any of the six former Soviet Union countries surveyed *(19)*. A subsequent study conducted in 2014 in Almaty city found that 19% (163 of 854) of the TB medicines sampled failed at least one test for quality *(20)*. Although both studies have limitations, they serve as important signals for the presence and availability of poor-quality TB medicines in Kazakhstan.

The continued availability of medicines of unverified quality in local markets, and the potential for life-saving TB medicines to degrade throughout the supply chain before reaching the patient, can negatively affect patient outcomes. Poor-quality medicines can lead to treatment failure, result in adverse events and contribute to the development of drug resistance. Beyond the effects that poor-quality medicines have on health, they also exacerbate the loss of productivity and income that individuals face due to illness, waste scarce resources, and erode public confidence in health systems.

Robust and effective quality control laboratories form the cornerstone of effective national medicines quality assurance systems, helping to detect poor-quality medicines and supporting national medicines regulatory authorities in taking evidence-based regulatory action. Recognizing this, Kazakhstan's national medicines regulatory authority – the National Centre for Expertise of Medicines, Medical Devices, and Medical Equipment (NCEM) – successfully supported the national quality control laboratory in Kazakhstan to become ISO 17025 accredited. Standards such as ISO 17025 and

WHO prequalification are internationally recognized benchmarks for quality and help confirm a laboratory's ability to reliably and accurately assess medicine quality. Although ISO 17025 accreditation had been achieved for the national quality control laboratory, in recognition of the need to expand the number of accredited laboratories, local authorities aimed to extend this level of quality to regional laboratories.

Description of the good practice

Strengthening laboratory networks to detect poor-quality medicines

To support the objectives and activities pertaining to quality-assured medicines outlined in WHO's Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7),* the Promoting the Quality of Medicines (PQM) Program, funded by the United States Agency for International Development (USAID) and implemented by United States Pharmacopeia, began working with three regional quality control laboratories in the cities of Astana, Karaganda and Kostanay in 2016 to build capacity to accurately and reliably test the quality of TB medicines.

Using a collaborative learning model, the PQM Program worked to build capacity rapidly and simultaneously across all three laboratories to attain compliance with WHO standards for medicines quality control laboratories and achieve WHO prequalification. The collaborative learning model encouraged open communication and learning among staff at all three laboratories so that lessons and best practices can be shared and standardized. After the PQM Program conducted an initial gap assessment at all three laboratories in 2016, the laboratories used the collaborative model to perform their own cross-audits of the quality management systems and worked together to revise appropriate documents based on the findings.

Working in close partnership with the NCEM, the PQM Program conducted follow-up assessments at all three laboratories to determine their readiness for WHO prequalification and held a five-day hands-on training course on essential testing methods for 17 laboratory analysts (Fig. 9). Based on the training and findings from the assessments, the PQM Program supported each laboratory in developing and beginning to implement appropriate corrective actions. Based on one of the PQM Program's recommendations following the assessments, the NCEM led the establishment of a Quality Team comprising members from each of the three laboratories. In line with the collaborative learning model, the Quality Team oversaw the revisions and standardization of quality management system documents and shared the updates with quality control laboratories nationwide. The Quality Team also developed the Laboratory Information File for submission to the WHO prequalification programme, while the PQM Program provided technical input, review and translation support. As the laboratories neared readiness for WHO prequalification, the PQM Program supported additional training needs, including conducting a training session on data integrity in early 2018.

Evidence of impact

With PQM Program support, Kazakhstan regional laboratories have strengthened their quality management system, which helps ensure that medicines can be accurately and reliably tested for quality. The regional laboratory in Karaganda, which will be the first laboratory to be considered for WHO prequalification, successfully strengthened its quality management system by addressing 98% of all corrective and preventive actions relevant to the anticipated scope of accreditation identified during PQM Program audits. The laboratory is anticipated to have addressed all corrective and preventive actions before WHO conducts its audit for prequalification.

In August 2017, the quality control laboratory in Karaganda took a major step towards accreditation by submitting its application for prequalification, which was accepted by WHO for consideration. As the laboratories in Astana and Kostanay were actively participating in training sessions with Karaganda and working simultaneously to build capacity at their respective laboratories, these two laboratories should be ready for prequalification as soon as Karaganda has successfully become prequalified. Having three regional laboratories prequalified by WHO will help protect the people of Kazakhstan from substandard medicines, including those procured for and used in TB treatment programmes.

Important factors for success

Strong commitment from the Kazakhstan Government combined with effective leadership from the NCEM helped to accelerate improvements across the laboratory network. Establishment of a cross-laboratory Quality Team fostered local ownership of the process

Fig. 9. Hands-on training for technicians, provided by the PQM programme, 2017

Technicians from regional quality control laboratories in Kazakhstan practice laboratory methods during a hands-on training provided by the PQM Program in 2017. Photo credit: Natalia Morozova, PQM Program.

and ensured that capabilities were reinforced across the network.

Sustainability of the good practice

The collaborative learning model encouraged lasting change and was made possible through strong participation on the part of the national regulatory authority. Parallel capacity-building of the three laboratories supported harmonized medicines quality testing throughout the country. As the PQM Program provided technical assistance to the strongest performing laboratory, staff from the other laboratories also participated in capacity-building activities, which amplified the PQM Program's technical assistance as laboratories worked towards complying with international accreditation requirements.

Kyrgyzstan. Development and implementation of a new system for sputum transportation in Kyrgyzstan

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Background

Kyrgyzstan is among 30 countries in the world with a high MDR-TB burden. It is therefore very important to ensure that drug-resistant forms of TB are identified as early as possible to initiate effective treatment.

Due to the remote location of the health-care facilities that perform the required tests, there is a need to ensure timely DST and coverage with the necessary laboratory methods of diagnosis. For example, according to 2016 data, coverage of GeneXpert MTB/RIF testing in the country was 16% among new TB cases and 21% among re-treatment cases.

GeneXpert platforms in the country were mostly distributed throughout primary health-care facilities, with the aim of providing proper coverage for all geographical areas. Because of the large distances between those facilities, sputum delivery to the laboratory is often problematic. A baseline situation analysis in the Chui region in January 2017 revealed that sputum specimens for GeneXpert MTB/RIF testing were transported by either medical staff (63%) or patients (27%) using public transportation. However, this was irregular, depending on the possibilities.

For rapid DST, patients have to go the regional TB control centre to collect sputum specimens on a certain day, which is often aligned with the scheduled sputum delivery to the NRL in Bishkek and Osh once or twice a month (with financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria). Vehicles purchased for regional TB control centres deliver sputum specimens, but do not completely cover the needs.

Therefore, there was a need to develop a financially sustainable system capable of the regular delivery of biological specimens from the primary health-care level to GeneXpert MTB/RIF laboratories and the NRL to meet existing needs.

Description of the good practice

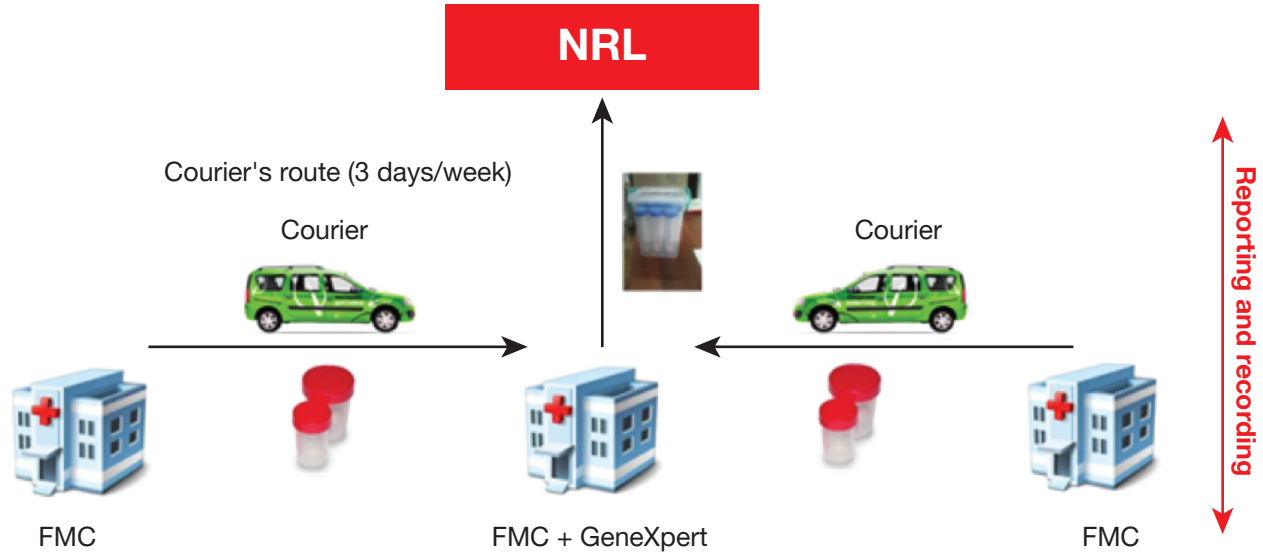
In 2016, the Ministry of Health of Kyrgyzstan requested technical assistance from the USAID Defeat TB project to develop an effective system capable of improving the coverage and availability of the required laboratory diagnostic methods, especially for early detection of MDR-TB. In the Chui region, the TB incidence is 135.2 cases per 100 000 population and MDR-TB prevalence is 21% (2016 data). Based on these data, the Chui region was selected for the pilot testing of this project. Of the nine family medicine centres in the region, only four had GeneXpert platforms. These were located at a distance of 20–30 km from each other, giving a catchment area of up to 70 km in diameter.

Following a preliminary analysis of the current sputum delivery situation at primary health-care facilities in the Chui region, a two-level model was developed: level I included the district family medicine centres, and level II included the laboratories engaged in GeneXpert MTB/RIF testing and the NRL in Bishkek (Fig. 10).

Level I. Since at the level of family doctor groups and feldsher-midwife stations no more than one to two patients per month per unit need sputum collection, it was decided that specimen transportation will be done by a nurse or a feldsher in compliance with the established requirements. In the past, their expenses were not reimbursed and so a reimbursement system for transportation costs was developed based on the existing legal framework.

Level II. At this level, it was decided to outsource sputum transportation. In order to launch the new system, the services of a transportation company were needed. The requirements for the company included: experience in providing transportation services, efficiency, operational transparency, presence of branches in other regions of the country and affordable services. Based on tender results, a choice was made in favour of the state Special Communication Service. Its experience in delivering important government documents, strict scheduling, punctuality, accuracy in actions, well-developed transportation routes, links with all regions of the country and, most importantly, pricing policy based on the government-controlled rates were the critical factors for selecting this company

Fig. 10. Developed and agreed procedures and routes for sputum specimen transportation, Chui region



FMC: family medical centre.

as a carrier agent. For example, its price offer for the Chui region in 2017 was 115 som per kg of transported materials, regardless of the delivery distance, while the price offers of other companies ranged from 309 to 3708 som per 1 kg, depending on distance.

After selecting the company, the Ministry of Health approved schedules for sputum transportation in two routes, standards and requirements for transportation, instructions for the couriers' response to accidents, and the composition of emergency kits. In each primary health-care facility, health workers responsible for sputum transportation were identified and trained in registration procedures, packaging of sputum specimens and filling out accompanying documents.

During implementation of the new system of sputum specimen transportation, there was no information system in place for reporting laboratory test results. Therefore, it was decided that the carrier agent would deliver the laboratory results back to the primary health-care facility.

Thus, a system was developed for the Chui region that ensures regular sputum specimens transportation from the primary health-care level to GeneXpert MTB/RIF laboratories and the NRL (Fig. 11). It meets the requirements of service quality and safety of the diagnostic specimens, follows the approved schedule and procedures, and functions promptly and accurately.

Evidence of impact

The introduction of the new transportation system contributed to improved coverage and availability of GeneXpert MTB/RIF testing among the populations of the pilot areas, where primary health-care facilities

Fig. 11. Sputum specimen transportation from the health-care facilities of the Chui region to the NRL in Bishkek

were not equipped with GeneXpert equipment. Thus, the proportion of pulmonary TB patients covered with this testing method after the introduction of the new transportation system increased from 0% to 25% in the Moskovsky region and from 18.2% to 76.9% in Panfilovsky district compared with the same period in 2016 (Fig. 12).

Following the introduction of the transportation system, primary health-care facilities in the pilot areas started sputum collection for culture and DST instead of sending patients to the TB hospital for the same purpose. The number of cases with confirmed TB diagnosis at the primary health-care level increased from 0% to 66% compared with the same period in 2016.

The actual costs of the carrier agent services of sputum delivery in 2017 in the Chui region amounted to 170 544 som ($2508). According to 2015 data, every primary health-care facility in the Chui region spent an average of 34 272 som on transportation services, excluding out-of-pocket expenses for medical workers. Thus, the total expenditure of the Chui region (i.e. the actual cost of fuel and lubricating materials) in 2015 (one year prior to the introduction of the transportation system) was 308 448 som ($4536).

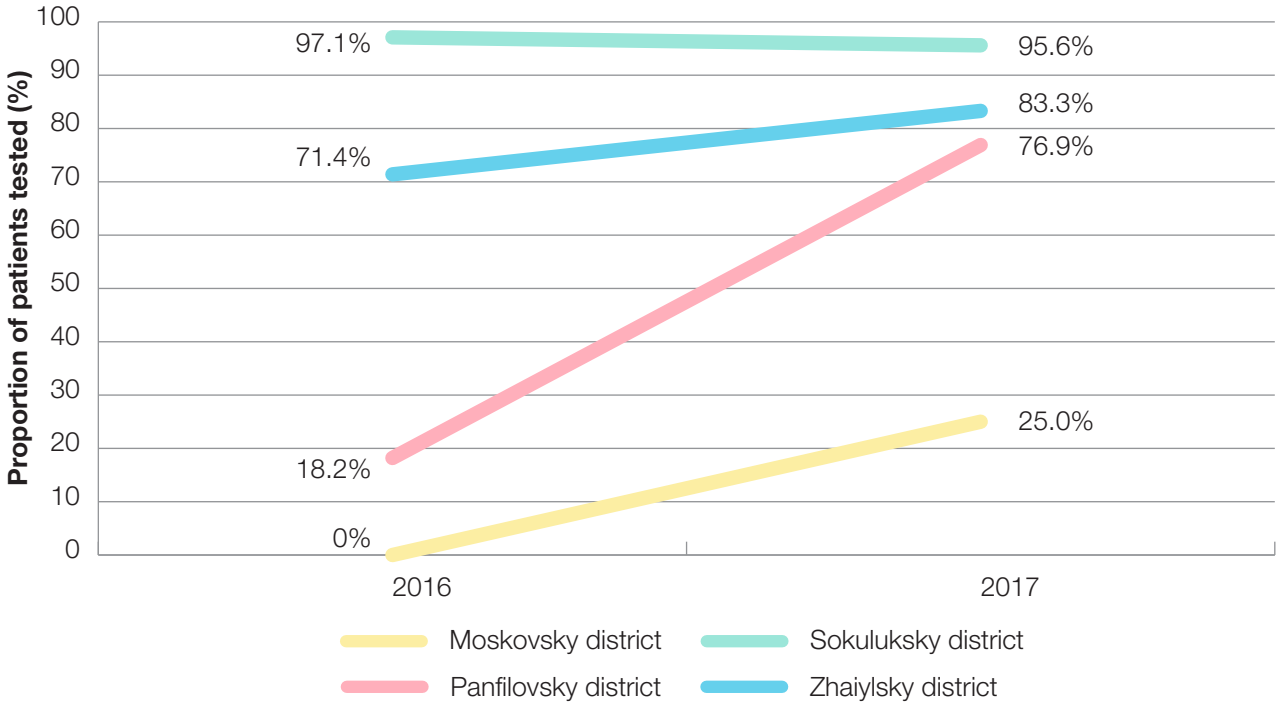
Thus, the first outcomes of the demonstrated that the sputum transportation system had a positive impact on the quality of services at primary health-care facilities, and improved and increased the involvement and commitment of primary health-care workers in the process of TB diagnosis, which was not observed earlier.

The new system for sputum transportation helped resolve the problem of specimen delivery but also (as the indicators showed) had a positive effect on the quality of TB services at the level of primary health-care. For instance, DST coverage and the bacteriological confirmation rates for TB cases were improved due to proper interactions with medical staff and on-the-spot training during monitoring missions at the level of primary health-care.

Sustainability of the good practice

During the pilot implementation, a number of regulatory documents were developed to ensure the quality and safety of sputum specimens during transportation, providing for the involvement of external players in the process of service delivery. In addition, a number of sensitive indicators were developed and tested to enable assessment of the quality and effectiveness of TB services at the level of primary health-care. At present, these are considered potential indicators

Fig. 12. Proportion of pulmonary TB patients with GeneXpert MTB/RIF testing before and after the introduction of the sputum transportation system in pilot districts, Chui region



for inclusion in the routine system of monitoring and evaluation (M&E) of service quality through the Mandatory Health Insurance Foundation. Development of the TB laboratory information system to include a section on specimen transportation is currently in progress. This will allow assessment of the timeliness of the necessary laboratory tests.

Portugal. Towards TB elimination: how to reach the homeless population in urban centres?

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Background

TB remains a major global health problem *(1)*. Although Portugal has recently reached the level of a low-incidence country *(21)*, it remains one of the countries with the highest TB burdens in the European Union. An action framework for the elimination of TB in low-incidence countries has been recently launched and, among other priorities, highlights the need to address the most vulnerable and hard-to-reach groups *(22)*. In addition to being hard to reach by conventional TB control methods, homeless people are considered vulnerable to TB because of several risk factors that affect transmission, diagnosis, treatment and outcome *(23)*. Data from 2011 shows that TB incidence was five times higher among the homeless population in Portugal than among the general population *(24)*.

In Portugal, a network of TB outpatient centres within the National Health Service is responsible for diagnosing and treating TB and for screening at-risk populations. There is no established active screening programme for homeless people. The existing strategies are based on passive screening and screening for TB before admission to a homeless shelter. The latter is based on referral of the homeless individual by these institutions to TB outpatient centres and participation in a scheduled appointment. Although recommended, it is neither mandatory nor routinely performed.

Description of the good practice

Porto, the second largest urban centre in Portugal, is considered a TB endemic area. As part of a public health initiative to develop TB eradication strategies in Porto, we designed an active TB screening programme for homeless people, in cooperation with local public health services, the TB outpatient centre and institutions dedicated to caring for the homeless population. These institutions help people in their facilities, such as shelters, social canteens and day care centres, as well as on the streets, and play a very important role in supporting the health-care of these individuals *(25)*.

The screening programme included several strategies: formal education and awareness campaigns; voluntary screening at a mobile X-ray unit (MXU); and screening upon admission to a shelter and periodically screening of homeless individuals living in shelters, both mandatory.

Formal training and awareness campaigns

The research team developed several educational workshops for workers in homeless care organizations, in which a basic approach to caring for TB patients was presented. This included education on the risk of different social groups, clinical symptoms that should prompt referral to the TB outpatient centre, diagnosis and treatment. Infection prevention measures with adequate face masks and procedures for transporting homeless persons with presumptive TB were also explained. The workers were also trained to cope with TB treatment adherence and possible side-effects in order to promote case holding and successful TB treatment.

In close cooperation with the above-mentioned institutions, we also performed direct actions to increase the awareness of homeless people of the programme and improve their compliance; these actions included the distribution of brochures explaining the benefits of a targeted TB screening programme and information on scheduled screenings.

To increase awareness of the general population, we also created a website and a Facebook page with periodic messages, newsletters and project updates. This information was also disseminated through local newspapers and social media websites.

MXU screening

Participation in MXU screening was voluntary. In order to achieve the highest possible coverage rate, screening locations, dates and times were selected based on information provided by the homeless care organizations related to the locations of the facilities, along with the areas occupied by homeless people and their daily routine. These screening details were announced in advance to homeless persons by workers from the organizations and other project partners.

The screenings were performed in an MXU; homeless individuals were observed by a nurse experienced in TB, completed a questionnaire and had a chest X-ray. The questionnaire collected demographic data, history of TB (personal history and history of closely related individuals), history of risky behaviours and the five main symptoms (persistent cough lasting at least three weeks; fever, usually mild and mostly at nights; weight loss resulting in a changed fit of clothing; night sweats; and bloody sputum). All chest X-rays were immediately reviewed by the radiology technician and afterwards by a medical radiologist. Individuals with a clinical suspicion of TB (two or more symptoms in the questionnaire) or a radiological suspicion of TB were asked to provide two sputum samples for fluorescence smear microscopy and mycobacterial culture, which were collected in an outdoor nearby place. All suspected cases were referred to the TB outpatient centre with a scheduled appointment and accompanied by a social worker who had received training from the research team.

Screening in shelters

The questionnaire was given to each homeless person before admission by the person in charge of the shelter. A chest X-ray was performed in the MXU within the next four weeks, according to schedule. For each resident in these shelters, the questionnaire was completed twice a year and the chest X-ray performed once a year.

Genetic characterization of Mycobacterium tuberculosis

In addition to the screening programme, all samples from TB patients diagnosed in Porto since 2014 have been genetically characterized to determine the transmission chains and improve TB control strategies *(26)*.

The screening programme we designed and implemented engages several areas of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*.

- Pillar 1:
  - Integrated, people-centred care and prevention – some components;
  - Systematic screening of contacts and high-risk groups;
  - Early diagnosis of all forms of tuberculosis; and
  - Equitable access to quality treatment and continuum of care for all people with tuberculosis, … and patient support to facilitate treatment adherence.

- Pillar 2:
  - Bold policies and supportive systems – some components;
  - Political commitment with adequate resources, including universal health coverage policy; and
  - Social protection, poverty alleviation and actions on other determinants of tuberculosis.

- Pillar 3:
  - Intensified research and innovation – one component; and
  - Discovery, development and rapid uptake of new tools, interventions and strategies (including new drugs and regimens).

This screening programme provides systematic TB screening and early TB diagnosis and facilitates access to health-care services.

The combination of homelessness with other risk factors, such as alcohol and drug abuse, may increase the risk of poor treatment compliance, with the associated risk of drug resistance development and disease transmission *(27)*. In addition, TB/HIV coinfection involves the presence of drug interactions and higher mortality rates, and may also lead to toxicity development *(28)*. The TB outcome also tends to be worse for homeless people *(29)*. The established partnerships with homeless care organizations are essential to support the management of possible side-effects and adherence to treatment.

For the success of the screening programme, a joint effort from several stakeholders is essential, including political commitment to allocate the necessary resources, a well-aligned local public health department and TB outpatient centre, and global commitment of all involved organizations. Thus, The *M. tuberculosis* genotyping research project represents an essential

tool for guiding and tailoring TB control strategies in Porto.

Evidence of impact

We first implemented the project in Porto, where the reported incidence was 1015 new cases per 100 000 homeless persons *(30)*. TB transmission in shelters is considered a common source of transmission among homeless people. The project minimized this problem: genetic characterization of TB strains among homeless people showed that the strains were not related, suggesting that this transmission route was blocked. In Porto, homeless individuals are reported to be diagnosed significantly faster than non-homeless people *(31)*. The screening programme was considered a feasible strategy by all concerned organizations and is now routinely performed among homeless people. the Genetic characterization of *M. tuberculosis*, along with epidemiological and georeferencing information, is an ongoing effort that provides a more detailed scenario of the dynamics of TB transmission between homeless individuals and their interaction with the general population affected by TB.

Sustainability of the good practice

We developed a screening programme for the homeless population that was integrated into the existing public health service system and coordinated with homeless care organizations. The programme contributed to the early detection of TB and to treatment compliance, as well as improving access to public health services for the homeless population.

The research team implemented and monitored the programme and social organizations that support this population provide ongoing continued support. The established partnerships are of paramount importance for the long-term maintenance of this screening programme, as well as for promoting adherence to treatment. Previous research indicated that this joint effort, with multiple local partners and stakeholders, yielded excellent results for other social groups at an increased risk of TB *(26)*. The screening programme has proven to be sustainable and effective, with no additional costs. We intend to extend it to other urban areas.

M. tuberculosis genotyping immediately after diagnosis would enable the identification and characterization of otherwise undetectable transmission chains, leading to the early detection of infected individuals. This would become an essential strategy to support refined TB control strategies in Porto, with sustainable costs for Public Health in Portugal.

Republic of Moldova. Use of the GeneXpert MTB/RIF assay decreased the treatment delay for MDR-TB patients in the Republic of Moldova

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Background

Through its End TB Strategy *(4)*, WHO aims to end the global TB epidemic by 2035. Even considering the current worldwide declining trend in TB incidence and mortality, achieving the 2035 elimination targets could be unrealistic if effective solutions for the current challenges are not found.

By far, MDR-TB is one of the hardest problems to be overcome on the way to TB elimination. The most critical aspects of efficient MDR-TB control are underdiagnosis, lack of effective drugs and an extremely long treatment duration, which together lead to a very low treatment success rate. Interventions for scaling up the early diagnosis of MDR-TB should have special priority because only 27% of all worldwide estimate MDR-TB cases are currently detected. Thus, early TB diagnosis including universal DST is a key component of the End TB Strategy. Prompt detection and assessment of the *Mycobacterium tuberculosis* resistance pattern could reduce the time to the initiation of adequate treatment and reduce the risk of spreading MDR-TB in the community. Therefore, implementation of rapid TB molecular diagnostics could be crucial for accelerating the current trend of decline in the TB epidemic.

In December 2010, WHO endorsed the use of the GeneXpert MTB/RIF assay for detecting *M. tuberculosis* and rifampicin resistance. GeneXpert MTB/RIF is a commercial diagnostic test based on the polymerase chain reaction (PCR) that has demonstrated high sensitivity and specificity in detecting *M. tuberculosis* and rifampicin resistance in an initial multicentre demonstration study and a later meta-analysis. Using

a cartridge-based technology, the GeneXpert machine can be placed in lower level laboratory facilities with similar requirements to those of smear microscopy. This should theoretically improve access to testing and reduce delays in diagnosis and adequate treatment initiation.

The Republic of Moldova is high burden TB and MDR-TB country, with a TB incidence of 83.3 cases per 100 000 population and an MDR-TB prevalence of 26.5% among new cases and 51.3% among re-treatment cases in 2017. Since 2012, the Republic of Moldova has received TB REACH support for the programmatic implementation of GeneXpert MTB/RIF rapid testing for TB diagnosis. One of the expected benefits from this intervention was to reduce the time from TB diagnosis to MDR-TB confirmation for prompt MDR-TB treatment initiation. The current study aimed to assess the length of treatment delay for MDR-TB patients before and after the implementation of GeneXpert MTB/RIF testing in the Republic of Moldova.

Description of the good practice

The treatment delay for all MDR-TB cases registered in the Republic of Moldova during the 2011–2015 period was assessed. Treatment delay was defined as the time between TB diagnosis (before confirmation of the drug-resistance pattern) and initiation of MDR-TB treatment. A yearly comparison of treatment delay was made before and after GeneXpert MTB/RIF assay implementation, involving more than 4000 MDR-TB cases. The median treatment delay in 2011 (the year prior to implementation of the GeneXpert MTB/RIF assay) was 42 days. In the first year of the introduction of GeneXpert MTB/RIF testing into clinical practice (2012), no significant reduction in the treatment delay was achieved (32 days). However, a progressive reduction in treatment delay was registered over next three years: the treatment delay was 20 days (range 5–53 days; $P < 0.001$) in 2013; eight days in 2014 (2–28 days; $P < 0.001$); and seven days in 2015 (2–18 days; $P = 0.02$). The number of GeneXpert MTB/RIF tests performed correlated strongly with the reduction in treatment delay.

Evidence of impact

Implementation of GeneXpert MTB/RIF rapid testing led to a significant reduction in treatment delay for MDR-TB cases in the Republic of Moldova, leading to better clinical management for these cases

Sustainability of the good practice

Implementation of GeneXpert MTB/RIF rapid testing will continue in the coming years to cover all territories of country. Financing of this activity is partially covered by the Global Fund to Fight AIDS, Tuberculosis and Malaria and will be fully covered by the Moldovan Government after 2020.

Russian Federation. Use of rapid molecular tests to increase the efficacy of M/XDR-TB treatment

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Central Tuberculosis Research Institute, Moscow

Background

Despite the declining trend in the TB epidemiological situation in the Russian Federation, WHO has included the Russian Federation in the list of countries with a high MDR-TB burden for the past 15 years.

Over the past 10 years, the proportion of newly diagnosed MDR-TB patients in the Russian Federation increased from 11.4% to 26.8%, and in some areas reached 30% or more. The most dangerous type of MDR-TB is XDR-TB. According to WHO data, 9.5–9.7% of all MDR-TB cases are XDR-TB. However, a sampling study showed that the proportion of XDR-TB patients in the Russian Federation exceeds the WHO estimate, at 14.3%.

Based on official statistics, the MDR-TB treatment success rate in the Russian Federation is currently not high enough, at 47.6%. The effectiveness of XDR-TB treatment, both globally and in the Russian Federation, is extremely low, at about 26%.

The low success rate for M/XDR-TB treatment is largely due to the late detection of drug resistance and, as a consequence, the late start of adequate chemotherapy. This leads to the development of disseminated destructive changes in the lungs, a lengthy time period needed for the cessation of bacterial excretion and the development of chronic conditions.

At the same time, owing to the achievements of molecular genetics, high-tech rapid methods for identifying *Mycobacterium tuberculosis* resistance to a number of FLDs and SLDs were developed. The tests are based on PCR-based detection of mutations associated with drug resistance.

The widespread use of rapid molecular tests in the diagnostic algorithm provides a timely indication of adequate chemotherapy regimens for M/XDR-TB patients and, thereby, significantly improves the treatment success rate.

Description of the good practice

All patients hospitalized in the inpatient units of the Central TB Research Institute (CTRI) undergo a mandatory diagnostic examination, which includes one of the molecular genetic tests (for two diagnostic specimens) designed to detect *M. tuberculosis* DNA and identify mutations associated with resistance to rifampicin (at least) and other anti-TB drugs. For this purpose, the CTRI uses cartridge-based GeneXpert MTB/RIF technology, line probe assays and domestic test systems based on real-time PCR technology.

In addition, liquid (MGIT) testing of the same specimens is done for all TB patients, with subsequent phenotypic DST using the proportion method in the automated BACTEC MGIT 960 system. the results of the rapid molecular DST of diagnostic material help in designing appropriate treatment regimens, which can be adjusted later, if needed, based on the results of MGIT liquid culture and DST. This practice can significantly improve the effectiveness of chemotherapy for M/XDR-TB patients through the timely indication of adequate treatment regimens. This practice is consistent with comprehensive people-centred TB care and prevention and is relevant to addressing the early diagnosis of all forms of TB and ensuring universal access to DST, including with the use of rapid methods.

Since the task of early TB diagnosis and ensuring universal access to DST with the use of rapid tests is part of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7),* in order to ensure the sustainable implementation of this practice, the CTRI administration purchased new equipment and provided an uninterrupted and sufficient supply of all necessary reagents and test systems to enable the microbiological laboratory to perform the required tests for all patients of the CTRI clinic.

In addition, in accordance with the TB Action Plan, the CTRI intensified research efforts to develop new domestic innovative molecular genetic test systems for the early detection of *M. tuberculosis complex* and non-tuberculous mycobacteria directly from the diagnostic material. At present, a domestic test system (based on real-time PCR technology to allow the detection of *M. tuberculosis* DNA in specimens and identify mutations associated with the resistance to isoniazid, fluoroquinolones and rifampicin) has been developed and is being introduced into daily practice.

Evidence of impact

To confirm the high efficiency of this practice, we conducted a number of studies and obtained the following results.

To study the impact of early detection of rifampicin resistance on MDR-TB treatment success, a benchmark assessment of chemotherapy effectiveness in in pulmonary DS-TB patients and RR-TB patients was performed using the cartridge-based GeneXpert MTB/RIF assay followed by regimen adjustment according to the liquid DST results obtained using the BACTEC MGIT 960 system. The collected data were compared with treatment outcomes for the control group of MDR-TB patients who did not undergo rapid molecular testing and liquid DST.

The study included 185 pulmonary TB patients, of whom 130 were examined by the GeneXpert MTB/RIF assay. All patients were divided into three groups.

- **Group 1** included 76 patients with rifampicin-susceptible TB, as identified by GeneXpert MTB/RIF testing. These patients were assigned a standard first-line chemotherapy regimen, which was subsequently adjusted based on the results of phenotypic DST on liquid medium in the BACTEC MGIT 960 system.

- **Group 2** included 54 patients with RR-TB, as identified by GeneXpert MTB/RIF testing. This group initially received the MDR-TB treatment regimen, with subsequent adjustment according to the results of the DST on liquid medium in the BACTEC MGIT 960 system.

- **Group 3** was retrospectively composed of patients (55 people) to whom the GeneXpert MTB/RIF assay and other molecular tests for diagnosing RR-TB

were not applied. This group of patients was initially assigned empirical first-line treatment regimens, with subsequent adjustment at two to three months after treatment initiation based on the results of DST on solid LJ medium by the method of absolute concentrations.

In Group 1, the treatment regimen was adjusted based on the results of MGIT liquid culture and DST (BACTEC MGIT 960) in 13 cases (17.1%). For seven patients, the chemotherapy regimen was changed because of detection of resistance to isoniazid and a combination of resistance to isoniazid and aminoglycoside. In patients diagnosed with ethambutol monoresistance, ethambutol was replaced by an aminoglycoside. Two patients were diagnosed with MDR-TB by phenotypic DST and started on MDR-TB treatment. The average time for chemotherapy adjustment for Group 1 patients was four weeks from treatment initiation.

In Group 2, the treatment regimens based on the results of liquid culture (BACTEC MGIT 960) and DST was adjusted for 24 patients (44.4%). Seven pre-XDR-TB patients with resistance to fluoroquinolones and 11 XDR-TB patients were detected; therefore, these patients were switched to the XDR-TB regimen. For six patients, owing to the detection of resistance to aminoglycosides (amikacin, kanamycin), these drugs were replaced with capreomycin. The average time for chemotherapy adjustment was four weeks, similar to in Group 1.

Group 3 patients initially received standard first-line treatment, but chemotherapy adjustment was required for all 55 patients (100%). For 31 MDR-TB patients and 14 pre-XDR-TB patients, the chemotherapy regimen was changed to the MDR-TB regimen. The XDR-TB regimen was administered to the remaining 10 XDR-TB patients. The average time for chemotherapy adjustment was 10 weeks.

An important component of the evaluation of treatment effectiveness was the trend in bacterial conversion. Prior to treatment initiation, the presence of bacterial excretion (confirmed by fluorescent microscopy) was reported in 64.5% of Group 1 patients (49 out of 76), 81.5% of Group 2 patients (44 out of 54) and 85.5% of Group 3 patients (47 out of 55). Bacterial excretion confirmed by sputum culture examination was reported in all Group 2 and 3 patients. A lack of bacterial excretion (according to culture results) was reported only in 6.6% of Group 1 patients (five out of 76), that is, the GeneXpert MTB/RIF assay results for those patients were the only source of information on rifampicin resistance.

The predominance of previously treated patients and patients with the disseminated destructive lung disease in Groups 2 and 3 can be explained by the higher proportion of patients with bacterial excretion in these groups compared with Group 1.

Sputum conversion (confirmed by fluorescence smear microscopy) was achieved more quickly in Group 1: in 80% of patients, AFB were not identified in sputum at two months after treatment initiation. Absence of AFB was reported in all patients in Group 1 after six months of treatment (Fig. 13). Slower rates of sputum conversion (confirmed by smear microscopy) were observed in Group 2: after two months of treatment, AFB were not identified in sputum samples from 64% of patients; however, after six months of chemotherapy, AFB were not reported in any of the patients. Therefore, the rates of sputum conversion confirmed by microscopy examination were comparable in Groups 1 and 2 ($P_{1-2} > 0.05$).

In Group 3, the situation was different. After one month of treatment, no sputum conversion (confirmed by microscopy examination) was reported for any patient; the sputum conversion rate was only 17% after two months of chemotherapy and 49% after six months. The difference in sputum conversion rates at two and six months was significant ($P_{1-3} < 0.01$, $P_{2-3} < 0.05$).

The sputum conversion rate for all groups was slower when confirmed by sputum culture examination than by microscopy examination. The best results were reported for Group 1 patients: after six months of treatment, no bacterial growth was present in any patients. In Group 2, the results were not as good, but by the end of six months of treatment all patients achieved complete bacterial conversion ($P_{1-2} > 0.05$) (Fig. 14). The rate of bacterial conversion was slower in Group 3 patients: after two months of treatment, bacterial conversion was achieved in only 5.5% of patients (compared with 72% and 52%, respectively, in Groups 1 and 2); and after six months of treatment, sputum conversion was reported only in 36.4% of patients ($P_{2-3} < 0.01$).

Therefore, bacterial conversion was reported to occur more quickly and at a higher frequently in

Fig. 13. Rates of and time for sputum conversion, as confirmed by fluorescence microscopy, Groups 1–3

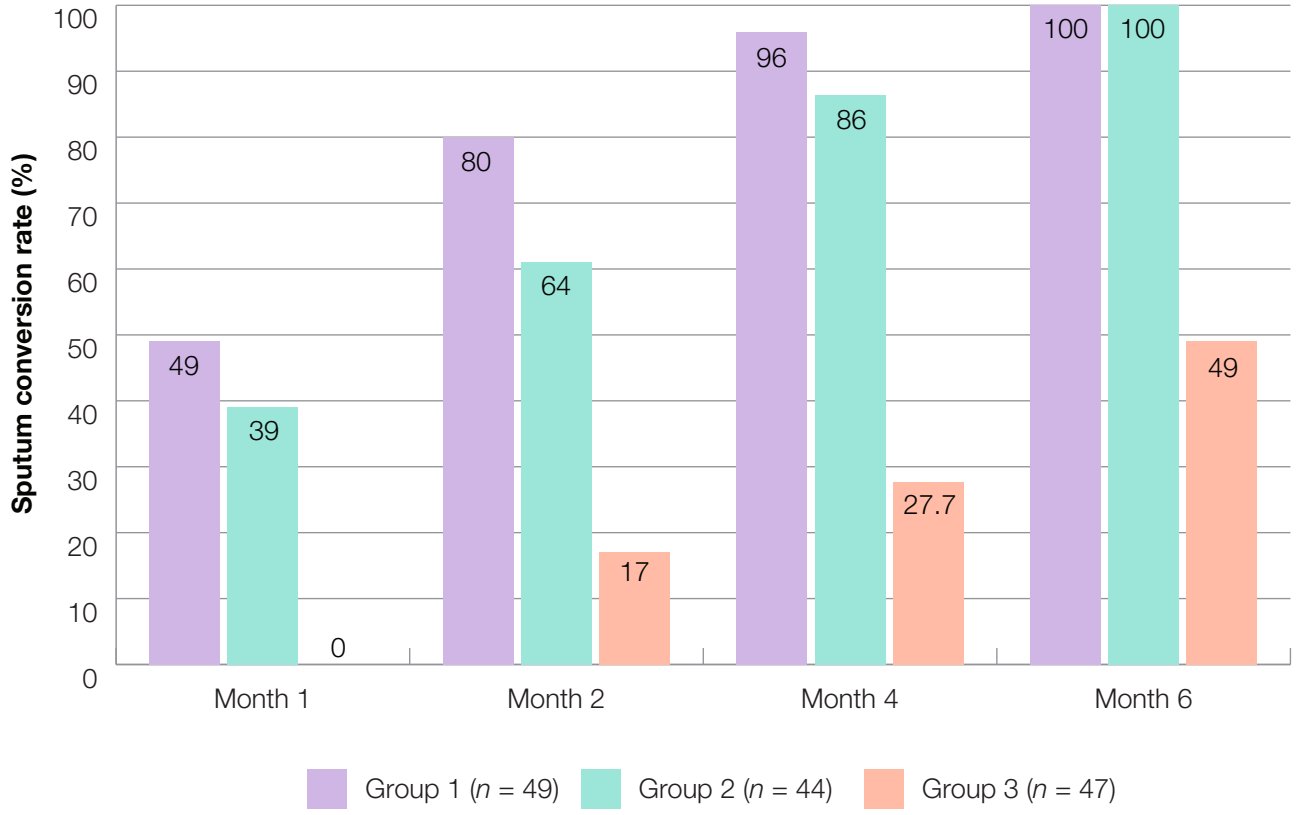
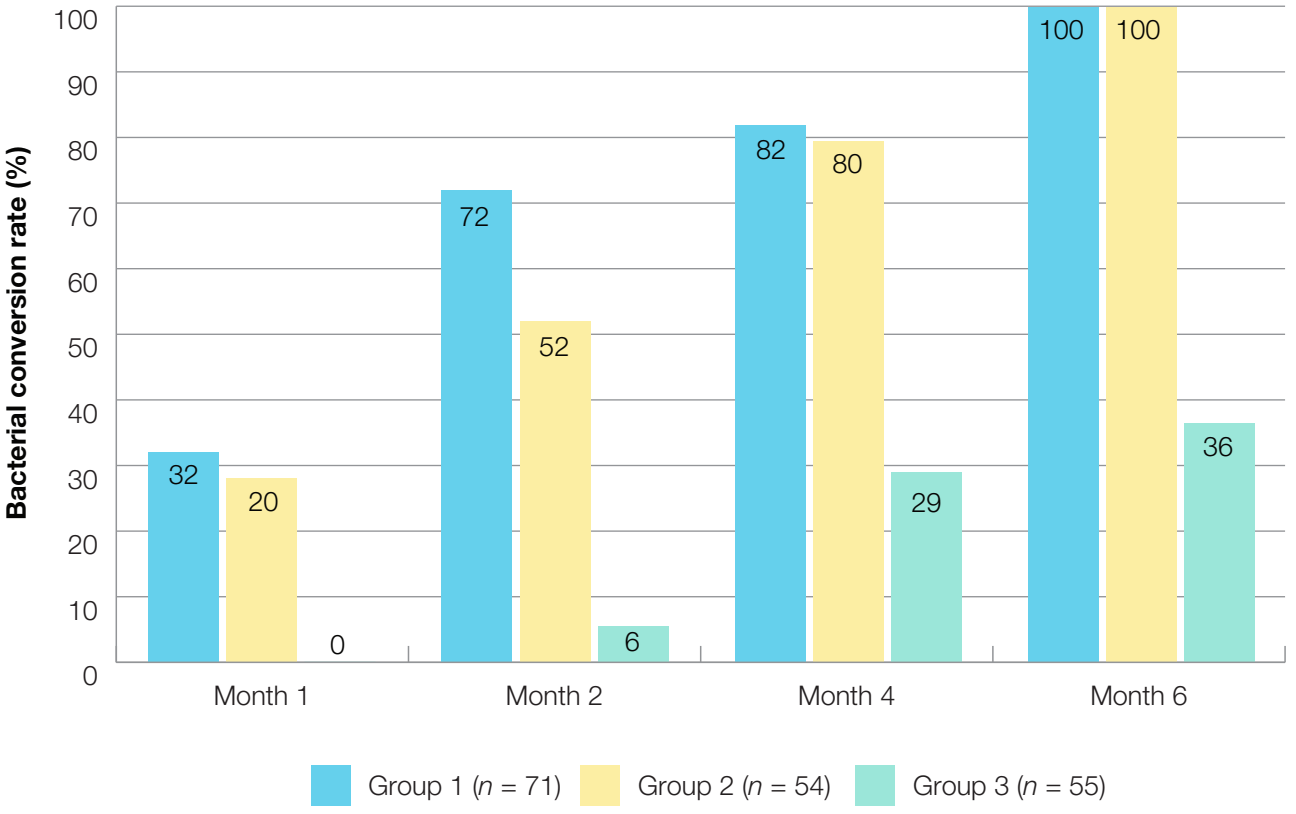


Fig. 14. Rates of and time for bacterial conversion, as confirmed by sputum culture examination, Groups 1–3



Group 2, in which MDR-TB patients were detected by the GeneXpert MTB/RIF assay and treated with the MDR-TB regimen from day 1 than in Group 3, in which MDR-TB patients had a delayed initiation of adequate chemotherapy based on the solid DST results: after six months of treatment, the sputum conversion rates in Groups 2 and II were 100% and 49% ($P < 0.05$), respectively, when confirmed by microscopy examination and 100% and 36.4% ($P < 0.05$), respectively, when confirmed by sputum culture examination.

It was also noted that destructive changes in the lungs healed more frequently in MDR-TB patients on an adequate chemotherapy regimen designed in accordance with rapid GeneXpert MTB/RIF testing results for rifampicin resistance (with subsequent adjustment of treatment regimens based on results of liquid culture (BACTEC MGIT 960) and DST) compared with the group of patients on empirical first-line chemotherapy with subsequent adjustment of treatment regimens based on the results of solid culture examination of sputum: after six months of treatment, healing was achieved in 92% and 63%, respectively ($P < 0.05$). Thus, based on the study results, it can be concluded that the initial rational treatment of DS-TB and MDR-TB patients leads to bacterial conversion and healing of destructive changes in the lungs in a high proportion of patients and within a shorter time period compared with cases with delayed initiation of adequate treatment.

It should be noted that during this study, there was 100% concordance between the rifampicin resistance results obtained by GeneXpert MTB/RIF testing and the frequency of MDR-TB detection by the DST in liquid medium of BACTEC MGIT 960. No RR-TB cases with resistance to isoniazid were detected.

A similar study was performed for line probe assays to assess the role of this DST method in the effective treatment of pulmonary XDR-TB patients. The retrospective study included 175 XDR-TB-patients who received SLD treatment from 2008 to 2015. Treatment regimens of this XDR-TB patients included 32 various combinations that were administered after DST results were obtained. On average, 6.1 TB medicine were used per regimen: *p*-aminosalicylic acid was in the regimen for 132 patients (75.4%), amoxicillin/clavulanate for 64 (36.6%), Bdq for 21 (12.0%), capreomycin for 175 (100%), clarithromycin for 64 (36.6%), cycloserine for 139 (79.4%), ethambutol for 49 (28.0%), levofloxacin for 21 (12.0%), linezolid for 77 (44.0%), moxifloxacin for 141 (80.6%), ofloxacin for 34 (19.4%), prothionamide for 58 (33.1%) and pyrazinamide for 105 (60.0%).

In 30 sputum smear-positive XDR-TB patients included in the study, line probe assays were used directly on diagnostic material to confirm XDR-TB and indicate adequate chemotherapy regimens. Based on the test results, all patients were assigned individualized treatment regimens which were later adjusted in accordance with the phenotypic DST results (liquid culture, BACTEC MGIT 960). After 12 months of treatment, 28 patients achieved bacterial conversion and only two had ongoing bacterial excretion.

For the remaining 145 sputum smear-positive patients, the individualized treatment of XDR-TB was assigned with a delay based on the DST results, obtained by culture method. Bacterial conversion after one year of treatment was achieved in 96 patients, while bacterial excretion persisted in 49 patients (Table 6).

Thus, the study into the impact of line probe assays on the effectiveness of chemotherapy showed that use of this method for rapid XDR-TB detection allows the timely initiation of adequate treatment, which significantly increases the chances of effective treatment, as defined

Table 6. Rates of bacterial conversion and bacterial excretion in XDR-TB patients based on sputum culture examination after 12 months of chemotherapy

Line probe assay	XDR-TB patients (*n* (%))			OR	95% CI	*P* value
	Total	Bacterial conversion	Bacterial excretion			
Applied	30 (100)	28 (93.3)	2 (6.7)	7.15	1.63 – 31.24	<0.05
Not applied	145 (100)	96 (66.2)	49 (33.8)			

CI: confidence interval; OR: odds ratio.

by bacterial conversion after 12 months of therapy confirmed by sputum culture examination.

In conclusion, the study highlighted that the use of rapid molecular genetic tests for detecting drug resistance in diagnostic material and the immediate initiation of individualized treatment with subsequent adjustment of treatment regimens based on the phenotypic DST in liquid medium ensures highly efficient M/XDR-TB treatment.

Sustainability of the good practice

Currently, this practice has been introduced into practice and is regularly used for all patients under treatment at the CTRI. As the National Centre of Excellence within the WHO network of supranational TB reference laboratories, the CTRI Microbiology Division shared its experience in the use of rapid methods of TB diagnosis with the Russian TB institutions.

Since 2015, molecular genetic methods (along with liquid sputum culture) have been officially included in the algorithms for microbiological TB diagnosis by the Executive Order of the Russian Ministry of Health and are mandatory for diagnostic TB examination throughout the country.

Tajikistan. Mentoring programme for quality improvement in the laboratories of eastern and south-eastern Europe

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Background

The burden of TB remains high in Tajikistan: the TB notification rate increased from 32.3 cases per 100 000 population in 1996 to 80.4 cases per 100 000 population in 2009. This was followed by a decrease to 59.8 cases per 100 000 population in 2017, made possible by comprehensive support from international partners.[6] The TB mortality rate was 3.0 cases per 100 000 population in 2000, 6.3 cases per 100 000 population in 2009 and 4.3 cases per 100 000 population in 2017. According to WHO estimates, the MDR-TB rate in 2015 was 22% and 45% among new and repeatedly treated TB cases, respectively.

The main reason for the high TB burden is thought to be a reservoir of infection in the population, the high drug resistance of *Mycobacterium tuberculosis* strains, and social factors including poor nutrition, migration and high HIV prevalence.

The state institution, the National Public Health Laboratory, was built with technical assistance from the United Nations Development Programme and financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria. In line with Executive Order No. 463 of 12 August 2013 and Ministry of Health and Social Protection Order No. 605 of 29 July 2014, the National Public Health Laboratory performs the following TB tests: iLED microscopy, GeneXpert MTB/RIF assay, GenoType MTBDR*plus* assay, and culture in liquid MGIT and solid LJ medium.

The National Public Health Laboratory provides diagnostic TB services to the population of Dushanbe, 13 Districts of Republican Subordination and the penitentiary institutions. A well-functioning, sustainable laboratory service that complies with international quality and safety requirements is an integral part of the strong health system and is essential for improving public health. Laboratory test results provide a reliable basis for the scientifically sound control of disease outbreaks, robust monitoring of adverse events related to the use of drugs and vaccines, and the early treatment of acute and chronic diseases.

In 2012, the WHO Regional Office for Europe, together with its partner – the WHO Collaborating Centre for Laboratory Strengthening at the Royal Tropical Institute, Amsterdam – developed and launched the Better Labs for Better Health project, focused on improving the laboratory services and thereby the health systems and health of the population in the countries of eastern Europe and central Asia. The first mission was conducted in July 2016 by technical staff of the WHO Regional Office for Europe, the coordinator of the Better Labs for Better Health mentoring programme and staff members of the WHO Country Office in Tajikistan.

[6] National TB statistics.

Description of the good practice

One of the activities within the framework of the Better Labs for Better Health initiative is the mentoring programme, aimed to support laboratories in implementation of the quality management system and preparation for accreditation according to the international quality standard ISO 15189. Within the framework of this programme, mentors visit selected laboratories in partner countries every three to four months for up to five days to provide mentoring support. During the visits, the mentors:

- train staff from participating laboratories;
- audit the current state of the laboratory quality system; and
- provide mentoring support and assistance in developing individual plans for further implementation of the laboratory quality system.

The National Public Health Laboratory performs different examinations and is interested in achieving accreditation for the following tests:

1. GeneXpert MTB/RIF assay
2. GenoType MTBDR*plus* assay
3. solid culture – LJ medium
4. liquid culture – BACTEC MGIT 960
5. iLED microscopy.

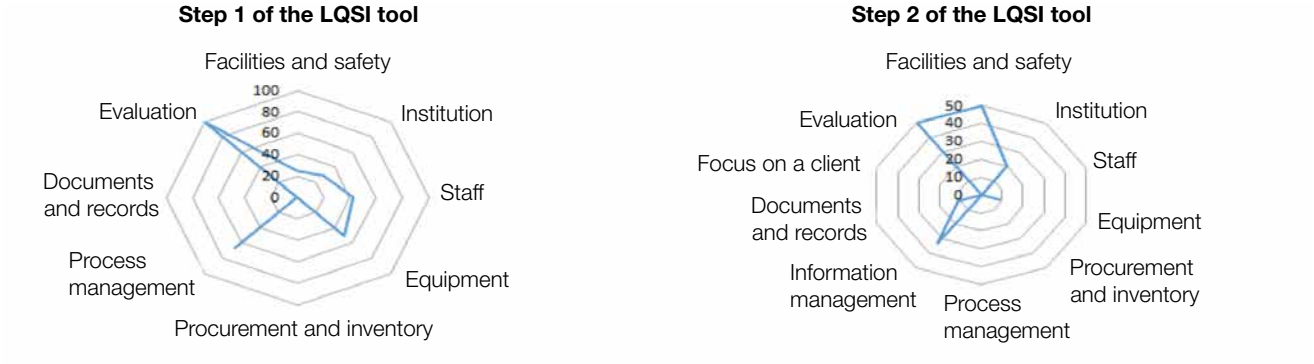
The audit was performed in line with the Laboratory Quality Stepwise Implementation (LQSI) tool. Results of the initial audit results show the percentage of confirmed and completed items in each section of the LQSI checklist (Fig. 15).

The perimeter of the National Public Health Laboratory is fenced and guarded; its rooms are spacious, with natural lighting, electrical wiring, ventilation, a cold and hot water (adapted) supply, a sewerage system, and appropriate fixtures.

The ventilation system was designed and installed in accordance with the international requirements of IS0-14644-4 (Clean Room Design Construction) and IS0-14644-1 (Classification of Air Cleanliness); a French company provides remote maintenance of the ventilation system. Air pressure in biosafety level 2 and 3 zones, as well as the temperature in refrigerators and freezers, are monitored daily and recorded on a special form. According to the available documentation and employee surveys, all laboratory premises comply with national standards and the laboratory activities are performed in line with national safety requirements. Waste disposal is in line with national standards. Laboratory technicians ensure that biosafety level 2 and 3 zones are cleaned following the approved schedule.

In line with staffing levels approved by the Ministry of Health and Social Protection of Population, the National Public Health Laboratory had 54 positions of employment as of April 2018. The laboratory equipment is appropriate for the tests being performed. However, maintenance of some equipment is unavailable due to a lack of both local companies and national

Fig. 15. Percentage of performed actions for each section according to the LQSI checklist, November 2016



Source: Internal WHO consultant report. Kalmambetova G. EECA mentoring program aimed to support the laboratories in the implementation of the quality management system and preparation for the accreditation according to the international quality standard ISO 15189.

standardization institutions capable of servicing the equipment. An equipment stocktaking schedule is in place. Every laboratory room has a list of equipment with assigned inventory numbers and laboratory staff ensure proper record keeping and storage of consumables and reagents.

The National Public Health Laboratory is equipped with computers and information can be kept in both paper and electronic format. Many standard operating procedures (SOPs) have been developed but need to be revised, updated and kept up to date.

Evidence of impact

Table 7 shows the trends in implementation of the quality plan. The total percentage of implemented activities is 64%.

In addition to the activities of the quality plan, the laboratory focused on the following aspects.

- Participation in the External Quality Assurance (EQA) programme: in 2017, the National Public Health Laboratory participated for the first time in proficiency testing, an annual event for the TB laboratory network within the framework of activities performed by the WHO Supranational Laboratories.

- A panel of 20 specimens was received from the Supranational Laboratories in Gauting, Germany. The tests were performed, and their results forwarded to the WHO Supranational Laboratories, which shared the validation results (Table 8).

Table 7. Progress in implementing activities towards LQSI

Quality plan	Activities *(n)*	Activities implemented according to the plan *((n)%)*	Activities in the process of implementation *((n)%)*	Activities pending implementation *((n)%)*
1	17	11 (65)	6 (35)	0 (0)
2	9	3 (33)	5 (55)	1 (11)
3	11	8 (72)	2 (18)	1 (9)
Total	37	24 (65)	10 (27)	3 (8)

Source: Internal WHO consultant report. Kalmambetova G. EECA mentoring program aimed to support the laboratories in the implementation of the quality management system and preparation for the accreditation according to the international quality standard ISO 15189.

Table 8. Results of the first proficiency testing in the National Public Health Laboratory, 2017

Result	LJ medium	MGIT
Number of EQA specimens	20	20
Total points	195	185
False positive	0	1
False negative	0	0
Contamination	1	1

Source: Internal WHO consultant report. Kalmambetova G. EECA mentoring program aimed to support the laboratories in the implementation of the quality management system and preparation for the accreditation according to the international quality standard ISO 15189.

According to the pilot EQA protocol, a satisfactory result is equivalent to 180 or more points. The National Public Health Laboratory demonstrated satisfactory results for both methods. However, despite this, the EQA programme revealed a serious problem of cross-contamination (false-positive results). The director of the laboratory noted that the NRL in Macheton and the National Public Health Laboratory will conduct an interlaboratory comparison of TB diagnostic methods.

The interlaboratory comparison protocol is expected to be finalized soon.

Progress has been made in several areas:

- SOPs:
  - Under the guidance of the laboratory director, the quality control team has almost completed revision of the analytical SOPs.
  - There is a need to develop SOPs for the new equipment – the GT BLOT 48 automatic hybridization device and the GenoScan reader.
  - A total of 40 SOPs have been developed and introduced into laboratory practice.

- Institution:
  - Regular meetings of the laboratory quality control team are held and minutes recorded.

- Staff:
  - The safety manager received appropriate training.
  - Training of trainers on use of the WHO LQSI tool was provided to the quality manager and a specialist responsible for equipment.
  - Four staff members of the laboratory had WHO Regional Office for Europe training on the safe transportation of infectious materials.
  - Laboratory staff participated in various training sessions on TB diagnostic methods and the quality manager took courses on computer literacy.

The biosafety officer trained in the framework of Project 53 of the European Union on Chemical, Biological, Radiological and Nuclear Risk Mitigation Centres of Excellence initiative on biosafety and biosecurity in Tajikistan and Afghanistan conducted an introductory session using training materials provided during the training courses. Training of National Public Health Laboratory staff is scheduled according to the six-month plan developed for internal training in 2018.

In addition, a training course based on eight training-of-trainer modules on transporting infectious materials and specimens is also planned. The quality manager who participated in the training of trainers course has made a commitment to training National Public Health Laboratory staff in quality control management.

Four new employees were hired, which facilitated the redistribution of time for routine tests and implementation activities of the quality management system.

- **Quality management system training:** an introductory training session on the internal audit was provided for staff of the National Public Health Laboratory. Staff members attended the presentation on the internal audit and learned about the definition of audit and the types, planning and conduct of audits.

- **Equipment and infrastructure:** the automated BACTEC MGIT 960 system was repaired and put into operation on 17 August 2017. In total, 35 SOPs (as of 18 December 2017) on the use of TB diagnostic equipment have been developed; those lacking are to be finalized and supported with maintenance documentation. SOPs are still to be developed for the multimixer, Priorclave (autoclave) and Sanyo refrigerator.

- **Evaluation:** The quality control team along with staff members received training on use of the LQSI checklist; the Gantt table with trends in the implementation of plan items and progress on use of the LQSI checklist was discussed with the head of the laboratory (Fig. 16).

Progress indicators

Based on the observed progress indicators, positive trends have become more visible. The quality control team under the guidance of the laboratory director ensured the implementation of quality plan items:

1. proportion of the developed (validated and approved) SOPs:

   a. 97.0% are analytical (48 out of 49), and there is a need to finalize and introduce SOPs for the GenoType MTBDR*s*l assay; and

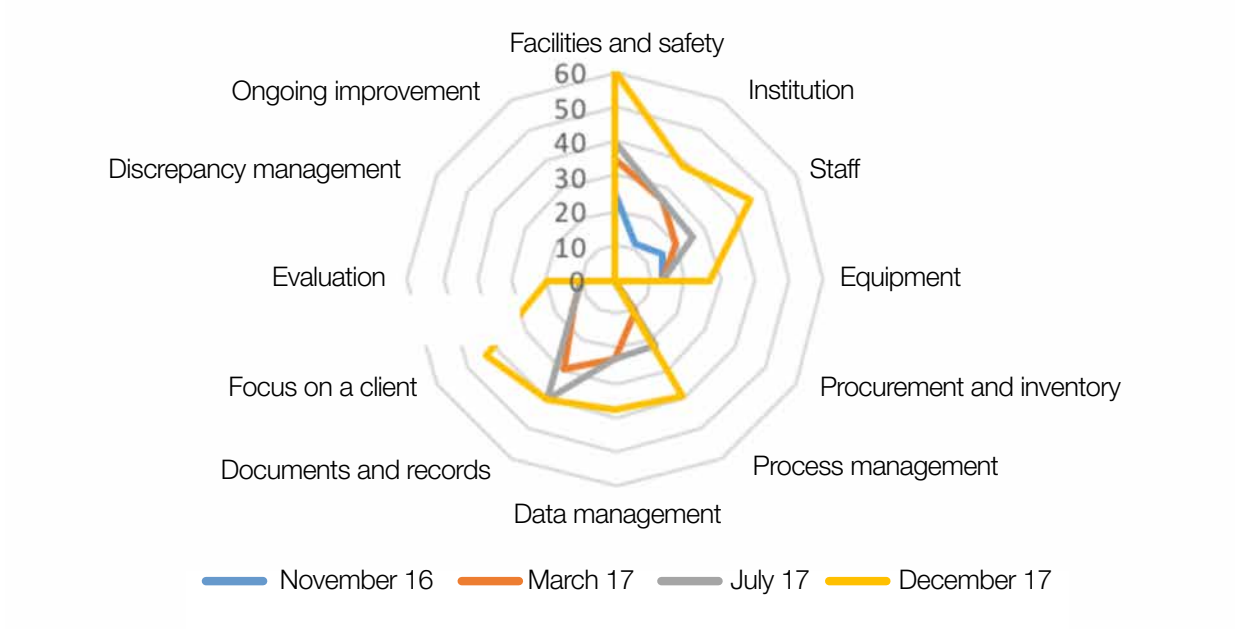
   b. 95.2% are for equipment (40 out of 42);

2. proportion of the timely implemented TB Action Plan items – 72% (Fig. 17); and

3. number of weekly meetings of the quality control teams since the third mentorship visit (on 17 July 2017) – 22 (Fig. 18).

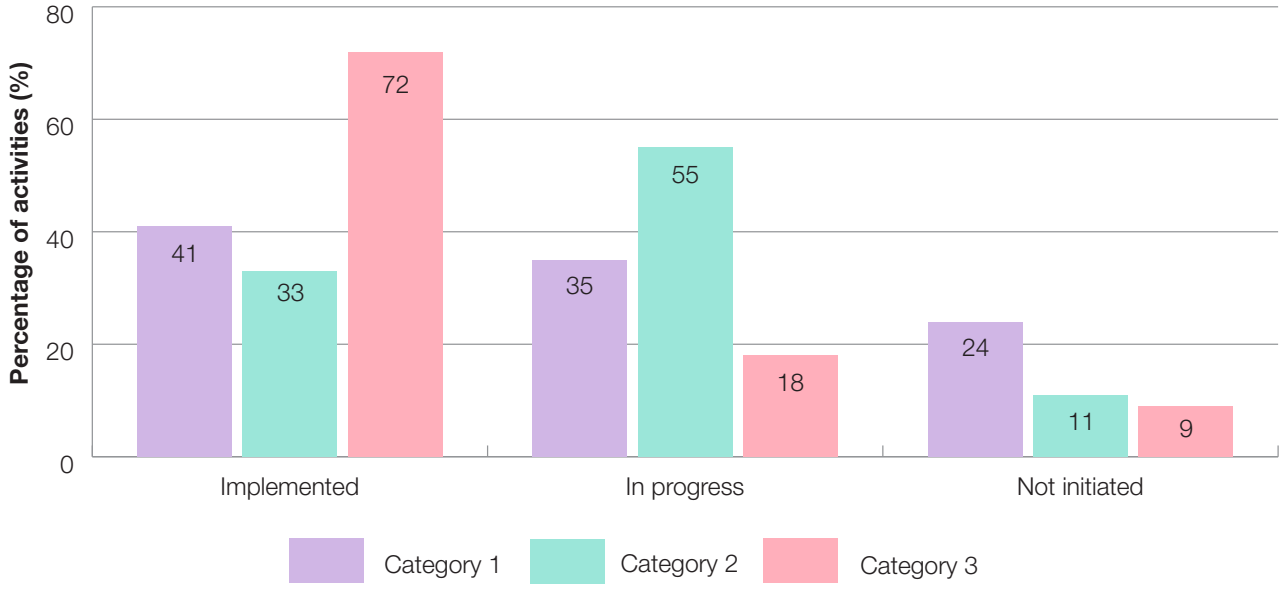
Fig. 19 shows the overall progress in implementing the LQSI checklist activities.

Fig. 16. Progress in the implementation of LQSI tool activities, all steps



Source: Internal WHO consultant report. Kalmambetova G. EECA mentoring program aimed to support the laboratories in the implementation of the quality management system and preparation for the accreditation according to the international quality standard ISO 15189.

Fig. 17. Proportion of quality plan activities implemented in a timely manner, categories 1–3

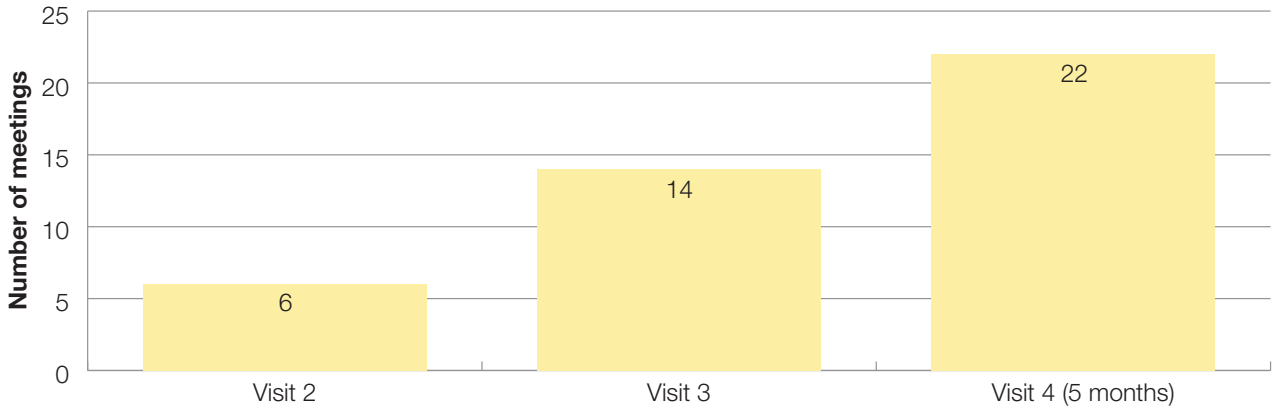


Sustainability of the good practice

Within the framework of the project, staff commitment to laboratory accreditation was demonstrated by implementation of the following activities.

- A Quality Management Team has been established and performs daily monitoring of the laboratory processes, including the infrastructure and maintenance of the available laboratory equipment. Training for staff of National Public Health Laboratory on laboratory quality management was organized, new employees received the instructions, and training on the use of all relevant documentation related to the quality control system was provided and will be repeated in the future as needed.
- SOPs for the analytical and post-analytical steps of examinations and for laboratory equipment have been developed and introduced into practice. All laboratory procedures comply with these documents, including all tests procedures for TB mycobacteria detection.

Fig. 18. Number of meetings held between visits[a]



[a] On average, every three months.

Fig. 19. Progress in implementation of the LQSI checklist activities[a]

[a] All steps.

- Quality management and policy is in place. There is no need to look for additional major resources for TB diagnostic services. It should be noted that even if the external audit and laboratory accreditation is delayed, the laboratory will be able to provide timely, safe, high-quality and reliable diagnosis in order to control TB and ensure protection against *M. tuberculosis*.

Ukraine. Expansion of access to anti-TB DST in Ukraine through the state budget

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Background

Ukraine is one of the countries with a high prevalence of MDR-TB among new and re-treatment cases (Fig. 20).

XDR-TB requires more costly treatment and has lower chances for successful outcome than MDR-TB. As approximately 15% of new MDR-TB cases are XDR-TB, it is very important to minimize the time to diagnosis and DST in order to design adequate treatment regimens.

Description of the good practice

A key factor in successful TB treatment is the availability of DST results for TB mycobacteria culture from each sputum sample. To ensure the availability of DST, all laboratories of regional TB facilities are equipped with a BACTEC MGIT 960 system, along with consumables and reagents. DST is conducted for all anti-TB drugs except for clofazimine, group D2 drugs (Bdq, Dlm) and group D3 drugs (*p*-aminosalicylic acid, amoxicillin/clavulanate, imipenem/cilastatin, meropenem).

In 2017, the level of DST coverage for laboratory-confirmed TB cases was 97%, and the level of laboratory confirmation of TB diagnosis was 67%. High rates of DST were achieved through compliance with standardized test method. The proportion method is used for DST in Ukraine – it shows the proportion of the mycobacterial population that is resistant to anti-TB drugs.

Internal quality control in TB microbiology laboratories is being performed on a regular basis to ensure reliable results of diagnostic testing. It covers media sterility, DST of control strains and check-ups of laboratory equipment.

DST procedures are also validated through regular external quality assurance of DST to FLDs and SLDs, performed by the Central Reference Laboratory for TB diagnostics of the Ministry of Health of Ukraine. Quality control for DST is regularly conducted by the Supranational Reference Laboratory in Lithuania.

Fig. 20. MDR-TB in Ukraine and other countries, 2016

Source: World Health Organization, 2017 *(1)*.

All laboratory specialists from level 3 microbiology laboratories have been trained in DST to FLDs and SLDs.

DST to linezolid was introduced into practice in 2017. In 2018, it is planned to perform DST to Bdq and Dlm.

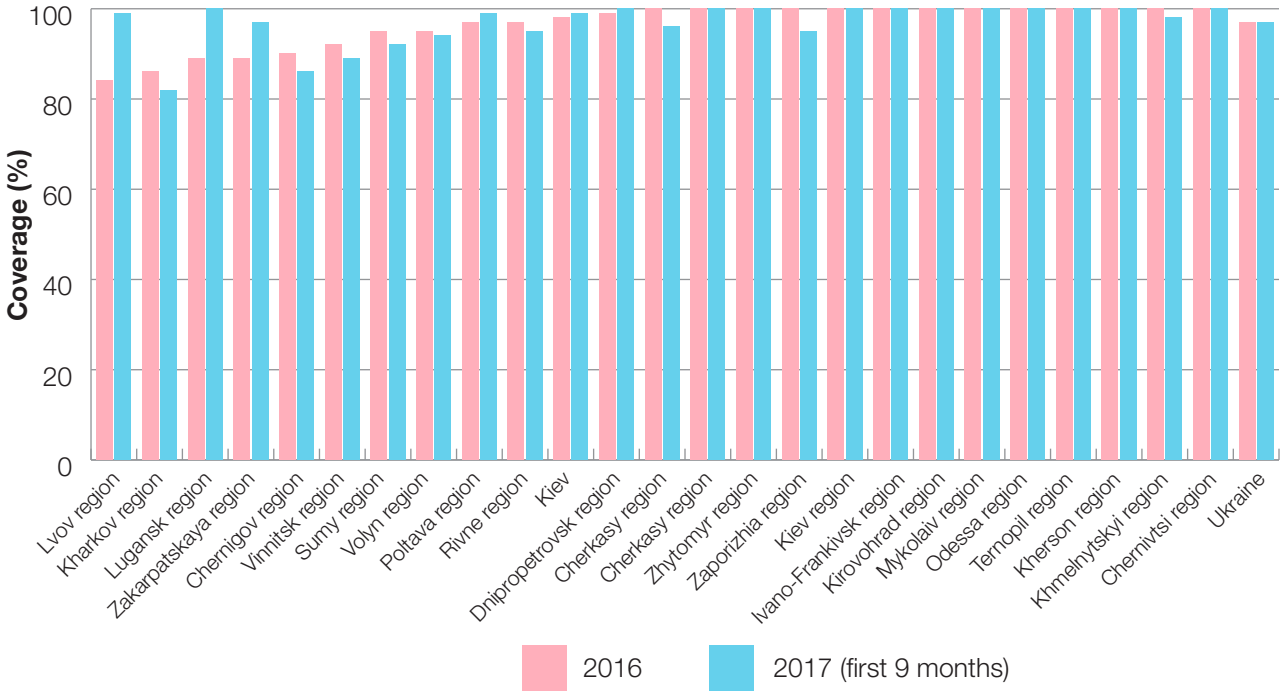
Evidence of impact

TB patients with a laboratory-confirmed diagnosis receive appropriate treatment regimens designed in line with the drug resistance profile (Fig. 21).

Sustainability of the good practice

Since 2017, the Ukrainian Government has allocated 100% of funding for the procurement of consumables for DST with the BACTEC MGIT 960 system, which guarantees the sustainability of this practice and independence from donor funding. Adequate funding is also planned for the next three years.

Fig. 21. Coverage with DST to FLDs among laboratory-confirmed TB cases



Uzbekistan. Integration of innovative technologies in TB and MDR-TB diagnosis in Uzbekistan

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Background

According to the Global Tuberculosis Report 2017, DR-TB remains a global threat *(1)*. Ten countries, including Uzbekistan, account for 75% of the difference between the number of people with DR-TB and those starting on treatment.

To ensure early diagnosis of TB and MDR-TB, the NTP introduced innovative, rapid methods for TB and DR-TB diagnosis. A plan for the phased integration of molecular methods was adopted in 2014. Since 2015, the USAID TB Control Program has provided technical assistance in training laboratory specialists and monitoring the effective use of GeneXpert MTB/RIF devices in all regions of the country. To support the effective implementation of the new methods and to monitor the overall laboratory performance, the NRL ensures regular visits by its experts to regional laboratories within the TB service. Regular, adequate maintenance and calibration of laboratory equipment

is in place; these services are being provided with the direct engagement of specialists trained by the USAID TB Control Program. Training was organized at Cepheid and the NRL, with the involvement of international experts and subsequent on-the-job training in the laboratories.

Description of the good practice

To achieve the targets of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7),* the NTP of Uzbekistan applies best practices and introduces innovative measures for TB and MDR-TB diagnosis, treatment and prevention that contribute to universal access to health-care and improvements in TB and MDR-TB diagnosis, prevention and treatment; prevent MDR-TB transmission; and achieve the Sustainable Development Goal targets.

Since 2015, the USAID TB Control Program has provided technical assistance to the NTP of Uzbekistan in implementing rapid diagnostic methods in TB laboratories, including standards for their use and the maintenance of GeneXpert devices. The USAID TB Control Program also supports the NTP in training laboratory specialists in the use of GeneXpert equipment throughout the country.

At present, the effective use of 28 GeneXpert MTB/RIF devices with a total of 104 modules is being monitored, covering up to 55% of the country's needs. A calibration plan is in place for all GeneXpert machines. Calibration is performed by self-trained regional laboratory specialists in coordination with the NRL. The test performance and requirements for maintenance of the devices are evaluated on a quarterly basis by trained specialists – NRL managers. These activities are aimed at improving access to high-quality rapid methods of the laboratory for TB and MDR-TB diagnosis. In 2017, a strategic plan for development of the TB laboratory network for 2017–2020 was developed, including scale-up of the rapid laboratory methods for diagnosis of TB and MDR-TB in TB laboratories at the district level. In 2015 and 2016, the MDR-TB detection rate was 6.8 and 6.2 cases per 100 000 population, respectively. The TB incidence and mortality rates were 46.8 and 3.1 cases per 100 000 population, respectively, in 2015 and 44.9 and 2.7 cases per 100 000 population, respectively in 2016. In the cohort of patients registered in 2013, the MDR-TB treatment success rate reported in 2015 was 54.3%; in the cohort of patients registered in 2014, the MDR-TB treatment success rate reported in 2016 was 61.4%.

Rapid GeneXpert diagnostic testing was introduced within the framework of an integrated, people-centred approach with the aim of ensuring early diagnosis of all forms of TB and improving access to the rapid tests for populations of all regions of the country.

Within the framework of GeneXpert implementation, the capacity for TB and MDR-TB diagnosis among laboratory specialists at TB institutions, as well as for the calibration and maintenance of GeneXpert devices was improved across the country. GeneXpert trainers were trained, and NRL specialists received training on the regular monitoring of GeneXpert use in practice. Special checklists are being used for monitoring and training at the workplace. These were approved by the Ministry of Health of Uzbekistan on 24 October 2014 by Executive Order No. 383.

At the level of regional TB institutions, access is provided to rapid diagnostic methods for TB and MDR-TB (in particular, GeneXpert). A comparison of laboratory performance showed an overall improvement in the bacteriological confirmation rates across all 17 laboratories that have been using GeneXpert since 2014. A 1% reduction in laboratory errors in TB and MDR-TB diagnosis and improved access to rapid tests led to a 1.4% increase in the case detection rate for DR-TB.

Early detection of TB and MDR-TB within the framework of a people-centred approach contributes to timely treatment and infection control and reduces the risk of TB and MDR-TB transmission and infection of contacts. Early detection and timely treatment of patients prevents the spread of TB, including MDR-TB.

Evidence of impact

The introduction of GeneXpert into laboratory practice as part of the comprehensive people-centred approach is aimed at achieving early diagnosis of all forms of TB and improving access to rapid testing in the regions. All laboratories of regional TB dispensaries which have successfully implemented GeneXpert testing, have reported improved access to testing and the efficient introduction of GeneXpert testing. Testing efficiency (calculated as the sum of *M. tuberculosis* positive/rifampicin susceptible and *M. tuberculosis* positive/rifampicin resistant test findings from the total number

of tests performed) improved from 27% in 2015 to 32% in 2016, with the test error rate staying below the threshold of 5% (4.8% in 2015 and 4% in 2016). Table 9 shows the results and quality of GeneXpert diagnosis for 2015–2016. The main difficulties in the implementation of rapid methods included the selection of patients for testing, the quality of the collected diagnostic specimens, compliance with standard operating procedures and the maintenance of laboratory equipment.

Table 9. TB and MDR-TB detection with GeneXpert MTB/RIF testing, Uzbekistan, 2015–2016

Tests	2015 (%)	2016 (%)
MTB+/RIF-S	16	18.5
MTB+/RIF-R	4.1	5.5
Error/invalid	4.8	3.8
Total MTB+	27	32

MTB+: *M. tuberculosis* positive; RIF-R: rifampicin resistant; RIF-S: rifampicin susceptible.

A significant improvement was achieved in the capacity of laboratory specialists, who use the new skills in practice and share their experience with colleagues from other regions.

The introduction of GeneXpert testing helped identify some challenges and problems in laboratory activity which had an impact on the vision, goals and objectives specified in the Strategic Plan for Tuberculosis Laboratory Network Development in Uzbekistan for 2017–2020.

In addition, a better understanding of the DR-TB diagnostic situation enabled projections of the laboratory equipment needs to be listed in the application to the Global Fund to Fight AIDS, Tuberculosis and Malaria, Unrequested funds 2017, to improve the laboratory diagnosis of TB and DR-TB and ensure universal access to TB diagnostic services.

Improvements were achieved in the clinical management of DR-TB, and interaction between laboratory and clinical specialists was strengthened. The laboratory specialists take an active part in the work of the regional councils, which ensure rational and targeted use of the equipment and consumables needed for rapid tests.

Sustainability of the good practice

The successful integration of rapid diagnostic methods into the TB laboratory service required careful planning and regular training, including training of national trainers in GeneXpert testing.

Regular monitoring, on-the-job training, and proper maintenance and calibration of the equipment are set up in the country. Trained laboratory specialists share their knowledge and skills in troubleshooting related to the equipment. This ensures sustainable and effective laboratory diagnosis of TB and MDR-TB in Ukraine.

1C. Equitable access to quality treatment and continuum of care for all TB (including DR-TB) patients and support for patients to facilitate their adherence to treatment

Azerbaijan. Treatment of XDR-TB in Azerbaijan

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Background

The current TB epidemiological situation worldwide is characterized by the spread of M/XDR-TB, leading to lower treatment success rates and increased TB mortality. In pulmonary TB patients, mycobacterial drug resistance develops during the long course of the disease due to non-compliance with treatment requirements and poor treatment adherence. Treatment of pulmonary MDR-TB with reserve drugs is long, expensive and often accompanied with more adverse events. The high incidence of DR-TB and the complexity of its treatment are relevant to TB epidemiology in Azerbaijan.

According to the drug resistance survey performed in Azerbaijan in 2013–2014, 12.4% of newly diagnosed TB patients have MDR-TB; of these, 9% have XDR-TB. Furthermore, 28.3% of previously treated TB patients have MDR-TB; of these, 13% have XDR-TB *(32)*.

MDR-TB treatment has been available in Azerbaijan since 2008. However, some pre-XDR-TB and XDR-TB patients have not received adequate treatment due to lack of access to new anti-TB drugs, which has led to increased TB mortality.

Description of the good practice

In April 2017, with support from the Global Fund to Fight AIDS, Tuberculosis and Malaria, new and repurposed anti-TB drugs (amoxicillin/clavulanate, Bdq, clofazimine, imipenem/cilastatin and linezolid) were procured and imported into the country. In this way, adequate, high-quality treatments to cover the full range of *Mycobacterium tuberculosis* drug susceptibility became available for XDR-TB patients. During preparation for the launch of the treatment programme for XDR-TB patients, the NTP's Working Group took a number of necessary measures. New protocols for DS-TB and DR-TB management were developed based on the most up-to-date WHO guidelines available. The responsibilities of the DR-TB Management Council for physicians at the Research Institute of Pulmonary Diseases of the Ministry of Health were expanded to include: confirmation of DR-TB diagnosis; indications for SLD treatment and for treatment with new and repurposed anti-TB drugs; adjustment of treatment regimens; decision-making on treatment tactics (duration of the intensive phase, transfer to the outpatient stage, completion of the treatment course); decision-making on patient transfer to symptomatic (palliative) treatment; assessment of the severity of adverse reactions and management of adverse events; decision-making on the need for surgical consultation and treatment; decision-making on case management in the presence of poor compliance with the treatment regimen or when patients are lost to follow-up; and presentation of the intermediate and final results of the cohort analysis (every six months). Patients are to be presented for review by the Council at least once every three months.

Lead specialists comprising members of the Council and practitioners were trained in Latvia and Belarus, where XDR-TB treatment is successful. Special directly observed treatment (DOT) sites were established to start and continue XDR-TB treatment on an outpatient basis. Particular attention was paid to ensuring all infection control measures are in place.

Phthisiologists, DOT nurses, doctors and nurses from the primary health-care sector, where treatment was planned to take place, participated in a training session

on TB detection and treatment, organized by experts from the Research Institute of Pulmonary Diseases. Training materials were developed based on the latest WHO protocols, as adapted to conditions in Azerbaijan. With support from the Global Fund and Ministry of Health, the necessary equipment and laboratory tests were purchased for treatment monitoring and the early detection of adverse reactions. At the final stage of preparation for the launch of treatment, readiness of the medical institutions specialized for XDR-TB treatment was reviewed and laboratory equipment and infection control measures were assessed.

Criteria for inclusion in the XDR-TB treatment programme included laboratory-confirmed XDR-TB diagnosis, patient consent and commitment to treatment. Given the toxicity of drugs used in XDR-TB treatment, patients aged over 65 years, with diabetes, HIV infection, hepatitis or severe renal failure, and with reported harmful use of alcohol or substance abuse were considered with caution.

On 6 June 2017, the first consultation on patient enrollment for XDR-TB treatment was held with the participation of international WHO experts. On 15 June, the first treatment programme for pre-XDR-TB and XDR-TB patients was launched.

From 15 June 2017 to 14 April 2018, 264 XDR-TB patients were presented to the Council: of these, 238 were started on treatment. As of 14 April 2018, 213 XDR-TB patients remain on treatment: of these, 45 (19%) are being treated in inpatient clinics and 168 (81%) receive outpatient care, with 59 patients receiving outpatient treatment from the start (i.e. 25% of all XDR-TB patients on treatment). It should be emphasized that outpatient treatment is available in all of the 47 regions of the country where XDR-TB patients reside.

Treatment of XDR-TB patients is monitored in both inpatient and outpatient settings. Primary health-care specialists are also involved in treatment monitoring and the early diagnosis of adverse reactions to anti-TB drugs. Thus, patients have the opportunity to be examined by a range of specialists including cardiologists, ear, nose and throat doctors, ophthalmologists, and neuropathologists, followed by the necessary clinical laboratory tests.

Evidence of impact

Before the introduction of new and repurposed TB medicines, the treatment success for XDR-TB patients was low at 23% (69 cases, 2014 cohort) *(1)*. Assessment of the first cohort of 47 patients who were started on treatment with new and repurposed TB medicines in June 2017 showed an interim treatment success rate of 62% based on culture conversion during the first six months of therapy. In addition, as noted by both patients and medical staff, TB treatment had a positive impact on the patients' quality of life and helped reduce the risk of TB infection.

Sustainability of the good practice

The Ministry of Health of Azerbaijan is supporting the provision of an uninterrupted supply with FLDs and SLDs via state funding. The registration process for new TB medicines has been initiated. The government plans to take over the procurement of new and repurposed TB medicines by 2021.

Belarus. Treatment of DR-TB in children and adolescents with new anti-TB drugs

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Background

In recent years, the TB epidemiological situation in Belarus has been characterized by a decreasing number of detected cases (from 5324 in 2012 to 3057 in 2017); over the same period, the incidence of all forms of TB decreased from 56.3 to 32.2 cases per 100 000 population. At the same time, the proportion of DR-TB cases is increasing among new TB cases, where the proportion of RR-TB increased from 33.6% in 2012 to 34.8% in 2017; the same time period among previously treated TB cases, the proportion of RR-TB ranged between 64.3% to 66.7% (65.2% in 2017).

Similar epidemic trends are also evident in children and adolescents: 54 TB cases were detected these age groups in 2012 and 38 in 2016, with most of these in adolescents aged 15–17 years (33 were aged 15 years and 25 were aged 17 years). In 2012, seven RR-TB

cases were detected among adolescents (while none were identified among children aged 0–14 years); in 2016, 18 RR-TB cases were detected among adolescents and four among children aged 0–14 years. In 2016, out of 22 registered patients aged 0–17 years, five had XDR-TB and seven had additional resistance to fluoroquinolones and second-line injectable drugs.

In June 2015, TB treatment with regimens containing new anti-TB drugs was launched in the country. Despite a lack of WHO recommendations at that time, the National Council on MDR-TB made the decision to use these drugs for TB treatment in children and adolescents.

Description of the good practice

The use of Bdq in children and adolescents started in September 2015, with the use of Dlm starting in December 2016. The indications for prescribing these drugs in each particular case was reviewed by the Council; all patients were included in the adverse events monitoring programme. The cohort of patients started on treatment with new anti-TB drugs from 1 January 2017 onwards included 16 patients on Bdq and 15 patients on Dlm. Currently, enrollment of new patients is ongoing. Cohort data collection was performed to assess the effectiveness and safety of the new anti-TB treatments in children and adolescents. Children and adolescents of both sexes aged 10–17 years (average age, 15 years) with DR-TB were included in the study. Pulmonary TB was detected in 29 patients and extrapulmonary TB in two patients. Except for one, all patients had a negative HIV status.

In the presence of clinical and radiological signs of TB combined with a lack of data on drug resistance of the pathogen (negative culture and rapid tests results were reported for three patients), indications for treatment were based on the drug-resistance patterns of patient contacts. The cohort included two MDR-TB patients, five patients with additional resistance to fluoroquinolones, five patients with additional resistance to injectable agents and 19 XDR-TB patients.

At least three new anti-TB drugs: Bdq (or Dlm), linezolid and clofazimine were added to the background treatment regimen. The basic regimen also included amoxicillin/clavulanate, moxifloxacin, prothionamide, pyrazinamide, terizidone and, less frequently, Imp. Cycloserine could also be present in regimens containing Dlm.

This practice covers at least two areas of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7).* First and foremost, it contributes to the provision of high-quality, effective treatment for children and adolescents with DR-TB and minimizes adverse drug reactions. In addition, due to the inclusion of patients in the adverse events monitoring programme, there is ongoing accumulation of knowledge about the consequences of using new anti-TB drugs in children and adolescents, specific drug indications and treatment regimen design (the latter an innovative activity).

Evidence of impact

Interim results showed a high efficiency for the new drugs in children and adolescents with DR-TB: no cases of treatment failure, loss to follow-up or death were reported during the observation. Culture conversion (in the presence of positive microscopy results at month 0 of treatment) was reported in 24 patients, occurring within one to three months.

Although all patients had adverse drug reactions during chemotherapy (mild in 68% of patients, $n = 21$; medium in 29% of patients, $n = 12$), treatment discontinuation was not required, except for the temporary withdrawal of drugs in one patient (due to the development of systemic vasculitis, a severe adverse reaction). In all cases, auxiliary medicines were used for adverse event management. Currently, eight patients have successfully completed the course of treatment: outcome for six patients, cure; and outcome for two patients, treatment completed.

In addition to building knowledge about the use of new anti-TB drugs in children and adolescents with DR-TB, this practice will contribute to at least two important aspects of TB control interventions. First, an increase in the proportion of patients with early culture and sputum conversion is expected in the evaluation of intermediate treatment outcomes in the national cohort of DR-TB patients aged 0–17 years. Second, the high quality of treatment and lack of resistance to Bdq and Dlm in the population of children and adolescents will help prevent TB relapse in treated patients, including in adulthood.

Data on the additional impact of this practice will be evaluated as information on treatment outcomes and occurrence of relapses accumulates over the next two to four years.

Sustainability of the good practice

Implementation of this practice does not require major costs. To date, the use of new anti-TB drugs is included in the National guidelines for treatment of drug-resistant tuberculosis and the Ministry of Health, together with the NTP, is taking measures to ensure an uninterrupted supply of these drugs. The drug procurement mechanism being improved to comply with the Sustainable Development Plan *(33)*, while ensure funding from the state budget for complementary purchases.

Owing to a relatively small annual number of DR-TB cases in children and adolescents registered in the country, as well the social and ethical priority to treat patients in this age group, these patients will have uninterrupted access to the new anti-TB drugs.

France. Multidisciplinary French Consilium for MDR-TB

Submitted by: Centre National de Référence des Mycobactéries et de la Résistance des Mycobactéries aux Antituberculeux (CNR-MyRMA)

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Background

The expertise needed to treat DR-TB is limited among physicians in low-incidence countries such as France. WHO recommends that multidisciplinary advisory bodies (consiliums) can help physicians to optimize the treatment of MDR-TB.

The French National Reference Centre for Mycobacteria and Resistance to anti-TB agents (CNR-MyRMA), located in Paris, surveys MDR-TB cases through a national laboratory network and receives MDR-TB strains for DST to SLDs.

In 1994, CNR-MyRMA showed that only 41% of MDR-TB patients achieved treatment success in France *(34)*. A subsequent prospective intervention study in 1998–1999 to evaluate potential interest in a TB consilium in the French setting showed that providing individualized patient management advice to physicians had a clear-cut benefit to outcomes *(35)*. Based on these results, CNR-MyRMA moved from the experimental consilium towards a permanent French TB Consilium for providing advice to physicians managing difficult-to-treat mycobacterial infection, including MDR-TB.

Description of the good practice

Cases are presented each month by physicians face to face (physically or via conference call) using a standardized case report form to the Consilium multidisciplinary team. which includes CNR-MyRMA microbiologists as well as pulmonologists, infectious disease practitioners, paediatricians, pharmacologists and social workers. Complete phenotypic and genotypic DST data obtained in the CNR-MyRMA laboratory on TB strains are discussed along with the clinical (e.g. comorbidities) and sociological status of each patient. Recommendations are based on national and WHO recommendations, and the consensual judgement of Consilium members. A written report is subsequently sent to the physician.

CNR-MyRMA, which set up the Consilium, continuously updates the molecular biology techniques (e.g. genomic tools such as whole-genome sequencing) to improve the quality of bacteriological data used by the Consilium.

The Consilium is also involved in approving the use of new anti-TB drugs within the compassionate use[7] programme, under the umbrella of the French drug agency (French National Agency for Medicines and Health Products Safety).

Evidence of impact

Between 2005 and 2016, the French TB Consilium organized 104 meetings (usually lasting for three to four hours and involving eight to 10 participants) and provided recommendations 786 times: 346 (44%) for treatment-naive MDR-TB cases, 323 (41%) for previously treated MDR-TB cases, 47 (6%) doe contacts of MDR-TB patients, 46 (6%) for non-MDR-TB cases and 24 (3%) patients with no available DST result. Each case was discussed by the Consilium during a mean of 2.5 meetings (3.4 for XDR-TB cases), enabling the outcome to be followed and treatment modified if needed (e.g. due to drug toxicity).

Overall, half of the MDR-TB cases diagnosed in France were submitted to the Consilium by physicians in 2005–2016 (26% in 2005, 55% in 2015), with the proportion reaching 68% in 2017. The proportion of

[7] The treatment of a seriously ill patient using a new, unapproved drug when no other treatments are available.

submitted cases was higher for the Paris region (64%) than for the rest of France (37%), and for XDR-TB cases (79%) than for pre-XDR-TB (58%) and simple MDR-TB (42%). In particular, complicated MDR-TB, pre-XDR-TB and XDR-TB cases in health-seeking migrants from eastern Europe *(36)* required numerous Consilium meetings. Since 2009, 42% of the submitted cases were prescribed treatment with new anti-TB drugs (mainly Bdq) for compassionate use.

It is notable that for an additional quarter of MDR-TB cases (the simplest ones), direct advice is provided to physicians by CNR-MyRMA members without requiring submission to the whole Consilium. Overall, for 80% of the MDR-TB cases diagnosed in France in 2017, physicians in charge of the patients had access to therapeutic counselling.

Based on regular meetings that allowed direct exchange with the physicians, work of the Consilium led to a collective increase of expertise on MDR-TB management in France.

Sustainability of the good practice

The French TB Consilium has worked continuously since 2005 and, so far, has been financially supported by French health authorities.

Remaining challenges are increasing the coverage of cases submitted to the Consilium (20% of MDR-TB cases diagnosed in France are still treated without counselling), obtaining exhaustive treatment outcome data and extending counselling to nontuberculous mycobacterial infections. An online registry is being implemented by CNR-MyRMA to facilitate patient follow-up and information sharing, including outcome monitoring.

Georgia. Introduction of new types of DOT in Georgia: video-observed treatment and a mobile outpatient clinic

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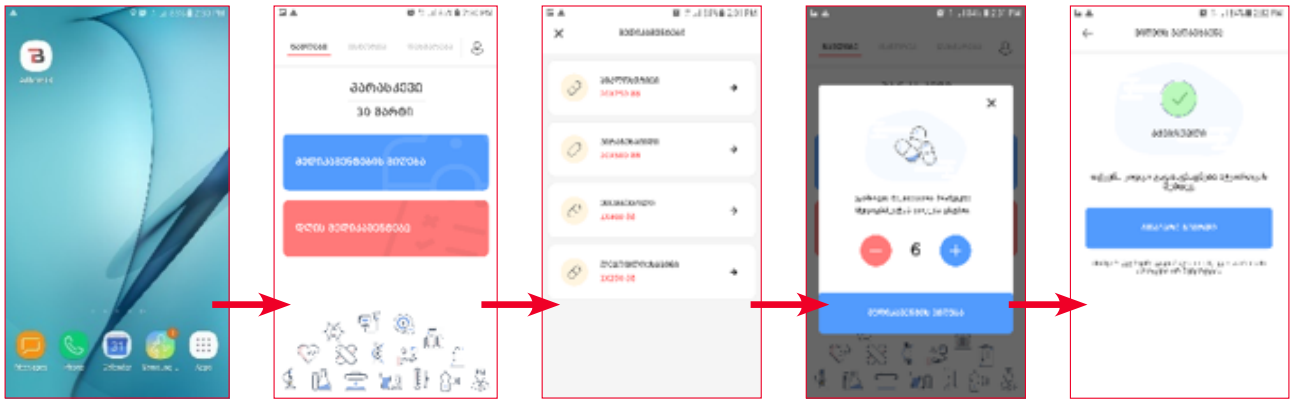
Background

New types of DOT were needed because of problems experienced by patients that prevent the adequate implementation of DOT, such as remoteness of the area, family circumstances, busy working hours and the need for twice daily DOT.

Description of the good practice

Video-observed treatment (VOT) was implemented in Tbilisi as a pilot project in patients treated for MDR-TB, pre-XDR-TB and XDR-TB. During the first phase, 80 patients were included in the project. A lack of injectable agents in treatment regimens was a prerequisite for inclusion in the VOT project. The VOT nurse performed video monitoring via Skype or a special mobile application (Fig. 22). The application enabled patients to record videos of self-administration of their drugs and send the recordings to the nurse. VOT was implemented with the use of mobile telephones purchased with financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria and provided to the patients for their temporary use during treatment.

Fig. 22. Mobile application



The method used was the most appropriate and convenient for patients because it allowed them to avoid daily visits to health-care facilities for DOT.

The mobile clinic is a specialized, high-tech minivan equipped with infection control measures and adapted for the adequate, on-the-spot DOT (Fig. 23). This mobile clinic served TB patients receiving treatment for DS-TB and MDR-TB. Medications were administered to patients under the direct supervision of DOT nurses. This service was available for the patients residing in remote areas and those with injectable agents in their treatment regimens, disabilities or no Internet access.

With the help of new types of DOT, the TB service facilitated adherence to treatment and adapted the treatment to patient needs, thereby reducing stigma, increasing adherence and improving the quality of treatment.

Evidence of impact

Currently, in Tbilisi, 36 of the 80 patients treated for MDR, pre-XDR-TB and XDR-TB included in the VOT project successfully completed the course of therapy, and the remaining 44 patients are still on treatment. This accounts for almost 30% of all outpatients with MDR, pre-XDR-TB and XDR-TB. The DOT rate among patients included in the VOT project was over 96%. These findings demonstrate that the new types of DOT contribute to reducing the TB burden and improving treatment adherence, leading to higher treatment success rates and minimizing treatment interruptions.

Sustainability of the good practice

Since the successful completion of the pilot phase of the project, full-scale implementation of this approach is currently being introduced throughout Georgia to cover all patients being treated for MDR-TB and DS-TB. The project is cost-effective and does not require additional human or material resources.

Fig. 23. Mobile clinic

Kazakhstan. VOT for M/XDR-TB patients receiving therapy with new anti-TB drugs in Kazakhstan

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Background

In Kazakhstan, treatment non-adherence is a critical obstacle to successful TB control and a leading factor in the amplification of drug resistance, treatment failure and the spread of TB. Despite positive reforms to the vertical TB system and the delegation of some responsibilities to the primary health-care level, the quality of DOT is not ideal. Currently, the NTP cannot ensure complete DOT coverage among large patient cohorts, especially for those with DR-TB (requiring longer therapy) and those being treated with new anti-TB drugs. As a result, self-administered therapy has become widespread. In 2016, Partners In Health introduced new anti-TB drugs for treating DR-TB and has now enrolled more than 320 patients to treatment with these drugs in nine regions across Kazakhstan. Therapy with new anti-TB drugs (e.g. clofazimine,

Dlm, linezolid) requires daily doses (seven days/week), without interruption. Partners In Health has introduced alternative ways to provide DOT with new anti-TB drugs in urban ambulatory settings, including VOT. Given the ongoing health reform focusing on decreasing hospitalization and strengthening ambulatory care, the NTP has shown great interest in introducing the new cost-effective alternatives for service delivery for larger patient cohorts.

Treatment duration is from six months for DS-TB up to two years for DR-TB. During the treatment period, it is extremely important to take drugs consistently and in a timely manner under direct observation by a health-care provider (i.e. DOT). Missing a dose of anti-TB drugs increases the risk of expanding the spectrum of resistance to anti-TB medicines and, as a consequence, of unfavourable treatment outcomes and ongoing infection transmission in the community.

Very often, the requirement for daily visits to a DOT venue cannot be met due to lack of resources, being busy at work, urgent household matters and emerging side-effects, leading to missed appointments. In a number of cases, drugs are dispensed to patients to be self-administered, which does not guarantee that the drugs are taken, thereby increasing the risk of poor treatment outcomes.

Switching to VOT alleviates the workload of health-care facilities, improve treatment adherence and reduce stigmatization for TB patients. VOT programmes have a number of advantages, including saving transportation costs (especially important for patients from more remote areas of the city) and freeing up patients' time; avoiding the inconveniences associated with long trips coupled with the side-effects experienced directly after taking drugs (e.g. on the way home); enabling more rational use of TB service resources; and ensuring patient adherence to treatment and thereby improving overall treatment outcomes. In VOT, patients take anti-TB drugs at a distance exactly like they take them while visiting a TB dispensary because it occurs under the direct observation of health staff. VOT provides health-care workers with the opportunity to watch their patients taking anti-TB drugs at home (or at school or work) in real time with the use of modern technology (such as Skype, WhatsApp, Viber) in order to be completely sure that all given drugs are taken as prescribed in a timely manner. Positive responses to VOT by patients were noted: patients appreciated saving the money and travel time allocated for daily visits to a DOT venue, especially those living in colder climates.

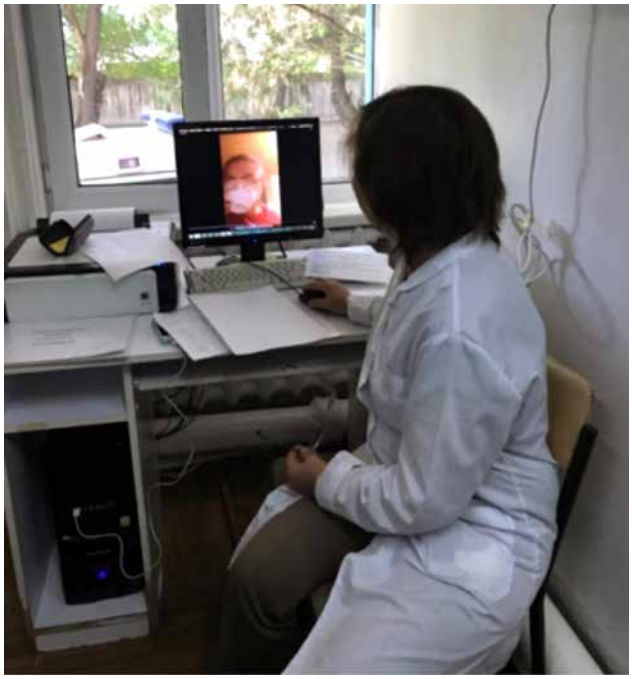
Description of the good practice

Partners In Health developed a working guideline on VOT for TB that described training for health-care providers and patients, VOT methodology, and M&E of results. The practice aims to enable supervised treatment of patients receiving therapy with novel anti-TB drugs in municipal setting at a number of pilot areas within the framework of the endTB project.

In pilot regions, health-care professionals of the TB control services responsible for providing DOT received training in VOT methodology in accordance with the guideline. Within regional TB control services, the following VOT components have been identified (Fig. 24):

1. an office equipped with a computer linked to the Internet;
2. a web camera to obtain webcam output;
3. Skype installed on the computer or WhatsApp/Viber installed on smartphones of health-care workers; and
4. containers to store the weekly supply of medicines.

Fig. 24. Office equipped for VOT



The VOT project enrolls DR-TB patients being treated with novel anti-TB drugs (endTB Project) on an ambulatory basis whose treatment regimens do not contain injectable medicines. Availability of a smartphone, tablet or computer at home and the technical ability to connect via Skype, WhatsApp or Viber are prerequisites. VOT sessions take place in real time six days per week. On Sundays, patients video-record the self-administration of medications via a smartphone/tablet/computer and send the recording to a health-care worker the next day via Skype, WhatsApp or Viber for documentation in Treatment Chart TB-01. Medication supplies are refilled once a week when patients visit their DOT venue. VOT enables the intake of anti-TB drugs to be tracked, thus increasing the patients' motivation for treatment by boosting trust between patients and health-care staff and significantly reducing the risk of missing anti-TB drug doses and/or medication self-management.

Evidence of impact

First launched by Partners In Health in urban settings in Astana and Almaty, VOT has already shown positive results for 64 patients on therapy with new anti-TB drugs (treated seven days/week, with 98% regimen compliance with the Unitaid-funded endTB project). Enrollment has rapidly scaled up and Partners In Health have helped regional TB services to start enrolling patients to VOT with the conventional MDR-TB regimen.

Sustainability of the good practice

The practice does not require a large amount of additional resources because it is possible to use the facilities already available in TB services (e.g. computer, Internet). In general, this technique reduces the costs associated with DOT provision for both patients and health-care professionals.

Portugal. Clinical management of M/XDR-TB in the Northern Regional Reference Centre

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Background

In Portugal, the TB notification rate has been steadily decreasing over the last five years (at a rate of 5% per year). In 2017, the TB notification rate was 16.9 cases per 100 000 population – with the urban centres of Lisbon and Porto being disproportionately affected. The proportion of TB patients with MDR-TB remains close to 1%, with most of these patients living in greater Lisbon or greater Porto. In 2017, 12 of the 1741 TB cases notified in Portugal were MDR-TB (0.7%). No XDR-TB cases were notified. TB cases are usually treated and followed up at the primary care level in specific units known as TB outpatient centres. Some TB cases with greater disease severity or a risk of complications/abandoning treatment might be followed up in hospitals. Since 2009, MDR-TB patients have been followed up in Regional Reference Centres.

Description of the good practice

In Portugal, the Regional Reference Centres for MDR-TB (RRC) were created in 2009 to support the implementation of standard procedures that facilitate rapid diagnosis and adequate treatment for MDR-TB patients. The Northern RRC started operating in July 2009, with standard procedures used for MDR-TB cases, as follows.

1. Whenever an MDR-TB case is identified based on molecular tests (GeneXpert or GenoType MDRTB*plus*) or DST to FLDs, the laboratory reports the case to the RRC, the clinician treating the patient and the Public Health Department. The system includes eight national health laboratories performing these tests, the results of which should be notified through notification form to the Public

Health Department in Northern Regional Health Administration. This process enables assessment of the efficiency of the laboratory notification system for DST in the early diagnosis of M/XDR-TB and in DR-TB case management in Northern Portugal.

2. For each patient, the therapeutic approach, decision on whether to hospitalize, and follow-up are discussed in the RRC. Hospitalization is the first choice at the start of treatment, and the patient remains hospitalized until smear sputum conversion.

3. Genotyping and DST to SLDs are systematically performed at the NRL (National Health Institute Doutor Ricardo Jorge). DST to FLDs is performed either in the laboratory associated with the patient's Health Care Centre or the NRL, if necessary.

4. The RRC is responsible for the clinical management of patients during the entire treatment course, including the choice of treatment regimen and the provision of medications to the health service where the patient is being treated (hospital, outpatient clinic), with periodic appointments with the patients to assess disease progression and the occurrence of adverse events to medication. The procedure is as follows:

    a. adequate treatment regimens are based on current MDR-TB guidelines and additional recommendations *(37,38)* on the use of new drugs (Bdq, Dlm) is proposed whenever necessary;

    b. treatment is adjusted at the RRC according to the clinical and microbiological response along with DST results;

    c. after discharge, local nurses provide the medication (supplied by the Pharmaceutical Department, Northern Regional Health Administration);

    d. the drugs prescribed for MDR-TB treatment are supplied at no cost to the patient;

    e. as for other TB patients, DOT for MDR-TB patients is administered at the primary care level (family doctor/nurse or TB outpatient centre);

    f. patient transport for regular consultation is provided by the National Health System at no costs to the patient;

    g. every adverse effect observed between appointments at the RRC is reported by nurses or the local TB outpatient centre's clinician to the RRC – therapy for symptoms relief and/or therapy modification or interruption is discussed in the RRC; and

    h. whenever necessary, nutritional and social support is provided through the RRC and/or local TB outpatient centres where the patient is registered.

5. The RRC, together with the clinician responsible for the TB outpatient centre (at the place of residence of the patient) and public health authority at the place of residence of the patient, identifies the best strategy for contact tracing, as follows:

    a. contact tracing follows national guidelines, according to WHO recommendations (37) and considers the time of exposure and individual risk for infection and disease;

    b. all contacts at risk undergo immunological testing (TST and/or interferon-gamma release assay) after the exclusion of active TB (via symptom questionnaires and chest X-ray);

    c. MDR-TB patient contacts with indications for preventive treatment are assessed and prescribed adequate treatment at the RRC and the medication is subsequently administered by local nurses; and

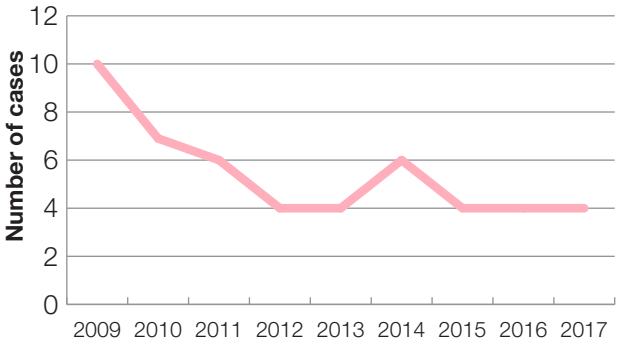
    d. adverse effects to preventive therapy are reported to the RRC by the physician in charge of the patient and symptomatic therapy and/or therapy interruption are decided in group discussions (RRC clinicians and physician responsible for the patient in the respective outpatient centre).

All TB cases, including M/XDR-TB cases, are notified through SINAVE (the National Epidemiologic Surveillance System) electronic platform and data is periodically analysed at regional and national levels.

Evidence of impact

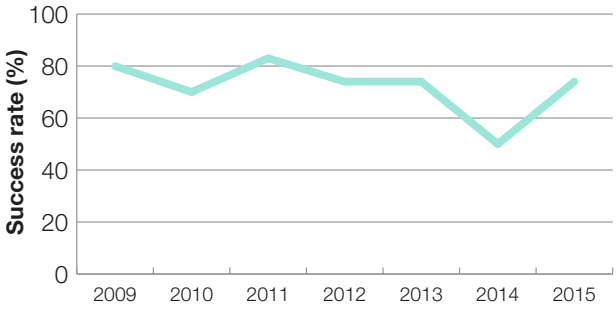
Since the Northern RRC started operating, the number of MDR-TB cases has diminished from 10 per year in 2009 to four per year since 2015 (Fig. 25). From to 2009 to 2015, only XDR-TB patient has been detected (still in treatment).

Fig. 25. MDR-TB cases, Northern RRC, 2009–2017



Use of this strategy also achieved a therapeutic success rate of 73.2% in MDR-TB patients followed by the RRC between 2009 and 2015 (Fig. 26), thus reinforcing the importance of ensuring surveillance and treatment of these patients by specialized reference centres.

Fig. 26. Therapeutic success rate for MDR-TB patients, Northern RRC, 2009–2015



Sustainability of the good practice

The Northern RRC was implemented in existing TB outpatient centres with clinicians namely pulmonologists and infectious diseases doctors) experienced in working with TB patients; clinicians continue to work in both the RRC and hospitals, which guarantees sustainability of the RRC. This interaction between primary and secondary care levels facilitates decision-making on the hospitalization of M/XDR patients.

As the results have been positive in terms of individual care and public health, reducing MDR-TB cases and optimizing treatment and follow-up, the maintenance of RRCs is crucial; therefore, this project has been included in the NTP.

Russian Federation. The system of coverage of TB patients by mobile communication (call centre) enables the remote monitoring of treatment in outpatient settings.

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Background

The current TB epidemiological situation in the Irkutsk region remains serious, with a current incidence of twice the national average. TB incidence in the region decreased 108.4 cases per 100 000 population in 2016 to 95.6 cases per 100 000 population in 2017. In the Irkutsk region, TB mortality in 2017 was 15.6 deaths per 100 000 population. In 2017, The TB mortality rate was 18.1% lower than in 2016 and 14.4% lower than the average over the 2015–2016 period. In comparison, the TB mortality rate in 2017 in the Russian Federation as a whole was 6.4 deaths per 100 000.

in the Irkutsk region, the proportion of MDR-TB patients among newly diagnosed TB patients was 17.8% in 2017 and 16.2% in 2016. The proportion of MDR-TB patients among all sputum smear-positive TB patients was 46.9% (n = 1053) in 2017 and 41.4% in 2016 (n = 1076). Therefore, the proportion of MDR-TB patients in the region has increased.

TB/HIV coinfection in the Irkutsk region

According to the annual analysis of Federal statistics forms, 652 patients with TB/HIV coinfection were identified in 2017 in the Irkutsk region (civil society). On 1 January 2018, a total of 1652 patients with TB/HIV coinfection were registered in the Irkutsk region. Despite the decreased the proportion of patients with TB/HIV coinfection among newly identified TB patients and all registered TB patients, the Irkutsk region has the highest rate of TB/HIV coinfection (incidence of TB/HIV coinfection, 27 cases per 100 000 population;

prevalence of TB/HIV coinfection, 68.6 cases per 100 000 population). The proportion of TB/HIV HIV-coinfected patients in Irkutsk region decreased slightly from 2015 to 2017 (Table 10).

It is also necessary to note the geographical and population characteristics of the Irkutsk region: despite a total area of 774 846 km^2 (representing 4.52% of the area of the Russian Federation), the region has a population of only 2 404 195 (2018) and a population density of 3.10 people/km^2 (2018). Thus, given the low population density and large area, the Irkutsk region has several hard-to-reach areas and territories, where access to medical care is low.

Description of the good practice

A call centre was established in the Irkutsk Regional Clinical Tuberculosis Hospital (IRCTH) for treatment monitoring and to increase the treatment adherence of TB patients at the outpatient stage. The call centre carries out daily telephone calls to notify patients of the need to self-administer anti-TB drugs.

Table 10. Proportion of TB/HIV-coinfected patients, Irkutsk region, 2015–2017

Indicators	2015 (%)	2016 (%)	2017 (%)	Percentage change (%): 2017 vs 2016
Proportion of TB/HIV-coinfected patients of the total number of newly diagnosed TB patients	32.2	33.4	30.4	–9.0
Proportion of TB/HIV-coinfected patients of the total number of TB patients	34.0	35.0	29.4	–16.0

Source: Vasilyeva, 2017 *(39)*.

Patients receiving chemotherapy on an outpatient basis are eligible for enrollment to treatment using the call centre. Patients receiving treatment in a day hospital in outpatient departments of the IRCTH and its branches are excluded, as are patients on the disability register (because they receive weekly visits from district TB specialist; but they can be included on request).

A medical registrar operates the call centre, keeping records of all calls sent and received. Each patient signs an agreement with a district TB specialist to receive daily calls with a reminder of the need to take a dose of anti-TB drugs agrees to answer the calls. Patients also have to provide telephone numbers of their close relatives or friends so that they can be contacted if information on anti-TB drug self-administration is missing. In addition to the agreement, patients receive a Memo for interaction with the call centre (Fig. 27), containing information on how to receive and reply to the telephone messages, and a questionnaire for evaluating the work of the call centre (Table 11).

Due to the prescription rules of anti-TB drugs for outpatient treatment, introduced in the Irkutsk region in 2014, patients are given the drugs in an amount corresponding to the primary packaging (usually at least 100 tablets, representing approximately one month's supply).

Every day between 9:00 and 12:00, patients receive an automatic telephone call reminding them of the need to take their anti-TB drugs. Upon receiving the call, patients confirm the drug intake by pressing a number on the telephone keypad or make a response call to the free Federal number 8-800-100-42-28 and use the interactive menu to confirm intake of the drug. After 12:00, the medical registrar at the call centre analyses the list of received calls from patients. In the absence of a response from the patient, the medical registrar makes a second call (in manual mode) with a notification to self-administer the anti-TB drugs. On weekends, the auto-call programme runs three times per day. Every Friday from 15:00 to 16:00, the medical registrar of the call centre presents a report to the head of the branch TB dispensary

Every Friday, a meeting of the Commission on treatment adherence is held, chaired by the head of the branch TB dispensary. Members of the Commission include the head of the outpatient department (if available), district TB doctors (paramedics) and district nurses (if necessary). During the meeting, each district TB doctor

(paramedic) provides information on patients who have interrupted their observation by the call centre and the measures taken to attract patients to the treatment and observation service.

Fig. 27. Memo for interaction with the call centre

Dear _____

1. Admission of anti-TB drugs must be confirmed daily.

2. Confirm the intake of anti-TB drugs in the following ways:

2.1. during the automatic call from the call centre, press “1”;

2.2. call on the toll-free number 8-800-100-42-28, after the start of the musical greeting, press “1”; or

2.3. confirm the intake of anti-TB drugs by a direct call to the medical registrar of the call centre.

3. To refuse the daily confirmation of taking medications you have to visit your TB doctor and fill out the application form.

breakout line _____

NOTIFICATION RECEIPT

I received and was acquainted with the Memo on interaction with the call-center.

Date: _____

Patient (legal representative): _____ / _____
Signature/Full name

TB specialist (paramedic): _____ / _____
Signature/Full name

Table 11. Patient questionnaire for evaluating the work of the call centre

No	Questions	Yes/No
1	Are you satisfied with the mode of operation of the service?	
2	Are you satisfied with the time of the call?	
3	During the last week, did you mostly answer the call in automatic mode or after the operator's call?	
4	Why did you not use the notification for taking anti-TB drugs in automatic mode?	……
5	What can we change to make it more comfortable for you to inform the operator about taking anti-TB drugs?	……..

Evidence of impact

Despite the fact that the call centre in Irkutsk has been working for less than a year, we can already note positive changes in the TB epidemiological situation Table 12).

According to the results of the questionnaire, patients treated with the help of the call centre noted that they received more attention from medical staff, felt more trusted and more confident in their ability to be cured. This indicates an increased likelihood of adherence to the TB treatment.

The findings of patients' positive experiences on the use of the call centre allowed the IRCTH to start a joint project with the University of Virginia (USA) in 2018 on an SMS alert system for TB/HIV-coinfected patients at the outpatient stage of therapy. Via a mobile application, patients receive a notification on the need to take antiretroviral and anti-TB drugs. In future, both projects will work in parallel.

Table 12. TB indicators in Irkutsk city

TB indicator	2016	2017
Interruption of chemotherapy in pulmonary TB patients	5.3%	3.8%
TB prevalence	263.8 cases per 100 000	197.2 cases per 100 000
Treatment success rate	41.9%	47.5%
Bacteriological conversion (by the end of the TB treatment course, among all TB/HIV-coinfected (DS-TB and DR-TB) patients)	49.9%	64.8%
Smear conversion by microscopy examination (by the end of the TB treatment course, among all TB/HIV-coinfected (DS-TB and DR-TB) patients)	65.9%	77.2%
Closure of cavities	61.1%	73.7%
TB mortality rate	15.1 cases per 100 000	13.5 cases per 100 000

Sustainability of the good practice

In March 2018, expansion of the call centre project to all IRCTH branches began. For this purpose, a 1.25 medical registrar position for the call centre was added to the staff schedule of the main outpatient department in Irkutsk (where a separate job description was developed and approved). When all IRCTH branches (nine, with a service radius of 1000 km) have been incorporated, it will be possible to add further medical registrar positions.

A separate, fully equipped office has been allocated for the call centre, with a separate telephone line (Federal number). Upon request from the branches, paper forms (informed consent, memos, questionnaires) are printed on a photocopier available in the IRCTH. The project is financed within the regional budget.

Russian Federation. VOT in the Voronezh region

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Background

Over the last 10 years, TB incidence in the Russian Federation has decreased but the annual number of notified TB cases caused by drug-resistant pathogens (i.e. DR-TB cases) has remained stable. The Voronezh region is no exception. The TB incidence decreased by 60.5% over this period (from 69.3 cases per 100 000 population in 2007 to 27.4 cases per 100 000 population in 2017) whereas the TB prevalence decreased by 69.4% (from 153.9 cases per 100 000 population in 2007 to 47.1 cases per 100 000 population in 2017). Over the same period, the MDR-TB incidence remained at the same level (at 4.2 cases per 100 000 population in 2007 and 3.9 cases per 100 000 population in 2017). From a clinical point of view, one of the reasons for the spread of MDR-TB is the complexity of organizing long-term daily monitoring of patients taking anti-TB drugs.

One of the most complicated problems in treating TB treatment is low treatment adherence, especially among outpatients. This leads to treatment inefficacy and broad proliferation of the *Mycobacterium tuberculosis* across society. Low treatment adherence among DR-TB patients is the leading challenge caused by prolonged treatment and more complex therapeutic regimens.

Description of the good practice

In March 2016 in the Voronezh region, a project on utilizing VOT for outpatients taking anti-TB drugs was launched for the first time in the Russian Federation. This project aims to enrol all patients with any TB type and achieving a treatment adherence rate of at least 75%. The main inclusion criterion is motivation for this treatment approach. The project is financed from the state budget of the Voronezh region.

Video monitoring at a distance of self-administration of anti-TB drugs by patients at home (or at school or work) allows medical staff to ensure that the patient has actually taken the drugs (i.e. has swallowed the pills with water).

During the first stage of the study, patients are surveyed in hospital to discover whether they agree to try VOT as a way of taking their anti-TB drugs and what devices they currently have for videoconferencing. Upon discharge, patients sign the consent form to participate in Skype sessions, after which they attend one to two training sessions on how to use the devices, how the video software works, how to correctly display a package and pills and the whole process of taking (swallowing) the pills. A designated person in the TB dispensary (usually a nurse) takes calls in accordance with the standard algorithm using a laptop equipped with a webcam and; records the video (or takes snapshots) after getting the pills ready and opens a patient treatment chart. Each patient shows the pill packet, names each pill and shows it to the camera before swallowing. During the subsequent conversation with each patient, adverse events, health status, previous (future) prescriptions and follow-up appointments are discussed, making it possible to verify that the patient has, indeed, swallowed the pills.

If the patient does not make contact at the appointed time, the nurse places a video call and then (if necessary) calls the patient's mobile phone. If the patient is not available, information is transferred to case management teams, which start looking for the patient; these teams are dispatched to patient's home to check whether conditions the patient is at home and, if possible, watch the patient taking the drugs.

On Sundays and holidays, or if there is no Internet connectivity, patients themselves may make video recordings of taking their TB medications and transmit these to the TB dispensary as a proof that the prescribed dose has been taken. Every two weeks, each patient visits the dispensary for clinical assessment and any necessary tests, and picks up a new supply of medication. At the end of treatment, the VOT record is reviewed by the medical commission.

VOT helps improve treatment adherence because it makes the treatment process more comfortable for patients for the following reasons.

- The patient does not need to go to the clinic every day to take TB medicines under direct observation of the health staff to prove treatment adherence

(which decreases a level of irritability and aggression in patients).

- The time saved can be used for other important matters.
- Money is saved on transportation costs associated with trips to the clinic for taking the medications.
- There are fewer chances for adverse events (such as nausea, vomiting, diarrhoea, dizziness, seizures) to occur in a vehicle on the way home, especially among MDR-TB patients.
- The level of confidentiality is higher with this approach to taking medications.
- Patients are interested in this new, innovative treatment modality that improves their self-esteem and gives a feeling of returning to normal life in the society.

Such approaches and technologies are becoming more broadly utilized as part of a significant trend in the worldwide phthisiatric community. Given the increasing use of various mobile communication gadgets among people of all age groups, this intervention should make a positive impact on treatment adherence to anti-TB regimens.

This project aims to introduce comprehensive, accessible and affordable people-centred approaches to improving treatment adherence in TB patients and preventing the further spread of TB and the emergence of the drug-resistant mycobacterial pathogens. It is impossible to implement this programme without political support because it requires both funding and interactions among and between members of the medical community.

Evidence of impact

Since March 2016, a total of 192 patients have been enrolled to the VOT project in the Voronezh region, of whom 155 completed the main therapeutic course (treatment success rate, 89.9%; treatment failure rate, 1.6%; switching to other treatment options, 1.6%), with 37 patients continuing their treatment. Thus, the therapy has significantly higher efficacy for this patient cohort compared with other available treatment options (treatment efficacy in the general 2016 cohort in Voronezh region, 84.8%). Treatment adherence among the patients recruited to the VOT project is 92–95%; the rate of missed doses is 1.9% and the cure rate is as high as 90%.

Figs 28 and 29 show the number of patients receiving VOT in city and rural/district areas of Voronezh and the treatment outcomes.

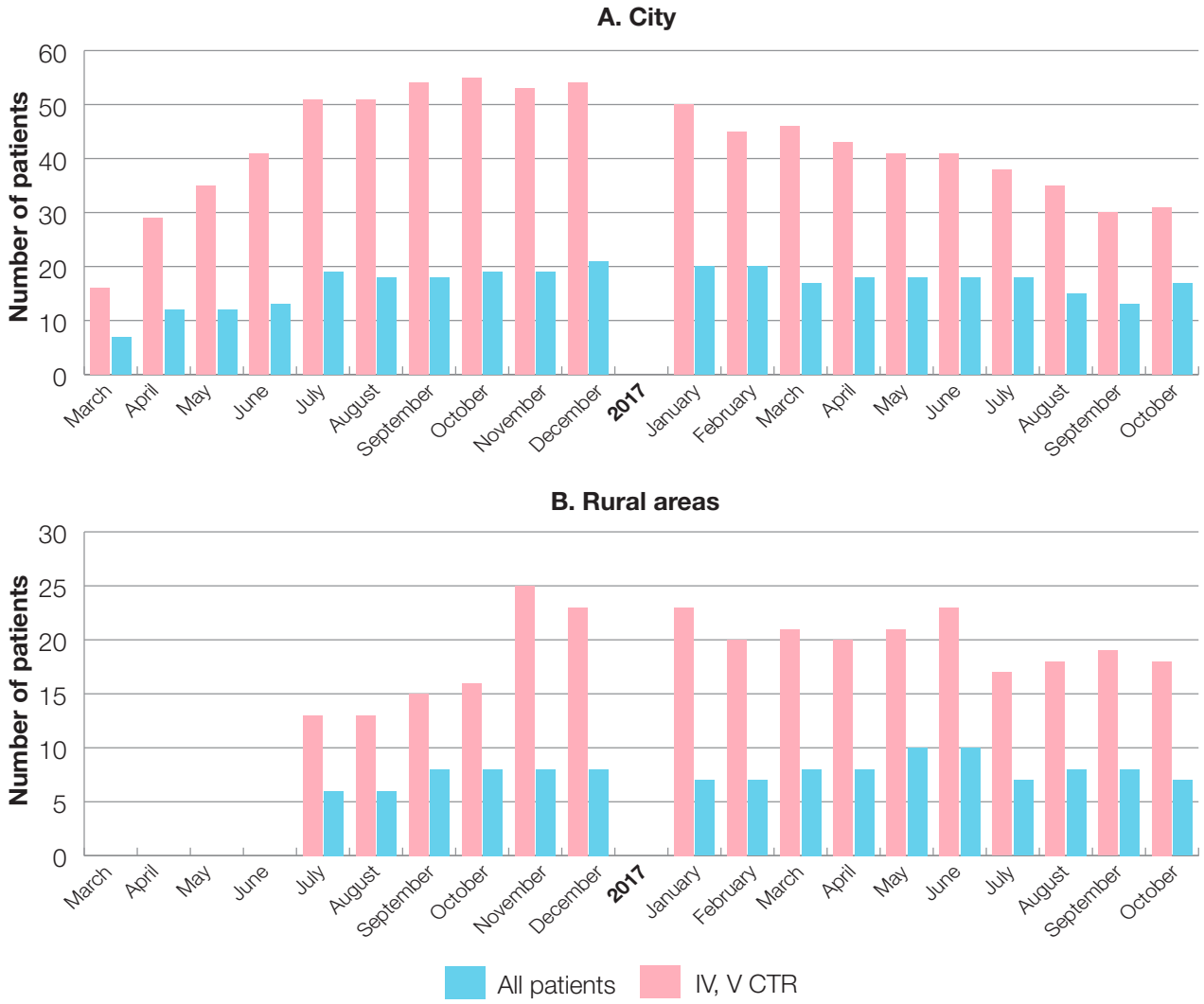
Implementation of this practice saved human resources and enabled them to be redirected to the treatment of more severely affected TB patients, thus improving the epidemiological situation by preventing the disease from spreading among exposed individuals.

Sustainability of the good practice

This project a long-term endeavour that does not require a massive influx of additional financial and human resources. The broader strategy is to disseminate existing practices among other districts in the region as well as expanding them to cover individuals with LTBI at a high risk of developing the disease (e.g. preventive treatment among adolescents and people living with HIV).

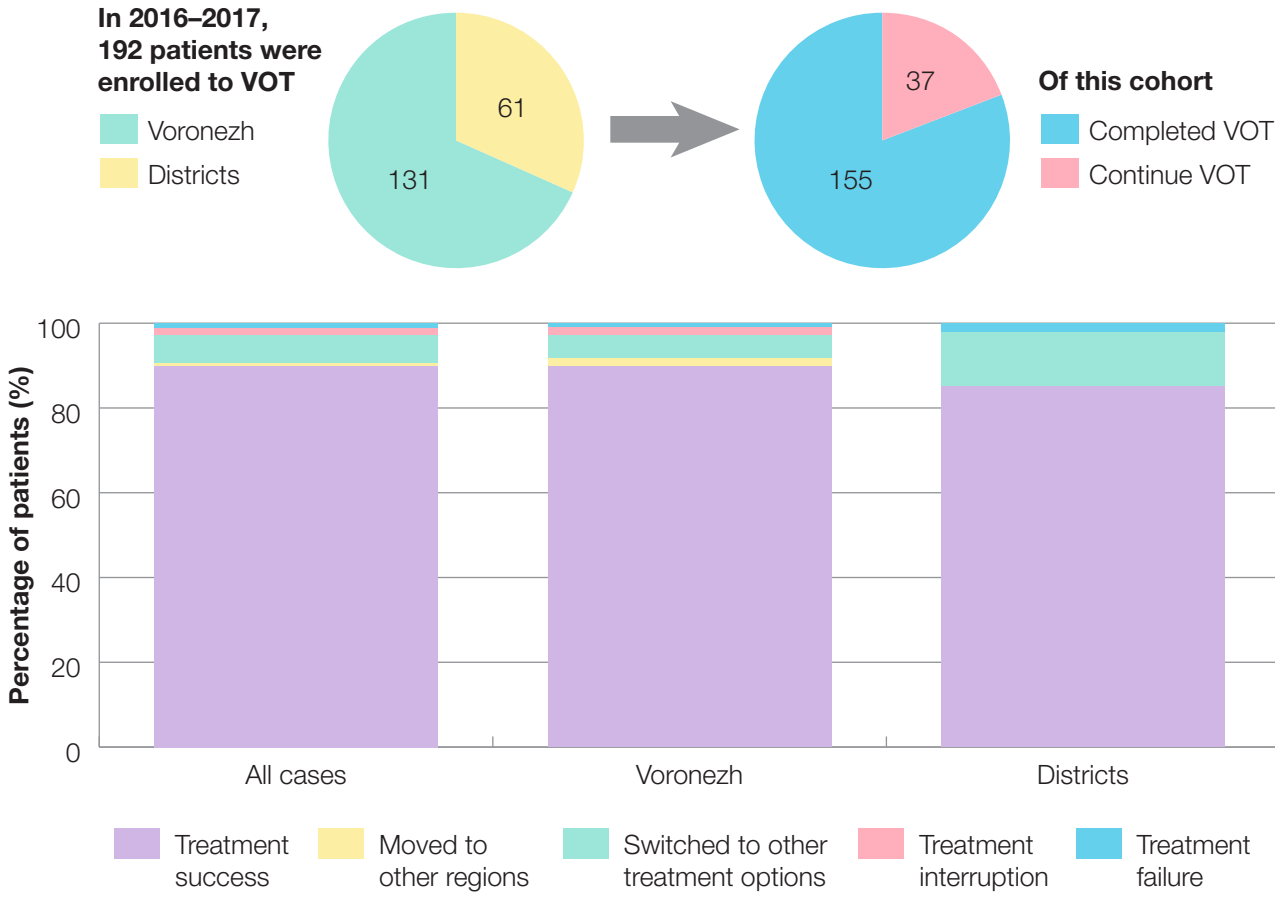
Evaluation of the project's strengths and the introduction of innovative technologies for TB diagnosis and treatment in the coming years in the Voronezh region suggest that this practice will make a significant contribution to reducing the TB incidence to 10 cases per 100 000 population by 2026–2029, in line with WHO recommendations in the context of the Sustainable Development Goals.

Fig. 28. Patients receiving VOT, Voronezh city and rural areas, 2016–2017 by month



CTR: individuals on chemotherapy regimens; IV: individuals in contact with people who have active TB or with TB-infected livestock; V: all extrapulmonary TB patients.

Fig. 29. VOT among TB patients, Voronezh city and rural areas, 2016–2017



Ukraine. Results-based social support of outpatient DS-TB treatment (with and without HIV coinfection)

Submitted by: Volodymyr Kurpita[1] | Viktor Lyashko[1] | Oxana Savenko[2] | Iurii Varchenko

[1]Public Health Centre, Ministry of Health, Kiev; [2]All-Ukrainian Network of People Living with HIV/AIDS

Background

TB incidence in Ukraine

As defined by WHO, Ukraine remains a country with high TB and MDR-TB morbidity rates. TB in Ukraine is characterized by widespread M/XDR-TB, a relatively high mortality rate due to an imperfect programmatic approach to managing DR-TB and a growing incidence of TB/HIV coinfection.

According to WHO estimates, the TB morbidity rate in Ukraine in 2016 was 87 cases per 100 000 population. According to Ukrainian Ministry of Health data, the TB morbidity rate (including new and relapsed cases) in the same year was 67.6 cases per 100 000 population. In 2016, 28 800 new cases of TB were reported (versus 30 151 in 2015), with a TB incidence of 54.7 cases per 100 000 population (versus 55.9 cases per 100 000 population in 2015). In all, 22.5% of TB diagnoses are missed in Ukraine every year, further contributing to the spread of TB among the population.

At-risk groups

The high TB morbidity rate in Ukraine strongly correlates with status of economic development and persistent military conflict in the country *(40)*. Therefore, in planning actions aimed at reducing TB morbidity at the national level and evaluating their effectiveness, it is necessary to take into account changes in gross domestic product per capita during these periods. The correlation between TB incidence and growth in gross domestic product per capita makes it obvious that overcoming the TB epidemic in Ukraine will only be possible if qualitative and positive changes are achieved in TB care and the health-care system as a whole, as well as in the national economy. This relationship

is supported by the consistently high proportion of unemployed individuals among TB patients (52–59%). This population remains the largest subgroup of TB patients, and the unemployment rate directly depends on the level of the economic development in the country.

According to regional demographic polls, in 2016 the TB prevalence per 100 000 population in the most at-risk groups was: 4384.54 for HIV-infected people; 1713.86 for homeless people; 1030.96 for detainees and incarcerated individuals (either in detention or discharged from detention facilities), convicts and prison inmates (including ex-prisoners, individuals followed up by law enforcement as convicts or those under surveillance); 972.04 for individuals exposed to TB patients (family contacts); 870.50 for unemployed and indigent people and those living below the poverty line; 654.28 for alcohol abusers; 587.71 for drug and substance users; 151.32 for individuals with conditions associated with suppressed immunity; 118.60 for psychiatric ward inmates; 111.27 for migrants and refugees; 66.59 for health-care workers; and 59.88 for other categories (key target groups were homeless people, migrants and refugees, and those living below the poverty line). Thus, among the most at-risk populations, TB incidence is the highest in people living with HIV.

According to surveys and questionnaires, in 2016 the TB patient profile was: unemployed and indigent people and those living below the poverty line, 52.1%; HIV-infected people, 19.8%; alcohol abusers, 12.8%; other categories, 5.5%; individuals with conditions associated with suppressed immunity, 4.5%; drug users, 2.9%; detainees and incarcerated individuals (either held in detention or discharged from detention facilities), individuals followed up by law enforcement agencies as convicts or those under surveillance, 2.4%; psychiatric ward inmates, 2.2%; homeless people, 2.1%; individuals exposed to TB patients (family contacts), 1.9%; health-care workers, 1.4%; and migrants and refugees, 1.2% (key target groups were homeless people, migrants and refugees, and those living below the poverty line).

Description of the good practice

This practice aims to establish a sustainable system to provide outpatient DOT for TB (including DR-TB and TB/HIV coinfection) to patients at risk of treatment interruption. The model necessitates the involvement of various DOT providers such as NGOs and primary health-care facilities. The basic principle of this model is based upon: an integrated people-centred approach to providing social and health-care services; daily delivery and control over taking anti-TB drugs by a DOT provider; and results-based financing. The integrated people-centred approach assumed a personalized approach to treating each individual patient in order to resolve sociopsychological issues such as document renewal, employment, legal advice, psychological counselling, housing, clothing and other needs, and linking these to health-care services. In is particularly relevant to patients with TB/HIV coinfection. Results-based financing envisages making incentive payments to DOT providers (social workers, nurses, family doctors) in two stages: (i) for ensuring uninterrupted treatment of the TB patient; and (ii) for successful completion of treatment, as to be confirmed by laboratory testing. Patients were encouraged to improve treatment outcomes via food incentives at three stages: (i) upon initiation of case management, (ii) upon completion of the treatment course and (iii) for laboratory investigation after treatment completion. Implementation of the project required coordinating action between health-care and local authorities, with the integration of social services.

The first model (Model 1) assumed NGO involvement. In 2017, this project was implemented by 21 NGOs in 17 regions of Ukraine. DOT services covered 2712 patients with DS-TB. Treatment efficacy in patients with known treatment outcomes at the end of 2017 was 96%.

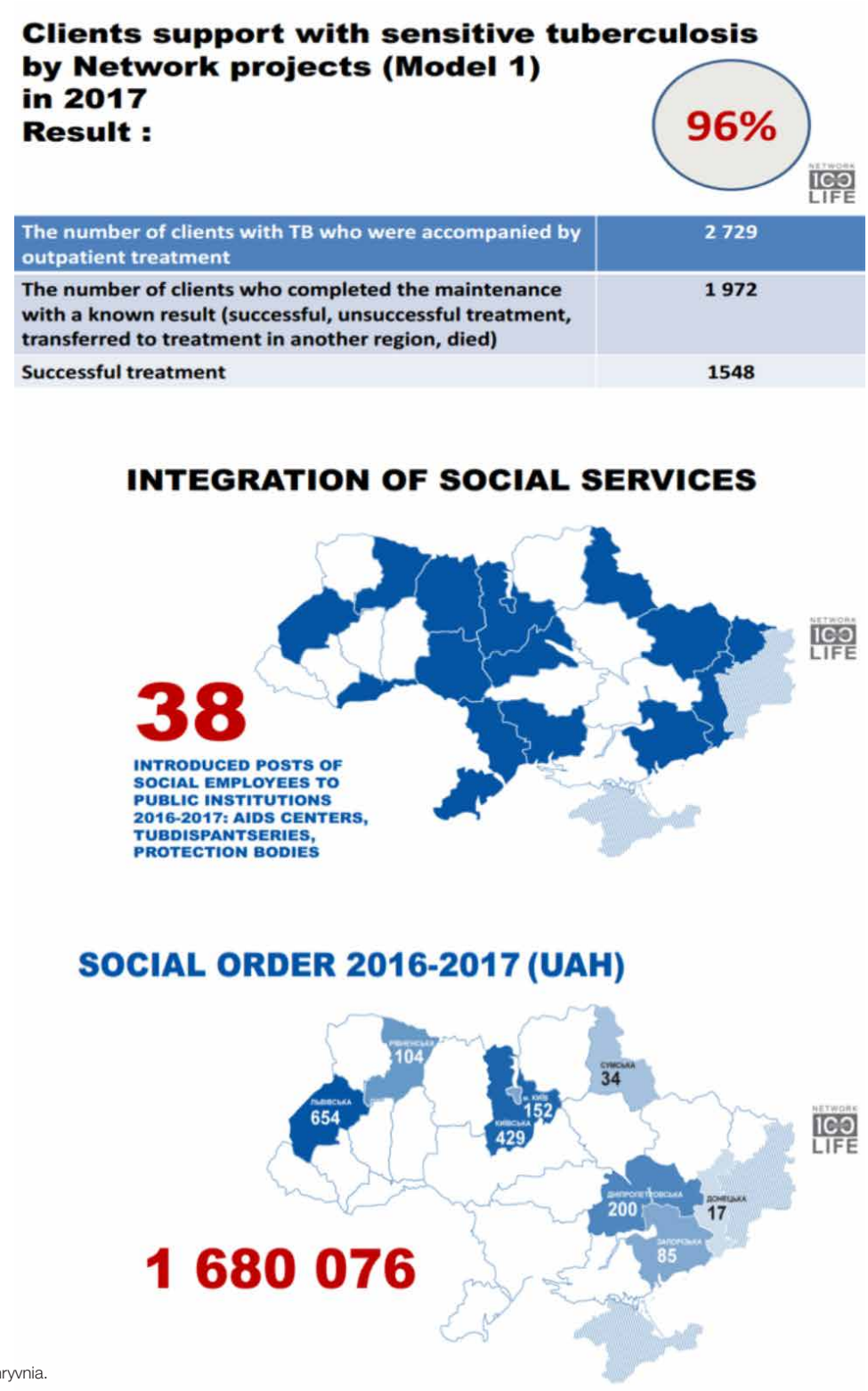
The second model (Model 2) assumed financing for DOT services would be provided through contracting primary health-care providers (family doctors, medical doctors) by the TB services. This model is important in Ukraine because DOT case management is not financed by the state. A gradual switch from funding by international donors to funding via state/local budgets is planned for 2018–2020. For the same purpose, building the capacity of TB services and primary health-care in providing DOT services within the scope of ambulatory care services is essential. The project was carried out in 2017 in the city of Zhitomir and the Chernigov region. This model complies with the principles outlined above but no additional social services except for the daily delivery of anti-TB drugs were offered to its patients.

Treatment efficacy was 96% for patients with known treatment outcomes at the end of 2017. Based on the programme's results for 2017, a range of DOT case management services were expanded for 2018–2020. Plans specifically include distributing supplies to ensure that patients and family members comply with infection control regulations during the course of TB outpatient treatment; screening for TB among patient contacts; delivering sputum samples; and paying the costs of fee-for-service diagnostic tests for low-income patients.

Evidence of impact

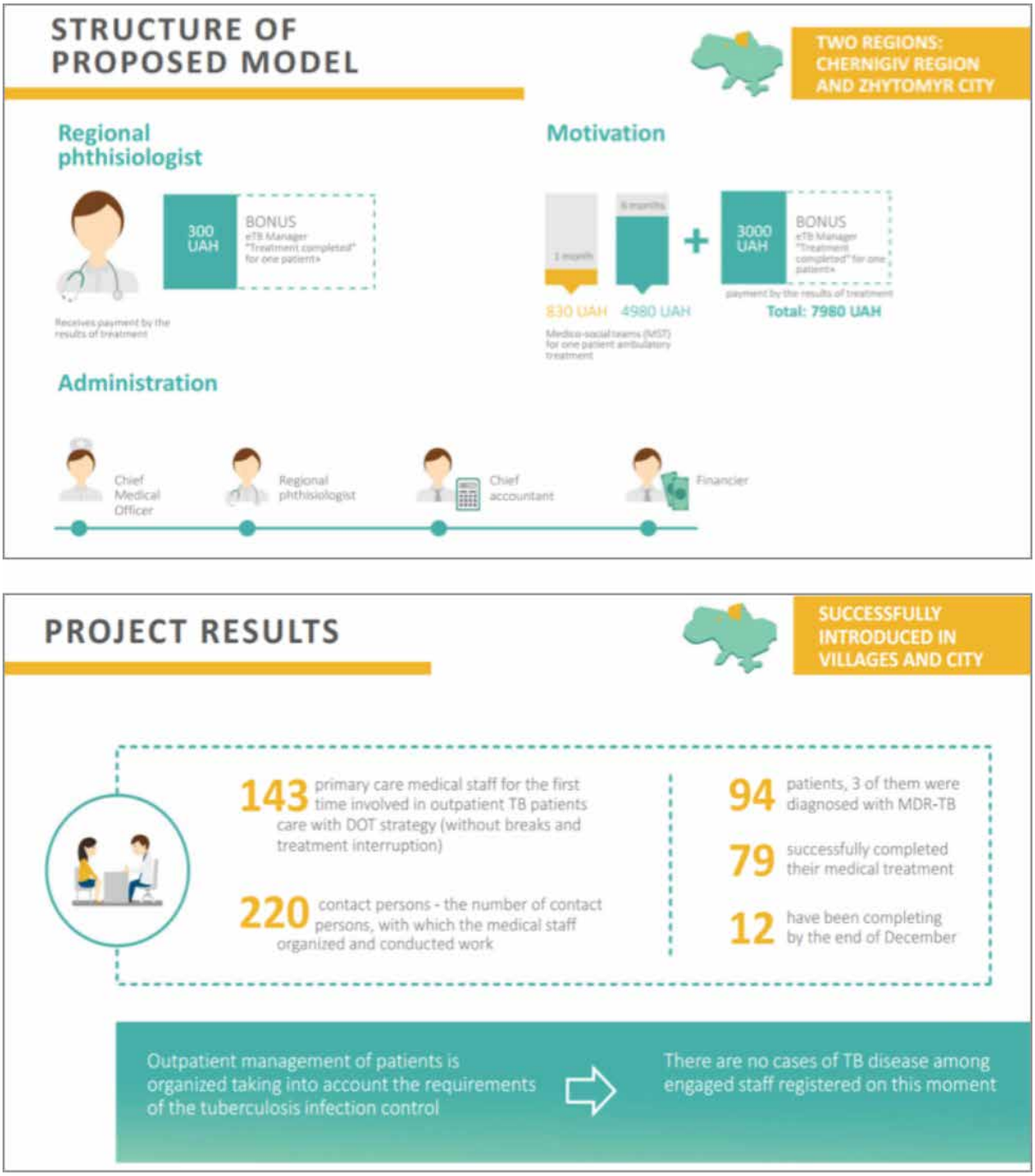
Figs 30 and 31 show the efficiency of Models 1 and 2, respectively.

Fig. 30. Efficiency of Model 1



UAH: Ukrainian hryvnia.

Fig. 31. Efficiency of Model 2



UAH: Ukrainian hryvnia.

Based on this practice:

- an efficient model of support for TB health services by NGOs has been developed and an effective collaboration between the state and NGOs has been demonstrated; and
- a system of infection control and monitoring of compliance with infection control measures by NGOs has been strengthened.

Sustainability of the good practice

Providing DOT services for TB outpatient treatment has proven effective in Ukraine. The state (in particular the Ukrainian Ministry of Health's Public Health Centre) made a commitment to providing political support and a guarantee to secure financing for DOT services as a part of TB outpatient treatment beginning in 2018. The stepwise transition to state and local budget funding for DOT services will take three years: 20% of funding in 2018; 50% in 2019; and 80% in 2020.

Reimbursement mechanisms were developed in 2018 and are already in place in two regions through the network of regional public health centres and involving regional administration. In the future, plans are to fund these activities from several sources, including state and local budgets and international organizations.

Ukraine. Use of international treatment protocols and best practices in care provision, including TB services, in Ukraine

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Background

The Ukrainian regulatory framework governing the provision of health-care is imperfect. According to national statistics, the combined incidence of new and recurrent TB was 63.9 cases per 100 000 population in Ukraine in 2017. Ukraine first entered the top five countries with the highest MDR-TB burden in 2014. In recent years, the number of MDR-TB cases has increased: from 3482 in 2009 to 6757 in 2017. Over the last five years, a decreasing tendency in TB mortality has been observed in Ukraine, with an average annual decline of 10.1% *(38)*.

Since 2012, only 123 unified protocols related to only a small proportion of diseases have been developed. At present, Ukraine has a Unified Protocol for TB Care, which was approved by Executive Order of the Ministry of Health in 2014. the development of unified clinical protocols often relies on the personal experience of Working Group members and is based on an outdated, not an evidence-based, framework. Until recently, unified clinical protocols and local clinical protocols were adapted to the capacity of the health-care system and not to the needs of patients; they violated patients' right of access to information about modern methods of treatment (e.g. available in another clinic, region, country).

Almost every year, new international recommendations based on evidence-based medicine become available but, since the development and approval of new medical standards is a long-term process, modern approaches remain inaccessible to physicians and patients, and sometimes lose their relevance.

Description of the good practice

The Ukrainian Ministry of Health made a political decision to allow the use of international clinical protocols in the work of physicians as an important component of progress towards health-care reform in Ukraine. After all, changes in the TB field are not possible without improving the quality of health-care. Transition from authority-based medicine to evidence-based medicine should be an integral part of national health system reform. This was made possible by Executive Order No. 1422 of the Ukrainian Ministry of Health of 29 December 2016, which entered into force in April 2017, allowing the use of international clinical protocols.

New clinical protocols are being developed and approved to accelerate the implementation of evidence-based principles in modern medical practice, with due consideration of international experience in the field of health-care.

A new clinical protocol, Clinical guidelines selected by the Ukrainian Ministry of Health for use in Ukraine without going through a procedure of adaptation, specifies the process of care provision in the context of certain diseases. The Ukrainian Ministry of Health approves it as the text of the new clinical protocol or as a reference to the source of its location or publication.[8]

To be approved as a new clinical protocol, clinical guidelines should be selected by the Ukrainian Ministry of Health and meet the requirements to be developed:

- by the national and/or professional medical associations of European Union Member States (Ukraine has membership as of 1 January 2017), the United States of America, Canada and the Australian Union;
- in line with the existing methodology and evidence-based medicine; and
- in English and/or Ukrainian.

[8] In Ukraine, it is now possible to approve international, European, American or any other clinical protocol or clinical guideline for use in Ukraine by approving a reference to the document or the text of the document

Protocols can be used immediately after the Ukrainian Ministry of Health approves their text or approves a reference to the source document. In addition, health-care institutions, including those providing TB care, have the right to choose and translate protocols from the list recommended by the Ukrainian Ministry of Health. Such protocols, approved by the internal order of a health-care institution, are allowed to be adopted for practical use.

If the application of a new clinical protocol is not possible due to inability to use appropriate medicines or lack of the necessary equipment/technology, the physician:

- informs the patient about other health-care institutions where the necessary care can be delivered in line with the new clinical protocol (if such information is available);
- chooses another similar drug or equipment/technology that is available and allowed for use (with informed consent from the patient); or
- notifies the health unit of the local administration in writing on the infeasibility to fully comply with the new clinical protocol in treating a certain disease and on the proposed alternative (the form of notification is arbitrary).

The use of new clinical protocols in medical practice is one of the most important ways to introduce evidence-based medicine into Ukraine. Evidence-based clinical protocols play a key role in the health-care system because they significantly benefit all players: patients, physicians and the state as a whole:

Benefits for the patients. International treatment protocols are people centred and their implementation will help improve patient health. Protocols on the use of effective, evidence-based diagnostic and treatment methods will have an impact on the treatment success rate, ultimately leading to a reduction in morbidity and mortality rates and improvement in patient quality of life. The protocols guarantee an equally high level of care to each patient, regardless of the hospital and physician providing it.

Benefits for health-care specialists. Treatment protocols provide clear recommendations for practitioners, as well as improving the quality of clinical decisions (including among those professionals used to outdated medical practices). Another important advantage of the clinical protocols is that they promote consistency in the delivery of care to the patients at all levels.

Benefits for the health-care system and state. For the health-care system, the introduced clinical protocols are associated with improvements in work performance (often through the standardization of care) and optimization of treatment costs. The introduction of the protocols can also contribute to raising confidence in the health system in particular and the state as a whole, since the provision of good quality, effective medical services creates a positive perception of both the system that delivers the services and the state guaranteeing them.

This practice is a bold political measure that covers several areas of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)* by contributing to the rapid introduction of new tools and strategies (including new drugs and treatment regimens) with an integrated, coordinated and people-centred approach to TB care and prevention.

Evidence of impact

The use of new clinical protocols provides an opportunity to introduce modern methods of diagnosis and treatment into medical practice (the efficiency of these methods has been demonstrated by numerous controlled studies), thereby improving the quality and effectiveness of health-care.

Sustainability of the good practice

Sustainability of this practice is based on policy management: the use of international protocols is in line with Executive Order No. 1422 of the Ukrainian Ministry of Health of 29 December 2016).

1D. Collaborative TB/HIV activities and management of comorbidities

Armenia. MDR-TB and hepatitis C virus coinfection: no longer an untreatable combination

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Background

In MDR-TB patients, hepatitis C virus (HCV) coinfection can put patients at risk of drug-induced hepatotoxicity, often resulting in recurrent TB treatment interruptions and, subsequently, poor TB treatment outcomes *(41,42)*.

Until recently, Armenia had no formal documented data/information on the prevalence of HCV coinfection among DR-TB patients. Since 2005, TB patients in Armenia are enrolled to MDR-TB treatment in the framework of the National TB Management Strategy with technical support of MSF. MSF collect data on all enrolled MDR-TB cases in the MSF and National TB Control Centre joint cohort from seven *marzes* (provinces) in Armenia. The results of anti-HCV antibody testing in high-risk or symptomatic DR-TB patients show that among 1540 DR-TB patients enrolled between 2005 and 2015, 86 had positive testing for anti-HCV antibody (approximately 6% of DR-TB patients). Other data from the Central Infectious Disease Hospital showed a prevalence of 9–10% for positive testing for anti-HCV antibody among all TB patients. MDR-TB patients were not systematically tested for HCV coinfection over this period.

Part of the reason for the lack of systematic testing for HCV coinfection was the impossibility of treating active hepatitis C in patients with active TB. Direct-acting antiviral agents are now available for treating HCV infection but drug interactions or contraindications for MDR-TB patients are not yet known. Therefore, MDR-TB patients have little access to diagnostic screening for HCV coinfection.

Description of the good practice

The main objectives of screening and treating DR-TB patients for active HCV coinfection in were to:

- determine the real prevalence of HCV coinfection among MDR-TB patients;
- determine the HCV genotypes most prevalent among MDR-TB patients in order to design a standardized treatment strategy; and
- improve access for eligible MDR-TB patients to the novel hepatitis C treatment regimen to contribute to better TB treatment outcomes.

During the screening process, a standard diagnostic algorithm for active HCV infection was developed and implemented (including genotype testing, PCR and FibroScan).

Starting in December 2016, direct-acting antiviral treatment was used to treat active HCV infection, based on a protocol developed by MSF and the National TB Control Centre as part of a joint HCV clinical guideline.

During the whole process, progress data was collected and interim data analysis was conducted. A total of 236 MDR-TB patients were screened actively for HCV coinfection from January 2016 to March 2017. HCV screening activities targeted a cohort of MDR-TB patients comprising patients enrolled to treatment in 2014 and 2015 and prospectively recruited patients who underwent treatment until June 2016.

The prevalence of active HCV coinfection was much higher than expected: 30% of MDR-TB patients had positive findings for anti-HCV serology and 20% had active hepatitis C (the most common genotype was 3a). The impact on MDR-TB treatment interruptions cannot be underestimated: hepatotoxicity is a common

adverse event experienced by MDR-TB patients and often leads to MDR-TB treatment interruption *(43,44)*.

Following HCV screening, direct-acting antivirals have been imported into Armenia: in 2017, 26 MDR-TB patients were treated for hepatitis C with no serious adverse events reported; of these, 58% received concomitant direct-acting antivirals and DR-TB treatment.

Evidence of impact

The screening, diagnosis and treatment of hepatitis C with direct-acting antivirals in MDR-TB patients represents a people-centred approach in which MDR-TB treatment is integrated with treatment of a common comorbidity, HCV infection. This approach contributes both to the quality of TB treatment and to hepatitis C treatment.

Treatment of hepatitis C in MDR-TB patients has led to greater knowledge about the epidemiology of hepatitis C in general in Armenia, well as the treatment of hepatitis C with direct-acting antivirals in the country – not only among TB patients. As expected, clinicians and public health experts in Armenia have benefited from this experience, which may lead to a national programme of treatment for hepatitis C in all affected persons.

Sustainability of the good practice

This practice has developed into a systematic practice in the NTP framework in which all new MDR-TB patients are screened for HCV coinfection. For those with positive test results, further diagnostic tests are conducted and direct-acting antiviral treatment is prescribed as appropriate.

For the first time in Armenia, GeneXpert testing was introduced within the scope of this project for implementation in diagnosing HCV coinfection in MDR-TB patients; this is planned to become a sustainable practice.

An increase in the number of patients treated for hepatitis C could lead to a real demand for direct-acting antivirals in Armenia and a reduction in the price of drugs for all those affected. For MDR-TB patients, the ability to continue MDR-TB treatment without interruption and without MDR-TB treatment failure due to hepatotoxicity will lead to both a reduction in MDR-TB transmission and improved outcomes for those affected.

To further investigate the efficacy of this project, an observational study is planned with the goal of assessing the safety, effectiveness and feasibility of treating chronic active hepatitis C with direct-acting antivirals in MDR-TB patients. The study will be implemented by the MSF Mission in Armenia in collaboration with the National TB Control Centre and the approval of MSF France and the National Ethical Review Board.

Kazakhstan. Improve access to high-quality TB and HIV care through engagement of the non-public sector

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Background

TB epidemiological situation

Kazakhstan is one of the 30 high MDR-TB burden countries in the world. Despite some improvements in the TB epidemiological situation and in provision of TB care, M/XDR-TB remains the main threat to TB control in the country. Recently, TB case notification has exceeded the estimated incidence, but cases of late diagnosis and an increase in TB among children are still observed. Although TB incidence and mortality rates in Kazakhstan have decreased over the last five years (2012–2016) from 81.7 to 52.7 cases per 100 000 population and 7.4 to 3.4 cases per 100 000 population, respectively, the incidence of DR-TB increased over the period: MDR-TB incidence increased from 20 to 25.7 cases per 100 000 population, respectively, and XDR-TB from 174 to 386 cases per 100 000 population.[9]

The TB epidemiological situation among key populations is even worse owing to other (social) external factors that make access to quality TB care

[9] National tuberculosis programme annual review report, 2017.

(diagnosis and treatment) difficult, such as: insufficient collaboration between public health programmes and between public and private health services; and limited involvement of local NGOs due to a lack of funding opportunities, insufficient knowledge about TB and insufficient experience in providing TB care.

Health care reforms

Over the last few years, the Ministry of Health has been working on health-care system reforms including HIV and TB programmes. One aspect of these reforms is to encourage collaboration between the government, civil societies and the private sector.

In Kazakhstan, TB care has traditionally been the responsibility of the public health-care sector (i.e. the TB service and primary health-care): private clinics were not allowed to provide TB care. Since 2014, the Ministry of Health has been expanding health-care provision through the guaranteed volume of free medical care (GVFMC) system that entitles public and private clinics to provide a package of free care, including ambulatory primary health-care, for which they are reimbursed by the government. In 2017, 16 private clinics were entitled to provide the ambulatory package in Almaty city. Although the ambulatory care package included TB care, private clinics were not aware of the regulations and organizational requirements to provide TB care. They assumed that they had to refer presumptive TB patients to the public sector for diagnosis and treatment, and that their clinics would not meet the specific requirements.

NGOs supporting HIV and TB patients

Although NGOs have been working with HIV-affected populations since 2005, they were barely involved in TB-related activities. No NGO was providing services to TB patients, owing to the stigma attached to TB and the reluctance of TB patients to remain engaged after being cured.

Collaboration between TB and HIV programmes

As the HIV service is centralized in Kazakhstan, with one HIV centre providing all services in each district, private and public providers are not entitled to offer antiretroviral therapy (ART). Anti-TB and antiretroviral drugs are provided free of charge by the government through the distribution channels of each programme. In the past, owing to a lack of collaboration between TB and HIV specialists in clinical management of patients with TB/HIV coinfection (including monitoring and management of adverse events to antiretroviral drugs), TB/HIV-coinfected patients did not receive proper care.

Description of the good practice

Positive effects of NGO engagement

Previous attempts to organize NGOs into a network in Kazakhstan have been unsuccessful. Within the framework of this project, the KNCV Tuberculosis Foundation (KNCV) and AIDS Foundation East-West in Kazakhstan (AFEW Kazakhstan) successfully established a network of NGOs whose work is already focused on HIV will be expanded to include TB. AFEW Kazakhstan has engaged with four NGOs in Almaty providing psychological, social and legal consultation support services to key populations (prisoners and ex-prisoners, people living with HIV and TB patients, drug users, internal migrants). These NGOs are currently forming a strong NGO Network, which is forming links with all existing service providers (public and private). They aim to ensure access to essential (support) services related to HIV and TB for all people in need and to augment the clinical services provided by regular health services. Since 2016, two of the NGOs have been involved in screening their patients for TB and referring presumptive TB patients to TB services for further assessment.

AFEW Kazakhstan developed a web platform to improve coordination of the NGO Network in providing patient support. The web platform provides information on the TB/HIV services offered by public and non-public organizations and includes a map with contact details for each organization. It also enables people to find and download information on TB and HIV and educational materials.

Two NGOs, Doverie Plus and Public Foundation Sanat Alemi, provide treatment adherence support to HIV and TB/HIV-coinfected patients. The Centre for Human Rights Monitoring NGO is dedicated to providing legal consultations.

Sanat Alemi is the most recently founded NGO in the Network, focusing specifically on TB patients and collaborating directly with the TB dispensary where all new TB patients initiate their treatment. It has worked successfully with a self-support group and on patient management. Other relevant activities include advocacy for TB patient rights through giving speeches at press-conferences and organizing anti-stigma flash mobs and videos. Recently, Sanat Alemi entered into

an agreement with the Employment Centre, entitling it to provide vocational training for TB patients. At the World TB Day conference, which took place this year (2018) in Almaty, the psychologist of the foundation received an award for providing the best psychosocial care for TB patients.

AFEW Kazakhstan provides regular training for members of the NGO Network on essential skills such as adherence support and counselling, psychological support, and the legal aspects of TB/HIV treatment. KNCV contributed to capacity development for the local NGOs in TB care and to establishing strong collaboration between local NGOs and both the public and private health-care sectors, thus improving TB detection and treatment adherence among key populations. They trained 15 representatives of local NGOs on providing TB care and on M&E. They provided psychological and social support to those of their patients receiving TB treatment.

In summary, NGOs have identified more people with presumptive TB and improved treatment adherence for TB and HIV among key populations at risk of HIV and TB.

Integrated TB and HIV care for key and general populations

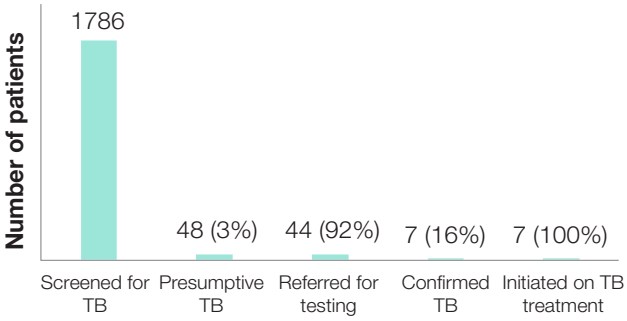
With support from the Almaty Health Department, KNCV carried out a qualitative survey in July 2016 of a selected sample of GVFMC-associated private clinics. The survey explored the experiences and interest of the private clinics in providing TB and HIV care. The survey found that the clinics had role in detecting patients with presumptive TB but had no referral system or link to TB services. According to local regulations, GVFMC-associated private clinics that had an ambulatory care package were eligible to provide TB care to the catchment population; however, the survey showed that doctors in the private clinics had limited knowledge in TB diagnosis and treatment. Nor was there collaboration between the private clinics and the TB service. Based on interpretation of the provisions under the GVFMC and the survey results, a strategic plan for public–private collaboration in TB care provision was developed by the TB service and approved by the Almaty Health Department at the start of 2017. The plan included activities related to capacity-building for medical doctors in private clinics, the development of a referral system for TB screening and diagnosis, integration of the private sector into the existing TB M&E system and the engagement of private clinics in ambulatory treatment for TB patients. Thus, all GVFMC-associated 16 private clinics were trained in different areas of TB care by specialists from the TB and HIV services with technical support from KNCV. Quarterly joint meetings under the leadership of the Almaty Health Department supported efficient collaboration and communication between the TB and HIV services and private clinics. To facilitate integration of private clinics into the national TB M&E system, KNCV and the TB service made the necessary adjustments to TB indicator, recording and reporting forms and added private clinics to the list of facilities for monitoring of TB activities.

The good practice covers several areas of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*, such as the systematic TB screening of contacts and high-risk groups, early diagnosis of all forms of TB and universal access to DST and good quality treatment. The engagement of non-public health-care providers in TB and HIV care (private clinics and NGOs) improved cross-sectoral collaboration in the provision of integrated TB and HIV care for key and general populations.

Evidence of impact

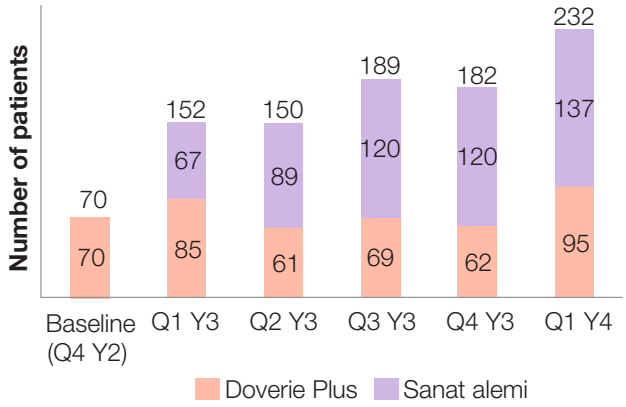
The NGO Network has already demonstrated its efficacy in providing patients with screening, referral and treatment adherence support. Two NGOs reported on the TB services cascade in year 3: Doverie Plus and Zabota. In all, 3% of screened individuals were identified as presumptive TB patients and referred for testing. Of these, 10% were confirmed as having TB. All confirmed patients were enrolled to TB treatment (Fig. 32). In total, Doverie Plus and Zabota, screened 1786 patients for TB in year 3 of the project (October 2016–September 2017), identifying 48 with presumptive TB, of whom seven (15%) were confirmed to have TB.

Fig. 32. TB services cascade, NGOs, year 3



The average number of patients who received support for treatment adherence per quarter in year 3 increased from 70 to 168. In year 3, Doverie Plus provided support for treatment adherence to 60 patients per quarter on average (baseline fourth quarter, year 2: 70 patients), while Sanat Alemi provided treatment adherence support to 99 TB patients on average. Thus, 2.5 times more people received treatment adherence support in the fourth quarter of year 3 than in the same period of the previous year (Fig. 33). Thanks to the intervention of local NGOs, the small number of patients with interrupted treatment (four in year 3) were all successfully encouraged to return to the project and continue treatment. The NGO Zabota received an award from the head of the TB service, naming it the NGO most active in TB screening and detection.

Fig. 33. Patients provided with treatment adherence support, by quarter

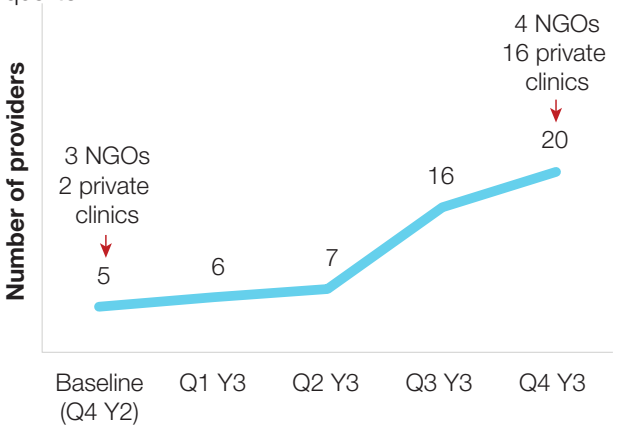


Q: quarter; Y2: year 2 (October 2015–September 2016); Y3: year 3 (October 2016–September 2017); Y4: year 4 (October 2017–September 2018).

All 16 private clinics now provide TB care, and four local NGOs (the NGO Network) were engaged in the public–private model of integrated TB care for key populations in Almaty, as developed by KNCV and AFEW Kazakhstan. In year 3, 1142 people from key populations (people who inject drugs, sex workers, (ex) prisoners, migrants) were screened for TB in private clinics, of whom 51 were positive and referred for TB diagnosis; of these, 16 (31%) had bacteriological confirmation of TB infection. All were enrolled to TB treatment provided by the TB service. In January 2018, an additional 14 clinics were engaged in the model and will participate in public–private activities.

A total of 20 non-public service providers had been engaged to the public–private model of integrated TB care for key populations in Almaty at the end of year 3 (baseline in the third quarter of year 2, five providers; Fig. 34). Fig. 35 shows various events of the project.

Fig. 34. Number of engaged non-public providers, by quarter



Q: quarter; Y2: year 2 (October 2015–September 2016); Y3: year 3 (October 2016–September 2017); Y4: year 4 (October 2017–September 2018).

Strong political commitment from the Almaty Health Department and the NTP led to increased recognition of the important role of the non-public sector in high-quality TB/HIV service delivery. They created an enabling environment for TB and HIV care, such as grants for NGOs. As a result, for the first time, the health-care authorities of Almaty created a Working Group on HIV and TB uniting all service providers: HIV, TB and drug-related medical services, international organizations and NGOs, in interacting with key populations at risk for HIV and TB.

There was a rapid positive change in attitude of the engaged private providers towards TB care. Currently, private clinics are creating conditions for the provision of TB diagnostic and treatment services. Private clinics have become more open to collaboration, resulting in smooth communication between the TB dispensary and private clinics in providing laboratory and instrumental diagnostic services, and in monitoring and supervising clinics.

The Stop TB Partnership in Kazakhstan was initially established in Almaty and then expanded to the national level, chaired by the NTP.

Sustainability of the good practice

From the start, the Almaty Health Department and TB service were involved in project implementation and played a key role in coordination and capacity-building to ensure sustainability of the practice. the Integration of private clinics into the TB service through adapting

Fig. 35. Photos showing various events that took place during the project

A. AFEW Kazakhstan. Action on TB Day

B. AFEW Kazakhstan. Training of primary health-care staff on stigma and discrimination

C. KNCV. Round table on initiation of the Stop TB Partnership in Almaty city

D. KNCV. Working meeting with private clinics and NGOs on development of public–private mix plan

the referral system for TB screening, diagnosis and treatment and the TB M&E system support sustainability of the practice. Signed agreements between private clinics and the TB dispensary on providing the necessary services to private clinics, such as TB laboratory diagnostics, clinical consultations by TB doctors and training, ensure the continuum of TB care.

During advocacy meetings with the Ministry of Religion and Civil Society and the Almaty Health Department, recommendations were formulated to enable access to government funding and training for NGOs on accessing these funds to sustain the role of civil society organizations in TB/HIV care provision.

Netherlands. The TB/HIV platform in the Netherlands: a network of clinicians and public health professionals discussing collaborative activities to monitor and control both diseases

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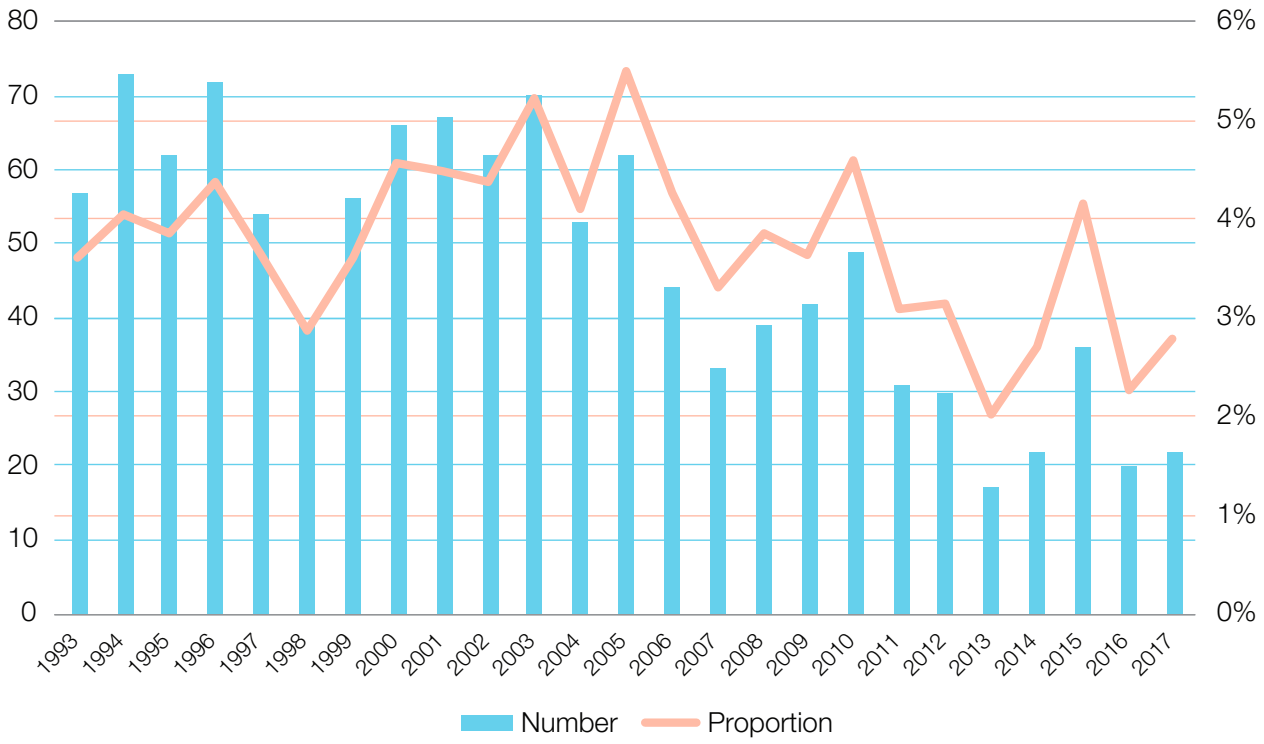
Background

The TB and HIV epidemics are closely linked because HIV infection is the main risk factor for progression from LTBI to active TB disease. Globally, 11% of the 10.4 million new TB cases in 2016 were HIV infected and 22% of the 1.7 million TB deaths were among HIV-

infected patients *(1)*. Both the absolute number and the proportion of HIV-infected TB patients are, however, declining worldwide due to successful HIV prevention programmes, including increased access to ART.

In the Netherlands, the number of TB patients declined from 1800 in 1994 to 787 in 2017, when the lowest number was recorded since notification became mandatory in the 1950s. Since 1993, HIV coinfection has been included as a variable in the Netherlands TB Register. Fig. 36 shows that an average 59 HIV-coinfected TB patients were notified per year during the 1990s, declining to an average of 23 per year over the last five years. The proportion of HIV-coinfected TB patients decreased from 3.9% in the 1990s to 2.8% in the last five years.

Fig. 36. Number and proportion of HIV-positive TB patients, Netherlands, 1993–2017



Sources: Netherlands TB Register and the National Institute for Public Health and the Environment (RIVM), Bilthoven.

WHO recommends undertaking collaborative TB/HIV activities to establish and strengthen the mechanisms for delivering integrated TB and HIV services; reduce the burden of TB in people living with HIV and initiate early ART; and reduce the burden of HIV coinfection in patients with presumptive and diagnosed TB (Table 13) *(45)*.

Description of the good practice

We started a TB/HIV Platform in the Netherlands, which held its first meeting on 1 December 2016 (World AIDS Day) involving 16 interested clinicians and public health professionals working in TB and HIV control. The Platform's objectives were defined as to: (i) share knowledge on both diseases; (ii) discuss the management of TB/HIV-coinfected patients; (iii) improve collaboration between professionals working in TB and HIV clinics and programmes; and (iv) systematically collect data for operational research *(46)*. In 2017, a second physical meeting and a teleconference were organized.

Following WHO recommendations for TB/HIV activities, the Platform's terms of reference, objectives and composition partly addressed activities A.1, A.3 and A.4 (Table 13). Three further topics researched by Platform participants were discussed during all three meetings:

- **HIV-coinfected TB patients** (Table 13, A.2). The proportion known to be HIV positive in 2011–2015 was 3.1% among all notified TB patients and 5.6% among those with a known HIV status. Study of the

Table 13. WHO-recommended collaborative TB/HIV activities

Category	Subcategory
A. Establish and strengthen the mechanisms for delivering integrated TB and HIV services	A.1. Set up and strengthen a coordinating body for collaborative TB/HIV activities functional at all levels
	A.2. Determine HIV prevalence among TB patients and TB prevalence among people living with HIV
	A.3. Carry out joint TB/HIV planning to integrate the delivery of TB and HIV services
	A.4. Monitor and evaluate collaborative TB/HIV activities
B. Reduce the burden of TB in people living with HIV and initiate early ART	B.1. Intensify TB case-finding and ensure high-quality anti-TB treatment
	B.2. Initiate TB prevention with isoniazid preventive therapy and early ART
	B.3. Ensure control of TB Infection in health-care facilities and congregate settings
C. Reduce the burden of HIV in patients with presumptive and diagnosed TB	C.1. Provide HIV testing and counselling to patients with presumptive and diagnosed TB
	C.2. Provide HIV prevention interventions for patients with presumptive and diagnosed TB
	C.3. Provide co-trimoxazole preventive therapy for TB patients living with HIV
	C.4. Ensure HIV prevention interventions, treatment and care for TB patients living with HIV
	C.5. Provide ART for TB patients living with HIV

Source: World Health Organization, 2012 *(45)*.

medical records of 123 TB/HIV-coinfected patients found that 66 (54%) had been diagnosed with HIV more than one month before the TB diagnosis, while the others had been diagnosed with both TB and HIV during the present disease episode *(47)*. Among the 66 patients with a known HIV infection, 29 (44%) had been diagnosed with HIV more than five years before the TB diagnosis, 46 (70%) were on ART, and 14 (21%) had a history of previous TB treatment *(47)*. Overall, 97% of patients are retained in HIV care in the Netherlands and 92% of those diagnosed and linked to care in the Netherlands are on ART (Table 14). Our data suggest that a higher proportion of TB/HIV-coinfected patients may not be on ART. Further study is needed to identify the underlying factors for the low ART coverage, but they could be related to a poor reporting system.

- **HIV testing for TB patients** (Table 13, C.1). The proportion of TB patients with known HIV status in the Netherlands TB Register increased from 20% in 2006 but stabilized at around 50–60% in 2013–2015, despite the National TB Control Plan and national guidelines recommending routine HIV testing *(48,49)*. Due to a study improving HIV data entry in the TB Register, the proportion of TB patients with a known HIV status in 2015 increased to 73.2% *(50)*. This higher proportion was sustained in 2016 and 2017 when reporting institutions were reminded about incomplete HIV data for TB patients; this effort will be repeated in the coming years.

- **LTBI screening for HIV-positive persons** (Table 13, B.2). This has been controversial in the Netherlands. The Dutch TB/HIV guideline was amended after research showed that clinicians did not agree with the recommendation to screen all newly diagnosed HIV-positive persons for LTBI. The current recommendation is to only screen HIV-positive persons from countries with a high

TB incidence or with known exposure to TB *(49)*. Currently, the new guideline is being implemented in several hospitals and supported by research documenting the challenges and yield of LTBI screening.

Several variables were recently added to the Netherlands TB Register to capture clinical management data for HIV-infected TB patients: the provision of co-trimoxazole preventive therapy and ART (Table 13, C.3 and C.5, respectively). Table 14 provides an overview of the key indicators collected in the Netherlands TB Register and the Dutch HIV Monitoring Register, enabling the country to monitor its WHO-recommended TB/HIV collaborative activities.

Conclusion

TB/HIV collaborative activities can be effectively implemented in a country where both diseases have a low prevalence. The most important factors are that surveillance systems are in place to monitor both diseases, including the WHO-recommended indicators, and that a TB/HIV Platform is available to discuss treatment of and efforts to further reduce both diseases.

Evidence of impact

We are currently discussing ways to improve collaboration between the Netherlands TB Register and the Dutch HIV Monitoring Register to increase collaborative efforts to further reduce both diseases.

Table 14. Key indicators and data on TB/HIV coinfection, Netherlands, 2016–2017

Indicator	*n*	Proportion
TB patients notified (2017)	787	4.6 per 100 000
Newly diagnosed persons with HIV (2016, projected)	816	4.8 per 100 000
Estimated number of persons with HIV (2016)	22 900	–
Persons with HIV, diagnosed and linked to care (2016)	20 264	94%
Persons with HIV, retained in care (2016)	19 136	84%
Persons with HIV, on ART (2016)	18 599	81%
TB patients with known HIV status (2017)	526[a]	68%[a]
TB patients coinfected with HIV (2017)	22	2.8%
TB/HIV-coinfected patients on ART (2017)	13[a]	59%[a]
TB/HIV-coinfected patients on co-trimoxazole preventive therapy (2017)	3[a,b]	14%[a]
Eligible individuals with HIV screened for LTBI	Unknown	Unknown
Eligible individuals with HIV diagnosed with LTBI	Unknown	Unknown

[a] Preliminary data. In five TB/HIV-coinfected patients, information on ART and co-trimoxazole preventive therapy was not known yet.
[b] In the Netherlands, co-trimoxazole preventive therapy is recommended for patients with a CD4 count of 200 cells/mm^3.
Sources: Netherlands TB Register; National Institute for Public Health and the Environment (RIVM), Bilthoven; and the Dutch HIV Monitoring Register, Stichting HIV Monitoring, Amsterdam.

Sustainability of the good practice

The TB/HIV Platform is a low-cost activity, which only requires a meeting room and an interesting, relevant agenda. Physical meetings are planned once a year, with the possibility of holding additional teleconference meetings.

Portugal. Active TB/HIV coinfection: description of outcomes in a setting of integrated TB, HIV and drug dependency care in the North of Portugal

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Background

Despite a declining trend in TB incidence, Portugal continues to be an intermediate TB incidence country, the only one in western Europe. In 2014, 2264 TB cases were diagnosed (20 cases per 100 000 population) and HIV was the most common comorbidity (present in 14.7% of cases).

HIV-infected patients have a higher risk of TB development compared with people without HIV infection; other risk factors include alcohol, malnutrition, homelessness and intravenous drug use. Despite a dramatic declined over the last few decades,[10] injecting drug use has been an important driver of the Portuguese HIV epidemic. TB treatment is more challenging in patients with overlapping health harms and is further complicated by therapeutic interactions between opioid substitution therapy (OST) and ART. Incomplete TB treatment can lead to drug resistance, continued transmission, morbidity and mortality, and all efforts should focus on maximizing treatment outcomes.

In Portugal, concerted efforts have been made to integrate HIV, TB, drug dependency and psychosocial care through collaboration between treatment centres and support services.

Description of the good practice

In Portugal, HIV care is delivered by hospital-based outpatient clinics. TB treatment centres provide TB screening, preventive therapy and directly observed treatment, short course (DOTS) for active disease; they can be accessed directly or by referral from hospitals, drug treatment centres, outreach teams or other health-care services. OST has been available since 1987 via public treatment units, where multidisciplinary teams of doctors, nurses, psychologists and social workers develop patient-tailored care programmes.

HIV, TB and drug dependency care are linked through collaboration between the relevant services: TB treatment centres, HIV outpatient clinics, drug treatment centres and outreach programmes. Two integration models for these services in Porto have previously been qualitatively described in a rapid assessment of the accessibility and integration of HIV, TB and harm reduction services for people who inject drugs in Portugal.[11] However, quantitative data related to this integrative approach are sparse.

Centro Hospitalar São João (Porto) has implemented a collaborative integration model providing a patient-centred approach in which the multiple health programmes work together to deliver co-located treatment at the most convenient venue to the patient (in a health-care or community setting, or at home). The integration of TB/HIV and OST services is aimed at facilitating access to and maximizing outcomes for TB treatment, particularly among socially vulnerable people.

This study describes the TB diagnosis and treatment characteristics of coinfected HIV patients admitted to a University Hospital in Porto between 2008 and 2014. Follow-up data were complemented by information provided by the Public Health Department because patients were discharged from hospital as soon as their clinical or social condition was favourable.

Evidence of impact

Among 2853 patients followed up at the HIV clinic from January 2008 to December 2014, 139 (4.9%) were admitted to hospital for TB treatment, representing 13% of all admissions in the Infectious Diseases Ward and about 5% of the population of patients followed up in the HIV clinic over the same period.

TB diagnosis was classified as possible in 47 patients (34%), probable in 12 (9%) and definitive in 80 (58%). One third of patients had disseminated TB (n = 46),

[10] In 2014, out of 1220 new HIV diagnosis notified to national surveillance systems, only 3.3% were attributed to injecting drug use.

[11] A rapid assessment of the accessibility and integration of HIV, TB and harm reduction services for people who inject drugs in Portugal. European Commission/WHO grant agreement on Scaling up access to high-quality harm reduction, treatment and care for injecting drug users in the European region. Work package 3: Integration of TB and HIV treatment services. April 2012.

and 79 (57%) patients had positive sputum culture examinations. MDR-TB was documented in one patient and XDR-TB in none. Most patients were male (*n* = 111; 80%). Sixty-two patients lived in a precarious social situation, defined as unemployment, economic insufficiency (mean monthly income per household member of less than 1.5 times the Portuguese social support index value), indigence (homeless), reclusion or residence in a shelter home.

At the time of TB diagnosis, 31 patients (22%) were current drug users (intravenous, inhaled or smoked) and 34 (24.5%) were former drug users. Sixty patients (43%) were coinfected with hepatitis C virus and 13 (9%) with hepatitis B virus.

Most patients (*n* = 107; 77%) had a CD4 count below 200 cells/mm^3 and 35% (*n* = 49) had a CD4 count of below 50 cells/mm^3. For 37% (*n* = 51), TB and HIV were diagnosed simultaneously (median CD4 count: 74 cells/mm^3, interquartile range 25–134 cells/mm^3; median HIV load: 307 500 copies/mL, interquartile range 120 839–906 000 copies/mL). Of the 88 (out of 139; 63%) patients with a previous diagnosis of HIV infection, 48 (55%) were on ART and only 13 (15%) patients had an undetectable viral load. Notably, the study took place before the present recommendation of universal ART regardless of CD4 cell count. Of those patients who already knew their HIV status, previous LTBI screening was registered for only 25% (22 patients).

The median elapsed between the beginning of symptoms and TB diagnosis and treatment was 47 days (interquartile range, 27–102 days), with a median interval of 11 days (interquartile range, 3–31 days) from the first medical observation to treatment initiation. Having a precarious social situation was not significantly associated with the time elapsed from the start of symptoms to the start of treatment (46 days versus 61 days; *P* = 0.076); however, the time elapsed between the first medical observation and the start of treatment was shorter in the group with a precarious social situation (eight days versus 14 days; *P* = 0.034). In addition, the time elapsed between the start of symptoms and TB diagnosis was shorter for those known to be HIV infected than for patients who did not know their HIV infection status (median: 39 days versus 65 days; *P* = 0.028).

TB treatment was initiated for all except one patient, who died shortly after admission. In 24% (*n* = 34) of patients, pharmacological toxicity was identified during the treatment course; in 23 of these patients (out of 34; 68%), treatment had to be temporarily halted. A total of 63 patients (51% of those who were not on ART before TB diagnosis) started ART during the TB treatment period. The median period between starting TB treatment and starting ART was 94 days (interquartile range, 51–168 days). Patients with a CD4 count of less than 100 cells/mm^3 started ART sooner (median: 71 versus 152 days; *P* = 0.005).

A total of 89 patients completed treatment (64%), 18 (13%) were lost to follow-up and five (4%) abandoned treatment. In all, 26 patients died during follow-up (mortality rate, 18.7%); for 12 (46%), TB was the attributed cause of death. Having a lower CD4 count at the time of TB diagnosis was related to mortality (median: 60 versus 96 CD4-positive cells/mm^3; *P* = 0.011). Neither the HIV viral load at the time of TB diagnosis (*P* = 0.525), disseminated TB (*P* = 0.167) nor a precarious social situation (*P* = 0.065) was significantly associated with mortality.

Highlights

In this study, the mean time elapsed between the start of symptoms and start of TB diagnosis was shorter than the national average (91 days versus 104 days for all TB cases). This difference may reflect both an earlier search for health-care and a lower threshold for suspicion of TB, particularly in patients with a previous HIV diagnosis. Importantly, the shorter time to TB diagnosis and treatment initiation experienced by those with a precarious social situation and active drug use suggests that access to health-care was not hampered by major barriers from health services. As we included only patients who were admitted to hospital, those with more serious clinical or social conditions might be an overrepresented. Nonetheless, a total of 89 patients (64%) completed treatment. This treatment success rate is lower than the national rate for all TB patients (82.5% in 2014) but higher than the rate reported for HIV-positive patients in Europe (57.9%) *(51)*.

Furthermore, the TB mortality rate was 8.6%, lower than the rate reported in Europe in 2014 (13.7%) *(51)*. Given the characteristics of our sample population (44.6% living in a precarious social situation and 21.8% being current drug users), our treatment and mortality rates

suggest that reasonable outcomes can be achieved for difficult-to-treat population with overlapping health harms through integrating TB/HIV and OST services.

Sustainability of the good practice

This practice has been set up and is planned to continue for years with regular public funding from the National Health Service.

Ukraine. Establishment of joint M&E units to improve intersectoral cooperation for TB/HIV activities

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Background

Ukraine has a high burden of HIV infection combined with TB or MDR-TB. The WHO Global Tuberculosis Report 2017 estimates Ukraine's incidence rate for all forms of TB at 87 cases per 100 000 population (range 56–124 cases per 100 000 population) and mortality rate at 9.5 deaths per 100 000 population (excluding HIV coinfection) and 14 deaths per 100 000 population (including HIV coinfection) *(1)*. The HIV epidemic in Ukraine coupled with poor coverage of antiretroviral drugs is contributing to the growing proportions of TB/HIV-coinfected patients. According to national data, the number of new and relapsed TB/HIV-coinfected cases was 5646 and 1663, respectively, and 30.2% of the total number of HIV-related deaths was due to TB/HIV coinfection in 2017. as of 1 January 2018, 4883 TB/HIV-coinfected patients were receiving anti-TB treatment. The cumulative number of TB/HIV cases has steadily increased over the past 10 years from 4.8 cases per 100 000 population in 2006 to 13.3 cases per 100 000 population in 2017. Although TB patient mortality from AIDS-related illnesses has decreased by an average of 7% annually since 2012, TB was the primary cause of death of all AIDS-related deaths (3.9 deaths per 100 000) in 2017.

TB and HIV/AIDS services reside in separate parallel systems which work independently with a lack of coordination. As a result, HIV detection in TB patients is challenging and the rate of TB detection among people with HIV is low. Very often, TB/HIV-coinfected patients fall between the two services, leading to insufficient health-care provision. Health-care workers are not well trained in TB/MDR-TB and HIV/AIDS, which causes problems in TB treatment, isoniazid preventive therapy and ART. A solution to these problems is needed to strengthen work on TB/HIV coinfection.

Description of the good practice

At the regional level, the implementers of the project are the Volyn Regional AIDS Centre, the Volyn Regional Medical Anti-TB Territorial Association, the Rivne Regional AIDS Centre and the Rivne Oblast TB Dispensary. In both regions (Volyn and Rivne), the project is implemented by following the same algorithm: organizational, methodical joining of M&E departments at regional AIDS centres without alterations to the staff list. In order to ensure that TB/HIV M&E units work efficiently and systematically, several regulatory documents have been prepared and approved.

Thus, in the Volyn region, the Regional Coordination Council on HIV, TB and Drug Regulations approved provisions of the regional M&E group on TB/HIV and the annual M&E programme for TB/HIV activities, the Health Care Department approved decrees on the Establishment of a joint unit for the monitoring and evaluation of programme measures against TB/HIV, Provision of a joint unit for the monitoring and evaluation of programme activities to combat TB/HIV, Interaction algorithm of the joint unit on monitoring and evaluation of programme activities to combat TB/HIV, Algorithm of interaction of regional territorial medical associations and the Regional AIDS Centre to provide medical care to TB/HIV-coinfected patients, as well as the patient evaluation route for TB/HIV.

In the Rivne region the Regional Coordination Council on HIV/TB approved the work plan of the joint HIV/TB M&E Unit and the development and sustainability plan of the unified M&E system for programme activities on TB and HIV in 2016. The list of members of the Working Group on HIV/TB M&E has been updated. The Health Care Department approved an order On creation of the joint TB/HIV M&E Unit to perform programme activities for TB and HIV/AIDS and the National AIDS Centre approved provision of the TB/HIV M&E Unit.

Each region developed and implemented recording and reporting forms to monitoring the incidence of TB/HIV coinfection and indicators for M&E of TB/HIV measures. Specialists at regional AIDS centres have been granted access to the register of TB patients to verify data on HIV-positive people with TB. A training system has been introduced for specialists involved in TB/HIV case management.

Evidence of impact

The above-mentioned measures have contributed to improving intersectoral cooperation, the effective use of statistical data to monitor implementation of TB/HIV activities, developing regional HIV/AIDS and TB programmes, improving population access to TB/HIV services (including TB and HIV diagnosis, isoniazid preventive therapy, ART, co-trimoxazole prophylaxis, social and psychological support).

Sustainability of the good practice

The national implementation of joint TB/HIV units with political commitment at the national and regional levels will create a sustainable, integrated system of TB and HIV/AIDS services.

1E. Management of LTBI, preventive treatment of persons at high risk and vaccination against TB

Netherlands. The clinical TB coordinator in hospitals in the Netherlands

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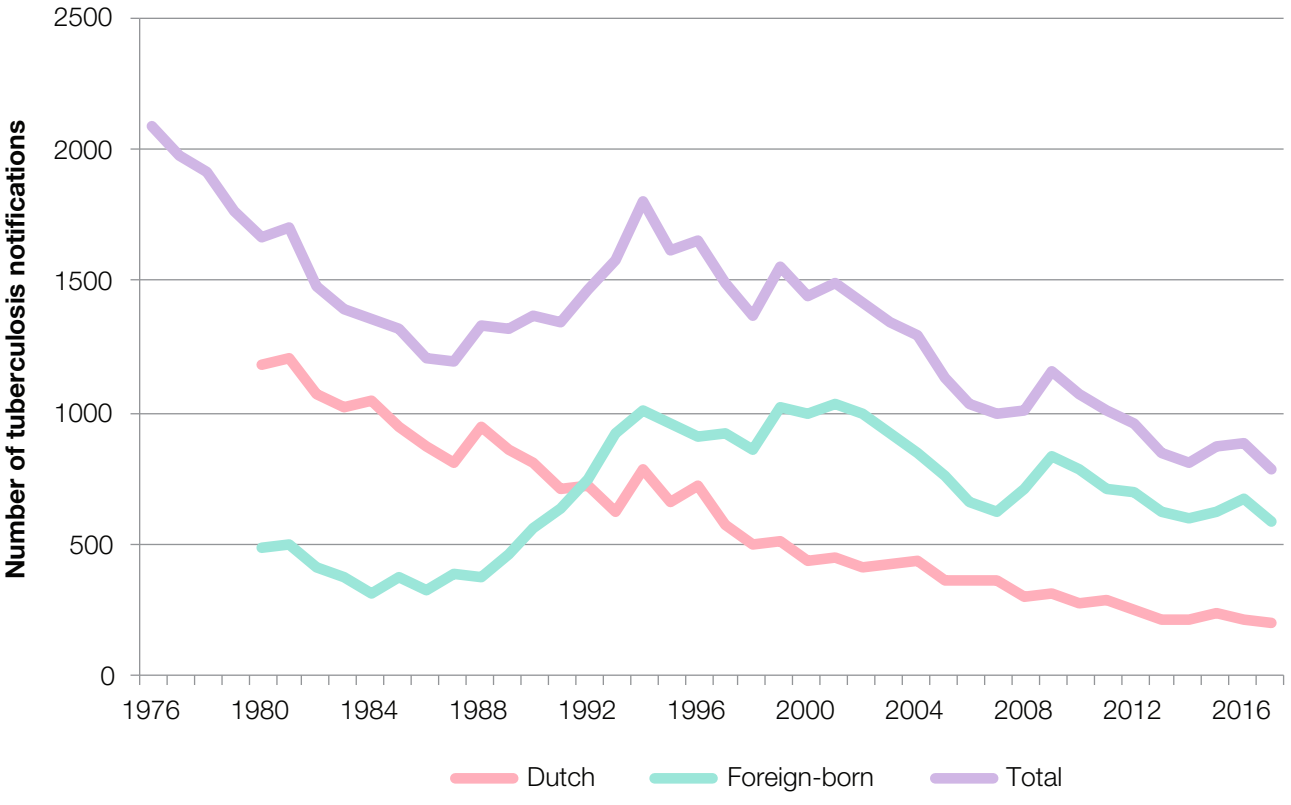
Background

The Netherlands is a high-income country with a total of 17 081 507 inhabitants and 12% (2 001 175) of its population born outside the country (foreign born; as of 1 January 2017) *(52)*. In 2017, the lowest number of TB patients (*n* = 787) was recorded since notification became mandatory in the 1950s. Fig. 37 shows that the steady decline that occurred since the 1950s stopped and then reversed in the 1980s, with proportionally more foreign-born TB patients. Since 1994, the downward trend has resumed (3.5% annual decline), although the country has occasionally experienced an increase for one or two years (e.g. related to a high influx of asylum seekers from countries with a high TB incidence) *(53)*. The TB incidence of 4.6 cases per 100 000 in 2017 was one of the lowest in the WHO European Region.

Description of the good practice

The National Tuberculosis Control Plan 2011–2015 stated that the decline in the number of patients and regional differences in number of TB cases would result in declining expertise among health-care professionals *(49)*. The Plan advised concentrating public health, laboratory and clinical care activities to maintain high-quality TB services. Treatment for MDR-TB and XDR-TB patients (annual average of 10–15 cases) was advised to take place only in one of the two TB centres (modern sanatoria). All hospitals were asked to make

Fig. 37. TB notifications, Dutch versus foreign born, 1976–2016



regional arrangements regarding clinical treatment for TB patients. In addition, establishment of the position of clinical TB coordinator was recommended. The tasks of clinical TB coordinators were formulated and endorsed by the Dutch Thoracic Society (NVALT). The clinical TB coordinator is to act as a reference consultant within a hospital for all TB-related questions, for all clinical specialists and for the hospital board and serves as the contact for the public health sector. The NVALT included the clinical TB coordinator as a required function during professional review visits to hospital pulmonology departments, which are conducted every five years.

TB Masterclass

The Erasmus University Medical Center, together with the GGD (Municipal Public Health Service) Rotterdam-Rijnmond and the KNCV Tuberculosis Foundation, developed a two-day training course for clinical TB coordinators. The training course is designed to facilitate interactive discussion and learning among a limited number of participants (15–20). The TB Masterclass has taken place eight times since 2011 (annually, and twice in 2013); 130 persons have been trained (121 clinical pulmonologists; eight TB doctors working at GGDs and one internal medicine infectious diseases specialist). Seventy-eight (89%) of the 88 Dutch hospitals now have a trained clinical TB coordinator.

Training starts with an overview of the specific activities and tasks of the clinical TB coordinator, who: (i) is responsible for the hospital's TB policy, including prevention and infection control (e.g. through setting up a Tuberculosis Advisory and Expert Group); (ii) is accountable to the Hospital Management Board on TB issues; (iii) has overview of all positive results for bacteriology tests (e.g. Ziehl-Neelsen/auramine stain, PCR, sputum culture), pathology investigations or other laboratory tests (e.g. positive interferon-gamma release assays); (iv) supervises or is responsible for the treatment and clinical management (including aerogenic isolation) of TB patients; (v) is consultant for questions on TB diagnosis; (vi) coordinates interventions for patients and staff exposed to an infectious TB patient in the hospital; (vii) coordinates multidisciplinary clinical case discussions; and (viii) organizes teaching and other educational sessions.

The first day of the training course involves updating basic TB knowledge, including TB epidemiology in the Netherlands, clinical presentation of a TB patient and TB diagnosis and treatment. An important take-home message is to work closely with microbiologists to recognize medical emergencies such as meningitis TB and TB in immunocompromised patients. The second day focuses on the legal framework and the role of public health based on the practices of clinical–public health cooperation gained in the Rotterdam setting. Interactive presentations cover the spectrum of preventing TB transmission/patient isolation within the hospital. The final topic in the course is the investigation of patients (who and how to test for LTBI) prior to the use of cellular immunosuppressants such as tumour necrosis factor (TNF-alpha) blockers.

The training course has created a network of clinical TB coordinators. Twice a year, the coordinators receive an email containing the latest developments in TB control in the Netherlands, such as the annual Tuberculosis Surveillance Report *(54)*. There is also an annual one-day refresher course for trained coordinators. The programme focuses on relevant clinical and public health literature related to TB (the year in review), new guidelines and case presentations by participants. Three times a year, a clinical case is presented in the Dutch journal, Tegen de Tuberculose. Trained coordinators also participate in working groups (such as the one that investigates TB mortality in the Netherlands) and the coordinator network is asked to share relevant cases.

Conclusion

Through the clinical TB coordinator role and continuous training, knowledge and awareness of TB are maintained in hospitals, despite a declining TB incidence.

Evidence of impact

Strengthening clinical care and creating the position of clinical TB coordinator have also had an impact on public health TB doctors, which have been declining in numbers for years. The annual refresher course for TB public health doctors now incorporates refresher training for clinical TB coordinators and strengthened collaboration between public health and clinical care, making these training courses more effective and efficient, with high attendance.

Sustainability of the good practice

NVALT formulated the tasks of the clinical coordinator, endorsed the position and included the position as a requirement during professional review visits to hospitals.

PART 2. BOLD POLICIES AND SUPPORTIVE SYSTEMS

2A. Political commitment with adequate resources, including universal health coverage policy in and health reform and penal reform aimed at improving TB control

Kazakhstan. Implementing activities aimed at cross-border control of TB among labor migrants in the Kazakhstan

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Background

Kazakhstan, as are most countries in central Asia, is among the 30 globally high MDR-TB burden. Although TB incidence and mortality rates in Kazakhstan have decreased over the last five years (2012–2016) from 81.7 to 52.7 cases per 100 000 population and from 7.4 to 3.4 deaths per 100 000 population, respectively, M/XDR-TB remains the main threat to TB control in the country (MDR-TB incidence increased from 20 to 25.7 cases per 100 000 population over the same period).[12]

In recent years, migration in the central Asian republics has increased dramatically; in conjunction with Kazakhstan's fast-growing economy, this has significantly impacted the growth of both internal and external migration. Information from available sources on the flow of migrants is limited and rather contradictory. TB is a social disease and migration, as a social determinant of health, increases TB-related morbidity and mortality among migrants and their surrounding communities. In this high-income country, TB prevalence in migrants from high TB burden countries is typically higher than in the local population and, reaching 3.3 cases per 1000 *(55)*.

By law in Kazakhstan, the detection of certain TB types in migrants requires treatment to be provided with free health-care guaranteed until the patient stops posing a threat to others or the disease stops threatening the patient's life. According to the 2012 WHO mission report on evaluation of the scientific and technical progress of the NTP, the system of TB care provision in Kazakhstan needed to be improved to address key issues of related to control of TB, M/XDR-TB and TB/HIV coinfection among internal and external labour migrants *(56)*.

In 2014, by decision of the In-Country Steering Committee of Kazakhstan, an international organization, Project HOPE, was designated the principal recipient of the Global Fund to Fight AIDS, Tuberculosis and Malaria grant for 2015–2017 to implement a programme addressing the cross-border control of TB, M/XDR-TB and TB/HIV coinfection among labour migrants in Kazakhstan within the framework of the Complex plan for tuberculosis control in Kazakhstan, 2014–2020 *(57)*, approved by Decree No. 597 of the Government of the Kyrgyz Republic on 31 May 2015.

Description of the good practice

Priority areas of the programme were the: (i) elimination of barriers that restrict access to health services for

[12] National tuberculosis programme annual review report, 2017.

internal and external migrants; (ii) prevention and treatment of TB among migrants; and (iii) strengthening community systems and reinforcing the role of civil society and NGOs. Major activities for this task have been devised in accordance with the minimum package for cross-border TB control and care in the WHO European Region *(58)* and have contributed to reinforcing the main provisions of the NTP envisaged in the Comprehensive Plan to Fight TB in the Republic of Kazakhstan for 2014–2020.

This practice has been promoted according to the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*, mostly in the domain of comprehensive, people-centred treatment and prevention (sections A–C), related to screening, access to diagnosis and treatment, with support for treatment adherence in this high-risk population: labour migrants and their family members.

Evidence of impact

During programme implementation, regulations on the access of migrants to diagnosis and treatment of TB were analysed and recommendations made for their improvement. Intersectoral plans have been developed and approved in pilot territories for the interdepartmental coordination of migration services, the health-care system, employers and other governmental entities involved in monitoring TB among migrants. Based on these activities, National guidelines on TB control among migrants in the Republic of Kazakhstan have been compiled (Fig. 38) and officially approved for use in the country.

Intercountry dialogue has also been initiated in the central Asian region through establishing the Regional Interagency Working Group on Cross-border Tuberculosis Control to draw up bilateral agreements between the Kazakhstan and Kyrgyzstan, as well as between Kazakhstan and Tajikistan. Together with the USAID Defeat TB project, three high-level regional meetings on migration and TB were convened in which representatives of the countries' ministries involved with migrants, donors, diasporas, and other international and local organization took part.

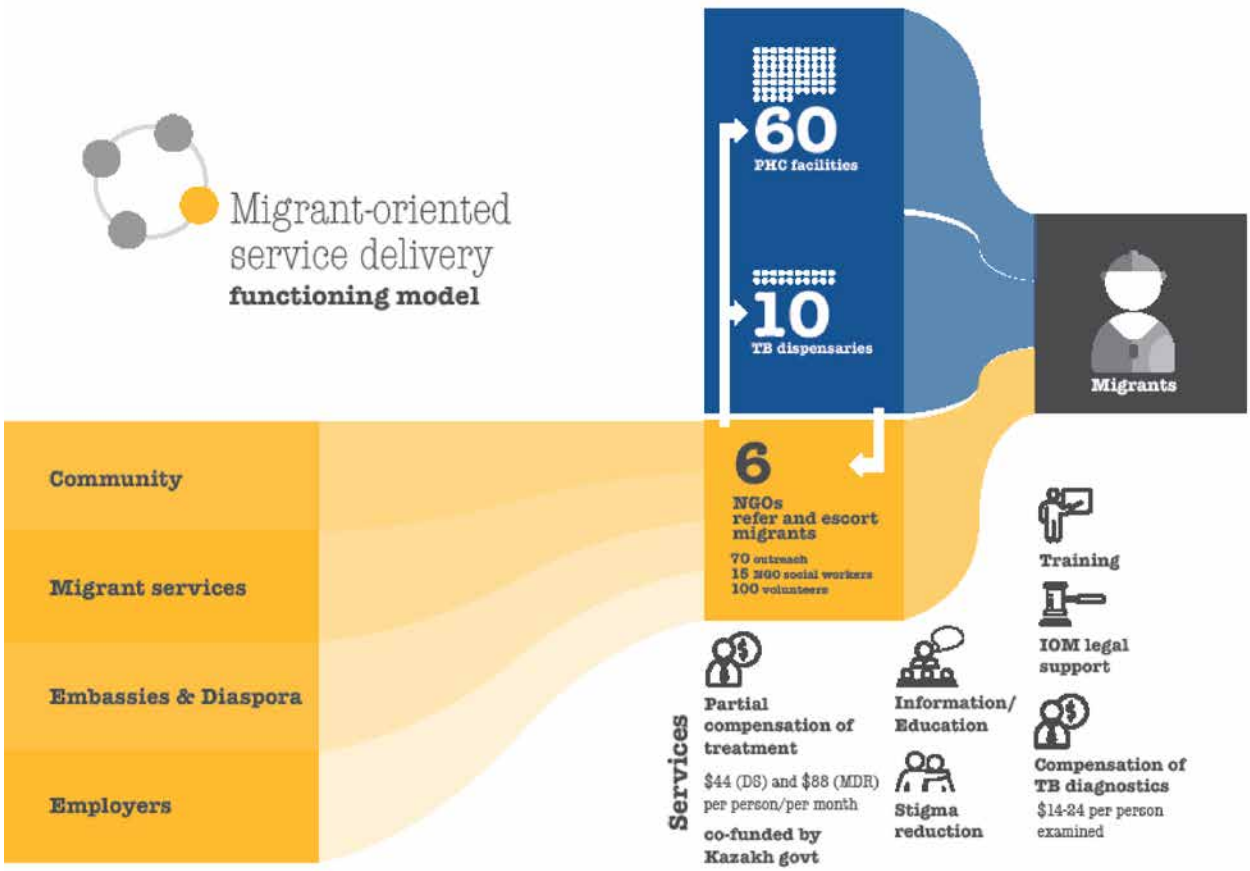
As a result of these meetings, a 12-month roadmap/Action Plan and relevant resolutions have been adopted and a functioning model of the migrant-oriented approach has been created, consisting of a migrant-friendly network of 60 general health-care institutions and TB dispensaries. All health-care institutions were reimbursed for providing services related to TB diagnosis and active screening in the target group, in addition to state co-funding for compensation for treatment of migrants with TB. The involvement of six local NGOs, including 70 outreach and 15 social workers, as well as over 100 volunteers, was instrumental in informing, referring and managing the target group, as well as providing motivational support to migrants receiving outpatient treatment (Fig. 39).

Fig. 38. Guidelines on tuberculosis control among migrants in the Republic of Kazakhstan

At the same time, active work on creating a supportive environment for this target group was carried out in order to conduct activities aimed at raising awareness and reducing stigma and discrimination to cover all strata from members of the target group to national and regional entities (Fig. 40).

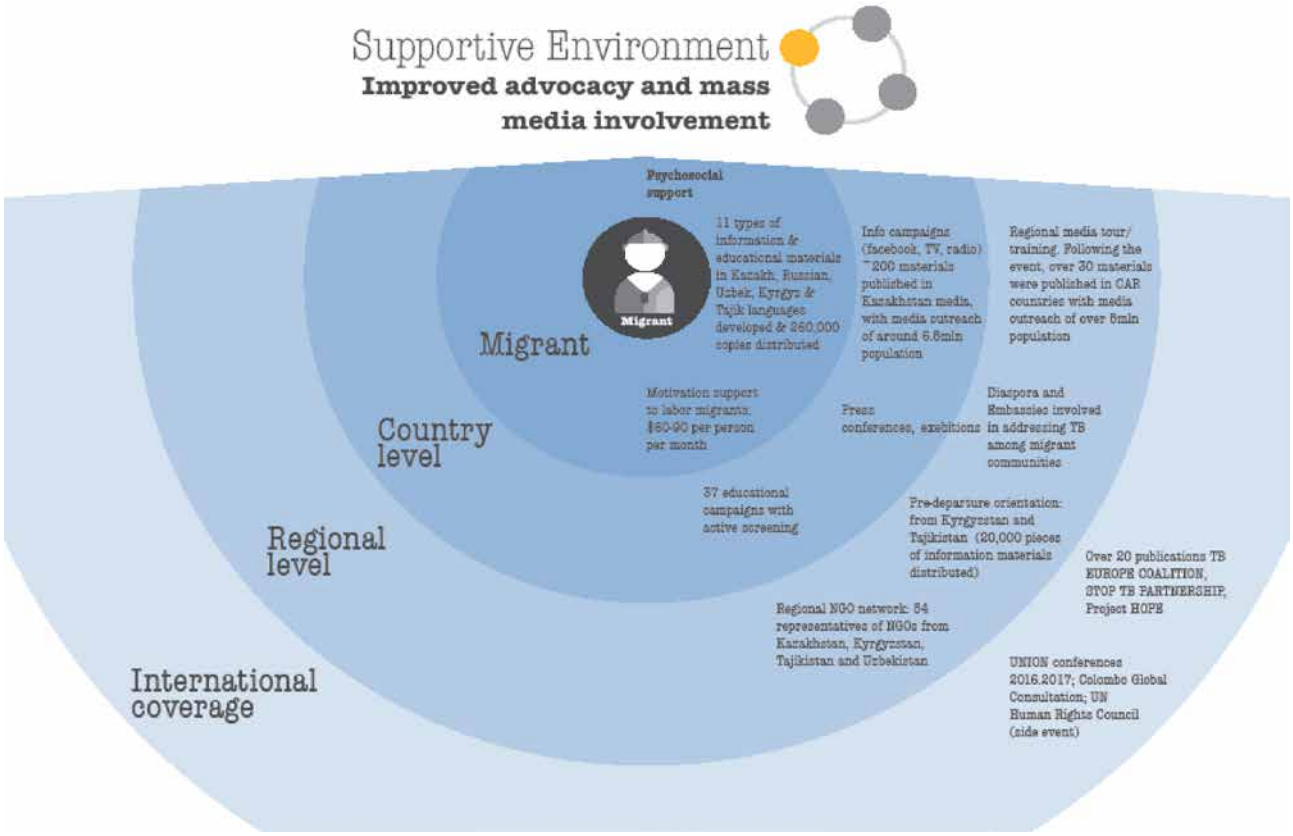
The system of TB case reporting and epidemiological surveillance among migrants became more sophisticated by refining the indicators, adding a module on TB notification and reporting among migrants to the National TB Electronic Register, and involving officials of the NTPs of Kyrgyzstan, Tajikistan and Uzbekistan

Fig. 39. Migrant-oriented service delivery functioning model



DS: drug-susceptible TB; govt: Government; M: million; MDR: multidrug-resistant TB; PHC: primary health care.

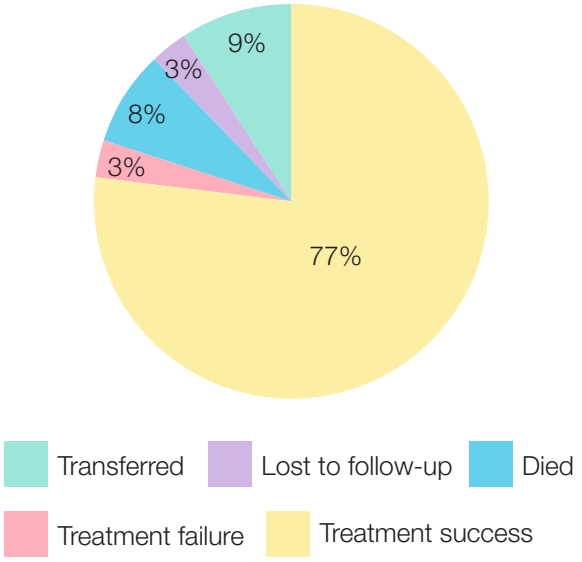
Fig. 40. Supportive environment: improved advocacy and mass media involvement



in cross-border data exchange on TB via the WHO European Region platform and the recommendations of the European Respiratory Society/WHO TB Consilium *(59)*.

During implementation of the programme, reported TB cases in external migrants increased several fold compared with 2014, whereas the number of TB cases declined among the citizens of Kazakhstan. During 2015–2017, activities carried out by outreach workers and volunteers to disseminate information, assure referrals and case management reached about 145 000 migrants and family members; more than 44 000 migrants were tested for TB, including sputum smear analysis with molecular genetic tests; and a total of 1607 TB cases among migrants were identified in the pilot territories. Of the 127 250 external migrants informed about TB, 401 TB patients were diagnosed during this period (>20% were MDR-TB cases). Analysis of treatment outcomes for DS-TB cases in 2015–2016 is shown in Fig. 41.

Fig. 41. Treatment outcomes for external migrants with DS-TB, 2015–2016



In addition to the detected TB cases among migrants, more than 100 individuals were suspected of having TB and 10 persons with smear-positive sputum samples had to leave Kazakhstan for further examination and treatment in their respective countries. These cases show a need for further improvement of regional dialogue and interaction related to cross-border TB control and data exchange. A project evaluation carried out by independent experts demonstrated the need for project activities, project continuation and developing good practices to be implemented at the country level.

As a result of implementing the programme and of advocacy for TB care provision, local authorities in Almaty bid for a state social order to enable local NGOs to carry out activities in the area of TB and HIV prevention among internal and external migrants in 2017; the Ministry of Health has also allocated resources from the state budget to state social order to be operated by local NGOs in performing TB preventive interventions in the three of Kazakh cities most attractive for labour migrants in 2018. The Ministry of Health made recommendations for changing the Code of the Republic of Kazakhstan on public health and the health-care system regarding migrant access to TB diagnosis and treatment depending on their immigration status in the country *(60)*.

Sustainability of the good practice

As a result of implementing the programme, plans on interdepartmental cooperation have been developed; the network of migrant-friendly health-care institutions is up and running; the reporting and accounting system is established; the National TB Patient Register was refined so that TB cases among migrants are reported and accounted separately; state allocations for the order for NGOs dealing with migrants are being made from both central and local budgets; the capacity of local NGOs to work with the target group has been built; more attention is paid to treating this target group; data exchange on TB cases in migrants in the central Asian region is being improved; and Guidelines on TB control among migrants in Kazakhstan have been developed.

Russian Federation. Organization and provision of measures for the social and psychological support for TB patients in the Republic of Khakassia

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Republican Clinical Tuberculosis Dispensary, Abakan

Background

The main reason for the low treatment effectiveness for TB patients is interruption of chemotherapy. Social support for TB patients has enabled increasing treatment adherence, by creating a system of material factors to encourage patients to comply with their prescribed medications. To optimize social support for TB patients and increase treatment effectiveness, additional funds must be allocated from regional and/or municipality budgets. Cooperation between TB control services and public organizations, along with the availability of psychological and legal counselling for patients, is the best option to provide of social support to improve patients' motivation for treatment. In the Republic of Khakassia (a Federal subject of the Russian Federation), the Russian Red Cross and the International Federation of Red Cross and Red Crescent Societies a joint project, Comprehensive model of the TB control programme in regions of the Russian Federation, was implemented from 2002 to 2004. The successful implementation of this project enabled a component of social support for TB patients to be included in the republican programme, Development of health in the Republic of Khakassia, since May 2005.

Description of the good practice

The Office of Health and Social Care at the Clinical TB Dispensary was established in 2014 to provide psychological and social assistance to TB patients. The Office's staff consists of a medical psychologist, a specialist in social work and an instructor in hygiene education. The primary selection for social support is based on data from a questionnaire completed by the patient and data from the district TB doctor, collected during a home visit to the TB patient. In the districts and cities of the Republic of Khakassia (except for Abakan), a decision on need for social assistance is made by the medical commission of a local health-care institution. For inclusion of TB patients in the target group, a combination of medical and social selection criteria is considered.

Medical selection criteria. The target group for social and psychosocial support includes TB patients registered with the regional TB dispensary and assigned to the course of TB outpatient treatment and hospital-at-home care (in which patients receive hospital-level care on an outpatient basis).

Social selection criteria. Social selection criteria need to be applied in resource-limited settings to provide the most expensive types of social support (food kits and coverage of transportation expenses) to render assistance to the patients with the most treatment interruption.

The types of psychosocial support for TB patients include:

- food kits;
- reimbursement of costs for return travel by public transport to the place of treatment (only for those days when the patient takes anti-TB drugs under direct observation by a health-care worker);
- legal and psychological assistance; and
- clothing and shoes (second hand).

Food kits

Food kits are delivered on a weekly basis or upon patient request once or twice a month. Patients receive food kits if they take all doses of their anti-TB drugs in a week under direct observation of a health-care provider or a person designated by the TB service to monitor their treatment.

An employee of the Russian Department of the Red Cross (Russian Red Cross) is responsible for the storage and distribution of food kits in large cities with a large number of TB patients. In all other cases, a health-care worker directly supervising treatment of TB patients is responsible on a voluntary basis.

If a TB patient receives treatment and psychosocial support in different places, the TB doctor gives a stamped, signed coupon with the date and the number of doses taken. The patient must then take this coupon to the psychosocial support venue. TB patients that

fail to take the prescribed doses of anti-TB drugs, for whatever reason, do not receive the weekly food incentives.

Reimbursement of travel expenses

Treatment sites are often located far from the places of patients' residence and patients may need to use a multistage transport route to reach them. In such cases, money is sought to compensate the travel expenses of the most socially disadvantaged TB patients included in the target group. An additional criterion for selecting TB patients for compensation of travel expenses is the distance from the patient's place of residence from the treatment site.

An employee of the Russian Red Cross responsible for compensating patients repays the patient's travel expenses upon receipt of the ticket(s). The patient then signs a financial statement confirming payment and the tickets are attached.

Support for patients with TB/HIV coinfection is organized to comply with infection control requirements. The social worker of the dispensary deals with the Pension Fund of the Russian Federation in Abakan upon registration of the appointed pension payments. Joint work with the Ministry of Internal Affairs is done on registration and the receipt of identity documents (passport). To assure infection control and convenience for inpatients, an agreement was reached to deliver pension payments to the TB dispensary (Table 15).

Legal and psychological assistance

Medical psychologists play an important role in providing patients with psychosocial support and facilitating preventive interventions by:

- preventing treatment interruptions and preventing bad habits during the therapy course (e.g. alcoholism, drug addiction); and
- identifying psychological factors that adversely affect treatment efficacy and adaptation to therapy (psycho-emotional disorders such as stress, anxiety, depression and suicidal thoughts).

Types of work for medical psychologists include:

- psychological counselling and psychodiagnostic surveys;
- conducting individual psycho-correctional activities;
- psychological education; and
- questioning patient groups to improve effective health-care provision.

The techniques used for psychological support include:

- cognitive behavioural therapy (to address psychological problems arising from a closed cycle of thoughts, emotions, feelings and behaviours), the only psychotherapeutic modality with a

Table 15. Types of assistance provided by a social worker, Republic of Khakassia, 2016–2017

Type of assistance (number of patients receiving support)	2016	2017
Obtaining an identity document	15	20
Obtaining mandatory health insurance policies	2	8
Obtaining the insurance number of individual personal account	4	20
Preparing documents for eligibility for a pension	21	38
Obtaining preferred drugs according to Federal and Republican programmes including at the AIDS Centre	8	25
Receiving the cards of a citizen who has the right to receive a set of social services to record the release of medicines, according to Federal and Republican programmes	3	8
Receiving and delivering pension payments to seriously ill patients	5	11

high efficacy, as confirmed by clinical trials, and supported by sound scientific evidence – this is the main approach to working with patients;

- art therapy (for patients with severe emotional disorders, difficulties in communication, social withdrawal or shyness);
- sand therapy (to stabilize the psycho-emotional state, improve movement coordination, improve finger mobility, stimulate sensory perceptual areas and tactile-kinesthetic sensitivity);
- autogenic training (to acquire skills related to self-control in critical situations, emotional stability, resilience to anger, resentment); and
- body-oriented therapy (to alleviate muscle tension).

The purpose of psychological support for TB patients is to:

- provide a socially acceptable way out of aggression and other negative feelings – psycho-correctional classes are a safe way to let off steam and defuse emotional stress;
- facilitate the process of psychotherapy;
- study the patients' suppressed thoughts and feelings– sometimes, strong emotions may only be expressed and clarified through verbalization;
- develop a sense of internal control; and
- focus on their sensations and feelings.

This type psychological support leads to changes in the psycho-emotional (improved mood, increased ability to respond appropriately to emotionally difficult situations, reduced emotional and physical stress) and the behavioural domains. To prevent suicidal behaviour among TB patients, lectures are delivered on the topic of Stop suicide!, explaining the reasons for, types of and signs of an impending suicide attempt and making recommendations for preventing prevention. A social video tape entitled Live! is shown at the end of the lecture.

Political support and commitment from the Government of the Republic of Khakassia has permitted the successful and consistent function of this practice for over 10 years.

Evidence of impact

Efforts to prevent the spread of TB in the Republic of Khakassia have significantly reduced the treatment interruption rate, especially in Abakan (the capital city): over the 2002–2016 period, the treatment interruption rate declined from 24% to 5% in Abakan; and over the 2014–2016 period the treatment interruption rate decreased by almost threefold to 1.4%. The lower treatment interruption rate has also improved treatment efficacy: the rates bacteriological conversion and cavity closure increased by 1.5 times the end of treatment (from 55.3% to 74.7% and from 43.8% to 66.2, respectively) among newly diagnosed TB patients. Treatment efficacy increased to 73.4% among all categories of TB patients (DS-TB and DR-TB) registered for therapy in 2015 who completed treatment by the end of 2016.

The TB epidemiological situation has also improved. The TB incidence rate in the Republic of Khakassia was 61.8 cases per 100 000 population in 2014 but had reduced to 52.9 cases per 100 000 population in 2016. TB prevalence over the same period decreased from 167.3 cases to 146.7 cases per 100 000 population. During this period, the TB mortality rate in the region (including in prisoners) decreased from 13.5 to 8.9 deaths per 100 000 population.

Since 2014, the TB Service of the Republic of Khakassia is working to meet the targets of the Roadmap to implement the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(8)*.

Every year, psychologists survey TB patient satisfaction with the quality of their health-care. Analysis of the results show that patients are satisfied with conditions in the TB hospital and the attitude of health-care staff: if problems are encountered, effective measures are taken to overcome them. Thus, the internal audit made it possible to increase patient satisfaction with their health-care.

Sustainability of the good practice

The practice of providing social and psychological support to TB patients in the Republic of Khakassia has been sustained and effective for 13 years (since 2005). Since this practice started, funding has come from the Republican budget within the framework of the state

programme, Health care development in the Republic of Khakassia until 2020.

Since the Office of Health and Social Care was set up in 2014, the demand for social services has significantly increased. TB patients have many social issues related to obtaining documents, obtaining preferred drugs from the AIDS Centre, pension payments, etc. Since its implementation, this practice has experienced only short-term financial constraints and temporary suspension of its work.

Ukraine. Parliamentary action advancing partnerships to end TB in Ukraine

Submitted by: Rosanna Flury[1] | Serhiy Kiral[2] | Andrii Klepikov[3] | Yuliya Chorna[4]| Aleksandra Vasylenko[4]

[1]Global TB Caucus; [2]Parliamentary Platform to Fight Tuberculosis, Government of Ukraine, Kiev; [3]International Charitable Foundation "Alliance for Public Health"; [4]"Alliance for Public Health" Ukraine

Background

Since 1995, the TB epidemic has been an urgent cause for concern in Ukraine. Each year, 4000 people die from TB in Ukraine *(61)*. Although progress has been made in tackling DS-TB, in 2017 alone 21 995 new TB cases were registered in the country. Furthermore, WHO estimates that about 20% of TB cases are missed by the health-care system. The main challenge for Ukraine is to combat DR-TB, both in terms of treatment success and new cases appearing. The treatment success rate for MDR-TB patients from the 2014 cohort was only 46%; therefore, urgent action is needed to improve this worrying statistic.

In Ukraine, addressing TB is a priority for state policy in the field of health-care and social development. Nonetheless, both a platform to consolidate the efforts of all stakeholders working to end TB by facilitating a multisectoral, participatory approach and the influence and power to help make the necessary changes are lacking.

Description of the good practice

Worldwide, members of parliament (MPs) play important role in fighting TB epidemics: they form the link between public and government and have unique tools available to them to drive change. For example, through budget allocations and follow-up and monitoring of government policy and legislation, they can help promote access to diagnostics, treatment and health-care for those who need it. MPs develop policies, form public opinion and represent their constituencies – thus, they have a great capacity to improve the models of TB care and the effectiveness of TB treatment. However, until recently, MPs have not been involved in addressing TB in Ukraine. In the past, TB was perceived as solely a medical issue under the auspices of the Parliament Health Committee; however, TB is heavily influenced by social determinants and therefore requires a broader approach. Exploring the risk factors associated with TB from different angles opens the door to a multistakeholder approach from both medical and social perspectives. With this in mind, and with the aim to bring on board all MPs with possible commitment, the interfactional Parliamentary Platform to Fight Tuberculosis was officially launched in Ukraine in October 2017. Currently, 47 Ukrainian MPs have joined the Platform.

The official launch of the Parliamentary Platform was preceded by a year of preparatory work. The idea of creating the Platform was conceived in September 2016, during a visit from Baroness Alison Suttie, Member of the United Kingdom House of Lords to Ukraine on behalf of the Global TB Caucus – a global parliamentary network which unites more than 2300 MPs across the world. Baroness Suttie's example in fighting TB through the United Kingdom All Party Parliamentary Group on TB was an inspiration for stakeholders in Ukraine. The Ukrainian Parliamentarian, the Honourable Mr Serhiy Kiral MP, who has been the rapporteur for a Council of Europe enquiry into DR-TB in Europe, took the initiative to take forward the launch of a Ukrainian Parliamentary Platform.

The Global TB Caucus supports the work of parliamentary platforms around the world, particularly through engaging civil society focal points within countries, to technically support the operation of the platforms. In Ukraine, the civil society focal point is the International Charitable Foundation "Alliance for Public Health", which is involved in supporting the ongoing functioning of the Parliamentary Platform through helping to organize meetings, sharing good practices and serving as a liaison with national and international stakeholders.

The work of the Parliamentary Platform is unique in that its mission is to consolidate the efforts of all stakeholders to end TB. It works closely with governmental institutions (particularly the Ukrainian Centre for Public Health, Ministry of Health) and MPs from different committees, civil society organizations, including organizations of TB-affected communities, and individual patient activists. It is also linked to international processes and networks through cooperation with the Global TB Caucus.

The Parliamentary Platform and its national and international partners were closely involved in the processes leading up to the United Nations General Assembly high-level meeting on ending TB in September 2018. Using participatory approaches and democratic procedures, and in close partnership with its governmental counterpart (the Ukrainian Centre for Public Health, Ministry of Health) and civil society organizations, it has agreed joint steps and taken actions to support Ukraine's position on the United Nations General Assembly high-level meeting on ending TB.

Evidence of impact

Evidence of impact of the good practice includes:

- a resolution for a public consultation for Ukraine's response to the United Nations General Assembly high-level meeting on ending TB;
- materials (releases, media monitoring, pictures) related to joint stakeholder activities of the Light Up the World in Red to End TB initiative *(62)* within the Stop TB Partnership's global campaign for World TB Day 2018 under the umbrella of the Parliamentary Platform;
- a press release on the events of World TB Day 2018;
- a resolution of the Parliamentary Assembly of the Council of Europe on antimicrobial resistance and DR-TB in Europe; and
- a Parliamentary Platform Facebook page.[13]

The most important positive impact, beyond engaging MPs in the fight against TB, is the strengthening of the intersectoral cooperation. So far, the Parliamentary Platform has served as a space for dialogue and actions of the legislative branch (Parliament), institutions of the executive power branch, including the Ministry of Health and the Ministry of Social Policy, civil society organizations, and affected communities, which are united to end TB.

Since the launch of the Parliamentary Platform, there have been three round table meetings organized at the Parliament (opened for the broad participation of the interested stakeholders), joint action for World TB Day 2018 and preparation for United Nations General Assembly high-level meeting on ending TB. As the result of the Platform's activity, Parliamentary hearings on TB were agreed and scheduled for October 2018.

Sustainability of the good practice

The Global TB Caucus secretariat will provide ongoing administrative support and technical support is ensured through the current activities of the civil society focal point, the International Charitable Foundation "Alliance for Public Health".

[13] Parliamentary Platform Facebook page (https://www.facebook.com/platformaborotbiTB/, accessed 21 September 2018).

WHO European Region. The Eurasian Parliamentary Group on TB: working together to create and sustain political will in the WHO European Region

Submitted by: Rosanna Flury

Global TB Caucus

Background

It is widely acknowledged that increased political will is needed to end TB in the WHO European Region and beyond. Although the Region has the lowest burden of TB worldwide, it has the highest rates of DR-TB, which poses a significant threat to global health security. Many countries in the Region have been struggling with their TB epidemics for decades and, although some good progress has been made, there is still a long way to go. Driving TB up the political agenda is recognized as a key element needed to accelerate the response. There is current global political momentum on the disease, such as an international focus on antimicrobial resistance through the G20 (Group of 20), the 2016 United Nations General Assembly high-level meeting on antimicrobial resistance, the foundations set by the 2017 Global Ministerial Conference on Ending TB, the United Nations General Assembly high-level meeting on ending TB, and a global push to increase the strength of health systems and move towards universal health coverage. In order to help accelerate the TB response in the Region, this momentum should be maximized through political engagement on the disease.

Description of the good practice

Parliamentarians are important decision-makers and play the critical role of linking the public with country governments and other decision-making bodies at the regional level. Parliamentarians influence national policy, budgets and legislation but also create public awareness and political momentum. They have a unique range of tools available to them (for example, asking parliamentary questions, launching enquiries, holding hearings) to hold governments to account on their promises at and regional levels.

One of the most important roles of parliamentarians is to encourage a sustained response to a certain issue by developing legislation, increasing funding, facilitating accountability and working in partnership with others to monitor successes and challenges. The Eurasian Parliamentary Group on TB, a network of over 200 parliamentarians from across the Region, exists to help cultivate political momentum to bring about the step-change that is needed and to facilitate a sustainable political response to TB in the Region through working in partnerships. The Eurasian Parliamentary Group on TB was launched in 2016 and is led by Mr Stephan Albani, member of parliament (MP; Co-chair, Germany), Ms Oxana Domenti (Vice-President, Republic of Moldova) and Baroness Alison Suttie (Vice-Chair, United Kingdom). Since the group was launched, many partnerships to help create a sustainable political response have been initiated. For example, Ms Oxana Domenti and Dr Akaki Zoidze MP (Georgia) worked with the Euronest Parliamentary Assembly to create a platform to focus on TB in the assembly itself: the group has since engaged new members of the Parliamentary Group and regularly discusses TB at Euronest meetings. Co-Chairs of the Euronest Parliamentary Platform on TB are Ms Malahat Ibrahimgizi, MP (Azerbaijan) and Mr Giorgi Pirinski, Member of the European Parliament (Bulgaria).

Baroness Suttie has worked closely with the International Charitable Foundation "Alliance for Public Health" in Ukraine and participated in the regional Cities project, funded by the Global Fund to Fight AIDS, Tuberculosis and Malaria, in which she visited Odessa to meet the city Mayor and other stakeholders, including representatives of civil society, and participated in signing the Zero TB Cities Declaration. Across the region, national parliamentary groups on TB have been launched in Azerbaijan, Georgia, Latvia, Kyrgyzstan, the Republic of Moldova (in collaboration with the Regional Eastern European and Central Asian Project (TB-REP)), Tajikistan, Ukraine and the United Kingdom. These groups help create a sustainable national parliamentary response to TB and help to facilitate multistakeholder participation, including with civil society and community representatives. The Parliamentary Group works closely with the TB Europe Coalition and TB People in facilitating engagement with civil society and community and former patient representatives.

Evidence of impact

Evidence of impact of the good practice includes:

- the Global TB Caucus website (www.globaltbcaucus.org) and Facebook and Twitter pages;
- media materials from the launch of the Eurasian Parliamentary Group on TB in Bratislava in 2016;
- media materials from the launches of national parliamentary working groups on TB across the Region;
- the website of the United Kingdom All Party Parliamentary Group on Global Tuberculosis[14];
- media materials from the Euronest Parliamentary Assembly regarding its Parliamentary Platform on TB;
- the Parliamentary Assembly of the Council of Europe Draft Report on MDR-TB in Europe (not publically available yet);
- media materials from the eastern Europe and central Asia TB Summit in Tbilisi in 2017;
- the European position on the United Nations General Assembly high-level meeting on ending TB; and
- evidence from the TB-REP on parliamentary engagement, including the launch of the Republic of Moldova National TB Caucus in 2017.

The good practice has resulted in an increase in collaborative activities with other areas of health, especially when working with MPs that also work in other areas of health, for example, HIV (in some countries, parliamentary working groups focus both on HIV and TB), tobacco control, hepatitis, antimicrobial resistance and noncommunicable diseases.

Sustainability of the good practice

The model of the Global TB Caucus is designed to gradually become self-sustaining, even without support from the Global TB Caucus secretariat: this is through the connection of parliamentarians with civil society and through collaborating with other regional bodies and networks (such as the Euronest Parliamentary Assembly) to facilitate including discussion of TB in their agendas, due to its importance in the Region. At the national level, parliamentary working groups on TB (or national TB caucuses) work with national partners and stakeholders, in particular with civil society focal points who are already working on TB on the ground in that country and, it is hoped, will continue to do so as long as TB still poses challenges. They also work with governments, NTP managers and other international organizations, such as the Global Fund, the Stop TB Partnership and WHO.

[14] United Kingdom All Party Parliamentary Group on Global Tuberculosis (https://www.appg-tb.org.uk/, accessed 21 September 2018).

2B. Strengthening of all functions of health systems, including well-aligned financing mechanisms for TB and human resources

Belarus. Implementing the World Bank's project: carrying out the Optima-TB study in Belarus

Submitted by: Alena Skrahina | Hennadz Hurevich | Dmitry Klimuk

Republican Scientific and Practical Centre of Pulmonology and Tuberculosis, Minsk

Background

The TB incidence, prevalence of active TB and TB mortality rate in Belarus declined between 2000 and 2015, while the relative proportion of TB patients with M/XDR-TB increased over the same period. In Belarus, the treatment success rate for TB was 88% for new and relapsed cases (2014 cohort), 54% for MDR-TB (2013 cohort) and 38% for XDR-TB (2013 cohort).

Ambitious national targets were set, including a 35% reduction in TB-related deaths, a 12% reduction in TB incidence and a 75% increase in the treatment success rate for MDR-TB by 2020. For the first time in the country (and in the whole eastern European Region), a group of international experts, under the auspices of the World Bank, conducted an Optima-TB study to evaluate the TB control programme, including the existing financial and resource opportunities, and their adequacy to meet the set goals.

Description of the good practice

Primary data included the number and profile of TB cases registered in the country between 2000 and 2015, as well as the scope of service provision related to TB diagnosis and treatment and associated costs.

Based on the collected data, a mathematical model (the Optima-TB model) was subsequently developed to predict changes in TB epidemic indicators until 2035 *(63)*. Th model also permitted incorporating a number of pre-set scenarios, including the impact of redistribution of the available financial resources in favour of priority areas such as prevention and therapy on the TB epidemiological situation.

Calculations made using this model showed that at the current level of expenditure on TB control activities (US$ 61.8 million in 2015) and the current resource allocations, the rates of TB incidence, prevalence and mortality will continue to decline moderately until 2035, but that no national goals, global milestones for 2020 or targets for 2035 will be achieved.

Analysis of the efficiency of resource allocation (based on the findings of the mathematical model) found that the country had some capacity to redistribute the financial resources available to the TB control programme. The existing budget for 2015 ($61.8 million) could be optimally reallocated to ensure changes in the TB epidemiological situation by 2035, such as reducing TB prevalence among the adult population by 45% and decreasing the total number of TB deaths by 60%. The most expensive interventions, for which about 40% of budget funds are spent, are: inpatient treatment for TB patients; compulsory hospitalization by court order; and the use of mass chest X-ray fluorography for population screening. Notably, there is no reliable data to support the effectiveness of these interventions.

The resources made available by reducing the amount of inefficient interventions can be channelled to maximize the effect of new or underfunded activities, such as: incentives to providers of TB outpatient treatments; procurement of new, more efficacious therapeutic regimens to treat M/XDR-TB; molecular diagnostic testing; intensified/active TB case-finding among high-risk groups and expanded monitoring of contacts; control of LTBI in the population; and

implementing projects to provide care for people with alcohol dependence.

The proposed practice covers two main areas of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*. Since ensuring effective mechanisms for financing TB control programmes is the most relevant area of reform, this study may be a source of primary data for political decision-making in this sector. Other components of a successful study, such as the methodology for building the mathematical model and collecting data, along with the results, will facilitate the progress of similar studies in high TB burden countries.

Evidence of impact

The results of the study were presented at a meeting attended by the Minister of Health and other Ministry of Health officials, principal staff of the TB Control Service and the WHO staff responsible for implementing the Regional Eastern European and Central Asian Project (TB-REP).

Sustainability of the good practice

For the proposed changes, redistributing the budget funds allocated to the TB Control Service is envisaged without increasing the amount of funding. Sustainability of transition to the people-centred model of TB care will be achieved through introducing more effective interventions and withdrawal of the hospital-based model of service funding.

Hungary. Improving service delivery for TB care using a bundled payment system in Hungary

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Background

In recent years, Hungary has reported several positive developments in the field of TB prevention and care. First, according to the recent surveillance report by the European Centre for Disease Prevention and Control and the WHO Regional Office for Europe *(2)*, Hungary had one of the best performances across the WHO European Region in reducing the number of new TB cases between 2012 and 2016. The mean annual reduction in new notified cases in Hungary (11%) was nearly triple the average annual reduction in European Union countries (4.1%), with a decrease in the estimated incidence rate to 8.8 cases per 100 000 population in 2016. However, performance indicators highlight several challenges in the care model related to both quality and efficiency: a relatively long length of hospital stay and a high hospital admission rate for DS-TB patients, with the relatively high loss to follow-up rate and a fairly low bacteriological confirmation rate for new and relapsed pulmonary TB patients (54.4%). These indicators clearly underline the need to strengthen the care model, including diagnostic testing. An important cause of such problems is that the current payment methods are clearly misaligned to the needs of people-centred care and are promoting the overuse of inpatient care with a focus on long-term hospitalization. This can be measured with indicators for the average length of stay and for hospital admission. A further cause is the organization of clinical governance, especially supervision of the quality of care provided.

Description of the good practice

The Hungarian Government has improved the performance of service delivery for TB care in Hungary by strengthening aspects of people-centred care, with a particular focus on improving quality and efficiency by a better alignment of payment methods across all service delivery categories. With this aim, the Hungarian Government initiated a pilot project in 2018, following a situation analysis and recommendations of the WHO Regional Office for Europe.

The pilot project applies a combination of policy tools to simultaneously address payment methods, clinical governance and the configuration of the model of care. The new payment mechanism, called a bundled payment, integrates the payments for hospital and ambulatory care into a single case payment with the hospital mandated as care coordinator. A particularly attractive aspect of this approach is that it can address weaknesses in payment methods and clinical governance not only for TB prevention and care but for the whole health system.

Evidence of impact

Only preliminary data are available on the performance of the pilot project. Evaluation will be needed after the projects ends next year.

Sustainability of the good practice

The set of policy tools implemented in the pilot aims to improve resource allocation of from hospital to ambulatory care without the need for additional financial resources. At the same time, the new care model increases the capacity of ambulatory care services.

Kyrgyzstan. A cascade training approach is helping to build a quality management system in the TB laboratories of Kyrgyzstan

Submitted by: Gulmira Kalmambetova[1] | Maka Akhalaia[2] | Altyn Iskakova[1] | Klara Takieva[2] | Dilorom Kosimova[2] | Meerim Sydykova[3]

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Background

Quality-assured laboratory services are critical for the provision of timely, accurate and reliable results to support the diagnosis of all forms of TB, DST, treatment monitoring and disease surveillance. Weak laboratory systems are error prone, which impacts patient care and undermines the confidence of health-care providers in laboratory services. Implementation of a quality management system improves the quality of diagnostic testing, leading to better patient care. The primary goal of quality management systems is to provide systematic, continuous improvement in laboratory services in compliance with a set of standards: Those standards are listed in the document, ISO 15189 Medical laboratories: requirements for quality and competence *(64)*.

Improvement in the quality of diagnostic testing services in TB laboratories is a high priority in many countries including Kyrgyzstan. Before implementation of the Defeat TB project, a quality management system had been introduced at TB laboratories in only one oblast in Kyrgyzstan. There was therefore a high need to build the capacity of laboratories so as to implement and strengthen quality management systems in all TB laboratories countrywide.

Description of the good practice

In order to build and strengthen the capacity of TB laboratories to manage and monitor the quality of their services, a comprehensive training course for implementing a quality management system countrywide was initiated by the NRL in Bishkek with support from Defeat TB project.

Training materials for three cascade training sessions was prepared using two approaches: (i) the Strengthening Laboratory Management Towards Accreditation (SLMTA) Training the Trainer teach back tool for TB laboratories (developed jointly by the SLMTA programme and Global Laboratory Initiative) and (ii) the Laboratory Quality Stepwise Implementation tool (developed by the Dutch Royal Tropical Institute) for WHO based on the Global Laboratory Initiative Stepwise Process towards Tuberculosis Laboratory Accreditation (Global Laboratory Initiative tool) and mentorship.

A total of 19 laboratory specialists from across the country attended the training course, which included all 12 modules combining the theoretical and practical aspects of implementing a high-quality management system.

- The first training session covered the following modules: Introduction of training, Introduction of a quality management system, Documents and records, Organization/personnel, Occurrence management, and Facility and safety.
- The second training session covered four additional modules: Equipment, Client management and customer services; Purchasing and inventory, and Corrective actions.
- The third training session focused on the following five modules: Control samples, Process control, Management review, Document and record management, and Information management.

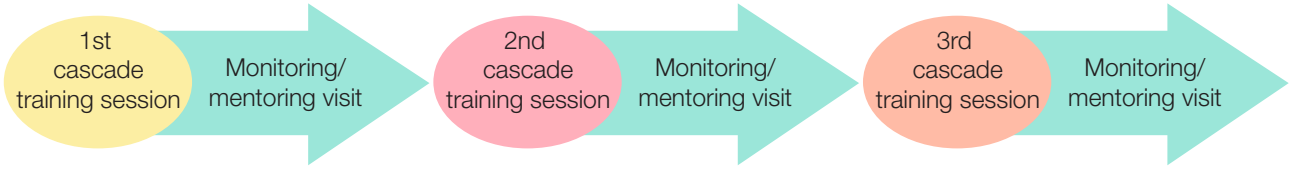
In the three months between training sessions, the participants had the opportunity to implement those elements of the quality management systems discussed at the training sessions using the PDCA

(plan, do, check, act) quality improvement project plan cycle; in the following training session, they gave presentations indicating what their situation had been, what actions had been taken and what had been achieved, according to the digital indicators.

The cascade training programme was followed by the regular quarterly monitoring visits and selected laboratory visits by a mentor (Fig. 42).

Assessments at baseline (in December 2015) and exit (in April 2017 for the NRL; in August 2017 for the Kara-Balta TB culture laboratory; and in October 2017 for the Bishkek city microscopy and GeneXpert laboratory) were conducted using the TB SLMTA Harmonized Checklist V2.1, based on the WHO Regional Office for Africa's guide for Strengthening Laboratory Quality Improvement Process Towards Accreditation (SLIPTA; based on ISO 15189 requirements) and incorporating

Fig. 42. Cascade training programme



TB laboratory-specific requirements (provided in the Global Laboratory Initiative tool) inserted as SLIPTA subclauses.

Differences between the overall scores and those obtained for each section served as a measure of impact for the programme. Assessors evaluated all laboratory operations in accordance with the TB Checklist, scored the assessment and documented their findings in detail for the next quality improvement plan. High-quality laboratory services are essential at all stages of the TB care cascade, from diagnosis and drug resistance testing to monitoring response to treatment.

Evidence of impact

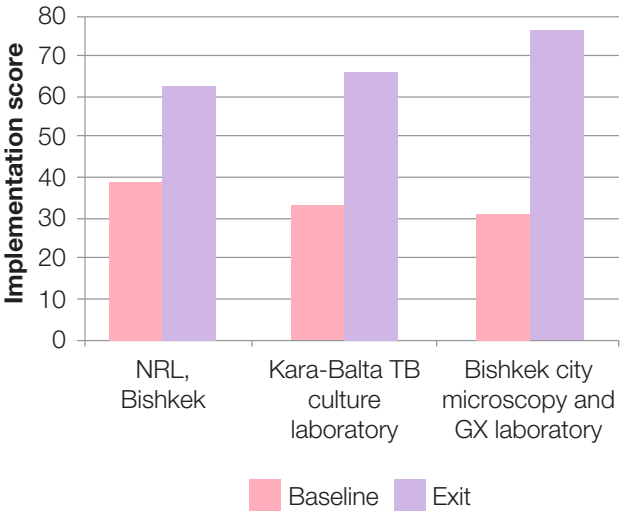
For the three pilot laboratories (NRL – Bishkek, Kara-Balta TB culture laboratory, Bishkek city microscopy and GeneXpert laboratory), the average baseline score was 86.7 out of a possible 252 (34.4%; range 78–99; see Table 16). At baseline, all three laboratories scored zero stars on the TB Checklist's star scale.

Table 16. Assessment score at specific time points

Laboratory name	Baseline	Exit
NRL, Bishkek	99	157
Kara-Balta TB culture laboratory	83	168
Bishkek city microscopy and GeneXpert laboratory	78	192

After cascade training and quarterly monitoring/ mentoring visits, the average score was 172.3 out of 252 (54.5%; range 157–92). After a year, the NRL scored one star on the TB Checklist's star scale, with a significant increase of 58 points on the average baseline score; the Kara-Balta TB culture laboratory achieved two stars, a significant increase of 85 points on the average baseline score; and the Bishkek city microscopy and GeneXpert laboratory had achieved three stars, a significant increase of 114 points on the average baseline score. Fig. 43 illustrates the progress made by the three pilot laboratories from baseline to the exit assessment.

Fig. 43. Implementation of essential components of the quality management system in three pilot laboratories, Kyrgyzstan



GX: GeneXpert.

The TB Checklist has 12 sections, each with scores of different weighting but adding up to 252. Figs 44–46 illustrate the progress made by the three pilot laboratories across all 12 sections of the TB Checklists.

Fig. 44. Implementation of the quality management system at baseline and exit, NRL

Fig. 45. Implementation of the quality management system at baseline and exit, Kara-Balta TB culture laboratory

Fig. 46. Implementation of the quality management system at baseline and exit, Bishkek microscopy and GeneXpert laboratory

Cascade training on quality management systems combined with monitoring/mentoring visits resulted in measurable improvement in laboratory performance, as measured by the TB SLMTA assessment tool. All pilot laboratories moved from zero stars on the TB SLMTA Checklist scale at baseline to two or three out of a possible five. Based on these findings, the cascade training model for quality management systems combined with regular monitoring/mentoring visits may be an effective mechanism to aid progress towards accreditation.

Sustainability of the good practice

A cascade training and mentoring programme customized to meet the needs of TB laboratories in resource-limited settings in a reasonably short time frame can build a firm foundation for further quality improvement through the implementation of ISO 15189 requirements. Such processes include tools, performance indicators and quality measures that are useful to produce meaningful improvements in the quality, reliability and timeliness of diagnostic testing.

Implementation of a quality management system helped to achieve targets for quality indicators, including reduced wastage due to expired supplies, a lower TB culture contamination rate, fewer unsuccessful molecular testing results, a lower sample rejection rate, less service interruption and a shorter turnaround time, and led to a high level of client satisfaction.

In addition, the trained national Quality Management Team is continuing to improve quality in TB laboratories towards international accreditation (ISO 15189) and to maintain its expertise in supporting the country's TB laboratory network.

Kyrgyzstan. Introduction of primary health-care financing for the successful completion of TB patient treatment in Kyrgyzstan

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Background

Although the TB incidence and TB mortality rates have been in steady decline since 2001, reaching 90.6 and 5.2 cases per 100 000 population, respectively, in 2017, TB remains a major public health issue in Kyrgyzstan.[15] In particular, MDR-TB presents a key challenge for the NTP because of suboptimal treatment success rates for MDR-TB of 53.7% (in 2015) and for DS-TB of 80.4% (in 2017). This is mainly caused by the high proportion of cases lost to follow-up: around 10% for DS-TB and 20% for MDR-TB. In 2016, 27% of new cases and 60% of re-treated TB cases were rifampicin resistant.

Within the framework of the National TB Control Strategy of Kyrgyzstan aims to expand ambulatory TB treatment for patients with the introduction of a people-centred approach. This will require greater involvement of health-care providers at the primary care level in managing TB patients, with the TB case management approach consisting of medical, psychological and social care provided to patients from the time of diagnosis to the completion of treatment. This approach will increase the workload of health-care providers in primary health-care, especially nurses and/or feldshers (physician assistants), requiring them to (i) perform new tasks beyond the conventional scope of their work and (ii) apply new knowledge and skills in practice.

Notably, the average salary of a family doctors is 12 000 Kyrgyz som (US$ 176) per month whereas primary health-care nurses and feldshers make about 9000 som ($132) per month: these figures are below the national average by 17% and 37%, respectively. Thus, in the context of low wages for primary health-care providers, devising and introducing incentives for performing extra work involving new tasks and functions has become an issue of the utmost importance.

Description of the good practice

In November 2017, the Mandatory Health Insurance Fund under the Government of Kyrgyzstan started piloting a new outcome-based payment method in addition to per capita reimbursement in the Chui region.

The main components of this method are that payments are made:

- for cure or treatment completion of TB patients; and
- to give financial incentives only to those health-care providers directly involved in managing TB patients.

The amount of payment for the successful completion of treatment by a TB patient depends on the whether the outcome is classified as cured or completed treatment, according to definitions provided in the approved clinical protocol. the incentive bonus for successful treatment completion by TB patients is given to primary health-care workers as a part of their monthly salary and cannot be redirected to pay for other needs of the health-care institution. The amount payable is calculated based on the time spent by health-care staff in working with each patient while applying the elements of TB case management (depending on case complexity): the payment was 12 000 som ($176) for DS-TB cases and 24 000 som ($353) for DR-TB cases.

Analysis of TB patient referrals from diagnosis to treatment completion revealed that the major burden of care was on family medicine providers, mostly nurses and feldshers. That is why a decision was made to allocate the bulk of payments for TB patients with an outcome of cured or treatment completed to family medicine providers (up to 85% of payments). However, it is envisaged to also pay district TB doctors and nurses (up to 10% of payments) to motivate them to monitor the quality of TB care and ensure they give methodological assistance to family medicine providers and primary health-care managers, thereby increasing their responsibility for the overall coordination of TB services at the primary health-care level (5% of payments).

[15] National Centre for Phthisiology of Kyrgyzstan, 2017.

Evidence of impact

The Chui region has been designated a pilot area for developing and introducing the practice of primary health-care reimbursement for the successful completion of treatment for TB patients. An average of 1200 new TB cases are reported annually in the Chui region, of which about 250 are MDR-TB.

Since November 2017, the Mandatory Health Insurance Fund has been making payments to primary health-care providers for the successful completion of treatment for TB patients at the primary health-care level. During the first three months of implementation (November 2017–January 2018), 294 TB patients successfully completed their treatment at primary health-care facilities in the Chui region: 233 with DS-TB and 61 with DR-TB. The total value of incentives paid so far to health-care workers involved in treatment provision for TB patients within primary health-care facilities is 4.26 million som ($62 647).

Notably, payments for the successful completion of treatment for TB patients are made from savings in the state budget made by restructuring TB care facilities. In 2018, a significant allocation of 30 million som ($441 200) was made for payments for successful TB treatment in an outpatient setting to include continuation of the practice in the Chui region and its expansion to the Talas region and the Kara-Suu districts of the Osh region.

The introduction of this method has changed the behaviour and attitude of family medicine providers towards TB patients. Providers have started looking for their patients at the expected arrival time, waiting for them after discharge from a TB hospital, filling out follow-up diaries more carefully and efficiently, and searching for the optimal way of arranging DOT using the case management tools. Before the introduction of the TB case management approach, over 60% of patients were followed up by a district phthisiatrician at a district centre, whereas since its introduction all TB patients returned to treatment at health-care facilities at their place of residence. As a consequence, district phthisiatricians have been able to switch from routine activities to coordinating TB control in the district, monitoring the quality of care and evaluating its outcomes.

Given the recent start of implementation and promotion of this practice, an in-depth study of its impact has not yet been done.

Sustainability of the good practice

Sustainability is ensured by the state budget being the source of payments to primary health-care providers for successful treatment completion for TB patients. The Mandatory Health Insurance Fund redirects the savings made in the course of restructuring TB hospitals to priority measures to improve TB control in the country.

A package of regulatory documents has been prepared, including the procedure, mechanisms, reporting forms authorizing payments for the successful completion of TB treatment at specialized health-care settings at the primary health-care level. Methodological recommendations for introducing the TB case management approach in an outpatient setting form the basis of the designed financing mechanism and will ensure its sustainable application in practice.

Republic of Moldova. Audit of TB control system in the Republic of Moldova

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Background

The Republic of Moldova has a high incidence of TB and MDR-TB; therefore, TB is a priority area of the health system. The Republic of Moldova continues to have a high level of TB morbidity and is included on the list of 18 high-priority countries for TB control in the WHO European Region and the global list of 30 countries with a high MDR-TB burden.

In recent years, following investment in TB prevention and treatment, a tendency towards stabilization of the TB epidemiological situation has been noted.

According to national statistics, the TB incidence in the country in 2017 was 83.3 cases per 100 000 population (3358 cases), 5.9% lower than in 2016 (88.5 cases per 100 000). The overall incidence among children increased by 15.9% in 2017 compare with 2016 (2017:

21.45 cases per 100 000 population, *n* = 166; 2016: 18.5 cases per 100 000 population, *n* = 143). However, according to the last reported data, the proportion of new and re-treatment MDR-TB cases is 26.6% and 63.8%, respectively. Over the last two years, the proportion of XDR-TB cases among registered MDR-TB cases was 6–8%.

A challenge to effective TB control is the association of TB with HIV infection. In 2017, the proportion of the new and re-treatment TB cases with TB/HIV coinfection decreased slightly to 8.2% compared with 2016 (8.5%). In 2017, the TB mortality rate decreased to 7.9 deaths per 100 000 population (*n* = 320) from 9.1 deaths per 100 000 population (*n* = 372 cases) in 2016.

Despite TB control interventions, including implementation of the new and rapid diagnostic methods for TB, new treatment options, incentive programmes for health providers and TB patients, diversification of service providers with involvement from communities, TB continues to affect society and remains a major challenge to the health-care system in the Republic of Moldova.

To obtain an independent, objective and comprehensive assessment of the country's TB control services, as well as to identify deficiencies and potential solutions to improve delivery systems to ensure high-quality TB control services, the Ministry of Health, Labour and Social Protection and the NTP agreed to perform an audit of TB control services in the Republic of Moldova.

Description of the good practice

Auditing is commonly implemented and undertaken by the internal auditing department of an institution. The health ministry and NTP acknowledged the need to comprehensively audit the TB control services, including auditing all systems involved in TB control within the same time frame using the same methodology and procedures. Generally, adequate assessments of the NTP have been predominantly held by international teams with participation of the national team. This comprehensive audit of TB control services was the first exhaustive, cross-sectoral examination of all TB-related systems involving national specialists from various levels of the health-care system, including public and non-government institutions and the academic sector.

Given the aim of a comprehensive audit of TB control services, the assessment focused on those dimensions deemed critical to successful TB control in the Republic of Moldova:

- the adopted strategies;
- the efficiency and effectiveness of TB control activities;
- the management of financial and non-financial resources; and
- compliance with regulatory acts and regulations.

TB control services were audited using specific methodology developed to facilitate efficient auditing and obtain concrete results. The methodology is specific to a risk-based audit, with the primary objective of improving performance and increasing control over activities within the NTP. The audit team comprised more than 30 specialists with extensive experience in all areas considered relevant for the audit. The audit strategy involved numerous field trips in various districts, direct discussions with representatives of medical institutions (from primary health-care to specialized TB services, NGOs, local public authorities and patients), verification of supporting documents and on-site assessments. The auditing team was composed of representatives of the diagnostic and clinical departments of TB health-care facilities, primary health-care facilities, funding and budgetary sectors, the Medical Ethics Committee, the National Council for Accreditation and Evaluation in Health, the National Centre for Health Management, the National Public Health Centre, the State University of Medicine and Pharmacy "Nicolae Testemițanu", the School of Public Health Management and principal recipients of the Global Fund to Fight AIDS, Tuberculosis and Malaria. The whole procedure took place between August and December 2017 and was supported by the Global Fund grant for 2015–2017.

The main elements of the approach used by the auditing team included:

- analysis of the organization framework of the National TB Control System in the Republic of Moldova;
- analysis of the policies, regulatory framework and procedures of the NTP;

- evaluation of the effectiveness and efficiency of activities within the National TB Control System;
- analysis of TB diagnosis and management;
- examination of TB clinical management;
- evaluation of infection control within the TB system;
- analysis of the supply of TB medicines and health-care products;
- analysis of the effectiveness of the M&E system of the NTP;
- evaluation of the quality assurance activities;
- examination of the human resources policies;
- evaluation of the budgetary system and of financing and financial management in the NTP; and
- assessment of how well information technology systems are tailored to the needs of the National TB Control System.

The auditing process had four key stages: (i) risk assessment of risks and the planning process; (ii) assessment; (iii) data processing and development of the report; and (iv) public presentation of the results.

The key elements that guided the auditing process were as follows.

- **Independence and objectivity.** Audit team members were selected to ensure their independence from the audited areas.
- **Risk-based audit.** The areas and institutions to be audited were selected following a risk assessment.
- **Planning the audit.** The audit was planned with consideration of the identified risks so as to be able to pay the greatest attention to critical issues within the National TB Control System.
- **Field visits.** The audit relied extensively on field visits to selected institutions, on a sampling basis. The field evaluation included visits to medical institutions at different levels of the health-care system, as well as visits to patients. This approach was critical to ensure understanding of the real problems faced by the National TB Control System.
- **Sampling.** Audits were conducted on a sampling basis.
- **Defining deficiencies.** The deficiencies outlined during the audit do not refer directly to individuals and do not establish the responsible persons because the purpose was to identify, first of all, solutions to systemic problems.
- **Developing the recommendations.** Recommendations were formulated in a more specific way to facilitate the definition of detailed plans for corrections and improvements.
- **Ensuring the quality of the audit.** To ensure a high-quality audit, a pyramidal structure was applied within the team as a principle for review. All audit documents and reports were reviewed by a supervisor within the team to ensure a high level of quality.

Visits to specialized TB service providers in two municipalities (Bălți and Chişinău) and six rayons (Anenii Noi, Cahul, Făleşti, Ialoveni, Nisporeni and Rezina), 28 primary health-care facilities at the rayon and rural levels, diagnostic and supply departments of the visited health facilities, Act for Involvement (NGO), and the central warehouse for TB medicines and laboratory consumables were undertaken for the implementation of planned activities.

Evidence of impact

To summarize the audit of TB control services, the national team synthesized a list of challenges common to all visited facilities and a list of specific institutional issues. Specific institutional challenges were recorded during audit and reflected in an action plan for every visited facility with a definite time frame for implementation. Moreover, the results of the audit visit were shared with the rayon (local) public administration for further discussion with all key stakeholders at the rayon level, such as the Social Assistance Department, Public Health Department, specialized TB services and primary health-care units, as well as with local public authorities in the rural settings.

The list of challenges in all visited facilities prompted the health ministry and NTP to further investigate whether

the issues were caused by gaps at the regulatory, operational level or by a lack of knowledge.

The final results of the audit consisted of practical recommendations to strengthen the fight against TB and increase the degree of monitoring and control over the activities being carried out. Beyond the recommendations related to diagnostic and clinical management, the list of recommendations included changes to policy-making and regulation, education (capacity-building), implementation and evaluation. Moreover, the team members improved their knowledge and skills in the cross-sectoral auditing of TB control services.

Through a comprehensive approach to TB control services, the intersectoral audit enabled the national team to simultaneously evaluate with multiple components using the same approach and to go beyond the common practice of in-depth assessment of the diagnostic, clinical and supply areas to include other areas such as regulation for the implementation of incentives by service providers and patients; M&E of the NTP architecture, which is currently distributed among several public institutions; introduction of standard operating procedures; activities of the quality councils of health-care facilities, to prioritize TB as a key topic in the agenda in internal medical auditing; strategy for further development of the electronic information system and related tools, along with a sustainability and security policy; involvement of services providers in different institutions; and functionality of the payment mechanism.

Sustainability of the good practice

The NTP and its partners will support the introduction into ordinary practice of cross-sectoral and inter-institutional auditing of the TB control services as an assessment tool to complement routine M&E procedures. Institutionalization of this methodology will empower the NTP to audit systems linked to the TB control programme at a predefined frequency, encompassing specialists with specific expertise from different health system levels and institutions, in addition to the current M&E team of the NTP.

Ukraine. Development and introduction of an optimal model for ambulatory treatment of TB patients and their social support as an effective way of improving TB treatment outcomes in Ukraine

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Background

According to national statistics or 2017, the combined incidence of new and recurrent TB cases was 63.9 per 100 000 population. The proportion of patients in the 2016 cohort with new TB outbreaks and recurrence with treatment interruption was 6.2%: treatment efficacy among these individuals reached 75.6% in 2017. Even though health-care is formally free in Ukraine, most Ukrainians live in fear of encountering the domestic health-care system. In addition to national taxes, citizens cover almost a half of their health-care costs with out-of-pocket payments; despite this, they are forced to accept services provision based on an outdated infrastructure with no quality assurance or respect for the rights and dignity of patients. The total health-care costs (state and private) in Ukraine is 7.8% of the gross domestic product. This value is lower than the average for European Union countries (which is 9.5% of the gross domestic product).

At present, Ukraine remains a country with the high prevalence of HIV infection and is one of the five countries with the highest MDR-TB incidence in eastern Europe and central Asia. This is because the system has failed to mobilize the available resources to implement a fully-fledged model of people-centred TB treatment.

Historically, the country's financial mechanisms have been designed to encourage the provision of inpatient services instead of stimulating patient management in all settings of health service provision.

Ukraine has the fourth highest number of hospital beds in the world and the second highest average length of stay in hospital in the WHO European Region (after the Russian Federation). With a large network of health-care institutions, with large numbers of hospital beds and doctors, Ukrainians seek medical attention much more often and stay in hospitals longer compared

with EU citizens; however, their health indicators are significantly worse, with a notably higher mortality rate and notably lower-than-average life expectancy. reasons for this are not the health infrastructure's quantitative shortages (such as number of hospitals, hospital beds and health-care providers) but rather its qualitative backwardness (lack of modern equipment, outdated approaches to treatment and care provision, insufficient workload) and, first and foremost, it is funded and managed within an extremely inefficient model of overall health system organization.

Description of the good practice

The state has made a commitment to reinforcing trust in the role of primary health-care as a foundation of the health-care system through introducing new incentive mechanisms for health-care workers and providing patients with competitive opportunities to select a doctor. This goal will be achieved by developing a package of guaranteed state obligations that treats all citizens of Ukraine equally regardless of their place of residence; introducing a new mechanism of primary care funding – risk adjusted per capita cost; designating a purchaser for the primary care services – the National Health Service will have the authority to conclude and execute contracts and control the quality of health-care, as well as introducing a reimbursement mechanism for medicines.

Within the framework of this reform, the public organization, Infection Control in Ukraine, piloted a model of financing TB outpatient care based on treatment outcomes between April and December 2017 involving two primary medical care facilities In Zhytomyr city and a regional anti-TB drug dispensary in the Chernihiv region. In total, the pilot supported 94 patients and examined 220 contact persons. An innovative aspect of this funding mechanism is that reimbursement depends on the final outcome; payments are made by the regional TB facilities to district phthisiatricians and primary care providers or social workers. According to these arrangements, incentives are simultaneously paid to phthisiatricians and family doctors to create a stronger interest in cooperation in managing TB cases and ensuring patient adherence to treatment.

The tangible incentives for primary care providers have significantly improved treatment adherence and indicators of treatment efficacy, leading to a cure rate for DS-TB patients was 95%.

During the transitional period of primary care development, the TB care services have an important coordinating role. The state intends to continue its efforts modernize this area of patient treatment, particularly through regional TB care facilities.

After considering worldwide experiences in reimbursement for primary care providers, a mixed payment method was introduced. The bulk of this payment is based on a per capita rate (i.e. a quota per citizen assigned to a relevant care provider, i.e. general practitioner/family doctor) and payment adjustment is envisaged depending on the risks posed by the age and sex of patients assigned to a particular doctor and whether the geographical area makes care provision more difficult (e.g. mountainous settlements and rural areas). The bonuses earned for achieving results specified in the contract for primary care provision are added to the basic salary. An example of a bonus is payment for success outcomes of TB treatment.

Evidence of impact

In all, 79 TB patients involved in the project had successfully completed treatment by the end of 2017, and 12 patients completed treatment after completing the project. No patient stopped treatment.

Sustainability of the good practice

The results of this practice have been included in a state policy for modifying approaches to funding services rendered to TB patients. The country is now ready to use this piloted model to reimburse primary care services.

Моксиф
таблетки по
Моксифлоксац
Каждая таблетка содер
Содержит паяктоу мон
Для приема внутрь.
Перед использованием
инструкцией по примен
Хранить в недоступном
Хранить в сухом/защи
Bullet
Universal
INTERNATIONAL PAPER
Vitamin B6
Pyridoxine
50 mg
500 Tablets
Vitamin B6
Pyridoxine
Number of treatment days (Число дней лечения)
Number of prescribed days (Число назначенных дней
Number of missed days (Пропущенные дней
Number of uncompleted days (Прерванные дней
Treatment adherence (to be filled out at the end of each month) (Выполнение
Drug (Препарат)
Days observed (Число дней наблюдения)
Missed days (Пропущенные дней)
Weight (Вес)
Date (Дата)

2C. Regulatory frameworks for case-based surveillance, strengthening of vital registration, quality and rational use of medicines, and pharmacovigilance

Belarus. Cohort monitoring of clinical events to assess the safety and efficacy of Bdq and Dlm combination therapy for TB

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Background

Over the past two decades, TB has persisted as a widespread disease in Belarus, significantly damaging the health of the population and the economy. The MDR-TB situation in Belarus is also disadvantageous. According to the WHO data, in 2015 the MDR-TB rate was 37% among newly diagnosed patients and 69% among those in treatment. Slightly over one half of patients diagnosed with MDR-TB in 2012 (54%) have been successfully treated. Fairly recently, an even more severe type of MDR-TB has emerged and proliferated: XDR-TB is characterized by additional resistance to any of the aminoglycosides and fluoroquinolones. The proportion of XDR-TB is 7.6% among newly identified TB patients and 16.1% among previously treated TB patients.

The options for treating M/XDR-TB are extremely limited. The treatment success rate varies from 22% to 68% and the mortality rate from 4% to 37%. In addition, the relapse rate is rather high. M/XDR-TB treatment is long, expensive and characterized by a high frequency of adverse events in patients, including serious adverse events. The major challenge to treatment initiation for M/XDR-TB patients is that at least four active anti-TB drugs need to be prescribed. Since June 2015, regimens including novel and repurposed anti-TB drugs such as amoxicillin/clavulanate, Bdq, clofazimine, imipenem/cilastatin and linezolid, have been in use for treating M/XDR-TB patients in Belarus. Since December 2016, Dlm started to be incorporated into TB treatment regimens. The current evidence base for the effectiveness and safety of regimens containing novel and repurposed anti-TB drugs has significant limitations because it is still limited to phase II clinical trials of relatively small cohorts.

The introduction of novel drugs with limited data to support their widespread use in health programmes is associated with a number of issues at country level related to the need to ensure the correct usage of new medicines; regular monitoring of patient safety; the timely detection of all negative changes in patient conditions; and taking appropriate measures to deal with adverse reactions and prevent serious undesirable outcomes in order to ensure that the application of novel drugs maximizes benefits to patients and health programmes, minimizes the risks to patients and prevents the further emergence of drug resistance. Fulfilment of these tasks requires implementation of a set of measures at country level, including refining the regulatory framework; ensuring the consistency of basic clinical and laboratory/equipment, staff training, devising new procedures for patient follow-up, developing and introducing the active monitoring of patient safety, and incorporating the pharmacological surveillance system into the NTP.

Description of the good practice

To introduce these new approaches into routine clinical practice for managing and following up patients and ensure continuous monitoring of patient safety while prescribing drugs with limited information in their safety profile, each novel anti-TB drug was introduced into the health-care programme within the cohort monitoring framework: one of the most intensive types of

monitoring the safety and efficacy of pharmacotherapy. Prospective cohort studies of patients receiving novel and repurposed anti-TB drugs have been conducted in Belarus since June 2015. From June 2015 to June 2016, 185 M/XDR-TB patients were enrolled to the cohort to monitoring the safety and efficacy of Bdq-containing treatment regimens. Since August 2016, cohort monitoring of patients receiving Dlm has been done, with 133 patients included so far. Upon completion of cohort monitoring, the prescription of novel drugs has been accompanied by active safety monitoring in accordance with an interim package of requirements for reporting adverse events. Until now, 640 M/XDR-TB patients have been enrolled to treatment with novel anti-TB drugs in Belarus, with a Bdq-containing treatment regimen prescribed to 507 patients; a Dlm-containing treatment regimen to 107 patients and a treatment regimen containing both Bdq and Dlm to 26 patients. Currently, Dlm treatment as a component of combination therapy to new patients is provided in the setting of cohort monitoring, whereas Bdq treatment is provided in the setting of active safety monitoring within the framework of routine pharmacological surveillance.

Treatment was prescribed based on a decision of the Republican of MDR-TB Council. The basis for referring patients to the Republican of MDR-TB Council is a laboratory-confirmed diagnosis of M/XDR-TB.

Patients in this cohort received combination therapy containing novel and repurposed anti-TB drugs. The patient treatment regimen was determined according to WHO recommendations for DR-TB patients in the Clinical guidelines for diagnosis and treatment of TB and its drug-resistant types, which was approved by Decree of the Ministry of Health of Belarus, with individual drug-susceptibility patterns also considered. In the intensive phase, as well as treatment continuation, ongoing laboratory, clinical, instrumental (e.g. ultrasound, bronchoscopy) and functional patient safety monitoring was done, including specific aspects of the safety profiles of novel anti-TB drugs. Each patient's condition was monitored by periodically completing data collection forms. Regular M&E of safety data significantly contributed to the early detection of all untoward effects in patients, enabling the adoption of appropriate measures to treat them and thereby prevent serious adverse outcomes, including treatment interruptions.

The efficacy profiles of novel anti-TB drugs comprised patient characteristics such as demographic data and medical data including the status of bacterial excretion, type of drug resistance of the *Mycobacterium tuberculosis* strain, type of case (new, relapsed) and the date of treatment initiation. Other characteristics included the rate and nature of adverse events and of serious adverse events and their degree of severity, preventability and reversibility; their risk factors; the efficiency of control measures; the efficiency of risk minimization measures; and the proportion of untoward effects necessitating modification to or discontinuation of TB therapy.

Evidence of impact

Preliminary results prove the high efficacy of novel anti-TB drug therapy for M/XDR-TB patients. Thus, in the patient cohort (185 individuals) receiving Bdq, 141 patients were successfully treated (76.2% versus 22–68% with conventional therapy); eight patients (4.3%) were lost to follow-up; two patients (1%) had treatment failure; three patients (1.6%) died; and 31 patients (16.9%) are continuing treatment. Notably, most patients in this cohort (58%) had previously been treated for TB and the XDR-TB rate was high (67%). Cohort monitoring allowed systematized data to be obtained, demonstrating a favourable safety profile for novel anti-TB drugs, including their use in patients with comorbidities and risk factors and in those with a different degree of disease severity from that of patients enrolled to clinical pre-registration trials. Adverse events were mild to moderate in most patients and the rate of serious adverse events did not exceed 10.33%, with most of these reversible. The monitoring process demonstrated the high efficacy of measures recommended within the framework of current WHO guidelines aimed at risk reduction, which include a specific safety monitoring plan and the introduction of active safety monitoring and guidelines for managing patients upon detection of disturbances associated with prescribed combination therapy with anti-TB drugs.

In addition to obtaining new data on the safety and efficacy profiles of novel anti-TB drugs, including increasing the amount of available information on specific patient subpopulations, this good practice improved the quality of health-care provision; strengthened the pharmacovigilance system at the health programme level; helped improved the professional skills of specialists to detect, verify and

report adverse events; increased patient adherence to treatment; facilitated interactions between the NTP and the national pharmacovigilance system, and expedited the introduction of optimal patient management approaches to routine clinical practice.

Sustainability of the good practice

Implementation of the additional measures for active safety and efficacy monitoring of novel anti-TB drugs received financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria in the initial stages. The necessary elements for patient monitoring have been incorporated into routine clinical practice and risk reduction measures have been adopted. The current practice of active safety monitoring of M/XDR-TB patients within routine clinical practice does not require additional financing.

Georgia. Implementation of the FAST strategy at the National Centre for Tuberculosis and Lung Diseases in Georgia

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Background

The number of TB cases in Georgia has substantially decreased over the past five years. In total, 3332 TB cases (all forms) were registered in the country in 2016 (including in the penitentiary sector), equivalent to 89.6 cases per 100 000 population; of these, 2465 were new cases (66.3 per 100 000 population). The NTP of Georgia, with support from the Government and international partners (mainly, the Global Fund to Fight AIDS, Tuberculosis and Malaria), has implemented every WHO-recommended intervention to produce the reduction in the number of TB cases; however, some bottlenecks in the overall set up of the health-care system in Georgia have the potential to unintentionally reduce the rate of TB case-finding and increase delays in TB referral and diagnosis. The TB case detection rate fell from 100% in 2006–2011 to 71% in 2016. Since 2012, all sectors of the Georgian health-care system have been privatized and most specialized TB units have (both organizationally and physically) become part of the inpatient and outpatient institutions/clinics run by private, multiprofile health-care providers. This has created an increased need to facilitate the delivery of TB services by private providers, including infection control measures, early case detection and diagnosis, and adequate treatment because a decrease in the detection rate is thought to be partly related to the health-care setup in Georgia. Thus, the National Strategic Plan for Tuberculosis Control in Georgia 2016–2020 has prioritized interventions directed towards strengthening the potential of private health-care providers to deliver the expected functions in Tuberculosis Control to increase the case detection rate, decrease the rate of delayed diagnosis and prevent the transmission of infection within multiprofile health-care facilities *(65)*. In response to these challenges, and with the support of the Global Fund's TB programme, a FAST strategy[16] has been implemented in 19 multiprofile health-care clinics, including the National Centre for Tuberculosis and Lung Diseases (NCTLD), a referral clinic for TB but and other pulmonary diseases, including respiratory disorders.

Description of the good practice

The FAST strategy includes a complex set of interventions aimed at decreasing TB transmission within a medical facility and at identifying patients with the symptoms and signs of TB *(66)*. This should involve active surveillance for cough because this is the leading symptom of TB and most TB transmission occurs between the onset of cough and start of treatment. Thus, the outcome of the FAST strategy is initiation of adequate anti-TB treatment, the most effective preventive measure for disease transmission. The availability of rapid diagnostic molecular methods (such as GeneXpert) is of key importance in this process. The intervention described here aims to isolate patients referred to the NCTLD with cough at admission and conduct GeneXpert MTB/RIF testing.

Implementation of the FAST strategy started in August 2017 in the NCTLD. A cough officer identifies self-reported patients with a productive cough and isolates them in a separate waiting room. The cough officer then informs patients of the importance of GeneXpert testing and if consent is given refers the patient to the microbiology laboratory for testing. The GeneXpert test result reaches the cough officer within 24 hours of

[16] FAST stands for Finding TB cases Actively, Separating safely, and Treating effectively.

submitting the sputum sample. Patients with positive test findings undergo an in-depth investigation for TB within the state TB programme. Patients who test positive for *Mycobacterium tuberculosis* infection are followed up by NCTLD epidemiologists, who inform the relevant TB facility about the patient's test results and treatment regimen.

This intervention addresses the two of the main components of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*. In terms of "integrated, patient-oriented care and prevention", the project aims to provide early diagnostic testing for all forms of TB and universal access to DST, including the use of rapid tests, along with systematic TB screening of patient contacts and high-risk groups, equitable access to high-quality treatment and the continuum of care for all TB patients (including those with DR-TB), and patient support to facilitate treatment adherence. In terms of "Bold policies and supportive systems", implementation of the FAST strategy provides airborne infection control, including regulated administrative, engineering and personal measures.

Evidence of impact

Between September 2017 and February 2018 inclusive, 1113 person with cough who self-reported to the NCTLD for various reasons related to coughing, have been tested with the FAST strategy. Of these, 932 patients had negative test results for *M. tuberculosis* infection, 76 patients could not provide an adequate quantity of sputum and 105 (9.4%) were diagnosed with active TB. Of the patients diagnosed with TB, 84 (80%) had rifampicin-susceptible TB, 19 (18%) had RR-TB, and drug resistance was not evaluated in two patients (2%).

The FAST strategy ensures that patients with presumptive TB are actively evaluated, separated and, if diagnosed, adequate treatment is initiated in a timely manner. Hence, in long run, this intervention is expected to improve the TB epidemiological situation in the country. However, an unexpected positive impact is the increase in referral of patients with cough (but not with presumptive TB) to the NCTLD from neighbouring health-care facilities that have learned that coughing patients will be investigated free of charge using rapid molecular methods.

Sustainability of the good practice

The FAST strategy is aimed at decreasing the burden and transmission of TB in Georgia The dedicated GeneXpert machine for the FAST strategy was procured by the Global Fund's TB programme and the cartridges are provided by the Global Fund. Costs of relevant staff (cough officers, epidemiologist, laboratory technicians) and machine maintenance/calibration are covered by the NCTLD budget. The current high level of government commitment ensures the sustainability of the practice.

Georgia. Implementation of the WHO framework for active TB drug safety monitoring and management in Georgia

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Background

M/XDR-TB remains a substantial challenge for NTP of Georgia, despite a steadily declining number of overall TB cases countrywide and universal access to quality SLD treatment since 2008. In 2016, the proportion of TB patients with MDR-TB was 10.3% for new cases and 38.4% for previously treated cases. In the same year, 33% of MDR-TB cases were resistant to fluoroquinolones, 41% were resistant to a second-line injectable agent and 17% were XDR-TB. In the 2013 cohort, the treatment success rate was poor for MDR-TB (49%) and even lower for XDR-TB (21%).

In response to the DR-TB crisis, the NTP started implementing new anti-TB drugs through the following mechanisms and chronology: Georgia started the compassionate use programme for Bdq in 2013; from 2014 to August 2015, the use of Bdq was expanded and Dlm was provided for compassionate use through the MSF programme. In April 2015, Georgia became a prime global candidate to receive life-saving access to Bdq for programmatic use through the joint USAID/ Janssen Therapeutics donation programme and the programmatic use of Bdq (through the USAID Bedaquiline Donation Program) and Dlm (through the Global Fund to Fight AIDS, Tuberculosis and Malaria/ Global Drug Facility) started in August 2015. Prior to

this, the Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs approved new per-patient funding for a comprehensive list of instrumental (e.g. ultrasound, bronchoscopy) and laboratory investigations needed for treatment safety monitoring linked to the use of new anti-TB drugs, such as electrocardiography investigations, liver function tests and electrolyte tests. In parallel to the implementation of new anti-TB drugs, a framework for active drug safety monitoring and management (aDSM) for new ant-TB drugs was introduced in Georgia.

Description of the good practice

Georgia was a pharmacovigilance-naive country in all disease contexts before 2015 and the programmatic introduction of new anti-TB drugs. In September 2015, shortly after the decision of the WHO and USAID partners' meeting in Geneva in July 2015 was reported, the National Centre for TB and Lung Diseases, called for an in-country stakeholder meeting with the goal to establish a new framework for introducing aDSM for new anti-TB drugs in line with recommendations of the WHO framework for aDSM for TB *(67)*. Representatives of the Pharmaceutical Department under the Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs, the NTP, the USAID-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program and MSF France took part in the discussions. It was agreed that Georgia would implement the core package of the aDSM framework as a mandatory requirement to monitor and report all serious adverse events (SAEs), as well as adverse events of special interest and other clinically important adverse events within frameworks of the MSF endTB output 1 operational research programme, with a plan for gradual takeover of the intermediate and advanced packages by the NTP after withdrawal of MSF from the country.

In collaboration with MSF France, an SAE recording and reporting form (with guidelines for its completion) and a document, Severity grading scale, were developed by the National Centre for Tuberculosis and Lung Diseases (NCTLD). Once these documents were ready, the NCTLD wrote the Minister of Health a letter summarizing the need for mandatory reporting rules and practices for SAEs in patients undergoing SLD treatment. In response, the health ministry issued in May 2016 Permanent Ministerial Decree No. 01-18/n on mandatory recording and reporting of the SAEs for all DR-TB patients, which came into force in June 2016.

The Ministerial Decree tasked the NCTLD with playing the central role in anti-TB drug pharmacovigilance countrywide and being responsible for the whole process, including data handling and causality assessment.

To facilitate the effective implementation of the Ministerial Decree on mandatory SAE reporting, training materials and lectures were developed for TB doctors and programmatic staff, with the participation of the NCTLD and MSF experts/consultants. Within the framework of the SIAPS Program, implemented by Management Sciences for Health, the Phthisiologists and Pulmonologists Association of Georgia, was engaged to conduct three-day training courses on aDSM (comprising 16 training sessions) for at least 200 TB doctors and TB programmatic staff. By 17 October 2016, the training course had taken place in Tbilisi and the regions: a total of 275 TB doctors and DR-TB programmatic management staff have received active pharmacovigilance training in over a period of three days, covering 100% of the human resource needs.

The Pharmacovigilance Committee (at central level, NCTLD), comprising a representative of the Pharmaceutical Department of the health ministry, members of the DR-TB consilium (a multidisciplinary advisory body), the pharmacovigilance focal point and the staff member responsible for pharmacovigilance data entry, has been established. District or regional TB doctors send the initial SAE report within one business day of becoming aware of the problem to the NCTLD pharmacovigilance focal point. Report completeness and data entry are checked at central level (NCTLD). The reporting doctors regularly receive feedback and/or requests for a follow-up report from the staff member responsible for pharmacovigilance data entry. Once per month (on the last Thursday of the month), the Pharmacovigilance Committee meets to review the full SAE reports (initial and follow-up sections) collected during the reporting month for causality assessment, using the criteria of the WHO Collaborating Centre for International Drug Monitoring in Uppsala, to evaluate the relationship between the SAE and each drug in the treatment regimen. Once per quarter, pharmacovigilance data are analysed by the Pharmacovigilance Committee and reports are prepared based on a predefined set of pharmacovigilance indicators.

The intervention addresses each of the main components of the Tuberculosis Action Plan for the

WHO European Region 2016–2020 *(7)*. In terms of "Integrated, patient-oriented care and prevention", the intervention aims to provide equitable access to high-quality treatment and the continuum of care for all TB patients (including those with DR-TB) and patient support to facilitate treatment adherence. In terms of "Integrated research and innovation", implementation of the aDSM framework ensures the regulation of case-based surveillance, strengthening vital registration, the rational use of high-quality medicines and pharmacovigilance. In terms of «Integrated research and innovation», the intervention supports the discovery, development and rapid uptake of new tools, interventions and strategies (including new anti-TB drugs and regimens).

Evidence of impact

Between April 2015 and December 2017 (2.8 years), a total of 141 SAEs were reported to the NCTLD Pharmacovigilance Committee. Overall, 102 out of 516 patients (19.8%) had at least one SAE: 70 patients (13.6%) had one, 25 patients (4.8%) had two and seven patients (1.4%) had three. Of the 102 patients with SAEs, 84% were men (mean age, 41 years), 36 were on Dlm (49 SAEs), 57 were on Bdq (70 SAEs) and nine were on other drugs (22 SAEs). Most patients who developed SAEs had bilateral XDR-TB (more than 60% had fluoroquinolone resistance), 41 (40%) had hepatitis C virus coinfection, 17 (17%) had HIV coinfection and eight (8%) had diabetes. In all, 78% of SAEs were of severity grade 3 or 4, 68% had resolved or resolved with sequelae, 15% had not resolved and 17% were fatal. In 66% of patients with SAEs to anti-TB drugs, the doses were changed or the drugs were permanently withdrawn. Table 17 shows the 10 commonest SAEs.

A total of 23 SAEs were fatal: of these, 14 were to Bdq-containing treatment regimens, seven were to Dlm-containing treatment regimen, one was to a Dlm-containing treatment regimen followed by a Bdq-containing treatment regimen, and one was to a linezolid-containing treatment regimen. The Pharmacovigilance Committee made the decision that:

- of the 14 deaths in patients receiving Bdq-containing treatment regimens:
  - 11 were unlikely to be related to Bdq;
  - one might be related to Bdq; and
  - two were unassessable;
- of the seven deaths in patients receiving Dlm-containing treatment regimens:
  - five were unlikely to be related to Dlm; and
  - two might be related to Dlm, along with other factors;
- the one death one death in a patient with consecutive use of Dlm- and Bdq-containing treatment regimens was unassessable.

Introduction of the aDSM framework has made Georgia a genuine leader in implementing the active pharmacovigilance strategy for TB patients in the WHO European Region and had highlighted the NTP

Table 17. Most common SAEs

Term	SAE (*n* (%))	Fatal outcome (*n* (%))	Median time to SAE (days)
Increased liver enzymes/hepatitis	48 (34)	3 (6)	132
QTcF interval	16 (11)	0 (0)	72
Respiratory insufficiency	3 (2)	3 (100)	264.5
Anaemia	4	1 (25)	101
Cardiac failure	5 (3.5)	5 (100)	89
Neuropathy	5 (3.5)	0 (0)	110
Renal insufficiency	6 (4)	1(17)	227.5
Sudden death	5 (3.5)	5 (100)	105
Allergic reaction	9 (6)	0 (0)	43.5
Gastrointestinal disorder	11 (8)	0 (0)	96

QTcF: corrected QT interval by Fredericia.

of Georgia. As a consequence, Georgia has hosted several study tours from countries within the eastern Europe and central Asia region at their request and is expecting several more this year.

Sustainability of the good practice

The introduction of aDSM in Georgia was based on in-kind contributions from NCTLD staff. Nevertheless, with the increased number of reported TB cases, there is a need for a permanent data entry staff position, which is currently covered by the Global Fund's TB programme. In addition, the technical expertise that is currently provided in kind to the programme might become exhausted or unavailable. Finally, there is increased need for refresher training for TB doctors: for 2018, this is budgeted in the Global Fund's TB programme but requires adequate planning to become sustainable in the long run. Airborne infection control, including regulated administrative, engineering and personal protection measures are also needed in all relevant health-care facilities and congregate settings.

Kyrgyzstan. TB infection control within the framework of introducing the outpatient TB treatment model in the Chui region of Kyrgyzstan

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Background

The TB Control Service of the Kyrgyz Republic during the Soviet era focused on isolating TB patients from society so that they spent the entire treatment period in a TB hospital or sanatoria. At present, the TB epidemiological situation in Kyrgyzstan is stable; however, TB incidence and mortality rates remained high in 2017, reaching 90.6 cases per 100 000 population and 5.2 deaths per 100 000 population, respectively. In particular, MDR-TB presents a key challenge for the NTP: with suboptimal treatment success rates of 53.7% in 2015 for MDR-TB and 80.4% in 2017 for DS-TB. Drug resistance has remained about the same since 2014, with drug resistance in approximately one quarter of new TB cases and more than half of formerly treated TB cases.[17]

Kyrgyzstan is among world's 30 countries with the highest MDR-TB burden. One reason for high MDR-TB rates is cross-infection between patients due to insufficient infection control measures in TB hospitals. However, there was low political commitment to the introduction of an outpatient treatment model to reduce the risk of transmission.

Of the regulatory documents governing infection control interventions, the TB Infection Control Instruction (Guideline) has been in operation targeting, first and foremost, compliance with TB infection control measures in inpatients settings; however, no instructions were in place for primary health-care facilities. Infection control issues at the primary health-care level were spread among small sections in various documents, with no unified approach to TB infection control activities in primary health-care organizations. Often, these recommendations were inconsistent with international recommendations, leading to misinterpretation and the improper adoption of infection control measures by primary health-care staff. These issues necessitated the development of a separate directive and an infection control activity evaluation form for use at the primary health-care level.

An important condition for compliance with infection control measures in primary health-care is rapid diagnosis and the early initiation of treatment for TB patients. The existing primary care system was not properly prepared for activities aimed at the rapid detection of patients with suspected TB, such as screening for TB symptoms, triage for cough patients, awareness of TB and counselling.

Another challenge was the poor involvement of the Sanitary and Epidemiological Service in the fight against TB. That is the main reason for uncoordinated actions among the various services involved in adopting the infection control measures in health-care institutions, including the Sanitary and Epidemiological Service. The results of monitoring infection control in health-care facilities were never discussed, with problems remaining unresolved. This problem required setting up a coordinating body to play the leading role as an independent entity in introducing the unified approach.

[17] National Centre for Phthisiology of Kyrgyzstan.

Description of the good practice

In Kyrgyzstan, infection control activities are carried out at four levels: managerial, administrative, environmental control (engineering–technical) and individual respiratory protection. Infection control measures at each level are established at different steps of infection transmission; however, the priority measures for TB infection control at the primary health-care level are managerial and administrative in nature; these do not require a large financial allocation but can make a significant impact on reducing the risk of infection transmission and spread.

In 2011–2014, the USAID TB CARE I Program provided technical support for improving infection control measures in TB hospitals to build the capacity of managers and staff, develop an infection control plan for each TB hospital and identify areas of risk. In conjunction with new strategies for TB diagnosis and treatment, Kyrgyzstan is switching to the outpatient care model, requiring a revision of infection control recommendations to improve compliance with infection control measures at the primary health-care level. Taking these considerations into account, the USAID Defeat TB project continued introducing infection control measures.

Priority managerial–administrative infection control measures are being adopted in primary health-care. In Kyrgyzstan, the system of screening and triaging cough patients includes screening for cough upon presentation at the Family Doctors Centre or feldsher-midwife stations, segregating patients with cough in a separate, specially designated room or seeing them without queuing if a primary health-care institution does not have enough rooms. An authorized health-care worker registers cough patients in a special logbook, indicating the cough duration. Patients with a cough lasting for longer than for two weeks are referred for sputum collection in a designated open-air area, after which they received TB counselling.

The processes of screening, triage, raising awareness and counselling influence the turnaround time to receive the results of laboratory tests (microscopy, GeneXpert), but a maximum of three days should be taken to diagnose TB and initiate adequate treatment to reduce the spread of infection.

The Defeat TB project has provided technical assistance in developing and introducing continuous quality improvement for TB services, with the use of self-assessment tools at the primary health-care level. This helps health-care institutions analyse problems and identify their main causes; it also makes the facilities less dependent on external monitoring and supports improvements in decision-making. Currently, staff at 275 primary health-care institutions in the Chui region have been trained in continuous quality improvement in TB service provision; 80.7% of facilities perform self-assessment on a monthly basis. Most quality indicators for TB service provision reflect the introduction of infection control measures such as triage of patients with respiratory symptoms, raising TB awareness, ensuring the results of sputum microscopy/GeneXpert are received in a timely manner (within three days) and testing patient contacts. Monthly self-assessment according to the quality indicators for TB service provision enables health-care workers to identify gaps in their routine work and the timely design of interventions for improvement.

Within the framework of the assistance, the Defeat TB project supplies individual protective equipment for health-care staff and patients, equipment for respirator fit testing, and medical devices for use in the safe performance of medical procedures.

Evidence of impact

Collaboration of the Defeat TB project with national partners has improved the adoption of priority infection control measures in primary health-care institutions. These institutions have guidelines for screening and triaging patients with respiratory symptoms. In all, 100% of health-care workers are screened for TB symptoms on a quarterly basis. Sputum is collected at specially designated open-air areas. Primary health-care institutions are supplied with individual protective equipment. As a result, pilot sites have improved the introduction of priority infection control measures at the primary health-care level approximately 1.7-fold (from 46% in 2014 to 82% in 2017; Fig. 47).

Rapid TB diagnosis of TB, particularly the different types of DR-TB, allows adequate treatment to be prescribed in a timely manner, thereby reducing the infectivity period of each patient and reducing the infection spread. Improvement has been seen in process indicators such as turnaround time for microscopy/GeneXpert testing: 90% of primary health-care institutions currently receive test results within three days (versus 34% in 2015; Fig. 48); and

the average turnaround time has also reduced from seven days in 2015 to 1.7 days in 2017.

Improvement of this indicator was influenced by introduction of a continuous monitoring system and self-assessment of the process by institutions, along with continuous external monitoring and mentoring from some members of the project and national partners.

Fig. 47. Proportion of primary health-care institutions adopting the priority TB infection control measures, Kyrgyzstan, 2015–2017

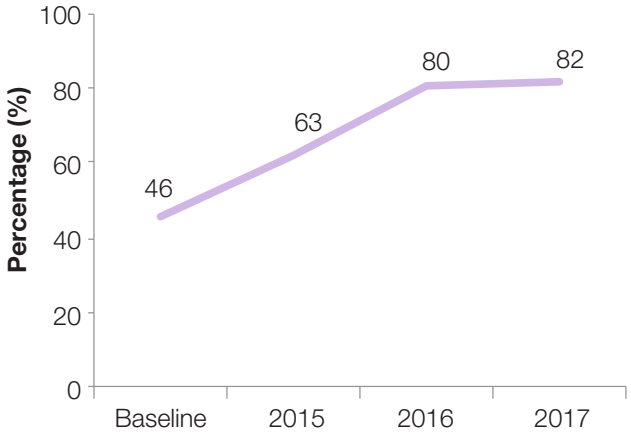
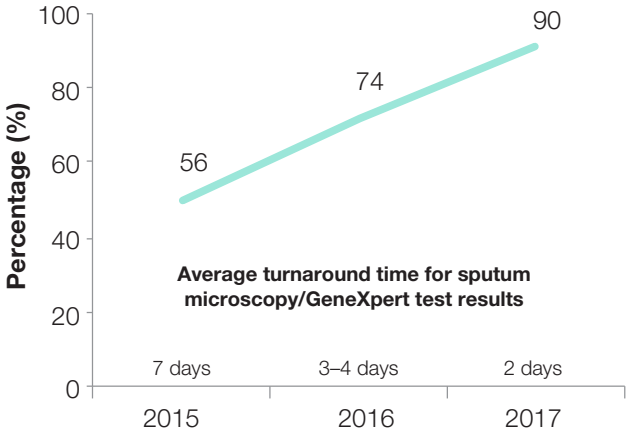


Fig. 48. Proportion of primary health-care institutions receiving the results of sputum microscopy/GeneXpert testing within three days

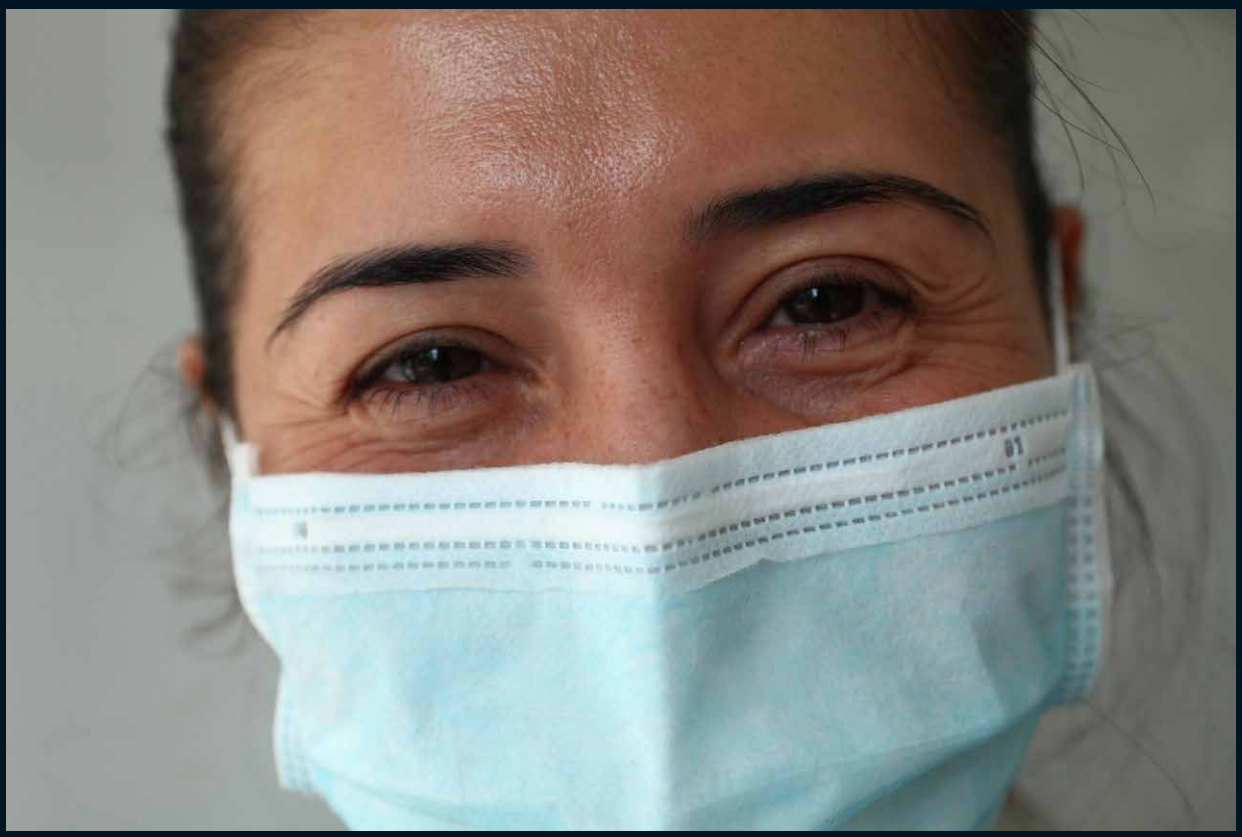


For the successful introduction of infection control measures at health-care institutions, gaining the understanding and support of institution managers is important to develop and implement the infection control plan; expand the capacity of health-care workers in infection control; continuously monitor compliance with infection control procedures; discus problematic issues with the steering committees for decision-making purposes; supply individual protective equipment. The infection control systems operating in primary health-care institutions create a safe environment for both patients and health-care workers in the provision of TB outpatient care.

The major indicator of the introduction of infection control measures is TB incidence among health-care providers. In 2010 and 2014, three and nine TB cases, respectively, were reported among staff of TB hospitals in the country. In the Chui region, no TB case was reported in 2015–2017 among TB hospital staff. Four cases of TB were reported in primary health-care institutions; after analysis, the affected individuals were proven to be at risk of infection in their respective communities and not at the workplace, demonstrating the need to strengthen contact tracing (looking for people who have been exposed to TB patients). Thus, if TB infection control measures are complied with, the risk of infection in primary health-care institutions should be the same as in TB hospitals.

Sustainability of the good practice

The project developed the TB infection control directives, accompanied by separate evaluation forms for primary health-care institutions and TB hospitals; these have been approved by an Order of the Ministry of Health. The documents enabled health-care institutions to systematize the implementation of infection control measures, including the targeted use of individual protective equipment, separation of cough patients upon presentation at primary health-care institutions, TB screening for health-care workers on a quarterly basis, sputum collection at specially designated areas in the open air, and monitoring of the rapid TB diagnosis process. As part of external monitoring, staff members of the Sanitary and Epidemiological Service participate in joint visits to health-care institutions to provide methodological assistance in infection control.



2D. Engagement of ministries, communities, civil society organizations and public and private care providers

Azerbaijan. Multidisciplinary approach to treatment of TB

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Background

Mycobacterium tuberculosis kills more people than any other pathogen. One third of the world's population, almost 2 billion people, is infected with *M. tuberculosis*, and the number of new TB cases each year climbed by 6% between 1990 and 1997, from 7.5 million to 8 million cases, and is currently 8.4 million *(68)*. TB is mostly prevalent among individuals of employable age. For this reason, TB is a global challenge for the world health system because it jeopardizes building a healthy society.

Together, TB and DR-TB remain a public health threat around the globe, including in Azerbaijan. In 2016, the TB incidence among HIV-negative persons in Azerbaijan was 66 cases per 100 000 population and the TB mortality rate was 6.4 deaths per 100 000 population *(1)*. Azerbaijan remains one of the globally high MRD-TB burden countries *(69)*. The national drug resistance survey, which was completed in 2013, showed that 13.1% of new and 27.5% of re-treatment TB patients had MDR-TB. Analysis revealed that a main cause of drug resistance in TB patients was treatment interruption among DS-TB patients. In 2016, the number of TB patients who interrupted their treatment was 8% among DS-TB cases and almost 8% among DR-TB cases. Experience has shown that the availability of medicines, modern laboratories and the well-established practices of health staff are insufficient for effective TB control. A new approach is needed with an emphasis on patients and their family and friends. The key to treatment adherence is a comprehensive, people-centred approach.

To improve treatment efficacy and boost treatment adherence for patients, the Public Organization of Phthisiatricians and Pulmonologists with financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria launched a project in January 2017 with a multidisciplinary approach to the treatment of TB patients. Notably, this is the first project to support patients in the civil sector in Azerbaijan. This project was carried out within the framework of the NTP of Azerbaijan in cooperation with the Scientific Research Institute of Pulmonary Diseases of the Ministry of Health of Azerbaijan.

Description of the good practice

The main objectives of the project were to implement interventions aimed at providing psychosocial support to patients and their family members throughout the treatment period by:

- assisting in solving the social and household problems of patients and their family members, such as obtaining welfare support and documents needed to resolve various household issues;
- promoting the need to complete the course of chemotherapy for increasing treatment adherence, informing patients about the consequences of unauthorized treatment interruption, and describing the consequences of treatment interruption for the patients themselves and for their family members;
- informing patients and their family members about infection control measures;
- supporting patients and their family members in networking and information exchange;
- setting up a telephone hotline to raise awareness among the general population; and

- performing activities aimed at fighting stigma in the population.

Social support also plays an important role in the project. The main tasks of social workers within the framework of this project are to assist indigent TB patients and their families in receiving social benefits. A total of 32 appeals were made to the Social Welfare Services, of which four were approved and the remaining ones were accepted for consideration. At the request of patients who find it difficult to travel every day for DOT, social workers bring medications to patients at home. All project activities are designed to meet patient needs and to persuade sick individuals to continue their course of chemotherapy.

The major challenges faced by psychologists were related to a loss of confidence in cure. This was especially true for inpatients. Acute problems were also associated with stigma. The reality in Azerbaijan is that patients and their families try to avoid the disclosure of TB diagnosis. A case from the practice of the project's psychologist is relevant. The father of an18-year-old girl was happy when a diagnosis of TB was ruled out and his daughter was instead definitively diagnosed with cancer. When asked why he was happy, he replied, "If she had tuberculosis, it would have ruined my family's reputation... But a tumour? Well, what can we do about that; perhaps, this is her fate...". This striking case confirms the need for interventions targeting stigma and raising public awareness of TB.

It should be emphasized that the Public Organization of Phthisiatricians and Pulmonologists provide support not only to patients but also to mid-level junior health staff. All health-care providers who deal with TB patients have attended training sessions on the multidisciplinary approach to treating TB patients, including the roles and responsibilities of all multidisciplinary team members in patient care. Within this framework, the first ever hotline dedicated to TB was set up in the country. From the very first weeks of its operation, the hotline received many calls – an "avalanche" – in relation to TB symptoms, aspects of TB diagnosis and treatment, and precautions needed during exposure to TB patients. Calls to the hotline were anonymous.

Evidence of impact

It is too early to say how the project is affecting the overall TB epidemiological situation in the country. However, one thing is clear: about 700 patients covered by the project in 2017 did not interrupt their treatment.

Figs 49 and 50 show examples of meetings between psychologists and patients during the project.

Fig. 49. Meeting between psychologist and patients, May 2017

Source: Public Organization of Phthisiatricians and Pulmonologists.

Fig. 50. Meeting between psychologist and patient, September 2017

Source: Public Organization of Phthisiatricians and Pulmonologists.

Sustainability of the good practice

The success of the project is the result of the thorough daily work of all partners – phthisiatricians, primary care providers and multidisciplinary team members – for sustaining the improving trend of the country's TB epidemiological situation; however, a lot of work is still ahead. All activities should meet the needs of TB patients.

The main tasks now for the Public Organization of Phthisiatricians and Pulmonologists is to find a sustainable funding source and to institutionalize the

multidisciplinary approach to treatment management for TB patients. The Organization provides stable policy advocacy with the main stakeholders for achieving the sustainable financing of multidisciplinary support for TB patients.

Kyrgyzstan. The role of religious leaders in informing the public about TB and reducing stigma and discrimination against TB patients

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Background

Informing the population about TB an important component of the NTP for curbing the TB epidemic in Kyrgyzstan. Insufficient knowledge of TB among the population and a high level of stigma against TB patients are contributing to the spread of this disease. A lack of awareness of new approaches to TB treatment and the possibility of outpatient treatment, as well as the negative attitude (stigma and discrimination) of society makes TB patients hide their disease, often resulting in late presentation of people with symptoms suggestive of Tb, the refusal of timely treatment and premature discontinuation of therapy, thus increasing the risk of infection transmission and leading to the emergence of DR-TB. Regrettably, the process of raising awareness of TB among the population was neither ongoing nor consistent; it was often limited to taking specific actions and one-time information campaigns. Modifying society's attitude to TB required a revision of existing practices of general public education.

Description of the good practice

To identify information gaps, an analysis of information flow was conducted within the framework of the USAID Defeat TB project in a pilot district in the Jalalabad region. The analysis showed that religious figures are among the most trusted leaders in the community. However, religious figures did not pay enough attention to TB because they were not aware of this challenge. In general, information circulating in society was inconsistent, intermittent and, sometimes, controversial. People were afraid of becoming infected with TB since most of the current information and rumours about TB were negative. A study of the specific ways in which men and women receive information revealed that women mainly trusted older women in their family, *aqsaqals* (male elders) and health-care providers, whereas men mainly trusted *aqsaqals*, village elders and religious leaders.

Religious leaders have an important role in informing men because the proportion of men among cases of treatment interruption remains significantly high. In addition, men form the greatest proportion of the most vulnerable populations, such as labour migrants and people who have served prison sentences.

Today, Kyrgyzstan is facing a TB epidemiological situation which religious leaders might be able to help combat. A sociological survey of the population of Kyrgyzstan conducted by staff of the Kyrgyz-Russian Slavic University in 2016 found that among those surveyed who were members of a particular religion, 81.2% considered themselves Muslims, 7.5% were Orthodox Christians and 12.3% were members of other religions that are relatively new to Kazakhstan. Given that Muslims make up the religious majority in Kyrgyzstan, collaboration with the Spiritual Directorate of Muslims of Kyrgyzstan (SDMK) was established with the support of the USAID Defeat TB project in order to encourage religious leaders, as opinion leaders, to become involved in raising awareness of TB among the population, as well as reducing stigma and discrimination against TB patients and providing them with care and support.

Jointly with SDMK, a methodological manual was developed for religious leaders, Prevention of tuberculosis in religious communities, which has so far formed basis of training in TB for 150 religious leaders. Ongoing training sessions target religious leaders of the country's largest mosques. Moreover, TB information sessions have been carried out in eight *madrasahs* (Islamic schools) in the city of Bishkek and the Chui region, reaching 993 boys and 65 girls (students of *madrasahs* and institutes of the Qur'an). Kyrgyzstan currently has 83 *madrasahs*, eight Islamic institutes and two universities.

To reach out more efficiently to religious communities, a package of information and educational materials was compiled: a booklet for religious populations on health issues, including the topic of TB; and calendars for 2018 including 12 key TB messages, each of which is accompanied by *ayat* (verses) and *surahs* (chapters) from the Hadith and the Holy Qur'an.

SDMK incorporated issues related to TB, such as reducing stigma and discrimination against TB patients and their families into the 2017–2018 plan for preaching before Friday prayers, which was approved by the Supreme Mufti of Kyrgyzstan; this provided a unique opportunity to deliver TB information to up to 1 million people at once. The text of the *Khutbah* (sermon) on health issues and TB was drawn up in collaboration between SDMK and the project. Thus, on 24 March 2017 and 23 March 2018, *Khutbah* dedicated to health issues in Islam, including TB, were conducted before Friday prayers in 1770 mosques in the country, and received broad national media coverage. A documentary film was produced on the TB-related *Khutbah* of 24 March 2017.

Notably, the project arranges for television and radio programmes with invited representatives of SDMK and the NTP to be broadcast during the annual Muslim fast of Ramadan in an attempt to prevent treatment interruption and refusal of treatment among fasting TB patients. In the programmes, the population receives information about the importance of completing the full course of treatment, the possible consequences of treatment interruption or discontinuation for both patients and their family and friends, and the importance of supporting TB patients. A representative of the SDMK appeals to Muslims not to interrupt treatment for TB in the holy month of Ramadan: "Health is a gift given by Allah, and it must be cherished. People who are sick and taking serious medication are freed from fasting [during Ramadan]".

Another significant event timed to coincide with World TB Day was a football tournament for religious leaders with the slogan: "Let's defeat tuberculosis: Islam against stigma!". The tournament took place on 24 March 2018 upon the initiative of SDMK and supported by the USAID Defeat TB project and the National Centre for Phthisiology of Kyrgyzstan.

In addition, the project has started actively cooperating with the Bishkek and Kyrgyz Diocese of the Russian Orthodox Church. Activities include information sessions on TB and having a tolerant attitude towards TB patients have been held for members of the Orthodox Church; a model of cooperation with Russian Orthodox religious leaders has been developed; and compilation of a methodological manual for training on TB and a package of information and educational materials for raising awareness of the public of TB.

Evidence of impact

The following photographs show examples of activities of the project (Fig. 51).

Sustainability of the good practice

Incorporating the activities into the Muftiate Action Plan to inform the general public about TB ensures sustainability of this practice. The information materials developed jointly with SDMK are carefully studied and kept for reference by the community. In turn, the leaders of the religious congregations of Kyrgyzstan make a significant contribution to raising awareness of TB at national and the international levels, reducing stigma and discrimination, and providing support and assistance to people affected by the TB epidemic.

Fig. 51. Examples of project activities

A. Seminar for imams, USAID Defeat TB project, Bishkek city, May 2016

B. Seminar for the women's religious organization Mutakallim, Jalalabad city, June 2016

C. Friday prayers, Jalalabad city, Jalalabad oblast, 24 March 2017

D. Friday Prayer, 24 March 2017, Suzak district, Jalalabad region

E. Friday Prayer, 24 March 2017, Bishkek city

F. Booklet entitled Know much for, for distribution to the general population during Friday prayers, USAID Defeat TB project

G. 2018 calendar with WHO key messages on TB and lines from *Hadises* (holy poems)

«Бекитемин»
Кыргызстан мусулмандарынын
[illegible] муфтийи
[illegible]бек ажы Токтомушев
[illegible] 2017

Кыргызстан мусулмандар дин башкармасынын 2017- жылга карата олко аймагындагы жума мечиттерде элге түшүндүрүү жана профилактикалык иш чараларынын планы.

№	Миладий жана хижрий жыл санактары.	2017-жылдагы ар бир айдагы жума күндөр.	Темалар
1	Январь. Рабиус-сании.	06-01-2017.м 08-04-1438.х	Илим алуу парз. Илимдин пазилеттери.
2	Январь. Рабиус-сании.	13-01-2017.м 15-04-1438. х	Акыйда жөнүндө. Ыймандын жети рукундеру.
3	Январь. Рабиус-сании.	20-01-2017.м 22-04-1438.х	Куран окуу жана анын сооптору.
4	Январь. Рабиус-сании.	27-01-2017.м 29-04-1438.х	Нике кыюунун эрежелери жана махр баяны. (18 жашка толо электерге нике кыйбоо мыйзамын түшүндүрүү).
5	Феврал. Жимад-ул- уула.	03-02-2017.м 06-05-1438.х	Өлгөн адамдын осуят кылуусу жана анын мурасын (байлыгын) бөлүп берүү эрежелери.
6	Феврал. Жимад-ул- уула.	10-02-2017. м 13-05-1438. х	Маркумду жерге берүү эрежелери.
7	Феврал. Жимад-ул- уула.	17-02-2017. м 20-05-1438. х	Өлгөн адамдын туугандарын зыярат кылуунун адеби. (Куран окутуу, Кудайыдагы ысрапкерчиликтер)
8	Феврал. Жимад-ул- уула.	24-02-2017.м 27-05-1438. х	Ички дүйнөнү оңдоо, мусулмандын адеби
9	Март. Жимад Ул-Сании	03-03-2017.м 04-06-1438.х	Адал эмгек, адал ырыскыга умтулуу. Арам иштен, арам ырыскы табуудан алыс болуу.
10	Март. Жимад Ул-Сании	10-03-2017. м 11-06-1438. х	Жакын туугандардын укугу жана жалпы коомдун укугу.
11	Март. Жимад Ул-Сании	17-03-2017. м 18-06-1438. х	Айлана чөйрөнү тазалоо, бак-дарак отургузуунун сооптору.
12	Март. Жимад Ул-Сании	24-03-2017. м 25-06-1438. х	Ислам дининде ден-соолукка кам көрүү жөнүндө.
13	Апрель. Ражап	31-03-2017. 03-07-1438. х	Радикалдык жана экстремистик көз караштардан алыс болуу жөнүндө.
14	Апрель. Ражап	07-04-2017. м 10-07-1438. х	Ыйман,адеп жана маданият жылына карата баян.
15	Апрель. Ражап	14-04-2017. м 17-07-1438.х	Туура жолго чакыруу жакшы жолдон токтотуу.

H. Annual plan of Friday Prayers, as endorsed by the Muftiate

Tajikistan. The role of local communities in detection of new TB cases in Sughd province, Tajikistan

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Background

Some characteristics of TB, such as the long latency period and low specificity of the clinical manifestations, make early diagnosis of the disease one of the most pressing challenges in the TB care system. According to the WHO Global Tuberculosis Report 2017 *(1)*, up to a third of all new TB cases worldwide remain undetected each year. This also applies to the WHO European Region and is emphasized in the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*, in particular for Tajikistan. Tajikistan has a high MDR-TB burden *(70)*, increasing the importance of interventions for early TB detection in the country's population. WHO estimates that Tajikistan has 7500 (range, 5700–9400) new TB cases per year, representing 85 (range, 65–108) cases per 100 000 population *(1)*. In 2016, approximately 6241 TB cases were notified in the country, of which 5695 were new and relapse cases.

Description of the good practice

This practice aimed to expand the capacity of local communities in Sughd oblast (province), Tajikistan to effectively identify people with TB symptoms and refer them for further examination and, if necessary, treatment. A policy document, National programme for formation of a healthy lifestyle in the Republic of Tajikistan for 2011–2020, supports this practice. The goal of the programme is to change the public attitude towards health through implementing the principles of a healthy lifestyle. Under this programme, Centres for the Formation of Healthy Lifestyle coordinates its activities with state agencies and local executive authorities. Implementation of the outreach activities in public health is coordinated by the National Centre for Healthy Lifestyle of the Ministry of Health and Social Protection of Tajikistan. The NTP has the following priorities: training of volunteers, promotion of a healthy lifestyle and prevention of communicable diseases, including TB. With this aim, and with USAID support, community health committees (CHCs) have been established: their activities are focused on TB prevention, including early TB detection, supporting patients during treatment and raising public awareness of a healthy lifestyle. CHCs were established in close coordination with local executive authorities at the *jamoat*[18] level (second level authority). The criteria for selecting CHC members were established through meetings with *jamoat* chairmen. A CHC member must be a *jamoat* resident and a respected person whose opinions and judgements are valued and heeded by their fellow villagers. They can be teachers, medical workers, religious leaders (clerics), female activists and youth representatives.

CHCs usually work directly with the general population in *jamoats* and districts, as well as with migrant workers returning home from working abroad. The main objectives for CHC members are to: (i) have a basic knowledge of TB (be familiar with symptoms and routes of transmission, know that TB is curable and that treatment is free and be aware of the treatment duration); (ii) raise public awareness about TB through holding information sessions; (iii) refer patients identified as having TB symptoms to the nearest health facility by filling out the voucher (all CHC members have these vouchers); (iv) ensure close interaction with local health-care providers; (v) provide psychosocial counselling to TB patients and their family members during treatment; (vi) reduce stigma and discrimination against TB patients; (vii) have a work plan and provide timely reports (all CHC members have registers/logs); and (viii) disseminate information, education and communication materials on TB during information and outreach sessions with local people.

Evidence of impact

Fig. 52 shows an example of the impact of the project.

Table 18 shows data generated for the period from July 2015 (when the first CHC started identifying individuals with TB symptoms) to December 2017 based on reports generated by CHC members and entered into the e-database, as well as the reports submitted by TB centres in Sughd province.

[18] *Jamoat* – a rural community or village council comprising part of a district of Tajikistan.

Fig. 52. CHC member talking to villagers about TB, Khatlon region

Table 18. TB cases notified by CHC members in Sughd province, 2015–2017

Notified TB cases	Period		
	July–December 2015	January–December 2016	January–December 2017
Total number	428	994	1025
Number notified through CHC referral	43	135	242
Percentage notified through CHC referral	10.0%	13.6%	23.6%

Through implementation of the CHC model in Sughd province, it was possible to increase the number of new TB cases notified via referral by CHC staff. At the start of implementation (July 2015), CHCs helped to detect 10% of all new TB cases in the Sughd province; by December 2017, the proportion had increased to 23.6%. These figures demonstrate that trained members of local communities can identify people with typical TB symptoms among the general public, effectively communicate to them information about the disease and the need for additional examination, and motivate them to seek further care from medical professionals. This is especially important for hard-to-reach groups with a low socioeconomic status.

Sustainability of the good practice

In Tajikistan, CHCs were established and promoted within the existing social and administrative model of *jamoats*, and have great potential to become a sustainable structure. Their focus on health and integration into a countryside network of centres for healthy lifestyle additionally contributed to their important role and sustainability at community level. Utilization of CHC capacities within current TB interventions is a promising approach, particularly in the areas of health education, basic symptom screening and further referrals to health facilities. Within the USAID TB Control project, the growing role of CHCs in early diagnostics was demonstrated in Sughd province; in 2017, CHCs helped to identify up to a quarter of all new TB cases in the region. Thus, through working on a voluntary basis, CHCs represent a sustainable, self-supported structure at the local level. Although the TB incidence did not significantly increase, CHCs have demonstrated their potential to become a key link in health education for TB and other pertinent public health issues in the country. Further studies will evaluate the potential of CHCs to combat TB in Tajikistan.

Ukraine. Advocacy for increased funding to purchase drugs

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Background

Since 2004, the expansion of HIV treatment programmes in Ukraine has been largely funded by the Global Fund to Fight AIDS, Tuberculosis and Malaria and other international donors. With the introduction of the new funding model and decreasing Global Fund funding, the Ukraine Government was expected to take over financial support for both HIV and TB treatment and prevention. Unfortunately, this transition seems impossible due to military conflict, political turmoil and a struggling economy.

In accordance with established practice, the funding level in the 2017 draft national treatment budget was similar to the funding level included in the 2016 budget, despite devaluation of the national currency and the expansion of TB treatment. The proposed budget for 2017 covered approximately 43% of the medication needs. In particular, treatment programmes for HIV, TB and viral hepatitis were critically underfunded (at 23%, 33% and 8% of the need, respectively). More than 50% of MDR-TB treatments were procured by the Global Fund principal recipient in 2016.

Ukraine has one of the highest rates of XDR-TB in the world, with treatment needed for more than 1500 XDR-TB patients. However, the introduction of new anti-TB drugs (Bdq and Dlm) into clinical practice for managing MDR-TB patients in Ukraine will significantly improve treatment outcomes (only 46% of MDR-TB patients have successful outcomes, against a WHO target value of at least 75%) and provide a significant number of patients with a better chance of recovery. However, Bdq and Dlm are not registered (i.e. have marketing authorization) in Ukraine. Bdq is currently entering Ukraine within the joint USAID/Janssen Therapeutics donation programme as a non-registered product and is reported to be imported for personal use from the Russian Federation.

Description of the good practice

Two examples of good practices are described: the first relates to advocacy for funding to treat patients with HIV infection, TB and hepatitis C and the second to advocacy for XDR-TB treatments.

In the first practice, the All-Ukrainian Network of People Living with HIV/AIDS and the Public Health Centre of the Ministry of Health of Ukraine lobbied the Prime Minister, Minister of Finance and Minister of Heath to ensure that much-needed funding for treatment programmes was provided in 2017. Following a meeting between patient organizations and the Ministry of Finance, the Ukrainian Government agreed to cover the deficit and ensure funding for life-saving medicines. The revised 2017 national budget was subsequently submitted to Parliament and approved: it included 50% more funding compared with 2016 for the procurement of medication for about 150 000 patients with HIV infection, TB and hepatitis C. The budget for TB treatment for TB was increased by 323 million Ukrainian hryvnia (approx. US$ 12.2 million), representing a 2.4-fold increase.

Budget planning should start well in advance of the budgetary process and community-based organizations and public health officials should be actively involved from the start. If necessary, direct actions involving mass media should be undertaken. In addition, to ensure Government willingness to involve them in the budgetary process, community-based organizations should provide the Government with solutions to the funding problems. A proactive approach by public health officials and community-based organizations, with a good understanding of the budgetary process, and with timely and professional communication with government authorities, can protect or increase the existing funding for treatment programmes, even under harsh economic and political conditions.

In the second example, the All-Ukrainian Network of People Living with HIV/AIDS in coordination with the Public Health Centre conducted an advocacy campaign in 2016–2017 targeting Janssen by sending several requests to its headquarters and regional offices in eastern Europe and central Asia to hold discussions with Janssen representatives in community advisory boards in eastern Europe and central Asia and with Janssen Ukraine with the aim of convincing the company to enter the Ukrainian market directly, and not through Janssen Russia. Janssen agreed to register Bdq in Ukraine through Janssen Ukraine and in

March 2018 an application for marketing authorization was filed with the Ukrainian drug regulatory authority, the Ministry of Health of Ukraine.

Evidence of impact

For the first example, many media publications covered the news of the budget increase, including:

- UNIAN: news about economy – Budget 2017: health-care costs increased by 6%, drug purchase – by 50% *(71)*;
- Apteka – State budget 2017: how much money is provided for health? *(72)*; and
- Ukrinform – infographic.[19]

The increased funding for the TB treatment programme guarantees uninterrupted, effective treatment. Delays in procurement and lack of funding in 2015–2016 meant risks were associated with switching patients to other regimens, which could undermine the treatment efficacy.

The second example was reported by the All-Ukrainian Network of People Living with HIV/AIDS – Bedaquiline is filed for registration in Ukraine *(73)*.

Responses from Janssen:[20]

- letter from Janssen Pharmaceutica on the channels available to access Bdq in Ukraine; and
- reply from Janssen Pharmaceutica to the enquiry regarding the registration of Sirturo (Bdq) in Ukraine and information on the decision to submit a Marketing Authorization Application in its own name, rather than in the name of Pharmstandard, as previously proposed.

Advocacy efforts encouraged Janssen to choose another strategy for entering Ukrainian market to avoid a political deadlock. The start of marketing authorization for Bdq is an important first step towards the future scale-up of treatment for XDR-TB patients in Ukraine via state and donor funding.

Sustainability of the good practice

Regarding example one, the All-Ukrainian Network of People Living with HIV/AIDS and the Public Health Centre are continuing their strategic collaboration to retain public and government focus on the importance of fighting TB in Ukraine and are technically supporting the process of creating the budget documentation.

Regarding example two, so far Ukraine has taken a number of politically important steps to ensure the possibility of introducing Dlm into Ukraine. In particular, Dlm is included in the draft of a new NTP for 2018–2021 and in the Nomenclature of drugs, and is planned to be procured centrally with funds from the state budget. Otsuka has informed the Government that it plans to file for Dlm registration in Ukraine through a Germany-based company.

[19] Infographic showing the main indicators of the main financial document of the country (https://www.ukrinform.ua/rubric-other_news/2139989-proekt-budzetu2017-osnovni-pokazniki-infografika.html, accessed 21 September 2018).

[20] These documents are available from the author on request (info@network.org.ua).

2E. Social protection, poverty alleviation and actions on other determinants of TB, such as migration and imprisonment

Belgium. BELTA-DOT: intensified and individualized case management for TB patients to improve compliance and treatment outcomes in Belgium

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Background

Belgium has a low incidence of TB (2016: 9.3 cases per 100 000 population, with 1047 cases) with typical characteristic of TB concentrated in big cities, in hard-to-reach populations and hard-to-hold at-risk groups. Although there is a declining trend in absolute numbers, cases are becoming increasingly complex, both socially and clinically. Managing these complex cases requires considerably more TB nurse time than routine therapy supervision allows for.

The treatment success rate among all notified cases has been rather disappointing for a high-income country, with a mean of 78.5% for the 2011–2013 period. The proportion of notified cases that abandoned treatment (due to loss to follow-up, refusal, non-compliance) was high, at 12.3% over this period. At the same time, treatment results have been much better: 86.8% of MDR-TB patients and 86.7% of XDR-TB patients were successfully treated *(74)*. This can be attributed to the quality of care (extra nurses for intensified MDR-TB case management), the ease of availability of SLDs and the possibility to enrol patients to the BELTA-TBnet project, an initiative supported by the National Health and Disability Insurance Institute (NHDII) and the Federal Public Service Health (health ministry) that ensures that TB treatment in general and MDR-TB treatment in particular is accessible to all patients. This project was cited as a best practice by WHO in 2013 *(75)*.

Experts of Belgian TB organizations have participated in several multicountry working groups for consensus papers and guidelines for urban TB *(76)* and vulnerable populations *(77)*. This exchange of best practices confirmed what could be observed in the field: first and foremost, the Belgian programme had to improve treatment results and lower the number of patients abandoning treatment. The most evidenced-based strategy to achieve this was to introduce intensified, individualized multidisciplinary case management. This could only be implemented by providing extra staff time, well-trained specialized TB nurses or social workers.

Description of the good practice

The health ministry and NHDII agreed to support the BELTA-DOT pilot operational research project, which started on 1 July 2014. All actions and interventions were based on best practices, scientific evidence and international guidelines. The project aimed to improve treatment results by intensifying case management and personalizing supportive interventions in a people-centred way. The target group comprised all TB patients with a risk of non-compliance.

All notified cases had to be seen by an experienced TB nurse. A standardized risk analysis was performed to score the risk of non-compliance. For each patient considered to be at risk of non-compliance, a personalized treatment supervision plan with specific interactions was developed. Supportive interventions included home visits of varying frequency (but could be as often as daily), telephone calls, pill boxes, and accompanying patients to the physician/pharmacy/X-ray facility. Each patient was appointed a TB case manager and, if possible, an ambulant care network was organized around the patient using family members, general practitioners, city social workers,

pharmacists and others, with the TB case manager being responsible for overall management.

Financial support by the NGO Damien Foundation enabled rental of beds in homeless shelters for patients with unstable housing conditions until treatment was completed successfully. Financial incentives such as a social cheque were used for patients in real need and in danger of becoming non-compliant. A social cheque is an existing system of distributing monetary payments that can only be spend on food or clothes. For every week the patient was compliant, a number of cheques were handed out. This turned out to be a cheap and easy to use motivator that is greatly appreciated both by patients and TB staff. Other enablers/incentives were also provided: bus/tram/train tickets, meal coupons for social restaurants, clothes and sleeping bags. When the pilot project ended on 31 December 2016, the health ministry and NHDII decided to continue funding BELTA-DOT within the framework of a budget stream earmarked for "universal access to health care for vulnerable groups".

The practice is fully in line with the "Equitable access to quality treatment and continuum of care for all people with TB, including DR-TB, and patient support to facilitate treatment adherence" component of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*, and also fits the component, "Political commitment with adequate resources, including universal health coverage policy". This combination of evidence-based good practices, political commitment and financing human resources for TB control has enabled excellent results to be achieved.

Regarding ethical appropriateness, it was decided not to work with a case–control design because withholding an evidence-based best practice from a control group was considered unethical. As a result, it was not possible to estimate the separate effects of the different interventions.

Evidence of impact

Treatment outcomes for pulmonary culture-positive TB patients of the cohort included in the pilot project were significantly improved compared with the 2011–2013 cohorts of the national TB registry (pre-BELTA-DOT cohort). The treatment success rate increased from 78.5% to 84.5%, while the proportion of patients abandoning treatment dropped from 12.3% to 6.3%. The improvement was observed in men and women, in nationals and non-nationals, within most risk groups, and in both pulmonary and extrapulmonary cases.

A total of 405 patients in the BELTA-DOT cohort were considered to present a moderate or high risk of non-compliance. To address this, more than 10 000 interventions were planned for these at-risk population groups; most patients benefited from a combination of different support activities tailored to their individual needs. Treatment outcomes before and after implementation of the BELTA-DOT are shown in Table 19.

The more individualized approach promoted by BELTA-DOT, together with the possibility to offer practical help such as lodging or social cheques, improved and strengthened the relationship of trust between TB nurses and patients, which had a very beneficial impact in terms of compliance. Nurses say they feel better armed to help patients with very complex

Table 19. Comparison of treatment outcomes for the BELTA-DOT (enrollment 1 October 2014–31 December 2015) and pre-BELTA-DOT 2011–2013 cohorts

Outcome	Mean for the 2011–2013 cohorts (%)[a]	BELTA-DOT patient cohort			
		TB patients with pulmonary data (*n* = 444)		Other patients (%)[b] (*n* = 402)	All patients (%) (*n* = 846)
		%	Difference from 2011–2013 cohorts		
Successful	78.5	84.5	*P* = 0.001	90.5	87.4
Treatment interrupted[c]	12.3	6.3	*P* = 0.001	5.5	5.9
Death	9.1	9.2		4.0	6.7

[a] Pulmonary culture and TB patients only; national TB registry. [b] Pulmonary culture and/or extrapulmonary TB. [c] Not treated for over two months (refusal, loss to follow-up).

social situations. Several TB-experts and physicians said they felt more comfortable discharging patients with complex social situations from hospital, knowing that intense ambulant care was available locally. This suggests that better ambulatory case management may lead to shorter hospitalization periods for these cases. However, as this finding was beyond the scope of the proposed research, it was not possible to quantify this observation.

The extra staff time provided in the context of the project strengthened the already strong collaboration with specialized hospitals and TB physicians, thus creating a direct link between outreach nurses operating at street level and the specialized tertiary care unit. This has improved information exchange, the opportunity for direct staff contacts, and patient referrals.

Sustainability of the good practice

The health ministry firmly adheres to the principles of evidence-based medicine and collaboration with WHO. The Country Cooperation Strategy (WHO – Belgium) 2016–2022 *(78)* states that TB is a priority topic. The Superior Health Council of Belgium issued a Position Paper on TB *(79)*, strongly advising that increased efforts should be made to improve treatment supervision. This advice was reaffirmed by the TB Working Group at the Interministerial Conference on Health in February 2017. Following this and the successful results of the project, the health ministry and NHDII agreed to extend the funding until mid-2020. This political commitment is the best guarantee for sustainability of the practice.

The practice is funded through the "access to health care" budget stream. This is a modest budget (in the context of the whole health-care budget) but was shown to be sufficient to obtain good results. Moreover, the project works closely with other initiatives delivering health-care to underserved population groups, enabling synergy (through a coordinating body, joint database and standard procedures) and more efficient use of the limited funds available, thus further improving sustainability of the practice.

Georgia. TB ECHO project: Extension for Community Healthcare Outcomes

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Background

The last few decades have seen major improvements in TB care and treatment in Georgia. However, significant work is still required to achieve the goals of the End TB Strategy *(4)*, and TB remains a major public health problem. The emergence of DR-TB has made TB care and treatment even more complex and costly, requiring the involvement of specialists and multidisciplinary teams for the successful management and care of TB patients.

Georgia has 10 principal TB facilities at regional level, with considerable capacity. These include the central facility in Tbilisi (National Centre for Tuberculosis and Lung Diseases), which serves as the national centre for clinical excellence, and a number of TB cabinets in rural areas of the country. Additionally, full access to TB services is provided in correctional facilities. Despite universal access to TB diagnosis and treatment and significant patient social support in Georgia, M/XDR-TB and TB patients with comorbidities from rural and underserved areas of Georgia are usually required to travel to central TB facilities to receive appropriate treatment. This creates a geographical barrier for some patients and, along with other factors, may contribute to the high rate of loss to follow-up in Georgia, one of the highest in the WHO European Region: 20% of MDR-TB patients and 11% of the overall cohort of TB patients enrolled to treatment in 2015 were lost to follow-up. In addition, the lack of specialists treating MDR-TB at the regional level leads to delays in initiating appropriate treatment. Given that the Central DR-TB Consilium is the only national entity eligible to assign appropriate M/XDR-TB treatment regimens and/or make clinical decisions in case of complications, the process of patient enrollment to MDR-TB treatment or appropriate treatment modification usually takes a considerable amount of time. The Committee previously conducted quarterly mobile consilium visits to regional TB facilities or patients themselves travelled to Tbilisi for treatment initiation. In both cases, travel for patient or the Committee was time consuming and costly; thus, an alternative solution was necessary.

Description of the good practice

The TB Extension for Community Healthcare Outcomes (TB ECHO) project was developed at the University of New Mexico Health Sciences Center and introduced at the National Centre for Tuberculosis and Lung Diseases in late 2016. This pioneering tele-monitoring and distance learning programme was designed to improve patient care in rural and underserved areas and to strengthen the capacity of the health-care workforce. Its mission is to democratize knowledge and collaborative problem solving and to develop and amplify capacity at the local level to safely and effectively treat chronic, common and complex TB cases, including paediatric TB. Through weekly tele-consiliums, the TB ECHO project offers an opportunity for the Committee to attend all regional sites simultaneously, thus saving time and money by reducing the need for travel. In addition, the TB ECHO project has solved the problem of patient access to specialty care and consultations, thereby minimizing the need for further patient referrals to such cases for which special multidisciplinary care and different-specialty consultations are necessary for their proper management.

The TB ECHO project addresses all three main components of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*. In terms of the first component,"Integrated, patient-oriented care and prevention", the project aims to provide equitable access to quality treatment and the continuum of care for all TB patients (including DR-TB patients) and patient support to facilitate treatment adherence. Another important objective is collaborative activities to provide proper management of TB and a variety of comorbidities. In terms of the second component, "Bold policies and supportive systems", the project aims to deliver social support, protection and poverty alleviation interventions and provide a high-quality service to those currently without sufficient means and access, and will greatly contribute to building the capacity of the health-care workforce. In addition to the weekly tele-consiliums, the project will conduct monthly tele-mentoring and distance learning sessions, thus supporting the third component, "Discovery, development and rapid uptake of new tools, interventions and strategies".

Evidence of impact

Comprehensive preparatory work was performed in 2017, including forming central and regional teams, procuring relevant telecommunication equipment, ensuring access to the Internet at all levels, developing the project's curriculum focusing on TB and DR-TB case management and active pharmacovigilance, and the developing the training curriculum and materials. Hence, full-scale implementation of the TB ECHO project started in 2018, when it fully replaced the concept of mobile consiliums, under the activities of the Global Fund to Fight AIDS, Tuberculosis and Malaria's TB programme (an example of a tele-consilium is shown in Fig. 53). Although the direct impact of the intervention has yet to be measured, the project is expected to have the following impacts.

- Amplification of human resources: the number of TB patients in Georgia with access to different types of specialty care will significantly increase.
- The time between TB diagnosis and the initiation of appropriate treatment and decisions on further treatment management, adverse event management and quality care will be significantly reduced. Therefore, the project is expected to result in a significantly increased number of favourable treatment outcomes.
- ECHO will be used as a tool for disseminating best practices and innovations and sharing knowledge.

With Global Fund support, new information technology equipment was purchased to support the project at all levels of TB care providers in Georgia, leading to an increase in overall accessibility to technology and innovations. Besides TB ECHO clinics, the project's platform has been used to conduct consultations on treatment adherence with providers in designated regions involving patient adherence units from all facilities and the different NGOs providing patient support.

Another significant and unexpected impact was the cost–effectiveness of the project. Besides making the process of case discussion much easier, the project has been highly cost-effective, requiring only a one-time purchase of technical equipment (costing a total of 12 000 Georgian lari, approximately US$ 5000) compared with mobile consiliums, which have an annual cost of 30 320 Georgian lari (approximately US$ 12 600).

Sustainability of the good practice

There is a high expectation that the TB ECHO project will be sustainable over time. The Global Fund made significant contributions in supporting the launch of the project by providing financial and technical support.

Fig. 53. Nine regional TB units participating remotely via the ECHO screen in the Central DR-TB Consilium

Source: National Centre for Tuberculosis and Lung Diseases.

From now on, the implementation and success of the project completely depend on human resources from the NTP, with no additional technical or financial input. The only further requirement of the project is for incorporation of additional medical specialists from different subspecialty areas.

Tajikistan. Improved treatment adherence via collaboration with local authorities

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[1]USAID TB Control Program – Tajikistan, [2]National Tuberculosis Programme

Background

Tajikistan is one of the five countries in central Asia that borders with Afghanistan, China, Kyrgyzstan and Uzbekistan. The country has five administrative regions: Gorno-Badakhshan Autonomous Oblast, Sughd and Khatlon oblasts (regions), Districts (Rayons) of Republican Subordination and the capital city of Dushanbe. In 2017, the population of Tajikistan reached 8742 million,[21] with almost three quarters of the country's population living in rural areas. According to the NTP, 5965 new and relapsed TB cases were notified in 2016 (70.6 per 100 000 population); of these, 5241 were new cases (62.0 per 100 000 population). During recent years, a decreasing trend in the number of notified TB cases (from 7641 in 2010 to 6232 in 2015) and TB mortality rate (from 6.2 deaths per 100 000 population in 2010 to 2.6 deaths per 100 000 population in 2015) has been observed. The treatment success rate for DS-TB patients increased over this period: the treatment success rate for new bacteriologically confirmed DS-TB cases was 89.4% in 2015 versus 76.9% in 2012.

The country remains one of the 30 globally high MDR-TB burden countries. In recent years, changes in the country's TB epidemiological situation have been observed with regard to the development of DR-TB evolution, in particular, increased notification of pre-XDR-TB and XDR-TB cases. The first nationwide surveillance of DR-TB in Tajikistan (for 2010–2011) reported an MDR-TB rate of 12.5% among new sputum culture-positive cases and 53.6% among re-treatment cases. Routine surveillance for drug resistance is not yet fully established in Tajikistan. However, in 2013 DST confirmed DR-TB in 34.9% of new cases and 66.7% in re-treatment cases.

Tajikistan's health system has evolved from the Soviet model of health-care, that is, vertical public health programmes with a clear distribution of roles and responsibilities between national, regional and district levels. The Ministry of Health and Social Protection is in

[21] Statistical Agency under President of the Republic of Tajikistan, January 2017.

charge of the public health programmes in the country and responsible for developing the national health policy and for overall coordination of public health programmes, with national health institutions directly accountable to the Ministry of Health and Social Protection. Local authorities (*Hukumats*) are responsible for most social services, including health-care and education. As in most post-Soviet countries, Tajikistan inherited an extensive hospital-based system, which has become increasingly hard to sustain. Therefore, in 2010 the country introduced an ambulatory model of TB treatment, with outpatient TB treatment reaching 70% of patients by the end of 2017.

Key risk factors for TB in Tajikistan are poverty, high migration/immigration rates, poor TB infrastructure, and a lack of human and financial resources for TB control activities. Although all population of Tajikistan has access to TB diagnostic testing and treatment, the NTP faces problems related to timely diagnosis and treatment, poor treatment adherence and suboptimal DOT.

Description of the good practice

Over 30% of the Tajik population are considered poor, with 13% living below the poverty line. Therefore, in Tajikistan TB is viewed as a social disease, or the disease of poor people. Preventing treatment interruption and improving treatment adherence are key challenges for the NTP. Given its existing challenges such as lack of financial and human resources for TB services and poor TB infrastructure, the NTP initiated advocacy activities to address problems faced by local authorities and communities. One solution was to use the existing benefit system that provides social support to poor families, people with limited opportunities and those in need. The USAID TB Control project supported establishment of a TB care system within the benefit package. It facilitated several advocacy and round table meetings with local authorities at district and rural levels, leading to an agreement to issue an official policy document, Regulations (*Qaror* in Tajik). In accordance with the document, TB specialists provide a list of their TB patients to the local authorities for inclusion in the social support system.

Advocacy meetings with district level local authorities in a few pilot districts resulted in issuance of the Regulations to provide social support to TB patients and their families during the TB treatment period in both inpatient and outpatient settings. In addition, the document describes the services and responsibilities of different agencies, including primary health-care and social services, to ensure that TB patients receive high-quality TB care and services based on a people-centred approach. In accordance with this document, TB centres provide lists of TB patients in need to local authorities each month. Local governments are responsible for implementing the system, together with *jamoats*[22] (second level authorities) and village management committees. By the end of 2017, 27 pilot districts had been issued the Regulations and had implemented the new approach, including establishing a social support system. The districts used different types of traditional and currently available support for patients, including exemption from electricity, land tax, water and sanitation, and other housing charges. In some districts, patients paid their own medical and transportation expenses, while some districts provided clothing and food support. Some districts use income generation support through allocating lands and stock. This practice helps TB centres to keep TB patients in treatment until its completion, thereby increasing the number of patients with treatment completion and cure, and reducing TB transmission among society.

Evidence of impact

Evidence of impact of the good practice are as follows.

- A total of 27 local authorities have demonstrated their understanding of and commitment to TB care by issuing the Regulation and establishing social support systems at a district level.
- A total of 27 local authorities have reviewed the local budget and increased funding for TB services from 45% to 65%, including funds for social support for TB patients.
- In 2015–2017, 2055 TB patients (1438 with TB and 617 with DR-TB) received different types of social support including monetary and food support, and exemption from land tax and housing charges such as water, sanitation and electricity. All patients completed the course of TB treatment and were cured.
- A total of 36 TB patients and 28 DR-TB patients from poor families were provided with housing and plots for building houses and gardening.

[22] *Jamoat* – a rural community or village council comprising part of a district of Tajikistan.

This practice directly improved treatment outcomes with increased the number of patients who completed the treatment and were cured. Fig. 54 shows the reducing trend of loss to follow-up, treatment failure and death after 2015 when the initiatives were implemented. The initiative also improved the response and commitment of local authorities to the challenges of TB and improved local ownership of the project's interventions. Using this model, the NTP and other TB projects are continuing advocacy activities in the remaining 39 districts of Tajikistan.

Over the last five years, the number of undesirable outcomes for TB patients such as loss to follow-up, treatment failure and death has declined considerably with psychosocial support interventions in pilot areas (Fig. 54), while the TB notification rate has remained steady (Fig. 55).

Fig. 54. Treatment failure, death and loss to follow-up for TB patients in 27 pilot districts, 2012–2016

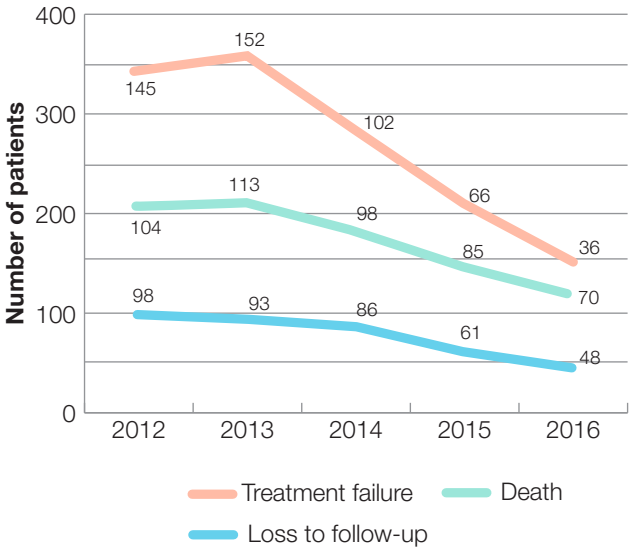
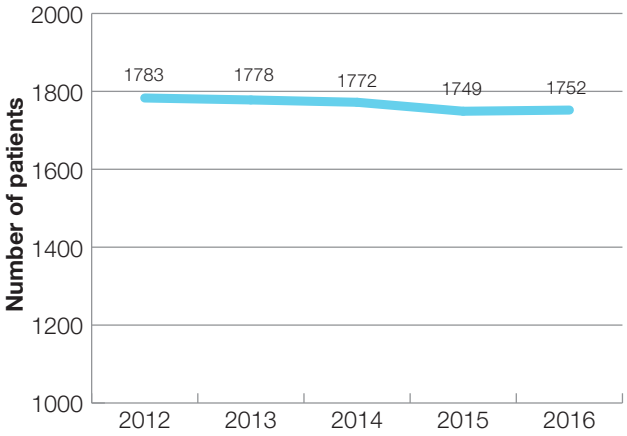


Fig. 55. Registered TB patients in 27 pilot districts, 2012–2016



Sustainability of the good practice

The programme used an existing benefits package that has been established in each district and city of the country. The programme helped to update health policy and add TB patients to the benefits list. In addition, TB centres will report to local authorities on the social support provided to TB patients, thereby helping the Government to in monitor the process and providing evidence of the sustainability of the practice.

Turkey. The Regular Financial Support Programme for Tuberculosis Patients with Psychosocial and Financial Loss in Turkey

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Background

Based on the global End TB Strategy *(4)*, the NTP aims to eliminate TB in Turkey. The results of the long-standing fight against TB in Turkey include an estimated reduction in TB incidence to 18 cases per 100 000 population in 2016. Currently, TB control strategies continue to be strengthened for TB elimination with the collaboration of public and private sectors, NGOs and philanthropic organizations.

TB diagnosis, care and treatment and anti-TB drugs are provided free of charge to all TB patients in Turkey through state funding. However, the disease brings an additional financial burden to TB patients (and their families) because of their inability to work when ill and the possibility that they may be the primary income earners of the household. Exposure to stigma and discrimination aggravates the situation and individuals can easily become vulnerable and disadvantaged.

In addition, adherence to conventional, clinic-based DOT under the supervision of a health worker is usually too difficult, even though full adherence to TB treatment is essential to prevent MDR-TB and increase the chances of cure.

The Turkish Government initiated the Regular Financial Support Programme for Tuberculosis Patients with Psychosocial and Financial Loss in Turkey to provide support, focus more attention on the social problems of TB patients and alleviate poverty.

Description of the good practice

Components of the NTP include people-centred care, social protection, support and poverty alleviation for TB patients. The Ministry of Health and Ministry of Family and Social Policy signed a joint protocol for providing conditional, regular financial social support and assistance services to TB patients to reduce poverty and increase their quality of life. The medical criteria and social criteria for financial support are determined by the Ministry of Health and Ministry of Family and Social Policy, respectively. TB patients are directed to apply to the Ministry of Family and Social Policy's Social Assistance and Solidarity Foundation by Ministry of Health TB dispensaries.

The conditions for financial social support are: being currently registered and treated by the TB dispensary; commitment to DOT under the supervision of health personnel, accepting one of the DOT applications approved by the dispensary physician and being a Turkish citizen. An additional support payment can be provided if a health or social worker determines that a TB patient is unable to perform medical self-care and is bedridden or their household living conditions are poor and should be improved.

A specific electronic social support module was developed within Public Health Management System and used by authorized users from the Ministry of Health and Ministry of Family and Social Policy for registering, management, approval and M&E of the status of each TB patient enrolled to the Programme (Figs 56 and 57).

The maximum duration of financial support depends on the type of TB treatment and is received by eligible patients until completion of treatment and then an additional six-month control period without medication and (Table 20).

Fig. 56. Electronic social support module for TB patients: main screen

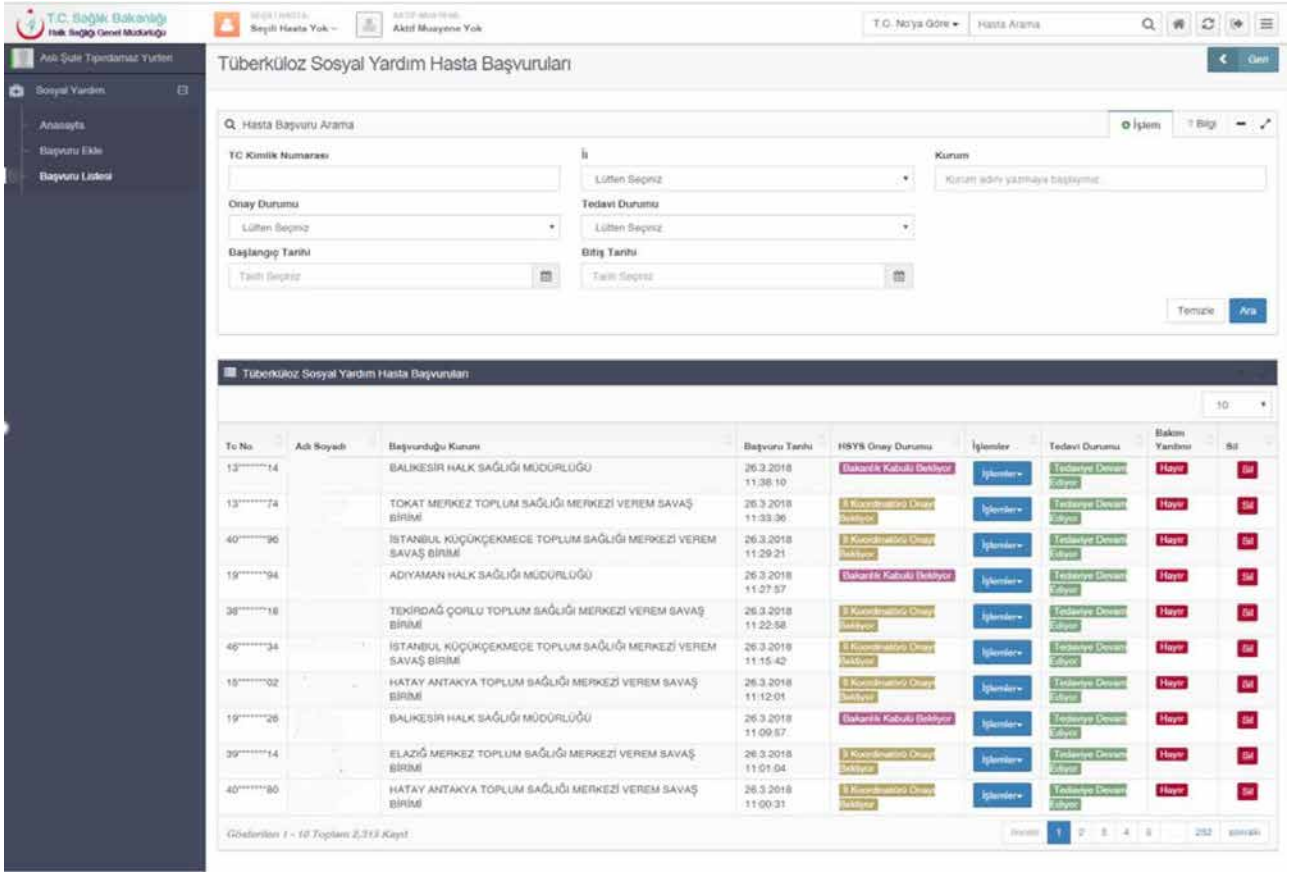

Fig. 57. Electronic Social Support Module for TB patients: application form

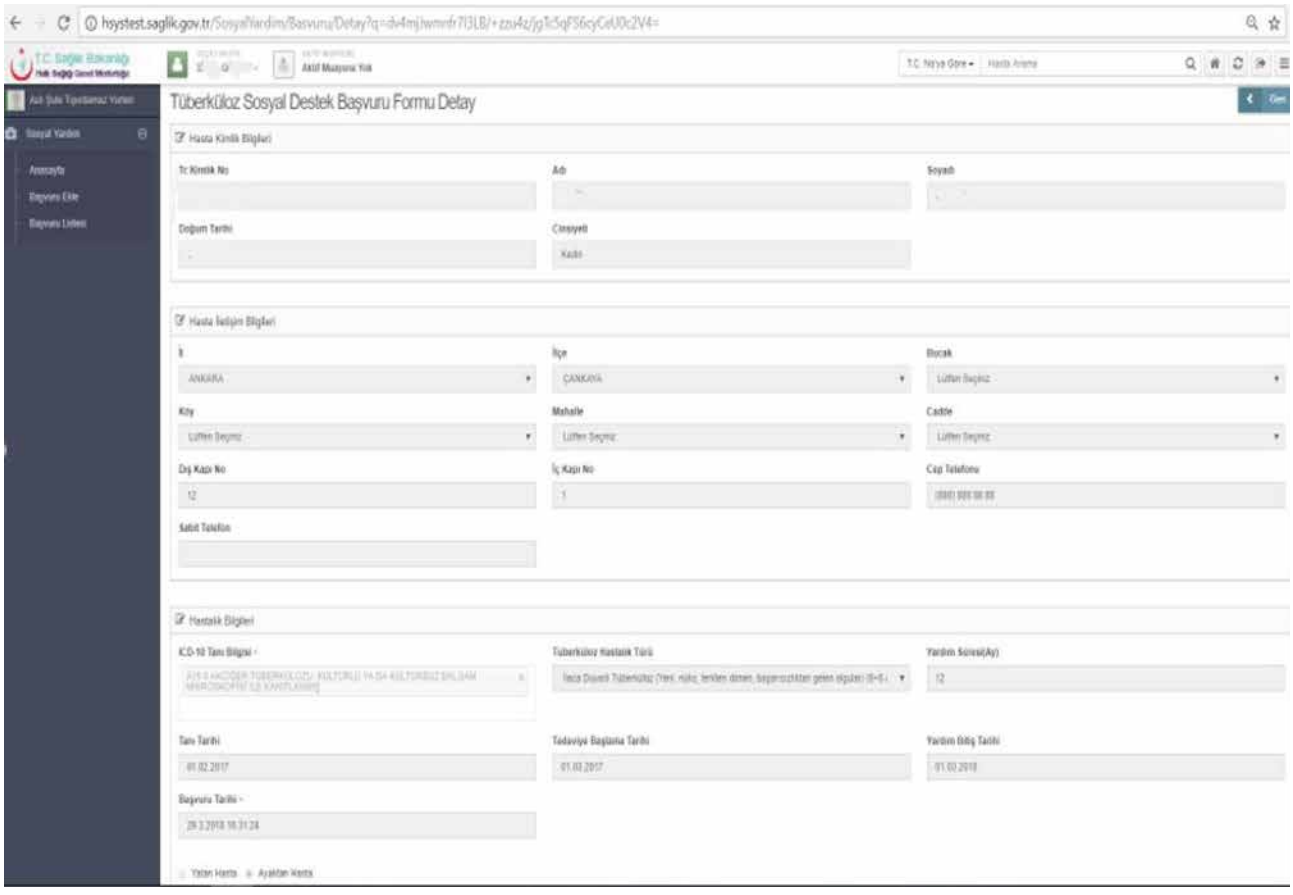

Table 20. Duration of financial support, by TB treatment

Treatment	Maximum duration of financial support
DS-TB treatment (patient type: new, relapsed, treatment after failure, lost to follow-up)	6 + 6 months
FLD-resistant TB (except for RR-TB)	9 + 6 months
RR-TB/MDR-TB/XDR-TB	24 + 6 months
Bone/central nervous system/miliary TB	12 + 6 months
SLD treatment (except for RR-TB/MDR-TB/XDR-TB)	24 + 6 months

Source: Based on Turkish Ministry of Health, 2011 *(80)*.

Evidence of impact

The press release and the announcement of the Programme raised public awareness of TB. Better adherence to clinic-based DOT, reinitiation of treatment for some patients who previously ceased treatment, and better treatment outcomes are expected. The Programme will lead to other similar programmes and better outcomes for chronic and neglected diseases.

Sustainability of the good practice

Article 5 of the Constitution of the Republic of Turkey describes one of the fundamental aims and duties of the state as: to safeguard the independence and integrity of the Turkish Nation, the indivisibility of the country, the Republic and democracy; to ensure the welfare, peace and happiness of the individual and society; to strive for the removal of political, social and economic obstacles which restrict the fundamental rights and freedoms of the individual in a manner incompatible with the principles of justice and of the social state governed by the rule of law; and to provide the conditions required for the development of the individual's material and spiritual existence.

The Law on Promoting Social Assistance and Solidarity (Law No. 3924) enacted in 1986[23] encourages the state to provide help and support for citizens in need and poverty, to take measures to reinforce social justice and to provide a fair income distribution. The Social Assistance and Solidarity Fund, which was established according to this Law also strengthens and ensures the sustainability of the other similar programmes. Thus, the Programme is secured and financed by laws which will ensure its sustainability.

Acknowledgements. We express our sincere thanks to the Ministry of Family and Social Policies and the Ministry of Health of Turkey and the General Directorate of Public Health and to staff of the Department of Tuberculosis for their immense efforts in actualizing the Programme.

[23] Published in the Official Gazette No. 19134, dated 14 June 1986.

PART 3. INTENSIFIED RESEARCH AND INNOVATION

3A. Discovery, development and rapid uptake of new tools, interventions and strategies (including new drugs and regimens)

Belarus. Use of a totally implantable central venous port system for treating M/XDR-TB

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Background

The current TB epidemiological situation in Belarus is characterized by a decreasing number of detected TB cases (from 5324 in 2012 to 3057 in 2017; over this period, the incidence of all types of TB decreased from 56.3 to 32.2 cases per 100 000 population). At the same time, proportion of DR-TB cases is increasing: the proportion of RR-TB cases increased from 33.6% in 2012 to 34.8% in 2017 among new infections ranged from 64.3% to 66.7% among re-treatment cases over the same period (65.2% in 2017). In all, 75% of TB patients with a treatment history had DR-TB. The treatment efficacy remains low for DR-TB: among patients who initiated treatment in 2014, the treatment success was as follows: 59% for MDR-TB patients; 36% for XDR-TB patients and 39% for MDR-TB/HIV-coinfected patients.

Totally implantable central venous port (TICVP) systems are widely used to provide long-term central venous access for the administration of intravenous antibiotics, chemotherapeutic agents and other medications. They are used in many domains of health-care (e.g. oncology, haematology) in both children and adults. TICVP systems may be used to avoid daily intramuscular and intravenous injections (infusions) through peripheral veins during the course of M/XDR-TB treatment, lasting for several months. The TICVP system has unquestionable advantages over other types of central venous access: it is not a subject to external influences; does not cause any discomfort or restrict the quality of life; and interferes with personal hygiene to lesser extent (taking a bath, shower). A pilot project supported by the international organization MSF; Doctors without Borders) was launched at the beginning of 2015; the project was then expanded with support from the Global Fund to Fight AIDS, Tuberculosis and Malaria at the beginning of 2017.

Description of the good practice

The TICVP system was offered to all patients whose treatment regimens included carbapenems (requiring two intravenous infusions a day over a period of several months). Two kinds of TICVP systems were used: Celsite (B Braun) and Seesite (Vygon). A total of 117 patients were enrolled to the study (41 women and 76 men; age range, 15–79 years), of whom 11 (9.4%) were HIV-infected and nine (7.7%) had drug dependence. The following vessels were used for the access: subclavian veins in 69 patients (59%), vena cephalica in 27 patients (23%), jugular veins in 15 patients (13%) and femoral veins in six patients (5%).

The practice covers at least two areas of the Tuberculosis Action Plan for the WHO European Region 2016–2020 *(7)*. First, it contributes to the provision of quality and effective treatment for DR-TB patients while minimizing drug-related adverse events. Introduction of the TICVP system improved both treatment adherence and quality of life for patients receiving treatment. Moreover,

their enrollment to the cohort monitoring programme enables the accumulation of knowledge on the use of TICVP systems and clarification of the indications for their use; these are innovative activities.

Evidence of impact

Complications of TICVP system were reported for seven patients (6%); of these, five (4%) requested its removal prior to the scheduled duration of its use but two (2%) had it re-implanted. In total, 113 (97%) patients had the TICVP system in place during the entire treatment duration.

Most patients who had previously experienced other types of venous access (74 out of 78, 95%), as well as health-care workers, reported that the TICVP systems had advantages compared with other types of venous access or intramuscular injections. Despite drug-related adverse events occurring in all patients receiving chemotherapy, discontinuation of TB treatment was not required through the use of TICVP systems to mitigate the adverse events. In all cases, medicines were given treating side-effects.

Preliminary results showed that using TICVP systems is safe and effective and that they are better than other types of venous access: they are preferred by both patients and health staff. Using TICVP systems improved the quality of life of M/XDR-TB patients and improved treatment adherence (including for those with HIV infection). These points are of the utmost importance, especially during the transition from predominantly hospital-based care to the outpatient model of managing TB patients.

Sustainability of the good practice

Implementation of this practice does not require a large expenditure. To date, TICVP systems have be in operation for long periods of time, up to a year, allowing a significant reduction in the costs associated with DR-TB therapy and fewer complications. These benefits are most relevant to HIV-infected patients. In accordance with the Sustainable Development Plan, TICVP systems are purchased from the state budget.

Norway. TB training programme targeting at-risk groups, the public and civil society, and health-care employees in Norway

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[1]Vestre Viken Hospital Trust; [2]LHL international, Oslo; [3]Drammen Municipality; [4]De Forente Somaliske Kvinner (Somalian women in Drammen), Drammen; [5]SOEEG (Somali Eagle Eyed Group), Drammen

Background

Norway is a low TB burden country in the pre-elimination phase of the epidemic (overall incidence of six cases per 100 000 population). Nearly 90% of incident TB cases are notified in immigrants from countries with a high TB incidence. Norway has mandatory TB screening at entry for all asylum seekers and refugees, and for other groups of migrants from high TB burden countries. Those diagnosed with LTBI and have certain defined risk factors are offered free preventive treatment. People diagnosed with active TB are offered treatment with all costs covered by national insurance.

As TB is a rare condition in Norway, general and specific knowledge are lacking in health and care services, schools, workplaces and the general public, as well as in at-risk groups. Misunderstandings caused by a lack of information and by linguistic and cultural barriers result in fear and stigma, causing suboptimal access to treatment and care, treatment adherence and outcomes.

A collaborative project to develop a TB teaching programme with multiple sets of tools aimed at different target groups and their needs was initiated in 2016. The collaboration is still ongoing, with members of the group consisting of the project initiators, a former TB patient, a patient organization, a public health nurse from the municipality, the TB coordinator from Drammen Hospital and two persons working with equitable health services at the hospital. Group members have complementary skills, knowledge and experience from both the user and system perspectives.

Description of the good practice

The TB training programme provides effective tools for health-care systems working with at-risk groups. It contains various written and visual information, including an animated film explaining TB in a simple

way (www.vestreviken.no/tuberculosis). The animated film is context neutral, is available in several languages and can be used in any country. The programme recommends including former patients in teaching sessions to create trust. The programme can be used in health and care services, reception centres, education services provided to immigrants, and contact tracing settings.

The aims of the teaching programme are to:

- transmit knowledge about TB symptoms and diagnostic procedures to health and care employees;
- transmit knowledge about TB to at-risk groups to enhance early diagnosis and better treatment adherence;
- create trust in the Norwegian health system;
- make people seek health-care if TB is suspected; and
- combat TB-related stigma and fear.

The main messages in the materials are:

- you will be cured of TB;
- consult a doctor if you have symptoms of TB;
- doctors and nurses are bound by confidentiality rules (professional secrecy); and
- treatment is free of charge.

The TB training programme materials include an information sheet[24]; a manual with stepwise instructions on organizing a teaching session[25]; a presentation containing facts about TB and the health system[26]; a script for the presentation; tasks for group work[27]; frequently asked questions about TB with answers; and films in several languages (available on YouTube)[28].

The training programme is supported by a range of written information resources provided by the NGO LHL international, the Norwegian institute of Public Health and others (translated into 10–20 languages) as pdfs to download and print. The programme and supportive materials are available through the websites of the Norwegian Public Health Institute (https://www.fhi.no/sv/smittsomme-sykdommer/tuberkulose/tb_skjema_maler/) and Vestre Viken Hospital Trust (www.vestreviken.no/tuberculosis).

The TB training programme is an innovative way to provide patient information and support in both the TB screening programme and general health and social care services. It provides better patient support to facilitate treatment adherence and reduce the time from symptom detection to diagnosis and treatment.

Evidence of impact

As the programme has only recently launched no systematical evaluation has yet been performed. As part of quality assurance, a small-scale Questback survey was conducted aimed at health professionals and teachers who have used the programme. The survey found that experiences with the programme are predominantly positive: it is easy to use and creates commitment to completing treatment among the audience.

The feedback from audits has been very positive: the programme promotes learning, reflection and a change of attitude towards TB. The programme, especially the animated films, are rather culture and system independent. They were assessed as useful tools that could be used by other countries to combat TB.

Sustainability of the practice

Development of the programme is a local initiative supported by a few grants. Most participants are health-care professionals dedicated to TB control and treatment, and their engagement will help in the further development and implementation of the tools, which is supported by central authorities in collaboration with civil society.

[24] You will be cured of tuberculosis (TB) (https://vestreviken.no/Documents/Helsefaglig/Tuberkulose%20undervisningspakke/Informasjonsark%20undervisningspakke_engelsk.pdf, accessed 20 January 2019).

[25] User's guide: tuberculosis (TB) teaching pack (https://vestreviken.no/Documents/Helsefaglig/Tuberkulose%20undervisningspakke/TB%20Teaching%20Pack%20Users%20guide.pdf, accessed 20 January 2019).

[26] Tuberculosis (TB) (https://vestreviken.no/Documents/Helsefaglig/Tuberkulose%20undervisningspakke/TB%20Teaching%20Pack%20Presentation.pdf, accessed 20 January 2019).

[27] TB teaching pack: group tasks (https://vestreviken.no/Documents/Helsefaglig/Tuberkulose%20undervisningspakke/TB%20Teaching%20Pack%20Group%20tasks.pdf, accessed 20 January 2019).

[28] Teaching pack: frequently asked questions (https://vestreviken.no/Documents/Helsefaglig/Tuberkulose%20undervisningspakke/TB%20Teaching%20Pack%20FAQ.pdf, accessed 20 January 2019).

Uzbekistan. Implementing a short course regimen in the Karakalpakstan region

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Background

Uzbekistan is among the 30 high MDR-TB burden countries worldwide. Current figures from the NTP estimate a DR-TB incidence of 44.9 cases per 100 000 population, representing 5.2% of new and 32.2% of TB cases.[29] Moreover, TB rates in the Autonomous Republic of Karakalpakstan are estimated to be twice the national average *(81)*. Conventional treatment for MDR-TB or XDR-TB involves taking drug combinations for up to 24 months. The significant levels of drug toxicity and personal sacrifice place an incredibly heavy burden on patients' motivation for treatment adherence, while also resulting in high costs for health systems and local economies through lost productivity. To support a more people-centred model of treatment delivery, MSF, in collaboration with the Ministry of Health, sought to evaluate a shorter treatment regimen for MDR-TB in the region as part of the Comprehensive TB Care for All programme.

Description of the good practice

In 2013, the Ministry of Health and MSF initiated a pilot programme of a short course regimen (nine to 11 months) for adults. The aim was to demonstrate the effectiveness of a treatment regimen which had been evaluated in Bangladesh, resulting in high cure rates; more specifically, the Ministry of Health and MSF sought to establish the levels of tolerance, safety and effectiveness of this standardized regimen in the setting of a background of high SLD resistance. Inclusion criteria for the cohort were RR-TB patients (confirmed by GeneXpert testing, Hain MTBDR testing and/or DST); if less than 14 years of age, confirmed close contact with a RR-TB case; and informed consent. Exclusion criteria were taking SLDs for more than one month; having a critical illness; meningeal/osteoarticular disease; resistance to ofloxacin or dual injectable agents (capreomycin/kanamycin); XDR-TB; creatinine clearance of less than 30 mL/minute, QTc interval of more than 500 ms; or pregnancy. The original cohort completed treatment in early 2016, with promising results at the 12-month post-treatment follow-up. A collaborative body established to monitor the pilot programme included the health ministries of Uzbekistan and of Karakalpakstan, Uzbekistan Tuberculosis Institute, WHO Country Office in Uzbekistan and MSF.

Evidence of impact

A total of 146 patients were enrolled to the original cohort, including five children. In all, 92 out of 128 (72%) of patients from the first cohort who met the inclusion criteria had a successful treatment outcome (cured or completed treatment). Those included in the study had good outcomes, with higher culture conversion rates at two months compared with conventional care (adjusted odds ratio 1.93 (95% confidence interval 1.08–3.43), $P = 0.026$). Final outcomes for the short course regimen were similar to those obtained with conventional care, despite the significantly shorter treatment duration.

Once the WHO DR-TB guidelines were released in 2017 *(82)*, the Ministry of Health together with MSF introduced the new WHO-approved guidelines in five out of 16 rayons (districts) in Karakalpakstan: Nukus (city), Shimbay, Khodejily, Takhiatash and Kegeyli. Four more rayons were approved for the expanded introduction in the spring of 2018 after successful results were obtained, bringing the number of rayons implementing the short course regimen in adults according to the new WHO guidelines to nine out of 16. In February 2018, following the experience in Karakalpakstan, Uzbekistan successfully approved the National DR-TB Guidelines for the Short Course Regimen and plans to implement it programmatically across Uzbekistan.

Sustainability of the good practice

To scale up the programme, its partners need to take a proactive approach at all levels of service delivery, thus making implementation feasible. Its expansion will depend on the availability of evidence, feasibility and resources to support increased activities.

[29] Unpublished poster presentation. MSF, Ministry of Health of Uzbekistan. Evaluation of the diagnostic accuracy of molecular methods for rapid identification of tuberculosis patients in Karakalpakstan, Uzbekistan. European Society of Clinical Microbiology and Infectious Diseases/American Society for Microbiology Conference on Drug Development to Meet the Challenge of Antimicrobial Resistance, 4–7 September 2018, Lisbon, Portugal.

Uzbekistan. Practices of expanding the distance training and monitoring approaches are the key to success in implementing the TB control measures

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Background

The Ministry of Health of Uzbekistan is supporting and implementing the Health 2020 policy framework for the WHO European Region and the Millennium Development Goals with the 2030 Agenda for Sustainable Development and prioritizing the aims "to significantly improve the health and well-being of populations, reduce health inequalities, strengthen public health and ensure people-centred health systems that are universal, equitable, sustainable and of high quality". The Ministry of Health has strong political commitment to all domains of the health-care sector, including support for national activities targeting the reduction of TB burden in Uzbekistan.

The successful implementation of national interventions aimed at reducing the TB burden is greatly appreciated by the international community. In 2017, Uzbekistan was ranked in the top three of the 53 Member States of the WHO European Region owing to the high rate of decline in TB incidence and mortality in the country.[30] National statistics in Uzbekistan indicate a decreasing trend in the TB notification and death rates, from 79.1 cases and 12.3deaths per 100 000 population, respectively, in 2002 to 44.6 cases and 2.2 deaths per 100 000 population, respectively, in 2017. However, drug resistance is still a challenge

These attainments were achieved through ensuring sustainability for the activities of the NTP. Significant support from various international partners (USAID, Branch Office of Project HOPE in Uzbekistan) aims to ensure broad access for all strata of the population to innovative TB diagnostic techniques combined with highly efficient approaches to patient treatment and treatment monitoring. The effectiveness of activities to overcome the challenges in combating TB such as expanding treatment with short course regimens using novel and repurposed anti-TB drugs, introducing international standards of pharmacological surveillance; and setting up a unified system of epidemiological and bacteriological control require dynamic decision-making and discussions.

Description of the good practice

The Centre for Innovative Distance Training and Monitoring was established at the at the Republican Specialized Scientific and Practical Medical Centre for Phthisiology and Pulmonology in accordance with the Decree of the Government of the Republic of Uzbekistan of 20 June 2017 No. PP-3071 on Measures for Further Development of Specialized Health Care to be Provided to the Population of the Republic of Uzbekistan for 2017–2020. Its purpose is to increase the efficiency of the specialty health-care system to meet modern requirements and improve the quality of health-care provided to the population, with technical support from USAID.

The Centre serves a base for best practices to train professionals in the area of phthisiology and respiratory medicine; provide methodological assistance to regional specialty care facilities and deliver high-quality specialized services to patients with TB and chronic nonspecific lung diseases in accordance with international standards. The Centre has a multilevel structure with the Republican Specialized Scientific and Practical Medical Centre for Phthisiology and Pulmonology on the top and four subsidiaries at regional TB control facilities in the Bukhara, Kashkadarya, Khorezm and Navoi regions; in the future, all other areas will be included.

The Centre led the activities and expanded access for regional providers in the field of phthisiology to new knowledge by attracting leading international specialists; arranging patient consultations and consiliums (multidisciplinary advisory bodies) at a distance; providing specialists of the central institution with the opportunity to monitor the management of complicated cases and the occurrence of adverse events during the treatment course.

[30] Wolfheze Workshops and WHO National Tuberculosis Programme Managers Meeting, 2017.

The main objectives of the Centre are to:

- assist national, regional and city institutions in organizing and carrying out training and retraining sessions for health-care providers to control TB at national and regional levels;
- conduct national and international conferences, meetings, workshops, seminars and master classes for all categories of health-care professionals and nonmedical staff involved in the provision of TB care to residents of Uzbekistan;
- arrange consultations and consiliums at a distance with the involvement of all national specialists; and
- incorporate a laboratory module to train both laboratory technicians (mid-level staff) and doctors-microbiologists at the Centre.

Evidence of impact

Figs 58 and 59 show examples of the impact of the project.

Sustainability of the good practice

The Centre for Innovative Distance Training and Monitoring has extended the capabilities for programmatic management of the TB Control Service by:

- introducing the tele-health-care system to TB control facilities, which has improved the quality of consultative care and the availability of modern therapeutic modalities and patient follow-up in at the regional level; and
- developing the standard operating procedures of the Unified National Consilium on M/XDR-TB treatment, drug quality monitoring and pharmacovigilance system.

A flexible approach has been used in compiling the modular training curriculums in various areas of phthisiology as a part of the online training system to meet the need for trained human resources in the regions.

Fig. 58. Opening ceremony of the Centre for Innovative Distance Training and Monitoring, Tashkent, April 2017

Left to right: Harry Robbins, Director of the USAID Office in Uzbekistan; Ilmira Basitkhanova, Deputy Minister of Health, Uzbekistan; and Professor Nargiza Parpieva, Director of the Republican Specialized Scientific and Practical Medical Centre for Phthisiology and Pulmonology.

Fig. 59. National consilium on MDR-TB treatment working online, Tashkent and Bukhara, April 2017

Uzbekistan. Using the quantification and early warning system (QuanTB) is the key to preventing stock-outs of anti-TB drugs in Uzbekistan

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Background

Uzbekistan is one of the top 18 high-priority countries included in the Plan to Stop TB in the WHO European Region *(83)* and in the top 30 countries with the highest MDR-TB rates in the world and the 15 countries with the highest MDR-TB rate in the WHO European Region.

The NTP has a complex vertical hierarchy, with the Republican Specialized Scientific and Practical Medical Centre for Phthisiology and Pulmonology under organizational and methodological guidance of the Ministry of Health of Uzbekistan at the central level; regional TB dispensaries at the regional level; and cabinets (rooms) in primary care facilities dedicated to continuous observed therapy at the district level; 100% access to treatment for both DS-TB and DR-TB patients is ensured.

Uzbekistan is implementing the ongoing provision of SLDs and reserve anti-TB drugs from the Global Fund to Fight AIDS, Tuberculosis and Malaria grant. The framework requires a high level of quantification of medication needs, as well as early warning indicators to improve the efficiency of procurement processes, orders and procurement plans to supply drugs for TB treatment.

Description of the good practice

A situation analysis of the anti-TB drug management system in Uzbekistan was performed in 2014 to determine the feasibility of achieving a high level of performance in pharmaceutical management by the NTP. This comprised expert evaluation of the domain of different drug management, including the rational use of medicines and compliance with national TB treatment protocols (with support from the USAID Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program).

The study outputs necessitated incorporating an electronic tool for forecasting, quantitative stock assessment and sending an early warning to the NTP. In 2015, QuanTB version 4 was implemented in four pilot regions in Uzbekistan (with support from the SIAPS Program) to for predicting the need for any TB therapeutic regimen or combination of anti-TB drugs over any period of time; notifying the upcoming need to replenish reserves, and the timing and maximum/minimum stock levels; and planning procurement (both scheduled and emergency orders) and the costs of medicines and other anticipated expenses. In 2016, with support from the SIAPS Program and Project HOPE, an electronic warning system was introduced across all 14 regions of the country. Both the quantitative assessment system and early warning system are now solely maintained by the staff of TB control services at national and regional levels, with technical support from the Global Drug Facility and the Stop TB Partnership.

As part of its commitment to raising the level of pharmaceutical management under the NTP, the Ministry of Health of Uzbekistan has equipped 14 regional TB dispensaries with new computers and installed the most recent version of QuanTB.

The electronic forecasting, quantification and early warning tool has permitted the NTP (central level) to analyse the early warning system reports regularly submitted by all 14 regions, thereby improving the countrywide system for the anti-TB drug procurement, supply and distribution and regional uptake. Regular quantitative assessments and the QuanTB early warning system option helped in making objective decisions on the amount of medicines to be ordered for the central and regional levels. The management system has improved coordination between the central and regional tiers to ensure optimal stock levels are maintained, including redistribution of medicines among districts and regions to prevent medicines being wasted due to expiry. Control over adherence to treatment regimens has also improved: both regional and central MDR-TB consiliums (multidisciplinary expert panels) warn of the improper use of anti-TB drugs based on data collected by the system.

A review of monthly reports of the QuanTB early warning system from all 14 regions covering the period from June 2016 to June 2017 showed that a proportion of regional warehouses experiencing a shortage of at least one anti-TB drug decreased by 57%. The proportion of district TB facilities across all regions with a shortage of at least one anti-TB drug decreased by an average of 35% between June and December 2016 and by a further 27% whereas from December 2016 to June 2017.

Evidence of impact

Fig. 60 shows that the proportion of district TB facilities with at least one anti-TB medicine stock-out dropped over the course of the project.

QuanTB was shown to be a sustainable and efficient tool for adequate quantitative assessment and the early prevention of managerial deficiencies in pharmaceutical coverage at all levels of the NTP. The QuanTB early warning system has been adopted as a single, unified standard to calculate the need for anti-TB drugs in Uzbekistan, by amendment of Executive Order No. 383.

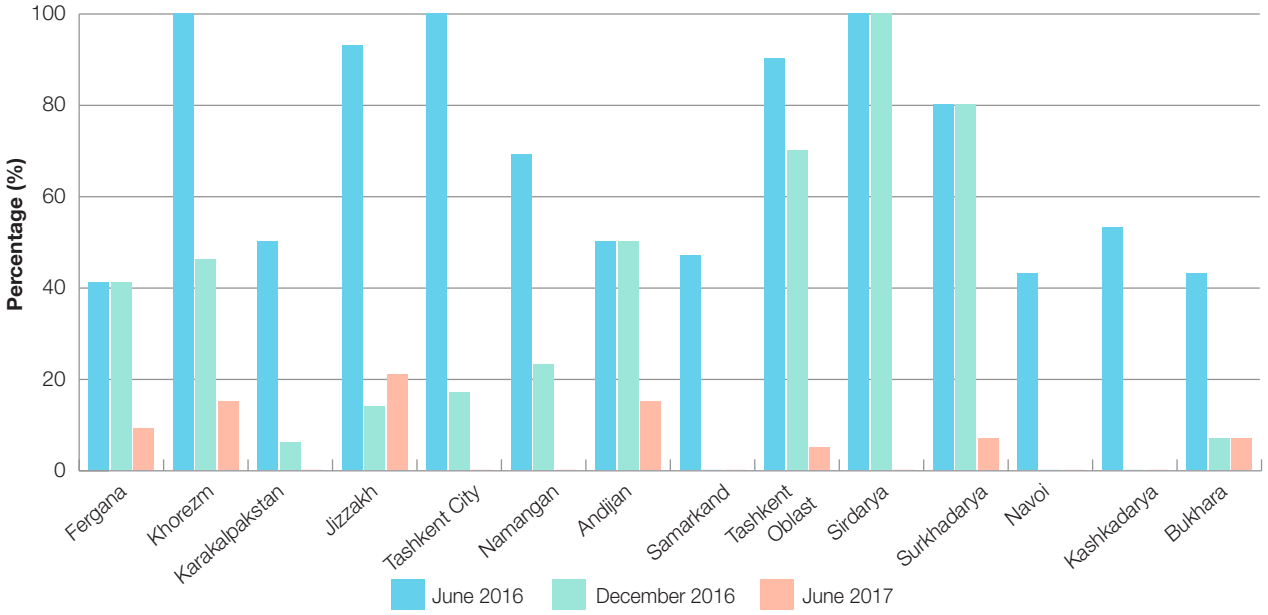
Nonetheless, a prerequisite for ensuring optimal stocks of anti-TB drugs in each institution is to strengthen current policies and practices in the programmatic management of anti-TB pharmaceutical coverage in the primary health-care system.

Sustainability of the good practice

Improvement in programmatic management requires:

- introducing the electronic TB surveillance system to improve the quality of TB patient data;
- developing standard operational procedures to process both scheduled and emergency requests for medicines at the national and regional levels in response to a QuanTB warning of potential stock-out;

Fig. 60. Proportion of district TB facilities in each region with at least one anti-TB medicine stock-out, 2016–2017



- ensuring close cooperation between pharmaceutical management and the MDR-TB Consilium at the regional (oblast) level to control treatment regimens and provide information on treatment for notified MDR-TB patients and drug stock levels;
- improving the system for distribution, redistribution and storage of TB medicines;
- strengthening links between primary care institutions and regional and district TB facilities to maintain optimal stocks of anti-TB drugs at all levels of health-care provision related to TB treatment; and
- annual monitoring visits to ensure the quality of the QuanTB data in all regions and evaluate functioning of the system.

As QuanTB is free of charge, no ongoing funding is needed for the software.

3B. Research to optimize implementation and impact of the End TB Strategy and to promote innovation

Armenia. Inpatient TB treatment in Armenia: a needs assessment for establishing a continuous quality improvement system

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Background

According to estimates for 2014, the TB (excluding HIV/TB) incidence rate in Armenia was 42 cases per 100 000 population and the TB mortality rate was 5.1 deaths per 100 000 population (including HIV-positive cases). The estimated proportion of new MDR-TB cases is 9.4% and of re-treated TB cases that develop MDR-TB is 43% *(84)*. Currently, 3800 people are estimated to be living with HIV/AIDS in Armenia. Among people aged 15–49 years, HIV prevalence is reaching 0.2%.

Of the 1099 TB patients tested for HIV infection from 2002 to 2007, 1.8% were reported to have HIV coinfection in 2002, increasing to 3.1% in 2007. Of the 1242 TB patients tested for HIV infection in 2010, the proportion with HIV coinfection dropped to 1.4%; however, the rate then dramatically increased, reaching 6.3% of 1342 HIV-tested patients in 2014.

In 2017, the Incidence of new TB cases in Armenia was 23.1 cases per 100 000 population and the mortality rate was 1.8 deaths per 100 000 population *(85)*.

High-quality TB care provision is an important step towards improving patient quality of life and decreasing TB morbidity and mortality. The introduction of international standards and guidelines for TB care provide an opportunity to ensure access to high-quality TB services by providing a benchmark for the performance assessment of the NTP. Assessment of diagnostic and treatment services for adherence to standards is an important component for defining the quality of care provision and then developing quality improvement programmes.

In collaboration with the National TB Control Centre, the Centre for Health Services Research and Development launched the project, In-patient Tuberculosis (TB) Treatment in Armenia: Establishment of Continuous Quality Improvement System *(86)*, which started with an initial needs assessment to develop a multiyear plan for collaboration to strengthen inpatient and outpatient TB care in Armenia. The needs assessment evaluated diagnostic and inpatient treatment services within the National TB Control Centre.

Description of the good practice

The study aimed to develop a multiyear plan to transform inpatient and diagnostic facilities at the National TB Control Centre into a modern mechanism for patient safety and a quality assurance system for care provision. This was to be achieved by implementing systematic measures for continuously improving its operations and the quality of care provision. The newly established quality assurance system will ensure that patients seeking health-care are protected from medical mistakes in the care they receive and create a safe environment for patients. During the first phase – the needs assessment – different aspects of the National TB Control Centre's diagnostic and inpatient operations were assessed, including both clinical and administrative functions, resulting in several recommendations for improvement. The study team (i) reviewed and summarized the literature on quality assessment of inpatient TB facilities; (ii) qualitatively explored the practices of health-care professionals in the National TB Control Centre and the experience of TB patients and their family members in inpatient treatment; (iii) assessed the documentation,

staff practices and environmental conditions of the inpatient facilities at the National TB Control Centre using standardized checklists; (iv) evaluated the level of compliance of TB diagnostic and treatment practices with internal policies and procedures, along with national and international guidelines and standards; and (v) made recommendations to the National TB Control Centre based on the findings for further improvement of TB diagnostic and treatment services.

The needs assessment generated evidence for improving the quality of care provision within the National TB Control Centre, which can be applied in other health-care facilities in Armenia.

Evidence of impact

The needs assessment identified deficiencies within the National TB Control Centre related to the standardization of processes and a lack of monitoring and follow-up mechanisms. The findings suggest that interventions are needed at two levels of operation: structure-related improvements (development of policies, procedures and written documentation, and establishment of modern infrastructures) and process-related improvements (actions towards improving patient care processes).

It was evident from the assessment that structured, up-to-date training courses and materials need to be developed to train health-care professionals in the latest techniques and treatment methods for TB. Hence, a training centre is needed, the main purpose of which would be to train health-care professionals from the central and regional levels. The training centre will also function as a research institution, where studies will be conducted to not only address the clinical aspect of TB as but also TB policy and management of TB care.

Sustainability of the good practice

Establishment of a quality assurance system within the National TB Control Centre is included in the Centre's development plan. After implementation of the quality assurance system (based on recommended standards of Joint Commission International), a gradual change in hospital-wide organization in line with the notion of high-quality health-care and patient safety will result in a routine standard procedure which will not require additional resources.

Georgia. Building clinical research capacity at the National Centre for Tuberculosis and Lung Diseases

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Background

After dissolution of the Soviet Union, the Georgian health-care system faced many challenges, including limited funding and a lack of institutional and individual capacity for clinical research. TB was a major public health problem in the country, and the initial lack of national treatment programmes and infrastructure contributed to the high rates of DR-TB still seen today.

As outlined in the recent End TB Strategy *(4)*, clinical research and implementation of new interventions are imperative to improve TB management. In 2004, through international partnership with Emory University School of Medicine in the United States of America, Georgia received a unique opportunity to train TB clinical research scientists. The Emory-Georgia TB Research Training Program (EGTB-RTP) was and continues to be supported by the Fogarty International Center, United States. National Institutes of Health through a Global Infectious Diseases Research Training Award. The National Centre for Tuberculosis and Lung Diseases (NCTLD), the main referral centre for TB diagnosis and treatment in Georgia, is the primary in-country partner; additional in-country partners include the Georgian National Centre for Disease Control and a school of public health. The EGTB-RTP has been successful in terms of establishing a cadre of highly trained clinical and translational researchers at the NCTLD, which has in turn has led to numerous publications, increased research funding and further collaborations with other institutions in Georgia and internationally. Experience in undertaking the EGTB-RTP is reported here with the goal of providing helpful guidance to other similar countries in building their research capacity.

Description of the good practice

The EGTB-RTP combines didactic and mentored research training for Georgian trainees (so-called Fogarty

trainees). Each trainee has a mentor form the United States one from Georgia. Didactic training courses in biostatistics, data management and scientific writing are provided by Emory University School of Medicine faculty members via real-time videoconferencing. Short courses in epidemiology, research ethics and mentor training have been conducted in Georgia, with English classes available for trainees as needed. Each trainee was required to carry out a research project and expected to submit their work to a scientific conference and for publication. A stipend was provided to cover at least 50% of the trainees' professional effort, along with a computer and support to attend an international conference to present the research work. From 2004 to 2017, a total 15 long-term (two years) and three short-term (six months) trainees from the National Centre for Tuberculosis and Lung Diseases were enrolled to the EGTB-RTP. Prior to implementation of the EGTB-RTP, only one peer-reviewed article had been published by the NCTLD; since initiation of the EGTB-RTP, trainees have published over 50 TB-related publications, including many in high-impact journals. The trainees have formed a critical mass of researchers at the NCTLD, leading to many direct and indirect benefits. Over half of the trainees have been recipients of at least one external peer-reviewed research grant following training and have been promoted to a leadership position; most former trainees are now serving as mentors of junior researchers at the NCTLD. Additionally, the first investigator-initiated TB-related randomized clinical trial in Georgia was led by five former trainees in collaboration with Emory University. Many opportunities have become available through having a strong core of researchers.

Capacity-building for individual research has been further strengthened from United States and European research centres through various additional programmes including: (i) the Field Epidemiology and Laboratory Training Program of the United States Centers for Disease Control and Prevention; (ii) postdoctoral training and doctoral programmes in infectious disease and epidemiology from the Swiss Tropical and Public Health Institute; (iii) postdoctoral programmes from the Royal Tropical Institute (KIT) of Amsterdam, the University of Leister (United Kingdom) and the Georgian Research & Development Foundation mini grants programme. Additional on- and off-site research-related training was provided by collaborative institutions in different fields such as molecular biology (including different typing methodologies), microbiology, immunology and clinical research. Altogether, these programmes have trained 11 persons in epidemiology and biostatistics and approximately 78 clinical and laboratory staff in different research methodologies and tests.

In 2014, the NCTLD established a clinical research unit led by a former Fogarty long-term trainee. All NCTLD research activities are run through the clinical research unit, which is staffed by five full-time researchers and administrators and predominantly supported through donor-funded projects. Research areas include operational research (evaluation of implementation of new diagnostic tools on patient treatment outcomes), clinical research (evaluation and demonstration studies for improved diagnostic tools for the early diagnosis and monitoring of infection, evaluation of adjunctive treatments and clinical trials) and translational research (antimicrobial drug resistance, biomarkers).

A total of 33 operational and clinical research projects are ongoing, most in collaboration with international partners. Local partners include the National Centre for Disease Control and Public Health and the Lugar Centre, Tbilisi, Georgia; and the Infectious Diseases, AIDS and Clinical Immunology Research Centre, Tbilisi, Georgia. International partners include the Health Science Research Institute of the Germans Trias I Pujol Foundation (IGTP), Catalunya, Spain, the Foundation for Innovative Diagnostics, Geneva, Switzerland, the Foundation of Mareux, Lyon, France, the International Union against Tuberculosis and Lung Diseases, and the Global Alliance for TB Drug Development (TB Alliance).

To enhance the clinical trial capacity, 17 researchers at the NCTLD have received training in Good Clinical Practice and Good Clinical and Laboratory Practice; with support from the Henry M. Jackson Foundation, ethics training was provided by international experts to Institutional Review Board members in 2015 and 2016. In 2018, the NCTLD is a site for three of the six phase III clinical trials in the TB drug development pipeline: Stream stage 2 (NCT02409290), ZeNiX (NCT03086486), STAND (NCT02342886) and one phase III post-marketing optimization trial, endTB (NCT02754765), with one phase 2c trial SimpliciTB (NCT03338621).

Additional achievements include being selected in 2014 as a Foundation for Innovative New Diagnostics site. Important new technology and diagnostic test

evaluation studies were carried through this partnership, including the GeneXpert MTB/RIF Ultra Trial at the NCTLD Mycobacteriological Reference Laboratory.

As a metric of academic productivity, the number of peer-reviewed publications in medium- and high- impact journals has been increasing yearly. Since 2011 (with one publication), NCTLD staff have published a total 57 manuscripts in Pubmed-listed scientific journals. In terms of research funding, the amount of annual TB research funding at the NCTLD has increased from 8500 Georgian lari in 2005 to 4.5 million lari in 2017. In 2018, the total anticipated TB research funding estimated at 5 million lari.

Research capacity-building has had a substantial impact on overall NCTLD infrastructure and human resource development impacting clinical care and enhancing people-centred approaches. Research evaluating novel TB diagnostics and treatment algorithms have facilitated rapid uptake of these tests and treatments into standard clinical care. We have also developed a weekly research conference and encouraged collaborations between investigators and clinicians which has helped to translated research findings into clinical care and vice versa has helped researchers address clinically relevant topics. Additionally, results from many clinical and operational projects have led to changes in the National TB Guidelines.

In summary, we presented our research capacity-building experience as evidence that investing in research and mentor training are crucial to building the necessary individual and institutional infrastructure to have a productive and impactful research enterprise which in turn helps improve patient care.

Evidence of impact

Capacity-building for research has increased the interest of staff in research, leading to increased interest in the Georgian pulmonary/phthisiology residency programme *(87)*.

Sustainability of the good practice

The established structure and ongoing capacity-building of the practice seem sustainable. The pool of former trainees has become in-country research mentors, which will facilitate continuous capacity-building.

Further development of the national research framework, strengthening national research ethics regulations in biomedical sciences, and opportunities for local funding would support sustainability of the practice.

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