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COUNTRY TECHNICAL SUPPORT MISSION REPORT

Country:	Moldova
Dates of the mission	4–16 October 2021
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Clearance of the report	The content of the report has been fully cleared by the National Tuberculosis Programme, Moldova.
Sharing of the report	1. The report has been shared with The Global Fund Portfolio Manager, Moldova and the TGF GLC Focal Point. 2. In-country circulation of the report done via WHO Country Office, Moldova.
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Abbreviations

ADR	adverse drug reactions
aDSM	active drug-safety monitoring
ART	antiretroviral therapy
Bdq	bedaquiline
BPaL	bedaquiline, pretomanid, linezolid
DR-TB	drug-resistant tuberculosis
Cfz	clofazimine
COVID-19	coronavirus disease 2019
Cs	cycloserine
Dlm	delamanid
DOT	directly observed treatment
DST	drug-susceptibility testing
FLD	first-line anti-TB drugs
FQs	fluoroquinolones
GDF	Global Drug Facility
HCV	hepatitis C virus
LTBI	latent TB infection
Lfx	levofloxacin
LPA	line probe assay
Lzd	linezolid
MAF-TB	Multisectoral Accountability Framework for TB
MDR-TB	multidrug-resistant tuberculosis
Mfx	moxifloxacin
MOH	Ministry of Health
MMDA	Medicines and Medical Devices Agency
MOTT	Mycobacteria other than TB
mSTR	modified all-oral shorter 9-month RR-TB regimen
NGO	nongovernmental organization
NRL	National Reference Laboratory
NTP	National Tuberculosis Programme
NPC	National Pharmacovigilance Centre
NNS	number need to screen
OR	Operational research
OST	opioid substitution therapy
PHC	primary health care
PLHIV	people living with HIV/AIDS
PS	penitentiary system
Rif	rifampicin
RR	relative risk
RR-TB	rifampicin-resistant tuberculosis
PV	pharmacovigilance
SLD	second-line anti-TB drugs
SNRL	Supranational Reference Laboratory

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TA	technical assistance
TB	tuberculosis
TBT	tuberculin skin test
TGF	The Global Fund Against AIDS, TB and Malaria
VOT	video-observed treatment
WHO	World Health Organization
XDR	extensive drug resistance

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1 Executive summary

Despite the significant progress achieved by the National Tuberculosis Programme (NTP) of the Republic of Moldova in 2019, the overall tuberculosis (TB) control system was significantly affected by the COVID-19 pandemic. As a result, the dramatic decrease in TB notification rates from 71.6 per 100 000 in 2019 to 43.9 per 100 000 in 2020 is more likely to be the result of underdiagnosis rather than a real improvement of the epidemiological situation.

Against this unfavourable background, the key achievements of the NTP of Moldova include consistent treatment success rates for new TB cases (a 85.9% success rate for new cases and 70.0% for relapses in the 2019 cohort, and a 72.8% success rate for new DR-TB cases and 47.2% for relapses in the 2018 cohort). The new mSTR (modified all-oral shorter 9-month RR-TB regimen) drug-resistant (DR)-TB treatment is being successfully implemented in the country under the operational research (OR) programme.

Approaches to case detection in Moldova in general are compliant with WHO strategic recommendations. In contrast with the overall TB notification rate, the proportion of laboratory confirmed cases.

of DR-TB is constant, confirming the resilience of the national laboratory networks.

The national guidelines on TB control are to be updated in line with the WHO Consolidated Guidelines on Tuberculosis (2020–2021) *.

As of 2020, the NTP's main funding came from the National Health Insurance Company (54%), the Global Fund to fight HIV/AIDS, Tuberculosis and Malaria (TGF) (29%) and the state budget (17%).

The NTP of the Republic of Moldova is currently implementing a TGF grant of around € 18 million, which is active from 1 January 2021 through to 31 December 2023.

Key recommendations

No.	Recommendation	Time frame	Responsible agency
1	To clarify the scope of the competencies of the national TB programme by clearly defining the mechanisms for their implementation, and providing the appropriate independent means for implementation.	2022	MOH
2	To identify the priority groups for TB screening based on the relative risks of each group. This will require measuring the target population size and monitoring risk factor prevalence.	2023	NTP, MOH, allied ministries (the Ministry of Justice and the Ministry of Labour and Social Welfare)
3	To ensure additional efforts for screening to compensate for the underdetection of TB during the COVID-19 pandemic, including collaboration with insurance companies, NGOs and TB awareness campaigns.	2022	NTP, MOH

4	To assess the potential for countrywide BPaL regimen implementation under the national OR programme supported by the Ministry of Health. To ensure the enrolment of incarcerated people onto the OR, if possible.	2023–2024	NTP. MOH, other partners
5	Taking into account the availability, experience and success of the implementation of the mSTR OR, invite the country's international partners (TGF, etc.) to support the NTP research group to finance the implementation of the BPaL research programme.	2023–2024	Local and international NGO's

2.Background

The Republic of Moldova is a landlocked eastern European country, bordering with Ukraine and Romania. The current administrative structure of the country is as follows: the capital city Chisinau; a total of 32 districts; one autonomous territorial entity (Gagauzia); one region with special status (Transnistria, which includes two cities and five districts). The total number of municipalities is 13, cities, 53; communes, 659; villages/towns, 916.

According to the official census data (2014), Moldova's total population is 3.5 million. Nevertheless, it is estimated that between 600 000 and 1 million citizens (or 25% of the population) work abroad. As a result, in 2021 the World Bank estimated a residential population of 2.6 million. The official statistics operate with a population size of 4 million. The latter figure has been used as the denominator for TB-related rates. These discrepancies are a serious concern as they suggest that the real TB burden in the country is underestimated.

Despite a solid economic performance over the past two decades, Moldova still remains among the poorest countries in Europe. Although a growth model reliant on remittance-induced consumption has generated high growth and reduced poverty, it had become less sustainable well before the COVID-19 pandemic. The decline in remittances, combined with a shrinking and ageing population, has resulted in low productivity growth, and a significant number of the lower-income population has become dependent on pensions and social assistance. In 2020 the pandemic and a severe drought starkly exposed the vulnerabilities of this growth model to shocks. With a subsequent decline in GDP of 7% in 2020, Moldova was among the countries in Europe most affected by COVID, which has significantly impacted households and businesses across the country. These unfavourable circumstances are potentially increasing the populations' vulnerability to TB.

In contrast, the data of TB case notifications presented in Table 1 demonstrate a significant drop in TB case notifications that could potentially lead to increased number of severe cases and a high mortality rate in the near future.

Table 1. TB case notifications, 2016-2021 Q1

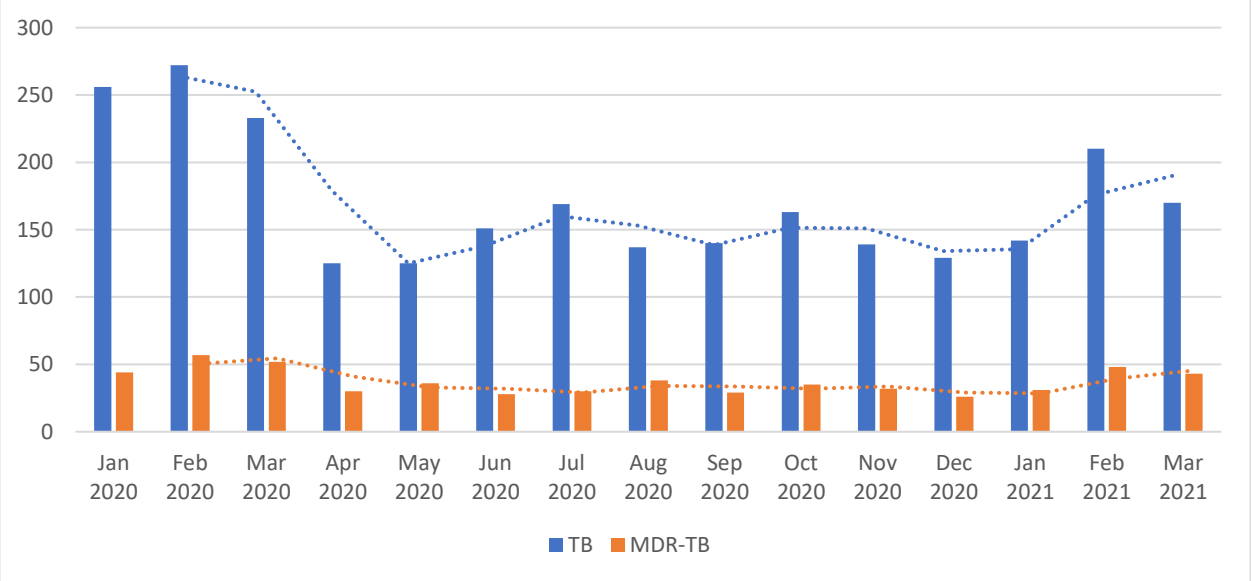
	2016	2017	2018	2019	2020	Q1 2021

New cases	2 844	2 681	2 451	2 280	1 375	352
Relapse cases	725	671	565	596	386	107
Previously treated cases other than relapse	557	504	441	432	278	63
All TB cases	4 126	3 856	3 457	3 308	2 039	522
TB mortality (absolute number)	372	320	304	248	210	82
Population for rate calculation	4 031 401	4 023 043	4 017 583	4 017 320	4 017 796	4 016 838
Incident (new and relapse) cases in children (0–14 years)	103	123	95	101	56	13
Notified RR-TB cases	788	737	719	695	437	122
TB/HIV cases out of all TB cases	372	355	320	345	195	18

Source: NTP data.

However, after the significant decrease in the TB notification rate in March 2020, which coincided with quarantine measures starting in Moldova, the rate is moving average is showing a recovery trend. The DR-TB notification rate appears less affected, and by the date of the mission, it was just slightly lower than the of the previous year's rate (Fig. 1).

Fig. 1 TB and MDR-TB notification rates during the COVID-19 pandemic with moving averages



Source: NTP data.

The main drug resistance patterns for newly detected and retreatment cases are presented in Tables 2–3.

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Table 2. FLD and SLD resistance profile among new TB cases, 2017–2021 Q1

		2017		2018		2019		2020		Q1 2021	
Line		***N***	***%***	***N***	***%***	***N***	***%***	***N***	***%***	***N***	***%***
1	Number of new TB cases notified	2 681		2 451		2 280		1 375		352	
2	Number of pulmonary cases from line 1	2 374	88.5%	2 187	89.2%	2039	89.4%	1 254	91.2%	311	88.4%
3	Number of laboratory confirmed cases from line 2	1 478	62.3%	1 414	64.7%	1 326	65.0%	822	65.6%	212	68.2%
4	Number of cases with DST result to rifampicin (Rif) from line 3	1 463	99.0%	1 383	97.8%	1 300	98.0%	804	97.8%	207	97.6%
5	Number of RIF-resistant TB (RR-TB) cases from line 4	438	29.9%	426	30.8%	372	28.6%	212	26.4%	68	32.9%
6	Number of cases with DST results to fluoroquinolones (fq) from line 5	385	87.9%	354	83.1%	313	84.1%	163	76.9%	53	77.9%
7	Number of cases sensitive to fq from line 6	328	85.2%	290	81.9%	267	85.3%	142	87.1%	50	94.3%
8	Number of cases resistant to FQ from line 6	57	14.8%	64	18.1%	46	14.7%	21	12.9%	3	5.7%
9	Number of cases with DST results both to linezolid (Lzd) and bedaquiline (Bdq) from line 8	17	29.8%	24	37.5%	19	7.1%	0	0.0%	0	0.0%
10	Number of cases sensitive to both Lzd and Bdq from line 9	2	11.8%	0	0.0%	1	2.2%	0	0.0%	0	0.0%
11	Number of cases resistant to both Lzd and Bdq from line 9	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
12	Number of cases resistant to Bdq and sensitive to Lzd from line 9	0	0.0%	0	0.0%!	0	0.0%	0	0.0%	0	0.0%

Table 3 FLD and SLD resistance profile among previously treated TB cases, 2017–2021 Q1

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		2017		2018		2019		2020		Q1 2021	
Line		*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*
1	Number of previously treated TB cases notified	1 175		1 006		1 028		664		170	
2	Number of pulmonary cases from line 1	1 122	95.5%	968	96.2%	989	96.2%	642	96.7%	161	94.7%
3	Number of laboratory confirmed cases from line 2	751	66.9%	699	72.2%	699	70.7%	407	63.4%	99	61.5%
4	Number of cases with DST result to rifampicin (Rif) from line 3	716	95.3%	667	95.4%	644	92.1%	353	86.7%	82	82.8%
5	Number of RIF-resistant TB (RR-TB) cases from line 4	483	67.5%	431	64.6%	378	58.7%	196	55.5%	43	52.4%
6	Number of cases with DST results to fluoroquinolones (fq) from line 5	443	91.7%	400	92.8%	334	88.4%	154	78.6%	33	76.7%
7	Number of cases sensitive to fq from line 6	263	59.4%	242	60.5%	223	66.8%	110	71.4%	25	75.8%
8	Number of cases resistant to fq from line 6	180	40.6%	158	39.5%	111	33.2%	44	28.6%	8	24.2%
9	Number of cases with DST results both to linezolid (Lzd) and bedaquiline (Bdq) from line 8	40	22.2%	38	24.1%	35	15.7%	0	0.0%	0	0.0%
10	Number of cases sensitive to both Lzd and Bdq from line 9	0	0.0%	1	2.6%	1	0.9%	0	0.0%	0	0.0%
11	Number of cases resistant to both Lzd and Bdq from line 9	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
12	Number of cases resistant to Bdq and sensitive to Lzd from line 9	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Source: NTP data

The National Strategic Plan (NSP) for 2021–2025 includes the following areas:

Early TB detection among the key populations:

- Improving financial incentives to primary health care (PHC) for active case finding (chest X-ray reimbursement, quality data coverage).
- Strengthening and diversifying active case-finding strategies at facility and community level: better definition/targeting of key populations, multidisciplinary teams (PHC and nongovernmental organizations (NGOs)).
- Implementing a nationwide training programme for paediatric TB.
- Rolling out Xpert MTB/Rif, culture &DST DST in prisons.
- Introducing incentives for mobile chest X-rays.
- Expanding NGO coverage (social contracting, capacity building).
- Active case-finding and contact investigation cascade reporting and analysis.
- Evidence generation through the national TB research agenda.

TB diagnosis:

- Strengthening the laboratory quality management system (including national assessment and action planning).
- Reforming the financing of labs.
- Gradual transitioning to domestic funding.
- Integrating the specimen transportation systems (TB, HIV, hepatitis C (HCV), COVID-19, non-communicable diseases).
- Introducing X-pert XDR, multi-disease platforms (TB, HIV, HCV, and COVID-19).

Treatment and support:

- Updating and implementing the TB hospital optimization plan.
- Scaling up outpatient treatment (PCMC, directly observed treatment (DOT)).
- Revising PHC incentives (per case holding).
- Improving clinical monitoring and management of adverse events.
- Patient care pathways/flows/referrals (guidelines and protocols).
- Scaling up new drugs/regimens, strengthening aDSM.
- Improving case management (needs assessment, multidisciplinary teams).
- Diversifying treatment administration (range of providers, home-based DOT).
- Scaling up video-observed treatment (VOT) (through the NGOs).
- Patient incentives and enablers.
- Developing and implementing integrated service delivery models.

Prevention

- Updating and implementing latent TB infection (LTBI) guidelines.
- Ensuring sustainable access to TB preventive treatment (TPT), tuberculin skin test. (TST), interferon-gamma release assay (IGRA).
- Patient incentives/enablers for TPT.

Policy:

- Establishment/implementation of the Multispectral Accountability Framework for TB (MAF-TB).
- Transition to domestic funding and addressing the financing gaps for TB services.
- Improving universal access, social protection and integration of TB diagnostic, treatment

and care services for the most prevalent comorbidities.

- NHAestablishment/reporting for TB.
- Obtaining evidence on the barriers (human rights, stigma, and discrimination), planning interventions and actions.

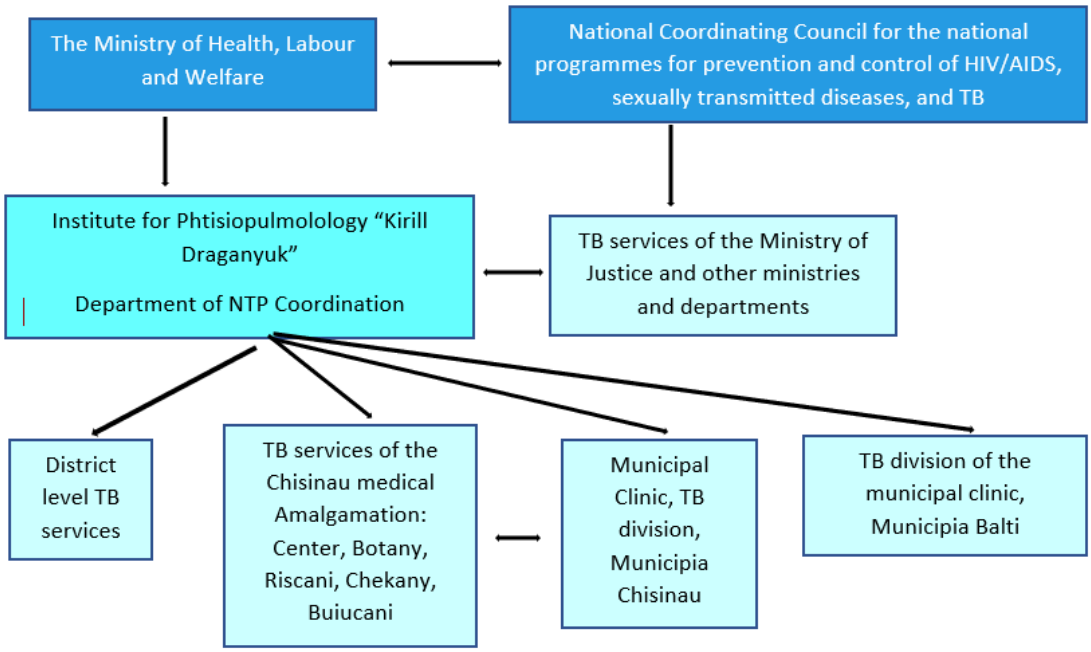
Supportive systems (Human Resources (HR), PSCM, NTP management):

- Developing/updating Human Resource Development (HRD) policies and plans.
- Updating integrated training curricula.
- Revise the national legislation/regulations to allow for procurement from the Global Drug Facility (GDF).
- Establishing a system for the joint procurement of anti-TB drugs.
- Strengthening the management of the NTP.
- Improving the TB monitoring and evaluation (M&E) system management, infrastructure and analytical capacity.

The region of Transnistria, which has a special status in the country, presents an important peculiarity of country-level TB control. The region reports to the NTP of Moldova. However, TB control approaches only partly parallel the NSP's: the regional TB managers are reluctant to implement the recent updates for TB control, such as selective TB screening and evidence-based practices of TB case management and support.

The structure of the NTP is presented in Fig. 2.

Fig. 2 Structure of the NTP



As of 2020, the main NTP funding comes from the National Health Insurance Company (54%), TGF

(29%) and the state budget (17%).

The NTP of the Republic of Moldova is currently implementing a TGF grant of around € 18 million, which is active from 1 January 2021 through to 31 December 2023.

3. DR-TB case-finding and diagnosis

The diagnostic algorithms for drug-susceptible and DR-TB in Moldova, in general, meet the latest WHO recommendations.

Total of 57 first-level laboratories provide sputum microscopy and X-pert MTB/RIF tests, including three laboratories in the penitentiary sector.Total of 59 X-pert machines operate in the country, including 48 at the primary care level, five in the NRL, three in the penitentiary sector, and three in TB services. Both the previous generation X-pert MTB/RIF cartridges and the new X-pert MTB/RIF Ultra cartridges are in use.

Three second-level laboratories operate as regional reference laboratories and provide all the services of third-level laboratories, including providing liquid medium culture tests and first- and second-line drug-susceptibility testing (DST) (Balti, Vorniceni, Bendery). The NRL, in addition to the functions above, provides testing for MOTTS (mycobacteria other than TB), training and M&E.

The NRL and the second-level laboratories have vehicles for sample transportation for culture testing and DST under cold chain conditions; each provides testing for a specified part of the country. The transportation frequency depends on the catchment area and varies from daily to biweekly. Civilian sector second- and third-level laboratories also provide DST for the penitentiary sector.

Line probe assay (LPA) is provided for all samples positive on microscopy or X-pert MTB/RIF. FLD LPA is done in all cases, and SLD LPA is done for all cases with resistance demonstrated in FLD LPA, and also for some other rifampicin-resistant cases detected by X-pert MTB/RIF.

The NRL has the capacity to perform X-pert MTB/RIF and culture testing for any extra-pulmonary samples, including blood and tissue samples and claims to have the necessary consumables and standard operating procedures (SOPs) in place. However, the diagnostic yield for the particular specimens is not assessed; and the patient and sample referral pathways are not clearly defined in the diagnostic algorithm.

The internal and external quality assurance (EQA) systems have been in place in Moldova for all testing types for almost 20 years. In particular, since 2005, EQA has been provided annually for DST to first-line and, for second-line drugs since 2009. According to this system, the average proportion of false results during the last 5 years has not exceeded 0.5%.

The COVID-19 pandemic significantly affected the laboratory throughput (Table 4). Against this background, the number of liquid media culture tests, DST and LPA performed showed a very small decrease.

Table 4 Number of microscopy, culture and DST investigations, countrywide, 2016–2021 Q1

	2016	2017	2018	2019	2020	Q1 2021
Direct smear microscopy (DSM)	121 368	111 998	96 162	141 124	101 187	24 623

Culture on solid media	65 073	67 148	67 907	68 316	48 981	11 562
DST to FLDs on solid media	1986	3 989	2 090	1 350	631	125
DST to SLDs on solid media	1964	4 121	2006	1 658	796	133
Culture in liquid media (automated MGIT)	26 197	24 119	25 401	27 392	24 828	8 285
DST to FLDs in liquid media (automated MGIT)	2 919	5 951	3 085	2 371	1 731	518
DST to SLDs in liquid media (automated MGIT)	1 560	3 259	1 577	1 017	955	300
LPA MTBDR-Plus	1 106	1 055	1 747	1 586	1 417	640
LPA MTBDR-sl	880	1 261	1 369	992	1 038	350

Source: NTP NRL Moldova data

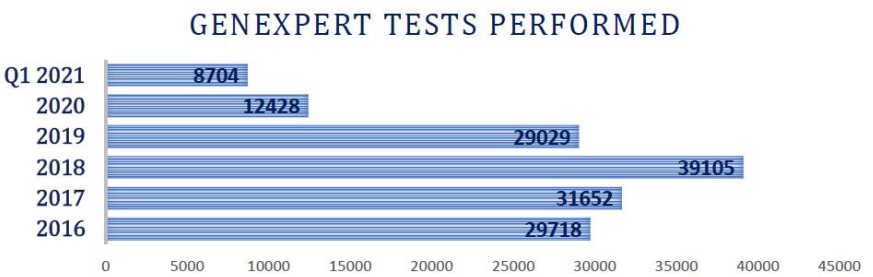
In 2021 there was a significant decrease in both the number of X-pert MTB/RIF tests performed and absolute diagnostic yield (Table 5). The increased X-pert positivity rate partly compensates for this gap (Fig. 3). Thus, the overall TB case detection has been more severely affected than the MDR-TB detection rate.

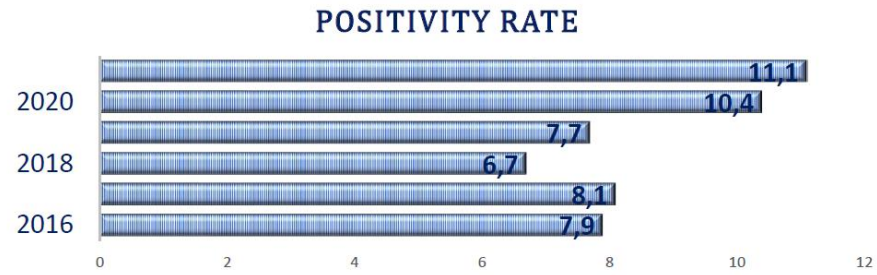
Table 5. Xpert MTB/RIF test results in the country, 2016–2021 Q1

Year	Total number of Xpert MTB/RIF tests	Invalid test results				Valid test results					
		Total invalid tests	"Test invalid"	"Test error"	"Test no result"	Total valid tests	MTB(-)	MTB(+)			
								MTB(+) total	MTB(+)/RIF sensitive	MTB(+)/RIF-Resistant	MTB+/RIF Inde-terminate
2016	31 831	562	35	442	85	31 269	28 751	2 518	1 627	824	67
2017	31 652	337	35	283	19	31 315	28 751	2 564	1 673	824	67
2018	39 105	981	56	823	102	38 124	35 493	2 631	1 627	924	80
2019	29 029	560	33	442	85	28 469	26 226	2 243	1 439	743	61
2020	12 428	307	27	249	31	12 121	10 827	1 294	778	446	70
2021 Q1	8 468	151	14	129	8	8 317	7 379	938	557	364	17

Source: NTP NRL data

Fig. 3 Number of Xpert MTB/RIF tests performed and positivity rate





Source:NTP data

Although laboratory confirmation rates of TB cases have been slowly increasing, they are still suboptimal with a 68.2% confirmation rate for new cases of pulmonary TB (Table 2).

The national TB screening algorithm needs improvement in line with Module 2 of the *WHO Consolidated Guidelines on Tuberculosis*.[1] Risk groups and screening algorithms need re-prioritizing. The NTP has requested the assistance required from the WHO Regional Office for Europe. The data on the sizes of at-risk populations, which are currently available to the NTP, are limited to people living with HIV (PLHIV) and incarcerated people. Nevertheless, data on the numbers of migrants, refugees, people who had been previously incarcerated, and immunocompromised individuals, other than PLHIV, are essential for relative risk (RR) calculations for each group, number needed to screen (NNS) estimates, and the selection of the most efficient screening algorithm. However, the overall situation with TB and COVID-19 has created other options for improving TB case detection.

Whereas the national TB standard does not specify approaches for screening, the physicians interviewed expressed various interpretations or perceptions on the screening algorithms. TB screening in the Transnistria region is of particular concern, as it is not based on risk assessments and the prioritization of key populations.

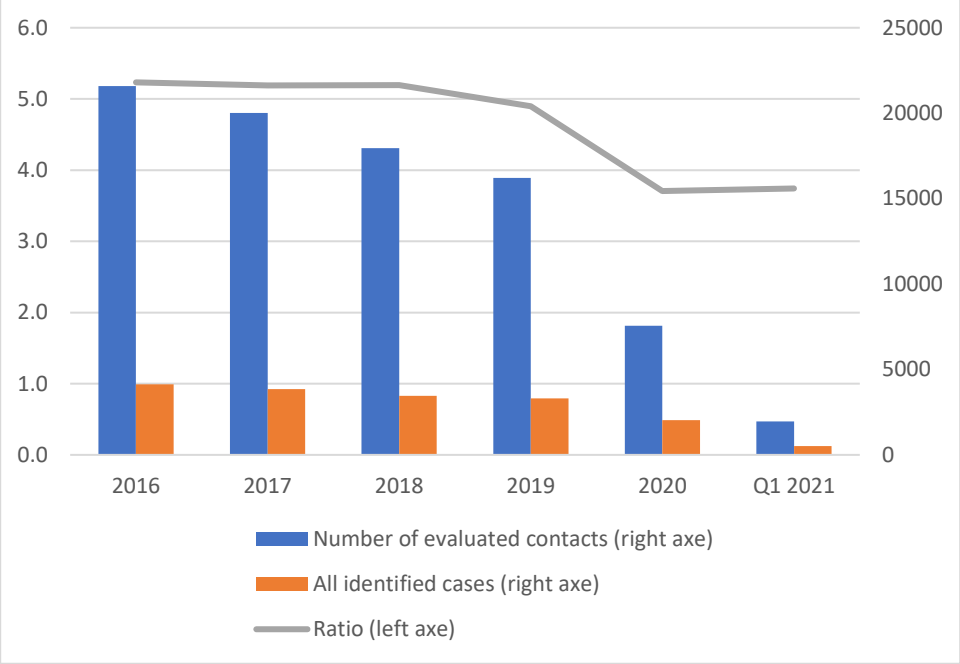
The physicians' reports and the statements suggest suboptimal funding and support for screening procedures. For example, no mobile X-ray screening was available in the penitentiary sector in 2020.

[1] WHO consolidated guidelines on tuberculosis Module 2: Screening – Systematic screening for tuberculosis disease. Geneva: World Health Organization; 2020. (https://www.who.int/publications/i/item/9789240022676, accessed 20 February 2022).

The NGOs, mainly within the TB-REP framework, provide the majority of the support for screening of key populations. For example, during 6 months of 2021, with NGO support, 6 261 alcohol users, injecting drug users, unemployed people, homeless people, PLHIV, and other representatives of key populations underwent symptom-based screening, and 7 026 had chest X-rays.

TB contact tracing was significantly less active in 2020, possibly due to the COVID-19 pandemic. The number of tested contacts due to one index case decreased in consort with the case notification rate (Fig. 4). Nevertheless, during discussions, TB physicians presented the results of contact tracing for each case study, suggesting that contact tracing is a routine approach.

Fig. 4 Ratio of tested contacts due to one index case



Source: NTP data

Recommendations

No.	Recommendation	Time frame	Responsible agency
1	Identify the priority groups for TB screening based on the relative risk in each group. This intervention will require measuring the target population size and monitoring prevalence of risk factors.	2023	NTP, MOH, allied ministries (the Ministry of Justice and the Ministry of Labour and Social Welfare)
2	To ensure additional efforts for screening to compensate for the under detection of TB during the COVID-19 pandemic, including collaboration	2022	NTP, MOH

	with insurance companies, NGOs and TB awareness campaigns.		
3	Conduct a study to analyse the reasons for the suboptimal level of pulmonary TB laboratory confirmations (a countrywide OR could be an appropriate format) and develop the national roadmap to address this gap.	2023	NTP
4	Develop SOPs on specimen collection and culture processing, X-pert MTB/RIF Ultra testing in children (stool and gastric aspirates) and in patients with possible extra-pulmonary TB. Provide training on the SOPs for clinical personnel.	2022	NTP, NRL, professional associations
5	Develop a mechanism for the sustainability of the laboratory network at the specialized and primary care levels, in particular for the maintenance of laboratory equipment and for regular EQA for Level I–III laboratories.	2022	NTP, NRL
6	Pilot active TB screening for patients with COVID-19-specific symptoms in PHC clinics and COVID-19 clinics using X-pert MTB/RIF sputum screening for cases in which patients produce sputum.	2022	NTP, NRL
7	Ensure regular X-ray TB screening in prisons.	2022	NTP

4.DR-TB treatment and case management

Although Moldova is no longer included in the WHO list of the top 20 MDR-TB countries, it is still in the. Despite great efforts were made by the country in the field of MDR-TB management in recent years, MDR-TB continues to be a health problem and it is important to maintain the political will to continue to provide adequate funding to the sector, ensuring the effectiveness and continuity of anti-TB activities. The management of MDR/RR-TB is one of the main components of the National TB Control Programme in Moldova.

In 2020, there were 212 (26.4%) notified MDR/RR-TB cases among the 822 new pulmonary TB bacteriologically confirmed cases. Of these, only 163 (76.9%) cases were tested for resistance to FQs, and resistance to FQ was detected in 21 (12.9%) cases. However, as a result of the relatively low rates for bacteriological confirmation and DST for FQs 65.5% in 2020, the actual number of MDR/RR-TB cases might be substantially higher. This is reflected in Tables 1 and 6.

Table 6. FLD and SLD resistance profile among new TB cases, 2017–2021 Q1

		2017	2018	2019	2020	Q1 2021

Line		N	%	N	%	N	%	N	%	N	%
1	Number of new TB cases notified	2 681		2 451		2 280		1 375		352	
2	Number of pulmonary cases from line 1	2 374	88.5%	2 187	89.2%	2039	89.4%	1 254	91.2%	311	88.4%
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4	Number of cases with DST result to rifampicin (Rif) from line 3	1 463	99.0%	1 383	97.8%	1 300	98.0%	804	97.8%	207	97.6%
5	Number of RIF-resistant TB (RR-TB) cases from line 4	438	29.9%	426	30.8%	372	28.6%	212	26.4%	68	32.9%
6	Number of cases with DST results to fluoroquinolones (fq) from line 5	385	87.9%	354	83.1%	313	84.1%	163	76.9%	53	77.9%
7	Number of cases sensitive to fq from line 6	328	85.2%	290	81.9%	267	85.3%	142	87.1%	50	94.3%
8	**Number of cases resistant to FQ from line 6**	57	14.8%	64	18.1%	46	14.7%	21	12.9%	3	5.7%
9	**Number of cases with DST results both to linezolid (Lzd) and bedaquiline (Bdq) from line 8**	17	29.8%	24	37.5%	19	7.1%	0	0.0%	0	0.0%
10	**Number of cases sensitive to both Lzd and Bdq from line 9**	2	11.8%	0	0.0%	1	2.2%	0	0.0%	0	0.0%
11	**Number of cases resistant to both Lzd and Bdq from line 9**	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
12	**Number of cases resistant to Bdq and sensitive to Lzd from line 9**	0	0.0%	0	0.0%!	0	0.0%	0	0.0%	0	0.0%

Source: NTP Moldova data

However, there were 196 (63.4%) notified MDR/RR-TB cases among the 407 retreatment pulmonary TB bacteriologically confirmed cases. Of these, 154 (78.6%) cases were tested for resistance to FQs, and resistance to FQ was detected in 44 (28.6%) cases (Tables 7). For the national TB program, it is important to explore the ways to increase the number of cases tested for FQ.

Table 7 FLD and SLD resistance profile among previously treated TB cases, 2017–2021 Q1

		2017		2018		2019		2020		Q1 2021	
Line		N	%	N	%	N	%	N	%	N	%
1	Number of previously treated TB cases notified	1 175		1 006		1 028		664		170	
2	Number of pulmonary cases from line 1	1 122	95.5%	968	96.2%	989	96.2%	642	96.7%	161	94.7%
3	Number of laboratory confirmed cases from line 2	751	66.9%	699	72.2%	699	70.7%	407	63.4%	99	61.5%

4	Number of cases with DST result to rifampicin (Rif) from line 3	716	95.3%	667	95.4%	644	92.1%	353	86.7%	82	82.8%
5	Number of RIF-resistant TB (RR-TB) cases from line 4	483	67.5%	431	64.6%	378	58.7%	196	55.5%	43	52.4%
6	Number of cases with DST results to fluoroquinolones (fq) from line 5	443	91.7%	400	92.8%	334	88.4%	154	78.6%	33	76.7%
7	Number of cases sensitive to fq from line 6	263	59.4%	242	60.5%	223	66.8%	110	71.4%	25	75.8%
8	**Number of cases resistant to fq from line 6**	180	40.6%	158	39.5%	111	33.2%	44	28.6%	8	24.2%
9	**Number of cases with DST results both to linezolid (Lzd) and bedaquiline (Bdq) from line 8**	40	22.2%	38	24.1%	35	15.7%	0	0.0%	0	0.0%
10	**Number of cases sensitive to both Lzd and Bdq from line 9**	0	0.0%	1	2.6%	1	0.9%	0	0.0%	0	0.0%
11	**Number of cases resistant to both Lzd and Bdq from line 9**	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
12	**Number of cases resistant to Bdq and sensitive to Lzd from line 9**	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Source: NTP Moldova data

DR-TB treatment is administered in both inpatient and outpatient settings in the civilian and in the penitentiary sectors. In the civilian sector, the treatment delivery model for DR-TB is a combination of hospitalization at inpatient TB facilities and therapy continuation at outpatient settings, which are widely available across the country.There are 12 hospitals in the country that provide TB medical care with 916 beds in total. The 7 hospitals out of these 12 hospitals are in civil sector with a total of 646 beds and five hospitals out of the 12 hospitals are in the penitentiary sector with a total of 185 beds. One hospital is located at the central level and six at the regional level. The total number of beds for DR-TB care is 470, of which 290 are in the civilian system and 180 in the prison sector. There is also a paediatric TB department with a total of 60 beds for children of which 10 beds are for children with DR-TB ; the number of surgical beds is 15.

Table 8. Number of TB inpatient facilities, number and profile of TB hospital beds, by sector and level of care, as of April 2021

Type of institutions and beds	**Country total**	**Breakdown by sector**		**Breakdown by level of care (civilian sector)**		
		Civilian sector	*Penitentiary sector*	*Central level*	*Regional level*	*District level*
Number of facilities providing hospital	**12**	**7**	**5**	**1**	**6**	

treatment of patients with active TB						
Total number of beds for treatment of active TB	**916**	646	270	185(130 (20 beds TB/COVID, 110 beds COVID)	461(80 beds COVID)	
• of which, for DR-TB patients	**470**	290	180	160	130	
• of which, for children	**60 (among them 10 beds for DRTB)**	**60 (among them 10 beds for DRTB)**)			**60 (among them 10 beds for DR-TB)**	
• of which, for extrapulmonary TB						
• of which, for surgery	**15**	15		15		
Number of facilities providing palliative care for TB patients						
Number of beds for palliative care						
Number of facilities providing involuntary isolation of TB patients						
Number of beds for involuntary isolation						

Source: NTP data

Due to the COVID-19 epidemic, 20 beds out of the 185 beds at the central level were repurposed for hospitalization and treatment of patients with TB/COVID co-infection and 110 beds were used for the treatment of patients with COVID-19; at the regional level, 80 beds from 461 were repurposed for the treatment of COVID-19 cases.

Hospitalization is not a mandatory TB treatment modality in Moldova; however, most patients are hospitalized at the start of the MDR-TB therapy. The main criteria for hospitalization are the clinical condition of the patient. Discharge from the hospital mostly takes place upon bacteriological

conversion (1 to 2 months of therapy), and adequate DOT treatment and care at the polyclinic closer to the patient's place of residence are provided for the patients.

One of the key components of the patient-centred approach is to reduce the frequency and duration of hospital stays and move towards outpatient care models. In 2019, the GLC mission recommended and which stays in National TB program activity plan that the hospital beds optimization plan should be updated to take into account the reduction of TB incidence and to give priority to outpatient treatment for TB and MDR-TB patients. For a variety of reasons, no official update of this plan has been made, but it is still actual for the national program and still in their further activities for 2022-2023. But the number of hospitalizations has actually decreased, these reductions are mainly due to the reduction of beds in the civilian sector, from 600 beds in Chiril Draganic Hospital to 185 in the first quarter of 2021, and from 265 to 120 in Chisinau Hospital. In the last 3 years, there has been no reductions in the number of beds in the prison system and the Transnistria region.

Table 9. Main activity indicators for institutions providing inpatient treatment of active TB cases, countrywide, 2016–2021 Q1

	2016	2017	2018	2019	2020	Q1 2021
Total number of beds for treatment of active TB						
IMSP IFP, Chiril Draganic, (Institut Medica Sanitaria Public , Institut Phthisiopneumology "Chiril Draganiuc")	600 (incluted in Vorniceni 110+(240 not functioning))	360 (included Vorniceni 110)	360	360	290	185
IMSP SCMF Chisinau (Institut Medica Sanitaria Public, Municipal Children's Clinical Infectious Diseases Hospital)	265	215	215	215	200	120
IMSP SCM Balti DFP Institut Medica Sanitaria Public "Spitalul Clinic Municipal Balti"	75	75	40	40	30	30
IMSP Spitalul Clinic de Psihiatrie secție psihoftiziatrie		40	40	40	30	30
Penitenciar Pruncul P16 Malul Drept	170	170	170	170	170	170
Spitalul de tuberculoza Rezina P17 Malul Drept		50	50	-	-	-
Transnistria (Region-level hospital)	200	200	200	200	200	200

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Transnistria (Pulmonary TB department, Dubăsari)	50	40	40	40	40	40
Transnistria (TB clinic for psychiatry patients, Slobozia)	15	15	15	15	15	0
Penitenciare Transnistria total		160	160	160	160	160
Total number of hospitalizations (discharges)						
IMSP IFP, Chiril Draganic'	1 377	1 414	1 501	1 801	1 243	250
IMSP SCMF Chisinau	916	889	887	808	790	144
IMSP SCM Balti DFP	427	375	286	254	169	34
Penitenciar Pruncul P16 Malul Drept	182	138	133	101	71	10
Transnistria (region-level hospital)	601	587	596.5	568	402	160
Transnistria (Pulmonary TB department, Dubăsari)	122	115	103.5	78	84	36
Transnistria (TB clinic for psychiatry patients, Slobozia)	31	52	33.5	32	8	0
Total number of patient-days						
IMSP IFP, Chiril Draganic'	120 750	132 921	118 292	101 622	67 374	12 258
IMSP SCMF Chisinau	58 361	51 667	50 253	50 853	48 334	9 797
IMSP SCM Balti DFP	26 245	22 108	14 554	12 653	9 434	1 669
Penitenciar Pruncul P16 Malul Drept	35 462	35 905	30 294	33 061	25 129	9 877
Transnistria (region-level hospital)	65 610	60 412	61 864	56 914	36 822	160
Transnistria (Pulmonary TB department, Dubăsari)	10 327	9 480	8 420	8271	-	-
Transnistria (TB clinic for psychiatry patients, Slobozia)	2 493	3 574	3 132	2 694	517	0
Average length of stay, days						
IMSP IFP, Chiril Draganic'	87.7	94.0	70.0	56.4	54.2	49.0
IMSP SCMF Chisinau	63.5	57.3	55.7	62.9	65.3	66.6
IMSP SCM Balti DFP	60.19	56.69	49.67	49.8	55.8	49.1

Penitenciar Pruncul P16 Malul Drept	366.3	489.8	248.15	155.85	166.6	90.85
Transnistria (region-level hospital)	110.2	102.2	103.3	99.9	91.5	81.7
Transnistria (Pulmonary TB department, Dubăsari)	92.25	72.45	72.95	90.75	-	-
Transnistria (TB clinic for psychiatry patients. Slobozia)	166.2	238.4	208.8	179.6	34.4	0
Bed occupancy rate, %						
IMSP IFP, Chiril Draganic'	95.4	94.0	85.4	77.3	63.6	73.6
IMSP SCMF Chisinau	64.6	70.0	67.6	65.9	68.6	72.2
IMSP SCM Balti DFP	86.83	94.99	100.45	128.8	85.15	89.8
Penitenciar Pruncul P16 Malul Drept	114.9	117.5	50.4	55.45	40.05	28.8
Transnistria (Region-level hospital)	113.3	104.2	106.3	97.8	63.5	45.1
Transnistria (Pulmonary TB department, Dubăsari)	62.6	48.2	51.3	49.1	-	-
Transnistria (TB clinic for psychiatry patients. Slobozia)	50.3	72.1	63.0	54.2	41.9	0
Number of surgical interventions, all types						
IMSP IFP, Chiril Draganic'	255	186	168	163	135	21
IMSP SCMF Chisinau	-	-	-	-	-	-
IMSP SCM Balti DFP	-	-	-	-	-	-
Penitenciar Pruncul P16 Malul Drept	-	-		-	-	-
Transnistria (Region-level hospital)	-	-	-	-	-	-
Transnistria (Pulmonary TB department, Dubăsari)	-	-	-	-	-	-
Transnistria (TB clinic for psychiatry patients. Slobozia)	-	-	-	-	-	-
Surgical activity, %						
IMSP IFP,Chiril Draganic'	78.1	66.9	55.4	56.0	41.9	16.6

Source: NTP Moldova data

In 2020, a 30% decrease in the total number of hospitalizations was registered compared with 2019, which is in line with the decrease in the number of TB cases detected. No significant changes were observed in lengths of hospital stay, which ranged from 2–3 months; longer hospitalizations remain in the Transnistria region. The bed occupancy rates in the repurposed COVID units in the IMSP IFP, Chiril Draganic Hospital and Chisinau hospital were approximately 75% and 82% (Table 10). However, the repurposing of beds did not limit access to TB patients' hospital care. The decrease is mostly due to the decrease in detection, the various epidemiological restrictions, and, of course, the wider application of remote treatment and follow-up technologies for TB patients.

Table 10. Main activity indicators for TB institutions/beds repurposed for COVID-19 countrywide, as of April 2021

	IMSP IFP, Chiril Draganic,	IMSP SCMF Chisinau	**Penitentiary sector**
Total number of beds repurposed from treatment of active TB to COVID-19	130 (20 beds for TB/COVID-19, 110 beds for COVID-19)	80	-
Total number of hospitalizations (discharges)	795	677	-
Total number of patient-days ("bed-days")	8 767	5 989	-
Average length of stay, days	11	11.7	-
Bed occupancy rate, %	74.9	82.3	

Source:NTP data

The number of the MDR/RR-TB cases enrolled in treatment decreased gradually from 1 033 cases in 2016 to 882 cases in 2019, but in 2020 the number of enrolled cases decreased dramatically, by about 30%. It is likely that low numbers of cases will be enrolled into MDR-TB treatment in first quarter of 2021 (Table 11). The number of MDR-TB cases enrolled decreased proportionally in the civilian and prison sector, and among children (Figure 5).

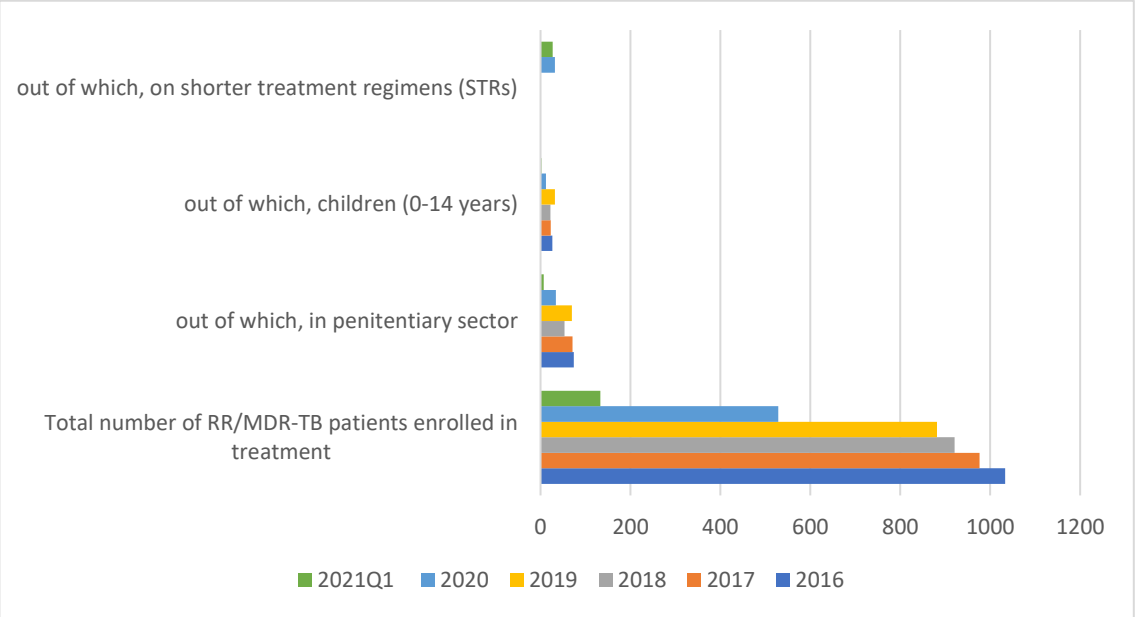
The reduction in the detection and inclusion of TB cases needs further investigation in order to elucidate the potential impact of Covid-19 epidemic.

Table 11. Number of MDR/RR-TB patients enrolled in treatment, 2016–2021 Q1

	2016	**2017**	**2018**	**2019**	**2020**	**Q1 2021**
Total number of MDR/RR-TB patients enrolled in treatment:	1 033	976	921	882	529	133
• out of which, in penitentiary sector	74	71	53	70	34	7
• out of which, children (0–14 years)	26	23	22	32	12	2
• out of which, on shorter treatment regimens (STRs)	0	0	0	0	32	27

Source: NTP Moldova data

Fig. 5. Number of MDR/RR-TB patients enrolled in treatment, 2016–2021 Q1



Source: NTP Moldova data

Despite the multiple interventions in the field of MDR/RR-TB in Moldova described in Table 12, the treatment success rate has not improved much during the last 5 years for MDR/RR-TB patients. According to NTP data presented in 2016, the success rate was 54.6% and 56.7% was reported in 2019. The cohorts of 2016, 2017, and 2018 are over and the treatment success rate is 54.6%, 55.1 and 58.7% correspondingly, and the cohort of 2019 is not over yet, 8.8% of patients are still in treatment, the cohort will end in 2021 and patients still in treatment are likely to complete the treatment successfully. For the same period, the lost to follow-up rate was about 20,1% among MDR/RR-TB cases, which decreased to 18.1% in 2019 (Table 12). The treatment failure rate decreased significantly from 13.1% in 2016 to 6.2% in 2019. A small decrease in mortality rate was observed in 2019, but the mortality rate for the first quarter of 2020 was already 14.1%, and this will require further monitoring. It will be useful to conduct a more qualitative analysis to understand and maintain these positive achievements.

Table 12. TB treatment outcomes, RR-TB cases notified, on longer treatment regimen, 2016–2020 cohorts

	2016		**2017**		**2018**		**2019**		**2020**	
	N	*%*	*%*	*%*	*N*	*%*	*N*	*%*	*N*	*%*
MDR/RR-TB cohort size	1 033		976		921		882		497	
Treatment success	564	54.6%	538	55.1%	541	58.7%	500	56.7%	77	15.5%

Treatment failed	135	13.1%	124	12.7%	111	12.1%	55	6.2%	19	3.8%
Died	126	12.2%	117	12.0%	98	10.6%	89	10.1%	70	14.1%
Lost to follow-up	208	20.1%	196	20.1%	166	18.0%	160	18.1%	64	12.9%
Still on treatment	0	0.0%	1	0.1%	5	0.5%	78	8.8%	267	53.7%

Source:NTP data

There was an increase of rate of successful outcomes for XDR-TB cases, from 19.3% in 2017 to 40.0% in 2019; this improvement could be due to decreases in treatment interruptions and lower mortality rates presented in Table 13.

Table 13. TB treatment outcomes, XDR-TB cases notified, 2017–2020 cohorts

	2017		**2018**		**2019**		**2020**	
	N	*%*	*N*	*%*	*N*	*%*	*N*	*%*
XDR-TB cohort size	57		44		25		6	
Treatment success	11	19.3%	14	31.8%	10	40.0%	0	0.0%
Treatment failed	23	40.4%	15	34.1%	8	32.0%	2	33.3%
Died	8	14.0%	8	18.2%	3	12.0%	1	16.7%
Lost to follow-up	14	24.6%	7	15.9%	3	12.0%	0	0.0%
Still on treatment	1	1.8%	0	0.0%	1	4.0%	3	50.0%

Source: NTP Moldova data

In September 2020, the Operational research for the mSTRs (modified short treatment regimens) for MDR/RR-TB cases was initiated in Moldova in the framework of WHO regional cohort. Between 15 September 2020 and 15 September 2021, total 226 MDR-TB patients were screened, and according to the operational study protocol inclusion criteria 111 patients were included in the study. The 12 patients out of 111 patients were excluded due to FQ resistance or unmanageable side effects or changes of treatment regimens, which were a deviation from the protocol, and 99 patients (of which one child) continued the treatment under study. So far, 20 patients have completed treatment (16 cases cured, 4 cases completed treatment) and 76 patients are still on treatment.

The introduction of the STRs (short treatment regimens like mSTRs or BPaL regimens) is an important approach for the country, but it is also challenging, as research implementation requires frequent monitoring of patients and increased levels of data collection. It is also challenging to monitor and evaluate the implementation of the study in peripheral facilities far from the central level.

4.1Regulatory framework and decision-making

The main regulatory documents for TB medical care in the country are two guidelines, which were revised in 2017 and in 2020. These documents include the organizational and clinical aspects of TB care.

- Tuberculosis in adults, December 2017;
- Tuberculosis in children, May 2020.

The clinical guidelines contain regulatory information on TB detection, treatment (hospitalization, outpatient treatment, medication management, descriptions of all TB drugs, side effects, etc.)Programme specialists and clinicians have developed . In addition to these key regulatory documents, additional documents and training materials. In particular, they refer to the policy of effective TB control strategy, training materials on the revised approaches to the main activities on TB care in the framework of the COVID-19 epidemic, and video materials. The national TB programme website contains all regulatory and educational documents and webinar materials. This makes the documents quite accessible for specialists and saves money on large-scale printing. The guidelines are usually reviewed on a 5-year basis or, if necessary, on a 3-year basis. At present, no new clinical guidelines are planned, according to the team. WHO makes changes very quickly, and intermediate operational documents are developed to follow them. The revision of the guidelines is quite laborious and, in addition, several procedures are required to approve them, so the national team plans to make their changes based on the recommendations of the WHO over the last 3 years.

The DR-TB Committee under the NTP carries out treatment initiation and clinical management of DR-TB patients at the central level.The DR-TB Committee's tasks include discussion of treatment strategies, regimen design, management of adverse events and serious adverse events, causality assessment, referrals between sectors, and assigning outcome definitions. While participating in the DR-TB Committee meeting, and based on the review of the cases presented by doctors from the regional TB medical facilities, it is apparent that cooperation with the central and peripheral specialists does take place. The specialists have a good understanding of the medical and paramedical-related problems that arise during the treatment and care of the patients. Regional physicians have appropriate proficiency to present their patients and patient's problems, receive appropriate support, guidance and follow the advice.

4.2 Clinical monitoring and pharmacovigilance (PV)

The country has a legal and reference basis for safety monitoring for the anti-TB drugs. In general, pharmacovigilance (PV) activities in the Republic of Moldova are carried out by the Medicines and Medical Devices Agency. There are four basic regulatory framework documents for drug management and pharmacovigilance:

1. Law on the Medicines Republic of Moldova, Nr 1409-XIII, 17 December 1997;
2. Law on Pharmaceutical activity Nr 1456-XII, 25 May 1993;
3. Order of MOH RM Nr 739_23.078.2012 "Regarding the regulation of the authorization of medical products for human use and variations";
4. Order of MOH RM Nr 358_1205.2017 "On the approval of the regulation on the pharmacovigilance activities".

To implement active PV for TB for the national programme, tools and methodologies are needed to monitor TB treatment and the detection and management of adverse events. Detection, monitoring of adverse events and reporting in the framework of PV and clinical trial activities are regulated by the

MOH order from 2017. The current national TB clinical guidelines for adults do include recommendations for drug-safety monitoring and reporting in various sections of the guidelines, but there is no comprehensive section covering the full package of PV measures in line with WHO requirements.In the future, the updated clinical guidelines should provide full, harmonized recommendations on PV in line with WHO recommendations.

The current strategy of aDSM includes active monitoring and management of the safety of anti-TB therapy for:

- ✓ groups of patients with MDR/XDR-TB who are prescribed new TB medicines, such as Bbq or Dlm;
- ✓ groups of patients with MDR-TB who are prescribed new shortened regimens of TB therapy;
- ✓ groups of patients with XDR-TB who are prescribing second-line drugs.

There are different ways to report adverse drug reactions (ADR): *electronic reports* that can be made directly on the Medicines and Medical Devices Agency (MMDA) website, or *ADR paper reports* that are filled in by patients or doctors. The ADR E-reporting system is a new platform for PV activities recording and reporting. The MMDA PV department is responsible for the collection, validation, analysis and evaluation of adverse reactions.

The national TB programme has established ADR reporting practices. ADRs are recorded in medical documentation, partially in statistical form. The doctor registers all ADRs in the SIME-TB information system with further reporting to MMDA.

The PV components are the reporting guidelines (manual/clinical guidelines), the ADR reporting forms and their availability, the collaboration with the MMDA for data assessment, safety management training for staff, the ADR/SIME-TB database, data submission to the MMDA database (aDSM), and periodic monitoring.

The national TB programme is to extend aDSM to other groups of TB patients receiving standard DR-TB treatment because of the effective PV activity implementation for the groups of patients listed above.

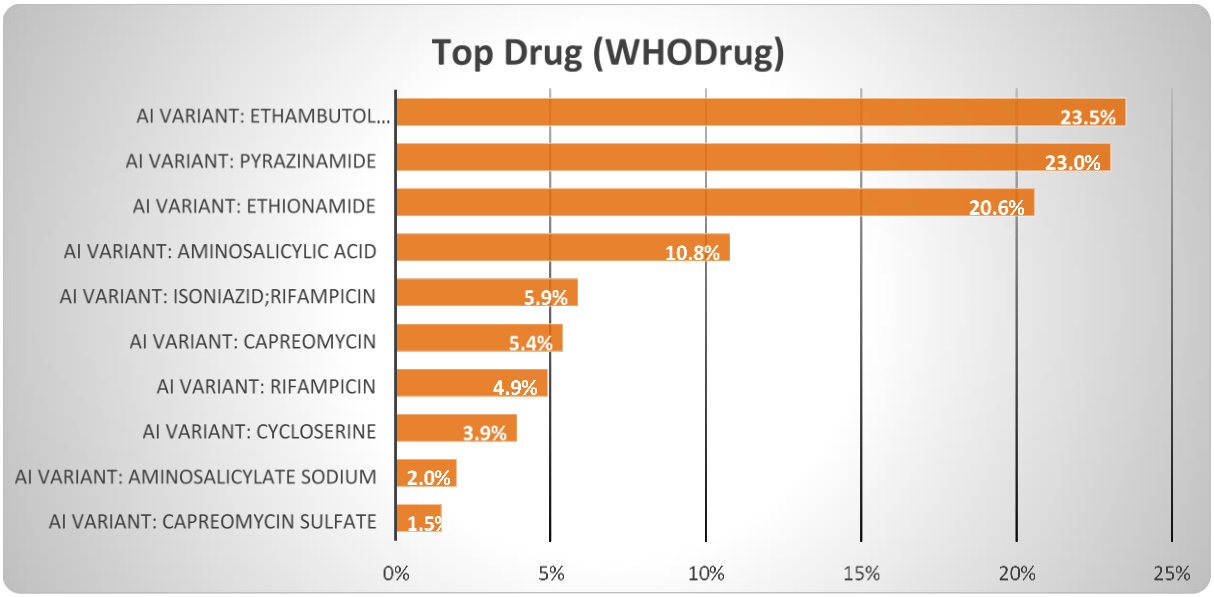
4.3 Available resources for sustainable implementation of PV in TB

As part of aDSM, the availability of systematic laboratory and clinical monitoring of patients is ensured at different levels of TB care in Moldova.
The TB cabinets responsible for the management of patients at the outpatient stage have different levels of equipment and resources available to meet the specific requirements for monitoring patients treated with the new and repurposed TB drugs. However, regular monitoring of biochemical parameters could be obstructed by interruptions in the availability of biochemical consumables. Continuous monitoring of the safety profile of medicines, including signal management and risk–benefit assessments of approved medicines, is part of current practice and is performed regularly.

Based on annual drug agency data for 2020–2021, about 1 721 signals were recorded, 12% (236) of which were related to anti-TB drugs. Reported ADRs were more specific to first-line and early-stage anti-TB drugs and were most likely to be related to ethambutol, pyrazinamide and ethionamide (Figure 6). It is important to note that the data generated do not contain reports on the new TB drugs, and it

is important to take into consideration that PV activities should be in line with the novel approaches to TB treatment.

Figure 6 . Vigilance on anti-TB drugs reports Reported Drugs



Source: Medicines and Medical Devices Agency data

Recommendations

No.	Recommendation	Time frame	Responsible agency
1	Evaluate the appropriateness of FQ use for drug-sensitive cases, assessing the risks and benefits.	2022	NTP
2	Assess the potential to expand the use of the MDR-TB short-term treatment regimens (based on mSTR) by identifying problems and possible solutions. Ensure the enrolment of incarcerated persons onto mSTR treatment.	2022–2023	NTP, MOH
3	Meanwhile take into account the mSTR mentors' recommendations on modified short treatment regimens implementation in the framework of WHO regional study initiation : consider that the NTP study team has already completed recruiting patients for the regional cohort, has received approval from the local ethics committee, and has begun recruiting the country cohort. Further funding should	2022	NTP. MOH

	consider necessary evaluations (electrolytes, ECG, etc.) at the expense of partners (GF, etc.), since they are not included in the national clinical guidelines so that this does not become an obstacle for the country mSTR OR.		
4	To assess the possibility of countrywide BPaL regimen implementation under the national OR programme supported by the Ministry of Health. Ensure the enrolment of incarcerated persons in the OR, if possible.	2023–2024	NTP. MOH, other partners
5	Taking into account the high availability, experience and success of the implementation of the mSTR OR, invite the country's international partners (TGF, etc.) to support the NTP research group in financing the implementation of the BPaL research programme.	2023–2024	Local and international NGO's
6	In the future, the updated clinical guidelines should provide full, harmonized recommendations on PV in line with WHO recommendations.	2023–2024	NTP. MOH
7	The goal of the national TB programme is to extend aDSM to other groups of TB patients receiving standard MDR-TB treatment because of the effective implementation of PV activities for the groups of patients listed above.	2023–2024	NTP. MOH
8	To ensure more active signal detection for the new TB drugs in the national TB programme and better communication with the NTP, ensuring proper evaluation of ADR data, causality assessment, signal detection and management is recommended.	2022–2023	NTP. MOH

5. Other programme areas

LTBI and preventive treatment

The Clinical Guideline on TB Management in adults and children contains a section on TB prevention. The section organized in line with WHO Guidelines of LTBI, updated and consolidated guidelines for programmatic management[2]. (2018).An update of the protocol in line with Module 1 of the *WHO*

Consolidated Guidelines on Tuberculosis is expected.[2] The guidelines presume the use of Interferon-Gamma Release Assay (IGRA) along with the TST for LTBI diagnosis, as well as rifampicin- and rifapentine-containing LTBI treatment regimens. Rifapentine has been available for LTBI treatment for the last 2 years.

However, the existing national TB register (SIME-TB) does not allow follow-up of patients enrolled into LTBI treatment; thus, the number of enrolled patients exposed to different TB risk factors and the use of particular treatment regimens remains underreported. IGRA use remains sporadic.

LTBI management in the Transistria region appears to be a mixture of gaps and conventional approaches. Mass non-selective TST is in place, the "Diaskintest" of unknown sensitivity and specificity is used. The 6-month isoniazid course was the only treatment regimen presented.

Recommendations

No.	Recommendation	Time frame	Responsible agency
1	For LTBI screening, consider using TST or IGRA among household contacts >5 years of age, health care workers working in TB clinics/units, candidates for organ and bone marrow transplantation, patients on TNF-alpha antagonist treatment, patients on dialysis and silicosis patients.	2022	NTP
2	Consider preventive treatment for child (0–15 years) household contacts (~80% of the target group for drug quantification purposes), adult household contacts (40% of the target group for drug quantification purposes), PLHIV, candidates for organ and bone marrow transplantation, patients on TNF-alpha antagonist treatment, patients on dialysis and silicosis patients in a staged manner.	2023	NTP
3	Consider the expansion of the shorter rifapentine-based preventive treatment regimens.	2022	NTP
4	Consider training of TB staff on LTBI screening and management, as per the guidelines referred to, and assign an LTBI coordinator.	2022	NTP

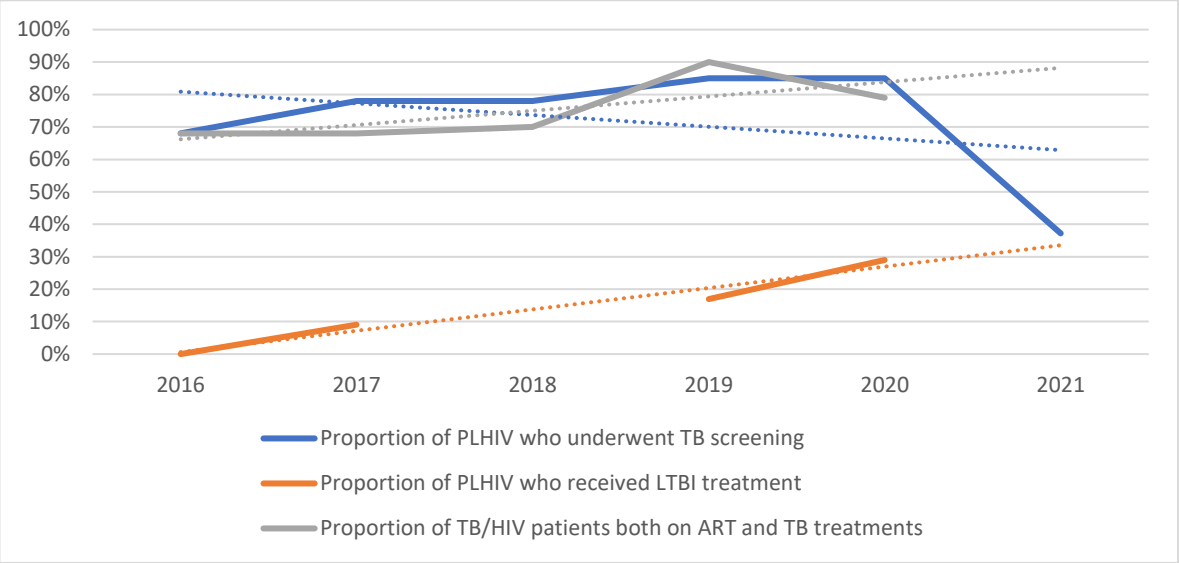
[2] WHO consolidated guidelines on tuberculosis: Module 1: Prevention: Tuberculosis preventive treatment. Geneva: World Health Organization; 2020. (https://www.who.int/publications/i/item/who-consolidated-guidelines-on-tuberculosis-module-1-prevention-tuberculosis-preventive-treatment, accessed 20 February 2022).

5.1 TB-HIV collaboration

By the date of the mission, the estimated number of PLHIV in Moldova was 14 538; 9 679 patients (66%) knew their status, of those 6 810 (70%) were on ART and 5 918 (87% of the latter group) had viral suppression.

Unlike the other lines of TB control, TB/HIV management demonstrated resilience during the COVID-19 pandemic. In particular, the TB screening proportion decreased only slightly, whereas LTBI treatment and coverage of TB/HIV patients by both antiretroviral therapy (ART) and TB treatment increased (Fig. 6).

Fig. 6 TB prevention, screening and treatment among PLHIV, with trends

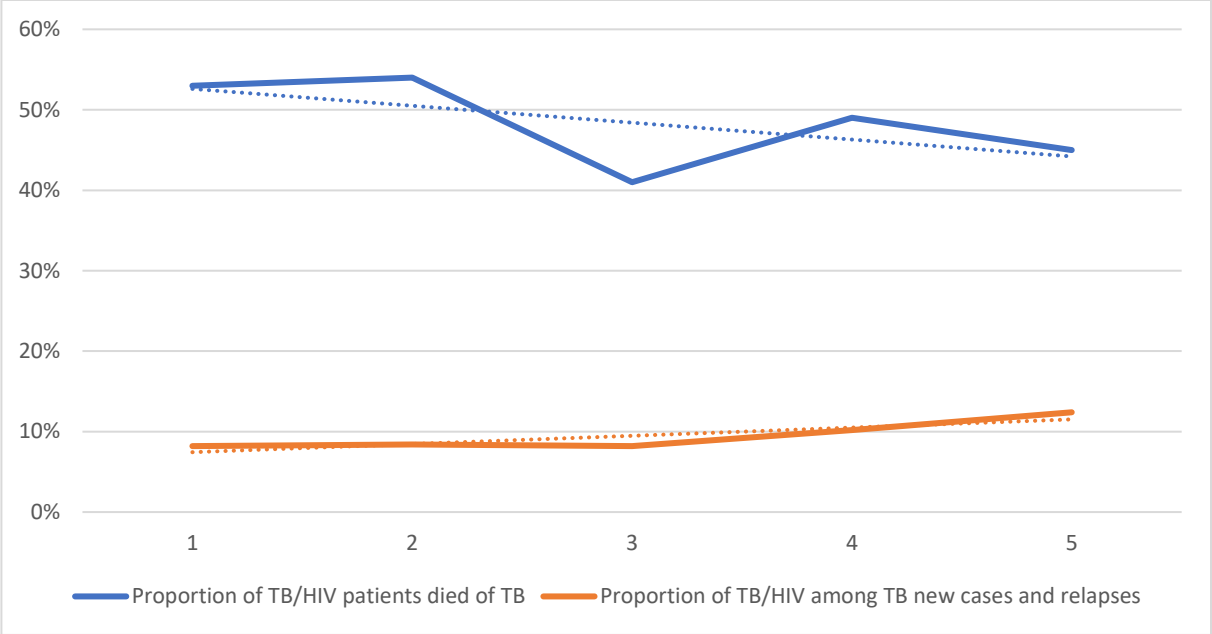


Source: NTP data

The national HIV Service has three X-pert MTB/RIF machines; therefore, 100% coverage of sputum samples by X-pert ensured. The NRL can identify non-tuberculosis mycobacteria, and thus, provide an additional diagnostic yield for HIV patients who were presumed to have TB but, in fact, have MOTT as an opportunistic infection.

Active case finding yielded an increased proportion of TB/HIV cases among all TB cases. Against the background of TB under detection, this effect was noticeable despite the absolute number of TB/HIV cases dropping almost twofold from 345 in 2019 to 195 in 2020. Increased ART coverage of PLHIV, and TB therapy and ART coverage for TB/HIV patients has led to a decreased role for TB as a reason of death for TB/HIV patients, as expected.

Fig. 7 TB/HIV among detected TB cases and TB as a reason of death among TB/HIV deaths, with trends



Source:NTP data

Nevertheless, the number of severe TB cases in PLHIV remains unknown. The TB LF-LAM lateral flow urine lipoarabinomannan assay) test for severely ill and severely immunocompromised patients is not in place. As a result, generalized TB cases, which are difficult to provide laboratory confirmation for, maybe underdiagnosed in Moldova.

Recommendations

No.	Recommendation	Time frame	Responsible agency
1	Ensure ART coverage for PLHIV to meet the 90% goal as a measure to decrease the TB/HIV incidence rate.	2023	NTP, National HIV programme MOH
2	Provide LF-LAM testing for all outpatient PLHIV with CD4 <100 cells/µl and inpatients with CD4 <200 cells/µl.	2023	NTP, National HIV programme MOH

5.2 PMDT in prisons

As of 1 January 2021, 6 429 people were incarcerated in Moldova (overall the prisons capacity is 6 735). Of these, 69 prisoners were treated for active TB in two penitentiary TB facilities with a total capacity of 170 beds. The TB care facilities are significantly understaffed with a 26.2% shortage of doctors and a 11% shortage of nurses.

The COVID-19 pandemic affected case detection in prisons, as the operation of mobile X-ray machines was stopped in 2020 and then resumed for only a short time because of the poor condition of the vehicles. As a results, nine facilities, which have not their own machines, were not able to organize screening X-ray.

These obstacles suggest significant TB underdetection in 2020–2021. The enrolment of incarcerated DR-TB patients in treatment dropped more than twofold in 2020 with 39 patients enrolled in 2019, 18 in 2020 and 14 for the first 9 months of 2021. Consequently, in 2021 the TB facilities were significantly underused: the total number of patients was 67. To some extent, this underuse enabled infection control requirements to be met, as it was possible to keep patients separated.

HIV, hepatitis treatment and opioid substitution therapy (OST) are also provided in prisons (as of 2021, to 12, 11 and 3 patients, respectively). TB is not a leading cause of death among incarcerated people. For example, in 2020 only 4 of 52 deaths were due to TB.

The NGOs have supported TB patients after their release: 24, 24 and 13 patients received this support in 2019, 2020 and 2021, respectively. As social support during TB treatment is available to all patients in Moldova after appealing to the civilian TB service, the needs of former inmates are completely met by this universal support package.

The TB services in the penitentiary sector are mainly funded by the NTP (70%). The separate drug procurements mechanisms are of concern because of the small amounts of drugs needed. These circumstances will potentially complicate the implementation of the STR and BPaL regimens.

5.3 Infection control

During the mission, the observations on infection control may be less accurate than for other issues. as the online mode does not allow for a complete assessment.

The national TB guidelines do not contain definitive criteria for hospitalization; thus, the priority for outpatient TB treatment is not articulated. There is no national IC standards for TB or other diseases. In the absence of national regulations, an outdated understanding of the modes of TB transmission and the prevention interventions is common. This gap was especially noticeable during the interview with the TB care providers from the Transnistria region.

However, as the NTP managers reported, the number of beds in TB clinic is currently excessive and the hospitals are underused which somewhat compensates for the infection control gaps, and allows patients to be separated.

Recommendations

No.	Recommendation	Time frame	Responsible agency
1	Develop the hospitalization criteria to ensure the prioritization of outpatient TB treatment.	2022	NTP
2	Incorporate TB infection control requirements into comprehensive national standards on Infection Prevention and Control.	2023	NTP, MOH

6. Human resources, capacity-building needs

A skilled, motivated and available workforce involved in TB prevention, diagnosis, treatment and care is an essential component of TB control. The National Strategy of Human Resource Development for TB Health in Moldova was developed in 2017 based on mapping for human resources (HR) involved in TB care and management (physicians, nurses, junior medical staff, and programme managers). Based on this, a regulatory document on the responsibilities of all specialists was developed and approved by the Ministry of Health Order 783, 110–2017 for the period of 2016–2020. This document continues to be an existing regulation; a new update of the mentioned policy is not planned, as the current situation is sufficient for effective programme implementation.

6.1HR provision

Vocational health education is provided in the medical and public health faculties of the university.

- ✓ Postgraduate professional education in phthisiology is a part of pulmonology postgraduate education and which lasts for 4 years.
- ✓ Other professionals study phthisiology for 2–4 weeks during residency.
- ✓ Advanced postgraduate education.
- ✓ At present, there are no problems with the level of physiatrist staff; however, in two regions there are no permanent doctors and part-time doctors carry out the work.

6.2 Programmatic education/training

The TB Management Programme provides ongoing training in various areas of TB management, organized for TB specialists, family physicians, narrow field specialists and nurses.
In addition, the educational component includes the guides and methodological manuals developed by the software team, which are available for TB specialists. The Phthisiopulmonology institute website contains all WHO and national (bilingual) guidelines and the materials of locally and internationally organized webinars and other seminars.

Training methods have changed during the COVID-19 pandemic and all training is now carried out remotely. Similarly, thematic seminars have been organized to improve TB specialists' analytical skills, as well as for training specialists.

Separate educational seminars are conducted on para-medical topics; in particular, social assistance to patients and legal aspects. It should be noted that the HR development actions have been effective, and the team working in the field of TB has a solid structure. However, the remote assessment method means that it is difficult to unequivocally draw conclusions about the skills of staff working in the peripheral levels. It was mentioned that the developed guidelines are available as electronic versions, which is an advanced approach. However, are all professionals able to use them effectively on electronic platforms? We think that such an assessment by the national team will be expedient for advocating the acquisition of knowledge in the future.

Recommendations

No.	Recommendation	Time frame	Responsible agency

1	Assess the theoretical knowledge and practical skills of TB specialists in line with the clinical and programmatic standards of TB management.	2022–2023	NTP
2	Evaluate and support the use of materials from electronic platforms by TB specialists.	2022–2023	NTP

7. Information system, programme monitoring and supervision

The national information platform, SIME-TB, has operated in the Republic of Moldova since 2009. To date, the system has provided a wide variety of TB-related analytics, legislation and educational materials. The governance and TB programme is moving forward to introduce innovative methods in various fields of TB management including the field of PV. In addition to ADR reporting through a phone application and the VigiFlow system, and reporting by scanning QR codes has been implemented since October 2021.

Nevertheless, the capacity of the register that SIME-TB provides lags behind the demands of the recent innovations in TB control. In particular, the laboratory module is outdated, LTBI management and contact tracing are not included, and the overall data protection and validation need significant improvement.

The programme monitoring operates with the following data flow.

- The Coordinating Unit of the NTP organizes data collection at three levels:
  - Primary care
  - Specialized outpatient care
  - Hospital care
- Monitoring takes place at:
  - National level: Coordinating Unit of the NTP
  - District level: Phthisiopneumologist, NTP coordinator.

The nonupgraded system of staff professional licensing is a substantial shortcoming of the NTP.

Recommendations

No.	Recommendation	Time frame	Responsible agency
1	Establish communication with the TB services in the Transnistria region to streamline the screening, diagnostic, treatment and prevention strategies with the last WHO guidelines.	2023	NTP, MOH, high level authorities
2	Ensure result-based competitive salaries for TB clinicians and programmatic personnel of the NTP.	2022	NTP, MOH

3	Continue reducing the number of beds and re-designation of redundant hospital facilities.	2022	MOH
4	Upgrade the national TB register (SIME-TB system). In particular, include the specific module on selective TB screening and LTBI treatment. Laboratory modules also need a significant upgrade to ensure follow-up of the results of the new techniques (LPA, Xpert MTB/XDR, etc.). Ensure the appropriate national registration of the register, and meet data protection requirements.	2023	NTP

8. Legal and ethical issues

The key ethical requirements, including equal access to TB care, are met in the Republic of Moldova. A total of nine NGOs (seven on the Left Bank of Dniester and two on the Right Bank) ensure provision of TB services to the hard-to-reach population.

In particular, a variety of TB-related services are provided for incarcerated people, including TB screening, all WHO-recommended LTBI treatment regimens, and TB and DR-TB treatment. OST, HIV testing, ART and co-trimoxazole preventive treatment are also available. The only issue is that, so far, the enrolment of the inmates onto the mSTR and BPaL OR programmes is impossible because of the aforementioned procurement issues and the inability to organize the required monitoring of adverse reactions. The rights of incarcerated people in the Transnistria region are of the most concern as the civil society and human rights supervisors have limited access to prisons.

9. Strategic planning, funding of PMDT interventions and partnerships

In Moldova, the main strategic direction for TB management in the country is to strengthen policies, practices and capacities to ensure effective TB control. At present, funding for scientific and technical progress comes from two main sources – the state budget of the Republic of Moldova and TGF grant. The gradual expansion of the public health insurance system to provide coverage for TB treatment is obviously happening.In 2020, for the first time, the TB Project “TB prevention among key populations and increasing adherence to DR and MDR-TB treatment” was funded by health insurance as a financial priority, which was implemented through local NGOs.

The involvement of local non-profit organizations in the provision of services for TB management is the strategic line for the TB programme. Over the past few years, there has been an increase in public funding for TB control; in particular, all first-line TB drugs are covered from the state budget and there is a significant increase of state quota for the coverage of second-line TB drugs. In 2020, the coverage was 63%.

The main goal of the Ministry of Health and the NTP is to develop NGCA action plan for 2021-2025 and implementation. The NGCA strategic objectives are the follows:

1) Ensuring the continuity of essential services for people affected by TB during the COVID-19 pandemic;

2) Mass screening for early detection of TB in PHC facilities, including the use of mobile radiology units;

3) Sustaining funding for diagnosis and treatment through continuous needs assessment, through universal access to diagnostics and treatment;

4) Supporting ongoing investments in TB control and progressive approaches to achieving sustainable TB control, financed primarily from domestic sources;

5) Optimization of the specialized hospital service in line with the goal of reducing the length and frequency of hospitalizations, merged into a single legal entity and with funding based on the global budget.

Strategic planning should involve the improvement of the patient-oriented approach for all sections of component 1 of WHO's End TB Strategy: in the diagnosis, treatment, prevention and care of TB coinfected patients. It is necessary to strengthen measures to improve the PV activities of TB care providers and at regulatory levels, and to establish legal bases and technical capacities for the wider application of research programmes for the implementation of short-term TB treatment approaches.

Annexes

Annex 1. Mission consultants

Consultant Name	Consultant Organization	email/cell phone
Naira Khachatryan	rGLC, WHO Euro	nairakhachatryan616@gmail.com
Maria Dolynska	rGLC, WHO Euro	dolynskamaria@gmail.com/+380500759513
Dilrabo Ulmasova	rGLC, WHO Euro	dulmasova@gmail.com
Sviatlana Setkina	rGLC, WHO Euro	setkina_lana@yahoo.com
Natavan Alikhanova	GDF, Stop TB Partnership	NatavanA@stoptb.org

Annex 2. Mission agenda

Joint regional Green Light Committee (rGLC) and Global Drug Facility (GDF) mission to Moldova

Agenda of the Assessment Component of the mission per TOR

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Dates: 4–16 October, 2021

WEEK 1 – CASE DETECTION

Date and proposed time (Yerevan time)	***Organization, participants***	***Discussion points***
Monday, 4 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the Ministry of Health representatives:** **Participants:** The TB focal point: Ministry of Health, Secretary of State, Public Health – Svetlana Nicolaescu, svetlana.nicolaescu@msmps.gov.md Ministry of Health, Head of the Public Health Policy Department – Daniela Demiscan, daniela.demiscan@msmps.gov.md Representative of CCM, secretary – Silvia Stratulat, ccm_secretariat@ms.md Public Institution "Coordination, Implementation and Monitoring Unit of the Health System Projects", TB Project Coordinator – principal recipient of the Global Fund grant "Strengthening Tuberculosis control and reducing AIDS-related mortality in the Republic of Moldova", Director – Nicolae Jelamschi, njelamschi@ucimp.md Project coordinator – Victoria Petrica, vpetrica@ucimp.md Director – Liliana Caraulan, liliana.caraulan@pas.md Project coordinator – Lucia Pirtina, lucia.pirtina@pas.md	• Overview of the state TB programme funding mechanism per programme areas. • Mechanism of reimbursement for inpatient and outpatient services, PHC level, TB diagnostics, treatment monitoring and follow-up, drug-safety monitoring, outsourced services. • Funding needs assessment. • List of items included in the TB management package at inpatient and outpatient level. • Procurement of drugs, consumable and services per funding source (Gov or GF). • Global Fund support and new funding proposal interventions. • Status of achievement of NSP targets and future targets. • Monitoring and quality assurance. • Challenges and room for improvement. GDF consultant specific discussion points

	Director of the Institute of Phthisiopneumology "Chiril Draganiuc" – Sofia Alexandru, sofi.alexandru@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP), Institute of Phthisiopneumology "Chiril Draganiuc" – Andrei Corloteanu, andreicorloteanu@mail.ru GLC and GDF consultants	
Tuesday, 5 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the NTP management –** **Director of the Institute of Phthisiopneumology "Chiril Draganiuc"; NTP Coordinator** **Participants:** Director of the Institute of Phthisiopneumology "Chiril Draganiuc" – Sofia Alexandru, sofi.alexandru@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP), Institute of Phthisiopneumology "Chiril Draganiuc" – Andrei Corloteanu, andreicorloteanu@mail.ru Head of NRL, Institute of Phthisiopneumology "Chiril Draganiuc" – Valeriu Crudu, valeriu.crudu@gmail.com Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com GLC and GDF consultants	• TB Programme Overview – TB epidemiology, impact of COVID-19 on TB control interventions. • TB case pathway – from symptoms to diagnosis and treatment. • MDR/RR-TB treatment organization (inpatient/outpatient) and strategy (DOT, VOT). • Funding of TB programmatic interventions, including diagnosis, treatment and the treatment safety tests/clinical monitoring at central and regional levels. • TB Contact Investigation – Policy, practice, implementation quality. • Active (systematic) Screening of TB. • LTBI screening and TB preventive Treatment (TPT). • Interventions under the Global Fund Proposal. • Challenges and room for improvement.

		• GDF consultant specific discussion points.
Wednesday, 6 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the NRL Head** **Participants:** Head of NRL, Institute of Phthisiopneumology "Chiril Draganiuc" – Valeriu Crudu, valeriu.crudu@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Microbiologist NRL – Nadejda Turcan, nadia.turcan@gmail.com Microbiologist NRL – Alexandru Codreanu, alexandru.codreanu@yandex.com Institute of Phthisiopneumology "Chiril Draganiuc", Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru GLC and GDF consultants	• National Tuberculosis Diagnostic and treatment monitoring algorithms. • Laboratory network. • Sample Transportation system. • Access to GeneXpert testing – number of modules, availability of cartridges, training of personnel, annual numbers of GeneXpert testing (2016–2020). • Line Probe Assay – access, kits, infrastructure, annual numbers of LPA investigations. • Culture and DST – tubes and reagents, biosafety cabinets, annual numbers of cultures disaggregated by result (positive, negative, contaminated). • TB suspects investigation. • Internal and EQA – last report. • Challenges and room for improvement. • GDF consultant specific discussion points.
13:00–14:30	**Meeting with NTP Coordination Department, NCP** Head of the Department of Coordinating of the National Tuberculosis Programme (NTP), Institute of Phthisiopneumology "Chiril Draganiuc" – Andrei Corloteanu, andreicorloteanu@mail.ru NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Institute of Phthisiopneumology "Chiril Draganiuc", Department of Coordinating of the	• Forecasting, quantification and early warning system, human resources, roles and responsibilities for each of these tasks, generation of the QuanTB reports (timeliness, completeness and accuracy). • Stock management at each level, drug distribution system for state and TGF funded TB medicines.

	National Tuberculosis Programme (NTP), Phtisiopneumologist – Tatiana Gulpe, gulpe@mail.ru Victoria Petrica	• Information management including LMIS and patient data for quantification, the data collection and reporting system, including the flow of patient related and PSM information (collection, reporting, consolidation, etc.) from the central level to the treatment sites.
Thursday, 7 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the representatives of the Prison Medical Centre of the Central Hospital for Detainees of the Ministry of Justice (MOJ)** National Administration of Penitentiaries, Head of the Medical Department – Irina Barbiros, email: i.barbirosh@anp.gov.md National Administration of Penitentiaries, Deputy Head of the Medical Department, TB programme departmental coordinator – Nelea Caras, n.caras@anp.gov.md P16-Pruncul (with hospital status), Deputy Director for curative activity – Natalia Gospodarenco, p16.adjunct.medicina@anp.gov.md P16-Pruncul, head of the Phthisiology II section – Elena Popovici, p16ftiziatrie2@anp.gov.md Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk	• Overview of the TB screening, prevention, diagnosis, and treatment services in penitentiary sector. • Number of detainees, number screened for TB each year, confirmed TB cases. • Systematic screening of detainees – screening algorithm, implementation, challenges. • TB diagnostic laboratory algorithm. • Management of other cross-cutting conditions – HIV, HCV, opioid substitution (OST) therapy, COVID-19. • Funding of TB services in penitentiary sector. • Active drug-safety monitoring and management in prison. • TB drug and diagnostic commodity management (storage, transportation, dispensing, ordering and reporting). • Challenges and room for improvement.
13:00–14:30	**Meeting with key in-country Partners and CSOs/NGOs (please add)**	• Overview of the various project goals and activities. • Funding sustainability and timelines.

	Participants: Representatives of the partner organizations/CSO/NGOs: Nicolae Jelamschi Victoria Petrica Liliana Caraulan Centre for Health Policies and Studies, Project coordinator – Lucia Pirtina, lucia.pirtina@pas.md Community representative, Vice President, AO Moldovan Patients Association SMIT (Society Against Tuberculosis), member of the National Council for the Coordination of the National Programmes for the Prophylaxis and Control of HIV/AIDS, Sexually Transmitted Infections and Tuberculosis Control (CCM) – Oxana Rucsineanu, oxana_rucs@yahoo.com International Organization for Migration (IOM), Mission to the Republic of Moldova Project Coordinator within "Enhancing Gender-Sensitive TB Detection, Surveillance, Treatment and Prevention among Mobile Populations from the Republic of Moldova" – Violina Nazaria, vnazaria@iom.int Director of the Institute of Phthisiopneumology "Chiril Draganiuc" – Sofia Alexandru, sofi.alexandru@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru GLC and GDF consultants	• The partners' prospective and views on how to improve the TB case detection and aDSM component, what gaps are still remaining that requires additional funding or management. • Collaboration with the NTP. • Challenges and room for improvement. • GDF consultant specific discussion points.
Friday, 8 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the City Outpatient Dispensary/clinic** **Participants:**	• Overview of the clinic catchment area. • Patient pathways to the clinic and from the clinic. • Access to rapid diagnostics.

	Representatives of the outpatient clinic administration and doctors: Territorial Medical Association Centru mun. Chisinau, Phtisiopneumologist – Caitaz Maria, pojamari@mail.ru Territorial Medical Association Botanica mun. Chisinau, Phtisiopneumologist – Ciubotaru Viorica, ciubotaru.viorica@mail.ru Territorial Medical Association Buiucani mun. Chisinau, Phtisiopneumologist – Sîrbu Petru, sirbupetru@gmail.com Territorial Medical Association Ciocana mun. Chisinau, Phtisiopneumologist – Pavliuc Carolina, corduleancarolina@mail.ru Territorial Medical Association Rîșcani mun. Chisinau, Phtisiopneumologist – Molodojan Aurelia, molodozhana@mail.ru Public Medical Sanitary Institution"The Municipal Clinical Hospital of Phthisiopneumology", Director – Vasile Popa, popa.vasile@mail.ru Public Medical Sanitary Institution"The Municipal Clinical Hospital of Phthisiopneumology",Medical vice-director – Marina Stanceva, marinastanceva@mail.ru Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com Head of the Department of the Consulting Polyclinic of Institute of Phthisiopneumology "Chiril Draganiuc", chairman of the management committee of TB DR – Aliona David, alionadavid@gmail.com Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk GLC and GDF consultants	• LTBI screening. • TB systematic screening. • Contact investigation. • Annual numbers – index cases, contacts investigated, TB confirmation. • 1 DS-TB and 1 MDR/RR-TB card review. • Challenges and room for improvement. • GDF consultant specific discussion points.

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WEEK 2

Monday, 11 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the Drug regulatory Authority/PV unit (MRA)** **Participants:** Medicines and Medical Devices Agency Deputy Director General – Lina Gudima, lina.gudima@amdm.gov.md NTP Pharmacist – Anghelina Djugostran, a.djugost@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com Institute of Phthisiopneumology "Chiril Draganiuc", Head of MDR-TB department – Olga Crasnova, olga.gulea@gmail.com Institute of Phthisiopneumology "Chiril Draganiuc", Department of Coordinating of the National Tuberculosis Programme (NTP), Phtisiopneumologist – Evgenia Cula, ecula@mail.ru Institute of Phthisiopneumology "Chiril Draganiuc", Department of Coordinating of the National Tuberculosis Programme (NTP), Phtisiopneumologist – Tatiana Gulpe, gulpe@mail.ru GLC and GDF consultants	• Overview of the PV activities countrywide. • Legal and policy aspect of TB-related PV in ARM. • Mandate, roles and responsibilities of the PV department. • Mandatory reporting criteria and requirement. • Causality assessment (who is responsible and has a capacity). • Reporting forms and modes (paper vs electronic). • Available PV and aDSM data and analysis (total spontaneous report, TB drug-related reports out of them, distribution of the reporting facilities, distribution of report by event, events severity, events seriousness, unexpected events, events outcomes, causal relationship). • Challenges and room for improvement. • GDF consultant specific discussion points.

13:00–14:00	**Meeting TB/HIV management team** NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru National AIDS Programme, HIV/AIDS treatment and care coordinator – Svetlana Popovici, svet.popovich@gmail.com Infectious disease specialist within ARV (antiretroviral) Treatment Department – Elena Golovco, elena-golovco@mail.ru	• TB screening among PLHIV. • TB case detection pathways. • Responsibilities for TB and HIV treatment. • Co-trimoxazole prevention. • LTBI management.
Tuesday, 12 October, 2021 (ZOOM link:)		
11:00–12:30	**Meeting with the Guideline Development Group (GDG) or equivalent and with the Central Clinical Consilium (DRC) chair and members** **Participants:** Representatives of the GDG and DRC: Director of the Institute of Phthisiopneumology "Chiril Draganiuc" – Sofia Alexandru, sofi.alexandru@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru Head of NRL, Institute of Phthisiopneumology "Chiril Draganiuc" – Valeriu Crudu, valeriu.crudu@gmail.com	• Overview of the current TB guidelines – diagnostic algorithm, treatment regimens and recommendations, treatment monitoring and follow-up, new definitions. • Availability of aDSM activities within TB guideline (mandatory monitoring schedule, AE reporting, forms). • Availability of drug toxicity management information in the guidelines/protocols. • Guideline revision and implementation plans (training?) • Central Clinical consilium – Overview of the consilium mandate and working SOP. • Consilium format, case presentation forms, interaction with regional and district level, frequency of meetings, etc.

	Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com Interim Deputy Director on science and innovation of Institute of Phthisiopneumology "Chiril Draganiuc" – Elena Tudor, eltudor@yandex.ru Head of the Department of the Consulting Polyclinic of Institute of Phthisiopneumology "Chiril Draganiuc", chairman of the management committee of TB DR – Aliona David, alionadavid@gmail.com Institute of Phthisiopneumology "Chiril Draganiuc", Department of Coordinating of the National Tuberculosis Programme (NTP), Phtisiopneumologist – Evgenia Cula, ecula@mail.ru Institute of Phthisiopneumology "Chiril Draganiuc", Head of MDR-TB department – Olga Crasnova, olga.gulea@gmail.com Institute of Phthisiopneumology "Chiril Draganiuc", Head of Phthisiology Department 2 – Liuba Nepoliuc, liuba_nepoliuc@yahoo.com GLC and GDF consultants	• Prescribed Treatment regimens/drugs – frequency distribution. • Coverage of the country with new treatment regimens. • Mentorship of the regional doctors. • Follow-up of discussed on treatment cases. • Room for improvement. • GDF consultant specific discussion points.
Wednesday, 13 October, 2021 (ZOOM link:)		
11:00–12:30	**Participation in the DRC meeting** **Participants:** Representatives of the GDG and DRC: Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com Head of the Department of the Consulting Polyclinic of Institute of	• Participation in case discussion. • Observation.

	Phthisiopneumology "Chiril Draganiuc", chairman of the management committee of TB DR – Aliona David, alionadavid@gmail.com Institute of Phthisiopneumology "Chiril Draganiuc", Department of Coordinating of the National Tuberculosis Programme (NTP), Phtisiopneumologist – Evgenia Cula, ecula@mail.ru Institute of Phthisiopneumology "Chiril Draganiuc", Head of MDR-TB department – Olga Crasnova, olga.gulea@gmail.com Institute of Phthisiopneumology "Chiril Draganiuc", Head of Phthisiology Department 2 – Liuba Nepoliuc, liuba_nepoliuc@yahoo.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru GLC and GDF consultants	
13:00–14:30	**Meeting with TB management team Transnistria region, RM** Director of the Tuberculosis Hospital from Tighina, coordinator of the territorial tuberculosis programme – Osadchyi Serhii, osadser@rambler.ru Deputy director of Hospital Department of the Tuberculosis Hospital from Tighina – Pankrushev Sergei, sergei_pankrushev@mail.ru Deputy director of Outpatient Department of the Tuberculosis Hospital	• Local TB data and vulnerable populations. • Local context of TB screening approaches, diagnosis and treatment. • Funding of TB programme. • Staffing. • Drug and diagnostics supply chain. • Challenges and room for improvement.

	from Tighina – Verchenco Nina, verchenko.nina@bk.ru Head of the regional reference laboratory – Maxim Tatiana, maksim_t.n@mail.ru Head of the Department of MDR-TB, Tuberculosis Hospital from Tighina – Gribanov Alexandr, shurik2008_85@mail.ru Director of the Institute of Phthisiopneumology "Chiril Draganiuc" – Sofia Alexandru, sofi.alexandru@gmail.com Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com Head of the Department of the Consulting Polyclinic of Institute of Phthisiopneumology "Chiril Draganiuc", chairman of the management committee of TB DR – Aliona David, alionadavid@gmail.com	
Thursday, 14 October, 2021 (ZOOM link:)		
11:00–12:30 12:30–13:00 Break 13:00–14:30 Continuation	**Interview with TB doctors from three different regions:** **Participants:** TB doctors: Clinical Hospital from Balti, Phthisiopneumology Department, Head	Review of one DS-case and one DR-case from each catchment area

	of Department – Petru Alexandriuc, petrualexandriuc@gmail.com Glodeni District Hospital, Phthisiopneumology Service, TB Coordinator – Guriev Ludmila, lguriev@yahoo.com Nisporeni District Hospital, Phthisiopneumology Service, TB Coordinator – Ioniță Nina, ms.nina.ionita@gmail.com Ștefan-Vodă District Hospital, Phthisiopneumology Service, TB Coordinator – Boian Parascovia, pboian855@gmail.com Deputy Director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com Head of the Department of the Consulting Polyclinic of Institute of Phthisiopneumology "Chiril Draganiuc", chairman of the management committee of TB DR – Aliona David, alionadavid@gmail.com Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk GLC and GDF consultants	
Friday, 15 October 2021 (ZOOM link:)		
11:00–12:30	**Wrap up the meeting of the GLC and GDF consultants with the NTP Coordinator** **Participants:**	• Verbal summary of the finding. • Discussion for the purposes of formulating the recommendations. • Drafting the recommendations.

	Director of the Institute of Phthisiopneumology "Chiril Draganiuc" – Sofia Alexandru, sofi.alexandru@gmail.com NTP Coordinator – Valentina Vilc, valentina_vilc@yahoo.co.uk Head of the Department of Coordinating of the National Tuberculosis Programme (NTP) – Andrei Corloteanu, andreicorloteanu@mail.ru Head of NRL, Institute of Phthisiopneumology "Chiril Draganiuc" – Valeriu Crudu, valeriu.crudu@gmail.com Deputy director of Institute of Phthisiopneumology – Ana Donica, annadonica741@gmail.com GLC and GDF consultants	

Annex 2 List of key people met

- Svetlana Cotelea, MOH Secretary of State.
- Daniela Demiscan, MOH Head of Public Health policy.
- Sivilia Statulat, Member of CCM.
- Sofia Alexandru, Director, Chiril Dragancuc Phthisiopneumology Institute.
- Valentina Vilc, Vice-Director for Strategy and Management, Chiril Dragancuc Phthisiopneumology Institute.
- Anna Donica, Medical Vice-Director, Chiril Dragancuc Phthisiopneumology Institute.
- Elena Tudor, Deputy Director of Science and Innovation, Chiril Dragancuc Phthisiopneumology Institute.
- Andrei Corloteanu, Head of the Department of Coordinating of the National Tuberculosis Programme (NTP).
- Crudu Valeriu, Chief of the National Reference Laboratory.
- Svetlana Popovici, National AIDS Programme, HIV/AIDS treatment and care coordinator.
- Lianna Caraulan, PAS Centre.
- Lucia Pirtina, PAS Centre.
- Nicolae Jalamshi, UCIMP, Project coordinator.
- Osadchyi Serhii, Director of the Tuberculosis Hospital from Tighina, coordinator of the territorial tuberculosis programme, Transnistria region.
- Pankrushev Sergei, Deputy director of Hospital Department of the Tuberculosis Hospital from Tighina, Transnistria region.
- Petru Alexandriuc, Clinical Hospital from Balti, Phthisiopneumology Department, Head of Department.
- Guriev Ludmila, Glodeni District Hospital, Phthisiopneumology Service, TB Coordinator.
- Ioniță Nina, Nisporeni District Hospital, Phthisiopneumology Service, TB Coordinator.
- Boian Parascovia, Ștefan-Vodă District Hospital, Phthisiopneumology Service, TB Coordinator.