World Health Organization
European Region

Tuberculosis Epidemiological Review
Republic of Moldova 2024

List of figures

List of tables

List of maps

Abbreviations

APC	Annual percent of change
ART	antiretroviral treatment
CAD	computer aided diagnostics
DST	drug susceptibility testing
eCMND	Electronic medical certificate of birth and death
EPT	Extrapulmonary tuberculosis
FLD	first-line TB drugs
GDP	gross domestic product
HIV	human immunodeficiency virus
IS	Information system
LTBI	latent TB infection
LPA	line probe assay
MDC	medical death certificate
MDR-TB	multidrug-resistant tuberculosis
MTB	Mycobacteria tuberculosis
M&E	monitoring and evaluation
NBS	National bureau of statistics
N&R	new and recurrent
NIPP	National Institute of phtysio-pulmonology after Chiril Draganiuc (currently Chiril Draganiuc Institute of pneumology)
NRL	National reference laboratory
NTP	National tuberculosis programme
OCHA	United Nations Office for the coordination of humanitarian affairs
OOP	out-of-pocket
PAF	population attributable fraction
PHC	primary health care
PIN	personal identification number
PLHIV	people living with HIV
PTB	pulmonary tuberculosis
R&R	recording and reporting
RR-TB	rifampicin-resistant tuberculosis
S&B	standards and benchmarks
SIME-TB	Sistem Informaţional de Monitorizare şi Evaluare a Tuberculozei - Informational System for TB Monitoring and Evaluation
SLD	second-line TB drugs
TB	tuberculosis
TPT	TB preventive treatment
TSR	Treatment success rate
U5	usnder 5 year of age
UI	uncertainty interval
VRS	vital registration system
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis
ZAGS	Zapis' aktov grazhdanskogo sostoiania, Registry of Acts of Civil Status

Summary

World Health Organization received a request from the Ministry of Health of Republic of Moldova to conduct a thorough review of the TB epidemiological situation in the country by assessing the available surveillance, survey, programmatic and other data. TB Epi-review has been conducted in November 2024 ahead of comprehensive external evaluation of National Tuberculosis Response program for period 2023-2024, to inform the mission as well as to feed into an update of the National Action Plan for TB and prepare new Funding Request to Global Fund for post 2026 period.

Current report provides an up-to-date assessment of TB epidemic in Republic of Moldova and progress in prevention, diagnosis and treatment of the disease at national and regional levels. This is done in the context of national and regional and global TB action plan strategies and targets. Data are based primarily on data extracted from national electronic surveillance system, reported by national reference laboratory and global TB database.

The purpose of the tuberculosis epidemiological review in Republic of Moldova was to assess the quality and coverage of routine tuberculosis surveillance and vital registration (VR) and to investigate the plausible drivers of the TB epidemic in the country.

The Republic of Moldova was one of the first countries in the region that introduced and successfully operated case-based real-time national electronic surveillance system, producing consistent reliable routine surveillance data and strong human resource capacity. Moldova NTP is well known for fast uptake of new recommendations into routine programming, innovative and sustainable solutions for people-centred care. However, despite of fast decline of TB burden in the country observed during pre-pandemic period, as of 2023 Moldova remains among five countries in the region with the highest TB mortality and incidence. COVID 19 pandemic and then armed conflicts between Ukraine and Russian Federation followed massive dislocation of people from conflict zone into Republic of Moldova creating and extra pressure for health systems in the country including TB service.

Case-definitions in Moldova are largely aligned with WHO recommended guidelines. Data quality assurance mechanisms are implemented at all stages of data processing and levels. All TB detected TB cases are notified across all country, including MDR/RR-TB cases, those diagnosed in private sector, penitentiary system, identified post-mortem, as well as those that didn't show up after diagnosed or refused to start the treatment. Electronic registration system is complete, consistent and allowable level of potential duplicates. VRS in Republic of Moldova has high coverage and quality. In mid of 2024 VRS moved from paper into real-time web-based electronic surveillance system interlinked with population registration system. HIV testing coverage among TB patients remains universal. Bacteriological confirmation among pulmonary TB case and routine drug-sensitivity testing coverage remarkably increased. There are several mechanisms in place to assure the validity of assignment of treatment outcomes. Preventive TB treatment surveillance relays on paper to aggregated electronic reporting. Overall surveillance system is well established to provide accurate and valid information related to size of people diagnosed with TB in the country. However, TB surveillance system is not strong enough to reflect all people with TB in the country. Because of restricted access to health care, still many people with TB remain not diagnosed or are diagnosed with delay, resulting continuous transmission of the infection in the population. There are areas with unacceptably high proportion of positive confirmation among people with presumptive TB. There are also areas with extreme low testing rate per capita population combined with hight positivity, suggesting under-detection of people with TB in the population. Therefore, the level of TB notification in Republic of Moldova cannot be considered as a good proxy of TB incidence due to possible under-detection. Overall, of the 15 WHO standards for TB surveillance that were assessed, ten were met and five were partially met (Table 1).

In 2023 there were an estimated 2,300 (95% uncertainty interval [UI]: 2,000-2,700) incident TB patients in Republic of Moldova, equivalent to 76 (95% UI: 64-88) cases per 100,000 population. Average annual decline of estimated TB incidence between 2019 and 2023 was only 1.3% in comparison of 6.1% annual reduction between 2015 and 2019. Thuse, cumulative reduction of TB incidence between 2015 and 2023 is 25.5% against 50% targeted reduction by 2025.

Table 1. Checklist results in 2016 and 2024 (preliminary)

Standard	2016	2024
B.1.1 Case definitions consistent with WHO guidelines		
B.1.2 TB surveillance system captures minimum set of variables for reported TB cases		
B.1.3 All scheduled periodic data received and processed at the national level		
B.1.4 Data in quarterly reports are accurate, complete, and internally consistent		
B.1.5 Data in national database are accurate, complete, consistent, and free of duplicates		
B.1.6 TB surveillance data are externally consistent		
B.1.7 Number of reported TB cases is internally consistent		
B.1.8 All diagnosed cases of TB are reported		
B.1.9 Population has good access to health care		
B.1.10 Vital registration system has high national coverage and quality		
B.2.1 Surveillance data provide a direct measure of drug-resistant TB in new cases		
B.2.2 Surveillance data provide a direct measure of the prevalence of HIV in TB cases		
B.2.3 Surveillance data for children reported with TB are reliable and accurate		
B.3.1. Treatment outcome is consistent with WHO guidelines		
B.3.2. R&R of treatment outcome are accurate, complete and consistent		
B.4.1. Monitoring of PMTPT are consistent with WHO guidelines		
B.4.2. PMTPT data are accurate, complete and consistent		

Green – met; yellow – partially met; red – not met

TB caused an estimated 200 deaths (95%UI: 180-220) in 2023 in the Republic of Moldova, including 140 deaths (95%UI: 130-160) among people with HIV. The number was down from best estimate of 240 in 2022 and below pre-pandemic level of 210 in 2019. However the reduction of TB mortality slowed significantly after COVID 19 pandemic. Cumulative reduction of number of TB death between 2015 and 2023 is 35% against 75% reduction by 2025 targeted by End TB strategy.

A total of 2,164 people were reported as newly diagnosed with TB in 2023 in Republic of Moldova, very small increase from 2,121 in 2022. The gap between estimated and notified cases is narrowed and targeted at least 85% case detection has been achieved.

In 2023 in total 264 people were diagnosed and treated for MDR/RR-TB. The treatment success rate was improved for both drug-susceptible TB (85% in 2022 cohort) and RR/MDR-TB without FQ resistance (70%), but remains insufficiently low for pre-XDR/XDR-TB (46%) and those with TB/HIV co-infection (67%).

Across rayons TB notification rates in 2023 varies in wide range from 28 to 166 per 100,000. This variation only partially reflects the difference in true TB burden, as across all area proportion of bacteriologically confirmed among presumptive patients varies in wide range. In addition, there is large variation in per-capita testing rate across sub-national units indicating that there are some areas with limited access to diagnosis.

Some of the external indicators are obviously have been improved in Republic of Moldova, which itself positively affects the TB epidemiology. Those include health system strengthening (demonstrated by decrease in under-5 mortality), access to health care and universal health coverage (expressed by decline in proportion of out-of-pocket payment of total health expenditure (THE OOP), improved economic status (expressed by increase of GDP per capita), reduction of incarceration rate, increase of ART coverage among PLHIV. Nevertheless, some of indicators that are known contributors to TB epidemic are persisting at a high level (high level of alcohol consumption, HIV incidence), or even on increase (e.g., smoking prevalence, diabetes prevalence, aging of population), most likely moderated the faster decline of TB burden in the population.

Key recommendations

- Upgrade electronic system in line with new requirement of electronic surveillance system by streamlining with other systems through MConnect governmental portal to receive and share the data. Establish automated connectivity solutions for peripheral GeneXpert machines to avoid manual data entry and ensure fast data transmission. Aim to establish connectivity to electronic system in all peripheral laboratories in the country. Implement national PIN for linkage of data, avoid duplicate entry and improve data quality.
- Introduce electronic case-based modules for contact tracing and TPT.
- Avoid repeat testing of people with presumptive TB. Monitor closely the trend in number of people with presumptive people tested for GeneXpert and positivity of tests result among people with presumptive TB. Monitor closely positivity rate by testing sites to identify hotspots for focused interventions as well areas requiring additional support.
- Improve the accuracy of indicators of number of people tested for TB and percentage positive by deduplication of the laboratory module externally at national level ideally applying probabilistic matching using relevant statistical programs.
- Improve the accuracy of drug-resistance surveillance.
- Adjust retrospectively annual population size at sub-national levels to allow accurate time-trend analysis.
- Undertake relevant measures to ensure reliable diagnosis of TB in children.
- Undertake relevant measures to ensure reliability of TB diagnosis among clinically diagnosed cases in areas with sub-optimal bacteriological confirmation (below 70% of bacteriological confirmation among pulmonary TB cases).
- NTP staff to be trained on advanced data management. Although currently deduplication is done on quarterly based, however, it involves deterministic deduplication resulting residual duplicates. NTP staff to use WHO guidance on internal and external probabilistic linkage for deduplication until new electronic system is developed and introduced.

1. Introduction

Having a robust disease surveillance and response monitoring system is essential to collect reliable data from the Member States, measure the indicators and monitor the progress towards the Regional and Global targets. It is important to make sure that the data collected by the member states and reported to the WHO is fully compliant with all elements of the data quality. The TB epidemiological reviews are part of the priority studies and aim to provide necessary background information to help understand the burden of TB disease and the characteristics of the TB epidemic in the country. It also seeks to provide an overview of the TB surveillance system and Monitoring and Evaluation (M&E) activities and evaluate its compliance to the TB case definitions and reporting framework, and check if the surveillance standards and benchmarks are met at the country level.

First standard and benchmark assessment in Republic of Moldova was conducted in late 2016. Current review aimed to assess the national surveillance system's ability to accurately measure TB incidence and TB deaths and identifying gaps in national surveillance systems that must be addressed in order to improve TB surveillance. The specific objectives of the review were:

- To describe and assess the current national TB surveillance and vital registration systems using the WHO checklist of standards and benchmarks
- To assess the progress made since the last S&B assessment conducted in 2014
- To assess the level of, and trends in, the TB disease burden (incidence, and mortality) using available surveillance, survey, programmatic and other data.

2. Methods

Methods of data collection included: (1) desk review of available TB control-related policy papers, manuals, guidelines and forms; (2) interviews and discussions with TB authorities and health care providers at national and district level; (3); review of electronic databases to assess the level of incompleteness of core variables, invalid entries, (4) analysis of notification/surveillance data over time and space to identify trends in disease burden and programmatic efforts.etc.

Most of the TB related data were provided by National tuberculosis program. We used also WHO global tuberculosis database for the national level data analysis. In addition, other resources were utilized to obtain data on TB determinants such as AIDS Info, WHO Global Health Observatory, World Bank, UNICEF, databases. All data sources are presented in the text and footnotes. Shapefile for admin 1 subnational level boundaries for Republic of Moldova was downloaded from OCHA Humanitarian data exchange repository[1].

The standard WHO-recommended assessment checklist and associated user guide, from S*tandards and benchmarks for tuberculosis surveillance and vital registration systems*,[2],[3] were applied. For analysis and interpretation of the influence of TB predictors and external factors, guidance from the handbook *Understanding and using tuberculosis data*[4] were followed.

We used WHO population estimates for the calculation of per capita indicators at national level. To calculate the rates for subnational level data we used NTP provided data exported from SIME-TB with additional adjustment for population size for 2018 and 2019. To make retrospective adjustment of population size at subnational level first

[1] The humanitarian data exchange (HDX) [online] available from https://data.humdata.org/
[2] WHO Global Task Force on TB Impact Measurement. Standards and benchmarks for tuberculosis surveillance and vital registration systems: checklist and user guide. WHO/HTM/TB/2014.02. Geneva: World Health Organization; 2014 http://www.who.int/tb/publications/standardsandbenchmarks/en
[3] Web Annex B. Standards and benchmarks for tuberculosis surveillance and vital registration systems: checklist, 2nd edition. In: Consolidated guidance on tuberculosis data generation and use. Module 1: Tuberculosis surveillance. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.
[4] WHO Global Task Force on TB Impact Measurement. "Understanding and using Tuberculosis data" WHO/HTM/TB/2014.09, Geneva: World Health Organization 2014, available from https://www.who.int/tb/publications/understanding_and_using_tb_data/en/

we computed annual growth rate for period between 2020 and 2023 for each of subnational unit using following formula:

$$r = \left(\frac{P_{2023}}{P_{2020}}\right)^{1/3} - 1$$

Where:
r = annual growth rate,
P_{2023} = population size in given subnational area in 2023
P_{2020} = population size in given subnational area in 2020

Population size for 2019 and 2018 in each subnational area was computed as quotient of population size in 2020 and 2019 respectively and (1+r)

We calculated TPT coverage for each of subnational unit as a quotient of total number of children under 5 enrolled into TPT and total number of children under 5 eligible for TPT expressed as proportion. The estimated number of household contacts aged under 5 years eligible for TPT was calculated for each of subnational area using the following formula

$$n = \frac{b}{c} HpL(1-t)$$

Where:

b = Number of notified bacteriologically confirmed pulmonary TB in 2023 in given rayon, differ by rayon
p = National proportion of children <5 in 2023 equal[5] to 7.2%
H = National average household size equal[6] to 2.89
L = Prevalence of TB infection among child household contacts aged <5years equal to 1
c = Average cluster size of active TB per household equal to 1.06
t = Proportion of children aged <5 years with active TB among TB household contact equal[7] 6.1%

To assess benchmark 1.5, the records of people registered with new and recurrent TB in 2023 were extracted from SIME-TB and checked for duplicates first using national identification number as well as SIME-TB generated id using excel "conditional formatting" -> "duplicate values" functions. Identified duplicates were sorted and reviewed manually to exclude multiple episode of the disease in one patients as duplicate considering other relevant fields such as proximity of registration and assigned treatment outcome of the previous episode.

Analysis conducted includes plotting of annual data followed by visual observation; computation of slopes by linear regression to describe/compare the speed of change of various indicators; and ecological analysis of TB case notification rates and trend of external factors. Province-level data were mapped using Stata software to identify spatial patterns.

[5] World Population Prospects 2024 [online] Available from https://population.un.org/wpp/
[6] The National Bureau of Statistics of the Republic of Moldova [online]. Available from https://statistica.gov.md/en/the-population-of-the-republic-of-moldova-at-the-time-12_896.html
[7] Dodd PJ, Gardiner E, Coghlan R, Seddon JA. Burden of childhood tuberculosis in 22 high burden countries: a mathematical modelling study. Lancet Glob Health [Internet]. 2014 Aug;2(8):e453–9. Available from: http://dx.doi.org/10.1016/S2214-109X(14)70245-1

3. Results

3.1. Description of TB surveillance system

3.1.1. Structure

Health care services in Republic of Moldova are delivered to the population by public and private facilities at primary, secondary and tertiary levels. TB services are integrated with in primary and secondary care general health service network.

PHC/ family doctors at primary care level conduct initial symptom screening, identification, testing and referral of people with presumptive TB for further diagnosis at the secondary level facilities, as well as contact investigation, referral, monitoring of TB treatment and, monitoring of preventive TB treatment of household contacts.

Secondary care at rayon or municipal level, including TB services, is provided by rayon hospitals and specialized ambulatory services. Specialized ambulatory services are often physically located in the rayon hospital to which they are subordinate.

Oversight of TB services is implemented by TB central unit hosted by Institute of Phtysio-pulmonology after Chiril Draganiuc (NIPP) in Chisinau (currently names Chiril Draganiuc Institute of pneumology) . Central unit comprises National Reference Laboratory (NRL) and department of program coordination. Functions of department of program coordination are developing policies and technical guidelines, planning, coordination with partners, surveillance, quality control, anti-TB drugs supply management, staff training, monitoring and technical supervision. Department is staffed by seven full-time specialists- TB doctors and coordinator.

TB Laboratory network follows similar structure and is organized at three levels: peripheral, inter-regional and national. 56 peripheral laboratories located at rayon central hospitals and municipal health centers serve as primary point of testing for people with presumptive TB. Peripheral laboratories perform direct sputum microscopy, rapid molecular diagnostic using Gene-Xpert and refer samples for upper level for more advanced diagnostics. Three inter-regional laboratories located in Balti, Vorniceni and Bender in addition to GeneXpert, perform culture, DST to first and second-line TB drugs, Line Probe Assays (LPA). NRL located in at the Institute of pneumology "Chiril Draganiuc" in Chișinău is responsible for the oversight of quality assurance for all laboratories, capacity building, supervision, technical laboratory guidelines, laboratory surveillance.

3.1.2. Data collection tools

Moldova TB surveillance system is based on paper to electronic case-based register designed for TB and M/XDR-TB individual case notification and treatment outcome monitoring as well as reporting aggregated data related to contact tracing, and preventive TB treatment.

Data are recorded for all individual TB cases at the service delivery points, using standardized TB data collection forms then are entered into case-based electronic system. All TB cases from all parts of the country are included in the national TB surveillance. Patient-level data are available at national level. Routine monitoring and quality control procedures are in place.

Once sputum is collected for examination, paper-based **Microscopy, Xpert MTB/RIF, LPA, culture and DST examination request** form is completed which accompanies a biological sample sent to a laboratory. Data from laboratory request form are used to complete paper-based laboratory registers (TB 04 and TB 06) as well as laboratory module of SIME-TB electronic register.

"SIME-TB" is real-time web-based application based on SQL Server 2000 with nation-wide coverage including penitentiary system. The electronic TB register ensures smooth flow of information between laboratory to clinical specialists and various levels of TB control system and is designed to generating national surveillance statistics on TB case notification.

Once a person is confirmed with TB, individual treatment card TB 01 is completed along with a case based TB notification form **N 089/e –Part A**, which serves as main data source for capturing patient information into SIME

TB. Simultaneously, the TB case is registered locally on the paper TB register and is assigned a serial number. In Moldova data into SIME-TB are entered by the doctor who diagnosed TB, regardless of residence of the patient and place of diagnosis. Such approach ensures that no diagnosed case is missed from the surveillance system and timely transmission of information from diagnostic unites to primary health care level. **N 089/e** form includes data related to patient's demographics, socio-economic and risk factors, disease characteristics and laboratory test results. Part B of this form is used to record the clinical progress, laboratory results and final treatment outcome results of regular TB cases. For the patient with RR/MDR tuberculosis form 090/e is completed and corresponding parts A1-3, B - that are designated to capture information related to details of treatment regimen, clinical progress, laboratory results, adverse reactions, as well as treatment outcomes. Part C is meant to document the discharge of the patient. Part F documents hospitalisation, H is for the active drug safety monitoring, and part G includes common data for F089/1e and F090. Also, part D includes post treatment follow-up.

3.1.3. Data flow and quality assurance

TB data flow is mostly carried out electronically, through SIME-TB with some paper-based components listed above. For each episode of TB separate record is entered in SIME-TB. In addition to national personal identification number (PIN) and TB-03 number, which serves as TB case identifier, the system automatically generates additional alphanumeric identifier for each patients consisting from first 2 letters of the name, first letters of family name and middle name, and date of birth (6 digits). This unique identifier as well as PIN allow identifying multiple episodes of disease in one patient. About 50-55 sites are entering the data into SIME-TB at rayon, laboratory, national levels as well as in penitentiary system. To ensure data security and confidentiality, users are authorized with different rights (access, modification, deletion) based on their responsibility. The system automatically generates electronic outputs in forms of standard tables, as well as customized tables using various filters.

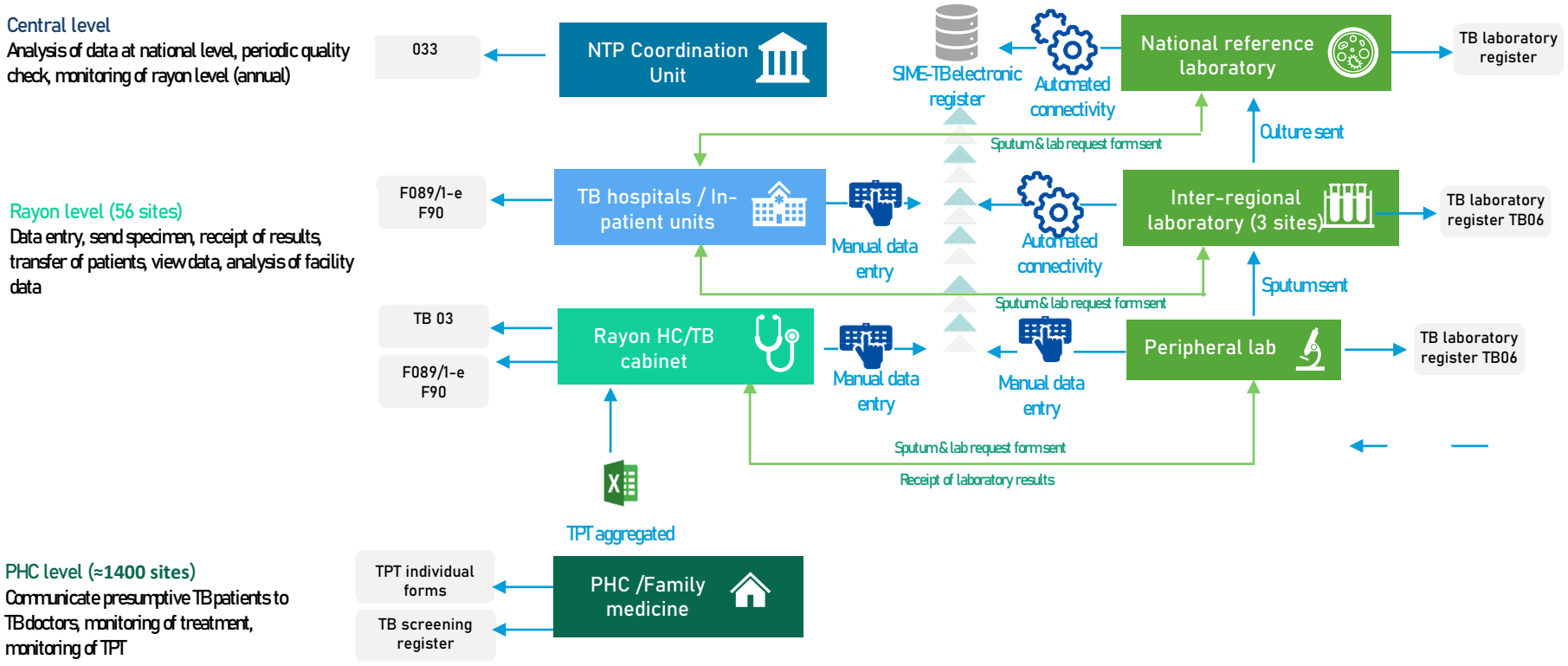
Laboratory module of electronic system is completed by all three level of laboratories and includes both presumed and confirmed TB cases. At peripheral laboratories and inter-regional laboratories the results of GeneXpert are entered manually into SIME-TB, while at NRL the results are transmitted by automated connectivity application "Doctor Eleks". Laboratory results are communicated back to the requestor by paper form, nevertheless, the results can be viewed from SIME-TB. To make the laboratory results seen at the patient's register treating doctor is supposed to search the laboratory results in laboratory module and link it with patient module.

Rayon hospitals (ambulatory service) and municipality health service departments annually submit TB-related report using form 33 in paper and excel format. This report includes information related to incident TB cases (page 1), prevalent cases and treatment outcomes (page 2), hospitalization by age, site of disease (page 3), patients that started treatment out-patient (page 4), household and close contacts investigation and preventive TB treatment (page 5). At national level a tool "centralisator" is used to aggregate data from 35 reporting units and submit this report by 3rd March to National Bureau of Statistics.

There are several procedures in place to ensure quality of collected data: This includes automated checks at data entry and batch checking, regular monitoring visits from national to rayon level using standard operating procedure for data validation and quality assurance. SIME-TB is designed in a way that during the data entry process data validation checks are undertaken to prevent errors. For most of variables (sex, geographical location, case type, previous history, laboratory results) only pre-defined options are allowed to enter that appear as a drop-down menu during the data entry. Fields are enhanced with the checks so, that only numbers are possible to enter into numeric fields and dates in date fields. Core variables are "must enter" fields; therefore, actually there are no missing values for core variables. System is enhanced with user-friendly instruction manual and dictionary located into web-site which is regularly updated once any change is made into the system.

Every quarter data are checked for duplicates.

Figure 1. Tuberculosis data recording tools and information flow



External quality control is implemented during the monitoring visits. Data quality specialists from the national centre are visiting each of reporting TB unites on annual basis and validate the data according to standard operating procedure. This includes cross-checking of paper electronic register, laboratory register, assessing consistency, and completeness of entered data. Every year on March the data entered in previous year are stagnated so it is no possible anymore make any changes in the database. Only limited number of users at national level are able to make changes in the records done in previous year after validation. Such approach protects historical data and prevents deleting and modification of historical data.

Annual validation meetings in December are used as an opportunity for refreshing face-to-face training on surveillance. Training is regarded as a part of each TB field visits.

Detailed annual surveillance report is produced and widely disseminated. It includes monitoring of progress of indicators of national strategic plan, discussion of the challenges and recommendations. Reports for previous year are available at SIME-TB repository. In addition, at NPT central level annually develops progress reports (including challenges and recommendations of TB care delivery) for each of sub-national unit which are communicated in written with both local government officials and local health authorities.

Challenges of the system

- TB electronic system allows calculations of the rates per capita at national and sub-national levels but population size projections changes from year-to-year. However, retrospective adjustment of population size is not implemented in TB surveillance system. Because of different projections, time series analysis of rates results misleading results.
- Due to high number of duplicate testing by Gene Xpert combined with sub-optimal quality of information of laboratory request forms, accurate calculation of number of presumptive TB cases, positivity, as well as accurate drug-resistance surveillance is cumbersome.
- PIN and other demographic information are entered into system manually. Errors in manual entry of PINs increase the risk of duplicate records in the dataset.
- Data analysis and visualization is still time-consuming.
- Peripheral laboratories are not enhanced with automated connectivity solutions.
- Data related to contact tracing and preventive TB treatment are collected on paper only. Only aggregated data are submitted. Individual records remains at PHC level.

3.2. Description of vital registration system

Starting from October 2024 Republic of Moldova transitioned from paper to electronic system for registering births and deaths[8]. The purpose of Information system "Medical certificate of birth and death" (eCMND) is to ensure digitisation of the processes of collecting, verifying, anonymising, analysing, interpreting and disseminating data on births and deaths of adults and children, and to improve the submission, recording, management, updating and reporting of information on natality and mortality. The Ministry of Health is the owner of the eCMND information system, while the National Public Health Agency is the holder of the eCMND and ensures its administration, maintenance and development.

The eCMND is designed as a modular system and is based on embedded components, compatible with cloud computing technology, which ensures that it can evolve without compromising continuity and allows for changes to be made and implemented. The eCMND IS architecture consists of three layers characterised by the following main components, which are interdependent, communicate with each other and are grouped as follows:

[8] Decision of government of Republic of Moldova No. HG278/2024 of 17.04.2024 on the establishment of the Information System 'Medical Certificates of Birth and Death' (eCMND) [online] link to access https://www.legis.md/cautare/getResults?doc_id=143322&lang=ru

1) data presentation layer - represents user interfaces;

2) application layer - designed to perform the business logic processes of the system, accessing data, processing, transforming data and ensuring its consistency and accuracy;

3) data level - designed to store and update data in the relational database management system.

The users of the eCMND IS are data providers, data recorders and data consumers. Data providers for the eCMND IS are providers of medical services regardless of organisational and legal form and form of ownership, namely:

- providers of primary medical care;
- providers of inpatient medical care;
- maternity hospitals;
- Forensic Medicine Centre.

eCMND registrars/data recorders are a category of users who are ex officio required to register/edit medical birth and death certificates. eCMND IS death registrar - a role that allows the registration of medical death certificates. Users holding this role can be:

- A family physician;
- Attending physician;
- A morphopathological doctor;
- A forensic medical expert.

Data registration in the IS eCMND is performed by the registrar. Each registrar is provided with secure access to the eCMND. Records are made in chronological order, with each record being assigned a date of entry into the system. Modification and/or addition of data in IS eCMND is performed by the registrar with special rights. After death if family doctors/attending physician knows the diagnose the he/she completes electronic Medication death certification directly in eCMND. If no FP, district police sent to autopsy. If non-natural death, forcenic autopsy.

Information is collected according to 10 ICD, cause of death is assigned, time from the start of disease to time of death. If cause of death is not known, autopsy is conducted (each PHC is connected to hospital with autopcy) along with the medical history. Medical certificate of death is completed. Necessary information is sent to ZAGS. Relatives directrly can go to ZAGS to take death certificate (this includes only personal information - without cause of death).

In order to ensure prompt and automatic updating of the IS eCMND information content with reliable information, interaction and synchronisation of data with other information systems can be carried out through automatic import or export of data to verify and/or supplement the IS eCMND information content. Data exchange between the eCMND IS and other state information systems and resources is carried out through the interoperability platform (MConnect). The IS eCMND exchanges data with the following state information systems:

- Information system 'State Register of Population';
- Information system 'State Register of Legal Units';
- Information system 'Compulsory Medical Insurance';
- Information system 'Inpatient Medical Care';

The eCMND IS interacts with the following public information systems:

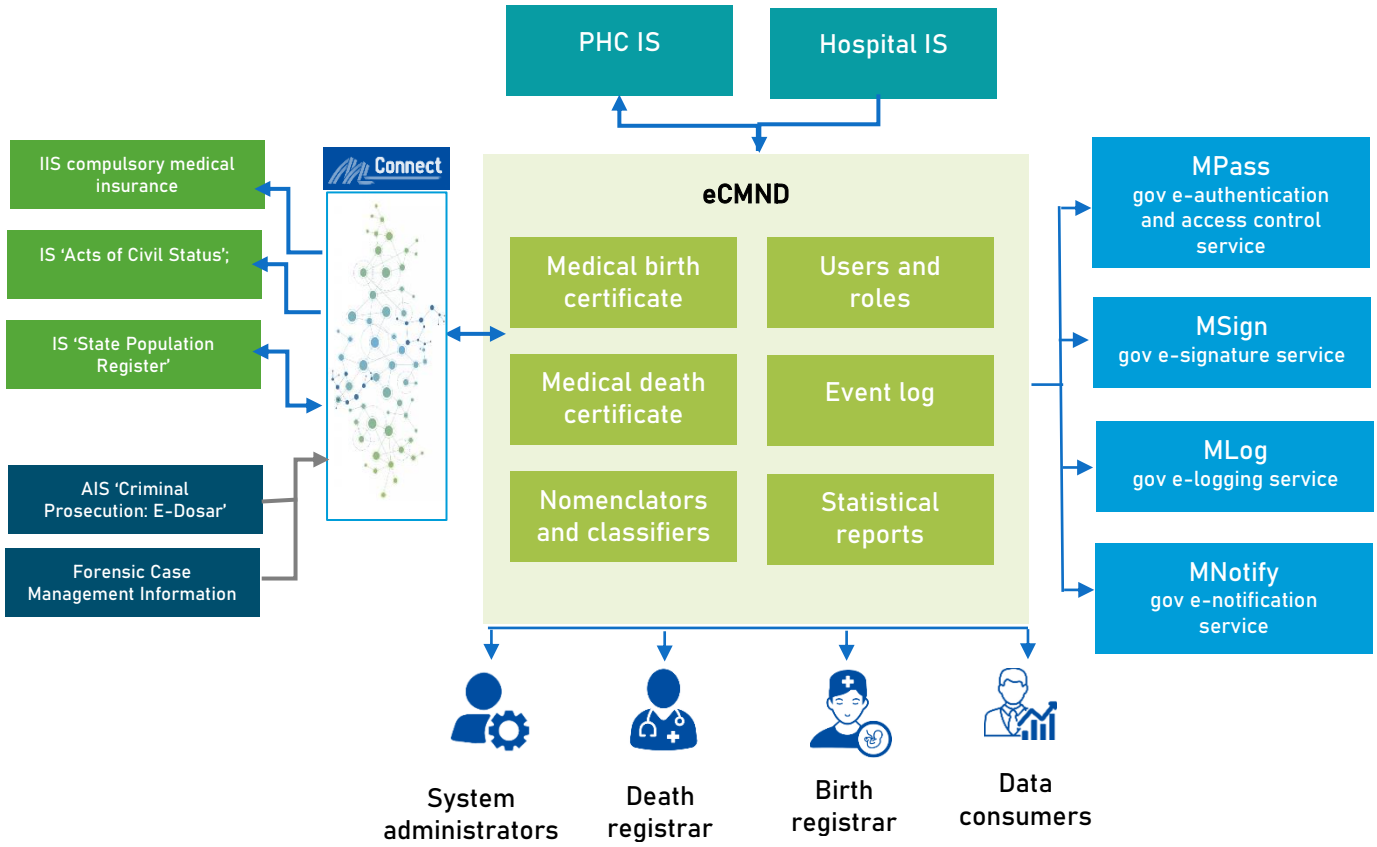
- government electronic service of authentication and access control (MPass);
- government electronic service of electronic signature (MSign);
- government electronic logging service (MLog);
- government electronic notification service (MNotify);
- interoperability platform (MConnect);

The eCMND IS data is categorised as data subject to data protection. User access to the eCMND IS is prioritised through the government's electronic authentication and access control service (MPass). Information exchange is carried out using software tools, only through secure channels, ensuring the integrity and safety of data.

The consumers of statistical data/recipients of the data contained in the IS eCMND are the Ministry of Health, National Agency of Public Health, National Health Insurance Company, Public Services Agency, National Bureau of Statistics, National Social Insurance Fund, health service providers and health units of local public administration, in accordance with the established data exchange procedure. Detailed diagram of eCMND is provided in Figure 2

Data related to number of deaths by cause of death, age group and sex are published annually by National Bureau of Statistics[9]. According to the most recent WHO report[10] the quality the completeness of death registration in the Republic of Moldova is 100% and percentage of ill-defined cause of deaths is 2.1%. This results to 97.9% data usability, defined as percentage of all deaths which are registered with meaningful cause-of-death information.

Figure 2. Diagram of information system of electronic medical certificate of birth and death (IS eCMND) interlinkage with other information systems



[9] National Bureau of statistics of the Republic of Moldova [online] https://statistica.gov.md/en/general-mortality-by-main-causes-of-death-in-2023-9696_61262.html
[10] WHO mortality database, Interactive platform visualizing mortality data [online] https://platform.who.int/mortality/about/data-quality

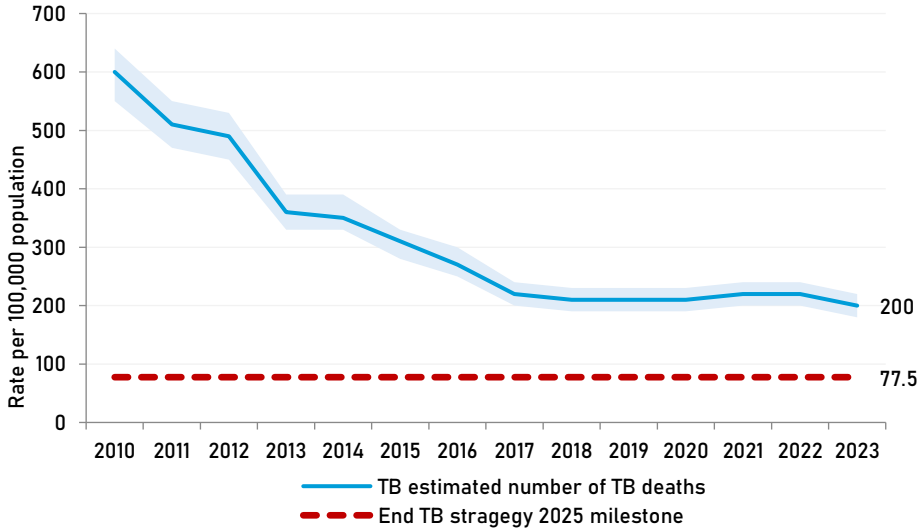
3.3. TB burden

3.3.1. Mortality

The source of TB mortality data in Moldova is the vital registration system (VRS), which is considered as the best source of information related to TB deaths, in cases when VRS has hight coverage and quality. According to WHO estimates in 2023 in total 61 (range 55-66) people died from TB disease. Another 140 (range: 130-160) deaths occurred among people with TB/HIV co-infection, resulting 200 (range: 180-220) total TB deaths which is equivalent to 6.7 (range 6-7.2) total deaths per 100,000 population. Despite historically this is lowest number of deaths observed in Moldova, nevertheless, this is very hight, to achieve End TB strategy milestone to reduce number of all TB deaths in 2025 by 75% in comparison to 2015 data (Figure 3). Main challenges of sub-optimal reduction of TB death was the disruption of TB services due to COVID-19 pandemic in 2020 and especially in 2021 when for the first time there was reversion of trend of TB mortality.

Figure 3. Estimated number of TB deaths, Moldova, 2010–2023

Shaded area around lines indicates uncertainty range



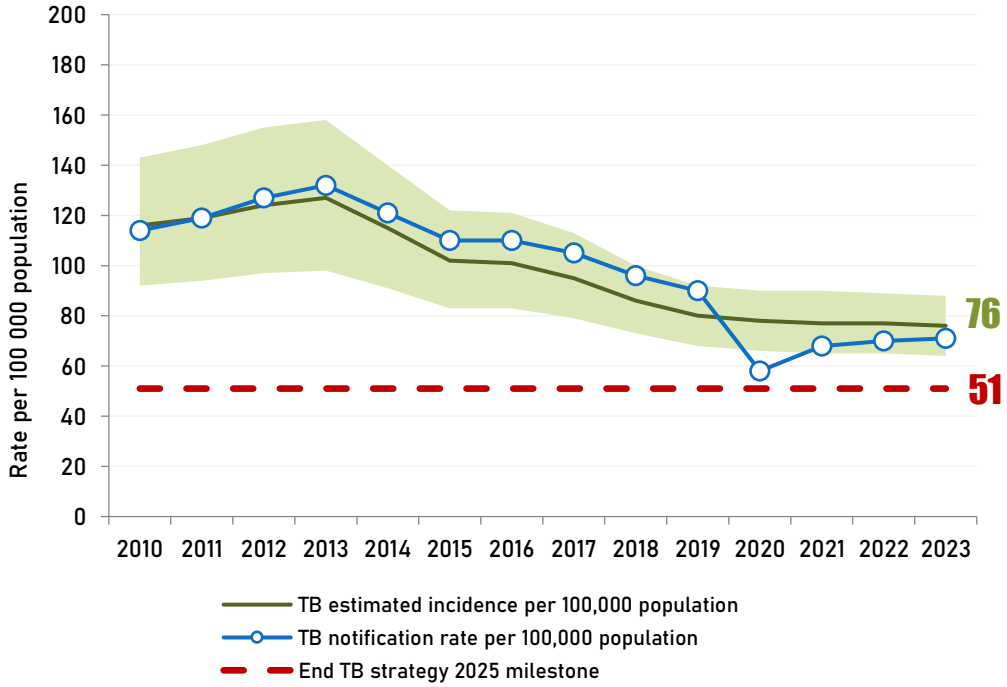
Given that TB deaths in the Republic of Moldova largely is attributed by HIV co-infection, interventions to detect people with HIV infection, early enrolment into ART and provision of TB preventive treatment should be prioritised to accelerate the reduction of TB death in the country.

3.3.2. TB incidence

The WHO-estimated incidence for 2023 was 76 (95% UI: 64–88) new and recurrent cases per 100,000 population. The mean annual decline over the last five years for estimated TB incidence was about 2.5% (Figure 4). Cumulative reduction of TB incidence between 2015 and 2023 is 25.5%. If the current trend of decline of TB incidence is sustained, Republic of Moldova most likely will not achieve End TB strategy milestone of 50% reduction of TB incidence by 2025 compared with 2015.

Figure 4. Estimated TB incidence and notification rate of incident TB cases, per 100,000, Moldova, 2010–2023

Shaded area around line indicates uncertainty interval



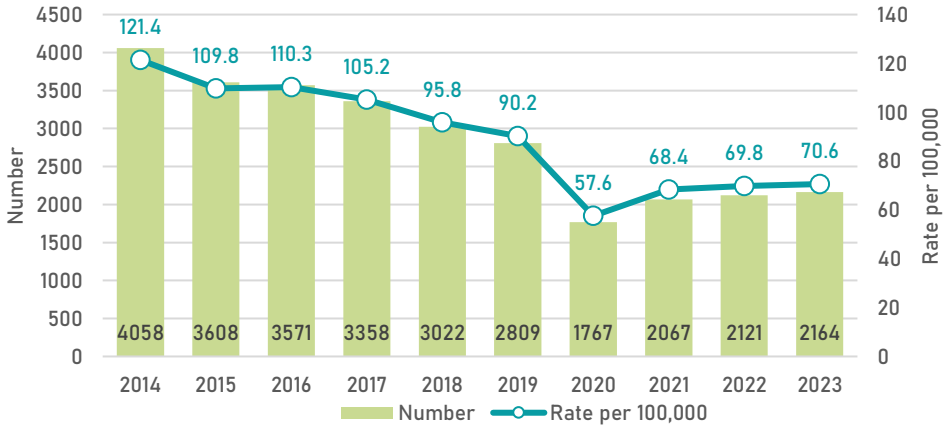
In 2023, the notification rate for people with new episode of TB cases in the country was 71 cases per 100,000 population using UN population estimates for Republic of Moldova. Gap between estimated and notified TB cases was narrowing between 2020 and 2023, implying increase of detection of TB cases in the population that previously went un-detected. Thuse, the estimated treatment coverage (previously known TB case detection rate) in 2023 was 93% (80-110%), up from 74% (range 64-87%) in 2020 (Figure 4). We can conclude that Republic of Moldova already achieved the 2025 milestone set by Regional action plan 2023-2030 of at least 85% case-detection rate in member states by 2025.

3.4. TB notification

3.4.1. Overall TB case notification and time trend

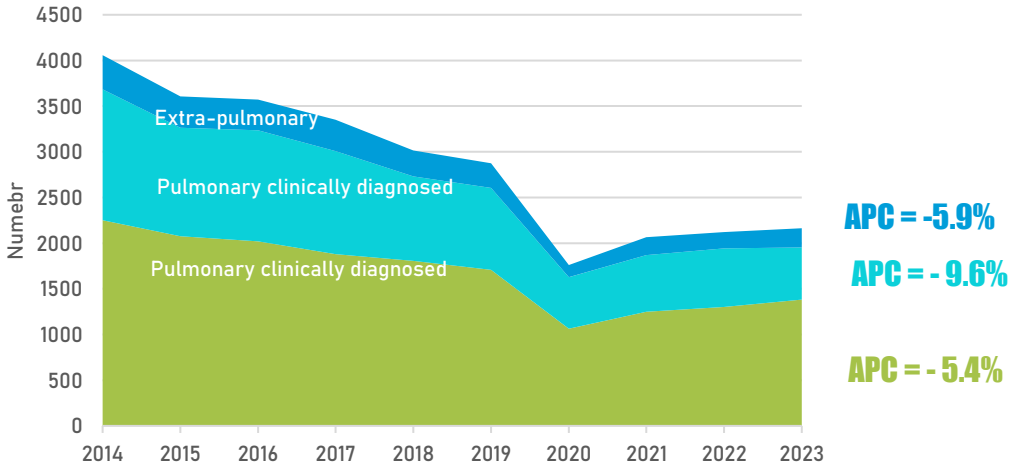
A total of 2,164 people were reported as newly diagnosed with TB in 2023 in Republic of Moldova, very small increase from 2,121 in 2022 and far below of 2,809 in 2019. Over five years period before the COVID pandemic TB notification rate in Republic of Moldova declined 5.9% annually, almost in parallel to estimated TB incidence. However, in 2020 because of disruption of routine health services and health care seeking the annual decline of TB notification in 2020 compared to 2019 made 45% (Figure 5). Following three consecutive years after COVID Moldova still recovering TB notification rate. This pattern in general reflect notification trend in WHO European regional.

Figure 5. TB notification number and rates per 100,000 population, 2014-2023



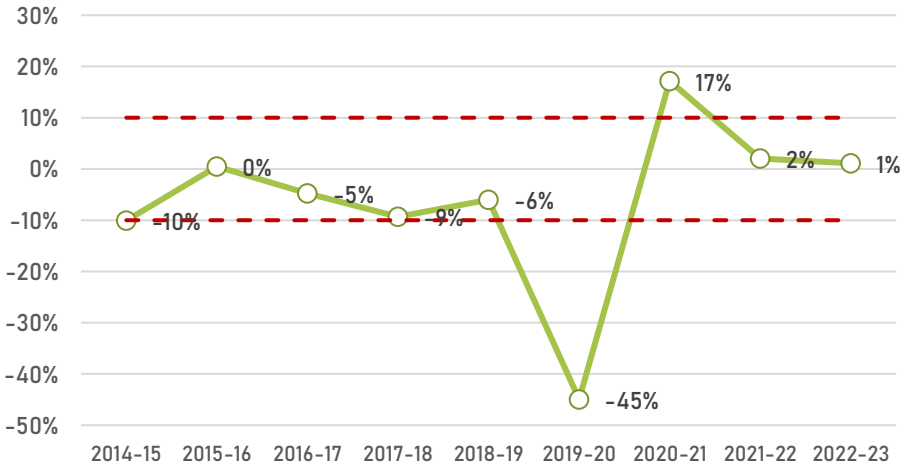
As shown in figure 6, the trend of TB notifications disaggregated by site of disease and bacterial confirmation follow the same trajectories, but with different pace: the fastest decline is observed in clinically diagnosed pulmonary TB cases, which decreased on average by –9.6% per year between 2018 and 2023 followed by extra-pulmonary TB cases with average annual decline of -5.9% during the same period. In comparison, the average annual decline of bacteriologically confirmed pulmonary TB cases over the same period was-5.4 % (Figure 9). Faster decline in clinically diagnosed patients might be explained by reduction of hyper-diagnosis. Improvement of laboratory testing most likely is not related to faster decline of clinically diagnosed, as Gene Xpert testing always is done in parallel to microscopy examination and Xpert testing coverage in Moldova over the time remains quite hight (Figure 6)

Figure 6. Notification number of new and recurrent TB cases per 100,000 population by laboratory confirmation and site of disease, and annual percent of change (APC) between 2018 and 2023



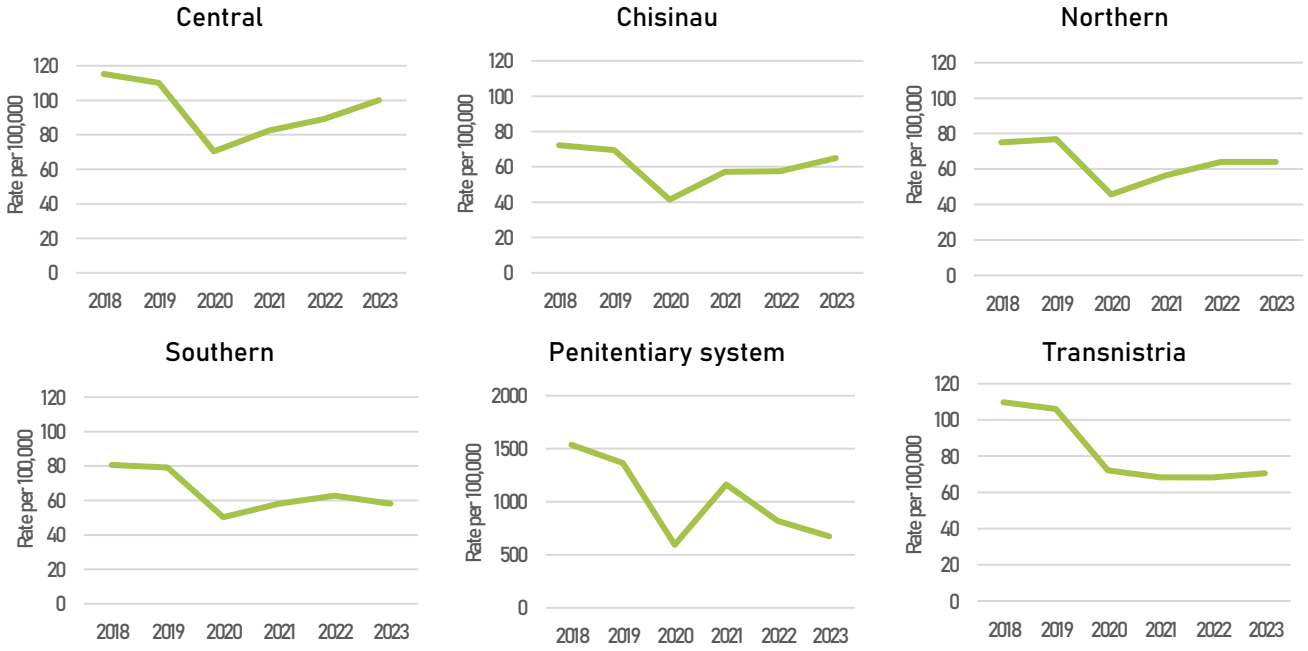
Interestingly, between 2019 and 2020 in context of COVID 19 pandemic the decline of TB among new episode of pulmonary bacteriologically confirmed, pulmonary clinically diagnosed and extra-pulmonary patients was 47%, 36% and 77% respectively, indicating that laboratory testing, was one of barriers of TB detection in 2020. (Figure 7).

Figure 7. Annual percent of change in TB notification



At regional level in 2023 TB notification rate was highest in Central region (100 per 100,000) and lowest in Southern region (58.1 per 100,000). All region and penitentiary system showed sharp drop in 2020 followed by recovery almost to the same level in the following year. Exceptions are Transnistria, where TB notification never recovered after sharp drop in 2020 and since then remain largely stable. While penitentiary system, again showed sharp drop in two consecutive years after recovery in 2021 (Figure 8).

Figure 8. New and recurrent TB notification per 100,000 population by region, from 2018 to 2023



TB notification rate in 2023 varied largely across the rayons from 28 (Vulkanesti) to 166 (Rezina) per 100,000 population. Of reporting units in 34 TB notification rate in 2023 compared to 2018 decreased, while in seven rayons TB notification rate increased (Figure 9). The largest increase of TB notification was observed in Floresti (91%), followed in Dnestrovsk (67%) and Rezina (21%). While Grigoropol, Criuleni, Vulcanesti, as well as penitentiary system on the right bank, reported rapid decline, which partially is explained by small absolute number of people notified. Variation in TB notification across the rayons most likely reflects the variation of true burden in TB across the geographic area as access to xpert testing in vast majority of rayons is hight and positivity of testing in majority of rayons is below 10% (Figure 35). However, the rayons with hight positivity of Xpert test results (Telenesti, Riskany, Edinet, Floresti, Singerei, Gubasaru, Bender) as well as those with low per-capita testing rate combined with above average Xpert testing positivity (Hinceti, Drochia) most likely have higher TB burden in the population compared to notification (Figure 9). The gap between TB burden and notification most likely is higher in rayons reporting excessive bacteriological confirmation (above 90%).

Map 1 below shows TB notification rate of people diagnosed with new episode of TB per 100,000 population in 2023 across first administrative level. There is some geographic pattern of TB notification: notification is high in the central part of the country and comparatively lower in norther and southern rayons.

Map 1. Notification of people diagnosed with new episode of TB per 100,000 population, 2023

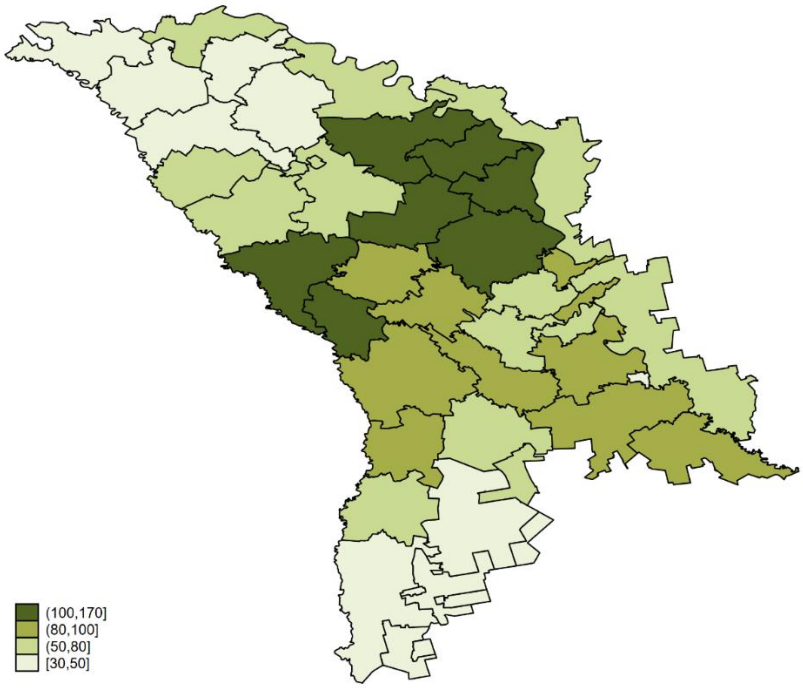
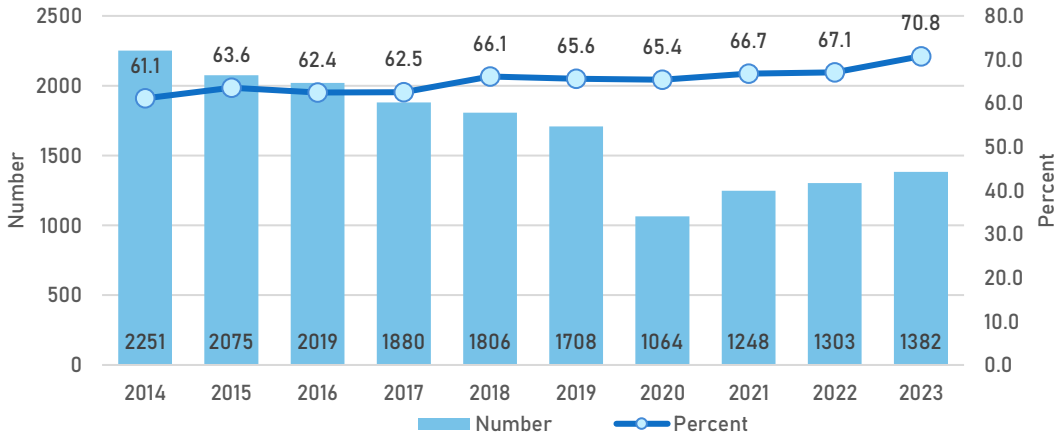


Figure 9. Notification of people with new episode of TB per 100,000 population by rayons in 2018 and 2023

3.4.2. Trend by bacteriological confirmation

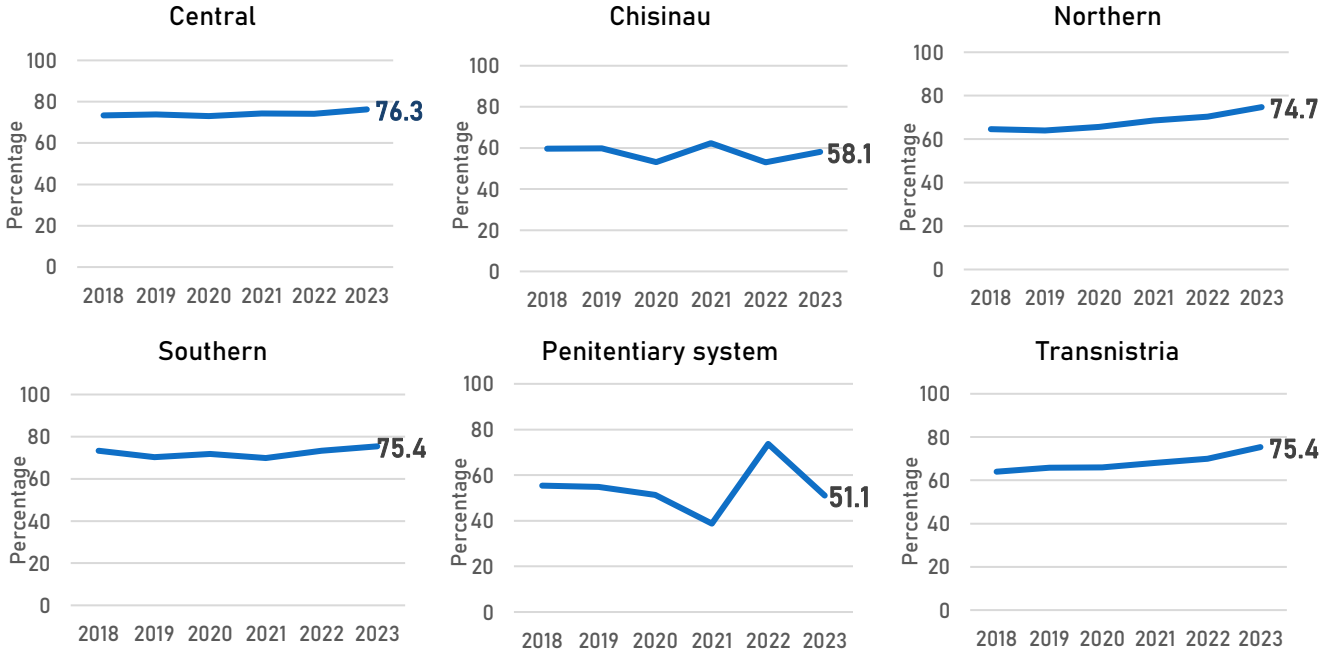
Between 2014 and 2023, both bacteriologically confirmed and clinically diagnosed PTB cases declined, however, decline in clinically diagnosed cases was slightly faster, which resulted that the percentage of bacteriologically confirmed slightly increased from 61% in 2014 to 73% in 2023. However, in 2020 most likely due to repurposed use of Gene Xpert the decline of bacteriologically confirmed was much sharper compared to clinically diagnosed resulting some drop of % of bacteriologically confirmed among new episode of pulmonary TB patients. (Figure 10).

Figure 10. Trend in notification of PTB by bacteriological confirmation and % of BC PTB



At regional level in 2023 TB bacteriological confirmation ranged 58% in Chisinau to 76% in central region. In penitentiary system bacteriological confirmation varied largely from year to year with 51% in 2023 (Figure 11)

Figure 11. Trend in percentage of bacteriologically confirmed new episode of PTB by regions



In 2023 the proportion of bacteriologically confirmed among people diagnosed with new episode of pulmonary TB ranged from 51% to 100% indicating variety in access and practice to TB diagnosis across the entire country. Of 47 subnational reporting units in 14 the percentage of bacteriologically confirmed was below 70% while in 2018 25 rayons reported below 70% bacteriological confirmation. Rayons with lowest bacteriologival confirmation in 2023 were Ialoveni, Comrat, Edinet as well as Chisinau municipality and penitentiary system. Sub-optimal bacteriological confirmation in those areas might indicate an over-diagnosis. In another six rayons the proportion of bacteriologically confirmed exceeded 90%. Dnestrovosk, Taraclia and Vulcanesti reported 100% bacteriological confirmation (Figure 12). Such extreme bacteriological confirmation might indicate that only patients in advanced stage of disease are diagnosed with TB and there is a risk that people with paucibacillary TB are missed to be diagnosed. Greater attention to the quality of TB case detection is warranted in rayons both with excessive lower (below 70%), as well as excessive higher (>90%) bacteriological confirmation.

Overall, there is no geographical pattern of bacteriological confirmation: rayons with highest confirmation are bordering with rayons with lowest level of confirmation (Map 2).

Map 2. Percent of bacteriologically confirmed among new episode of pulmonary TB, 2023

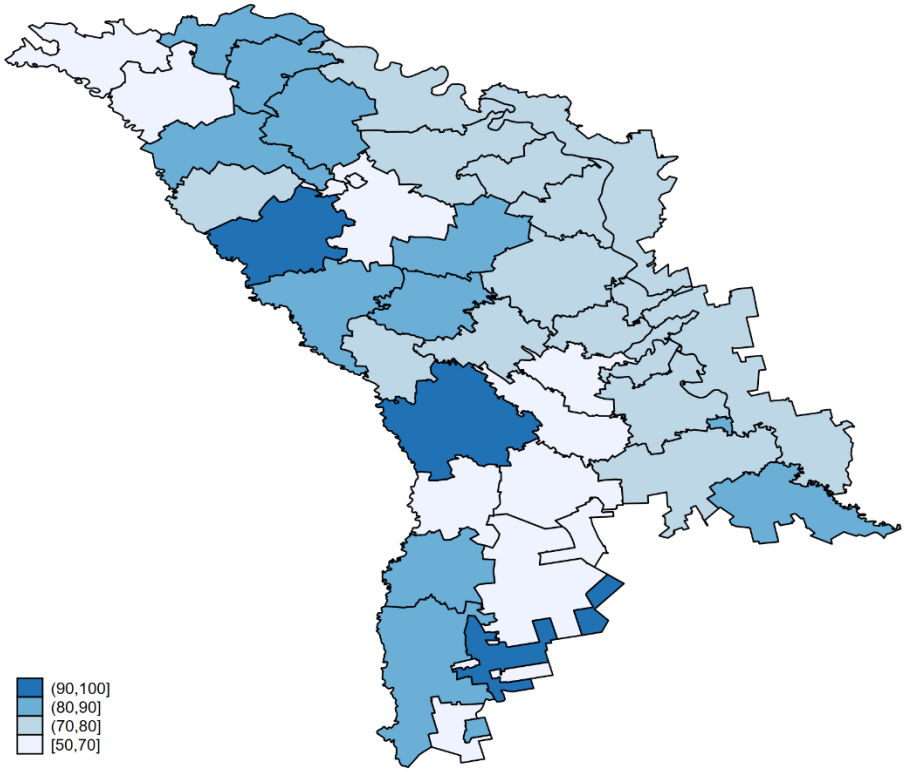
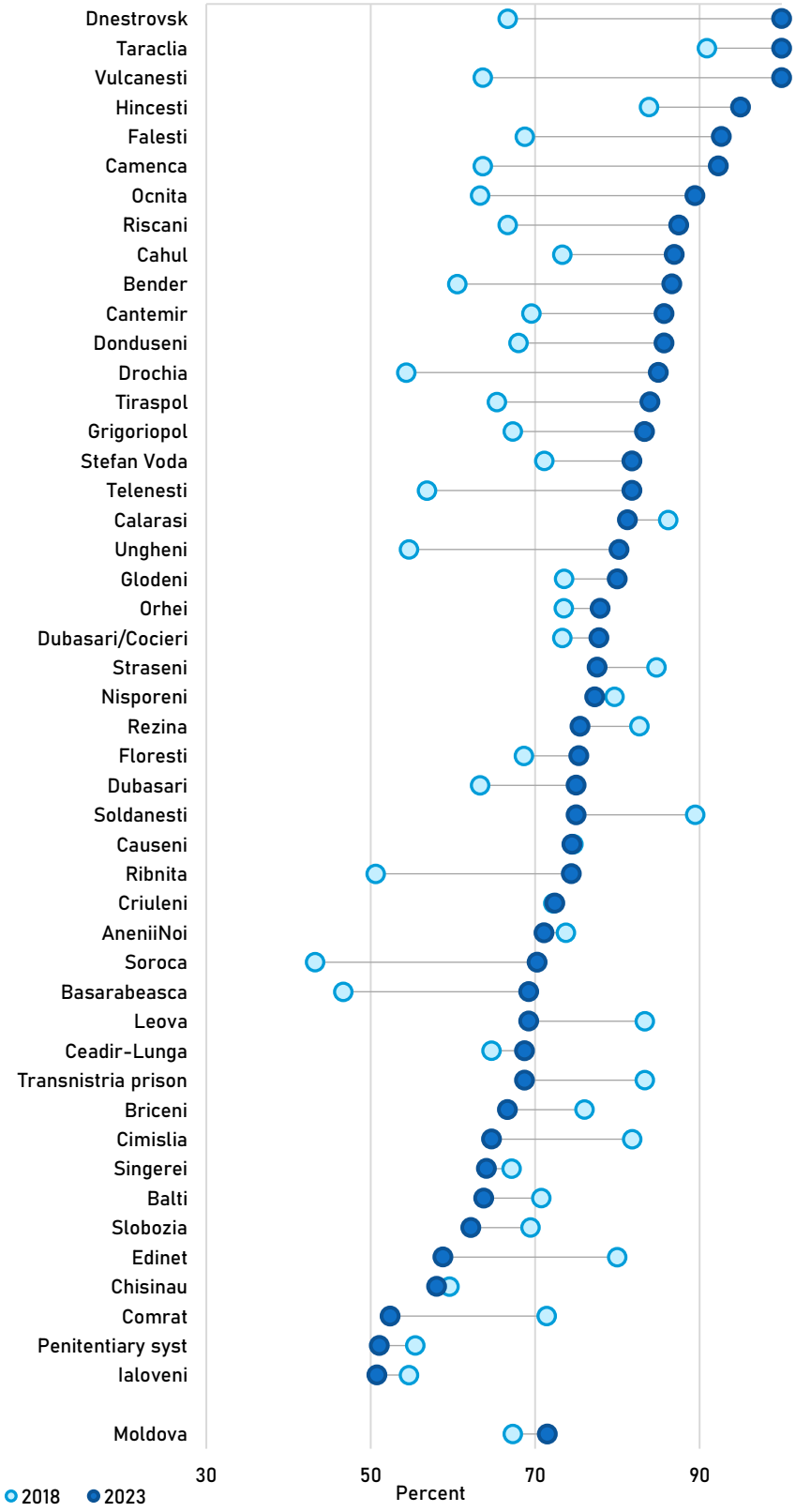


Figure 12. Proportion of bacteriologically confirmed TB cases N&R PTB patients by rayon in 2018 and 2023



3.4.3. Trend by site of disease

In 2024 9.7% of people diagnosed with new episode of TB had extrapulmonary localization. Since 2014 proportion of people TB with extrapulmonary localization of disease in the Republic of Moldova remains largely stable ranging between 7.6 to 10.3 (Figure 13). Notable drop in TB notification in 2020 was more pronounced extrapulmonary cases compared to pulmonary, resulting sharp decline in proportion of extrapulmonary, which was recovered in 2021 to pre-pandemic level.

Figure 13. Number and percent of people diagnosed with new episode of extrapulmonary TB, 2014-2023

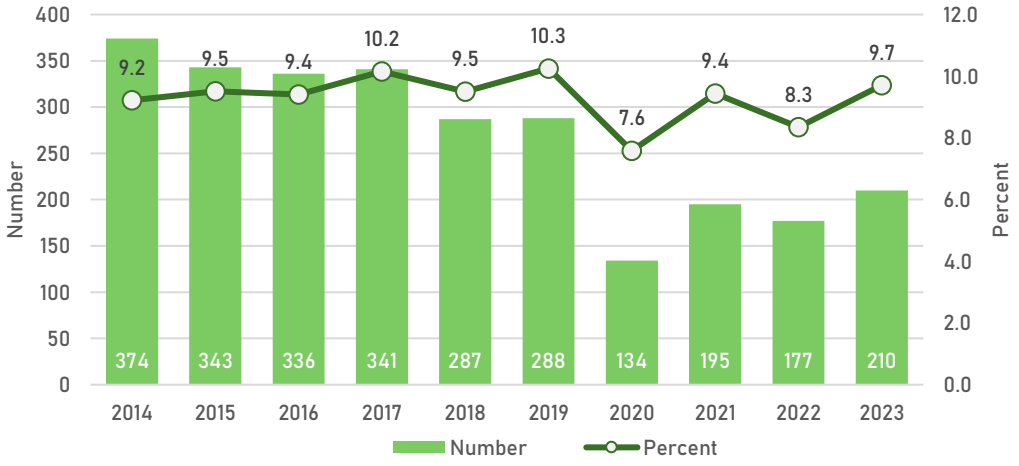
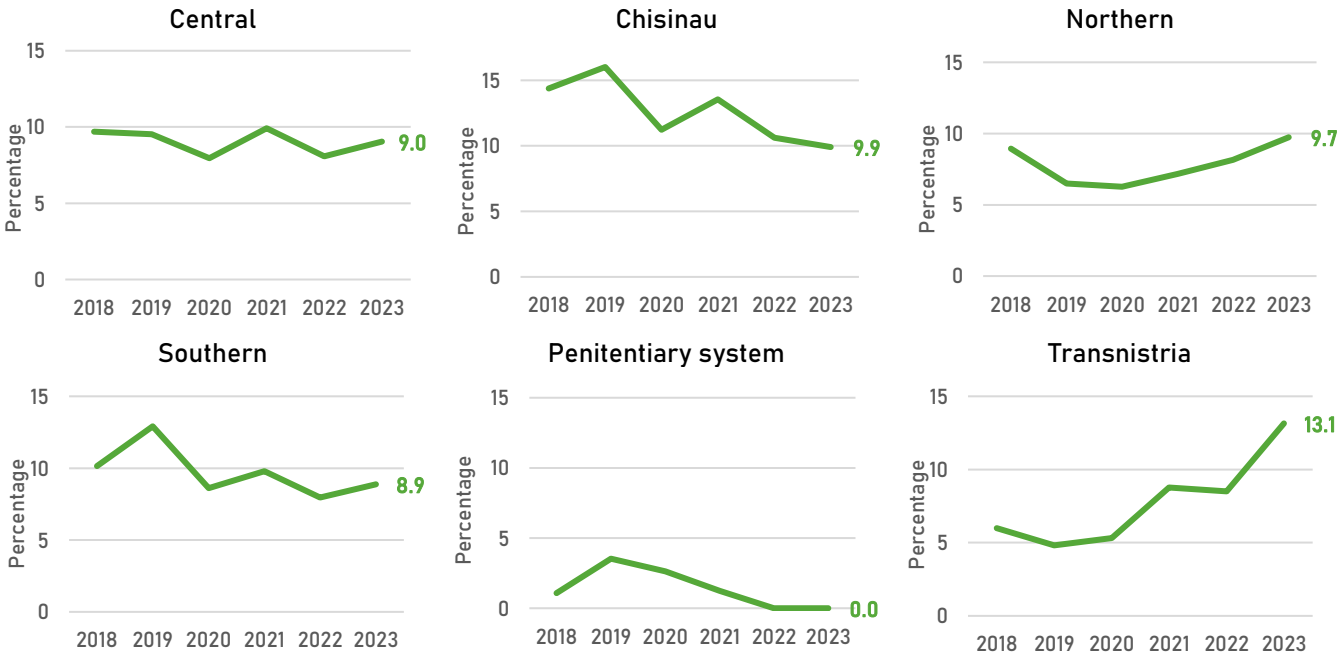


Figure 14. Trend the proportion of EPTB by regions, 2018-2023



In 2023 the proportion of extrapulmonary TB cases varied largely from 0% in penitentiary system to 13.1% in Transnistria (Figure 14). This may reflect under-lying differences in TB epidemiology, attributed by proportion of child TB cases, proportion of TB/HIV co-infected, which have higher risk of extrapulmonary localization, as well

as diagnostic practices. Although the national proportion of notified cases accounted for by extrapulmonary TB has been relatively stable over time (exception is 2020), there is considerable year-to-year variation at the regional levels such as in Transnistria between 2022 and 2023, Chisinau between 2021-2022. Such sharp year-to-year variation might suggest unstable diagnostic practice and greater attention to quality of diagnosis of extrapulmonary cases is warranted.
At rayon level the percentage of people with extrapulmonary localization of disease in 2023 varied from 0 to 25.6% (Figure 15). Nine rayons as well as penitentiary system reported no case of extrapulmonary TB in 2023, while in 2018 only two rayons reported 0 cases of extrapulmonary TB, indicating that over time less rayons are diagnosing EPT and diagnosis of EPT over time is centralized. Such observation partially is explained by the small absolute number of cases and decline in number of notified TB cases.

There was no geographic pattern of special distribution of people with extrapulmonary TB: rayons with highest notification border with the rayons with the lowest notification (Map 3).

Map 3. Percent of extrapulmonary TB cases among new episode of TB, 2023

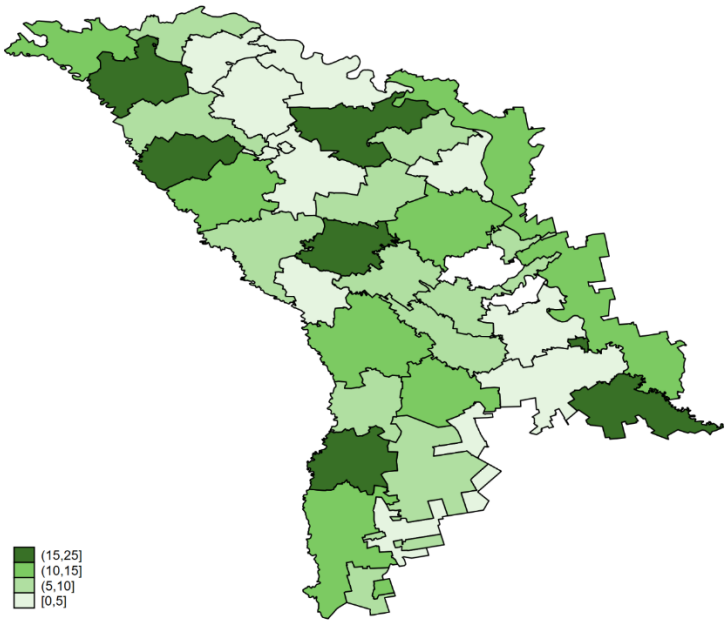
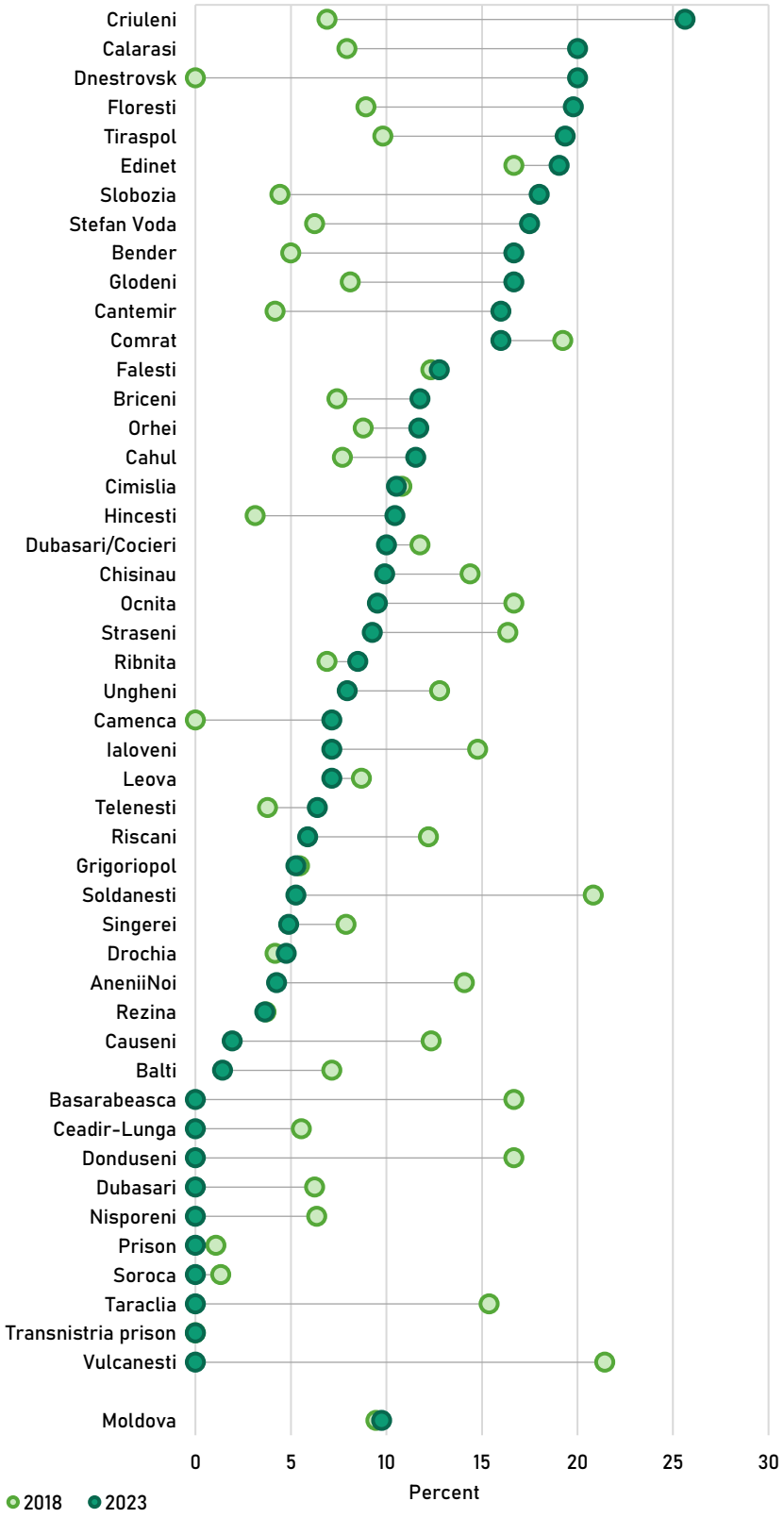


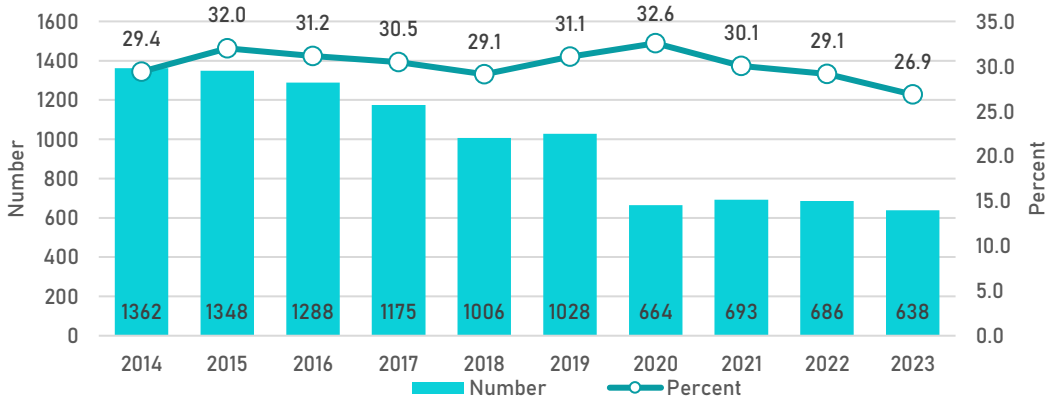
Figure 15. Percentage of ETP in 2018 and 2023 by rayons



3.4.4. Trend by history of treatment

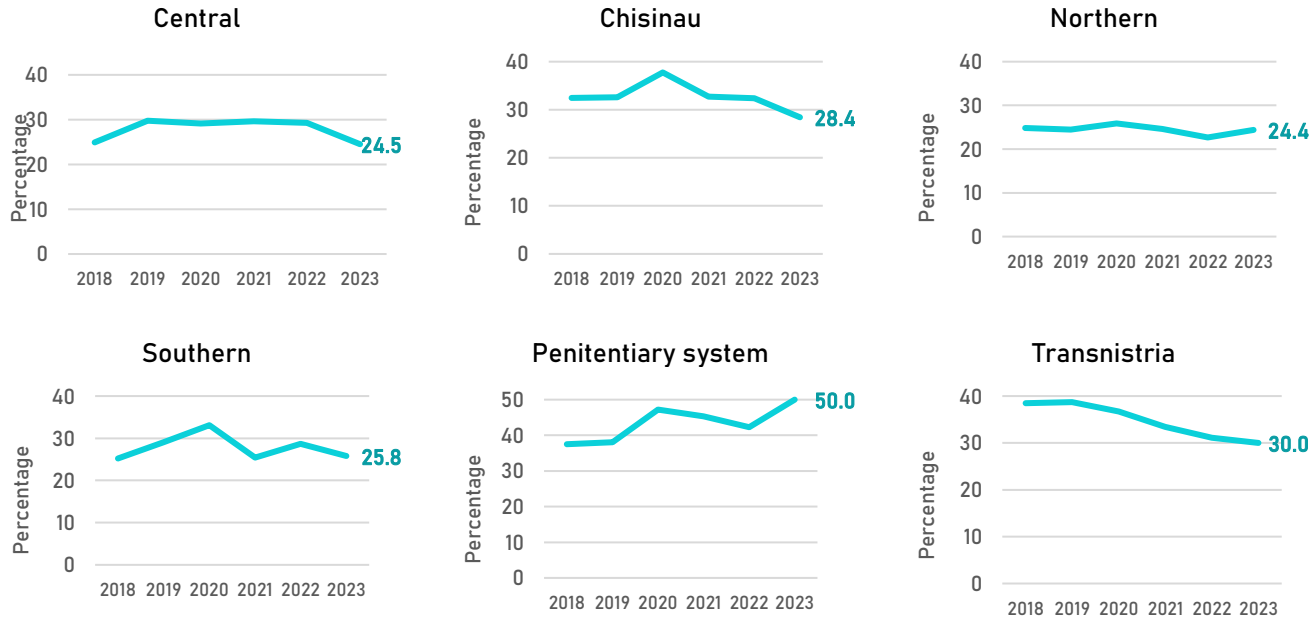
Between 2014 and 2020, the percentage of retreated cases in the Republic of Moldova was largely stable accounting about third of notified TB cases. Absolute number of retreated cases sharply dropped in 2020, almost proportional to TB cases, but subsequent recovery was much slower compared to new TB cases resulting in a gradual relative decrease in the proportion of retreated cases from 32.6% in 2020 to 26.9% in 2023 (Figure 16). This pattern partially might be explained by the improvement of effectiveness of TB treatment, such as introduction of all-oral and shorter treatment regimens thus preventing disease re-occurrence.

Figure 16. Trend in number and proportion of retreated TB cases, 2014-2023



The proportion of retreated cases by regions in 2023 varies from 24.4% in Northern region to 30% in Transnistria and 50% in penitentiary system. There was no clear trend across the rayons: in Chisinau and Transnistria proportion of retreated declined, in penitentiary system increased, while in rest of regions remained largely stable (Figure 17).

Figure 17. Proportion of previously treated TB cases by region



At rayon level percentage of retreated ranged from 7.1 in Donduseni to 57.1% in Vulcanesti. Regions reporting excessive variation of proportion of previously treated between 2018 and 2023 were Vulcanesti, Dnestrovsk, Transnistria prison. In 20 rayons proportion of previously treated decreased, while in another 12 rayons proportion of people of previously treated TB cases increased (Figure 18).

Mapping indicated no geographic pattern in the distribution of proportion of previously treated case (Map 4).

Map 4. Percent of previously treated among all notified, 2023

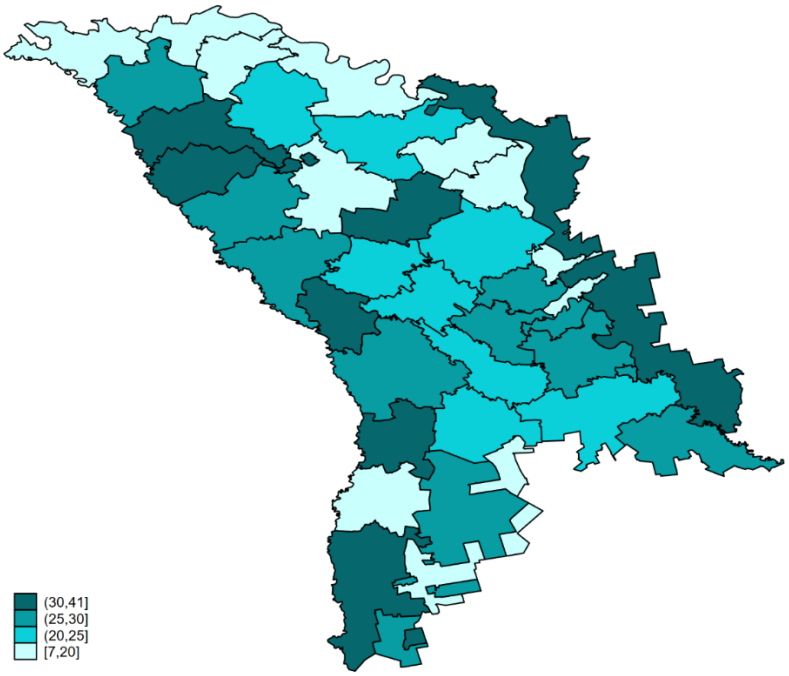
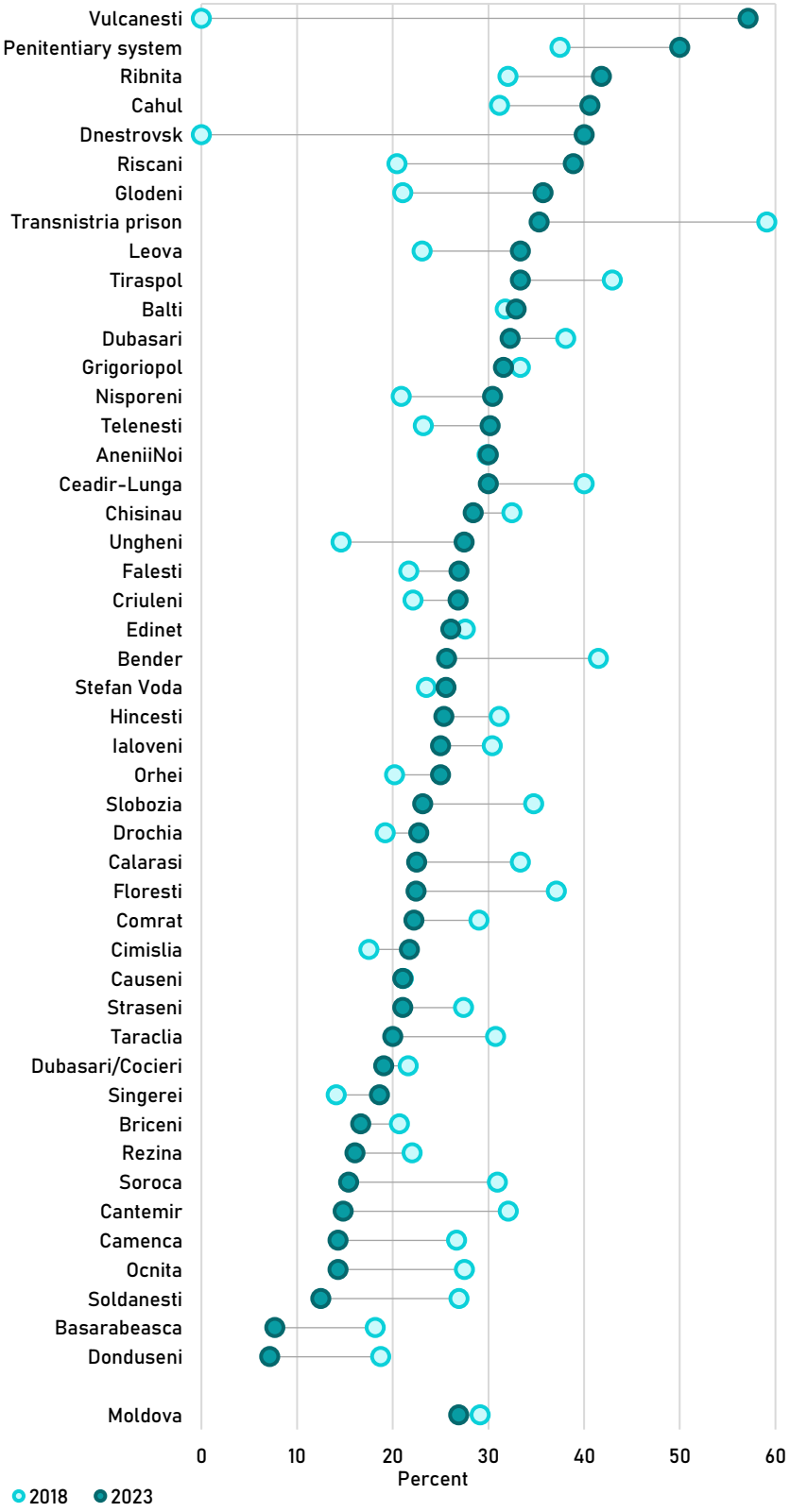


Figure 18. Proportion of previously treated TB cases by rayon



3.4.5. Trend by childhood TB notification

Between 2014 and 2022 the proportion of child TB cases among people diagnosed with new episode of TB was largely stable ranging between 2.8 and 3.7% without any clear trend. In 2023 there was a sharp increase of children from 83 to 153, equivalent to 7,1% of all notified. (Figure 19). There were recognized issues in the diagnosis of TB in children, and most likely reason according to NTP was the over-diagnosis of child TB cases.

Figure 19. Trend in number and percent of child TB cases among all new and relapse TB patients

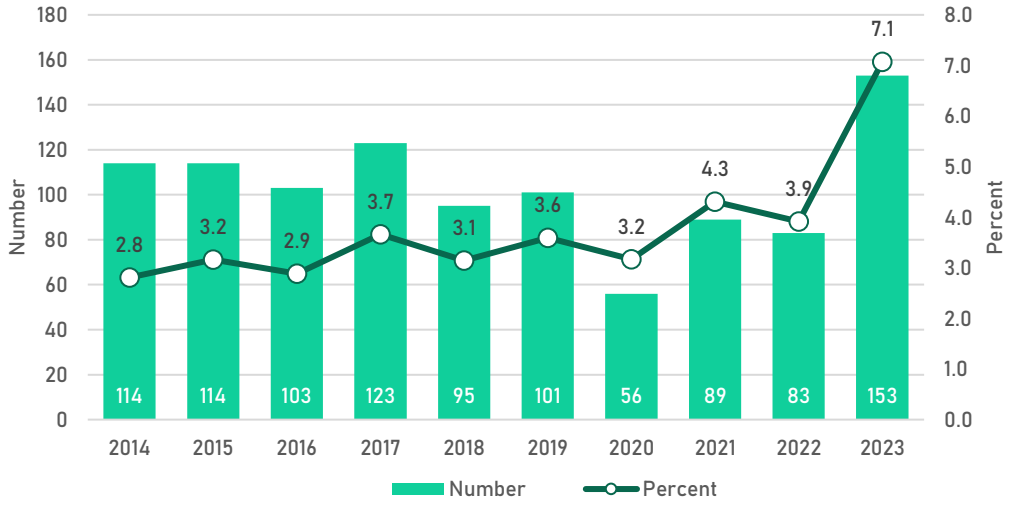
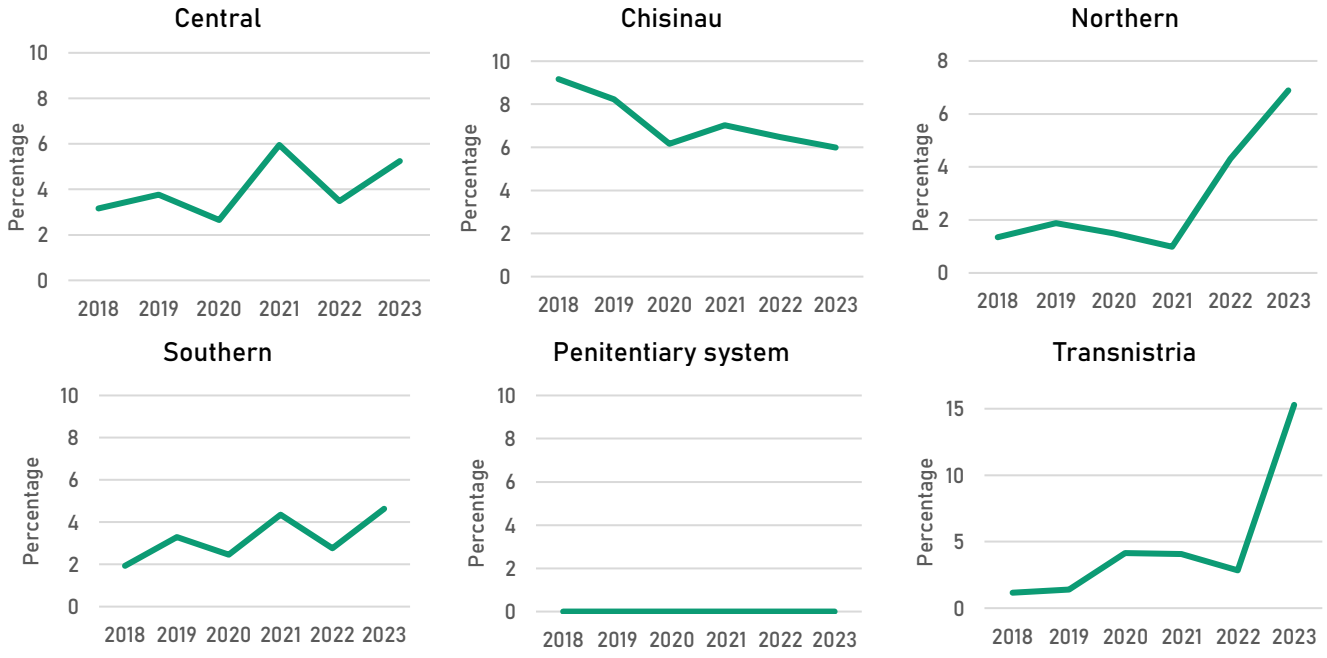


Figure 20. Percent of child TB cases among new and relapsed



Observation of notification child tuberculosis cases disaggregated by rayons shows quite sharp year to year variation in percentages of child tuberculosis case, however, this is most likely due to small absolute number of

cases. At the rayon level, in 2023 no child TB cases were reported in 17 rayons and in the remaining rayons the proportion of child TB cases ranged from 1.4% to 29.0%. (Figure 21). 11 rayons reported above 10% child notification, with the highest percentage in Slobozia (29%), followed in Criuleni (23%), Floresti (21%) and Dnestrovsk (20%).

Mapping indicates some geographic pattern of childhood TB, with more frequent pattern in eastern rayons and less frequencies in north and south (Map 5).

Map 5. Percent of children among people diagnosed with new episode of TB, 2023

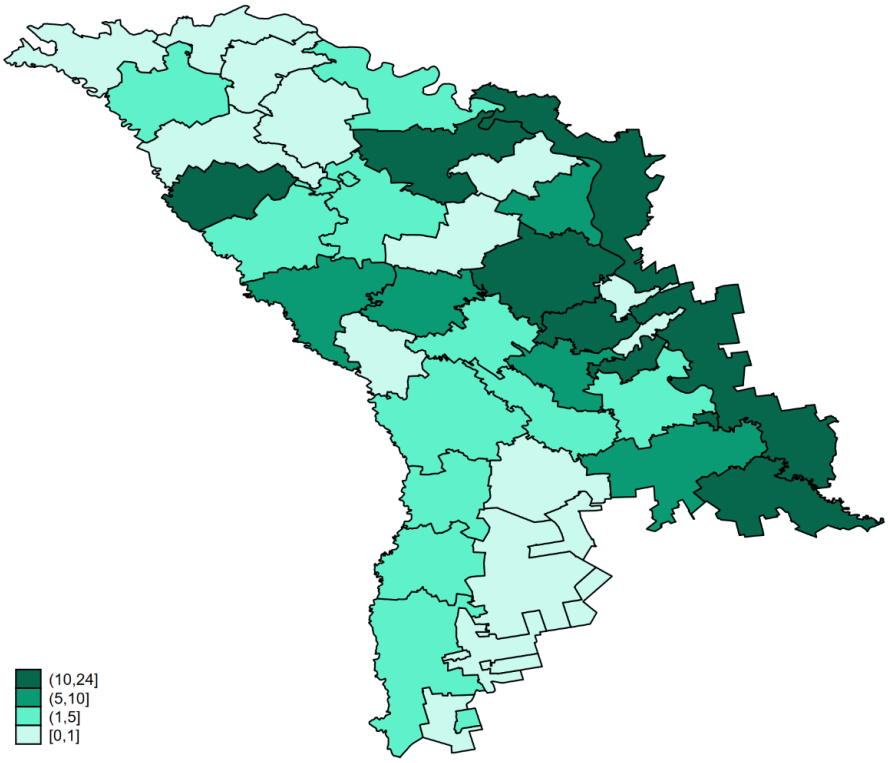
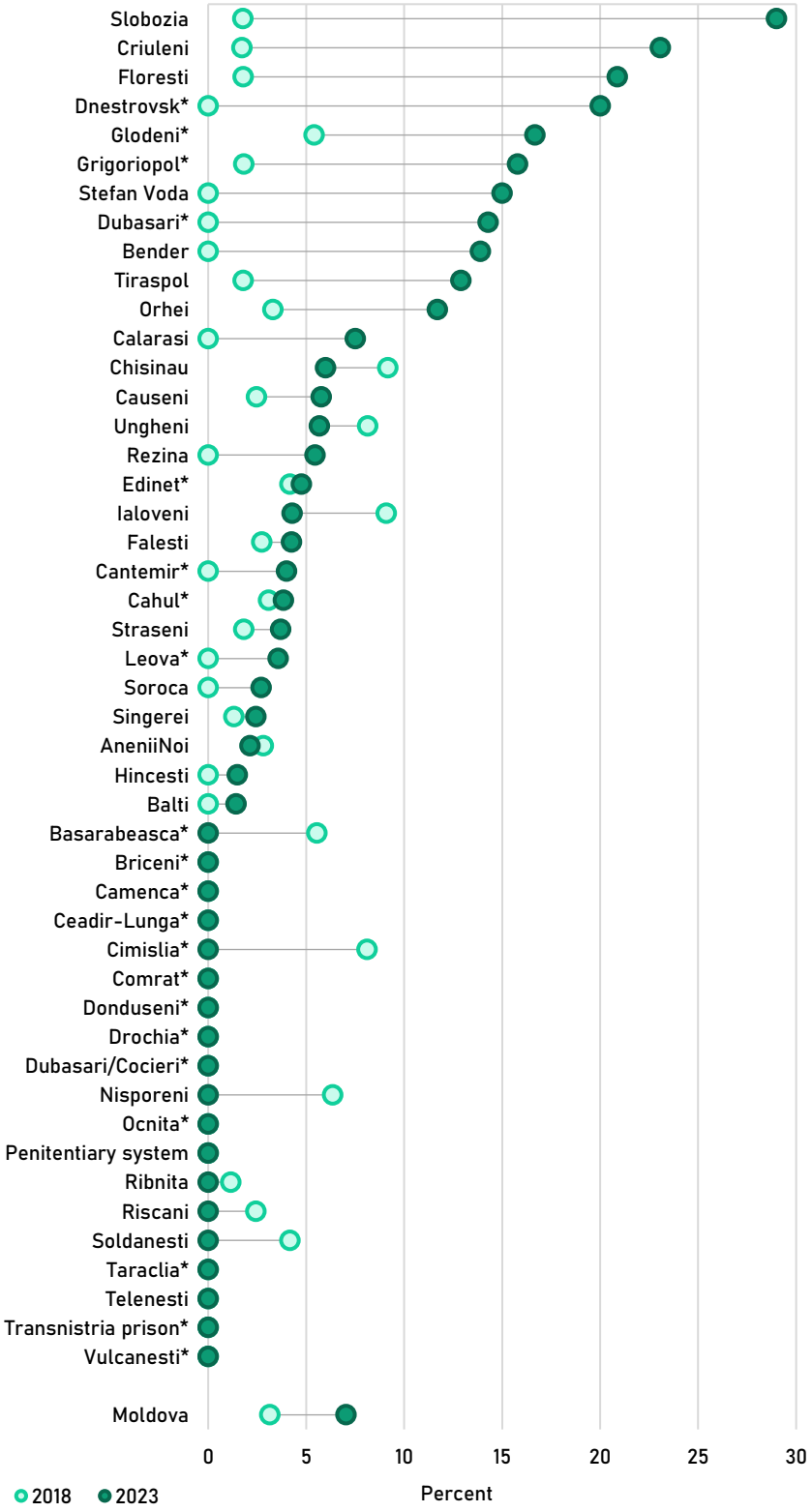


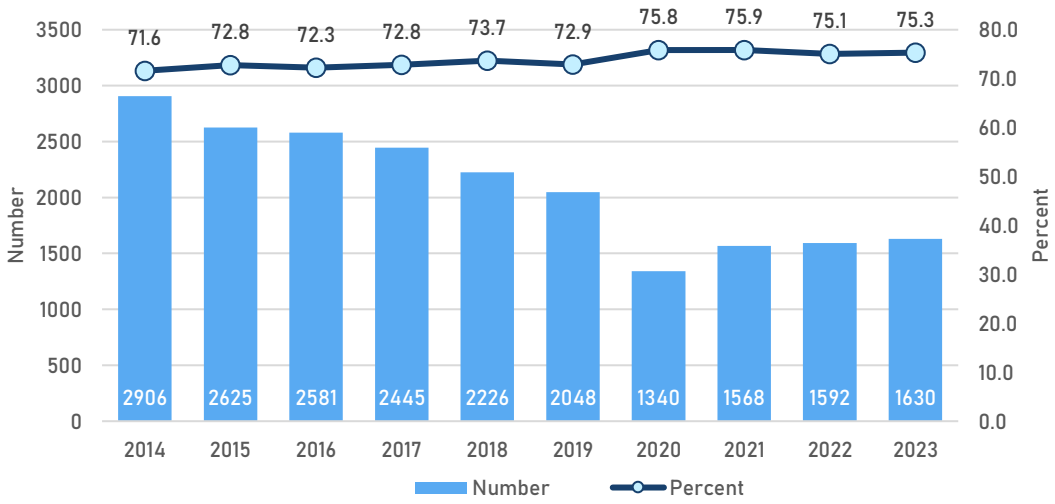
Figure 21. Percent of child TB cases among people with new episode of TB in 2018 and 2024 by rayons



3.4.6. TB notification trend by sex

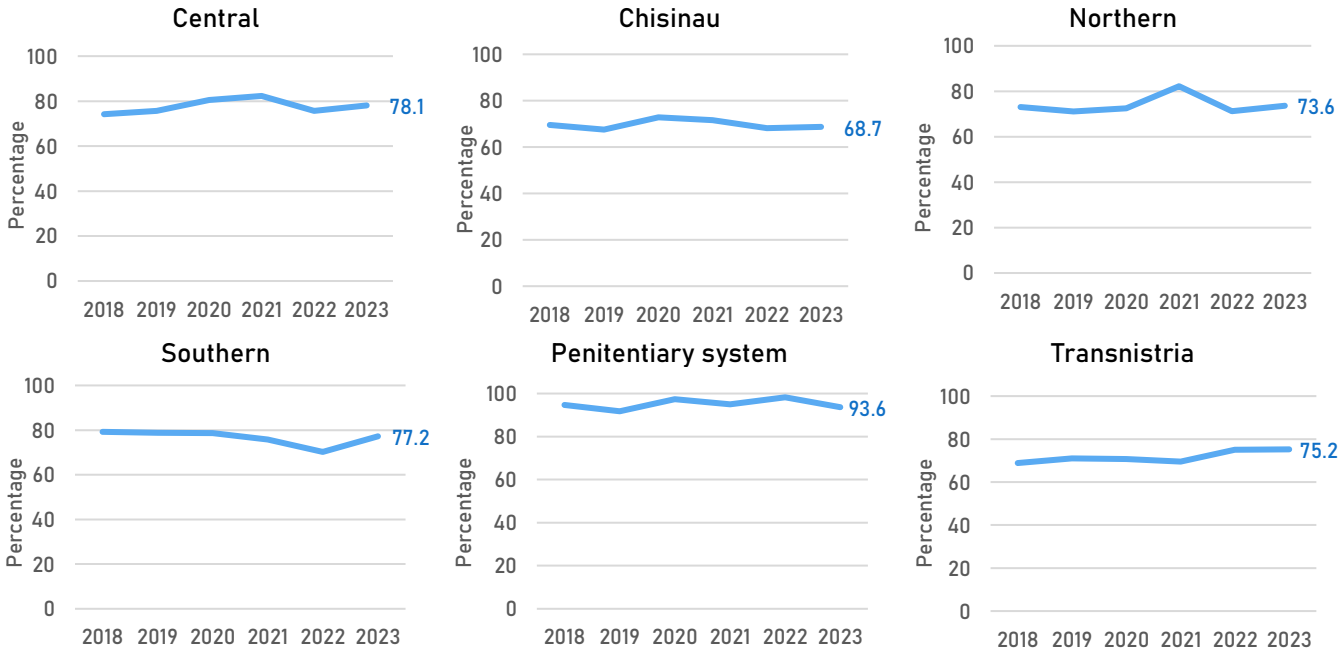
Between 2014 and 2023 the proportion of males among notified new and recurrent TB patients slightly increased from 72% to 75%, without any major year-to-year variation (Figure 22).

Figure 22. Trend in number N&R TB by sex and proportion of males



At regional level proportion of males ranged from 69% in Chisinau municipality to 78% in Central region (Figure 23).

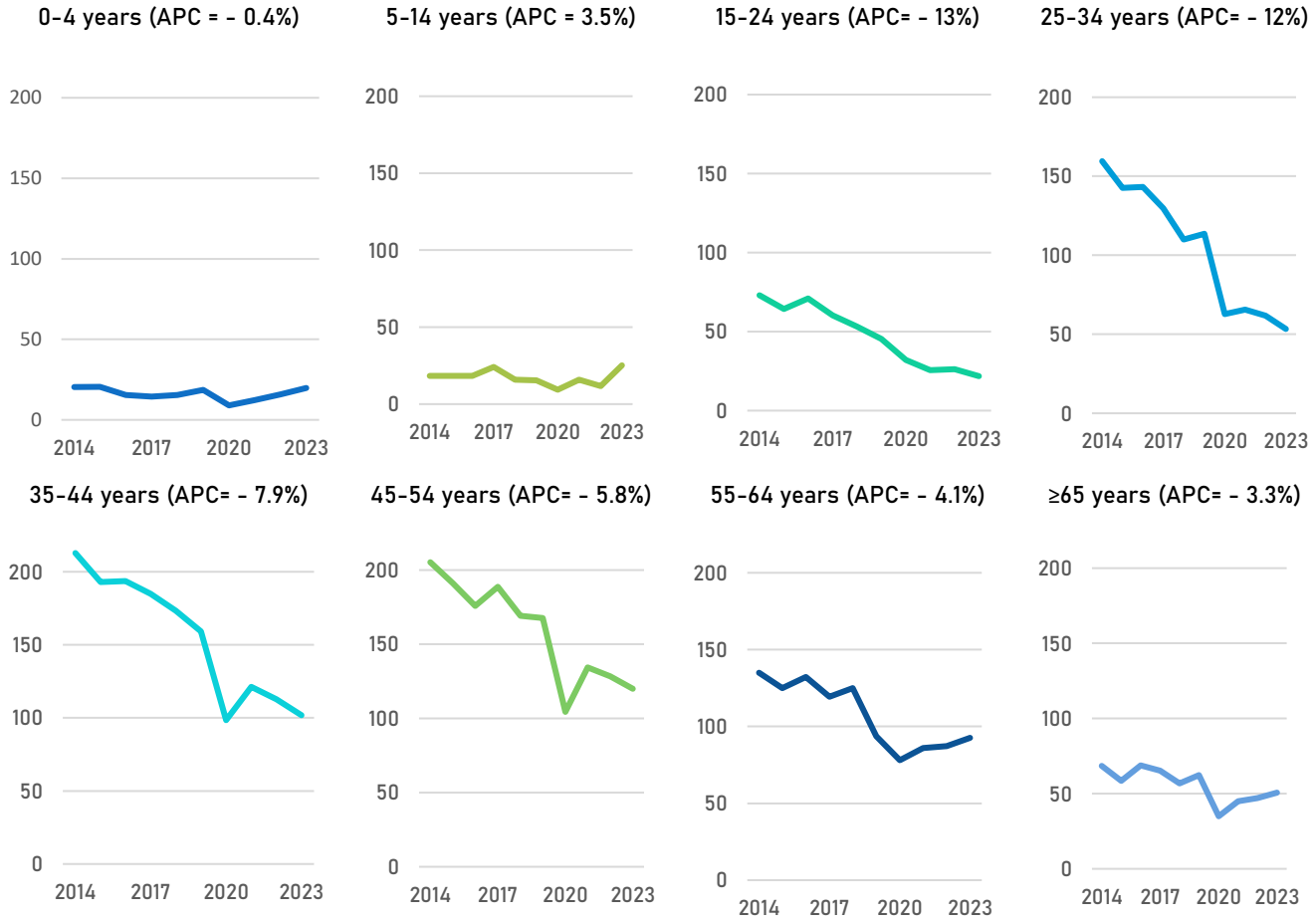
Figure 23. Proportion of male TB patients among new and relapse in 2015 and 2020



3.4.7. Trend of TB notification by age

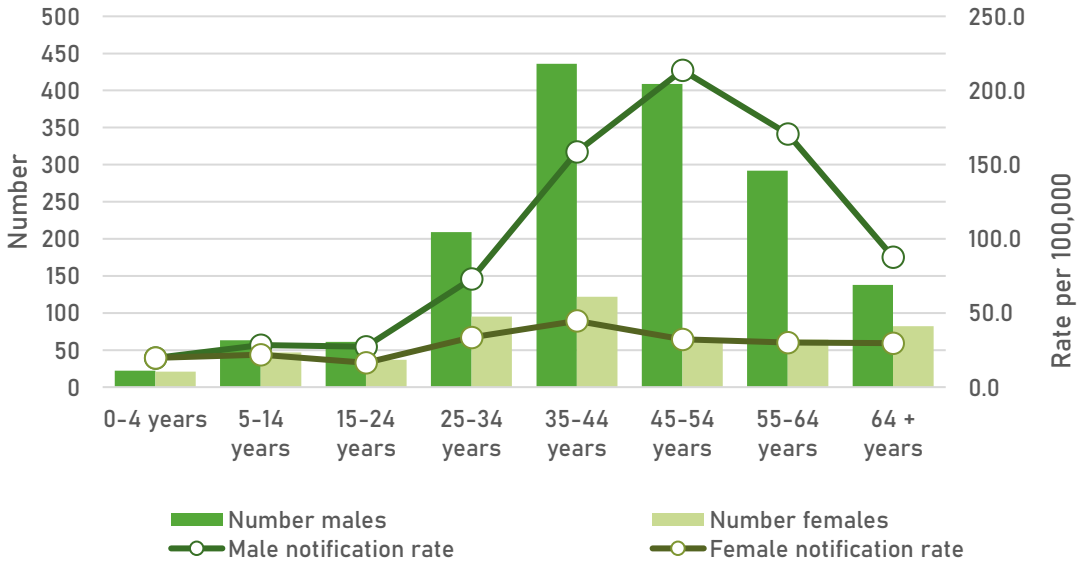
Figure 24 shows the trends in notification rates for new and recurrent TB cases disaggregated by age group. Between 2014 and 2023, the TB notification rate declined for all age groups except the children aged 5-14 years. The fastest decline was observed among young adults aged from 15 to 34 years (-13% annually) followed by 25-34 years (-12% annually) and 35-44 (-7.9% annually) (Figure 22). Thuse, among adults, the speed of decline was negatively associated with the age almost in linear pattern. This pattern of temporal change is consistent with the general understanding of TB epidemiology- "aging of the epidemic", which is a sign of the true decline of TB burden in the population. Because TB in the elderly mostly results from the reactivation of latent infection, the decline in transmission rate has little effect on TB incidence in this age group. In contrast, TB in younger age groups is the result of recent infection, and decreased TB notification in this age group suggests a decline in the annual risk of infection and therefore, a decline of TB transmission in the general population. Ideally, we should expect faster decline of TB notification in children, however, striking increase of TB notification in 2023 resulting inconsistent trend by age-group.

Figure 24. Trend in age-specific TB notification rates in Moldova, 2014-2023



The most populated age group of TB patients in 2023 are males aged 35-44 years; however, the highest age and sex-specific notification rate is observed among males aged 45-54. In males, the TB notification rate increases with age and peaks at 45-54 and then declines. Among females, the notification rate peaks in the 35-44 age group and then slightly declines, with stable notification rates until the elderly age group (Figure 25).

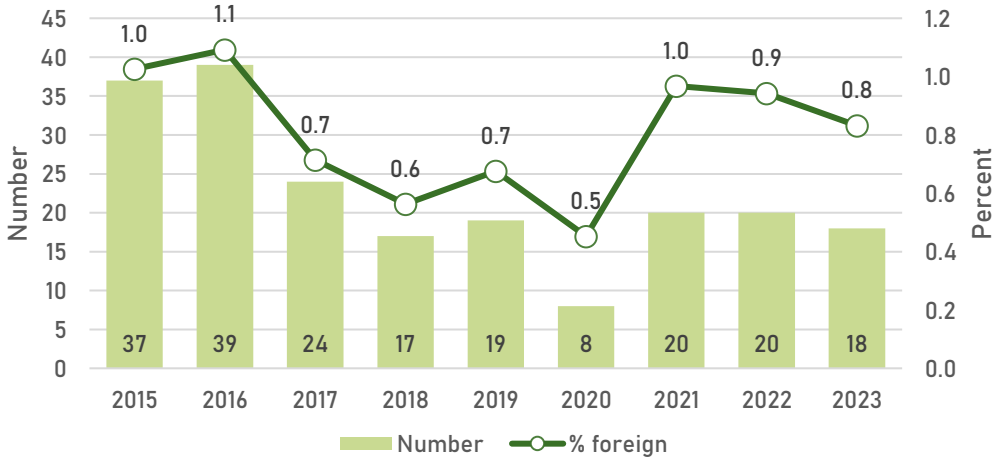
Figure 25. TB number and rates disaggregated by age group and sex, 2023



3.4.8. Trend by of TB by foreign population

In Moldova the people of foreign origin make only small proportion of people with TB. After Russian- Ukrainian war started in February 2022 Moldova became one of key host country of people leaving zone of conflicts. However, there is no evidence of increase in absolute number of TB notified among people of foreign origin. (Figure 26).

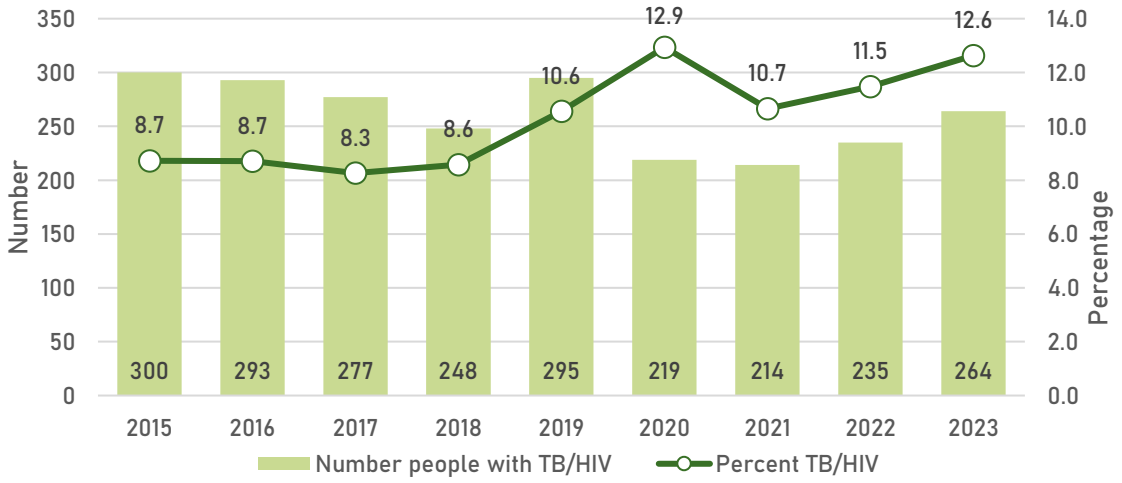
Figure 26. Trend in number and percent of people notified with TB of foreign origin



3.4.9. TB/HIV co-infection trend

According to routine surveillance, over the recent decade the absolute number of people notified with TB/HIV co-infection ranged from 2014 to 300. Expressed as percentage it TB/HIV co-infection varies between 8.6 to 12.9% (Figure 27).

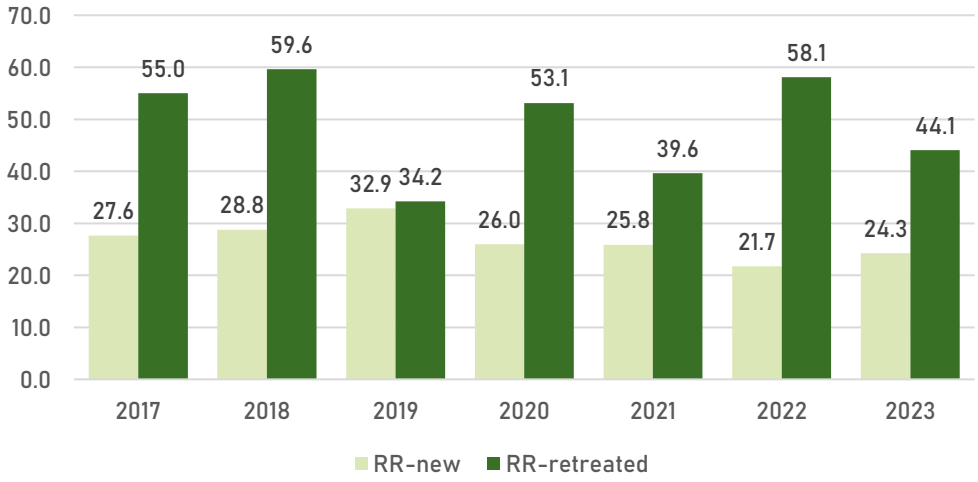
Figure 27. Trend in number and percent of notified TB/HIV patients



3.4.10. Trend of RR/MDR-TB

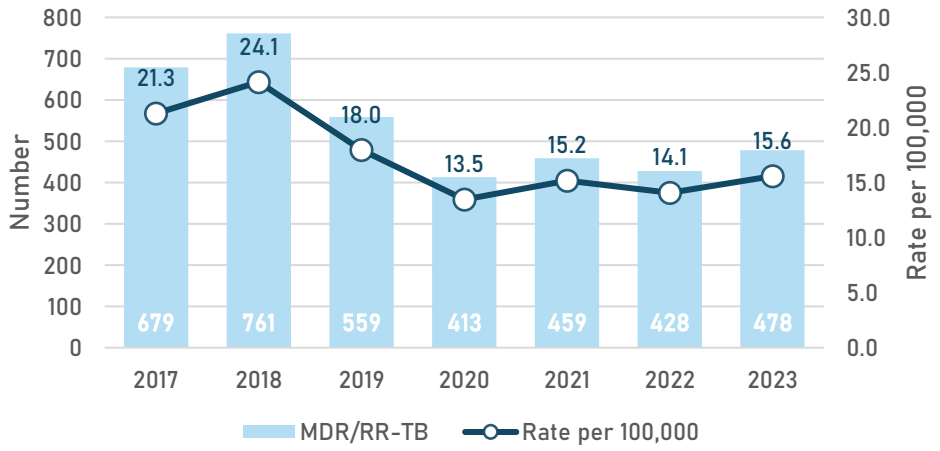
In 2023 the percentage of RR/MDR TB among people with new and retreatd TB was 24.3 and 44.1% respectively. Moldova has all pre-requisits for the high quality of routine drug-resistance surveillance, including high bacteriological confirmaiton, universal access to testing for drug-resistance and quality ensured laboratory service. However, large year-to-year variation of percentage of RR-TB implyes some issues in recording and/or reporting, which might related to incorrect classification of people with history of TB treatment or double counting of the resutls.

Figure 28. Trend in percentage of RR/MDR TB among new and previously treated patients with DST results



Between 2017 and 2023 total number of people notified with RR-TB in Moldova varied largely from year-to-year. There was sharp decline between 2018 and 2019. Another sharp decline in 2020 due to COVID pandemic followed slow recovery, which continued up to 2023. Expressed as relative to population, this translates to a decline from 21.4 in 2018 to 15.6 in 2023 per 100,000 population (Figure 29).

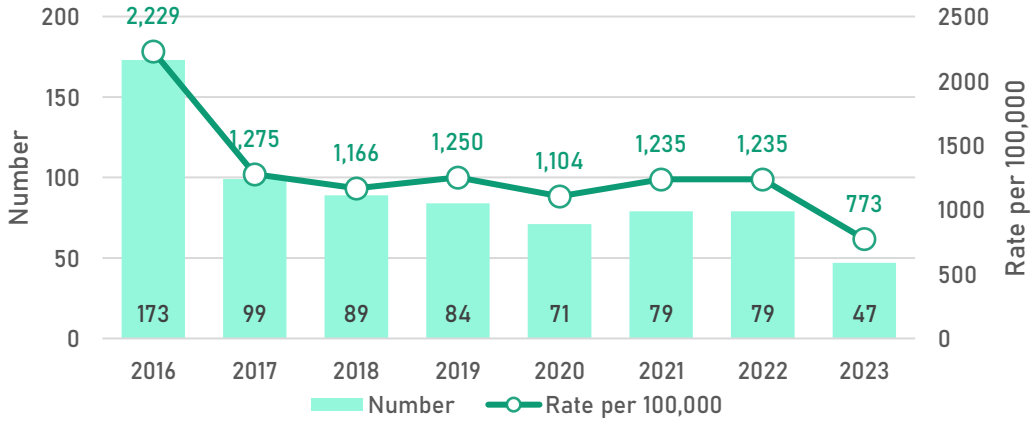
Figure 29. Trend in number of RR-TB and rate per 100,000 population



3.4.11. Trend of TB among prisoners

TB notification rate in 2023 in penitentiary system was 773 per 100,000, which is over ten times higher compared to notification in civilian population. From 2016 to 2023, notification of new and recurrent TB cases in prison decreased from 173 to 47 (Figure 30). Relative to size of penitentiary population the TB notification rate declined from 2,229 per 100,000 in 2016 to 773 in 2023. The decline of TB cases in prison was much faster than in civilian population, which resulted to decline of relative contribution of new episode of prison TB cases among all notified from 4.8% to 2.2%.

Figure 30. Trend in number of prison TB cases and rate per 100,000 population



3.5. Determinants of TB: programmatic factors

3.5.1. TB diagnostic facilities

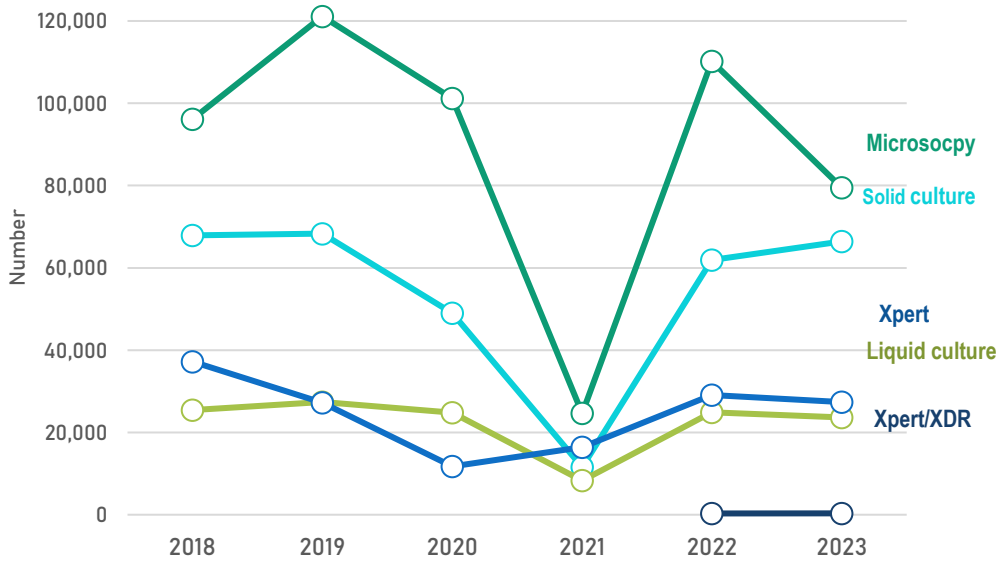
Shortening the duration of disease through detection and treatment of cases will also reduce the prevalence of TB disease, and therefore, transmission. Moldova has well-functioning TB laboratory network organized on three diagnostic levels. The first level consists of 50 GeneXpert/smear microscopy centres, located at outpatient TB facilities (serving 77 000 population per facility on average). The second level includes three reference laboratories (in Vorniceni, Balti and Bender) that in addition to Xpert and microscopy, perform culture, first-line LPA, second-line LPA, and phenotypic DST for FLD, SDL as well as for Mfx, BDQ and LZD. These laboratories are responsible for quality control of first level laboratories in respective areas. The third level is represented by NRL, located at Institute of pneumology. NRL has the leading role in organization of TB laboratory service, development of protocols for laboratory diagnosis, training and supervision. (Table 3).

Table 2. Number sites providing smear, Xpert, culture and DST services, 2023

Sector	Number of TB diagnostic facilities	DSM	Xpert MTB/RIF	Solid media investigations (e.g. LJ)			Liquid media investigations (automated MGIT)			Line Probe Assays (LPA)	
				Culture	DST to FLDs	DST to SLDs	Culture	DST to SLDs	DST to FLDs	GenoType MTBDR-Plus	GenoType MTBDR-sl
Civilian sector total	54	54	54	4	4	4	4	4	4	4	4
Penitentiary sector	3	3	3	0	0	0	0	0	0	0	0
Country total	**57**	**57**	**57**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**

Between 2018 and 2023, the laboratory TB laboratory testing varied year-to-year with the sharp reduction in 2020 and especially in 2021, followed further recovery. However, almost none of the tests. However, up to 2023 the volume of xpert tests and liquid media didn't regain to pre-pandemic level (Figure 31).

Figure 31. The trend in number of microscopy, Xpert, and culture examinations, 2018-2023



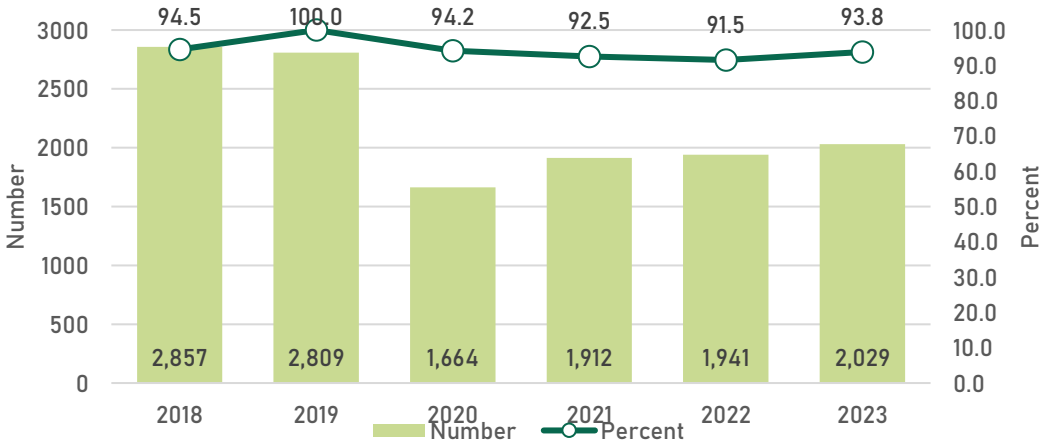
Laboratory data should be interpreted cautiously, as repeat diagnostic testing was common practice, and actual number of people with presumptive TB tested actually might be much lower. To avoid un-necessary testing, NRL

undertake measure to refuse to do the test the person already has laboratory test result recorded in SIME-TB. Therefore, the reduction of the Xpert tests might reflect above efforts.

3.5.2. Xpert testing coverage among people with new and recurrent TB

In 2023, Xpert testing in Republic of Moldova was used as the initial diagnostic test for of the people newly diagnosed with TB in 2023, up from 91.5% in 2022. Since 2018, Xpert testing coverage in Moldova has remained above 90%, indicating almost universal access to WHO recommended rapid diagnostic testing (Figure 32).

Figure 32. Trend in Xpert testing coverage among people diagnosed with new episode of TB



3.5.3. Trend in number of people tested for TB

The number of people tested for TB in Republic of Moldova over the recent years largely varied between 12K to 37K with sharp reduction in 2020 and 2021 and comparatively slow recovery in 2022 and 2023. Trend in the percentage of people initially tested with Xpert who had positive test results provides an indication of the trend in the burden of disease in the population in case of stable testing rate. However, because number of Xpert tests in Moldova from year-to-year varies over 3 times, also there are concerns of repeat testing, therefore, monitoring of positivity trend becomes less informative for the underlying TB burden. At national level positivity ranges from 6.7% up to 10.5% and negatively associated with the absolute number of tests performed (Figure 33).

Figure 33. Trend in number of xpert tests for diagnostic purpose and percent of positives

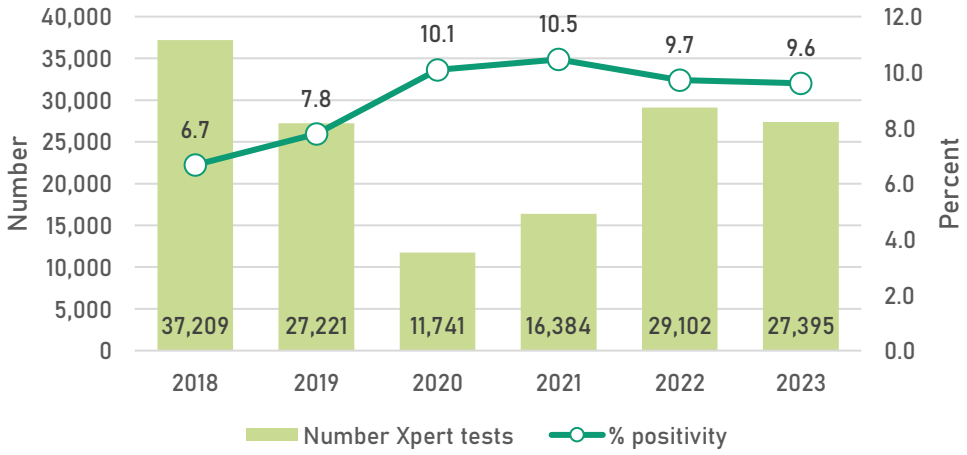
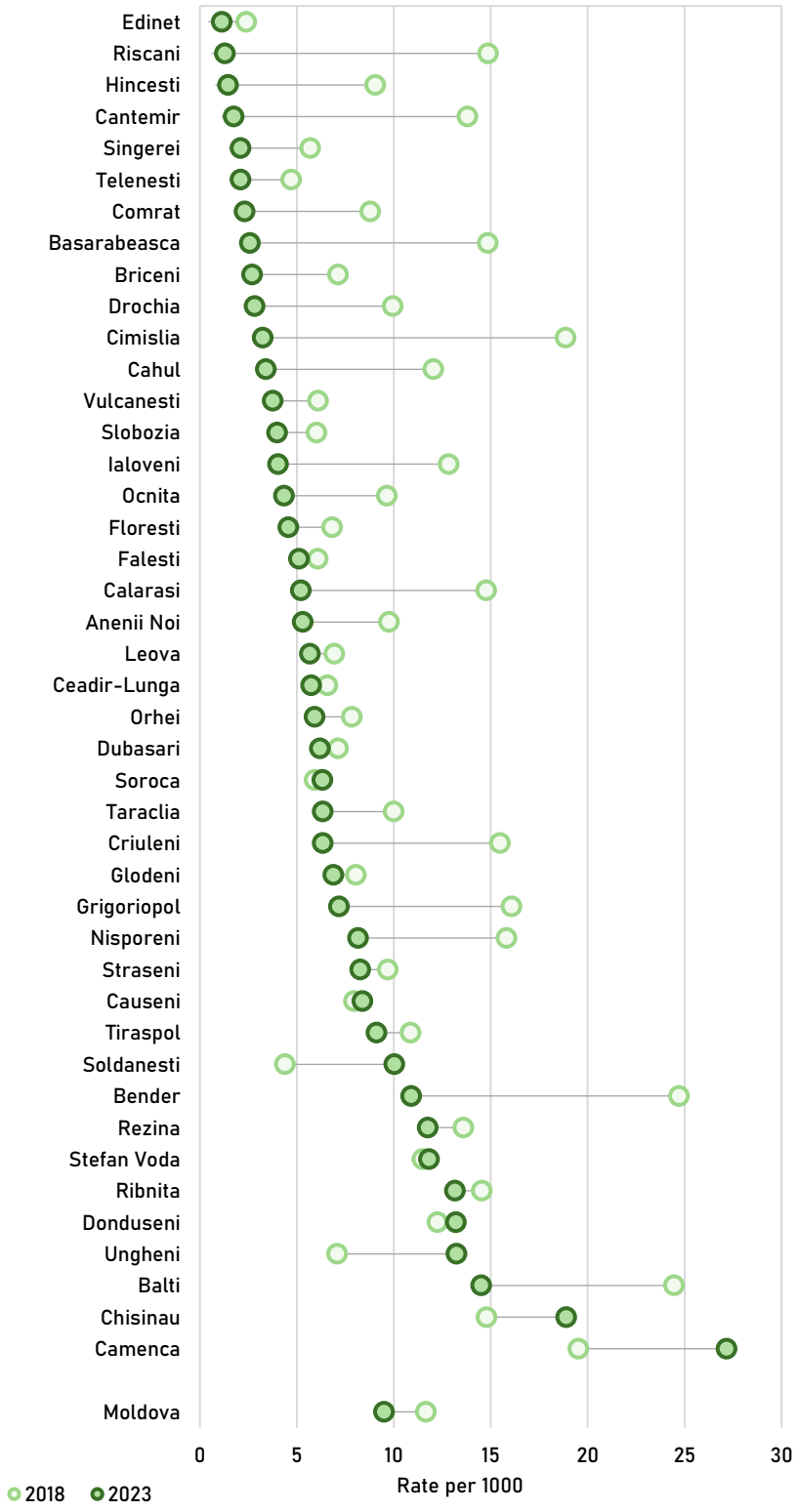


Figure 34. Xpert testing rate per 1,000 population by rayons in 2018 and 2023

Chisinau testing rate is calculated as the sum of all municipal laboratories and NRL testes over Chisinau population * 1000, which results to an over-estimation as NRL performs tests for entire country. Likewise, RRL testing rates also is assumed to be inflated.



While at national level Xpert testing was 9.5 per 1000 population, down from 11.6 in 2018, there was substantial variation in Xpert per capita testing rate ranging from 1.1 in Edinet to 27.2. in Camenca (Figure 34). It is noteworthy that most of sub-national unites reported decline of testing in 2023 compared to 2018 in relation to population with few exception. It is noteworthy that few rayons with low testing rate also report very low notification rate (Edinet, Riskani, Vulcanesti). This might hint that low notification is due to low testing/referral. Other rayons although have low testing rate compared to national average, report higher notification rates (Floresti, Slobozia, Telenesti). Both types of outliers have potential to increase notification rate and improve case detection just by increasing the number of presumptive people to be tested for TB (Figure 35)

Figure 35. Scatterplot of TB notification rate per 100,000 population against Xpert population testing rate per 1000 population by rayon, 2023

Each circle represents pair of level data point. Size of circle is proportional to rayon population. Chisinau testing rate is calculated as the sum of all municipal laboratories and NRL testes over Chisinau population * 1000, which results to an over-estimation as NRL performs tests for entire country. Likewise, RRL testing rates also is assumed to be inflated

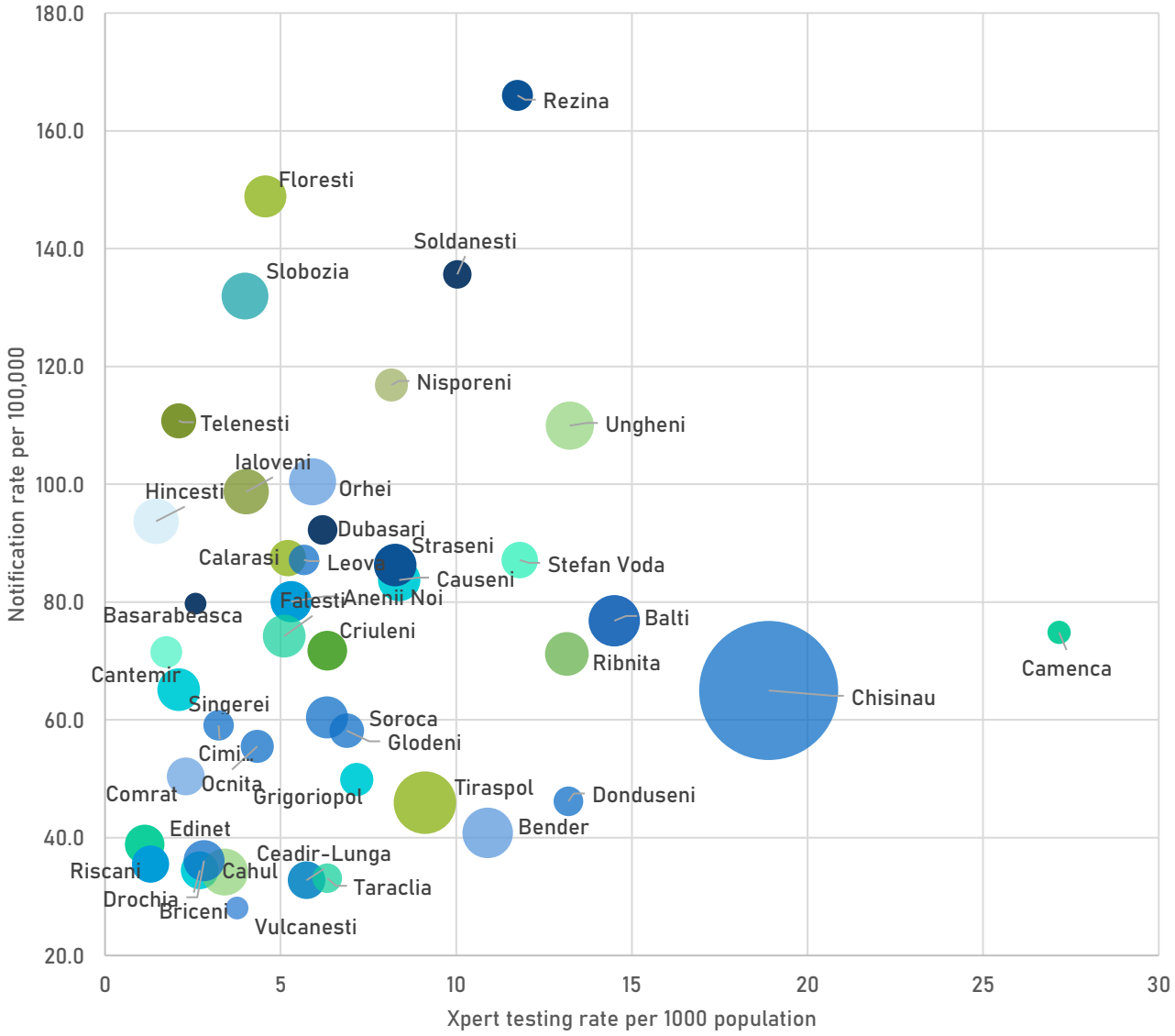
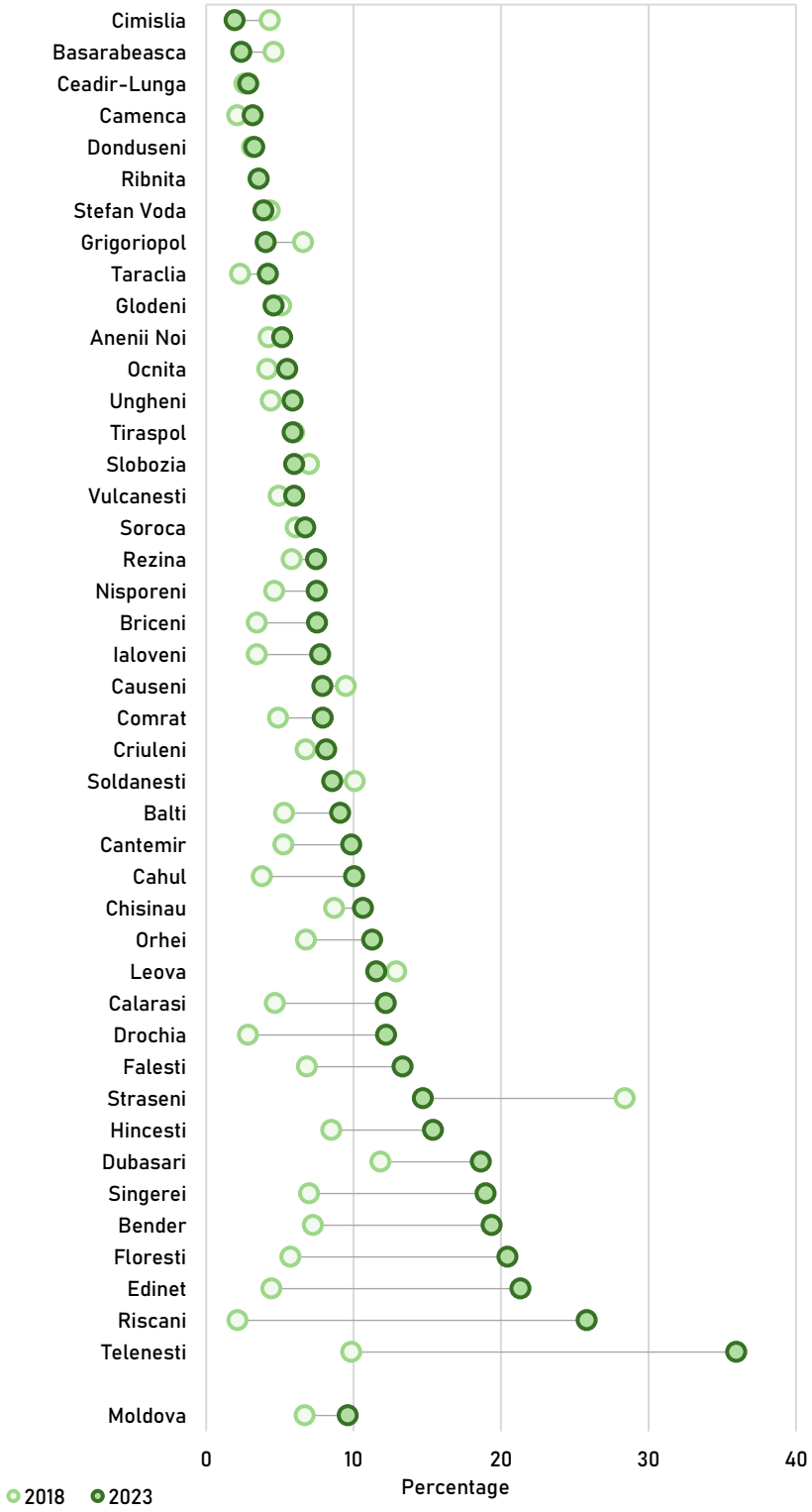


Figure 36. Percentage of people with positive MTB tested by GeneXpert by rayons, 2018 and 2023

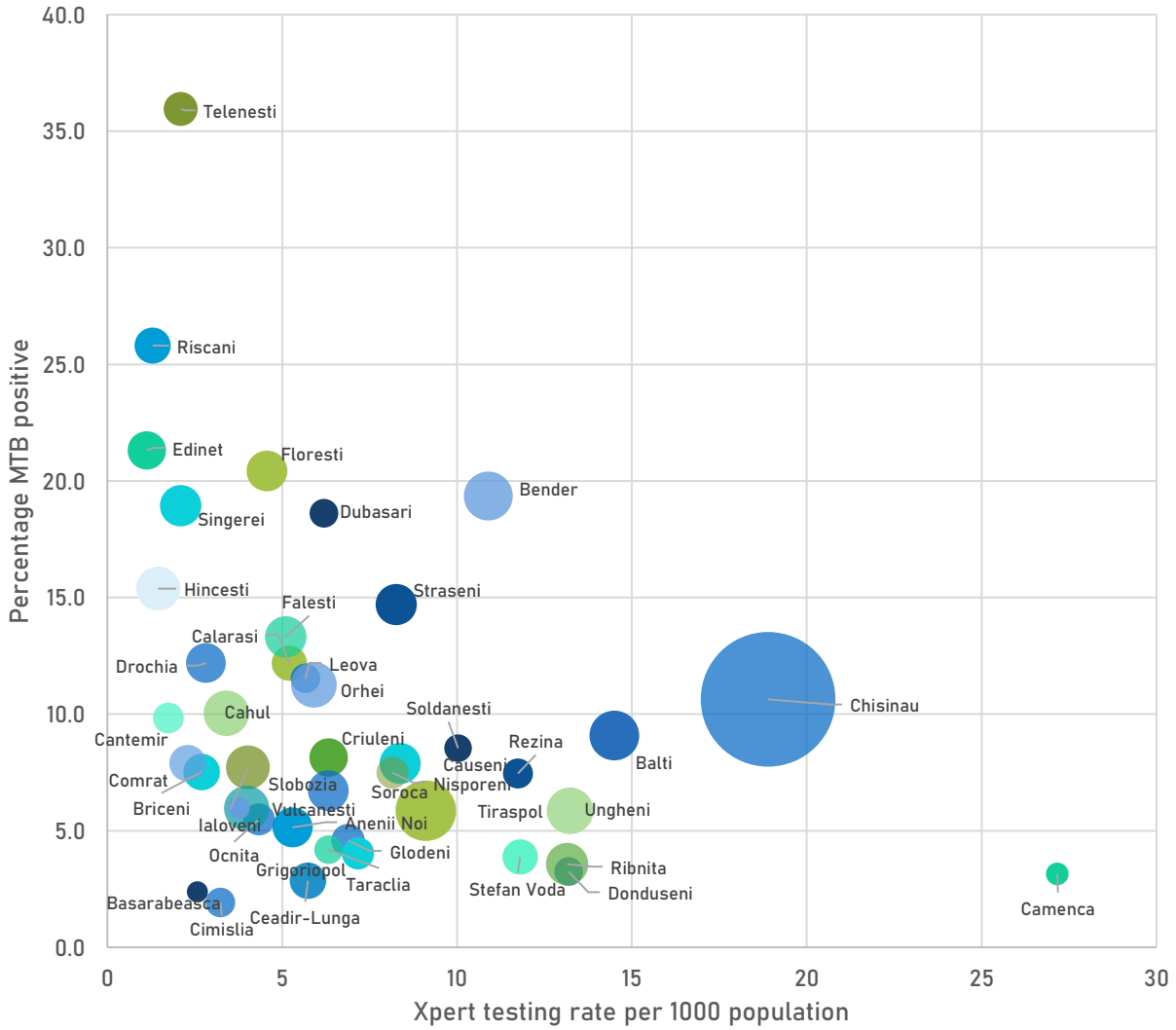
Chisinau result include sum of tests of NRL and municipal laboratories in Chisinau



GeneXpert test positivity also provides an indication of the level of diagnostic effort in relation to TB burden among tested. Low positivity suggests a lack of precision in deciding who to test, while high positivity among tested suggests suboptimal efforts to detect people with TB in communities. In 2023 Xpert positivity across sub-national unites ranged substantially from 1.9% to 36%. Ten sub-national units reported below 5% positivity, while another eight sub-national units percentage of people with positive MTB was above 15%, including, HInceti, Dubasari, Singerei, Bender, Floresti, Edinet, Riscani and Telenesti (Figure 36). It is noteworthy that many of listed with high positivity also report low Xpert testing rate per capita population (Telenesti, Riscani, Edinet, Floresti, Singerei) indicating that those areas have a good potential to increase TB notification (Figure 37).

Figure 37. Scatterplot of percentage of people MTB positive among those tested with Xpert against Xpert testing rate per 1000 population by rayon, 2023

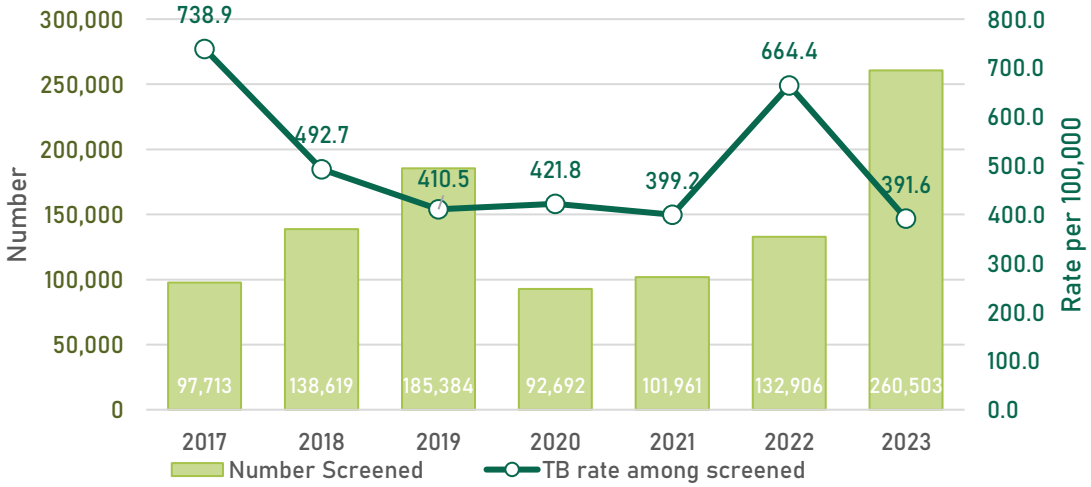
Each circle represents pair of level data point. The size of circle is proportional to rayon population. Chisinau testing rate is calculated as the sum of all municipal laboratories and NRL testes over Chisinau population * 1000, which results to an over-estimation as NRL performs tests for entire country. Likewise, RRL testing rates also is assumed to be inflated



3.5.4. Trend in number of people screened for TB

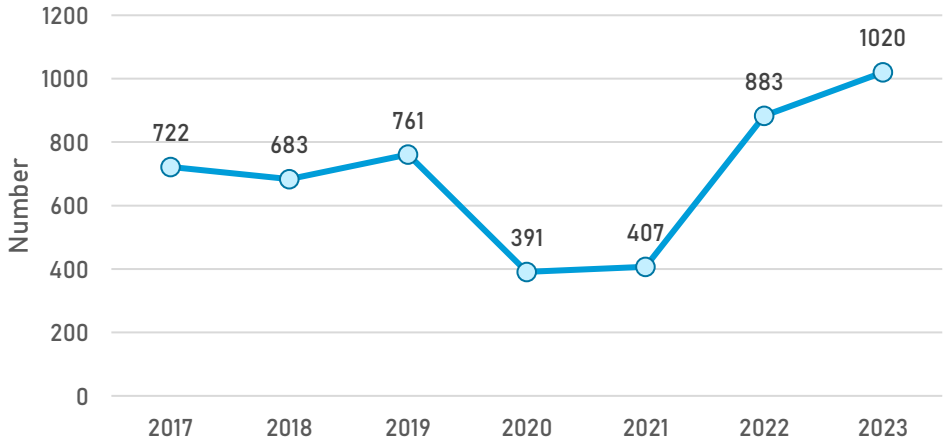
National guideline define 18 groups of people at risk to be systematically screened for TB, TBI and TPT, including household contacts, close contacts of people with TB, prison population, PLHIV, homeless people, active smokers, IDUs, alcohol abusers, people with diabetes etc[11]. To reach the people at risk in remote communities National TB program since 2018 mobile radiological installations (machine-based) have been used, which were equipped with CAD in 2022. Since 2023, ultra-portable radiological installations equipped with CAD have also been used. Number of people screened for TB disease increased over the time with some variation reaching 260,000 in 2023 which is the highest level ever recorded over the recent seven years but still 74,8% of planned[12] (Figure 38).

Figure 38. Number of people at risk screened for TB and prevalence of TB among screened, 2017-2023



Number of people detected among those screened follow the same trajectory as number of people screened, with lowest level in 2020 and reaching to its peak in 2023 with 1020 people detected among those screened (Figure 39). This makes about 43% of all people notified with TB disease.

Figure 39. Number of people with TB detected by ACF, 2017-2023



[11] Tuberculosis in adults: National clinical protocols, 6th edition, PCN-123, Ministry of Health of Republic of Moldova, Chisinau, 2024. [online] Accessed from https://simetb.ifp.md/Download/oficial_docs/Ordin_MS_2024_01_31_nr_121_protocol.pdf

[12] Report on implementation of national Tuberculosis program 2023 "Realizarile Programului national de raspuns la tuberculoza pentru anul 2023 (in Romanian) [online]. Accessed from https://simetb.ifp.md/Download/tbreps.excel/

3.5.5. Contact tracing and LTBI treatment coverage

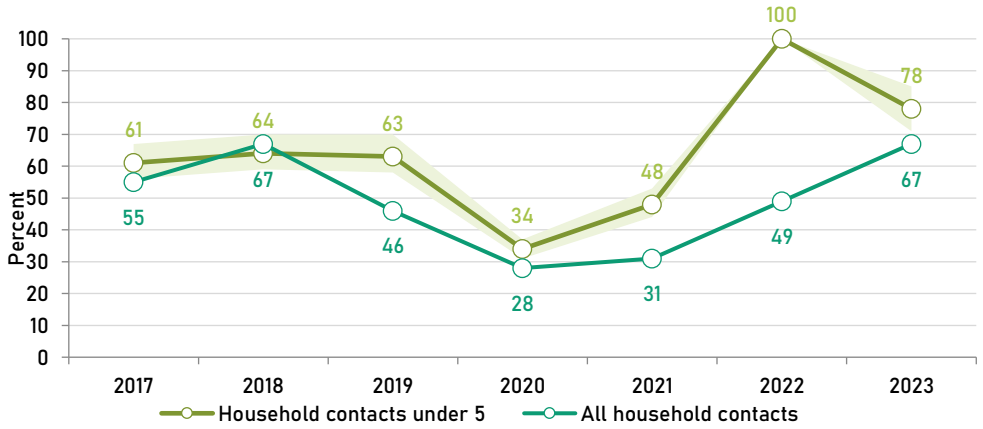
According to national guidelines, all household and close contacts of TB patients, regardless of site if disease and bacteriological confirmation are subject of active screening for TB in Republic of Moldova. Total number of identified contacts and contacts U5 between 2019 and 2023 largely varied from year-to-year with sharp decline in 2020 and 2021. Considering the average number of household size in Moldova is about 2.89, the average number of 6.8 contacts per index case as of 2023 surveillance results is an indication of extensive contact tracing coverage. Between 2019 and 2023 the percentage of people diagnosed with TB among the contacts screened ranged from 1.3% to 7.4% among all age groups and 3.9-10% among children U5. There was no clear trend of TB yield among the contacts. Number of child TB cases among contacts remains largely stable. TB prevalence among contacts in Republic of Moldova is higher compared to the finding in other settings (Table 4). A meta-analysis based on 203 published studies showed about 3.1% TB prevalence among contacts in low and middle countries and 1.4% (95%CI 1.1-1.8%) among high income countries[13]. The possible reason for the high yield of TB among contacts might be delay in TB detection, as well as the high prevalence of alcohol abuse, smoking, poor health care seeking behavior, limited access to health care services

Table 3. Number of TB contacts screened and yield of TB cases among contacts

Year	People with new episode of TB	Number of contacts identified		Mean N contacts identified per index case	TB cases detected among contacts				U5 TPT enrolled	
		<5 yr.	all ages		<5 yr.	%	all ages	%	<5 yr.	all ages
2019	2,809	562	8,031	2.9	35	6.2%	387	4.8%	471	2,134
2020	1,767	241	4,026	2.3	24	10%	299	7.4%	106	550
2021	2,067	316	5,812	2.8	32	10.1%	337	5.8%	109	735
2022	2,121	824	8,037	3.8	32	3.9%	432	5.4%	380	1,435
2023	2,164	465	14,636	6.8	31	6.7%	195	1.3%	195	2,387

According to WHO estimates accounting total number of pulmonary bacteriologically confirmed cases, households size and percentage of children under 5 years of age among the population, there are about 210 (range 190-230) children under 5 eligible for preventive TB treatment. Thuse TPT coverage among children as of 2023 is estimated 78% (71-85), down from 100% in 2022, but higher than recorded between 2017-2022 (Figure 40)

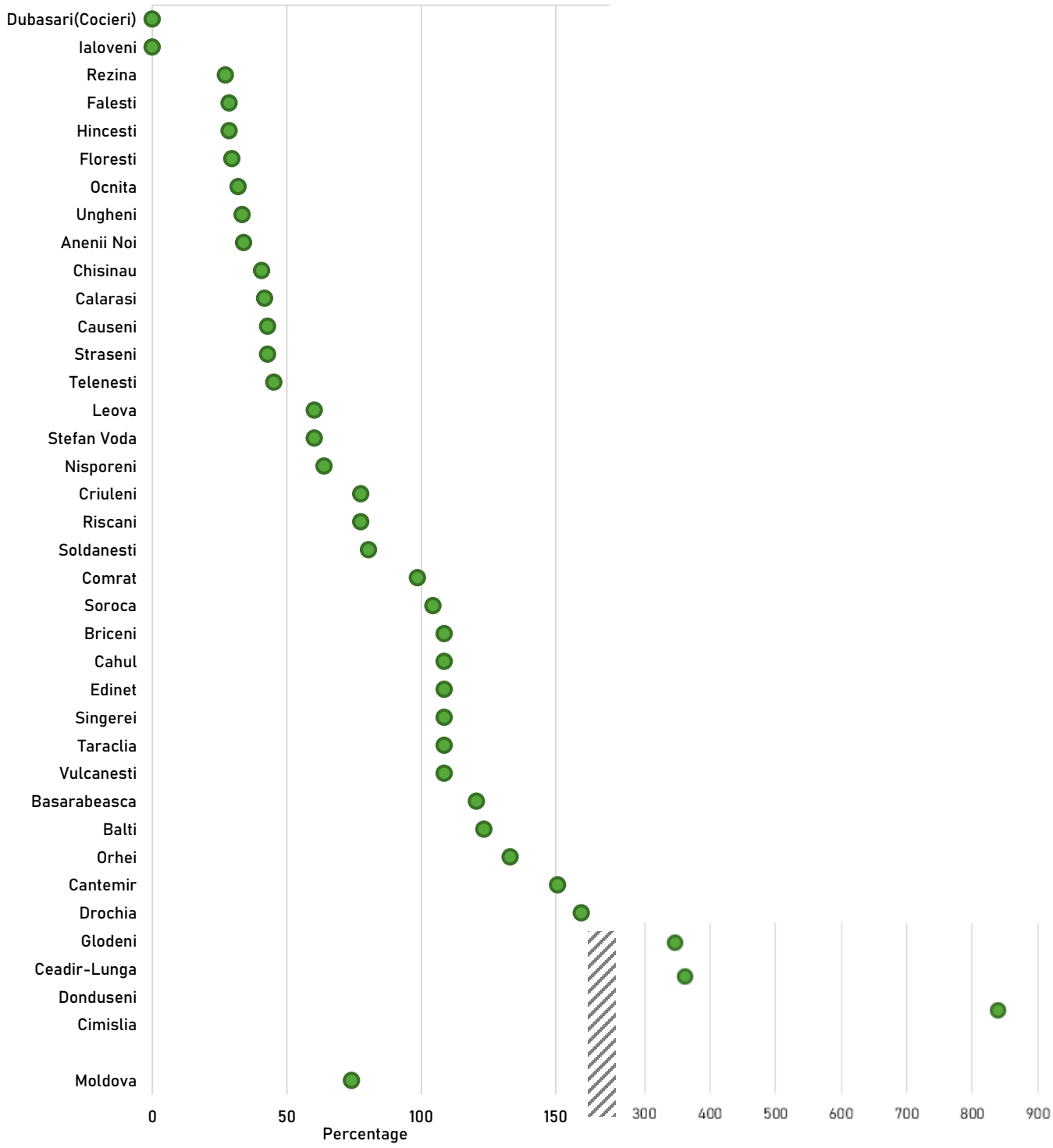
Figure 40. TPT coverage among children under 5 years of age, 2017-2023



[13] Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: A systematic review and meta-analysis. *Eur Respir J*. 2013;41(1):140-156. doi:10.1183/09031936.00070812

Total number of household contacts of bacteriologically confirmed PTB cases eligible for TPT treatment according to WHO estimates in 2023 was 2,500 (UI: 2,400-2,500). TPT coverage among all household contacts is 67% (65-69%), up from 49% recorded in 2022.

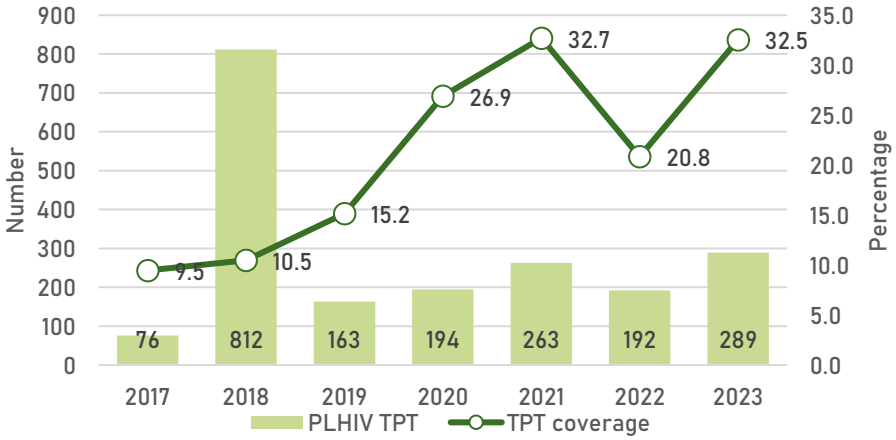
Figure 41. TPT coverage among children under 5 years of age in rayons with available data, 2017-2023



At subnational level in rayons with reported data on TPT coverage among children under 5 years of age ranged from 0 (Dubasar/Cocieri, Ialoveni) to 838% (Cimislia). Overall, in 14 of 37 rayons with TPT related data, TPT coverage was below 50% (Figure 41).

Moldova has progressively scaled up access to TPT for people living with HIV, aligning with WHO guidelines. These efforts aim to reduce the risk of TB infection progressing to active TB, which is a significant risk factor in immunocompromised individuals. To enhance uptake and completion rate Moldova introduced and scaled up shorter and more tolerable rifampicin-containing TPT regimen. TPT coveage among PLHIV in 2023 was 32.5%, up from 9.5% reported in 2017 (Figure 42). Challenge faced to achieve higher coverage includes burden of RR-TB, as well as stigma associated with HIV, high prevalence of alcohol abose socially dis-advantaged people among PLHIV and high hindering uptake of TPT.

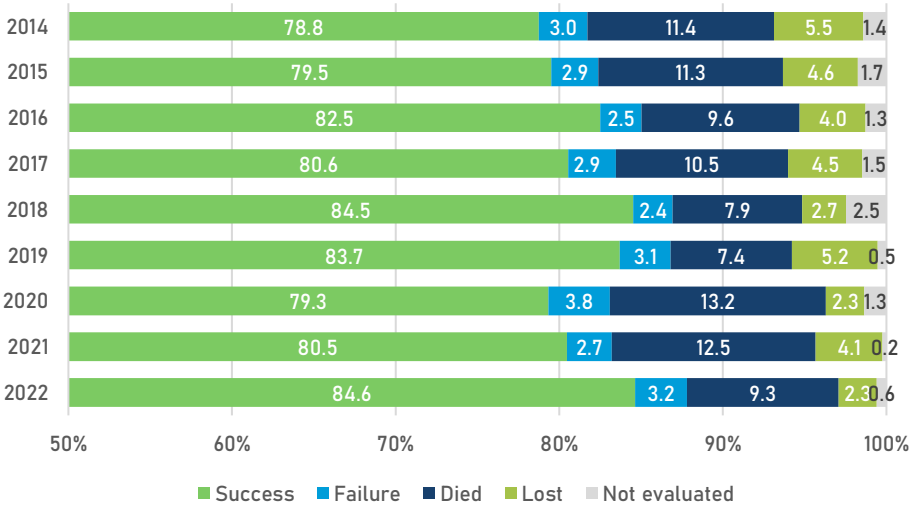
Figure 42. Number of PLHIV newly enrolled into ART and started TPT and TPT treatment coverage, 2017-2023



3.5.6. TB treatment outcome

TB treatment is one of the most effective interventions in TB control to reduce the prevalent cases in the population and reduce the transmission of infection. Between 2014 and 2022 the treatment success rate among new and recurrent TB eligible for first-line treatment slightly increased from 78.8 to 84.6%. This is higher compared to 75.3 TSR reported in WHO European region, but somewhat below of Regional target of strategy target of 90% TSR.

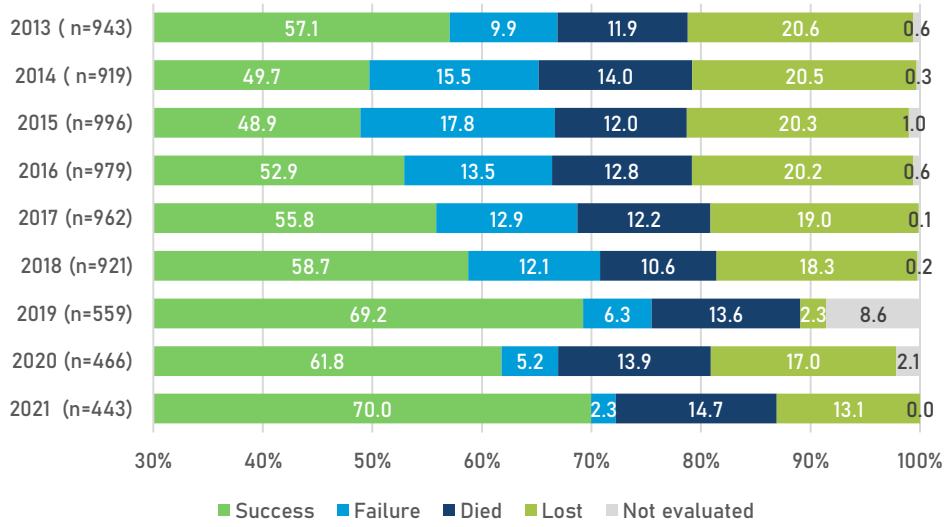
Figure 43. Treatment outcomes of people with new and recurrent TB, 2014-2022



Main reason of unfavourable outcome is death, which over the time steadily increased. Of positive note, the proportion of lost to follow-up over time steadily declined which might reflect patient-centred efforts, such as video-supported treatment, social support in form of vouchers for food conditional to treatment adherence etc. High death rate can hint that most likely the patients with TB are detected at the advances stage of disease. Other common reason of increased fatality is low access to ART among PLHIV (Figure 43).

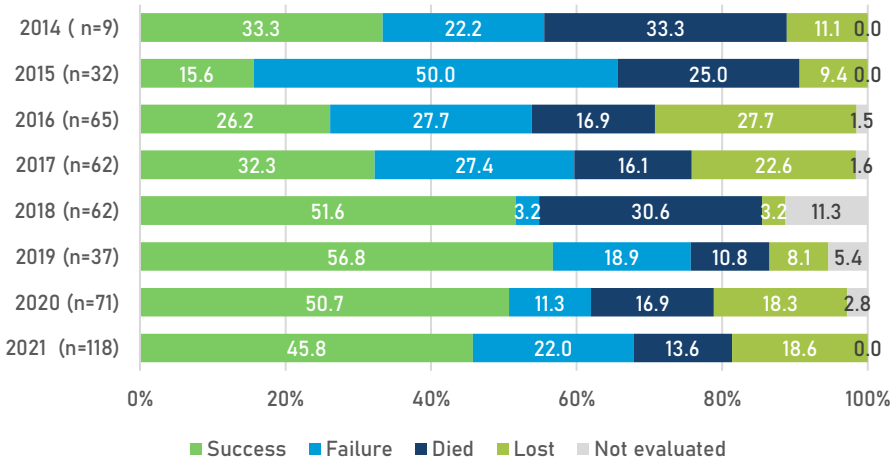
Between 2015 and 2021 treatment success rate among RR/MDR-TB patients without FQ resistance gradually increased from 49.7 to 70% (Figure 44). Improvement of treatment outcome was attributed largely by the impressive reduction of treatment failure (from 17.8% in 2015 to 2.3% in 2023) and partially by the reduction of lost to-follow-up, most likely related to introduction and scale up new fully oral-shorter treatment regimens and rapid methods of testing for FQ resistance.

Figure 44. Treatment outcomes of RR-TB patients without FQ resistance 2013-2021



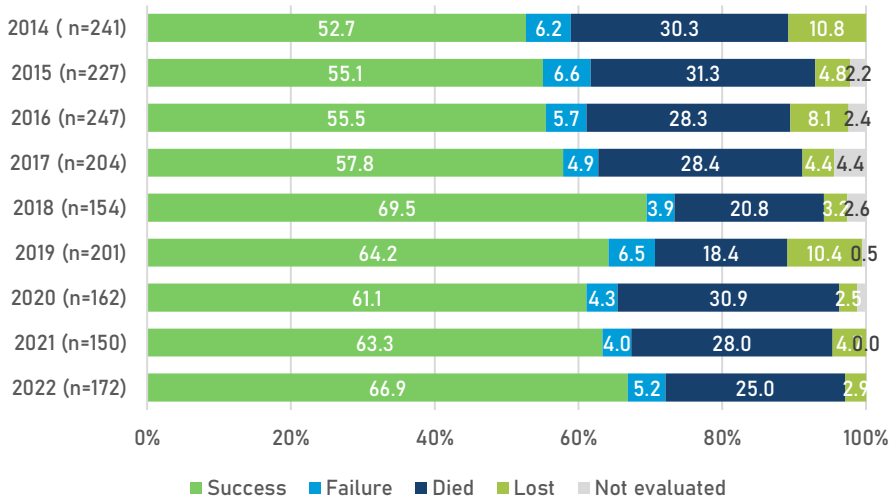
Treatment outcome among people treated for pre-XDR/XDR-TB was 45.8% in 2021 cohort, down from 50.7% reported in 2020 and 56.8% in 2019 treatment cohorts. Main reason of unfavourable treatment outcome is treatment failure, followed by lost to follow-up and death (Figure 45).

Figure 45. Treatment outcomes of people treated for pre-XDR/XDR-TB 2014-2021



Treatment success rate among HIV/TB patients in 2022 cohort was 66.9%. Although there is a slight improvement over the time, and this level is higher compared to 54.5% European average reported in 2022, nevertheless, there is an ample room for the improvement. Main reason of unfavorable outcome in TB/HIV cohort is death, which commonly is related to low ART coverage among PLHIV, due to lack of adherence or late detection. (Figure 46).

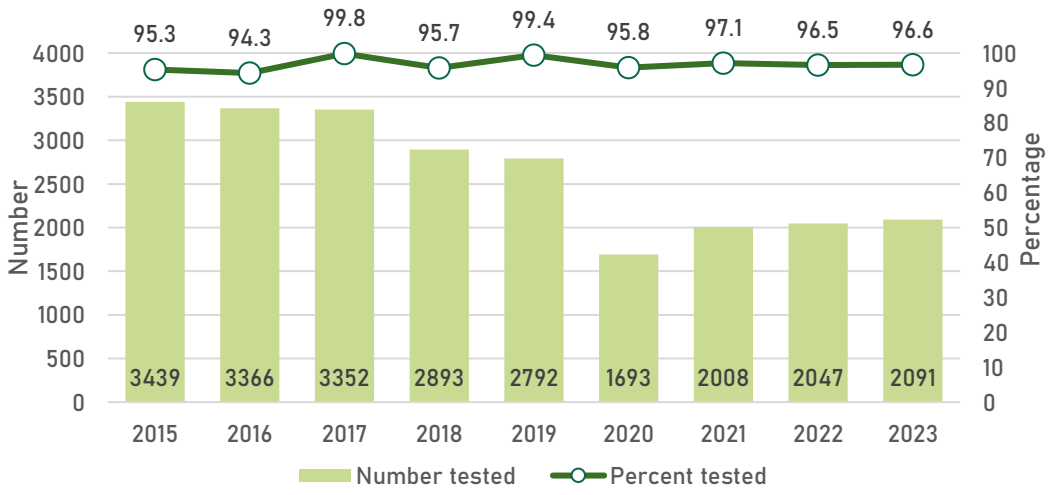
Figure 46. Treatment outcomes of new and recurrent HIV/TB cases 2014-2022



3.5.7. HIV testing and ART coverage people with new episode of TB

To ensure effective and integrated TB and HIV service delivery, WHO recommends HIV testing for all people diagnosed with TB; provision of antiretroviral treatment (ART) to those who are HIV-positive; as well as regular TB screening for PLHIV; and offer of preventive TB treatment to PLHIV who do not have active TB. HIV testing of among people diagnosed with TB over last 10 years in the republic of Moldova consistently exceeded 90% and in 2023 was 96.6% (Figure 47).

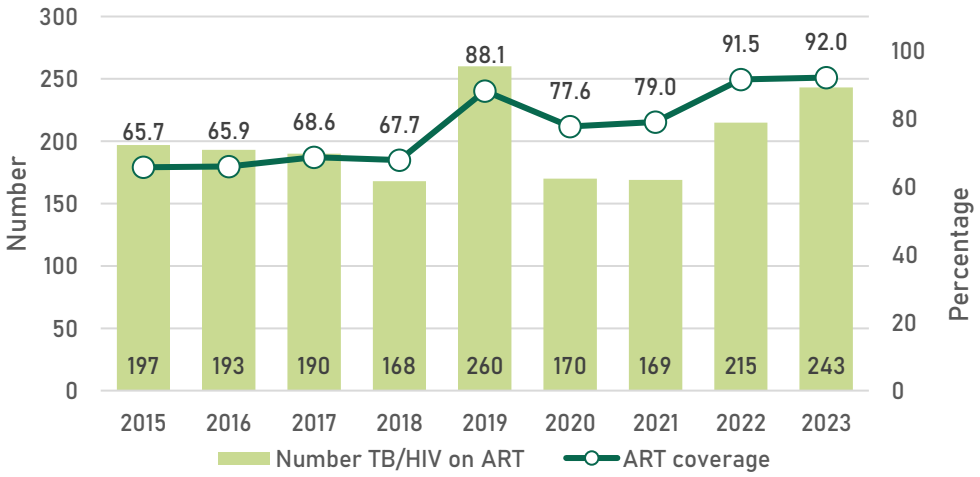
Figure 47. HIV testing coverage among people with new episode of TB, 2015-2023



ART coverage among people with TB/HIV co-infection has been improving in recent years in the Republic of Moldova. In 2023 ART coverage people co-infected with TB/HIV has been over 92%, up from 67.7% reported in 2018

(Figure 48). Additional efforts will be needed to achieve Regional Action plan 2025 milestone of at least 99% TPT coverage among PLHIV by 2025.

Figure 48. ART coverage among people with TB/HIV co-infection, 2015-2023

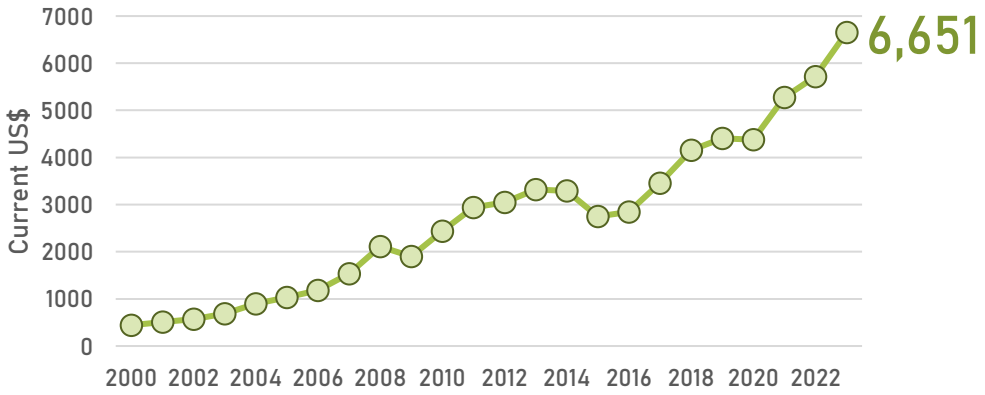


3.6. TB determinants: External factors

3.6.1. Per capita gross national product

Economic growth is expected to drive TB epidemic to downward. It may affect numerous TB determinants such as overcrowding, education, nutrition and health care-seeking behaviour, and thus contribute to reduced transmission of infection and a reduced risk of progression from infection to disease and Gross National Domestic Product (GDP) per capita is the most commonly used measures of county economic status. As of 2023, according to WB classification Republic of Moldova belongs to the upper middle-income countries. In recent years Republic of Moldova has experienced a notable upward trend in its GDP per capita rising approximately 52% over three-year period from 2020 to 2023, which indicates a positive economic trajectory. (Figure 49)

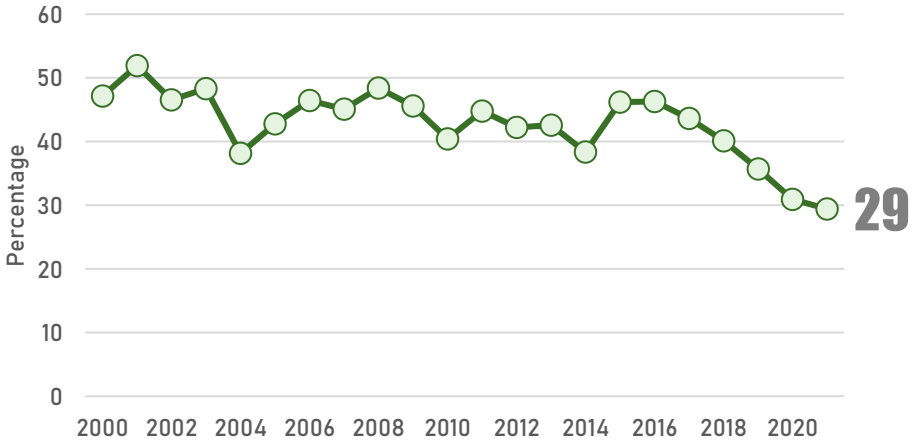
Figure 49. GDP per capita (current US$), 2000–2023



3.6.2. Coverage of financial protection for health care costs

As of 2021, 29% of total health expenditure in Republic of Moldova was covered by out-of-pocket (OOP)[14]. Between 2000 and 2016, the proportion covered by OOP has been largely stable. Starting 2016 percent of OOP gradually declined from 46% to 29% (Figure 50). However, it is still high. According to WHO general benchmarks for middle-income countries OOP should ideally be kept below 20%. Therefore, despite of improving trends access to quality health care still might be not affordable for many vulnerable people at highest risk of TB in Moldova.

Figure 50. Out-of-pocket expenditure as a percentage of current health expenditure, 2000–2021



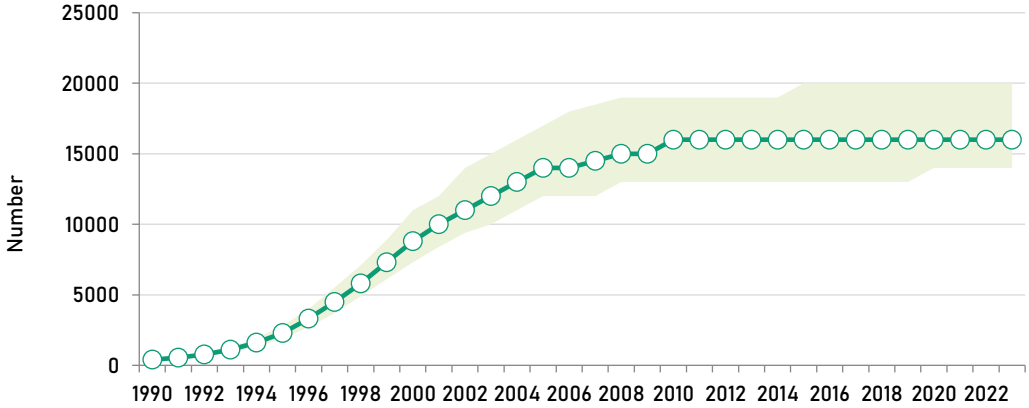
[14] Out-of-pocket expenditure (% of current health expenditure) [online]. Washington, DC: World Bank (https://data.worldbank.org/indicator/SH.XPD.OOPC.CH.ZS accessed 24 November 2024)

Data source: https://data.worldbank.org/indicator/SH.XPD.OOPC.CH.ZS

3.6.3. Prevalence of HIV in the general population and ART coverage

Between 1990 and 2010 the number of PLHIV in Republic of Moldova increased and since then remained relatively stable reflecting on-going prevention and treatment efforts. In 2023 there were an estimated 16,000 PLHIV (range: 14,000 – 20,000). In 2023 the estimated prevalence of HIV was below 0.9% (range: 0.7-1.1) among the adults aged 15 to 49 years[15] . In 2023 only 69% (57-84%) of PLHIV knew their status.

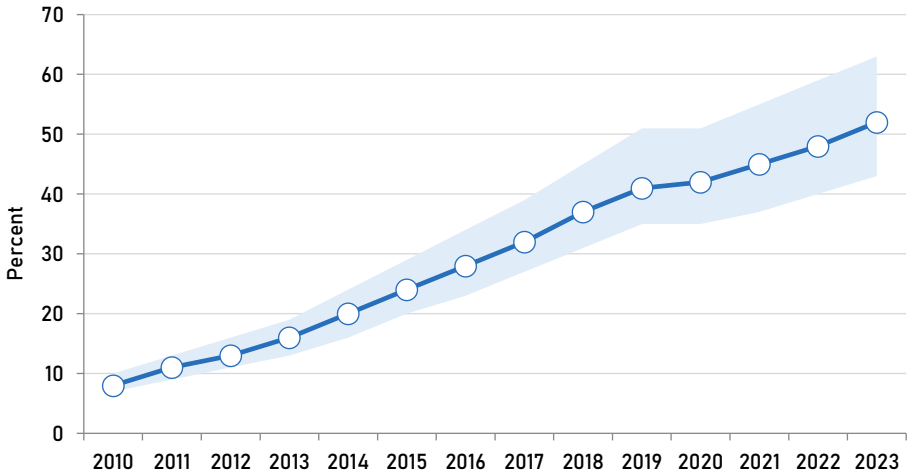
Figure 51. Trend number of people living with HIV (all ages)



Data source: https://aidsinfo.unaids.org/

There is strong evidence that ART and preventive TB treatment initiated in good time may reduce the risk of progression from infection to disease. Figure 52 shows the trend in access to ART showing gradually increase from 8% in 2010 to 52% (range: 43-63%) in 2023, which is far below of 90-90-90 target. Ongoing HIV transmission HIV combined with low ART coverage and makes HIV infection as one of key contributing factors of TB burden in Republic of Moldova.

Figure 52. Coverage of people receiving ART (all ages), 2010–2023



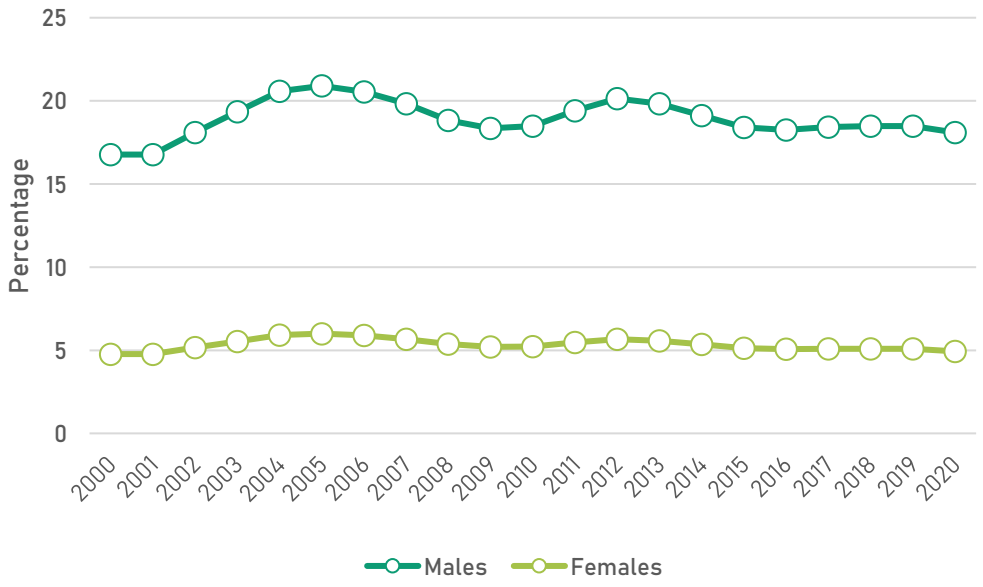
[15] Country data: Republic of Moldova [online]. Geneva: UNAIDS. (https://www.unaids.org/en/regionscountries/countries/republicofmoldova accessed on 25 November 2024).

3.6.4. Alcohol consumption

Alcohol consumption has been shown to increase the risk of infection and subsequent mortality from tuberculosis and lower respiratory infections by suppressing a wide range of immune responses via multiple biological pathways, particularly in people who engage in heavy episodic drinking or who chronically consume large amounts of alcohol. The risk rises with the increase in levels of alcohol consumption. There is a three-fold increase in the risk of tuberculosis associated with a diagnosis of alcohol use disorder. People with alcohol use disorders are at greater risk for delayed health-seeking behaviour, poor treatment adherence, treatment failure, and drug-resistant tuberculosis infection. According to WHO estimates in Republic of Moldova, about 260 (100-490) TB cases estimated to occur in Moldova in 2023 are attributed to alcohol use disorder.

Alcohol per capita (15+) consumption (in liters of pure alcohol) in 2020 was 11.1 liters (18.9 liters among males and 4.9 among women), which much higher compared to the European average of 8.9 liters recorded in 2020 (Figure 53)[16].

Figure 53. Total alcohol consumption per capita, (liters of pure alcohol) male and females 15+ years of age)

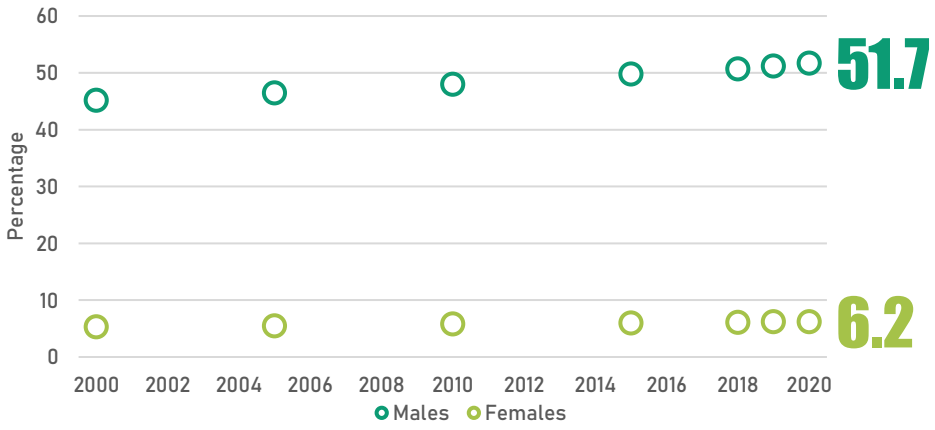


[16] Alcohol consumptions, males (% adults) Washington, DC: World Bank (https://data.worldbank.org/indicator/SH.ALC.PCAP.MA.LI. accessed 24 November 2024) and Alcohol consumptions, females (% of adults) [online]. Washington, DC: World Bank (https://data.worldbank.org/indicator/SH.ALC.PCAP.FE.LI accessed 24 November, 2024)

3.6.5. Smoking

Tobacco consumption doubles the risk of developing TB and remains a serious public health issue in the Republic of Moldova. Smoking prevalence since 2007 declined slightly in females but remain comparatively high. In 2020, the prevalence of male and female smokers in the country was 51.7% and 6.2%, respectively[17] (Figure 54).

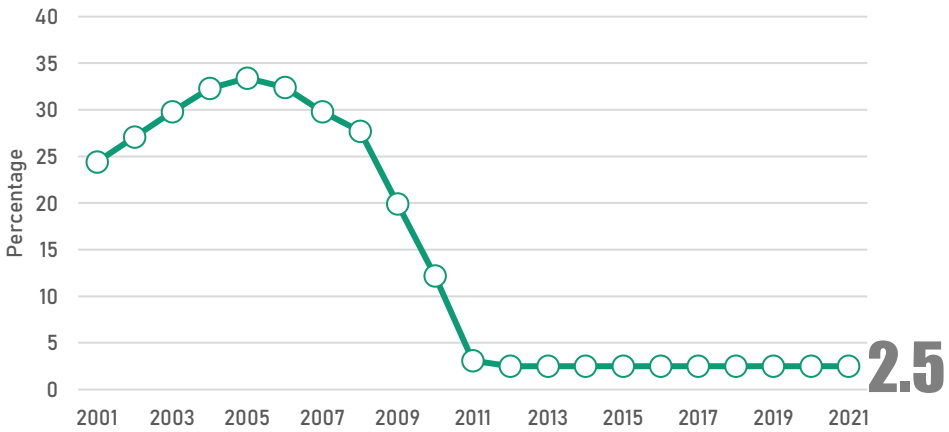
Figure 54. Trend in prevalence of smoking in adult males and females



3.6.6. Malnutrition

Malnutrition almost triples the risk of TB. It is a proximate risk factor for TB with its effect of impairing the host defence against infection. Up to 2011 the prevalence of malnutrition in Republic of Moldova sharply decreased and since then remailed low. As of 2021 it was estimated that only about 2.5% of the population was undernourished (i.e., they received below the minimum level of dietary energy consumption, also referred to as 'prevalence of undernourishment')[18]. (Figure 55)

Figure 55. Trend in prevalence of undernourishment, Republic of Moldova, 2001–2021



Data source: https://data.worldbank.org/indicator/SN.ITK.DEFC.ZS

[17] Smoking prevalence, males (% of adults) [online]. Washington, DC: World Bank (https://data.worldbank.org/indicator/sh.prv.smok.ma accessed 25 November 2024) and Smoking prevalence, females (% of adults) [online]. Washington, DC: World Bank (https://data.worldbank.org/indicator/sh.prv.smok.fe accessed 25 November 2024)

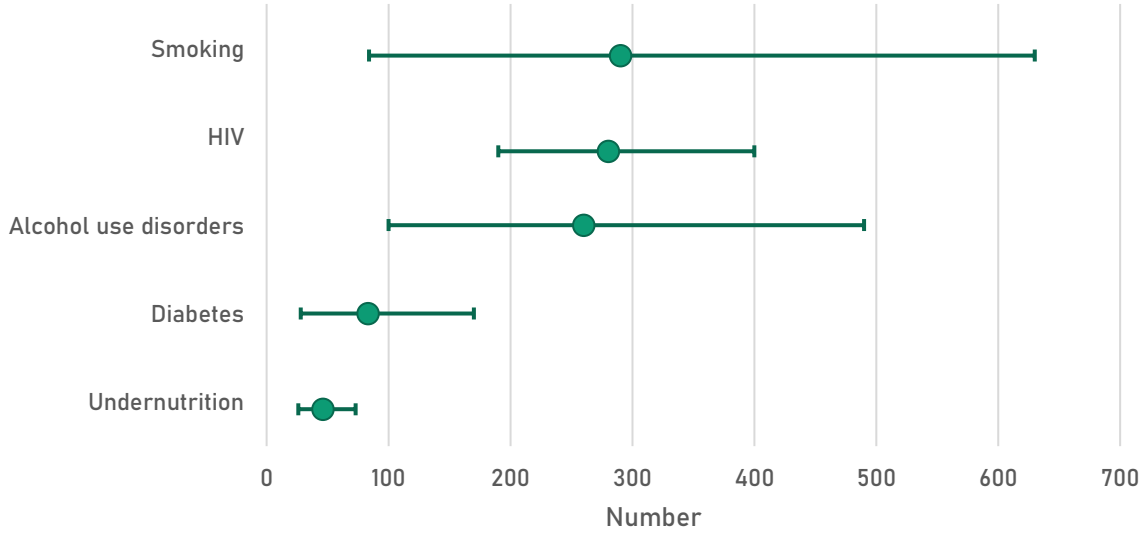
[18] Prevalence of undernourishment (% of population) [online]. Washington, DC: World Bank (https://data.worldbank.org/indicator/SN.ITK.DEFC.ZS accessed 25 November 2024)

3.6.7. Diabetes Mellitus

Diabetes triples a person's risk of developing TB. In 2021 according to the International Diabetes Federation (IDF) 5.6% of population aged 20-79 years in Republic of Moldova had diabetes[19]. Almost one in five adults with diabetes in Republic of Moldova are undiagnosed (82 thousand people). According to IDF estimates, the prevalence of diabetes in Republic of Moldova between 2011 and 2021 almost doubled. Given that a considerable number of people with diabetes are not diagnosed in Moldova, the prevalence is increasing, diabetes prevalence might be one factor moderating decline of TB burden in Republic of Moldova.

The relative contributions of key risk factors of tuberculosis are presented in the figure 56 which could be considered in prioritizing TB control interventions. As it is shown above the risks of TB in Republic of Moldova are associated with so-called modern risk risks such as smoking, HIV, alcohol use, while "traditional risks" which are associated with poverty, such as undernutrition has little contributing impact on TB burden in the country.

Figure 56. Estimated number of TB cases attributable to five risk factors, 2023

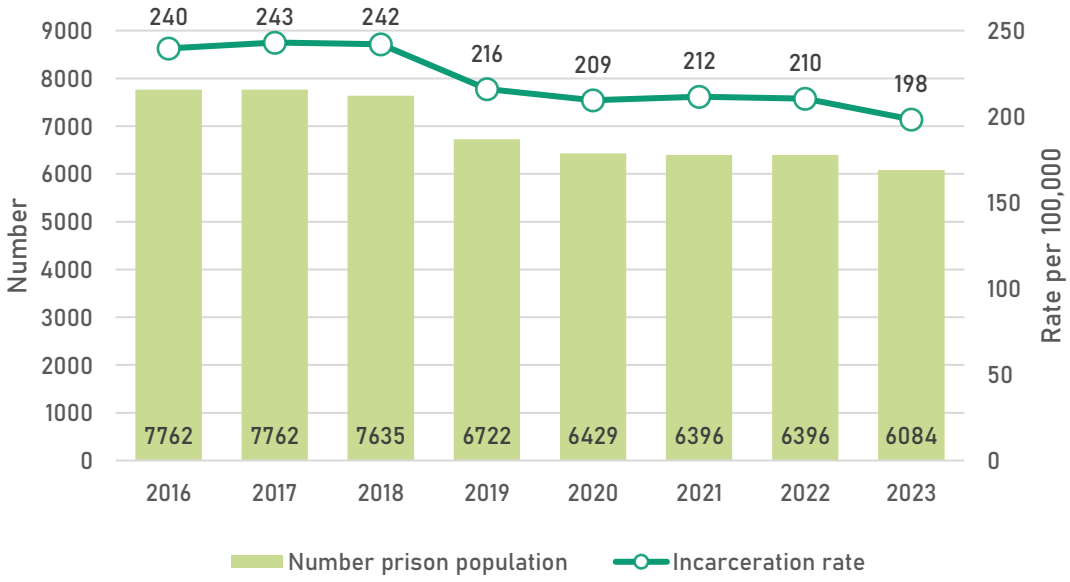


[19] IDF Diabetes Atlas 10th edition 2021: [online] (https://www.diabetesatlas.org/en/resources/)

3.6.8. Incarceration rate

The level of TB in prisons has been reported to be up to 100 times higher than that of the civilian population[20]. Therefore, the changes in incarceration rates might notably affect county TB epidemic. Between 2016 and 2023 both incarceration rate and absolute number of prison population declined in Republic of Moldova (Figure 57). As of 2023 the incarceration rate in Moldova was 198 per 100,000, which is higher than the global median incarceration rate of 149 per 100,000 population[21].

Figure 57. Trend in number and rate of prisoners per 100,000 population



3.6.9. Demographic changes

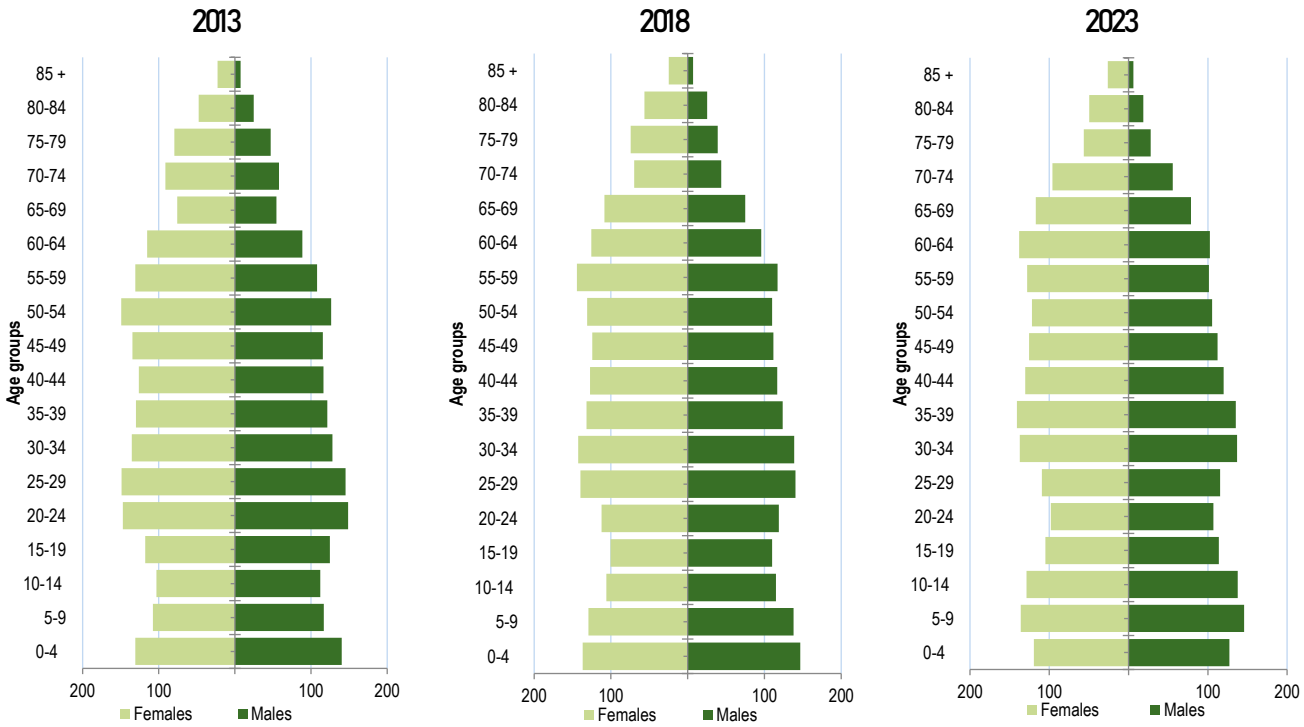
TB is strongly associated with age and sex, being more common in the population aged 25–55 years and in males. Therefore, demographic changes caused by natural movements or migration can drive the TB epidemic in a country upwards or downwards, depending on changes in the proportions of different age groups. Figure 53 shows the age pyramids for Republic of Moldova in 2013, 2018 and 2023. Each pyramid shows the distribution of the population by age and sex.

Over the past decade, Moldova's population pyramid has shifted significantly, reflecting demographic changes such as population decline, aging, and migration trends (Figure 58). Moldova's population has decreased substantially from approximately 3.41 million in 2013 to about 3.07 million in 2023 according to UN estimates and 2.51 mil according to the national estimates. This decline is due to both negative net migration (more people leaving than arriving) and a natural population decrease (more deaths than births). The proportion of people aged 60 and older has increased. By 2023, individuals aged 64+ constituted over 20% of the population, compared to 13.5% a decade ago. This reflects declining birth rates and increased life expectancy. Fertility rates have fallen steadily, with fewer births per year and a declining number of women of childbearing age. For instance, in 2022, the fertility rate was about 1.69 children per woman, compared to 1.78 in 2013.

[20] Tuberculosis in prisons. Fact Sheet. https://www.who.int/tb/areas-of-work/population-groups/prisons-facts/en/

[21] World Prison Brief Data, [online]. https://www.prisonstudies.org/highest-to-lowest/prison_population_rate?field_region_taxonomy_tid=All

Figure 58. Population pyramid (number in thousands) in Republic of Moldova in 2013, 2018 and 2023



Data source: https://population.un.org/wpp/

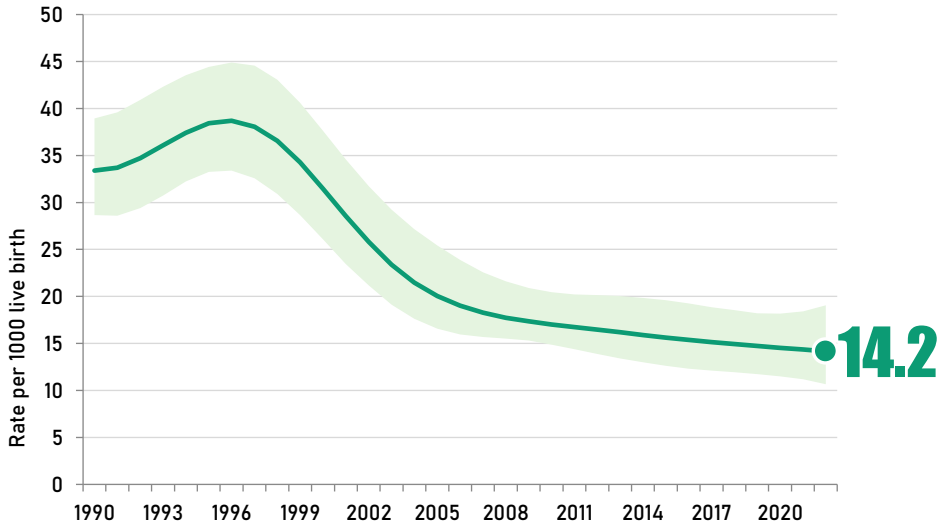
In addition, Moldova continues to experience high emigration rates, especially among younger age groups, which exacerbates the demographic imbalance. Over 43,000 people emigrated in 2022 alone[22]. These trends have resulted in a pyramid with a shrinking base (younger population) and a widening top (older age groups), highlighting the challenges Moldova faces in terms of population sustainability. Such changed in the population can moderate the decline of TB in the population.

3.6.10. Under-5 mortality

It is assumed that an improvement in the general population's health is associated with a decreased TB burden. Under-five mortality is commonly used as a proxy indicator of overall population health and therefore for access to health services. The figure below shows the estimated trend in under-five mortality in Republic of Moldova since 1990. Under-five mortality in Republic of Moldova steadily declined, and decline was accelerated especially between 2000 and 2008 reaching an average rate of decline over 5% annually. (Figure 59). This suggests that population health and access to health care have improved in Moldova over this period, which could contribute to reductions in the burden of TB. In 2022 under-five mortality in Republic of Moldova was 14.2 per 1000 live birth, which indicates that access to hight quality health care is still limited in Republic of Moldova.

[22] Moldova in figures: Statistical summary / National Bureau of Statistics of the Republic of Moldova ; editorial board: Oleg Cara (president) [et al.]. – Chişinău : [S. n.], 2023 – . – (Statistica Moldovei / Biroul Naţional de Statistică al Republicii Moldova

Figure 59. Under-five mortality rate in Republic of Moldova, per 1000 live births, 1990–2022



Data source: https://data.unicef.org/topic/child-survival/under-five-mortality/

Compared to other countries with the similar income under-five mortality in Moldova in 2022 is close median, or to what it would be expected from the size of the economy expressed in GDP per capita (Figure 60)

Figure 60. Scatterplot of under-5 mortality rate against GDP per capita (2022)

Each green circle represents a country pair of data points. Republic of Moldova is shown in red

Data sources: https://data.worldbank.org/indicator/SH.DYN.MORT,
https://data.worldbank.org/indicator/NY.GDP.PCAP.CD

4. Synthesis

4.1. Strengths of Surveillance system

Quality of surveillance

- TB surveillance system in Republic of Moldova is designed to capture all core variables recommended by WHO. There is a smooth data flow across the primary, rayon and national levels. Data transmission is implemented on continuous basis. Data verification is implemented at all levels. There are clear standard operating procedures to be implemented for each level of data verification and quality assurance.
- Since 2005 Republic of Moldova maintains nominal web-based electronic register. Presence of an established electronic system at rayon and national levels is one of the key achievements of the surveillance system in country. System is enhanced with numerous validation checks and functionalities to ensure data completeness and accuracy in the electronic system. All core variables are 100% complete, valid and internally consistent for the 2023 reporting year. The level of potential duplicate records is acceptably low (<1%). The system allows the identification of patient-level data at the national level (identify multiple episodes of TB in the same person). Transmission of data from the first subnational administrative level to the national level is implemented on real-time basis.
- Routine surveillance data produced by NTP are characterized with moderate internal consistency at national levels, most of indicators are free of implausible year-to-year variation.
- Bacteriological confirmation among pulmonary TB case in recent years increased and at national level reached to WHO set benchmark of for bacteriological confirmation of 70% for 2023 reporting year.
- There are several mechanisms in place to assure the validity of assignment of treatment outcomes, including review of steering committee the monitoring of RR/MDR/XDR, checklist of monitoring visits, annual review at national level.
- Other important strength of surveillance quality is the high access to HIV testing, Xpert testing, drug-susceptibility testing to second-line drugs which allows to monitor the trends of TB epidemic over the time and area for the timely and tailored interventions.

Coverage of surveillance system

- TB notification in Republic of Moldova is legal requirement. All bacteriologically confirmed presumptive TB cases regularly are checked to ensure that they are included into notification.
- All TB detected TB cases are notified across all country, including MDR/RR-TB cases, those diagnosed in private sector, penitentiary system, identified post-mortem, as well as those that didn't show up after diagnosed or refused to start the treatment.
- There was an improvement of access to health care services expressed by decline of child mortality, decline of OOP which is an indirect indication of improved access to TB care.
- Vital registration system has high coverage and quality. Recently it moved from paper to electronic web-based systems mainstreamed with other relevant systems and government services to send and receive data, ensure data protection and confidentiality.

Use of data and informed decision making

- NTP central team is staffed by highly skilled and motivated staff members.
- There are numerous operational studies based on routine surveillance data conducted at national and sub-national level published in peer-reviewed articles. Routine surveillance data are used for informed decision making, identification of area with issues, targeted interventions.
- Data from routine surveillance by rayon levels are thoroughly analyzed and in writing are communicated with rayon health authorities, and administration highlighting the area that needs improvement.
- Detailed annual surveillance report with analysis against the target and is produced and available online for the wide public.

4.2. Challenges of surveillance system

Quality of surveillance

- TB electronic system is stand-alone, without any interoperability with other systems. The system has no dashboard, and there are no built-in features to produce time-series analysis tables, figures. Modules are missing for nominal presumptive TB patient, close contacts and preventive TB treatment.
- Linkage between TB patients register and lab registers is not adequate. Currently automated linkage is executed if the TB patient is registered and has a TB number. For the presumptive TB patients, without TB number, laboratory data should be manually re-entered,
- Diagnosis of childhood TB presents a challenge in Moldova. The benchmark of rate ratio of children U5 to those 5-14 years is much lower than expected, indicating that either children U5 are overlooked or/and those who aged 5-14 are over diagnosed. Also, there was unplausible variation of child TB notification in 2023.
- Suboptimal bacteriological confirmation in some of area noted, suggesting possible over-diagnosis or issues in bacteriological confirmation.
- Duplicate Xpert testing
- No designated field in electronic surveillance system to assign DST status.
- It is challenging to compute the number of presumptive TB cases tested accurately using current methods
- No connectivity solutions for Gene Xperts

Coverage of surveillance system

- Although the gap between estimated and notified TB cases in the Republic of Moldova is narrowing, however TB notification can't be considered as a good proxy of TB incidence due to possible and under-detection and possible over-diagnosis. Health services have sub-optimal capacity to detect all TB patients because of limited access to health care services and high prevalence of risk factors (such as alcohol use) preventing timely health care seeking and adherence to long-lasting treatment.
- Analysis of data of number of people tested with Xpert indicates that there is a wide disparity between rayons in terms of practice of presuming of TB, testing for active TB in reference to both per capita population as well as to number of people notified with TB. Regions with a low per-capita testing rate and those with high positivity most likely have the potential to increase TB notification by referring more people for TB testing and using Xpert as the initial test for TB diagnosis.
- Under five mortality and proportion of out-of-pocket expenditure out of total health expenditure in Republic of Moldova despite of reducing trends, still remain much higher compared to WHO benchmarks, indicating that access to quality health care services in Republic of Moldova is sub-optimal. This means that there might be people with TB that are not detected by health systems due to financial barriers and/or health system capacity.
- Because of repeat Xpert testing practice, calculation of exact number of unique people tested for TB as well as prevalence of RR-TB among new and previously treated TB cases is challenging.
- Excessive percentage of positivity in some subnational area suggests that in those areas only people with obvious clinical signs and symptoms are diagnosed and there might be people with TB who are not presumed to have TB the disease and are missed by systems.
- Notification of TB among children under five years of age is below what would be expected in reference to knowledge of TB epidemiology and evidence demonstrated in high-performing countries with good TB surveillance systems, suggesting that most TB cases among children under five years of age are under-detected.
- No case-based data related to TPT and contact tracing at national and rayon level.

4.3. Recommendations

Strengthen quality of the TB surveillance system

Many of the above listed challenges of surveillance system quality will be resolved once new electronic system mainstreamed with other systems is developed and rolled-out. However, some manual additional works might be carried out to improve the quality of surveillance for upcoming transition period.

- Given that laboratory module contains numerous types of drug-resistance tests, computation of drug-resistance surveillance using this source without throughout deduplication and analysis is challenging. In addition, the source of history of previous TB treatment in laboratory module is laboratory request forms, which might be not as accurate as TB register. Therefore, to improve the quality of drug-resistance surveillance in the country, consider using TB register, instead of laboratory module as a source of drug-resistance surveillance. Consider introducing a new field in TB register to denote drug-resistance profile of individuals registered with TB. Ideally, this field might be autocompleted based on the other fields (similar to the field of bacteriological confirmation, which is automatically generated based on fields of microscopy, Xpert, liquid and solid culture test results) or can be completed manually but enhanced with validation checks with other relevant fields (GeneXpert tests and DST-results).
- Improve the accuracy of indicators of number of people tested for TB and percentage positive by deduplication of the laboratory module externally at national level ideally applying probabilistic matching using relevant statistical programs. For this purpose follow WHO guidance on internal and external linkage[23] (Russian version will be available during the first quarter of 2025).
- Adjust retrospectively annual population size at sub-national levels to allow accurate time-trend analysis. Retrospective data might be requested from NBS, otherwise, annual population growth might be calculated for each rayon and applied retrospectively as described above in Methods section of current report.
- Upgrade electronic system in line with new requirement of electronic surveillance system by streamlining with other systems through MConnect governmental portal to receive and share the data. Establish automated connectivity solutions for peripheral GeneXpert machines to avoid manual data entry and ensure fast data transmission. Aim to establish connectivity to electronic system in all peripheral laboratories in the country. Implement national PIN for linkage of data, avoid duplicate entry and improve data quality.
- Introduce electronic case-based modules for contact tracing and TPT.

Strengthen coverage of the TB surveillance system ("missed" TB cases)

- Possible reasons for under-detection of childhood TB cases in the age group 0–4 years should be investigated by paediatric international and national experts, discussed with pediatricians, intensive care physicians from pediatric hospitals, pulmonologists, family practitioners and all those who make, and report diagnoses of childhood TB. After these discussions, it may be necessary to take corrective actions, including training of health care providers, revision of the differential diagnostic algorithm adopted at general hospitals, etc.
- Assess the reasons for the disparity in access to TB testing across rayons. Monitor relevant indicators for assessing the efforts of TB detection such as percentage of positivity among people tested for Xpert, number of tests in reference to per capita population as well as per notified TB cases. Provide feedback to rayons with extremely high and low data.
- Undertake relevant measures to ensure reliability of TB diagnosis among clinically diagnosed cases in areas with sub-optimal bacteriological confirmation (below 70% of bacteriological confirmation among pulmonary TB cases). Currently NTP delegates the confirmation of diagnosis of child TB and clinically diagnosed TB to TB steering committee to eliminate possible over-diagnosis.
-

[23] Web Annex C. Record-linkage exercises. In: Consolidated guidance on tuberculosis data generation and use. Module 1: Tuberculosis surveillance. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.

- Use of data and informed decision making
  - To improve the usability of data generated by laboratory services, monitor the scale of laboratory services by the number of people tested by Xpert and the number of positives among those tested. Monitor the Xpert positivity across the regions using laboratory data. This might require linkage of the laboratory register with the TB register and deduplication of the laboratory register. Avoid massive double testing by Xpert.
  - NTP staff to be trained on advanced data management. Specifically, use WHO guidance on internal and external probabilistic linkage for deduplication until new electronic system is developed and introduced

References

1. Tuberculosis in adults: National clinical protocols, 6th edition, PCN-123, Ministry of Health of Republic of Moldova, Chisinau, 2024 [Romanian]. Accessed from https://simetb.ifp.md/Download/oficial_docs/Ordin_MS_2024_01_31_nr_121_protocol.pdf
2. Guidelines for completion of the " Notification of the patient with established diagnosis of new/recurrent active tuberculosis case and restart of treatment and its results" (Form no. 089 - 1/e) accessed from https://simetb.ifp.md/Download/ghiduri_tb/
3. Decision of government of Republic of Moldova No. HG278/2024 of 17.04.2024 on the establishment of the Information System 'Medical Certificates of Birth and Death' (eCMND) [online] link to access https://www.legis.md/cautare/getResults?doc_id=143322&lang=ru
4. National Bureau of statistics of the Republic of Moldova [online] https://statistica.gov.md/en/general-mortality-by-main-causes-of-death-in-2023-9696_61262.html
5. Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: A systematic review and meta-analysis. Eur Respir J. 2013;41(1):140-156. doi:10.1183/09031936.00070812
6. IDF Diabetes Atlas 10th edition 2021: [online] (https://www.diabetesatlas.org/data/en/)
7. Lönnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P, et al. Tuberculosis control and elimination 2010-50: cure, care, and social development. Lancet. 2010;375(9728):1814–29.
8. Realizarile Programului national de raspuns la tuberculoza pentru anul 2023 (in Romanian) [online]. Accessed from https://simetb.ifp.md/Download/tbreps.excel/
9. UNAIDS, Geneva [online] https://www.unaids.org
10. World Health Observatory [online]. Geneva: https://www.who.int/data/gho
11. WHO Consolidated guidance on tuberculosis data generation and use. Module 1. Tuberculosis surveillance. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.
12. WHO, Global tuberculosis report 2024. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.[online] https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2024
13. Web Annex B. Standards and benchmarks for tuberculosis surveillance and vital registration systems: checklist, 2nd edition. In: Consolidated guidance on tuberculosis data generation and use. Module 1: Tuberculosis surveillance. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.
14. Web Annex C. Record-linkage exercises. In: Consolidated guidance on tuberculosis data generation and use. Module 1: Tuberculosis surveillance. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.
15. WHO Global Task Force on TB Impact Measurement. "Understanding and using Tuberculosis data" WHO/HTM/TB/2014.09, Geneva: World Health Organization 2014 https://www.who.int/tb/publications/understanding_and_using_tb_data/en/
16. World Bank database, Washington, DC [online] https://data.worldbank.org
17. World Prison Brief Data, [online]. https://www.prisonstudies.org
18. World Population Prospects 2024 [online] Available from https://population.un.org/wpp/

Annex 1. Checklist for TB surveillance and vital registration system

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
TB SURVEILLANCE SYSTEM DATA QUALITY				
B1.1 Case definitions are consistent with WHO guidelines	All three benchmarks should be satisfied to meet this standard: • laboratory-confirmed cases are distinguished from clinically diagnosed cases; • new cases are distinguished from previously treated cases; • pulmonary cases are distinguished from extrapulmonary cases.	☑ **Met** ☐ Partially met ☐ Not met	To assess the benchmark the following tools were reviewed: National clinical protocol on tuberculosis in adults[24] SIME-TB electronic register, recording forms 089-1e (part A), recording form TB -090 (part A2), guidelines for the completion of TB recording forms[25], as well as surveillance data submitted to WHO global TB database. Definitions of laboratory-confirmed cases are distinguished from clinically diagnosed cases by all available laboratory confirmation methods (smear, culture, X-pert) and there are designated fields New cases are distinguished from previously treated cases. We noted that in paper and electronic registers there is no option for patients with "unknown history" of treatment. However, because in Moldova there is electronic register with the case-based records since 2005, which implies that type of any patients residing in Moldova could be accurately identified by searching the electronic register in case when need. Therefore, this gap actually has little impact for the surveillance in Moldova. Pulmonary cases are distinguished from extra-pulmonary cases in all reviewed tools mentioned above. This standard is **met**. Recommendations: Consider update TB terminology in-line with the newest WHO surveillance guidance: "recidiva" (relapse) to re-occurrence.	

[24] Tuberculosis in adults: National clinical protocols, 6th edition, PCN-123, Ministry of Health of Republic of Moldova, Chisinau, 2024 [Romanian]. Accessed from https://simetb.ifp.md/Download/oficial_docs/Ordin_MS_2024_01_31_nr_121_protocol.pdf

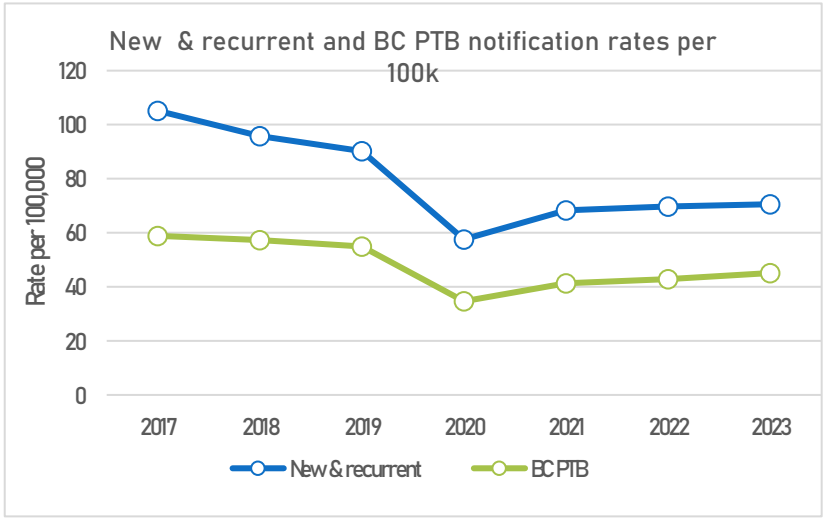
[25] Guidelines for completion of the " Notification of the patient with established diagnosis of new/recurrent active tuberculosis case and restart of treatment and its results" (Form no. 089 - 1/e) accessed from https://simetb.ifp.md/Download/ghiduri_tb/

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
B1.2 TB surveillance system is designed to capture a minimum set of variables for reported TB cases	Data are routinely collected for at least each of the following variables: • age or age group; • sex; • year of registration; • bacteriological results; • history of previous treatment; • anatomical site of disease; • for case-based systems, a patient identifier.	☑ **Met** ☐ Partially met ☐ Not met	Individual treatment cards, and the electronic register captures all core variables, including patient identifier, age, sex and year of registration; bacteriological results of TB tests (microscopy, culture, GeneXpert MTB/RIF and LPA results); history of previous treatment; site of disease for all people notified with TB. Moreover, in addition to core data detailed information on socio-economic status and under-lying risk factors are collected including area of residence (urban vs rural), occupation, living conditions, history of incarceration, number of household contacts,_comorbidities as well as DST results, HIV status and ART treatment. SIME-TB records have unique identifiers allowing identifying multiple episode of diagnosis in one patient. National personal identification number (PIN) are entered into system for all patients that have it. Another unique identifier is generated automatically by system once patient data are entered into the database. It consists of eight alphanumeric characters: first 2 characters come from first 2 letters of patient family name, 3rd character from patient first name 4th character from surname following four numeric characters indicating patient's date of birth. In addition, patient TB03 registration number as well as which also is largely used to search and identify the patients. This standard is considered **met**.	

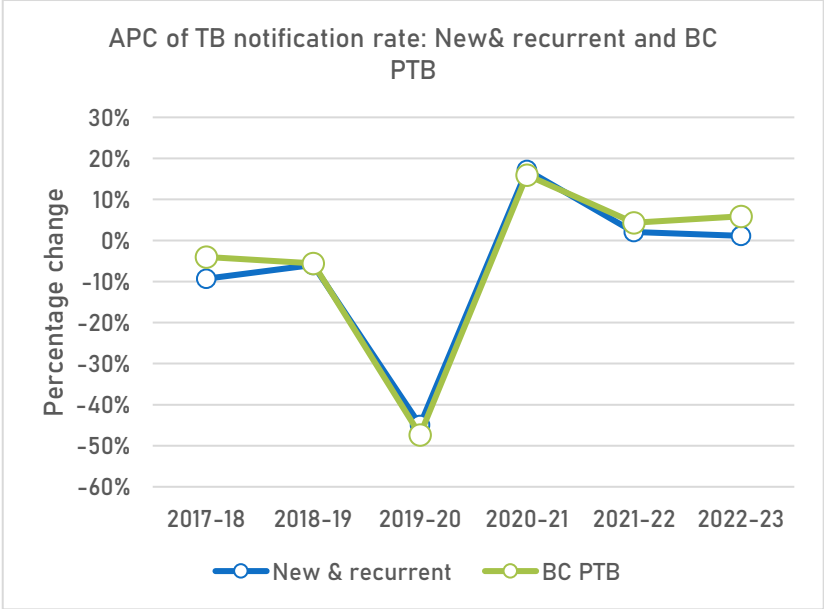
STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
B1.3 All scheduled periodic data submissions have been received and processed at the national level	For paper-based systems: • 100% of expected reports from each TB basic management unit have been received and data aggregated at national level. For national patient-based or case-based electronic systems that import data files from subnational (e.g. provincial or regional) electronic systems: • 100% of expected data files have been imported.	☑ **Met** ☐ Partially met ☐ Not met ☐Not applicable	Case-based electronic system. In Republic of Moldova reports are generated from case-based electronic system which are entered on daily basis; therefore, no file import is expected. Completeness of the reporting is ensured and validated by quarterly review (when laboratory results are checked against electronic register) and annual monitoring visits, (when all patients from individual treatment card and TB register are checked against the electronic system). Reporting of TB data by health facilities is monitoring closely by the NTP. This standard is considered fully met.	
B1.4 Data in quarterly reports (or equivalent) are accurate, complete, and internally consistent *(For paper-based systems only)*	All benchmarks should be satisfied to meet this standard: • Subtotals of the number of TB cases by age group, sex, and case type equal the total number of reported TB cases in ≥95% of quarterly reports (or equivalent) from BMUs; • The number of TB cases in ≥95% of quarterly reports (or equivalent) matches the number of cases recorded in BMU	☐ Met ☐ Partially met ☐ Not met ☑Not applicable		N/A

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	TB registers and source documents (patient treatment cards and laboratory registers); • Data for a minimum set of variables are available for ≥95% of the total number of reported TB cases in quarterly reports.			
B1.5 Data in national database are accurate, complete, internally consistent, and free of duplicates *(For electronic case-based or patient-based systems only)*	All benchmarks should be met to reach this standard: • Data validation checks are in place at national level to identify and correct invalid, inconsistent, and missing data in the minimum set (B1.2); • For each variable in the minimum set (standard B1.2), > 90% of case records are complete, valid and internally consistent for the year being assessed; • < 1% of case records in the national dataset for the year being assessed are unresolved potential duplicates.	☑ Met ☐ Partially met ☐ Not met ☐ Not applicable	SIME-TB is enhanced with range of data validation checks to prevent, identify and correct invalid, inconsistent and missing data. Most of core variables, such as name, surname, date of birth, sex, region, type of TB and site of disease are "must enter" fields, therefore without completing those variables the record could not be saved. Secondly, for most of variables (sex, geographical location, type, previous history, laboratory results) only pre-defined options are allowed to enter that appear as a drop-down menu during the data entry. In addition, fields are enhanced with the checks so, that only numbers are possible to enter into numeric fields and dates in date fields. Several fields that are supposed to be entered manually, there are no restrictions to values within plausible ranges (like registration or date of birth or diagnosis could not be in the future). SIME TB is enhanced with logical check to minimize the inconsistency, such as if the date of start of treatment is earlier than date of registration a pop-up window will appear to ask if the user wants to save the record containing error. Or once date of start of treatment is entered, a reminder appears to enter start date of treatment. Once record with incomplete data is saved a pop-up windows appears with message "do you want to save with error?" For users there is an automated option to assess the completeness and consistency of the record by pressing bottom "check for errors", which generate pop-up window highlighting all missing and inconsistent field. After the 3rd month the records became stagnated for users and it is not possible any more to make any back dated changes in the database. Only limited number of data quality specialist at the national level are authorized to make back date changes. Each year at first of March the	

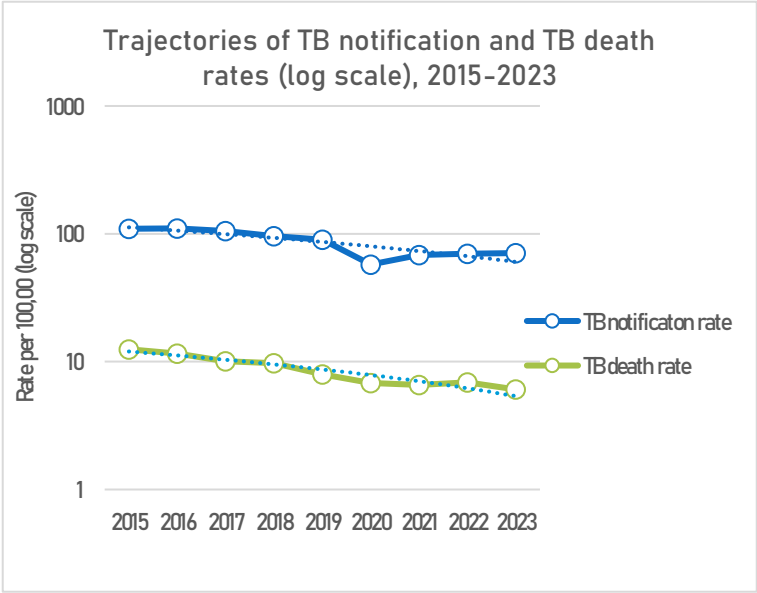
STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
			data from the previous year become blocked. Thus, the first benchmark is deemed to be ***met.*** For the assessment of second benchmark we explored the national electronic dataset TB patients for 2023 and we found that the fields age, site of disease, and previous treatment were 100% complete and consistent (free of unfeasible results). For the bacteriological confirmation SIME-TB automatically populated a field for bacteriological confirmation which was positive when any of fields of microscopy, GeneXpert or culture were positive. This field also was 100% complete and free of unplausible values. Hence, the second benchmark also is considered to be satisfied. To assess the level of unresolved potential duplicates we exported all records for 2023 containing core variables into excel sheet and sorted alphabetically using system generated ID and looked for potential duplicates by applying excel conditional formatting "detect duplicate value" function. We identified 45 pairs of potential duplicate records using system generated ID. All 45 pairs of highlighted duplicates were explored one-by-one manually, comparing the category of disease, date of registration and date of start of treatment. Following manual review, we identified in total 5 pairs of unresolved potential duplicate records while the rest of 40 pairs were multiple episodes of the individual. Identified potential duplicates makes only 0.2% of total records, therefore we can conclude that the third benchmark also is met. Considered above mentioned it could be concluded that Moldova surveillance system satisfied all three benchmarks and therefore the standard B 1.5 has **been *met* for 2023**. Overall, all 3 standards are met, therefore benchmark is **met** Recommendations: Although current system is good enough to ensure good data quality, however, there is a room to improve it to facilitate data analysis and use. NTP to consider enhancing the new electronic system with dashboard to allow time series analysis of data and computation of rates at national and sub-national level. WHO has a recommended set of dashboards	

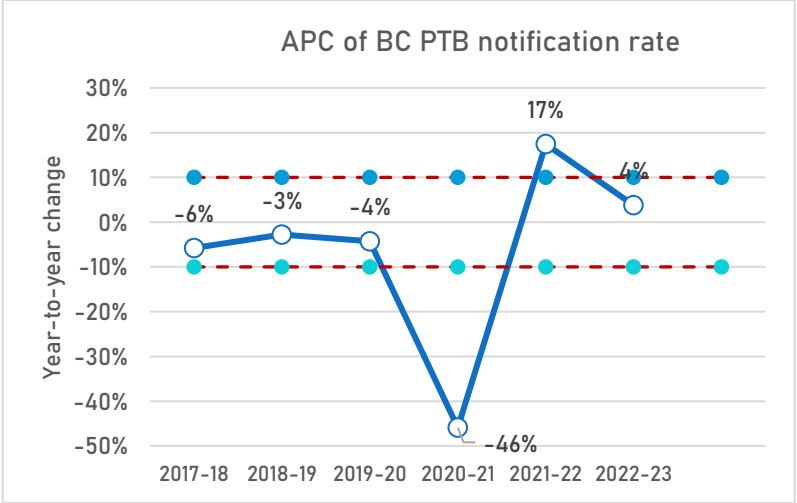
STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
			for programmatic management of TB control program[26]. NTP should aim to establish interlinkage with other systems, such as vital registration system, civil register. Interlinkage with other systems using PIN would allow to autocomplete demographic data, avoid entering error, duplicate entries, ensure smooth linkage with laboratory data.	
B1.6 TB surveillance data are externally consistent	All benchmarks should be met to reach this standard: • Percentage of bacteriologically confirmed cases among pulmonary new and recurrent cases ranges between 70% and 90% • Year-to-year change of TB notification rates (new and recurrent, all forms) is consistent with the year-to-year change in bacteriologically confirmed notification rates for pulmonary TB (i.e. the trajectories are in the same direction) • Overall percentage of decline in proportion of bacteriologically confirmed pulmonary TB cases over the 5 years preceding the year of the assessment does not exceed 5%	☑ **Met** ☐ Not met	Percentage of bacteriologically confirmed TB case among new and recurrent pulmonary cases over the past 5 years ranged between 65.4 and 70.8%. Only in 2023 bacteriological confirmation reached lower level of benchmark of 70-90% laboratory confirmation. Thus, as of 2023 the first benchmark is **met**. Despite of large variation of overall TB notification over the past five years, the bacteriological confirmation largely followed the same direction of the trend, indicating that the practice of diagnoses over the time was largely consistent towards the improvement. Thuse, the second benchmark also is **met**. 	

[26] World Health Organization. Analysis and use of health facility data: Guidance for tuberculosis program managers. https://www.who.int/healthinfo/FacilityAnalysisGuide_TB.pdf?ua=1, WHO 2018

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
			 Percentage of bacteriologically confirmed TB cases among people with new episode of pulmonary TB in Moldova in 2019 was 65.6% and improved to 70.8% in 2024. This makes 7.9% increase over the five years. Because there was no decline, this benchmark also can be considered as **met**. Thuse all three benchmarks are met, therefore standard of external consistency is **satisfied.**	
B1.7 Number of reported TB cases is internally consistent	If vital registration data are available, then the following benchmark should be satisfied for this standard to be met: 1. Year-to-year change in the national number	☐ **Met** ☑Partially met ☐ Not met	According to the most recent WHO report[27] the completeness of death registration in the Republic of Moldova is 100% and percentage of ill-defined cause of deaths is 2.1%, indicating high data of data. Therefore, only the first standard is assessed. Annual percent of change of TB deaths reported to Global TB database from the national system of mortality from 2015 and 2024 was -9%. Annual change of TB notification rate for the same period	N/A

[27] WHO mortality database, Interactive platform visualizing mortality data

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	of reported TB cases is consistent with year-to-year change in national TB mortality (HIV-negative, from national vital registration) i.e. trajectories with the same direction. If vital registration data are not available, then the following benchmarks should be satisfied for this standard to be met: 2. Proportion of extrapulmonary TB cases out of all TB cases; 3. Ratio of male-to-female TB cases; 4. Proportion of childhood TB out of all TB cases; 5. Year-to-year change in the case notification rate for new bacteriologically confirmed TB; 6. Ratio of the number of people with presumptive TB to total notifications of TB cases.		was -5.5%. Trajectories of TB notification and TB mortality follow the same direction and benchmark **is met**.  Proportion of extrapulmonary cases out of total (Figure 10) as well as proportion of males (Figure 13) also are consistent of the last 10 year. Proportion of childhood TB cases between 2014 and 2022 was largely stable, ranging between 2.8 and 4.3% with sudden increase up to 7.1% in 2023, indicating internal inconsistency. Year-to-year change of bacteriolgocially confirmed pulmonary TB notification rate was -46% between 2020-2021, and 17% between 2021-2022 period, explained by COVID-related disruption of services. Data exceed expected +/-10% indicating internal inconsistenty.	

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
			 Thus, some of the benchmarks of internal consistency are not met, therefore standard is partially met. Recommendations: (1) Possible reasons for inconsistency of childhood TB cases should be investigated by paediatric and TB experts, discussed with paediatricians, intensive care physicians from paediatric hospitals, pulmonologists, family practitioners and all those who make and report diagnoses of childhood TB. (2) After these discussions, it may be necessary to take corrective actions, including training of health care providers, revision of the differential diagnostic algorithm adopted at general hospitals, delegation of confirmation of diagnosis of childhood TB to a steering committee a etc.	
B1.8 All diagnosed cases of TB are reported	Both benchmarks should be satisfied to meet this standard:	☑ **Met** ☐Partially met ☐ Not met	Reporting of TB cases is mandatory by law passed from Moldova parliament in 2009 (Law № 10/2009 about state surveillance on public health) and Law on control and prevention of TB (Law № 153/2008).	

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	• TB reporting is a legal requirement; • ≥90% of TB cases are reported to national health authorities, as determined by a national-level investigation (e.g. inventory study) conducted in the last 10 years		Although no formal inventory study or external audit was conducted in the country, however, current procedures of recording and reporting and monitoring ensure that all diagnosed cases in the country are reported, including those diagnosed in private sector, initial lost to follow-up, and people who died before the start of treatment. All people confirmed bacteriologically are monitored at facility, regional and national level to ensure completeness of registration of bacteriologically confirmed cases. In addition, laboratory register and TB register are linked at national level regularly. Thus, both benchmarks are considered to be **met**.	
B1.9 Population has good access to health care	UHC index score is ≥80 (SDG Indicator 3.8.1)	☐ Met ☑ Partially met ☐ Not met	According to the Global health observatory UHC score in Republic of Moldova improved since 2015 up to 72 in 2019. In 2021, which is the latest year with available data, the UHC score was 71 which is below of threshold set[28]. There is a need for further investments in improving the accessibility and affordability of healthcare, however this standard is beyond of scope of NTP.	
B1.10 Vital registration system has high national coverage and quality	• Vital registration data provided by CRVS is evaluated either "1-Hight" or "2-Medium"	☑ Met ☐Partially met ☐ Not met	According to the most recent WHO report[29] the completeness of death registration in the Republic of Moldova is 100% and percentage of ill-defined cause of deaths is 2.1%, indicating high data of data. Standard is considered fully **met**.	N/A
SURVEILLANCE OF DRUG RESISTANT TB				
B2.1 Surveillance data provide a direct measure	One of the two benchmarks should be satisfied to meet this standard:	☑ **Met** ☐ Partially met ☐ Not met	Per the 2023 routine surveillance report, in total 1,637 bacteriologically confirmed pulmonary TB cases were notified in Republic of Moldova.	

[28] WHO Global Health Observatory. Geneva World Health Organization https://data.who.int/indicators/i/3805B1E/9A706FD [accessed on December 09, 2024]
[29] WHO mortality database, Interactive platform visualizing mortality data

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
of rifampicin-resistant TB in bacteriologically confirmed pulmonary cases	• Rifampicin susceptibility testing results are documented for ≥80% of all bacteriologically confirmed pulmonary TB cases; • Rifampicin susceptibility testing results are documented for a nationally representative drug-resistance survey conducted in the past 5 years.		Among them 1,584 (97%) had documented DST results for RIF. This is above 80%, thus the standard could be assumed fully met.	
B2.2 Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases	One of the two benchmarks should be satisfied to meet this standard: • HIV status (positive/negative) documented for ≥80% of all notified TB cases; • HIV status is available from a representative sample from all TB cases notified in settings with a low-level epidemic state where it is not feasible to implement routine surveillance.	☑ Met ☐Partially met ☐ Not met	According to surveillance reports into the WHO global TB database, in 2023 a total of 2,164 new and recurrent TB cases were notified in Republic of Moldova. Among them 2,091 TB patients had their HIV status documented, which is 97% of total cases, thus the standard could be assumed fully met.	

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
B2.3 Surveillance data for children reported with TB (defined as ages 0–14 years) are reliable and accurate AND all diagnosed childhood TB cases are reported	Both of the benchmarks should be satisfied to meet this standard: • Ratio of age groups 0–4 to 5–14 years is in the range 1.5–3.0; • ≥90% of childhood TB cases are reported to national health authorities, as determined by a national-level investigation (e.g. inventory study) conducted in the last 10 years.	☐ Met ☑ Partially met ☐ Not met	In 2023 in Republic of Moldova the number of children notified with TB aged 0-4 and 5 – 14 years were 43 and 110 correspondingly. Expressed as rate ratio this makes 0.8, which is not within the expected range, Because Moldova has strong system of TB notification, which involves routine cross-check of registration system with laboratory and vvital registration system, at all levels, under-reporting of child TB cases in Moldova is unlikely to due established functional system of registration and notification, therefore, we consider the second benchmark to be met although there was no formal inventory study conducted in the past 10 years. **Recommendations**: (1) Possible reasons for under-detection of childhood TB cases in the age group 0–4 years should be investigated by paediatric international and national experts, discussed with paediatricians, intensive care physicians from paediatric hospitals, pulmonologists, family practitioners and all those who make and report diagnoses of childhood TB. (2) After these discussions, it may be necessary to take corrective actions, including training of health care providers, revision of the differential diagnostic algorithm adopted at general hospitals, etc.	
B3.1 Monitoring treatment outcomes is consistent with WHO guidelines	Both these benchmarks should be satisfied to meet this standard: • Treatment outcome definitions for all TB cases are consistent with WHO guidelines. • Treatment outcomes of TB patients at national level can be disaggregated by at least	☑ Met ☐ Partially met ☐ Not met	To assess the first benchmark the following tools were reviewed: National clinical protocol on tuberculosis in adults (Table 26, page 130)[30] SIME-TB electronic register, recording forms 089-1e (part C), recording form TB - 090 (part B), guidelines for the completion of TB recording forms[31] as well we discussed with national experts. Discussions with national experts indicated that people diagnosed with TB, but not started TB treatment, as well as those identified post-mortem are notified and included into treatment outcome. While definitions in National Clinical protocol correspond to the latest WHO definitions, instructions to complete forms 089 requires minor updates to align with the national protocol. We can	

[30] Tuberculosis in adults: National clinical protocols, 6th edition, PCN-123, Ministry of Health of Republic of Moldova, Chisinau, 2024 [Romanian]. Accessed from https://simetb.ifp.md/Download/oficial_docs/Ordin_MS_2024_01_31_nr_121_protocol.pdf

[31] Guidelines for completion of the " Notification of the patient with established diagnosis of new/recurrent active tuberculosis case and restart of treatment and its results" (Form no. 089 - 1/e) accessed from https://simetb.ifp.md/Download/ghiduri_tb/

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	the following variables: treatment history, HIV status and drug resistance status		conclude that country treatment outcome definitions and actual practice are in-line with WHO recommendations. As Republic of Moldova implements case-based electronic surveillance system, therefore, treatment outcome at national level is dis-aggregated for all required variables (by HIV, treatment history, and drug-resistance profile) and reported to GTB accordingly. Both benchmarks related to treatment outcome consistency to WHO guidelines are met, therefore standard is assumed to be **fully met.** **Recommendations:** In new electronic surveillance system still in pipeline, NTP and system developers should consider that there are new definitions of "treatment outcome" (reserved for people with TB who actually started TB treatment) and "case outcome" (all people diagnosed with TB including those who didn't start the treatment). Definitions, new electronic system, reporting forms as well as M&E plan, should be updated accordingly for 2025 reporting year.	
B3.2 Recording and reporting of TB treatment outcomes are accurate, complete and consistent	All these benchmarks should be satisfied to meet this standard: *For paper-based systems:* • Assignment of treatment outcomes is correct for >95% of TB patients recorded in the facility register • Number of treatment outcomes (for each outcome category) in >95% of quarterly reports (or equivalent) matches the number recorded in BMU TB registers • Reported number of the cohort of patients with an expected assigned2	☐ Met ☑ **Partially met** ☐ Not met	NTP Republic of Moldova implements case-based electronic surveillance system and currently is in transition from stand alone web-based TB database into a system mainstreamed into overall health information system. Old system didn't have any capabilities for automated validation checks to ensure the validity of treatment outcome data, while this feature still be developed into new system. Therefore, this benchmark is assumed **not met.** To assess the second benchmark we compared TB/HIV as well as RR-TB cohorts notified and size of corresponding treatment cohorts in the corresponding year using global TB database. In 2021 in total 214 new episode of TB were notified in Moldova. The sizes of TB/HIV and RR-TB/HIV cohorts in 2021 were correspondingly 150 and 87. The cohort size was larger by 23 compared to those notified as expected, because RR-TB/HIV cohort includes retreated non-recurrent cases as well, indicating **good match**. In 2021 in total 459 people with RR-TB were notified in Moldova among bacteriologically confirmed pulmonary TB cases against 559 people with	

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	treatment outcome in any given year matches the number of patients notified the year before • <1% of cases are assigned an outcome of not evaluated *For case-based or patient-based digital systems:* • Data validation checks are in place to ensure validity of assigned treatment outcome for individual cases • Reported number of the cohort of patients with an expected assigned1 treatment outcome in any given year matches the number of patients notified the year before • <1% of cases are assigned an outcome of not evaluated.		RR-TB reported with treatment outcome (443 MDR/RR-TB and 116 preXDR/XDR-TB) in 2023 for 2021 cohort. Cohort size is larger compared to notified, as it includes the people without laboratory conformation of RR-TB, extrapulmonary cases as well as people after RR-TB treatment failure, and lost to follow-up. Thuse, the second benchmark also is **met**. In the latest cohorts the proportion of people not evaluated for treatment outcome was as follow: new and recurrent eligible for first-line TB treatment 0.6% (2022), RR-TB without FQ resistance 0%(2021 cohort), RR-TB with FQ resistance 0% (2022) Overall percentage of those who are lost to follow-up is below 1%, therefore benchmark is **met.** Of three benchmarks related to TB treatment outcome quality two are met and one is not met, therefore the standard is considered partially met. Recommendations: consider introducing automated validation checks in the new system to ensure the quality of treatment outcome data.	
B4.1 Monitoring indicators for PMTPT are consistent with WHO guidelines	All these benchmarks should be satisfied to meet this standard: • M&E indicators for PMTPT are consistent with WHO guidelines in terms of: (1) Contact investigation coverage (2) TPT coverage (disaggregated by PLHIV, contacts <5 years of age	☐ Met ☑ Partially met ☐ Not met	To assess the first benchmark we reviewed Annex 3 of National TB action plan for 2022-2025 period. According to indicator 1.2. contact investigation coverage is "Total number of people who were screened for TB among total number of people who were exposed to people with active TB disease". Definition adopted by Moldova NTP is not restricted to the contacts of bacteriologically confirmed pulmonary TB, resulting an over-estimation of data reported to Global TB database. M&E indicators for the calculation of TPT coverage follow follows WHO recommendations, however targets are defined for PLHIV and children under 5 years of age. Indicator related to TPT completion is not included in M&E plan. Reporting of TPT coverage among PLHIV is the mandated of	

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	and ≥5 years) (3) TPT completion (disaggregated by regimens lasting 6 months or more and others lasting <6 months) • PMTPT dataset contains the minimum variables for monitoring TPT at three important instances of PMTPT: (1) Assessment of contacts of TB patients (2) Assessment of PLHIV and other at-risk groups (3) Initiation and completion of TPT		national HIV program. TB program document data related to TPT only for those PLHIV who were referred to TB program for TB testing. Guidance of assignment of TPT completion (page 44) follow WHO recommendations Recording and reporting form related to TPT include designated fields to record and report TPT regimen. In Republic of Moldova data related to screening of people with HIV and other risk groups, assessment of contacts, initiation and completion of TPT is implemented using paper registers at PHC level. Data from paper records are aggregated and submitted to rayon TB centres on quarterly basis. At rayons level data from all PHC centres are aggregated and entered into SIME-TB. At national level reports from multiple excel sheet are summarized and aggregated using special electronic tool (excel macro?). **Recommendations:** NTP should consider mainstreaming the household contacts and people started on TPT into electronic surveillance system to have unified surveillance system along pathway of prevention and care. Indicators related to TPT completion should be monitored on annual basis. Improve collaboration and data sharing with HIV program. This might include establishment of committees with representatives from both HIV and TB programs to regularly discuss and coordinate activities, policy and guidelines harmonization, Implement collaborative monitoring and evaluation frameworks to track TPT initiation coverage and completion.	
B4.2 PMTPT data are accurate, complete and consistent	All the benchmarks should be satisfied to meet this standard: For paper-based systems: • Number of individuals evaluated for TB disease and TB infection and recorded in the source registers at the health facility matches the number reported (disaggregated by	☐ Met ☐ Partially met ☐ Not met	Standard was not assessed as data are collected at PHC level.	

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET TO ADDRESS KEY ACTION(S)
	PLHIV, contacts aged <5 years and those aged ≥5 years) • Number of individuals started on TPT in the source register at the health facility matches the number reported (disaggregated by PLHIV, contacts aged <5 years and ≥5 years) • Number of individuals who completed TPT in the source register at the health facility matches the number reported (disaggregated by PLHIV, and household contacts of all ages combined) For case-based or patient-based digital datasets: • Data validation checks are in place at national level to identify and correct invalid, inconsistent and missing PMTPT data in the minimum set of variables (B4.1) • For each variable in the minimum set (B4.1), ≥90% of individual records are complete, valid and internally consistent for the year being assessed			