World Health Organization
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Analysis of the epidemiological impact of tuberculosis in the Republic of Moldova

ABSTRACT

An excellent understanding of the level of, and trends in, disease burden and how these have been (and can be) influenced by the implementation of prevention and treatment interventions is of considerable importance to national health programmes, as well as international donor agencies. It can help to ensure the appropriate allocation of funding and ultimately help to save more lives in the future. This report delivers tuberculosis epidemiological and impact analyses, conducted as part of tuberculosis programme reviews, as inputs to health sector reviews and for the "epidemiological stage" of the Global Fund's when supported by the CCM of Republic of Moldova.

Keywords

Tuberculosis - epidemiology

Tuberculosis - prevention and control

Surveillance

National Health Programs

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Moldova

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Abbreviations

ART	**Antiretroviral treatment**
DST	Drug susceptibility testing
GDP	Gross domestic product
GNI	Gross national income
ICD	International Classification of Diseases
IPT	Isoniazid preventive therapy
MDR-TB	Multidrug-resistant tuberculosis
NBS	National Bureau of Statistics
NCHM	National Centre for Health Management
NRL	National Reference Laboratory
NTP	National Tuberculosis Programme
OOP	Out-of-pocket
PAF	Population-attributable fraction
PLWHIV	People living with HIV
RR	Rifampicin resistant
SIME TB	Sistem Informaţional de Monitorizare şi Evaluare a Tuberculozei [Information system for TB monitoring and evaluation]
SOP	Standard operating procedure
TB	Tuberculosis
THE	Total health expenditure
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

Summary

In September 2016, the World Health Organization (WHO) Regional Office for Europe conducted an epidemiological review of the National Tuberculosis Programme (NTP) in the Republic of Moldova using the standard checklist and terms of reference to assess the reliability of routine tuberculosis (TB) surveillance data. There was a particular focus on the country's capacity to measure the level of, and trends in, TB disease burden. The review also explored the potential influence of a range of external and internal factors on recent trends in the TB burden.

Epidemiology

In the last decade, substantial investments were made in the Republic of Moldova to improve surveillance, diagnosis and treatment of TB. These efforts resulted in a decline in trends of disease epidemiology in key indicators: TB mortality and notification.

By the end of 2015, TB mortality was estimated at 7.7 per 100 000 population and, though this rate is almost three times higher than Millennium Development Goal 6 target of halving TB mortality by 2015 compared with 1990, the analysis of TB mortality trends shows that it is steadily declining. Starting from 2005, when the TB mortality rate reached its highest point since 1990, the mortality rate has decreased, with an average annual decline of 11.2%. Changes in postmortem TB notification provide more evidence for a decline in TB mortality: TB is diagnosed post-mortem in about one in seven TB deaths and this proportion has remained stable over time; however, the absolute number of TB cases diagnosed postmortem has decreased by about twofold since 2009.

The estimated number of incident TB cases in the Republic of Moldova in 2015 was 6200, equivalent to a rate of 152 per 100 000 population. The increasing trend in TB incidence observed since the early 1990s was reversed in 2006; however, the rate of decline in TB incidence between 2006 and 2015 was only −1.5%.

The number of notified new and relapse incident TB cases also has declined since 2007: from 5325 (equivalent to 129 per 100 000) in 2007 to 3608 (88.7 per 100 000) in 2015, with an average rate of decrease of 5.0% per year. Notifications disaggregated by disease site and bacterial confirmation follow the same pattern of decline, although with different trajectories: the sharp decline observed in the last 2–3 years was driven by clinically diagnosed pulmonary TB cases, which decreased on average by −8.7% per year between 2011 and 2015. The rates of annual decline of bacteriologically confirmed pulmonary and extrapulmonary TB cases over the same period were −1.9% and −4.7%, respectively. The comparatively slow decline in bacteriologically confirmed pulmonary TB cases might be explained by the roll-out of GeneXpert MTB/RIF testing from 2013, which improved bacteriological confirmation of TB cases. The sharp decline in clinically diagnoses cases may also be caused by a decline in overdiagnosis of suspected cases. The notification rate shows a stable year-on-year decline of within 10%, indicating no evidence of problems in reporting and recording at the national level.

The proportion of bacteriologically confirmed TB cases between 2007 and 2013 was stable at 55–58%. Between 2013 and 2015, there was sharp decrease in clinically diagnosed new and relapse TB cases, which resulted in a relative increase in the proportion of bacteriologically confirmed TB cases from 57% in 2013 to 65% in 2015. The likely causes of these changes are improved laboratory diagnostics due to roll-out of the GeneXpert MTB/RIF test and a decreased TB burden in the total population.

Disaggregation of TB notification data from 2007–2015 by site of disease reveals a declining trend in both pulmonary and extrapulmonary TB. The proportion of extrapulmonary TB cases among new TB cases notified in 2007–2015 ranged between 9% and 12%.

Over the last 9 years, the absolute number of both new and retreated TB cases decreased. Between 2007 and 2011, the decline was faster for retreated than for new TB cases, resulting in a relative decrease in the proportion of retreated cases from 35% in 2007 to 28% in 2011.

The absolute number of child TB cases between 2007 and 2015 gradually decreased from 176 to 111. The decreased number of TB cases after 2010 was driven mainly by a decrease in the number of TB cases in children aged 5–14 years, while the absolute number of TB cases in children aged 0–4 years was comparatively stable. This suggests a slight improvement in the diagnosis of child TB cases. These trends indicate that TB notification in children is more or less stable, except for a sharp decline in the number of TB cases in children aged 5–14 years from 95 to 67 between 2013 and 2014.

The recent decline in TB notification and mortality rates reflects a true decrease in the TB burden of the population. A notable and consistent decrease in TB mortality over time, along with a comparatively consistent pattern of new TB notifications across the regions, a decrease in the age-specific notification rate in younger age groups and a gradual increase in the mean age of new TB cases, supports the hypothesis that the TB burden in the Republic of Moldova is decreasing in the total population. The decline in TB burden is related to both TB-specific interventions and external factors.

Key findings

The Republic of Moldova has a well-established and smoothly operating national vital registration system, with a coverage of >90%. There are mechanisms in place to check the completeness and consistency of death records, and the proportion of so-called ill-defined and unknown causes of mortality within the last 10 years was below 5%; these combined factors indicate that mortality data are sufficiently accurate and complete to measure the mortality rates and trends. However, since 1997, the annual death counts do not cover the Transnistria region, which contains about 15% of the total population of the Republic of Moldova.

The TB surveillance system is based on paper and electronic case-based registers designed for individual TB and multidrug-resistant and extensively drug-resistant TB (MDR/XDR-TB) case notification and treatment outcome monitoring. TB case definitions are in line with WHO-recommended definitions. The database contains all core variables recommended by WHO, as well as the results of drug susceptibility testing (DST) and HIV testing, underlying risk factors, comorbidities and treatment outcomes. About 55 data entry sites across the Republic of Moldova contribute to data entry into the Sistem Informaţional de Monitorizare şi Evaluare a Tuberculozei (Information system for TB monitoring and evaluation (SIME TB)) database at the district, laboratory and national levels, as well as in the penitentiary system. Several mechanisms are in place to ensure the quality of the collected data. The existing strong link between the TB surveillance and the vital registration system provides an additional mechanism for ensuring the quality of TB surveillance data.

To assess the quality of data produced by the Moldovan TB surveillance system, the WHO *Checklist of standards and benchmarks for TB surveillance and vital registration systems* was implemented in September 2016. Of the 12 standards for TB surveillance applicable for the Republic of Moldova, eight were met, two were partially met and only two were not met.

Observation of data in the electronic register at the national level and during field visits indicated that the records do not contain invalid or implausible values for any of the variables in the minimum dataset, and proportion of observations with missing information was very low or non-existent. Cross-checking of laboratory and TB registers indicated no evidence of undernotification. Postmortem cases were included in TB registers and accounted for in cohort analyses, indicating that the Moldovan TB surveillance system captures all notified TB cases. However, because the population has limited access to health care (under-five mortality is >10% and out-of-pocket (OOP) payments are >25%), it may be assumed that some TB cases in the Republic of Moldova are not detected by health systems.

Routine TB surveillance in the Republic of Moldova provides reliable information related to drug resistance as a result of universal DST coverage and a strong quality-assured laboratory system. HIV testing coverage was consistently above 95% in the last 5 years; therefore, routine surveillance data provide a direct measure of HIV prevalence in TB patients.

The main weakness of the Moldovan surveillance system relates to TB detection in children. In recent years, around 4% of all new cases were in children. This is slightly lower than the expected range of values (5–15%) for a middle-income country. In addition, the ratio of children aged 0–4 to 5–14 years in 2015 was 0.7, which is far below the expected ratio of 1.5–3, indicating that TB cases in children aged under 5 years are probably overlooked.

The following factors may have influenced the trend in TB burden in the Republic of Moldova.

- The main TB programming-related factors that have contributed to the decreased TB epidemic are the introduction and scale-up of rapid diagnostic tests and second-line TB treatment, improved outcomes for second-line treatment and focusing efforts on the most vulnerable sectors of the population, as well as applying innovative methods to ensure patients support the programme and adhere to treatment. These actions were supported by increased government and donor funding for the NTP.
- Among the external factors expected to contribute to driving the TB epidemic downwards in the population by reducing TB transmission, population vulnerability and increasing protection and prevention at the health system level were economic growth (increased gross domestic product (GDP) per capita), poverty reduction, increased health financing (reduced OOP payments as a percentage of the total health expenditure (THE)), health system strengthening (decrease in under-five mortality) and increased antiretroviral treatment (ART) coverage among people living with HIV (PLWHIV).
- Despite the increasing trends in ART coverage among TB/HIV co-infected patients, the overall effect of this intervention on the TB epidemic is probably limited by the very rapid growth of HIV infection in the general population and in TB patients, variable year-on-year ART coverage and short follow-up for periods with high ART coverage. Contact tracing and treatment outcomes have not changed notably over time; therefore, their effects on the observed trend remain important but not decisive. High rates of alcohol abuse and tobacco use are likely to contribute to the persistence of the TB epidemic; however, these rates have not changed over time so are not likely to have played a role in the observed decline in TB.

K**ey recommendations**

Review of the TB surveillance system of the Republic of Moldova and analysis of the epidemiological situation show notable achievements made by the NTP in strengthening the country's TB surveillance. The slow decline in TB is due to the high rate of MDR-TB and HIV coinfection, as well as to other TB-associated risk factors such as high rates of smoking and alcohol misuse and a growing number of PLWHIV in the general population, comparatively low ART coverage and a growing prevalence of diabetes. The NT should continue its efforts toward sustainable TB control in the Republic of Moldova. Addressing the following recommendations will advance TB control in the Republic of Moldova.

- To address the issue of possible underdiagnosis of paediatric TB cases, the NTP should analyse and discuss potential reasons for the underdetection of child TB cases with paediatricians, intensive care physicians from paediatric hospitals, pulmonologists, family practitioners and all those who make and report the diagnosis of childhood TB.
- The Ministry of Health should continue prioritizing TB surveillance in the Republic of Moldova and insure that TB surveillance mechanisms institutionalized by NTP continue to receive adequate support and full-scale implementation. This will ensure that the reversed trends of the disease are sustainable.
- Addressing some of the gaps of TB surveillance, such as access to care, is beyond the influence of a TB surveillance system and NTP. These activities are long term, including strengthening health care services, increasing financial investments and introducing mandatory national health insurance. The Ministry of Health should continue implementation of health policies to improve general access to health care, leading to further strengthening of the TB system.
- WHO should revise the estimated TB incidence in the Republic of Moldova. The case detection rate is underestimated and needs to be increased from the current 60% to 81%. The estimation of TB incidence should be amended from 152 to 110 new TB cases per 100 000 population. The reduction in TB burden was achieved through revision of the national TB protocols, strengthening health care practices in the provision of TB prevention and care to the population, and improved surveillance.

Introduction

The Republic of Moldova is one of the 18 high-priority countries for tuberculosis (TB) control in the WHO European Region and the one of the highest MDR-TB burden countries worldwide. According to WHO, estimated TB incidence and mortality rates in 2015 were 152 and 7.7 per 100 000 population, respectively. Although these figures have decreased notably in recent years, TB control efforts in the Republic of Moldova are hampered by the high level of multidrug resistance and growing burden of TB/HIV coinfection. The Republic of Moldova is among the countries with the highest MDR-TB prevalence, reaching 31.8% of newly diagnosed and 69.1% of previously treated TB patients, according to 2015 routine surveillance results. In 2011, 95% of all new and relapse TB cases were tested for HIV, and 8.6% were HIV positive. Treatment success rates are consistently low: in 2014, 79% patients were successfully treated, 3% had treatment failure, 11% died and 5.5% were lost to follow-up.

In the last decade, substantial investments were made in the Republic of Moldova to improve TB diagnosis, surveillance and treatment. The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) ranks the Republic of Moldova second out of 110 countries for the level of per capita funding. Notable achievements of TB control in the Republic of Moldova include updating national policies and guidelines, universal DST coverage and introducing rapid diagnostics, piloting innovative approaches (including m-health) to support patient adherence, and the developing an online data collection system that incorporates laboratory, clinical and demographic information. TB epidemiology and treatment response in the Republic of Moldova is strongly influenced by high poverty, alcohol consumption, tobacco smoking and migration rates and the growing HIV epidemic.

TB notification and mortality rates in the Republic of Moldova have continuously decreased in recent years. An epidemiological review was therefore important to determine the reliability of routine surveillance data and identify which programmatic and external factors are influencing these trends.

Objectives

The objectives of current review are to:

- Describe and assess the current national TB surveillance and vital registration systems, with a particular focus on their capacity to measure the level of, and trends in, TB disease burden (incidence and mortality), through implementing a checklist for TB surveillance.
- Assess the level of, and trends in, TB disease burden (incidence, prevalence, mortality) using available surveillance, survey, programmatic and other data.
- Assess whether recent trends in TB disease burden indicators might be related to changes in TB-specific interventions, taking into account external factors such as economic or demographic trends.

Methods

Methods for data collection included a desk review of available TB control-related policy papers, manuals, guidelines and forms *(1)*; interview and discussions with TB authorities and health care providers at national and district level *(2)*; and reviewing and cross-checking TB records, laboratory registers and electronic surveillance system at TB dispensaries *(3).* The SIME TB database *(4)* was also reviewed to assess the completeness of core variable data and detect invalid entries, duplicate entries and inconsistencies. This included producing summary and frequency reports, exporting data into

Microsoft Excel spreadsheets and sorting variables, looking into extreme values, calculating the time between the date of registration and date of treatment outcome, and other types of data tabulation.

Most TB control data were obtained from the SIME TB database. Information from statistical yearbooks and databases of the National Bureau of Statistics of the Republic of Moldova were heavily used to obtain data on population size, mortality, TB determinants and other health issues *(5)*. Other resources were AIDSinfo *(6)*, the WHO Global Health Observatory *(7)* and World Bank Open Data *(8)*.

The analysis involved plotting annual data followed by visual observation, computation of slopes by linear regression to describe and compare the rates of change of various indicators, and an ecological analysis of the TB notification rate and trends in external factors.

The standard WHO-recommended checklist, S*tandards and benchmarks for tuberculosis surveillance and vital registration systems: checklist and user guide*, were used for the assessment *(1)*. Analysis and interpretation of the influence of TB predictors and external factors were based on instructions in the *Understanding and using tuberculosis data* handbook *(2)*.

1. Assessment of Moldovan TB surveillance and vital registration systems, and their capacity to measure the TB burden

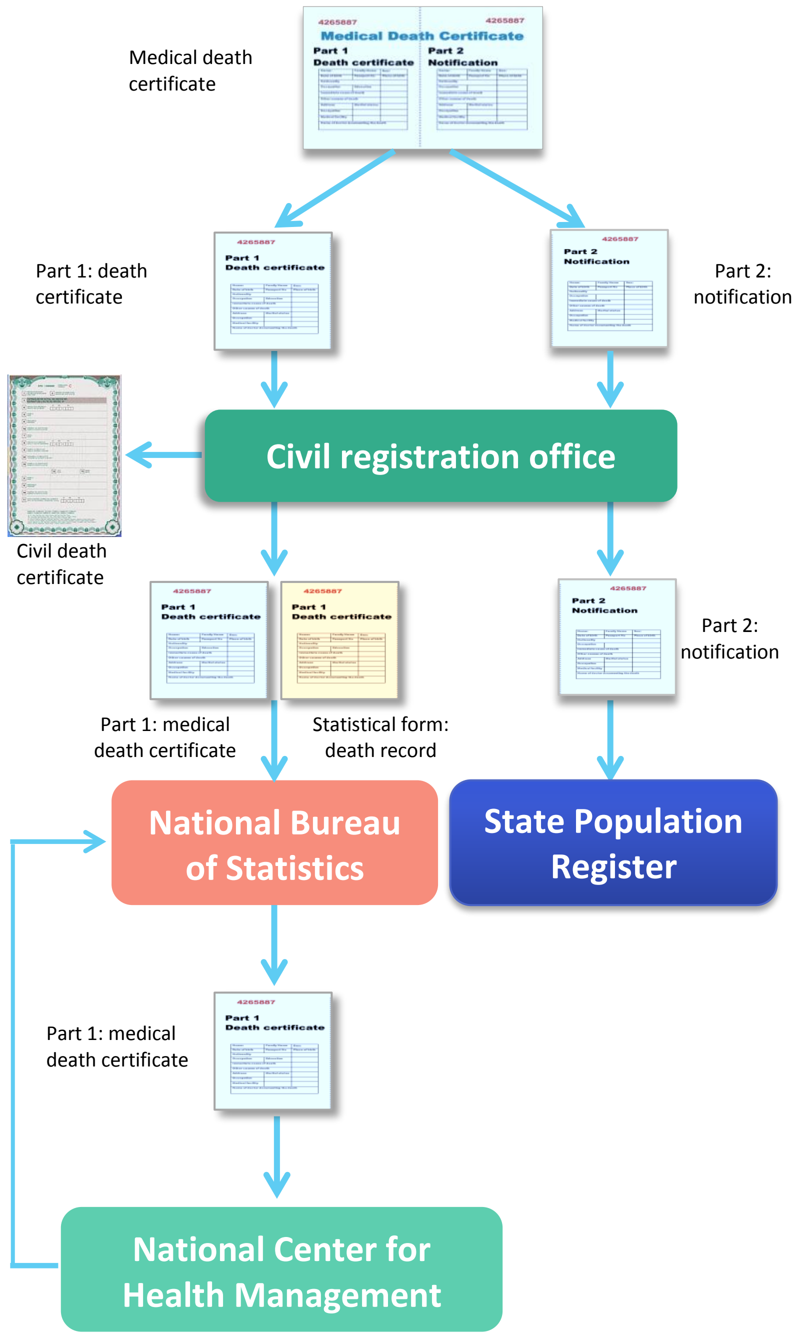
1.1 The vital registration system

Data on vital statistics in the Republic of Moldova are generated by an integrated information flow process administered jointly by the Ministry of Justice, Ministry of Health, Ministry of Information Technology and Communications and the National Bureau of Statistics (NBS), the institutions responsible for carrying out specific stages of the integrated information flow, as stipulated in Joint Order no. 44/347/100 of 11 October 2005. The Ministry of Health is responsible for issuing civil status acts (health records confirming death), the Ministry of Information Technology and Communication is responsible for registering civil status documents and the NBS is responsible for recording natural movement of the population in the statistics system.

The flow of information on vital statistics relies primarily on a hand delivery system[1]: once a death occurs, relatives of the deceased person apply to their physician for official documentation of the cause and time of death. After examination of the body, the physician issues a medical death certificate. A postmortem is only conducted when the death occurs in hospital or when there is suspicion of a violent death. The medical death certificate, which is prefilled with a serial number, consists of two parts: a death certificate and a notification document. The death certificate is given to the relatives of the deceased, who must submit it to the local civil registration office within 72 hours (Fig. 1.1). In exchange, they receive a civil death certificate that serves as both a burial permit and a legal document for inheritance purposes. The notification section of the medical death certificate is sent to the civil registration office by the physician or medical institution that certified the death (this is done in batched on the 10th of each month). A check is made at the civil registration office that the medical death certificate matches the notification received from the medical institution. The death is registered if the information on both documents coincides. This procedure guarantees that all deaths are recorded at the civil registration office. Death notification forms are then sent to the Centre for State Information Resources, which is in charge of population registries (or *Registru*), and a record of the deaths is made in the State Register of Population. The medical death certificate and an additional statistical form (the death record, completed by the civil registration office) are sent to the NBS. The death record is completed based on the medical death certificate: it does not include the cause of death, but covers 17 sociodemographic variables. The NBS manages the database of all death records; it verifies and processes the statistical data, and then forwards the medical death certificate to the National Centre for Health Management (NCHM). The NCHM is responsible for checking the completeness and consistency of all death records and for coding the causes of death according to the 10th revision of the International Classification of Diseases and Causes of Death (ICD-10) *(9)*, based on the diagnosis made by the physician who certified the death. If case of any inaccuracy or contradictory data, the NCHM contacts the treating physician for clarification and correction. At the NCHM, data are entered into the database. Aggregated data with cause-of-death statistics from the NCHM are returned to the NBS for publication and dissemination.

[1] According to Common Order no. 132/47/50, dated 29 April 2004, of the MITC, NBS and Ministry of Health regarding the issuance of death certificates.

Fig. 1.1. Flow of information on vital registration statistics



The medical death certificate is prefilled with a serial number for inclusion in the Population Register and completed by a doctor. It is composed of two parts: part 1 (death certificate) and part 2 (notification).

Both parts of the death certificate are sent to the district civil registration office. Part 1 is submitted by a relative of the deceased within 72 hours. Part 2 is sent by the medical institution (10th day of each month).

The civil registration office checks that the information is the same on both parts of the medical death certificate; if not, it must inform the police.

Part 2 is sent to the State Population Register.

The civil registration office completes the death record on the basis of the death certificate. This form does not include the cause of death.
The death certificate and the death record are both sent to the NBS.

The NBS manages the database of all death records. It is in charge of verifying and processing all statistical data.

The NBS transmits the death certificate to the NCHM.

The NCHM assigns four-digit ICD-10 code(s) to the cause(s) of death.

The NCHM manages the database of all death certificates and sends aggregated cause-of-death statistics to the NBS for official dissemination.

Source: Penina et al. *(3)*.

Vital statistics in the Republic of Moldova are considered to be complete. According to the evaluation of the Moldovan Health Information System conducted by the Health Metrics Network in 2007, coverage of the vital registration system for deaths is >90% *(10)*. However, since 1997, annual death counts do not cover the Transnistria region, which contains about 15% of the total population.

Data quality is checked and analysed at the NBS, especially for internal and temporal consistency with other data. To ensure the accuracy of the received information, the NBS verifies civil status data on the statistical forms, for example, the person's age and training level or occupation. If there is any inconsistency, the NBS contacts the civil registration Office for explanation and correction. The proportion deaths classified with an “ill-defined and unknown causes of mortality” (as defined in ICD-10 Chapter XVIII, Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified) in the last 10 years in the Republic of Moldova was below 5%.

National and regional statistics are generated for annualized death counts and for the primary cause of death by sex and age. Vital statistics are available in database form and published in NBS statistical yearbooks *(11)* and in NCHM-produced yearbooks on health statistics *(12)*.

The World Bank estimates that completeness of death registration in the Republic of Moldova is close to 91% (see details in standard B1.10) *(13)*. According to a recent study, the Republic of Moldova is classified as one of 46 countries in the world with a very high vital statistic performance index, with a satisfactory death registration system capable of producing data with sufficient quality for public health research and planning purposes *(13)*. In 2010–2012, the average vital statistic performance index score for the Republic of Moldova was estimated as 93.2%. This is consistent with findings of another in-depth assessment of the completeness and quality of death registration in the Republic of Moldova by a group of international and national experts, who concluded that death certification and vital statistics reporting were effective *(15)*. Mortality data in the Republic of Moldova were deemed to be sufficiently accurate and complete for measuring levels of and trends in mortality.

1.2 TB surveillance system

Oversight of the overall TB surveillance system in the Republic of Moldova is implemented by the monitoring subunit of the NTP, which operates under the National Tuberculosis Institute “Chiril Draganiuc” in Chişinău. In parallel, the Ministry of Internal Affairs provides health care, including TB services, in the penitentiary system.

The Moldovan TB surveillance system is a paper and electronic case-based register designed for TB and MDR/XDR-TB individual case notification and treatment outcome monitoring. Paper-based recording forms include TB notification form N 089/e, TB facility register (TB-03), second-line treatment register for TB facilities (TB-02) and laboratory register (TB 04)**.** Paper-based registers are mainly used for data verification, while reporting is generated based on the electronic register. The SIME TB was developed in 2005 with financial support from the World Bank, WHO and the Global Fund *(4)*. It is a real-time web-based application running on SQL Server 2000 with nationwide coverage that includes the penitentiary system. The electronic TB register ensures smooth information flow between laboratory and clinical specialists and various levels of the TB control system, and is designed to generate national surveillance statistics on TB case notification, disaggregated by core variables, MDR-TB notification and treatment outcomes for regular and rifampicin-resistant (RR)/MDR-TB and XDR-TB patients.

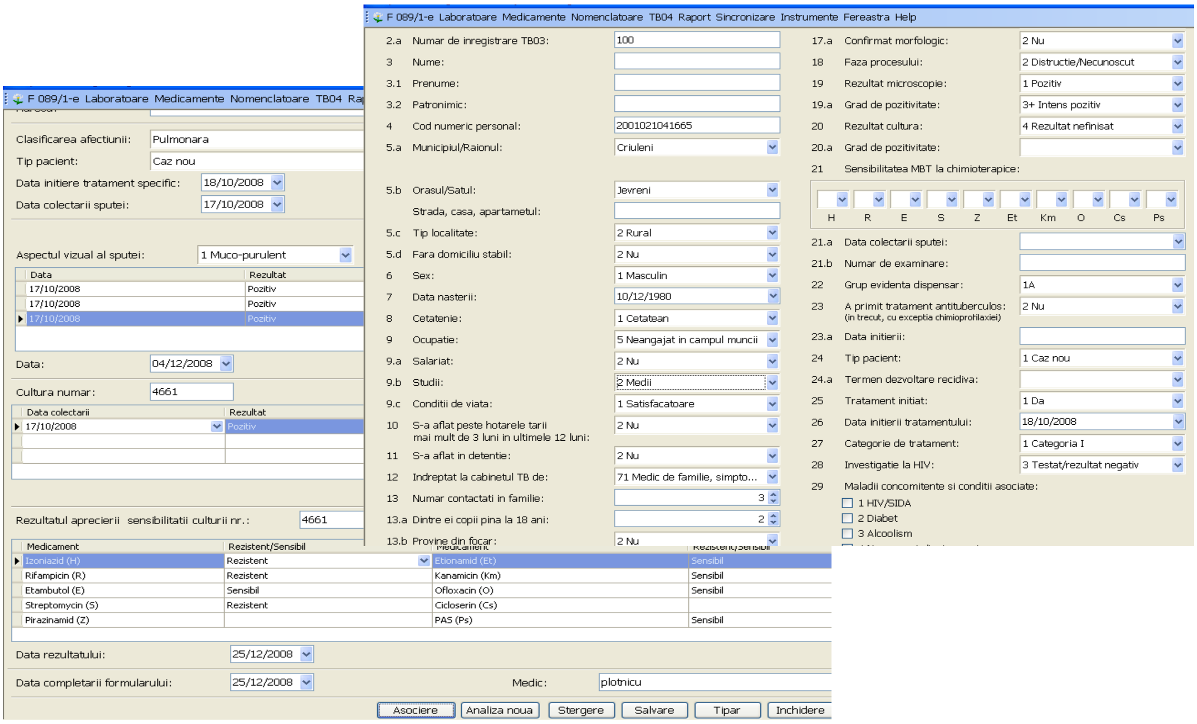
The electronic TB register, SIME TB, has three main modules:

1. a patient module, which is used to generate reports on TB notification by core variables (age, site of disease, bacteriological confirmation, sex, treatment history, HIV status), and treatment outcome for TB patients treated with first-line TB drugs (drug-susceptible) and for those notified with RR/MDR-TB and enrolled into second-line treatment;
2. a laboratory module, which includes all laboratory test results (microscopy, bacterial culture, GeneXpert MTB/RIF, DST by line probe assay, Löwenstein Jensen and BACTEC) for both suspected and confirmed cases; and

3. a drug management module.

Once TB is confirmed, a case-based TB notification form N 089/e part A is completed, which serves as main data source for capturing patient information in the SIME TB. Data are entered by the doctor who diagnosed TB, regardless of the patient's residence and place of diagnosis. This approach ensures that no diagnosed case is missed from the surveillance system and the timely transmission of information from diagnostic units to the primary health care level. TB notification form N 089/e includes data related to the patient's demographics, socioeconomic status and risk factors, disease characteristics and laboratory test results (Fig. 1.2). TB notification form N 089/e part B is used to record clinical progress, laboratory results and final treatment outcome results for regular TB cases. For patients with RR/MDR-TB, form 090/e is completed: parts A1–3 and B record details of the treatment regimen, clinical progress, laboratory results, adverse reactions and treatment outcomes; part C records patient discharge information; part F records hospitalization, Part H records active drug safety monitoring and part G records data common to F089/1e and F090. Part D records post-treatment follow-up.

Fig. 1.2. Screenshots of the SIME TB patient module (left), showing associated variables, and the laboratory module (right)



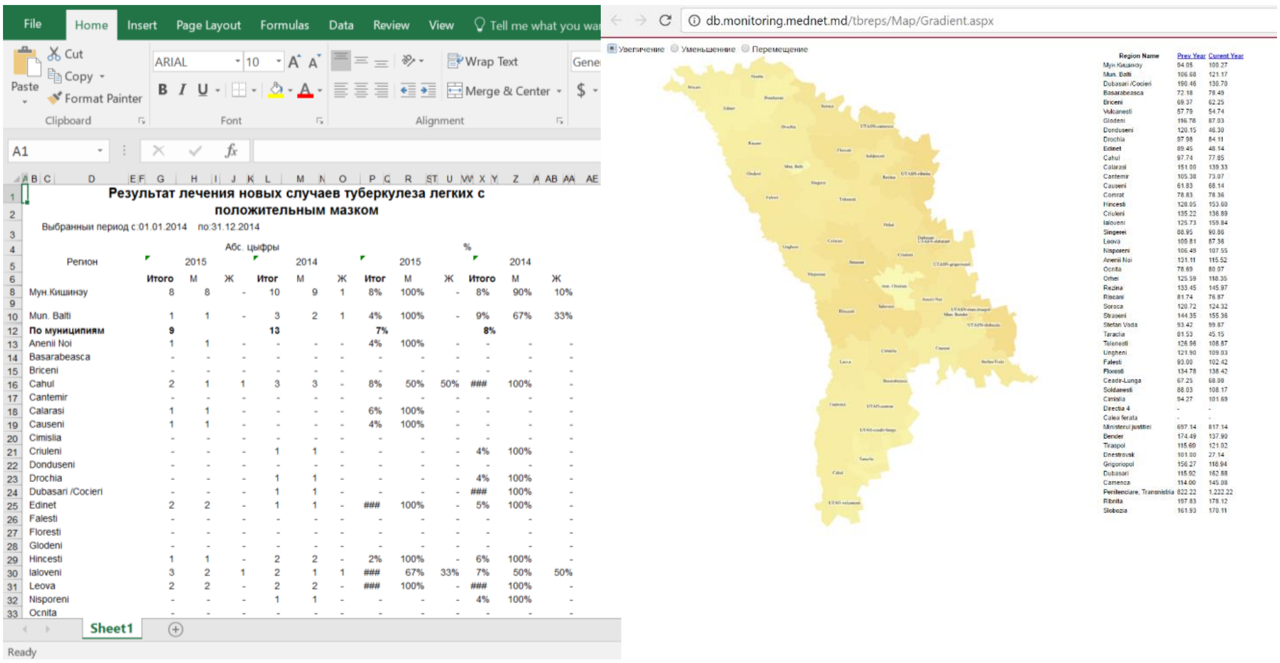
Source: SIME TB *(4)*.

A separate entry is made for each TB episode. However, the system automatically generates a unique alphanumeric identifier for each patient, which enables the identification of multiple episodes of disease affecting a single patient. Currently, about 50–55 sites enter data into the SIME TB at district, laboratory, national levels, including the penitentiary system. To ensure data security and confidentiality, the server is located at the NCHM to ensure restricted physical access. Data are backed up regularly according to an agreed schedule. Different categories of authorization provide different access rights (viewing, modification, deletion). The system automatically generates electronic outputs in the form of fixed standard tables and maps, in line with the WHO definitions and reporting framework, revised in 2013 *(16)*.

The laboratory module is completed by all third-level laboratories performing culture tests. The TB laboratory register includes both suspected and confirmed TB cases. To view the laboratory result in the patient's register, the treating doctor should search for the laboratory results in the laboratory module and link them to the patient module.

Several procedures are in place to ensure the quality of collected data. These include automated checks at data entry and batch checking, regular monitoring visits at national to district levels at least once a quarter using a SOP for data validation and quality assurance. The SIME TB is designed so that data validation checks are undertaken during data entry to prevent errors. For most variables (sex, geographical location, case type, previous history, laboratory results), only pre-defined options are allowed; these appear in a drop-down menu during data entry. Fields are enhanced with checks so that only numbers can be entered into numeric fields and dates into date fields. Core variables are "must enter" fields, so there are no missing values for them. In several fields with manual data entry, there were no restrictions on values within plausible ranges (e.g. the registration date could be after the treatment start date). However, this was done deliberately to enable data entry for patients who started treatment outside of the Republic of Moldova (in such cases, the registration date is after the treatment start date). The SIME TB is enhanced with feature to validate the entered data. By pressing the "validate" button, system users can generate a report of inconsistencies and missing values in a separate window to inform them about potential errors. The system is enhanced with a user-friendly instruction manual and dictionary within the website, which is regularly updated to incorporate changes made to the system.

Fig. 1.3. Screenshots of the SIME TB database, showing an analysis of internal consistency by comparing notification data in consecutive years (in percentages; left) and a generated map showing an area with excessive year-on-year change in selected indicators

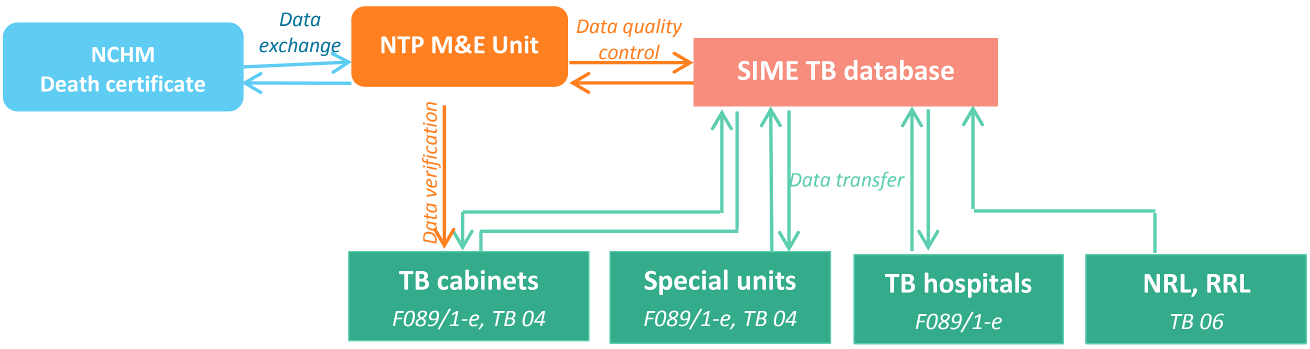


External quality control is ensured by regular monitoring visits. Data quality specialists from the national centre regularly visit each of the reporting TB units and validate the data using a SOP. The SOP includes cross-checking the paper, electronic and laboratory registers, and assessing the consistency and completeness of entered data. Every year in March, data entered in the previous year are locked to prevent changes being made to the database. Only a limited number of users at national level can make changes to the previous year's records after validation. This approach protects historical data by preventing its deletion and modification. In addition, at the Monitoring and Evaluation Unit, data consistency within reporting units is analysed by comparing notification rates between two consecutive years.

Another important characteristic of the Moldovan TB surveillance system is its strong link with the vital registration systems. At the central level, there is monthly exchange of data between the TB surveillance system and Demography Department of the NCHM on recorded TB deaths. Cases of TB diagnosed postmortem are notified to the TB surveillance system following verification with health care providers and included in cohort analyses. The NTP might correct the cause of death in the vital registration system if there is insufficient evidence that the death was caused by TB (e.g. cured TB patients). In addition, TB deaths recorded in the TB surveillance system but with a missing cause-of-death record in the vital registration system are corrected. This approach ensures that all TB cases diagnosed postmortem are included in the surveillance system and that all causes of death (whether TB or not) are corrected in the vital registration system (Fig. 1.4).

Moldovan routine surveillance data have been extensively used to produce peer-reviewed scientific articles. Aggregate surveillance data are accessible on the website. However, the most recent narrative surveillance report was produced in 2012.

Fig. 1.4. Flow of information in the Moldovan TB surveillance system



1.3 Capacity of the national TB notification and vital registration system to provide a direct measure of TB disease burden

Standard B1.1

Case definitions are consistent with WHO guidelines.

Benchmarks

All of the following benchmarks should be satisfied to meet this standard.

- *Laboratory confirmed cases*[2] *are distinguished from clinically diagnosed cases.*
- *New cases are distinguished from previously treated cases.*
- *Pulmonary TB cases are distinguished from extrapulmonary TB cases.*

[2] By sputum smear, bacterial culture or a WHO-endorsed molecular test e.g. GeneXpert MTB/RIF.

The following documents were reviewed to assess these benchmarks:

- *Monitoring and evaluation plan of the national tuberculosis control programme (2011–2015) (17)*
- *National health statistics report, (17)*
- *Manual of SIME TB application*
- *Guide for completing recording and reporting forms*
- Notification form on the diagnosis of active TB in new and relapse patients and those undergoing treatment (form 089/1e parts 1 and 2)
- TB registers (paper and electronic) and surveillance data submitted to the WHO global TB database.

Performance indicators and recording and reporting forms distinguish bacteriologically confirmed from clinically diagnosed cases, new from previously treated cases, and pulmonary from extrapulmonary TB cases. The forms were updated long before the launch of the WHO revised definitions and reporting framework in 2013. Electronic registers and laboratory request forms contain designated fields for entering the results of GeneXpert MTB/RIF and culture tests. Annual surveillance data submitted to the WHO global TB database from the Republic of Moldova are distinguished by all available laboratory confirmation methods (sputum smear, culture and GeneXpert MTB/RIF tests), as well as by patient history and site of disease. It should be noted that classification of patients by previous treatment history is not fully in line with WHO recommendations: in paper and electronic registers there is no option for patients with an "unknown treatment history"; and in patients with a previous treatment history, there is no option for an "unknown treatment outcome". However, because an electronic register has operated for over 10 years in the Republic of Moldova, these data can be accurately identified for any patient residing in the Republic of Moldova by any TB health care provider. Therefore, lack of these options has little impact.

Conclusion

Key policy documents, as well as the data management system, provide disaggregation of cases by laboratory confirmation results, TB treatment history and site of disease, in line with WHO guidelines. Therefore, the Moldovan system fully satisfies all three benchmarks.

Standard B1.2

The TB surveillance system is designed to capture a minimum set of variables for all reported TB cases.

Benchmarks

Data are routinely collected for at least each of the following variables for all TB cases:

- *age or age group*
- *sex*
- *year of registration*
- *bacteriological results*
- *history of previous treatment*
- *anatomical site of disease*
- *a patient identifier (for case-based systems).*

The Republic of Moldova uses both paper and electronic case-based surveillance systems. Core data are collected and recorded on individual TB case registration forms (form 089/1e part 1: Notification form on the diagnosis of active TB in new and relapse patients and those undergoing treatment) and facility TB registers (TB 03). Once a patient is diagnosed with TB, all core information is captured on an individual copy of form 089/1e, which is sent for data entry into the SIME TB electronic register. A national report is prepared based on the national electronic register. Both paper and electronic TB registers record all essential variables, including age, sex, year of registration, bacteriological results, history of previous treatment and site of disease for all notified TB patients. Moreover, in addition to core data, detailed information on socioeconomic status and underlying risk factors is collected, including area of residence (urban vs rural), occupation, living conditions, history of incarceration, number of household contacts and comorbidities, as well as DST results, HIV status and ART treatment.

All TB patients have a unique identifier that enables identification of multiple episodes of diagnosis in a single patient. The unique identifier is generated automatically by the system once patient data are entered into the database: the first two characters of the identifier are generated from first two letters of patient name, two characters from patient family name, six digits of the patient's birth date and the patient's sex. Review of national reports and electronic registers for 2015 and 2016 indicated that all core variables are consistently recorded, few data entry errors for the dates of registration and diagnosis. Thus, we conclude that this standard is fully met.

Standard B1.3

All scheduled periodic data submissions have been received and processed at the national level.

Benchmarks

- *For paper-based systems: 100% of expected reports from each TB basic medical unit have been received and data aggregated at the national level.*
- *For national patient-based or case-based electronic systems that import data files from subnational (provincial or regional) electronic systems: 100% of expected data files have been imported.*

The Moldovan electronic registration system is real-time and web-based; data for each notified case are entered at regional TB facilities and in the prison system, so no import of data file is needed. The autonomous Transnistria region also provides surveillance data. The completeness of notification data is assessed on a quarterly basis (twice a year starting from 2016) by the Monitoring and Evaluation Unit by comparing outputs of notification data from the electronic surveillance system and paper-based TB registers.

Conclusion

Because all expected data submissions from TB reporting units (including Transnistria and the prison system) are received and processed at the national level, the standard could be assumed to be met.

Standard B1.5

Data in the national database are accurate, complete, internally consistent and free of duplicates (for electronic case-based or patient-based systems only).

Benchmarks

All of the following benchmarks should be met to reach this standard.

- *Data validation checks are in place at the national level to identify and correct invalid, inconsistent and/or missing data in the minimum set (standard 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.*

The SIME TB is enhanced with a range of data validation checks to prevent, identify and correct invalid, inconsistent and missing data. Most core variables (name, surname, birth date, sex, region, TB type and site of disease) are "must enter" fields, so the record cannot be saved without adding these variables. For most variables (sex, geographical location, type, previous history, laboratory results) only pre-defined options can be entered; these appear as a drop-down menu during data entry. In addition, fields are enhanced with checks, so that only numbers can be entered into numeric fields and dates into date fields. Several fields that are supposed to be entered manually, there are no restrictions to values within plausible ranges (e.g. the date of registration, birth or diagnosis cannot be in the future). The SIME TB is enhanced with a logic check to minimize inconsistencies. For example, if the treatment start date is earlier than the registration date, a pop-up window will appear to ask whether the user wants to save the record. Once record with incomplete data is saved, a pop-up window 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 the "check for errors" button, which generates a pop-up window highlighting all missing and inconsistent fields. After the third month, records are locked to users and it is no longer possible to make back-dated changes to the database. Only a limited number of data quality specialists at the national level are authorized to make back-dated changes. On 1 March each year, data from the previous year is locked. Thus, the first benchmark is deemed to be met.

To assess the second benchmark, we reviewed the national electronic dataset of TB patients for 2015. The fields for age, site of disease, microscopy results for pulmonary TB patients and previous treatment were 100% complete and consistent (i.e. free of unfeasible results). In all, 10 out of 4203 records (0.2%) did not include the treatment start date and in 71 (1.7%) the treatment start date was earlier than the date of diagnosis. This inconsistency was explained by removal of the validation check to allow data entry for cases transferred from abroad, for which the treatment start date is actually earlier than the registration date. Hence, the second benchmark also is considered to be satisfied.

To assess the level of unresolved duplicates, we exported all records containing core variables into a Microsoft Excel spreadsheet, sorted alphabetically by name and looked for potential duplicates using Excel conditional formatting for "detect duplicate value". All highlighted duplicates were assessed separately by comparing the category of disease, registration date and treatment start date. All cases with the same unique identifier and same name, surname or birth date were multiple episodes of the same cases, and duplicate records were found.

Conclusion

Based on these findings, it could be concluded that the Moldovan TB surveillance system satisfied all three benchmarks. Therefore, standard B 1.5 has been met for 2015.

Standard B1.6

TB surveillance data are externally consistent.

Benchmark
Among new TB cases, the percentage of children diagnosed with TB is between 5–15% in low- and middle-income countries and <10% in high-income countries.

The World Bank classifies the Republic of Moldova as a country with a lower-middle-income economy *(18)*. Therefore, the expected percentage of children diagnosed with TB in the Republic of Moldova should be 5–15%. Of the 2863 new TB cases notified in 2015, 114 were children aged 14 years and below, representing 4.0% of the total. This is slightly below the acceptable range of values for a middle-income country. Thus, this benchmark is not satisfied and the standard is not met.

Standard B1.7

TB surveillance data are internally consistent over time.

Benchmark
If vital registration data are available, then the following benchmark should be satisfied for this standard to be met.

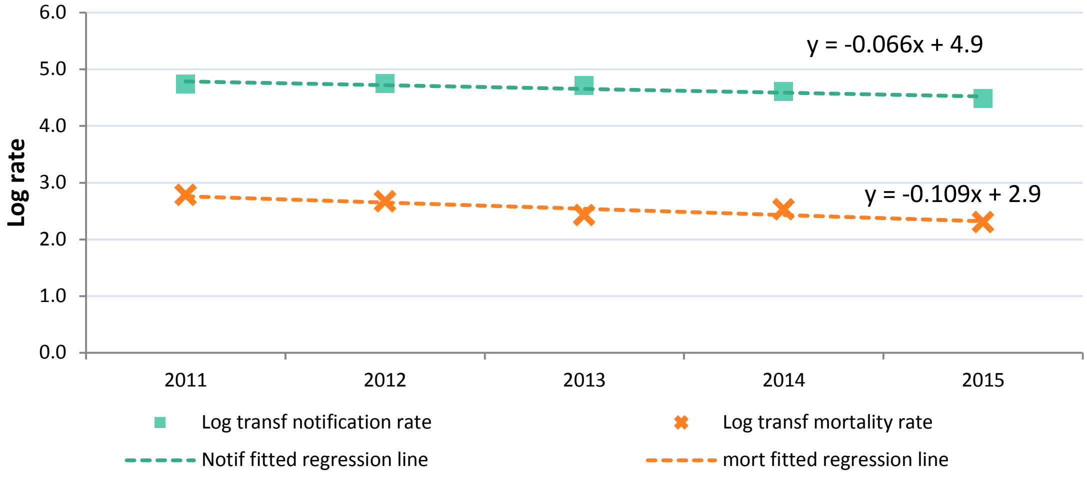
- *The year-on-year change in the national number of reported TB cases is consistent with the year-on-year change in national TB mortality (HIV-negative, from national vital registration) i.e. the trajectories are moving in the same direction.*

If the surveillance and vital registration system are of an acceptable quality, trends in TB case counts are expected to follow the same trajectory as trends in TB mortality. Table 1.1 shows the TB (all forms) case notification and mortality rates based on data reported by the vital registration system for 2011–2015. The average rate of change was calculated using a linear regression model fitted to log-transformed case notification rates and log-transformed TB mortality rates. The slope was calculated for each model. The average annual percentage change in the TB notification rate over this period was −6.6%, and the average annual percentage change in mortality rate was −10.9%. These data suggest that notification and mortality are moving in the same direction, but that mortality is decreasing faster than notification, as expected (Fig.1.5). Thus, this benchmark is considered to be satisfied.

Table 1.1. TB case notification and mortality rates per 100 000, Republic of Moldova, 2011–2015

Year	Notification rate (per 100 000)	TB mortality rate (per 100 000)	Log-transformed notification rate	Log-transformed mortality rate
2011	114.5	16.1	4.7	2.8
2012	114.7	14.4	4.7	2.7
2013	110.3	11.3	4.7	2.4
2014	99.7	12.5	4.6	2.5
2015	88.4	10	4.5	2.3
Slope	–	–	−0.066	−0.109

Fig. 1.5. Log-transformed TB notification rate (new and relapse) and TB mortality rate fitted with linear regression line, the Republic of Moldova, 2011–2015



Source: SIME TB *(4)*.

Standard B1.8

All diagnosed cases of TB are reported.

Benchmarks

Both of the following benchmarks should be satisfied to meet this standard.

- *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. an inventory study conducted in past 10 years).*

According to law LPM10/2009 On the state surveillance over public health, ratified on 3 February 2009 by the Parliament of the Republic of Moldova, TB is subject to compulsory notification *(19)*.

Although no formal inventory study has been conducted in the Republic of Moldova, routine data quality control mechanisms in place since 2007 ensure external data validation using a SOP on a quarterly basis across all 56 basic medical units. This includes cross-checking laboratory registers with the TB register, cross-checking the TB register with an inventory of patient incentives and cross-checking form 089/1e with the electronic register at both local and national levels. In addition, death certificates containing a diagnosis of TB are checked with the TB electronic register on monthly basis; each case of postmortem TB diagnosis is added to the electronic register and action is taken to identify contacts.

During the epidemiological review, the team of reviewers visited randomly selected TB facilities in Cimișlia, Hincești, Comrat, Orhei and Soroca, and one of the five polyclinics in Chişinau Municipality. Cross-checking the TB and electronic registers for 2015 indicated a >99% agreement in results. From the laboratory register, we identified patients with positive GeneXpert MTB/RIF or microscopy results in 2016, and checked whether these patients were included in the TB register (SIME TB). Of the 144 bacteriologically confirmed TB cases recorded in the laboratory registers of these facilities, 143 (99.3%) were included in the TB register. An explanation for this minor discrepancy is that we reviewed the most recent records, which had not yet been validated by the Monitoring and Evaluation Unit. We were impressed by the proficiency of all TB doctors at these facilities in using the SIME TB to search for information in the database. Importantly, data entry was not a passive, one-way process for them; they were interested in data quality and could describe the benefits of the real-time web-based system for accomplishing their tasks. We therefore conclude that the existing system of data quality control fully replaces periodic investigations; therefore, this benchmark is deemed to be satisfied and the standard is met.

Standard B1.9

The population has good access to health care.

Benchmarks

Both benchmarks should be satisfied to meet this standard.

- *The under-five mortality rate (i.e. the probability of dying by age 5 years per 1000 live births) is <10.*
- *<25% THE is OOP.*

For notification data to provide a direct measurement of TB incidence, apart from the accurate reporting of diagnosed TB cases (standard B1.8), the number of undiagnosed cases must be a small or negligible fraction of the total number of TB cases. To ensure that all TB cases are diagnosed and reported (i.e. that notification is a proxy of incidence), the population must have good access to a well-functioning health care system. The under-five mortality rate and the percentage of health expenditure that is OOP provide a very broad overall indication of the quality and coverage of health care, as well as the affordability and accessibility of services.

According to the WHO Global Health Observatory data repository, the under-five mortality rate in the Republic of Moldova in 2015 was 13.6 per 1000 live births, suggesting some suboptimal access to quality health care *(20)*. Moreover, in 2014 OOP expenditure was 38.4% of THE *(21)*, suggesting the existence of notable financial barriers to health services.

In these conditions, it is likely that there are people with TB in the Republic of Moldova who are not being diagnosed with the disease. Therefore, TB notification data are not a good proxy for TB incidence. Thus, neither of the two benchmarks is satisfied and the standard is not met.

Recommendations

The action needed to address the gaps is beyond the influence of a TB surveillance system and is long-term in nature, including strengthening health care services, increasing financial investments and introducing mandatory national health insurance.

Standard B1.10

The vital registration system has high national coverage and quality.

Benchmarks

Both of the following benchmarks should be satisfied to meet this standard.

- *Cause of death documented in >90% of total deaths recorded in (i) national vital registration system or (ii) sample vital registration system.*
- *<10% of deaths have ICD codes for ill-defined causes (defined as ICD-9 780–799 and ICD-10 R00-R99).*

The World Bank estimated that 90% of death records in the Republic of Moldova in 2012 (latest available data) included information on the cause of death *(22)*.

According to the WHO mortality database, from 2005 to 2013 the total number of deaths with ill-defined causes with codes R00–R99 ranged between 217 and 277, or consistently below 1% *(23)*. In 2014, according to the database of the Demography Department of the NCHM, only 301 deaths had ill-defined causes, which is about 0.8% of the total TB deaths. This suggests satisfactory data quality on cause of death.

Conclusion
Both benchmarks are considered to be satisfied and the standard is met.

Standard B2.1

Surveillance data provide a direct measure of drug-resistant TB in new cases.

Benchmarks
One of the following benchmarks should be satisfied to meet this standard.
- *Rifampicin susceptibility status (positive/negative) documented for ≥75% of new pulmonary TB cases.*
- *Rifampicin susceptibility status (positive/negative) documented for a nationally representative drug resistance survey of new pulmonary TB cases.*

All bacteriologically confirmed pulmonary TB cases in the Republic of Moldova are tested for drug resistance. Concordance for first-line TB drugs in the most recent round of proficiency testing conducted by the supranational reference laboratory was 100% for both isoniazid and rifampicin.

According to the Moldovan surveillance report for 2015 in the WHO global TB database, 2553 new pulmonary TB cases were notified *(24)*. Of these, 1623 patients (63.6%) had a positive culture or positive findings in WHO-recommended rapid diagnostic tests such as GeneXpert MTB/RIF. Of the 1623 bacteriologically confirmed patients, 1292 (79.6%) had documented DST results for both rifampicin and isoniazid. Another 252 patients (15.5%) had only GeneXpert MTB/RIF test results. Thus, the percentage of new pulmonary TB patients with documented rifampicin DST results in 2015 was 60.5% (1544/2553), which is within the 50–75% range. Thus, the standard is only partially met.

Standard B2.2

Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases.

Benchmarks
One of the following benchmarks should be satisfied to meet this standard.
- *HIV status (positive/negative) is 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[3] or where it is not feasible to implement routine surveillance.*

[3] In which HIV prevalence has not consistently exceeded 5% in any defined subpopulation.

WHO recommends that all patients with presumptive or diagnosed TB should receive HIV testing and counselling to ensure early case detection and rapid initiation of treatment *(25)*. Data on HIV status among TB cases should be collected through routine surveillance in all settings regardless of HIV epidemiology.

In 2015, a total of 3608 new and relapse TB cases (all forms) were notified in the Republic of Moldova. Of these, HIV status documented for 3439 (95.3% of total cases), so the standard could be assumed fully met.

Standard B2.3

Surveillance data for children reported with TB are reliable and accurate, and all diagnosed childhood TB cases are reported.

Benchmarks

Both of the following benchmarks should be satisfied to meet this standard.

- *The ratio of the age group 0–4 years affected by TB to those aged 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. an inventory study conducted in the past 10 years).*

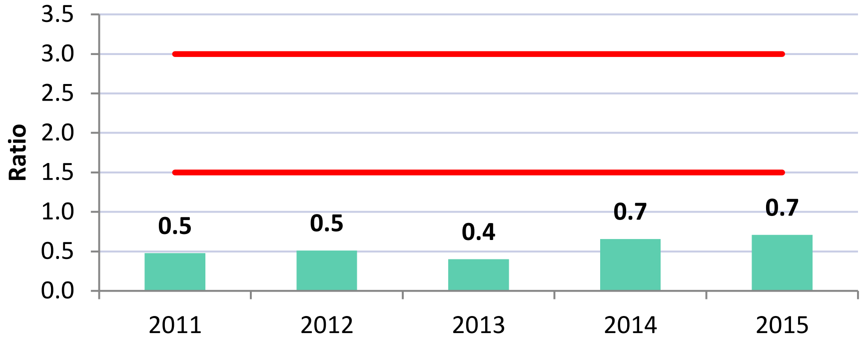
TB is often not considered as a possible diagnosis in case of child diseases and therefore often goes undetected. It is difficult to establish a definitive diagnosis of TB in children because it is rarely laboratory confirmed. Children can present with TB at any age, but the most common age is between 1 and 4 years. Children aged 0–4 years are at the highest risk of contracting TB; therefore, TB is more common in this age group than in children aged 5–14 years. The lowest risk of TB is observed at age 5–10 years, known as the safe school years. According to routine notification data for the Republic of Moldova in 2015, of the 114 children diagnosed with TB, 46 were aged under 5 years and 68 were aged 5–14 years. Thus, the number of children with TB aged 0–4 years is much lower than number of children aged 5–14 years, suggesting that many cases of TB in children aged <5 years in the Republic of Moldova remain undetected and/or underreported. The ratio of TB cases in children aged 0–4 years to those aged 5–14 years in 2015 was 0.7, far below the expected level. Thus, the first benchmark is considered not satisfied (Fig 1.6). No inventory study has been undertaken in the previous 10 years in the Republic of Moldova; however, given the exceptional internal and external data quality of the routine data collection system, the second benchmark is considered to be satisfied. As a result, standard B 2.3 is partially met.

Recommendations

Potential reasons for the underdetection of child TB case should be considered and discussed with paediatricians, intensive care physicians from paediatric hospitals, pulmonologists, family practitioners and all those who make and report the diagnosis of childhood TB.

Corrective actions may be required, including training of health care providers and revising the differential diagnostic algorithm adopted at the general hospital.

Fig. 1.6. TB ratio of the 0–4 age group to the 5–14 year aged group, the Republic of Moldova, 2010–2015



Horizontal red lines indicate the range of the benchmark at levels of 1.5 and 3.0.

Source: WHO global TB database *(24)*.

1.4 Strengths and weaknesses of the TB surveillance system

Of the 12 standards for TB surveillance, eight were met, two were partially met, and only two were not met (Table 1.2), indicating that the TB surveillance system is operating quite effectively. We can therefore assume that the surveillance system provides a direct measure of the number of TB patients detected; nevertheless, notification is not a good proxy for TB incidence because of limited access of the population to health care services and/or weaknesses of the health care system.

Table 1.2. Summary of standards for TB surveillance, the Republic of Moldova, September 2016

Standard	Met	Partially met	Not met	Not applicable
B1.1 Case definitions consistent with WHO guidelines	X			
B1.2 TB surveillance system designed to capture a minimum set of variables for reported TB cases	X			
B1.3 All scheduled periodic data submissions received and processed at national level	X			
B1.4 Data in quarterly reports are accurate, complete and internally consistent				X
B1.5 Data in national database are accurate, complete, internally consistent and free of duplicates	X			
B1.6 TB surveillance data are externally consistent			X	
B1.7 Number of reported TB cases is internally consistent	X			
B1.8 All diagnosed cases of TB are reported	X			
B1.9 Population has good access to health care			X	
B1.10 Vital registration system has high national coverage and quality	X			
B2.1 Surveillance data provide a direct measure of drug-resistant TB in new cases		X		
B2.2 Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases	X			
B2.3 Surveillance data for children reported with TB are reliable and accurate		X		

Based on the WHO TB surveillance checklist, the strengths of the TB surveillance system in the Republic of Moldova include:

- an established web-based real-time electronic database at all levels
- availability of effective data quality assurance mechanisms
- universal access to culture testing, DST and HIV testing
- linkage between the vital registration system and TB surveillance system
- adequate numbers of highly skilled staff both at national and district levels;

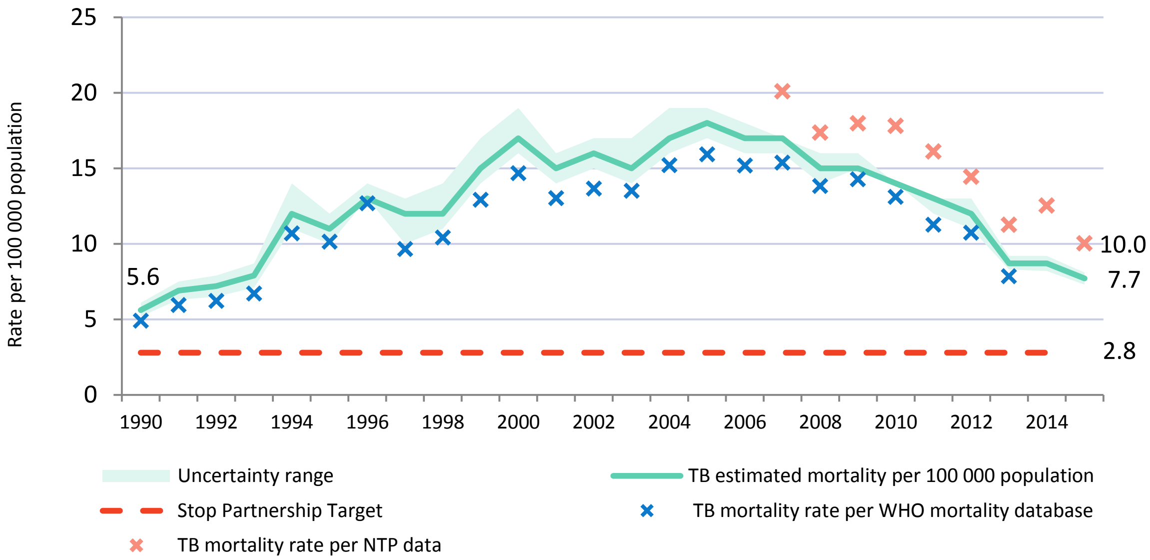
and the weakness include:
- lack of external consistency
- limited validity of surveillance data for childhood TB.

2. Assessment of the level of, and trends in, TB disease burden

2.1 Analysis of the level of, and trends in, TB mortality

Estimates of TB mortality for the Republic of Moldova are based mainly on information from the vital registration system *(24)*. Thus, in 1990 TB mortality rate was estimated 5.6 per 100 000 population. Between 1990 and 2005, the rate gradually increased with some fluctuations from 5.6 to 18. Starting from 2005, the mortality trend has been decreasing, with an average annual decline of 11.2%. By the end of 2015, TB mortality in the Republic of Moldova was estimated at 7.7 per 100 000 population, which is almost three times higher than Millennium Development Goal 6 target of halving TB mortality by 2015 compared with 1990 (Fig. 2.1). There was a large discrepancy in the number of TB deaths in the WHO mortality and SIME TB databases: numbers of TB deaths in the SIME TB database are about 30% higher than in the TB mortality database. The reason of this discrepancy is that NTP data include TB deaths from Transnistria, whereas mortality data reported in the WHO global TB database do not.

Fig. 2.1. Estimated TB mortality rate (excluding TB/HIV mortality) per 100 000 population, the Republic of Moldova, 1990–2015

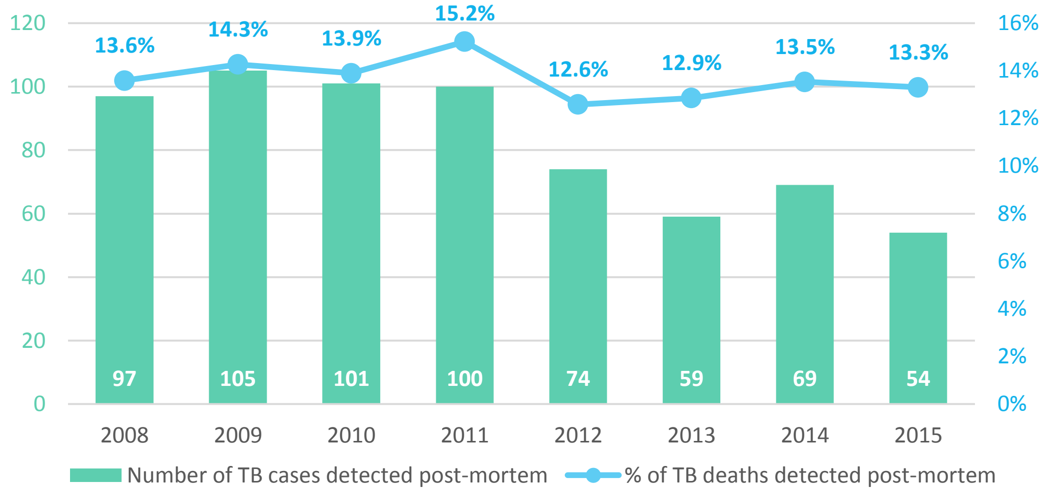


Blue crosses represent TB mortality rates reported in the WHO global TB database, which does not include data on Transnistria, red crosses represent TB mortality rates in the SIME TB database (including TB deaths in Transnistria) Shaded areas represent the uncertainty band for WHO-estimated TB mortality. The horizontal dashed line represents the MDG 6 target of a 50% reduction in TB mortality rate by 2015 compared with 1990.

Sources: WHO mortality database, WHO global TB database *(24)* and SIME TB *(4)*.

In the Republic of Moldova, TB is diagnosed postmortem in about one in seven TB deaths and this proportion has remained stable over the time; however, the absolute number of TB cases diagnosed postmortem has decreased by about twofold since 2009 (Fig. 2.2). This is another indication that TB mortality in the Republic of Moldova has fallen sharply in recent years.

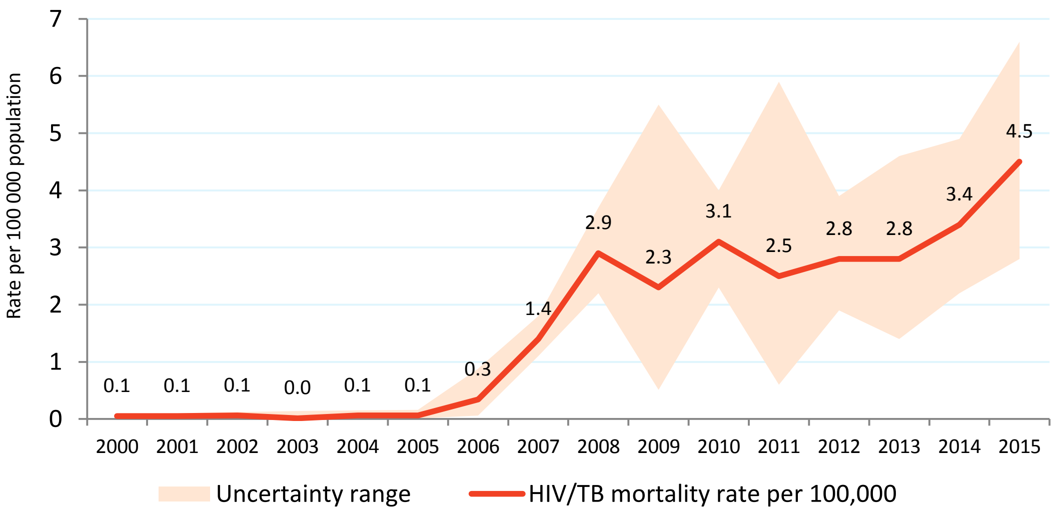
Fig. 2.2. Number and proportion of TB deaths detected postmortem among all TB deaths, the Republic of Moldova, 2008–2015



Source: SIME TB *(4)*.

WHO started estimating the number of deaths due to HIV/TB coinfection in 2011. As shown in Fig. 2.3, deaths due to HIV/TB coinfection have increased rapidly, especially in recent years. In 2015, WHO estimated 4.5 HIV/TB deaths per 100 000 population, equivalent to an absolute number of 180 deaths (range 110–270 deaths).

Fig. 2.3. Estimated HIV/TB mortality rate per 100 000 population, the Republic of Moldova, 2000–2015



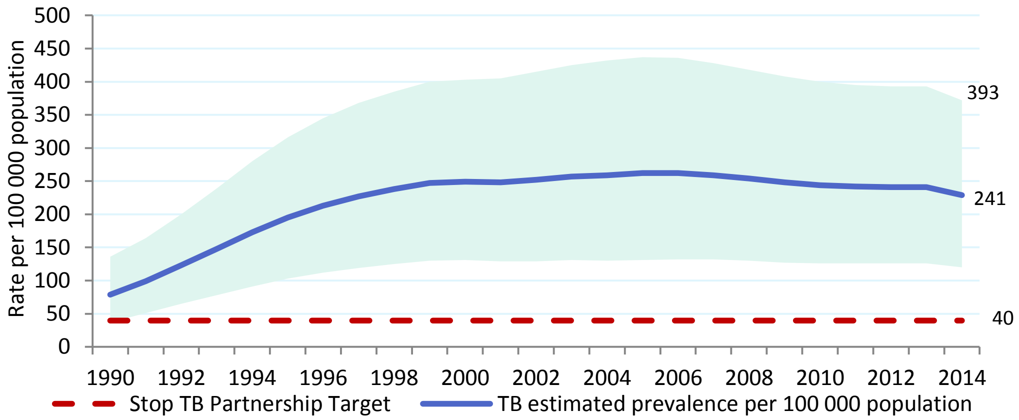
Shaded areas represent the uncertainty band.

Source: WHO global TB database *(24)*.

2.2 Analysis of the level of, and trends in, TB prevalence and incidence

There are no data from direct measurement of TB prevalence in the Republic of Moldova. The only available information on TB prevalence comes from WHO indirect estimates. The last estimate of TB prevalence was produced for 2014. Thereafter, WHO stopped producing estimates for TB prevalence because this is no longer a target indicator for sustainable development goals. According to the WHO *Global tuberculosis report 2014*, TB prevalence in the Republic of Moldova rapidly increased from 79 cases per 100 000 population in the early 1990s and peaked at 262 (131–437) cases per 100 000 population in 2005–2006 *(26)*. TB prevalence then slowly decreased by an average of 1.5% per year to 229 (120–372) cases per 100 000 population in 2014 (Fig. 2.4). As for TB mortality, the Republic of Moldova did not achieve the Stop TB Partnership Goal of halving TB prevalence by 2015 compared with the estimate of prevalence in 1990.

Fig. 2.4. Estimated TB prevalence, the Republic of Moldova, 1990–2014

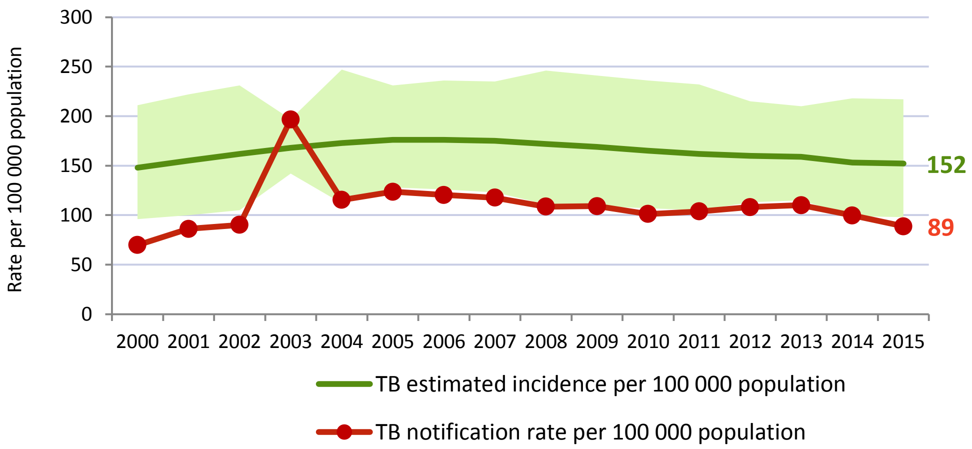


Shaded areas represent the uncertainty band. Horizontal dashed line represent Stop TB Partnership target of a 50% reduction in prevalence rate by 2015 compared with 1990.

Source: WHO global TB database *(24)*.

In the Republic of Moldova in 2015, there were an estimated 6200 incident cases of TB (uncertainty range 4000–8800), equivalent to a rate of 152 (98–217) per 100 000 population. The increasing trend in TB incidence observed since the early 1990s was reversed in 2006; however, the rate of decline of TB incidence between 2006 and 2015 was only −1.5%, compared with the mean annual decline of −5.5% recorded for the WHO European Region over the same period (Fig. 2.5).

Fig. 2.5. Estimated TB incidence rate and notification of incident TB cases (new and relapse) per 100 000 population, the Republic of Moldova, 2000–2015



Shaded areas represent the uncertainty band.

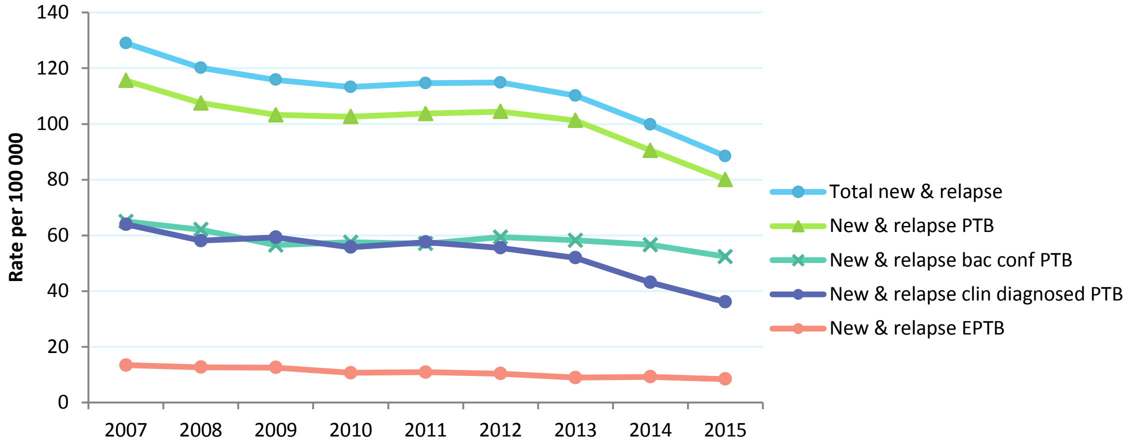
Source: WHO global TB database *(24)*.

2.3 Analysis and interpretation of the level of, and trends in, TB case notifications

2.3.1 Overall TB case notifications and time trends

In the Republic of Moldova, the number of notified incident TB cases has declined since 2007. The number of notified new and relapse TB cases decreased from 5325 (equivalent to 129 per 100 000) in 2007 to 3608 (88.7 per 100 000) in 2015, with an average rate of decrease of 5.0% per year. The decline was especially sharp between 2007 and 2009, and between 2013 and 2015 (Fig. 2.6).

Fig. 2.6. Notification of new and relapse TB cases, the Republic of Moldova, 2007–2015

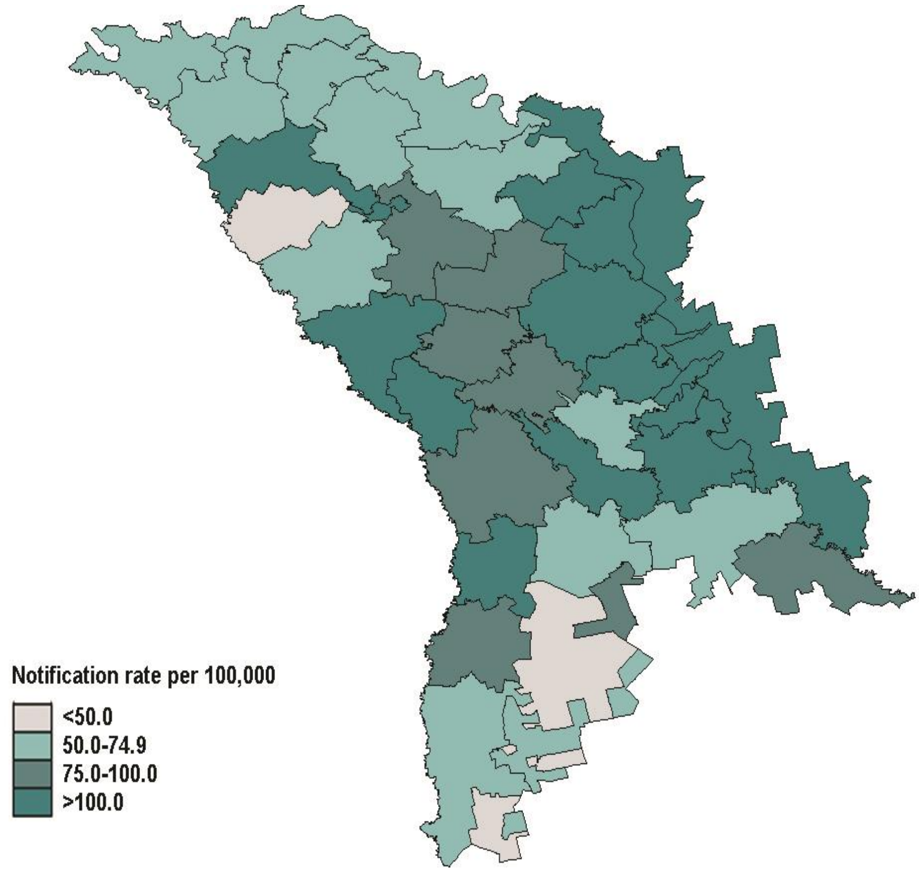


Clin: clinically; EPTB: extrapulmonary TB; PTB: pulmonary TB.

Source: SIME TB *(4)*.

As shown in Fig. 2.6, notifications disaggregated by site of disease and bacterial confirmation follow the same pattern of decline, but with different trajectories: the sharp decline observed in the last 2–3 years was driven by clinically diagnosed pulmonary TB cases, which decreased on average by −8.7% per year between 2011 and 2015. In comparison, the rate of annual decline of bacteriologically confirmed pulmonary and extrapulmonary TB cases over the same period were −1.9% and −4.7%, respectively. The comparatively slow decline in bacteriologically confirmed pulmonary TB cases may be explained by the roll-out of GeneXpert MTB/RIF testing from 2013, which improved bacteriological confirmation of TB cases. The sharp decline in clinically diagnoses cases may also be caused by a decline in overdiagnosis of suspected cases.

Fig. 2.7. Notification rate for new and relapse TB cases by districts and municipalities, the Republic of Moldova, 2015



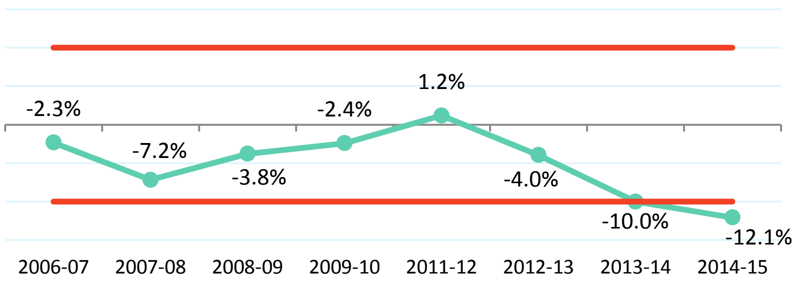
Source: SIME TB *(4)*.

Analysis of annual changes in the notification rate at national level shows a stable year-on-year decline of within 10%, indicating no evidence of problem in reporting and recording at national level.

2.3.2 TB notification and trend by geographical area

Mapping the distribution of TB notification in the Republic of Moldova shows a clear pattern, with the highest notification rate in the central part of the country and Transnistria, and lowest in the northern and southern regions (Fig. 2.7). TB notification rates vary in magnitude vary by geographical area notably from 42 per 100 000 in Gagaúzia to 122 per 100 000 in Transnistria (Fig. 2.8). Access to TB diagnostic services is unlikely to have a substantial impact on case notification rates as the Republic of Moldova is a small country with well-distributed TB diagnostic facilities. The variation is more likely to be true differences in TB burden across the regions, consistent with the striking MDR-TB heterogeneity shown in earlier studies *(27)*. Variations in the TB burden across districts could be due to differences in socioeconomic factors, population age structure, population density, MDR-TB burden and HIV burden. Thus, Transnistria has the highest TB notification rate as well as the highest MDR-TB burden and HIV/TB coinfection rate compared with other regions. In contrast, Gagaúzia has the lowest TB notification rate and also the lowest HIV and MDR-TB rates in the country.

Fig. 2.8. Annual changes in notification rate of incident TB, the Republic of Moldova, 2006–2015

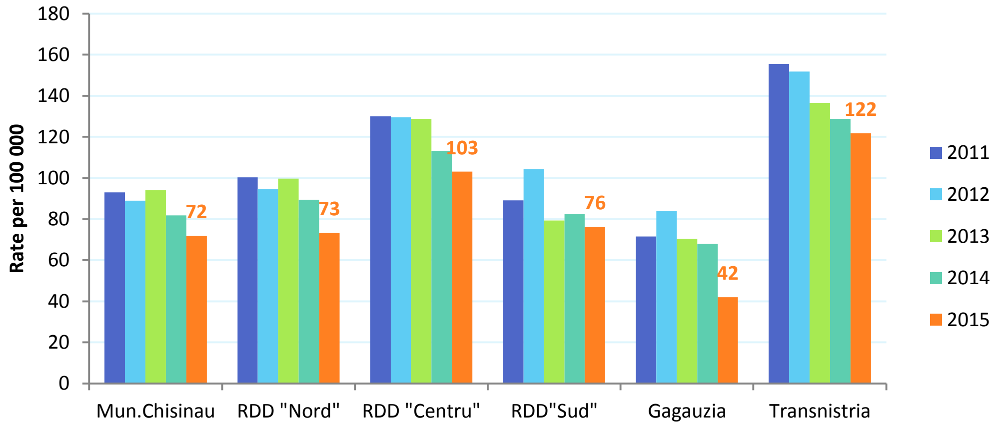


Red lines indicate ±10% limits.

Source: SIME TB *(4).*

As shown in Fig. 2.9, trajectories for notification rates across all areas are following the same direction, but at different paces. The fastest annual decline over the last 5 years was observed in Gagaúzia and in penitentiary system, reaching an average of 10% annually between 2010 and 2015. In contrast, in RDD "South", the average annual decline was as low as 0.7%.

Fig. 2.9. Notification rate of new and relapse TB cases per 100 000 population by region, the Republic of Moldova, 2011–2015

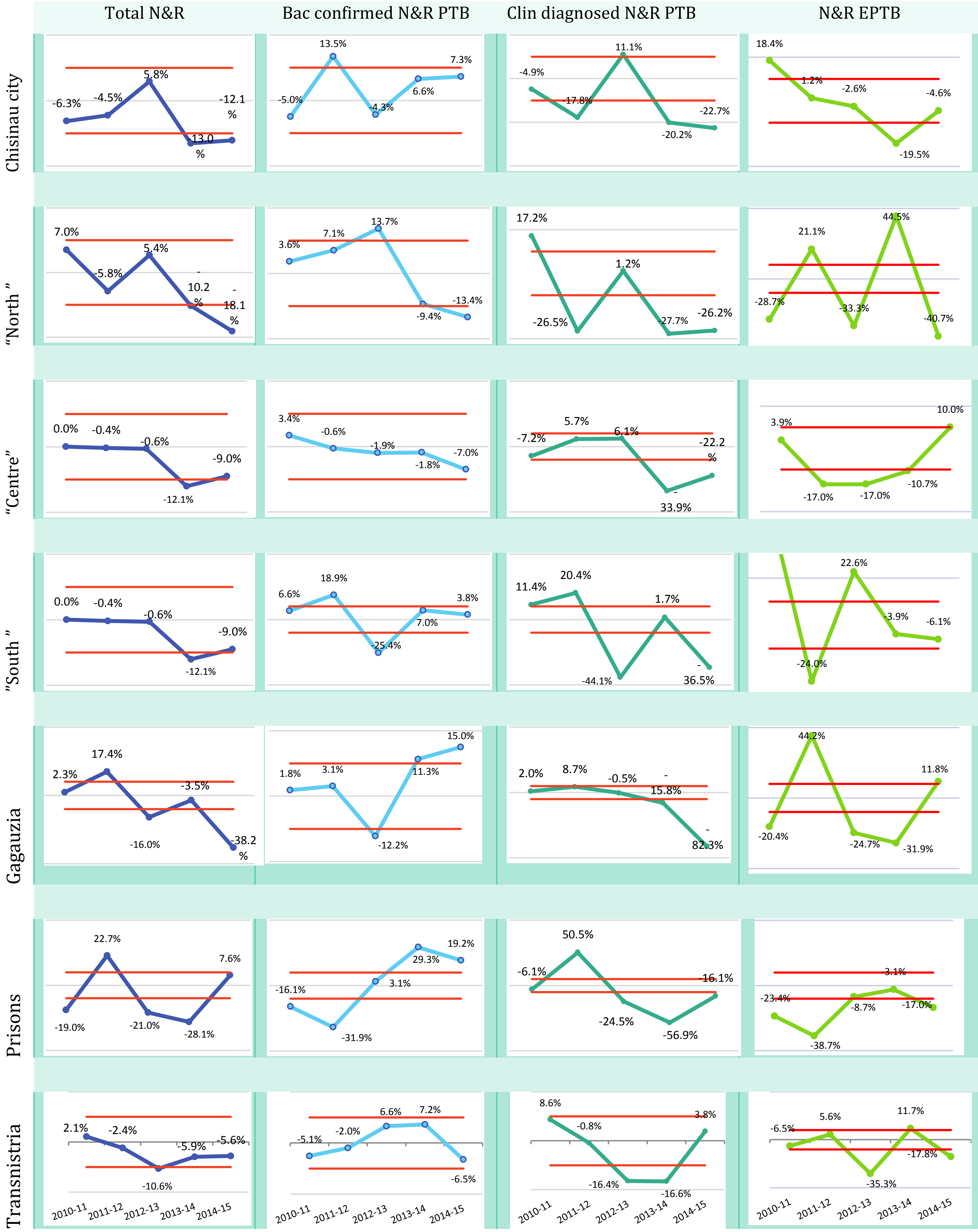


Mun: Municipality.

Source: SIME TB *(4).*

Year-on-year changes in routine TB notification from 2011 to 2015 obtained from the surveillance system and stratified by geographical area and the prison system were plotted by bacteriological confirmation and site of disease and assessed visually (Fig. 2.10). Any variation above or below 10% was considered overdispersion (i.e. variability above the expected level). Graphs show that notification of total new and relapse TB cases is more or less stable across regions, with clear trends over the years and no overdispersion. In contrast, notification of bacteriologically confirmed and clinically diagnosed TB cases increases and decreases over consecutive years, with excessive variability indicating a variable capacity for TB diagnosis. This could be explained by the roll-out of GeneXpert MTB/RIF starting from 2013, as well changes in TB screening policy. There is excessive variability in notification of extrapulmonary TB cases, suggesting that extrapulmonary TB diagnosis presents a challenge. Thus, during 2012–2014 no extrapulmonary TB was diagnosed in the penitentiary system.

Fig. 2.10. Year-on-year change in TB notification rate by geographical area, the Republic of Moldova, 2010–2011 to 2014–2015



Bac: bacteriologically; clin: clinically; EPTB: extrapulmonary TB; Mun: Municipality; N&R: new and relapse; PTB: pulmonary TB.

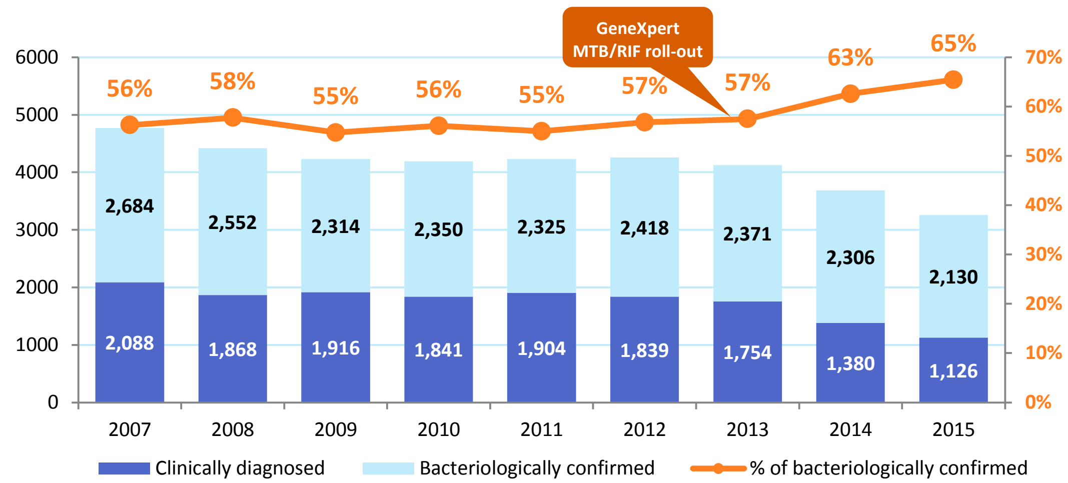
Red lines indicate ±10% limits.

Source: SIME TB *(4)*.

2.3.3 Trend in new and relapse TB notification by bacteriological confirmation

As shown in Fig. 2.11, the proportion of bacteriologically confirmed TB cases was stable between 2007 and 2013 at 55–58%, while the absolute number of TB cases decreased proportionally over the same period. Between 2013 and 2015, there was sharp decrease in clinically diagnosed new and relapse TB cases, which resulted in a relative increase in the proportion of bacteriologically confirmed TB cases from 57% in 2013 to 65% in 2015. The likely causes of these changes are improved laboratory diagnostics in the Republic of Moldova due to roll-out of the GeneXpert MTB/RIF test, as well as a decreased TB burden in the total population.

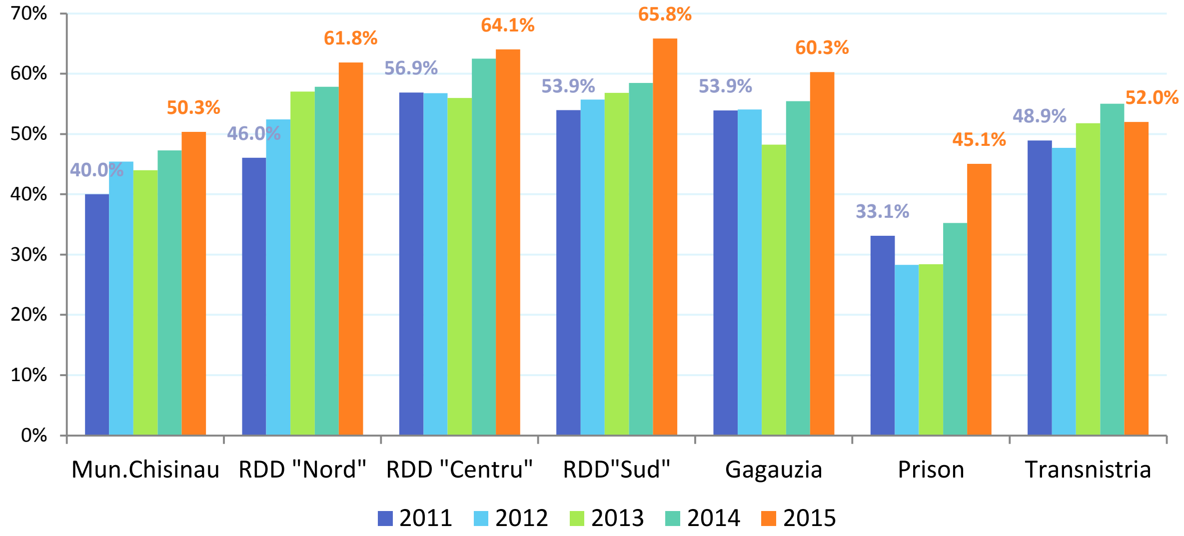
Fig. 2.11. Notification of bacteriologically confirmed and clinically diagnosed TB among incident pulmonary TB cases and the proportion of bacteriologically confirmed TB cases, the Republic of Moldova, 2007–2015



Source: SIME TB *(4)*.

The trend showing a gradual increase in the proportion of bacteriologically confirmed cases at the national level was maintained when data were disaggregated by geographical area and the prison system (Fig. 2.12).

Fig. 2.12. Trend in proportion of bacteriologically confirmed TB cases among new and relapse TB cases disaggregated by geographical area and the prison system, the Republic of Moldova 2011–2015

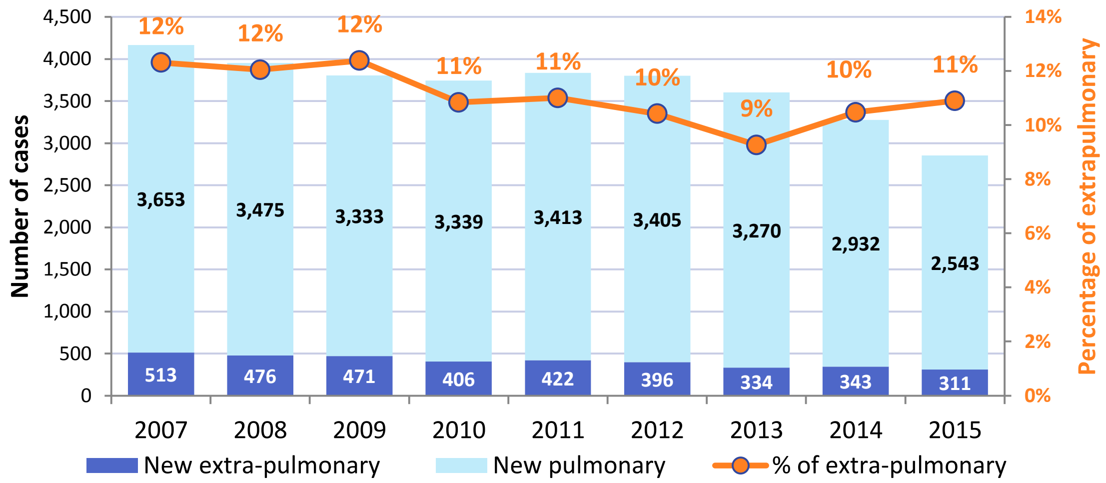


Source: SIME TB *(4)*.

2.3.4 Trend in new and relapse TB notification by site of disease

Analysis of TB notification data from 2007–2015 by site of disease reveals a declining trend in both pulmonary and extrapulmonary TB (Fig. 2.13). The proportion of extrapulmonary TB cases among new TB cases notified in 2007–2015 ranged between 9% and 12%. Overall, TB notification by site of disease has been stable, except for between 2012 and 2013, when there was an unusually sharp decline in extrapulmonary TB notification rate of >10%.

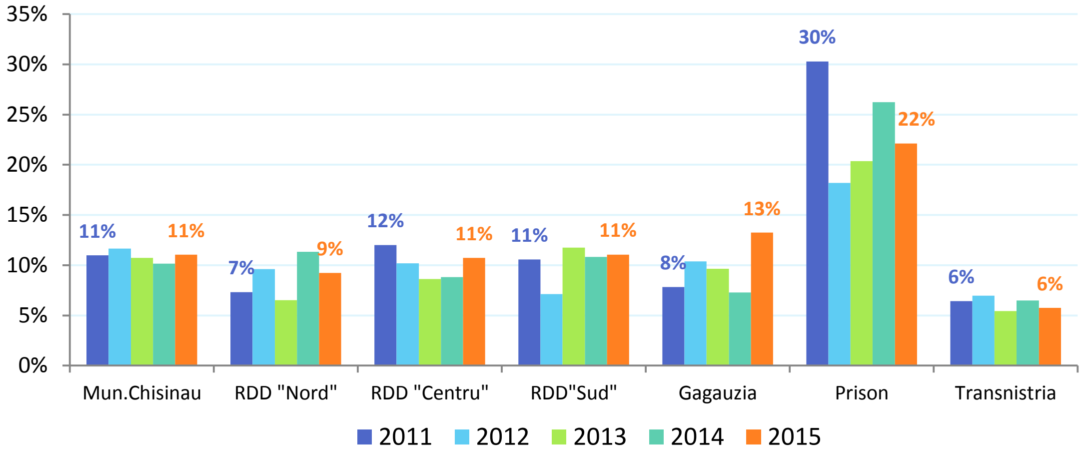
Fig. 2.13. Notification of new pulmonary and extrapulmonary TB cases and the proportion of extrapulmonary TB among new TB cases, the Republic of Moldova, 2007–2015



Source: WHO global TB database *(24)*.

The proportion of extrapulmonary TB cases among new and relapse TB cases is about twice lower in Transnistria than in other regions, but is about twice higher in the prison system compared with the national average, indicating inconsistencies in TB diagnosis or case definitions. Further investigations are needed to establish the cause(s) of these inconsistencies. There is also notable year-on-year variation, especially in Gagaúzia; however, this is probably related to small absolute number of cases.

Fig. 2.14. Proportion of extrapulmonary TB cases among new and relapse TB cases, disaggregated by geographical area and the prison system, the Republic of Moldova, 2011–2015

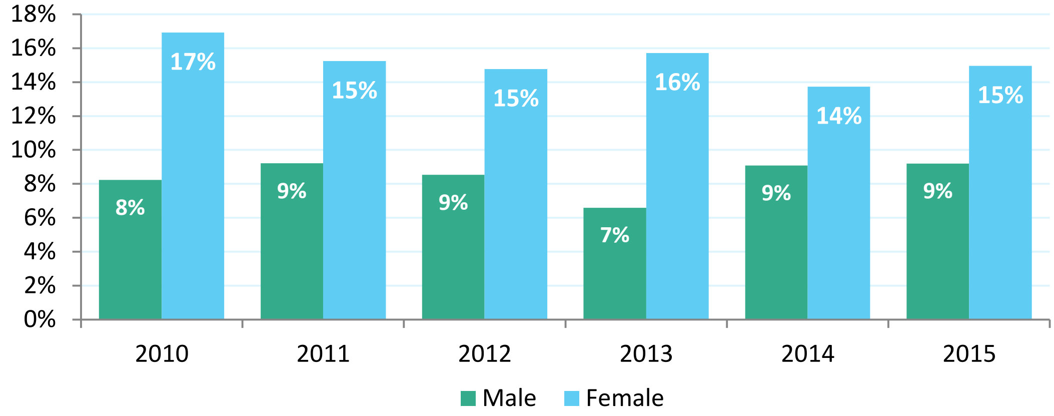


Source: SIME TB *(4)*.

Disaggregation of the trend in the proportion of extrapulmonary TB cases by sex shows striking variability: the proportion of extrapulmonary TB in male TB patients varies between 7% and 9%, whereas the proportion of extrapulmonary TB cases in female TB patients is about twice as high, ranging from 14% to 17% over the last 6 years (Fig. 2.15). The large variation in the proportion of extrapulmonary TB cases is unusual and should be explored further. Further disaggregation of the proportion of extrapulmonary TB cases by sex and age group showed[4] that there are equal proportions of extrapulmonary TB in males and females at ages up to 44 years; the difference appears after age 45 years. Another unusual feature of the TB surveillance data is the very high proportion of extrapulmonary TB cases in the population aged below 25 years. Recent epidemiological data for all age groups suggest that the proportion of pulmonary TB cases should be higher than the proportion of extrapulmonary TB cases, even in children *(28)*. The distribution of extrapulmonary TB cases in the Moldovan population and reasons for the unusual distribution according to sex, age, geographical area and the prison system should be further explored.

[4] As the Global TB database has not included disaggregation of extrapulmonary TB cases by age and sex since 2012, this analysis was not possible using the data available for 2013–2015, but was instead done using NTP data.

Fig. 2.15. Trend in the proportion of extrapulmonary TB cases disaggregated by sex, the Republic of Moldova, 2010–2015

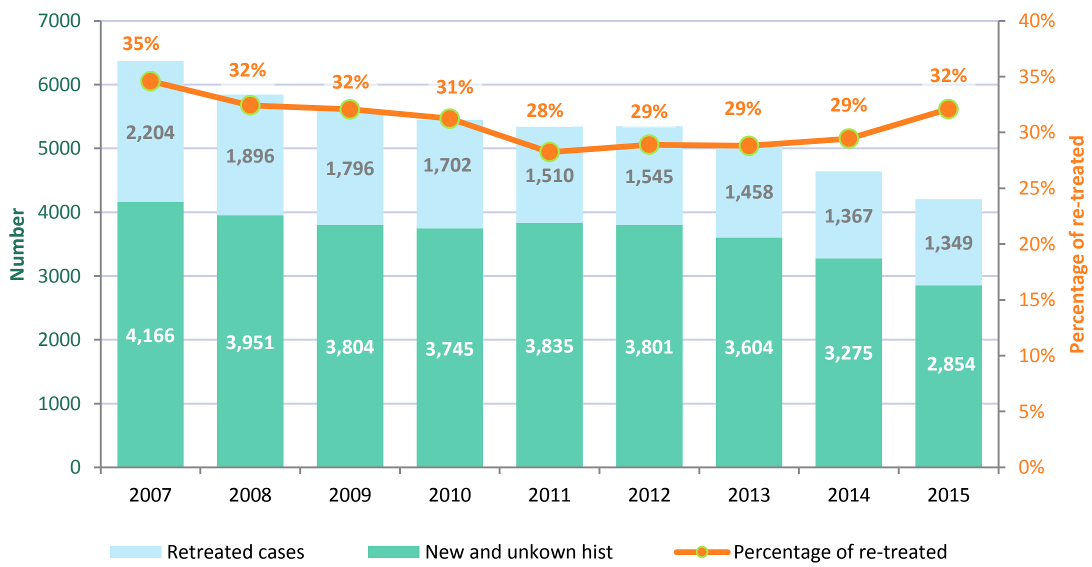


Source: SIME TB *(4)*.

2.3.5 Trend in TB notification by category

Over the last 9 years, the absolute number of both new and retreated TB cases decreased. Between 2007 and 2011, the decline was faster for retreated than for new TB cases, resulting in a relative decrease in the proportion of retreated cases from 35% in 2007 to 28% in 2011. In contrast, between 2013 and 2015, the decline was faster for new cases than for retreated cases, which led to an increase in the proportion of retreated cases from 29% in 2013 to 32% in 2015. In general, the year-on-year proportions of TB cases by category are stable at the national level. Any changes are likely to be due to increased access to diagnosis for MDR-TB patients, and increased survival of MDR-TB patients contributing to the number of retreated TB cases (Fig. 2.16).

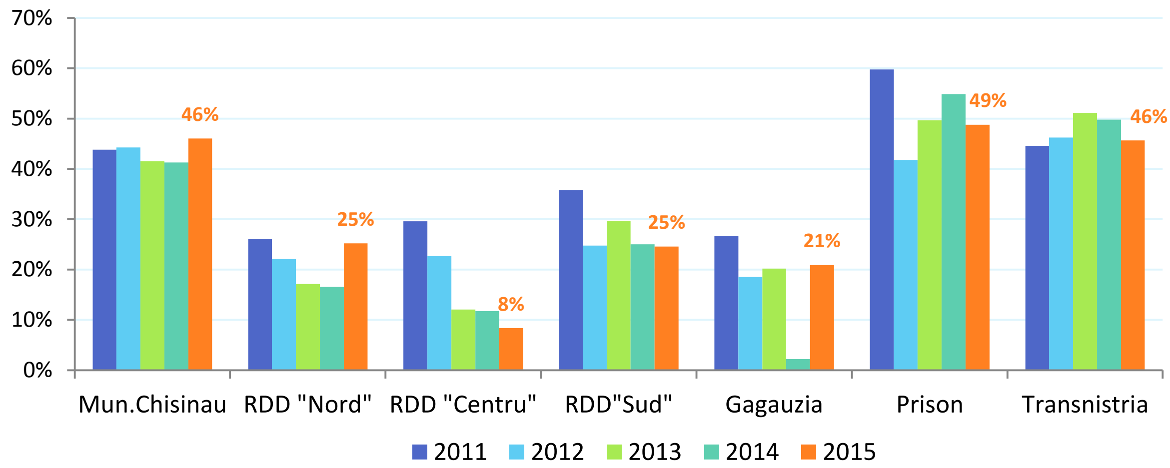
Fig. 2.16. Notification of new and retreated TB cases and the proportion of retreated among all TB cases, the Republic of Moldova, 2007–2015



Hist: history.

The proportion of retreated cases by geographical area varies greatly, from 8% in Centru to 46% in Chişinău and Transnistria, and 49% in the prison population (Fig. 2.17). This wide variation reflects the geographical heterogeneity of MDR-TB and HIV/TB coinfection. There is also notable year-on-year variation in the proportion of retreated TB patients in almost all areas without any clear trend. However, it is impossible to state with certainty that the variation is due to a weakness in surveillance (except in Gagaúzia in 2014) because retreated TB episodes could be notified several times within a single reporting year. Therefore, the variation could be related to programmatic performance and interventions focused on increasing adherence and reducing loss to follow-up and treatment failures.

Fig. 2.17. Trend in proportion of retreated TB patients among all notified disaggregated by geographical areas, the Republic of Moldova, 2011–2015

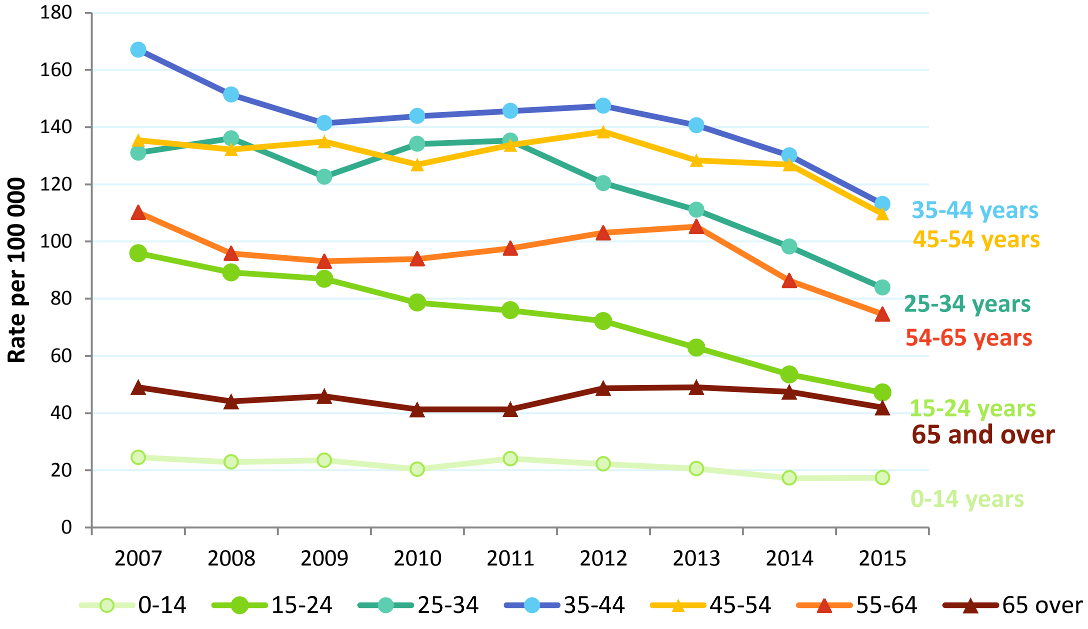


Source: SIME TB *(4)*.

2.3.6 Trends in TB notification by age group

Fig. 2.18 shows the trends in notification rates for new TB cases disaggregated by age group. Between 2007 and 2015, the TB notification rate declined for all age groups, but at different paces: thus, the fastest decline was observed in the 15–24, 25–34 and 35–44 year age groups, while the decline in notification rate of TB among the elderly (aged >65 years) has been relatively slow. This pattern of temporal change is consistent with our general understanding of TB epidemiology: TB in the elderly mostly results from the reactivation of latent infection; therefore, 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 these age groups suggests a decline in TB transmission in the general population.

Fig. 2.18. Trend in notification of new TB cases by age groups, the Republic of Moldova, 2007–2015



Source: WHO global TB database *(24)*.

According to current knowledge of TB epidemiology, TB notification rates among young adults are high in areas with a persistently high annual risk of infection. This is because TB cases in young age groups indicate recent transmission. Once TB is controlled and the annual risk of infection starts to fall, TB incidence declines and there are relatively more cases in older individuals, which are mainly due to reactivation. To assess the trend in the mean age of TB patients over time, the age distribution of new TB cases first was checked for normality and the mean age of new TB cases of annual cohorts were fitted with a linear regression line. Fig. 2.19 shows the mean age of new TB patients by sex in the Republic of Moldova for the period 2007–2015. This mean age increased from 39.3 to 42.6 years in males and from 36.0 to 38.1 years in females. Thus, between 2007 and 2015, the average annual increase in the mean age was 0.25 years in male TB patients and 0.17 years in female TB patients. In both sexes, the correlation between time and mean age is strong: 96% of the variance in males and 83% of variance in females is explained by the regression model. The increasing trend in mean age supports the hypothesis that the risk of contracting TB in the Republic of Moldova is decreasing. Although the Moldovan population is ageing, the change in mean age of TB patients is related to a decreased TB burden rather than to demographic changes, as indicated by the clear decline in TB notification in younger age groups (Figs 2.20 and 2.21).

Fig. 2.19. Trend in mean age of new TB patients by sex over time

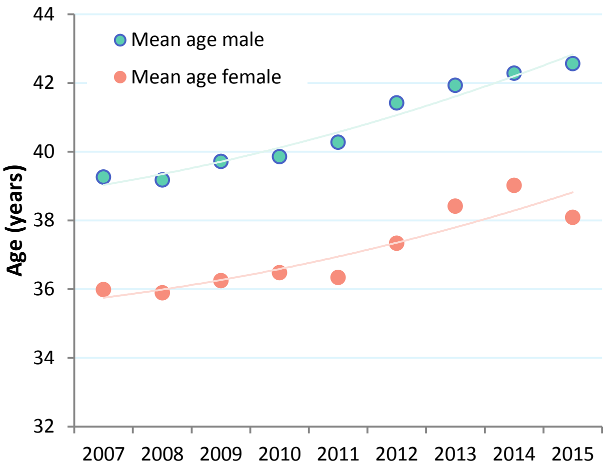


Fig. 2.20. Age-specific notification rates for new TB cases, 2007, 2011, 2013 and 2015

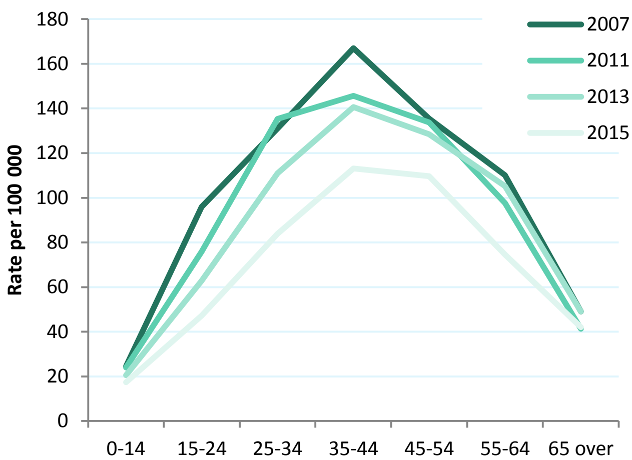
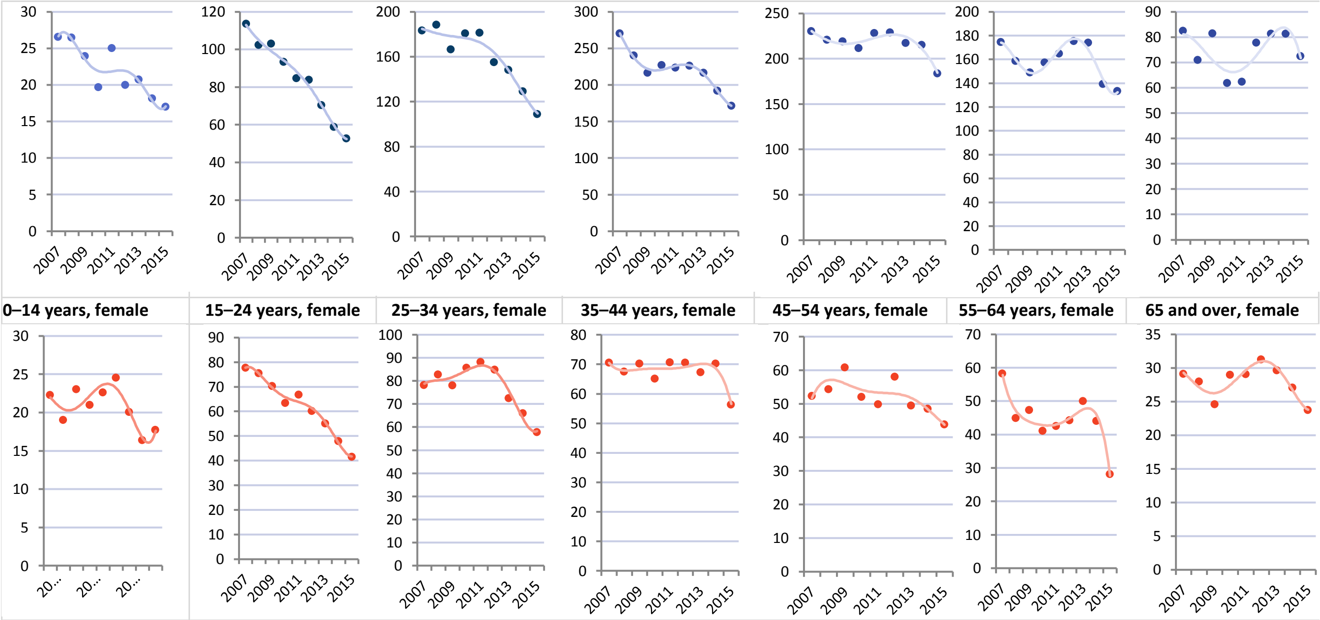


Fig. 2.21 shows notification rates for new TB cases (all forms) in 2007–2015 disaggregated by age group and sex. Notification rates for new TB cases are decreasing sharply in young male and female age groups. However, with increasing age, the decline of notification rates gradually become slower, and there is no clear trend in the 65 years and over age groups. Thus, we conclude that the trends in TB notification are consistent across age groups and sex and that the TB burden is declining in the population.

Fig. 2.21 Age and sex specific TB notification rate among new cases, the Republic of Moldova, 2007–2015

0–14 years, male	15–24 years, male	25–34 years, male	35–44 years, male	45–54 years, male	55–64 years, male	65 and over, male

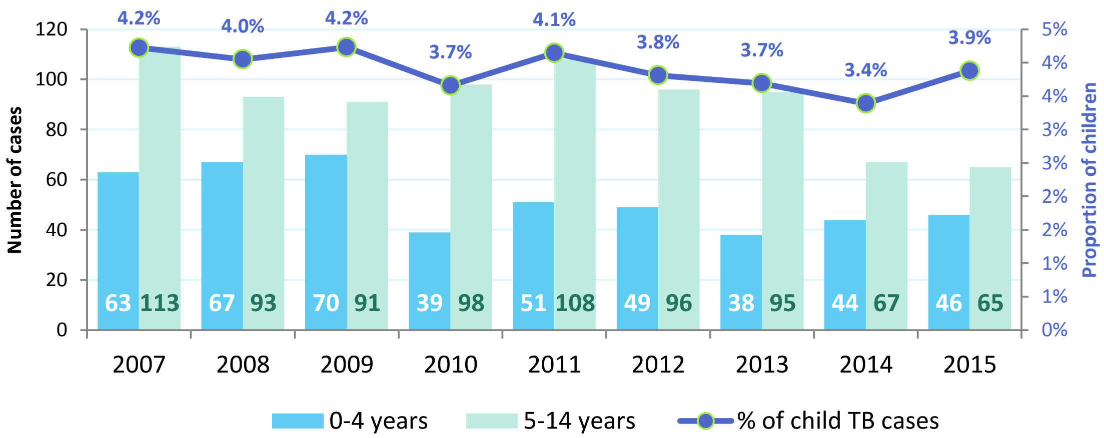


Source: WHO global TB database *(24).*

2.3.7 Trends in childhood TB

The absolute number of child TB cases between 2007 and 2015 gradually decreased from 176 to 111. However, the proportion of child TB cases among all new TB case remained stable at around 4% (Fig. 2.22). The decreased number of TB cases after 2010 was driven mainly by a decrease in the number of TB cases in children aged 5–14 years, while absolute number of TB cases in children aged 0–4 years was comparatively stable. This suggests a slight improvement in the diagnosis of child TB cases as, according to current knowledge of TB epidemiology, the number of TB-affected children aged 0–4 years should exceed the number of those aged 5–14 years. However, trends indicate that TB notification in children is more or less stable, except for a sharp decline in the number of TB cases in children aged 5–14 years from 95 to 67 between 2013 and 2014.

Fig. 2.22. Trend in notified number of TB cases in children and proportion of child TB among all new pulmonary TB cases, the Republic of Moldova, 2010–2015

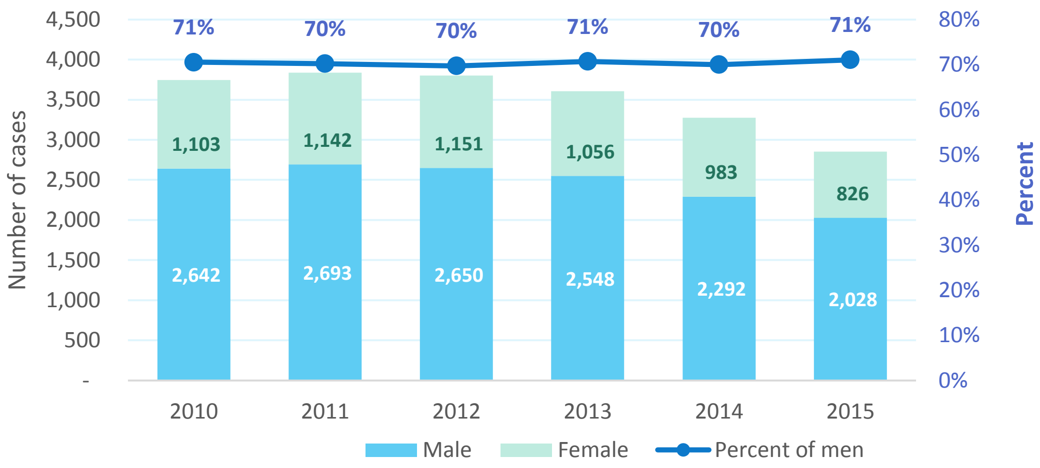


Source: WHO global TB database *(24)*.

2.3.8 Trend in TB notification by sex

From 2010 to 2015 in the Republic of Moldova, the proportion of all new TB cases who were men remained stable at around 70% (Fig. 2.23).

Fig. 2.23. Number of notified new all TB cases by sex and the proportion of male patients, the Republic of Moldova, 2010–2015



Source: WHO global TB database *(24)*.

2.3.9 Trend in TB case notification in prisons

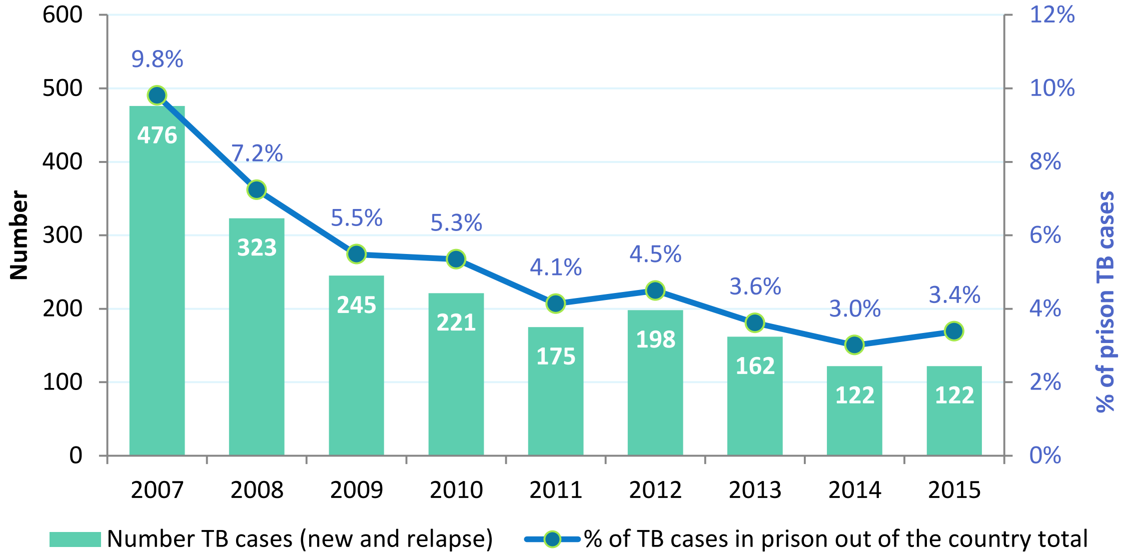
Over the past 9 years, the prison population in the Republic of Moldova gradually decreased from 8876 in 2007 to 6853 in 2014 but then increased to 7872 in 2015 *(29)*. From 2007 to 2014, TB case notification decreased by almost four times from 476 (5.4%) to 122 (1.5%; Table 2.2).

Table 2.2. TB in prisons, the Republic of Moldova, 2007–2015

Year	Prison population	TB cases (all forms)	TB notification (all forms) (%)	TB cases in prisons (out of the country total) (%)	TB relative risk in prisons
2007	8876	476	5.4	9.8	45.6
2008	7895	323	4.1	7.2	37.7
2009	7215	245	3.4	5.5	31.1
2010	6535	221	3.4	5.3	33.4
2011	6506	175	2.7	4.1	25.9
2012	6476	198	3.1	4.5	28.3
2013	6583	162	2.5	3.6	22.4
2014	6853	122	1.8	3.0	17.9
2015	7872	122	1.5	3.4	17.5

The observed TB rate of 1.5% in 2015 in prisons (still about 18 times higher than the risk of TB in the general population) makes up 3.4% of the total TB cases in the Republic of Moldova (Fig. 2.24). Thus, the decline of TB in the prison population made a notable contribution to overall TB case notification in the Republic of Moldova.

Fig. 2.24. Time trend in number of TB cases in prisons and the proportion of the total notified new and relapse cases, the Republic of Moldova, 2007–2015

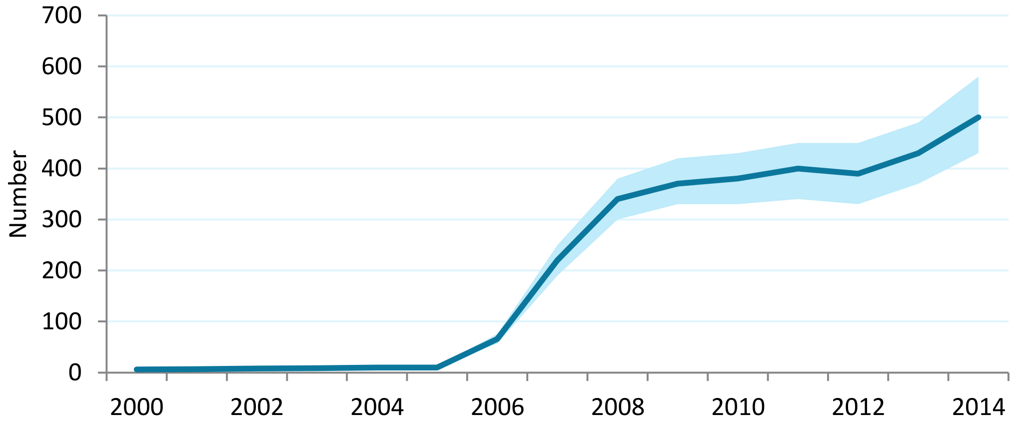


Source: WHO global TB database *(24)*.

2.3.10 Trends in TB in PLWHIV

According to Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates, the number of TB cases in PLWHIV has increased sharply since 2014. In 2014, the estimated number of TB cases among PLWHIV was 500 (uncertainty range 430–580) compared with 300 cases (range 300–340) reported in 2008, suggesting that HIV could be a leading factor driving the TB epidemic (Fig. 2.25).

Fig. 2.25. Estimated number of TB among PLWHIV, the Republic of Moldova, 2000–2015



Shaded area represents the uncertainty band.

Source: AIDSinfo data repository *(6)*.

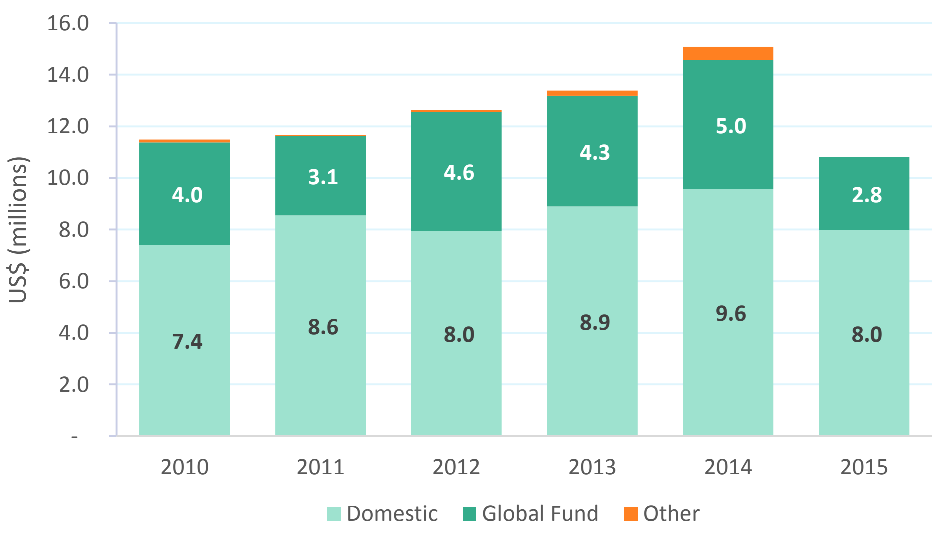
3. Are recent trends in TB disease burden related to changes in TB-specific interventions caused by external factors?

3.1 Factors related to the NTP

3.1.1 Government and donor funding for TB care and control

Funding for and implementation of high-quality TB-specific interventions should result in the detection of people with TB and curative treatment for them. In turn, these actions should have a direct impact on TB mortality through reducing case fatality rates compared with no or substandard treatment. TB services in the Republic of Moldova are financed by two sources: the Government of the Republic of Moldova and the Global Fund. Between 2010 and 2014, TB control funding increased from US$ 11.5 million to US$ 15.0 million, representing an overall increase of about 31% during this period (Fig. 3.1). Both donor and domestic funding increased proportionally, demonstrating government commitment. As increased TB funding coincided with decreases TB notification in the country, it can be concluded that increased funding has contributed to driving the TB epidemic downwards. However, the rapid decline in actual expenditure reported in 2015 is a concern. The most notable difference in expenditure in 2015 compared with 2014 was on items related to laboratory infrastructure, equipment and supplies.

Fig. 3.1 Actual expenditure on TB control interventions in US$ (millions), the Republic of Moldova, 2010–2015



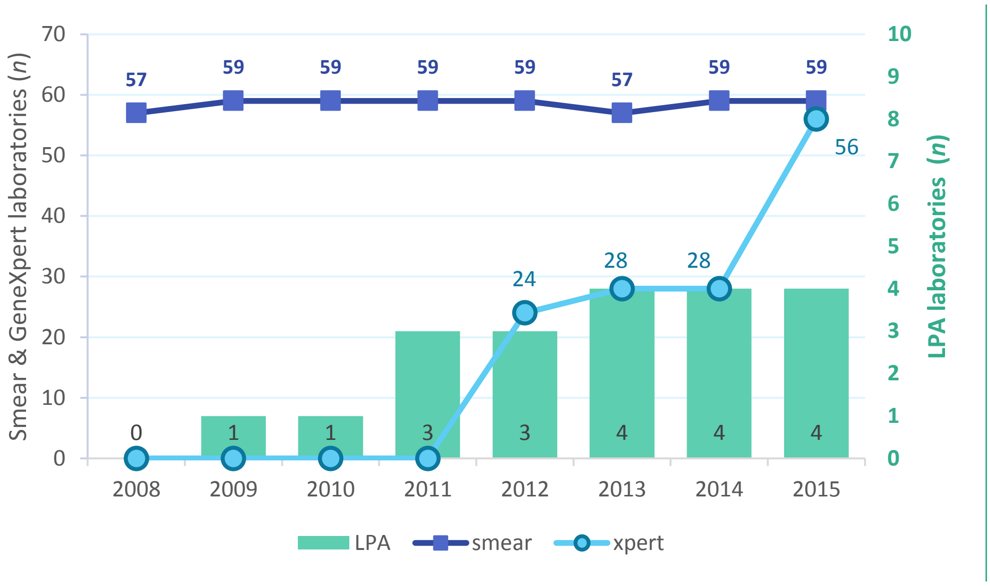
Source: WHO global TB database *(24)*.

3.1.2 Number of health facilities providing TB diagnostic services

Shortening the duration of TB disease through detection and treatment will also reduce its prevalence and, therefore, transmission. The Republic of Moldova has a well-functioning TB laboratory network organized into three diagnostic levels. The first level consists of 59 smear microscopy centres, located at TB outpatient facilities (each serving a population of 77 000 on average) and 70 sputum collection points. The microscopy laboratories undergo proficiency testing organized by the National Reference Laboratory (NRL) and regional laboratories, which is performed on-site during monitoring visits. The second level includes three reference laboratories (in Vorniceni, Balti and Bender) that perform culture tests and DST, and report the results to the NRL. These laboratories are responsible for quality control of microscopy centres in their respective areas. The third level is represented by the NRL, located at the National Tuberculosis Institute "Chiril Draganiuc". The NRL has the leading role in organizing TB laboratory service and developing protocols for laboratory diagnosis, training and supervision.

The number of microscopy laboratories has not changed over the last 8 years. The line probe assay was introduced in 2009, and by 2013 four laboratories were using the line probe assay for the rapid diagnostic of drug-resistant TB. GeneXpert MTB/RIF was introduced in the Republic of Moldova in 2012, and 56 out of 59 laboratories were equipped with GeneXpert MTB/RIF by 2015, so coverage is now almost universal (Fig.3.2). The introduction and widespread use of GeneXpert MTB/RIF has improved diagnostic testing and reduced both the time to start treatment and time to detection of drug-resistant cases, hence reducing TB transmission in the general population and hospital settings. Thus, we can conclude that improvement in diagnostic services could also play an important role in reducing the TB burden.

Fig. 3.2. Laboratory diagnostic services, the Republic of Moldova, 2010–2015



3.1.3 Case-finding

There will be an impact on TB incidence if transmission can be reduced sufficiently and/or if preventive treatment of people with latent TB infection is effectively implemented on a large scale. Increased of screening of the at-risk population can increase case detection, thus reducing TB transmission in the general population.

TB cases are mainly detected through passive case-finding, that is, investigation of individuals seeking health care for symptoms. Active case-finding is conducted among population groups at risk for TB (i.e. close contacts of TB patients, detainees and ex-detainees of the penitentiary system, PLWHIV, homeless people and other population groups as per current regulations) *(30)*.

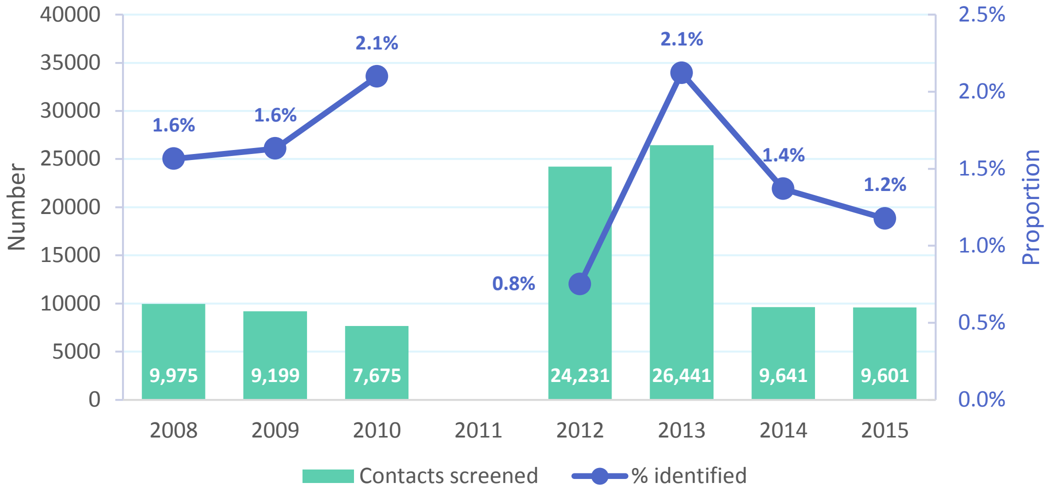
All close contacts of TB patients are subject to active screening for TB in the Republic of Moldova. According to Moldovan reports to the WHO global TB database over the last 8 years, the number of TB contacts ranged from 7675 to 26 441, with the trend increasing and then decreasing over the time. The average number of contacts screened per notified laboratory confirmed pulmonary TB case between 2008 and 2015 showed no clear trend but fluctuated notably between 2.7 and 11.0. In 2012 and 2013, there was a sudden sharp increase in the number of contracts screened (Fig.3.3). In 2012, this intensified screening effort yielded only 0.8 TB cases per 100 contacts screened, while in 2013 about three times more TB cases were identified among the contacts. In the last 2 years, fewer TB cases were identified among contacts. However, because of the large fluctuations in the number of contacts screened and in detection, it is not possible to assume that that fewer TB cases are detected among the contacts over time or that TB transmission has decreased. Thus, the decrease in TB notification cannot be explained by changes in active screening practices.

Practices in isoniazid preventive therapy (IPT) have changed several times over the past 8 years (Table 3.2). According to national TB reports, only 1.6% of contacts received IPT in 2008–2009, while over 60% received IPT in 2010 and about 10–18% received IPT between 2012 and 2015. Overall, starting from 2010, the number of contacts receiving IPT increased by >10 times. It can be assumed that increased coverage of IPT has also contributed to the reduction in TB burden in the Republic of Moldova.

Table 3.2. Number of TB contacts screened and yield of TB cases among contacts, the Republic of Moldova, 2008–2015

Year	Laboratory confirmed TB cases in civilian population (*n*)	Contacts screened (*n*)	Contacts screened/case, mean (*n*)	TB cases detected among contacts (*n* (%))	Contacts who received IPT (*n* (%))
2008	2161	9975	4.6	156 (1.6)	156 (1.6)
2009	1766	9199	5.2	150 (1.6)	150 (1.6)
2010	2833	7675	2.7	161 (2.1)	4630 (60.3)
2011	2852	NA	NA	NA	NA
2012	2896	24 231	8.4	182 (0.8)	3934 (16.2)
2013	2407	26 441	11.0	561 (2.1)	2771 (10.5)
2014	2251	9641	4.3	132 (1.4)	1751 (18.2)
2015	2075	9601	4.6	113 (1.2)	1226 (12.8)

Fig. 3.3. Trend in number of TB contacts screened and percentage of TB diagnoses among TB contacts, the Republic of Moldova, 2008–2015



Source: WHO global TB database *(24)*.

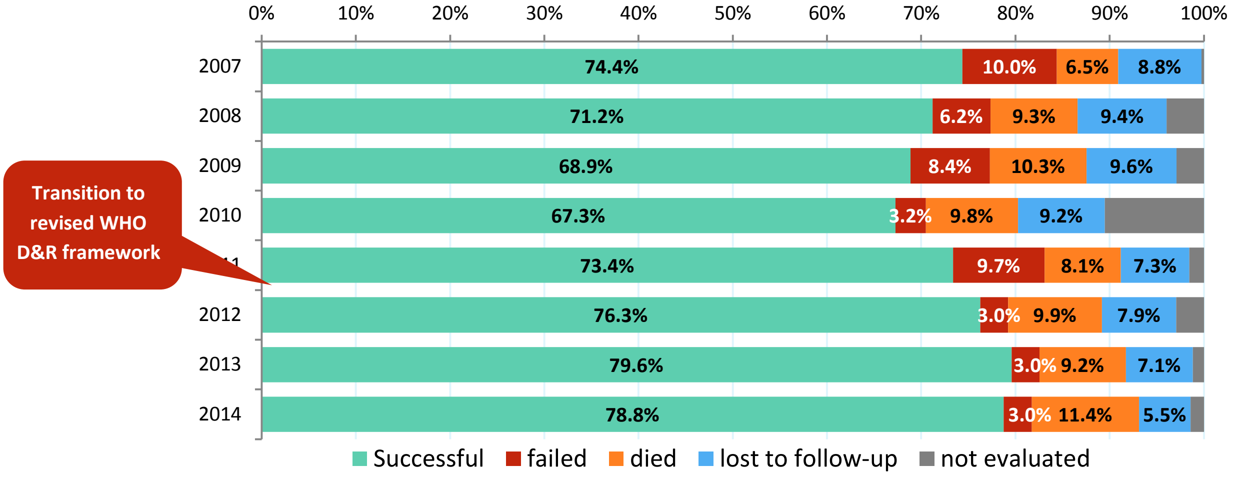
3.1.4 Delay in diagnosis and treatment

Delays in TB diagnosis result in patients remaining infectious for prolonged periods, which increases the risk of transmission to contacts. Roll-out of GeneXpert MTB/RIF in 2012 and the rapid increase in coverage shortened the time to MDR-TB detection and treatment (data are available at the NTP). This could be an important factor driving the TB epidemic downwards.

3.1.5 Treatment outcomes

TB treatment is one of the most effective interventions in controlling TB to reduce the prevalence of cases in the population and the transmission of infection. Fig. 3.4 shows a cohort analysis of treatment outcomes for TB patients. Cohorts from 2007 to 2011 include both new and MDR-TB cases. According to previous guidelines, cases in which MDR-TB was detected were classified as treatment failure. With transition to the revised WHO definitions and reporting framework for TB, the proportion of successfully treated patients among new and relapse TB cases is higher because newly detected MDR-TB cases are now excluded from the cohort. This change probably explains why treatment outcome for new and relapse TB patients has not improved over the time and remains below the target treatment success rate of 85%. Thus, there is no evidence that treatment outcome for new and relapse TB patients has improved or decreased.

Fig. 3.4. Treatment outcomes of new and relapse TB patients, the Republic of Moldova, 2007–2014

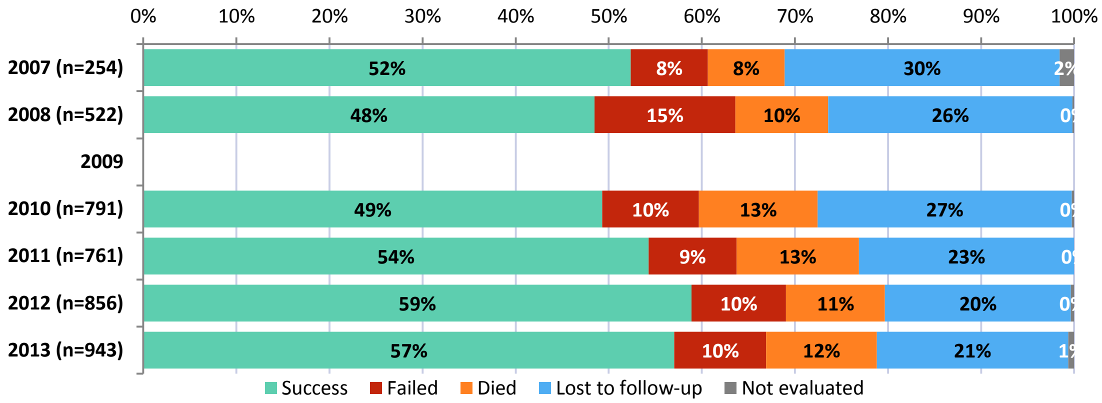


D&R: definitions and reporting.

Source: WHO global TB database *(24)*.

Notable progress has been made in improving the effectiveness of RR/MDR-TB treatment. In the 2013 cohort, 57% of RR/MDR-TB cases were successfully treated vs 48% in the 2008 cohort (Fig. 3.5). The improvement was due to a decrease in the proportion of patients lost to follow-up. The proportion of those who failed treatment or died remained stable. Over the last 3 years, the treatment success rate for MDR-TB in the Republic of Moldova has been much higher than the regional average of 50%.

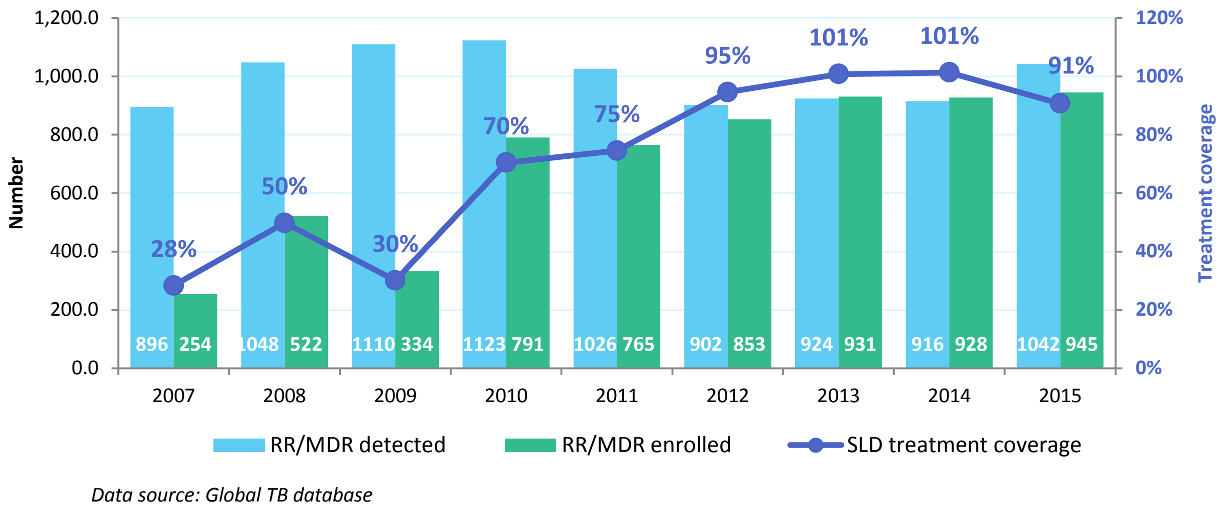
Fig. 3.5. Treatment outcomes of confirmed RR/MDR-TB patients enrolled into second-line treatment, the Republic of Moldova, 2007–2013



Source: WHO global TB database *(24)*.

It is noteworthy that the increase in treatment effectiveness was combined with an impressive increase in second-line treatment coverage. Thus, in 2007 only 28% of RR/MDR-TB cases were enrolled into the second-line treatment programme. Coverage of second-line treatment gradually increased and became universal in 2012 (Fig. 3.6).

Fig. 3.6. Number of pulmonary RR/MDR-TB cases detected and number and proportion of these enrolled into second-line treatment, the Republic of Moldova, 2007–2015



Source: WHO global TB database *(24).*

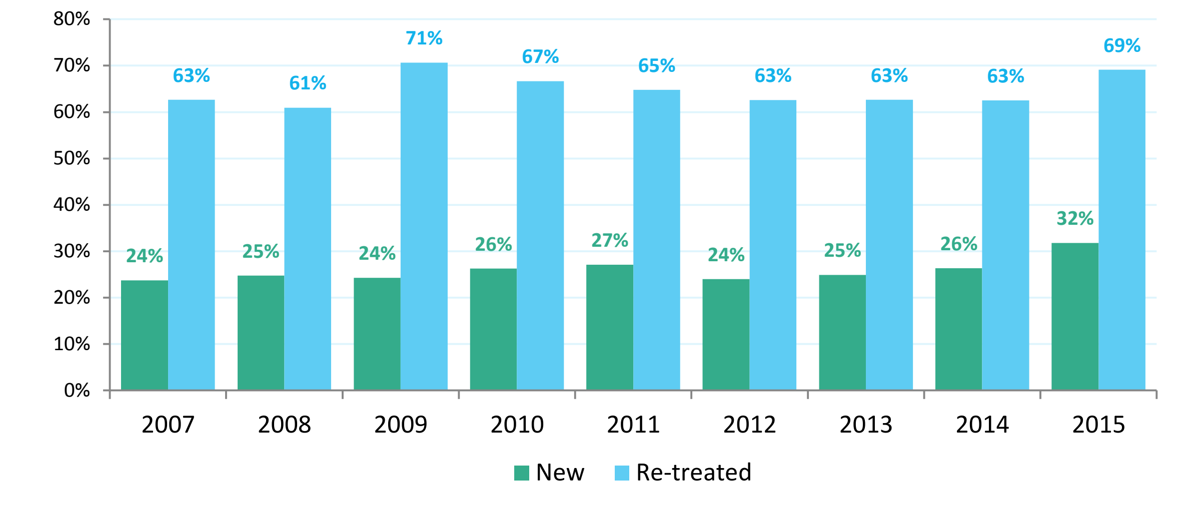
As shown in Fig. 3.6, before the introduction of second-line treatment, quite a large number of drug-resistant cases (producing TB bacilli) remained untreated, thus spreading the infection to the general population. The introduction of second-line treatment, however, largely removed the source of TB infection. Thus, recent improvements in access to second-line TB treatment in years and in the effectiveness of second-line treatment could be key factors in attenuating the TB epidemic in the Republic of Moldova.

3.1.6 RR/MDR-TB

RR/MDR-TB represents a challenge due to the long duration and low effectiveness of available treatments. The increased RR/MDR-TB burden can be considered one of the key factors driving the TB epidemic upwards. The Republic of Moldova is one of 15 countries with a high MDR burden among the 53 Member States of the WHO European Region. The NTP of the Republic of Moldova has established a strong routine drug resistance surveillance system in line with WHO recommendations, including quality-assured drug sensitivity testing, universal access to DST or GeneXpert MTB/RIF for all bacteriologically confirmed pulmonary TB cases and a comparatively high level of bacteriological confirmation among pulmonary TB cases with reliable classification of patients by treatment history.

According to routine drug resistance surveillance results, the proportion of RR/MDR-TB among new TB cases increased from 23.7% in 2007 to 31.8% in 2015. In the same period, the overall proportion of RR/MDR-TB cases increased from 62.6% to 69.1%. This suggests an increased MDR-TB burden of about 30% among new TB cases within the last 9 years. This increase was especially sharp between 2014 and 2015 (Fig. 3.7).

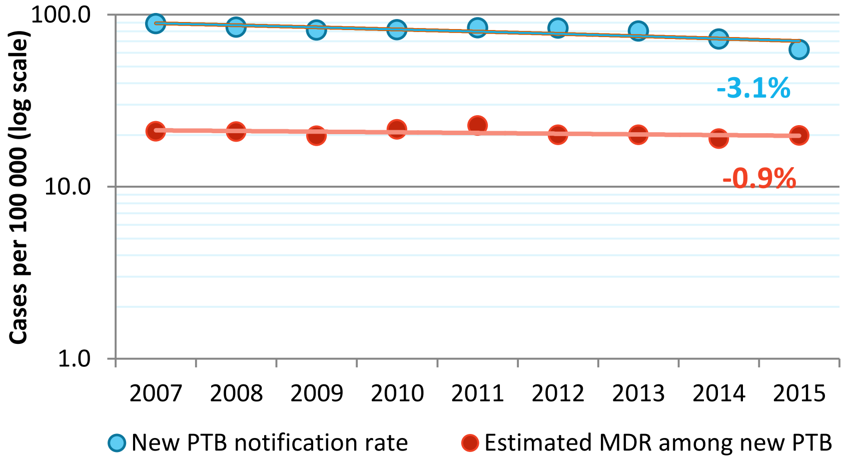
Fig. 3.7. Proportion of RR/MDR-TB patients among new and retreated pulmonary TB patients with DST/GeneXpert results based on routine surveillance, the Republic of Moldova, 2007–2015



Source: WHO global TB database *(24)*.

To assess the variation in the estimated number of MDR-TB cases among notified new TB cases, the proportion of MDR-TB among new TB cases was multiplied by the number of notified new pulmonary TB cases and the rate of estimated MDR-TB cases was calculated per 100 000 population for each year. The results were plotted on a log-scale per year and the slope was calculated from the fitted regression line (as shown in *Understanding and using tuberculosis data*, p. 140) *(2)*. The results of the analysis indicated that the estimated number of MDR-TB cases per 100 000 population within the last 9 years decreased by −0.9% on average, while the average decrease in new pulmonary TB cases was notably faster at 4.4% per year (Fig.3.8). Non-resistant strains in the Moldovan population were eliminated much faster than RR/MDR-TB strains. In any case, the burden of MDR-TB in the population has a decreasing trend, especially after 2011. The average decline in the estimated RR/MDR-TB rate between 2011 and 2015 was −3.1% annually.

Fig. 3.8. Rates per 100 000 populations of notified new pulmonary TB cases and estimated MDR-TB cases among notified new TB patients over time fitted with a linear trend-line, the Republic of Moldova, 2007–2015



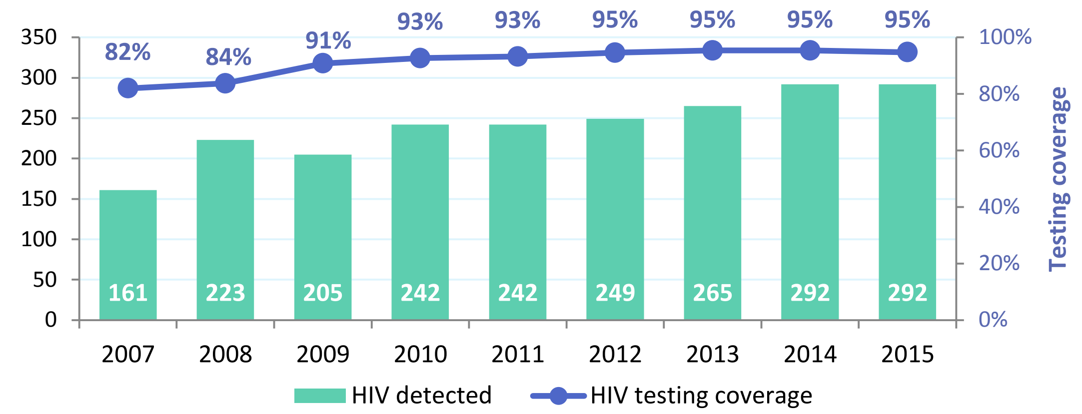
PTB: pulmonary TB.

Source: WHO global TB database *(24)*.

3.1.7 TB/HIV

To ensure effective and integrated TB and HIV service delivery, WHO recommends HIV testing for all TB patients, provision of ART and co-trimoxazole preventive treatment to HIV-positive TB patients, regular TB screening for PLWHIV and the offer of IPT to PLWHIV who do not have active TB *(25)*. In 2007, only 82% of incident TB patients had a documented HIV test result. From 2009 onward, HIV testing coverage was consistently reported at >90%. The absolute number of HIV cases among TB patients increased gradually from 161 in 2007 to 292 in 2015 (Fig. 3.9)

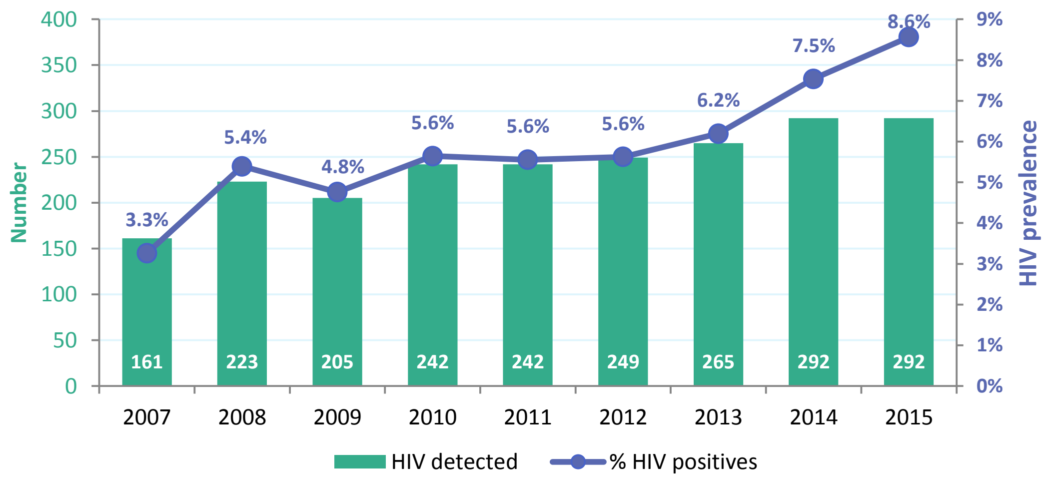
Fig. 3.9. Number of notified TB/HIV coinfections and HIV testing coverage among notified new and relapse TB patients, the Republic of Moldova, 2007–2015



Source: WHO global TB database *(24)*.

The relative proportion of HIV cases among TB patients was only 3.3% in 2007. According to national surveillance data, the HIV burden has sharply increased over the past 7 years (especially in the last 3 years), reaching 8.6% in 2015 (Fig 3.10).

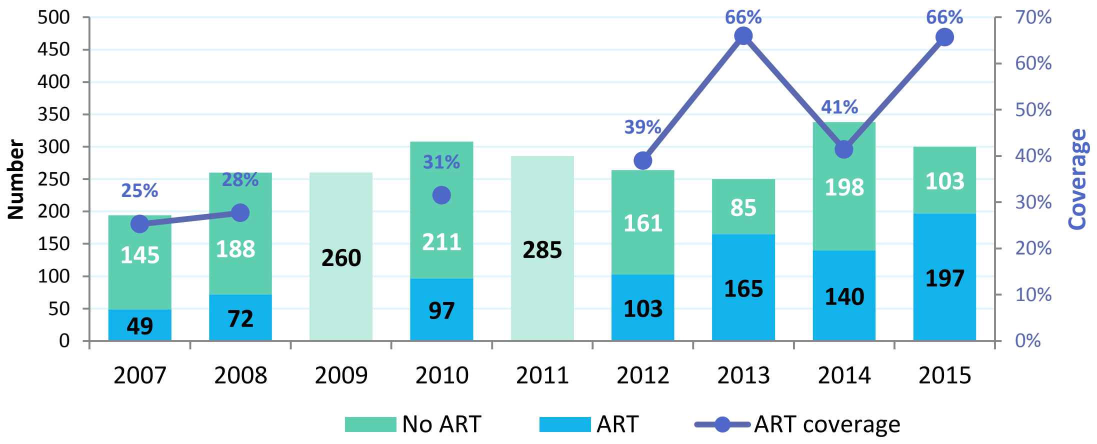
Fig. 3.10. Prevalence of HIV among incident TB patients, the Republic of Moldova, 2007–2015



Source: WHO global TB database *(24)*.

In the Republic of Moldova over the last 9 years, ART coverage has fluctuated greatly, but increased from 25% in 2007 to 66% in 2015 (Fig. 3.11). This is far below the WHO-recommended level of universal ART coverage.

Fig. 3.11. Number and percentage of HIV-positive TB patients enrolled in ART, the Republic of Moldova, 2007–2015



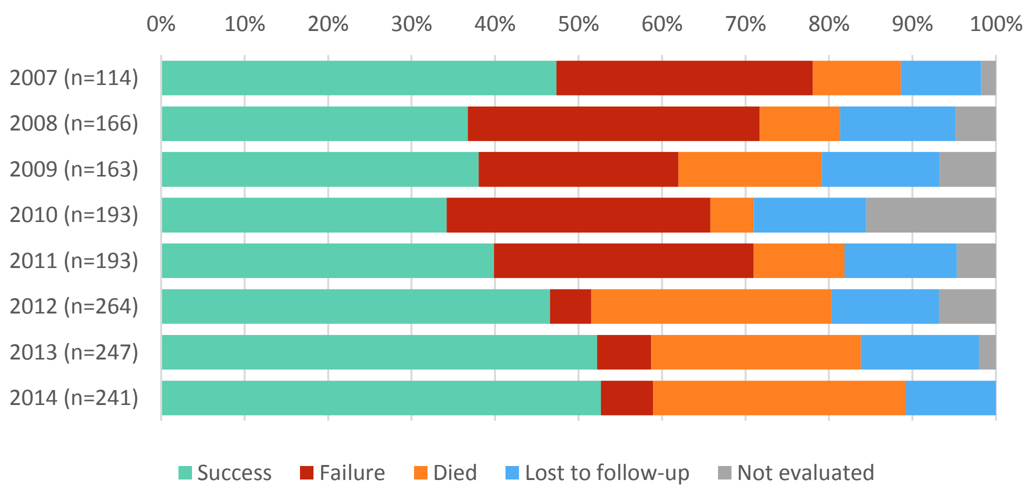
No data on ART coverage is available for 2009 and 2011.

Source: WHO global TB database *(24)*.

IPT coverage among HIV patients in the Republic of Moldova is currently 14%. However, no historical data is available to assess the trend.

According to NTP data, the treatment success rate for new HIV/TB co-infected patients increased from 37% in 2008 to 53% in 2014. This is a notable improvement, but it is possible that transition to the revised definitions and reporting framework, as well as incompleteness of the data (difference between the number of HIV/TB cases detected and cohort size) might bias the overall analysis and interpretation of the trend in treatment outcome (Fig. 3.12).

Fig. 3.12. Treatment outcomes for TB/HIV patients, the Republic of Moldova, 2007–2014



Note that 2007–2011 cohorts include new TB/HIV cases and 2012–2014 cohorts include all new and relapse TB/HIV cases.

Source: WHO global TB database *(24).*

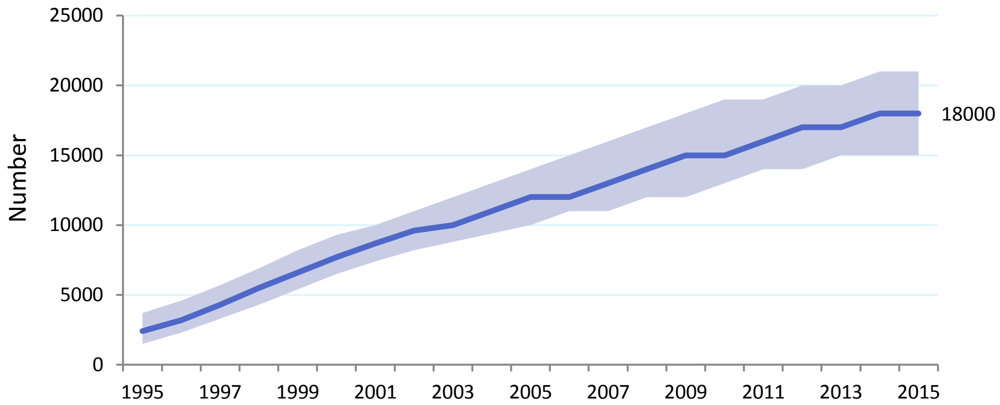
Given that the Republic of Moldova is low HIV epidemic country, and considering that ART coverage among TB patients and IPT coverage among PLWHIV were suboptimal until recently, these findings suggest that HIV/TB collaborative activities are unlikely to substantially affect TB epidemiology in the Republic of Moldova. Thus, the recent decrease in TB notification is not likely to be related to TB/HIV collaborative activities.

3.2 External factors not related to the NTP

3.2.1 HIV prevalence among the general population and ART coverage

HIV is the most potent risk factor for TB within the individual; therefore, an increase in number of PLWHIV can drive TB epidemic upwards. The number of PLWHIV is increasing in the Republic of Moldova. The estimated number of PLWHIV increased from 12 000 (range 10 000–14 000) in 2005 to 18 000 (range 15 000–21 000) in 2015, according to UNAIDS estimates, with an estimated prevalence of 0.6% (range 0.6–0.8%) among the population aged 15–49 years *(31)*. Fig. 3.13 shows the estimated numbers of PLWHIV in the Republic of Moldova over the last decade.

Fig. 3.13. Estimated number of PLWHIV (adult and children), the Republic of Moldova, 1995–2015



Shaded areas represent the uncertainty band.

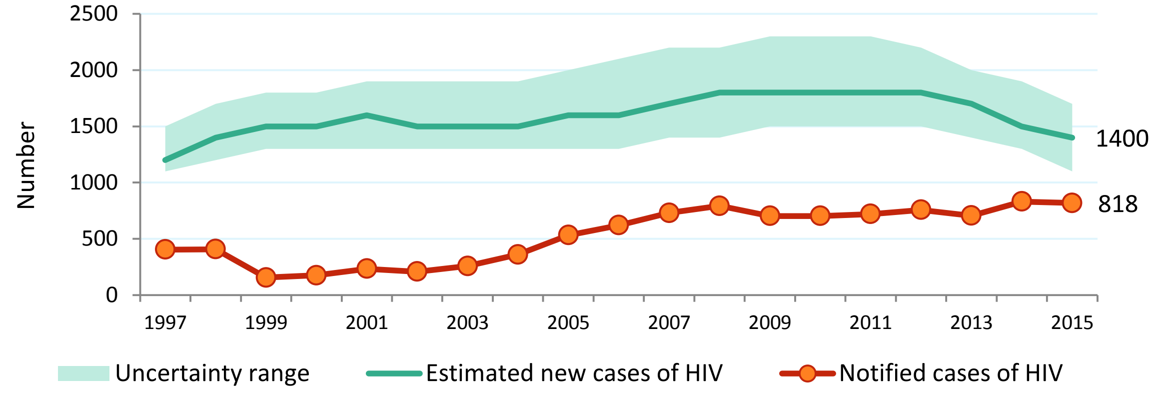
Source: AIDSinfo data repository *(6)*

The estimated number of incident HIV cases in the Republic of Moldova increased from the beginning of the epidemic until 2008 and then remained stable until 2012 at about 1800 new HIV infections annually. HIV incidence started to reverse in 2013, and in 2015 about 1400 (range 1100–1700) new HIV infections were estimated in the Republic of Moldova. Similar to the estimated number of incident TB cases, notification of new HIV cases increased progressively between 1999 and 2008. Since then, around 800 HIV cases have been recorded annually, without any clear trend over time (Fig. 3.14). Thus, the growing prevalence of HIV, with an average rate of increase of 4.6% per year between 2007 and 2015, is likely to drive the TB epidemic upwards.

The HIV epidemic is largely concentrated among high-risk groups such as injecting drug users, men who have sex with men, and sex workers, with estimated prevalences of 8.5%, 5.7% and 11.6%, respectively

(32). The HIV epidemic is more severe on the left bank of the Nistru River, where the coverage of prevention programmes is lower.

Fig. 3.14. Estimated number of incident HIV cases and number of newly notified HIV cases, the Republic of Moldova, 1997–2015

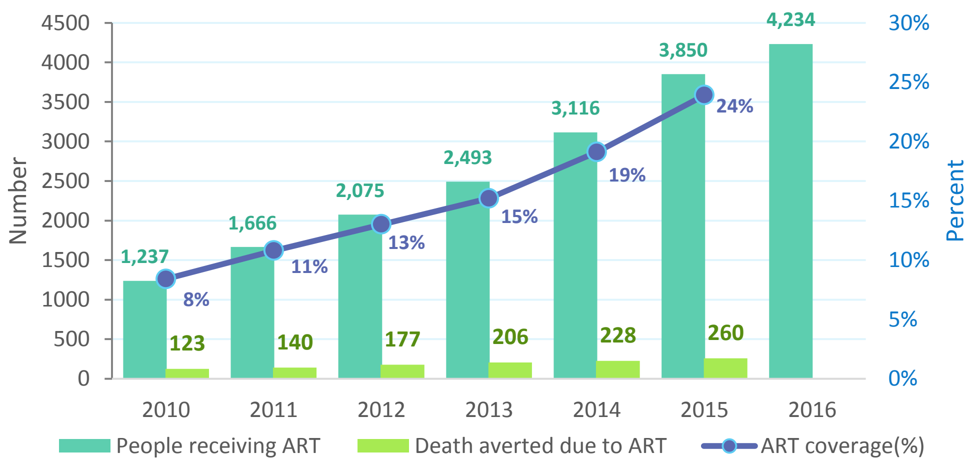


Shaded area represents the uncertainty band.

Sources: AIDSinfo data repository *(6)*, and HIV/AIDS surveillance in Europe, 2007 and 2016 *(33)* and AIDS center statistics (http://aids.md).

There is strong evidence that timely initiation of ART and preventive isoniazid therapy may reduce the risk of progression from infection to disease, thus driving the TB epidemic downwards. According to the Republic of Moldova Progress Report on HIV/AIDS, support from the Global Fund has ensured free access to antiretroviral therapy since 2004 *(34)*. Between 2010 and 2015, the absolute number of people receiving ART tripled. At the end of 2015, 3850 PLWHIV were on ART, representing about 24% coverage among those who are diagnosed with HIV *(32)*. This is still far below the current recommendation of universal ART coverage regardless of CD4 cell count (Fig. 3.15) *(35)*.

Fig. 3.15. Time-series change in number of PLHIV receiving ART, number of deaths averted due to ART and ART coverage, the Republic of Moldova, 2010–2016

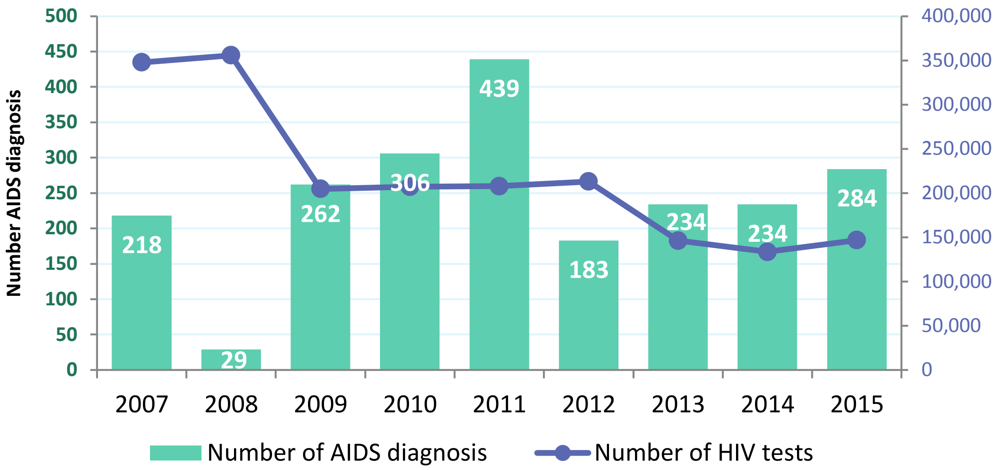


Source: AIDSinfo data repository *(6)*

In the Republic of Moldova, IPT coverage is quite low: only 14–15% of PLWHIV received IPT in 2014 and 2015 because of concerns about the high prevalence of isoniazid resistance in the country *(36)*.

HIV surveillance data indicate sharp fluctuations in the number of AIDS cases over time, which results from late HIV diagnosis (i.e. when disease is detected at an advanced stage) and/or inefficiency of ART. Fig. 3.16 shows the number of recorded AIDS cases and number of HIV tests performed in the Republic of Moldova since 2007 *(37)*.

Fig. 3.16. Number of AIDS cases notified by health systems and number of HIV tests performed, the Republic of Moldova, 2007–2015



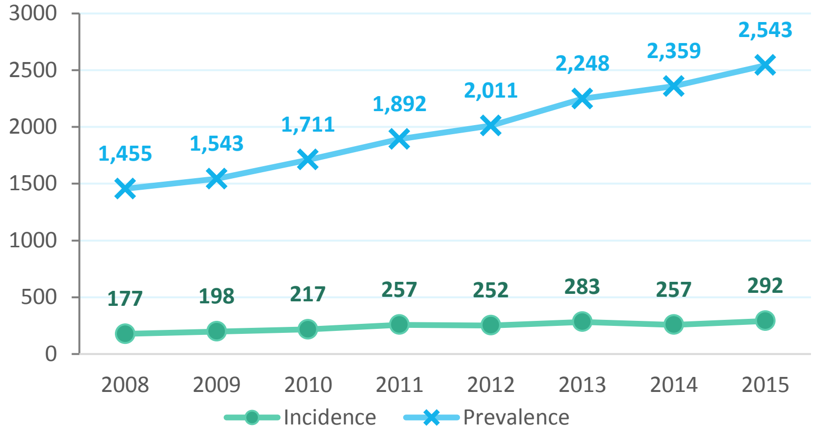
Source: HIV/AIDS surveillance report in Europe 2016 *(33)*.

The increased ART coverage is probably driving the TB epidemic downwards. However, because of the growing trend towards an HIV epidemic (with low HIV case detection, modest ART coverage and limited use of IPT), the aggregate effect of the HIV epidemic and its response is driving the TB epidemic in the Republic of Moldova upwards. This is reflected by an increasing burden of TB/HIV coinfections and lack of a decreasing trend in AIDS notification.

3.2.2 Trend in diabetes

Diabetes triples the risk of developing TB. The increasing prevalence of diabetes is therefore threatening a resurgence of TB. According to national statistics, the Republic of Moldova is experiencing a growing burden of diabetes (similar to many other countries in the European Region), mostly due to increases in overweight and obesity, unhealthy diets and physical inactivity *(38)*. The registered number of diabetes cases increased from 1455 per 100 000 in 2008 to 2545 per 100 000 in 2015 (Fig. 3.17). According to the International Diabetes Federation, the estimated prevalence of diabetes in 2015 in the Republic of Moldova was 7.7% (uncertainty range 6.7–11.0%) *(39)*. Although the total number of newly registered cases per year increased by 65% between 2008 and 2015, the International Diabetes Federation estimates that about 43% of diabetes cases in adults (aged 20–79 years) remain undiagnosed. This poses a number of challenges for TB control.

Fig. 3.17. Time-series change in incident and prevalent cases of diabetes per 100 000 population, the Republic of Moldova, 2008–2015



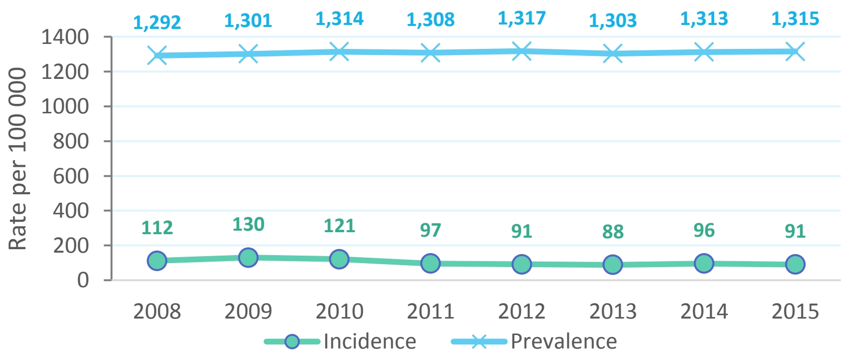
Source: NBS of the Republic of Moldova *(5).*

3.2.3 Trend in alcohol consumption

Heavy alcohol use and alcohol-related disorders increase the risk of active TB, due to the increased risk of infection in the drinking environment and alcohol-related downward social drift, as well as an increased risk of progression to disease due to the direct effect of alcohol on immunity and the indirect effect of immunity on alcohol-related disorders, including malnutrition, malignancy and chronic disease (Fig. 3.18).

According to the WHO Global status report on alcohol and health 2014, the Republic of Moldova has one of the highest levels of alcohol consumption, reaching 16.8 litres per person per year *(40)*. This is nearly three times the global average of 6.1 litres per person per year. The country is a major wine producer, and many people drink cheap homemade wine, vodka and other spirits. According to official statistics, the rate of newly recorded cases of alcohol-related disorder decreased between 2008 and 2015 *(41)*. However, the total number of registered cases increased slightly. As the changes are minor with a wide uncertainty range, there is no evidence that alcohol consumption has changed in recent years in the Republic of Moldova. Nevertheless, alcohol consumption remains a major contributory factor to the TB burden in the Republic of Moldova.

Fig. 3.18. Time-series change in incident and prevalent cases of alcoholism and alcohol-related disorder per 100 000 population, the Republic of Moldova, 2008–2015

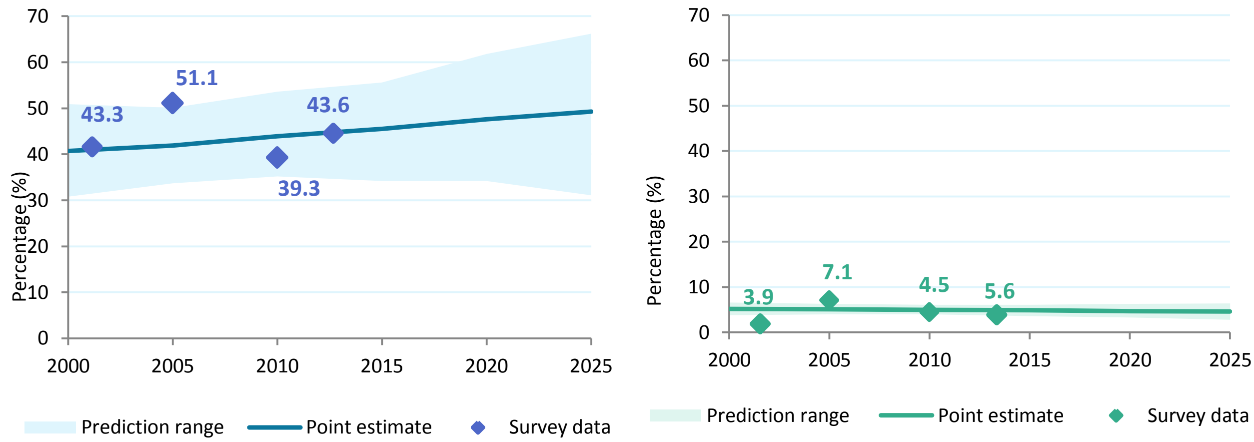


Source: NBS of the Republic of Moldova *(5).*

3.2.4 Trend in tobacco consumption

Tobacco smoking remains a serious health issue in the Republic of Moldova: according to WHO estimates, 45.5% of the male population and 4.9% of the female population aged 15 years and over are current smokers *(42)*. Several studies conducted over the last 15 years in the Republic of Moldova showed no evidence of a significant change in the pattern of smoking in the country (Fig. 3.19). A recent knowledge, attitude and practice survey conducted in Transnistria reported comparable results *(43)*.

Fig. 3.19. Fitted trends in current tobacco smoking among persons aged 15 years and over, the Republic of Moldova, in men (left) and women (right)



Source: WHO Global report on tobacco consumption 2015

The relative contributions of key risk factors for TB could be considered in prioritizing TB control interventions. The population-attributable fraction (PAF) of each of risk factors was calculated using the formula:

$$PAF = \frac{Prevalence * (RR - 1)}{Prevalence * (RR - 1) + 1}$$

The PAF is a statistic used to estimate the proportion of cases that would be prevented if the risk factor were eliminated. Given that over 95% of TB cases in the Republic of Moldova occur in the population aged >14 years, the PAF calculated for the population aged >15 years is very close to the population PAF. The highest PAFs for TB are associated with alcohol misuse, smoking, diabetes, HIV and indoor air pollution (in that order; Table 3.3).

Table 3.3. Prevalence and PAF of selected TB risk factors, the Republic of Moldova

Risk factor	Prevalence of risk factor in the Republic of Moldova (%)	Relative risk[a]	PAF in population aged >15 y (%)
HIV (15–49 y)	0.6[b]	26.7	13.4

Diabetes (20–79 y)	7.7[c]	3.1	13.9
Smoking (>15 y)	23.7[d]	2.0	19.2
Percentage of population using solid fuel (%)	8.0[e]	1.4	3.1
Percentage of heavy episodic drinkers (>15 y)	32.2[f]	2.9	38.%

Y: years.

[a] Lönnroth et al. *(44)*.

[b] UNAIDS *(31)*.

[c] International Diabetes Federation *(39)*.

[d] WHO *(42)*.

[e] WHO *(45)*.

[f] WHO *(40)*.

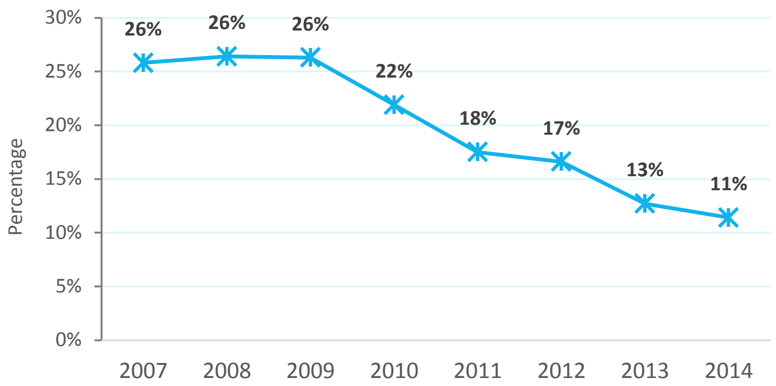
3.2.5 Gross national income per capita and poverty

Economic growth may have an important effect on 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. According to the World Bank, the Republic of Moldova is lower-middle-income country *(18)*. Although it is the poorest country in Europe, it has made superb progress in reducing poverty and promoting inclusive growth since the early 2000s. The economy has grown by an average of 5% per year, driven by consumption and fuelled by remittances *(46)*. Gross national income (GNI) per capita increased almost twofold from US$ 1160 in 2007 to US$ 2560 in 2014, and then dropped to US$ 2220 in 2015 (Fig. 3.20). In a similar trend, the proportion of population living under the national poverty line decreased from 26% in 2007 to 11% in 2014 (Fig. 3.21).

Fig. 3.20. GNI per capita (current US$), the Republic of Moldova, 2007–2015

Source: World Bank *(18)*.

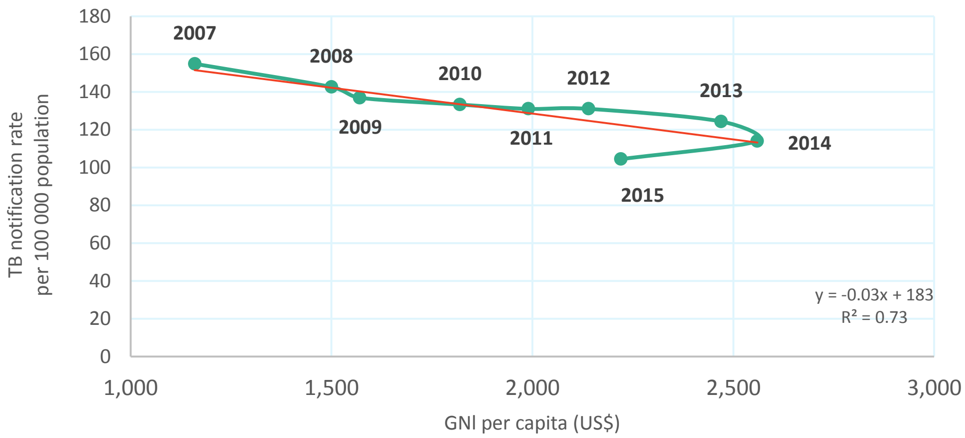
Fig. 3.21. Population living under national poverty line (%), the Republic of Moldova, 2007–2014



Source: World Bank *(18)*.

Economic growth is expected to drive the TB epidemic downwards. Fig. 3.22 shows the well-established tendency for TB notification to decrease with increasing GNI per capita. The decreasing trend continued in 2015, despite a decrease in GNI *(46)*. Linear regression analysis showed that an increase in GNI per capita by each US$ 100 is associated with a decreased in the TB notification rate of 2.7%. Thus, the improvement in socioeconomic conditions in the population might be an important contributory factor in the observed decrease in TB notification. It is notable that the economic crisis had no impact on either GNI per capita or the TB burden in the Republic of Moldova.

Fig. 3.22. Relationship between GNI per capita (US dollars) and TB notification rate (all forms), the Republic of Moldova, 2007–2015



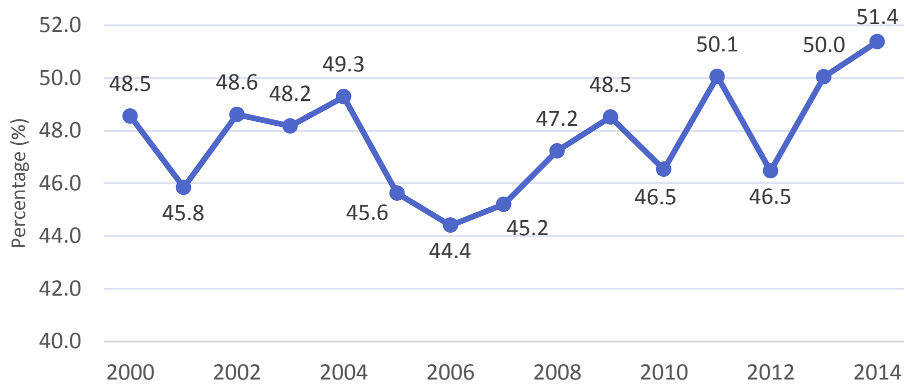
Source: SIME TB *(4)*.

Poor socioeconomic status is also a known risk factor not only for TB infection and for progression of infection to active TB but also for poor treatment outcome as well. A recent study conducted in the Republic of Moldova indicated that lower household income was independent risk factor for unfavourable TB treatment outcome *(47)*.

3.2.6 Coverage of financial protection for health care costs

The Republic of Moldova has a high THE as a percentage of GDP, which increased from 6.7% in 2000 to 12.5% in 2012 (a 70% increase), and then decreased slightly to 10.3% in 2014. This level of spending is one of the highest in the European Region. The Government of the Republic of Moldova is committed to ensuring access to affordable health care through health reforms that improve financial protection. General government health expenditure as a percentage of THE increased from 45.2% in 2007 to 51.4% in 2014 (Fig. 3.23) *(21)*.

Fig. 3.23. Trend in GGHE as a percentage of THE, the Republic of Moldova, 2000–2014



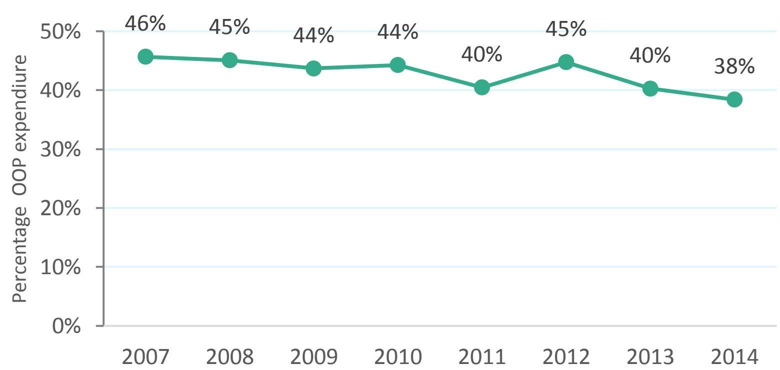
GGHE: General government health expenditure.

Source: WHO Global Health Observatory data *(7)*.

Moldovan legislation provides all citizens with access to free primary health care. About 80% of the population is enrolled in the Unified Programme of Mandatory Health Insurance, which provides access to a defined benefit package. This includes emergency care, primary care, secondary and tertiary care, emergency and preventive dental care, medical transportation, laboratory, radiology and other diagnostic testing, and home care. Inpatient services are provided without coinsurance, deductibles or copayments. Some medicines are also provided to inpatients. The National Health Insurance Company has a clear strategy, approved in 2012, to improve financial protection and reduce OOP payments *(48)*.

Between 2007 and 2014, OOP health expenditure varied between 38% and 46%, but a decreasing trend was recorded only during the last 2 years; therefore, it is unlikely that these minor changes could have an impact on TB burden. Compared with most high-priority countries in the region, the Republic of Moldova has a comparatively low level of OOP expenditure; however, ensuring universal access to health services remains a high priority.

Fig. 3.24. OOP expenditure as a percentage of THE, the Republic of Moldova, 2007–2014

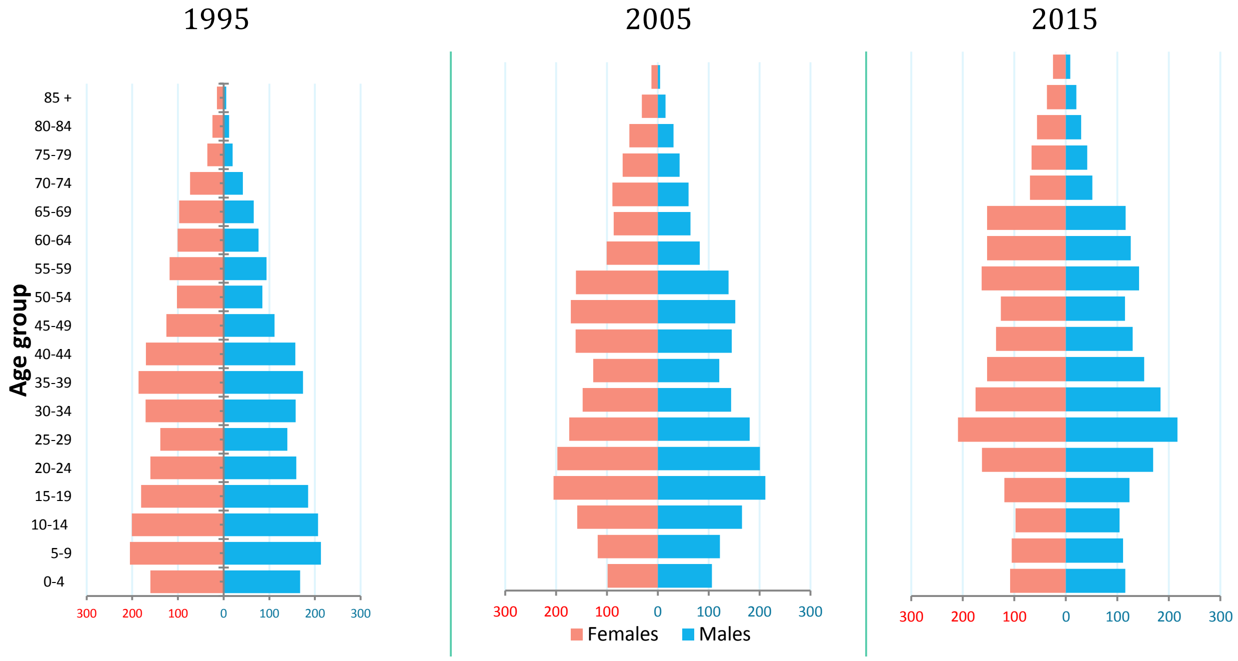


Source: WHO Global Health Observatory data *(7)*.

3.2.7 Demographic changes

TB is strongly associated with age and sex, being more common in the population aged 35–55 years and in males. Therefore, demographic changes caused by natural movements or migration could drive the TB epidemic upwards or downwards in a country, depending on changes in proportions of different age groups. Fig. 3.25 shows the age pyramids for the Republic of Moldova in 1995, 2005 and 2015, indicating rapid changes in the size and structure of the population. Each pyramid represents the distribution of the population by age and sex. According to United Nations estimates for the last 20 years, the population of the Republic of Moldova shrunk from 4339 million in 1995 to 4069 million in 2015 due to decreased fertility and outmigration. Combined with an increase in life expectancy, these factors changed the shape of the population pyramid over time: the pyramid for 2015 is narrower at the bottom and wider in the middle compared with the pyramids for 1995 and 2005.

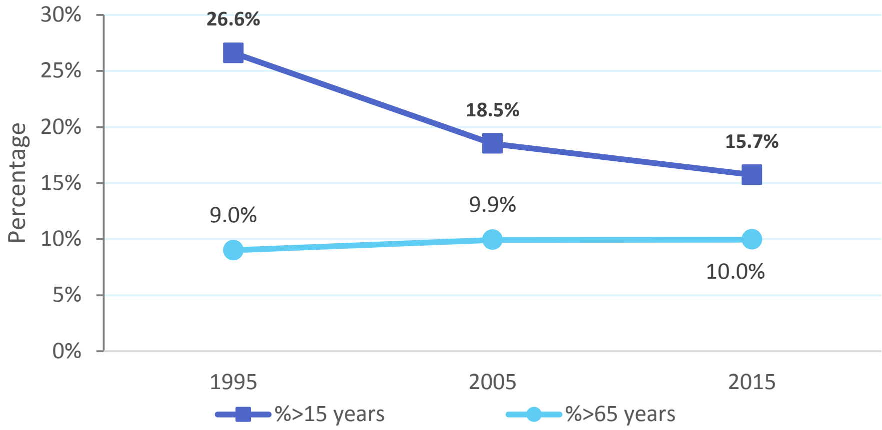
Fig. 3.25. Population structure (in thousands), the Republic of Moldova, 1995, 2005 and 2015,



Source: United Nations *(49)*.

Thus, the relative proportion of children (aged <15 years) decreased from 26.6% in 1995 to 15.7% in 2015, while the proportion of the elderly population (aged >65 years) only increased slightly from 9.0% in 1995 to 10.0% in 2015 (Fig. 3.26). Such changes in the population structure could drive the TB epidemic upwards as TB is less common in children and the elderly population, and TB prevalence and incidence are expected to be much higher in the increasing middle-aged population. However, as these changes are taking place quite slowly in the Republic of Moldova, especially in recent years, the impact of demographic changes on the pattern of TB epidemic is likely to be low.

Fig. 3.26. Percentage of the population aged <15 years and >65 years, the Republic of Moldova, 1995, 2005 and 2015



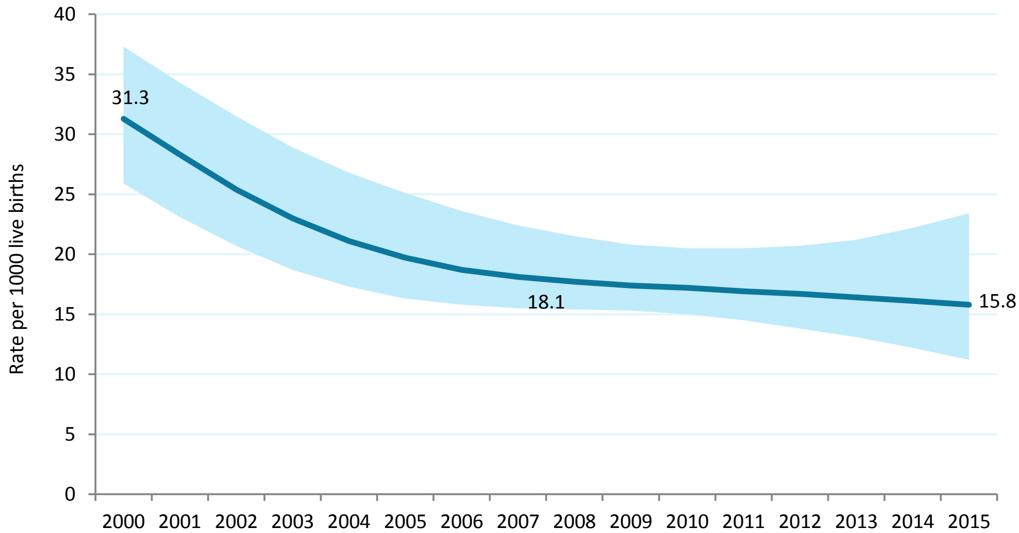
Source: United Nations *(49)*.

3.2.8 Under-five mortality

It is assumed that improvement in 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 could, therefore, serve to assess progress in the general population's health and access to health services. Fig. 3.27 shows the time trend in estimated under-five mortality in the Republic of Moldova since 2000. The average annual change in under-five mortality between 2000 and 2015 was −4.6%, demonstrating improvement in overall population health. The rate of decline was especially fast from 2000 to 2008 and comparatively slower thereafter. However, the slower decline in under-five mortality in recent years is because most easily preventable deaths have been avoided using existing technologies, and a further reduction will require technological advances and more resources

.

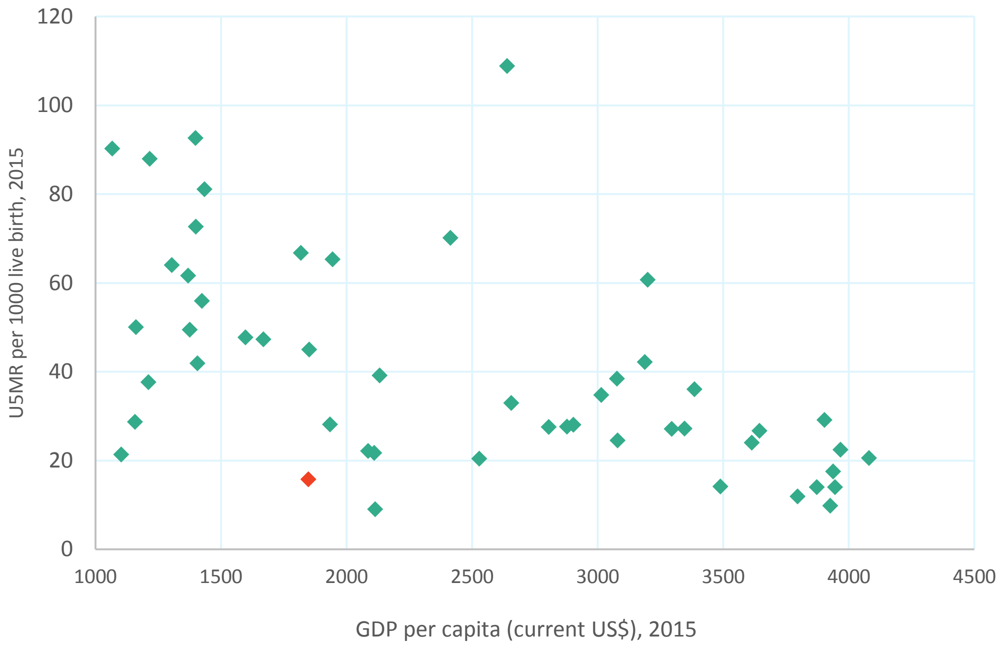
Fig. 3.27. Trend in under-five mortality rate per 1000 live births, the Republic of Moldova, 2000–2015



Source: WHO Global Health Observatory data repository *(50)*.

Compared with other countries with similar incomes, under-five mortality in the Republic of Moldova was lower in 2015 than it would be expected from the size of the economy expressed in GDP per capita, suggesting a comparatively better performance of the health system (as measured through the under-five mortality indicator) (Fig. 3.8).

Fig. 3.28. Scatterplot of the under-five mortality rate against GDP per capita, the Republic of Moldova, 2015



U5MR; under-five mortality rate.

Note that green dots represent country pairs of data points. The Republic of Moldova is shown in red.

Sources: The World Bank *(51)*.

Key findings for Section 3.1

Factors driving TB epidemic downwards

TB expenditure

2010 **US$ 11.4** million
2014 **US$ 14.6** million

Diagnostic services

2010 0 GeneXpert MTB/RIF
2015 **58 GeneXpert MTB/RIF**

Second-line treatment coverage

2008 **28% coverage**
2015 **91% coverage**

Factors with little impact on observed trend

Contact tracing

2008 **9975** contacts
2015 **9601** contacts

Treatment outcome: new & relapse

2012 **76.3%** treatment success
2014 **78.8%** treatment success

TB/HIV ART coverage

2007 **25%**
2015 **66%**

Factors driving TB epidemic upwards

RR/MDR-TB prevalence

2007 **23.7% of new TB cases**
2015 **31.8% of new TB cases**

HIV/TB prevalence

2007 **3.3%**
2015 **8.6%**

External factors not related to the NTP

Factors driving TB epidemic downwards

ART coverage

2010 **8%**
2015 **24%**

Economic growth
(GNI per capita)

2007 US$ **1160**
2015 **US$ 2220**

Poverty reduction
(% of poor)

2007 **26%**
2015 **11%**

Health financing
% of OOP THE

2007 **46%**
2014 **38%**

Health system
Under-five mortality

2007 **18.1** per 1K live births
2014 **15.8** per 1K live births

Factors with little impact on observed trend

Alcohol consumption

2008 **1291** per 100K
2015 **1315** per 100K

Tobacco smoking
(in males)

2008 **43.9%**
2015 **45.5%**

Demographic changes

1995 **26.6%** aged <15 y
2015 **15.7%** aged <15 y

Factors driving TB epidemic upwards

HIV prevalence

2007 **13 000 PLWHIV**
2015 **18 000** PLWHIV

Diabetes prevalence

2007 **1455** per 100K
2015 **2545** per 100K

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