ANALYSIS OF DETERMINANTS AND BARRIERS IN THE CASCADE OF CARE FOR PEOPLE WITH DRUG-RESISTANT TUBERCULOSIS IN MOLDOVA AND TAJIKISTAN

CONSOLIDATED REPORT

2026

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Acknowledgments

The authors would like to thank, first and foremost, all focus group participants, including healthcare and social workers, as well as patients, who shared their experiences, opinions, and valuable advice, as well as the leadership of the SMSI Institute of Pulmonology (Ministry of Health of the Republic of Moldova) and the Republican Center for Protection of Population against TB (Ministry of Health and Social Protection of the Population of the Republic of Tajikistan) for their assistance in organizing and conducting the study, as well as for their valuable comments during preparation of the study report. Also, special thanks are extended to the national consultants, coordinators, and experts who were involved in implementation of this study at every stage.

Citation reference:

Analysis of Determinants and Barriers in the Cascade of Care for People with Drug-Resistant TB in Moldova and Tajikistan. Consolidated Report. TB Europe Coalition, 2026

This study was conducted by TB Europe Coalition (TBEC) in partnership with SMIT (Moldova) and KNCV (Tajikistan) within the interregional project COMBAT DR-TB under financial support from UNITAID.

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Table of contents

List of abbreviations

aMDS	Active Monitoring and Management of Drug Safety
ART	Antiretroviral therapy
EECA	Eastern Europe and Central Asia
HIV	Human immunodeficiency virus
WHO	World Health Organization
SMSI	State medical-sanitary institution
CI	Confidence interval
TBEC	TB Europe Coalition
MDR/RR-TB	Drug resistant tuberculosis
MoH	Ministry of Health
NGO	Non-governmental organization
CSO	Civil society organization (including communities)
UN	United Nations Organization
OR	Odds ratio
PHC	Primary health care services
RRJ	Regions under the jurisdiction of the Republic of Tajikistan
TB	Tuberculosis
DST	Drug Sensitivity Test
CLM	Community-Led Monitoring
COMBAT DR-TB	The Community-Based Approaches to Transformative Change in the Fight Against Drug-Resistant Tuberculosis Project
Open MRS	Open Medical Records System
SIME TB	Electronic Information System for Tuberculosis Surveillance and Monitoring
SMIT	«Societatea Moldovei Împotriva Tuberculozei», a nongovernmental organization

The List of Tables and Diagrams

INTRODUCTION

To date, sufficient data has been gathered indicating that in the countries of Eastern Europe and Central Asia (EECA), the main barriers to providing care for people with drug-resistant tuberculosis (MDR/RR-TB) are stigma, insufficient coordination between medical and social services, limited access to public services in rural areas, and burnout among healthcare workers *(1, 2)*. Studies show that community-based interventions – such as counseling on treatment adherence, home visits, and motivational support – can significantly improve retention in treatment and treatment outcomes *(3–5)*.

This study was aimed at a systematic analysis of the barriers faced by people with MDR/RR-TB in accessing care services and retention in treatment – from the onset of symptoms through completion of treatment and subsequent reintegration into society. The comprehensive analysis helped identify key gaps in the cascade of care, covering both medical and non-medical aspects, with a particular focus on the role of community-based support services and taking into account firsthand experiences of the patients.

Use of a mixed method approach provided meaningful evidence, on the basis of which practice oriented recommendations were formulated, aimed at:

- improving access to services and increasing patient retention in the care system;
- reducing interruptions and delays in initiating treatment;
- capacity building for healthcare workers;
- integrating medical and social services within a personalized model of care.

Moreover, the analysis included results of community-led monitoring (CLM) regarding implementation of a standardized package of support services at the local community level in six countries in the EECA region conducted by TBEC in 2024 *(2)*.

About the Project

The *Community-Driven Approaches for Transformative Change to Combat Drug-Resistant Tuberculosis* (COMBAT DR-TB) Project is a three-year initiative implemented by the coalition comprising KELIN (Kenya), the TB Europe Coalition (TBEC), and O'Neill Institute for National and Global Health Law at Georgetown University, with financial support from UNITAID. The Project aims to transform response to MDR/RR-TB through advocacy, ensuring accountability, and creating demand for new, vital treatment regimens for MDR/RR-TB – initiated by communities and civil society while ensuring equal access to them.

Implemented in six countries with a high burden of MDR/RR-TB – Kenya, Nigeria, Zimbabwe, Moldova, Tajikistan, and Ukraine – it focuses on four key areas: ensuring policy ecosystems that facilitate access to MDR/RR-TB treatment, strengthening civic advocacy, promoting a multisectoral accountability mechanism, and scaling up community-led responses. It aims to support implementation of shorter, fully oral treatment regimens for MDR/RR-TB to eliminate systemic barriers such as stigma and poor-quality care, and to align with the WHO Global Strategy for the Elimination of Tuberculosis and the Second UN High-Level Meeting on Tuberculosis in 2023.

The project is coordinated at the regional level by: KELIN in Africa and TBEC in Eastern Europe and Central Asia (EECA) while global collaboration is led by O'Neill Institute and the Tuberculosis Community Advisory Board (TB CAB). COMBAT DR-TB reinforces UNITAID's commitment to people-centered and rights-based approaches and to the central role of communities in transforming the health care system.

RATIONALE

Despite positive trends, tuberculosis (TB) and MDR/RR-TB remain a serious threat to public health in the WHO European Region, particularly in the EECA region, which includes the Republic of Moldova and the Republic of Tajikistan. The both countries are among the 30 countries worldwide with the highest burden of MDR/RR-TB, as the prevalence of MDR/RR-TB significantly exceeds the global average for the burden of MDR/RR-TB *(6)*. Key challenges still include the need for early diagnosis of MDR/RR-TB, implementation of shortened oral treatment regimens, ensuring access to necessary medications, and the importance of supporting patients throughout their treatment, as well as providing follow-up rehabilitation and resocialization.

Factors that will influence progress toward ending the TB epidemic include: optimizing current strategies and measures for TB treatment and prevention; ensuring universal access to TB treatment and support through universal health coverage and social protection measures; and investing in research aimed at developing new, human rights-based, and more effective methods and strategies for the diagnosis, treatment, and prevention of TB.

The WHO identifies "comprehensive care tailored to the needs of people with TB" as one of the key components of the Global Strategy for the Elimination of Tuberculosis, which is also reflected in the regional action plan for the European Region *(7)*. The TB cascade of care, also known as the continuum, is an important model for systematically evaluating effectiveness of service delivery at each stage necessary to achieve the ultimate goal. The cascade helps quantify gaps in care delivery highlighting areas where the quality of care needs to be improved. Originally used in HIV prevention programs, this model was subsequently applied on a wide scale to other diseases, including TB.

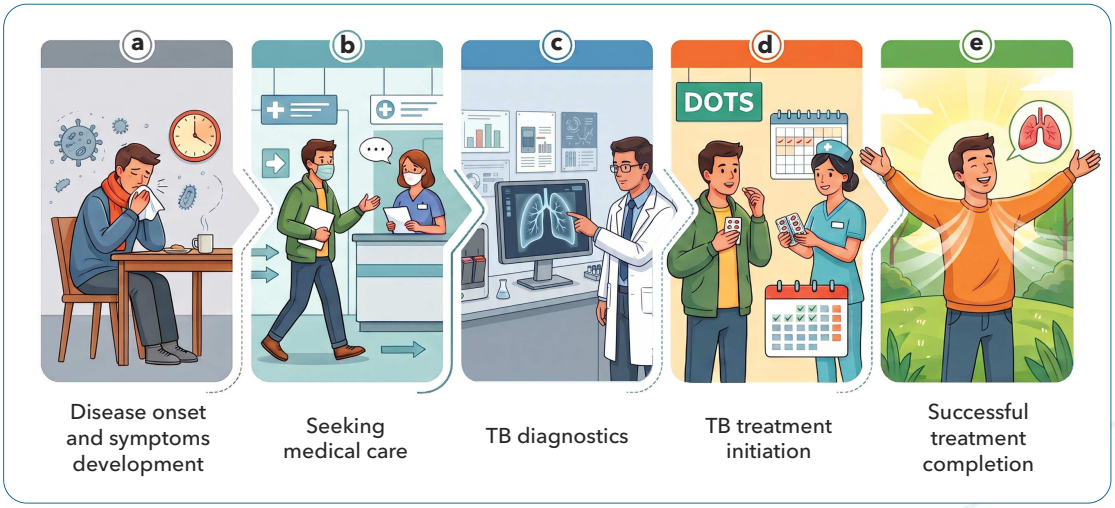
The cascade approach has only recently been used to evaluate TB screening, diagnosis, treatment, and care, although cohort analysis and, more recently, patient pathway analysis were already well established and had been used to understand the reasons for treatment discontinuation. Moreover, the WHO has developed an "onion-layer" model, where patient losses at different stages of treatment are visualized as a series of concentric circles, and this conceptual model informs the approach to the cascade of care.

The TB Cascade of Care

The TB cascade of care is a model for providing medical care to the population with TB, in which distinct phases, or stages, are identified that each individual goes through, starting from the moment of probable infection and the onset of TB until successful completion of a course of TB therapy. In other words, it is a sequence of stages during the specific period of a person's life that involve receiving medical care aimed at TB diagnosis, treatment, and prevention.

The level of detail in the TB cascade of care may vary. At a minimum, the cascade consists of five stages:

a) onset of the disease and development of symptoms;
b) seeking medical care;
c) TB diagnosis;
d) initiation of TB treatment; and
e) successful completion of treatment.



Sometimes another stage is added to these five – preventing relapses or deaths among patients after treatment is completed. In 2019, the WHO also proposed a framework for identifying key challenges in the TB cascade of care to provide meth-odological support for planning of national programs *(8)*.

The analysis covers 9 stages across three key categories:
1) before seeking medical care,
2) at the time of seeking care and before a diagnosis is made, and
3) during treatment.

Table. 1. **The TB cascade of care proposed within the WHO framework approach**

People who do not have access to the healthcare system		
People at high risk of developing the disease.	People with asymptomatic TB who do not seek medical care.	People with TB symptoms who do not seek medical care.
People with TB who have sought care but have not been diagnosed or are not recorded		
Those seeking help but who have not been diagnosed.	The diagnosis was not made at a TB organization and was not recorded.	The diagnosis was made at a TB organization but was not recorded.
People diagnosed with TB who have not received effective treatment		
The diagnosis has been made but treatment has not yet begun.	The treatment is ineffective.	The treatment was successful, but there was a relapse.

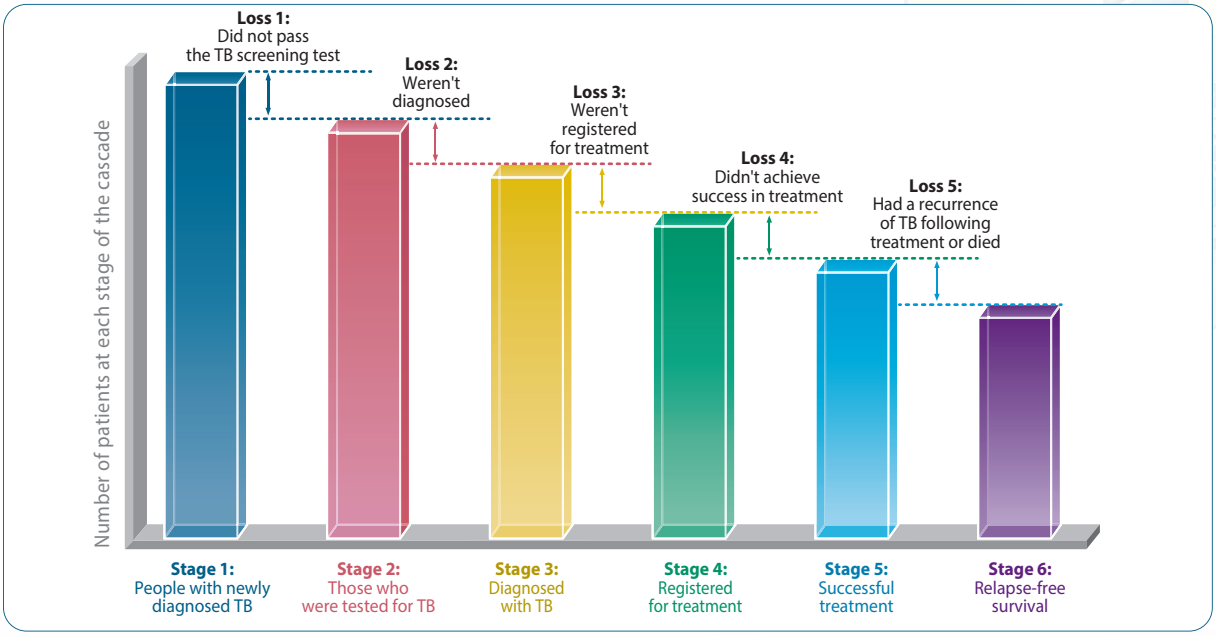
Source: WHO, 2019 (8)

The TB cascade of care is a valuable and feasible approach to analyzing the quality of services. The approach to developing a TB cascade of care depends on the primary objective of the assessment, which may include:

(1) large-scale assessments to monitor treatment outcomes for patients covered by national programs, or

(2) smaller-scale assessments to identify gaps in the quality of care at the municipal and/or regional level.

Chart 1. **A TB cascade of care with an assessment of losses at each stage**



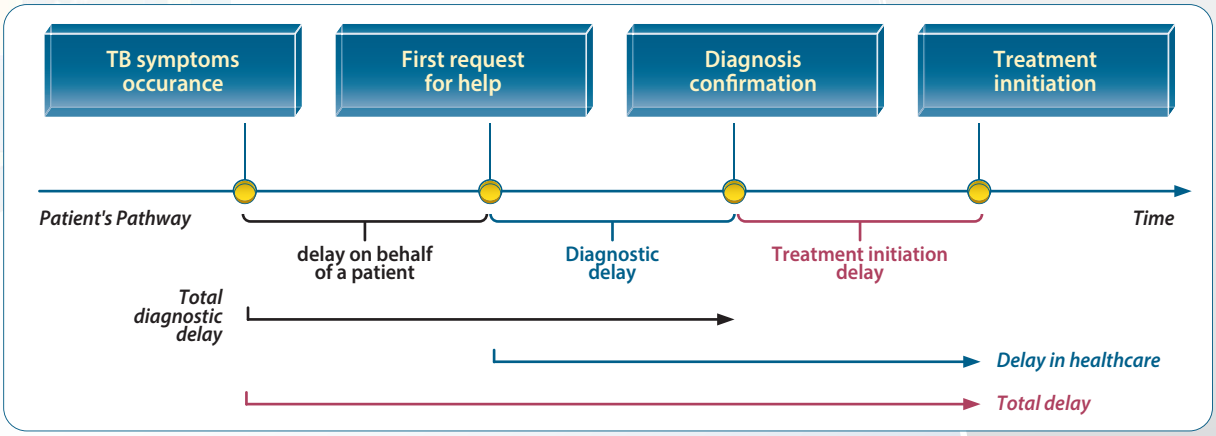
Source: Subbaraman et al., 2019 (9)

A cascade of care is a model for assessing patient support and retention at successive stages of care necessary to achieve the successful treatment outcome. This approach was first used to assess HIV programs and has since been applied to other diseases. TB surveillance experts have also begun using cascade of care analysis to quantify gaps in quality of treatment.

The TB cascade of care identifies gaps at each stage of a patient's TB journey, from the moment they seek medical care upon the onset of the first symptoms of the disease to their cure. The essence of the TB cascade of care is identifying gaps at all stages of medical care, particularly during screening, diagnosis, initiation of treatment, and completion of treatment. The cascade makes it possible to determine the percentage of patients who drop out of the diagnostic and treatment process.

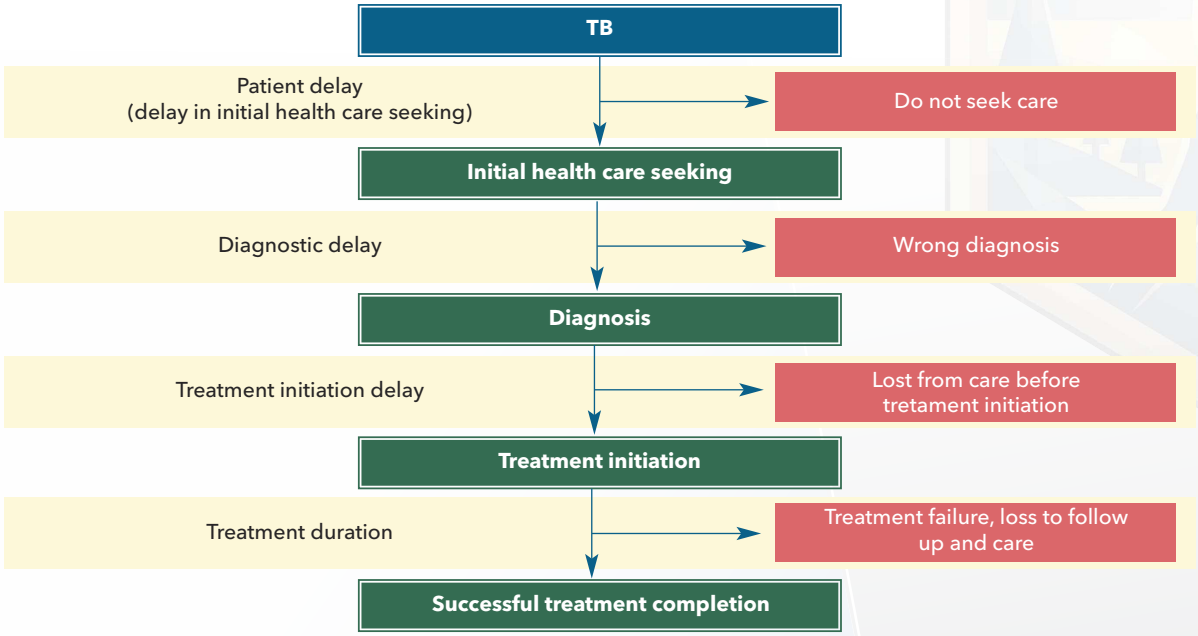
In addition to quantifying losses, the cascade also makes it possible to assess time-related losses – so-called "delays" – that occur as a person moves from one stage to another. Consequently, new concepts have emerged: delay in seeking care, diagnostic delay, delay before the start of treatment, and so on.

Chart 2. **The TB patient's path and identification of major delays at stages of the cascade of care**



Conducting a study such as a "patient pathway analysis" makes it possible to collect and examine important data needed to better understand the factors that influence the likelihood of losing a specific proportion. The cascade of healthcare, which assesses outcomes at different stages of patient engagement in the healthcare system, serves as an important foundation for evaluating the quality of TB care. In recent years, some progress has been made in studying the cascade of care, raising hopes for a better understanding of the factors that cause patients to fall through the cracks of the healthcare system at various stages. Nevertheless, research into such factors (such as those related to patients being lost to follow-up before treatment begins or to relapses following successful treatment) is severely hampered by a lack of quality evidence base. Collecting and analyzing such data will provide a better understanding of the cause-and-effect links making it possible to develop and implement respective measures. In this regard, a study such as a "patient pathway analysis" makes it possible to collect and examine important data needed to better understand the factors that influence the likelihood of losing a certain proportion of patients at various levels of the TB cascade of care.

Chart 3. **The TB cascade of care and major losses and delays by stage**



Source: Vesga et al., 2019 (10)

Key Definitions

Delay in seeking care (delay on the part of the patient) – the time that elapses from the onset of the first symptoms indicating a possible case of pulmonary tuberculosis until the date of the first contact with a healthcare provider regarding those symptoms.

Diagnostic delay – the period of time between a patient's first contact with the healthcare system and the date of laboratory confirmation of the diagnosis.

Delay until treatment begins – the time from the moment the diagnosis is laboratory-confirmed until the start of TB treatment.

Delay in the healthcare system – the time from the patient's first contact with the healthcare system until the start of treatment.

Total delay – the time from the onset of the first TB symptoms to the start of TB treatment.

Factors such as social inequality or health-related behaviors may have a greater impact on the burden of TB among vulnerable groups than the endemic nature of TB. Indeed, prevalence and incidence of TB will vary significantly depending on the context, including geographic, cultural, sociopolitical, and medical factors.

Many people with TB do not experience any symptoms in the early stages of the disease, do not seek medical care in a timely manner, and may not be tested for TB. Other population groups may lack access to health care for financial reasons, due to geographic isolation, or because of other factors. Identifying high-risk groups and carefully planning systematic screening – whether within or outside the healthcare system – can help improve the situation regarding early diagnosis of TB.

The cascade of care for people with MDR/RR-TB cannot be separated from the cascade for all forms of TB during the initial stages, until the results of drug susceptibility testing (DST) are available. Nevertheless, a retrospective analysis makes it possible to specifically identify barriers to delivery of services provided to patients with MDR/RR-TB, which was the objective of this study.

This study makes it possible to conduct an assessment of the number of people with TB lost to follow-up at each stage of the TB cascade of care. It also discusses the steps involved in cascade reconstruction: from the onset of the first symptoms and seeking help to completion of treatment. Based on the study's findings, recommendations are provided regarding the potential use of this model to assess the impact of interventions aimed at improving disease detection, diagnosis, referral to treatment, retention in the treatment system, and follow-up care for patients after treatment is completed.

GOALS AND OBJECTIVES

The objective of the study was to conduct a comprehensive analysis of critical gaps in service delivery within the MDR/RR-TB cascade of care in Moldova and Tajikistan. This includes identifying barriers at every stage of the TB care pathway – from case finding and diagnosis to successful completion of treatment and rehabilitation, encompassing both medical and non-medical components – as well as ensuring that the analysis is evidence-based, context-specific, aligned with national TB priorities, and grounded in results of community-led monitoring of progress in implementing the Standardized Community-Based Support Package in six EECA countries in 2024 *(1, 11)*.

Study objectives:

1. 1. Build the MDR/RR-TB cascade of care in Moldova and Tajikistan for the period of 2021–2023.
2. Identify gaps in both medical and non-medical components at each stage of service delivery within the cascade of care for people with MDR/RR-TB.
3. Explore the possibility of quantitatively assessing the prevalence of specific gaps in care using retrospective patient-related data.
4. Examine perceptions and experiences of people with MDR/RR-TB and community-level workers.
5. Compile examples of effective interventions that have improved access, retention, and treatment outcomes for MDR/RR-TB.

The findings will be used to develop practical recommendations for enhancing delivery of MDR/RR-TB services, including both medical and non-medical components, to improve patient treatment outcomes and enhance effectiveness and accountability of national TB programs in the both countries.

MATERIALS AND METHODS

This study employed a mixed-method (combined) design, which integrated quantitative and qualitative methods to ensure a comprehensive analysis of the phenomena under study and to enhance reliability of the data obtained.

The study was conducted from November 2025 to February 2026, which provided sufficient time to carry out all the stages in sequence – from planning and data collection to data analysis and interpretation.

Quantitative study

This phase involved a retrospective analysis of the pathway for patients with MDR/RR TB, from the onset of the first symptoms through completion of TB treatment. Throughout their pathway, patients interacted with various levels of the healthcare system, including community and support services.

The study focused on assessing coverage with healthcare services, as well as analyzing time intervals between the initial contact with the healthcare system (including community support services) and completion of treatment. The analysis included an assessment of key intermediate steps, such as symptom screening, laboratory testing, diagnosis confirmation, initiation of treatment, and monitoring of treatment progress.

Study type: observational, cohort, retrospective.

Sample: The study included all patients with laboratory-confirmed MDR/RR-TB diagnosed and registered in the national surveillance system between 2021 and 2023; thus, it covered the entire population of MDR/RR-TB cases confirmed with laboratory testing during that period.

Sub-cohort: For an in-depth analysis, a sub cohort of 295 patients with MDR/RR-TB was formed, consisting of patients who met the following additional inclusion criteria: patients registered as new cases or relapses between 2021 and 2023; who had started treatment for MDR/RR-TB; who were enrolled in support programs throughout the course of treatment; who were over 18 years of age; the civic sector.

Qualitative study

The study aimed to examine perceptions and experiences of patients with MDR/RR-TB, as well as community-level staff, including primary health care (PHC) providers and civil society organizations (CSOs), involved in providing care and support to patients with MDR/RR-TB. To this end, focus group discussions were organized (in Tajikistan), or an online survey was conducted (in Moldova).

Selecting a location for the study. A targeted location selection strategy was used to ensure a balanced geographic distribution across the three regions of the Republic of Moldova (North, Central, and South). In each of the three regional zones, 4 to 5 settlements were selected, including two urban and three rural settlements. For each selected settlement, the strategy of exhaustive (total) inclusion was applied, which involved including all respondents who met the predetermined selection criteria. In Tajikistan, the study was conducted in five settlements including both urban and rural populations. As part of

the study, three focus groups were organized, each consisting of 10–20 people, including:
1) PHC workers (in Moldova and Tajikistan);
2) representatives of civil CSOs providing support to patients with TB (in Moldova only).

Inclusion criteria for focus group participants:

1) Healthcare personnel meeting the following criteria: work within the PHC system and interacting with patients with MDR/RR-TB; provided written informed consent to participate in focus group discussions.
2) Representatives of CSOs who meet the following criteria: work at the CSO that provide support services to people with TB; have at least one year of experience in providing support services to patients with TB; have provided written informed consent to participate in focus group discussions.
3) 3) People diagnosed with MDR/RR-TB who meet the following criteria: have undergone treatment within the last 24 months; completed treatment no more than 12 months ago; received treatment on an outpatient and/or inpatient basis; have the physical and cognitive capacity to understand questions and provide answers; are over 18 years of age; reside on the right bank of the Dniester River (for Moldova); civic sector; have provided written informed consent to participate in focus group discussions.

Data collection

The study employed several data collection methods, including extraction and systematization of information, as well as data obtained during focus group discussions.

The following sources were used for the quantitative analysis: the national electronic registry SIME TB (Moldova) and OpenMRS (Tajikistan), individual medical records of patients with MDR/RR-TB, and community service provision logs at the NGO level. The study involved direct contact with patients with MDR/RR-TB through focus group discussions.

Lists of individuals who met the inclusion criteria and sampling principles were extracted from the SIME TB registry. After data extraction, a unique anonymous identifier was generated for each study participant, preventing both direct and indirect identification of the individuals. The anonymous identifier was used when coding the study questionnaire, which included variables extracted from SIME TB and was supplemented with additional data from the medical records of the enrolled participants, as well as from other relevant sources listed above.

The coded and completed questionnaires were collected by the NGO SMIT and forwarded to the Monitoring and Evaluation Department at the SMSI Institute of Pulmonology for centralized processing. The questionnaires (completed and coded) underwent a verification and validation process. Only validated questionnaires were entered into the database, which was developed on the EpiData platform specifically for this study, with double data entry. Validated questionnaires were entered twice to ensure data quality. The final database underwent data entry quality control procedures and verification to ensure the questionnaires were filled out correctly.

Data analysis

Quantitative study. The data obtained were subjected to the following analytical methods: synthetic, comparative, and prognostic analysis, as well as methods for assessing reliability. The data extracted from SIME TB, along with additional information collected, were imported into SPSS for further statistical analysis. The analysis included generation of simple frequency distributions and cross tabulations. Moreover, statistical tests were conducted to identify possible correlations among the variables. Continuous variables were described using the mean (standard deviation) or the median (IQR, interquartile range). The odds ratio (OR) was used to assess risk factors. A p-value of less than 0.05 was considered the threshold for statistical significance. The analytical phase focused on obtaining the minimum necessary set of results, including: a stratified analysis based on sociodemographic characteristics, comorbid conditions, and social determinants; quantification of gaps in the cascade of care, including an assessment of the proportion of patients with MDR/RR-TB who received delayed or incomplete care or who discontinued treatment; and reconstruction of the cascade of care for patients with MDR/RR-TB.

Qualitative study. The collected information was converted into text format through decoding, transcription, and triangulation. Based on transcripts of the focus group discussions, a thematic content analysis was conducted using specialized software for processing audio recordings. The qualitative findings obtained were subjected to triangulation with quantitative data, which made it possible to reinforce, refine, or compare the patterns identified during the study. The analytical process was aimed at identifying barriers, unmet needs, and factors that facilitate provision of medical and community services to patients with MDR/RR-TB. The analysis took into account the perspectives of both beneficiaries and representatives of medical personnel and community-based CSO staff.

Ethical considerations

The study was designed and conducted in strict accordance with the fundamental ethical principles applicable to studies involving human subjects, in accordance with the Declaration of Helsinki, the Guidelines on *Good Clinical Practice*, as well as the valid national laws of the Republic of Moldova and the Republic of Tajikistan governing protection of personal data and patients' rights.

To ensure confidentiality, all collected data were encrypted and anonymized. The interviewers received training on confidentiality and signed non-disclosure agreements. Audio recordings, written notes, and electronic files were stored under high-security conditions, and access to the data was restricted to authorized members of the study team only. Once the study is complete, the data will be stored for 12 months, after which it will be destroyed in accordance with standard procedures.

The questionnaires used to collect data during the focus group discussions were adapted and translated into the national language.

The study protocols were reviewed and approved by the National Committee for the Ethical Review of Clinical Trials of the Republic of Moldova (Decision No. 2019 of October 29, 2025) and by the Ethics Committee of the Ministry of Health and Social Protection of the Republic of Tajikistan (No. 2–7/4619 of December 27, 2025).

STUDY RESULTS CONDUCTED IN THE TWO COUNTRIES OF EECA: THE REPUBLIC OF MOLDOVA AND THE REPUBLIC OF TAJIKISTAN

MDR/RR-TB cascade: from laboratory confirmation to successful completion of treatment in the Republic of Moldova

The analysis of the service cascade allows us to trace the sequence of steps – from identification and laboratory confirmation of MDR/RR-TB to completion of treatment – providing a comprehensive understanding of the patient's journey through the care system (**Chart 4**). Of the initial group of 1,276 individuals classified as suspected cases of MDR/RR-TB, the diagnosis was confirmed for 1,222 patients (95.8%). This indicates that the diagnostic system is functioning reliably and that the follow-up examination procedures are effective in promptly ruling out cases that are not true episodes of TB or MDR/RR-TB. Unconfirmed cases are generally associated with clinically sound decisions based on additional examinations, which indicates a high standard of care at the diagnostic stage.

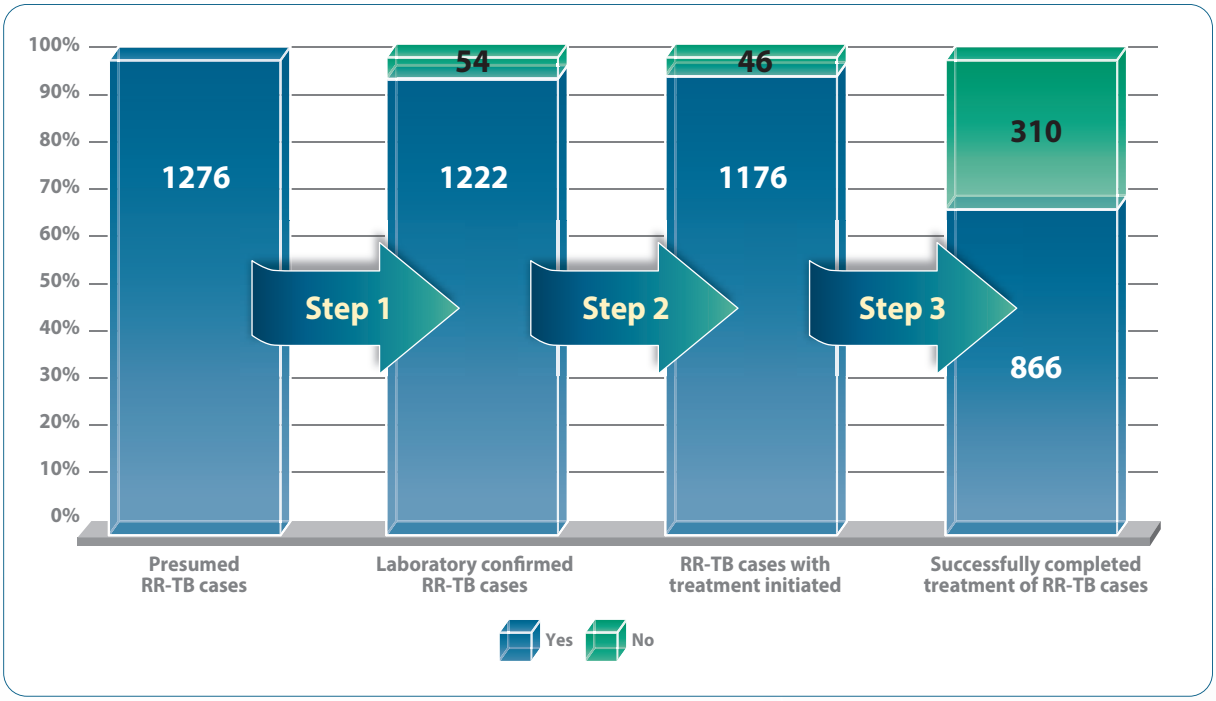
Once the diagnosis is confirmed, the next step in the process is to begin treatment. Of the 1,222 confirmed cases of MDR/RR-TB, 1,176 patients (96.2%) were en-rolled in MDR/RR-TB treatment, indicating a high level of coverage and effective patient referral systems.

The cases in which treatment was not initiated were primarily due to the patients' severe condition and late diagnosis of the disease, when clinical decompensation results in death before treatment can even be started. Despite these losses, the high treatment initiation rate confirms that the system provides timely access to therapy for the vast majority of patients with laboratory-confirmed MDR/RR-TB (**Chart 4**).

The final and most vulnerable stage of the cascade is related to treatment outcomes. Among the 1,176 patients who began treatment for MDR/RR-TB, 866 (73.6%) achieved a successful outcome, while treatment was unsuccessful for 310 patients (26.4%). It is at this stage that the highest dropout rates occur, highlighting the need to strengthen measures to retain patients during long-term therapy, including expanding comprehensive support and improving treatment adherence (**Chart 4**).

Overall, the presented cascade confirms effectiveness of the key components of the national TB control program, including the quality of diagnosis, timely initiation of treatment, and access to health care services. At the same time, the findings show that the success of long-term treatment for MDR/RR-TB depends largely on a combination of clinical management, sustained psychosocial support, and timely enrollment of patients in a structured care model – the factors that form the foundation for success-ful treatment and for reducing the risk of adverse outcomes.

Chart 4. **The cascade of care for MDR/RR- TB: from a suspected case to completion of treatment**



Step 1. Laboratory confirmation of the MDR/RR-TB diagnosis

As part of the study, data from 1,276 individuals classified as "suspected cases of MDR/RR-TB" during the 2021–2023 period were analyzed. In the first stage of the analysis, it was determined that 1,222 individuals had a laboratory-confirmed diagnosis of MDR/RR-TB, accounting for 95.8% of all those examined. For the remaining 54 individuals (4.2%), resistance to rifampicin – and, in some cases, TB as such – was not confirmed. An analysis of clinical–diagnostic trajectories shows that the reasons for non-confirmation were documented and can be grouped into several categories **(Chart 5).**

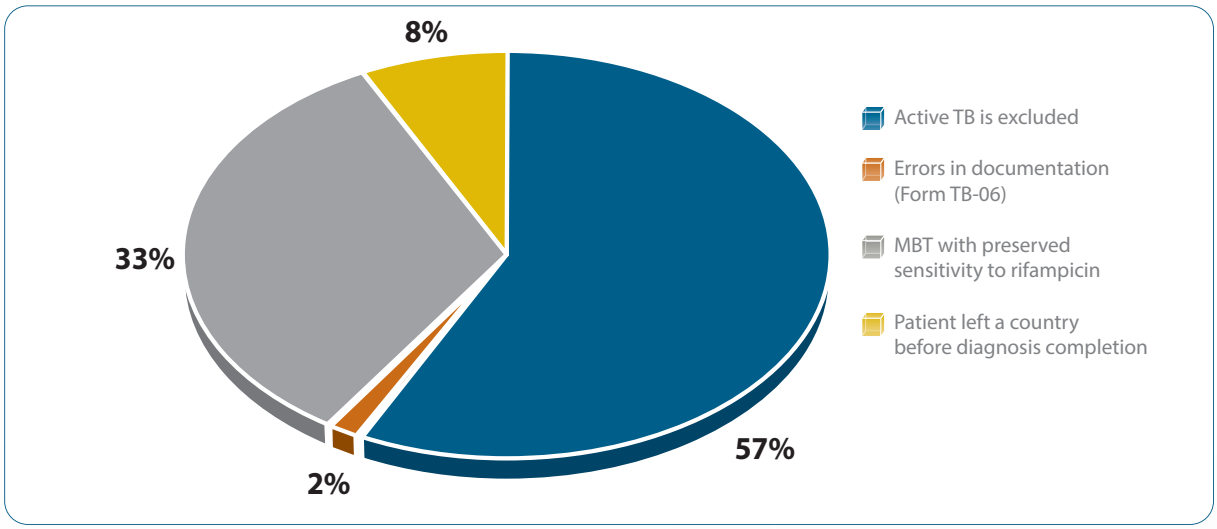
In most cases (83.7%; 31/54), the failure to confirm MDR/RR-TB was due to the fact that active TB had been ruled out based on results of additional testing conducted by the MDR/RR-TB Case Management Committee. Clinical and laboratory data did not confirm the disease, indicating that the mechanisms for further examination and screening of suspected cases were appropriate.

A separate subgroup of unconfirmed cases of MDR/RR-TB was attributed to errors in completing documents (form TB-06) – 1 case (1.9%) – as well as detection of M. tuberculosis with preserved susceptibility to rifampicin upon retesting, which rules out the diagnosis of MDR/RR-TB (33.3%; 18/54).

Moreover, a small proportion of the cases was due to non-medical reasons that made it impossible to complete the diagnostic algorithm (7.4%; 4/54): patients left the country on the day of their examination (cases of departure to France, Ukraine, Belgium, and Italy were recorded). Under these circumstances, the full diagnostic algorithm was not completed, and confirmation of the diagnosis of MDR/RR-TB was not possible for procedural reasons **(Chart 5).**

Overall, the results underscore the importance of consistent verification of suspected cases of MDR/RR-TB and demonstrate robustness of the diagnostic component of the care cascade, which ensures accurate identification of true cases of MDR/RR-TB and prevents excessive diagnoses.

Chart 5. **Results of follow-up examinations of patients with suspected MDR/RR-TB**



The profile of individuals with laboratory confirmed MDR/RR-TB

Analysis of the sociodemographic characteristics of patients with MDR/RR-TB for 2021–2023 reveals a consistent epidemiological profile of the disease. A total of 1,222 people were included in the analysis. The sample was heterogeneous but structured. Men accounted for the overwhelming majority of participants – 80% – while women accounted for 20%, corresponding to the approximate male-to-female ratio of 4:1 **(Table 2).**

The mean age of the participants was 44.8 years, and the median was 44 years (range 18–89 y.o.; standard deviation 12.05), indicating moderate variability in age and a comparable representation of young people and middleaged and older adults. This is also reflected in the breakdown by age group: 52.3% of the participants were younger than 44, while 47.7% were 45 or older.

The distribution by place of residence was even: 50% of cases occurred in urban areas and 50% in rural areas, indicating a comparable epidemiological burden in the both settings.

From the geographical perspective, cases from the right bank of the country predominated (74.9%), while the eastern region accounted for 25.1% of the total. The regional distribution was as follows: the central area – 43.7% (534 cases), the northern part – 17.3% *(211)*, the southern part – 11.8% *(144)*, and the eastern region – 25.1% *(307)*; the penitentiary system, although relatively small – 2.1% (26 cases) – remains epidemiologically significant.

In most cases, the process leading to laboratory diagnosis began at the local level: 74.9% *(933)* of the referrals were processed by regional services, 25.1% *(289)* were processed at the national level.

Overall, the profile of participants shows predominance of males, with a relatively balanced age distribution and equal representation of urban and rural areas, with a predominance

of right-bank territories and a significant contribution from the eastern region. Access to diagnostic services and follow-up care was primarily provided at the local level **(**see **Table 2)**.

Table. 2. **Key characteristics of patients with laboratory-confirmed MDR/RR-TB**

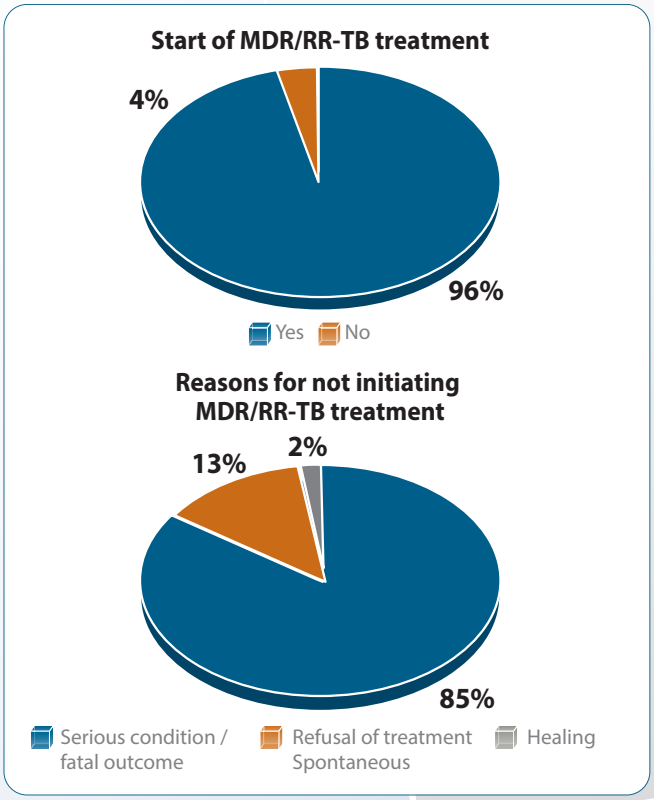
Variable	Laboratory-confirmed MDR/RR-TB n (%)
Total	**1222**
Sex	
man	977 (80,0)
woman	245 (20,0)
Age	
under 44 y.o.	639 (52,3)
45 years and older	583 (47,7)
Place of residence	
urban area	611 (50,0)
rural area	611 (50,0)
Geographic region	
right bank	915 (74,9)
left bank (eastern region)	307 (25,1)
Level of referral for laboratory testing	
national level	289 (23,6)
local level	933 (76,4)

Step 2. From confirmation of the diagnosis of MDR/RR-TB to the start of treatment

The proportion of patients who began treatment among confirmed cases of MDR/RR-TB was 96.2% (1,176 out of 1,222), which indicates a high level of access to therapy. Nevertheless, 46 patients (3.8%) did not begin treatment, and an analysis of the reasons for non-inclusion revealed a clear distinct structure **(Chart 6).**

The main reason for not initiating treatment was the patient's critical condition, which resulted in death (84.8%; 39/46). This emphasizes the fact that a significant proportion of patients were diagnosed at late stages of the disease, when their clinical condition did not allow for initiation of TB therapy. Six patients (13.0%) refused treatment, indicating persistent individual and behavioral barriers that affect access to therapy and acceptance of medical care. Spontaneous remission/regression of the disease without initiation of

Chart 6. **Initiation of treatment for people with confirmed MDR/RR-TB**



treatment was observed in 1 case (2.2%), which represents a rare exception and does not have a significant impact on the overall pattern of reasons for not initiating treatment **(Chart 6).**

Analysis of factors associated with the start of treatment

Analysis of **socio-demographic characteristics** of patients, compared with the probability of initiating treatment of MDR/RR-TB, shows that the variables under consideration do not demonstrate a statistically significant association with transition from diagnosis to initiation of therapy. Gender differences (80.0% among those who did not begin treatment vs 82.6% among those who did; OR = 1.19; p = 0.812), age groups (50.0% vs 52.3%; OR = 0.91; p = 0.866), type of place of residence (60.9% vs 49.6%; OR = 1.58; p = 0.175) and geographic area (76.1% vs 74.8%; OR = 1.07; p>0.999) were not found to be statistically significantly associated with the probability of initiating treatment. Similarly, a history of migration (OR = 1.22; p = 0.760) and a history of incarceration (OR = 0.91; p>0.999) also showed no statistically significant effect on initiation of therapy **(Table 3)**.

The source of income is a factor that draws particular attention, as significant differences were identified in this regard. No statistically significant differences were found between the "employed" and "no income" groups. However, the group of patients with "other types of income" shows a significantly higher risk of not initiating treatment (OR = 24.13; p<0.001). This odds ratio is extremely high and may indicate the presence of specific characteristics in this subgroup, including irregular income, social instability, and dependence on allowances or temporary earnings. Such conditions have the potential to reduce adherence to treatment initiation and limit access to health care, especially in the presence of financial barriers, transportation costs, and general social vulnerability **(Table 3).**

Thus, findings of the analysis show that most traditional sociodemographic determinants (gender, age, type of settlement, geographic region, migration history, and history of incarceration) do not have a statistically significant effect on the probability of initiating treatment for MDR/RR-TB (all p>0.05). This indicates that various patient subgroups have relatively equal access to treatment initiation.

At the same time, one key socioeconomic factor was identified – **unstable sources of income** – which is associated with a significantly higher risk of not initiating treatment or initiating it late. The findings underscore the need to strengthen social support mechanisms for groups in precarious financial situations in order to reduce barriers to treatment and minimize the risk of patients dropping out in the early stages of the cascade of care.

Table. 3. **Social-demographic factors associated with the start of treatment for MDR/RR-TB**

Variable	Start of «RR-therapy», n (%)		OR [95% CI]	P value
	No	Yes		
Total	**46**	**1176**		
Sex				
man	38 (80,0)	939 (82,6)	1,19 [0,55–2,60]	0,812
woman	8 (20,0)	237 (20,2)	1 (реф.)	
Age				
under 44 y.o.	23 (50,0)	616 (52,3)	0,91 [0,50–1,63]	0,866
45 years and older	23 (50,0)	560 (47,6)	1 (реф.)	

Variable	Start of «RR-therapy», n (%)		OR [95% CI]	P value
	No	Yes		
Place of residence				
urban area	28 (60,9)	583 (49,6)	1,58 [0,86–2,89]	0,175
rural area	18 (39,1)	593 (50,4)	1 (реф.)	
Geographic region				
right bank	35 (76,1)	880 (74,8)	1,07 [0,53–2,13]	>0,999
left bank (eastern region)	11 (23,9)	296 (25,2)	1 (реф.)	
Sector				
civil	46 (100,0)	1133 (96,3)	-	-
penitentiary	0 (0,0)	43 (3,7)	-	-
History of migration				
yes	7 (15,2)	144 (12,2)	1,22 [0,53–2,78]	0,760
no	39 (84,8)	1032 (87,8)	1 (реф.)	
History of incarceration				
yes	7 (15,2)	192 (16,4)	0,91 [0,40–2,08]	>0,999
no	39 (84,8)	982 (84,8)	1 (реф.)	
Has income				
yes / employed	15 (32,6)	362 (30,8)	1 (реф.)	
yes / other income	28 (60,9)	28 (60,9)	24,13 [11,57–50,36]	<0,001
no	3 (6,5)	3 (6,5)	1,0 [0,18–5,38]	>0,999

The breakdown by **programmatic factors** shows that the method for detecting MDR/RR-TB (mWRD/Xpert or other laboratory tests), year of TB case notification, or the type of the TB case (new or relapse) do not have a statistically significant effect on the probability of initiating treatment (all p>0.05). Proportions of patients who began therapy remain comparable across all subgroups **(Table 4).**

A referral for a consultation with the TB and pulmonology service is the only programmatic factor that showed a statistically significant association. Patients referred by a medical specialist were more than twice as likely to not start treatment compared with patients referred by a family doctor (OR = 2.07; p = 0.032). This may reflect later diagnosis, presence of comorbidities, as well as possible delays in referral at the secondary care level. At the same time, patients who sought care on their own did not differ from the reference group in terms of the probability of initiating treatment (OR = 1.40; p = 0.554), which confirms consistency of the mechanisms for enrollment in treatment regardless of the method of referral to the TB and pulmonology service.

Overall, the results show that – with the exception of referral by a medical specialist – none of the programmatic indicators examined constitutes a statistically significant barrier to initiation of treatment for MDR/RR-TB, which indicates a high degree of standardization and consistency in referral processes and ensures timely transition of patients to treatment.

Table. 4. **Programmatic factors associated with initiation of treatment for MDR/RR-TB**

Variable	Start of «RR-therapy», n (%)		OR [95% CI]	P value
	No	Yes		
Total	**46**	**1176**		
Referred to the TB unit for a consultation by				
Family doctor	15 (32,0)	551 (46,9)	1 (реф.)	
Medical specialist	22 (47,8)	390 (33,2)	2,07 [1,06–4,04]	0,032
Self-referral	9 (19,6)	235 (20,0)	1,40 [0,60–3,26]	0,554

Variable	Start of «RR-therapy», n (%)		OR [95% CI]	P value
	No	Yes		
Method for detecting MDR/RR-TB				
mWRD / Xpert	36 (78,3)	910 (77,4)	1,05 [0,51–2,14]	
Other methods*	10 (21,7)	266 (22,6)	1 (реф.)	>0,999
Year of the TB case report				
2021	18 (39,2)	425 (36,1)	1,20 [0,58–2,44]	0,747
2022	14 (30,4)	354 (30,1)	1,12 [0,52–2,38]	0,913
2023	14 (30,4)	397 (33,8)	1 (реф.)	
Type of TB case				
New case	31 (67,4)	774 (65,8)	1,07 [0,57–2,01]	0,962
Relapse	15 (32,6)	402 (34,2)	1 (реф.)	

Other methods – includes all laboratory tests used to confirm TB and determine drug susceptibility, except for the mWRD/Xpert test.

Analysis of clinical **characteristics shows** that two factors – problematic alcohol use and HIV-positive status – are associated with a statistically significant increase in the likelihood of not initiating treatment for MDR/RR-TB. The proportion of patients with problematic alcohol use among those who failed to initiate treatment is more than double that among those who did begin treatment (23.9% vs 12.8%), as confirmed by an elevated odds ratio (OR = 2.15; p = 0.043). HIV infection is also associated with a significantly higher risk of not initiating treatment (30.4% vs 15.1%; OR = 2.43; p = 0.016). The results obtained indicate presence of significant vulnerabilities among these groups and underscore the need to strengthen intersectoral collaboration – including coordination between TB and HIV services – as well as to implement interventions aimed at improving treatment adherence among patients with harmful habits **(Table 5).**

At the same time, diabetes, mental disorders, and drug use do not show a statistically significant association with the likelihood of initiating treatment for MDR/RR-TB. The prevalence of these conditions among patients who failed to initiate treatment is comparable to their prevalence among those who initiated treatment, and the odds ratios do not reach statistical significance (p>0.05). These results indicate that the clinical conditions in question do not as such pose significant barriers to initiating treatment for MDR/RR-TB in the sample analyzed **(Table 5).**

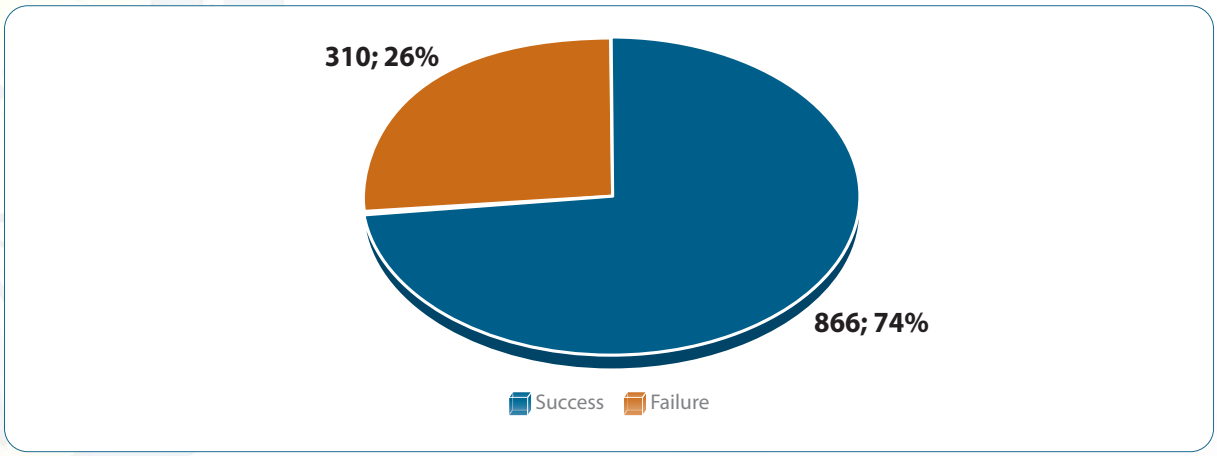
Table. 5. **Clinical factors associated with case reporting as MDR/RR-TB**

Variable	Start of «RR-therapy», n (%)		OR [95% CI]	P value
	No	Yes		
Total	**46**	**1176**		
Problem alcohol use				
Yes	11 (23,9)	150 (12,8)	2.15 [1.06–4.32]	**0,043**
No	35 (76,1)	1026 (87,2)	1 (реф.)	
Diabetes				
Yes	0 (0,0)	54 (4,6)	-	
No	46 (100,0)	1122 (95,4)	-	
Mental illnesses				
Yes	1 (2,2)	34 (2,9)	0.74 [0.099–5.57]	>0,999
No	45 (97,8)	1142 (97,1)	1 (реф.)	
Drug use				
Yes	1 (2,2)	19 (1,6)	1.35 [0.17–10.33]	>0,999
No	45 (97,8)	1157 (98,4)	1 (реф.)	
HIV				
Positive	14 (30,4)	178 (15,1)	2.43 [1.27–4.64]	**0,016**
Negative	32 (69,6)	998 (84,9)	1 (реф.)	

Step 3. Outcomes of MDR/RR-TB treatment

Among the 1,176 patients who began treatment for MDR/RR-TB, 866 patients (73.6%) achieved a successful treatment outcome, while treatment was unsuccessful in 310 patients (26.4%) due to treatment discontinuation, death, or other adverse outcomes **(Chart 7).**

Chart 7. **Treatment outcomes among people who started MDR/RR-TB treatment**



Analysis of factors associated with outcomes of MDR/RR-TB treatment

The study's results show that analysis of **socio-demographic characteristics** helped identify factors influencing the likelihood of an adverse outcome of MDR/RR-TB therapy. Gender is a significant determinant: men have approximately 1.4 times higher chances of failing treatment compared to women (OR = 1.43; p = 0.037). A significant factor is also being in the group of patients with "other sources of income" – their probability of an unfavorable outcome is approximately 1.6 times higher than among employed patients (OR = 1.59; p = 0.002). Thus, the results highlight vulnerability of socially and economically unstable groups of population and the need for strengthening targeted measures of social support aimed at reducing the financial burden during the course of treatment and increased resistance to treatment **(Table 6).**

At the same time, most of the sociodemographic characteristics examined do not show a statistically significant effect on the final treatment outcome. Age, type of settlement, geographic area of residence, sector (civil or penitentiary), history of migration and previous incarceration (all p>0.05) do not have a significant effect on the probability of successful completion of therapy. The proportions of successful and unsuccessful outcomes in the respective subgroups are virtually identical, indicating equal access to MDR/RR-TB treatment and absence of systemic differences in treatment outcomes across these groups **(Table 6).**

Overall, results of the analysis show that the key socio-demographic risk factors of failure remain as follows: male gender and unstable sources of income, while the other studied characteristics do not have a statistically significant effect on the outcome of treatment, which highlights the need for targeted attention to socially vulnerable patients and development of additional measures to improve retention and adherence to therapy.

Table. 6. **Social-demographic factors associated with outcomes of MDR/RR-TB treatment**

Variable	Results «RR-therapy», n (%)		OR [95% CI]	P value
	Failure	Success		
Total	**310**	**866**		
Sex				
man	260 (83.9)	679 (78.4)	1.43 [1.02–2.02]	**0.037**
woman	50 (16.1)	187 (21.6)	1 (реф.)	
Age				
under 44 y.o.	162 (52.3)	454 (52.4)	0.99 [0.76–1.28]	>0.999
45 years and older	148 (47.7)	412 (47.6)	1 (реф.)	
Place of residence				
urban area	154 (49.7)	429 (49.5)	1.01 [0.77–1.30]	>0.999
rural area	156 (50.3)	437 (50.5)	1 (реф.)	
Geographic region				
right bank	226 (72.9)	654 (75.5)	0.87 [0.64–1.17]	0.363
left bank (eastern region)	84 (27.1)	212 (24.5)	1 (реф.)	
Sector				
Civil	302 (97.4)	831 (96.0)	1.59 [0.72–3.46]	
Penitentiary	8 (2.6)	35 (4.0)	1 (реф.)	**0.242**
History of migration	44 (14.2)	100 (11.5)	1.26 [0.86–1.85]	
Yes	266 (85.8)	766 (88.5)	1 (реф.)	0.226
No				
History of incarceration	60 (19.4)	132 (15.3)	1.33 [0.95–1.87]	
Yes	249 (80.6)	733 (84.7)	1 (реф.)	0.094
No				
Has income	75 (24.3)	287 (33.1)	1 (реф.)	
Yes / employed	210 (68.0)	504 (58.2)	1.59 [1.18–2.15]	**0.002**
Yes / other income	24 (7.8)	75 (8.7)	1.22 [0.724–2.07]	0.530

The study provided for a comprehensive assessment of the impact of **programmatic factors on treatment outcomes** and the likelihood of successful completion. The most significant factor is the source of the patient's referral to the TB and pulmonology service. It was found that patients referred by specialists are nearly twice as likely to experience an adverse treatment outcome vs patients referred by primary care physicians (41.9% vs 30.0%; OR = 1.96; p<0.001). A similar, though less pronounced trend is observed among patients who sought care at a TB and pulmonology clinic on their own: their likelihood of an adverse outcome is 1.4 times higher compared to the group referred by PHC providers (OR = 1.42; p = 0.009). The results obtained indicate that patients entering the system through alternative channels (medical specialists or self-referral) are likely to begin treatment at later stages of the disease, with more pronounced clinical symptoms or presence of additional risk factors, which negatively affects treatment outcomes for MDR/RR-TB. Thus, timely identification and referral of patients through primary health care remains a critically important element of the referral pathway ensuring more favorable treatment outcomes **(Table. 7).**

The "type of TB case" variable warrants special attention. Among patients with a relapse, the proportion of adverse outcomes is higher than among new cases (38.4% vs. 32.7%); however, the observed differences are on the borderline of statistical significance (OR = 1.28; p = 0.047). This suggests that a relapse may be a potential risk factor for an adverse outcome, requiring cautious interpretation and further confirmation in future studies, including consideration of the influence of concomitant clinical and social factors **(Table. 7).**

At the same time, most of the programmatic variables analyzed do not show a statistically significant effect on the probability of successful completion of treatment for MDR/RR-TB. In particular, the method used to detect MDR/RR-TB (mWRD/Xpert or other laboratory methods) is not associated with differences in treatment outcomes (OR = 0.88; p = 0.439), indicating that the diagnostic approaches used are comparably effective. Similarly, the year in which a case was reported (2021, 2022, or 2023) had no statistically significant effect on treatment outcomes (all p>0.05), indicating that the organization of the treatment process remained consistent across different periods **(Table 7).**

Overall, the findings of the analysis show that the key programmatic risk factor for an adverse outcome is the patient's pathway into the healthcare system. The "type of TB case" is also significant: a relapse is associated with an increased likelihood of treatment failure and can be considered a risk factor. The results obtained support the need to strengthen the role of PHC, standardize patient referral pathways, and ensure their early inclusion in structured care models. Implementing these measures could significantly increase the proportion of successful treatment outcomes for MDR/RR-TB.

Table. 7. **Programmatic factors associated with MDR/RR-TB treatment outcomes**

Variable	Results «RR-therapy», n (%)		OR [95% CI]	P value
	Failure	Success		
Total	**310**	**866**		
Referred to the TB unit for a consultation by				
Family doctor	112 (36,1)	439 (50,7)	1 (реф.)	
Medical specialist	130 (41,9)	260 (30,0)	1,96 [1,45–2,63]	**0,000**
Self-referral	68 (21,9)	167 (19,3)	1,42 [1,09–1,84]	**0,009**
Method for detecting MDR/RR-TB				
mWRD / Xpert	235 (75,8)	675 (77,9)	0,88 [0,65–1,20]	0,439
Other methods	75 (24,2)	191 (22,1)	1 (реф.)	
Year of the TB case report				
2021	122 (39,4)	303 (35,0)	1,21 [0,88–1,65]	0,224
2022	89 (28,7)	265 (30,6)	1,01 [0,72–1,40]	0,948
2023	99 (31,9)	298 (34,4)	1 (реф.)	
Type of TB case				
New case	191 (61,6)	583 (67,3)	1 (реф.)	
Relapse	119 (38,4)	283 (32,7)	1,28 [0,98–1,68]	**0,047**

Other methods – includes all laboratory tests used to confirm TB and determine drug susceptibility, except for the mWRD/Xpert test.

Assessment of clinical characteristics of patients identified two factors that significantly increase the risk of an adverse outcome of MDR/RR-TB treatment. Problematic drinking has the most significant impact: among these patients, the likelihood of treatment failure is approximately 2.4 times higher here than among patients with-out this characteristic (21.0% vs 9.8%; OR = 2.43; p<0.001). Similarly, the HIV-positive status also statistically significantly increases the risk of an adverse outcome – by approximately 1.8 times (21.0% vs 13.0%; OR = 1.76; p = 0.002). The findings highlight the need to strengthen support measures for these patient groups, including multidisciplinary care and more intensive monitoring throughout the course of treatment **(Table 8).**

The other clinical determinants examined did not show a statistically significant effect on the likelihood of successful completion of therapy. In particular, the presence of diabetes, mental illness, and drug use was not associated with an increased likeli-hood of an adverse outcome (all p>0.05). The proportions of successful and unsuccessful outcomes

in the respective subgroups remain comparable, which may indicate the consistency of clinical management for these patient categories **(Table 8).**

Taken together, the results show that, among clinical factors, problematic alcohol use and HIV infection are the key determinants of the risk of an adverse outcome. This underscores the need to prioritize comprehensive support for patients with problematic alcohol use and HIV coinfection, including intersectoral collaboration, early detection and intervention, and targeted measures to improve treatment adherence.

Table. 8. **Clinical factors associated with MDR/RR-TB treatment outcomes**

Variable	Results «RR-therapy», n (%)		OR [95% CI]	P value
	Failure	Success		
Total	**310**	**866**		
Problem alcohol use				
Yes	65 (21,0)	85 (9,8)	2,43 [1,71–3,47]	**0,000**
No	245 (79,0)	781 (90,2)	1 (реф.)	
Diabetes				
Yes	18 (5,8)	36 (4,2)	1,42 [0,79–2,54]	
No	292 (94,2)	830 (95,8)	1 (реф.)	0,242
Mental illnesses				
Yes	11 (3,5)	23 (2,7)	1,34 [0,64–2,79]	0,531
No	299 (96,5)	843 (97,3)	1 (реф.)	
Drug use				
Yes	6 (1,9)	13 (98,5)	1,29 [0,48–3,43]	0,768
No	304 (98,1)	853 (98,5)	1 (реф.)	
HIV				
Positive	65 (21,0)	113 (13,0)	1,76 [1,26–2,47]	**0,002**
Negative	245 (79,0)	753 (87,0)	1 (реф.)	

The profile of determinants influencing the probability of a failure of MDR/RR-TB treatment

This subsection presents a comprehensive profile of the factors influencing the likelihood of treatment failure in MDR/RR-TB, based on an indepth analysis of data from an additional sample of 295 patients with MDR/RR-TB who met the established inclusion criteria.

The analysis showed that men were in the majority, accounting for about four-fifths of the entire cohort (80.7%). The percentage of women is significantly lower – 19.3%. This ratio reflects the overall epidemiological situation regarding MDR/RR-TB in the country, where the disease is more commonly diagnosed among men, and underscores the need to develop gender-sensitive approaches that take into account differences in the healthcare-seeking behavior and adherence to treatment **(Table 9)**.

The distribution of patients by age is relatively balanced: 52.2% are under 45 years of age, while 47.8% are 45 years of age or older. The mean age of the patients was 44.68 years, and the median was 43 years, indicating a distribution close to symmetric. The standard deviation (11.62 years) indicates moderate variability, which is typical of an adult population. The participants' age ranged from 18 to 81, reflecting the wide age range of patients undergoing treatment for MDR/RR-TB. The data obtained confirm that MDR/RR-TB affects both younger and older age groups equally, which requires adapting patient care approaches to take agerelated characteristics into account **(Table. 9).**

In terms of the place of residence, the subcohort is also characterized by relative uniformity: 48.1% of patients live in urban areas, while 51.9% live in rural areas. This distribution confirms that issues regarding access to diagnosis and treatment of MDR/RR-TB remain relevant for the both population groups. The geographic distribution of patients highlights predominance of right-bank areas: 74.6% of the participants live on the right bank of the Dniester, while 25.4% live in the eastern region. This ratio corresponds to the overall pattern of MDR/RR-TB incidence **(Table. 9).**

Table. 9. **Key characteristics of the sub-cohort**

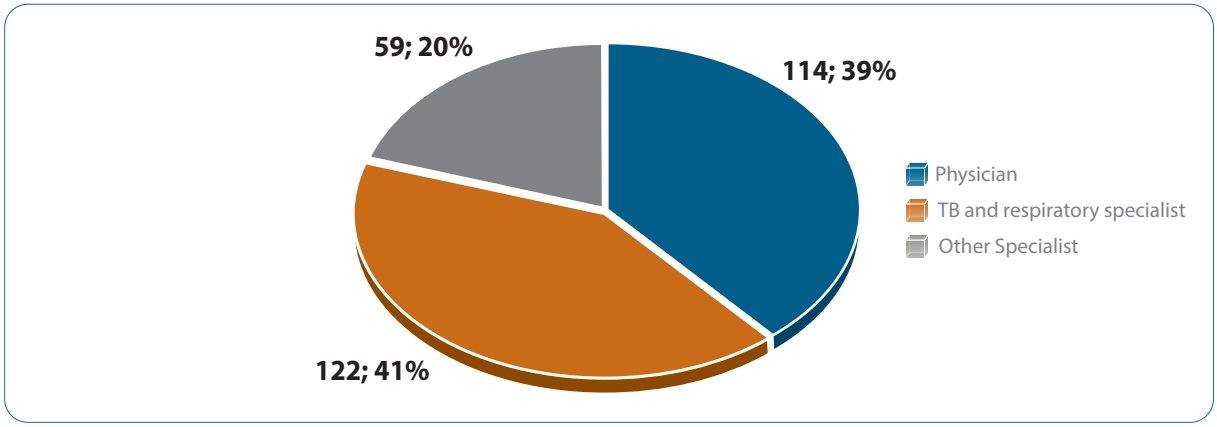
Variable	n (%)
Total	**295**
Sex	
man	238 (80,7)
woman	57 (19,3)
Age	
under 44 y.o.	154 (52,2)
45 years and older	141 (47,8)
Place of residence	
urban area	142 (48,1)
rural area	153 (51,9)
Geographic region	
right bank	220 (74,6)
left bank (eastern region)	75 (25,4)

The distribution of initial visits for TB symptoms indicates existence of two "entry points" into the system that are comparable in scale: 41.4% of patients first sought care directly from a pulmonologist specializing in TB, while 38.6% saw a family doctor; another 20.0% were seen by other specialists. Thus, patients use both specialized services and primary care to roughly the same extent, while onefifth follow "scattered" pathways beyond these two main channels **(Chart 8)**.

The near parity between PHC and the TB and pulmonology service can be viewed as an indicator of accessibility of specialized care and, at the same time, as confirmation of the significant role of family doctors in early detection of TB. Given the previously reported minimal delay before screening (median = 0 days) and the high proportion of prompt referrals, this distribution of initial contacts generally does not hinder rapid initiation of the diagnostic process. At the same time, the presence of the group of "other specialists" (20.0%) potentially increases the risk of fragmentation in the patient's care pathway and of missing the "window of opportunity" for timely testing.

From the programmatic perspective, these data support the need to strengthen the standardized "TB trigger" at all points of first contact, not just in PHC and the TB and pulmonology services. For family doctors, it is advisable to maintain and expand existing algorithms for managing patients with suspected TB, including immediate referral for mWRD/Xpert testing and/or chest X-rays where symptoms are present, as well as clear coordination of the patient's subsequent pathway. It is important for the TB and pulmonary service to maintain the practice of conducting examinations on the day of the patient's visit and to provide prompt feedback to PHC facilities in order to close the information loop and coordinate the patient's further care. For "other specialists," it is necessary to implement standardized, concise TB vigilance checklists (cough, fever, weight loss, etc.) that require immediate referral for screening and referral to the TB and pulmonology service. This will help reduce the proportion of late referrals and shorten the "long tail" of diagnostic delays.

Chart 8. **Initial medical contact regarding TB symptoms, sub-cohorts**



Analysis of time intervals in the diagnostic pathway for patients with MDR/RR-TB reveals significant variability in the duration of individual stages and indicates that the stages contribute unevenly to the overall delay before the start of MDR/RR-TB treatment **(Chart 9)**.

Stage 1 – from the initial visit to the doctor to Tb-screening-screening – is characterized by a relatively short duration: the median is 0 days, the average duration is 3.29 days. Thus, the high standard deviation (12.96) and the maximum of 144 days indicate the presence of a small group ofpatients with extremely long intervals between the stages. For most patients access to primary screening is provided promptly.

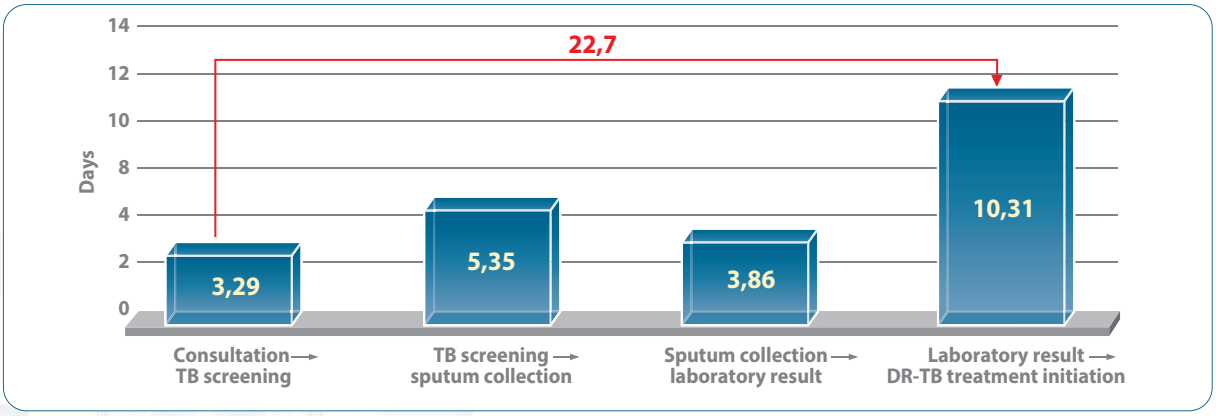
Stage 2 – from TB-screening to collection of sputum – shows an increase in the average time to 5.35 days with the median of 1 day, and reflects more pronounced organizational differences and possible delays related to logistics for collection of the biological sample, working hours of laboratory services, or availability of transportation for samples.

Stage 3 – from sputum collection to receiving the lab results – remains relatively short (average duration: 3.86 days; median: 0 days), which indicates high efficiency of laboratory processes. At the same time, the range of values up to 55 days indicates presence of rare but clinically significant delays at this stage.

Stage 4 – the period from receiving the laboratory results to the start of treatment for MDR/RR-TB – is the longest. The average duration is 10.31 days, and the median is 5 days. This stage represents the longest segment of the diagnostic pathway, as evidenced by the high variability of the indicators, including the maximum value of 129 days and the highest variance among all the stages (268.6). The data obtained underscore the need to optimize coordination between diagnostic services, clinicians, and patients, as well as to streamline the administrative procedures that precede the start of treatment.

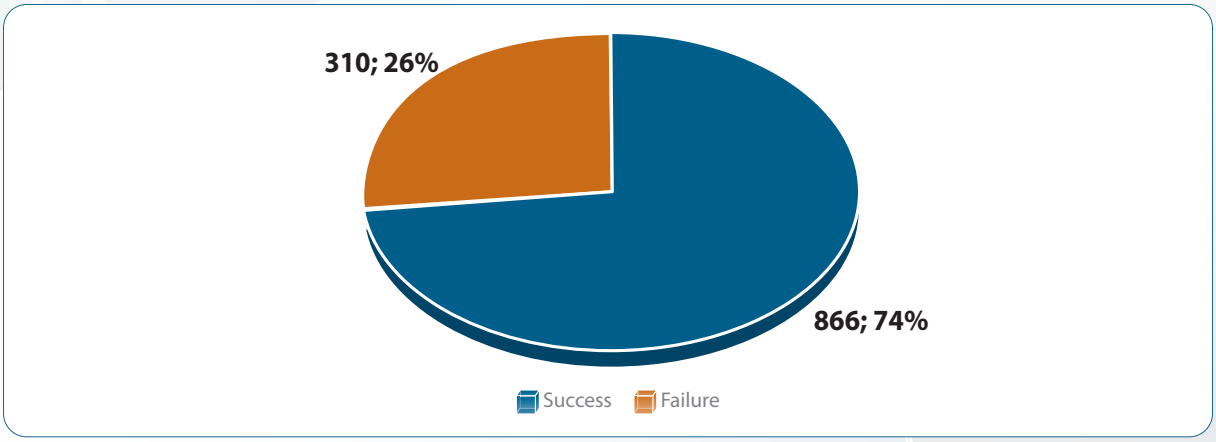
The total interval from the first visit to seek medical care to the start of MDR/RR-TB treatment averages 22.70 days (median: 12 days). Thus, the total duration of the patient's care pathway is not due to uniform accumulation of minor delays between stages, but rather results from a combination of predominantly short intervals with one or two critical "bottlenecks," the most significant of which is the stage between diagnosis confirmation and the start of treatment **(Chart 9)**.

Chart 9. **Average duration of key stages in the diagnostic pathway prior to the start of MDR/RR-TB treatment**



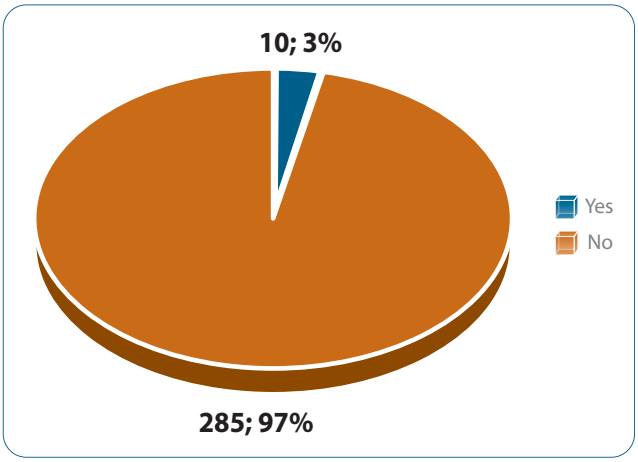
The distribution of treatment regimens in the analyzed cohort shows a predominance of long-term treatment regimens (68.8%; 203) **(Chart 10)**. In the clinical and organizational context, this may reflect both clinical and microbiological selection criteria (drug resistance profile, tolerability, comorbidities) and organizational factors (availability of medications, experience of multidisciplinary teams, referral standards). Given the high rates of timely access to screening demonstrated earlier and the significant role of PHC in organizing the patient pathway, the current ratio of regiments can be viewed as reflecting a balance between clinical safety requirements and programmatic feasibility. At the same time, about onethird of patients receiving short-course therapies constitute an important subgroup for targeted monitoring. A comparative assessment of adherence, the frequency of adverse events, and outcomes in this group will help determine under what conditions short treatment regimens are most effective, as well as which factors (selection criteria, community-based care, and PHC support) increase the likelihood of successful completion of therapy.

Chart 10. **Treatment regimens**



Analysis of patient distribution based on whether outpatient treatment began on the first day of therapy shows that this practice is used extremely rarely. Only 10 patients (3.4%) began treatment on the outpatient basis from the first day, while the vast majority of patients (96.6%; 285) began treatment in a hospital and were subsequently transferred to outpatient care **(Chart 11)**. This distribution indicates that the model of initiating treatment on an outpatient basis – recommended in international practice as a means of speeding up the start of therapy and reducing the burden on hospitals – is used only to a limited extent.

Chart 11. **The proportion of patients who began outpatient treatment on the first day**

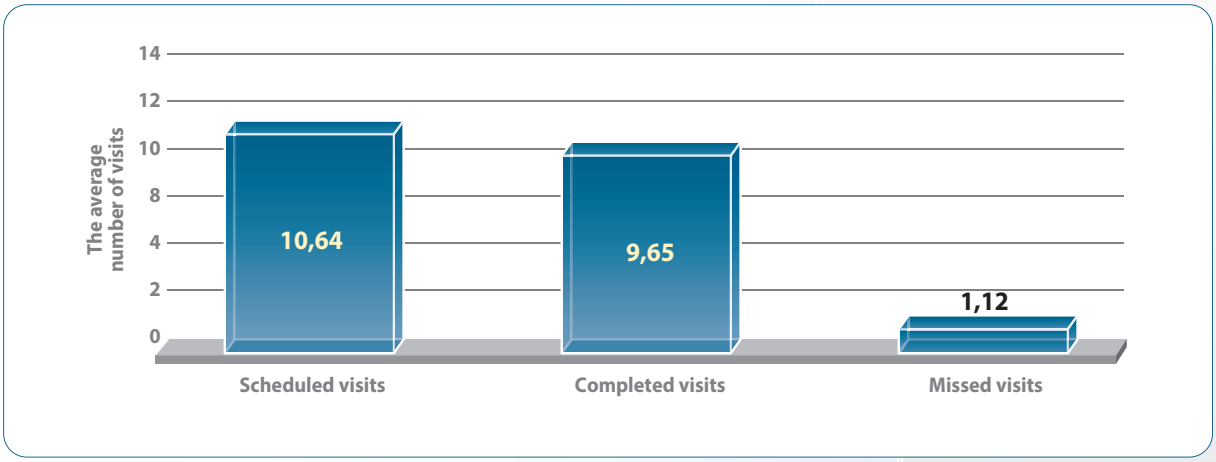


Analysis of data reflecting completion of scheduled visits to a TB doctor during treatment of MDR/RR-TB reveals certain discrepancies between the planned and actual number of visits. With an average of 10.64 scheduled visits, the median is 10, indicating a relatively stable recommended follow-up schedule. In fact, an average of 9.65 visits were made (median: 9), meaning that most visits took place, although the number was slightly lower than planned **(Chart 12).**

The number of missed visits remains relatively low: the mean is 1.12, and the median is 0. At the same time, the wide range of values (from 0 to 18) indicates presence of a small but clinically significant group of patients with marked irregularities in their attendance. This may reflect a combination of factors, including social vulnerability, unstable employment, low adherence to treatment, mobility barriers, and possible organizational constraints on outpatient care **(Chart 12).**

Overall, the data indicate that the system ensures a relatively high rate of completion of scheduled visits. At the same time, there remains a group of patients with significant gaps in their treatment, which could potentially have a negative impact on treatment outcomes and requires additional monitoring and targeted support measures.

Chart 12. **Comparison of the number of scheduled, completed, and missed visits to a TB doctor**



The additional analysis of the sub-cohort of patients revealed a number of clinical and organizational factors that contribute to the likelihood of successful completion of treatment for MDR/RR-TB. Although most of the variables studied do not show a statistically significant association with treatment outcomes, certain factors have been identified that require increased attention from the National Tuberculosis Control Program **(Table 10).**

First and foremost, attention should be paid to the category of healthcare professional who the patient first consulted regarding TB symptoms. Although the differences between consulting a family doctor and a pulmonologist are not statistically significant, consulting "another specialist" is associated with a trend toward an almost

twofold increase in the odds of an adverse outcome (OR = 2.02; p = 0.057). This finding may indicate possible fragmentation of the patient's care pathway and longer intervals before symptoms are recognized and specific examination begins **(Table 10).**

Indicators reflecting the duration of individual stages of the diagnostic pathway – from the initial visit through screening, sputum collection, and receipt of laboratory results – did not show a statistically significant association with treatment outcomes. The data obtained are consistent with findings in the previous sections of the analysis and indicate that, when considered in isolation, time intervals are not independent determinants of treatment success.

The borderline trend observed for the total time from the first visit to the start of MDR/RR-TB treatment (OR = 0.50; p = 0.065) may reflect the influence of clinical severity: it is possible that patients with more severe symptoms begin treatment sooner but have less favorable outcomes. This underscores the need for careful interpretation of temporal metrics and the importance of a multifactorial analysis that takes into account the patient's clinical condition and comorbidities **(Table 10).**

Table. 10. **Additional analysis of determinants associated with outcomes of MDR/RR treatment**

Variable	Results «RR-therapy», n (%)		OR [95% CI]	P value
	Failure	Success		
Total	**71**	**224**		
Category of healthcare professional at the initial visit for TB symptoms				
General practitioner (Family doctor)	23 (32,4)	91 (40,6)	1 (реф.)	
Pulmonologist specializing in TB	28 (39,4)	94 (42,0)	1,17 [0,63–2,19]	0,720
Another specialist	20 (28,2)	39 (17,4)	2,02 [1,00–4,11]	**0,057**
Average duration (in days) from the initial visit to TB screening				
≤ 3.29 days	62 (87,3)	197 (87,9)	1 (реф.)	
> 3.29 days	9 (12,7)	27 (12,1)	1,05 [0,47–2,37]	0,871
Average duration (in days) from TB screening to sputum collection				
≤ 5.35 days	53 (74,6)	159 (71,0)	1 (реф.)	
> 5.35 days	18 (25,4)	65 (29,0)	0,83 [0,45–1,52]	0,661
Average time from sputum collection to receipt of laboratory results				
≤ 3.86 days	60 (84,5)	190 (84,4)	1 (реф.)	
> 3.86 days	11 (15,5)	34 (15,2)	1,02 [0,48–2,14]	1,000
Average time from receipt of laboratory results to the start of MDR/RR-TB treatment				
≤ 10.31 days	56 (78,9)	167 (74,6)	1 (реф.)	
> 10.31 days	15 (21,1)	57 (25,4)	0,78 [0,41–1,49]	0,568
Total interval (in days) from the initial visit to the start of MDR/RR-TB therapy				
≤ 22.70 days	59 (83,1)	160 (71,4)	1 (реф.)	
> 22.70 days	12 (16,9)	64 (28,6)	0,50 [0,25–1,01]	0,065
Treatment regimen				
long	56 (78,9)	147 (65,6)	1,95 [1,03–3,68]	
short	15 (21,1)	77 (34,4)	1 (реф.)	**0,043**
Outpatient treatment starting on the first day of therapy				
Yes	4 (5,6)	6 (2,7)	1 (реф.)	
No	67 (94,4)	218 (97,3)	0,46 [0,12–1,68]	0,399
Missed appointments with a TB doctor				
No	51 (71,8)	187 (83,5)	1 (реф.)	
Yes	20 (28,2)	37 (16,5)	1,98 [1,06–3,70]	**0,046**

The factor related to the treatment regimen had a statistically significant effect on treatment outcomes. Patients who received long treatment regimens had a higher risk of an adverse outcome compared with patients on short regimens (OR = 1.95; p = 0.043). This association does not necessarily reflect negative characteristics of long regimens per se, but may rather indicate selection effects: patients with more complex drug resistance profiles, comorbidities, and/or significant social risk factors are typically placed on long regimens. In this regard, strengthening clinical support and measures to maintain patient adherence to long treatment regimens is of particular importance **(Table 10)**.

Another important aspect is the format in which therapy begins. Although the initiation of outpatient treatment on the first day was observed in an extremely small number of patients in the sample and did not show a statistically significant association with treatment outcomes (p = 0.399), its low uptake points to persistent organizational constraints, including insufficient readiness of PHC facilities, logistical delays, and the lack of a standardized model for early initiation of therapy **(Table 10).**

> Missed appointments with a TB doctor remain the most significant modifiable factor. The presence of even a single missed visit nearly doubles the risk of an adverse outcome (OR = 1.98; p = 0.046), underscoring the critical importance of continuous follow-up during treatment **(Table 10).**

Overall, results of the additional analysis suggest that the key determinants of treatment success are not so much time delays or individual clinical and demographic characteristics as the quality of referral and continuity of patient care. Special attention should be given to patient groups showing signs of adverse progression, including those first seeking care from non-specialist physicians, patients on long treatment regimens, and patients who miss scheduled appointments. Strengthening interdisciplinary collaboration, standardizing early detection algorithms, and implementing adherence support programs at the PHC and CSO levels can help improve sustainability of treatment outcomes in these groups and reduce the proportion of adverse outcomes across the cascade of care.

Focus groups with primary care providers and representatives of civil society organizations

The qualitative component of the study involved conducting focus group discussions with primary health care workers and representatives of civil society organizations directly involved in supporting patients with MDR/RR-TB at the community level. This phase was designed to conduct an indepth study into the practical experience of the specialists, their professional observations, their perceptions of the system's barriers and resources, as well as the mechanisms that either facilitate or, conversely, hinder patient retention in treatment. The interviews made it possible to identify key elements of interaction between the health care system and community organizations, assess coordination of service delivery, and understand how organizational, social, and motivational factors influence effectiveness of patient support programs.

The participant profile in the focus group comprising PHC workers and CSO representatives

The profile of participants in the qualitative component provides a comprehensive picture of perspectives on MDR/RR-TB care at the community level. Of the 32 respondents,

the majority were PHC workers – 21 people (65.6%) – while 11 people (34.4%) represented CSOs, which allows for a combination of the primary care level clinical perspective with the experience of community support services. Geographically, the sample covers all the three regions of the country: Central region – 14 participants (43.8%), Northern region – 12 (37.5%), Southern region – 6 (18.8%); in terms of the setting, urban practice predominates, with 22 participants (68.8%), while 10 (31.3%) work in rural areas. The gender age structure corresponds to the current staffing profile of the PHC system: among those surveyed, there were 27 women (84.4%) and 5 men (15.6%), and the "core" of the sample consists of professionals aged 45–59 – 19 people (59.4%); while the 25–44 age group – 5 people (15.6%) – and the 60 and older age group – 8 people (25.0%) – provide for additional diversity in terms of experience. Taken as a whole, the respondent group provides a reliable basis for interpreting clinical and programmatic aspects of the service cascade.

Most participants have documented clinical experience working with patients with MDR/RR-TB: 65.6% (21) reported having at least one year of experience providing medical services, while 34.4% (11) do not have such experience. In contrast, the situation is opposite when it comes to supportive (non-medical) services: only 11 participants (34.4%) have ≥1 year of experience, while 21 participants (65.6%) have not accumulated such a profile

Analysis of Focus Group Discussions

Training on managing MDR/RR-TB cases. Discussions in the focus groups revealed a high level of training coverage in managing MDR/RR-TB cases: of the 32 participants, 30 (93.8%) reported having received relevant training, and only 2 (6.3%) had no such experience. At the same time, the range of training formats proved to be diverse, reflecting both institutional practices and individual professional development paths. The most frequently mentioned formats were inperson sessions – seminars, workshops, and lectures – which underscores the importance of practice oriented activities and exchange of experiences within the group. Participants also highlighted online modules (including webinars and courses), which points to sustained adoption of remote formats and their role in ensuring timely access to updated clinical guide-lines. Mentions of continuing professional education (professional development courses) were a separate theme, as were institutional training providers (such as professional associations and specialized institutions), which were mentioned only sporadically.

> During the discussions, participants noted that, despite having completed training courses and regularly updating their knowledge, there are still areas in which they do not always feel confident. First and foremost, the discussion focused on managing adverse drug reactions: experts described the challenges of early detection of toxicity, selecting strategies for adjusting treatment regimens, and communicating the risks and expected effects of treatment in a way that patients can understand it.

Another recurring theme relates to mental health. Participants discussed the challenges of assessing patients' emotional states, recognizing anxiety and depression, managing crisis situations, and maintaining motivation during long treatment regimens. Particular emphasis was placed on the need for clearer protocols for collaborating with psychologists and social workers, as well as practical tools for day-to-day work – such as short questionnaires, conversation scripts, and referral procedures.

Other topics were occasionally raised as well: managing clinically complex cases, working with socially vulnerable groups, and issues requiring sensitivity to gender-specific considerations. In these situations, professionals often rely on personal experience and

informal support from colleagues, which underscores the need for standardized guidelines and coordinated protocols. At the same time, some participants found it difficult to specify the areas where they lacked competencies, which can be interpreted as an indication of an implicit request for a "diagnostics" of their own educational needs through supervision and case discussions.

> Overall, the discussions showed that strengthening practice oriented modules on managing adverse reactions and mental health, implementing brief screening tools and clear referral pathways, as well as conducting regular intersectoral case reviews involving PHC providers, TB specialists, psychologists, and CSOs can significantly boost professionals' confidence and improve the quality of patient care throughout the entire course of treatment.

Professional training and competency development. During the discussions, participants emphasized that regularly updating their knowledge and receiving professional mentorship have become an integral part of managing MDR-TB/RR-TB cases. Most respondents cited regular professional development formats: inperson seminars and training sessions involving analysis of clinical cases, lecture series, and hands-on workshops focused on application of updated protocols and on coordinating decisions within a multidisciplinary team. The role of online training was high-lighted – webinars, distance learning courses, and modular programs made it possible to quickly master new developments and revisit the material as needed, which is especially convenient for teams with heavy workloads and geographically dispersed members.

Participants cited "horizontal" and "vertical" mentorship as important resources. On the one hand, this involved support from experienced colleagues in the workplace – joint rounds, discussions of complex cases, and prompt consultations in cases of drug intolerance or suspected drug interactions. On the other hand – expert support from specialists in the national TB program, relevant institutions, and professional associations: such sessions helped standardize approaches across different levels of care, refine protocols for selecting short and long treatment regimens, and strengthen collaboration with laboratory services and PHC.

Participants also found targeted updates on key topics to be useful: implementation of changes to clinical protocols, toxicity monitoring algorithms, criteria for progression between treatment phases, as well as organizational guidelines on referral and communication among services. At the same time, the value of a mixed format was emphasized – one where theoretical sessions are supplemented by supervision, case conferences, and "quick" consultations on specific patients. According to participants, this approach increases confidence in decisionmaking, improves coordination within the team, and helps retain patients in treatment throughout the entire continuum of care.

Tools and resources for everyday practice. During the discussions, participants noted that in their work they rely primarily on national clinical protocols, regulatory documents, and practice guidelines, which serve as the basis for decisionmaking and ensure a consistent approach within the team. Moreover, training activities – such as seminars, webinars, courses, and regular updates – provided by the national program, professional platforms, and specialized institutions remain an important source of support. Many also mentioned the support they received from colleagues: consultations with more experienced specialists, joint discussions of complex cases, and on-the-job mentoring allow them to quickly resolve issues as they arise and boost their confidence in their work.

There were also mentions of organizational resources – a stable supply of medications, the opportunity to quickly get advice by phone, and access informational materials and presentations. In some cases, participants emphasized the role of donor programs and platforms that provide methodological and informational support. At the same time, several respondents noted a lack of structured support, which underscores the need to further strengthen systems for collaboration and support.

Challenges in providing services. During the discussions, participants described a range of challenges they face when working with patients with MDR/RR-TB. At the clinical level, confirming the diagnosis is challenging for individuals with inconsistent engagement with the healthcare system and multiple social risk factors; situations were also mentioned where a prompt reassessment of treatment strategies is required due to comorbidities and unpredictable clinical episodes.

> During treatment, adherence remains a key challenge: professionals face patients who refuse treatment, distrust medical recommendations, and resist care services offered. In a number of cases, the limited "leverage" over patients with high levels of stigma, substance use disorders, or difficult life circumstances – ranging from poverty and unstable employment to a lack of family support – was highlighted.

Organizational barriers include staff overload and time constraints, staff shortages, bureaucratic procedures, and infrastructure deficiencies, such as cramped facilities and inconsistent communication among levels of care. Gaps in cross-sectoral coordination were specifically noted: wariness on the part of some primary care physicians or local administrations, difficulties with patient referral, and feedback between services that was not always timely. Some teams face financial constraints – ranging from occasional disruptions in supply of resources to a lack of rapid and sustainable support mechanisms to meet patients' social needs.

At the same time, there were also positive observations: a number of experts report no significant difficulties and emphasize that any issues that arise are success-fully resolved through team coordination and well-established working channels. Overall, participants agree that the most effective measures are practical ones that are "close to the patient": simple and quick referral pathways, reduction of excessive bureaucracy, regular communication among services, as well as targeted social support and psychological counseling integrated into daily practice.

Stigma and rejection: experiences and response strategies. During the discussions, it was noted that some participants had experienced stigma and rejection, both from individual healthcare professionals, and at the community level. These episodes most often manifested in subtle ways – through wariness, distancing, or doubts about appropriateness of services provided. In response, the participants described a set of practical strategies: calmly and systematically explaining the nature of the disease and goals of the interventions; brief informational discussions and reasoned debates within teams; mediating conflicts; and appealing to professional standards. When necessary, administrative and local authorities were brought in to support the process and strengthen commitment; in situations that did not require immediate action, experts preferred not to escalate tensions and instead allowed time and facts to "take their course." At the same time, many emphasized that systematic, respectful communication, a reserved tone, and coordination within a multidisciplinary team make it possible to gradually reduce bias and foster more constructive interactions with patients and those around.

Systematic and coordination issues, as well as managing inadequate commitment. During the discussions, participants noted that, at the system level, glitches occur periodically that can complicate patient care: delays in receiving lab results, limited access to certain types of diagnostic tests, gaps in information flow among services, as well as instances of excessive hospitalization – all within the context of a hospital funding mechanism in which the number of beds determines the facility's annual budget, even when there are sound grounds for effectively organizing outpatient care from the moment the diagnosis is confirmed. Organizational bottlenecks further complicate the picture – including a lack of coordination among organizational levels, varying degrees of involvement by local authorities, and a shortage of resources, which makes it difficult to plan support activities. At the same time, some experts emphasized that in a number of contexts, the processes operate smoothly, and any difficulties that arise are localized and can be managed at the team level.

During the discussion of situations involving inadequate adherence and "loss to follow-up," the focus was on personalized and cross-sectoral approaches. In most cases, the specialists began by establishing direct contact with the patient and their family and providing them with information, reinforcing their motivation and agreeing on a realistic schedule of visits. As needed, colleagues from primary care, social services, and local government were brought in; in cases of significant social risk, law enforcement agencies were involved, solely to ensure safety of the route and connection with the system. The role of psychological counseling and mediation in conflict situations was specifically emphasized. In a number of cases, the impact of collaboration with external partners was limited, which participants attributed to the lack of uniform regulations and clear "entry points"; a possible solution proposed was to formalize fasttrack communication channels and establish schedules for "fast-track windows" to resume treatment without bureaucratic delays.

> Overall, the discussions converged on the view that the greatest impact is achieved when clinical interventions are complemented with predictable coordination across services and targeted social support, and when communication with the patient remains consistent, respectful, and focused on informed consent and shared decisionmaking.

Focus groups with patients with MDR/RR-TB

Perception of the diagnosis of MDR/RR-TB

Patients describe receiving the diagnosis of MDR/RR-TB as an experience marked by shock, fear, and confusion, which is exacerbated by a lack of information about drug-resistant forms of the disease. *"At first, I was completely shocked… I just couldn't pull myself together"* (M 34).

Some had never heard of drug-resistant TB before, while others viewed this diagnosis as a form of the disease "that cannot be treated." Strong emotional reactions – such as panic, fear of death, and anxiety – are common, and they are intensified by witnessing severe cases in the hospital and by associating the disease with high mortality rates. *"I was afraid I would die – I'd heard that many people die"* (W 34).

At the same time, misconceptions about the causes of the disease (colds, diet, stress, hygiene) persist, indicating significant gaps in knowledge about TB. *"I thought it was because of a cold, or because I wasn't eating on time… but the doctor explained to me that I need to follow his advice, or I might die young."*

Some patients reported not understanding the reasons for repeated X-ray examinations and expressed concern about the potential harm of frequent use of X-ray machines, which increased their anxiety and reduced their trust in medical prescriptions. *"Could you please explain me why so many X-rays are needed? They did it twice at the district level, and then again at the hospital when I was admitted. Is it really necessary to do that so often? Will this hurt me?"*

Despite initial negative reactions, some patients were able to adapt and accept the need for treatment due to explanations provided by the medical staff.

Patient interaction with medical staff

Patients generally describe their interactions with medical staff as positive, noting their professionalism and clear explanations, especially in the inpatient setting. Many say they did not encounter any problems and received the necessary information about their diagnosis and treatment, including the need for daily monitoring of their medication intake.

However, patients' experiences differed significantly between the hospital and their local community: while they felt safe and well cared for in the hospital, at home they faced gossip, mistrust, and a lack of understanding from their fellow villagers, which negatively affected their overall perception of their treatment. *"Everything is fine at the hospital. While in the village – nothing but talk and gossip"* (M 28). Despite the care provided by the medical staff, a prolonged hospital stay and isolation caused psychological distress and anxiety in some patients.

Patients also noted that the large number of pills and the strict treatment regimen were difficult at first, but due to the support and explanations from their doctors, they were able to adapt and adhere to their prescribed treatment. *"At first it was really hard – so many pills – but then I pulled myself together; there was no other way."*

Challenges in obtaining medications and receiving home care

Patients generally report that access to medications has been consistent, with medications dispensed daily and without interruption. Despite this, home care was virtually nonexistent: healthcare workers did not visit patients, which intensified their sense of isolation and mistrust from those around them. As one patient noted: *"There were no problems – they gave me my pills on time, but no one ever came to my home; everyone kept their distance"* (V 54).

Many patients note that their daily visits to the clinic went smoothly, and any brief interruptions were due to personal reasons rather than system malfunctions. This is well reflected in the patient's words: *"I went to the clinic every day – everything was fine, and there were rarely any interruptions"* (B 28).

One of the main challenges for patients was the large number of pills and the need to take them all at the same time. For some, the start of treatment proved to be particularly difficult and required time to adjust. Nevertheless, after a few days, many people managed to get used to it, as evidenced by the following remark: *"At first, I couldn't take all the pills at once, but after a week I got used to it – then they went down easier."*

The impact of the TB diagnosis on work capacity and the ability to support one's family

The diagnosis of TB significantly reduced the patients' ability to work, led to a marked loss of physical strength, and, as a result, to a loss of the income needed to support their families. Most participants note that weakness, shortness of breath, and severe symptoms prevented them from continuing their previous work. Some of the patients who used to work as day laborers in rural areas emphasize that their condition deteriorated to such an extent that they have completely lost the ability to perform even simple physical tasks. *"I worked on the day-pay basis in the village. I can't do it right now. I don't have the strength."*

For those who worked abroad, the disease had even more serious consequences – they were forced to return home, having lost their stable income. Significant weight loss and lack of energy were the key factors that made it impossible to continue working. *"I was in Italy. I couldn't work… I lost a lot of weight and had no strength."*

Some patients highlight the stark contrast between their former physical abilities and their current, significantly weakened condition, which profoundly affected their quality of life. *"I used to lift 100 kilograms and run up to the third floor… but now, just two buckets of water – and I'm already out of breath."*

Others describe severe symptoms – episodes of shortness of breath and severe cough – that forced them to stop working entirely and seek medical care. *"At first I couldn't breathe – I was coughing so hard I felt like I was going to throw up… they told me I needed to go to the hospital"* (W 34).

There are also patients who, upon returning to the country for treatment, began to notice an improvement in their condition; however, it remains uncertain whether they will regain their previous ability to work. *"I wasn't feeling well, so I came to Moldova for treatment. I'm feeling better now."*

Types of support received (financial, emotional, social)

Patients receiving outpatient care noted the importance and role of "food assistance cards," while pointing out that these are not sufficient to meet their families' needs: *"How can you get by having 53 lei a day – when you have a family... children..."* (M 34).

Patients noted that social support during treatment was limited and largely in-consistent. Many said that the situation was "difficult" and hard to describe, emphasizing lack of structured assistance from the system, while actual, meaningful support came mainly from family members or those closest to them. Some patients received some minimal financial assistance – money or food – from family members or acquaintances. This helped them cope with the difficulties arising from the loss of their ability to work and their reduced income. As one participant noted: *"Money, food… I want people to understand that I didn't mean to get sick – it just happened."*

Emotional support provided by the family played a key role in helping patients stay motivated to continue their treatment. Some participants said that, due to fatigue and the demanding treatment, they wanted to stop taking their medication, but it was their spouses or relatives who convinced them to continue. One patient described how her husband stood by her and supported her during the most difficult moments: *"I didn't want to go there, but he came with me… he encouraged me – I need to keep moving, I need to get treatment"* (W 34).

Overall, patients emphasized that their main source of support came almost exclusively from their families. The lack of organized support exacerbated the emotional and economic vulnerability of people with MDR/RR-TB.

The impact of stigmatization and, conversely, the support received for completing treatment and the ability to successfully complete it

Patients noted that stigmatization made their emotional distress much more difficult and affected their confidence in their ability to complete treatment. Many described experiences related to the feelings of guilt, fear of judgment, and the sense of being constantly under the judgmental gaze of those around them. One participant expressed this feeling succinctly: *"I felt guilty. Everyone was looking at me"* (M 31).

For some, the pressure of public opinion served as an additional incentive to continue treatment in order to avoid being ostracized by others. As one patient pointed out: *"If you don't get treatment, everyone will run away from you"* (M 35).

At the same time, not all of the patients' expectations regarding stigma were met. Some participants admitted that they had expected a negative reaction from their loved ones, but instead received support and acceptance. One of the patients noted: *"I thought they would keep their distance and look down on me. No – nothing like that happened"* (M 39).

However, in small communities, patients were more likely to encounter spread of rumors and increased attention to their condition. One participant said that even before he was hospitalized, there had already been talk in the village, with people asking why he was getting X-rays so often. *"When I left the hospital, it seemed to me that people were looking at me as if something wasn't quite right…"* (M 41).

Stigma also manifested itself in the form of actual avoidance. One participant said that after she was discharged, people around her were afraid to even be near her: *"I couldn't go into a store – everyone was afraid… I couldn't even ask anyone for a glass of water – everyone kept their distance"* (W 34). In other cases, interaction with neighbors continued, but only from a noticeable distance – "one or two meters ."

Overall, patients emphasize that stigmatization exacerbated their emotional and social vulnerability, which could undermine their confidence in the treatment process. At the same time, instances in which family and loved ones showed acceptance and support significantly contributed to maintaining motivation and successfully completing treatment.

Necessary interventions and forms of support

Patients emphasized that financial difficulties were one of the most serious problems they faced during treatment. Loans and debts exacerbated stress, and in some cases people were even unable to receive the food assistance they were entitled to because their bank accounts had been frozen (M 45). The payments provided were considered insufficient: "53 lei [1] a day isn't enough" (M 34).

Some participants also noted problems related to disability status: patients had to choose between working or retaining their disability status, which exacerbated their economic instability.

[1] $1 is approximately 17 lei.

In addition to financial support, patients expressed the need for psychological support and follow-up care after completing treatment due to fears of a relapse: *"I have concerns that the disease might return."* (M 39)

> All in all, patients find the following helpful: stable financial support (for food and to cover basic expenses); access to social assistance that is not contingent on debt; more flexible rules for assigning and maintaining disability status; and psychological support during and after treatment.

Discussion

This study presents the first comprehensive analysis of the determinants and barriers to provision of medical and social services within the care cascade for patients with MDR/RR-TB in the Republic of Moldova. The combination of quantitative and qualitative methods made it possible to assess the systemic, clinical, and social factors that influence detection, registration, initiation and completion of treatment.

The study's findings provide a **comprehensive assessment of the resilience of the cascade of care in the context of MDR/RR-TB,** identifying both the system's strengths and the structural limitations that lead to patient loss at various stages. The quantitative analysis demonstrated relatively high effectiveness of such stages of the treatment process as laboratory confirmation, registration, and initiation and completion of treatment. In turn, quality data made it possible to gain a deeper understanding of the mechanisms underlying patient loss during notification, retention, and successful completion of therapy stages. Combined interpretation of the results provides a comprehensive understanding of the key barriers that limit achievement of higher treatment success rates and highlights the critical role of social, psychological, and organizational factors that cannot be fully assessed using quantitative methods alone.

As part of the analysis of the results obtained, the cascade approach made it possible to assess sustainability of the care system for MDR/RR-TB and to identify the stages at which the greatest number of patients are lost to follow-up. The data obtained indicate that the system for providing care to patients with MDR/RR-TB in the Republic of Moldova is relatively stable in the early stages of the cascade – from laboratory confirmation of the diagnosis to the start of treatment. This pattern is generally consistent with international observations, according to which the key losses among MDR/RR-TB patients typically occur not at the diagnosis stage, but during the course of long treatment and its completion *(9, 12–14)*.

WHO estimates of the burden of MDR/RR-TB in the Republic of Moldova provide additional context for interpreting the cascade of care. According to WHO estimates, during the period 2021–2023, the projected number of MDR/RR-TB among bacteriologically confirmed TB cases (approximately 480–610 cases annually) exceeds the number of registered patients with pulmonary MDR/RR-TB (about 430–480 cases per year). These differences should be interpreted in light of the methodological differences between model-based estimates and data from routine registration reports. Given the consistently high coverage with drug susceptibility testing and the near-complete enrollment of identified patients in treatment, the persistent discrepancy between estimated and reported figures may indicate potential losses at the precascade stage, primarily at the level of case detection and referral of patients with suspected drug-resistant tuberculosis (15–17). At the same time, this discrepancy may reflect characteristics of data collection and reporting systems, including incomplete capture

of some clinically diagnosed cases, differences in definitions between model estimates and registry criteria, and time lags in data updates. Thus, the observed differences should be viewed as the combined effect of epidemiological and registration factors, requiring further analysis through integration of surveillance data and disease burden modeling.

> Analysis of the **first stage** of the healthcare delivery chain indicates that the diagnostic component is highly effective in detecting drugresistant TB. The proportion of laboratory-confirmed MDR/RR-TB cases among patients with suspected TB (96%) is comparable to the high rates described in the international literature for national TB programs with advanced systems for case selection and diagnostic quality control (18–19), and may indicate an effective system for referring patients to the indepth examination stage. The results obtained are consistent with the WHO's findings, according to which high coverage with molecular diagnostics (Xpert) and the presence of functioning mechanisms for clinical and laboratory verification reduce the likelihood of both missed cases of drug-resistant tuberculosis and of overdiagnosis *(20)*.

The reasons for the failure to confirm MDR/RR-TB in a small subgroup of suspected cases are primarily of a clinical and diagnostic nature and reflect functioning of mechanisms for additional verification of results *(21)*. The fact that medical consultation decisions to rule out active tuberculosis are based primarily on a comprehensive assessment of clinical and laboratory data indicates existence of a secondary clinical validation stage for primary screening results. Thus, the data obtained underscore the need to interpret molecular results within a broader clinical and diagnostic context, especially given the widespread use of rapid tests *(21–23)*.

The identified cases of retesting in which susceptibility to rifampicin was subsequently confirmed are consistent with scenarios described in the literature and associated with preanalytical and analytical factors *(21,24)*. The low proportion of documented errors and non-medical causes (including patient migration) indicates that the process is stable and that the patient's journey is sufficiently traceable at this stage. Overall, the diagnostic component of the cascade was highly reliable during the period under review, reducing the likelihood of patients being unjustifiably included in treatment for MDR/RR-TB *(23)*.

The sociodemographic profile of laboratory-confirmed TB cases is consistent with long-standing epidemiological trends characteristic of both the Republic of Moldova and other countries in the WHO Europe Region *(25, 26)*. The predominance of men of working age and the relatively even distribution of cases between urban and rural areas reflect both the cumulative risk of infection and recurrence, as well as comparable access to diagnostic services in different types of settlements *(25)*.

The prevalence of cases identified at the local level further underscores effectiveness of primary and district-level facilities in identifying suspected cases of MDR/RR-TB and their timely inclusion in the diagnostic algorithm *(8, 27)*. In the context of the cascade analysis, this may indicate a low rate of patient loss at this stage. Thus, the first stage of the cascade establishes a relatively stable foundation for subsequent stages of care and confirms that the key challenges to sustainability of the MDR/RR-TB cascade lie beyond laboratory diagnostics – in the areas of patient retention and successful completion of treatment.

> Results of analysis of the **second stage** of the MDR/RR-TB care pathway indicate high effectiveness and organizational readiness of the healthcare system to initiate treatment following laboratory confirmation of the diagnosis *(23)*. The proportion of patients who initiated treatment (over 95%) is comparable to or exceeds the figures reported in international reports for countries in the WHO Europe Region *(26)*, and

indicates that formal barriers at the treatment initiation stage have been largely mitigated *(25)*.

At the same time, the pattern of reasons why some patients were not included in MDR/RR-TB treatment points to a potential vulnerability in the treatment cascade – **late clinical detection.** The high rate of deaths prior to initiation of treatment may indicate that these deaths are due to the patients' severe condition at the time of diagnosis. Thus, despite high diagnostic coverage, some patients seek medical care only in late stages of the disease, which limits the possibility of starting treatment in a timely manner *(25)*.

Absence of a statistically significant effect of most sociodemographic characteristics (gender, age, type of residence, geographic region, migration history, and criminal history) on the likelihood of starting treatment may indicate relatively equal access to initiation of MDR/RR-TB therapy for various population groups *(28, 29)*.

At the same time, identification of an unstable source of income as a factor associated with an increased risk of failure to initiate treatment for MDR/RR-TB indicates existence of socioeconomic barriers that cannot be fully overcome with measures taken by the healthcare system alone. Financial instability and dependence on irregular income may limit patients' willingness to begin longterm treatment in a timely manner, given the additional indirect costs, temporary loss of earning capacity, and increased social vulnerability *(5, 30)*.

The identified determinants of vulnerability – such as problematic alcohol use and HIV-positive status – deserve special attention, as they are statistically significantly associated with an increased risk of failure to initiate MDR/RR-TB treatment. Such patterns have been repeatedly described in international studies and are considered key determinants of vulnerability of the cascade of care for MDR/RR-TB *(31–33)*.

Overall, analysis of results of the **second stage of the cascade** shows that dropouts on the path to the start of MDR/RR-TB treatment are largely associated with clinical severity of the condition and socioeconomic vulnerability of certain patient groups. In this regard, further reductions in mortality at this stage can be achieved primarily through earlier detection of cases, strengthening the role of primary health care, and expanding social support mechanisms for clinically and socially vulnerable population groups.

The final stage of the care continuum – achieving a successful **treatment outcome for MDR/RR-TB** – is characterized by the highest patient loss rates. The data obtained indicate that, given the current level of organization and coverage of TB care, the health care system ensures successful completion of treatment for approximately threequarters of patients who have started their MDR/RR-TB therapy. According to the WHO, the global average treatment success rate for MDR/RR-TB is approximately 63%, whereas in the WHO Europe Region it more often reaches 70–75%, particularly in countries with access to modern, alloral treatment regimens *(26, 34)*.

At the same time, the proportion of adverse outcomes remains significant and exceeds onequarter of all cases, including treatment discontinuation, fatalities, and other forms of failure. The persistence of a relatively high rate of adverse outcomes likely reflects the combined effect of the duration and complexity of treatment for MDR/RR-TB, severity of patients' clinical condition, as well as social and behavioral factors that limit patient retention in treatment *(23, 25, 26)*.

The identified sociodemographic determinants of adverse outcomes underscore the role of social vulnerability *(35)*. The higher risk of treatment failure among men is consistent with international findings linking male gender to later seeking for medical care, a higher

prevalence of behavioral risk factors, and reduced adherence to long treatment regimens (36). Similarly, unstable sources of income represent a significant risk factor, reflecting the impact of economic vulnerability, catastrophic expenses, and social instability on patients' ability to complete long MDR/RR-TB treatment *(5.37)*.

Programmatic factors indicate that a patient's initial contact with the healthcare system is of fundamental importance for the subsequent success of MDR/RR-TB treatment *(29)*. The higher risk of an adverse outcome among patients referred by specialists or those who sought care on their own appears to reflect not the referral pathway itself, but rather later presentation, presence of risk factors, or a more severe initial condition. The data highlight the key role of PHC as the optimal point for early referral for MDR/RR-TB treatment and the need to strengthen PHC as the "anchor" link in the TB cascade of care *(38)*.

The association between a TB relapse and poor treatment outcomes deserves special attention. Although the observed effect should be interpreted with caution, it is consistent with the literature, which indicates that patients with relapse episodes of the disease have more complex clinical and social profiles, including more pronounced drug resistance, comorbidities, and accumulated social vulnerabilities. This underscores the need for tailored care models for patients with relapses of MDR/RR-TB *(39)*.

Risk factors for treatment failure, such as problematic alcohol use and HIV coinfection, had the greatest impact and represent key modifiable determinants. Their contribution to poor treatment outcomes is detailed in international guidelines, which emphasize the need for integrated and intersectoral approaches to management of patients with MDR/RR-TB, involving a combination of TB therapy with psychosocial support, substance use treatment, and coordination between TB and HIV services *(23, 31, 40)*.

Results of an extended analysis of the MDR/RR-TB subgroup led to a more comprehensive understanding of the mechanisms underlying adverse outcomes in the final stage of the cascade of care. The data confirm that the likelihood of treatment failure is determined not so much by isolated clinical and demographic characteristics or time delays as by the quality of patient referral and the continuity of care throughout the entire treatment process *(8,29)*.

Analysis of initial points of contact with the healthcare system reveals an important structural issue: fragmentation of the patient's care pathway. The near parity between visits to PHC and the TB and pulmonology service indicates that the both points of entry are accessible and confirms the key role of the family doctor in early detection. At the same time, a significant proportion of patients who first seek care from other specialists constitute a group at increased risk of adverse outcomes. These findings underscore that lack of standardized "TB triggers" across all clinical disciplines may lead to diagnostic delays, disruptions in the care pathway, and reduced effectiveness of subsequent treatment, even when laboratory processes are relatively efficient *(38)*.

An analysis of time parameters of the diagnostic pathway revealed that, despite prompt access to screening and sputum collection, the most significant delays occur between receiving the laboratory results and the start of MDR/RR-TB treatment. The average delay at this stage was more than ten days, and in some cases the delay exceeded several months. Such delays can contribute to progression of the disease, increase the risk of further transmission of the infection, and reduce patient motivation, especially in the absence of timely information support and clearly organized referral pathways. In this regard, optimizing communication between laboratory services, PHC, and specialized institutions is one of the key areas for improving effectiveness of the MDR/RR-TB cascade *(41)*.

[1] One USD is equal to approximately 17 Lei.

The results also indicate that patients receiving longterm treatment regimens are more likely to experience adverse outcomes, which is likely due to a more severe drug resistance profile and presence of comorbidities requiring more intensive monitoring *(23, 42)*.

The low proportion of patients who begin treatment on an outpatient basis from the first day reflects persistent structural and organizational barriers, including prevalence of a hospital-centered model, insufficient preparedness of PHC facilities, and the features of existing financing mechanisms. Given international data on safety and effectiveness of outpatient models for clinically stable patients, expanding the practice of early outpatient treatment initiation offers a significant opportunity to optimize the service cascade and reduce the risk of patient loss before and during treatment *(43)*.

Behavioral factors also had a significant impact on treatment outcomes: missing even one scheduled visit to a pulmonologist specializing in TB nearly doubled the risk of an adverse outcome. This finding underscores the critical importance of continuous monitoring, as well as the need to implement flexible support models (including remote care), transportation assistance, and psychological support *(44, 45)*.

> Taken together, results of the **third stage of the cascade** confirm that the success of treatment for MDR/RR-TB is determined not so much by availability of therapy, but rather by the quality of care pathways, the extent of social support, and continuity of care for the patient. The greatest potential for reducing adverse outcomes is linked to strengthening the role of PHC, standardization of first point-of-contact, targeted interventions for socially vulnerable patients, as well as scaling up outpatient and patient-centered treatment models.

Qualitative data support these findings, showing that it is during the long-term treatment phase that patients face the greatest number of barriers. The diagnosis of MDR/RR-TB causes shock, fear, anxiety, and prolonged emotional distress in many patients. Low awareness about TB, misconceptions about causes of the disease, and distrust for frequent procedures (especially X-rays) create an additional psychological barrier to treatment adherence. At the same time, professionalism of the medical staff, their clear explanations, and the sense of security they provide – especially in a hospital setting – are noted. However, returning home after hospitalization is often accompanied by social isolation, stigmatization, and a lack of regular contact with community-based healthcare facilities. Home medical visits are generally not provided, and the primary burden of care falls on the family, which often faces significant emotional and financial strain.

Stigma is one of the key cross-cutting factors that influence all stages of the care continuum. It manifests itself at the family and community levels and, in some cases, at healthcare facilities *(4)*. Patients report fears of judgment, spread of rumors, and being shunned by their neighbors, which exacerbates social isolation and may reduce their motivation to continue treatment. Healthcare workers and CSO representatives also confirm existence of stigmatizing attitudes among their colleagues and the general public. In situations of emotional vulnerability, family support becomes one of the key factors influencing adherence; without it, the risk of treatment discontinuation increases significantly.

The socioeconomic barriers identified in the quantitative analysis as determinants of poor treatment outcomes (unstable income, unemployment) were further explained within the qualitative component. Patients report a significant reduction in income due to loss of their ability to work, the need to take loans, and the limited effectiveness of social food vouchers (53 lei/day), which do not even cover the minimum costs of food and transportation *(5)*. Under these circumstances, some patients are forced to resort to informal

and irregular employment, which leads to missed appointments, disruptions in treatment adherence, and an increased risk of adverse outcomes. Patients in rural areas are particularly vulnerable, as their transportation costs and time commitments are significantly higher.

Determinants such as problematic alcohol use and the HIV-positive status were also identified in both methodological clusters as key factors contributing to dropout from the cascade. Healthcare professionals emphasize that patients with substance use disorders are more difficult to retain in treatment, more likely to miss appointments, they have reduced self-control and often experience severe side effects, all of which increase the risk of treatment discontinuation. In the context of HIV coinfection, there is a need for ongoing multisectoral collaboration between TB and HIV services, which not always happend consistently and in a timely manner. This leads to delays in prescribing or adjusting ART, insufficient coordination in management of adverse reactions, and additional organizational challenges. The quantitative data show a significant increase in the risk of adverse outcomes in both groups, underscoring the need for integrated patient management models.

> Organizational gaps in routing remain a significant challenge. The quantitative analysis showed that referrals to the TB and pulmonology service by a specialist or a patient's self-referral are associated with a higher risk of an adverse outcome compared to referrals by a family doctor. Qualitative data confirm that primary care plays a key role in early detection, explaining the diagnosis, building trust, and providing regular follow-up care for patients, whereas "fragmented" care pathways lead to delays in diagnosis, a lack of continuity of care, and reduced adherence. PHC professionals emphasize the need to implement standardized "TB triggers" for all clinical specialties, as well as standardized referral algorithms.

Delays at various stages of the diagnostic pathway – particularly between receiving laboratory results and starting treatment – are confirmed by both quantitative and qualitative data. Patients report a lack of information about the next steps after receiving their results, uncertainty regarding when treatment will begin, and a lack of timely communication among facilities. Experts point to bureaucratic burden, staff shortages, overburdened laboratories, and logistical constraints – including transportation of biological samples – as factors that increase the risk of losing a patient before treatment begins.

An important outcome of the qualitative component was identification of a need for standardized and regular training for healthcare workers. Although most PHC and CSO staff have received training on MDR/RR-TB, the training is fragmented and often does not focus sufficiently on practical aspects of managing adverse reactions, psychosocial support, and intersectoral coordination. Healthcare professionals have expressed the need for regular refresher training, supervision, interdisciplinary case discussions, and accessible tools for quickly assessing a patient's condition.

Qualitative data also clearly show that patients view socioeconomic support – including food packages, reimbursement for transportation costs, and flexibility in the disability determination process – as a key factor in treatment retention. Many empha-size the need for ongoing psychological support not only at the time of diagnosis, but also throughout the course of treatment and after its completion, during the reintegration period, when patients face anxiety about relapse and social difficulties. These needs are consistent with the quantitative findings regarding the significance of missed appointments and the need for a sustainable patient follow-up system.

Overall, the results obtained suggest that the MDR/RR-TB care system in the Republic of Moldova has made significant progress in the early stages of the cascade but remains vulnerable at the final stage – retaining patients until they successfully complete treatment. Clinical, socioeconomic, and organizational determinants have a complex impact on adherence, which requires a cross-sectoral approach that includes integration of TB, HIV, and substance use disorder services; strengthening social interventions; expanding outpatient models; implementing "rapid initiation" mechanisms for treatment; and systematic use of CLM to identify and promptly address barriers.

Given the identified risk factors, special attention should be paid to patient groups with alcohol addiction, HIV coinfection, unstable income, and a history of relapse, as well as to patients entering the system through fragmented pathways. Strengthening targeted support for these groups, along with further standardization of the patient pathway and enhanced coordination across all levels of the system, has the potential to improve treatment completion rates and ensure sustainability of the cascade of medical and social care.

Limitations of the study

This study has a number of methodological and practical limitations that must be taken into account when interpreting the results and formulating policy recommendations.

Registry limitations and data completeness

The sources of information were data from the SIME TB information system and primary medical records. Despite the validation procedures in place, registry systems may be subject to incomplete records, variability in variable coding, and delays in data updates. Moreover, certain clinical and sociodemographic characteristics may have been missing, aggregated, or recorded inconsistently across different institutions, which could potentially lead to bias in estimates of treatment effects (underestimation or overestimation).

Small subgroups and statistical power

A number of sub-analyses focused on small subgroups (e.g., drug use, specific mental disorders, diabetes at specific stages of the cascade, outpatient initiation on the first day), which widens the confidence intervals and increases the likelihood of Type I and Type II errors. Accordingly, lack of statistical significance for certain factors does not rule out their practical significance and requires confirmation using larger samples.

Limitations of the qualitative component

Focus groups provided deep insights into participants' experiences and barriers, but they are subject to social desirability bias, dominance by active participants, and selection bias (participation by individuals who are more accessible or motivated). Conversion of audio recordings into text and the subsequent interpretation may also introduce subjectivity, despite use of triangulation. Furthermore, qualitative data are not intended for quantitative extrapolation of the frequency of events, but rather serve to interpret and contextualize quantitative findings.

Differences in cross-level practices and measurement of stigma

The differences observed in referral practices (PHC, specialists, self-referral) and manifestations of stigma within families, communities, and institutions may have varied by region. Since the measurement of stigma and discrimination relied primarily on participants' self-reports and experts' assessments, there remains the risk that hidden forms of stigmatization and micro-aggression may be overlooked. Standardized stigma scales were not used universally, which limits comparability with international assessments.

Community-level monitoring tools

Although CLM is being developed in the country, in this study its results were used primarily to provide context and qualitative feedback, rather than as a comprehensive dataset for analytical comparison; this limits the possibility to accurately quantify the impact of specific public interventions (VST, navigation, support) on cascade outcomes without additional analytical designs.

Measures to mitigate limitations. To mitigate the impact of these limitations, the following methods were employed: standardized data collection and double data entry, validation procedures, thematic content analysis involving triangulation of qualitative and quantitative results, and a comparison of findings from different sources. However, to further improve reliability of the data, prospective studies and economic evaluations are needed, along with an expansion of the set of clinical and social variables in SIME TB, regular use of validated scales (stigma, addiction, mental health), as well as implementation of analytical causal inference approaches when evaluating effectiveness of program interventions.

Key findings

The MDR/RR-TB cascade of care in Moldova shows high effectiveness rates in the early stages; however, the major decline in effectiveness occurs after treatment is initiated. The study showed that more than 95% of patients complete the stages of laboratory confirmation and initiation of MDR/RR-TB treatment, but only 74% of those who begin therapy achieve a successful outcome. Thus, the overall losses in the cascade of care occur primarily during the phase of retaining patients in treatment, indicating that the healthcare system is effective at ensuring access but remains vulnerable when it comes to providing ongoing support and maintaining adherence throughout the treatment course.

Key adverse determinants of treatment outcomes – problematic alcohol use, HIV coinfection, and economic vulnerability – consistently increase the risk of dropout during the notification, treatment initiation, and completion stages. Patients with alcohol addiction and the HIV-positive status are less likely to be included in the registry as MDR/RR-TB cases, less likely to begin treatment, and are significantly more likely to experience adverse treatment outcomes. Unstable sources of income are also associated with an increased risk of adverse outcomes, underscoring the need to integrate programs addressing TB, HIV, and substance use disorders, as well as to strengthen targeted social support, as key priorities.

Gaps in care pathways and insufficient coordination across levels of care – particularly when referrals come from narrow specialists and in cases of self-referral – significantly increase the risk of adverse outcomes and underscore the key role of PHC in ensuring continuity of the cascade of care. Patients referred to the TB and pulmonology service by

medical specialists or who sought care on their own are more likely to complete treatment with unfavorable outcomes compared to patients referred by a family doctor. This reflects fragmentation of care pathways, delayed seeking of care, and a lack of consistent link to the healthcare system, whereas referral through PHC ensures a more consistent patient pathway and is associated with better treatment outcomes.

Delays in the diagnostic pathway – particularly during the period between receiving laboratory results and starting treatment – remain a significant systemic bottleneck that limits timeliness of the therapy and creates the risk of patients dropping out before treatment is initiated. The longest stage is the "lab result → start of treatment" interval, which averages more than 10 days and, in some cases lasts several weeks, whereas the other stages are characterized by a swifter course. These delays point to a lack of coordination among laboratory, clinical, and administrative processes and call for improved communication, implementation of mechanisms to expedite initiation of treatment, and standardization of pathways among the levels of care.

The low prevalence of outpatient treatment initiation and the limited use of "accelerated treatment initiation" models (same-day/next-day) hinder reduction of delays and retention of patients, despite clinical applicability of this approach in stable patients. The proportion of patients who began outpatient treatment on the first day was only 3.4%, even though the greatest delay in the cascade occurs precisely between receiving the lab results and starting treatment. Expanding outpatient models for rapid initiation of treatment – provided there are clear selection criteria and standardized care pathways – can reduce dropouts and improve adherence.

Missed scheduled appointments and inconsistent psychosocial support are key behavioral and organizational factors that influence treatment adherence and significantly increase the risk of adverse outcomes. The quantitative analysis showed that even a single missed appointment nearly doubles the likelihood of an adverse outcome, underscoring the critical role of continuous monitoring and early intervention in addressing adherence issues. Qualitative data support these findings, pointing to emotional exhaustion, high levels of anxiety, stigmatization, and a lack of regular psychological and social support as key barriers to patient retention in treatment.

Qualitative data also highlight that stigma, emotional vulnerability, and a lack of patient awareness significantly reduce adherence to treatment and increase losses in the cascade, particularly during long-term therapy. Receiving a diagnosis is often accompanied by shock, anxiety, and severe stress, which are exacerbated by the fear of judgment and negative reactions from family and the community. A lack of knowledge about the disease, doubts about the need for frequent checkups, and no consistent psychological support contribute to emotional exhaustion and increase the risk of treatment discontinuation. Stigma remains the systemic barrier that affects treatment-seeking behavior, trust in the healthcare system, and patients' capacity to complete a long treatment course.

Limited standardization of specialist training and a lack of practical tools for managing complex cases of MDR/RR-TB reduce the quality of care for patients and lead to variability in practices between levels of the healthcare system. The qualitative survey showed that, although most PHC and CSO workers have undergone training on MDR/RR-TB, the training remains fragmented, irregular, and insufficiently focused on practical application: healthcare workers report difficulties in managing adverse reactions, assessment of the mental health status, supporting adherence, and referral of patients in complex situations. The lack of standardized clinical algorithms, supervision, regular refresher–modules, and interdisciplinary case discussions leads to different approaches to

treatment and care reducing coordination of the cascade and increasing the risk of losses at long therapy stages.

Service integration (TB–HIV), expansion of outpatient models, and systematic use of CLM (communityled monitoring) are key strategies for improving treatment effectiveness and patient retention. The key losses in the cascade occur after treatment is initiated and are due to a combination of clinical and social vulnerabilities, as well as organizational gaps. The greatest potential for improvement lies in integrated patient care models, scaling up initiation of outpatient treatment while adhering to safety criteria, and implementing CLM as a continuous feedback mechanism to promptly address barriers.

Recommendations

Enhancing the package of interventions for patients with problematic alcohol use and for individuals with HIV co infection as groups at high risk of loss to follow-up and treatment failure. To mitigate the key source of loss identified in the cascade of care – the phase between initiation of treatment and its completion – it is recommended to implement a structured, differentiated, and enhanced package of interventions targeting two key groups: patients with problematic alcohol use and people living with HIV – the groups that consistently demonstrate a high risk of adverse treatment outcomes, treatment discontinuation, and loss to follow-up at all stages of the medical care cascade.

Strengthening the system for early detection and patient referral at the initial contact level. It is recommended to enhance the unified algorithm for early detection of TB at all initial contact points, including PHC and specialists in other fields, to ensure that patients are referred for molecular genetic testing in a timely manner and to prevent delays in early stages of the cascade. It is recommended to implement a standard clinical "TB trigger" when suspicious symptoms are present, ensure mandatory referral for the WHO-recommended rapid diagnostic test (Xpert testing) on the day of presentation, and strengthen coordination between PHC and the TB service through a clear mechanism for information sharing and rapid organization of the next steps. Additional short-term training for physicians in related specialties and improvements in the logistics of collecting biological samples and transferring results will help reduce diagnostic delays and improve efficiency of patient referral.

Strengthening social and economic support for patients to improve treatment adherence and prevent treatment discontinuation. It is recommended to expand and structure measures of socio economic support for patients with MDR/RR-TB, with a particular focus on groups with unstable sources of income who are at an increased risk of failing to complete treatment.

Strengthening continuous clinical monitoring and preventing missed appointments during treatment. It is recommended to strengthen the system of regular clinical follow-up for patients with MDR/RR-TB, with a particular focus on preventing missed appointments, which significantly increase the risk of an adverse treatment outcome. To ensure a stable course of treatment, it is necessary to implement mechanisms for promptly responding to a patient's absence on a scheduled appointment day, including automatic notifications, active follow-up through PHC and CSOs, flexible appointment scheduling, and expansion of remote monitoring options (RMOs). Improved access to monitoring, timely communication among services, and personalized patient support will help improve treatment adherence and reduce the likelihood of treatment discontinuation.

Expanding outpatient treatment models and creating conditions that allow clinically stable patients to begin therapy on an outpatient basis. It is recommended to expand implementation of outpatient treatment models for MDR/RR-TB and make sure that clinically stable patients can begin treatment on an outpatient basis. Given the extremely low proportion of cases where treatment is initiated outside of a hospital setting, it is necessary to remove organizational barriers related to referral pathways, prompt prescribing of medications, and availability of support teams at the community level. Optimizing the process of transferring patients from the diagnostic setting to outpatient care, strengthening the role of PHC in organizing follow-up care from the first day of treatment, and ensuring that CSOs are prepared to provide timely support will help reduce delays, ease the burden on hospitals, and improve adherence to treatment. Establishing clear criteria for clinical stability, standardized protocols for outpatient initiation of treatment, and an efficient decisionmaking process will facilitate a broader and safer use of outpatient treatment models. At the same time, it is essential to ensure that all patients, without exception, are informed of the option of receiving treatment at home from the moment of diagnosis, especially in cases where the start of treatment is delayed due to the patient's reluctance to be hospitalized.

Revising the funding mechanism for TB care and preserving and specifically protecting TB financial resources. There is an urgent need to reform the mechanism for financing TB care, as a result of transition from a funding model based primarily on the number of hospital beds and the length of hospitalization to a blended model that takes into account the entire continuum of tuberculosis care, including out-patient treatment. At the same time, it is absolutely essential to ensure that the funds freed up by reducing unnecessary hospitalizations are "protected" and subsequently used exclusively for the national TB control program.

Strengthening integration of medical and non-medical services through systematic development of partnerships between PHC, TB services, and civil society organizations. It is recommended to strengthen coordination between clinical services and CSOs to ensure continuity of care for patients with MDR/RR-TB at all stages of treatment. It is necessary to formalize and expand the mechanisms for collaboration among PHC, TB clinics, and CSOs, including regular data exchange, coordinated planning of interventions, and joint management of patients requiring intensive follow-up. Enhancing sustainability of the partnership involves establishing standards for provision of public services, ensuring predictable contracting, strengthening the role of CSOs as part of the care system, and implementing standardized quality monitoring tools. Developing such a model will enable a personalized approach, timely response to emerging barriers, and improved patient retention in treatment through a combination of medical, social, and psychological support.

Expanding and institutionalizing the communityled monitoring (CLM) mechanism as a tool for providing timely feedback and improving service quality at all stages of the cascade. It is recommended to strengthen and systematically integrate the CLM mechanism into the national model for providing care to patients with MDR/RR-TB. Use of CLM makes it possible to identify barriers to access, delays in diagnosis, referral issues, missed appointments, and gaps in outpatient care in a timely manner, thereby ensuring continuous and reliable feedback between among, CSOs, and the healthcare system.

Strengthening competencies and working conditions of PHC and CSOs to improve the quality of care for patients with MDR/RR-TB at the community level. It is recommended to strengthen support for PHC and CSO workers, taking into account the needs identified in the focus group discussions for additional training, standardized support

tools, and improved conditions for interagency collaboration. Expanding organizational and professional support will improve the quality of patient navigation, increase treatment adherence, and ensure sustainability of medical and nonmedical services provided at the community level.

Results of the study conducted in the Republic of Tajikistan

A qualitative study was conducted based on individual interviews with healthcare workers and patients with MDR/RR-TB, using standardized question-naires that covered key stages of the patient pathway and aspects of accessibility and quality of medical care. The study included representatives from various levels of the healthcare system as well as patients, which guaranteed that a variety of perspectives were taken into account.

As part of the study, 56 semistructured interviews were conducted. The study was conducted in collaboration with a national consultant, subject to obtaining an informed consent from all participants.

The sample included: 28 healthcare workers and 28 patients with drug-resistant TB. This ensured a balanced representation of the key groups, making it possible to conduct a comparative analysis of how both service providers and patients perceive the healthcare delivery system.

The study covered various regions of the country in order to take into account regional differences in organization of healthcare. The sample includes participants from the following administrative units: Dushanbe, Khujand, Vahdat, Bokhtar, and Kulob. This geographic scope ensured that both the urban and regional contexts were represented, including differences in access to medical services and the healthcare infrastructure.

When forming the sample, the principle of maximum variability was followed:

- healthcare workers were distributed across various workplaces (different levels of the healthcare system and facilities);
- among patients – by place of residence.

Healthcare workers included professionals involved in providing care to patients with TB, including staff of specialized TB services and primary healthcare facilities. This makes it possible to account for the various levels of medical care – from initial diagnosis to specialized treatment

Patients included individuals with the confirmed diagnosis of MDR/RR-TB who live in various regions of the country. Their experience reflects the various stages of the patient's pathway, including diagnosis, the start of treatment, and its continuation. This approach helped reduce the risk of systematic bias and ensured a broader representation of experiences of interaction with the healthcare system.

Focus group discussions with healthcare workers involved in care of patients with MDR/RR-TB

During focus group discussions with healthcare workers involved in providing care to patients with MDR/RR-TB, the focus was on their practical experience, as well as on identifying systemic barriers and factors affecting accessibility and continuity of treatment. In this regard, particular attention was paid to views of healthcare professionals as key actors in the system who directly influence screening, diagnosis, treatment, and care of patients.

The profile of participants of the focus group discussion with healthcare professionals

A total of 28 respondents participated in the survey; all of them are healthcare workers in the TB service (100%). This indicates a targeted selection of specialists directly involved in diagnosis, treatment, and follow-up of patients with MDR/RR-TB, which enhances practical significance of the data obtained.

Geographically, the sample covers all regions of the country except for the Gorno-Badakhshan Autonomous Oblast (GBAO): Dushanbe – 10 participants (35.7%), Districts of Republican Subordination (DRS) – 5 participants (17.8%), Sughd Region – 5 participants (17.8%), and Khatlon Region – 8 participants (28.5%). In terms of work settings, urban practice predominates – 15 participants (53.6%) – while 13 participants (46.4%) work in rural areas. This ratio indicates that urban and rural healthcare contexts are represented almost equally. This is an important advantage of the sample, as it allows for identification of differences in the conditions under which healthcare is provided, access to diagnosis and treatment, and organizational barriers, depending on the context.

Table. 11. **Geography and demographics of the interview participants among healthcare workers**

№	Region	City/district	Healthcare facility	Number of interview participants
1.	Dushanbe	Dushanbe	City Center for Protection of the Population Against TB, PHC facilities	10
2.	DRS	Vahdat	Center for Protection of the Population Against TB, PHC	5
3.	Sughd Region	Khujand	City Center for Protection of the Population Against TB	5
4.	Khatlon Region, Kulyab Region	Kulob	Center for Protection of the Population Against TB	0
5.	Khatlon Region, Bokhtar	Bokhtar	Center for Protection of the Population Against TB	8

The gender and age distribution corresponds to the current staffing profile of the PHC system: among those surveyed, there were 11 women (39.3%) and 17 men (60.7%). By age groups, there were 8 participants (28.6%) aged 25–44, 13 participants (46.4%) aged 45–59, and 7 participants (25.0%) aged 60 and older. The ratio of men to women reflects the current workforce profile among healthcare professionals in the country. The predominance of men may reflect the historically established staffing structure of the TB control service.

It is also worth noting that the inclusion and participation of women ensures a diversity of perspectives, particularly on issues related to interacting with patients with MDR/RR-TB. The majority of respondents (46.4%) are in the 45–59 age group – these are the most experienced professionals with many years of work experience. Young professionals (ages 25–44) make up nearly one-third of the sample, which allows us to take into account current practices and new approaches to treatment. Participants over the age of 60 bring in a historical perspective and experience from long-term work within the system, which is important for analyzing changes in the organization of TB care. Taken as a whole, the respondent group provides a reliable basis for interpreting clinical and programmatic aspects of the service cascade.

Most participants have a proven track record of significant clinical experience working with TB patients, ranging from 8 to 42 years. Such a wide range of professional experience indicates that the respondents are highly qualified and have a good understanding of the processes involved in the detection, diagnosis, and treatment of TB, including MDR/RR-TB. Involvement of specialists with varying levels of experience allows for a more comprehensive analysis of the evolution of the TB care system and helps identify both persistent and new systemic barriers. The participants have between 5 and 10 years of experience in the field of MDR/RR-TB, which corresponds to the period during which treatment programs for drug-resistant forms of TB have been implemented in the Republic of Tajikistan (beginning in 2016 on a pilot basis). This indicates that a significant proportion of the respondents were directly involved in the processes of implementing and scaling these approaches. Thus, their existing experience allows participants not only to evaluate current treatment practices but also to analyze trends, including effectiveness of implemented care models, as well as factors affecting patient adherence to treatment and retention in therapy.

Results of the discussions

Training on managing MDR/RR-TB Cases

Results of the focus group discussions indicate a high level of training coverage among healthcare workers regarding management of MDR/RR-TB cases. Virtually all participants (all 28 respondents) confirmed that they had completed the relevant training, which indicates that professional development initiatives in this area are systematic. At the same time, a variety of training formats used was identified, reflecting both institutionalized approaches to staff training, and individual career development paths. Face-to-face learning formats – such as seminars, workshops, and lectures – remain the most common ones, which underscores their key role in developing practical skills and facilitating exchange of professional experience.

At the same time, participants actively noted that remote learning formats, including webinars and online courses, have been used ever more widely in recent years, which indicates their gradual integration into the system of continuous medical education and their importance for promptly updating knowledge in accordance with current clinical guidelines. Moreover, respondents mentioned participating in continuous professional development programs, including professional development courses.

> Overall, the data obtained demonstrate a wellestablished training system for management of MDR/RR-TB that combines traditional and modern educational approaches, thereby laying the foundation for maintaining a high level of professional competence among healthcare workers.

Nevertheless, despite the high level of training coverage, results of the discussions point to a number of potential areas for further improvement. In particular, the report notes that there is limited information on a systematic assessment of the quality and effectiveness of the training activities conducted, as well as the extent to which they influence patient care practices. Moreover, the variety of instructional formats may indicate a lack of a unified approach to content and program standardization. The issue of regularly updating knowledge and ensuring equal access to training opportunities deserves special attention, especially for professionals working in remote and rural areas.

Thus, while a high level of educational coverage has been achieved, the ongoing challenge remains to further improve the workforce training system, with an emphasis on quality, standardization, and the practical applicability of the knowledge gained.

During the discussions, participants noted that, despite having completed training courses and regularly updating their knowledge, there are still areas in which healthcare workers lack confidence when managing patients with MDR/RR-TB. In particular, the most frequently mentioned challenges were those related to management of adverse drug reactions, including early recognition of toxicity, selection of strategies for adjusting treatment regimens, and effective communication with patients regarding the risks and expected effects of therapy. The participants also emphasized that the training programs in place do not always fully cover all relevant topics and practical aspects necessary for comprehensive management of patients with MDR/RR-TB. This may lead to inconsistencies in the level of training among professionals involved in the various stages of care.

An additional challenge is the constant updating of international guidelines, particularly those issued by the WHO, which requires regular and timely training for healthcare workers. At the same time, some of these specialists completed their training quite some time ago, and since then there may have been significant changes in approaches to diagnosis, treatment, and monitoring of patients, which could potentially affect relevance of their current knowledge.

Special mention was made of the need to adopt a systematic approach to tracking and monitoring training of healthcare workers. Currently, there is no single mechanism for tracking which specialists have completed training, the extent of that training, and topics covered. This makes it difficult to assess the extent of coverage and identify gaps in training, and it also limits the ability to plan targeted educational activities.

Thus, while training coverage is high, there is a need to enhance its systematic approach, relevance, and comprehensiveness, including regular updates of knowledge, expansion of subject matter, and implementation of mechanisms to monitor and track workforce training, to ensure high-quality care for patients with MDR/RR-TB.

During the focus group discussions, additional priority thematic areas were identified that require strengthening as part of training of healthcare workers involved in care of patients with MDR/RR-TB. In particular, participants identified the need to deepen their knowledge and practical skills in the following areas:

- management of patients with comorbidities, including coordination of care and accounting for drug interactions;
- identification and management of adverse events associated with use of TB drugs (aMBDs), including early diagnosis, monitoring, and adjustment of therapy;

- issues related to patients' mental health, including identifying psychological problems, supporting patients throughout long-term treatment, and improving treatment adherence.

> Discussions of these topics have shown that they are among the most challenging ones in practical work and are not always adequately covered by the training programs in place. The participants emphasized that these specific aspects directly affect the quality of care, safety of treatment, and patient retention in the treatment program.

Moreover, it was noted during the discussions that, at present, a significant portion of the systematic training on management of patients with MDR/RR-TB has been and continues to be implemented with the support of international organizations. Thus, planning and the content of training activities are largely determined by the priorities and objectives of the relevant projects.

The participants emphasized that, on the one hand, this approach provides access to up-to-date knowledge and international experience; on the other hand, however, it may lead to fragmented learning experience. In particular, topics covered in the training programs do not always address the full range of practical needs of healthcare workers, and the scope of the training may be limited to the framework of individual projects. This, in turn, creates the risk of uneven professional development among specialists involved in care of patients with MDR/RR-TB and underscores the need to develop a more coordinated and sustainable national training system that addresses comprehensive needs of the healthcare system throughout the country.

Professional training and competence development

During focus group discussions with healthcare professionals involved in care of patients with MDR/RR-TB, key elements, limitations, and best practices in professional training were identified.

Currently, inperson seminars and training sessions form the basis of the training, but online formats (webinars, remote learning courses, and modular programs) are gradually being introduced. These formats allow participants to quickly learn new concepts and review the material as needed, which is especially important when teams have heavy workloads and are geographically dispersed. However, the reach of online training is fragmented and largely depends on international organizations, with topics determined by project priorities and not always ensuring uniform coverage of all professionals.

Given the current circumstances, with nearly universal Internet coverage in the country, it seems possible to expand this format of training. This nationwide expansion and reach will allow professionals to acquire new knowledge anytime, anywhere – which is especially important for employees in remote areas or those with heavy workloads – and will provide access to the content that they can review and revisit as needed.

Participants cited “horizontal” and “vertical” mentorship as important resources. On the one hand, this involved support from experienced colleagues in the workplace – joint rounds, discussions of complex cases, and prompt consultations in cases of drug intolerance or suspected drug interactions. On the other hand – expert support from specialists in the national TB program, relevant facilities, and professional associations. One such resource could be a monitoring and evaluation system that can provide on-the-job training during site visits. Previously, this methodology was used nationwide to help standardize

approaches across different levels of care, refine algorithms, and strengthen coordination with laboratory services and PHC.

> Systematic training, mentoring, and blended learning formats (theory, practice, and supervision) are key elements in development of healthcare professionals' competencies. To improve the quality of care for patients with MDR/RR-TB, it is necessary to transition to a systematic, standardized, and sustainable model of professional training that includes planning, standardization of programs, implementation of training, monitoring, and ensuring retention of knowledge.

Challenges in providing services

Healthcare workers face a range of clinical, organizational, educational, and social challenges that directly affect the quality of care for patients with MDR/RR-TB. Effectively addressing these issues requires a systematic approach that includes strengthening human resources capacity, standardizing training, improving patient referral processes, and expanding access to diagnostics and specialized care.

During the discussions, participants noted that although many of these challenges are being resolved in practice, a number of problems remain:

1. Patient referral – delays in transitioning between levels of care, and insufficient coordination between the hospital, PHC, and laboratory services.
2. Stigma and discrimination – patients and healthcare workers face lack of public understanding, fear of infection, and social isolation.
3. Patient resistance to treatment – low adherence, missed doses, and difficulty maintaining long treatment regimens.

These challenges underscore the need for systematic planning and integration of clinical, educational, and social components into the service delivery process to ensure high-quality, safe, and accessible treatment for all patients with MDR/RR-TB.

Conclusions

The discussions have shown that effectiveness of patient management for MDR/RR-TB depends significantly on systemic organization and coordination across different levels. Major systemic barriers include delays in laboratory testing, limited access to diagnostics, and gaps in information flows caused by funding mechanisms.

Problems with patient adherence and loss to follow-up require personalized, cross-sectoral approaches: direct contact with patients and their families, involvement of PHC, social services, and local authorities, and psychological support. It is noted that the limited impact of collaboration with external partners is often due to the lack of uniform regulations and clear "entry points."

> The greatest success is achieved when clinical interventions are combined with predictable coordination across services, targeted social support, and consistent, respectful communication with the patient that focuses on informed consent and shared decisionmaking. This underscores the need for standardized routing protocols, formalized communication channels, and a systematic approach to social support as key factors in improving the quality of care for patients with MDR/RR-TB.

Problems

First, the content of training programs does not always fully cover all key aspects of patient care. The most significant gaps are observed in management of comorbid conditions,

management of adverse drug reactions (aMBDs), as well as provision of psychosocial support and mental healthcare for patients.

Second, there are disparities in the level of training among specialists. This is due both to differences in access to training and to the fact that some healthcare workers received their training a long time ago. Given that international guidelines – including those from the World Health Organization – are regularly updated, there is a risk of using outdated approaches to diagnosis, treatment, and monitoring of patients.

Third, there is no systematic mechanism for tracking and monitoring training of healthcare workers. This makes it difficult to assess the scope, quality, and comprehensiveness of training, as well as to identify specific gaps in knowledge and skills.

It was also noted that a significant proportion of training activities are carried out with the support of international organizations. Despite their important role, the topics and scope of the training are often determined by the framework of individual projects, which may lead to fragmented training and incomplete coverage of all categories of professionals.

Taken together, these factors limit effectiveness of the training system and may affect the quality of care provided to patients with MDR/RR-TB.

Recommendations

1. First and foremost, it is necessary to develop and implement a unified national approach to training in accordance with current international recommendations – including those of the WHO – that ensures standardization of the curriculum content and covers all key aspects of patient care, including management of side effects, comorbidities, and mental health.

   Part of this approach involves development of standardized training modules covering the full patient care cycle, including early detection and diagnosis, current treatment regimens, monitoring of treatment efficacy, management of adverse drug reactions (aMBDs), management of patients with comorbidities and mental health issues, and psychosocial support. It would be advisable to incorporate aspects of integration and cross-sectoral collaboration (between civil society organizations, mental health services, and social services) into the training.

   Moreover, a unified approach will involve strengthening coordination between national agencies and international partners to align the topics and content of training programs, taking into account actual needs of the healthcare system.
2. These training modules should be used to provide regular training for healthcare professionals, with an emphasis on practical application of new approaches through clinical case discussions, mentoring, and supervision, as well as on-the-job training. Such training should become part of a system of continuous professional development: professional development programs, certification courses, and mandatory refresher training when protocols change.
3. Plan for widespread adoption of digital and distance learning formats through online courses and webinars, and develop platforms featuring up-to-date clinical materials and protocols. This will also help expand access to training for professionals working in remote and rural areas.
4. Implementation of a training tracking and monitoring system will make it possible to assess specialists' participation in educational activities and the extent of training coverage, as well as to identify gaps in training. This will make it possible to plan training more effectively and ensure equal access to it in the future.

Focus groups with patients with MDR/RR-TB

As part of the study, focus group discussions were conducted with 28 MDR/RR-TB patients, with their consent. The geographic scope included 2 cities and 3 districts of the country (Dushanbe, Khujand in Sughd Region, and the Vahdat District of the Republic of Tajikistan, as well as Bokhtar and Kulob districts of Khatlon Oblast). Whenever possible, the principle of geographical dispersion based on patients' places of residence was maintained **(Table 12).**

Table. 12. **Geography and composition of interview participants among people with MDR/RR-TB**

№	Region	City/district	People with MDR/RR-TB	Interview
1.	City of Dushanbe	Dushanbe	10	10
2.	DRS	Vahdat	5	5
3.	Sughd Region	Khujand	5	5
4.	Khatlon Region, Kulob Region	Kulob	0	0
5.	Khatlon Region, Bokhtar	Bokhtar	8	8

Perception of the diagnosis of MDR/RR-TB

Patients with MDR/RR-TB describe the diagnostic process as *a complex, emotionally stressful, and often protracted* stage of treatment. It is specifically emphasized that the moment the diagnosis is communicated is a critical juncture that influences the patient's continued adherence to treatment. Supportive communication from healthcare providers, a clear explanation of the diagnosis and next steps, and emotional support help build trust and prepare the patient to be ready for treatment. Patients emphasize that they often feel fear and confusion at the time of diagnosis. *"I was scared, I was worried, and I was afraid of dying," "When I heard about it, I was very upset and shocked to find out that I had been diagnosed with this disease"* (M-40).

Analysis of the statements shows that such strong emotional reactions are largely due to a lack of awareness prior to the onset of the disease, as well as insufficient information provided at the time of diagnosis. Many patients noted that even before receiving the diagnosis, they had encountered the widespread belief that this disease is incurable and often fatal. Such attitudes intensify fear and a sense of hope-lessness at the time of diagnosis, leading to negative expectations regarding treatment and its outcomes. When healthcare providers fail to provide sufficient explanation, this leads to increased anxiety and mistrust and can negatively affect adherence to treatment.

When a person is diagnosed with MDR/RR-TB for the first time, the reaction is almost always emotionally difficult. This isn't just medical news – it's a major psychological blow. Some responses indicated that the diagnosis was met with shock and denial. Especially if the person used to think of TB as *"a disease that affects other people." "It must be a lab error – how could I possibly have this disease?"*

There were also reports of feeling fear and anxiety. Often, these fears were not related to one's own health, but rather to the fear and anxiety of infecting one's loved ones: *"What will happen to my family now?".*

When a patient first hears the diagnosis of MDR/RR-TB, anxiety about the long treatment is very common. There are several reasons for this. First of all, the mere news that treatment will be long creates a feeling of losing control over one's life. The patient begins to think about how this will affect their work, family, income, and daily activities. Second, duration of treatment is associated with severity of the disease. Many people take this as a sign: "if treatment takes so long, it must mean the illness is very serious," which intensifies fear and uncertainty. Third, patients often lack prior information about MDR/RR-TB. Therefore, long-term treatment is perceived not as a medical necessity, but as something frightening and unknown, especially when potential side effects are also mentioned. *"When they told me about the diagnosis and the need for continued treatment, I felt fear and anxiety about how long the treatment would take."*

Concerns about duration of treatment are some of the key initial reactions most patients experience when first informed of MDR/RR-TB. Moreover, anxiety may increase as patients receive more information about their diagnosis and the duration of treatment, stemming from concerns about whether they will be able to complete the treatment, whether they will recover from the disease, and the need to change their usual lifestyle.

> It should also be noted that a significant factor contributing to psychological distress in patients with MDR/RR-TB is the persistent social stigma associated with this disease. Despite advances in medical approaches to diagnosis and treatment, TB is still associated with social disadvantage in the public perception and remains a socially sensitive diagnosis.

As a result, patients often develop fears of being rejected or isolated by those around them. Many people express the fear of being judged negatively by society, which is accompanied by thoughts of possible judgment (*"What will people think of me?"*). Such feelings may lead to the diagnosis being kept secret not only from a wide range of people, but also from one's own family members.

Patient interaction with medical staff

Patient/healthcare provider interaction is one of the key factors determining effectiveness of treatment for MDR/RR-TB. Given the duration of therapy, the need for strict adherence to treatment regimens, and potential side effects, the quality of communication between patients and healthcare providers acquires particular importance. For people with MDR/RR-TB, regular contact with healthcare providers becomes an important part of their daily lives. Against this backdrop, the level of trust in doctors and nursing staff, availability of information, and willingness of healthcare professionals to answer questions and take patients' individual needs into account directly influence adherence to treatment.

Lack of information, a formal approach to communication, or lack of emotional support can contribute to increased anxiety, reduced motivation for treatment, and, as a result, poorer treatment outcomes. At the same time, a respectful, attentive, and supportive attitude on the part of healthcare providers helps patients feel safe, increases their engagement in the treatment process, and improves their adherence to treatment recommendations. In this context, analyzing patients' experiences when interacting with healthcare personnel is particularly important for identifying current barriers and determining ways to improve the quality of care for patients with MDR/RR-TB.

Patients generally describe their interactions with medical staff as positive, noting their professionalism and clear explanations, especially in the inpatient setting. Many people say

they did not encounter any problems and received the necessary information about their diagnosis and treatment, including the need to monitor their medication intake daily: *"The staff at the center give practical advice and are never rude," "I have no negative feelings toward the medical staff; on the contrary, I'm glad I started treatment on time."*

Besides, some patients report a lack of information about possible side effects of treatment and how to manage them, which may cause additional anxiety and undermine their confidence in the treatment process. In some cases, there is a lack of emotional support from medical staff, which is particularly important in the early stages following diagnosis. There may also be communication barriers related to use of medical terminology that is not sufficiently adapted to the patient's level of under-standing, or to cultural and social factors. This may lead to an incomplete understanding of the recommendations and reduced adherence to treatment.

Thus, despite the generally positive overall context of collaboration, the aspects listed above point to the need for further improvement of a patient-centered approach to the care of patients with MDR/RR-TB.

Challenges in obtaining medications and receiving home care

Issues related to obtaining medications and organizing home care play a significant role in the experiences of people with MDR/RR-TB, given the long-term nature of treatment and the need for regular therapy.

Patients generally report that access to medications has been consistent, with medications dispensed daily and without interruption. Many patients note that their daily visits to the clinic went smoothly, despite the additional costs: *"I didn't have any problems with either the medication or the treatment"* (M-35).

Among patients with MDR/RR-TB, there are a number of patient-related issues that may make it difficult to obtain and take medications regularly. These aspects are usually related not to the healthcare system, but to personal, lifestyle, or psychological factors.

"Due to financial difficulties, I was unable to receive home care in a timely manner, so I had to go to the hospital" (M-56).

The impact of the diagnosis on work capacity and the ability to support one's family

The diagnosis of MDR/RR-TB has a significant impact on patients' ability to work and support their families. Long treatment, the need for regular visits to medical facilities, side effects of therapy, and temporary limitations on daily activities lead to a decrease in physical and occupational activity. Many patients note that, because of their illness, they have to reduce their working hours, temporarily stop working, or change the type of work they do, which affects their income and their family's financial stability. The fear of infecting loved ones and isolation requirements also limit participation in social and economic life: *"TB has affected my family's livelihood"* (M-42).

The TB diagnosis significantly reduced patients' ability to work, led to a marked loss of physical strength, and, as a result, to a loss of the income needed to support their families.

"With this diagnosis, it became difficult to continue working at my old job, but I need to support my family" (M-59).

These data highlight the need for a comprehensive approach to supporting patients with MDR/RR-TB, including social assistance, adjustments to work schedules, and psychological support to maintain the family's financial and emotional stability. *"When I got tuberculosis, I could no longer work and was forced to rely on the support of my family and relatives"* (M-28). *"Because of financial difficulties, I had to work while undergoing treatment to support my family."*

Types of support received (financial, emotional, social)

In the context of treating patients with MDR/RR-TB, "types of support received" refer to the categories of assistance that help patients cope with the disease, ensure adherence to treatment, and maintain their quality of life. Patients emphasize the importance of social and psychological support throughout their course of treatment. The most sought forms of assistance are food aid, reimbursement of transportation costs, and regular psychological support. It is noted that such support helps increase adherence to treatment and reduce the risk of treatment discontinuation.

For many patients, family and relatives become the primary or only source of financial support during treatment. Given the need for long-term treatment, frequent visits to medical facilities, and a possible weakening of the ability to work, support from loved ones plays a key role in ensuring access to medications, covering transportation costs, and meeting basic living needs. Direct statements from study participants confirm this: *"When I got TB, I could no longer work and was forced to rely on the support of my family and relatives"* (M-28). *"Due to financial difficulties, I had to work while undergoing treatment to support my family"* (M-44).

Thus, financial support from the family becomes an important factor in ensuring continuity of treatment and maintaining the stability of the patient's living conditions. Some patients received minimal financial assistance (money or food) from representatives of Khukumats, mosques, and acquaintances. This helped them cope with the difficulties arising from the loss of their ability to work and their reduced income.

Support from family, friends, and healthcare providers helps patients cope with stress, anxiety, and the fear of stigma. Emotional support increases motivation to adhere to treatment and promotes more successful adaptation to the long-term treatment. Many noted that the emotional support they received – in most cases, primarily from family and relatives – helped patients stay motivated to continue their treatment.

Assistance with organizing daily living, inhome care, help with transportation to medical facilities, and adjustments to work schedules enable patients to adhere to their treatment and maintain social connections. Social support makes it easier to adhere to treatment and improves patients' quality of life. However, social assistance is fragmented in nature; for the most part, such assistance is provided by international organizations or civil society organizations as part of their own programs.

Patients with MDR/RR-TB face prolonged treatment, reduced work capacity, and social stigma. In these circumstances, comprehensive support plays a key role. Financial assistance from family members ensures access to coverage for medical expenses; emotional support from loved ones and medical staff reduces anxiety and increases motivation for treatment;

and social support helps patients organize their daily lives and adhere to their treatment regimen. This set of measures promotes the patient's successful adaptation and increases adherence to treatment.

The impact of stigmatization and, conversely, the support received for completing treatment and the ability to successfully complete it

The stigma associated with the diagnosis of MDR/RR-TB has a significant impact on the treatment process and its outcomes. Fear of judgment, social isolation, and negative attitudes from those around them may lead to concealing the diagnosis, limiting social contact, and to reduced adherence to treatment. In some cases, this manifests itself in missed doses of medication, irregular visits to medical facilities, and a refusal to fully cooperate with medical staff.

At the same time, having support – from family, loved ones, and healthcare professionals – plays the opposite, protective role. Emotional, social, and financial support helps reduce anxiety, strengthen motivation, and build trust in treatment. Support helps patients adapt more easily to long-term treatment, follow medical recommendations, and remain resilient in the face of challenges.

> Thus, stigmatization and support are factors with opposite effects: the former may hinder successful treatment, while the latter significantly increases the likelihood of completing treatment and achieving positive outcomes.

Overall, patients emphasize that stigmatization exacerbated their emotional and social vulnerability, which could undermine their confidence in the treatment process. At the same time, instances in which family and loved ones showed acceptance and support significantly contributed to maintaining motivation and successfully completing treatment.

Here are some quotes regarding stigmatization: *"I didn't want my relatives to find out about my disease" (F-33), "At the beginning of treatment, I felt fear and judgment"* (M-37).

The statements presented here demonstrate that stigmatization has a significant negative impact on patients' behavior, including concealing their diagnosis, avoiding medical care, and reduced adherence to treatment. At the same time, emotional and social support helps foster motivation for treatment, increases resilience in the face of treatment challenges, and improves the likelihood of successful completion.

Discussion and key issues identified

The survey provided an opportunity to examine experiences of patients and healthcare workers, as well as to identify key barriers and factors affecting progression through the cascade of care for MDR/RR-TB in the Republic of Tajikistan.

> The data show that patients experience the greatest difficulties during the long-term treatment phase. At the same time, communicating the diagnosis of MDR/RR-TB is a complex and sensitive step in clinical practice that has a significant impact on the patient's subsequent attitude toward treatment and adherence to therapy. For most patients, receiving the diagnosis is a major psychological stress,

accompanied by shock, fear, denial, and concerns related to the social stigma associated with the disease. Many patients have a low level of awareness about the disease, which leads to misconceptions about its causes and a lack of trust in medical procedures, including regular checkups.

Under these circumstances, not only the content of the information conveyed but also the way it is presented become particularly significant. Effective communication of the diagnosis requires adherence to a number of principles: ensuring a private and calm setting, assessing the patient's level of understanding beforehand, presenting information clearly and in an accessible manner without excessively using medical terminology, and allowing the patient time to process the information emotionally. An important element is acknowledging and supporting the patient's emotional state, which helps build trust in the healthcare provider.

When communicating the diagnosis, it is important to emphasize that MDR/RR-TB is a curable disease provided that the prescribed treatment is followed, despite its duration and potential challenges. Providing structured information about the next steps in treatment and verifying that the patient has understood the information help reduce anxiety and increase the patient's willingness to cooperate.

Thus, the process of communicating the diagnosis of MDR/RR-TB should be viewed not only as transmission of medical information, but also as a key step in fostering patient adherence to treatment, which is particularly important in the context of further analysis of the issues identified during patient interviews in the Republic of Tajikistan.

As patients come to terms with the diagnosis of MDR/RR-TB, they eventually reach the stage of gradual acceptance of their illness. With the support of healthcare professionals and loved ones, intensity of initial emotional reactions decreases, and a more rational understanding of the illness emerges. Patients start realizing that MDR/RR-TB is curable if they adhere to their treatment; they adapt to long-term treatment, and learn to structure their daily lives in accordance with medical recommendations. At the same time, patients feel a greater sense of control over their own lives and become more engaged in the treatment process. At this stage, a clear and understandable explanation of the diagnosis, as well as support from family and medical staff, play a key role in reducing anxiety and increasing adherence to treatment.

Although patients generally view their interactions with medical staff positively, noting the professionals' expertise and clarity of their explanations, a number of issues are still observed in this area. First, some patients may feel that they are not receiving personalized care, as evidenced by the formal nature of interactions and limited time allotted for consultations. This may make it difficult to ask questions and receive detailed answers, especially during the course of long-term and complex treatment for MDR/RR-TB. Second, patients report a lack of community-based support, infrequent home visits by healthcare providers, and limited interaction with primary care providers. Under these circumstances, the primary burden of care and support falls on family members.

Socioeconomic barriers also play a significant role. Patients describe a decline in income due to their loss of their ability to work, the need to take on informal employment, as well as financial difficulties related to transportation costs and food. Patients living in rural areas are particularly vulnerable, as access to medical services requires additional time and financial resources. These factors often lead to missed appointments and non-compliance with treatment regimens.

Moreover, stigma remains one of the most significant factors influencing patient behavior at all stages of treatment. It manifests itself both within the family and in the community, and in some cases, in the medical setting as well. Patients report fears of judgment, social isolation, and being shunned by those around them, which negatively affects their motivation to continue treatment; this must be taken into account when organizing medical and psychological care. At the same time, having a supportive family significantly increases the likelihood of maintaining adherence to treatment.

Clinically vulnerable groups, such as patients with problematic alcohol use and HIV coinfection, face additional challenges. According to healthcare professionals, these patients tend to show lower adherence to treatment, miss appointments, and experience more severe side effects from therapy. There is also a lack of coordination among services providing care for tuberculosis, HIV, and substance use disorders, which complicates comprehensive management of such patients.

> Organizational barriers manifest themselves as lack of coordination among different levels of the healthcare system and absence of clear patient pathways. Patients often feel uncertain after receiving the diagnosis; they do not always understand the next steps or when treatment will begin.

Despite the mechanisms for providing patients with TB medications in place, difficulties may arise in some cases due to logistical challenges in obtaining medications, the need for frequent visits to healthcare facilities, and temporary delays or disruptions in the medication distribution schedule. Patients who live in remote areas or have limited mobility and cannot afford transportation may face additional challenges.

Organizing home care is also a significant aspect of treatment of MDR/RR-TB. Not all patients receive sufficient support from their families or close circle of friends, which can make it difficult to adhere to their treatment regimen, especially when side effects occur or their condition worsens.

Thus, difficulties related to accessing medications and receiving home care can affect treatment adherence and patients' overall wellbeing, underscoring the need for further improvements to organizational and support mechanisms within the system of care for patients with MDR/RR-TB.

Healthcare workers, for their part, point to the system's overload, staff shortages, and limited resources, which affect the quality of patient care. An additional challenge is lack of training for healthcare workers in the areas of psychosocial support and management of complex cases. Although some training programs are available, they are fragmented and do not always provide the practical skills needed to effectively work with patients who have multiple vulnerabilities.

Overall, the qualitative analysis shows that the barriers faced by patients with MDR/RR-TB in Tajikistan are multifaceted and include psychological, socioeconomic, clinical, and organizational aspects. This underscores the need to implement patient-centered and crosssectoral approaches aimed at providing comprehensive support to patients throughout the entire cascade of care.

Table. 13. **Key issues identified during the focus group discussions**

Problem	Description	Consequences
Decreased adherence during long-term treatment	A significant proportion of patients may discontinue treatment in the later stages due to the length of therapy, side effects, and lack of comprehensive support.	A decrease in treatment success rates and an increased risk of community transmission of MDR/RR-TB.
Insufficient psychosocial support	Patients experience anxiety, fear, and stress, but regular psychological support is not available.	Low adherence, social isolation, and the risk of treatment discontinuation.
Socio-economic vulnerability	Loss of income, transportation and food costs, especially for rural patients.	Missed appointments and irregular treatment are associated with a high risk of poor treatment outcomes.
High levels of stigma	Stigmatization at the family, community, and sometimes healthcare provider levels leads to concealment of the diagnosis and social isolation.	Patients avoid appointments, and their motivation to complete treatment decreases.
Clinically vulnerable groups		Treatment discontinuation, delayed diagnosis, increased risk of complications.
Insufficient coordination and routing	Lack of standardized pathways, gaps between levels of the system, and delays between diagnosis and the start of treatment.	Patients "get lost" in the system, and treatment begins late, which worsens the prognosis.
Inadequate training of healthcare workers	Fragmented training, lack of skills in providing psychosocial support, and managing complex cases.	Ineffective patient follow-up, failure to detect side effects, and the risk of treatment discontinuation.
Lack of comprehensive support after treatment is completed	Patients face challenges with reintegration and anxiety about relapse.	An increased risk of relapse, poor social adjustment, and a decline in long-term outcomes.

Recommendations

Support for adherence during long-term treatment, including psychological and social support. Effective treatment of patients with MDR/RR-TB requires not only drug therapy but also a comprehensive approach that includes medical, psychological, and social interventions. Given duration of treatment, severe side effects, and the impact of the disease on daily life, patients need comprehensive support at every stage of the therapy. Comprehensive interventions that combine medical, psychological, and social support are essential for improving treatment adherence and ensuring successful completion of therapy among patients with MDR/RR-TB.

> The key areas of intervention include ensuring availability and continuity of drug therapy, providing clear and timely information about the disease and its treatment, and offering regular follow-up by healthcare professionals. An important component is psychological support aimed at reducing anxiety, overcoming stigma, and strengthening motivation to complete treatment.

Equally important is social and financial assistance, including support from family members, reimbursement of transportation and living expenses, and assistance in maintaining of or adapting to employment. Organizing home care, when necessary, and developing community-based care services make it easier for patients to adhere to their treatment regimens and improve their quality of life. Access to food aid and reimbursement of transportation costs are particularly important for patients living in rural areas. Mechanisms

for temporary financial support should be developed for patients who lost income during their treatment, and opportunities for flexible social assistance should be expanded.

This necessitates targeted identification of patients at high risk of treatment discontinuation before therapy begins and implementation of a system for ongoing patient support throughout the entire treatment period. Given adoption of innovations, treatment can be conducted remotely, for example, through telemedicine platforms. Psychological support should also be integrated into the standard of care for patients with TB. It is recommended to provide counseling at all stages of treatment, including the outpatient phase, and to expand involvement of social workers and non-governmental organizations in patient care.

Improving coordination and referral of patients to reduce delays and enhance effectiveness of care for specific vulnerable patient groups. It is recommended to optimize coordination between laboratories and clinical services, implement mechanisms for a "quick start" to treatment, and streamline the bureaucratic procedures involved in confirming the diagnosis. Standardized referral protocols should also be developed, and the role of primary health care in coordinating treatment should be strengthened. It is also necessary to ensure that patients are informed about each stage of treatment and its duration.

Patients from clinically vulnerable populations must receive multidisciplinary care, including support from addiction specialists, infectious disease specialists, and social workers.

Expansion of outpatient treatment models. It is necessary to gradually transition from a hospital-centered model to a patient-centered one, inform patients about the possibility of outpatient treatment, and revise funding mechanisms that encourage excessive hospitalizations.

Reducing stigma and discrimination. To reduce stigma, it is necessary to conduct public awareness campaigns, train healthcare workers in the principles of non-discrimination and patient-centered approaches, and develop community-based support programs for patients and their families.

Continuous education for healthcare professionals. Regular educational programs and training sessions should be implemented, with an emphasis on practical skills, including management of side effects, psychosocial support, and coordination of interdisciplinary care. It is also necessary to develop mentoring and supervision systems. This recommendation is closely linked to the recommendations based on findings of *focus group discussions with healthcare workers involved in care of patients with MDR/RR-TB* (see above).

CONCLUSIONS

This study was the first one to analyze determinants and barriers in the healthcare cascade for people with drug-resistant tuberculosis in the Eastern Europe and Central Asia region. Based on the examples of two countries – the Republic of Moldova and Tajikistan – critical stages were identified: from delays in TB diagnosis to treatment discontinuation and loss to follow-up.

> A key element was the quantitative assessment of losses in the specific cohort of patients with MDR/RR-TB, based on observations in the Republic of Moldova. It made it possible to identify the most important determinants associated with the highest risk of loss at various stages of the cascade of care and to identify groups of patients who need the most support, both during early detection of TB and in subsequent stages, including support for treatment adherence and relapse prevention. Specifically, these groups include people living with HIV and people with alcohol use disorders.

An additional advantage was use of a quality component designed to examine experiences of both those involved in implementing activities under national TB control programs (healthcare and social workers), and patients who had been treated for MDR/RR-TB or who were receiving such treatment at the time of the study. This provided a deeper understanding of the causes of losses and delays at various stages of the cascade, as well as an opportunity to explore respondents' views on what steps would be appropriate to take to improve the situation.

The authors hope that these findings will help highlight the importance of regularly evaluating the TB care continuum in order to improve the quality of care and adopt a more targeted approach to needs of the most vulnerable patient groups. Moreover, the study highlights the importance of meaningful engagement with civil society organizations and communities, which can play a key role in collecting and analyzing the data needed to make evidence-based decisions.

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