Original Article

Risk factors for treatment failure of drug-resistant pulmonary tuberculosis: results from a two-decade data analysis

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Background: Drug-resistant tuberculosis (DR-TB) remains a major public health challenge worldwide, particularly in Eastern Europe, where high disease burden and complex treatment regimens contribute to suboptimal outcomes. Lithuania has historically reported high rates of pulmonary DR-TB; however, data on long-term treatment outcomes and their determinants over extended periods are limited. This study evaluated long-term treatment outcomes among adults with pulmonary DR-TB in Lithuania over a 22-year period and assessed associations between treatment outcomes, individual risk factors, and temporal trends.

Methods: A retrospective cohort analysis was conducted using data from the National Tuberculosis Information System for 2000–2021. The study included 5,761 adults with DR-TB, categorized into three periods: Period I (2000–2007), Period II (2008–2015), and Period III (2016–2021). Treatment outcomes were classified as successful (treatment completion with recovery) or unsuccessful [treatment failure, progression to chronic TB, death before completion, or transition from multidrug-resistant tuberculosis (MDR-TB) to extensively drug-resistant tuberculosis (XDR-TB)]. Associations between outcomes and risk factors such as smoking, alcohol and substance use, comorbidities, and sociodemographic variables were examined using multivariate analysis.

Results: Treatment success rates increased steadily across periods (66.2%, 68.5%, and 79.5%), while mortality rates declined (30.7%, 29.5%, and 20.1%). Non-lethal treatment failure rates decreased markedly (3.0%, 2.0%, and 0.3%). Treatment failure was significantly associated with low body mass index, male gender, unemployment, homelessness, tobacco and alcohol use, substance abuse, and comorbidities including cancer, cardiovascular and chronic lung disease, diabetes mellitus, human immunodeficiency virus (HIV) infection, and renal failure.

Conclusions: Treatment outcomes of DR-TB in Lithuania have shown improvement over a 22-year period. Successful treatment outcomes were strongly influenced by a combination of clinical, behavioral, and socioeconomic factors, underscoring the complexity of DR-TB management. The relative importance of these components may vary for each individual patient. Incorporating multifaceted strategies, such as psychological support, social assistance (including access to food and shelter), and employment opportunities, into the national DR-TB control framework could enhance health system responsiveness and reduce inequities in care.

Keywords: Drug-resistant tuberculosis management (DR-TB management); tuberculosis risk factors; drug-resistant tuberculosis treatment outcome (DR-TB treatment outcome)

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Introduction

Tuberculosis (TB) continues to pose a significant global public health concern, especially in low- and middle-income countries where healthcare infrastructure and resources are frequently inadequate (1,2). The World Health Organization (WHO) provides standardized definitions and reporting guidelines to improve the classification and monitoring of TB cases and outcomes. "Drug-resistant TB (DR-TB)" refers to infections caused by *Mycobacterium tuberculosis* strains resistant to one or more anti-TB drugs.

Highlight box

Key findings

- Report here about the key findings of the study. Pulmonary drug-resistant tuberculosis (DR-TB) treatment failure was significantly associated with several categories of risk factors, including socioeconomic factors (male gender, unemployment, homelessness), behavioral factors (tobacco and alcohol use, substance abuse), nutritional status (low body mass index), and clinical comorbidities, such as cancer, cardiovascular and chronic lung disease, diabetes mellitus, human immunodeficiency virus (HIV) infection, and renal failure.

What is known and what is new?

- Treatment failure in pulmonary DR-TB patients arises from a complex interplay of biological, clinical, behavioral, and socioeconomic factors. While established risk factors such as HIV co-infection, diabetes, malnutrition, and substance abuse have been linked to poor treatment outcomes, their relative significance in the setting of pulmonary DR-TB has not been thoroughly investigated.
- This study investigates long-term treatment failures among adult pulmonary DR-TB patients in Lithuania from 2000 to 2021, utilizing a uniquely extensive dataset rarely available in other European countries with a medium tuberculosis incidence, and aims to identify key demographic, clinical, and social factors associated with unsuccessful treatment outcomes.

What is the implication, and what should change now?

- This study highlights the multifactorial nature of treatment outcomes among patients with DR-TB in Lithuania. Unsuccessful treatment was strongly associated with a combination of clinical, behavioral, and socioeconomic risk factors. Multivariate analysis indicated that the presence of multiple comorbidities—such as HIV infection, cancer, chronic lung disease, coronary heart disease, diabetes mellitus, and renal failure—substantially increased the likelihood of poor treatment outcomes.

DR-TB includes several subtypes: "rifampicin-resistant TB (RR-TB)", characterized by resistance to rifampicin detected by phenotypic or genotypic methods; "multidrug-resistant TB (MDR-TB)", which is resistant to at least both rifampicin and isoniazid; and "extensively drug-resistant TB (XDR-TB)", defined as MDR-TB with additional resistance to any fluoroquinolone and at least one second-line injectable agent (amikacin, kanamycin, or capreomycin) (3).

Treatment outcomes are also clearly defined by the WHO. A "successful treatment" outcome includes patients who are cured (with bacteriological confirmation of cure) or who have completed the full course of treatment. In contrast, "unsuccessful treatment" outcomes include treatment failure, death during treatment, loss to follow-up, or cases that were not evaluated (3). To improve clarity and facilitate interpretation, we present a summary table of outcome categories according to WHO definitions (*Table 1*), illustrating the composition of successful and unsuccessful outcomes.

In 2023, approximately 8.2 million new TB cases were recorded worldwide, marking an increase from 7.5 million in 2022 and reflecting a continuing rise in incidence since 2021 (4). MDR-TB/RR-TB remains a major global public health concern. According to the World Health Organization Global Tuberculosis Report 2024, the highest MDR-TB/RR-TB rates in 2023 were reported in Kazakhstan (19 cases per 100,000 population), the Russian Federation (18 per 100,000), and the Republic of Moldova (16 per 100,000) (5).

Within the European Union and European Economic Area (EU/EEA), 1,032 MDR-TB/RR-TB cases were reported in 2023, with the highest numbers observed in Romania, Germany, and Lithuania. Despite its smaller population, Lithuania reported 116 cases, corresponding to an incidence of approximately 4 cases per 100,000 population, and continues to have a TB prevalence more than three times the EU/EEA average (5). Notably, the proportion of MDR-TB among TB cases in Lithuania reaches 18%, exceeding the regional average more than fivefold (5).

Lithuania has achieved a threefold reduction in MDR-TB/RR-TB incidence over the past eight years, decreasing from 264 cases per 100,000 in 2017 to 91 cases per 100,000

Table 1 The WHO definitions

Outcome category	WHO definition/criteria	Classification
Cured	Patient completed treatment and had bacteriological confirmation of cure	Successful
Treatment completed	Patient completed treatment but without bacteriological confirmation of cure	Successful
Treatment failure	Patient's treatment regimen failed, evidenced by bacteriological persistence or worsening	Unsuccessful
Death	Patient died for any reason during TB treatment	Unsuccessful
Loss to follow-up	Patient interrupted treatment for ≥2 consecutive months	Unsuccessful
Not evaluated	Outcome unknown or patient outcome not assessed	Unsuccessful

TB, tuberculosis; WHO, World Health Organization.

in 2024, according to available data (6). Nevertheless, the improvement in the epidemiological situation of MDR-TB/RR-TB in the country has been influenced using rapid molecular diagnostics for drug resistance detection, quality case management, social support measures, and the inclusion of new and repurposed drugs in treatment regimens. Despite this progress, MDR-TB/RR-TB remains a persistent public health challenge in Lithuania.

The approval of novel anti-TB agents, including bedaquiline, delamanid, and pretomanid, has complemented substantial revisions in treatment guidelines and therapeutic regimens for DR-TB (7). These innovations have the potential to significantly strengthen TB control efforts, provided they are accessible to both patients and national programmers. Ensuring equitable access through affordable pricing of new anti-TB drugs is essential and remains a central focus of ongoing political discussions and global advocacy (8). Limited information is available regarding the availability of new and repurposed anti-TB drugs, as well as access to corresponding drug susceptibility testing (DST). Similarly, data on the cost of these medications and treatment regimen remain scarce (9,10).

Treatment failure in pulmonary DR-TB patients arises from a complex interplay of biological, clinical, behavioral, and socioeconomic factors. While established risk factors such as HIV co-infection, diabetes, malnutrition, and substance abuse have been linked to poor treatment outcomes, their relative significance in the setting of pulmonary DR-TB has not been thoroughly investigated.

In Lithuania, both drug-sensitive and DR-TB treatment are fully reimbursed, both in inpatient and outpatient settings. This discrepancy is particularly evident in medium-burden countries, such as Lithuania, where long-term data on treatment outcomes and related risk factors remain limited. Understanding these trends and associations is essential for guiding targeted interventions and improving patient management.

Therefore, this study investigates long-term treatment failures among adult pulmonary DR-TB patients in Lithuania from 2000 to 2021, utilizing a uniquely extensive dataset rarely available in other European countries with a medium TB incidence, and aims to identify key demographic, clinical, and social factors associated with unsuccessful treatment outcomes. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1-2548/rc).

Methods

Study design

Data for this study were prospectively collected through the State Tuberculosis Information System (TB Registry) beginning in 2000. The registry is managed by a dedicated team responsible for case verification and data entry, ensuring consistency, accuracy, and reliable control of potential confounders. For this analysis, data from 2000 to 2021 were extracted. In total, 37,713 patients with registered pulmonary TB were identified. The inclusion criterion was a confirmed diagnosis of DR-TB. Patients with unclear treatment outcomes, those who initially had drug-susceptible TB but later developed drug resistance, and cases with incomplete or missing data were excluded. The final analytical cohort consisted of 5,761 patients who met the inclusion criteria.

To assess temporal trends and risk factors for treatment outcomes, DR-TB cases were grouped into three periods: 2000–2007 (Period I), 2008–2015 (Period II), and 2016–2021 (Period III). The Tuberculosis Registry in Lithuania began collecting data in the year 2000. Therefore, we

selected the longest possible study period, ending in 2021, which corresponds to the timeframe during which this study was conducted. This broad timeframe was then divided into three distinct periods based on key developments in TB management: the introduction of new diagnostic methods (which improved case detection), the implementation of new laws, and improved funding for patients with TB. These changes marked important shifts in TB care and were used as criteria for defining the periods. The grouping of time periods was guided by these contextual factors, and the differences between the groups were tested for statistical significance where appropriate. Treatment outcomes were classified as successful (treatment completion with recovery) or unsuccessful (treatment failure, chronic disease, death before treatment completion, or progression from MDR-TB to XDR-TB).

Operational definitions

TB cases, medication resistance, and treatment outcomes were classified by the WHO's definitions and reporting guidelines for TB (3). The following standardized clinical definitions were applied in the Table S1.

Study population

The sociodemographic and clinical characteristics of the study population are presented in Table S1, which summarizes data from 5,039 individuals diagnosed with DR-TB in Lithuania between 2000 and 2021. The cohort is stratified into three time periods: Period I (n=2,099), Period II (n=1,869), and Period III (n=1,071).

The mean age of patients increased modestly across periods, from 46.4 years in Period I to 47.6 years in Period III (P=0.03). The proportion of younger patients (0–30 years) declined over time, and age stratification into 0–29, 30–49, and 50+ years categories revealed a statistically significant shift in age distribution (P=0.008). Gender distribution remained stable, with approximately 75% male and 25% female participants across all periods (P=0.77). A slight but statistically significant increase in rural residence was observed in Period III (42.6% *vs.* 36.7% in Period I; P=0.005) (Table S1).

All patients had culture-confirmed TB. Smear microscopy results were consistent across the three periods, with no significant differences in positivity rates (P=0.54). Comorbidities were identified using International Classification of Diseases (ICD) codes: coronary heart disease (CHD) (codes starting with I), chronic lung diseases (J44, J40, J42, J43, J47), diabetes mellitus (E10–E14), oncological conditions (codes starting with C), liver diseases (K71, K72), and kidney diseases (codes beginning with N). However, the prevalence of several comorbidities increased notably in Period III. These included CHD (3.1% *vs.* 1.9% in Period I; P<0.001), chronic lung diseases (2.8% *vs.* 3.8%; P<0.001), diabetes mellitus (3.5% *vs.* 1.9%; P=0.005), oncological diseases (3.2% *vs.* 0.1%; P<0.001), liver diseases (0.4% *vs.* 0.0%; P=0.01), and kidney diseases (1.2% *vs.* 0.2%; P<0.001). HIV positivity also increased significantly, from 0.5% in Period I to 3.7% in Period III (P<0.001) (Table S1).

Lifestyle and socioeconomic factors showed notable variation over time. Educational attainment differed significantly across periods (P<0.001). Secondary education remained the most common level attained by participants, peaking at 48.5% in Period III. Conversely, the proportions of participants with higher education or vocational training decreased during the same period. There was a slight improvement in employment status; in Period III, 26.4% of individuals reported being employed or engaged in irregular work, compared to 20.3% in Period I (P<0.001). The prevalence of smoking has remained consistently high at around 71% across all periods, showing no significant temporal variation (P=0.18). In contrast, patterns of alcohol consumption have changed: the proportion of non-drinkers increased from 18.2% in Period I to 27.9% in Period III, while heavy drinking decreased from 46.3% to 36.3% (P<0.001). Substance use also increased over time, rising from 1.1% in Period I to 3.6% in Period III (P<0.001) (Table S1).

Significant changes in TB-related indicators were also observed. The proportion of new TB cases increased substantially over time—from 58.4% in Period I to 81.0% in Period III (P<0.001). However, contact tracing remains suboptimal. The proportion of patients with a known source of TB contact decreased over time, with the highest rate of unknown contact status reported in Period II (92.0%; P<0.001) (Table S1).

Statistical analysis

All collected data were anonymized and entered into a Microsoft Excel database. Statistical analyses were performed using R statistical software version 4.5.1. Descriptive statistics—frequencies, proportions, medians, and interquartile ranges (IQRs)—were used to summarize sociodemographic and clinical characteristics.

Categorical variables were compared using Pearson's

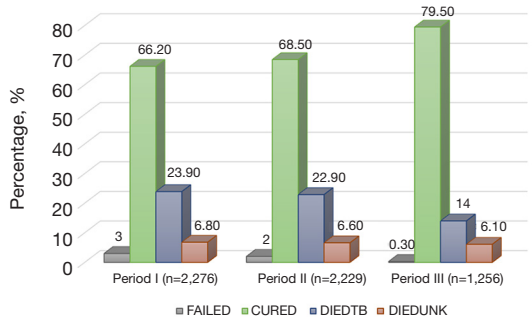

Figure 1 Drug-resistant pulmonary tuberculosis treatment outcomes. Period I: 2000–2007; Period II: 2008–2015; Period III: 2016–2021. CURED, completed tuberculosis treatment; DIEDTB, died from tuberculosis; DIEDUNK, died from other causes; FAILED, tuberculosis treatment failure.

Chi-squared test or Fisher's exact test, as appropriate. Continuous variables were analyzed using the Student's *t*-test or the Mann-Whitney U test for two-group comparisons, depending on the distribution of data. For comparisons involving more than two groups, one-way analysis of variance (ANOVA) was used; when normality or homoscedasticity assumptions were violated, the Kruskal-Wallis test was applied.

Univariable logistic regression was performed to evaluate associations between treatment outcomes and potential explanatory variables, including age, sex, smoking status, alcohol misuse, substance use, comorbidities, HIV status, education level, prior TB treatment, and drug susceptibility. Variables with P<0.05 in univariable analysis were included in multivariable logistic regression, restricted to patients with complete data. Collinearity was assessed using the variance inflation factor (VIF), and variables with high collinearity (VIF >5) were excluded from the model simultaneously. Demographical variables (age, sex) were included in the final model regardless of univariable P value. The analyses were stratified by study period to reflect changes in treatment regimens. Subsample analyses were conducted using hospital routine data for variables not available in the national database. Firth's logistic regression was applied in subsample analyses with small sample sizes to ensure robust estimation. Additionally, odds ratios (ORs) with 95% confidence intervals (CIs) were presented. An OR >1 indicates increased odds of the outcome compared to the reference group, while an OR <1 indicates reduced odds. A 95% CI excluding 1 denotes statistical significance. The TB registry is managed by the same team responsible for verifying each case and entering the data, which helps ensure consistency and accuracy in handling potential confounders.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This study was approved by the Regional Biomedical Research Ethics Committee of Vilnius University (approval date: March 30, 2023; Protocol No. 158200-13-652-210; Addendum No. 2023-LP-28). In accordance with the Lithuanian Law on Biomedical Research Ethics, the requirement for informed consent was waived due to the study's retrospective nature. To maintain anonymity, the data were encrypted, and access was restricted to authorized personnel only, ensuring patient confidentiality after anonymization.

Results

Sociodemographic and clinical attributes of study participants

The treatment outcomes for pulmonary DR-TB showed a consistent and encouraging improvement across the three study periods. In Period I, 1,507 of 2,276 patients (66.2%) successfully completed treatment. This proportion increased in Period II, with 1,526 of 2,229 patients (68.5%) achieving treatment success, and further improved in Period III, where 999 of 1,256 patients (79.5%) completed treatment (*Figure 1*).

Conversely, the mortality rate among pulmonary DR-TB patients showed a gradual decline. In Period I, 700 patients (30.7%) died during treatment, compared to 658 (29.5%) in Period II and 253 (20.1%) in Period III (*Figure 1*).

The incidence of treatment failure remained low and stable across all periods: 69 cases (3.0%) in Period I, 45 cases (2.0%) in Period II, and 4 cases (0.3%) in Period III (*Figure 1*).

Further analysis identified several risk factors significantly associated with treatment failure in DR-TB patients. These include older age, co-infection with HIV, a history of previous TB treatment, and socioeconomic factors such as malnutrition and substance use. A comprehensive summary of treatment outcomes across the three periods is illustrated in *Figure 1*, providing a visual depiction of trends to enhance interpretability.

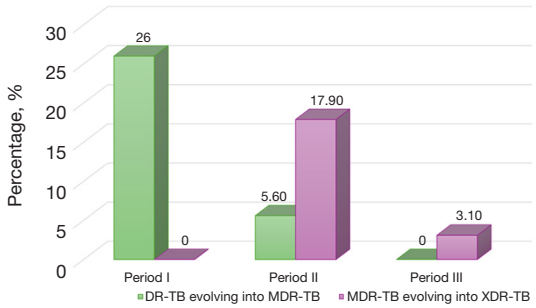

Figure 2 Trends in the progression of drug-resistant tuberculosis to MDR-TB and XDR-TB across the three study periods. Period I: 2000–2007; Period II: 2008–2015; Period III: 2016–2021. DR-TB, drug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis; XDR-TB, extensively drug-resistant tuberculosis.

Moreover, the progression of DR-TB cases to MDR-TB demonstrated a marked reduction, declining from 26% in Period I to 5.6% in Period II, and reaching 0% in Period III. However, no consistent trend was observed in the progression from MDR-TB to XDR-TB, which increased from 0% in Period I to 17.9% in Period II, before declining to 3.1% in Period III (*Figure 2*).

Factors associated with TB unsuccessful treatment

A comparative analysis of sociodemographic, clinical, behavioral, and social characteristics was conducted among patients with successful and unsuccessful TB treatment outcomes in Lithuania across three time periods (2000–2008, 2009–2015, and 2016–2021; in the Tables S2-S5). Across all periods, multiple statistically significant differences were observed between the two outcome groups, highlighting persistent and evolving risk factors associated with unsuccessful treatment.

- Age and gender: patients with treatment failure were consistently older than those with treatment success, with mean age increasing over time (49.9 → 51.2 → 54.9 years). Male sex was more prevalent in the failure group, significantly so in the first two periods.
- Microbiological indicators: microscopy positivity was higher among patients with successful treatment, particularly in 2000–2008, while culture positivity was universal due to inclusion criteria.
- Comorbidities: CHD, cancer, kidney disease, and HIV co-infection were consistently associated with treatment failure, with some conditions (e.g., kidney disease) emerging as significant only in later periods. Diabetes and liver disease were not significant predictors.
- Social factors: low educational attainment, unemployment, and homelessness were strongly linked with treatment failure in all periods. Place of residence (urban *vs.* rural) did not show consistent effects.
- Harmful habits: alcohol abuse, smoking, and non-alcohol substance use were more common in patients with unsuccessful treatment, with some risk factors becoming more pronounced in recent years.
- TB history and drug resistance: relapse or return TB cases, as well as MDR-TB and extensively XDR-TB, were significantly associated with treatment failure. XDR-TB rates increased over time in the failure group.
- Risk factors from multivariable analysis: univariate logistic regression identified older age, male sex (Period I–II), comorbidities (CHD, cancer, kidney disease, HIV), harmful habits, low education, unemployment, homelessness, and prior TB treatment as significant predictors of unsuccessful treatment (*Table 2*). Overall, the proportion of unsuccessful treatment declined over time (33.8% → 31.5% → 20.5%), reflecting improvements in TB management, though vulnerable subgroups remained at high risk.

This analysis demonstrates a multifactorial landscape of risk for pulmonary DR-TB unsuccessful treatment, emphasizing the importance of personalized interventions targeting clinical, behavioral, and social determinants.

Body mass index (BMI)

Because BMI and duration of hospitalization were not available in the national database, subsample analyses were conducted among patients with available hospital routine data, using a limited set of variables and the same modeling approach. These analytical steps have been clarified in the Methods section to improve transparency. To maintain focus on the primary study objectives, the additional multivariable model including all patients was removed, as BMI analyses were restricted to the subsample. The complete subsample results are now provided in Tables S6,S7.

In univariate Firth's logistic regression analysis, low BMI (<18 kg/m^2) was significantly associated with the outcome in Period I (OR =14.49; 95% CI: 2.56–112.73; P=0.002) and

Table 2 Demographic, clinical, and laboratory characteristics of the study patients: univariate logistic regression (N=5,761)

Risk factor	Period I (N=2,276)		Period II (N=2,229)		Period III (N=1,256)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age (OR per 1-year increase)	1.03 (1.02–1.04)	<0.001	1.03 (1.03–1.04)	<0.001	1.05 (1.04–1.06)	<0.001
Age (OR per 10-year increase)[†]	1.33 (1.25–1.42)	<0.001	1.4 (1.32–1.5)	<0.001	1.56 (1.41–1.74)	<0.001
Aged 50 years and above	1.87 (1.57–2.23)	<0.001	2.16 (1.8–2.59)	<0.001	2.52 (1.9–3.35)	<0.001
Coronary heart disease	–	–	8.82 (2.79–38.8)	<0.001	7.38 (3.90–14.5)	<0.001
Chronic lung disease	1.74 (1.12–2.69)	0.01	1.78 (0.92–3.38)	<0.001	–	–
Diabetes mellitus	1.50 (0.81–2.73)	0.19	–	–	1.58 (0.77–3.06)	0.19
Cancer disease	–	–	3.76 (1.74–8.55)	<0.001	14.0 (6.79–31.7)	<0.001
Kidney disease	–	–	5.46 (1.17–38.2)	<0.001	3.98 (1.45–10.9)	0.006
Liver disease	–	–	–	–	–	–
HIV	2.96 (1.06–8.87)	0.040	3.58 (2.10–6.24)	<0.001	2.77 (1.50–5.01)	<0.001
Smoking	2.21 (1.80–2.72)	<0.001	1.88 (1.51–2.34)	<0.001	–	–
Excessive alcohol consumption	4.38 (3.32–5.84)	<0.001	2.90 (2.19–3.88)	<0.001	1.93 (1.37–2.74)	<0.001
Moderate alcohol consumption	–	–	–	–	–	–
Substance use	2.78 (1.24–6.47)	0.01	2.81 (1.62–4.94)	<0.001	2.15 (1.10–4.03)	0.02
Low level of education[‡]	1.62–2.79 (1.03–4.77)	<0.001	3.61–4.57 (2.14–6.53)	<0.001	1.94–4.12 (0.96–10.6)	<0.001
Unemployment	4.98 (3.70–6.84)	<0.001	4.29 (3.17–5.93)	<0.001	4.78 (3.04–7.92)	<0.001
Homelessness	4.59 (2.79–7.79)	<0.001	2.41 (1.61–3.62)	<0.001	3.01 (1.76–5.06)	<0.001
Living in a rural area	–	–	–	–	–	–
TB relapse	5.29 (4.39–6.40)	<0.001	4.71 (3.90–5.72)	<0.001	1.99 (1.50–2.64)	<0.001
Male sex	2.40 (1.40–1.82)	<0.001	2.02 (1.61–2.55)	<0.001	1.47 (1.06–2.08)	0.03
Unsuccessful treatment, n (%)	769 (33.8)	–	703 (31.5)	–	257 (20.5)	–

[†], the underlying variable is identical to that reported above; only the unit of increase (per 10 years) differs for interpretability of the OR; [‡], indicates a range of ORs in this row. CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; TB, tuberculosis.

Period III (OR =7.86; 95% CI: 1.64–46.19; P=0.009), whereas the association in Period II did not reach statistical significance (OR =3.10; 95% CI: 0.63–19.86; P=0.17) (Table S6). After adjustment for age, duration of hospitalization, TB relapse, and sex, low BMI remained independently associated with the outcome in Period I (OR =7.80; 95% CI: 1.24–68.7; P=0.03) and Period III (OR =5.62; 95% CI: 1.20–31.8; P=0.03), but not in Period II (OR =1.87; 95% CI: 0.20–18.8; P=0.56) (Table S7).

Risk factors for unsuccessful drug-resistant pulmonary TB treatment outcomes: an univariable analysis across three periods

This study presents a univariable analysis of risk factors associated with unsuccessful treatment outcomes in patients with pulmonary DR-TB in Lithuania across three distinct time periods: 2000–2007, 2008–2015, and 2016–2021. The results highlight consistent and evolving predictors across clinical, behavioral, and socioeconomic domains, offering insight into the changing epidemiological and healthcare landscape. Additionally, ORs with 95% CIs were presented. An OR >1 indicates increased odds of the outcome compared to the reference group, while an OR <1 indicates reduced odds. A 95% CI excluding 1 denotes statistical significance.

In the first period (n=2,276), older age (OR =1.03; 95% CI: 1.02–1.04; P<0.001), male sex (OR =2.40; 95% CI: 1.92–3.03; P<0.001), and a positive microscopy result (OR =2.61; 95% CI: 2.08–3.28; P<0.001) significantly increased

the risk of treatment unsuccess. Social factors played a crucial role: unemployment (OR =4.98), homelessness (OR =4.59), and low education levels (e.g., no schooling or primary education: OR =2.79) were all strongly associated with poor outcomes (P<0.001). Additionally, heavy alcohol use (OR =4.38), drug use (OR =2.78), HIV infection (OR =2.98), and smoking (OR =2.21) were statistically significant behavioral risk factors. Among comorbidities, liver disease, kidney disease, and cardiovascular disease were not statistically significant during this period (Figure S1).

In the second period (n=2,229), the strength of association increased for multiple comorbidities. CHD was associated with poor outcomes in a powerful manner (OR =8.82; 95% CI: 2.79–38.8; P<0.001). Cancer (OR =3.76), kidney disease (OR =5.46), and HIV infection (OR =3.58) also emerged as significant predictors. Socioeconomic vulnerabilities remained critical: unemployment (OR =4.29), homelessness (OR =2.41), and lower education (OR range, 2.91–4.57) were all independently associated with an increased risk of treatment failure (P<0.001). Behavioral risks included heavy alcohol use (OR =2.90), smoking (OR =1.88), and drug addiction (OR =2.81), while rare alcohol use was not statistically significant. Patients with relapsed TB had 4.71 times higher odds of poor outcomes compared to new cases (Figure S2).

In the most recent period (n=1,256), the risk associated with age remained consistent (OR =1.05; P<0.001), while cancer (OR =14.0; 95% CI: 6.79–31.7) and CHD (OR =7.38; P<0.001) became even more prominent as predictors. Additional significant comorbidities included liver disease (OR =11.8; P=0.03) and kidney disease (OR =3.98; P=0.006). Behavioral risk factors such as heavy alcohol consumption (OR =1.93; P<0.001) and drug addiction (OR =2.15; P=0.02) continued to show strong associations. Male sex remained a risk factor (OR =1.47; P=0.03), though the effect size decreased compared to earlier periods. Unemployment (OR =4.78; P<0.001), homelessness (OR =3.01; P<0.001), and low education (OR for no schooling =4.12) were again significantly linked to poor outcomes. Patients with previous TB treatment (relapses) had twice the odds of treatment failure (OR =1.99; P<0.001). Living in a rural area, diabetes, and smoking were not significantly associated with poor outcomes in this period (Figure S3).

Across all three periods, older age, male sex, relapsed TB, low education, unemployment, homelessness, heavy alcohol use, and drug addiction consistently emerged as key risk factors. However, the strength of association for clinical comorbidities, particularly cancer, cardiovascular disease, and kidney disease—increased over time. There were noticeable improvements in TB care overtime, reflected in reduced treatment unsuccess rates and better health indicators (e.g., lower alcohol use, improved education, increased employment). This analysis underscores the complex interplay between clinical, behavioral, and social factors in determining DR-TB treatment outcomes. The growing influence of comorbidities over time emphasizes the need for integrated care approaches, while the sustained association of social determinants necessitates targeted public health interventions aimed at addressing structural inequalities.

Discussion

Trends in pulmonary DR-TB cases and treatment outcomes

Over the past 22 years, our study demonstrates a consistent decline in pulmonary DR-TB cases. In parallel, the treatment failure rate for DR-TB fell from 3% in the initial Period to 2% in the second, and further to just 0.3% in the most recent phase. These trends reflect significant progress in TB management, with fewer treatment failures and steadily improving outcomes for patients with pulmonary DR-TB.

Key clinical risk factors

The composite outcome of "unsuccessful treatment" follows WHO surveillance definitions, it combines heterogeneous events (including treatment failure, death during treatment, and progression from MDR-TB to XDR-TB) with distinct etiologies. As a result, outcome-specific associations may be masked, and findings should be interpreted as relating to overall unfavorable treatment outcomes rather than specific causal pathways. The key findings of our study are that the leading associations of pulmonary DR-TB treatment failure are low BMI, male sex, older age, comorbidities (CHD, chronic lung disease, diabetes mellitus, oncological diseases, kidney disease, HIV), social factors (low education, lack of employment, lack of housing, smoking), and TB relapse. Other important risk factors: substance use, excessive alcohol consumption (less significant than the leading associations). These are discussed below.

Low BMI: our findings further underscore that low BMI (<18 kg/m^2) substantially contributes to treatment failure in DR-TB. A meta-analysis of DR-TB patients in Ethiopia

found that a BMI below 18.5 kg/m^2 was associated with more than double the risk of poor treatment outcomes (risk ratio ≈2.45, 95% CI: 1.16–5.17) (11). An extensive cohort study from China on MDR- and XDR-TB reported that BMI <18.5 kg/m^2 independently increased the odds of poor outcomes (OR ≈2.19, 95% CI: 1.37–3.48) (12). In Uganda, among patients with DR-TB and BMI <18.5 kg/m^2, all cases of treatment failure occurred in those with severe undernutrition—highlighting the critical impact of low BMI on failure risk (13). A Korean study of 89,150 TB patients found that male sex, current smoking, and multiple underlying diseases were associated with lower treatment success [adjusted OR (aOR) 0.66 for men *vs.* women] and that drug-resistant status and multiple comorbidities were significant predictors of unfavorable outcome (14). Another study analyzing the overweight status in pulmonary TB patients also highlighted the importance of BMI in treatment outcomes (15)—emphasizing that both low and high extremes of body mass can influence prognosis. We recommend that patients with low BMI receive nutritional support, particularly increased high-quality protein intake.

Male sex and older age: male sex and advancing age, particularly among patients aged over 40–45 years, were significant predictors of treatment failure in DR-TB. These findings align with previous research from Xi'an, China, where male patients had approximately 2.5 times the odds of unfavorable outcomes, and individuals over 40 had more than triple the risk (aOR ≈3.25) (14). Systematic reviews have similarly identified male sex [hazard ratio (HR) ≈1.25] and older age (HR ≈2.13) as independent risk factors for poor DR-TB outcomes (16,17). Additionally, cohort data from the Kyrgyz Republic reported increased rates of unsuccessful treatment among men and patients aged 45 years and above (18). A retrospective study of MDR/RR-TB patients treated between 2011–2017 found older age and comorbidities to be key predictors of death during treatment [median age of deaths 62 years, adjusted HR (aHR) for age 1.06] (19). In addition, a Korean cohort of MDR/RR-TB patients found that older age and multiple comorbidities increased mortality during treatment (20). Another study of patients lost to follow-up and not evaluated compared to MDR/RR-TB cases highlighted male predominance and older age as risk factors for adverse outcomes (21). These results underscore the importance of implementing directly observed treatment (DOT) and enhanced adherence strategies, particularly for older adults and male patients, to improve outcomes.

Comorbidities: several comorbidities emerged as significant risk factors for TB treatment failure in our study. For example, in our study, HIV co-infection was identified as an important independent predictor of treatment failure in DR-TB. This finding is consistent with data from the Eastern Cape, South Africa, where untreated HIV infection was associated with a markedly lower treatment success rate and nearly a tenfold reduction in the odds of success compared to HIV-negative individuals (OR =10.24) (22). Similarly, cohort studies from Johannesburg highlighted additional risk factors among HIV-positive patients with MDR-TB, including severe anemia and the presence of comorbidities, which further compromised treatment outcomes (23). Systematic reviews conducted across Africa and Asia have also reported significantly lower treatment success rates and higher mortality among HIV co-infected patients (24). Furthermore, a large meta-analysis confirmed a strong association between HIV infection and MDR-TB (OR ≈1.42), with an even greater risk observed among patients over 40 years of age (OR ≈1.56) (25). These findings reinforce the importance of integrated TB-HIV management strategies, with particular emphasis on early antiretroviral therapy initiation, close clinical monitoring, and nutritional and psychosocial support to improve treatment adherence and outcomes in this high-risk population.

In our study, chronic kidney disease (CKD) emerged as a significant independent predictor of treatment failure in DR-TB. This is consistent with findings from a cohort in West Java, Indonesia, where CKD was associated with a significantly reduced likelihood of successful MDR-TB treatment [risk ratio (RR) ≈0.62; P=0.02] (26). Similarly, a study in Taiwan (China) reported a 3.65-fold increased risk of severe drug-related adverse events and mortality among MDR-TB patients with CKD (95% CI: 1.71–7.76) (27). In Japan, advanced renal dysfunction [estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2] was independently linked to poor TB treatment outcomes, with an aOR of ~0.20 for treatment success and ~2.99 for mortality (28). Chinese cohort data further demonstrated that CKD stages 4–5 and hemodialysis were significantly associated with higher treatment failure and mortality rates (HR ≈4.7–6.1), particularly in patients with hypoalbuminemia and older age (29). These findings highlight the importance of renal function monitoring, individualized drug dosing, and comprehensive supportive care in improving treatment outcomes among DR-TB patients with CKD.

Diabetes mellitus co-infection was identified as a significant independent predictor of treatment failure in patients with DR-TB. This finding aligns with existing

literature, including a meta-analysis of 25 studies involving 16,905 DR-/MDR-TB patients—1,952 of whom had diabetes mellitus—which reported that diabetes was associated with increased odds of treatment failure (OR 1.28, 95% CI: 1.03–1.58), as well as significantly lower cure and treatment completion rates (30). In MDR-TB subgroups, the pooled OR for treatment failure was 1.37 (95% CI: 1.08–1.75), and for overall unsuccessful outcomes, 1.57 (95% CI: 1.20–2.04) (30). Similarly, a cohort study from Armenia found that diabetes mellitus was strongly associated with treatment failure, with an aOR of 8.99 (95% CI: 2.51–32.23) (31). These findings reinforce the evidence from our study that diabetes is a critical risk factor for poor TB treatment outcomes and underscore the need for integrated management strategies addressing both TB and metabolic comorbidities.

Cancer comorbidities emerged as independent predictors of both treatment failure and increased mortality among DR-TB/MDR-TB patients. This finding is supported by national cohort data from Poland, where cancer was significantly associated with reduced treatment success and higher mortality rates, even after adjusting for other comorbidities such as HIV, diabetes, alcoholism, and immunosuppressive therapy (32). Similarly, a cohort of 228 MDR/XDR-TB patients assessed using the Charlson Comorbidity Index—which assigns high weights to cancers, including leukemia, lymphoma, and metastatic tumors—demonstrated that the presence of malignancies substantially contributed to poor treatment outcomes and elevated mortality risk, despite specific ORs not being reported (33). Together, these converging lines of evidence reinforce our results and underscore the urgent need for integrated management approaches that address both DR-TB and cancer.

In our study, chronic pulmonary disease was identified as an independent predictor of treatment failure and adverse outcomes among patients with DR-TB/MDR-TB. This finding aligns with broader respiratory disease literature, which has shown that chronic obstructive pulmonary disease (COPD) is independently associated with an elevated risk of developing active TB, with adjusted HRs ranging from 1.4 to 3.1 in cohort studies controlling for age, sex, and other comorbid conditions (34). Supporting this, data from Zhejiang Province, China, demonstrated that chronic lung disease remained significantly associated with poor DR-TB treatment outcomes even after adjustment for confounding variables such as age, previous TB treatment, and disease severity (35). Further evidence from China indicates that among pulmonary TB patients with coexisting COPD, the risk of MDR-TB and fluoroquinolone resistance is significantly increased, independent of classical risk factors such as cavitary lesions and prior treatment history (36). Additionally, a cross-sectional study of MDR-TB survivors in Uganda reported a high prevalence of COPD (23%), with many patients experiencing substantial physical and psychological impairment due to persistent airflow limitation, despite achieving microbiological cure (37). Collectively, these findings support our results and underscore the need for integrated clinical strategies that address the dual burden of chronic pulmonary disease and DR-TB.

CHD and broader cardiovascular comorbidities were identified as independent predictors of treatment failure and adverse outcomes among patients with DR-TB/MDR-TB. This finding is supported by an extensive cohort analysis involving 9,600 TB patients, which demonstrated that individuals with cardiovascular disease complications, including CHD, had significantly lower odds of achieving treatment success (aOR 0.59; 95% CI: 0.42–0.83) compared to those without chronic comorbidities (38). Additionally, meta-analytic evidence indicates that TB is associated with a 1.76-fold increased risk of developing CHD (95% CI: 1.05–2.95) (39). Studies conducted in TB-endemic regions further support this association, revealing that latent TB infection is independently linked to a higher prevalence of subclinical coronary artery disease, with an aOR of 4.96 (95% CI: 1.05–23.44) after adjusting for conventional cardiovascular risk factors (40). Collectively, these findings highlight CHD as a clinically significant comorbidity in the context of DR-TB and underscore the importance of integrated care models that address both cardiovascular and infectious disease management to improve patient outcomes.

Based on these findings, we advocate for the integration of comprehensive comorbidity management, especially targeting CHD, chronic pulmonary disease, cancer, diabetes mellitus, CKD, and HIV—within standard TB treatment protocols. Our results are consistent with prior studies and underscore the critical importance of personalized, multidisciplinary care strategies in mitigating treatment failure and improving outcomes among high-risk populations.

Social and behavioral determinants

Low education

A low level of education was found to be an independent predictor of treatment failure among patients with pulmonary DR-TB. This finding is consistent with evidence

from multiple settings. For example, a cohort study from Ghana reported that patients with less than a high school education had reduced odds of treatment success (aOR ≈1.12) (41). Similarly, a Chinese cohort study showed that individuals with at least a junior high school education were significantly more likely to achieve favorable outcomes (aOR =3.60; 95% CI: 1.04–12.5) (42). Furthermore, a multivariable risk model developed across the Asia-Pacific region identified low education as one of the strongest predictors of poor outcomes in DR-TB patients, suggesting that it is closely linked to lower financial resources and poor treatment adherence (43). Together, these findings reinforce our own results, underscoring that limited education is a significant and independent risk factor for unsuccessful DR-TB treatment outcomes.

Unemployment

Unemployment was identified as a significant independent predictor of treatment failure among pulmonary DR-TB patients. This finding is consistent with several international studies highlighting the socioeconomic challenges faced by unemployed individuals during TB treatment. For instance, a study conducted in Thailand found that unemployment was associated with a 3.12-fold increased risk of unsuccessful treatment outcomes (aHR =3.12; 95% CI: 1.41–6.86) (44). Similarly, research from Sudan reported that unemployment was a significant risk factor for treatment default, with an OR of 1.9 (45). Additionally, a study in Poland observed that over 60% of DR-TB patients were unemployed, and this group experienced more advanced disease, higher rates of treatment interruption, and increased mortality (46). These findings underscore the substantial influence of socioeconomic factors, including employment status, on treatment outcomes. Unemployment often correlates with limited access to healthcare, financial constraints, and reduced adherence to treatment protocols, all of which can contribute to unfavorable TB treatment outcomes. Addressing these socioeconomic factors through targeted interventions could enhance treatment success rates and reduce the burden of DR-TB.

Homelessness

Homelessness was identified as a significant independent predictor of treatment failure among pulmonary DR-TB patients. This finding is consistent with several international studies highlighting the challenges faced by individuals experiencing homelessness in adhering to TB treatment regimens. For instance, a survey conducted in Busan, South Korea, found that homeless patients had a treatment failure rate 4.77 times higher than those residing in shelters or facilities (OR =4.77; 95% CI: 2.05–11.10; P<0.001) (47). Similarly, research from São Paulo, Brazil, reported that homelessness was associated with a 4.96-fold increased risk of unsuccessful treatment outcomes (aOR =4.96; 95% CI: 4.27–5.76; P<0.001) (48). A scoping review further supports these findings, indicating that homelessness is associated with a 3.2-fold increase in the odds of unsuccessful treatment outcomes (OR =3.23) (49). These studies underscore the vital role of stable housing in achieving successful TB treatment outcomes. Homeless individuals often face barriers such as limited access to healthcare, poor nutrition, substance abuse, and lack of social support, all of which can impede treatment adherence and increase the risk of treatment failure. Addressing these social factors through integrated healthcare and social support services is crucial for improving treatment outcomes among this vulnerable population.

Tobacco smoking

Tobacco smoking was identified as a significant independent predictor of treatment failure in pulmonary DR-TB patients. This finding aligns with a global meta-analysis showing that smoking increases the odds of DR-TB (OR ≈1.57; 95% CI: 1.33–1.86) and MDR-TB specifically (OR ≈1.49; 95% CI: 1.19–1.86) (50). A study of 89,150 TB patients found that current smoking status was associated with lower treatment success (aOR 1.40 for never smoker's *vs* current smokers) (14). Consistent with this, a cohort study in Georgia reported an elevated risk of poor TB treatment outcomes among current smokers (adjusted RR ≈1.70; 95% CI: 1.00–2.90) (51). While a case–control study in Brazil found that smoking more than doubled the odds of treatment failure (aOR ≈2.1; 95% CI: 1.1–4.1) (52). Similarly, a Moroccan cohort study found an aOR of 2.25 (95% CI: 1.06–4.76) for failure among smokers (53). These findings underscore the detrimental impact of tobacco use on TB treatment success. We therefore recommend that TB treatment programs integrate targeted behavioral and psychological support for smoking cessation, as part of a comprehensive strategy to improve treatment adherence and outcomes among patients with pulmonary DR-TB.

Substance use

Substance use was identified as a significant independent predictor of treatment failure among pulmonary DR-TB patients. This finding is consistent with a retrospective cohort study conducted in Tel Aviv, Israel, which reported that

substance use was associated with 4.0-fold increased odds of treatment failure (OR =4.0; 95% CI: 1.0–16.0) (54). In Korea, an extensive online data analysis of public perceptions and barriers between 2002 and 2024 highlighted increased queries relating to substance use and TB treatment adherence, indicating persistent behavioral risk factors (55). Furthermore, a study in Ethiopia identified that khat chewing was independently associated with unfavorable treatment outcomes, with an aOR of 3.01 (95% CI: 1.06–8.59) (56). These studies underscore the critical role of substance use in influencing treatment outcomes for DR-TB patients. Addressing substance use through integrated care models that combine TB treatment with substance use treatment and support services is essential to improve treatment adherence and overall success rates.

Excessive alcohol consumption

Excessive alcohol consumption emerged as a significant independent predictor of treatment failure among pulmonary DR-TB patients. This aligns with findings from a comprehensive meta-analysis, which reported that alcohol use more than doubles the odds of poor outcomes in DR-TB (OR ≈2.00; 95% CI: 1.73–2.32) and increases the likelihood of treatment failure (OR ≈1.54; 95% CI: 1.09–2.17) (57). Another cohort of TB survivors found that incident depression was significantly associated with past heavy drinking and prior TB treatment—underscoring the interplay between alcohol use, mental health, and TB outcomes (58). Additionally, a prospective cohort study of Indian male TB patients found unhealthy alcohol use independently elevated the risk for unfavorable outcomes [adjusted incidence rate ratio (aIRR) ≈1.47; 95% CI: 1.05–2.06] and death (aIRR ≈1.90; 95% CI: 1.08–3.34) (59). Furthermore, a Georgian cohort demonstrated that excessive alcohol uses significantly increased the risk of loss to follow-up—a key contributor to treatment failure—in DR-TB cohorts (60). These findings underscore the substantial impact of alcohol use on treatment adherence and outcomes. As such, we recommend integrating structured psychological counseling and addiction support into DR-TB care for individuals with alcohol use disorders. In severe cases, inpatient management may be necessary to ensure adherence and optimize treatment success.

Programmatic and national TB control implications

In the Lithuanian context, several concrete and actionable steps have already been implemented through national policy frameworks. By implementing Lithuania's 2014–2025 National Progress Program for Health (61) and the 2014–2023 Action Plan for Reducing Health Inequalities (62), substantial improvements in TB care have been achieved. These initiatives strengthened TB diagnostics and treatment delivery, including the introduction and expansion of the Directly Observed Treatment, Short course (DOTS) strategy, improved access to social support services for vulnerable populations, and enhanced coordination between health and social care sectors. Our findings support the continued prioritization of these programs, particularly focusing on early identification of socially vulnerable patients, integration of targeted social support measures, and monitoring measurable treatment outcome indicators to further improve DR-TB control.

This study evaluated DR-TB treatment outcomes across three defined periods, providing valuable insights into the evolving epidemiological and programmatic landscape of TB control in Lithuania. By analyzing all nationally registered DR-TB cases over the past two decades, the study offers a comprehensive assessment of treatment effectiveness and identifies systemic gaps in care delivery. Key risk factors and barriers to treatment success—particularly among patients with MDR-TB and XDR-TB—were identified and examined. Given the paucity of research focusing on DR-TB outcomes in Lithuania, these findings represent a significant contribution to understanding the factors of treatment success and failure, as well as to guiding future strategies for improved case management, targeted resource allocation, and sustained strengthening of the national TB control program.

Despite advances in diagnostic technologies and expanded access to second-line treatment regimens, DR-TB control in Lithuania remains constrained by limited integration between clinical services and broader social support systems. Persistent socioeconomic challenges—such as unemployment, unstable housing, and substance use disorders—continue to hinder treatment adherence and contribute to suboptimal outcomes. While addiction treatment and psychosocial support services are available, their integration into the national TB framework remains insufficient, limiting their potential impact on improving DR-TB management.

Future directions

To further improve treatment outcomes and reduce the burden of DR-TB, future control strategies in Lithuania should prioritize comprehensive, patient-centered, and

contextually tailored interventions. Key priorities include:

- Integration of DR-TB services with social and mental health programs that address housing instability, unemployment, and substance use.
- Expansion of community-based adherence supports mechanisms, including peer counseling and mobile outreach for individuals facing barriers to consistent care.
- Provision of targeted nutritional and psychological assistance to improve treatment tolerance and patient well-being throughout lengthy therapeutic regimens.
- Development of multidisciplinary care models to manage comorbidities and overlapping social vulnerabilities among DR-TB patients.
- Strengthening of infection prevention and control measures alongside systematic contact investigation to curb the spread of resistant strains.

The adoption of these multifaceted strategies is essential to addressing the complex interplay between biological, clinical, and social factors of DR-TB outcomes. A more integrated and holistic approach—linking biomedical interventions with social and community-based support—will be pivotal to accelerating Lithuania's progress toward the national and global goals of TB elimination.

Strengths and limitations

Strengths of the study

- Large national cohort with an extended observation period;
- Use of registry-based data, reducing the risk of selection bias;
- Combined analysis of temporal trends and individual-level risk factors;
- High practical relevance for TB control and healthcare policy.

Limitations

The main limitations of the study include its retrospective design and the potential incompleteness of registry data, particularly regarding behavioral risk factors. Important markers of baseline TB severity, such as radiological extent, cavitary disease, smear grading, and detailed resistance patterns, are not included in the multivariable models. Their absence raises concern for residual confounding, particularly for variables such as low BMI and comorbidities, which may act as proxies for disease severity. The study reveals that it is necessary to adjust the information collected for the Registry. In addition, a more detailed description of changes in treatment regimens and diagnostic approaches across the different time periods would further strengthen the interpretation of the observed trends. These factors should be considered when interpreting the study's findings and when assessing their generalizability.

Conclusions

This study highlights the multifactorial nature of treatment outcomes among patients with DR-TB in Lithuania. Treatment outcomes of DR-TB have improved over a 22-year period. Successful treatment was strongly associated with a combination of clinical, behavioral, and socioeconomic risk factors. This is a complex issue, and the individual components may carry different weights for a specific patient. Multivariate analysis indicated that the presence of multiple comorbidities—such as HIV infection, cancer, chronic lung disease, CHD, diabetes mellitus, and renal failure—substantially increased the likelihood of poor treatment outcomes.

Furthermore, patients characterized by low BMI, unemployment, unstable housing, and substance use (including alcohol and drug dependence) were found to be particularly vulnerable to unfavorable outcomes.

These findings underscore the importance of adopting a comprehensive, patient-centered approach that extends beyond pharmacological management alone. Interventions that integrate medical care with social and behavioral support—such as targeted nutritional assistance, addiction treatment, and housing support—are likely to enhance adherence and improve treatment outcomes.

Incorporating multifaceted strategies such as psychological support, social assistance (access to food and shelter), and employment opportunities into the national DR-TB control framework could enhance health system responsiveness, reduce care inequities, and ultimately contribute to improved treatment outcomes and progress toward the elimination of TB in Lithuania.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study received approval from the Regional Biomedical Research Ethics Committee of Vilnius University (approval date: March 30, 2023; Protocol No. 158200-13-652-210, Addendum No. 2023-LP-28). The Regional Biomedical Research Ethics Committee of Vilnius University has exempted the necessity for informed consent in retrospective studies, in compliance with Lithuanian Law on Biomedical Research Ethics. To maintain anonymity, all collected data were anonymized and deidentified before analysis.

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