

Rapid assessment of the country tuberculosis emergency response and preparedness in mitigating the impact of cross-border migration on the tuberculosis epidemic in Czechia

#### **ABSTRACT**

An increase in tuberculosis (TB) and drug-resistant TB notifications was reported by Czechia to WHO in 2022 and observed over the first 10 months of 2023. This pointed to a recovery of the country's health system from the impact of COVID-19, in addition to increased migration processes across the region, mainly heightened by the war in Ukraine. The WHO mission to Czechia addressed reported cases of multidrug-resistant TB (MDR-TB), particularly among children. Mission outcomes indicate that most of the notified MDR-TB cases have a foreign origin, largely from Ukraine. Available evidence suggests that most cases likely resulted from the reactivation of latent infection or a new exposure to TB before migration, rather than from recent transmission occurring in the host country.

WHO/EURO:2024-9561-49333-73749

#### **KEYWORDS**

TUBERCULOSIS, DRUG-RESISTANT TUBERCULOSIS, MIGRANTS, CZECHIA, UKRAINE

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Cataloguing-in-Publication (CIP) data. CIP data are available at <a href="http://apps.who.int/iris">http://apps.who.int/iris</a>.

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# Contents

Acknowledgements	
Authors	
Funding	
Abbreviations	
Executive summary	
Goal, objectives and methodology	
Country context	
Achievements	5
Challenges	6
Opportunities	7
Recommendations	
References	<u>C</u>
Annex 1. Composition of the joint review mission	10
Annex 2. Mission programme	11
Annex 3. Review mission snapshots (©WHO)	12

## Acknowledgements

The WHO Regional Office for Europe would like to thank colleagues from the Ministry of Health (MoH), Thomayer University Hospital, and the National Public Health Center (SZU) for the collaborative work on planning, reviewing and developing the report.

Special recognition goes to Professor Martina Koziar Vasakova (Head of the Department of Pulmonology at Thomayer University Hospital), Ms Gabriela Pilková (focal point for WHO at the MoH of Czechia) and Dr Jiri Wallenfels (country TB counterpart, TB surveillance and response mentoring focal point at the MoH of Czechia).

## **Authors**

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## **Funding**

This work was supported by the United States Department of State in the Framework Agreement REM-USA-360 (SPRMCO23VC0073) to support refugees from Ukraine across Europe.

## **Abbreviations**

COVID-19 coronavirus disease 2019

CI Confidence Interval

CSO civil society organization

DR-TB drug-resistant tuberculosis

HIV human immunodeficiency virus

MDR-TB multidrug-resistant tuberculosis

MoH Ministry of Health

NGO nongovernmental organization

TB tuberculosis

WHO World Health Organization

XDR-TB extensively drug-resistant TB

# **Executive summary**

An increase in tuberculosis (TB) and drug-resistant TB (DR-TB) notifications was reported by Czechia to WHO in 2022 and observed over the first 10 months of 2023. This information has been reported in a series of publications from Czechia and other European countries. This pointed to a recovery of the country's health system from the impact of COVID-19, in addition to increased migration processes across the region, mainly heightened by the war in Ukraine. The WHO mission to Czechia (4–6 December 2023), initiated at the request of the Ministry of Health (MoH), addressed reported cases of multidrug-resistant TB (MDR-TB), particularly among children. Mission outcomes indicate that most of the notified MDR-TB cases have a foreign origin, largely from Ukraine. Available evidence suggests that most infections likely resulted from the reactivation of latent disease or exposure to TB before migration, rather than from recent transmission occurring in the host country. Despite the crisis, Czechia has successfully coordinated the national response and expanded diagnostic and treatment initiatives to ensure control over the situation with efficient actions. Furthermore, including TB elimination in the national health priority agenda will ensure a sustainable rapid response to the health security threats that challenge the WHO European Region.

# Goal, objectives and methodology

An increase in TB and MDR-TB cases notified to WHO in 2022 and observed by country TB counterparts over the first 10 months of 2023 warranted the establishment of a joint mission with the goal of provisionally identifying the reasons for the increased MDR-TB notifications in children, which may qualify as an outbreak that requires an emergency response (1–3). In addition, the following complementary objectives were identified for the mission:

- assess the country's response to and preparedness for large numbers of refugee arrivals in terms of ensuring continuity of TB care; and
- recommend people-centred emergency interventions to address the needs of refugees and other vulnerable groups (EPIC-Czechia project).

The joint review mission, composed of a group of experts from the WHO Regional Office for Europe and the MoH, was established by the WHO Country Office in agreement with the MoH (Annex 1. Composition of the joint review mission). The mission members had an opportunity to (a) review the epidemiological landscape and dynamics notified in the national TB register and genotyping results of the clustered strains, (b) interview representatives of TB care providers within the main health system building blocks, (c) visit sites with an increased number of TB cases in vulnerable groups, and (d) discuss the funding and follow up on joint interventions to ensure country preparedness and response to an increased TB burden in Czechia (Annex 2).

A TB outbreak is generally defined as a situation where there are more TB cases than expected within a geographic area or population during a particular time period, and there is evidence of recent transmission of *Mycobacterium tuberculosis* among those cases (1). An outbreak of TB can be defined as a cluster of cases that includes three or more active cases with evidence of serial transmission (2). A possible cluster is defined as any two or more active cases with the same genotype, where temporal and geospatial association is plausible, but no direct epidemiological link is identified (2). In low-incidence jurisdictions, any temporal cluster of cases is suspicious for an outbreak (3).

## Country context

Czechia remains a low TB incidence country, with 440 newly-emerged<sup>ii</sup> TB cases in 2022, as estimated by WHO, which represents a rate of 4.2 cases per 100 000 people (4–6). Meanwhile, the country's health system was able to detect 379 new and relapsed TB cases, showing a case detection rate of 87% (CI: 75–100%) at the borderline target of 90% (7). This constitutes a slight increase as the health system capacity recovers from the impact of the COVID-19 pandemic, when case notifications dropped by 20%, from 464 in 2019 to 368 in 2020 (8). An estimated uptick in TB notifications in 2023 to 450 newly emerged TB cases may be due to the impact of the war in Ukraine and increased migration in the region.<sup>iii</sup> Overall, TB notifications in migrants increased from 126 cases in 2020, which was the lowest number reported in the last five years, to 166 cases in 2022. Eighty-eight (53%) of all TB patients of foreign origin notified in 2022 were Ukrainian, most of them labour migrants. However, provisional notifications in 2023 rose by 122, mostly in refugees. This is an increase of over 450% since 2020, when 27 TB cases, the lowest number in patients of Ukrainian origin, were detected.

WHO estimates that there have been 162 TB cases (including 23 in children under 15 years of age) among the 375 000 refugees from Ukraine currently residing in Czechia since the start of the war in Ukraine in February 2022 (9,10). The estimated TB incidence in Ukrainian refugees residing in Czechia is 42 cases per 100 000, which is less than half of the 90 cases per 100 000 rate in Ukraine. This might be explained by the profile of the refugees, largely comprising women, children and elderly people, who are at lower risk of developing active TB than their fellow citizens remaining in Ukraine (5,9).

Nineteen MDR-TB cases were estimated by WHO to emerge in 2022, of which 17 were detected by the health system of Czechia. This indicated a good detection rate at the recommended target of 90%. Meanwhile, provisional notifications as of November 2023 indicated 28 MDR-TB patients, which is a 60% increase from 2022. This suggests the impact of the migration processes experienced by Czechia. Overall, since the start of the war in Ukraine, WHO has estimated that there have been 67 MDR-TB cases (including 14 cases of extensively drug-resistant TB (XDR-TB)) in Ukrainian refugees, which is a projected 400% increase from the 17 MDR-TB cases notified in 2022 (including four XDR-TB cases).

Data from a recent analysis conducted by a group of national counterparts suggest that most infections were likely the result of reactivation of latent infection or exposure to TB before migration, rather than recent transmission occurring in the host country (11).

Treatment outcomes are well monitored and documented in the national TB register. The treatment success rate of drug-susceptible TB reported in 2022<sup>iv</sup> for 365 patients remains at 66%, which is well below the 90% target. This is due to the high death rate of 18%, of which half is due to conditions other than TB. Such a high lethality rate in the treatment cohort could be explained by the prevalence of dementia among TB patients in Czechia. Other significant reasons are high loss of follow-up (9%) and patients still undergoing treatment (4%).

<sup>&</sup>quot; New TB cases and relapses.

Estimates based on TB case notification trends in 2023, as of three out of four quarters of the year. A final annual data snapshot and validation is planned for the end of March 2024, which is a customary time frame for data reporting.

<sup>&</sup>lt;sup>iv</sup> Patient cohort notified in 2021. Their treatment outcomes were reported 12 months later, in 2022.

### **Achievements**

In response to the ongoing humanitarian crisis, a united national response has been implemented, deploying effective measures to combat communicable diseases, with a focus on tackling TB. This comprehensive effort, encompassing acknowledgement, prevention, diagnosis, treatment and care demonstrates a commitment to addressing the multifaceted challenges posed by the crisis.

As strides are made in mitigating the heightened prevalence of MDR-TB, progress is evident, especially in the context of children and adolescents. This is a positive development in the battle against a form of TB that poses unique challenges due to its resistance to conventional treatments.

A key pillar supporting the national response is the exceptional technical capacity for the prevention, diagnosis, treatment and care of both TB and DR-TB, underlining the country's commitment to staying at the forefront of medical advancements in the field.

The efficacy of the national response is further bolstered by the establishment of effective coordination and information-sharing mechanisms among key stakeholders. Public health services at regional level actively participate in this effort, supporting swift and well-informed decision-making.

At the heart of the response is the National Reference Laboratory, showcasing commendable diagnostic capabilities for TB. Employing a diverse array of testing methods, including cutting-edge genome sequencing in collaboration with Slovakia, the laboratory plays a pivotal role in ongoing research initiatives.

Clinical and patient management strategies align with the latest WHO recommendations for the treatment of TB and DR-TB across all age groups. Designated as the national centre for managing DR-TB, which allows for streamlined treatment initiation and coordination, Thomayer University Hospital has 15 beds allocated for MDR-TB patients and maintains up-to-date infection prevention and control standards.

Another key component of the national response is accessibility of medicines, with TB and DR-TB medications provided free of charge for insured residents of Czechia. However, people with uncertain health insurance status due to factors such as legal residency, undocumented migrant status or unemployment find themselves in a state of limbo when it comes to the country's universal health coverage. This poses a challenge for health and social care providers in effectively managing service delivery.

Health-care facilities in Czechia are reimbursed by the National System of Health Insurance. Despite the high local market costs, the range of medicines for DR-TB includes WHO-recommended six-month regimens featuring bedaquiline, pretomanid, linezolid and moxifloxacin.

A hybrid approach to patient-centred management, integrating both inpatient and ambulatory phases, enables the continuation of treatment and adherence to it at home for the majority of patients diagnosed with TB, including those with DR-TB. This model prioritizes people-centred delivery of care and services, while maintaining the necessary level of medical supervision. By blending inpatient and outpatient components, health-care providers ensure a balanced and personalized treatment experience for patients and remove a considerable financial burden from the health-care system,

creating an opportunity to redirect resources to the engagement of TB communities and civil society organizations (CSOs).

Crucial in national response monitoring is a comprehensive cloud database, which provides immediate access to critical information and response interventions, and enables prompt and necessary measures. This data-driven approach ensures that the response remains agile and adaptive to the evolving dynamics of the humanitarian crisis.

# Challenges

Accessing medications for DR-TB, including paediatric formulations, presents difficulties considering the reported increase in TB and DR-TB notifications. The numbers emphasize the need to comprehensively address challenges in drug availability. Drug supply and management is decentralized, and the sudden influx of patients may jeopardize health-care facility budgets, making it difficult to meet the medication needs.

The prolonged hospitalization period, averaging between three and five months for DR-TB patients, underscores the necessity to shift towards outpatient management for TB and DR-TB. This transition should embrace people-centred modalities of service delivery, actively involving CSOs, community health workers, and mediators to enhance patient care and support.

A notable challenge involves non-insured patients, particularly Ukrainian refugees residing in Czechia who have not applied for or received temporary protection. The lack of insurance complicates their access to medical care, accentuating the need for cross-border collaboration and prioritized information sharing to meet the health-care needs of this vulnerable population.

Specific challenges in the local context further compound the situation, such as the absence of a governance framework for TB prevention and control as a national strategic plan toward TB elimination, aligned to the Global End TB strategy and the European Region Action Plan 2023–2030 (4,5,12,13). This highlights a significant shortcoming, in which the TB national focal point faces limitations in influencing decision-making processes. Addressing this imbalance is crucial for enhancing the overall effectiveness of TB management strategies.

Moreover, national capacities in emergency preparedness and response require additional reinforcement. While the TB focal point is adept in the field, integrating TB-specific expertise into broader emergency response strategies remains an area for improvement. Strengthening these capacities will enable a more holistic and effective response to the multifaceted challenges posed by TB and DR-TB.

Collaboration and coordination, especially the involvement of CSOs and community health workers in the outpatient management of TB and DR-TB, are critical in navigating these challenges. Additionally, fostering cross-border collaboration, particularly with respect to health-care access for non-insured people, demands a coordinated effort to streamline information sharing and facilitate necessary interventions.

Addressing the noted challenges requires a comprehensive strategy that not only tackles immediate concerns but also addresses underlying structural issues. Strengthening governance structures for TB

prevention and control, empowering key stakeholders, and integrating TB expertise into broader emergency response frameworks will contribute to a more resilient and effective health-care system.

In conclusion, the current landscape presents intricate challenges in the management of TB and DR-TB. However, with strategic interventions focusing on medication access, outpatient care modalities, cross-border collaboration, and strengthened governance structures, there exists a pathway towards improving the overall response and mitigating the impact of TB in the context of Czechia.

## Opportunities

Prioritization of active engagement with CSOs, nongovernmental organizations (NGOs) and health and community mediators is underscored, specifically targeting clusters of potential TB infection hotspots within the population (14).

A fundamental step involves the integration of genome sequencing by adopting a two-pronged approach: (i) a prospective application covering all patients with confirmed rifampicin-resistant cases, with a focus on medications integral to DR-TB regimens (bedaquiline, linezolid, clofazimine, pretomanid, delamanid and moxifloxacin); and (ii) a retrospective analysis spanning isolates from the available bank since 2005, aimed at identifying mutations associated with certain TB medications, notably bedaquiline, pretomanid and delamanid. Collaboration with the WHO Regional Office for Europe in this genomic exploration is strongly encouraged.

Genotyping results reveal an absence of transmission within identified clusters. The predominance of infections is likely attributed to latent disease reactivation or prior exposure to TB pre-dating migration, as opposed to recent transmissions in the host country.

The exemplary coordination among relevant stakeholders, thoroughly documented for future reference, should be recognized and potentially emulated by other European countries in the management of TB-related challenges.

The imperative nature of a national emergency preparedness and response plan cannot be overstated. Thoughtful considerations within this plan should encompass communicable diseases, notably TB and the human immunodeficiency virus (HIV), thereby establishing a strategic framework and operational plan to address the re-emerging demands associated with TB and DR-TB prevention and control. This strategic vision is particularly pertinent considering the humanitarian crisis unfolding in Europe.

#### Recommendations

- 1. Collaborate with the WHO Regional Office for Europe to refine the epidemiological projections of TB burden for the period 2024–2030. This effort aims to provide a comprehensive understanding of the evolving landscape of TB and DR-TB within the specified time frame, incorporating potential scenarios and epidemiological insights to guide strategic planning and resource allocation (15). Develop a national TB elimination strategy and operational plan for its implementation by 2030 (16).
- 2. Sustain the genome sequencing of isolates from patients with confirmed rifampicin resistance, employing both prospective and retrospective approaches. Collaboration with WHO and European countries is needed to determine subsequent steps in this critical area of research. Financial support

from the MoH is required to ensure the continuation of ongoing research in this specialized field of genomics (17).

- 3. Investigate alternatives to hospitalization, embracing people-centred models of service delivery such as video-supported treatment and ambulatory care (18).
- 4. Explore the involvement of CSOs, NGOs and community mediators in augmenting the management of TB and DR-TB patients in outpatient settings. This collaborative approach emphasizes the integration of community-based support to enhance patient care, aligning with epidemiological strategies that acknowledge the role of community engagement in improving health outcomes. Use WHO's guidance for affected community and civil society organizations, national TB programmes and policy-makers in eastern Europe and central Asia entitled "Standardized package of community-based support services to improve tuberculosis outcomes" (14).
- 5. Harness the WHO Regional Office for Europe's support to reassess risk groups for TB screening, fostering a targeted approach to identifying latent infection, particularly among vulnerable groups like migrants, refugees, asylum seekers, Roma communities, people living with HIV, prisoners, and people experiencing homelessness. These epidemiologically informed directions aim to bridge gaps in intensified case finding through systematic screening and TB preventive treatment, emphasizing inclusivity and equity in health-care delivery (19–21).
- 6. Continue to enhance the national electronic TB register, with a focus on incorporating monitoring mechanisms for (a) DR-TB treatment enrolment and outcome monitoring; and (b) TB contact tracing and TB preventive treatment, including regimen details and therapy completion.
- 7. Perform a TB medicine forecast for 2024 and 2025, safeguarding a six-month centralized buffer stock to respond to emergency needs. Explore alternative mechanisms for procuring WHO-prequalified TB and DR-TB medicines through international sources such as the Global Drug Facility of the Stop TB Partnership (22). For a more sustainable solution, collaborate closely with the WHO Regional Office for Europe to improve accelerated registration of prequalified finished pharmaceutical products in Czechia approved by another relevant regulatory authority, such as the European Medicines Agency or the US Food and Drug Administration. This is to ensure access to and availability of medicines for TB and DR-TB treatment and prevention across all age groups in European Union countries (23).
- 8. Conduct a thorough assessment of immediate equipment needs at Thomayer University Hospital, ensuring the capacity to manage paediatric TB, and the National Reference Laboratory, to optimize TB and DR-TB case management, diagnostics and surveillance. Explore local procurement options and leverage the WHO catalogue for cost-effective acquisitions. Maintain transparent communication with all stakeholders, especially in the context of available funding as part of the Ukraine refugee response, aligning with epidemiological imperatives to enhance diagnostic and management capabilities.

<sup>&</sup>lt;sup>v</sup> Cost accessed via the WHO Country Office in Ukraine.

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vi All references accessed 11 December 2023.

## Annex 1. Composition of the joint review mission

Listed below in alphabetical order are the members of the joint review mission:

- 1. DADU, Andrei (Medical Officer, Epidemiologist, focal point for TB essential service delivery in emergency settings and for the Balkan and Visegrad Group countries, TB Unit of the WHO Regional Office for Europe)
- 2. KULCHYNSKA, Roksolana (Health Operations Officer, WHO Country Office for Czechia)
- 3. PILKOV, Gabriela (Focal point for WHO at the MoH of Czechia)
- 4. SELINGER, Elika (Consultant, WHO Country Office for Czechia)
- 5. WALLENFELS, Jiri (Country TB counterpart, TB surveillance and response mentoring focal point at the MoH of Czechia)
- 6. YEDILBAYEV, Askar (TB Regional Adviser at the WHO Regional Office for Europe, review mission team lead)

# Annex 2. Mission programme

Monday, 4 December 2023		
09:00-10:00	Meeting with MoH representatives: Mr. Jakub Dvoracek, Deputy	
	Minister, Mgr. Zdenek Kysely, International Health Regulations	
	focal point, Dr Jozef Dlhy, Senior Epidemiologist	
10:00–12:00	Meeting with Mgr. Jiri Wallenfels, national TB surveillance focal point	
14:00–17:00	Meeting at Thomayer University Hospital: Professor Martina	
	Koziar Vadakova, Head of the Department of Pulmonology, Dr	
	Karolina Dolezalova, Chief Medical Officer of the Pulmonary	
	Outpatient Clinic, Dr Emilia Kopecka, Chief Medical Officer of the	
	Pulmonary Bed-Unit	
Tuesday, 5 December 2023		
09:00–12:00	Field trip to Benatky nad Jizerou, visiting families affected by TB	
14:00-17:00	Meeting at Regional Hygiene Station, Mlada Boleslav: Michaela	
	Honegerova, Head of the Antiepidemic Department, Dr Beatrix	
	Maliakova, Medical Officer in the Paediatric Pulmonary Unit,	
	Lilian Rumlova, Director of the Antiepidemic Department,	
	Nymburk location	
Wednesday, 6 December 2023		
09:00–14:00	Meeting at the National Institute of Public Health: Dr Barbora	
	Mackova, Director of the Institute, Věra Dvorakova, Director of	
	the National Reference Laboratory, Jana Kozakova, Head of the	
	Epidemiology and Microbiology Unit at the Institute	

Annex 3. Review mission snapshots (©WHO)











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