

INFORMATION NOTE

Testing for tuberculosis infection and screening for tuberculosis disease among refugees arriving in European countries from Ukraine

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Key messages

Testing for tuberculosis (TB) infection

Universal testing of refugees arriving in European countries from Ukraine for TB infection is not recommended.

Specific groups should be considered for TB testing, such as household contacts of bacteriologically confirmed pulmonary cases or immunocompromised individuals (e.g. those preparing for dialysis).

Screening for TB disease

Universal screening for TB disease of refugees arriving in European countries from Ukraine is not recommended.

In certain groups at risk of TB, such as people living with HIV or those who are contacts of TB patients, screening for TB disease is important, while in those without disease, assessment for TB preventive treatment is recommended.

Scope and audience

This document provides an overview of public health guidance on testing for TB infection, TB preventive treatment and screening for TB disease, in the context of the mass influx of people arriving in European countries from Ukraine.

The target audience for this technical report includes national policymakers, public health and healthcare planners, staff working in reception centres, and healthcare staff caring for refugees.

Background

Since 24 February 2022, when the Russian invasion of Ukraine began, large numbers of people have left Ukraine. As of 7 April 2022, more than four million people have fled to Hungary, Poland, Romania, Slovakia, and the Republic of Moldova, and from there they are dispersing to other European countries [1]. This number is expected to increase in the coming months. To date, mainly women, children and men aged over 60 years have been arriving in European countries.

The European Council has adopted a Decision on the temporary protection of displaced persons from Ukraine fleeing to neighbouring EU Member States [2]. This Decision provides immediate protection and rights, including residency rights, access to the labour market, schools, housing, social welfare assistance, medical or other assistance and means of subsistence. For refugees from Ukraine, access to healthcare services (including TB testing and treatment) in other European countries is the same as for the citizens of those countries.

Tuberculosis epidemiological situation in Ukraine [3]

Ukraine is one of the TB high-priority countries in the WHO European Region and one of nine countries globally with a high burden of rifampicin-resistant or multidrug-resistant TB (RR/MDR-TB) [4]. The estimated TB incidence is 73 per 100 000 population, compared to 9.5 per 100 000 in the EU/EEA. In 2020, 19 521 TB cases were notified, 44.6 per 100 000 population. The incidence of TB in children is low. The total number of TB cases in the EU/EEA was 33 148 in the same period, 7.3 per 100 000 (ranging from 2.9 per 100 000 in Slovakia to 39.8 per 100 000 in Romania).

In 2020, 32.6% of all bacteriologically confirmed pulmonary TB cases in Ukraine were RR/MDR-TB and 4 117 MDR/RR-TB cases were notified. In 2020, the total number of RR/MDR-TB cases in the EU/EEA was 595. It should be noted that the male/female ratio in Ukraine is 2.4, meaning that the majority of TB cases are diagnosed in men. Furthermore, only a small proportion of RR/MDR-TB cases are diagnosed in children since laboratory confirmation in children is challenging [5].

Testing for TB infection

Neither ECDC [6] guidance nor WHO [7,8] guidelines recommend universal testing of migrants and refugees for TB infection. Certain at-risk populations are priority target groups for TB preventive treatment (TPT):

- People with elevated risk of progression from infection to TB disease
- People with increased likelihood of exposure to TB disease.

The WHO recommendations set out below may be considered with regard to testing for TB infection and TB preventive treatment (Table 1).

Table 1. Identifying at-risk populations to test for TB infection and TB preventive treatment [7]

People living with HIV
1. Adults and adolescents living with HIV who are unlikely to have active TB should receive TB preventive treatment as part of a comprehensive package of HIV care. Treatment should also be given to those on antiretroviral treatment, to pregnant women and to those who have previously been treated for TB, irrespective of the degree of immunosuppression and even if LTBI testing is unavailable.
2. Infants aged < 12 months living with HIV who are in contact with a person with TB and who are unlikely to have active TB on an appropriate clinical evaluation or according to national guidelines should receive TB preventive treatment.
3. Children aged ≥ 12 months living with HIV who are considered unlikely to have active TB on an appropriate clinical evaluation or according to national guidelines should be offered TB preventive treatment as part of a comprehensive package of HIV prevention and care if they live in a setting with high TB transmission, regardless of contact with TB.
4. All children living with HIV who have successfully completed treatment for TB disease may receive TB preventive treatment.
Household contacts (regardless of HIV status)
5. Children aged < 5 years who are household contacts of people with bacteriologically confirmed pulmonary TB and who are found not to have active TB on an appropriate clinical evaluation or according to national guidelines should be given TB preventive treatment even if LTBI testing is unavailable.
6. Children aged ≥ 5 years, adolescents and adults who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have active TB by an appropriate clinical evaluation or according to national guidelines may be given TB preventive treatment.
7. In selected high-risk household contacts of patients with multidrug-resistant tuberculosis, preventive treatment may be considered based on individualised risk assessment and a sound clinical justification.

Clinical and other at-risk population groups

8. People who are initiating anti-TNF treatment, or receiving dialysis, or preparing for an organ or haematological transplant, or who have silicosis should be systematically tested and treated for LTBI.
9. Systematic LTBI testing and treatment may be considered for prisoners, health workers, immigrants from countries with a high TB burden*, homeless people# and people who use drugs.
10. Systematic LTBI testing and treatment is not recommended for people with diabetes, people who engage in the harmful use of alcohol, tobacco smokers and underweight people unless they also belong to other risk groups included in the above recommendations.

* Countries with a TB incidence > 100/100 000 population are considered high TB burden countries. Ukraine has an estimated TB incidence of 73/100 000 population.

Prior to displacement from Ukraine to other European countries

LTBI – Latent Tuberculosis Infection;
Active TB = TB disease; LTBI = TB infection

Testing for TB infection can be considered for populations from countries with a high TB incidence [9]. Ukraine is not considered a high-TB incidence country since the common threshold for high-TB incidence is a TB incidence above 100 per 100 000 population. Several EU/EEA countries apply different thresholds [10]. A lower threshold can be applied in countries that are aiming to eliminate TB in their national TB strategy [11].

Countries that apply a threshold incidence lower than the estimated TB incidence in Ukraine (73 per 100 000) to test for TB infection should also test refugees from Ukraine following their national guidelines.

Testing for TB infection can either be done using the tuberculin skin test (TST) alone, an interferon-gamma release assay (IGRA) alone or by integrating both tests in the screening strategy. Alternatively, TB antigen-based skin tests can be used [12]. The most appropriate test or combination of tests depends on the resources available and the target group. According to WHO guidelines [7] testing is not a requirement for people living with HIV or children under five years who are household contacts of people with bacteriologically confirmed pulmonary TB. These groups could be provided with TB preventive treatment directly (Table 1).

Ukraine provides Bacille Calmette–Guérin (BCG) vaccination at birth and had reached a coverage of 84% in 2019 [13]. In addition, until 2018, children received a booster dose at the age of seven years. BCG vaccination, and especially recent BCG vaccination, may result in false positive TST test results. Therefore testing using IGRAs or a combination of both tests may be more appropriate for refugees from Ukraine.

Table 2 provides an overview of the considerations for ruling out TB disease among various target populations before starting TPT. While effective TB symptom screening forms the backbone of TPT services, tests for TB infection, chest radiography and diagnostic testing may be used [14].

Table 2. Key steps for ruling out TB and considering TPT [14]

	Adults and adolescents living with HIV ^b	Children living with HIV ^a	HIV-negative/close contacts of TB patients	Clinical at-risk populations
Clinical symptom-based screening	Current cough, fever, weight loss or night sweats	Absence or poor weight gain, fever or current cough or history of contact with a case of TB, reduced playfulness, night sweats.	Cough of any duration, haemoptysis, fever, night sweats, weight loss, chest pain, shortness of breath, fatigue	
Frequency of symptom screening	At every visit to a health facility or contact with a health worker			
Chest radiography	Not mandatory although desirable. May be considered among PLHIV on ART; among symptomatic adolescent and adult contacts and clinical at-risk groups			
Diagnostic testing for TB if screen test is positive	WHO recommends rapid diagnostics (such as Xpert MTB/Rif, Urine LAM among seriously ill PLHIV) or as per national guidelines			
Test for TB infection (TST/IGRA)	Not required among PLHIV and contacts below five years of age. In other populations these tests limit unnecessary treatment of uninfected individuals (such as settings with low prevalence of TB infection) Unavailability of tests should not be a barrier to provision of TPT to those in need			
Contra-indication to TPT	<ul style="list-style-type: none"> Active hepatitis (acute or chronic), regular and heavy alcohol consumption and symptoms of peripheral neuropathy Concurrent use of other hepatotoxic medications (such as nevirapine) History of hypersensitivity to TPT 			
Counselling	Information of TB infection, need for TPT, schedule of medication collection, medication adherence support and follow up visits, benefits from completing the course, adverse events, actions on development of TB symptoms or adverse events			

ART = antiretroviral therapy; PLHIV = people living with HIV; TB = tuberculosis; TPT = TB preventive therapy

^a Screening for children and pregnant/breastfeeding women may be integrated into various entry points for care (such as maternal and child health, immunisation, well-baby clinics, nutrition clinics).

^b Among PLHIV, all the above steps should be incorporated if differentiated service delivery models are implemented. Active case finding and TPT should be an integral part of the care package for PLHIV.

Those eligible should receive TPT [7]. Different preventive treatment regimens can be considered (daily isoniazid for 6–9 months or rifamycin-containing regimens [e.g. weekly rifapentine + isoniazid for three months from age 2 upwards; or isoniazid + rifampicin daily for three months for all ages; or rifampicin daily for four months for all ages]). The preventive treatment provided should be based on an individual risk assessment, including a drug resistance profile of the TB case for household contacts, and availability of drugs, especially rifapentine.

Screening for TB disease

Universal screening for TB disease is an option for people arriving from high-TB incidence countries [9,15]. The threshold for high-TB incidence is often defined as a TB incidence above 100 per 100 000 population. This is higher than the current incidence in Ukraine. In the past, European countries have applied different thresholds for screening migrants [16].

Systematic screening for TB disease should be conducted in people living with HIV, household contacts and other close contacts of individuals with TB disease (Table 3). It may also be conducted in other populations such as those with structural risk factors for TB - i.e. poverty; malnutrition; overcrowded and poorly ventilated living and working conditions. These populations can include poor communities in urban areas, homeless communities (prior to displacement from Ukraine to other European countries), communities in remote or isolated areas, indigenous communities and other vulnerable or marginalised groups with very limited access to healthcare. Systematic screening of these populations is important to ensure that people have access to prevention and care services.

Table 3. Systematic screening for tuberculosis disease in targeted populations [15]

1. Systematic screening for TB disease may be conducted among the general population in areas with an estimated TB prevalence of 0.5% or higher.
2. Systematic screening for TB disease may be conducted among subpopulations with structural risk factors for TB. These include urban poor communities, homeless communities, communities in remote or isolated areas, indigenous populations, migrants, refugees, internally displaced persons and other vulnerable or marginalised groups with limited access to health care.
3. People living with HIV should be systematically screened for TB disease at each visit to a health facility.
4. Household contacts and other close contacts of individuals with TB disease should be systematically screened for TB disease.
5. Systematic screening for TB disease should be conducted in prisons and penitentiary institutions.
6. Current and former workers in workplaces with silica exposure should be systematically screened for TB disease.
7. In settings where the TB prevalence in the general population is 100/100 000 population or higher, systematic screening for TB disease may be conducted among people with a risk factor for TB who are either seeking health care or who are already in care.
8. People with an untreated fibrotic lesion seen on chest X-ray may be systematically screened for TB disease.

Studies have shown that there is no clear evidence of benefits or cost-effectiveness from screening [17]. Screening can cause anxiety and stigmatisation in individuals and the wider community. Screening may also deter people from asking for medical check-ups, thereby jeopardising the identification of high-risk patients.

Screening for TB disease can be done by screening for symptoms such as cough, fever, or poor weight gain; or alternatively by means of chest radiography; or both [15]. Chest radiography will improve the screening sensitivity. Those with a positive symptom screen or abnormal chest radiography should be referred for assessment of TB or other diseases and have a sputum culture examined for *Mycobacterium tuberculosis*, if they can expectorate.

When TB disease is diagnosed, it is important to get results from drug susceptibility testing to guide the treatment regimen [18,19].

A programme of systematic screening for TB disease should ensure that those who are diagnosed with TB disease receive adequate treatment and support. For refugees from Ukraine with TB disease, continuation of treatment with an adequate regimen should be ensured, and a mechanism should be put in place to enable a person to continue receiving treatment when moving to another area.

Conclusion

Systematic testing of all refugees from Ukraine for TB infection and screening for TB disease is not recommended, and only certain groups need to be tested and screened. The yield and overall effect of systematic testing on TB control is likely to be modest and testing and screening may divert attention from other, more immediate public health needs, such as mental health issues.

The implementation of a testing or screening programme needs to balance the benefits against potential harm, such as stigmatisation, discrimination, resource use, opportunity costs for other interventions and prompt management of other conditions, such as malnutrition, or mental health issues. Before a testing or screening programme is implemented access to healthcare for those with symptoms of TB should be guaranteed.

Initial health checks should be offered to refugees from Ukraine, to check for both communicable and non-communicable diseases. Any initial health checks of refugees arriving from Ukraine should be followed up with proper diagnosis and treatment and the necessary healthcare provided, particularly for vulnerable groups, such as the elderly, those with underlying health conditions, pregnant women and children under the age of five years.

References

1. The UN Refugee Agency (UNHCR). Operational data portal. Ukraine Refugee Situation. [Last updated 4 April 2022]. Available at: <https://data2.unhcr.org/en/situations/ukraine>
2. Council Implementing Decision (EU) 2022/382 of 4 March 2022 establishing the existence of a mass influx of displaced persons from Ukraine within the meaning of Article 5 of Directive 2001/55/EC, and having the effect of introducing temporary protection ST/6846/2022/INIT, OJ L 71;4.3.2022:1–6. Available at: https://eur-lex.europa.eu/eli/dec_impl/2022/382/oj
3. European Centre for Disease Prevention and Control (ECDC)/World Health Organization Regional Office for Europe (WHO Europe). Tuberculosis surveillance and monitoring in Europe 2022 – 2020 data. Copenhagen: WHO Regional Office for Europe and Stockholm: ECDC; 2022. Available at: www.ecdc.europa.eu/en/publications-data/tuberculosis-surveillance-and-monitoring-europe-2022-2020-data
4. World Health Organization (WHO) Global list of high burden countries for TB, TB/HIV and MDR/RR-TB. Geneva: WHO; 2021. Available at: <https://www.who.int/news/item/17-06-2021-who-releases-new-global-lists-of-high-burden-countries-for-tb-hiv-associated-tb-and-drug-resistant-tb>
5. Ködmön C, van den Boom M, Zucs P, van der Werf MJ. Childhood multidrug-resistant tuberculosis in the European Union and European Economic Area: an analysis of tuberculosis surveillance data from 2007 to 2015. *Eurosurveillance*. 2017;22(47):17-00103. Available at: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2017.22.47.17-00103>
6. European Centre for Disease Prevention and Control (ECDC). Programmatic management of latent tuberculosis infection in the European Union. Stockholm: ECDC; 2018. Available at: www.ecdc.europa.eu/en/publications-data/programmatic-management-latent-tuberculosis-infection-european-union
7. World Health Organization (WHO) consolidated guidelines on tuberculosis. Module 1: prevention – tuberculosis preventive treatment. Geneva: WHO; 2020, <https://www.who.int/publications/i/item/9789240001503>
8. Tuberculosis Prevention and Care Among Refugees and Other Populations in Humanitarian Settings. An interagency field guide. US CDC, UNHCR, WHO. 2022. Available at: <https://www.who.int/publications/i/item/9789240042087>
9. European Centre for Disease Prevention and Control (ECDC). Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA. Stockholm: ECDC; 2018. Available at: <https://www.ecdc.europa.eu/en/publications-data/public-health-guidance-screening-and-vaccination-infectious-diseases-newly>
10. Margineanu I, Rustage K, Noori T, Zenner D, Greenaway C, Pareek M, et al. Country-specific approaches to latent tuberculosis screening targeting migrants in EU/EEA countries: A survey of national experts, September 2019 to February 2020. *Eurosurveillance*. 2022;27(12):2002070. Available at: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.12.2002070>
11. World Health Organization (WHO). Towards tuberculosis elimination: an action framework for low-incidence countries. WHO; 2014. Available at: <https://www.who.int/publications/i/item/9789241507707>
12. World Health Organization (WHO). Rapid communication: TB antigen-based skin tests for the diagnosis of TB infection. Geneva: WHO; 2022 (WHO/UCN/TB/2022.1). Available at: <https://apps.who.int/iris/bitstream/handle/10665/352802/WHO-UCN-TB-2022.1-eng.pdf>
13. The BCG World Atlas, third edition. Available at: <http://www.bcgatlas.org/index.php>
14. World Health Organization (WHO) Operational Handbook on Tuberculosis. Module 1: prevention – tuberculosis preventive treatment. Geneva: WHO; 2020. Available at: <https://www.who.int/publications/i/item/9789240002906>
15. World Health Organization (WHO) consolidated guidelines on tuberculosis. Module 2: systematic screening for tuberculosis disease. Geneva: WHO; 2021. Available at: <https://www.who.int/publications/i/item/9789240022676>
16. Dara M, Solovic I, Sotgiu G, D'Ambrosio L, Centis R, Tran R, et al. Tuberculosis care among refugees arriving in Europe: an ERS/WHO Europe Region survey of current practices. 2016:[808-17]. Available at: <https://erj.ersjournals.com/content/48/3/808>
17. Greenaway C, Pareek M, Abou Chakra C-N, Walji M, Makarenko I, Alabdulkarim B, et al. The effectiveness and cost-effectiveness of screening for latent tuberculosis among migrants in the EU/EEA: a systematic review. *Eurosurveillance*. 2018;23(14):17-00543. Available at: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2018.23.14.17-00543>
18. World Health Organization (WHO) Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment. WHO, 2020. Available at: <https://www.who.int/publications/i/item/9789240007048>
19. World Health Organization (WHO) Consolidated Guidelines on Tuberculosis Module 5: Management of tuberculosis in children and adolescents. WHO, 2022. Available at: <https://www.who.int/publications/i/item/9789240046764>