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REVIEW ARTICLE

Tuberculosis screening in vulnerable populations

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ABSTRACT

Tuberculosis (TB) remains a global public health challenge. In countries with low annual incidence (≤ 10 cases/100,000 population), it mainly affects vulnerable populations with difficult access to care. In this context, passive case-finding systems may not be effective in detecting and treating all cases. Active case finding (ACF) strategies in these at-risk groups are essential to detect active or latent TB cases, improve treatment outcomes, and prevent transmission. This review addresses current ACF strategies in vulnerable populations, drawing on recent international guidelines. In addition, a focus on the situation in Barcelona is provided as an example of local implementation.

Keywords: Tuberculosis. Screening. Vulnerable population.

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INTRODUCTION

According to the latest the World Health Organization (WHO) report, 10.8 million people were diagnosed of tuberculosis (TB) in 2023, and it is again the infectious disease with the highest mortality globally, after 3 years in which it was COVID-19 with more than 1.2 million deaths[1].

In middle and high-income countries, TB is concentrated in vulnerable and socially disadvantaged populations[2]. Structural risk factors, present in vulnerable people, such as poverty, malnutrition, housing problems, and difficulty in accessing health care, lead to an increased risk of infection and active TB. Structural risk factors may overlap with other clinical factors (HIV infection, diabetes, smoking, alcoholism, and drug use), and increase the risk of developing active disease[2,3].

Diagnosing symptomatic people who consult health services is not enough to detect all existing TB cases[4]. Difficulty of access to medical care, prioritization of other social problems, misinformation, stigma and language and cultural barriers can lead to late diagnosis in vulnerable groups with the consequent impact on prognosis and transmission to the community[5]. Active TB screening and early diagnosis active case finding (ACF) strategies are therefore needed in populations at higher risk[6]. ACF in vulnerable populations with difficult access to the health system allows for the detection of asymptomatic disease, reducing delays in diagnosis, early initiation of specific treatment, which reduces transmission, improves treatment outcomes, and has a positive impact on local epidemiology[7]. In 2015, the WHO, in its End TB Strategy, established the objective of reducing the number of TB cases worldwide by 80% by 2030. To achieve these objectives, and in accordance with its guidelines updated in 2021, it proposed implementing active TB screening strategies in populations with structural risk factors as an essential component to achieve early diagnosis of all TB cases, as well as to act against the reservoir, the cases of TB infection[6]. In the same vein, in 2023, the Department of Health of the Generalitat de Catalunya drew up a document recommending screening for TB infection in various vulnerable population groups, such as drug users, homeless people, and recent immigrants from areas with a high TB burden[8]. However, the implementation of these recommendations is not yet widespread, and there is no record of the activities carried out in the territory. The Drassanes TB Clinic Unit of the Vall d'Hebron University Hospital of Barcelona in collaboration with the TB Program of the Barcelona Public Health Agency, primary health care, various social institutions and non-governmental organizations, is responsible for carrying out ACF in vulnerable populations in the city, which in its 30 years of history has been adapting to the important socials and demographic changes experimented of the city[9] (Fig. 1).

OBJECTIVES AND PRINCIPLES OF ACF

ACF aims to detect TB cases early in vulnerable and hard-to-reach populations, ensuring initiation and completion of treatment while reducing transmission and improving local epidemiology. Strategies must be ethically sound, accessible regardless of administrative status, and adapted to the social and cultural needs of each risk group.

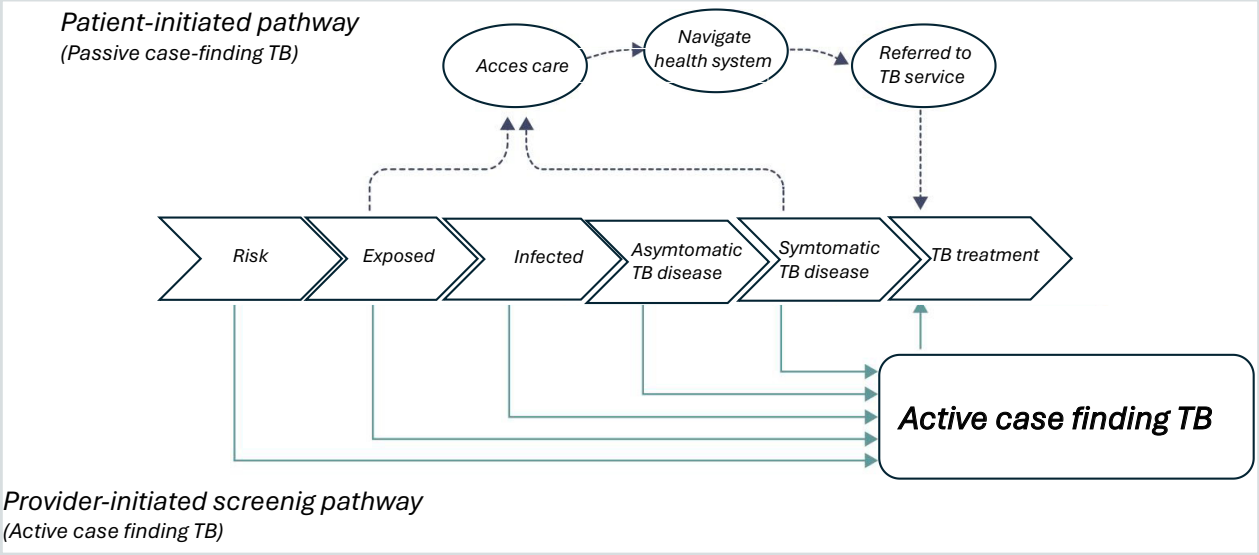

Figure 1. Comparison of provider-initiated TB screening pathway with the patient-initiated health care pathway for TB (*adapted from the WHO Consolidated Guidelines, 2021*[6]).

Key principles include: prioritizing high-risk populations; integrating screening with other health and social services and minimizing stigma or discrimination; and tailoring diagnostic algorithms to specific risk groups. A positive screening result must always be confirmed before starting treatment. Continuous monitoring and evaluation are essential to optimize resources, adapt approaches, and discontinue activities when appropriate. Collaborative work between health, social, and community actors is critical to maximizing the impact of ACF interventions.

VULNERABLE POPULATIONS

Populations vulnerable are those that have an increased risk of contracting TB and of having poorer treatment outcomes due to structural factors in their environment (e.g., poverty, malnutrition, overcrowding, poorly ventilated housing or workplaces, and limited or no access to health services). These risk factors are not exclusive, nor do they exclude the clinical risk factors, and they often compound one another. The list of potential populations affected by structural risk factors included in this review is not exhaustive, may include other groups with a high risk of TB and who have poor access to health care (Table 1).

HOMELESS PEOPLE OR PEOPLE WITH A HISTORY OF HOMELESSNESS

There is no common, generalized definition of homelessness. The European Federation of National Organizations Working with the Homeless proposes a broad definition that includes not only people who are roofless but also those who are homeless and those living in temporary, insecure, and inadequate housing (ETHOS classification)[10].

Table 1. Objectives and guiding principles of ACF in vulnerable populations

Objective	Guiding principle
1. Early detection of TB cases in vulnerable and hard-to-reach populations	Prioritizing groups with high TB risk and prevalence
2. Ensuring access to treatment and follow-up	Providing care regardless of administrative status; adapt interventions to social and cultural needs, including directly observed treatment when indicated
3. Improving treatment outcomes	Confirming diagnosis before treatment; ensure adherence through patient-centered approaches
4. Reducing TB transmission and improve local epidemiology	Integrating TB screening with other health and social services to address structural barriers
5. Promoting coordinated multisectoral action	Fostering collaboration between health, social, and community services.
6. Optimizing resources and adapt interventions	Regular monitoring and evaluation to prioritize risk groups, refine approaches, and discontinue ineffective activities

ACF: active case finding; TB: tuberculosis.

The homeless population has much higher mortality and morbidity rates than the general population, is at greater risk of psychiatric disorders, chronic diseases, and communicable diseases, and also has high rates of substance addiction (tobacco, alcohol, drugs)[11].

The prevalence of TB in homeless people published in a systematic review in 2023 was 1,100 cases/100,000 inhabitants, which is 10-30 times higher than in the general population of high- and middle-income countries. In Barcelona, the incidence of TB in homeless people is 10 times higher than in the general population[12-14].

MIGRANTS AND REFUGEES

Migrants from countries with high TB rates are at high risk of developing active disease due to the possible reactivation of TB infection acquired in their country of origin, frequent travel to high-incidence areas, and transmission within migrant communities in the receiving country. A significant proportion of TB cases in many low-incidence countries occur in migrants from high-incidence areas. In 2020, one-third of TB cases reported in European Union/European Economic Area countries were diagnosed in people of foreign origin[15-16], and in Catalonia in 2022, the rate was 32.5/100,000 inhabitants (5 times higher than the native population)[13].

Although there is no pre-migration screening policy in Spain, it is recommended that migrants from areas with a high incidence of TB be screened for TB infection and active TB when they first access primary care[17]. However, in many cases, administrative, language, and cultural barriers make it difficult to access healthcare and lead to delays in diagnosis.

DRUG USERS AND PROBLEMATIC ALCOHOL CONSUMPTION

This group includes people with problematic alcohol consumption and users of other illicit drugs (injectable, oral, inhaled, and smoked). This population is at significant risk of infection and progression to active TB due to multiple factors: precarious socioeconomic conditions, overcrowding, frequent presence of comorbidities (such as HIV), barriers to

accessing health services, lack of recognition of symptoms, and difficulties in adhering to treatment[18].

PRISON POPULATION

People in prisons and other penitentiary institutions are at an increased risk for TB compared with the general population. The estimated incidence of TB among people residing in prisons is 23 times higher than that among the general population[19].

Previous observational studies demonstrated showed that TB screening in prisons may reduce TB prevalence in the facilities[20,21]. One trial showed that screening in prisons may increase case detection by more than 50%[22].

TOOLS FOR ACF TB AMONG VULNERABLE POPULATIONS

TB screening tools should identify individuals with a high probability of having disease and those with a low probability of having it. Screening tests are not intended for diagnostic purposes. The various screening tools should be part of a detection and diagnosis algorithm, so that if a person tests positive in a screening test, they are referred to the next step in the algorithm to confirm or rule out TB.

TB screening tools should be easy to use, provide rapid results, and indicate whether further diagnostic evaluation is necessary. The optimal screening strategy should achieve high detection of true cases (high sensitivity), low false positives (high specificity), it should require testing few people to find a case, be inexpensive, rapid, and accepted by users. According to the WHO, an ideal screening test should have at least 90% sensitivity and 70% specificity for pulmonary TB. Based on these parameters, different tools are considered:

SYMPTOM SCREENING

According to WHO guidelines (2021), the main symptoms associated with active pulmonary TB include persistent cough (usually ≥ 2 weeks), fever, night sweats, and weight loss. Screening is recommended to be considered positive when the person has one or more of these symptoms. Screening for symptoms offers the advantage of being low-cost, feasible in community settings, and applicable by non-healthcare personnel. However, its sensitivity is limited, so it may not detect subclinical cases, especially in immunocompromised individuals. Specificity is relatively high, although it decreases in contexts with a high prevalence of other respiratory diseases.

CHEST RADIOGRAPHY (CXR)

CXR is a key tool for TB screening. It has high sensitivity for detecting abnormalities suggestive of pulmonary TB (around 94%) and also high specificity (89%), if any abnormal image is considered. It allows for the identification of both symptomatic and some asymptomatic cases, making it useful for reducing transmission in the community and detecting the disease early.

CAD-assisted radiology (computer-assisted detection) uses artificial intelligence to automatically analyze chest X-rays and detect signs suggestive of TB. This technology allows images to be automated and interpreted without the need for expert radiologists, making it particularly useful in resource-limited settings. Its sensitivity and specificity meet the WHO minimum standards for screening tests, improving detection, especially where there is a shortage of specialized personnel or large volumes of patients.

The results of CAD-assisted radiology must always be complemented by clinical evaluation and, in the case of positive findings, by confirmatory diagnostic tests.

RAPID MOLECULAR TESTS (RMTS)

RMTs for TB use molecular biology techniques to detect *Mycobacterium tuberculosis* (MTB) DNA and possible drug resistance, such as Rifampicin (RIF).

The tests recommended by the WHO commonly used include Xpert® MTB/RIF y Xpert MTB/RIF Ultra (Cepheid, EEUU), These tools provide high sensitivity and specificity, accurately detect both TB and drug resistance, and allow treatment to be started quickly, reducing transmission; however, they require equipment, trained personnel, and are significantly more expensive than traditional techniques.

Although not recommended as an initial screening tool, RMTs are essential after a positive screening for symptoms or CXR. Their inclusion significantly improves the performance of the diagnostic algorithm (Table 2).

Table 2. Diagnostic accuracy of symptoms, chest X-ray, and a rapid molecular test for screening for TB

Screening test	Sensitivity (%)	Specificity (%)
Prolonged cough (> 2 weeks)	42	94
Any cough	51	88
Any TB symptom (cough, fever, night sweats, weight loss)	71	64
Chest X-ray (any abnormality)	94	89
Rapid molecular test	69	99

TB: tuberculosis. *Adapted from the WHO Consolidated Guidelines, 2021*[6].

TUBERCULIN SKIN TEST (TST) INTERFERON GAMMA RELEASE ASSAYS (IGRAS)

Both tests are used to detect TB infection, not active disease. They identify an immune response to MTB and are fundamental in strategies for screening for TI in at-risk populations.

TST consists of an intradermal injection of purified protein derivative. Induration is measured at 48-72 h, and interpretation depends on the size of the induration and the risk of the person being studied. It is an inexpensive, readily available, and useful test in settings without access to a laboratory. Its limitations include false positives in people vaccinated with Bacille Calmette-Guérin (BCG) or exposed to non-tuberculous mycobacteria and false negatives in immunocompromised individuals or those with advanced TB. Furthermore, it requires two visits, and interpretation varies depending on the technique used and the reading.

IGRAs measure the release of interferon-γ in blood after stimulation with specific MTB

antigens (ESAT-6, CFP-10, TB7.7). The main tests used are: QuantiFERON-TB Gold Plus (QFT-Plus) and T-SPOT.TB.

Their advantages are that they are not affected by BCG vaccination or by most environmental mycobacteria, which means greater specificity, especially in vaccinated individuals, and they only require one medical visit. However, they are more expensive techniques and require laboratories with trained personnel. The use of either test is recommended, but in people vaccinated with BCG, IGRAs are preferred.

NEW TESTS FOR DIAGNOSING TB INFECTION

C-Tb is a new generation skin test for TB infection that combines the logistical simplicity of the TST with the specificity of IGRAs. C-Tb uses the same antigens as IGRAs tests (ESAT-6 and CP10), which are specific to MTB and are not present in BCG or in most non-tuberculous mycobacteria, thereby reducing false positives due to vaccination. It is administered intradermally (like TST) on the anterior aspect of the forearm and read after 48-72 h by measuring the induration (in mm). The proposed positivity threshold is ≥ 5 mm, regardless of vaccination status. It may be particularly useful in settings with widespread BCG vaccination and where resources for IGRAs are limited[23]. At the end of 2024, the European Medicines Agency approved its marketing in Europe under the name SIIL-BIVCY®[24], and it is expected that it will be available for use in clinical practice in the near future, most likely replacing the traditional tests for TB infection, TST and IGRAs.

SCREENING ALGORITHMS

Screening algorithms for TB are ordered sequences of actions that guide the selection and application of tools to detect cases in different contexts and populations. Depending on how the screening tools are combined, algorithms can be classified into:

Single screening

A single screening test, followed by a diagnosis test if positive. For example: CXR only.

Parallel screening

Two simultaneous tests (for example: symptoms and CXR). If either is positive, the patient is referred for diagnostic evaluation. Parallel screening is more sensitive, but less specific and more expensive.

Sequential screening

Sequential positive

If the first test is positive, a second test is performed; only if both are positive is the patient referred for diagnosis: lower sensitivity, but higher specificity.

Sequential negative

If the first test is negative, a second test is performed; if this is positive, the patient is referred for diagnosis. It has similar sensitivity/specificity to parallel screening, but it is less expensive and has fewer potential delays (Fig. 2).

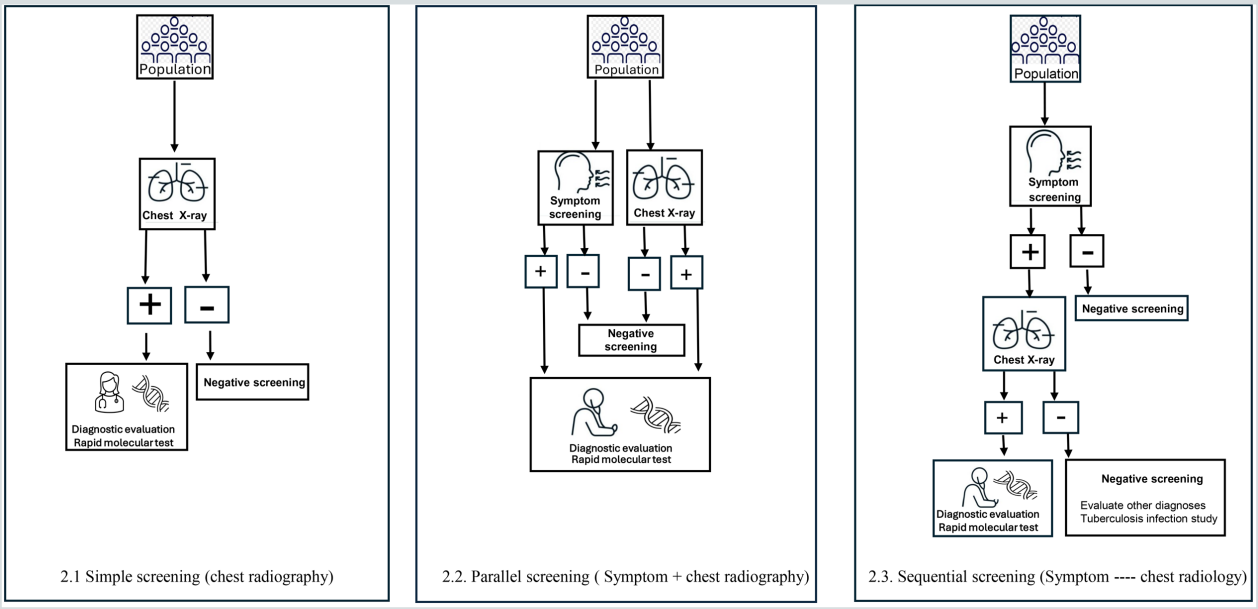

Figure 2. Screening algorithm (*adapted from the WHO Consolidated Guidelines, 2021*[6]).

MONITORING AND EVALUATION

Monitoring and evaluating ACF strategies in populations with structural risk factors is essential to ensure that interventions are effective and efficient, and to adapt them to emerging needs. Specific indicators should be studied at each stage of care, as well as the identification of vulnerable groups eligible for screening, the number of people to be screened, the performance of screening tests, diagnostic confirmation, initiation and adherence, and treatment outcomes (cure, failure, dropout, and mortality), and the impact on reducing transmission and the emergence of secondary cases.

In summary, an effective monitoring and evaluation system must be dynamic, adaptive, and based on clear and regularly audited indicators, including both processes (screening coverage) and treatment outcomes for diagnosed cases, with a special focus on social and structural barriers specific to structurally at-risk populations.

IMPLEMENTATION OF ACF FOR TB STRATEGIES IN VULNERABLE POPULATIONS IN BARCELONA

The Vall d'Hebron-Drassanes TB Unit, in collaboration with the TB Program of the Barcelona Public Health Agency, primary care services, and various social institutions and non-governmental and refugee aid organizations, has been running a TB ACF program for vulnerable populations in the city since the 1990s. At present, active TB screening is targeted at the following population groups:

— People with a history of homelessness and people with financial difficulties are referred to soup kitchens because they

are unable to meet their basic food needs, referred by social services.
— People with problematic alcohol consumption and drug users, referred from Care and Follow-up Centers (CAS) and harm reduction centers (REDAN).
— Vulnerable migrants from countries with a high incidence of TB, referred from primary care and various entities.

The study algorithm includes two parts: (1) structured clinical history with TB-specific symptoms questionnaire (cough, expectoration, hemoptysis, night sweats, and weight loss), as well as a previous history of TB and toxic habits, and (2) digital CXR with anteroposterior projection and profile. Both interventions were performed on the same day, and the radiology assessment was performed by a pulmonologist with experience in TB diagnosis. CXR were classified as normal, compatible with TB diagnosis, residual, and other pathologies.

In individuals with clinical or radiological compatible with TB, microbiological studies to confirm the diagnosis were requested on the same day of the visit, including smear microscopy and RMTs (GeneXpert MTB/R) on sputum or induced sputum.

Clinical, social, and housing status were assessed in all reported cases. In those cases in which a correct treatment follow-up could not be guaranteed due to their social situation or their complexity, mainly drug-resistant TB, they were proposed as candidates for directly observed treatment (DOT) in a specialized social-health center. In cases of TB reported in migrant populations, community health workers from the Barcelona Public Health Agency in their community collaborated to facilitate communication, accompany them throughout the treatment, to mediate in conflict situations, active search, and facilitate administrative regularization procedures. TI is studied in those subjects, mainly immigrants, minors, and people with clinical risk factors, by performing TST and IGRA tests, and TB preventive treatment is indicated in cases that meet the criteria for treatment. Free health care and pharmacological treatment were guaranteed for all the people attended, regardless of their administrative status.

A review of ACF TB studies conducted in Barcelona between 1 January 2018 and 31 December 2024, which analyzed more than 10,000 people in socially vulnerable situations (51% has housing problems and 69% were born outside Spain), diagnosed 73 cases of active TB (prevalence 0.72%). DOT was established in 52% of cases, with overall compliance of 87.7%[25]. These excellent results demonstrate the usefulness of ACF strategies for diagnosing cases of TB, some of which are asymptomatic, that would not have been detected by standard passive diagnostic procedures. The integration and coordinated work of multiple health and social actors made it possible not only to recruit vulnerable people for the study, diagnosis, and treatment follow-up but also to cure a very high percentage of cases, comparable to those obtained for the general population in our environment.

However, ACF strategies currently only cover a small proportion of vulnerable people in our environment, as they are carried out on a regular basis in the TB Clinical Units of some health centers and their implementation in the territory remains a challenge. The integration of ACF strategies in at-risk

populations into primary care protocols could respond to this strategic need and have an impact on the local epidemiological situation.

CONCLUSION

ACF strategies in vulnerable populations are not only a health priority, but also an ethical and social imperative. Early detection, appropriate treatment, and the removal of structural barriers are key components in reducing transmission and moving towards the global elimination of TB.

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CONFLICTS OF INTEREST

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript.

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Each of the authors of the article has contributed substantially to the elaboration of the manuscript. All authors have read and agreed to the published version of the manuscript.

ETHICAL CONSIDERATIONS

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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