









Active Case-Finding: An Effective Solution for Tuberculosis Detection in Vulnerable Groups – The Romanian Experience

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Introduction: Tuberculosis (TB) remains a global health challenge, requiring enhanced active case finding (ACF) through screening strategies. This study assesses the effectiveness of such an approach in locating TB cases among vulnerable groups, such as homeless persons, injecting drug users, those detained in prison, and people living in rural areas.

Methods: The study focuses on socio-economic characteristics and TB detection rates across Romanian counties using modern techniques including computer-aided detection of lesions on chest X-ray and GeneXpert tests.

Results: The results highlight the disproportionate burden of TB in vulnerable groups, by revealing significant differences in TB detection rates between regions. Notably, the TB detection rates among these vulnerable groups (250.85 per 100,000 population) are five times higher than the national incidence rate (46.1).

Discussion: These findings underscore the imperative integration of ACF into National TB Program to provide customized and efficient solutions for diverse vulnerable groups, thereby informing crucial public health initiatives and interventions.

Keywords: active screening, vulnerable populations, socio-demographic analysis, GeneXpert, intervention health strategies, tuberculosis

Introduction

With an estimated 10 million cases of tuberculosis (TB) worldwide in 2019 and 7.1 million notified, this disease remains a major public health concern. The numbers estimated and notified differ significantly, and this discrepancy has gotten worse during the COVID-19 epidemic. Another area of concern is drug-resistant tuberculosis (DR-TB), especially multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB). Early diagnosis of TB, prompt detection of drug resistance, and the start of an appropriate treatment plan are necessary for the proper management of TB.¹ An important measure in the management of TB is routine disease screening, which is a key element of the End TB Strategy’s first pillar, which aims to guarantee early detection for all TB patients.² The overall objective of the United Nations and World Health Organization (WHO) aligns with that of the END TB strategy, specifically aiming to reduce the incidence to less than 20 cases per 100,000 population by 2030.^{3,4} Systematic TB screening is described as

the systematic identification of people with presumed TB disease, in a predetermined target group, using tests, examinations, or other procedures which can be applied rapidly

According to the guidelines on TB screening released by WHO and its partners.² Among the instruments used for TB screening is chest radiography (CXR), which has been used on a number of populations. These groups include the general public, human immunodeficiency virus (HIV)-positive individuals, children who are in close contact with TB patients, and other high-risk individuals. All groups examined showed that CXR was a sensitive screening tool, with the potential to lower the prevalence of TB when used in conjunction with early treatment. However, it did not have enough specificity to confirm a TB diagnosis, but it was useful in identifying TB early in children and adults who are more susceptible to the disease.²

CAD software automates processing of digital CXR images for TB screening, generating a risk score. Its accuracy and effectiveness resemble human interpretation, indicating the need for CAD calibration to be adapted to the intended use and environment for effective TB screening.²

The WHO recommends molecular quick diagnostic tests (mWRDs) like Xpert MTB/RIF for TB. The efficacy of these TB screening tests was carefully assessed. Diverse populations with high TB risk were prioritized. Recent study shows that HIV patients and other high-risk populations can improve precision and efficacy. Symptom screening alone may not be enough to detect TB in this group of individuals, emphasizing the need for more complete screening. These patients may suffer serious consequences if TB treatment is delayed, underscoring the urgency of implementing effective screening protocols.^{5–8}

Screening interventions for infectious diseases like TB improve individual health and help communities address the disease's epidemiology. By efficiently identifying and treating TB patients, the goal is to significantly reduce TB prevalence, transmission, and future occurrence in a community.²

Romania's National Tuberculosis Control Strategy 2022–2030 aligns with the WHO's End TB Strategy 2030, demonstrating the disease's continued importance. These strategies outline the global and national steps needed to eliminate TB worldwide.⁹ In the past 15 years, our country has made significant progress in combating TB. The latest data reveal a remarkable 72.4% decrease in the incidence of TB, including both new cases and relapses. This positive trend is particularly noteworthy when we consider that in 2002, our country had the highest global incidence of TB within the Europe/ East European Area (EU/EEA) and ranked among the highest in the WHO European Region. The decline is truly remarkable, with the incidence dropping from a peak of 142.9 cases per 100,000 people in 2002 to 39.7 cases per 100,000 people in 2021.^{9,10} However, the number of notified cases remains a concern, with over 11,000 cases reported annually, although there has been a decrease during the pandemic years. In 2020, the number dropped to 7693, and in 2021, it slightly increased to 7979. Romania's National TB Program (NTP) reports a significant decrease in RR-TB and MDR-TB cases over the past few years, with a significant decrease from 602 cases in 2014 to 263 in 2021 for RR-TB cases and from 532 in 2014 to 193 in 2021 for MDR-TB cases, highlighting the country's ongoing efforts to combat DR strains.¹⁰

It is noteworthy that our study marks the inaugural endeavor to fill the existing gap in TB screening in Romania. We are conducting a thorough evaluation to detect TB patients within vulnerable population groups, with a particular focus on rural areas. This approach presents an innovative method yet to receive global recognition from the WHO.

The primary objective of our study is to assess the TB detection rate among four vulnerable groups using CAD on CXRs and GeneXpert tests, alongside exploring the socio-demographic characteristics of screened individuals with active TB.

Materials and Methods

A retrospective cohort analysis had been performed using data from the Romanian TB screening program implemented by the "Marius Nasta" Pneumology Institute in Bucharest, under the coordination of the Ministry of Health (MoH), between November 2019 and October 2023. The research was conducted in Romania, a high-income country situated in South-Eastern Europe, with a population of 19.3 million inhabitants.

The study focused on individuals aged 18 and above, who were subjected to TB screening.

Participants were selected from four vulnerable populations:

- Homeless People (HP): This category encompassed those without a consistent source of income, or none at all. They are typically uninsured and lacked social support. Screening-targeted individuals showing signs of TB as determined by the medical service provided;
- People who inject drugs (PWID): This group is at heightened risk for infections as hepatitis, HIV and TB;
- Rural residents (RR): This category included individuals residing in rural areas characterized by lower income levels, limited access to healthcare, insufficient health education, and lack of awareness regarding effective prevention methods;
- People deprived of liberty (PDL): Incarcerated individuals or under court supervision. This group faces unique challenges due to the confined living conditions, increased comorbidity risks, and limited access to intensive medical care;

Certain categories have been excluded from the study:

- Non-Romanian Speakers: Individuals who did not communicate effectively in Romanian were excluded due to potential language barriers that could hinder accurate assessment;
- Pregnant Women: Pregnant individuals were excluded, particularly during the first trimester, to ensure the safety of both the mother and the unborn child;
- Refusals: Participants who chose not to participate in the screening process.

These specific inclusion and exclusion criteria have been established to ensure a targeted and representative sample for the study, focusing on those most vulnerable to TB.

The precise choice of the rural intervention area was determined by the local tuberculosis incidence over the previous 5 years, entailing a careful selection of the highest-incidence localities from each county.

The screening activity covered the medical procedures leading to the diagnosis of TB, according to WHO standards, including:

- A medical questionnaire, to identify people likely to have TB and their contacts;
- The CXR has embraced CAD technology using the locally certified Conformité Européenne software – Xvision, specially calibrated for detecting lesions compatible with TB. It operates based on a set of artificial intelligence algorithms, extracting information from a digital CXR and providing specialists with both information about TB and additional images to aid in specific aspects of the imaging process. The screening process involved the use of a lesion score, considered in the screening steps;

The screening procedure was as following:

1. Individuals selected for screening have been fully informed about the project and signed an informed consent form and a GDPR form, then completed a questionnaire, which gather essential general, clinical, demographic and social data for subsequent characterization of the groups;
2. Individuals without contraindications underwent CXR;
3. Based on the results of the medical questionnaire and radiological examination:
 - Those without symptoms or risk factors and normal CXR concluded screening (stopped);
 - Those with at least one symptom or risk factor and/or a CXR with a lesion score of less than 20% were referred to the territorial TB dispensary for evaluation;
 - Those with at least two symptoms/risk factors and/or a CXR with a lesion score of 20% or higher were asked to provide sputum at the mobile caravan for GeneXpert examination and referred to the pulmonologist for further investigations to establish the diagnosis;

4. Individuals at high risk of infection (eg, HIV-infected) had their sputum taken for laboratory examination (ie: GeneXpert, microscopy and culture) regardless of symptomatology or radiological scoring;
5. Individuals with TB have been advised to start treatment, and they contacts were assessed for active or latent TB (LTB) at territorial TB dispensaries. Those with active/latent TB followed treatment according to national standards.

This comprehensive approach ensures a thorough and effective response to TB infection within the vulnerable populations.

Results

The data, systematically collected from November 2019 to May 2023, covers a cohort of active TB cases identified through the screening program. This subset comprised 218 individuals, stratified across distinct vulnerable groups (VG): 89.4% (N = 195) people from rural areas – RR, 2.8% (N = 6) persons who inject drugs – PWID, 6.4% (N = 14) homeless people – HP, and 1.4% (N = 3) people deprived of liberty – PDL.

Incidence Analysis of the Total Screened Participants

The TB detection rates in the screened individuals (per 100,000 population) were determined through the application of the subsequent formula:

$$\frac{\text{Screened participants with active TB}}{\text{Total screened participants}} * 100,000$$

In Table 1 we present the data results from rural residents from all counties.

Table 1 Data Results from Rural Residents from All Counties

County	Screened participants	Sputum/ GeneXpert tests		Referrals to the Specialist		Persons diagnosed with active TB	Incidence of TB cases (per 100,000 population)	Official Global TB Incidence by county in 2022 (NTP) ¹⁰
		Number of persons	%	Number of persons	%			
Alba	1083	48	4.4%	210	19.4%	1	92.34	24.1
Arad	1320	29	2.2%	67	5.1%	3	227.27	47.4
Arges	1612	36	2.2%	105	6.5%	2	124.07	42.5
Bacau	1780	125	7.0%	430	24.2%	4	224.72	57.2
Bihor	768	43	5.6%	188	24.5%	4	520.83	36.5
Bistrita-Nasaud	1984	86	4.3%	170	8.6%	4	201.61	28
Botosani	2031	70	3.4%	96	4.7%	14	689.32	82.7
Braila	2528	64	2.5%	126	5.0%	6	237.34	56.5
Brasov	736	10	1.4%	169	23.0%	2	271.74	25.7
Buzau	1503	12	0.8%	30	2.0%	10	665.34	46
Cluj	1209	80	6.6%	194	16.0%	2	165.43	26
Dambovita	460	22	4.8%	94	20.4%	2	434.78	40.2
Dolj	2365	315	13.3%	53	2.2%	4	169.13	70.1
Galati	3024	76	2.5%	225	7.4%	5	165.34	60.5
Giurgiu	2467	115	4.7%	40	1.6%	6	243.21	64.9
Iasi	2364	140	5.9%	370	15.7%	12	507.61	59.7
Maramures	2042	43	2.1%	87	4.3%	4	195.89	42.8
Mehedinti	2296	61	2.7%	772	33.6%	3	130.66	64.2
Prahova	1473	50	3.4%	162	11.0%	2	135.78	37.5
Salaj	876	22	2.5%	150	17.1%	2	228.31	30.8
Teleorman	1403	13	0.9%	83	5.9%	6	427.66	78.6

(Continued)

Table 1 (Continued).

County	Screened participants	Sputum/ GeneXpert tests		Referrals to the Specialist		Persons diagnosed with active TB	Incidence of TB cases (per 100,000 population)	Official Global TB Incidence by county in 2022 (NTP) ¹⁰
		Number of persons	%	Number of persons	%			
Tulcea	2829	274	9.7%	241	8.5%	17	600.92	64.4
Valcea	1878	50	2.7%	207	11.0%	3	159.74	38.4
Caras-Severin	1599	139	8.7%	356	22.3%	7	437.77	48.1
Constanta	3570	58	1.6%	190	5.3%	11	308.12	54
Gorj	2791	10	0.4%	351	12.6%	5	179.15	57.5
Ialomita	1789	250	14.0%	260	14.5%	4	223.59	60.9
Neamt	3778	123	3.3%	292	7.7%	17	449.97	57.1
Olt	2050	300	14.6%	287	14.0%	4	195.12	72.9
Suceava	2777	110	4.0%	212	7.6%	7	252.07	46.4
Vaslui	3973	73	1.8%	389	9.8%	13	327.21	65.9
Vrancea	1712	14	0.8%	524	30.6%	1	58.41	51.6
Ilfov	4064	268	6.6%	185	4.6%	8	196.85	42.3
Calarasi	1956	46	2.4%	258	13.2%	0	0	68.8
Covasna	594	11	1.9%	89	15.0%	0	0	20.1
Harghita	1222	47	3.8%	208	17.0%	0	0	13.4
Hunedoara	1017	2	0.2%	264	26.0%	0	0	45.9
Mures	1102	79	7.2%	201	18.2%	0	0	32
Satu-Mare	1945	0	0.0%	0	0.0%	0	0	47.7
Sibiu	1119	1	0.1%	221	19.7%	0	0	20.7
Timis	833	46	5.5%	200	24.0%	0	0	38.7
TOTAL	77,922	3361	4.3%	8756	11.2%	195	250.25	-

From a total of 77,922 screened individuals in rural areas, 3361 (4.3%) underwent GeneXpert testing, revealing 195 cases of active TB. The utilization of GeneXpert tests varied, with the highest percentages observed in Dolj (13.3%), Ialomita (14%), and Olt (14.6%) counties. The incidence rates range from 58.41 per 100,000 inhabitants in Vrancea to 689.32 in Botosani, highlighting significant disparities among the assessed counties. Notably, these values surpass the reported incidence at the county level. Furthermore, it is noteworthy that in eight counties, no cases of active TB were identified.

Table 2 evaluates data related to the four targeted vulnerable groups. Out of a total of 86,911 screened participants, 3555 (4.1%) underwent GeneXpert tests, resulting in 218 cases diagnosed with active TB. Regarding the TB incidence calculated per 100,000 population, a notable pattern emerges: the highest incidence was observed among the homeless population, 1113.76, followed by PWID with 576.37, RR with 147.6, and PDL with an incidence of 44.84. The overall TB detection rate (per 100,000) for the study was 250.85, which is over 5 times higher than the incidence rate reported at the country level (46.1).

Detected Cases with Active TB by County

Analysis of screening locations reveals significant patterns. Counties with a high proportion of active TB cases ($\geq 5\%$ of the sample) include Bucharest-Ilfov (12.8%), Neamt (7.8%), Botosani (6.4%), Vaslui (6%), and Iasi (5.5%) in the North-East, and Tulcea (7.8%) and Constanta (5%) in the South-East. These counties also reported TB incidence in 2022 exceeding the national average. In contrast, Alba and Vrancea counties have a lower percentage, each at 0.5% of total active TB individuals ($N = 218$). Notably, while Vrancea's TB incidence in 2022 surpassed the national average, Alba's rate is below (Table S1).

Table 2 Analysis of Incidence in the Screened Vulnerable Groups

Vulnerable group targeted	Screened persons	Sputum/ GeneXpert tests		Referrals to the Specialist		Persons diagnosed with active TB	Incidence of TB cases (per 100,000 population)	Official Global TB Incidence by county in 2022 (NTP) ¹⁰
		Number of persons	%	Number of persons	%			
RR: all counties	77,922	3361	4.3%	8756	11.2%	195	250.25	–
PDL: all counties	6691	118	1.8%	774	11.6%	3	44.84	–
HP: Bucharest+ Ilfov	1257	54	4.3%	199	15.8%	14	1113.76	–
PWID: Bucharest + Ilfov	1041	22	2.1%	181	17.4%	6	576.37	–
TOTAL PARTICIPANTS	86,911	3555	4.1%	9910	11.4%	218	250.83	46.1

Notes: RR, Rural residents; PDL, People deprived of liberty; HP, Homeless people; PWID, People who inject drugs.

Socio-Demographic Analysis of Rural Residents Detected with Active TB, by Socio-demographic profile

In persons with active TB from rural area (N = 195), no significant differences by sex were found, compared with distribution of TB in general population. Of the 195, the majority (73.3%, 143) were male, aligning with the national trend. The regional distribution mirrors the overall pattern, explained by the higher national TB incidence among males. The age distribution aligns with the national norm as well, ranging from 19 to 91 years, with a mean of 55 years. The 45–54 age group recorded the highest values for both sexes ([Table S2](#), [Figure S1](#)).

Concerning marital status, 48.2% (N = 94) were single, while 50.8% (N = 99) were married or in a cohabiting relationship, with two participants not responding to the question. Cohabitation analysis indicated that the majority live with one (29.7%, N = 52) or two persons (29.1%, N = 51), while 6.3% (N = 11) live alone. In terms of employment, 45.1% (N = 88) were inactive, 16.4% (N = 32) were employed, of which only 68.8% (N = 22) declared their workplaces, and others fall into categories such as social assistance beneficiaries (7.2%, N = 14), retirees (29.7%, N = 58), and unemployed (1.5%, N = 3). To comprehensively assess the medical profile of TB cases, their access to medical services was examined. Regarding insurance status, 68.7% (N = 134) were insured, 24.6% (N = 48) were not and 6.7% (N = 13) did not respond. Enrollment with a family doctor, a key indicator of access to essential medical services, was declared by 90.3% (N = 176) ([Table S2](#)).

Health status and risk factors

Regarding the number of symptoms, 71.8% (N = 140) reported at least one characteristic TB symptom. Only one participant reported experiencing all listed symptoms, while 55 (28.2%) did not report any. No statistically significant differences were noted in the number of symptoms declared by respondents. In case of individuals who exhibited two specific TB symptoms, over 80% were smokers or former smokers (72.7% and 9.1%, respectively) and 68.2% reported alcohol consumption ([Tables S3](#), [S4](#), [S5](#)).

The severity of TB symptoms is influenced by the patient's immune status and age. Analysis of TB cases by age and symptoms showed no statistically significant differences related to sex. With age, patients are more likely to exhibit three or more TB symptoms. Notably, in the age group with the highest number of positive persons (45–54 years old), the majority reported no symptom ([Figure S2](#)). Thus, the results highlight that there is insufficient evidence to conclude that there are significant differences between men and women regarding age or the number of symptoms within the studied population.

To provide a deeper insight into the magnitude of differences between groups, we calculated the effect size.^{11,12} The analysis revealed that the variations related to age between sexes demonstrate a relatively small effect size (Cohen's d =

0.33). The result shows that age discrepancies between gender groups are minor and most likely devoid of significance from a practical application perspective. However, the difference in the number of symptoms manifested between the sexes highlighted a significantly more pronounced effect size, with Cohen's $d = 0.89$. Although statistical significance was not achieved for any variable, this result indicates considerably more accentuated variability, signaling a potential area of interest for future research.

Regarding the addictions and chronic conditions, from the total sample of 195 positive TB subjects, smoking (55.4% smokers and 12.3% former smokers) and alcohol consumption (52.8%) were prevalent. The majority of smokers and alcohol consumers were male (62.2% and 66.4%, respectively). Notably, 12.8% reported daily alcohol consumption, with 1.9% female and 16.8% male participants. Regarding drug consumption, 98.5% declared non-use, while 3 participants (1.5%) did not respond. The 45–54 age group has the highest proportion of alcohol consumers (33%) and smokers (35.2%), with variations among males (33.7%) and females (42.1%). Significantly, 21.5% ($N = 42$) of the total sample did not declare any addiction, with approximately 60% being over 65 years old (Table S6).

When considering comorbidities, 23.1% ($N = 45$) reported a history of TB, 16.4% ($N = 32$) reported arterial hypertension, 4.6% ($N = 9$) chronic respiratory diseases, and 4.1% ($N = 8$) diabetes (Figure S3).

Among the 23.1% of individuals with a previous episode of TB, the majority (42.2%, $N = 19$) were within the 55–64 age group, with an average age of 57 years. Surprisingly, over 50% of those individuals remain active in the labor market. Additionally, addiction analysis revealed that 66.7% were smokers, with 11.1% admitting past smoking and 64.4% alcohol consumption (Table S7). When examining the TB-related family medical history, out of 195 individuals, 25 (12.8%) mentioned family members with a TB history and 13 (6.7%) reported personal experience or acquaintance with someone affected by TB (Table S8).

Socio-Demographic Analysis of Other Vulnerable Groups (PDL, HP, PWID)

These three vulnerable groups comprise in total 23 individuals, with PDL accounting for 3, HP for 14, and PWID for 6. Examining marital status, 99.9% of HP and 66.7% of PDL were single, contrasting with PWID, among whom 66.7% stated being married or in a concubinage relationship. Regarding household size, 50% of TB positive HP live alone, 33.3% with one person and 16.7% with 5 people, while PWID share their residence with 1 or 5 people (33.3%) or 2 or 4 people (16.7%). PDL declared living with 5, 11, and 40 people in the same space. Importantly, none of the individuals in these three categories were active in the labor market (Table S2).

Discussion

The implementation of active TB detection is an essential step for any country that is witnessing a decrease in the occurrence of this disease, as is currently observed in Romania. Countries with a high prevalence of TB implement national screening programs in diverse formats.^{13,14} In the current screening program, we implemented ACF through the integration of radiological examination and GeneXpert testing. The inclusion criteria in the program focused on belonging to a vulnerable category (RR, PWID, HP, and PDL) and the existence of risk factors for TB.

ACF for TB is a growing priority in the South East Asia Region amid the COVID-19 pandemic. Many countries have integrated ACF into national plans, overcoming challenges through community mobilization. Despite the overlap with the pandemic, careful planning ensured continuous case identification.^{15,16} An example from rural India demonstrated ACF success, identifying over 8700 symptomatic cases among 65,000 individuals, with 17% (964) confirmed positive for TB through smear tests.¹⁷ A separate ACF initiative targeted households in urban slums, tribal areas, and remote rural regions. Approximately 4.9 million households, encompassing around 20 million people, underwent screening. Out of 350,047 presumptive pulmonary TB cases (individuals with a cough lasting ≥ 2 weeks), 187,586 (54%) underwent sputum smear examination, leading to the identification of 14,447 (8%) smear-positive TB cases.¹⁸ In another study, Shewade et al primarily emphasized the screening of susceptible persons, such as individuals undergoing immunosuppressive therapy, the elderly population, individuals lacking adequate housing and residing in night shelters, nursing homes, and orphanages, as well as incarcerated individuals and street children. It was found that TB was detected in 3.4% of homeless individuals. Furthermore, in areas that are difficult to access, the frequency of TB detection varied between 4.5% and 6.3%. Moreover, 2.6% of the incarcerated population under evaluation exhibited a diagnosis of TB, while 5.8%

of individuals aged 60 and above were identified as having TB.¹⁹ A study from South Africa by Churchyard suggests that screening every 12 months is generally sufficient for identifying TB cases in vulnerable communities, emphasizing the importance of adaptation to specific demographic and epidemiological factors for optimal accuracy.²⁰

Data from Romania between 2015 and 2017 highlights a concerning increase in TB cases among vulnerable populations. Individuals in specific categories, making them more susceptible to the disease, were found to have TB rates significantly higher, up to 7 to 18 times, compared to the general population.²¹

The effectiveness of TB screening can be evaluated using a key metric, namely the detection rate. To contextualize this, we examined the overall TB incidence (per 100,000 individuals) in Romania, which was reported as 57.1 cases in 2020, decreasing to 39.7 in 2021, and slightly increasing to 46.1 in 2022. In contrast, our study revealed a remarkable TB detection rate of 250.83 per 100,000 individuals, which is more than 5 times higher compared to the official national incidence reported by NTP.¹⁰ Notably, the homeless population emerged as the most affected group, exhibiting an alarming incidence rate of 1113.76 per 100,000. Following closely behind are individuals who inject drugs, with a detection rate of 576.37 per 100,000. Additionally, those residing in rural areas had been reported a detection rate of 147.64 per 100,000. Individuals in incarceration had a detection rate of 44.84 per 100,000, as a result of NTP efforts and the prior E-DETECT screening initiative, targeting this category.²²

Furthermore, based on our study's results, there was a notable escalation in TB incidence across specific counties. Particularly, Tulcea witnessed a remarkable surge, surpassing 600, reaching a detection rate of 600.92 per 100,000. Similarly, Buzău and Botoșani recorded a substantial increase in cases, reporting detection rates of 665.34 and 689.32 per 100,000, respectively. However, it is important to note that eight counties, including Calarasi, Timis, Satu Mare, Hunedoara, Mures, Sibiu, Harghita, and Covasna, reported no instances of TB during the study period, as indicated in [Table 1](#). These results prompt an analysis in three main directions, when examining the detection data.

Firstly, our study remarkably uncovered a notable similarity between higher incidence rates in specific counties and the national level, albeit at significantly lower values. This emphasizes the consistency of our study's results.

Secondly, the issue of TB detection within the screening program is particularly concerning in three counties: Calarași, Timiș, and Satu Mare. These counties, identified with high or average TB incidence by NTP, reported incidence rates of 68.8, 38.7, and 47 per 100,000, respectively. Recognizing these limitations prompts a closer examination of the community selection process for screening and the execution of mobilization efforts during the screening caravan.

Thirdly, a significant disparity emerged between the reported incidence and the actual detection rate during screening in Bihor County. While the reported incidence is relatively low, at 36.5, the screening process has revealed a substantially higher detection rate of 520.83 per 100,000. This raises questions about the accuracy of reported incidence rates and underscores the importance of comprehensive screening measures in identifying health conditions.

Analysis of symptoms revealed that 71.8% of participants reported at least one TB symptom, while 28.2% reported none. Notably, a high prevalence of smoking (55.4% smokers and 12.3% former smokers) and alcohol consumption (52.8%) was observed, particularly in the 45–54 age group. Noteworthy comorbidities included a history of TB (23.1%) and arterial hypertension (16.4%). This underscores the imperative of integrating socio-economic and environmental considerations into screening strategies to effectively address the complex challenges presented by TB in diverse populations.

The analysis of other vulnerable groups (PDL, HP, PWID) highlights unique socio-demographic characteristics, with distinctive marital statuses and household sizes. Importantly, none of these individuals were active in the labor market, revealing potential barriers to healthcare access.

The inclusion of these details in the analysis emphasizes the nuanced socio-demographic landscape of TB and underscores the necessity for targeted interventions and comprehensive public health strategies to address the specific challenges presented by these vulnerable populations. This aligns with WHO recommendations, emphasizing the importance of tailoring screening methods to the socio-demographic particularities of the implementing country.^{2,23}

Our study mainly focused on assessing vulnerable groups according to socioeconomic conditions, whereas other studies, such as Nunemo's study, targeted populations with specific comorbidities such as hypertension and diabetes. Interestingly, Nunemo et al found that the majority of TB patients had no comorbidities with noncommunicable diseases, and among TB patients, the prevalence of hypertension was 6.55% and diabetes 5.64%. This highlights the limited

presence of comorbidities among TB patients and underlines the effectiveness of our approach in targeting vulnerable groups, mainly based on socio-economic factors. However, it also highlights the importance of exploring different approaches to address the complex landscape of public health challenges.²⁴

The limitations of this study include the focus on data from the past 5 years to select localities with high TB incidence, which may underestimate or overestimate the current epidemiological landscape. Additionally, while the inclusion and exclusion criteria are established to ensure a representative sample, they might exclude certain vulnerable groups that do not strictly fit within these categories. It is important to note that the innovative approach, concentrating on the rural area, may not be directly comparable to similar studies, making it challenging to generalize the results globally. Another inherent limitation lies in the predominantly descriptive nature of the study, without clearly defined correlations. Future steps involve a nuanced analysis of the population's structure and risk factors, paving the way for subsequent exploration of correlations between socioeconomic criteria and risk factors. It is noteworthy to underline that within our study, we did not collect specific data regarding the direct and indirect costs associated with TB diagnosis. However, the literature indicates that ACF, when implemented in marginalized and disadvantaged communities, has led to a decrease in overall costs and the occurrence of additional costs associated with TB diagnosis. It is important to highlight that, despite these financial benefits, ACF has not effectively addressed social inequalities in these communities. Thus, there is considerable interest in continuing to explore and evaluate the potential implications of ACF strategies for prioritizing and managing TB in various populations, considering the complexity of socio-economic factors and access to healthcare services.

The strengths of the study are represented by the following: The implementation of a systematic screening process for TB in Romania marked the first instance of such a project in our country. This initiative was motivated by the benefits it offers to individuals who are at risk of contracting TB. Timely identification and initiation of treatment can improve their prognosis and reduce their costs. Additionally, our study had a positive impact on entire communities that were more susceptible to TB by decreasing the occurrence of the disease and averting future instances. Moreover, screening can circumvent the obstacles that individuals have when seeking healthcare, by offering a straight route to receiving medical attention, especially in the vulnerable groups that we conducted the study upon and who did not have access to medical professionals. The detection of TB is contingent upon individuals seeking medical attention at healthcare facilities in the absence of screening. Screening has the potential to mitigate delays in the diagnosis of TB and thus decreases expenses and the likelihood of severe financial burdens for individuals affected by TB. An important direction of the health policies drawn by this research resides in the recommendation to evaluate the risk of tuberculosis within the administrative-territorial units as an optimal solution for evaluating the control of tuberculosis.

Conclusion

Our data strongly support the necessity of reassessing the selection process for TB screening settings, according to risk categories. This research provides a comprehensive understanding of the complex socio-demographic factors and health difficulties faced by populations affected by tuberculosis. It is important to emphasize the importance of customized interventions and support services that are inherent in national tuberculosis initiatives, especially in vulnerable groups. The use of this strategic ACF screening method not only assists in saving important resources by optimizing staff, medical equipment, and infrastructure but also improves efficiency in the detection and subsequent treatment of tuberculosis. It propels us closer to reducing the incidence and ultimately eradicating this disease.

Abbreviations

TB, tuberculosis; ACF, active case finding; DR-TB, drug-resistant tuberculosis; MDR/RR-TB, multidrug- or rifampicin-resistant tuberculosis; WHO, World Health Organization; CXR, chest radiography; HIV, human immunodeficiency virus; CAD, computer-aided detection; mWRDs, WHO recommended molecular rapid diagnostic tests for tuberculosis; EU, Europe; EEA, East Economic Area; NTP, National TB Program; MoH, Ministry of Health; HP, homeless people; PWID, people who inject drugs; RR, rural residents; PDL, People deprived of liberty; LTB, latent tuberculosis; VG, vulnerable groups; ATU, administrative-territorial unit.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of “Marius Nasta” Institute of Pneumology (No.: 23935/25.10.2023).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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Disclosure

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References

1. World Health Organization (WHO). Module 3: diagnosis - rapid diagnostics for tuberculosis detection, 2021.
2. WHO. WHO Consolidated Guidelines on Tuberculosis Module 2: Systemic Screening for Tuberculosis Disease. 2020.
3. Stop TB Partnership. UNHLM on TB political declaration: key targets & commitments for 2022; 2018.
4. World Health Organization. The end strategy TB. *End TB Strateg*. 2015;53(9):1689–1699.
5. Nurwidya F, Handayani D, Burhan E, Yunus F. Molecular diagnosis of tuberculosis. *Chonnam Med J*. 2018;54(1):1. doi:10.4068/cmj.2018.54.1.1
6. Woods GL. Molecular methods in the detection and identification of mycobacterial infections. *Arch Pathol Lab Med*. 1999;123(11):1002–1006. doi:10.5858/1999-123-1002-MMITDA
7. Kunduraciocğlu A, Karasu L, Biçmen C, Özsoz A, Erbaycu AE. Yayma Negatif Tuberkuloz Olgularinin Tanisinda MTD Gen-Probe® Testi, BACTEC 960™ Sistemi ve Löwenstein-Jensen Kultur Yöntemlerinin Performansinin Karşılaştırılması. *Mikrobiyol Bul*. 2013;47(3):417–431. doi:10.5578/mb.5728
8. Papaventsis D, Ioannidis P, Karabela S, et al. Impact of the Gen-Probe Amplified MTD® test on tuberculosis diagnosis in children. *Int J Tuberc Lung Dis*. 2012;16(3):384–390. doi:10.5588/ijtld.11.0276
9. Strategia Na țională pentru Controlul Tuberculozei în România 2022-2030. Available from: <https://sgg.gov.ro/1/wp-content/uploads/2022/09/ANEXA-Strategia-Nationala-.pdf>. Accessed 2 May, 2024.
10. Ghid Metodologic de Implementare a Programului Național de Prevenire, Supraveghere și Control al Tuberculozei și altor Micobacterioze, București 2023, ISBN: ISBN 978-973-0-38231-0. Available from: <https://marius-nasta.ro/wp-content/uploads/2023/04/Ghid%20metodologic%20TB.pdf>
11. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Routledge; 2013.
12. Perez-Navarro LM, Restrepo BI, Fuentes-Dominguez FJ, et al. The effect size of type 2 diabetes mellitus on tuberculosis drug resistance and adverse treatment outcomes. *Tuberculosis*. 2017;103:83–91. doi:10.1016/J.TUBE.2017.01.006
13. Shargie EB, Mørkve O. Tuberculosis case-finding through a village outreach programme in a rural setting in southern Ethiopia: community randomized trial. *Bull World Health Organ*. 84:112–119. doi:10.2471/BLT.05.024489
14. Hanrahan CF, Nonyane BAS, Mmolawa L, et al. Contact tracing versus facility-based screening for active TB case finding in rural South Africa: a pragmatic cluster-randomized trial (Kharitode TB). *PLoS Med*. 2019;16(4):e1002796. doi:10.1371/journal.pmed.1002796
15. Singh AA, Creswell J, Bhatia V. Framework for planning and monitoring active TB case finding interventions to meet the global targets in the COVID-19 era and beyond: south-East Asia perspective. *PLOS Glob Public Heal*. 2021;1(11).

16. Burke RM, Nliwasa M, Feasey HRA, et al. Community-based active case-finding interventions for tuberculosis: a systematic review. *Lancet Public Heal.* 2021;6(5):e283–e299. doi:10.1016/S2468-2667(21)00033-5
17. Vyas A, Creswell J, Codlin AJ, et al. Community-based active case-finding to reach the most vulnerable: tuberculosis in tribal areas of India. *Int J Tuberc Lung Dis.* 2019;23(6):750–755. doi:10.5588/ijtld.18.0741
18. Prasad BM, Satyanarayana S, Chadha SS. Lessons learnt from active tuberculosis case finding in an urban slum setting of Agra city, India. *Indian J Tuberc.* 2016;63(3):199–202. doi:10.1016/j.ijtb.2016.08.006
19. Shewade HD, Kiruthika G, Ravichandran P, et al. Quality of active case-finding for tuberculosis in India: a national level secondary data analysis. *Glob Health Action.* 2023;16(1). doi:10.1080/16549716.2023.2256129
20. Churchyard GJ, Fielding K, Roux S, et al. Twelve-monthly versus six-monthly radiological screening for active case-finding of tuberculosis: a randomised controlled trial. *Thorax.* 2011;66(2):134–139. doi:10.1136/thx.2010.139048
21. Munteanu I, Cioran N, van Hest R, et al. Tuberculosis surveillance in Romania among vulnerable risk groups between 2015 and 2017. *Ther Clin Risk Manag.* 2022;18:439–446. doi:10.2147/TCRM.S347748
22. de Vries G, Gainaru D, Keizer S, et al. Human reading versus computer-automated reading of chest radiographs in a tuberculosis screening programme in Romania. *Eur Respir J.* 2021;58(1):2004628. doi:10.1183/13993003.04628-2020
23. World Health Organization RO for SEA. Optimizing Active Case-Finding for Tuberculosis; 2019.
24. Nunemo MH, Gidebo KD, Woticha EW, Lemu YK. Integration challenges and opportunity of implementing non-communicable disease screening intervention with tuberculosis patient care: A mixed implementation study. *Risk Manag Healthc Policy.* 2023;16:2609–2633. doi:10.2147/RMHP.S432943

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