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Tran Duc Anh Ly, Floriane Holi-Jamovski, van Thuan Hoang, Ndiaw Goumballa, Meriem Louni, et al.. Screening Strategy of Active Pulmonary Tuberculosis in Sheltered Homeless People in Marseille, 2019. Journal of Epidemiology and Global Health, 2021, 11 (1), pp.124. 10.2991/jegh.k.201009.001. hal-03243172

HAL Id: hal-03243172 https://amu.hal.science/hal-03243172

Submitted on 1 Jun 2021

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Journal of Epidemiology and Global Health Vol. 11(1); March (2021), pp. 124–131 DOI: https://doi.org/10.2991/jegh.k.201009.001; ISSN 2210-6006; eISSN 2210-6014 https://www.atlantis-press.com/journals/jegh



Research Article

Screening Strategy of Active Pulmonary Tuberculosis in Sheltered Homeless People in Marseille, 2019

Tran Duc Anh Ly^{1,2,1}, Floriane Holi-Jamovski³, Van Thuan Hoang^{1,2,4,1}, Ndiaw Goumballa^{1,2,5}, Meriem Louni^{1,2}, Thi Loi Dao^{1,2,6,1}, Michel Drancourt^{2,7}, Philippe Gautret^{1,2,*}, D

¹Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France

ARTICLE INFO

Article History

Received 05 July 2020 Accepted 19 September 2020

Keywords

Active pulmonary tuberculosis tuberculosis-screening questionnaire chest X-ray microscopical testing GeneXpert MTB/RIF assays culture

ABSTRACT

We aimed to assess the reliability of a screening questionnaire for Active Pulmonary Tuberculosis (APTB) in a population of sheltered homeless persons (HP). Participants from two homeless shelters completed a questionnaire specially designed to identify patients at highrisk of APTB (available at www.tb-screen.ch), underwent a Chest X-ray (CXR), and provided sputum samples. Computed Tomography (CT) scanning was subsequently performed on those which had images consistent with APTB. Microscopical examination, real-time polymerase chain reaction (qPCR) and culture testing were applied for $Mycobacterium\ tuberculosis$ complex detection. Additionally, we retrospectively selected 16 HP hospitalised in our hospital between 2017 and 2019 with biologically confirmed tuberculosis and typical CXR images, and retrospectively documented a screening questionnaire by reviewing their medical files. Overall, the population ($n = 383\ HP$) was predominantly migrants (87%). Forty-seven individuals (11.7%) had positive screening questionnaire scores and four (2.4%) displayed abnormal CXR features consistent with APTB. Three of them three underwent CT scanning that ruled out APTB and one was lost to follow-up. None tested positive through microbiological investigation. Fifteen (of 16, 93.8%) hospitalised patients with biologically confirmed APTB had a positive screening questionnaire score. The sensitivity and specificity of questionnaire for confirmed APTB were 93.8% and 87.7%, respectively. Screening questionnaires can be used as a first assessment tool in people arriving at homeless shelters and to refer those screening positive for a CXR.

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1. INTRODUCTION

In France, the annual incidence of Active Pulmonary Tuberculosis (APTB) in 2018 was 5.4 per 10⁵ individuals, and the trend of morbidity and mortality regularly decreased over the past 20 years [1,2]. Nevertheless, concentrated epidemics continue to occur among hard-to-reach groups such as homeless people and migrants [1,2]. Homeless people accounted for 7% of all new ATPB cases in Marseille (France) in 2016, while the homeless population in Marseille represents only around 0.2% of the population [3]. Over the past two decades, we have seen a change in the sheltered homeless population in Marseille, with a rising proportion of migrants [4]. All of the nine homeless APTB patients hospitalised at our hospital between 2017 and 2018 were migrants [5]. Screening for APTB in homeless people is, therefore, of major importance in terms of public health.

*Corresponding author. Email: philippe.gautret@club-internet.fr

Data availability statement: All data generated or analysed during this study are included in this published article.

In a preliminary study conducted by our team in 2018, in two Marseille homeless shelters, we showed that the use a short questionnaire aiming at screening for APTB [6] was well accepted by both homeless persons and medical staff during Chest X-ray (CXR)-based TB screening campaigns [3]. In this paper, we report the results of cross-sectional 1-day surveys conducted at these two Marseille homeless shelters in 2019, where all participants were investigated using questionnaire, chest radiography and microbiological examination of respiratory samples, with the aim of assessing the reliability of this screening questionnaire in a population of sheltered homeless people.

2. MATERIALS AND METHODS

2.1. Ethics

Ethical approval was obtained from the Marseille Institutional Review Board and Ethics Committee (Protocol number: 2010-A01406-33). Written informed consent was obtained from the survey participants.

²IHU-Méditerranée Infection, Marseille, France

³Centres de Lutte Antituberculeuse, Marseille, France

⁴Family Medicine Department, Thai Binh University of Medicine and Pharmacy, Vietnam

⁵VITROME, Campus International IRD-UCAD de l'IRD, Dakar, Senegal

⁶Pneumology Department, Thai Binh University of Medicine and Pharmacy, Vietnam

⁷Aix Marseille Univ, MEPHI, Marseille, France

2.2. Setting, Study Design and Population

In this cross-sectional 1-day survey, adult homeless people housed in shelters A and B in Marseille were recruited on a voluntary basis during three campaigns conducted in March, May, and December 2019. Participants were systematically asked to provide basic demographic information and information on their smoking habits, and to complete a questionnaire specially designed to identify patients at a high risk of APTB [6]. Mobile CXR were systematically performed on site at enrolment and analysed by a pneumonologist. Finally, two sputum samples were systematically collected from each participant, including one in a sterile vial for microscopic examination and real-time PCR, and another in a vial containing transport medium (C-Top TransBK liquid medium, Eurobio Scientific, Ulis, France) for mycobacterial culture. Samples from patients testing positive through the questionnaire screening and/ or CXR with images consistent with APTB, and/or with a positive microscopic examination were further tested by qPCR (Figure 1).

In addition, we retrospectively selected sixteen homeless patients hospitalised in our hospital between 2017 and 2019 with biologically confirmed tuberculosis and typical CXR images, and retrospectively documented a screening questionnaire by reviewing their medical files.

2.3. Questionnaire

The questionnaire is designed to identify patients at high risk of APTB, based on their country of origin, clinical data, history of TB, and contact with TB patients (www.tb-screen.ch, version 4.3.1 updated 3 January 2018) [6]. The questionnaire comprised nine closed simple questions available in 32 differences languages (together with visual and audio formats) that takes a short time to complete. Participants with a score ≥10 are considered likely to be suffering from APTB. Questionnaires were administered by nurses under the supervision of medical doctors.

2.4. Chest Radiography

All CXRs with images consistent with APTB were double-checked by radiologists within 48 h and patients with abnormal findings underwent a Computed Tomography (CT) scan within 2 weeks, when possible.

2.5. Laboratory Procedure

Quality of expectorated sputum specimens was assessed using quantification of squamous epithelial cells and polymorphonuclear

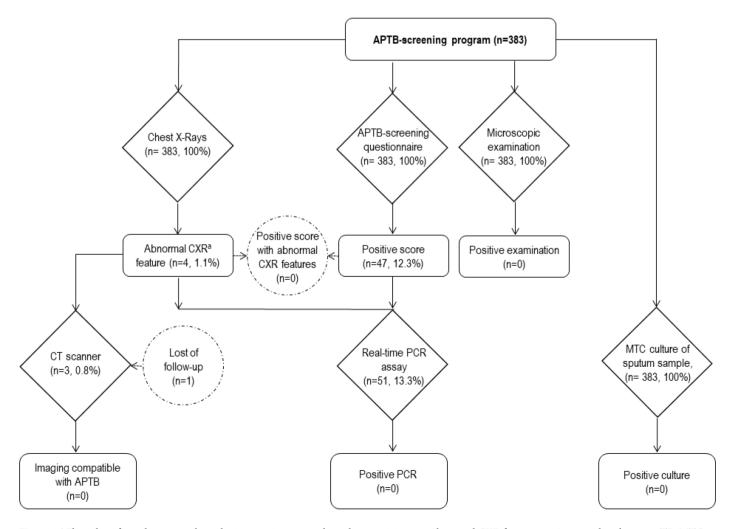


Figure 1 | Flow chart for pulmonary tuberculosis screening among homeless participants. ^aAbnormal CXR feature consistent with pulmonary TB. MTC, *Mycobacterium tuberculosis* complex.

cells per low-power field, in a Gram-stained smear of the specimen. Sputum samples were stained using a kit featuring Kinyoun staining (Cold ZN, RAL, Toulouse, France) and scanned by automated microscopy (Axio Scan Z1 Digital Slide Scanner, Zeiss, Germany) [7]. Positive results were confirmed by classical microscopic examination after Ziehl-Neelsen staining, qPCR (GeneXpert MTB/ RIF assays, Cepheid, Sunnyvale, CA, USA) was performed to detect Mycobacterium tuberculosis and rifampicin resistance genes, according to the manufacturer's recommendations. Participants were informed of their microscopy and qPCR results within 72 h of recruitment. Culture of M. tuberculosis Complex (MTC) organisms was carried out on solid culture media including Coletsos medium (bioMérieux, France) for all samples for up to 6 weeks. The case definition for confirmed APTB was a positive qPCR (highly sensitive detection method) and/or a positive culture for MTC organisms which is considered the gold standard. If an individual was confirmed to have APTB, they were referred to hospital.

2.6. Statistical Analysis

Data were collected and analysed using SPSS (version 23.0, IBM, USA). Percentage differences were tested using Pearson's chi-square or Fisher's exact tests when appropriate. The theoretical normal distribution of quantitative data was assessed using Shapiro–Wilks test and means of quantitative data were compared using the Wilcoxon signed-rank test when samples were not normally distributed. A p-value <0.05 was considered to be statistically significant. The sensitivity and specificity of questionnaire for confirmed APTB were also calculated.

3. RESULTS

3.1. Characteristics of Individuals Participating in Screening Campaigns

Overall, 383 subjects volunteered to participate in this study, accounting for an estimated 40% of homeless people sheltered within in two shelters at the time of enrolment (Table 1). About two-thirds were recruited from shelter A. All subjects were male, and their mean age was 40 years. The majority of participants were migrants and had settled in France approximately 6 years before the survey took place. Two-thirds had health insurance when they were recruited. A proportion of 53.5% of patients reported that they smoked tobacco.

3.2. Screening Questionnaire

The results of the screening questionnaires are summarised in Tables 2 and 3. Forty-seven participants (12.3%) screened positive (with a score \geq 10), and 336 (87.7%) screened negative (with a score \leq 10). Five (of 383, 1.3%) participants came from countries with a national TB incidence over 500/100,000 inhabitants or a national Multidrug-resistant Tuberculosis (MDR-TB) incidence higher than 20/100,000 inhabitants, including Russia (n=2), Georgia (n=2), and Somalia (n=1). Regarding alleged symptoms, 21.7% of individuals reported recent weight loss; 21.4% currently felt ill; 21.1% reported a productive cough and 13.3% reported a prolonged cough; 11.0% reported sweating at night. A proportion of 4.7% of participants reported previous TB treatment and 3.1%

Table 1 Characteristics of homeless population (n = 383 individuals) participating in screening campaigns

Characteristics	Total	Positive screening according to questionnaire	Negative screening according to questionnaire	p-value ^a
Total	383	47	336	_
Shelter				
A	266 (69.5)	36 (76.6)	230 (68.5)	0.26
В	117 (30.5)	11 (23.4)	106 (31.5)	-
Sex				
Male	383 (100)	47 (100)	336 (100)	1.00
Female	0 (0)	0 (0)	0 (0)	-
Mean age (years, SD)	40.0 ± 16.6	40.0 ± 15.0	40.0 ± 16.8	0.76°
Age range (years) ^b	18-90	22-82	18-90	_
≤34 years of age	196 (53.3)	22 (46.8)	174 (51.9)	0.51
>34 years of age	186 (48.7)	25 (53.2)	161 (48.1)	-
Unknown	1 (-)	_	-	-
Geographical origin				
France	50 (13.1)	6 (12.8)	44 (13.1)	N/A
Other countries	333 (86.8)	41 (87.2)	292 (86.9)	-
Mean duration of residence in France for migrants (SD)	6.1 (0-19.1)	6.6 (0-19.9)	6.0 (0-18.9)	0.68°
Range of duration of residence in France for migrants ^b	1 week to 59 years	1 month to 48 years	1 week to 59 years	_
≥10 months	154 (50.8)	20 (57.1)	134 (50.0)	0.43
<10 months	149 (49.2)	15 (42.9)	134 (50.0)	-
Health insurance				
Yes	254 (66.3)	34 (72.3)	220 (65.5)	0.35
No	129 (33.7)	13 (27.7)	116 (34.5)	-
Tobacco consumption	205 (53.5)	24 (51.1)	181 (53.9)	0.72

^{*}Comparison between positive questionnaire group and negative questionnaire group. bMedian of the variable is used for analysis. Wilcoxon signed-rank test was used. SD, standard deviation; N/A, not applicable.

 Table 2 | Tuberculosis screening questionnaire

Items	Total	Positive screening	Negative screening
Total	383	47	336
Mean of score (SD, range)	$4.9 \pm 3.5 (0-16)$	$11.7 \pm 1.7 \ (10-16)$	$4.0 \pm 2.5 (0-9)$
Part 1. (Q0) Country of origin (0–8 points)			
0 if national TB incidence <20/100,000	67 (17.5)	7 (14.9)	60 (17.9)
1 if 20–49/100,000	32 (8.4)	0 (0)	32 (9.5)
2 if 50–99/100,000	123 (32.1)	11 (23.4)	112 (33.3)
3 if 100–149/100,000	38 (9.9)	0 (0)	38 (11.3)
4 if 150–199/100,000	50 (13.1)	10 (21.3)	40 (11.9)
5 if 200–299/100,000	5 (1.3)	0 (0)	5 (1.3)
6 if 300–399/100,000	63 (16.4)	18 (38.3)	45 (13.4)
7 if 400–499/100,000	0 (0)	0 (0)	(0)
8 if \geq 500/100,000 or if national MDR-TB incidence \geq 20/100,000	5 (1.3)	1 (2.1)	4 (1.2)
Part 2. Interview questions (0–16 points)			
Q1. Cough (4 points if positive answer: have you been coughing for more than 3 weeks?)	51 (13.3)	26 (55.3)	25 (7.4)
Q2. Cough with phlegm (2 if positive answer)	81 (21.1)	30 (63.8)	51 (15.2)
Q3. Weight loss over the last 3 months (1 if positive answer)	83 (21.7)	34 (72.3)	49 (16.4)
Q4. Sweat at night (1 if positive answer)	42 (11.0)	18 (38.3)	24 (11.2)
Q5. Previous TB treatment (1 if positive answer)	18 (4.7)	4 (8.5)	14 (4.2)
Q6. TB in member of immediate family (1 if positive answer)	12 (3.1)	7 (2.1)	5 (10.6)
Q7. Currently feeling ill (3 if positive answer)	82 (21.4)	35 (74.5)	47 (14.0)
Q8. Impression of poor health by the examiner (3 if positive answer)	31 (8.1)	14 (29.8)	17 (5.1)

Q0-Q8, question from 0 to 8.

Table 3 Details of 47 participants screening positive by questionnaire

ID code Participant		Score												
	Country of origin (Q0)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	- Total score	CXR ^a	ME	qPCR ^b	Culture ^c
N°1	Ivory Coast (4)	4	2	1	1	0	1	3	0	16	Normal	NEG	NEG	NEG
N°2	Nigeria (6)	4	2	1	0	0	0	0	3	16	Normal	NEG	NEG	NEG
N°3	Russia (8)	4	2	1	0	0	0	0	0	15	Normal	NEG	NEG	NEG
N°4	Algeria (2)	4	2	1	0	0	0	3	3	15	Normal	NEG	NEG	NEG
N°5	Algeria (2)	4	2	1	0	0	0	3	3	15	Normal	NEG	NEG	NEG
N°6	France (0)	4	2	1	1	0	0	3	3	14	Normal	NEG	NEG	NEG
N°7	Algeria (2)	4	2	0	1	0	1	3	0	13	Normal	NEG	NEG	NEG
N°8	Nigeria (6)	0	2	1	1	0	0	3	0	13	Normal	NEG	NEG	NEG
N°9	Nigeria (6)	0	2	1	1	0	0	3	0	13	Normal	NEG	NEG	NEG
N°10	Niger (6)	4	2	0	1	0	0	0	0	13	Normal	NEG	NEG	NEG
N°11	Nigeria (6)	0	2	1	1	0	0	3	0	13	Normal	NEG	NEG	NEG
N°12	Nigeria (6)	0	0	1	0	0	0	3	3	13	Normal	NEG	NEG	NEG
N°13	France (0)	4	2	1	0	0	0	3	3	13	Normal	NEG	NEG	NEG
N°14	Guinea (4)	0	0	1	0	0	1	3	3	12	Normal	NEG	NEG	NEG
N°15	Guinea (4)	4	2	1	1	0	0	0	0	12	Normal	NEG	NEG	NEG
N°16	Algeria (2)	4	0	0	0	0	0	3	3	12	Normal	NEG	NEG	NEG
N°17	Algeria (2)	4	2	1	0	0	0	3	0	12	Normal	NEG	NEG	NEG
N°18	Algeria (2)	0	2	1	1	0	0	3	3	12	Normal	NEG	NEG	NEG
N°19	Nigeria (6)	0	2	1	0	0	0	3	0	12	Normal	NEG	NEG	NEG
N°20	Nigeria (6)	0	2	0	1	0	0	3	0	12	Normal	NEG	NEG	NEG
N°21	Algeria (2)	4	2	1	0	0	0	3	0	12	Normal	NEG	NEG	NEG
N°22	France (0)	0	2	1	0	1	1	3	3	11	Normal	NEG	NEG	NEG
N°23	Guinea (4)	4	2	1	0	0	0	0	0	11	Normal	NEG	NEG	NEG
N°24	Guinea (4)	4	2	1	0	0	0	0	0	11	Normal	NEG	NEG	NEG
N°25	Guinea (4)	0	2	1	1	0	0	3	0	11	Normal	NEG	NEG	NEG
N°26	Niger (6)	4	0	0	1	0	0	0	0	11	Normal	NEG	NEG	NEG
N°27	Algeria (2)	4	2	0	0	0	0	3	0	11	Normal	NEG	NEG	NEG
N°28	France (0)	4	2	1	1	0	0	3	0	11	Normal	NEG	NEG	NEG
N°29	France (0)	4	2	1	1	0	0	3	0	11	Normal	NEG	NEG	NEG
N°30	Algeria (2)	4	2	0	0	0	0	0	3	11	Normal	NEG	NEG	NEG
N°31	Nigeria (6)	0	0	1	1	0	0	3	0	11	Normal	NEG	NEG	NEG

(Continued)

Table 3 Details of 47 participants screening positive by questionnaire—Continued

ID code Participant		Score												
	Country of origin (Q0)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total score	CXR ^a	ME	qPCR ^b	Culture
N°32	Nigeria (6)	0	0	1	1	0	0	3	0	11	Normal	NEG	NEG	NEG
N°33	Algeria (2)	0	2	1	0	0	0	3	3	11	Normal	NEG	NEG	NEG
N°34	Guinea (4)	4	0	1	0	0	1	0	0	10	Normal	NEG	NEG	NEG
N°35	Guinea (4)	4	0	0	1	1	0	0	0	10	Normal	NEG	NEG	NEG
N°36	Nigeria (6)	4	0	0	0	0	0	0	0	10	Normal	NEG	NEG	NEG
N°37	Guinea (4)	0	0	0	0	0	0	3	3	10	Normal	NEG	NEG	NEG
N°38	Romania (0)	4	2	0	0	1	0	3	0	10	Normal	NEG	NEG	NEG
N°39	Guinea (4)	4	2	0	0	0	0	0	0	10	Normal	NEG	NEG	NEG
N°40	Nigeria (6)	0	0	1	0	0	0	3	0	10	Normal	NEG	NEG	NEG
N°41	Algeria (2)	4	0	1	0	0	0	3	0	10	Normal	NEG	NEG	NEG
N°42	Nigeria (6)	0	0	1	0	0	0	3	0	10	Normal	NEG	NEG	NEG
N°43	Nigeria (6)	0	0	0	0	1	0	3	0	10	Normal	NEG	NEG	NEG
N°44	Nigeria (6)	0	0	1	0	0	0	3	0	10	Normal	NEG	NEG	NEG
N°45	Nigeria (6)	0	0	1	0	0	0	3	0	10	Normal	NEG	NEG	NEG
N°46	France (0)	0	2	1	1	0	0	3	3	10	Normal	NEG	NEG	NEG
N°47	Nigeria (6)	0	0	1	0	0	0	3	0	10	Normal	NEG	NEG	NEG

*Chest X-rays. *Real-time polymerase chain reaction (Xpert MTB/RIF) of *Mycobacterium tuberculosis* complex DNA. *Culture of *Mycobacterium tuberculosis* complex organisms. ID, identity; Q0–Q8, question from 0 to 8; NEG, negative; ME, microscopic examination.

reported TB in close relatives. The investigators considered 8.1% of the participants to be in poor health.

Questionnaire scores ranged from 0 to 16 with an average $[\pm$ Standard Deviation (SD)] of 4.9 $(\pm$ 3.5). No significant differences were observed between patients having a score >10 and others, regarding sex, age, duration of stay in France for migrants, and health insurance coverage (Table 1).

Fifteen (of 16, 93.8%) hospitalised patients with biologically confirmed tuberculosis had a screening questionnaire score >10 (ranging from 11 to 19) (Table 4), one (patient TB°15) had a screening questionnaire score = 2.

3.3. Imaging

Four screened participants (2.4%) had abnormal CXR features consistent with APTB (Table 5). Of the four, three underwent a CT scan and one was lost to follow-up. The CT scan was considered normal in two participants and revealed signs of bronchiolitis in the other (Table 5). Questionnaire scores ranged from 2 to 5 in these patients with abnormal radiographies.

Fifteen (of 16, 93.8%) hospitalised with biologically confirmed APTB had both CXR and CT scan features consistent with APTB (Table 4), one (patient TB°9) had no feature consistent with pulmonary TB on both CXR and CT scan.

3.4. Microbial Investigations

The results of the direct microscopic examination of sputum samples were negative for all screened participants. Fifty-one participants (including 47 with a positive questionnaire and four with abnormal CXRs) were tested with GeneXpert assays and no MTC-DNA was detected. All cultures were negative 6 weeks after recruitment in screened individuals. Hence, no

case of APTB was diagnosed based on microbiological criteria in screened people.

Of 16 patients hospitalised with biologically confirmed APTB, 10 (62.5%) had positive direct microscopic examination, 16 (100%) had positive PCR, and four (25%) had positive culture testing (Table 4).

The sensitivity and specificity of the questionnaire for confirmed APTB were 93.8% (15/16) and 87.7% (336/383), respectively.

4. DISCUSSION

In our study, homeless people were characterised by a high proportion of migrants, a high proportion of smokers, and one third lacked health insurance coverage which is in line with previous surveys conducted in Marseille homeless shelters [3–5] and with surveys conducted in others European cities such as Frankfurt (Germany) [8] and Geneva (Switzerland) [6].

For migrants and refugees in reception or detention centres, crowded living conditions, poor environmental conditions (poor ventilation, lack of sufficient food) and lack of continuity of care (delayed diagnosis, interrupted or poor quality treatment) may increase their vulnerability to TB [9]. Our APTB screening strategy was designed in accordance with European recommendations [10] and French guidelines for the 2019-2023 period [2], promoting decentralisation and intersectional collaboration between regional tuberculosis control centres, acute care and follow-up care structures, medical biology laboratories and medical staff in shelters. The key strength of our study is the large population (>380 people) enrolled over a 1-year period. In spite of our efforts, no confirmed cases of active TB were diagnosed in the target population. In 2005, an APTB screening campaign was conducted among 221 homeless people in Marseille, using CXRs, and reported a 0.9% rate of infection [11]. During the 2013-2018 period, we conducted 1-day cross-sectional surveys among 617

 Table 4 | Detail of 16 patients with biologically-confirmed active pulmonary tuberculosis with retrospective evaluation using the screening questionnaire

*Chest X-rays. *Real-time polymerase chain reaction (Xpert MTB/RIF) of Mycobacterium tuberculosis complex DNA. *Culture of Mycobacterium tuberculosis complex organisms. ID, identity; Q0-Q8, question from 0 to 8; POS, positive; NEG, negative; ME, microscopic examination.

 Table 5 | Imaging results of four screened participants with abnormal CXR features consistent with APTB

ID code		Score								T 1			
Participant	Country of origin (Q0)	Q1	Q2	Q3	Q4	Q5	Q6	Q 7	Q8	- Total score	CXR ^a	CT scanner ^b	
N°1	Algeria (2)	0	0	0	0	0	0	0	0	2	Rounded opacity of the right lung apex	N/A	
N°2	France (0)	4	0	0	0	0	0	0	0	4	Well-circumscribed opacity of the left lung apex + micro nodule in the left mid lung zone	Bronchiolitis, CT scanner control in 3 months	
N°3	France (0)	0	0	1	1	0	0	3	0	5	Apical micronodular in two lungs	Normal	
N°4	France (0)	4	0	1	0	0	0	0	0	5	Apical micronodular in two lungs	Normal	

^aChest X-rays. ^bThoracic computed tomography scanner. ID, identity; Q0-Q8, question from 0 to 8; N/A, not applicable.

sheltered homeless people, using various microbiological investigations (qPCR of sputum or stools, sputum culture), and found no cases of APTB [3]. These results are in line with the 0–2% APTB prevalence reported among homeless populations in western European countries during the 2000–2019 period [3,6,12]. As in our preliminary survey, conducted in 2018, we found a higher prevalence of participants with a positive screening result (9.2% and 12.2%, respectively) than in the study by Janssens et al. (4.1%). One major finding of our survey is a higher sensibility of screening questionnaire (93.8%) for confirmed ATPB when applicated for homeless persons in Marseille, as compared to previous study conducted on asylum individuals in Switzerland during the period 2007–2008 (55%, p = 0.008) [13].

Our study has several limitations. Notably, the population was not randomly and homogenously recruited. Only homeless people present in the shelters were enrolled on a voluntary basis leading to a 40% participation rate and we cannot exclude the possibility that those harbouring respiratory symptoms (cough, expectoration) might have been more likely to enrol in the survey, given that a medical examination was offered, while in the Janssens's study, 87% of homeless people present in the shelter were enrolled [6].

We propose that medical staff in homeless shelters use screening questionnaires as a first assessment tool for each person arriving at the shelters and refer those screening positive to the regional tuberculosis control centres for a CXR. This strategy, which is cost-effective and easy to implement, may complete 1-day cross sectional CXR screening campaigns that are currently conducted twice a year in shelters.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTION

TD and PG contributed to the experimental design, data analysis, statistics, interpretation, and writing. TD, VT, TL, ML and NG administered questionnaires, examined patients, and collected samples. FH analysed the results of the chest X-rays. MD contributed to critically reviewing the manuscript and PG coordinated the work.

ACKNOWLEDGMENTS

No potential conflict of interest relevant to this study was reported. We thank the "Centre de lutte antituberculeuse à Marseille" and the "Oeuvre Antituberculeuse des Bouches-du-Rhône à Marseille" for their cooperation.

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