# Active tuberculosis case finding interventions among immigrants, refugees and asylum seekers in Italy

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## Abstract

In Italy tuberculosis (TB) is largely concentrated in vulnerable groups such as migrants and in urban settings. We analyzed three TB case finding interventions conducted at primary centers and mobile clinics for regular/irregular immigrants and refugees/asylum seekers performed over a four-year period (November 2009-March 2014) at five different sites in Rome and one site in Milan, Italy. TB history and presence of symptoms suggestive of active TB were investigated by verbal screening through a structured questionnaire in migrants presenting for any medical condition to out-patient and mobile clinics. Individuals reporting TB history or symptoms were referred to a TB clinic for diagnostic workup. Among 6347 migrants enrolled, 891 (14.0%) reported TB history or symptoms suggestive of active TB and 546 (61.3%) were referred to the TB clinic. Of them, 254 (46.5%) did not present for diagnostic evaluation. TB was diagnosed in 11 individuals representing 0.17% of those screened and 3.76% of those evaluated. The overall yield of this intervention was in the range reported for other TB screening programs for migrants, although we recorded an unsatisfactory adherence to diagnostic workup. Possible advantages of this intervention include low cost and reduced burden of medical procedures for the screened population.

## Introduction

Tuberculosis (TB) notification rates are declining to less than 20 per 100,000 population in most European Union countries, however, TB rates in big cities remain higher than the national notification rate, and the majority of TB cases are concentrated among certain high-risk groups, including migrants from high-incidence countries, homeless people and drug and alcohol users.[1]

In Italy in 2013 TB incidence rate was 5.3/100.000, with 3153 cases.[2] In Latium region notification rates among foreign born in 2013 were 62.2/100,000 while among Italian born were 4.2/100,000 (data provided by Latium Regional Health Authority – SeReSMI – infectious diseases regional surveillance system). In Lombardy region the overall incidence in 2011 was 8.8/100,000 with 56.6% of the cases in foreign born subjects (Lombardy Regional Health Authority, personal communication). The percentage of notified TB cases of foreign origin among all notified TB cases in Italy has considerably increased during the past decade passing from 39.4% in 2004 to 62.6% in 2013,[2] and this increase has paralleled the rise in the proportion of the immigrant population in Italy from 1.5 million (2.7%) in 2002 to more than 5 million (8.1%) in 2014.[3]

Systematic screening for active TB for populations groups that have poor access to health care, such as vulnerable or marginalized groups including migrants and refugees has been recommended in 2013 by the World Health Organization (WHO).[4,5]

Recently, the adaptation of the new global TB strategy – approved by the World Health Assembly in May 2014 – to low-incidence settings,[6] outlined eight priority action areas that can be considered key interventions for accelerating progress towards pre-elimination (<10 cases per million population) and, ultimately, elimination of TB (<1 case per million population). *Addressing special needs of migrants and cross-border issues* and *undertaking screening for active TB and LTBI in TB contacts and selected high-risk groups* are two of these eight priority action areas.[7] TB control in urban risk groups in E.U., with special attention to congregate settings, social disadvantage, and economic/cultural barriers, was addressed in a Consensus statement by Van Hest *et al.*[8]

Italy has no TB national screening policy for new entrants,[9] but according to National recommendations issued by the Consensus Conference on TB in migrants, access to TB specialized care through active offer of infor-

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Contributions: EG conceived of the study and its design, and coordinated it, with the collaboration of MSS. PP was in charge of the database. MSS performed the statistical analyses. All of them drafted the manuscript. GG, under the supervision of FP performed the diagnostic workup at INMI, and LRC coordinated the diagnostic workup performed by MF at Villa Marelli. Enrolment and symptom questionnaire administration were performed by GR under the supervision of FG at SaMiFo, AUSL RM A, by FF at MEDU, and by MM and DDA at Cittadini del Mondo.

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mation and anticipated diagnosis at public health care or at NGOs sites should be promoted.[10] During years 2009 and 2010 we performed a TB case finding program based on verbal symptom screening conducted at primary centers for regular and irregular immigrants and refugees/asylum seekers at three different sites in Rome.[11] During subsequent years we then tailored this intervention to other settings (temporary settlements reached by mobile-units) and implemented a similar program in two primary health care centers in Rome and Milan.

The objective of the present study is to compare adherence and yield of this first intervention with the two subsequent ones.

## Materials and Methods

### Study area and population

Details on the methodology of the first intervention (Phase I) performed in three primary care centers for migrants in Rome province along years 2009-10 have already been published elsewhere.[11] Study sites were: *SaMiFo – Health for forced migrants*, a health service that mainly cares for asylum seekers and refugees (center A); *Caritas* Health Service, a non-governmental out-patient clinic who provides primary and specialized medical care for regular and irregular immigrants (center B), both in Rome; and an outpatient's health clinic for irregular migrants in Nettuno – town located 60 km south of Rome, run by the Regional Health Service Unit (center C).

The second intervention (Phase II) along years 2010-11 focused on outreach program in the city of Rome by mobile units run by two non-governmental services *MEDU – Medici per i diritti umani*, for irregular migrants (center D), and *Cittadini del MONDO*, for regular and irregular migrants (center E).

The last intervention (Phase III, years 2012-14) involved again *SaMiFo – Health for forced migrants*, a health service that mainly cares for asylum seekers and refugees health service in Rome (center F) and a *NAGA*, a non-governmental out-patient clinic for irregular migrants, in Milan (center G).

All individuals presenting to these services along years 2009-2014 (in the following study periods: Phase I: November 2009-December 2010; Phase II: November 2010-February 2012; Phase III: January 2013-March 2014), were considered for inclusion in this study. Subjects were eligible if foreign-born and aged 18 or more. The study population included regular migrants, irregular migrants – defined as persons whose entry, stay or work in the country is illegal, refugees and asylum seekers – defined as persons wishing to be admitted to the country as refugees and awaiting decision on their application.[12]

### Screening and diagnostic procedures

The aims and methods of the study were explained to participating individuals in a printed leaflet written in eleven languages. Cultural mediators were present at primary care centers when the questionnaire was administered and provided further information about the study in the patients' own language or in a vehicular language. Written consent was obtained from all subjects before enrolment. Ethical approval was provided by the Ethical Committees at the National Institute for Infectious Diseases L. Spallanzani (INMI) in Rome, and at Villa Marelli Institute (VMI) - Niguarda Hospital in Milan.

Eligible individuals underwent symptom screening which was performed through a standardized verbal questionnaire investigating on the presence of the following symptoms and signs: fever of more than one week duration, cough of more than two weeks duration, night sweating, weight loss, and hemoptysis. Chest pain was added as sixth symptom in the third intervention. These symptoms were chosen because previous studies in settings with low incidence of HIV had shown that the presence of any of them provided 70% (95% CI 58-82) sensitivity in active TB screening programs in adults.[4,13] Information on prior diagnosis and treatment for TB, on contact with TB patients, BCG vaccination, and on social and demographic characteristics was collected.

Individuals presenting one of the previously listed symptoms/ signs were referred to the TB clinic at INMI in Rome, or Villa Marelli in Milan, for diagnostic workup. TB history and previous contact with TB patients were included as items for referral in the third intervention.

Referred individuals were given instructions verbally and in printed leaflets on when and how to reach the TB clinic and they were informed that all examinations were free of charge; no support such as free transportation or monetary incentives was provided. Patients reporting cough were instructed to carry an early morning sputum sample collected on the day of the visit. During the visit, a clinical examination and a chest radiograph were performed and a second sputum sample was collected. Further investigations were performed in selected cases if deemed necessary by the attending physician to confirm or rule out the diagnosis of TB.

For the purpose of the analysis, patients were considered as having completed diagnostic evaluation if they performed all the investigations considered necessary by the attending physician.

A case of TB was defined as a physician's diagnosis of TB in a person who has bacteriological evidence of active disease and/or signs and symptoms compatible with TB and has completed diagnostic evaluation, and a physician's decision to start treatment with a full course of antituberculosis chemotherapy.[14]

### Statistical analysis

Descriptive statistics are reported as proportions for categorical data or median (and interquartile range, IQR) for continuous variables. Chi-square test (or Fisher's exact test when applicable) or Mann Whitney non-parametric test were used to compare groups respectively for categorical or continuous variables and to test their association. Data management and statistical analysis was performed using SPSS v. 22 statistical package (SPSS Inc, USA).

For individuals reporting at least one TB symptom, we investigated the association with refusal or non-attendance to diagnostic evaluation of relevant characteristics using logistic regression analysis through odds-ratio (OR) and their 95% confidence intervals (95% CI). Gender, age and other variables found to be associated with refusal or non-attendance ($P<0.1$) in the first intervention were included in the multivariable logistic regression (MLR-OR) final models for the second and third intervention.

Confidence intervals (95% CI) reported in Figure 1 were calculated through the adjusted Wald method.

## Results

Characteristics of the individuals enrolled are summarized in Table 1. Overall, the median age of the participants (4964 males, 78.2%) was 32.3 years (IQR: 26.2-41.5). Migrants enrolled in phase II were significantly younger (median age 27.9 years, IQR 22.7-33.8) than those enrolled in phase I and III (respectively 32.3, IQR 26.2-41.9 and 34.3, IQR 22.7-44.0).

The four most frequently reported countries of origin according to study phase were Romania (293/2142, 13.7%), India (220, 10.3%), Eritrea (190, 8.9%), and Afghanistan (138, 6.4%) during Phase I; Afghanistan (437/1177, 37.1%), Eritrea (242, 20.6%), Somalia (100, 8.5%) and Ethiopia (84, 7.1%) during Phase II and Egypt (346/3028, 11.4%), Morocco (327, 10.8%), Senegal (246, 8.1%), and Romania (190, 6.3%) during Phase III.

Many patients were from Sub-Saharan Africa (37.3%, 40.1% and 31.1%, respectively in phase I, II or III) or from Asia (27.7%, 48.3%, 16.2%, respectively in phase I, II or III). Overall, more than 50% came from countries with a TB incidence of 100 per 100.000 or higher. The median length of time spent in Italy varied from 0.7 (IQR 0.1-2.6) for center D to 5.4

(IQR 2.2-9.9) for center F, and the differences found [shorter periods for phase I, 2.1 (1.1-4.9) and II, 2.3 (0.4-4.5) compared to phase III, 3.3 (1.1-7.6)] were statistically significant.

Overall, 2170 (34.2%) subjects did not have a residence permit, but this proportion varied widely among centers and reached 71.3% and 79.0% in centers C and F, respectively. Patients enrolled in phase III were mostly unemployed (70.1% in center F and up to 91.2% in center G); regular registration with the Italian National Health Service was very low (0, center C; 3.8% center F; and 11.0% center B) when migrants enrolled were mainly irregular, and very high when migrants were asylum seekers/refugees (97.8% center G, and 99.9% center A), due to differences in entitlement to NHS registration (*i.e.* they are entitled to access health care on equal grounds as Italian nationals in regards to coverage and conditions).

Among 6347 enrolled individuals, 891 overall (14.0%), 11.9%, 10.4% and 17.0% respectively in phases I, II and III, reported at least one positive item (TB history or symptom suggestive of active TB). Most of them, 60.2% (Phase I), 49.8% (Phase II) and 75.4% (Phase III), sought primary medical care due to symptoms other than protocol-defined TB symptoms.

Based on the judgment of the attending physician at the primary care centers, 30.7% of 254 (Phase I), 39.5% of 122 (phase II) and 42.5% of 515 (Phase III) individuals with protocol defined TB symptoms were not referred for TB diagnostic evaluation (Figure 1).

Among a total of 891 subjects positive to the questionnaire (14.0% of all subjects interviewed), 546 (61.3%) were referred to the TB clinics. Of them, 254 (46.5%) did not present for evaluation. This proportion varied widely across study sites, ranging from 20.5% (center A) to 86.7% (center D).

We then compared some factors (*e.g.*, age, gender, birth country, length of stay in Italy) between those who attended the diagnostic evaluation and those who did not attend it. For Phase I, in multivariable analysis, the probability of not attending TB clinic for diagnostic evaluation among symptomatic patients was higher in younger individuals and in irregular migrants or asylum seekers compared to regular migrants, and it also varied for patients seen in different primary care centers. The positive association -although not statistically significant- with irregular legal status was found also for Phase III. Besides, during Phase II, those who received previous healthcare in Italy were less likely to refuse further diagnostic evaluation at the TB clinic. Other examined

**Table 1. Demographic and social characteristics of 6347 screened individuals.**

| | All (n=6347) | Phase I | | | Phase II | | Phase III | |
|---|---|---|---|---|---|---|---|---|
| | n (%) | A (n=700) n (%) | B (n=951) n (%) | C (n=491) n (%) | D (n=731) n (%) | E (n=446) n (%) | F (n=2046) n (%) | G (n=982) n (%) |
| Gender, male | 4964 (78.2) | 584 (83.4) | 616 (64.8) | 351 (71.5) | 710 (97.1) | 350 (78.5) | 1492 (72.9) | 861 (87.7) |
| Age, median (IQR) | 32.3 (26.2-41.5) | 28.9 (24.4-3.9) | 38.0 (29.4-9.1) | 32.2 (26.9-9.9) | 25.3 (20.8-32.4) | 30.5 (26.6-35.3) | 37.4 (29.6-47.3) | 30.0 (25.1-36.0) |
| Length of stay in Italy (yrs), median (IQR) | 2.6 (1.0-6.0) | 1.5 (1.0-2.4) | 3.0 (1.3-6.8) | 3.2 (1.2-5.8) | 0.7 (0.1-2.6) | 4.1 (2.9-5.7) | 5.4 (2.2-9.9) | 1.3 (0.3-3.0) |
| Education (yrs) | | | | | | | | |
| None/Not available | 875 (0.3) | 104 (14.9) | 155 (16.3) | 182 (37.1) | 360 (49.2) | 74 (16.6) | - | - |
| 1-8 | 1096 (0.3) | 290 (41.4) | 341 (35.9) | 94 (19.1) | 231 (31.6) | 140 (19.2) | - | - |
| 9+ | 1348 (0.4) | 306 (43.7) | 455 (47.8) | 215 (43.8) | 97 (21.7) | 275 (61.7) | - | - |
| Country of origin | | | | | | | | |
| New EU | 711 (11.2) | 0 | 308 (32.4) | 96 (19.6) | 47 (6.5) | 9 (2.0) | 251 (12.3) | 0 |
| Other European non EU/Western | 384 (6.1) | 2 (0.3) | 94 (9.9) | 27 (5.5) | 34 (4.6) | 4 (0.9) | 174 (8.5) | 49 (5.0) |
| Northern Africa | 939 (14.8) | 1 (0.1) | 57 (6.0) | 103 (21.0) | 29 (4.0) | 2 (0.4) | 737 (36.0) | 10 (1.0%) |
| Sub-Saharan Africa | 2211 (34.8) | 548 (78.4) | 211 (22.2) | 40 (8.1) | 80 (10.9) | 392 (87.9) | 186 (9.1) | 754 (76.8) |
| Asia | 1652 (26.0) | 148 (21.1) | 227 (23.8) | 219 (44.6) | 538 (73.6) | 30 (6.8) | 341 (16.6) | 149 (15.2) |
| Other/Not available | 448 (7.1) | 1 (0.1) | 54 (5.7) | 6 (1.2) | 3 (0.4) | 9 (2.0) | 357 (17.5) | 20 (2.0) |
| TB incidence rate in the country of origin*° | | | | | | | | |
| <25 | 716 (11.3) | 12 (1.7) | 108 (11.4) | 31 (6.3) | 37 (5.0) | 1 (0.2) | 453 (22.1) | 74 (7.5) |
| 25-49 | 415 (6.6) | 6 (0.9) | 39 (4.1) | 56 (11.4) | 60 (8.2) | 6 (1.3) | 235 (11.5) | 13 (1.3) |
| 50-99 | 1493 (23.5) | 158 (22.6) | 190 (20.0) | 76 (15.5) | 65 (8.9) | 285 (63.9) | 482 (23.6) | 262 (26.8) |
| 100-299 | 3325 (52.4) | 292 (41.7) | 558 (58.6) | 326 (66.4) | 567 (77.6) | 154 (34.6) | 851 (41.6) | 552 (56.2) |
| 300+ | 373 (5.9) | 232 (33.1) | 56 (5.9) | 2 (0.4) | 0 | 0 | 19 (0.9) | 64 (6.5) |
| Occupation,° yes | 1508 (29.2) | 373 (53.3) | 229 (24.1) | 282 (57.4) | - | - | 594 (29.0) | 33 (3.4) |
| Migration pattern | | | | | | | | |
| Regular | 1078 (17.0) | 6 (0.9) | 462 (48.6) | 100 (20.4) | - | - | 502 (24.5) | 8 (0.8) |
| Irregular | 2170 (34.2) | 3 (0.4) | 319 (33.5) | 388 (79.0) | - | - | 1458 (71.3) | 2 (0.2) |
| Asylum seeker/refugee | 1780 (28.0) | 614 (87.7) | 161 (16.9) | 1 (0.2) | - | - | 49 (2.4) | 955 (97.3) |
| Other/Not available | 1319 (20.8) | 77 (11.0) | 9 (0.9) | 2 (0.4) | 731 (100) | 446 (100) | 37 (1.8) | 17 (1.7) |
| Place of residence | | | | | | | | |
| Apartment | 3497 (55.1) | 193 (27.6) | 433 (45.5) | 482 (98.2) | 15 (2.1) | - | 1856 (90.7) | 518 (52.7) |
| Immigration center | 615 (9.7) | 285 (40.7) | 246 (25.9) | 1 (0.2) | 82 (11.2) | - | 0 | 1 (0.1) |
| Homeless/dormitories | 1682 (26.5) | 221 (31.6) | 240 (25.2) | 5 (1.0) | 604 (82.6) | - | 180 (8.8) | 432 (44.0) |
| Prison | 1 (0.0) | 0 | 0 | 0 | 1(0.1) | - | 0 | 0 |
| Not available | 552 (8.7) | 1 (0.1) | 32 (3.4) | 3 (0.6) | 29 (4.0) | 446 (100) | 10 (0.5) | 31 (3.2) |
| NHS registration,# yes | 2390 (37.7) | 699 (99.9) | 105 (11.0) | 0 | 205 (28.0) | 343 (76.9) | 78 (3.8) | 960 (97.8) |
| Previous healthcare in Italy, yes | 3305 (52.1) | 259 (41.3) | 228 (24.0) | 60 (12.2) | 161 (22.0) | 115 (25.8) | 1906 (93.2) | 546 (55.6) |

Centers: A) NGO-public health service for asylum seekers/refugees (years 2009-10, Rome); B) NGO-public health service for migrants (years 2009-10, Rome); C) Public health service for migrants (years 2009-10, Rome); D) NGO-public health service MEDU Mobile Medical Clinic Units for irregular migrants (years 2010-2011, Rome); E) NGO-public health service CITTADINI DEL MONDO Mobile Medical Clinic Units for regular and irregular migrants (years 2010-2011, Rome); F) NGO health service for irregular migrants (years 2012-2014, Milan); G) NGO-public health service for asylum seekers/refugees (years 2009-2010, Rome). *According to WHO estimates (http://www.who.int/tb/publications/global_report/2015/en/index.html). °The sum could not add up to the total because of missing values. #Registration with the Italian National Public Health Service.

factors were not significantly associated to refusal or non-attendance during Phases II and III (Table 2).

Overall, thirteen patients were diagnosed as active TB, of which two extrapulmonary case and eleven pulmonary cases. These eleven cases were diagnosed among individuals with protocol defined TB symptoms at screening, representing 0.17% of the individuals who underwent symptom screening, and 3.76% of those who completed diagnostic evaluation. The number needed to screen (NNS) to diagnose one case of active TB was 306 for Phase I, 1177 for Phase II, and 1009 for Phase III. Diagnosis of pulmonary TB was confirmed by sputum smear microscopy and culture in four (two of Phase I, one in Phase II and one of Phase III) individuals, and by DNA-PCR on the bronchoalveolar lavage fluid in one case (Phase I), while it was based on clinical/radiological findings in the remaining six (four of Phase I and two of Phase III) pulmonary cases.

Among the individuals referred for diagnostic evaluation without protocol-defined TB symptoms, 50% (5/10) in Phase I, 11.1% (2/18) in Phase II and 61.5% (16/26) in Phase III completed diagnostic evaluation and two (one of Phase I and one of Phase III) extrapulmonary TB cases were diagnosed by DNA-PCR assay on a lymph node aspirate. All patients with a TB diagnosis started treatment.

Adherence to these interventions was different among the three Phases: 96/176 (54.5%) participants accepted referral to TB clinic during, while the percentage decreased to 16.2% (12/74) during Phase II, and was highest during Phase III (62.2%, 184/296). Yield of the programs, defined as the number of active TB cases diagnosed among those screened, ranged from 0 to 0.53 (center B), and overall was 0.17.

## Discussion

The first TB case finding program we performed during years 2009-2010 provided evidence that a non-negligible number of TB cases in migrants might be identified through verbal screening and then linked to care.[11] During subsequent years this intervention was proposed to migrant populations reached by mobile-units services in temporary settlements in the city of Rome (Phase II) and to migrants presenting themselves to primary health centers, in Rome and Milan (Phase III).

**Table 2. Factors significantly associated with refusal or non-attendance to diagnostic evaluation for tuberculosis at multivariate analysis.**

| | Phase I | | Phase II | | Phase III | |
|---|---|---|---|---|---|---|
| | Refusal or non-attendance, n/total (%) | MLR-OR, (95% CI) | Refusal or non-attendance, n/total (%) | MLR-OR, (95% CI) | Refusal or non-attendance, n/total (%) | MLR-OR, (95% CI) |
| Total | 80/176 (45.5) | | 62/74 (83.8) | | 112/296 (37.8) | |
| Gender | | | | | | |
| Male | 62/143 (43.4) | 1 | 56/68 (82.4) | - | 91/240 (37.9) | 1 |
| Female | 18/33 (54.5) | 1.9 (0.8-4.4) | 6/6 (100.0) | - | 21/56 (37.5) | 1.1 (0.6-2.1) |
| Age each 10-year increase, median (IQR) | 34.8 (28.0-40.3) | 0.7 (0.5-0.9)[a] | 30.3 (23.4-35.5) | 1.1 (1.0-1.2) | 35.2 (26.8-42.3) | 1.0 (1.0-1.0)[a] |
| Length of stay in Italy (yrs)* | | | | | | |
| <2 | 30/65 (46.2) | | 25/28 (89.3) | | 41/119 (34.5) | |
| 2+ | 49/106 (46.2) | | 30/39 (76.9) | | 68/166 (41.0) | |
| TB incidence rate in the country of origin (/105)° | | | | | | |
| <25 | 7/11 (63.6) | | 1/2 (50.0) | | 14/44 (31.8) | |
| 25-99 | 17/36 (47.2) | | 26/33 (78.8) | | 39/93 (41.9) | |
| 100+ | 56/129 (43.4) | | 35/39 (89.7) | | 59/148 (39.9) | |
| Occupation* | | | | | | |
| No/NA | 61/131 (46.6) | | - | | 93 /241 (38.6) | |
| Yes | 19/45 (42.2) | | - | | 19/112 (35.4) | |
| Legal status* | | | | | | |
| Regular | 25/90 (27.8) | 1 | - | | 15/49 (30.6) | 1 |
| Irregular | 32/56 (57.1) | 1.9 (0.9-4.0)[b] | - | | 60/139 (43.2) | 1.7 (0.8-3.7) |
| Asylum seeker/refugee | 52/136 (38.2) | 1.3 (0.3-7.2) | - | | 36/94 (38.3) | 1.4 (0.6-7.3) |
| Place of residence | | | | | | |
| Apartment | 38/83 (45.8) | | 2/2 (100.0) | | 90/223 (40.4) | 1 |
| Immigration center | 20/40 (45.5) | | 5/6 (83.3) | | 0 | 0.8 (0.4-1.5) |
| Homeless/dormitories | 20/44 (45.5) | | 30/35 (85.7) | | 21/60 (35.0) | - |
| Other/NA | 2/5 (40.0) | | 25/31 (80.6) | | 1/13 (7.7) | |
| NHS registration# | | | | | | |
| No/NA | 67/126 (53.2) | 1 | 31/36 (86.1) | 1 | 76/205 (37.1) | 1 |
| Yes | 13/50 (26.0) | 0.8 (0.2-2.9) | 31/38 (81.6) | 0.9 (0.2-4.5) | 36/91 (39.6) | 0.9 (0.2-4.5) |
| Previous healthcare in Italy | | | | | | |
| No/NA | 64/125 (51.2) | 1 | 42/47 (89.4) | 1 | 23/61 (37.7) | 1 |
| Yes | 16/51 (31.4) | 0.7 (0.3-1.5) | 20/27 (74.1) | 0.3 (0.1-1.0)[b] | 89/235 (37.9) | 6.1 (0.6-65.3) |
| Education (yrs) | | | | | | |
| None/NA | 19/38 (50.0) | | 2127 (77.8) | | - | |
| 1-8 | 28/62 (45.2) | | 15/17 (88.2) | | - | |
| 9+ | 33/76 (43.4) | | 26/30 (86.7) | | - | |

MLR-OR, multivariate-logistic regression odds ratio; CI, confidence interval. [a]P<0.05; [b]P<0.10. *The sum could not add up to the total because of missing values. °According to WHO estimates (http://www.who.int/tb/publications/global_report/2015/en/index.html). #Registration with the Italian National Public Health Service.

In spite of the overall sub optimal adherence to diagnostic procedures the yields of the three programs were both in the inter quartile range (0.10-0.38) reported for community post-arrival screening programs for migrants using chest radiography as a primary method of screening in combination with other tools, such as symptom screening,[12] and in or above the inter quartile range (0.08-0.15) found by Alvarez *et al*. in their recent international survey.[9]

Migrant screening approaches in low TB incidence areas vary widely in Western Europe, and heterogeneity exists in screening location, including pre-departure screening,[15,16] on arrival port of entry screening or post-entry screening,[17] selection criteria for which immigrant subgroups are screened, and screening methods used.[9,18,19] Among migrants, asylum seekers and refugees are often targeted as a high priority group for screening, as being recognized as having higher risk for TB.[18,20,21] With regard to screening strategies there is evidence that eliciting the presence of the main TB symptoms (fever of more than one-week duration, cough of more than two weeks duration, night sweating, weight loss and hemoptysis) may represent a simple and sensitive method for screening of active TB, although this approach may have a low specificity.[22,4]

The main difference between the program described in the present paper and the vast majority of the TB screenings directed at new immigrants is that we did not include any laboratory or imaging tool in the first part of the screening, and these diagnostic interventions were only applied to those reporting TB history or at least one symptom suggestive of active TB. This approach is attractive because it may significantly reduce the use of resources and it may be applied when radiographic facilities are not available at the sites where target population is first screened. On the other hand, we cannot rule out that some prevalent TB cases were not identified by verbal screening.[5]

Available evidence from active case finding studies, conducted in different settings and populations,[22-25] suggests that sensitivity of a symptom-based screening may be significantly lower than sensitivity of traditional radiographic screening and in low-incidence counties, radiological screening for TB targeting specific high-risk groups has re-emerged as a viable approach.[26]

Other possible explanations for the low yields recorded in our program are the increased incidence of mixed or extrapulmonary forms in migrant populations and the need for invasive test to obtain a microbiological diagnosis, as described in other studies,[28-30] and the fact that, more often than in the general population, among hard-to-reach groups, individuals may have chronic cough or weight loss for other co-morbidities.

In our study, among 891 individuals positive to the questionnaire, 30.7 to 42.5% were not referred for further diagnostic evaluation, mainly because the caring physician considered an alternative diagnosis more likely. As expected this proportion was higher during Phase III, as the symptom *thoracic pain* was

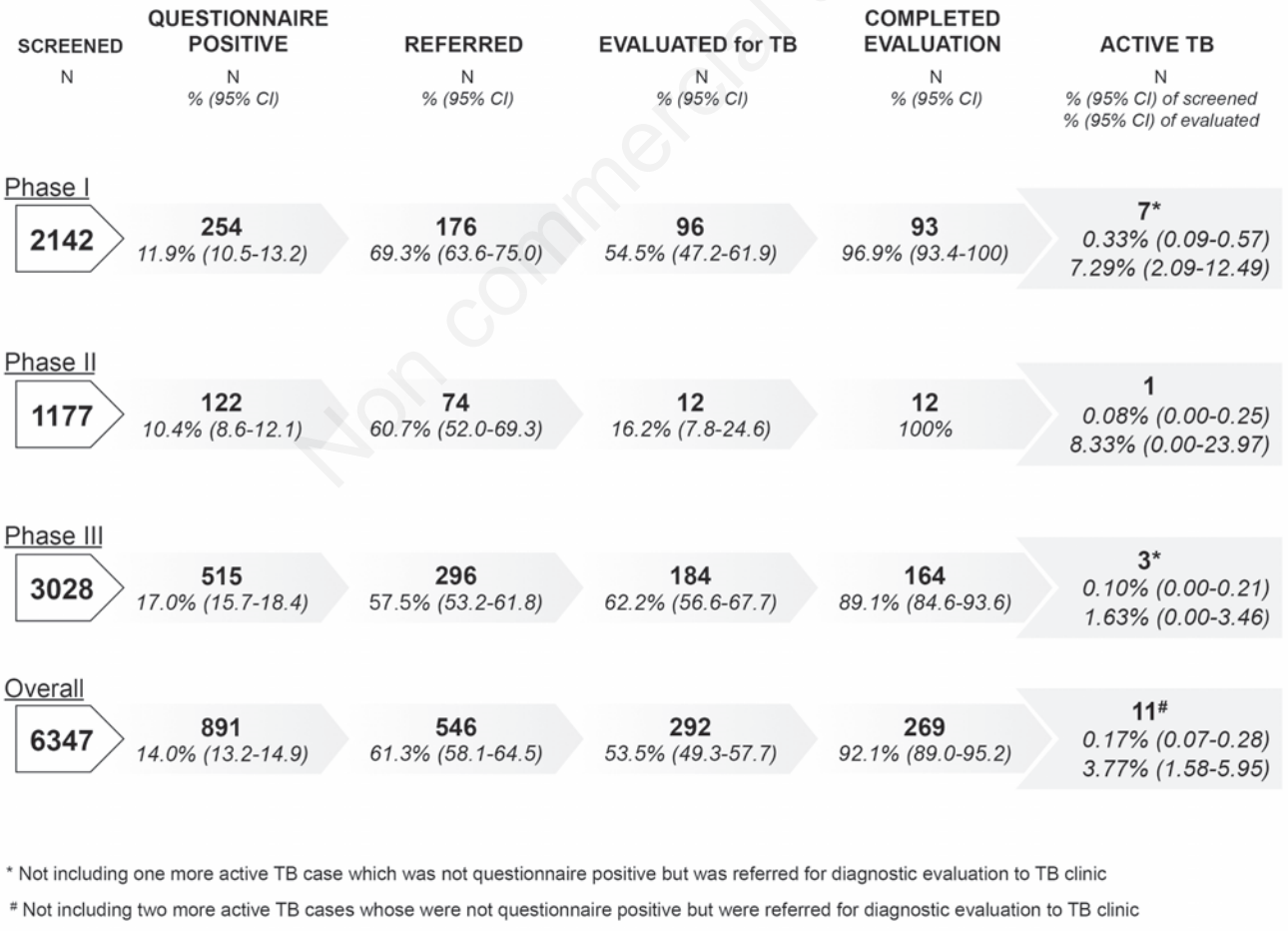


**Figure 1. Flow diagram by study phase.**

often caused by a trauma.

Among the population studied in Phase I almost half did not present to the TB clinic, being the probability of not attending diagnostic evaluation lower for younger patients and higher for males and for irregular migrants. To try to increase completion of screening, the TB clinic staff tried to contact directly by phone individuals which did not show up for diagnostic evaluation and provided information of non-attendance to the participating centers, that could in turn reinforce the invitation to adhere to their clinic appointment. We could not provide any monetary incentives, known to be effective in favoring the acceptance of TB screening in other population groups.[30,31]

The percentage of those evaluated among those referred decreased to 16.2% (12/74) during Phase II, and was highest during Phase III (62.2%, 184/296). A similar active TB screening program performed in 2010 at NAGA (center F) on 1005 migrants from high endemic countries, reached an attendance proportion similar to the one obtained in the same center during this program, in 2013-4 (45.3% *vs.* 60.4%).[32] This percentages were lower than the one reported (82.8%) by Jimenez-Fuentes in a study carried out in Barcelona from 2009 to 2012 among drug-users, economically disadvantaged and recent immigrants from hyper-endemic countries through symptom screening and Chest X-ray.[23]

In our study, migration pattern and consequently, legal status, length of stay in Italy and access to public healthcare of the target population groups influenced adherence to the screening interventions, so, as expected, only a small proportion of migrants referred to diagnostic evaluation during Phase II, which were mostly young Afghans transiting through Italy to reach other EU countries, was able and willing to accept the referral proposal. Irregular legal status, characterized by unstable access and link to public healthcare was also found to be associated to refusal or non-attendance. One possible approach to address this issue has been suggested by Story *et al*., which performed a pulmonary TB screening intervention through the use of mobile digital chest radiography in London among homeless populations, persons accessing drug treatment services and prisoners.[33]

A series of limitations of this study need to be mentioned. Our study design did not allow measuring to what extent verbal symptom screening may have increased the detection rate of active TB and/or reduced diagnostic delay compared to traditional passive case finding: we could not retrieve data on the number and on the clinical presentation at diagnosis of passively identified TB cases (before or after the intervention, during a similar period of time) at the enrolment centers; we did not cross-check our findings with TB notification records linked to those which resulted questionnaire negative and in subsequent years for all the study population. The effects of risk factors on active TB diagnosis were not explored due to the overall low number of TB cases.

The diagnosis of pulmonary TB has been confirmed by microbiological examinations only in five of the eleven patients observed in the program, possibly due to the fact that active screening may allow the detection of TB at an earlier stage, with a lower mycobacterial burden, compared to passive case finding. This is in line with previous studies suggesting that active screening is associated with a reduction in the severity or infectivity of identified cases, with a lower proportion of cases who were symptomatic or smear or culture-positive.[34-36] On the other hand, we cannot rule out a diagnostic bias due to the inclusion in a TB screening program.

Another limitation of the study is that we do not have information on the prevalence of HIV infection in the population studied, which may influence the clinical presentation of TB. However, in the context of active case finding there is no evidence of a different sensitivity of symptom-based screening in HIV infected and non-infected persons.[37,38]

To our knowledge, this study reports data on the largest and longest active TB case finding program for migrants performed in Italy. The main public and private sector health services dedicated to migrants in Rome and in Milan have been engaged in order to raise awareness about symptoms and risk factors for TB both among subpopulations most vulnerable to the disease and among frontline staff. Peers from these subpopulations, which acted as cultural mediators, have been trained and have contributed to awareness-raising activities. A closer relationship between the medical services from voluntary sectors, the migrant communities and the TB referral hospitals in the two largest cities in Italy has been built. Arising out of this program, a collaboration between INMI and Médecins Sans Frontières – Rome was established and, and using the same screening tool, a further program was implemented in closed immigration centers located in Rome (central Italy), Milan (Northern Italy), and in Trapani and Caltanissetta (Sicily) during 2012-3.[39]

This feasible low cost approach, with reduced burden of medical procedures for the screened population, once adapted to reach different groups of migrants, can contribute to disease control by diagnosing TB among hard to reach subpopulations with difficulties in accessing specialized healthcare services, who would otherwise not have sought prompt medical care.

Further operational research on how to improve TB screening effectiveness and how to integrate it with migrant health programs including testing for blood-borne viruses is needed.[40] Evidence-based guidance to be used by policy makers, public health experts and practitioners working with newly arrived migrants on the screening of migrants for a range of infectious diseases, including TB is currently being formulated by ECDC.[41]

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