\

Early Detection and Integrated Management of Tuberculosis in Europe

PJ-03-2015
Early diagnosis of tuberculosis

D5.1
Temporary migrant screening set up

WP 5–Migrant TB detection, prevention and treatment

Due date of deliverable	Month 1 – 27th january 2017
Actual submission date	22 / 01/ 2017
Start date of project	3 May 2016
Duration	8 months
Lead beneficiary	OSR
Last editor	Daniela Maria Cirillo
Contributors	Partners' acronyms
Dissemination level	*Pubblic*

This project E-DETECT TB has received funding from the European Union's Health Programme (2014-2020) under grant agreement N°709624.

History of the changes

Version	Date	Released by	Comments
2	22-02-16	DANIELA MARIA CRILLO	- Background information on TB among migrants in South of Italy - Questionnaire in English, French and Arabic added in Appendix 1 - Management of the refusals: information sheet and patient's education - Description of EdetectTB App - D5.1 postponement's reason - CARE project implementation - English editing

Table of contents

Key word list

Tuberculosis, Migrants, TB screening

Definitions and acronyms

Acronyms	Definitions
TB	Tuberculosis
LTBI	Latent Tuberculosis Infection
CARA	Centro Accoglienza per Richiedenti Asilo, Centre for Accomodation of Asylum-seeker
CSPA	Centro Primo Soccorso e accoglienza, First Aid and Reception Centre
Usmaf	Uffici di sanità marittima, aérea e di frontiera
OSR	Ospedale San Raffaele
POC	Point of Care
CARE	Common Approach for Refugees and other migrants' health
INMP	National Institute for Health Migration and Poverty

1. Introduction

The scope of **work-package 5 (WP5) - Migrant TB detection, prevention and treatment,** is to establish a mechanism to ensure that health services delivering TB care are accessible to asylum seekers at the point of arrival.

The aim of deliverable **5.1-Temporary migrant screening set up** was to develop, in collaboration with local and national health and immigration authorities, a coordinated protocol of intervention within *a selected sample of* CARA (Centro Accoglienza per Richiedenti Asilo, Centre for Accomodation of Asylum-Seekers) centre.

and to identify the asylum seekers as a relatively stable population who offer the opportunity of screening and treatment interventions for both active TB and LTBI.

1.1. General context

In recent years, there has been a surge in the number of asylum seekers arriving via the Mediterranean route, with an ever-increasing number of people arriving on Sicilian shores. It is estimated that 170,100 people arrived in Italy by sea in the year 2014, 153,842 in the year 2015 and more than 180,000 in the year 2016 (www.interno.gov.it)**.** Italy is a country with a low-incidence of TB cases, with incidence below 10 per 100,000[1]. Since 2009, more than 50% of cases reported each year (and most MDR TB cases) have occurred in foreign-born persons[1]. Although TB diagnosis and treatment are offered for free to all those who report to a public hospitals (regardless of their legal resident status), symptomatic migrants tend to report late, increasing the chance of complications and TB transmission.

To date, little data has been published on the incidence of TB amongst migrant populations and the majority of reports available concern northern European countries, where the context is significantly different to the Mediterranean one in terms of features and number of arrivals.
Recently, Schepisi et al published data from three TB case finding interventions conducted at primary centres and mobile clinics for migrants and asylum seekers (performed at five different sites in Rome and one site in Milan, Italy) [2]. Out of a population of 6347 migrants screened over a 4 years' period (2009-2014) by verbal screening through a structured questionnaire, TB was diagnosed in 11 persons representing 0.17% of the screened population. A similar incidence rate was reported in the Italian guidelines [3]for TB screening among migrants published in 2010, which states that "*active TB screening yield (number of identified cases over 100000 persons screened) is very low corresponding in mean to 272 cases per 100000 persons-year".*

The data from TB notification system shows that between 2010 and 2013, 876 new TB cases were reported in Sicily (median 4.4 cases per 100.000 persons-year). TB incidence rate (4.4 cases per 100.000 persons-year) is almost doubled when compared to incidence rate reported in the decade 1999-2008 (2.6 cases per 100.000 persons-year)[4]. Since July 2015 local health authorities (Usmaf) in collaboration with Garibaldi Hospital in Catania have been carrying out the active TB case finding at the Port of Catania. From July 2015 until July 2016, 11804 migrants have been screened at the point of arrival by means of a multi-step questionnaire. Eighty-eight (88) individuals resulted questionnaire-positive and out of them twenty-nine (29) where referred to further analysis. Eleven (11) TB cases were diagnosed by geneXpert and culture (estimated incidence 93 per 100.000 person-year).
Italian data on TB screening among migrants is limited and therefore does not allow for an exhaustive evaluation of different screening approaches. Most of the case-finding interventions are performed in symptomatic migrants who report themselves to health centres or who visit outpatient clinics for unrelated medical conditions. Moreover, due to the low resource setting of the centres, case finding investigations for TB are rarely provided by local health services. Microbiological and radiological investigations of suspected cases, when performed, require authorized transport of this population to local hospital. CSPA (Centro di Primo Soccorso e Accoglienza, First Aid and Reception Centre) and CARA (fully explanation of Migrants' reception facilities in Italy available in appendix A) in the south of Italy are well recognised patterns in migration routes[5] and focusing intervention in these structures will allow early detection of infection and spread prevention. Therefore, we plan to implement a locally-based intervention in selected sample of CARA.

2. Methodological approach

The analysis of data collected by the Catania Prefecture and the consultation of the public and local health authorities lead to the identification of two lines of action:

1) The implementation of the Usmaf initiative "TB on port" by giving an on-spot tool for active TB diagnosis: GeneXpert Omni (Cepheid).
   Rationale: empowering the real-time active TB detection at point of arrival (Port of Catania), avoiding the need for transport to local hospitals, which entails government directed police escort and support.
   OSR will provide: the GeneXpert Omni, once available; GIV cartridges for sputum analysis; local staff training on the GIV, Ultra and Omni expert laboratory procedures.

2) The implementation of an active case finding strategy in a selected CARA centre in Sicily.
   Rationale: targeting the population within the CSPA and the CARA centres will allow an accurate screening of individuals whose point of arrival is not monitored by Usmaf and who therefore have yet to receive TB screening. It will additionally allow health personnel to monitor and screen the cases that develop TB during the stay in the centre. The active approach of this initiative will ensure an early identification of cases and avoid the incidence of individuals falling critically ill and reporting themselves to the health authorities when the disease is in an advanced stage.

3. Summary of activities and research findings

3.1. Screening strategies set up

Identification of lines of action:
1) Implementation of the Usmaf initiative "TB on port",
2) Implementation of an active case finding strategy in a selected CARA centre in Sicily

3.1.1 TB on port implementation

In accordance with the Italian Ministry of Health and with local authorities, the team will contribute and provide assistance to the initiative "TB on port" carried out in the port of Catania by the Sicilian government and the Italian MoH. This initiative screens for TB cases in migrants who arrive directly at the quayside. Screening time will be extended from 1 year to 1.5 years to allow for a minimum of 10 months of continuous use of the Xpert OMNI platform, which will be available next September.

3.1.2 Active case finding in CARA centre

The strategies for conducting the active screening of TB cases at CARA and CSPA have been widely discussed between WP5 partners and the local health authorities. All those arriving at the centres will be offered the opportunity to participate in a voluntary screening by completing a questionnaire provided (in different languages and with the support of an interpreter if necessary). The study is approved by San Raffaele Ethic Committee (Protocollo 709624 E-DETECT TB (02052016). Informed written consent will be obtained from each study subjects, before starting

data collection. Informed consent is in Italian as approved by the Ethic Committee; a simplified information sheet is provided in English French or Italian (Appendixes D, E and F) to each study subjects. Whenever the individual is not able to achieve full understanding of the study procedure in the vehicle languages (English and French) the intervention of local cultural mediators will be required. If illiterate a literate witness must sign (the witness will be selected by the participant and with no connection to the research team). All signed forms will be stored at Emerging Bacterial Pathogen Unit at OSR, Milano.
Refusal to participate in the initiative will not impact a person's eligibility for the all other services available. In addition, information will be provided on the main symptoms of TB disease and individuals will be encouraged to contact the local health centres (Red Cross outpatient service) should these symptoms present themselves.

Based on the score obtained in the questionnaire, health personnel will be able to quickly identify those with suspected pulmonary TB. This will prompt the collection of sputum on site and the performance of a rapid test using GeneXpert. Individuals identified as MTB positive will be immediately transferred for treatment initiation and further testing at the infectious disease service of the Garibaldi Hospital in Catania. Agreement with the general director of the Garibaldi Dr Santonocito, the head of the Infectious Diseases department Prof. Caccopardo and the head of the emergency service Dr Pintaudi, has been reached to provide a fast-track hospitalization for detected cases.

3.2. Active TB screening tools

3.2.1 Questionnaire

Trained medical staff will verbally carry out the screenings with the use of a structured questionnaire. The questionnaire (appendix B) has been drafted following the WHO[6] and the ECDC[7] recommendations. It will collect information including individuals' personal data, date of arrival in the centre, past medical history, past TB history and risk factors for TB (including HIV/AIDS). Symptoms suggestive of TB, such as cough, fever, haemoptysis, night sweats and weight loss will be also recorded. WP5 partners have agreed that a sputum sample will be requested if at least one of the above-mentioned symptoms is present. This strategy will also allow the evaluation of each symptoms sensitivity and specificity for active TB disease in migrant population. The questionnaire is available in three languages (English, French, and Arabic) and the support of an interpreter will be available when requested. The three vehicles languages cover over 90% of the spoken languages of the migrant population within the centre.

3.2.1.1 Ethics committee

The study entitled **EARLY DETECTION AND INTEGRATED MANAGEMENT OF TUBERCULOSISIN EUROPE: E-DETECT TB** (WP5 Migrant TB detection, prevention and treatment) was presented to the San Raffaele Institute Ethic Commission (protocol number 709624) and the 25th October 2016 was approved the 10th November 2016. Informed written consent (Appendixes G and H) will be obtained from each subject before data collection.

3.2.2 EDETECT APP

As a part of **D5.8- Development of an effective, digital recording tool for CPSA and CARA residents**, we plan/propose to substitute the paper questionnaire with a digital recording tool. The use of a digital tool to preform active TB screening will allow the standardization of the TB screening practice and the possibility to record and share all the patient's information in a common database which, once adequately evaluated, could be shared by different CARA and CSPA centres. APP contents have been widely discussed amongst WP5 partners. The design of the APP has been subcontracted. Selection of the subcontractor has been performed.
A preliminary App containing all the information needed for active TB screening has been already designed. After revision by all the WP5 partners it was found that this preliminary APP will greatly benefit from the adding of a second track for LTBI screening.
Edetect app is a mHealth system which includes:
-a Phone application. This is a touch screen icon-based application for Android smartphone designed and developed following the WHO guidelines for active TB and LTBI screening. The app is available in English, and is structured in five modules. To record information, a user can click on the relevant icons or take photos. The application additionally allows the user to verbally record and save any further comments if necessary. At the end of the questionnaire all data collected is automatically sent via network to the Medical Unit. If the app-user is out of cellular network coverage, it is still possible to use the application and store the data locally until an area with network coverage is reached. The phone would then synchronize and send the details of the questionnaire to the medical unit based in the referral hospital.
-***Medical Unit***. This is a java-based software system hosted inside a referral hospital. The system receives all information registered by the phone application and allows clinical staff to monitor the data collected.
-**Data Exportation system**. All data collected will be directly exported into an excel database for scientific and epidemiological purposes.

When GeneXpert OMNI will be available, Edetect App and GeneXpert OMNI technology will provide a complete point of care (PoC) in the CARA, CSPA centers allowing evidence-based standardized screening data collection and microbiological analysis on spot.

4. Conclusions and future steps

The implementation of active TB screenings for the migrant population in Sicily was fully achieved on time (the deadline was postponed to M8 as requested by the ethical committee to approve the project and to set up the process). Active TB screening at CARA of Mineo started on schedule in November 2016. We have at present already screened around 1600 subjects.
We are in contact with staff working on the CARE project (Common Approach for Refugees and other migrants' health) Dr Valentina Marchese (INMP, National Institute for Health Migration and Poverty), which is following WP6 (Tracking and monitoring health status) of CARE projects. Currently the CARE project is not implemented from a practical standpoint at CARA in Mineo, where our action is now focusing. Red Cross is responsible for Health care services and organisation in Mineo centre, and Italian Red Cross is an also one of the partners of the CARE project. Dr Cirillo is part of the group, headed by Istituto Nazionale Migrazione e Povertà (Italian main partner of the

CARE) responsible for establishing a consensus panel for next Italian guideline on TB screening among migrants. The first meeting will take place in March (appendix C). During this meeting, we will discuss the implementation of CARE interventions in the CARA centres in Sicily and how to best integrate the data collected during Edetect screening intervention and CARE USB medical recording tool (WP6).

5. Reference

[1] ECDC, *Tuberculosis surveillance and monitoring in Europe 2016*. 2016.

[2] M. S. Schepisi, G. Gualano, P. Piselli, M. Mazza, D. D'Angelo, F. Fasciani, A. Barbieri, G. Rocca, F. Gnolfo, P. Olivani, M. Ferrarese, L. R. Codecasa, F. Palmieri, and E. Girardi, "Active Tuberculosis Case Finding Interventions Among Immigrants, Refugees and Asylum Seekers in Italy," *Infect. Dis. Rep.*, vol. 8, no. 2, p. 6594, 2016.

[3] "AGGIORNAMENTO DELLE RACCOMANDAZIONI PER LE ATTIVITÀ DI CONTROLLO DELLA TUBERCOLOSI 'Gestione dei contatti e della tubercolosi in ambito assistenziale' ." [Online]. Available: http://www.salute.gov.it/imgs/c_17_pubblicazioni_1221_allegato.pdf. [Accessed: 15-Apr-2016].

[4] C. Mammina, C. Bonura, M. Barchitta, A. Quattrocchi, M. Palermo, and A. Agodi, "Tuberculosis surveillance in Sicily, Italy," *Epidemiol Prev*, vol. 38, 2014.

[5] A. Barbieri, G. Cannella, L. Deotti, and M. Peca, "Migratory Routes from Sub-Saharan Countries to Europe SUMMARY, MEDU Medici per i Diritti Umani."

[6] WHO, "Systematic screening for active tuberculosis," 2013.

[7] ECDC, "Guidance on tuberculosis control in vulnerable and hard-to-reach populations," 2016.

6. Appendix A

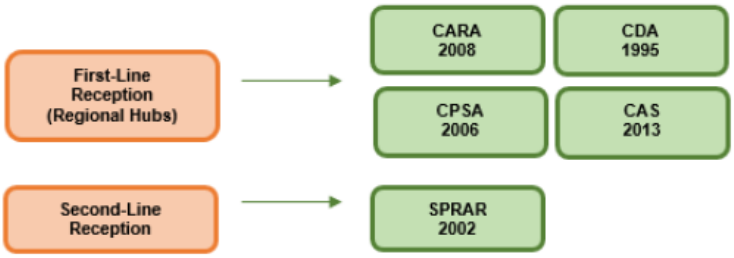
aida Asylum Information Database

Published on *Asylum Information Database* (http://www.asylumineurope.org)

Short overview of the Italian reception system

In Italy, there is no uniform reception system. LD 142/2015 has amended the Procedure Decree 25/2008 and has repealed the previous Reception Decree 140/2005 (with the exception of the financial provisions), without substantially modifying the previous reception system. Articles 20 and 21 of the Procedure Decree, respectively on reception and administrative detention, have also been repealed by LD 142/2015.

The reception system is in theory distinguished between first reception and second reception.[1]



Upon arrival, asylum seekers and migrants may be placed in the following first reception centres:

- Centres for Accommodation of Asylum Seekers (**CARA**). CARA were established in 2008 and replaced previous identification centres;[2]
- Accommodation Centres (**CDA**), created in 1995 for general purposes of accommodation of migrants and also used for asylum seekers;
- First Aid and Reception Centres (**CPSA**), created in 2006 for the purposes of first aid and identification before persons are transferred to other centres;
- Emergency Reception Centres (**CAS**), introduced in October 2013 upon the launch of the *Mare Nostrum* Operation in response to the increasing influx of sea arrivals in Italy.[3]

At the same time, temporary reception centres have also been established for persons returned to Italy under the Dublin Regulation through specific projects.

According to LD 142/2015, first reception is guaranteed in the governmental accommodation centres in order to carry out the necessary operations to define the legal position of the foreigner concerned.[4] It is also guaranteed in the temporary facilities, specifically set up by the Prefect upon the arrival of a great influx of refugees, due to unavailability of places in the first and second level accommodation centres.[5] Indeed, accommodation in temporary reception structures is limited to the time strictly necessary for the transfer of the applicant in the first or second reception centres.[6] LD 142/2015 provides also first aid and accommodation structures[7] and clarifies that the current governmental reception centres (CARA) have the same functions of CPA.[8]

According to the Italian Roadmap the first reception centres (CARA/CDA and CPSA) are turning into Regional Hubs, which are reception structures where the applicants will formalise their

asylum requests through the form C3. Generally the asylum seekers can stay in these centres for a period ranging from 7 to 30 days and thus ensure a fast turnover of guests.

Second-line reception is mainly provided under the System for the Protection of Asylum Seekers and Refugees (**SPRAR**). The SPRAR, established in 2002 by L 189/2002, is a publicly funded network of local authorities and NGOs which accommodates asylum seekers and beneficiaries of international protection. It is formed by small reception structures where assistance and integration services are provided. In contrast to the large-scale buildings provided in CARA, CDA, CPSA and CAS, SPRAR is composed of over 430 smaller-scale decentralised projects as of May 2015.

SPRAR accommodates those destitute asylum seekers that have already formalised their applications. Therefore, asylum applicants already present in the territory may have access directly to the SPRAR centres.[9]

Coordination and monitoring

The overall activities concerning the first reception and the definition of the legal condition of the asylum applicant are conducted under the programming and criteria established by both National and regional Working Groups (*Tavolo di coordinamento nazionale e tavoli regionali*).[10] In first and second accommodation centres special reception services are ensured to vulnerable asylum seekers.[11]

Without prejudice to the activities conducted by the Central Service of the SPRAR, the Civil Liberties Department of the Ministry of Interior conducts, also through the Prefectures, control and monitoring activity in the first and second reception facilities. To this end, the Prefectures may make of use of the municipality's social services.[12]

Moreover, the LD 142 has introduced a more protective norm concerning the trafficked asylum seekers who can now be channelled to a special programme of social assistance and integration under Article 18(3-bis) of LD 286/1998.[13]

The Minister of Interior adopted on 4 August 2015 a Directive on the implementation of activities aimed to control the managing bodies of reception services for non-EU citizens,[14] transmitted through the Circular 11209 of 20 August 2015 to all Prefectures. Specifically, the directive aims to strengthen the control system on the subjective requirements of the bodies managing reception centres and to set out specific clauses aiming at protecting the overwhelming public interest in preserving legality and transparency.

1. Article 8 (1) LD 142/2015.
2. Article 20 LD 25/2008, replacing the Centri di identificazione with the CARA; Article 9 LD 142/2015.
3. Their legal basis is now provided in Article 11 LD 142/2015.
4. Article 9(1) LD 142/2015.
5. Article 11(1) LD 142/2015.
6. Article 11(3) LD 142/2015.
7. Article 8(2) LD 142/2015.
8. Article 9(3) LD 142/2015.
9. Article 14 LD 142/2015.
10. Article 9 (1) LD 142/2015.
11. Article 17(3) (4) LD 142/2015.
12. Article 20(1) LD 142/2015.
13. Article 17(2) LD 142/2015.
14. Available at: http://bit.ly/21VEjkD [1].

7. Appendix B

DETECTTB
early detection & treatment of tuberculosis in europe

Nom _____ **Date:** _____

DonnHeA perAonne::eA

DaBe dI arriDHe en IBa:ie _____ SeEe: F ☐ M ☐ DaBe de naiAAance_____

PaFA dI origine _____ BH:Hphone _____

Fami::e oCi ☐ non ☐ Sco:ariAaBion oCi ☐ non ☐

nBHcHdenBA

nBHcHdenBA de TB oCi ☐ non ☐ En qCe::e annHe _____

ConBacB TB oCi ☐ non ☐ En qCe::e annHe _____

GroAAeAAe oCi ☐ non ☐ MoiA de groAAeAAe _____

CigareBBeA
oCi ☐ non ☐

:coo:
oCi ☐ non ☐

DrogCe
oCi ☐ non ☐

DiabGBeA
OCi ☐ non ☐

VIH
oCi ☐ non ☐

CBre ma:adieA
oCi ☐ non ☐

DEPIST GE DES SYMPTOMES

ToCE
OCi ☐ non ☐

fiGDre
oCi ☐ non ☐

CrachaBA AangCino:enBeA
oCi ☐ non ☐

SCeCrA nocBCrneA
OCi ☐ non ☐

PerBe de PoidA
oCi ☐ non ☐

Co::ecBion dC crachaB
oCi ☐ non ☐

DETECTTB
early detection & treatment of tuberculosis in europe

!NOME%_____!BADGE_____DATE:%_____%

PERSONAL DATA
!
DaG: Cf aEEiI:!iB IGaIL _____ S:x: F M M M DaG: Cf BiEGh _____

CCHBGEL _____ PhCB: _____

FaAiIL L:F M BC M EdHcaGiCB L:F M BC M

MEDICAL HISTORY

PE:IiCHF TB L:F!M BC!M If L:F L:aE _____

TB CCBGacG L:F!M BC!M If L:F L:aE _____

PE:gBaBcL L:F!M BC!M If L:F ACBGh _____

SACkiBg
L:F!M BC!M

Alcohol
L:F!M BC!M

IDU
L:F!M BC!M

Diab:G:F
L:F!M BC!M

HIV
L:F!M BC!M

OGh:EF
L:F!M BC!M

TB SYMPTOMS SCREENING

CCHgh
L:F!M BC!M

F:I:E
L:F!M BC!M

Ha:ACDGLFiF
L:F!M BC!M

NighG Fw:aGF
L:F!M BC!M

W:ighG ICFF
L:F!M BC!M

SDHGHA CCII:cGiCB
L:F!M BC!M

تاريخ_____BADGE_____اسم_____

المعلومات الشخصية

يوم الوصول الى ايطاليا _____ جنس ☐ M ☐ F تاريخ الميلاد _____

البلد _____ الهاتف _____

العائلة ☐ نعم ☐ لا الدراسة ☐ نعم ☐ لا

التاريخ الطبي

مرض السل في الماضي نعم☐ لا☐ السنة_____

معرفة شخص مصاب بمرض السل نعم☐ لا☐ السنة_____

الحمل نعم☐لا☐ الشهر_____

تعاطى المخدرات
☐ لا ☐ نعم

الكحول
☐ لا ☐ نعم

التدخين
☐ لا ☐ نعم

اخر
☐ لا ☐ نعم

HIV
☐ لا ☐نعم

مرض السكر
☐ لا ☐ نعم

اعراض السل

البلغم الدموي
☐ لا ☐نعم

الحمى
☐ لا ☐نعم

السعال
☐ لا ☐ نعم

جمع البلغم
☐لا ☐نعم

فقدان الوزن
☐ لا ☐ نعم

التعرق ليلا
☐لا ☐نعم

8. Appendix C

Istituto Nazionale per la promozione della salute delle popolazioni Migranti e per il contrasto delle malattie della Povertà INMP NIHMP National Institute for Health Migration and Poverty

Il Direttore Generale

Alla c.a. della Dott.ssa Maria Luisa Moro
Agenzia Regionale Sanitaria
Emilia Romagna

Alla c.a. del Dott. Salvatore De Masi
Azienda ospedaliero universitaria Meyer

Alla c.a. della Dott.ssa Antonietta Filia
Istituto Superiore di Sanità

Alla c.a. della Dott.ssa Daniela Cirillo
Ospedale IRCCS San Raffaele - Milano

Trasmessa via mail

Oggetto: Linee guida per il contrasto della tubercolosi tra gli immigrati in Italia – designazione esperti panel per la ReNIP.

L'Istituto Nazionale per la promozione della salute delle popolazioni Migranti e per il contrasto delle malattie della Povertà - INMP ha avviato, una specifica attività finalizzata all'elaborazione di linee guida clinico-organizzative sulla tutela della salute e l'assistenza socio-sanitaria alle popolazioni migranti.

Per la realizzazione di tale attività, ha sottoscritto, in data 3 luglio 2015, un Accordo di collaborazione con l'Istituto Superiore di Sanità, in ragione dell'esperienza maturata nell'ambito del Sistema Nazionale Linee Guida, e con la Società Italiana di Medicina delle Migrazioni, in quanto impegnata anche a sostenere le buone pratiche nell'assistenza ai migranti, sia a livello nazionale sia locale (attraverso i Gruppi territoriali Immigrazione e Salute - GrIS).

Tra gli argomenti prioritari da affrontare con le linee guida, è stato individuato – mediante consultazione dei principali stakeholder dell'Istituto – il tema della tubercolosi. Su questo argomento, nel giugno 2008 è stata tenuta a Roma una *Consensus Conference* che ha coinvolto un gruppo qualificato di esperti, le cui raccomandazioni sono state recepite dal Ministero della Salute nel documento di indirizzo "*Politiche efficaci a contrastare la tubercolosi negli immigrati da paesi ad elevata endemia tubercolare*" (2010). Tale documento rappresenta una base

Istituto Nazionale per la promozione della salute delle popolazioni Migranti e per il contrasto delle malattie della Povertà (INMP)
National Institute for Health, Migration and Poverty (NIHMP)

Via di S. Gallicano 25/a 00153 Roma
Tel. +39 06/58558201 Fax 06/58558401 - info@inmp.it - www.inmp.it
Codice Fiscale e Partita IVA 09694011009

9. Appendix D

==========

INFORMATION SHEET
E-DETECT TB STUDY

==========

Dear Madam or Sir,

San Raffaele Scientific Institute, was invited to participate in an European study, named E-Detect TB, that has the primary purpose of contributing to definitive elimination of tuberculosis (TB) in the European Union (EU).
To carry out this research, we need the cooperation and willingness of people who, like you, meet the scientific requirements appropriate to the evaluation that will be performed. The research project that we present here is aimed to obtain clinical-epidemiological data related to TB screening in migrant population through the Mediterranean routes.

If you take part in this study, it will be asked you to answer, voluntarily, to a questionnaire containing information on previous history of TB and TB symptoms and risk factors. Based on the questionnaire's response, if a pulmonary TB will be suspected, we will ask you to produce a sputum sample. The sputum samples will be shipped at Emerging Bacterial Pathogen Unit (EBPU) at San Raffaele Hospital where the microbiological analysis will be carried out (solid and liquid culture, Xpert MTB / RIF and the new version Xpert MTB/RIF ULTRA). The results of those tests performed at EBPU will be managed and stored by EBPU laboratory staff. The datasets and case report forms (CRF) will be stored in either electronic or paper format. Data will be collected in a database managed by EBPU. The information that we collect from this research project will be kept confidential. Your personal information that will be collected during the research will be put away and no-one but the researchers will be able to see it. Data collected and entered into the CRF are property of San Raffaele Institute. In the event of any publication regarding this study, your identity will remain confidential.

Participation in the study is not dangerous since it is an observational study that only requires the collection of data.
Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will be offered the treatment that is routinely offered for TB disease but data will not be used for the study. Your adherence to this study is completely voluntary and you can change your mind and stop participating at any time

If you have any questions, complaints or feedback about this research study, you may contact the Principal Investigator or the EBPU staff.

Dott.ssa Daniela Maria Cirillo tel 0226437947
Dott. Emanuele Borroni tel 0226435684

10. Appendix E

==========

FOGLIO RIASSUNTIVO
E DICHIARAZIONE DI CONSENSO
per un paziente adulto capace di dare personalmente il consenso

==========

Gentile signora/e,

Questo nostro Istituto di Ricovero e Cura a Carattere Scientifico, Ospedale San Raffaele, è stato invitato a partecipare ad uno studio internazionale che ha lo scopo primario di contribuire all'eliminazione definitiva della tubercolosi (TB) nell'Unione Europea (UE)

Per svolgere tale ricerca abbiamo bisogno della collaborazione e della disponibilità di persone che, come Lei, soddisfino i requisiti scientifici idonei alla valutazione che verrà eseguita. In particolare, con la ricerca che qui Le presentiamo, si intendono ottenere dati clinici-sanitari ed epidemiologici relativi allo screening per TB della popolazione dei migranti dell'area del Mediterraneo.

Nel caso decida di partecipare, lo studio prevede quanto segue:
Verrà proposto a tutti i migranti ospitati presso i CPSA o nei CARA di rispondere, in modo volontario, ad un questionario richiedente informazioni su storia precedente di TB e fattori di rischio. In base alle risposte ottenute dal questionario, se si sospetta una TB polmonare, sarà richiesto alla persona di produrre un espettorato. I campioni di espettorato verranno spediti presso Emerging Bacterial Pathogen Unit (EBPU) dell'Ospedale San Raffaele per l'esecuzione dei test Xpert MTB/RIF e presso le strutture sanitarie locali per la routine diagnostica convenzionale.
I risultati dei test eseguiti presso EBPU e presso le strutture sanitarie locali saranno gestiti ed archiviati da EBPU. I dataset e le schede di raccolta dati (CRF) saranno conservati sia in formato elettronico che cartaceo. I dati verranno raccolti in un database gestito da EBPU.

Se accetta di partecipare a questo studio Lei sarà sottoposto/a ad una prima visita per verificare che le sue condizioni soddisfino i criteri richiesti dallo studio. In occasione di tale visita: saranno eseguiti: i controlli di routine previsti e le sarà proposto un questionario. La collaborazione che Le viene richiesta consiste nel di produrre un espettorato (4 ml). Inoltre è prevista la compilazione di una scheda raccolta dati contenente dati personali, dati relativi a storia tubercolare e fattori di rischio per TB e dati relativi agli esami effettuati per la diagnosi di TB.
La partecipazione allo studio non comporta rischi trattandosi di uno studio osservazionale che richiede solo la raccolta dei dati.
Lei è libero/a di non partecipare allo studio. In questo caso riceverà le terapie standard previste per la patologia da cui Lei è affetto ed i medici continueranno a seguirla con la dovuta attenzione assistenziale, ma i suoi dati non saranno utilizzati per lo studio.
La sua adesione a questo programma di ricerca è completamente volontaria e **Lei si potrà ritirare dallo studio in qualsiasi momento**.
Per **ulteriori informazioni** e comunicazioni durante lo studio potrà contattare il seguente personale:

Dott.ssa Daniela Maria Cirillo tel 0226437947
Dott. Emanuele Borroni tel 0226435684

11. Appendix F

==========

FOURMULAIRE D'INFORMATION
E-DETECT TB

==========

Chère Madame,
Cher Monsieur,

L'Institute Scientifique San Raffaele (Milan) a été invité à participer à une étude européenne qui a pour but principal de contribuer à l'élimination définitive de la tuberculose (TB) dans l'Union européenne (UE).

Á ce propos, nous avons besoin de la coopération des personnes qui, comme Vous, soient répondent aux exigences scientifiques appropriées pour l'évaluation qui sera effectuée. En particulier, pour la recherche que nous présentons ici, nous avons l'intention d'obtenir des données cliniques et épidémiologiques liés au dépistage de la tuberculose dans la population des migrants.
Si Vous participez à cette étude, il vous sera demandé de répondre, volontairement, à un questionnaire contenant des informations sur votre antécédents médicaux, sur les facteurs de risque et sur les symptômes principaux de TB. Sur la base de la réponse au questionnaire, si on a des suspicions de TB pulmonaire, on vous demandera de produire un échantillon d'expectoration. Les échantillons de crachat seront expédiés à l'unité Emerging Bacterial Pathogen (EBPU) de l'hôpital San Raffaele où sera effectuée l'analyse microbiologique (culture solide et liquide, Xpert MTB / RIF et la nouvelle version Xpert MTB / RIF ULTRA). Les résultats de ces tests effectués à l'unité EBPU seront gérés et stockés par le personnelle de laboratoire EBPU. Les ensembles de données et les formulaires de rapport de cas (CRF) seront stockés sous format électronique ou papier. Les données seront collectées dans une base de données gérée par EBPU. Tous les renseignements recueillis au cours du projet de recherche demeureront strictement confidentiels. Le chercheur principal de l'étude utilisera les données à des fins de recherche dans le but de répondre aux objectifs scientifiques du projet de recherche décrits dans ce formulaire d'information. Les données du projet de recherche pourront être publiées dans des revues scientifiques ou partagées avec d'autres personnes lors de discussions scientifiques. Aucune publication ou communication scientifique ne renfermera d'information permettant de vous identifier.
La participation à l'étude n'est pas dangereuse car il s'agit d'une étude observationnelle qui ne nécessite que la collection de données.
Votre participation à cette recherche est entièrement volontaire. C'est votre choix de participer ou non. Que vous choisissiez de participer ou non, tous les services que vous recevez dans cette clinique se poursuivront comme d'habitude. Si vous choisissez de ne pas participer à ce projet de recherche, on vous offrira le traitement qui est couramment offert pour la tuberculose, mais vos données ne seront pas utilisées pour l'étude. Votre adhésion à cette étude est entièrement volontaire et vous pouvez changer d'avis et arrêter de participer à tout moment.
Pour plus d'informations au cours de l'étude vous pouvez contacter les personnes suivantes :

DR Daniela Maria Cirillo tel 0226437947
DR. Emanuele Borroni tel 0226435684

12. Appendix G

OSPEDALE SAN RAFFAELE	**INFORMED CONSENT FORM** **E-DETECT TB** 12.1. San Raffaele Scientific Institute	OSPEDALE SAN RAFFAELE 13.

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the research with you)**
- **Certificate of Consent (for signatures if you agree to take part)**

You will be given a copy of the full Informed Consent Form

Dear Sir or Madame,

1) San Raffaele Scientific Institute, was invited to participate in an international study that has the primary purpose of contributing to definitive elimination of tuberculosis (TB) in the European Union (EU) according to the European Center for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) Europe (www.euro.who.int) "TB Action Plan 2016 to 2020".
The title of the study is "Early Detection and Integrated Management of Tuberculosis in Europe: E-DETECT TB (709,624). In particular, San Raffaele Institute is involved in Work Package 5 (WP5 Migrant TB detection, prevention and treatment).
This is a multicenter research study involving other Hospitals and Health-Care Centers in Italy and abroad.
To carry out this research, we need the cooperation and willingness of people who, like you, meet the scientific requirements appropriate to the evaluation that will be performed. We kindly ask you to agree to participate in this project. You have already had detailed information about this project by Dr. _____
Before making any decision about whether to participate or not, please read carefully these note and ask for any further clarification. Moreover, if you wish, before deciding feel free to request your family's or your doctor's opinion.

2) The aim of this research study is to contribute to Tuberculosis elimination through the development of interventions that ensure early diagnosis and integrated care especially in vulnerable populations (migrant, homeless, drug addicts) in low and high TB incidence countries. Our Institute aims to develop a common protocol to ensure accessible screening for active and latent TB at the point of arrival, at the CPSA (Center of First Aid and Accommodation) and at CARA (Center for asylum seeker accommodation). Information collected within the research study presented here, will allow better understanding of TB epidemiology in migrant population and the evaluation of the best screening practice among migrants.

3) If you take part in this study, we will ask you to answer, voluntarily, to a questionnaire containing information on previous history of TB and TB symptoms and risk factors. Based on

the questionnaire's responses, if a pulmonary TB will be suspected, we will ask you to produce a sputum sample. The sputum samples will be shipped at Emerging Bacterial Pathogen Unit (EBPU) at San Raffaele Hospital where the microbiological analysis will be carried out (solid and liquid culture, Xpert MTB / RIF and the new version Xpert MTB/RIF ULTRA). The results of those tests performed at EBPU will be managed and stored by EBPU laboratory staff. The datasets and case report forms (CRF) will be stored in either electronic or paper format. Data will be collected in a database managed by EBPU. The information that we collect from this research project will be kept confidential. Your personal information collected during the research will be safely and confidentially stored and will be available only to the researchers involved in the study. Data collected and entered in the CRF are property of San Raffaele Institute. In the event of any publication regarding this study, your identity will remain confidential.

4) The study includes the following investigation:
Sputum samples collected from symptomatic patients will be shipped at the Emerging Bacterial Pathogens Unit of San Raffaele Hospital. Each sample will be analyzed by Xpert MTB/RIF test (Cepheid - Sunnyvale CA - USA) and the new version of the test Xpert MTB / RIF ULTRA, solid and liquid culture.

5) From your participation in this study are expected the following benefits:
Early detection and treatment of tuberculosis disease
In addition:
-The development of a standardized protocol for TB screening
-The development of a digital information recording system
-The creation of a dataset where information from different EU countries are shared.

6) Your participation in the study should not result in risks since it is an observational study that only requires data collection

7) This study does not provide a specific insurance coverage, as it does not entail risks for the individual.

8) If you are a woman of childbearing age the study is not dangerous.

9)Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will be offered the treatment that is routinely offered for TB disease but data will not be used for the study. Your adherence to this study is completely voluntary and you can change your mind and stop participating at any time.

11) The study protocol has been prepared in accordance with the current revision of the Declaration of Helsinki and was approved by the Ethics Committee of t San Raffaele Institute. Feel free to contact the San Raffaele Ethics Committee for any facts regarding the study that

concerns you, by contacting the Chair of the Committee: Chairman of the Ethics Committee - San Raffaele Hospital - Via Olgettina, 60, 20132 Milano.

If you have any questions, complaints or feedback about this research study, you may contact the Principal Investigator or the EBPU staff.

Dott.ssa Daniela Maria Cirillo tel 0226437947
Dott. Emanuele Borroni tel 0226435684

CERTIFICATE OF CONSENT

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant_____

Signature of Participant _____

Date _____
Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands.
I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____
Date _____
Day/month/year

14. Appendix H

OSPEDALE SAN RAFFAELE	**INFORMED CONSENT FORM** **E-DETECT TB** 14.1. San Raffaele Scientific Institute	OSPEDALE SAN RAFFAELE 15.

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the research with you)**
- **Certificate of Consent (for signatures if you agree to take part)**

You will be given a copy of the full Informed Consent Form

Dear Sir or Madame,

1) San Raffaele Scientific Institute, was invited to participate in an international study that has the primary purpose of contributing to definitive elimination of tuberculosis (TB) in the European Union (EU) according to the European Center for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) Europe (www.euro.who.int) "TB Action Plan 2016 to 2020".
The title of the study is "Early Detection and Integrated Management of Tuberculosis in Europe: E-DETECT TB (709,624). In particular, San Raffaele Institute is involved in Work Package 5 (WP5 Migrant TB detection, prevention and treatment).
This is a multicenter research study involving other Hospitals and Health-Care Centers in Italy and abroad.
To carry out this research, we need the cooperation and willingness of people who, like you, meet the scientific requirements appropriate to the evaluation that will be performed. We kindly ask you to agree to participate in this project. You have already had detailed information about this project by Dr. _____
Before making any decision about whether to participate or not, please read carefully these note and ask for any further clarification. Moreover, if you wish, before deciding feel free to request your family's or your doctor's opinion.

2) The aim of this research study is to contribute to Tuberculosis elimination through the development of interventions that ensure early diagnosis and integrated care especially in vulnerable populations (migrant, homeless, drug addicts) in low and high TB incidence countries. Our Institute aims to develop a common protocol to ensure accessible screening for active and latent TB at the point of arrival, at the CPSA (Center of First Aid and Accommodation) and at CARA (Center for asylum seeker accommodation). Information collected within the research study presented here, will allow better understanding of TB epidemiology in migrant population and the evaluation of the best screening practice among migrants.

3) If you take part in this study, we will ask you to answer, voluntarily, to a questionnaire containing information on previous history of TB and TB symptoms and risk factors. Based on the questionnaire's responses, if a pulmonary TB will be suspected, we will ask you to produce a sputum sample. The sputum samples will be shipped at Emerging Bacterial Pathogen Unit (EBPU) at San Raffaele Hospital where the microbiological analysis will be carried out (solid and liquid culture, Xpert MTB / RIF and the new version Xpert MTB/RIF ULTRA). The results of those tests performed at EBPU will be managed and stored by EBPU laboratory staff. The datasets and case report forms (CRF) will be stored in either electronic or paper format. Data will be collected in a database managed by EBPU. The information that we collect from this research project will be kept confidential. Your personal information collected during the research will be safely and confidentially stored and will be available only to the researchers involved in the study. Data collected and entered in the CRF are property of San Raffaele Institute. In the event of any publication regarding this study, your identity will remain confidential.

4) The study includes the following investigation:
Sputum samples collected from symptomatic patients will be shipped at the Emerging Bacterial Pathogens Unit of San Raffaele Hospital. Each sample will be analyzed by Xpert MTB/RIF test (Cepheid - Sunnyvale CA - USA) and the new version of the test Xpert MTB / RIF ULTRA, solid and liquid culture.

5) From your participation in this study are expected the following benefits:
Early detection and treatment of tuberculosis disease
In addition:
-The development of a standardized protocol for TB screening
-The development of a digital information recording system
-The creation of a dataset where information from different EU countries are shared.

6) Your participation in the study should not result in risks since it is an observational study that only requires data collection

7) This study does not provide a specific insurance coverage, as it does not entail risks for the individual.

8) If you are a woman of childbearing age the study is not dangerous.

9)Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will be offered the treatment that is routinely offered for TB disease but data will not be used for the study. Your adherence to this study is completely voluntary and you can change your mind and stop participating at any time.

11) The study protocol has been prepared in accordance with the current revision of the Declaration of Helsinki and was approved by the Ethics Committee of t San Raffaele Institute. Feel free to contact the San Raffaele Ethics Committee for any facts regarding the study that

concerns you, by contacting the Chair of the Committee: Chairman of the Ethics Committee - San Raffaele Hospital - Via Olgettina, 60, 20132 Milano.

If you have any questions, complaints or feedback about this research study, you may contact the Principal Investigator or the EBPU staff.

Dott.ssa Daniela Maria Cirillo tel 0226437947
Dott. Emanuele Borroni tel 0226435684

CERTIFICATE OF CONSENT

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant_____

Signature of Participant _____

Date _____
Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands.
I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____
Date _____
Day/month/year