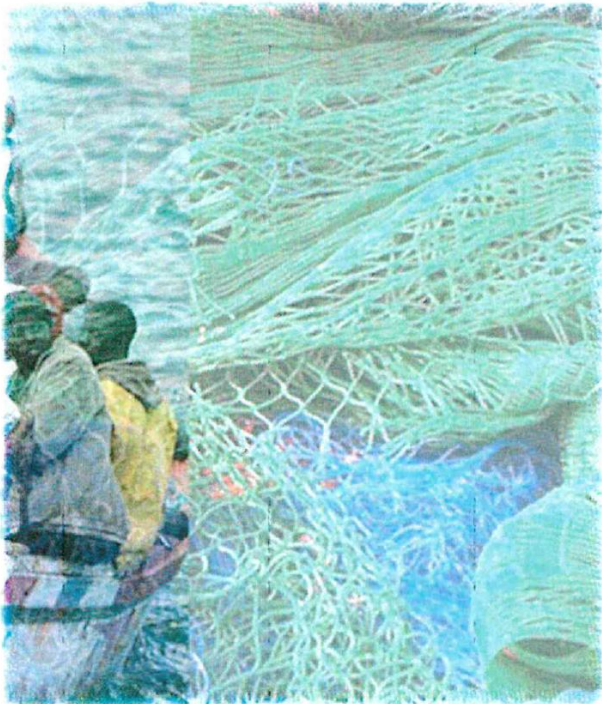


**AGGIORNAMENTI IN TEMA
DI MEDICINA DEI VIAGGI E
DELLE MIGRAZIONI
(1°evento)**

*Gestione sanitaria dei richiedenti
asilo: tubercolosi e le altre*



Lo screening per TBC e il trattamento dell'infezione latente: le indicazioni europee

Alberto Matteelli
Brescia, Italy



Institute of Infectious and Tropical
Diseases - University of Brescia



WHO Collaborating Centre for
TB/HIV collaborative activities
and for TB elimination

Venezia, 25 maggio 2017

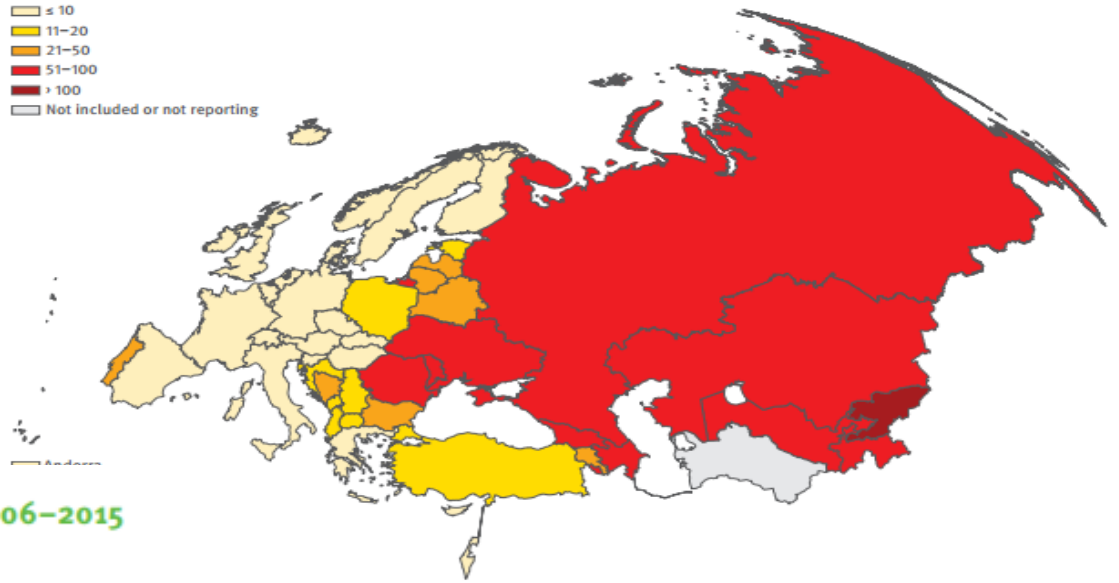
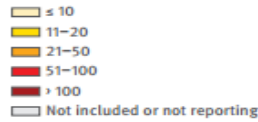
*Sala Polifunzionale del Palazzo Grandi Stazioni
Regione Veneto, Cannaregio 23*

Punti per discussione

- Ruole dell'immigrazione nell'epidemiologia della TB
- Emergenza immigrati in Italia
- Linee guida OMS su screening (ECDC non disponibili ancora)
- Esperienza a Brescia

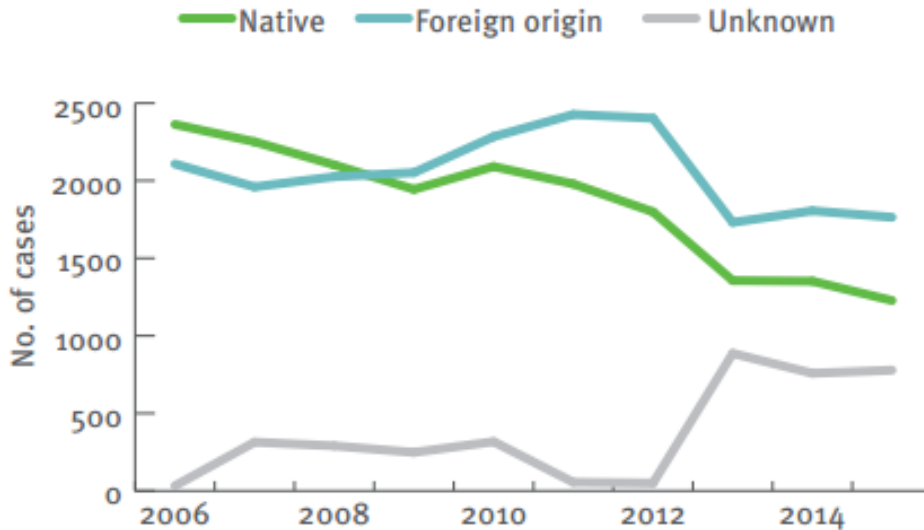
Tubercolosi in Italia 2015

Map 1: TB notification rates of new TB cases and relapses per 100 000 population, European Region, 2015



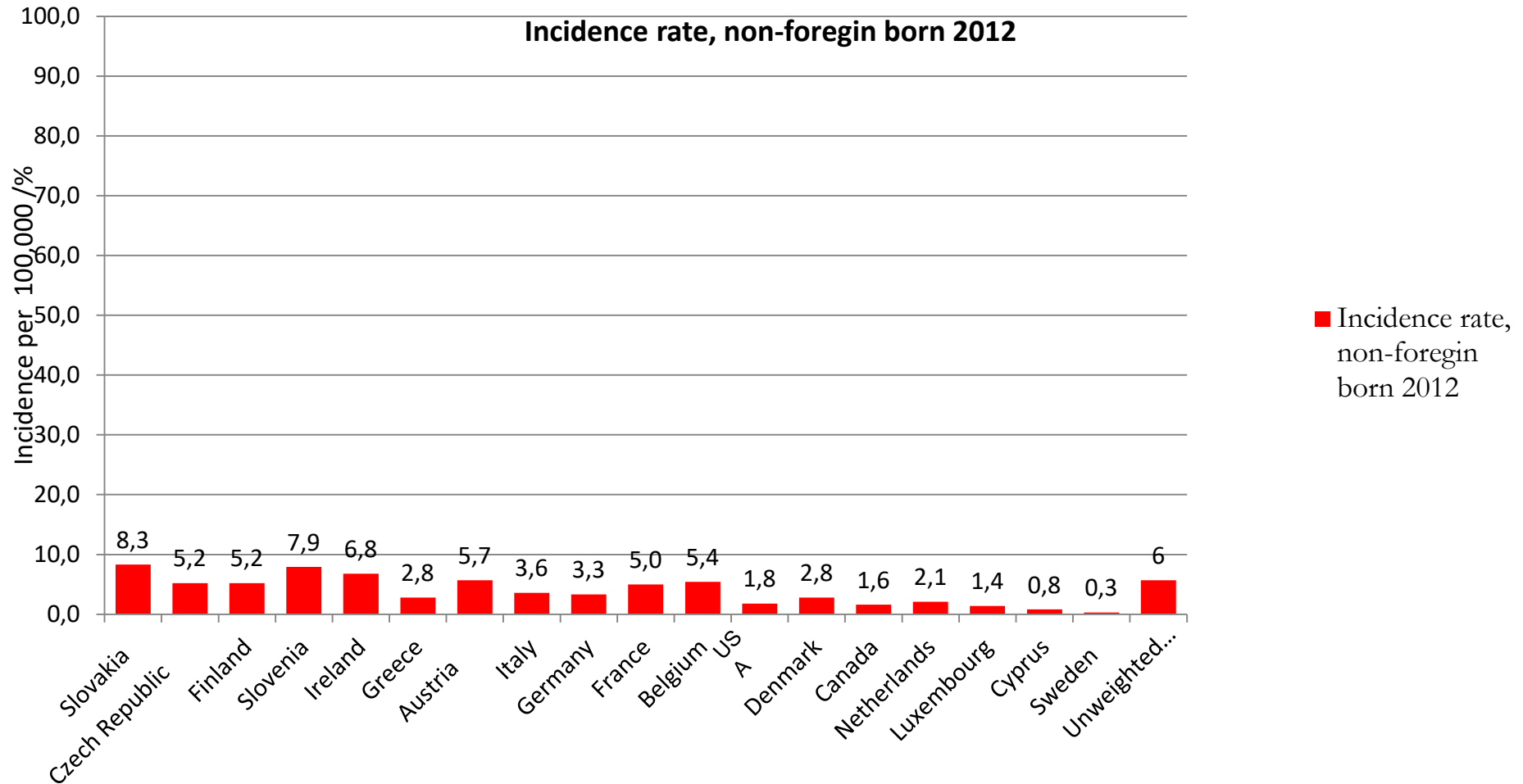
N. Totale di casi notificati: 3769
Incidenza 6.2/100.000

Tuberculosis cases by geographical origin, 2006–2015

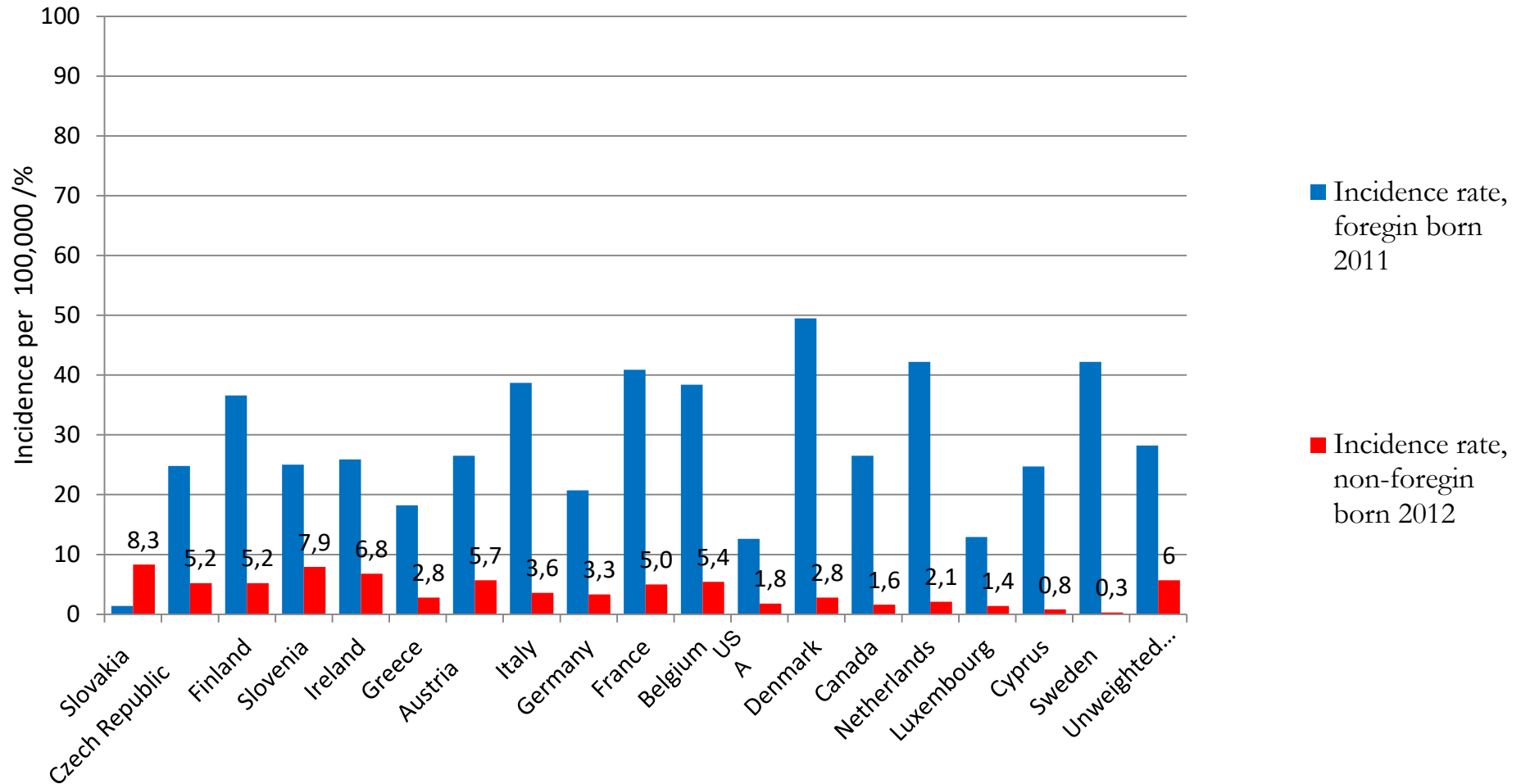


46,8% (1764 casi)

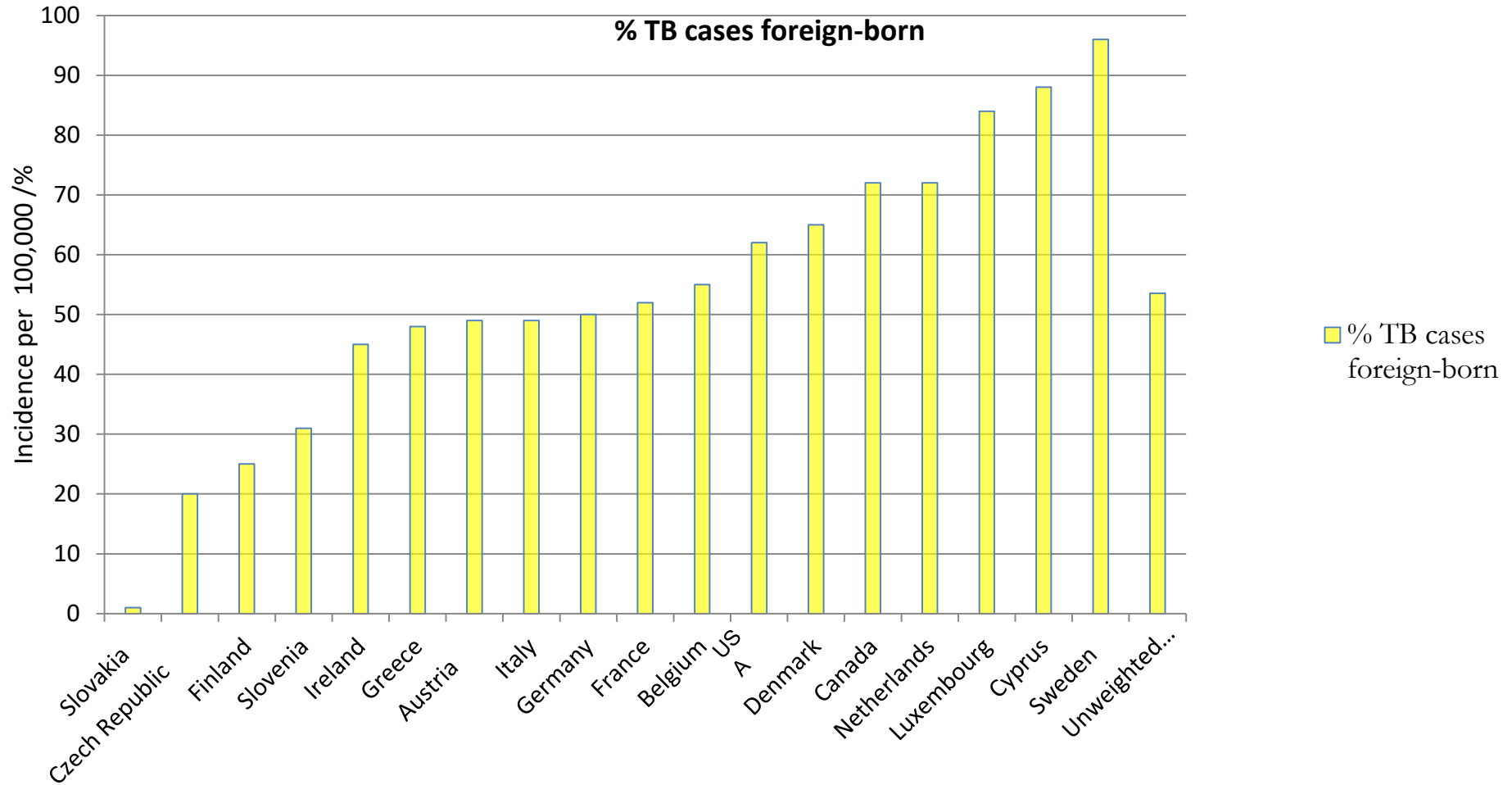
TB in foreign borne in low incidence countries



TB in foreign borne in low incidence countries



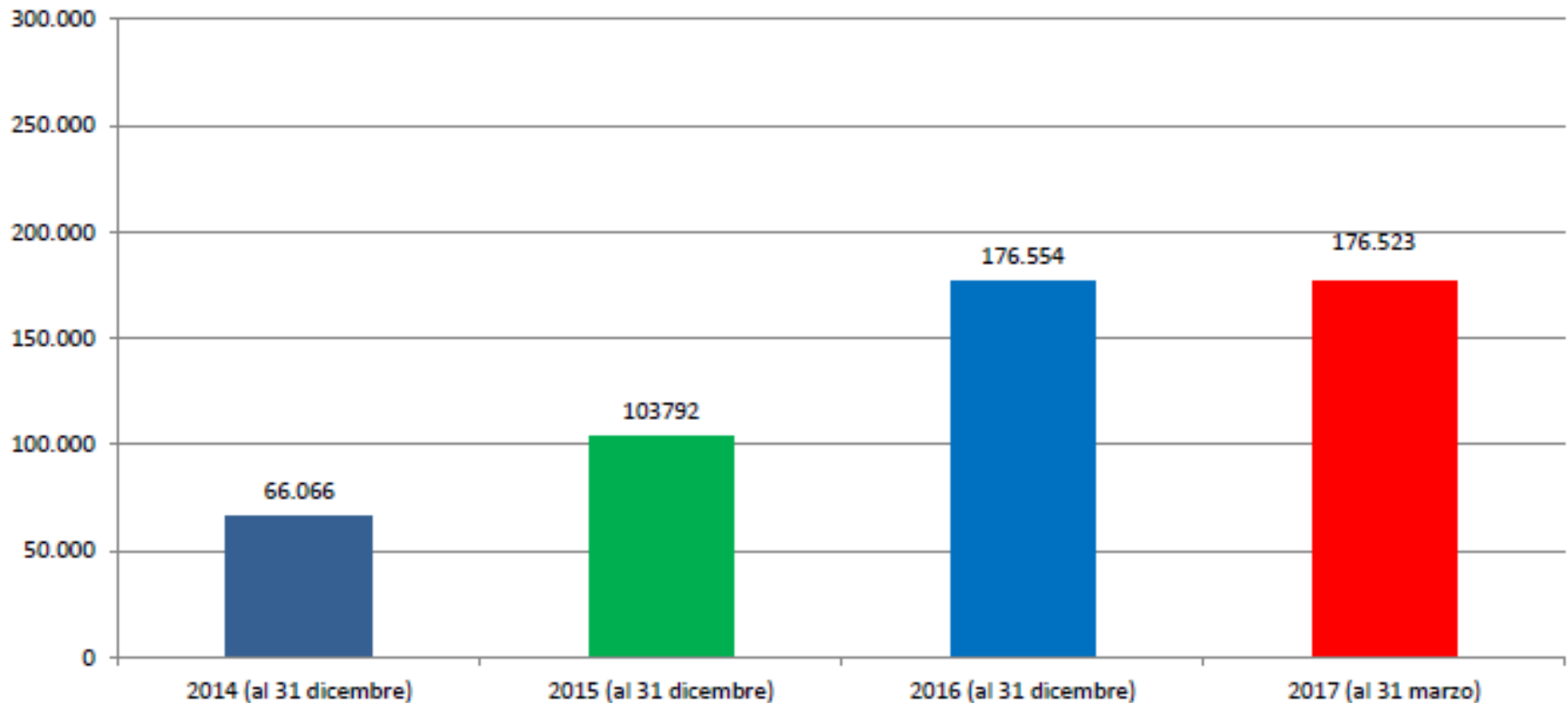
TB in foreign borne in low incidence countries



Emergenze Richiedenti Asilo in Italia

Numero degli sbarchi sulle coste italiane in netto aumento dal 2014
181mila migranti sbarcati in Italia nel 2016

Trend dell'accoglienza anni 2014 - 2015 - 2016 - 2017



Arrivano dal mare



Trapani

Porto Empedocle

Lampedusa



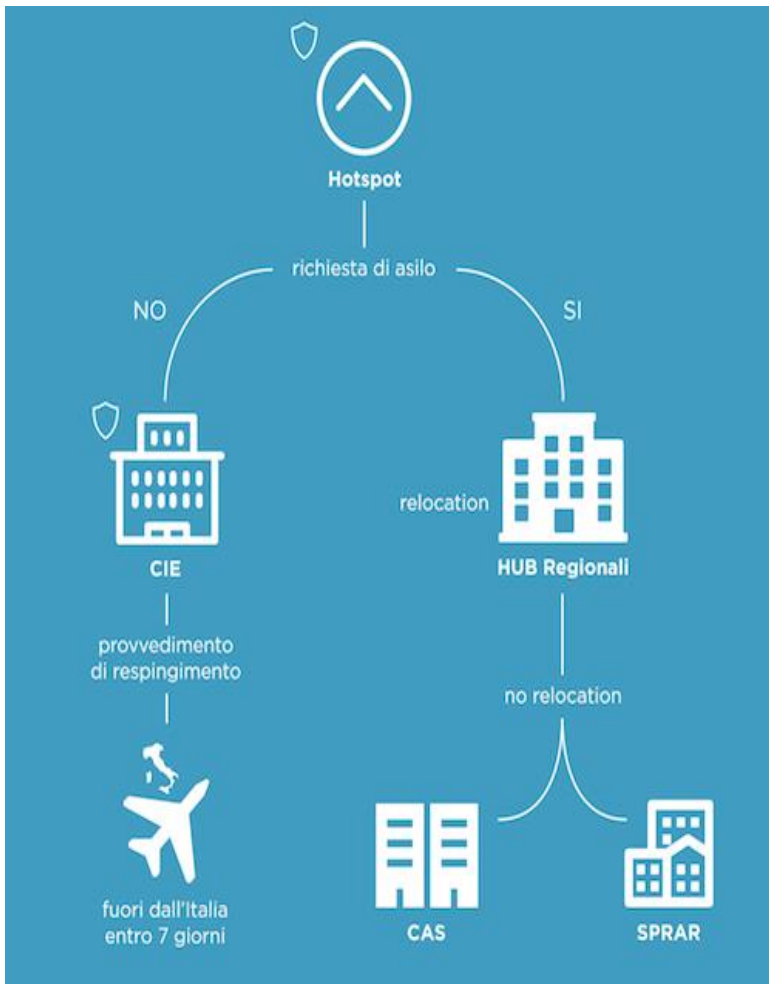
Routes variations over time

Country	Total 2014	Total 2015	1 Jan – 13 Apr 2016
Greece	34,442	853,650	153,362
Italy	170,100	153,842	23,170

Cosa succede dopo lo sbarco

181mila migranti sbarcati in Italia nel 2016 →
176mila richiedenti asilo a Dicembre 2016

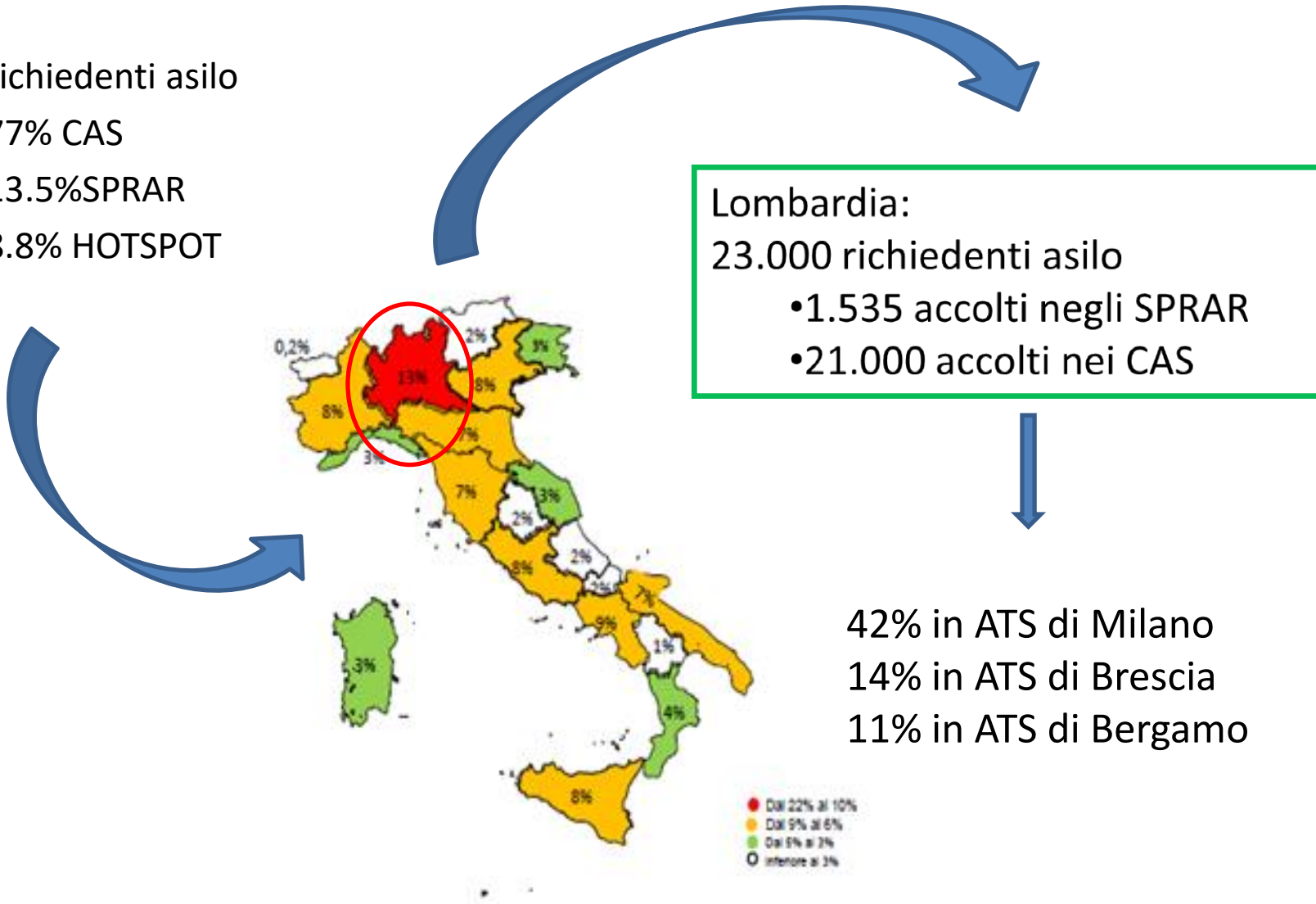
L'accoglienza è articolata in 3 fasi (d.lgs. 142/2015):



1. Subito dopo lo sbarco sul territorio italiano gli stranieri sono accolti nei centri di primissimo soccorso e accoglienza (**Hotspot**) dove vengono identificati e fotosegnalati
 2. Gli stranieri che manifestano la volontà di richiedere la protezione internazionale vengono ricollocati negli **Hub** regionali, dove rimangono per il tempo necessario alla formalizzazione della domanda (non più di 30 giorni).
 3. Infine, vengono trasferiti nei centri di seconda accoglienza (nel **sistema SPRAR**) in cui rimangono fino alla decisione dell'istanza da parte della Commissione territoriale per il riconoscimento della protezione internazionale.
- Chi non fa richiesta di asilo viene spostato nei **CIE** (Centri di identificazione ed espulsione) e riceverà un decreto di respingimento.

I centri di seconda accoglienza

- 176.000 richiedenti asilo
 - 77% CAS
 - 13.5% SPRAR
 - 8.8% HOTSPOT



ACTION FRAMEWORK

8 priority actions for elimination in low-incidence countries



Vulnerable and hard-to-reach groups

TB risk groups are all those with an elevated incidence. Hard-to-reach groups are those whose socioeconomic conditions or lifestyle makes it difficult to recognize TB symptoms, access health services, self-administer treatment and attend regular health care appointments.

Basic requirements

Mapping of TB risk is necessary in order to:

- design interventions to **improve access**,
- tailor treatment and social protection interventions for TB-affected people and households
- plan activities to diminish the underlying TB risk factors.

The health response requires:

- Regulation based on **human rights**
- **Adaptation** of services to special needs.

Implementing social protection

- Schemes for **compensating** the financial burden, such as sickness insurance, disability pension, social welfare payments, other cash transfers
- **Housing support, vouchers or food packages;**
- **Legislation** to protect people with TB from **discrimination**, such as deportation, expulsion from workplaces or housing, educational or health institutions;
- **Instruments** to protect and promote human rights, including addressing **stigma** and discrimination, with attention to gender,

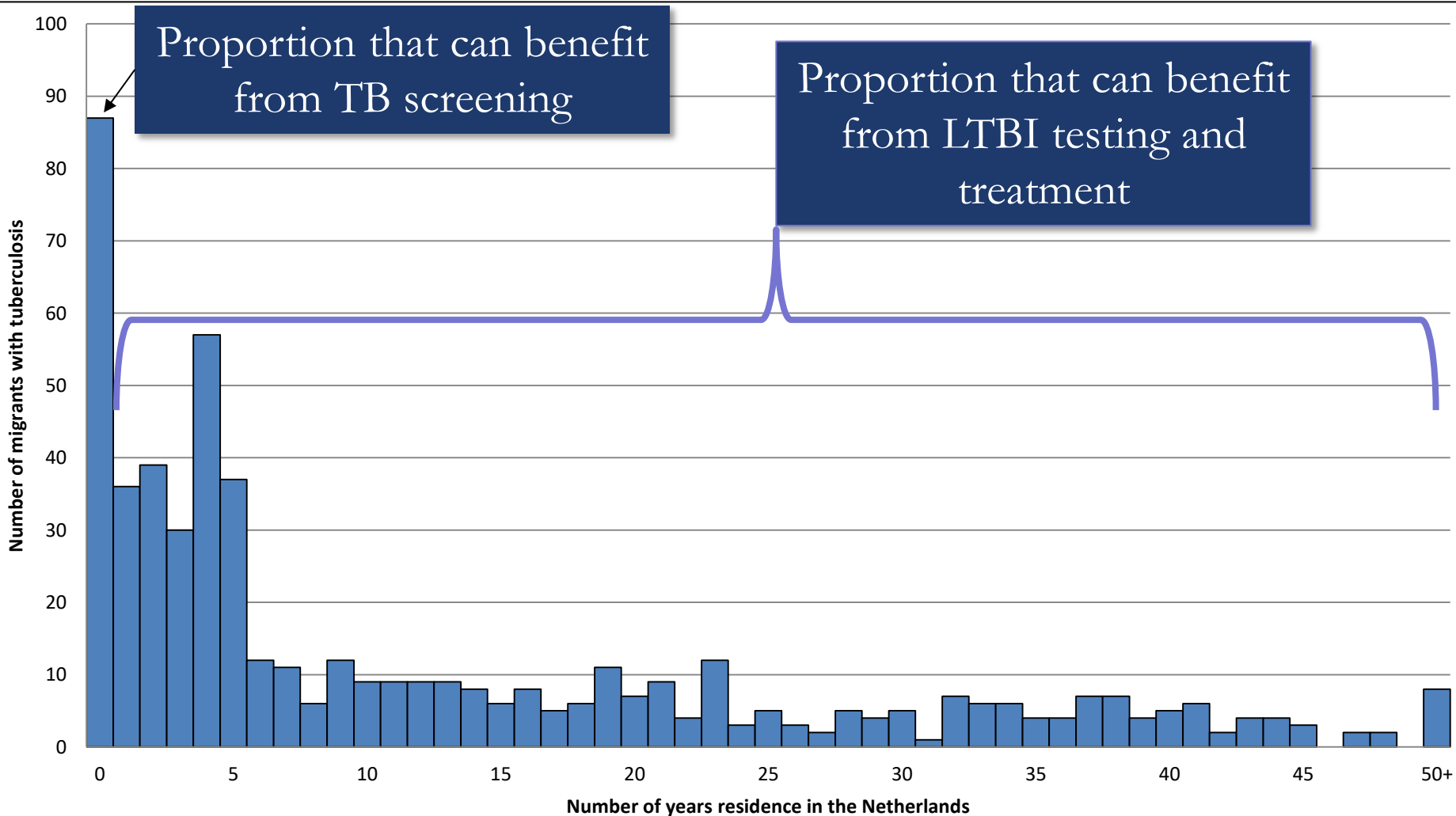
Special needs of migrants

- Migrant communities should be **empowered** through social mobilization and health communications.
- TB diagnosis, treatment and care for migrants should be **integrated** within general health services
- **Reach** migrants in centres for refugees and asylum seekers, situations of displacement and other special settings, such as shelters for undocumented migrants.

Special needs of migrants

- Consider systematic screening for active TB in migrants, either before migration, at the point of arrival or after arrival.
- Consider systematic testing and treatment of LTBI for specific subgroups

TB among migrants 2013, years residence in the Netherlands (550 with known duration of residence)



Screening of tuberculosis disease and infection in asylum seekers



In hot spots upon arrival
Screening for active TB



In CAS/SPRARS
Screening for active TB
and for LTBI

Conditional recommendations, cont.

7. ***A. Systematic screening may be considered for geographically defined sub-populations with extremely high levels of undetected TB (>1% prevalence)***

B. Systematic screening may be considered also for other sub-populations with very poor health care access, such as urban slum dwellers, homeless people, people living remote areas with poor access, indigenous populations, migrants, and other vulnerable groups.

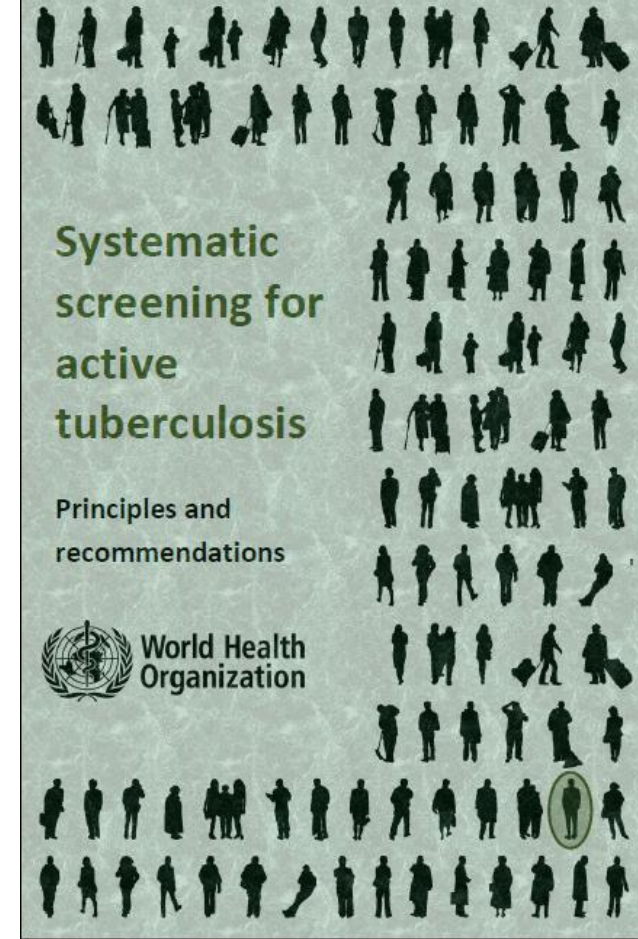


Algorithms for screening and diagnosis

Screening tools:

1. Symptoms (questionnaire)

2. Chest X-ray (either as first step or as a follow-on step for symptom positive persons)



Setting the option according to TB incidence in screened population



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Low yield of screening asylum seekers from countries with a tuberculosis incidence of <50 per 100000 population

Gerard de Vries, Job van Rest, Wieneke Meijer, Bert Wolters, Rob van Hest

DOI: 10.1183/13993003.00099-2016 Published 1 June 2016

Evaluation of screening asylum seekers (by chest X-ray) in the period 2011 through September 2015 in the Netherlands

12 cases detected over 45,439 screened, for an incidence rate of 26.4 (CI:14.3-44.9).

Policy to stop screening asylum seekers from countries with TB incidence < 50/100,000 approved in The Netherlands

De Vries G. et al. Eur Respir J 2016

Recommendations on at-risk populations



Risk population groups	Strength of recommendation
<ul style="list-style-type: none">• People living with HIV• Adult and child PTB contacts• Patients initiating anti-TNF treatment• Patients receiving dialysis• Patients preparing for transplantation• Patients with silicosis.	Strong: systematic testing and treatment should be performed (Low to very low quality of evidence)
<ul style="list-style-type: none">• Prisoners• Health workers• Immigrants from high burden countries• Homeless persons• Illicit drug user	Conditional: Systematic testing and treatment should be considered (Low to very low quality of evidence)
<ul style="list-style-type: none">• Patients with diabetes• People with harmful alcohol use• Tobacco smokers• Under-weight people	Conditional: systematic testing and treatment is not recommended unless they belong in the upper two groups (Very low quality of evidence)

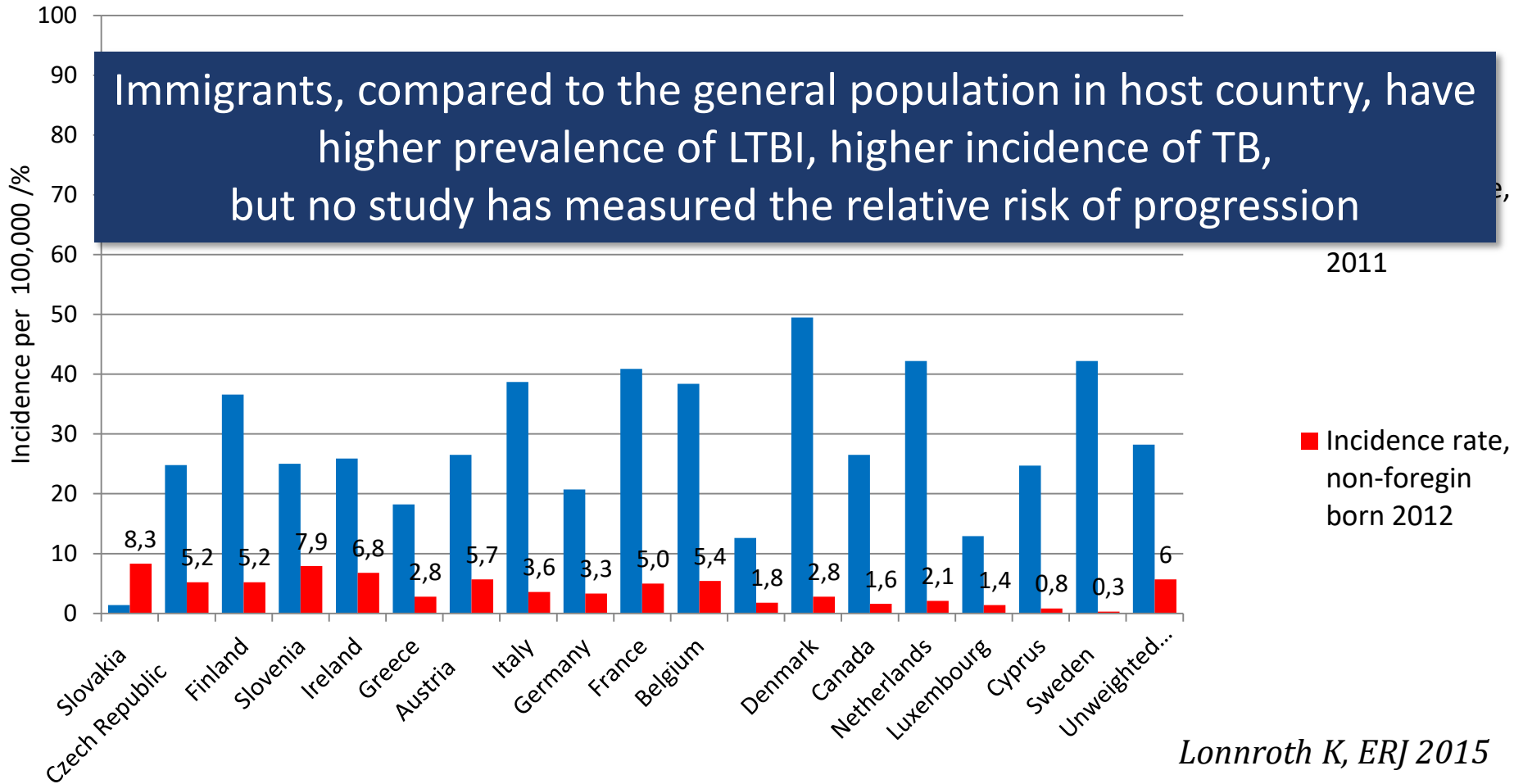
Why conditional ?



Pooled LTBI risk estimates across risk groups, compared to general population, low burden countries

Risk group	Low TB burden			
	TST		IGRA	
	n*	Pooled estimate risk ratio (range)	n*	Pooled estimate risk ratio (range)
Immigrants and refugees (n=23)	17	3.27 (1.00-8.31)	13	2.26 (0.79-8.08)

TB in foreign borne in low incidence countries



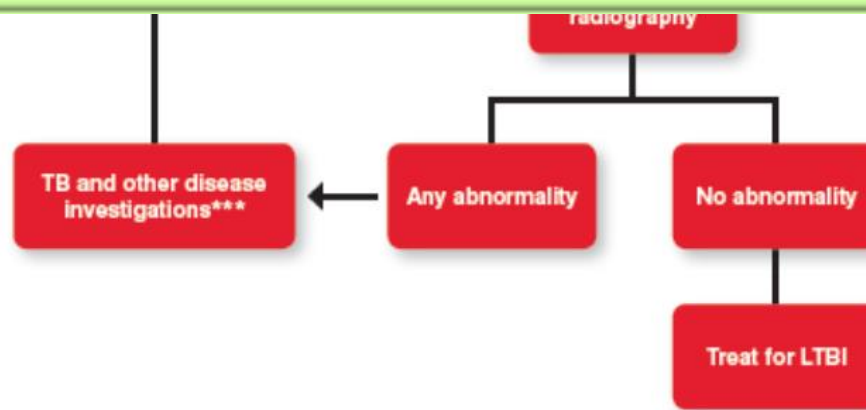
Lonroth K, ERJ 2015

Algorithmic approach to diagnosis and treatment of LTBI in at-risk populations

Ask for any symptoms of tuberculosis in individuals from the risk groups*

Either TST or IGRA can be used to test for latent TB infection. IGRA should not replace TST in low and middle income countries¹.

(Strong recommendation, very low quality of evidence)



Comparison of TST and IGRA for prediction of progression of TB disease

Eight head-to-head studies

Outcome (# of studies)	Pooled estimate of TST (95% CI)	I ² (P-value)	Pooled estimate of IGRA (95% CI)	I ² (P-value)
Risk ratio (8)	2.58 (1.72-3.88)	14% (0.32)	4.94 (1.79-13.65)	72% (0.001)
IRR (3)	2.07 (1.38-3.11)	0% (0.60)	2.40 (1.26-4.60)	41% (0.18)

Estimate of PPV of commercial IGRA 0.03 (range 0.00 -0.13)
and TST 0.03 (range 0.01-0.07)

Comparison of TST and IGRA for prediction of progression of TB disease

823 asylum seekers screened with QTF and TST and followed for 23–32 months in Norway, 2005-2006.

Test	PPV (CI 95%)	NPV (CI 95%)
Quantiferon Gold	3.3 % (1 – 5)	99.8% (99 – 100)
TST > 15 mm	2.3 (0 – 5)	99.1% (98 – 100)

Other alternatives ?

- A two step approach: first testing all subjects with TST, then retesting all TST positive subjects with IGRA, then treating only double positive subjects
- Decreases the number of tested with a costly IGRA, and the number of treated if only TST is used
- Limited and discordant data on cost-effectiveness

Recommendation on LTBI treatment

The following treatment options are recommended for the treatment of latent TB infection:

- 6 months isoniazid (6H)
- 9 months isoniazid (9H)
- 3 months weekly rifapentine plus isoniazid (3HP)
- 3 to 4 months isoniazid plus rifampicin (3-4HR)*
- 3 to 4 months rifampicin alone (3-4R)**

(Strong recommendation, moderate to high quality of evidence)

* Voted by 53% of panel and ** voted by 60% of panel as equivalent options for 6H

Comparison of 6 months INH with other regimens for the incident TB and hepatotoxicity

Comparator	Intervention	Development of incident TB		Hepatotoxicity	
		OR (95% CI)	Quality of evidence	OR (95% CI)	Quality of evidence
Isoniazid 6 m	Rifampicin 3-4 months	0.78 (0.41-1.46)	Moderate	0.03 (0.00-0.48)	Low
Isoniazid 6 m	Rifampicin and isoniazid 3-4 months	0.89 (0.65-1.23)	Low	0.89 (0.52-1.55)	Very low
Isoniazid 6 m	3 months weekly rifapentine plus isoniazid*	1.09 (0.60-1.99)	Low	1.00 (0.50-1.99)	Low
Isoniazid 9m	3 months weekly rifapentine plus isoniazid	0.44 (0.18-1.07)	Low	0.16 (0.10-0.27)	Moderate

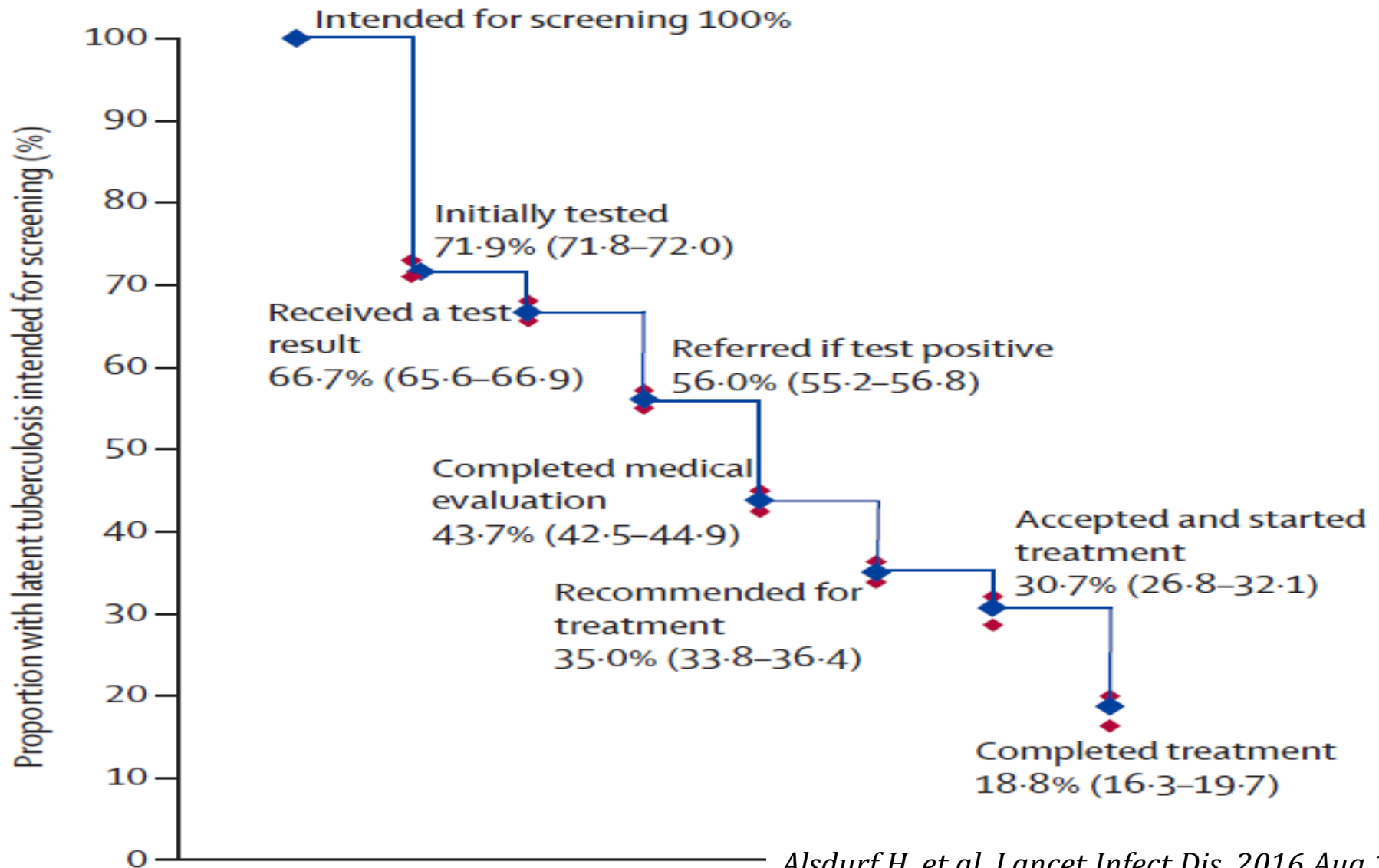
*exclusively among people living with HIV

Two relevant questions

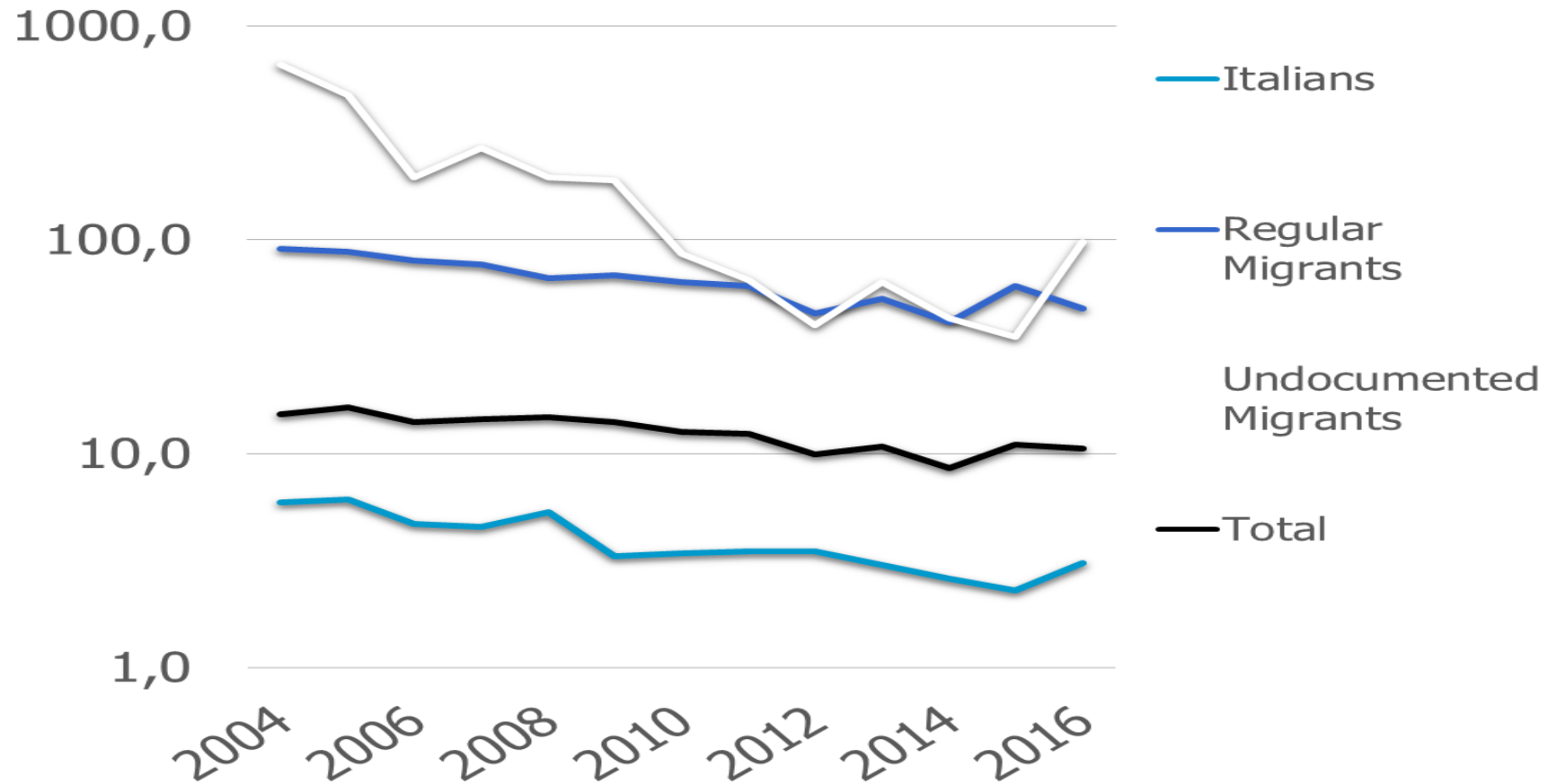
- Effectiveness
 - Can screening and treatment be done?

- Cost-effectiveness
 - If screening is feasible, does it worth the money?

Losses and drop-outs at each stage of the cascade of care in latent tuberculosis

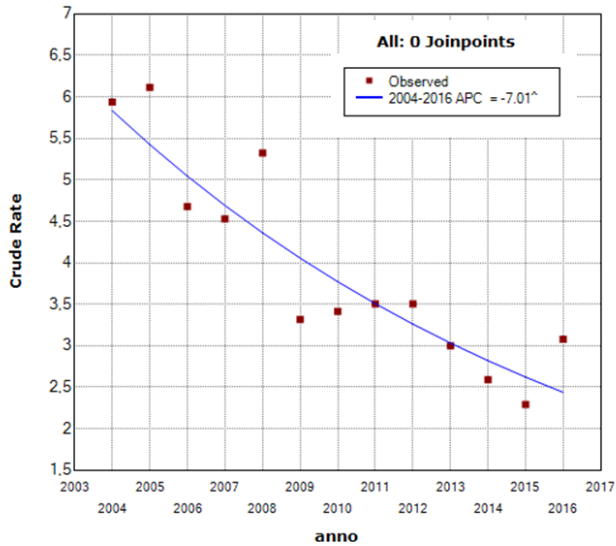


TB notifications in Brescia, 2004-2015

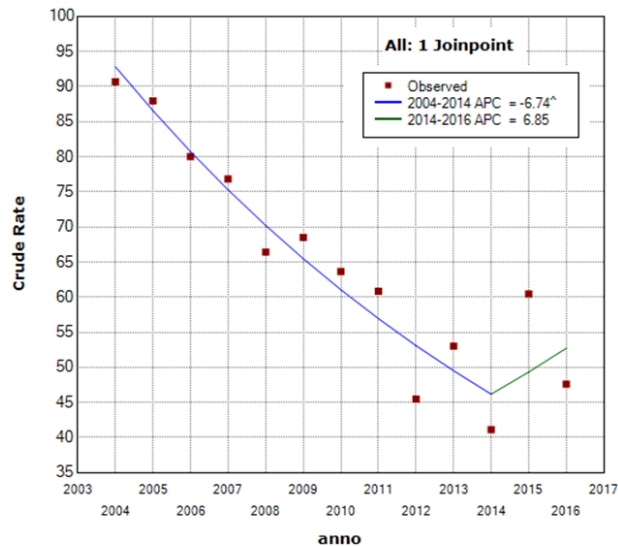


TB notifications in Brescia, 2004-2015

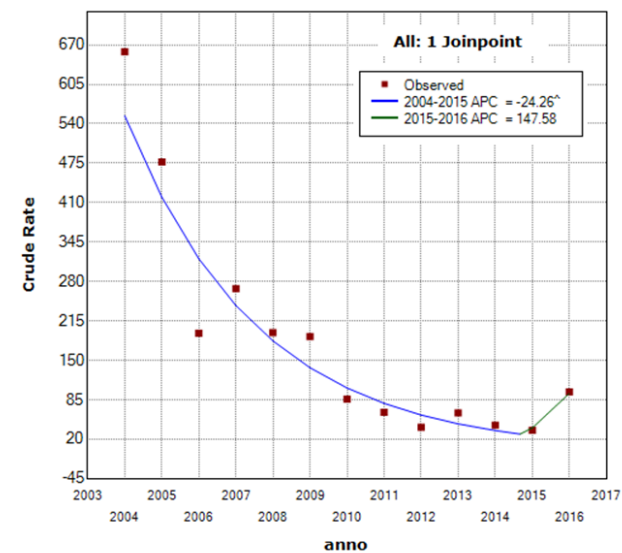
ITA



REGMIG



UNDMIG



Temporal trends were performed using Joinpoint Trend Analysis Software

The local health network

Retrospective analysis of cascade of care and cascade of prevention among 3,169 asylum seekers displaced in Brescia in 2015-2016



**ASST Spedali Civili di Brescia –
Clinica di Malattie Infettive**



**Poliambulatorio pneumologico
territoriale – Via Corsica**

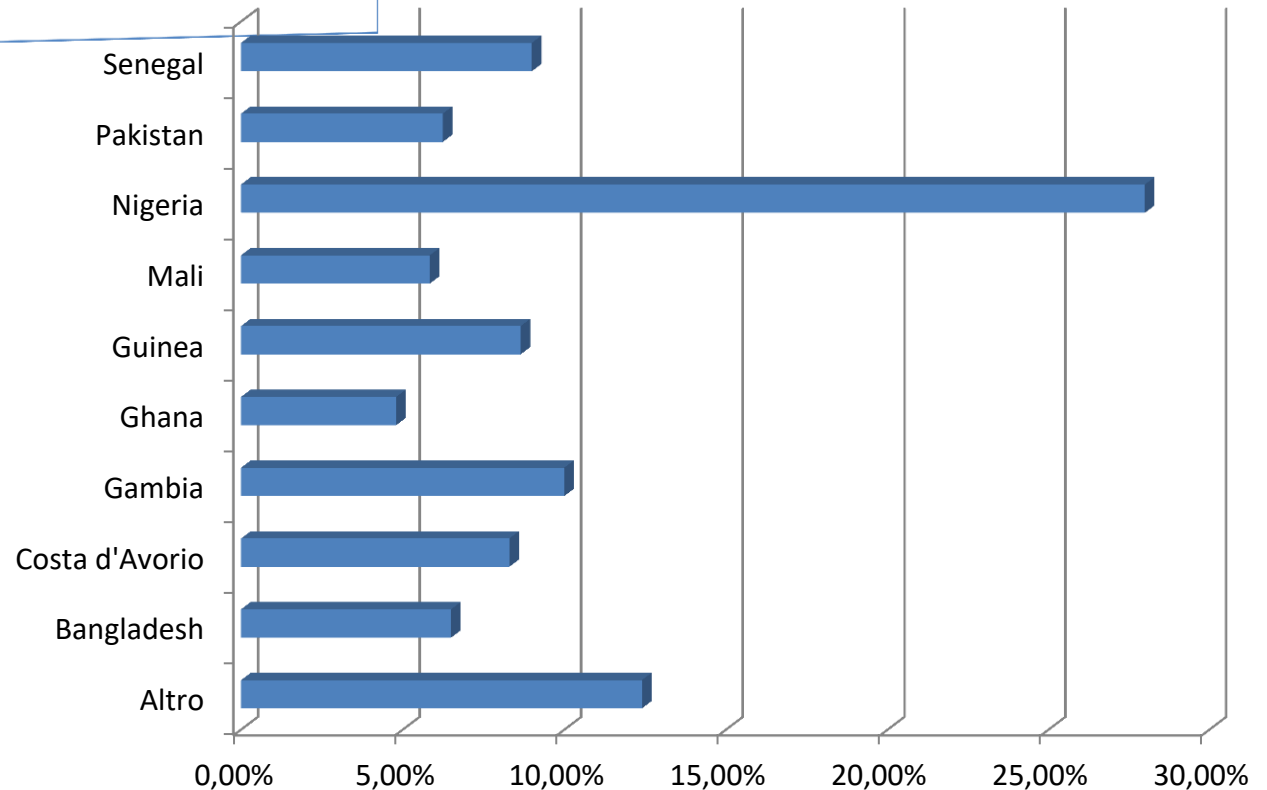


**Ambulatorio Migranti –
Viale Piave**

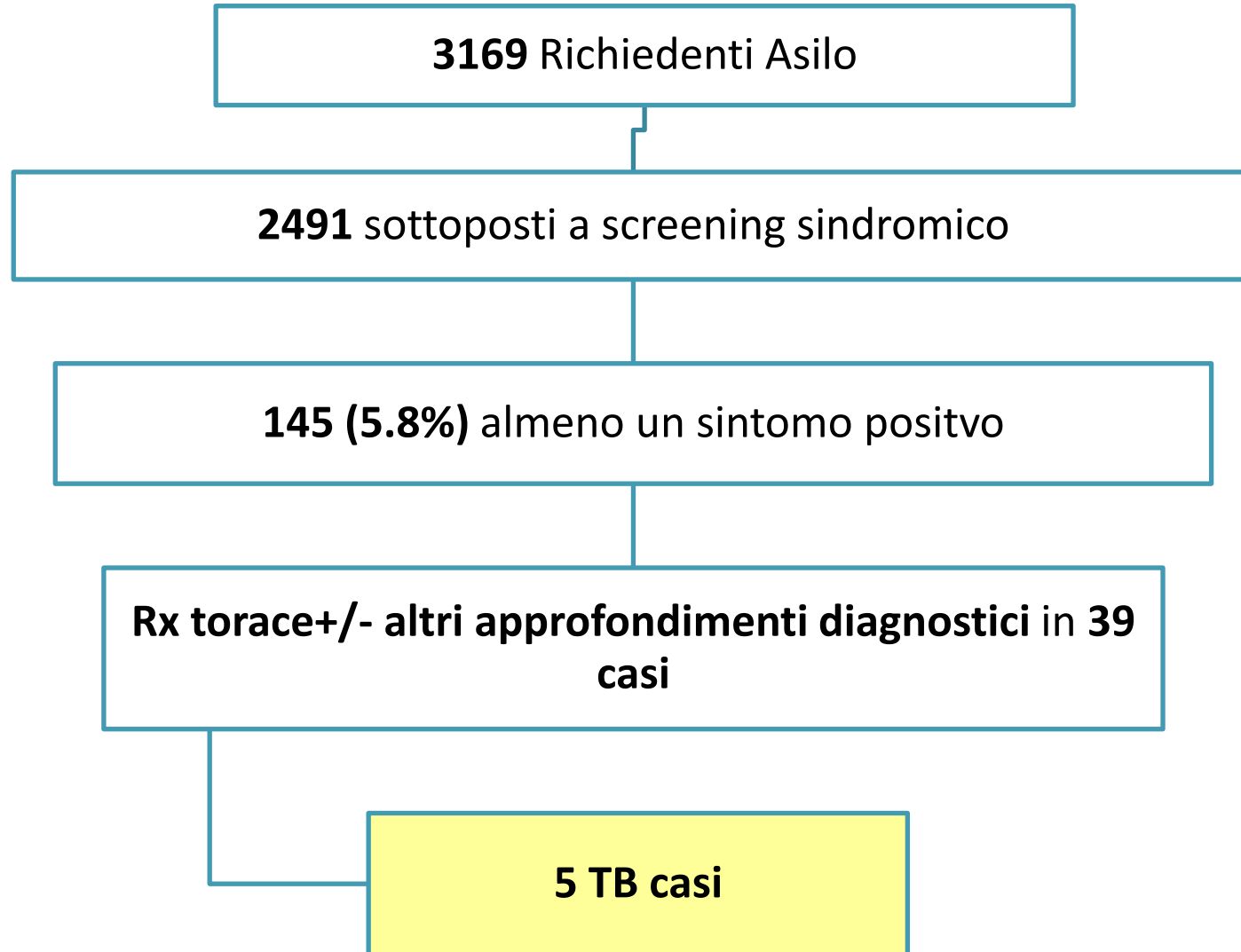


Richiedenti Asilo 2015-2016, Brescia

- Popolazione: 3169
- 83% maschi
- 22 anni età mediana
- 84% africani



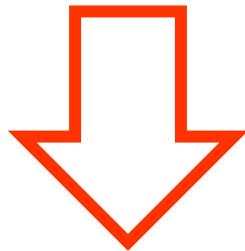
Active TB case finding



Estimated TB incidence among asylum seekers, 2015-2016

5/3,169 → 0.2 % screening yield

13 TB cases out of 3,169 asylum seekers*

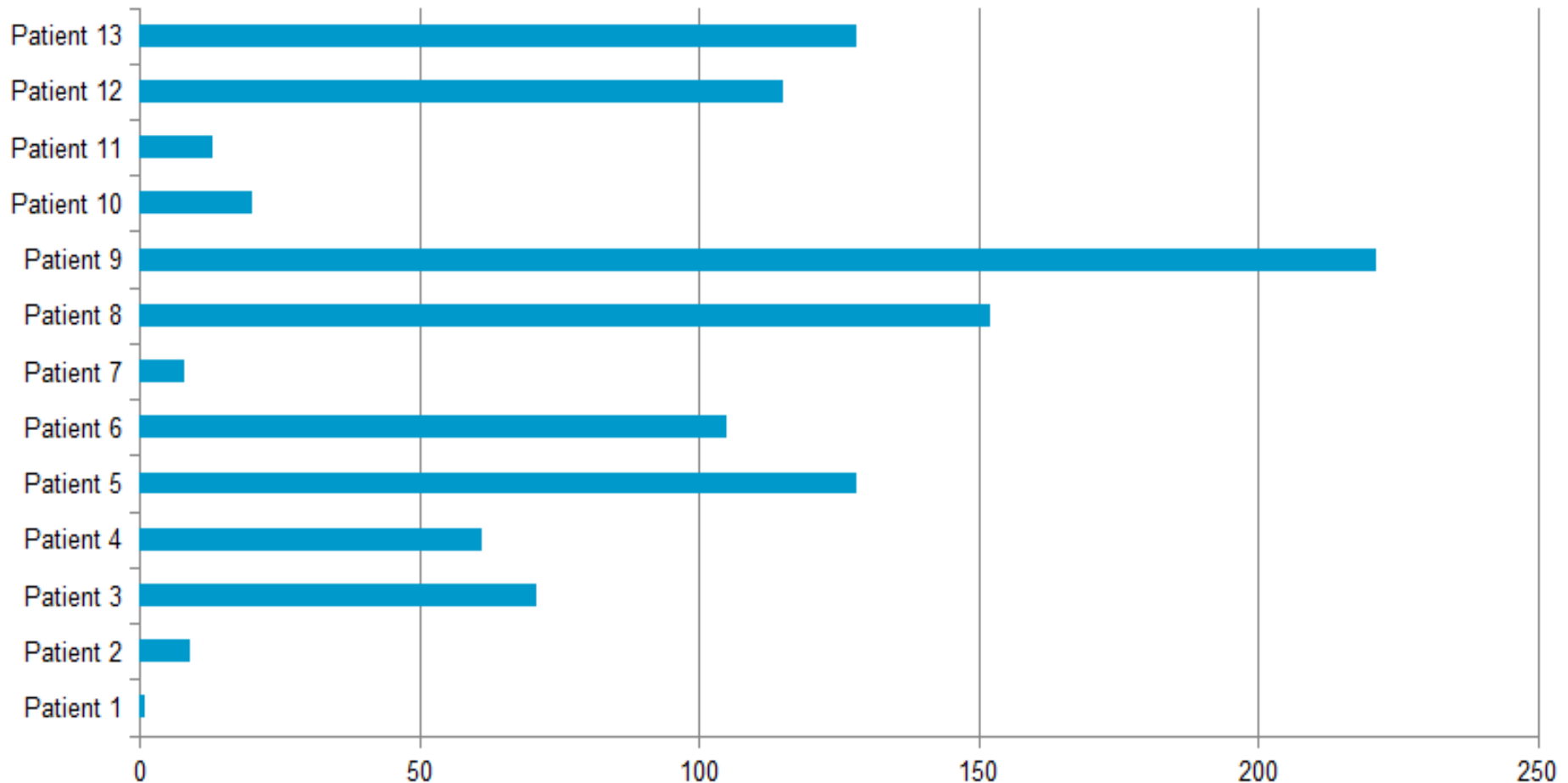


200 cases per 100,000

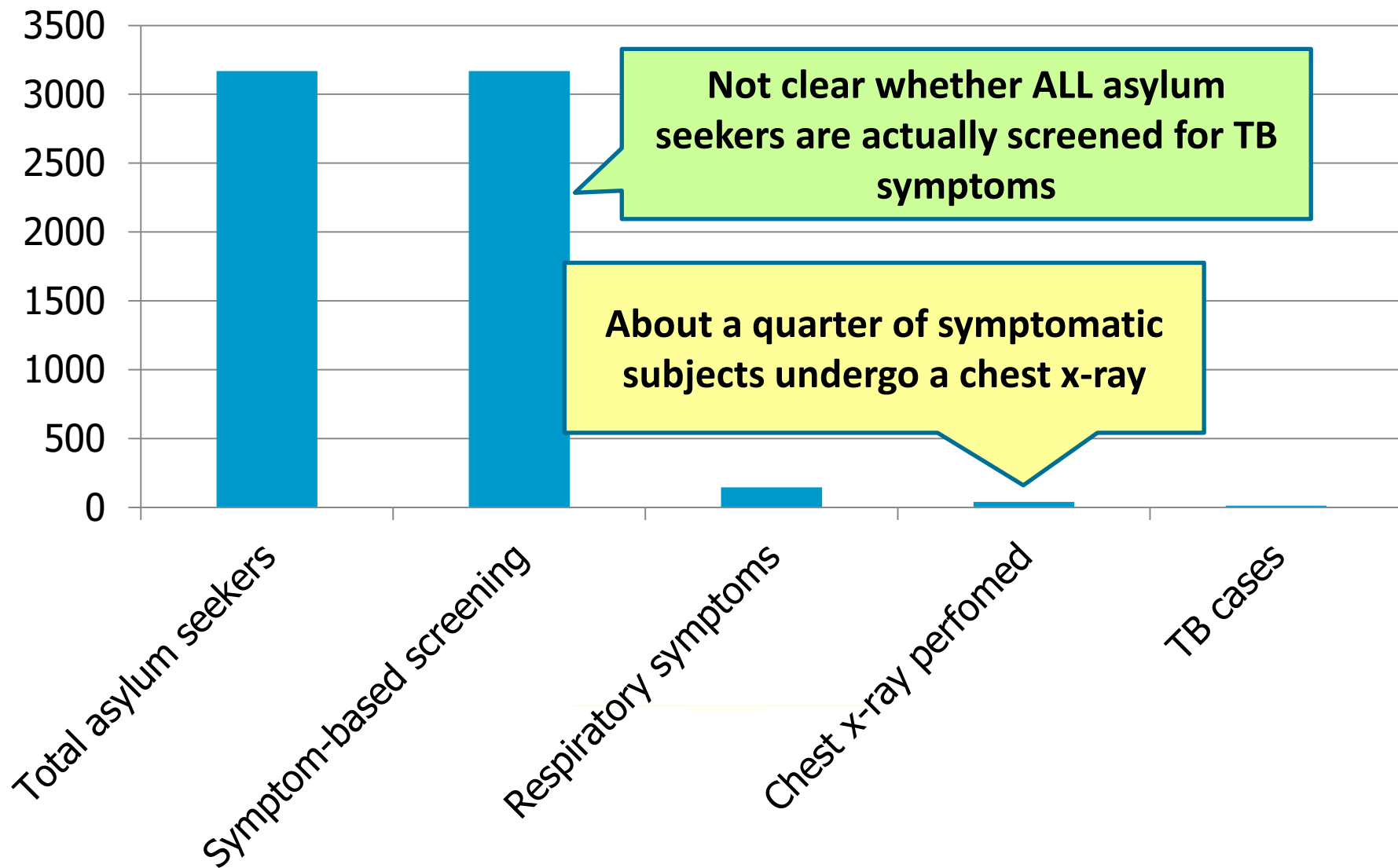
*Denominator is uncertain

Time from arrival to treatment initiation

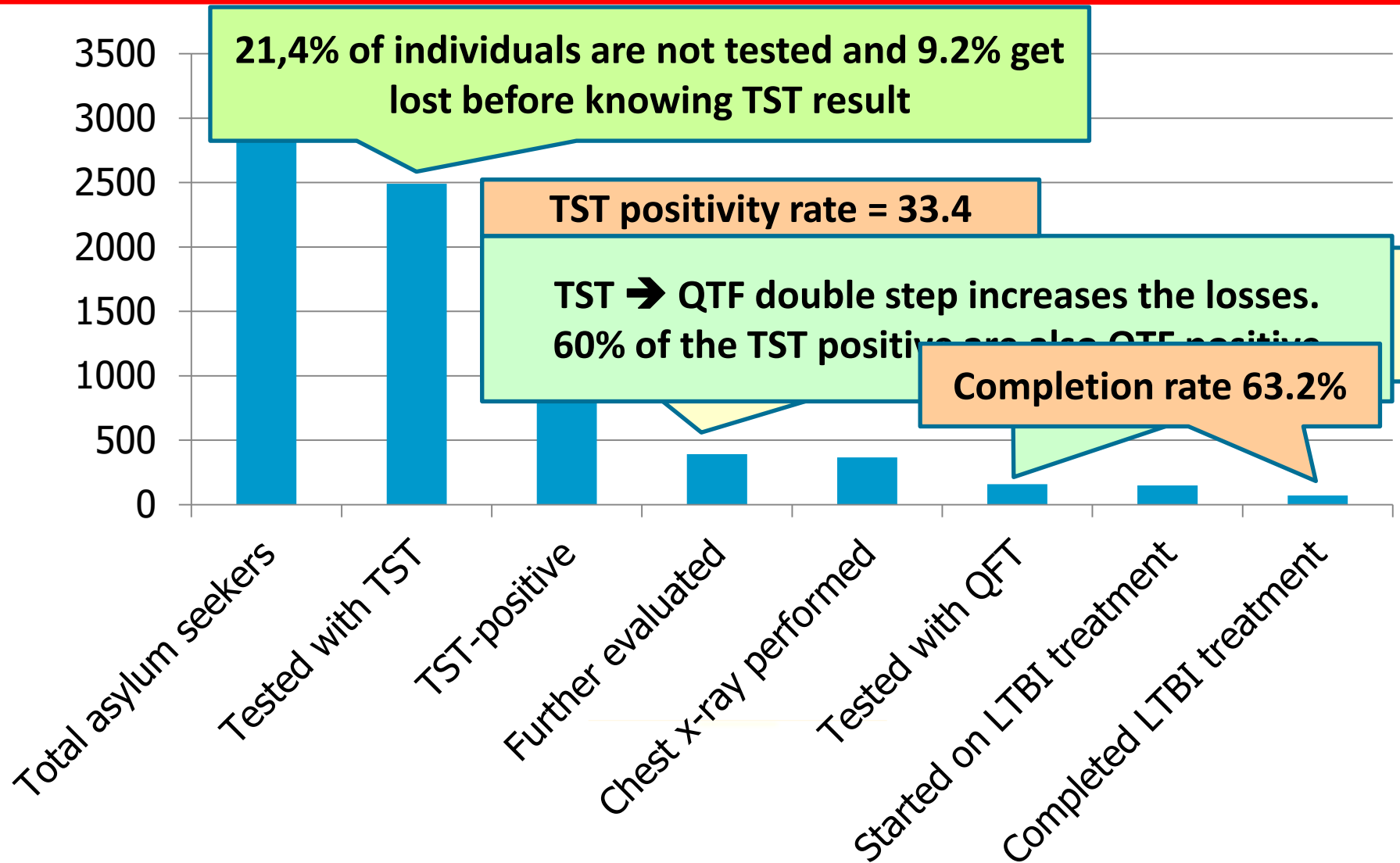
Time to treatment initiation (days) for 13 TB cases



Active TB case finding among asylum seekers in Brescia, 2015-2016



LTBI screening among asylum seekers in Brescia, 2015-2016



EARLY DETECTION AND INTEGRATED MANAGEMENT OF TUBERCULOSIS IN EUROPE: E-DETECT TB

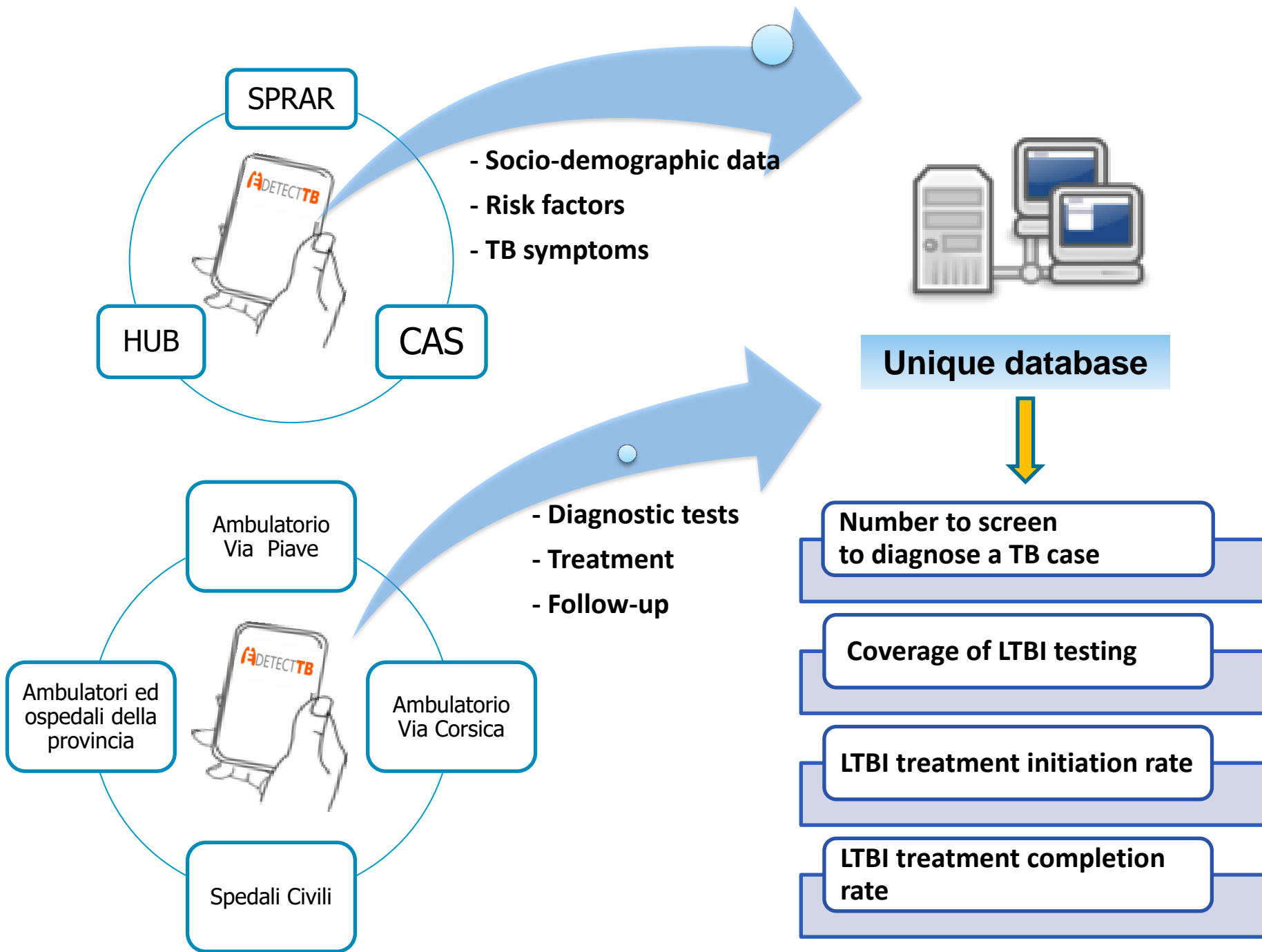
Work-package 5: To reduce the TB prevalence in asylum seekers at their first arrival on Italian coasts by early TB detection (active TB and LTBI)

Rationale

No M&E and R&R systems of screening activities among asylum seekers are currently in place

Objectives

- To develop and implement a **digital recording and reporting system on TB and LTBI screening activities among asylum seekers** in the Province of Brescia:
 - Indicators of performance
 - Indicators of impact
- To identify the **strengths and weaknesses** of the process





Questionnaire



Smear



GeneXpert
X-Ray
Culture



Treatment
Follow-up

LTBI

A user-friendly device

Privacy protection and correct patient identification are pivotal



I have received information regarding the objectives, advantages and risks of the TB Programme. I give my consent to share my personal and clinical data.

Name and Surname:

SIGNATURE



Scan the CARA barcode



Take a photo of the CARA card



← TB Symptoms screening

Cough for more than
2 weeks ?



Fever for more than
7 days ?



Haemoptysis



Night sweats

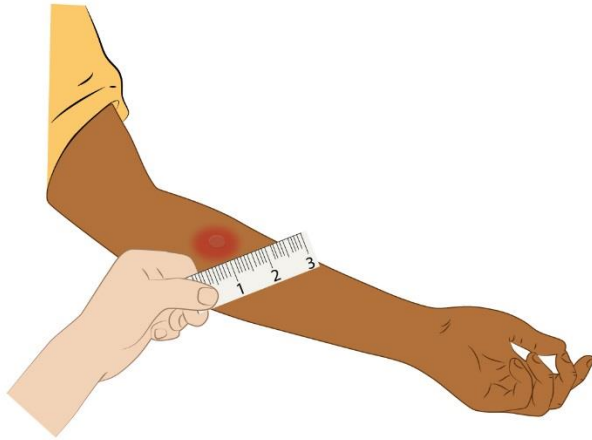


Weight loss



**Symptom-based
screening
is the first step**





Yes

No

Data administration PPD _____

Data reading _____

no induration

induration of 5 mm or more _____mm

induration of 10mm or more _____mm

induration of 15mm or more _____mm

**TST is offered to all
asylum seekers**





Yes

No

Date:

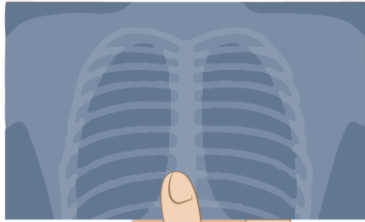
Positive

Negative

Other

**A two-step approach
for LTBI testing is
adopted: only TST-
positive subjects are
tested with QFT**





Yes

No

Date:

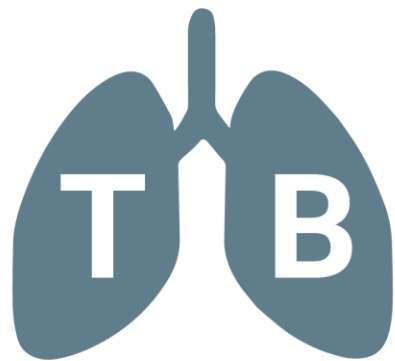
Positive

Negative

Other

Chest x-ray is performed on all TST/IGRA-positive subjects to rule out active TB even if no symptoms are present





Eligible for LTBI treatment?

Yes

No

Finally, a decision can be done on eligibility to LTBI treatment





Yes

No



Starting
treatment data

Treatment regimen: _____

(drop down menu with the different regimens + other)

NOTES _____

**Monthly visits are
performed during LTBI
treatment until
completion**



Acknowledgements

Dr. Issa El Hamad & team,

*Ambulatorio Migranti U.O. di Medicina Transculturale e
Malattie a Trasmissione Sessuale*

Dr. Rolando Moioli & team,

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Dr. Agostina Pontarelli & Dr Valentina Marchese,

Dpt. Infectious and Tropical Diseases, University of
Brescia

grazie

