

Herzlich Willkommen zum 28. Tuberkulose-Symposium in Magglingen

Bienvenue au 28e Symposium Tuberculose de Macolin

Mit Unterstützung von / Avec le soutien de

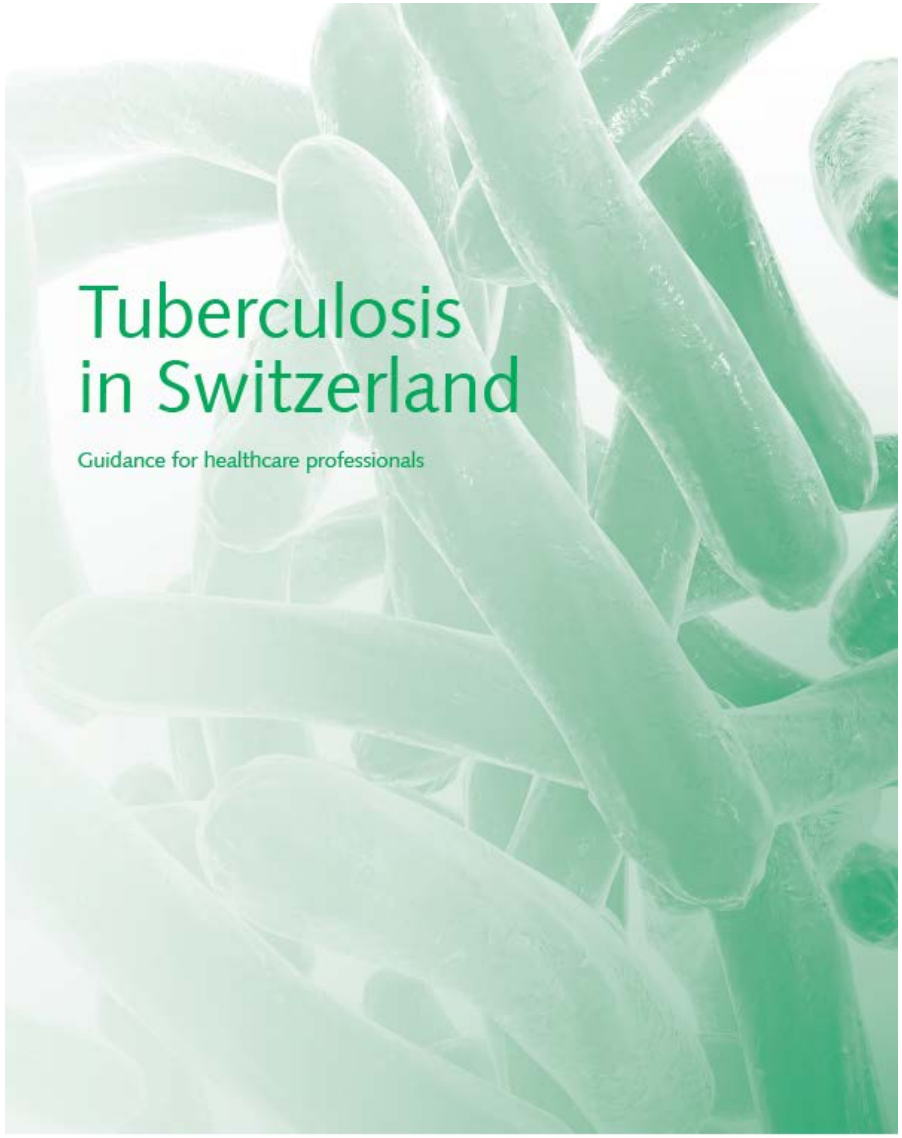
Cepheid
A better way.

Oxford Immunotec

QIAGEN

LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Kompetenzzentrum Tuberkulose
Centre de compétence tuberculose



Ausgabe 2019
Edition 2019

www.tbinfo.ch

Willkommensgruss

Mot de bienvenue

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Swiss Centre for International Health

Bundesamt für Gesundheit (Office Fédéral de Santé Publique)

TB Delay Studie in der Schweiz

Resultate einer Studie unter Erwachsenen mit Lungentuberkulose: verschiedene Verzögerungen und deren Determinanten

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Übersicht

- TB in der Schweiz
- Ziele der TB Delay Studie
- Methodik, Ansätze
- Die verschiedenen Arten von “delay”
- Rekrutierung der Fälle
- Beschreibung der Stichprobe
- “Help seeking” Verhalten und die verschiedenen Verzögerungen (delay)
- Prädiktoren von delay
- Ergebnisse der qualitativen Studien
- Schlussfolgerungen

Tuberkulose in der Schweiz

Anzahl Fälle pro Jahr zwischen ca. 450 und 600 während der letzten zehn Jahre

~ 75% im Ausland geboren
~ 35% unter Flüchtlingen

Anzahl Todesfälle rund 20 pro Jahr

1947: 3055
1957: 869
2008: 20

Zum Vergleich: in Belarus ca. 130;
in Papua New Guinea ca. 3800

Ziele

- Charakteristika von TB-Patienten in der Schweiz
- Erkennen vom:
  - “help seeking behaviour”: Beschreibung des Weges vom Beginn der Symptome bis zum Beginn der TB-Behandlung
  - Patientendelay (Zeitspanne vom Beginn der Symptome bis zur Erstkonsultation) und die Determinanten (Prädiktoren) dazu
  - Der “health system delay” (“provider delay”), d.h. Zeitspanne von der Erstkonsultation bis zum Beginn der TB-Behandlung und die Determinanten (Prädiktoren) dazu.

Methodik

1. Quantitativer Ansatz: Patientenbefragungen durch Lungenligen.
2. Qualitativer Ansatz: Gespräche mit elf TB-Patienten und acht Vertretern des Gesundheitssektors
3. Datenanalyse
    1. Beschreibend (Häufigkeiten)
    2. Analytisch (Assoziationen, Regressionen): Beschreibung von Determinanten von Verzögerungen (determinants of delay).

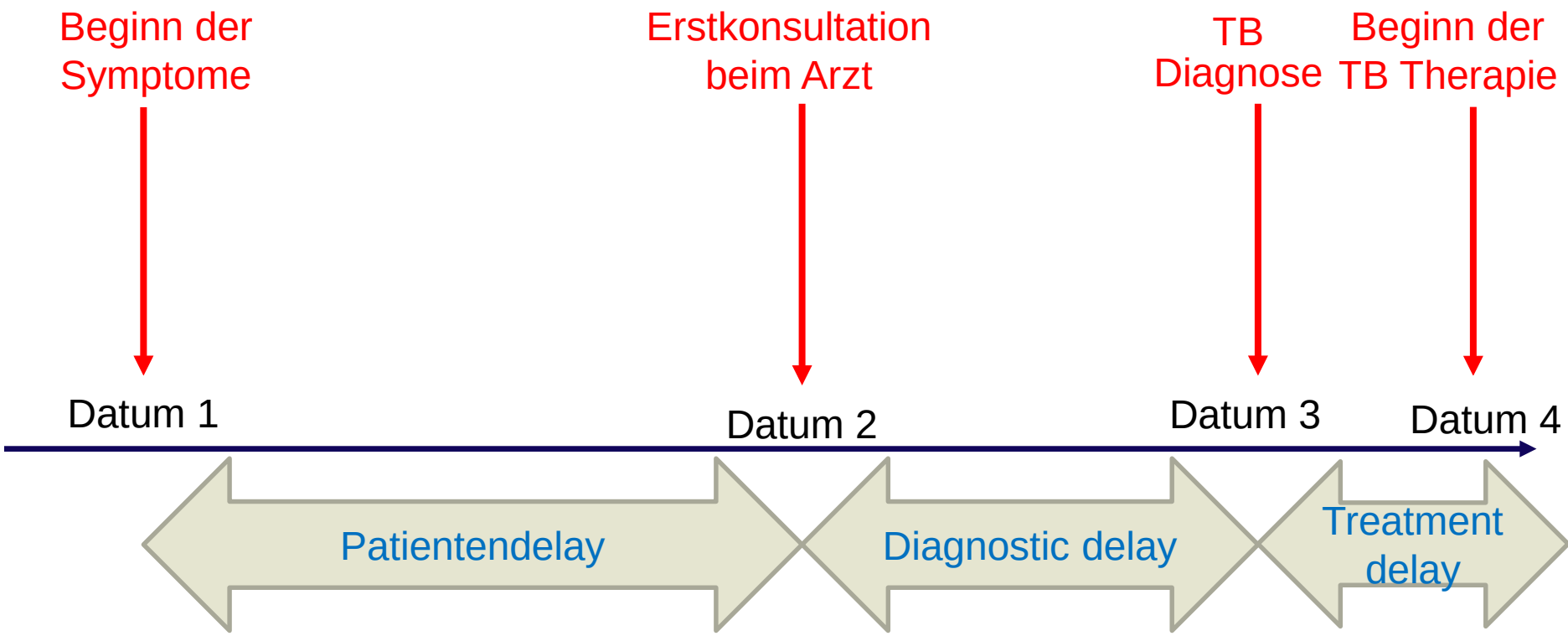
       Regressionen von Quantilen (P50, P75)

Studienansatz

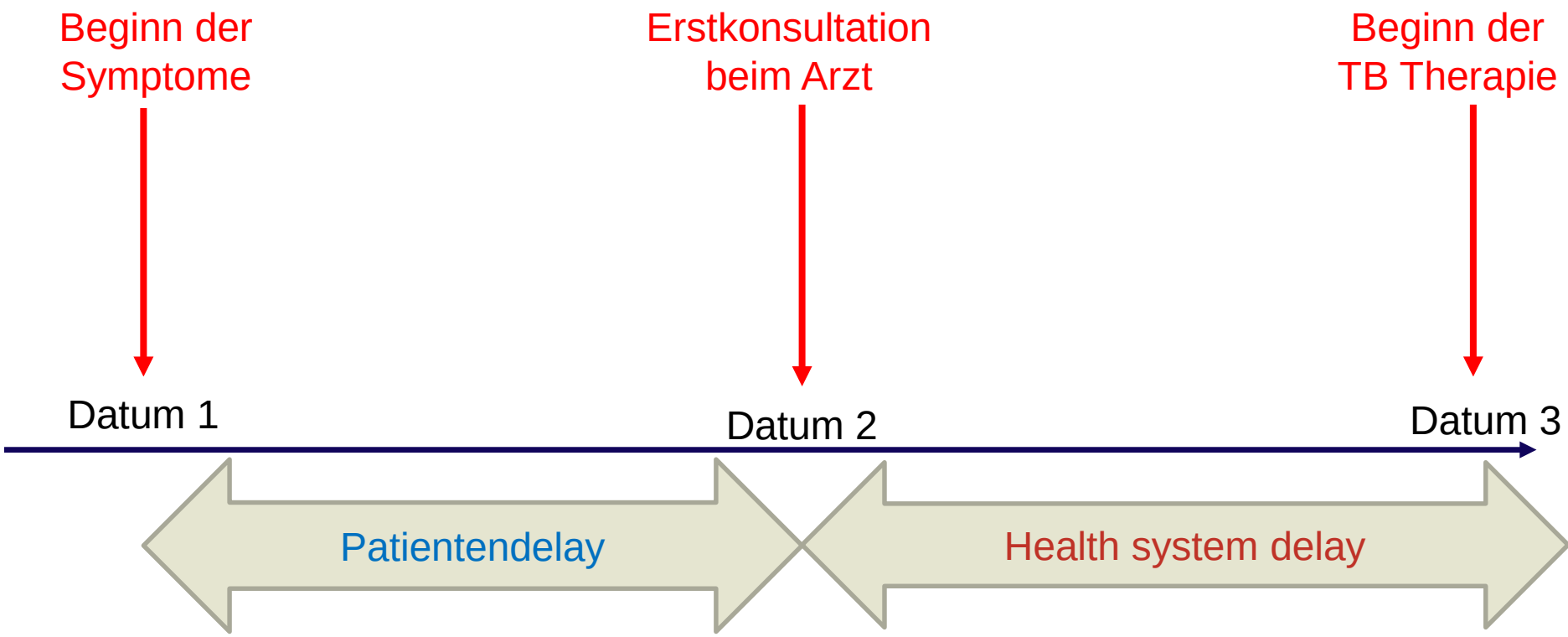
- Ursprünglicher Plan: Telefonbefragung
- Befragung von Patienten durch Angestellte der Lungenligen. Nur Patienten mit Lungentuberkulose und Mindestalter von 18 Jahren.

Fokussierung auf die verschiedenen Schritte im "help seeking process" and auf Daten (wann geschah was?)

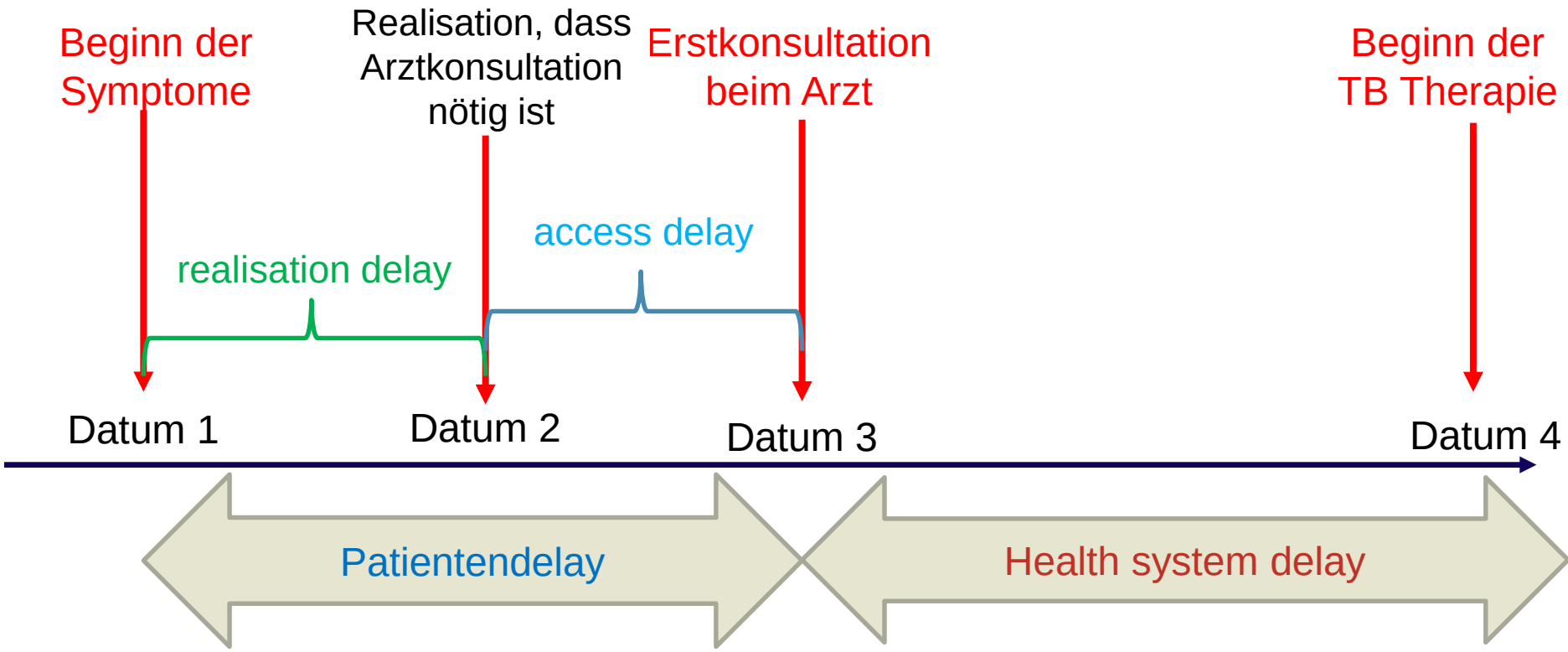
Die verschiedenen Zeitspannen (delays)



Die verschiedenen Zeitspannen (delays)



Die verschiedenen Zeitspannen (delays)



Rekrutierung der Fälle

- Von den Kantonen AG, BL, SO, ZH, GE, VD (fünf Lungenligen)
- Patienten, die von diesen fünf Lungenligen im Zeitraum vom 1. Nov. 2014 bis 31. Mai 2016 registriert wurden.
- In diesen sechs Kantonen leben rund 53% der TB Fälle der Schweiz.
- Antwortquote: 64% (162/252).

Registriert und befragt pro Kanton

	Registriert	Befragt	Nicht befragt
AG	27	25 (92.6)	2 (7.4)
BL	8	6 (75.0)	2 (25.0)
SO	8	7 (87.5)	1 (12.5)
ZH	90	51 (56.7)	39 (43.3)
GE	59	33 (55.9)	26 (44.1)
VD	60	40 (66.7)	20 (33.3)
Total	252	162 (64.3)	90 (35.7)

Nicht befragt: verweigert, zu alt, zu schwach, verstorben.

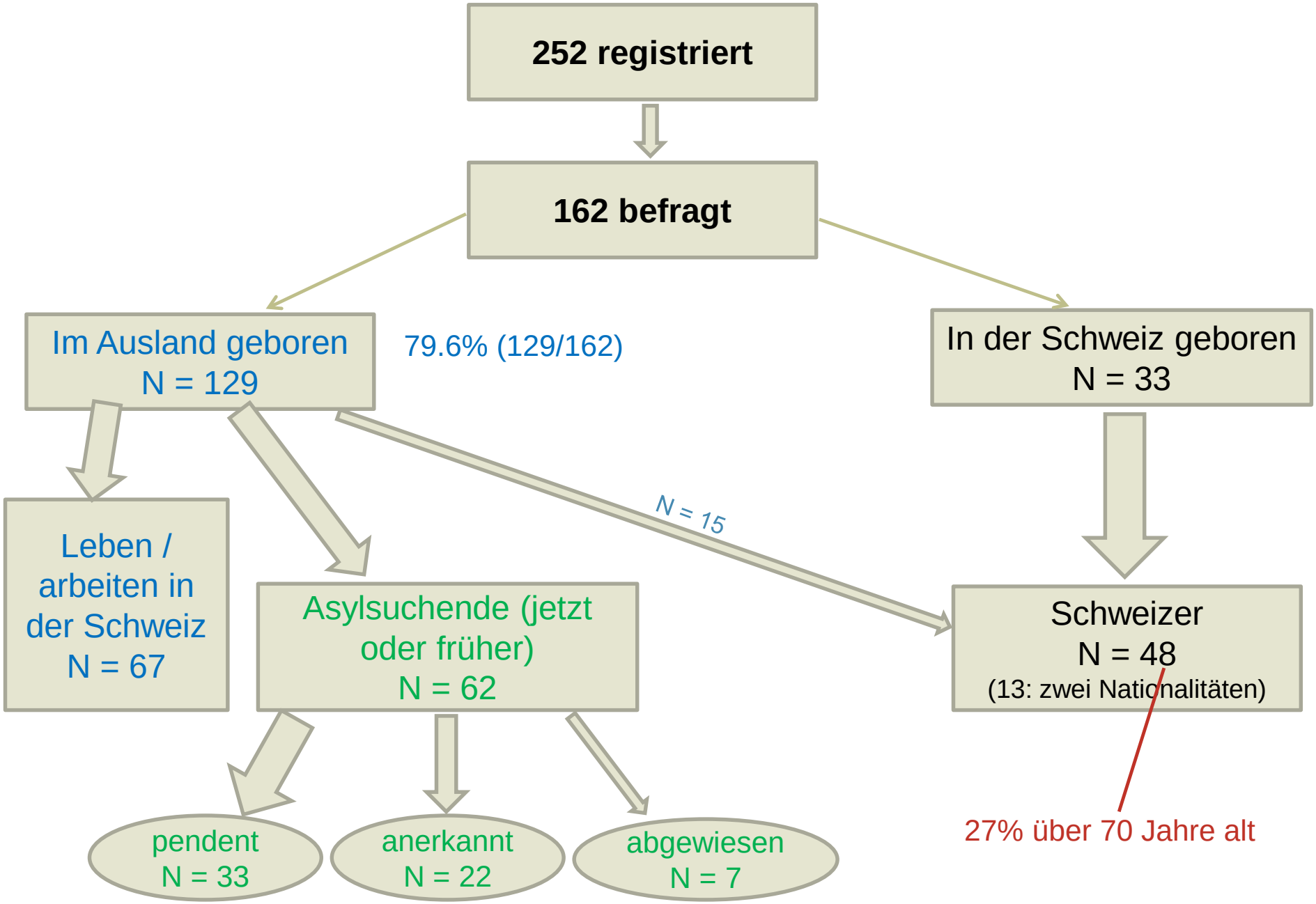
Beschreibung unserer Stichprobe

Demographische Indikatoren		
GESCHLECHT	N	%
Männlich	107	66.0%
Weiblich	55	34.0%
ALTER		
Median: 35 Jahre		
18-29 Jahre	56	34.6%
30-44 Jahre	57	35.2%
45-59 Jahre	21	13.0%
60-74 Jahre	16	9.9%
75-90 Jahre	12	7.4%
ANZAHL JAHRE AUSBILDUNG		
Bis 5 Jahre	29	17.9%
6 bis 9 Jahre	56	34.6%
Mind. 10 Jahre	74	45.7%

In der Schweiz:
62.4% männlich
37.6% weiblich

CH, 2015: 34 Jahre

Nicht-Teilnehmer: 41 Jahre
(p = 0.02)


252 registriert
162 befragt
Im Ausland geboren
N = 129
79.6% (129/162)
In der Schweiz geboren
N = 33
Leben / arbeiten in der Schweiz
N = 67
Asylsuchende (jetzt oder früher)
N = 62
N = 15
Schweizer
N = 48
(13: zwei Nationalitäten)
pendent
N = 33
anerkannt
N = 22
abgewiesen
N = 7
27% über 70 Jahre alt

Wissensstand und Erfahrung zu TB

Wissensstand zum Zeitpunkt, als “help seeking” begann		
	Ja	*%*
TB ist ansteckend	122	**75.3%**
TB kann behandelt werden	121	**74.7%**
TB kann zum Tod führen	115	**71.0%**
Kannte Leute mit TB	78	**48.1%**
Kannte Leute, die an TB starben	27	**16.7%**

Zwischen den 48 Schweizern und den anderen 114 Befragten gab es hinsichtlich dieser Fragen keine signifikanten Unterschiede (alle p-Werte > 0.1)

“Help seeking” Verhalten: erste “Tätigkeit”

- Nur 8% hatten zuerst medizinische Hilfe im Ausland aufgesucht
- Ort der Erstkonsultation in der Schweiz:

Ort	*N*	*%*
Hausarzt	74	45.7%
Spital	42	25.9%
Permanence/"Drop-in"	14	8.6%
Praxis im Empfangszentrum	10	6.1%
Pneumologe / Kinderarzt	4	2.5%
Anderes	18	11.1%

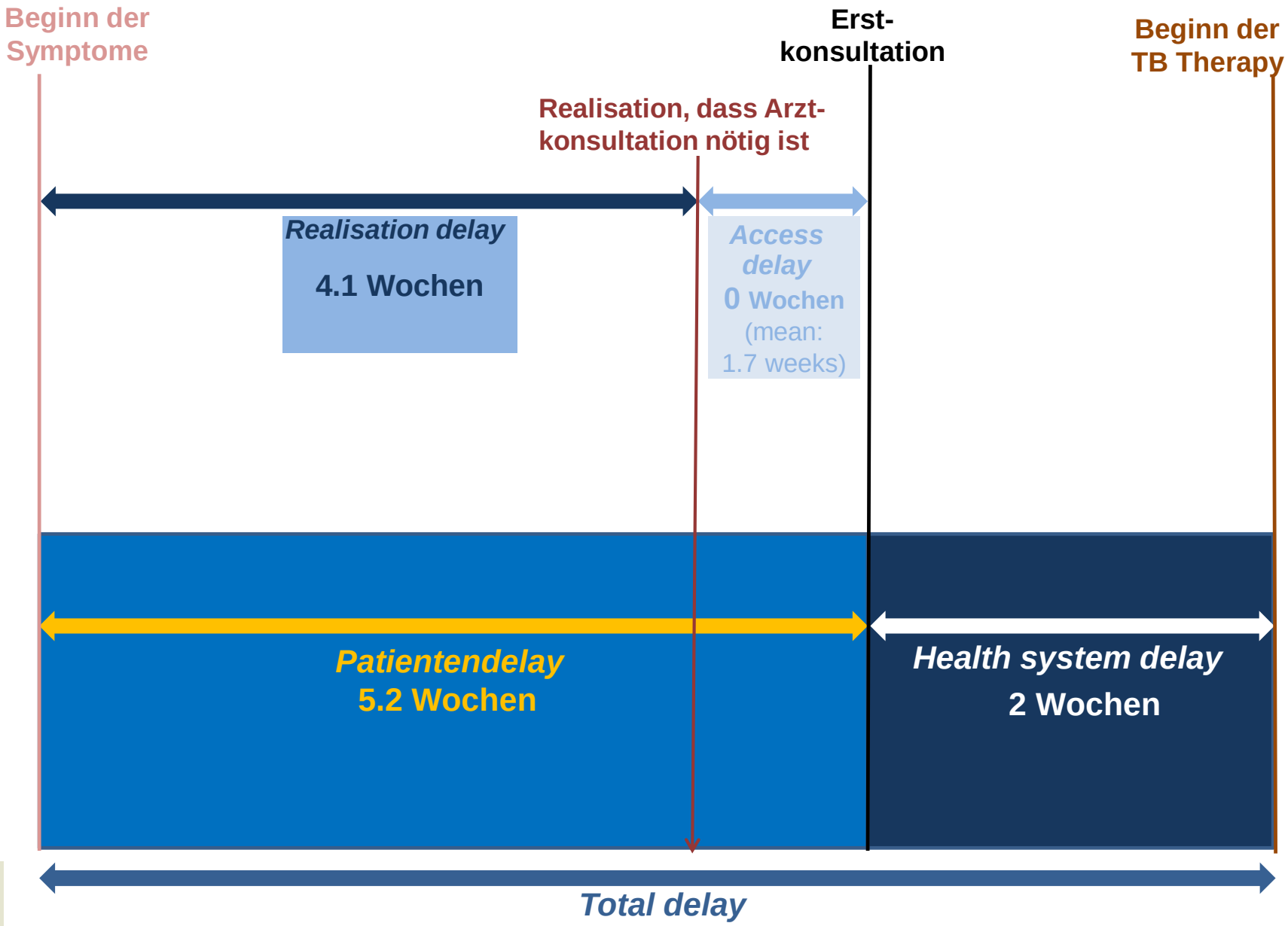
9 Flüchtlinge, 1 Gefangener

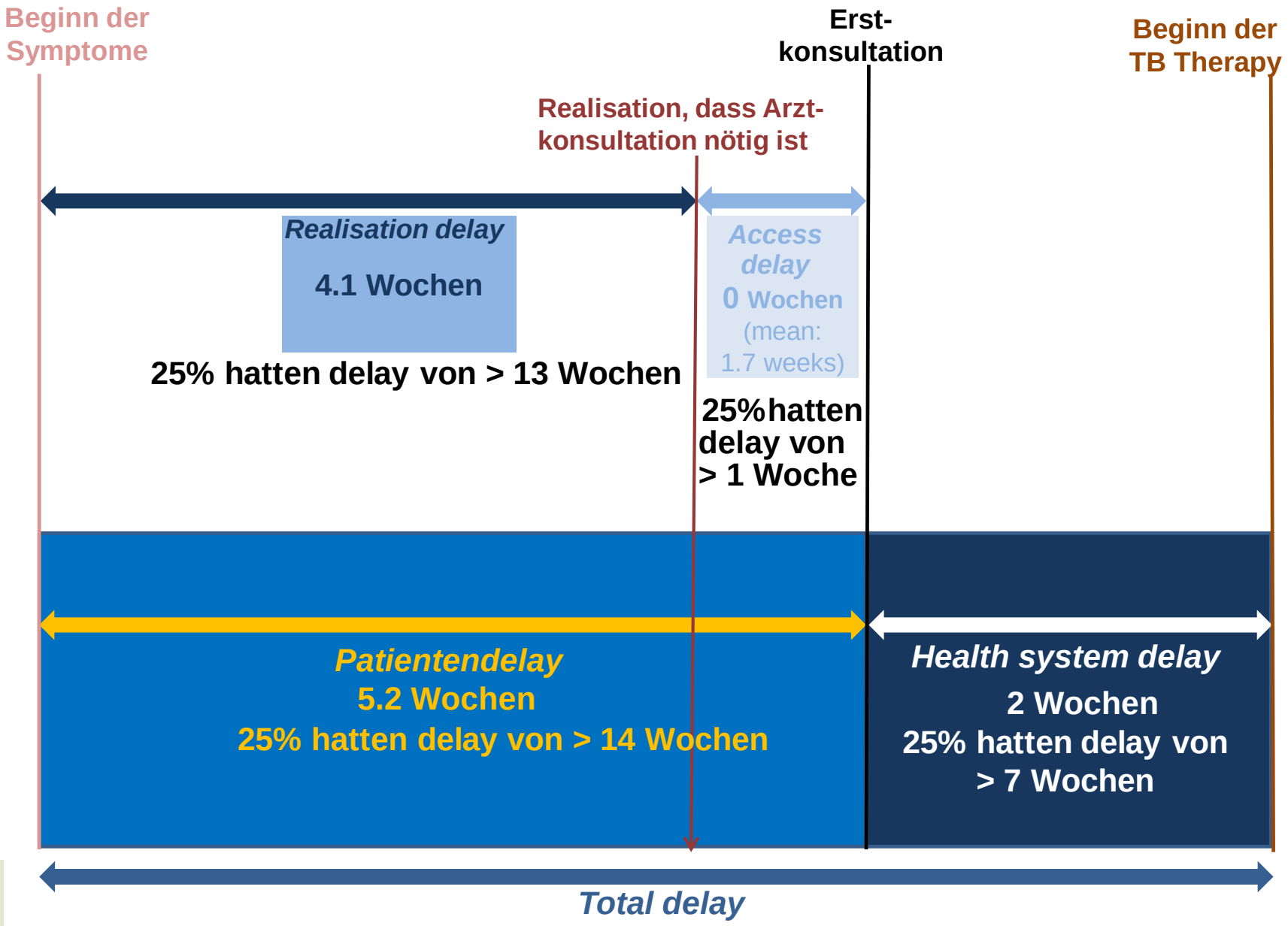
Andere Merkmale des “help seeking”

Anzahl konsultierter Ärzte, von Erstkonsultation bis Beginn der TB-Therapie

Anzahl konsultierter Ärzte	*N*	*%*
1	19	11.7%
2	56	34.6%
3 oder 4	63	38.9%
5 oder 6	12	7.4%
Mehr als 6	3	1.9%
Unklar	9	5.6%

Resultate zu den «delays» (in Wochen, median)


Beginn der Symptome
Erst-konsultation
Beginn der TB Therapy
Realisation, dass Arzt-konsultation nötig ist
Realisation delay
4.1 Wochen
Access delay
0 Wochen
(mean: 1.7 weeks)
Patientendelay
5.2 Wochen
Health system delay
2 Wochen
Total delay


Beginn der Symptome
Erst-konsultation
Beginn der TB Therapy
Realisation, dass Arzt-konsultation nötig ist
Realisation delay
4.1 Wochen
25% hatten delay von > 13 Wochen
Access delay
0 Wochen
(mean: 1.7 weeks)
25% hatten delay von > 1 Woche
Patientendelay
5.2 Wochen
25% hatten delay von > 14 Wochen
Health system delay
2 Wochen
25% hatten delay von > 7 Wochen
Total delay

Determinanten von Verzögerungen: Patientendelay

keine statistisch signifikante Resultate.

Determinanten von Verzögerungen: health system delay

Prädiktor	*Effekt (95% CI) (in Wochen)*	*P-Wert*
Health system delay (n = 154)		
A) Prädiktoren für einen langen delay		
Fieber	1,6 (0,5 to 2,6)	0,004
Erstkonsultation bei einem Haus- oder Kinderarzt	1,0 (0,1 to 1,9)	0,024
3 bis 4 Ärzte gesehen bis Beginn der TB-Therapie (statt nur 1 or 2)	2,9 (0,7 to 5,1)	0,01
Im VD (verglichen mit AG)	1,9 (-0,004 to 3,8)	0,051
In ZH (verglichen mit AG)	1,7 (-0,2 to 3,7)	0,083
Brustschmerzen	1,8 (-0,2 to 3,7)	0,071
Komorbidität COPD	3,7 (-0,7 to 8,0)	0,098
B) Prädiktoren für einen kurzen delay		
X-ray bei Erstkonsultation	-2,9 (-4,8 to -0,9)	0,004
Patient männlich	-2,6 (-5,4 to 0,1)	0,060

Determinanten von Verzögerungen: health system delay

Prädiktor	*Effekt (95% CI) (in Wochen)*	*P-Wert*
Health system delay (n = 154)		
A) Prädiktoren für einen langen delay		
Fieber	**1,6 (0,5 to 2,6)**	**0,004**

Sogar Patienten, die unter Fieber *und* Schwitzen/Nachtschwitzen *und* Gewichtsverlust litten (n = 45), hatten einen langen health system delay (p = 0.003)!

Ein paar Befunde von den qualitativen Studien

Ein junger Mann aus dem Tibet (lebt mit einer Schweizer Familie)

Wann?	Durch wen?	Diagn.?	Rx	Wirkung
Mitte März ‘16	Anruf HA			3 Tage später Termin beim HA
«In März» (Brustschm., Fieber?)	HA	Stethoskop	Dafalgan	“Es ist wegen des Wetters” (Patient hatte X-ray erhofft)
5.4.2016	HA	Nichts (?)	Ibuprofen, Hustensyrup, Protonenpumpenhemmer	Keine Besserung Kein Sprachproblem
unklar	Caritas in Aarau	Patient bat um Rat		→ Zu Praxis in Aarau
unklar	Grosse Praxis in Aarau	Stethoskop, Blutuntersuch.	Dafalgan	Keine Besserung. Patient hatte seine frühere TB-Erkrankung erwähnt
23.4.2016	Grosse Praxis in Aarau	Rö’bild	Ciprofloxacin	«Geh ins Spital». Versprechen, das Spital würde anrufen, verpuffte
Ende Apr.	“Swiss Vater” rief Spital an	Spital erbat Dokumente von der Praxis. < 1 Woche später: Spital rief Patienten an. 2 Tage darauf ging Patient ins Spital für Bronchoskopie		
~ 30.4	Spital	Sputum, Blutunters. Bronchoskopie: TB!		**TB-Therapie beginnt (zu Hause) am 3. Mai**

Andere Ergebnisse von den 11 Patientengesprächen und den 8 Gesprächen mit Gesundheitsversorgern

Patienten

- Stigma nur ein geringes Problem
- Die Dienste der Lungenliegen werden geschätzt.
- DOT in Apotheken scheint gut zu funktionieren.

Hausärzte

- Einige haben die Gesinnung “Think TB!”, andere nicht.
- Einige HA seien schwarze Schafe (ein paar Ergebnisse der Patientengespräche deuten dies ebenfalls an).
- Was Migranten/Flüchtlinge betrifft: Mangelndes Bewusstsein und Klarheit über die bestehenden Übersetzerdienste (inkl. Finanzierung).
- Kommunikation zw. den Lungenligen und den Hausärzten könnte besser sein; sollte evtl formalisiert werden. Z.B. wenn bei einem Patienten TB diagnostiziert wurde, feedback an dessen Hausarzt geben (→ mehr “Think TB”).

Schlussfolgerungen

1) Patientendelay eher lange, health system delay eher kurz (Europa)

	Delay in Tagen (Median)	
	Patientendelay	Health system delay
Schweiz (diese Studie)	36.5	14
Italien (Pezotti et al 2015)	31	15
Frankreich (Tattevin et al 2012)	14	25
Spanien (Diez et al 2004)	22	NA
England (Sultan et al 2012)	29	34
England, Thames valley (Saldana et al 2013)	29	39
Norwegen (Farah et al 2006)	28	33

2) Kanton AG: sehr hohe Antwortquote, kurzer health system delay:

können wir (bzw. die anderen Lungenligen) ertwas lernen von AG?

3) Flüchtlinge: Kann die Versorgung organisatorisch und logistisch noch verbessert werden (z.B. Übersetzungsdienst)? Wie sieht dies mit dem neuen Ansatz aus?

»Gesundheitsversorgung für Asylsuchende in Asylzentren des Bundes

und in den Kollektivunterkünften der Kantone»

4) Wie kann die Zusammenarbeit zwischen den Lungenligen und den Ärzten (v.a. Hausärzten) optimiert werden?

5) Warum wurden Patienten, die unter Fieber und Schwitzen/Nachtschwitzen und Gewichtsverlust litten, nicht gleich als potentielle TB Fälle erkannt?

(sie hatten einen langen health system delay)


Merci beaucoup
Vielen Dank
Grazie mille
Cordial engraziament / Grazia fitg!

Tuberculose chez les personnes âgées

Journée de Maccolin 27.03.2019

Jesica Mazza-Stalder

LIGUE PULMONAIRE VAUDOISE

CHUV

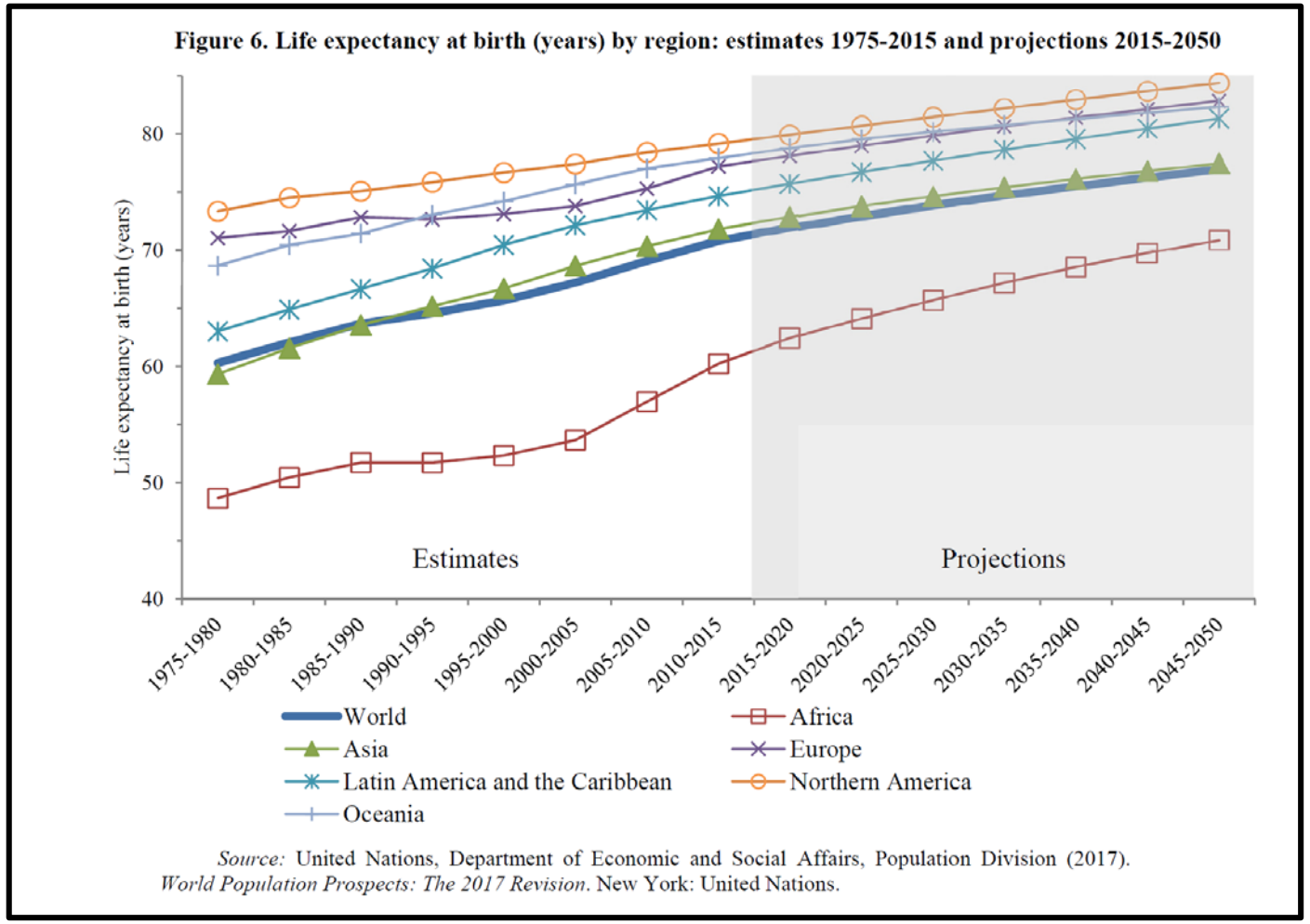
Policlinique Médicale Universitaire CH-Lausanne

canton de vaud

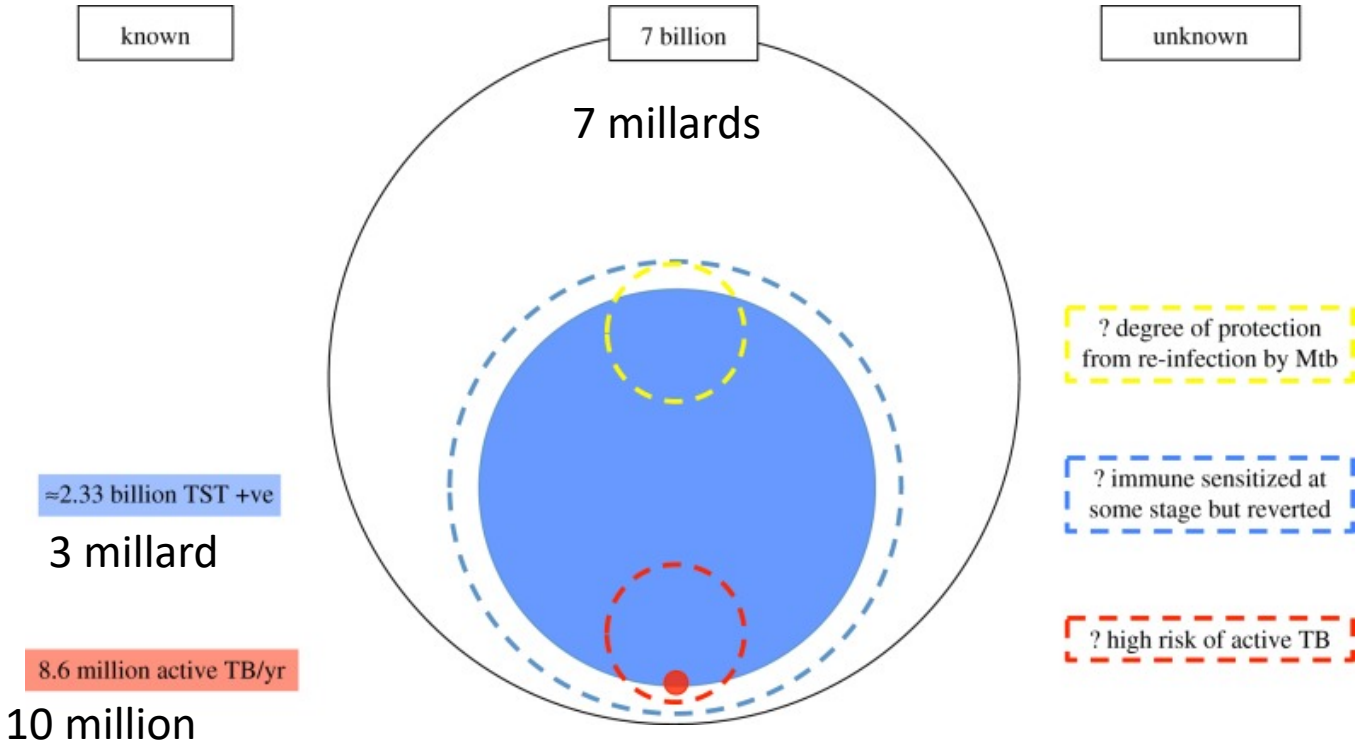
La tuberculose chez les personnes âgées

- Epidémiologie
- Réactivation versus infection (nosocomiale)
- Formes de présentation clinique
- Facteurs de Risque de réactivation et Comorbidités
- Traitement spécifique
- Intérêt du screening ou «active case finding»
- Conclusions

Population mondiale Esperance de vie et projections 2050



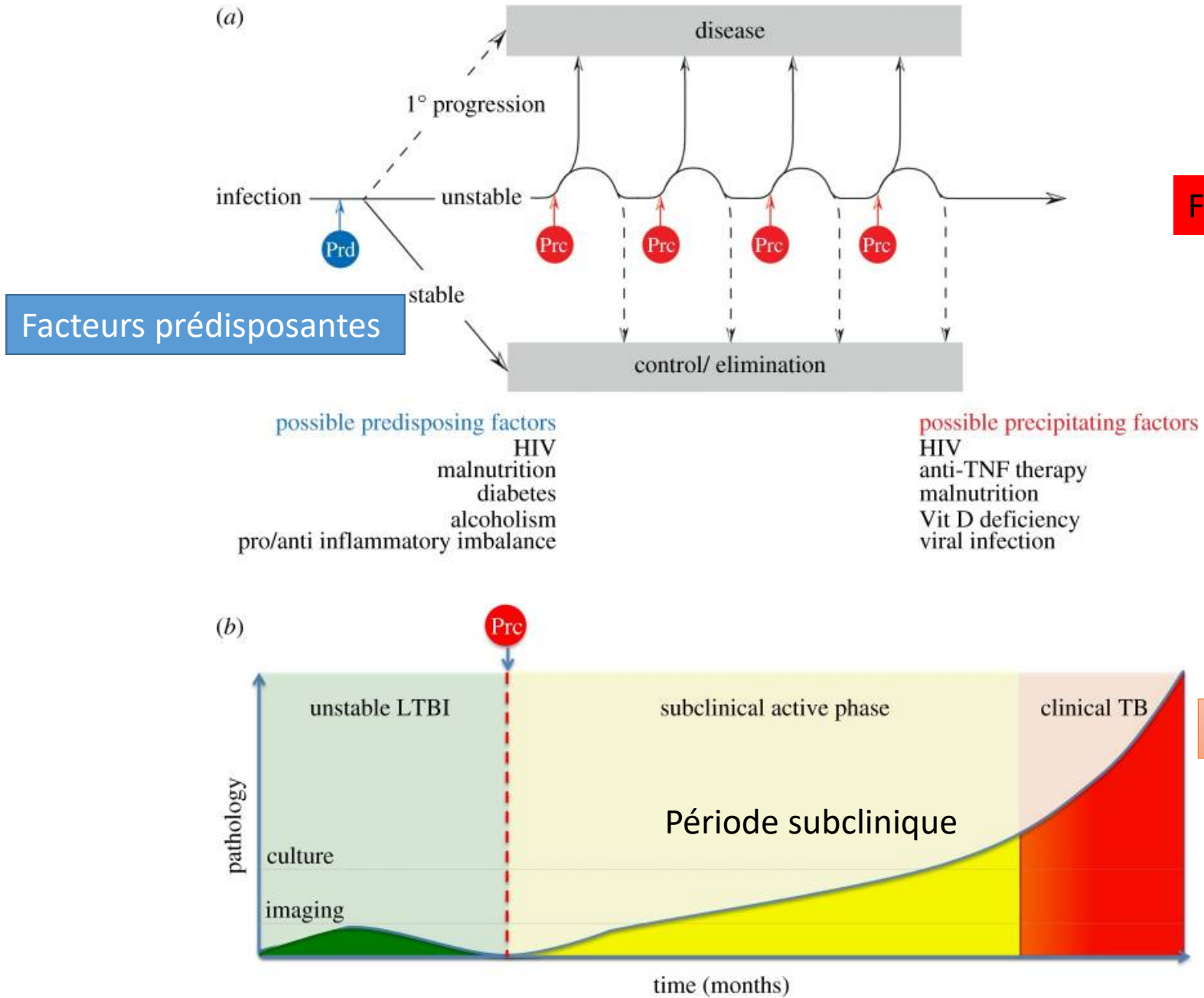
Réactivation ou infection par Transmission



Réactivation endogène le plus souvent chez la personne âgée
(90% Yoshikawa et al 1992)

Infection exogène dans des pays à faible endémie comme la Suisse c'est surtout en institution
(Maladie nosocomiale)

Esmail, Barry and Wilkinson 2014 rstb.royalsocietypublishing.org Phil.Trans.R.Soc.B 369:201304

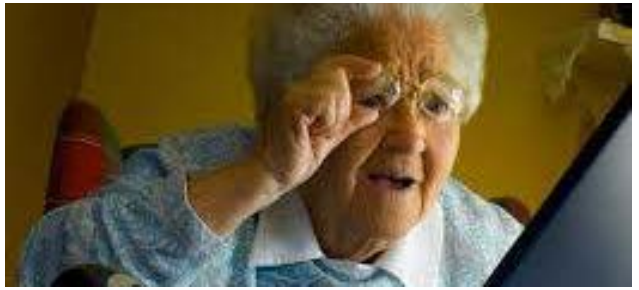


Facteurs prédisposantes

Facteurs précipitantes

Progression de la maladie

Epidémiologie



- USA (1985-1988) *Hans Rieder (Chest 1991)* reporté que 5,1% de cas de TB été déclaré et diagnostiqué au moment du décès (60% de ces cas chez le > de 65 ans)

- Plus TB-EP 18% TB miliaire ou péritonéal

- Tb non diagnostiqué chez la personne âgée plus de morbidité/ mortalité si pas détecté précocement et plus de risque de transmission

Epidémiologie

- Global Burden of Disease 2010: **57%** de tout les **décès** dues à la Tb arrivent chez les personnes **de >50 ans** plus de la moitié chez le **>65 ans**

- Israël une étude sur 11 ans de surveillance 4555 TB mortalité 9.9% (patients âgées >65 ans **70% of TB-related deaths**)

- Europe occidental et en Australasie aussi la plus part de décès arrivent chez les personnes agées

- Brésil la mortalité n'était pas lié à l'âge mais a une manque de diagnostique indépendamment de l'âge 34% de décès chez les personnes de >75 ans

Chez les **>75 ans** la Tb se voit **quadrupler** dans cette catégorie d'âge en **Chine**

14% de Tb en Chine arrive chez les adultes âgées, pareil Amériques, et en Inde

Global Burden Disease 2014
Shuldiner J et al 2014 IJTLD
Simoni Pimena de Oliveira 2019 IJID
Xia et al Tb nation wide prevalence in China 2010

Epidémiologie

- En Amérique latine 2,3% de personnes âgées entre 50 et 59 et 3,4% chez les >60 ans aurait eu un diagnostique de TB (Platino) TB rates deux fois plus élevé que chez le 40-49 ans. (Platino study)
- Similaire aux USA avec incidence plus élevé et plus de mortalité observé chez le plus de 65 ans (Pratt et al)

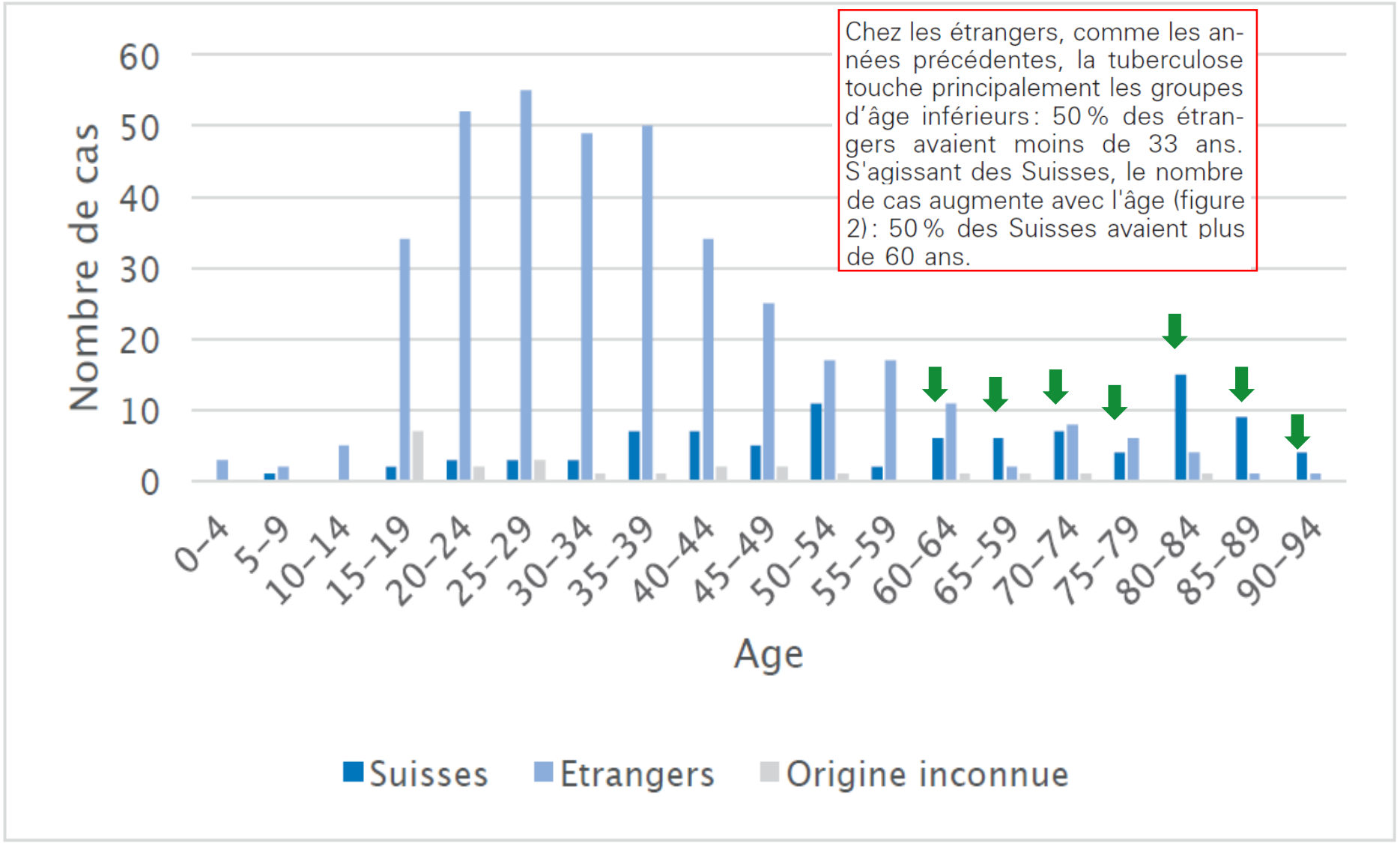
- Afrique du SUD (Soweto) chez les personnes âgées 5.8% des tous les adultes avec une TB (50% EPTB 37% EP seul 13% les deux le reste pulmonaire seul)

- Tanzanie étude national a montré un shift dans prévalence de Tb chez les HIV jeûnes à non-HIV plus âgées (plus de 45 ans) (2012)

Panamerican Health organisation Tb *in Americas 2011 WHO /****Menezes et al ERJ 2007*** *Platino study /* ***Pratt*** *et al 2011 Journal of American Geriatrics/* ***Karstaedt et Bolhaar 2014 IJTLD/ Law et al Tb*** *prevalence surveys WHO 2012*

Figure 2 :

tuberculose en Suisse en 2014, répartition par tranche d'âge et selon l'origine



Canton de Vaud

VD période 2010/2015

- 375 patients
- 65 p ont >65 ans 17% de cas de tous le cas de TB : 56 tt accompli ou guérison 9 **DCD**
- 3.5% mortalité global (10 suisses) la plus part chez de personnes âgés (9/11) 13% mortalité chez le >65 ans
- 6 due à Tb l'autre et 5 au comorbidités associés + TB

Immunosuppression, BPCO, Cancer, maladies CV

Patient décédés avant le diagnostique

2 patients suisses âgée de 85 ans ont été diagnostiqué seulement à l'autopsie

Les deux patients auront transmis la Tb à deux soignants

La personne âgée est le plus souvent



- Multiples comorbidités
- Consultent tardivement isolement difficulté au déplacement
- Les symptômes sont confondus avec des Sy plus lié à la vieillesse
- Troubles cognitives moins facile de décrire les symptômes
- Transmissions au sein des EMS connu depuis long date (USA)



Ann Intern Medicine Stead et al 1981
NEJM Stead et al 1985 (Arkansas)

Formes de présentation clinique

Formes de présentation atypiques

- Moins de nodules, moins de masses moins de cavitation
- Souvent EP-TB
- Méningite
- Tb rénal
- Spondylodiscite TB ou articulaire
- Symptômes pris comme lié à l'âge et investigué tardivement
- Anémie, hypo-albuminémia, plus perturbation de test hépatiques

Vulnérabilité

- Majoration de décès
- Majoration de DALY (disability adjust life years)
- Comorbidité augmenté
- Difficulté en diagnostique car moins de symptômes classiques fièvre, toux, hémoptysies

Pratt et al 2011 Journal of American Geriatrics
Yoshikawa 1992 Journal of medical Geraitrics



Facteurs de Risque x réactiver une TB

- Plus de Susceptibilité aux infections respiratoires
- Altération de l'immunité inné et adaptative
- Plus de risque d'infection tout court
- Formes sans symptômes classiques
- Formes EP assez fréquentes

Facteurs de Risque

- L'utilisation de stéroïdes inhalées
  > 500 ug de fluticasone (inutiles dans la BPCO) est un facteur de risque pour réactiver une TB (Shu et al)
- Le diabète mal contrôlé augmente le risque de Tb de **3 X** chez le population âgée
- Une étude montre un score de prédiction de mortalité > chez le patient avec **TB-DM** âgée
- La prednisone oral **(7,5 mg ou plus)** souvent utilisé pour tt des affections rhumatismales
- TT Anti-TNF (FR élevé)

Nguyen BMC 2019

Facteurs de Risque

Table 1 Risk factors for TB activation

Risk factor	TB risk[a]	Reference(s)	WHO's recommendation for screening and treatment for LTBI[41]	
			Country A[b]	Country B[c]
High-risk factors				
HIV/AIDS	10–100	Landry *et al.*,[4] Hourburgh *et al.*[9] and WHO[14]	Required	Required
Close contacts	15	Landry *et al.*[4] and Sutherland *et al.*[15]	Required	Required for close contacts (<five years old)
Organ-transplantation recipients	20–70	Aguado *et al.*[16] and Sakhuja *et al.*[17]	Required	Not mentioned
Chronic renal failure requiring dialysis	6.9–52.5	Andrew *et al.*,[18] Lundin *et al.*,[19] Belcon *et al.*[20] and Hussein *et al.*[21]	Required	Not mentioned
TNF-alpha blockers	1.6–25.1	Solovic *et al.*[22]	Required	Not mentioned
Silicosis	2.8	Cowie *et al.*[23]	Required	Not mentioned
Moderate-risk factors				
Fibronodular disease on chest x-ray	6–19	Grzybowski *et al.*[24]	Not mentioned	Not mentioned
Immigrants from high-TB-prevalence countries	2.9–5.3	Baussano *et al.*[25]	Options to be considered	Not mentioned
Health-care workers	2.55	Chu *et al.*[26]	Options to be considered	Not mentioned
Prisoners, homeless persons, illicit drug users	–	–	Options to be considered	Not mentioned
Low-risk factors				
Diabetes mellitus	1.6–7.83	Harries *et al.*,[27] Dobler *et al.*,[28] Jeon *et al.*,[29] Boucot *et al.*,[30] Kim *et al.*[31] and Baker *et al.*[32]	Not recommended	Not mentioned
Smoking	2–3.4	Altet *et al.*,[33] Slama *et al.*[34] and Maurya *et al.*[35]	Not recommended	Not mentioned
Use of corticosteroids	2.8–7.7	Jick *et al.*[36]	Not recommended	Not mentioned
Underweight	2–3	Palmer *et al.*[37] and Comstock *et al.*[38]	Not recommended	Not mentioned

[a] Relative risk of TB compared to the general population.
[b] In high- and upper-middle-income countries with an estimated TB incidence less than 100/100,000 population.
[c] For resource-limited countries and other middle-income countries that do not belong to country A.

Ai et al Emerging Infectious Diseases 2016

BPCO et TB

Patient de 77 ans BPCO hospitalisé aux SI : Origine espagnol, en Suisse depuis 50 ans. Diabétique, sous CSI inhalées et Systémiques.

Décompensation BPCO et Foyer bilatérale de condensations bilatérales sous VNI en raison de insuffisance respiratoire.

Dyspnée et toux depuis 2 ans.

Perte pondérale d'environ 12-15 kg sur ces 2 ans

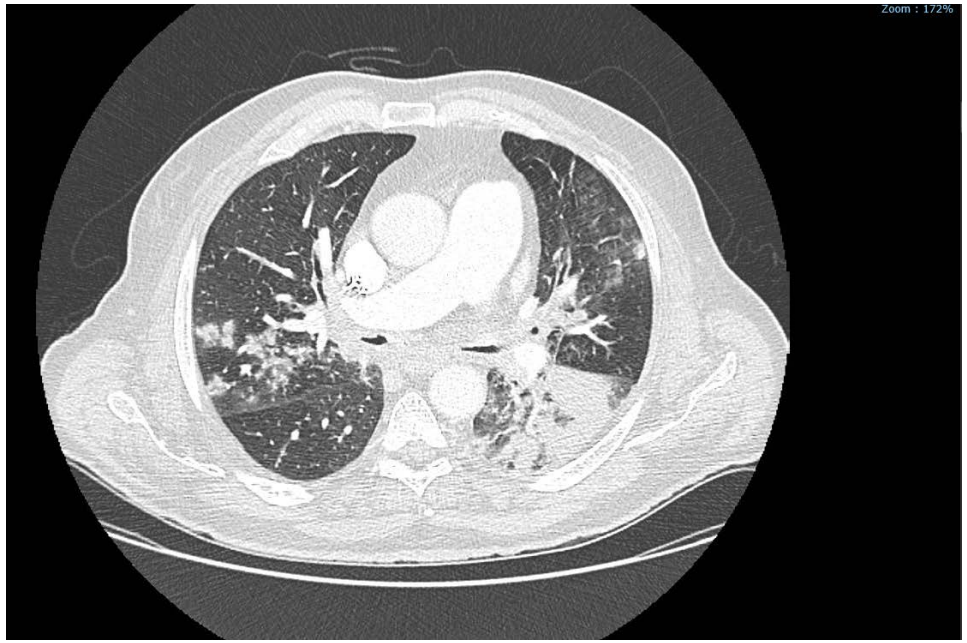
Sudations nocturnes présentes. Pas d'hémoptysie

Recherche de BAAR qui reviennent ++ PCR+ mtbc Rpo B négative

Enquête d'entourage en cours

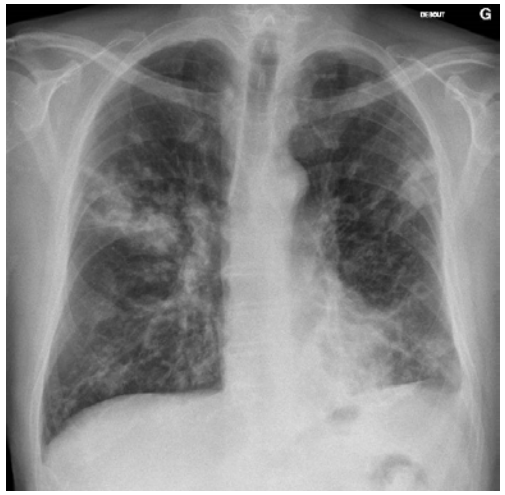
15 cas y/c de patients

9 cas non hospitalisée enquête en cours



BPCO +Bronchectasies + TB

Patient de 76 ans **BPCO** et **asthme bronchique** et Bronchectasies origine Suisse hospitalisé pour une Bronchopneumonie en décembre 2018 sous CSI inhalées (Budesonide 400 2 inh 2 x jour) sortie sous tt de Augmentin



Le patient toussait toujours perte de 7 kilos de poids. Bronchoscopie et Recherche de **BAAR** qui reviennent ++ PCR+ mtbc Rpo B néG Enquête d'entourage en cours : 2 petits enfants de 6 et 10 ans Mantoux et IGRA pos sous INH. Le patient évolue bien sous tt classique avec guérison

6 mois après



BPCO et Risque de Tb

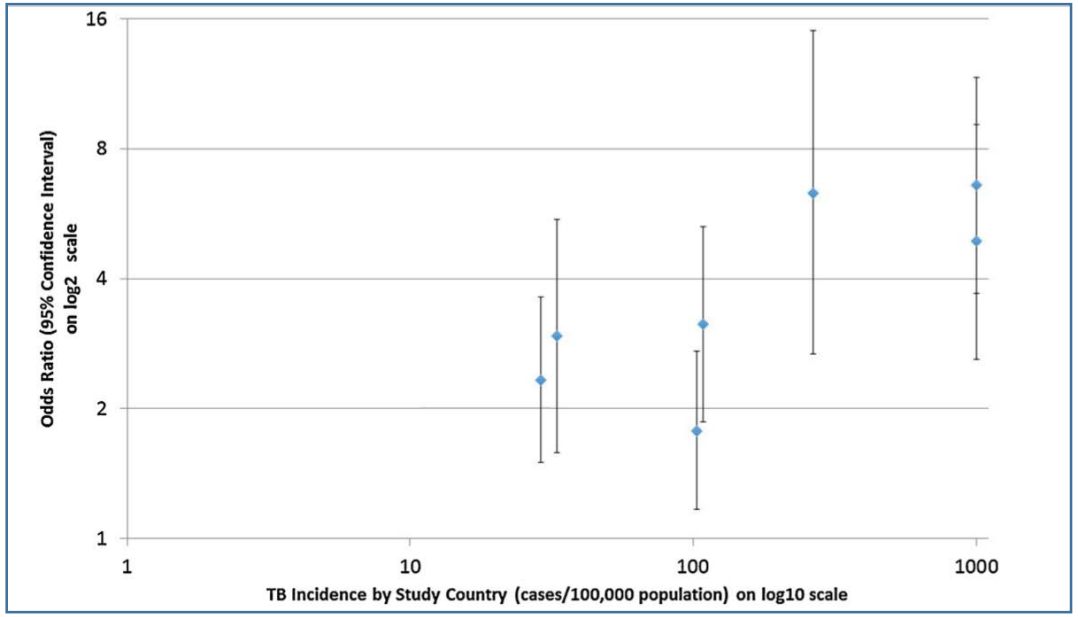
- Les deux affectent le poumon
- Facteurs de risque communs
- Status socioéconomique (tabac + TB)
- Consommation de tabac
- Altération de défenses immunitaires
- Bas BMI, altération de clearance mucociliaire, colonisation a d'autres bactéries, utilisation de stéroïdes systémiques ou inhalées

- 115000 patients BPCO
- Risque plus important de développer une TB dans les années qui suit comparé à la population générale
- TB avec BPCO 2 fois plus de risque de décéder comparé à des patients tuberculeux sans BPCO

Inghammahr et al Plos One 2010
A Population-Based Cohort Study

Comorbidités: BPCO et TB

- Review systématique multicentrique
- Forte association entre BPCO et TB
- Plus évident dans le pays à forte endémie de TB
- Bold and Platino studies (Amérique latine)
- Non fumeurs et association avec BPCO chez de patients jeunes

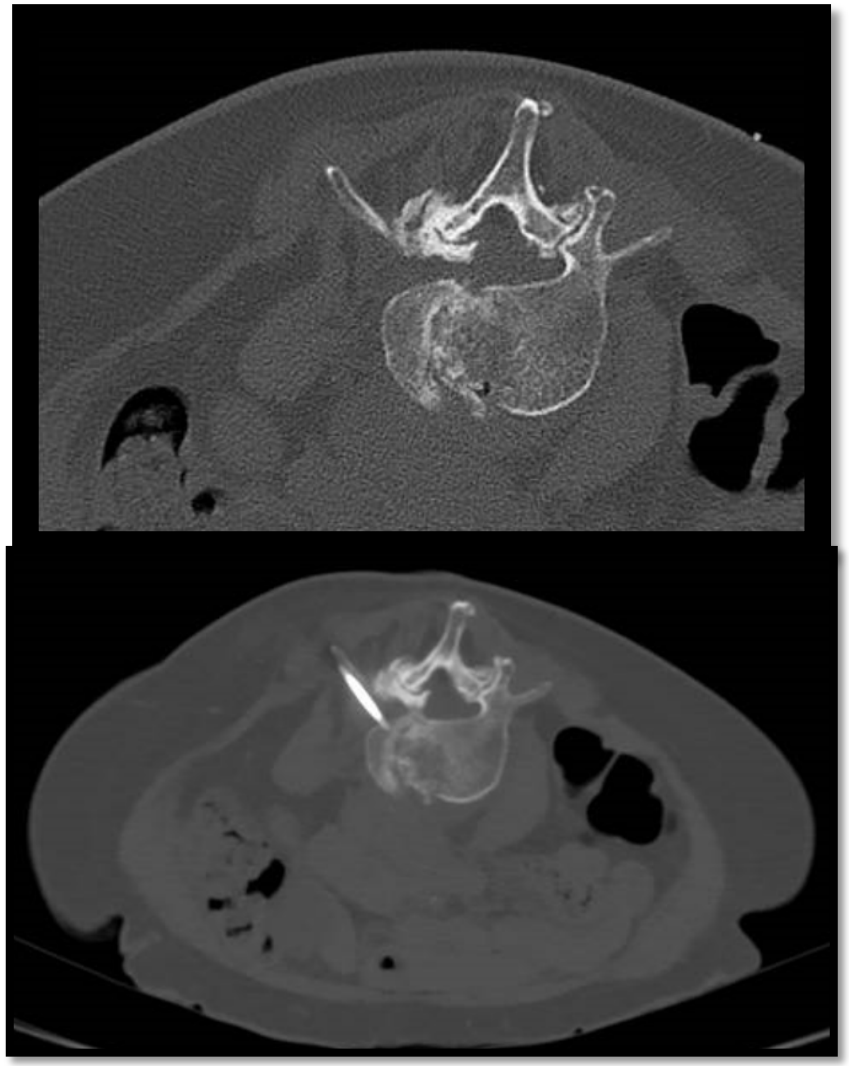


- Etonnamment dans un étude on trouve une corrélation plus importante de BPCO chez les adultes de < de 40 ans ayant eu une TB
- BPCO associé à la TB (les séquelles pulmonaires dues à TB)
- Dommage pulmonaire qui se cumule a d'autres facteurs de risques environnementales pour développer BPCO (pauvreté, pollution)
- Utilisation de CSI a haut doses s'associe a Tb (Shu et al)

Byrne et al International Journal of Infectious Diseases 2015
SHU et al Taiwan 2010

Spondylodiscite L3-L4

- Patiente de 84 ans sous **anti-TNF (adalimumab)** pour une maladie auto-immune
- Lombosciatalgies invalidantes
- Perte de 7 kilos de poids
- Dépression sévère
- Ponction du Disque L3-L4
- Pcr mtbc Pos
- Culture pos en 13 jours
- Tt 1 année: excellente évolution



PR et son traitement

- Personnes âgées de plus de > 67 ans avec PR (n=56.260) avec PR

(étude canadienne)

- 57 cas de TB et 211 de NTM

- Plus de risque de TB (OR 5,2) anti-TNF * et plus de risque de souffrir d'une maladie pulmonaire à MNT (OR 2.19)

*infliximab, etanercept, adalimumab

- Corticostéroïdes oraux, Méthotrexate, Leflunomide et Ciclosporine (risque moindre)

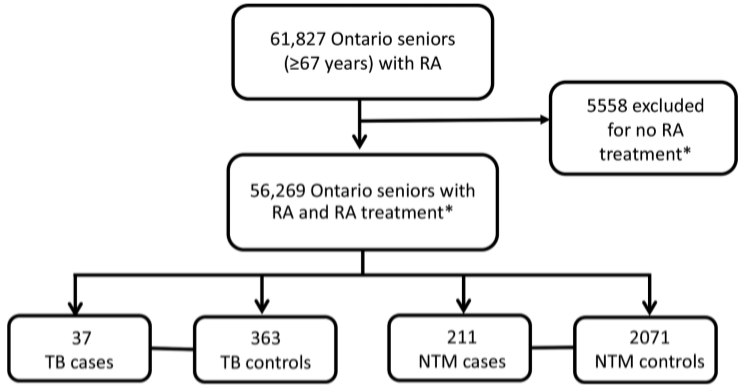


Figure 1 Study population. TB cases defined by any culture positive for *Mycobacterium tuberculosis* complex organisms; NTM disease cases defined by ≥2 sputum, or ≥1 bronchoscopy or lung biopsy specimen, or any positive culture from a normally sterile body site, including pleura. DMARD, disease modifying anti-rheumatic drug; NSAID, non-steroidal anti-inflammatory drug; NTM, nontuberculous

Brode et al Thorax 2015
Brassard et al Arthrit. Rhumat 2001

DBT et TB

- Review systématique (13 études)
- Diabètes augmente le risque d'avoir une Tb (OR 3. 11)
- Améliorer contrôle de diabète chez la personne âgée
- Garder un haut indice de suspicion de TB chez de personnes DBT
- Active case finding ?
- Y/c TT de Tb latente chez le DBT ?
- Dans les études qui ont ajusté pour l'âge le RR semble plus élevé chez le groupe de < de 40 ans que chez les personnes âgées

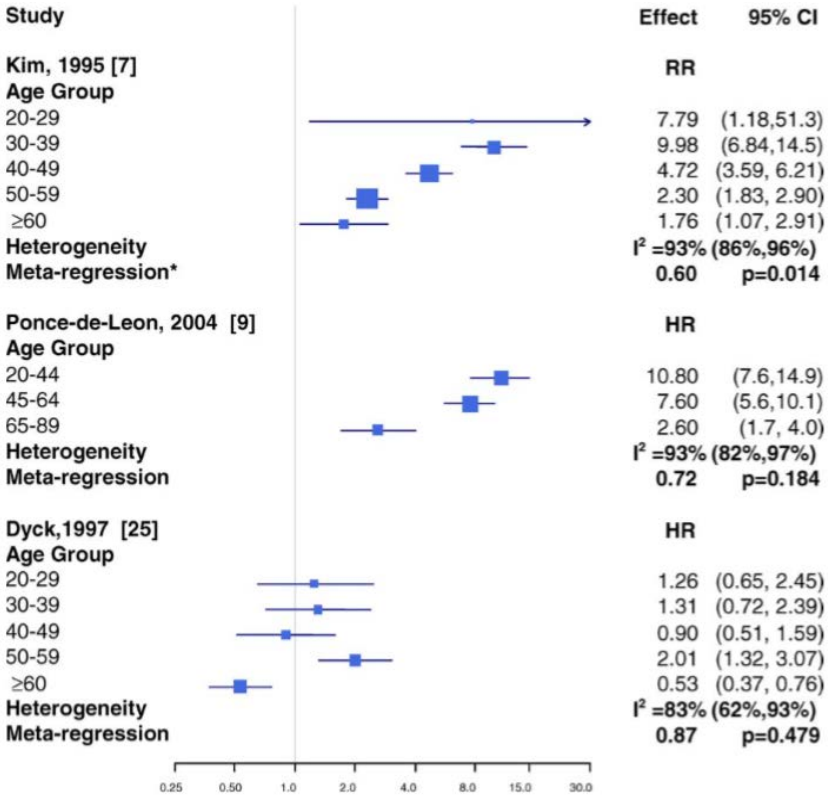
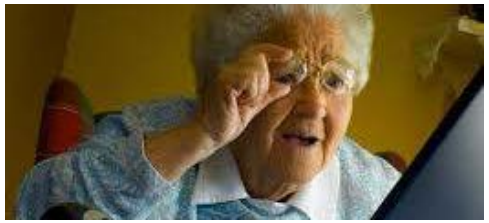


Figure 3. Forest Plot of Age-Specific Association between Diabetes and Active Tuberculosis from Kim et al. [7], Pc

Murray et al One Harvard School of Public Health 2008 Plos
Riza et al Lancet Endocr 2014

Traitement





Toxicité

- Âge plus de risque de Hépatotoxicité
- Plus de comorbidités
- Fonction rénal et hépatique plus défaillantes
- Enlever toute les médicament non indispensables (cave interactions Rif)
- Mesure de taux sériques
- Plus de éruptions cutanées
- Plus de arthralgies
- Mortalité plus élevé (jusqu'à 30% chez le > 70 ans même si bien traité)

En Ems s'assurer que les médicaments soit pris et pas posé sur la table de nuit …DOT

- En première intention, on peut proposer le traitement classique:
- INH 3 à 5 mg/kg + RIF 10 mg/kg + PZA 15-25 mg/kg pendant 2 mois puis INH + RIF pendant les 4 mois qui pyridoxine (vit B6), en prévention du risque de neuropathie.
- Si le PZA est contre-indiqué, le traitement est de 9 mois avec INH+ RIF +EMB pendant les 2 premiers mois puis INH + RIF ensuite

Gisselbrecht et al La tuberculose chez les personnes âgées en institution RMR 2003
Davies et al Drugs aging 1996

Tb Screening chez les personnes âgées

ORIGINAL ARTICLE | https://doi.org/10.4046/trd.2018.0063
ISSN: 1738-3536(Print)/2005-6184(Online) • Published online Feb. 28, 2019

A Pilot Project of Systematic Tuberculosis Screening in the Elderly in a South Korean Province

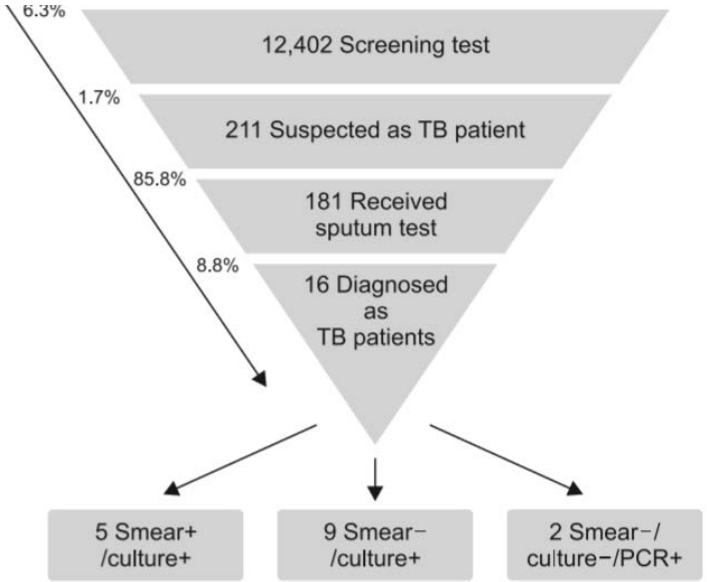


Figure 1. Cascade analysis of tuberculosis (TB) screening project involving the elderly who live in the Jeollanam-do region. PCR: polymerase chain reaction.

16 cas de tuberculose active retrouvé parmi 12402 personnes

Number needed to screen = 775

Incidence en Corée du Sud chez le plus de 65 ans 146/100 000 habitants chez les plus de 65 ans

La prévalence de TB augmente avec l'âge la TB est >12 fois plus fréquent chez les plus de 85 ans

Screening chez cette population maintenant recommandé en Corée du Sud

Screening indépendamment de symptômes est recommandé prévention de transmission (early case detection)

Limitation pas de correction par status socio économique ou isolement

Kim et al Tuberculosis and Respiratory diseases 2017

«active case finding» ?

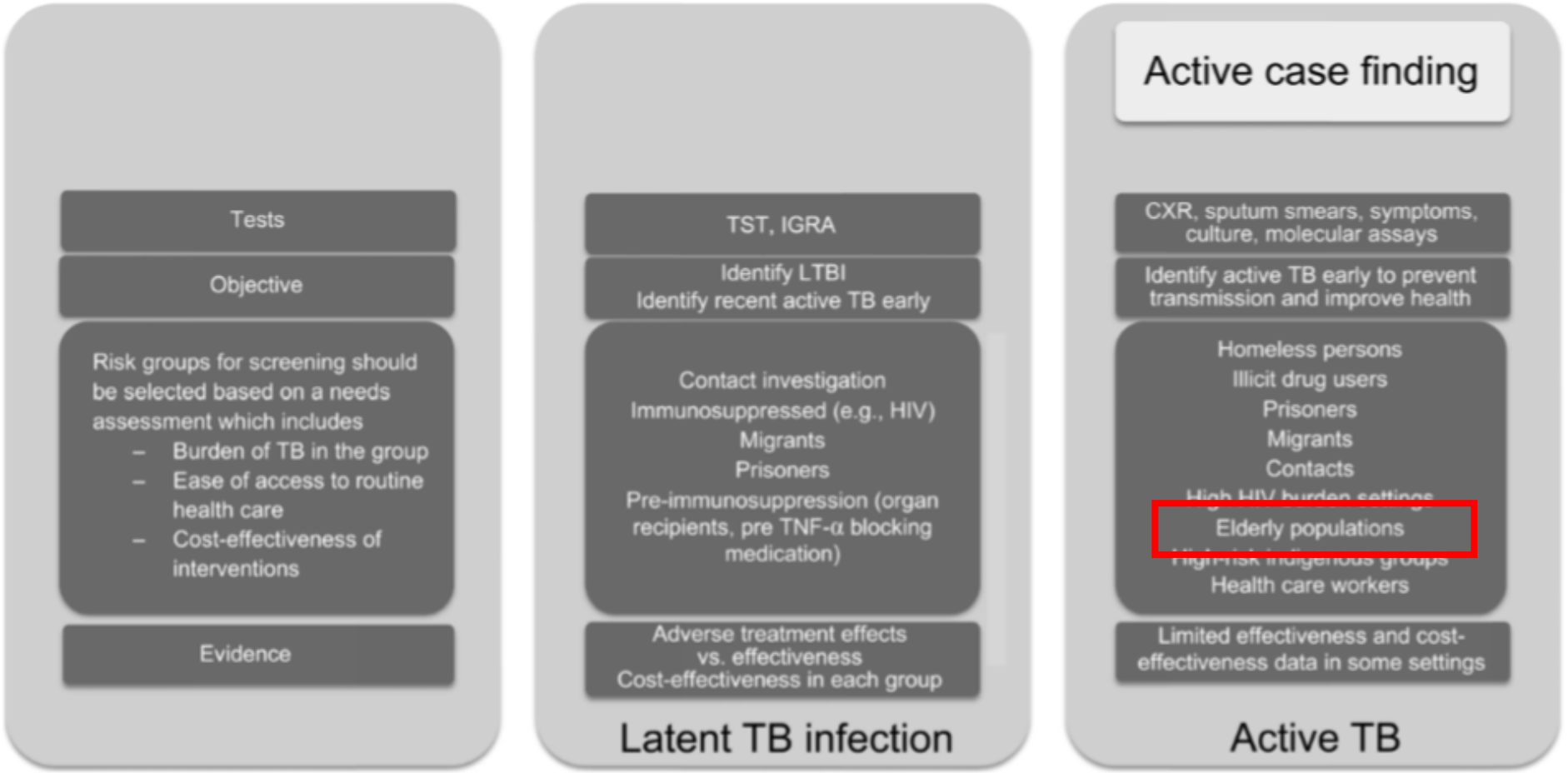


Figure Conceptual model based on the natural history of TB illustrating opportunities for active case finding. TB = tuberculosis; TST = tuberculin skin test; IGRA = interferon gamma release assay; LTBI = latent tuberculosis infection; HIV = human immunodeficiency virus; TNF = tumour necrosis factor; CXR = chest X-ray.

Negin et al IJID 2015
Tuberculosis among older adults Time to take notice

Active case finding for tuberculosis among high-risk groups in low-incidence countries
D. Zenner,*† J. Southern,* R. van Hest,‡ G. deVries,§ H. R. Stagg,† D. Antoine,¶ I. Abubakar*

Dépistage en Institution (EMS)

- Arkansas: une patiente en EMS atteinte d'une tuberculose pulmonaire non diagnostiquée aurait infecté 80 personnes
- À l'EMS 5% de risque par année de virer une Mantoux si cas de TB détecté + (dans les 3 années précédentes)
- Le risque annuel dans les institutions sans identification de cas est de 3,5%
- Taux de conversion tuberculinique de 4,7 % dans l'année qui suit l'admission en institution
- Bénéfice en terme de survie de la chimioprophylaxie par l'INH paraît réduit chez le sujet de plus de 80 ans
- Mais ce traitement préventif contribue à prévenir l'extension de la maladie au sein des institutions
- Un dépistage à l'admission en EMS légitime mais pas obligatoire

Stead et al 1985
Welty C A*m Rev Respir Dis* 1985

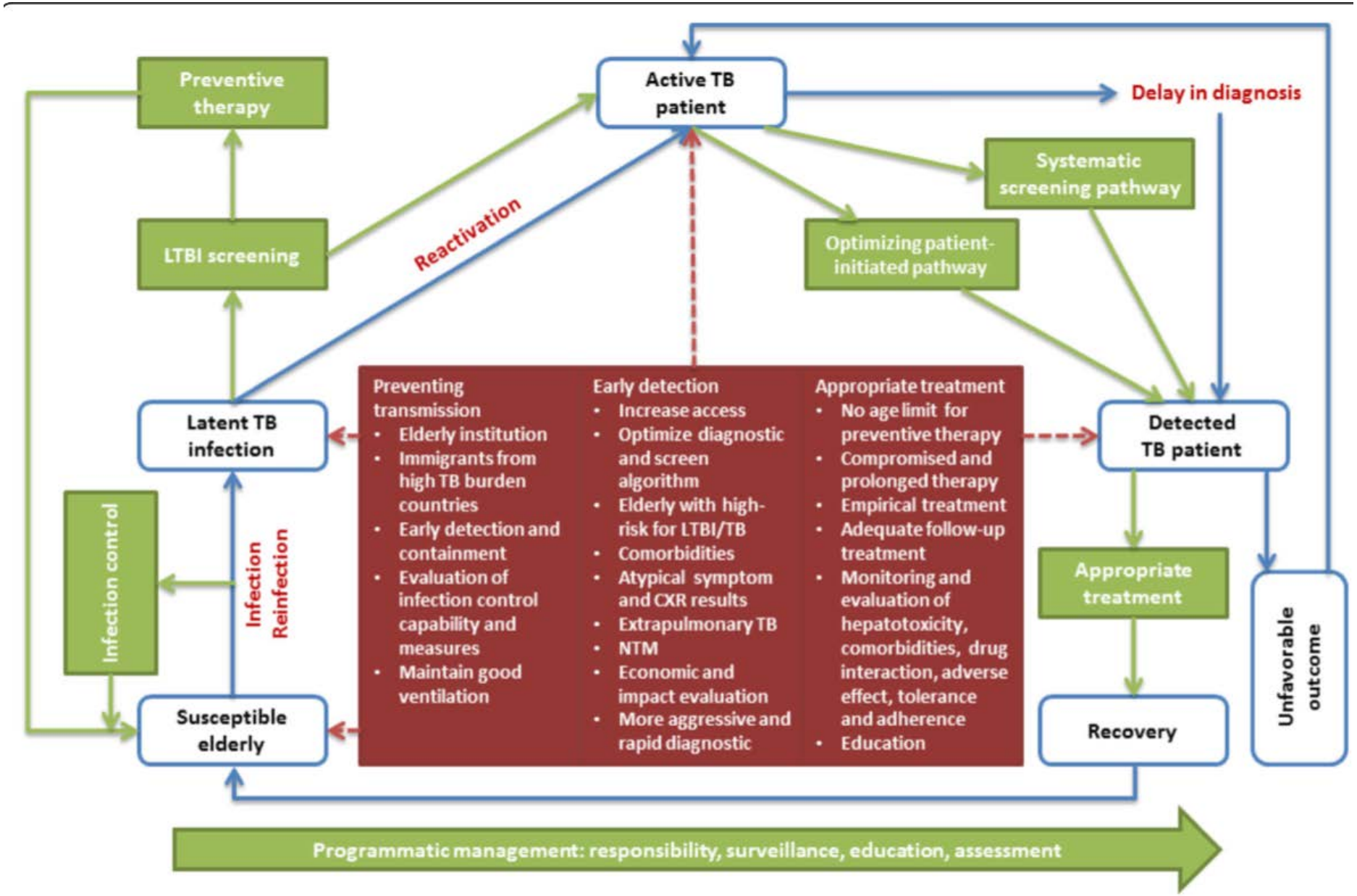


Fig. 2 The conceptual strategic framework of TB control and prevention in the elderly

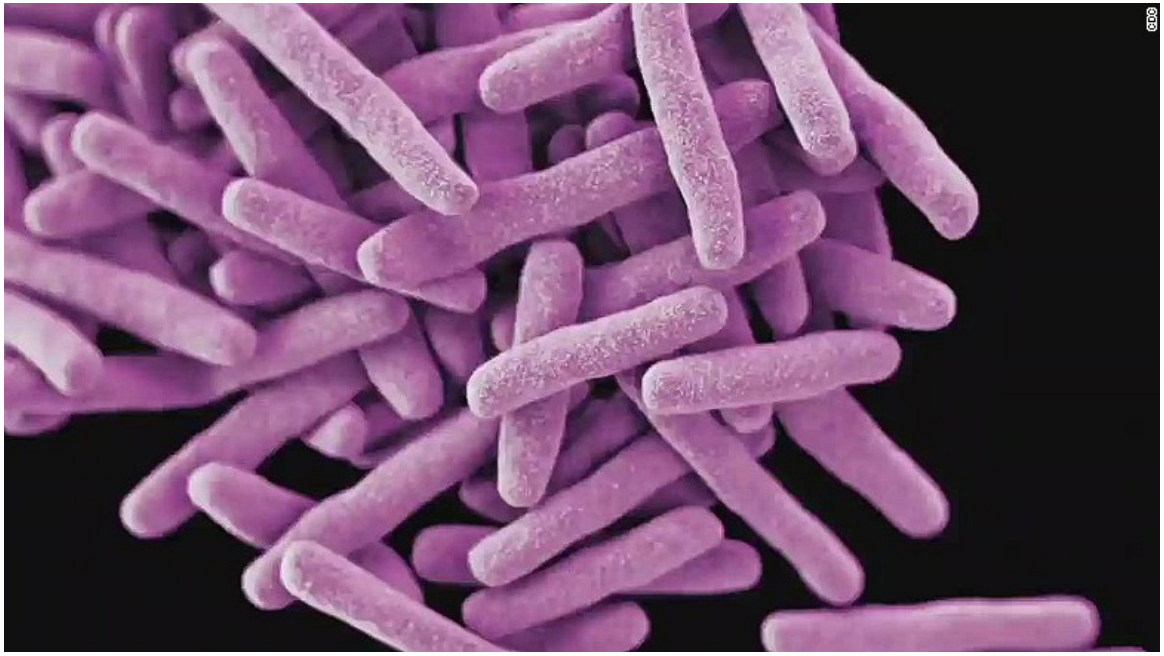
Li et al Infectious Disease for Poverty 2017

Conclusions

- Tb et sa problématique chez la personne âgée n'est pas encore assez apprécié
- Reconnaitre qu'il existe un problème c'est un premier pas
- En 2012 L'OMS a donné une priorité chez les enfants
- Il est temps qu'on consacre plus de réflexion à la TB chez les personnes âgées
- Savoir reconnaitre les facteurs de risques, diagnostiquer sans délai et traiter les personnes âgées est prioritaire
- Mesures de tb contrôle / Eviction de transmission au sein des institutions et protection du personnel soignant
- Evaluer la place du «active case finding»


WORLD
TB DAY
March 24
IT'S TIME!

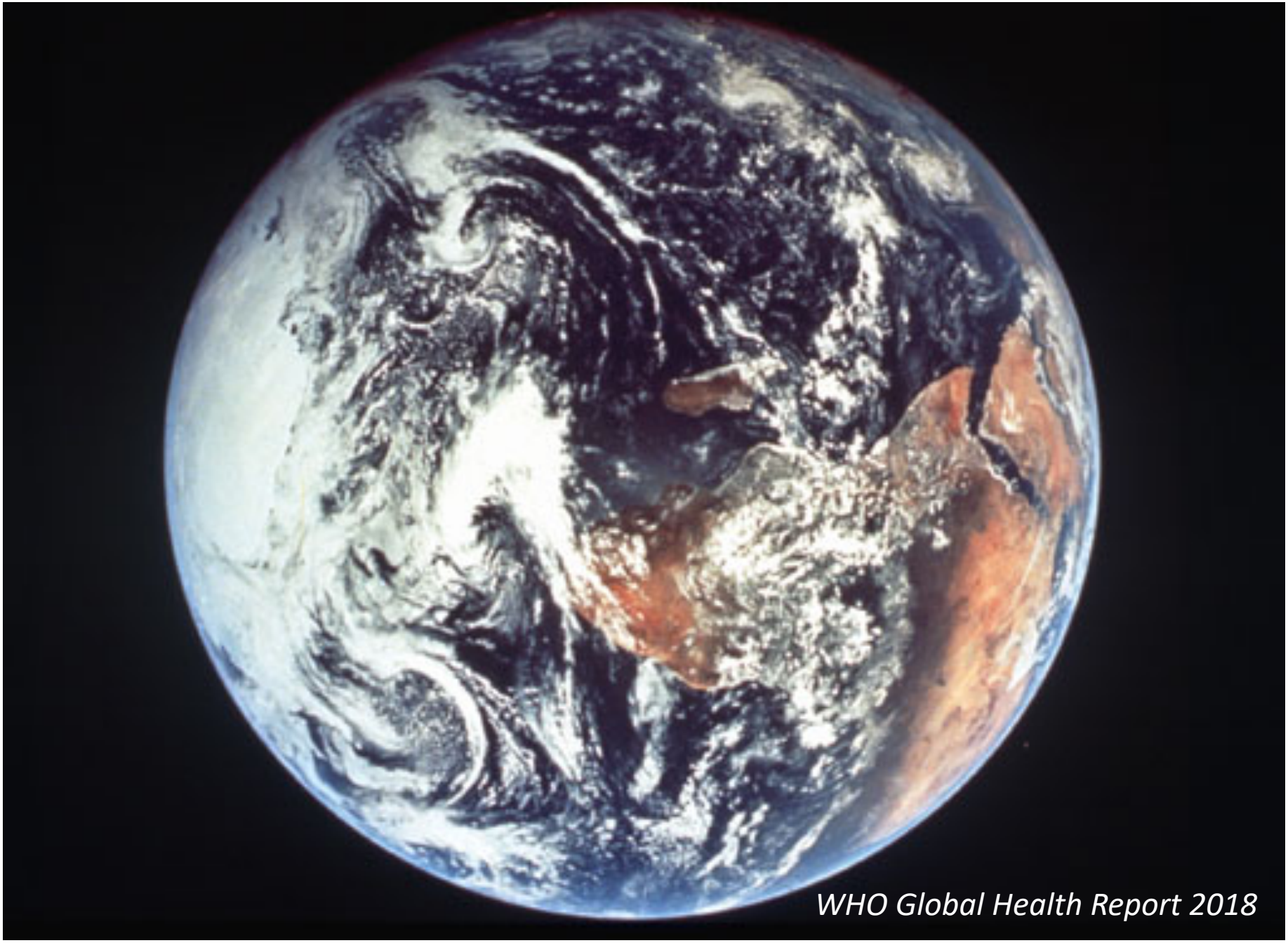
Tuberculose extra-thoracique: évolution des modalités diagnostiques



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Service de Pneumologie, HUG, Geneva
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Hôpitaux Universitaires Genève

Service de Pneumologie


WHO Global Health Report 2018

Tuberculoses extrathoraciques (TB-ET): monde

Proportion des patients avec TB ayant une atteinte extra-thoracique:

- USA: 20%; GB: 40%; F: 25%; CH: 37%
- Atteinte exclusivement extra-thoracique: 14% (OMS, 2009)

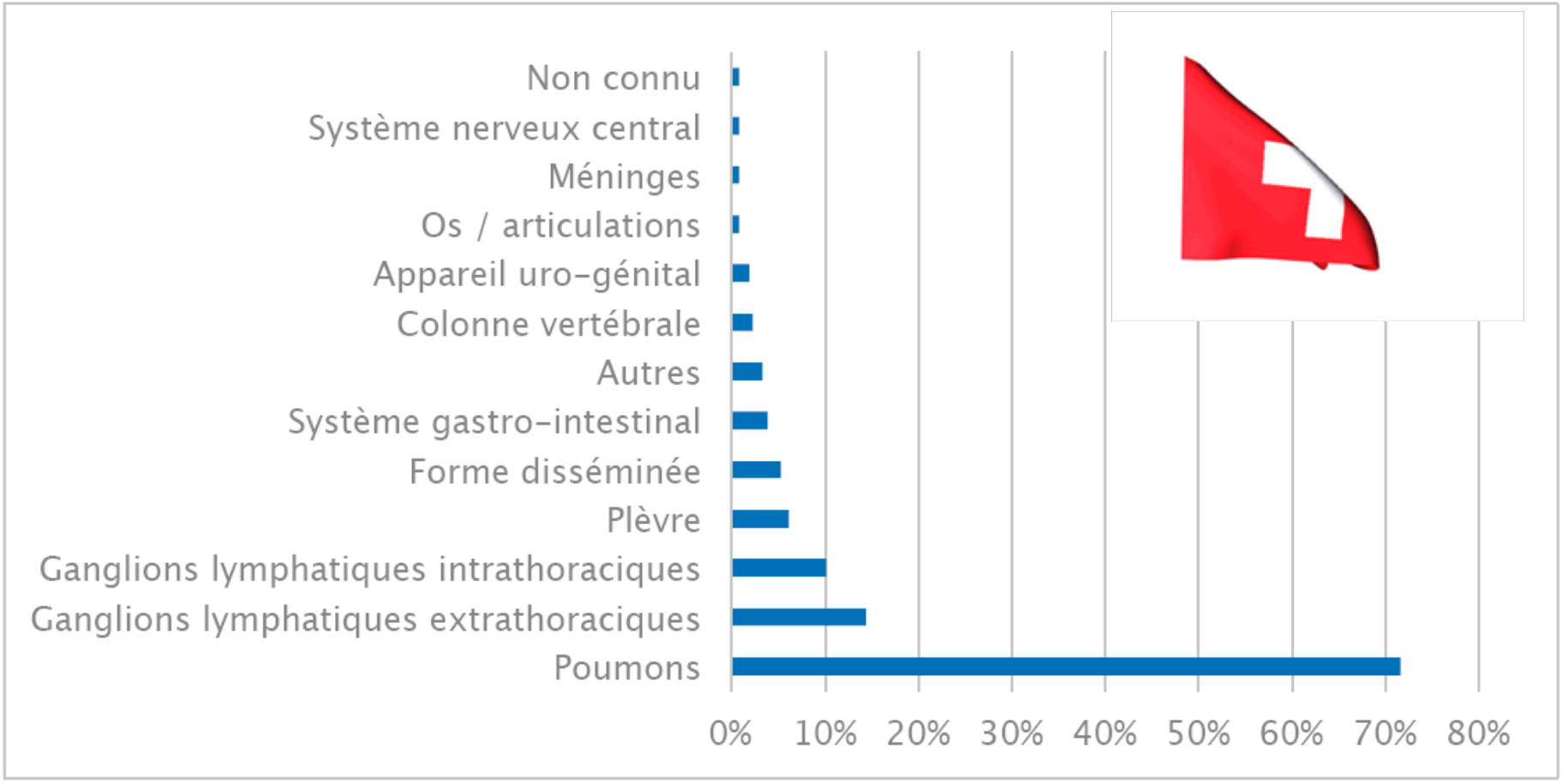
Facteurs associés à une prévalence plus élevée d'atteintes ET:

- Ethnicité (noirs, asiatiques), femme vs. hommes, HIV+, souche « Beijing »

Diagnostic des TB extra-thoraciques souvent plus tardif et difficile

J Mazza-Stalder et al; Rev Mal Respir 2012

Figure 4 :
tuberculose en Suisse en 2014, organes atteints (plusieurs réponses possibles)



Disséminée: miliaire ou touchant plus de deux organes



Tableau 1
Tuberculose, 2005–2011

	2005	2006	2007	2008	2009	2010	2011	Total	%
Nombre total de cas	564	520	478	520	556	548	577	3763	*100,0*
Taux de déclaration pour 100 000 habitants	7,5	6,9	6,3	6,7	7,1	6,9	7,2	7,0	
Origine									
Suisse	178	159	156	129	134	150	127	1033	*27,5*
Etrangers	385	354	318	389	412	377	429	2664	*70,8*
dont requérants d'asile	97	72	73	109	159	108	131	749	
non connue	1	7	4	2	10	21	21	66	*1,8*
Organe atteint									
Forme pulmonaire	307	320	270	273	278	291	289	2028	*53,9*
Forme extrapulmonaire	170	123	135	156	165	152	180	1081	*28,7*
Combinaison des deux formes	87	77	73	91	113	105	108	654	*17,4*

Et à Genève…..



Table 2: Clinical presentation

n = 252	n (%)
Pulmonary TB	158 (63)
• Smear +/Culture +	93 (59)*
• Smear -/Culture +	58 (37)*
• Smear -/Culture -	7 (4)* #
• Cavitary disease	36 (23)*
• New TB cases	151 (96)*
Extrapulmonary TB	137 (54)
• Adenitis	74 (29)
• Pleuritis	18 (7)
• Abdominal TB	17 (7)
• Osteo-articular TB	17 (7)
• Urogenital tractus TB	16 (6)
• ENT TB	4 (2)
• Other	21 (8)

O Kherad et al; BMC Infect Dis, 2009

Augmentation des tuberculoses extra-thoraciques?

Aux USA, la proportion des TB-ET est passée de 16% en 1993 à 20.4% en 2008, avec 41% d'atteintes ganglionnaires, 18% d'atteintes pleurales, 11% d'atteintes péritonéales, 5.3% d'atteintes uro-genitales, 4.7 % d'atteintes meningées..

CDC report, 2009

Système Xpert MTB/RIF test

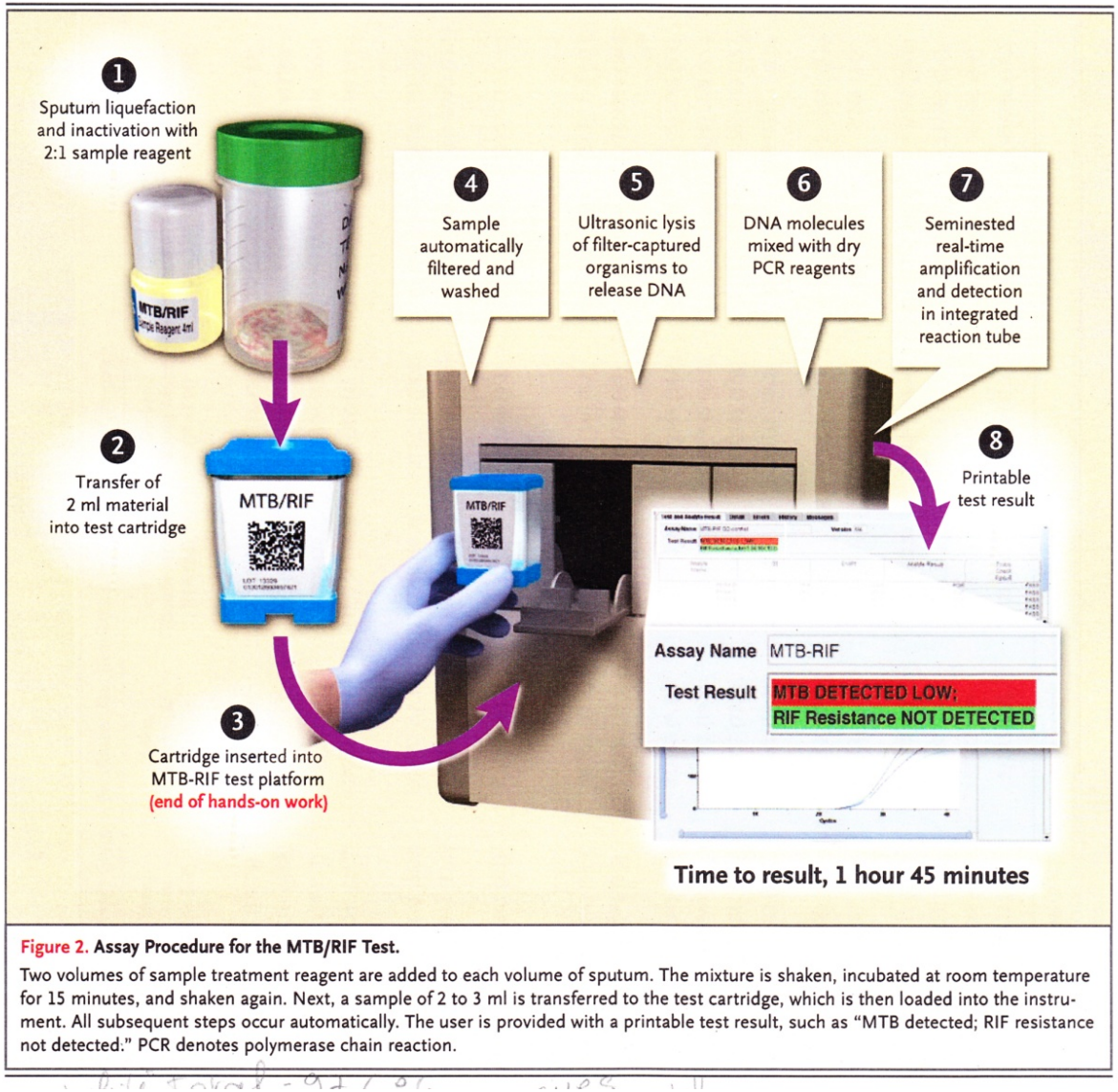


Figure 2. Assay Procedure for the MTB/RIF Test.

Two volumes of sample treatment reagent are added to each volume of sputum. The mixture is shaken, incubated at room temperature for 15 minutes, and shaken again. Next, a sample of 2 to 3 ml is transferred to the test cartridge, which is then loaded into the instrument. All subsequent steps occur automatically. The user is provided with a printable test result, such as "MTB detected; RIF resistance not detected." PCR denotes polymerase chain reaction.



Lima,Baku,Mumbai, Cape Town

C. Boehme et al. Sept. 2010. New Engl J Med; FIND & Bill and Melinda Gates Foundation



The times they are a'changin……

Bob Dylan, 1963, Columbia studios…

Le nec plus ultra…..



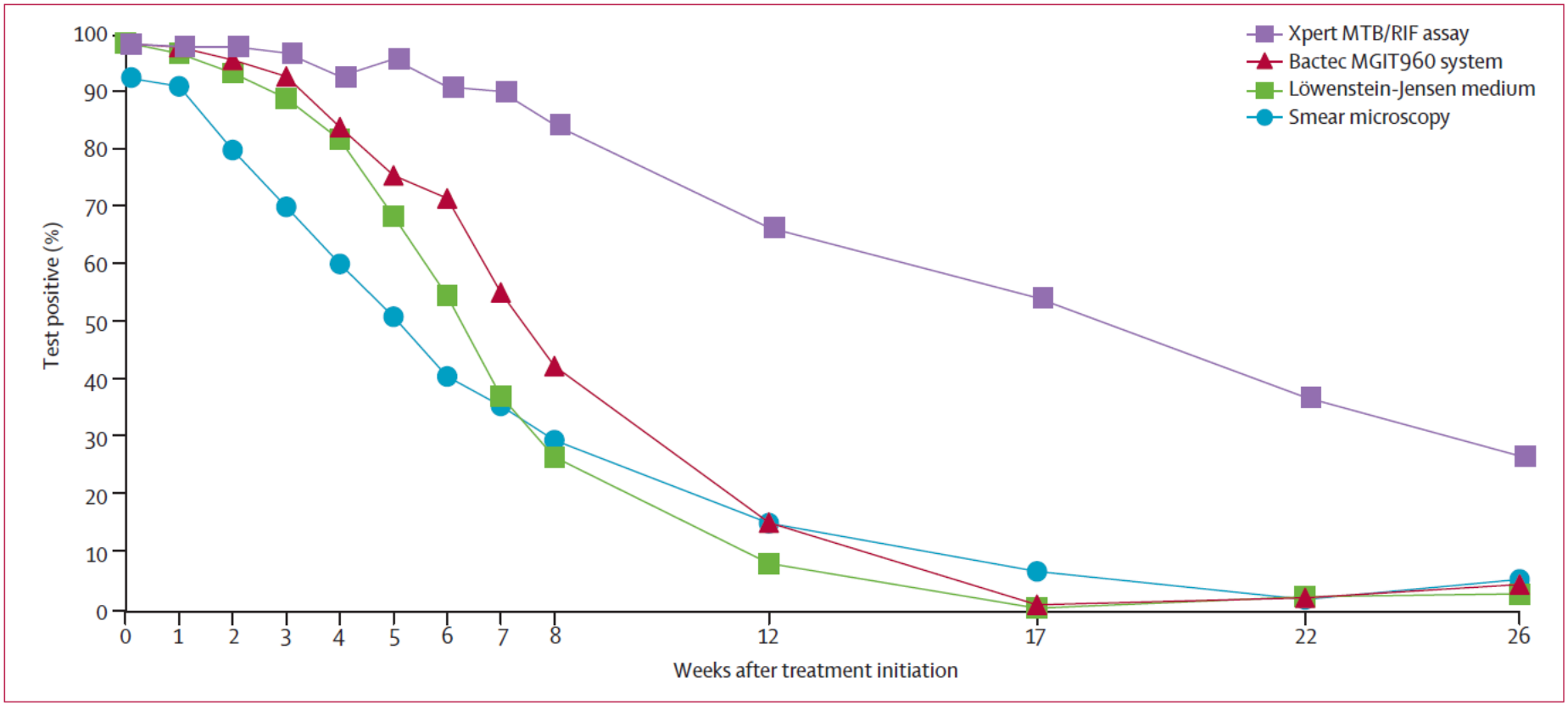


Figure 1: Qualitative data for all tests at baseline and follow-up visits

SO Friedrich et al; Lancet Respir Med 2013

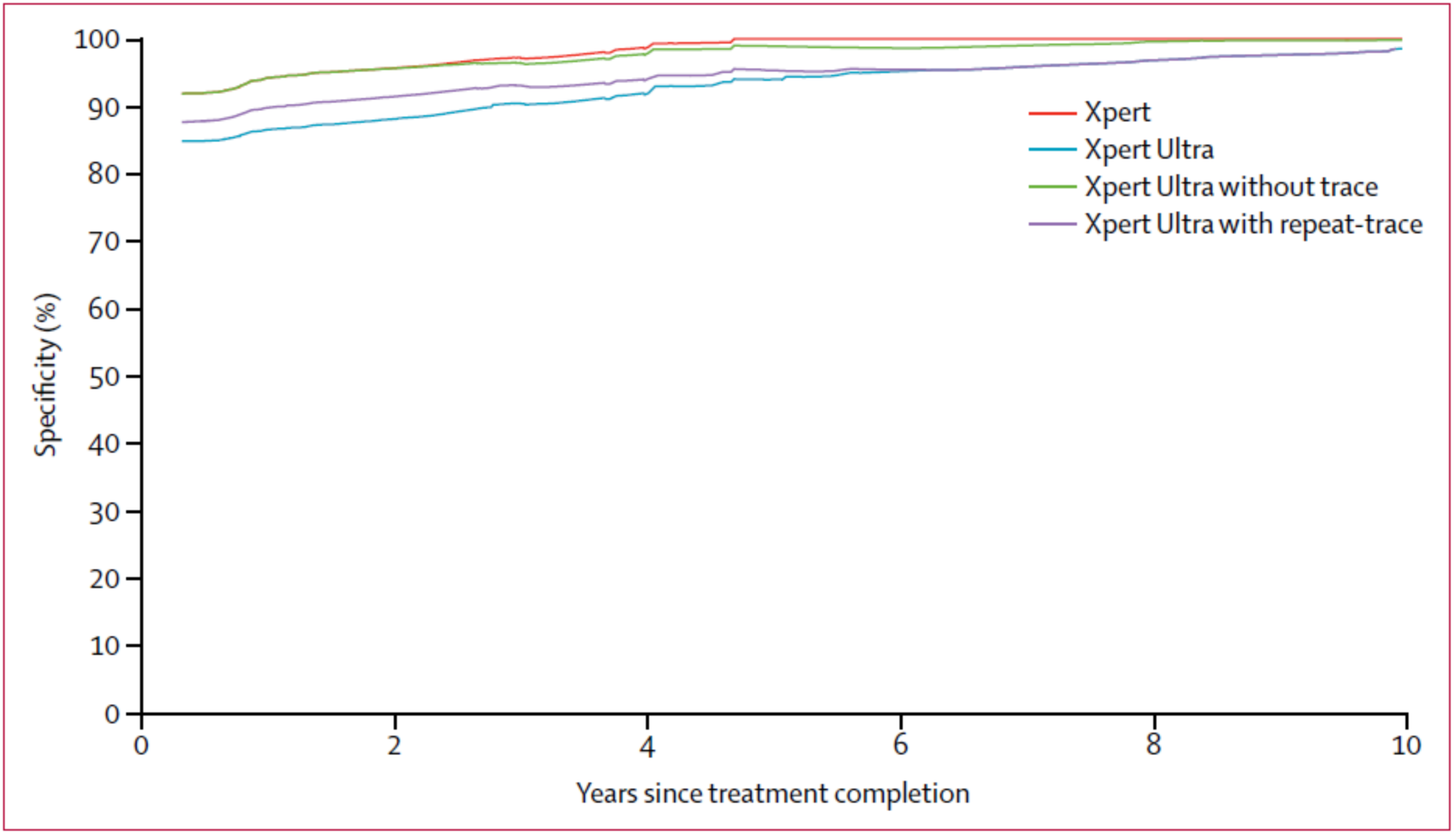


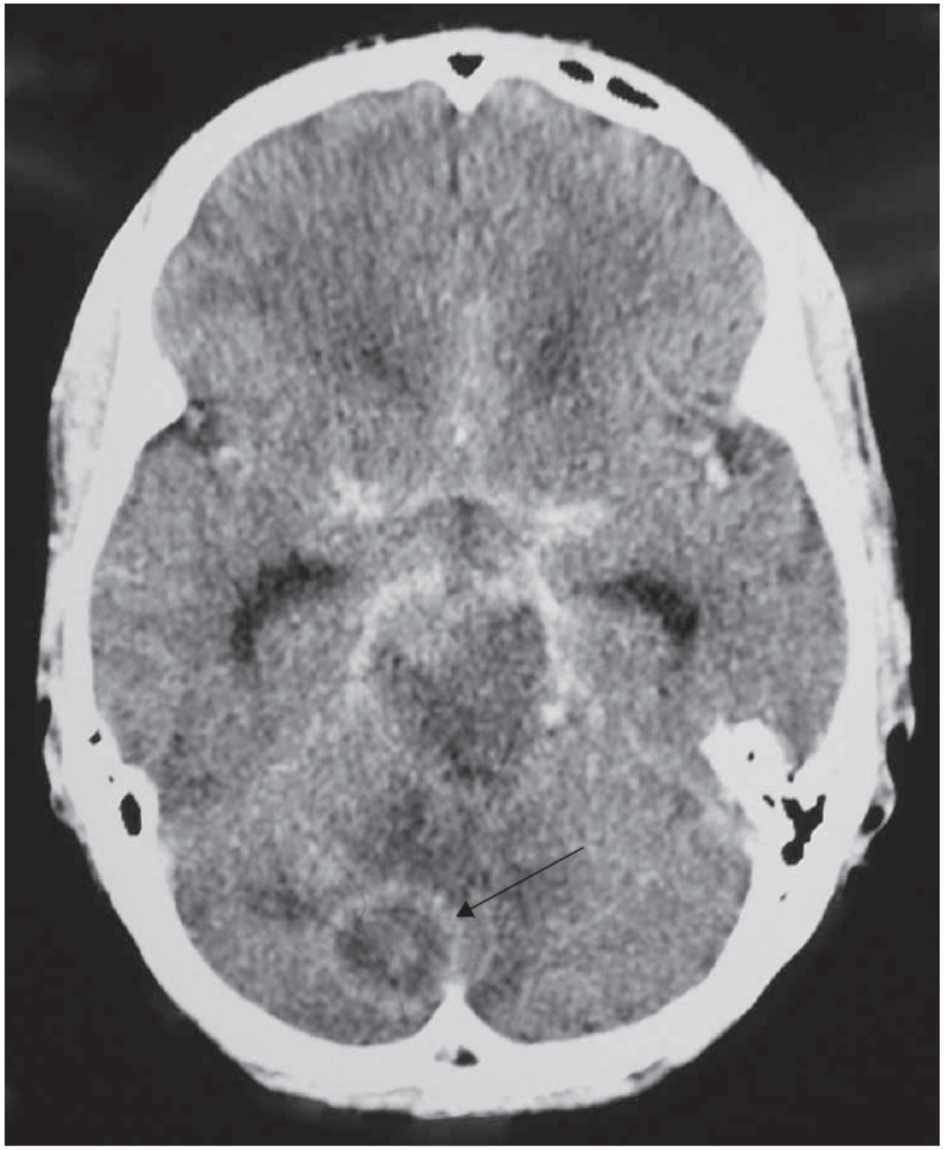
Figure 2: Specificity estimates of Xpert MTB/RIF and Xpert MTB/RIF Ultra (Xpert Ultra) for tuberculosis case detection in patients with a tuberculosis treatment history and for different approaches to handling an initial Xpert Ultra trace-positive result

SE Dorman et al; Lancet Infect Dis 2018

Quelques illustrations



Tuberculose meningée et/ou du SNC

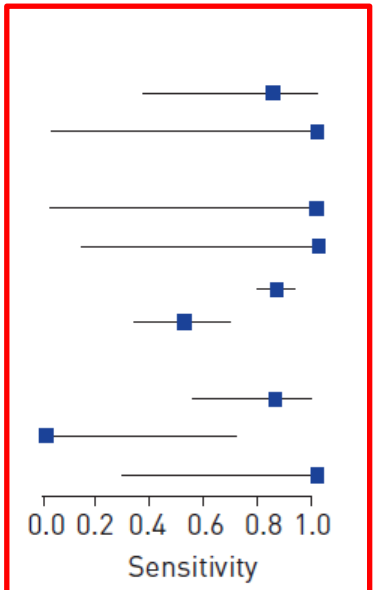


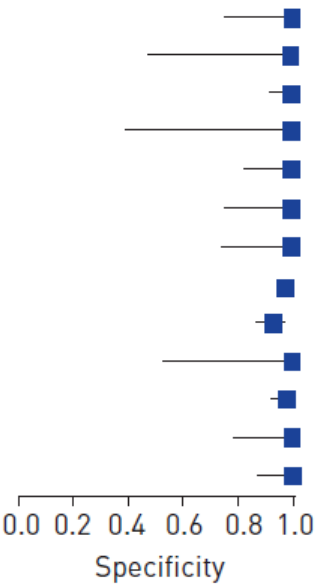
Tuberculose meningée et/ou du SNC

- *Touche avec prédilection les enfants très jeunes, les sujets immunosupprimés, les personnes âgées*
- *Forme la plus grave de TB ET, avec une mortalité dans les pays émergeants de l'ordre de 44 – 69%*
- *LCR: lymphocytose > 60%, hyperprotéinorachie, hypoglycorrachie (< 50% du taux plasmatique)*
- ***BAAR +: 5-20% des cas; Culture +: ≈40% des cas***
- *PCR: Sensibilité insuffisante pour exclure la maladie; excellente spécificité*

J Mazza-Stalder, L Nicod, JP Janssens, Rev Mal Respir 2012

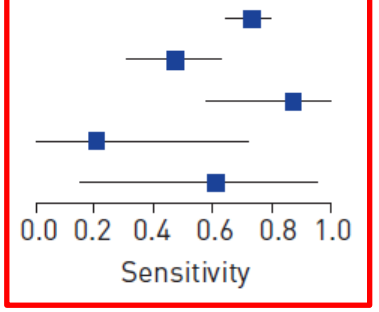
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Al-Ateah [14]	0	0	0	14	Not estimable	1.00 (0.77–1.00)
Armand [15]	0	0	0	5	Not estimable	1.00 (0.48–1.00)
Causse [16]	5	0	1	44	0.83 (0.36–1.00)	1.00 (0.92–1.00)
Hanif [19]	1	0	0	4	1.00 (0.03–1.00)	1.00 (0.40–1.00)
Hillemann [20]	0	0	0	19	Not estimable	1.00 (0.82–1.00)
Malbruny [22]	1	0	0	14	1.00 (0.03–1.00)	1.00 (0.77–1.00)
Moure [23]	2	0	0	12	1.00 (0.16–1.00)	1.00 (0.74–1.00)
Nhu [24]	103	6	18	252	0.85 (0.78–0.91)	0.98 (0.95–0.99)
Patel [25]	18	7	17	107	0.51 (0.34–0.69)	0.94 (0.88–0.97)
Safianowska [27]	0	0	0	6	Not estimable	1.00 (0.54–1.00)
Tortoli [28]	11	2	2	118	0.85 (0.55–0.98)	0.98 (0.94–1.00)
Vadwai [29]	0	0	3	16	0.00 (0.00–0.71)	1.00 (0.79–1.00)
Zeka [31]	3	0	0	28	1.00 (0.29–1.00)	1.00 (0.88–1.00)





b)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Nhu [24]	108	1	43	227	0.72 (0.64–0.79)	1.00 (0.98–1.00)
Patel [25]	20	5	23	101	0.47 (0.31–0.62)	0.95 (0.89–0.98)
Tortoli [28]	12	1	2	118	0.86 (0.57–0.98)	0.99 (0.95–1.00)
Vadwai [29]	1	0	4	14	0.20 (0.01–0.72)	1.00 (0.77–1.00)
Zeka [31]	3	0	2	26	0.60 (0.15–0.95)	1.00 (0.87–1.00)



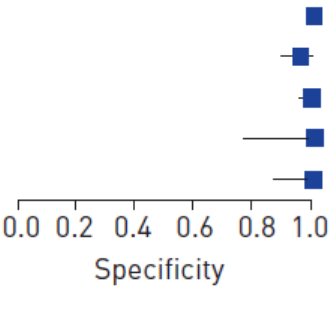


FIGURE 5 Forest plot of Xpert sensitivity and specificity for tuberculosis detection in cerebrospinal fluid with a) culture reference standard and b) composite reference standard. The squares represent the sensitivity and specificity of one study, the black line its confidence interval. TP: true positive; FP: false positive; FN: false negative; TN: true negative.

Claudia M Denkinger et al; Eur Respir J, 2014

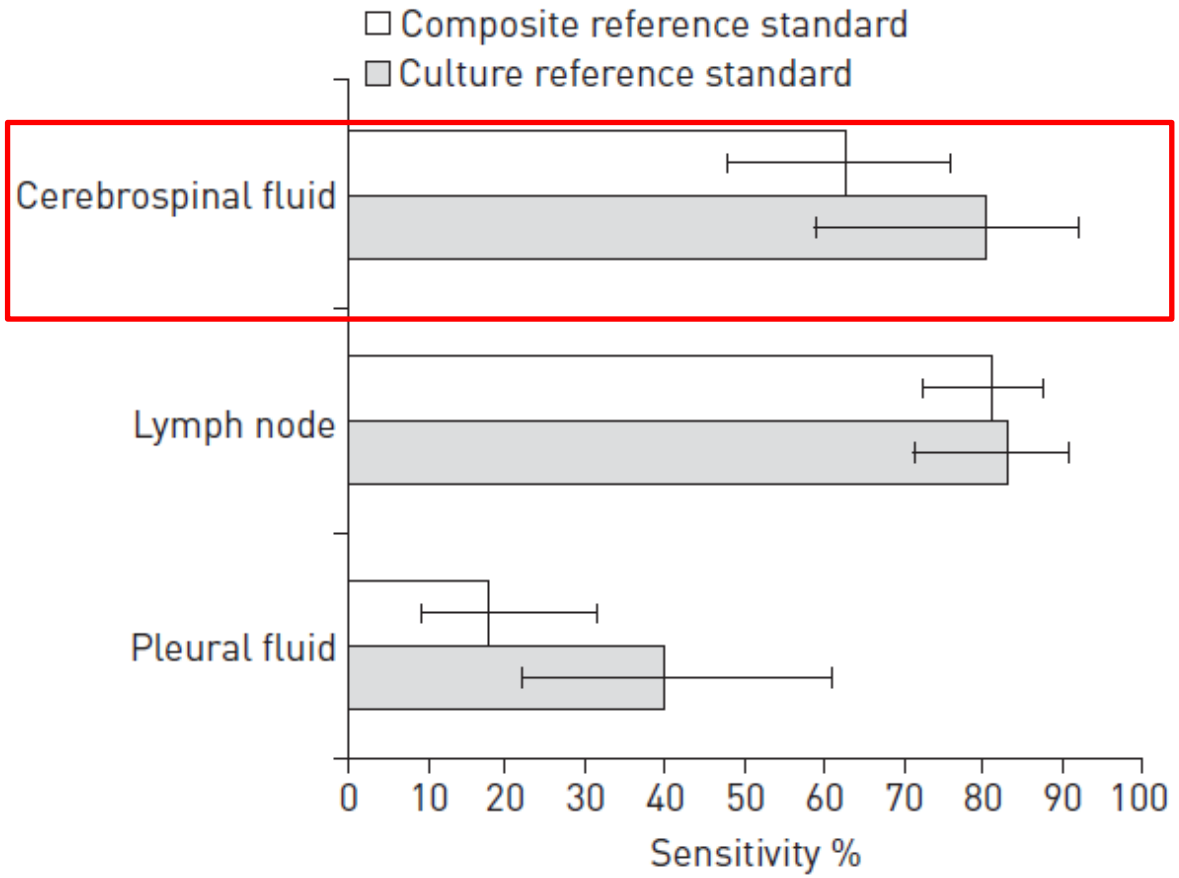


FIGURE 6 Pooled sensitivity estimates across sample types.

Claudia M Denkinger et al; Eur Respir J, 2014

Diagnostic accuracy of Xpert MTB/RIF Ultra for tuberculous meningitis in HIV-infected adults: a prospective cohort study

Nathan C Bahr, Edwin Nuwagira, Emily E Evans, Fiona V Cresswell, Philip V Bystrom, Adolf Byamukama, Sarah C Bridge, Ananta S Bangdiwala, David B Meya, Claudia M Denkinger, Conrad Muzoora, David R Boulware, on behalf of the ASTRO-CM Trial Team

	Sensitivity *vs* composite endpoint (95% CI; n/N)	Sensitivity *vs* case definition (95% CI; n/N)	Assay error rate
Xpert Ultra	95% (77–99; 21/22)	70% (47–87; 16/23)	2·3% (3/129)
Xpert	45% (24–68; 10/22)	43% (23–66; 10/23)	4·7% (6/129)
MGIT culture	45% (24–68; 10/22)	43% (23–66; 10/23)	1·6% (2/129)

All three tests were done in all 129 participants. Composite endpoint included any positive CSF Xpert Ultra, Xpert, or Bactec960 MGIT culture. Sensitivity *vs* uniform clinical case definition for definite (n=14) or probable (n=9) tuberculous meningitis excluded Xpert Ultra results in defining case status.[10] Error in culture reflects contamination with non-tuberculous mycobacterium growth. Xpert=Xpert MTB/RIF. MGIT=mycobacteria growth indicator tube. CSF=cerebrospinal fluid.

Table 3: **CSF diagnostic performance for tuberculous meningitis of Xpert, culture, and Xpert Ultra**

Lancet Infect Dis 2018

n=292 n=108 n=43

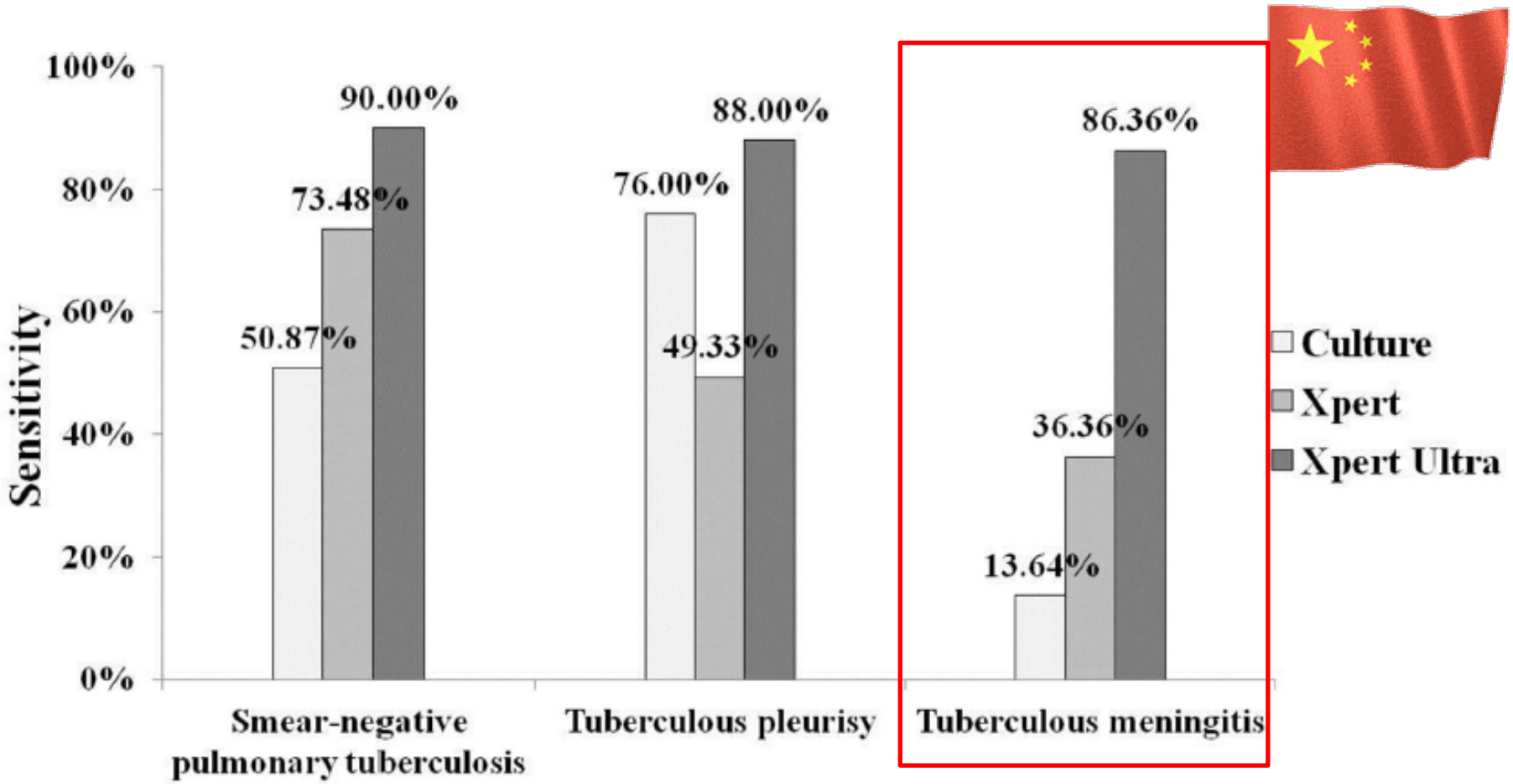


Fig. 2. The sensitivity of each method among bacteriologically confirmed tuberculosis.

G Wang et al; J Infect 2019

Tuberculose pleurale



Tuberculose pleurale

- *Plus fréquente chez l'adulte jeune, lors de co-infection VIH et chez l'enfant*
- *Survient classiquement 3- 6 mois après la primo-infection*
- *Le plus souvent unilateral; Exsudat lymphocytaire (93%)*
- *Pauci-bacillaire;* ***culture + dans ≈1/3 des cas***
- *ADA élevée : Sensibilité ≈90-93%%; Spécificité ≈90%*
- *PCR: sensibilité variable*

J Mazza-Stalder, L Nicod, JP Janssens, Rev Mal Respir 2012

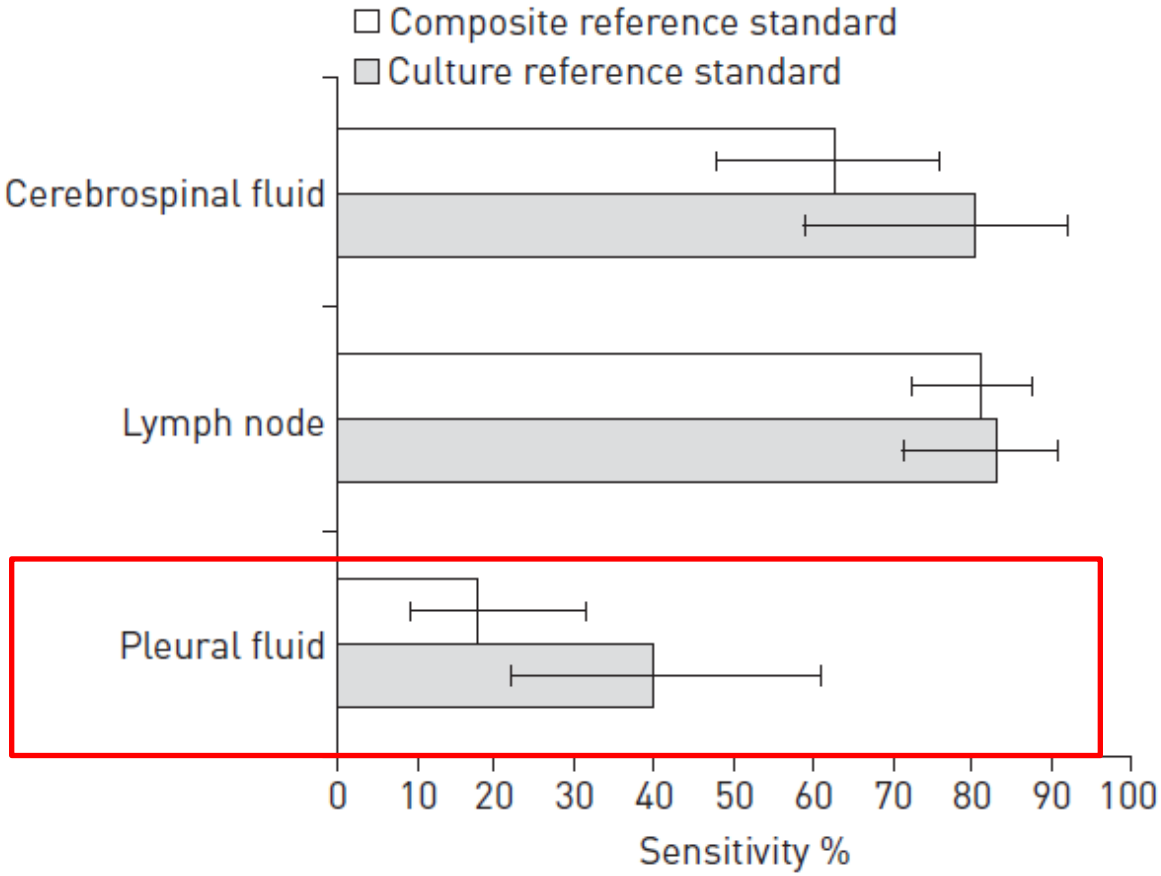
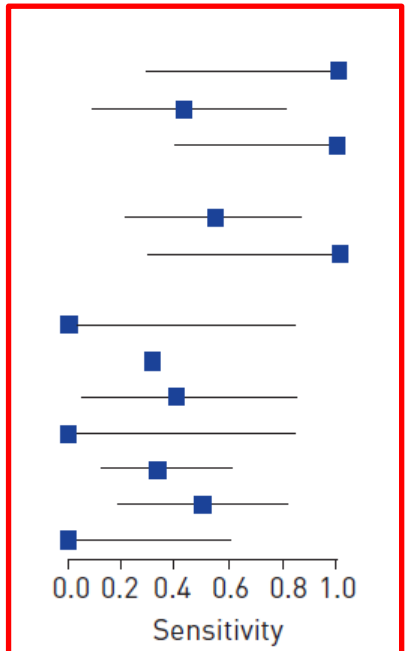
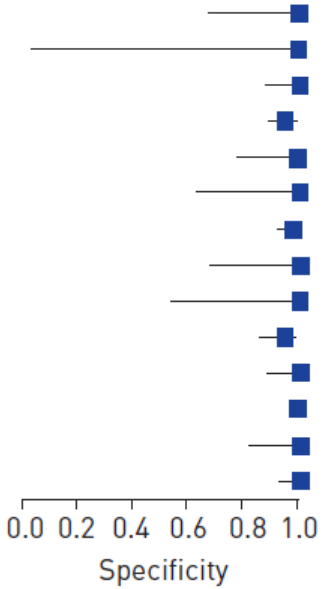


FIGURE 6 Pooled sensitivity estimates across sample types.

Claudia M Denkinger et al; Eur Respir J, 2014

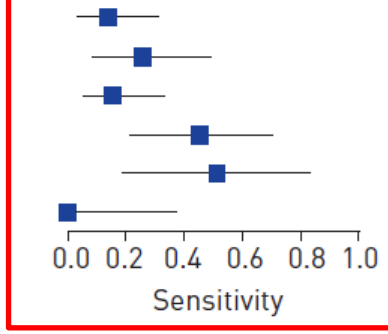
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Al-Ateah [14]	3	0	0	10	1.00 (0.29–1.00)	1.00 (0.69–1.00)
Armand [15]	3	0	4	1	0.43 (0.10–0.82)	1.00 (0.03–1.00)
Causse [16]	4	0	0	30	1.00 (0.40–1.00)	1.00 (0.88–1.00)
Christopher [17]	0	4	0	83	Not estimable	0.95 (0.89–0.99)
Friedrich [18]	5	0	4	15	0.56 (0.21–0.86)	1.00 (0.78–1.00)
Hanif [19]	3	0	0	8	1.00 (0.29–1.00)	1.00 (0.63–1.00)
Hillemann [20]	0	2	0	103	Not estimable	0.98 (0.93–1.00)
Malbruny [22]	0	0	2	10	0.00 (0.00–0.84)	1.00 (0.69–1.00)
Moure [23]	9	0	19	6	0.32 (0.16–0.52)	1.00 (0.54–1.00)
Porcel [26]	2	3	3	58	0.40 (0.05–0.85)	0.95 (0.86–0.99)
Safianowska [27]	0	0	2	30	0.33 (0.12–0.62)	1.00 (0.88–1.00)
Tortoli [28]	5	3	10	312	0.00 (0.00–0.84)	0.99 (0.97–1.00)
Vadwai [29]	5	0	5	19	0.50 (0.19–0.81)	1.00 (0.82–1.00)
Zeka [31]	0	0	4	52	0.00 (0.00–0.60)	1.00 (0.93–1.00)





b)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Christopher [17]	4	0	26	61	0.13 (0.04–0.31)	1.00 (0.94–1.00)
Friedrich [18]	5	0	15	5	0.25 (0.09–0.49)	1.00 (0.48–1.00)
Porcel [26]	5	0	28	34	0.15 (0.05–0.32)	1.00 (0.90–1.00)
Tortoli [28]	8	0	10	312	0.44 (0.22–0.69)	1.00 (0.99–1.00)
Vadwai [29]	5	0	5	19	0.50 (0.19–0.81)	1.00 (0.82–1.00)
Zeka [31]	0	0	8	48	0.00 (0.00–0.37)	1.00 (0.93–1.00)



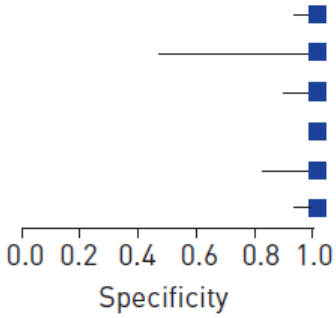


FIGURE 4 Forest plot of Xpert sensitivity and specificity for tuberculosis detection in pleural fluid with a) culture reference standard and b) composite reference standard. The squares represent the sensitivity and specificity of one study, the black line its confidence interval. TP: true positive; FP: false positive; FN: false negative; TN: true negative.

Claudia M Denkinger et al; Eur Respir J, 2014

Table 2 - Sample distribution for materials and statistical features.

Sample type (n°)	*Respiratory specimen (12257)*	*Extrapulmonary specimen (2818)*	*Gastric aspirate (375)*	*CSF (160)*	*Biopsy (744)*	*Urine (235)*	*Pus (336)*	*Total cavitary fluid (968)*	*Only pleural fluid (714)*	*Other cavitary fluid (254)*
Sensitivity %	87.1	83.6	81.8	100	83.6	88.2	95.6	53.6	38	70
Specificity %	99.9	99.9	99.7	100	100	100	100	100	100	100
Positive LR	2460.1	2035.1	252.8	∞	∞	∞	∞	∞	∞	∞
Negative LR	0.13	0.16	0.18	0	0.16	0.12	0.04	0.46	0.62	0.3
PPV %	99.5	99.7	98.2	100	100	100	100	100	100	100
NPV %	98.9	97.5	96.2	100	95.7	99.1	98.4	98	98.1	97.5

Ester Mazzola et al; 2016

n=292 n=108 n=43

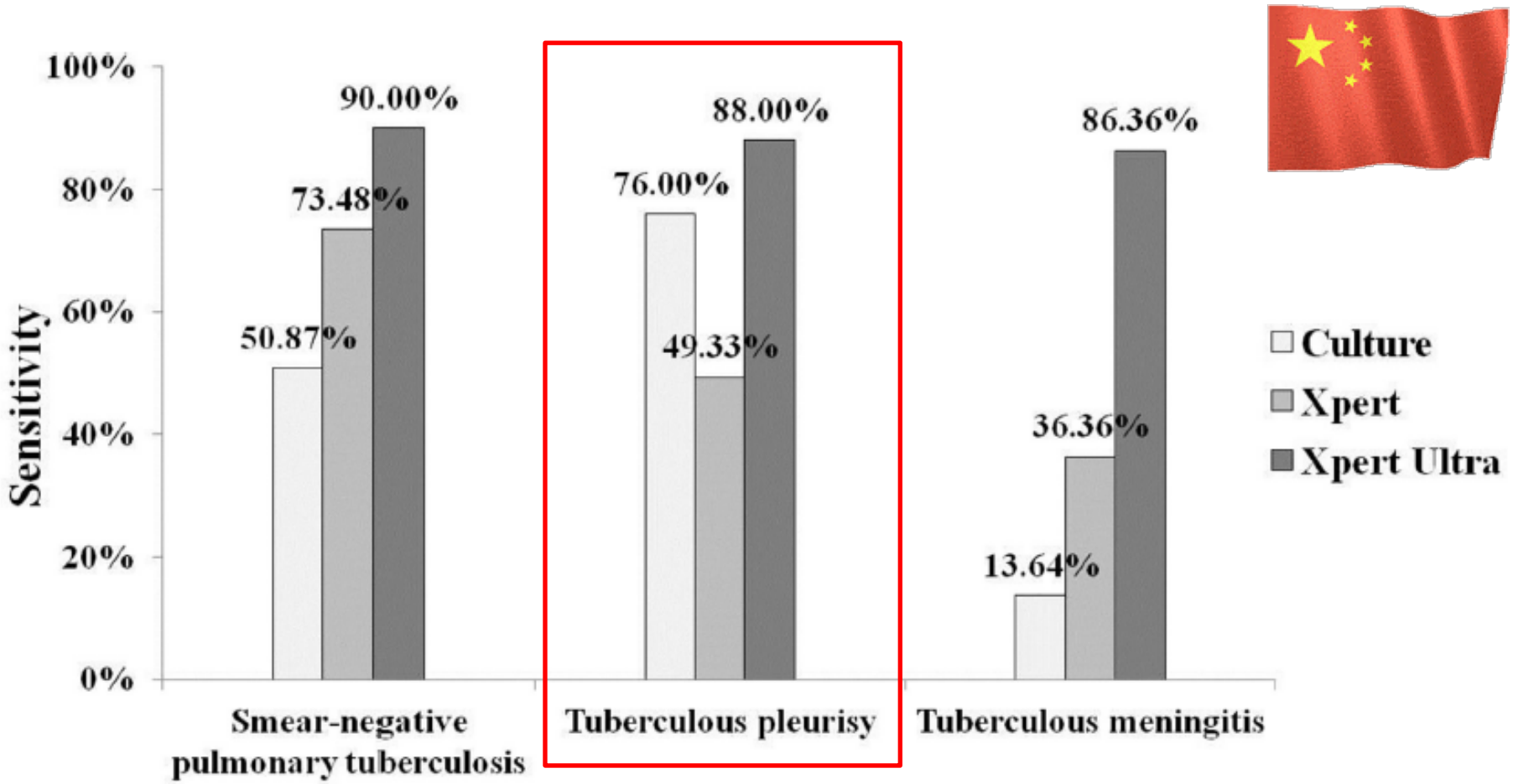


Fig. 2. The sensitivity of each method among bacteriologically confirmed tuberculosis.

G Wang et al; J Infect 2019

Les adénites tuberculeuses

- *Le plus souvent: cervicales (57%), supra-claviculaires (26%), sous-mandibulaires (13%), puis axillaires (12%)*
- *Plus rarement: sous-mentonnières, inguinales, auriculaires postérieures*
- *TB pulmonaire associée dans 15 - 40% des cas*
- *Δ: Ponction fine à l'aiguille*
- ***BAAR: 15 - 40%; PCR: 50 – 100%***


A

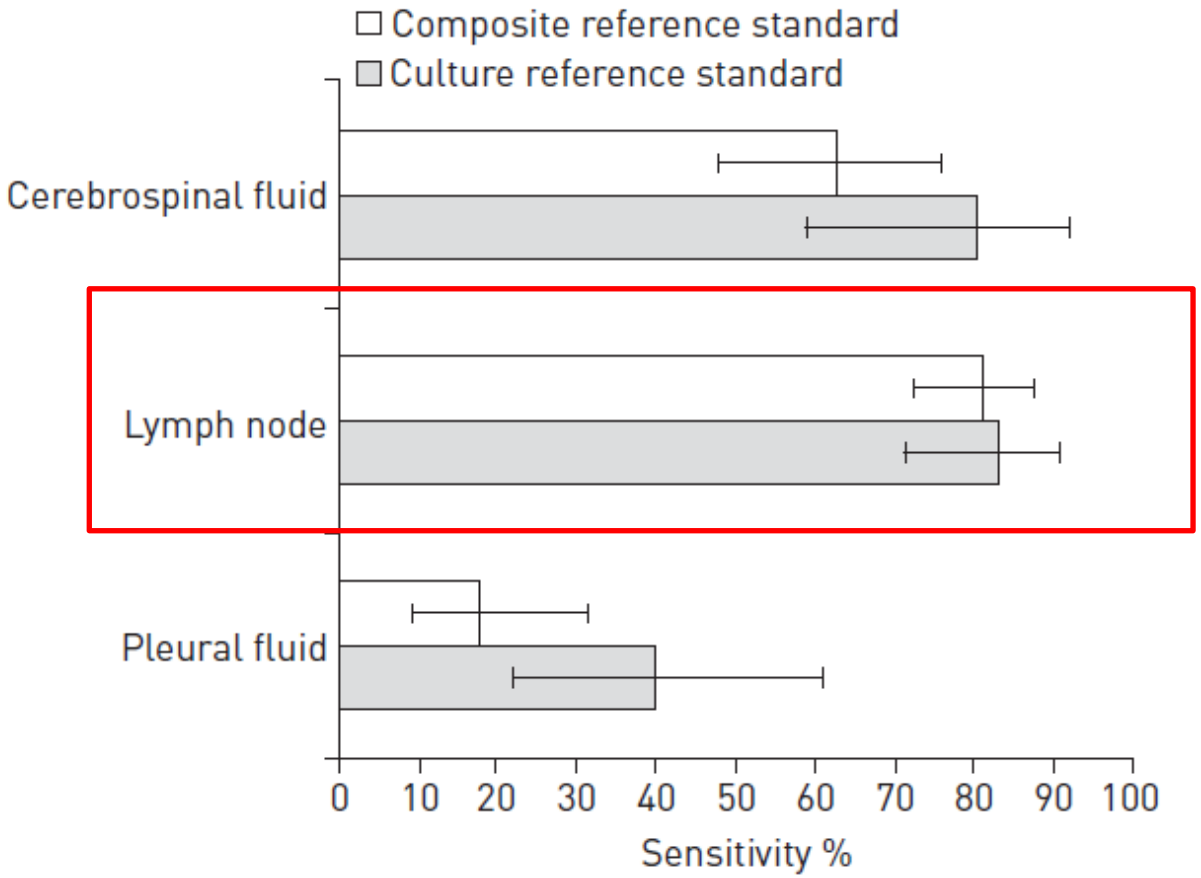
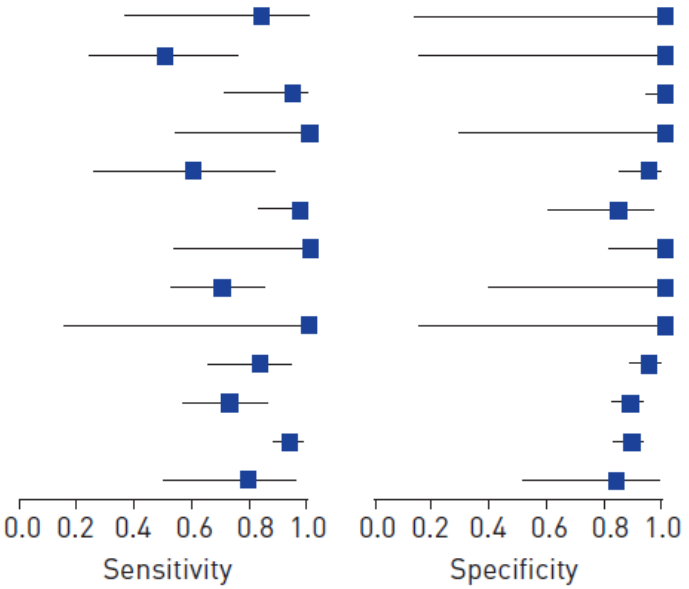


FIGURE 6 Pooled sensitivity estimates across sample types.

Claudia M Denkinger et al; Eur Respir J, 2014

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Al-Ateah [14]	5	0	1	2	0.83 (0.36–1.00)	1.00 (0.16–1.00)
Armand [15]	8	0	8	2	0.50 (0.25–0.75)	1.00 (0.16–1.00)
Causse [16]	16	0	1	70	0.94 (0.71–1.00)	1.00 (0.95–1.00)
Hanif [19]	6	0	0	3	1.00 (0.54–1.00)	1.00 (0.29–1.00)
Hillemann [20]	6	3	4	52	0.60 (0.26–0.88)	0.95 (0.81–0.99)
Ligthelm [21]	28	3	1	16	0.97 (0.82–1.00)	0.84 (0.60–0.97)
Malbruny [22]	6	0	0	17	1.00 (0.54–1.00)	1.00 (0.80–1.00)
Moure [23]	24	0	10	4	0.71 (0.53–0.85)	1.00 (0.40–1.00)
Safianowska [27]	2	0	0	2	1.00 (0.16–1.00)	1.00 (0.16–1.00)
Tortoli [28]	24	4	5	85	0.83 (0.64–0.94)	0.96 (0.89–0.99)
Vadwai [29]	32	17	12	127	0.73 (0.57–0.85)	0.88 (0.82–0.93)
Van Rie [30]	139	23	10	176	0.93 (0.88–0.97)	0.88 (0.83–0.93)
Zeka [31]	11	2	3	10	0.79 (0.49–0.95)	0.83 (0.52–0.98)



b)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ligthelm [21]	29	2	1	16	0.97 (0.83–1.00)	0.89 (0.65–0.99)
Tortoli [28]	28	0	5	85	0.85 (0.68–0.95)	1.00 (0.96–1.00)
Vadwai [29]	49	0	17	122	0.74 (0.61–0.84)	1.00 (0.97–1.00)
Van Rie [30]	160	2	42	144	0.79 (0.73–0.85)	0.99 (0.95–1.00)
Zeka [31]	13	0	4	9	0.76 (0.50–0.93)	1.00 (0.66–1.00)

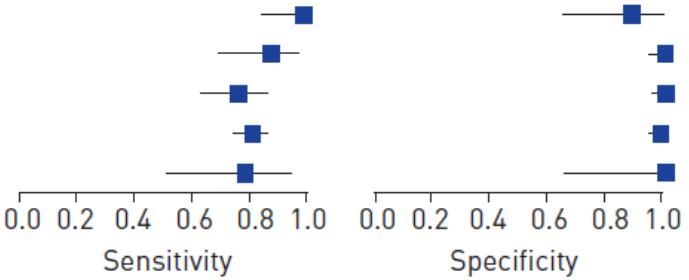


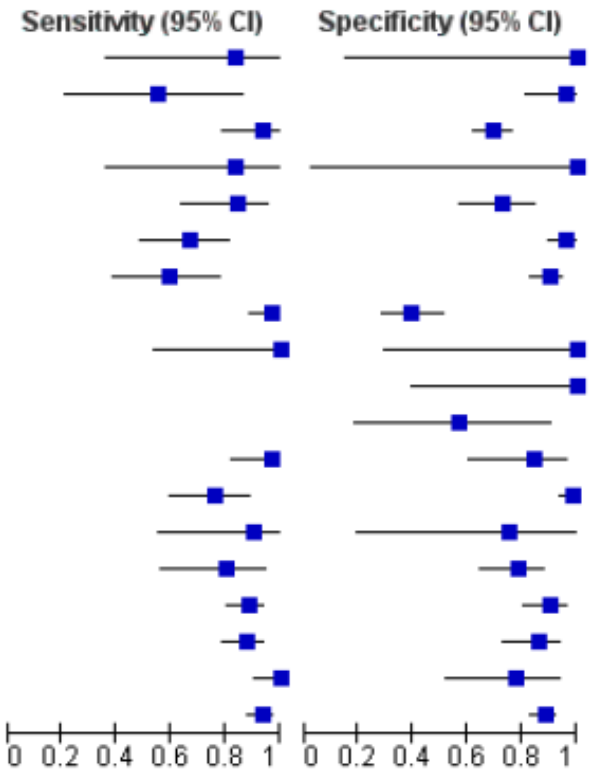
FIGURE 3 Forest plot of Xpert sensitivity and specificity for tuberculosis detection in lymph node samples (tissue or aspirate) with a) culture reference standard and b) composite reference standard. The squares represent the sensitivity and specificity of one study, the black line its confidence interval. TP: true positive; FP: false positive; FN: false negative; TN: true negative.

Claudia M Denkinger et al; Eur Respir J, 2014

Tuberculose des voies urinaires

Figure 7. Forest plot of Xpert® MTB/RIF sensitivity and specificity in lymph node aspirates with respect to a culture reference standard. The squares represent the sensitivity and specificity of one study, the black line its confidence interval. FN: false-negative; FP: false-positive; TN: true-negative; TP: true-positive.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Al-Ateah 2012	5	0	1	2	0.83 [0.36, 1.00]	1.00 [0.16, 1.00]
Bholla 2016	5	1	4	26	0.56 [0.21, 0.86]	0.96 [0.81, 1.00]
Biadglegne 2014	29	56	2	126	0.94 [0.79, 0.99]	0.69 [0.62, 0.76]
Blaich 2014	5	0	1	1	0.83 [0.36, 1.00]	1.00 [0.03, 1.00]
Coetzee 2014	21	13	4	34	0.84 [0.64, 0.95]	0.72 [0.57, 0.84]
Dhasmana 2014	24	3	12	77	0.67 [0.49, 0.81]	0.96 [0.89, 0.99]
Dhooria 2016	16	12	11	108	0.59 [0.39, 0.78]	0.90 [0.83, 0.95]
Ghariani 2015	58	48	2	31	0.97 [0.88, 1.00]	0.39 [0.28, 0.51]
Hanif 2011	6	0	0	3	1.00 [0.54, 1.00]	1.00 [0.29, 1.00]
Ioannidis 2011	0	0	0	4	Not estimable	1.00 [0.40, 1.00]
Kim 2015a	0	3	0	4	Not estimable	0.57 [0.18, 0.90]
Ligthelm 2011	28	3	1	16	0.97 [0.82, 1.00]	0.84 [0.60, 0.97]
Nataraj 2016	29	1	9	87	0.76 [0.60, 0.89]	0.99 [0.94, 1.00]
Pandey 2017	9	1	1	3	0.90 [0.55, 1.00]	0.75 [0.19, 0.99]
Scott 2014	16	12	4	43	0.80 [0.56, 0.94]	0.78 [0.65, 0.88]
Sharma 2014	85	7	11	63	0.89 [0.80, 0.94]	0.90 [0.80, 0.96]
Tadesse 2015	76	7	11	42	0.87 [0.79, 0.94]	0.86 [0.73, 0.94]
Ullah 2017	36	4	0	14	1.00 [0.90, 1.00]	0.78 [0.52, 0.94]
Van Rie 2013	139	23	10	172	0.93 [0.88, 0.97]	0.88 [0.83, 0.92]



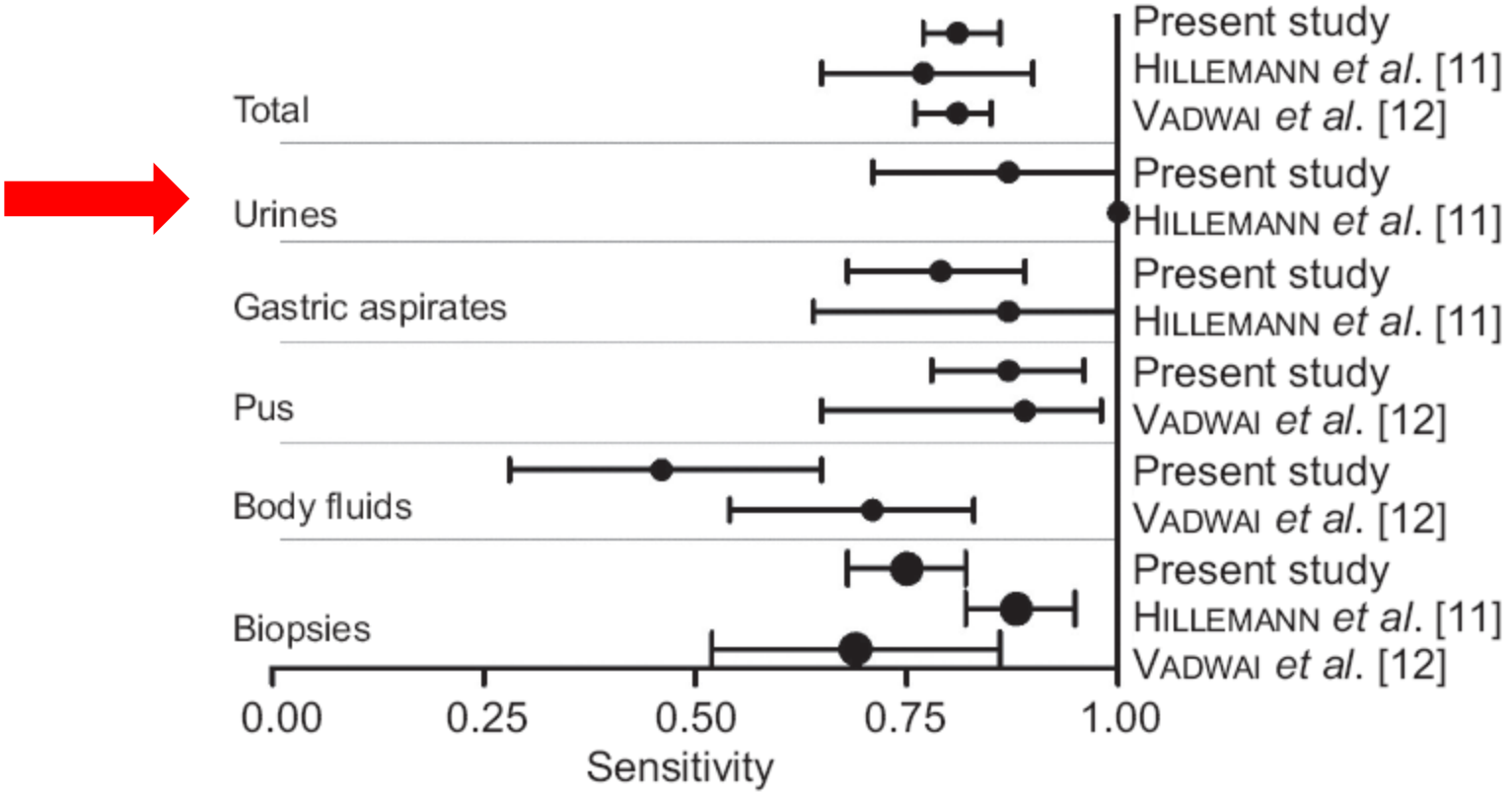


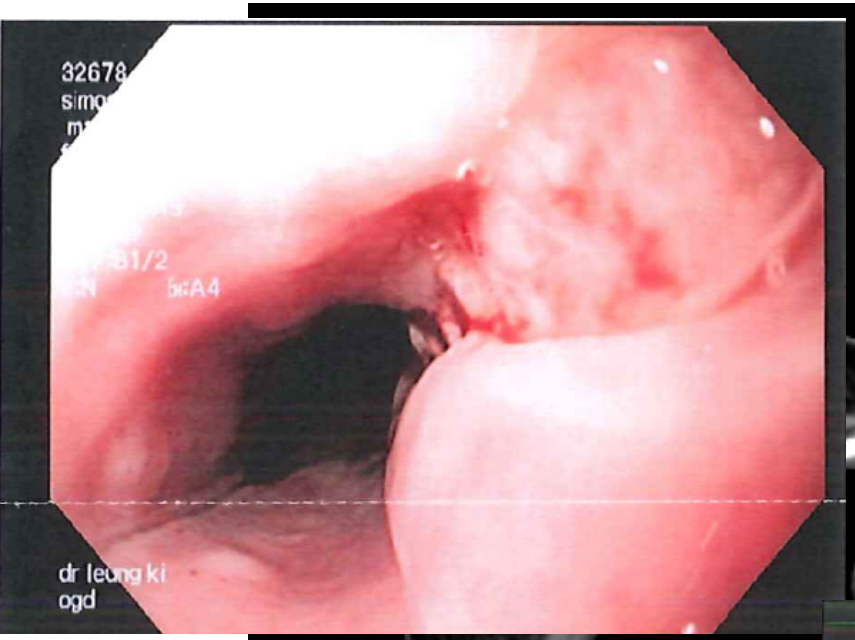
FIGURE 1. Forest plot comparing sensitivity estimates for *Mycobacterium tuberculosis* complex detection in different types of extrapulmonary samples. Three studies, including the present: only specimen types represented by at least 25 samples have been included.

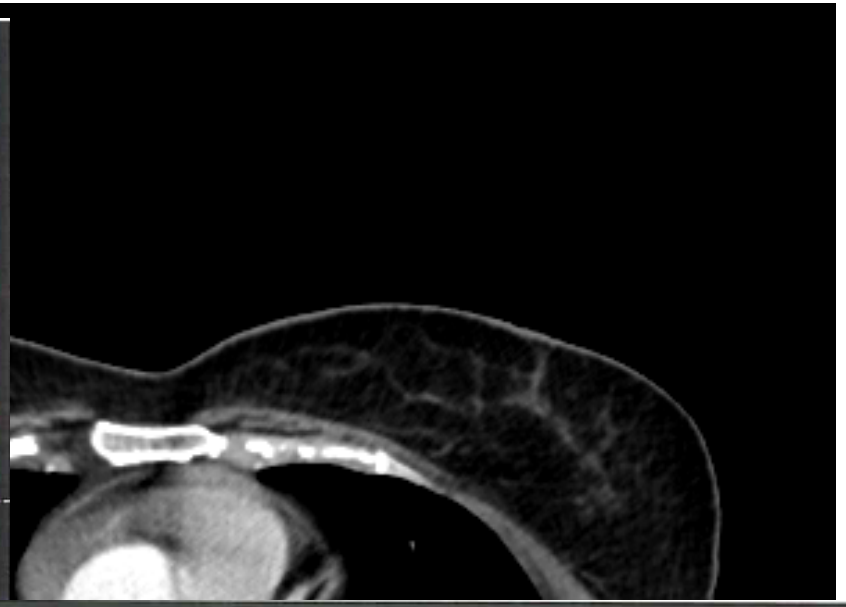
E Tortoli et al; Eur Respir J 2012

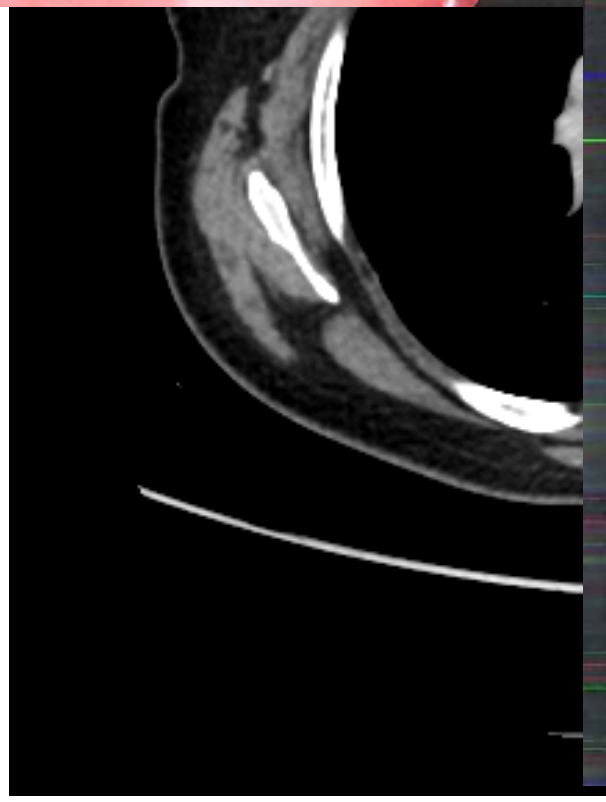
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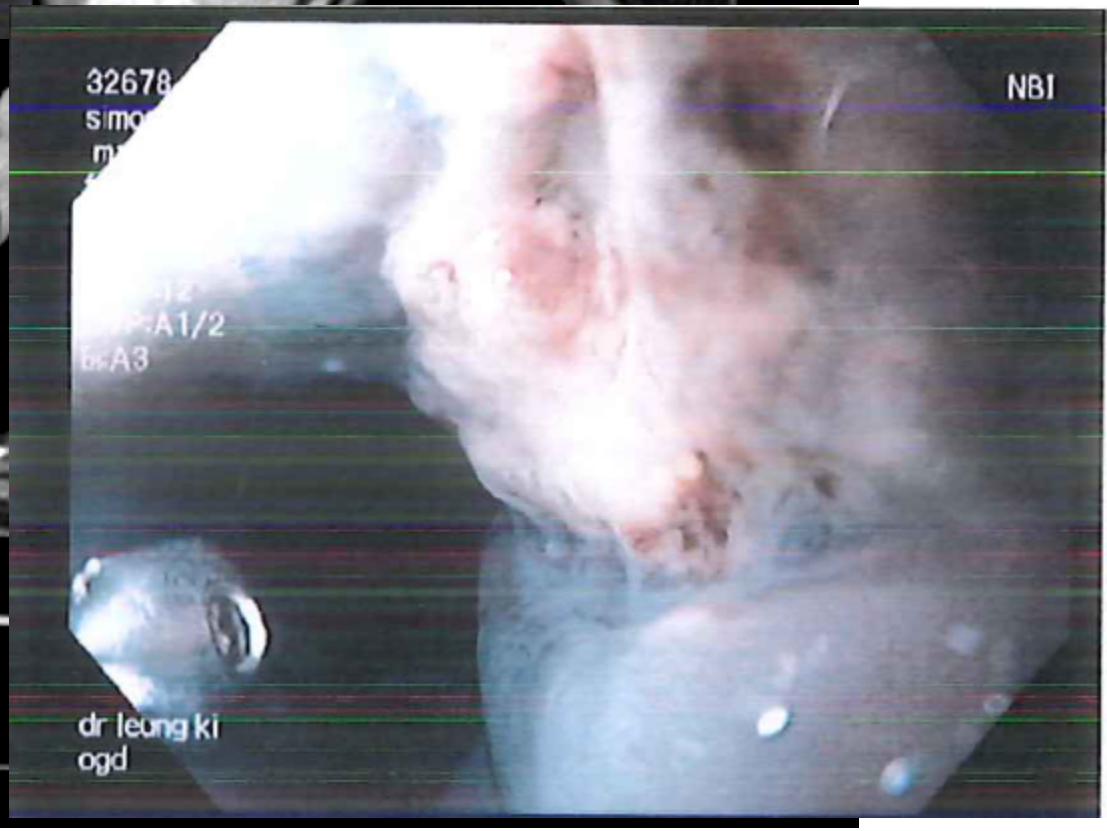
- *Atteinte pulmonaire concomitante (≈ 1/3 des cas)*
- *Plus fréquent lors de co-infection VIH*
- *Ascite: exsudat lymphocytaire*
- *CA-125 élevé lors d'atteinte péritonéale**
- *Diagnostic histo-pathologique le plus souvent par endoscopie (OGD, colonoscopie) ou par laparoscopie*

**: Younossian AB, Scand J Infect Dis 2006*


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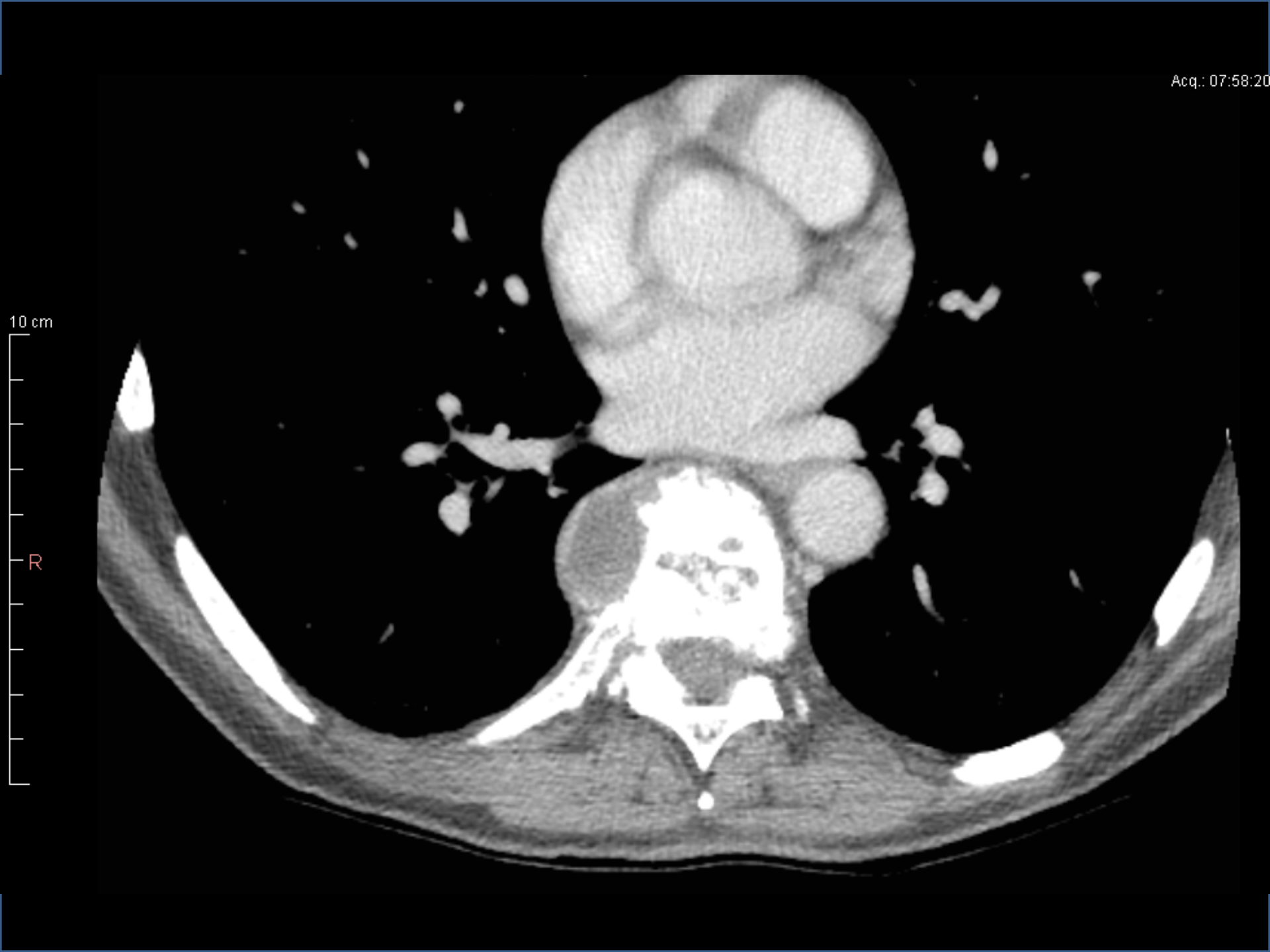


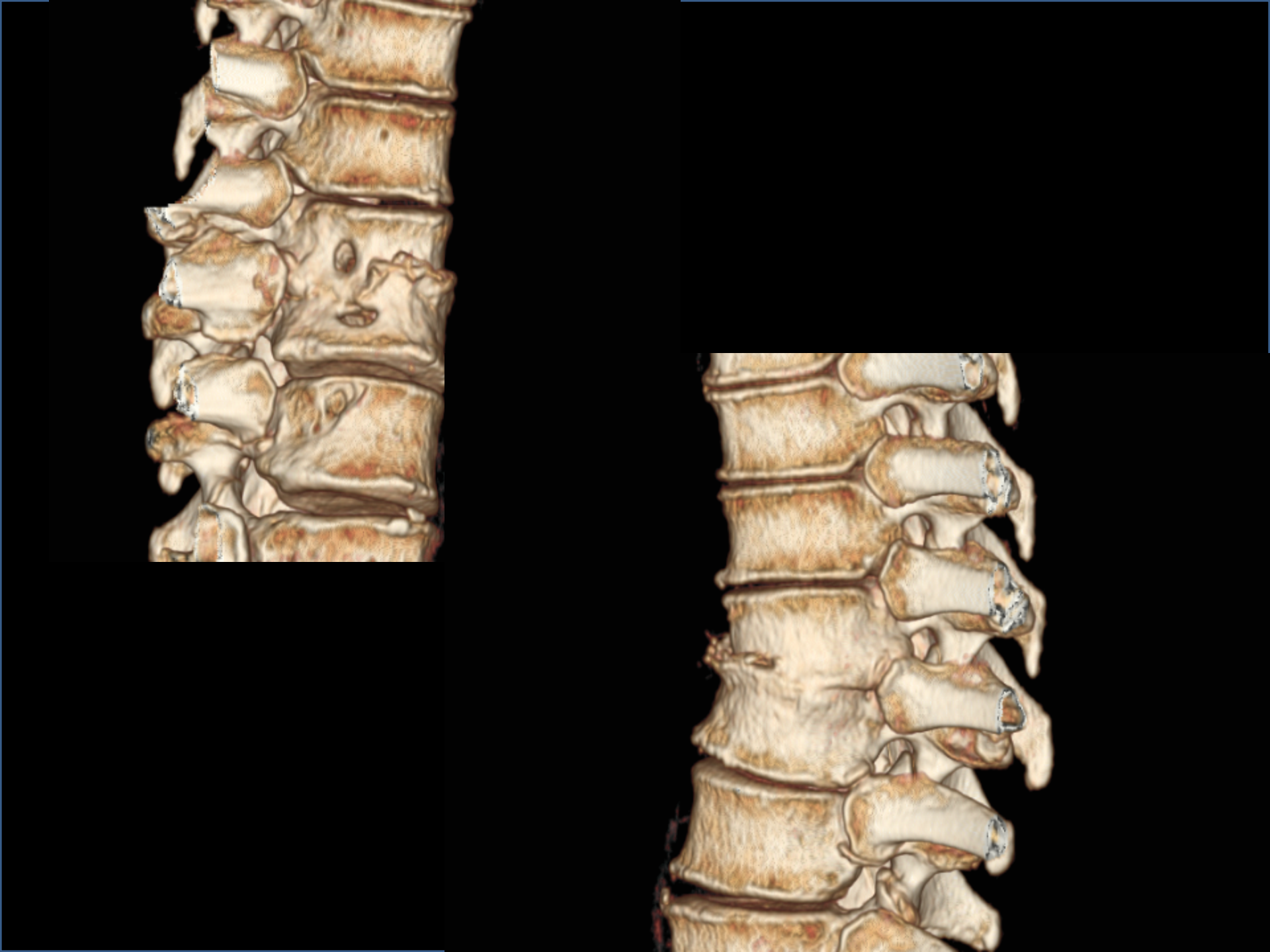



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NBI
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ogd



Sir Percival Pott
1714-1788


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Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis

Enrico Tortoli*, Cristina Russo#, Claudio Piersimoni¶, Ester Mazzola+, Paola Dal Monte§, Michela Pascarella/, Emanuele Borroni*, Alessandra Mondo**, Federica Piana##, Claudio Scarparo¶¶, Luana Coltella#, Giulia Lombardi§ and Daniela M. Cirillo*

- Biopsy specimens: Se: 86.6; Sp: 95.5; Positive LR: 19.1; Negative LR: 0.1
- Pleural fluid: Se: 33.3; Sp:99.0; Positive LR: 35.2; Negative LR: 0.7
- Pus Se: 85.1; Sp: 94.6; Positive LR: 15.7; Negative LR: 0.2
- Cavitary fluids: Se: 50.0 ; Sp: 100; Positive LR: --; Negative LR: 0.5
- All (Adults): Se: 79.0; Sp: 97.3; Positive LR: 28.8; Negative LR: 0.2

Eur Respir J 2012; 40: 442–447

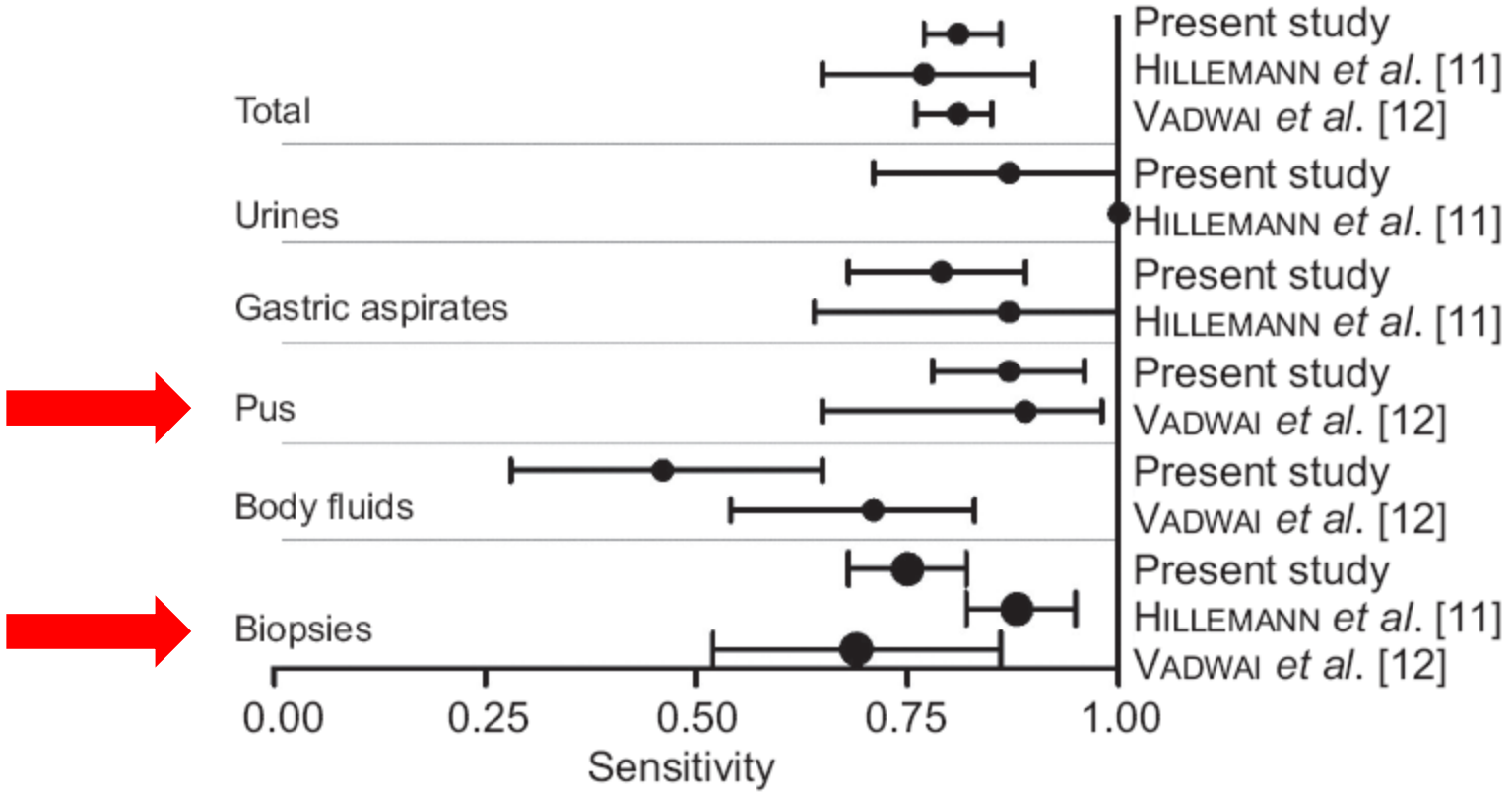


FIGURE 1. Forest plot comparing sensitivity estimates for *Mycobacterium tuberculosis* complex detection in different types of extrapulmonary samples. Three studies, including the present: only specimen types represented by at least 25 samples have been included.

E Tortoli et al; Eur Respir J 2012

Impact pour le traitement et pour le suivi d'un diagnostic de tuberculose extra-thoracique

- *<u>Réactions paradoxales</u>: plèvre, péricarde, adénites, SNC, voies urinaires, abcès sur Mal de Pott*
- *<u>Durée du traitement</u>: par ex: SNC: 9 – 12 mois*
- *<u>Surveillance radiologique spécifique</u>: plèvre, voies urinaires, spondylites (abcès), SNC (IRM), (adénites)*

Peut-on accepter un diagnostic de tuberculose sans confirmation microscopique et/ou par la culture ?

TB S-/C-

- La notion de tuberculose « abacillaire » (S- et culture négative, ou ∅ culture) est un concept bien accepté par les sociétés savantes et l'OMS

Case of TB A definite case of TB (defined above) or one in which a health worker (clinician or other medical practitioner) has diagnosed TB and decided to treat the patient with a full course of TB treatment.

Smear-negative pulmonary case of TB A patient with pulmonary TB not meeting the above criteria for smear-positive disease. Diagnostic criteria should include: at least two sputum smear examinations negative for AFB; radiographic abnormalities consistent with active pulmonary TB; no response to a course of broad-spectrum antibiotics (except in a patient for whom there is laboratory confirmation or strong clinical evidence of HIV infection); and a decision by a clinician to treat with a full course of anti-TB chemotherapy. A patient with positive culture but negative AFB sputum examinations is also a smear-negative case of pulmonary TB.

- Même la biologie moléculaire n'a pas une sensibilité (ni une spécificité) de 100%
- L'histopathologie permet parfois de confirmer un diagnostic S-/C-

Extrapulmonary case of TB A patient with TB of organs other than the lungs (e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges). Diagnosis should be based on one culture-positive specimen, or histological or strong clinical evidence consistent with active extrapulmonary disease, followed by a decision by a clinician to treat with a full course of anti-TB chemotherapy. A patient in whom both pulmonary and extrapulmonary TB has been diagnosed should be classified as a pulmonary case.

« Take home messages »

- Les TB-ET représentent ≈ 30% des TB; les adénites sont les TB-ET les plus fréquentes
- Leur diagnostic est souvent malaisé: il dépend beaucoup de la suspicion clinique qui elle dépend avant tout de l'épidémiologie (incidence de la TB dans le pays d'origine)
- La confirmation bactériologique et/ou par PCR n'est pas la règle car les TB-ET sont le plus souvent pauci-bacillaires
- Les systèmes Xpert TB/RIF Ultra ont révolutionné le diagnostic de la plupart des formes de TB ET, mais ont souvent une sensibilité insuffisante pour exclure la maladie



Lagos, Nigeria

LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Difficultés dans le suivi des patients tuberculeux

Jean-Pierre Zellweger
Ligue pulmonaire Suisse

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Traitement de la tuberculose en pratique

Le traitement de la tuberculose est efficace mais

- long (6 mois)
- compliqué (4, puis 2 médicaments)
- coûteux (franchise, participation, déplacements, contrôles)
- décourageant (à suivre malgré l'amélioration des signes de maladie)
- pas toujours bien toléré

Quelques problèmes de suivi:

Erreurs de traitement

Tolérance du traitement

Interruptions et abandons

Mobilité des patients

Supervision

Les risques d’erreurs:

Sélection volontaire ou involontaire de médicaments

Sous-dosage (même avec les préparations combinées)

Malrésorption (surtout rifampicine)

Interactions médicamenteuses

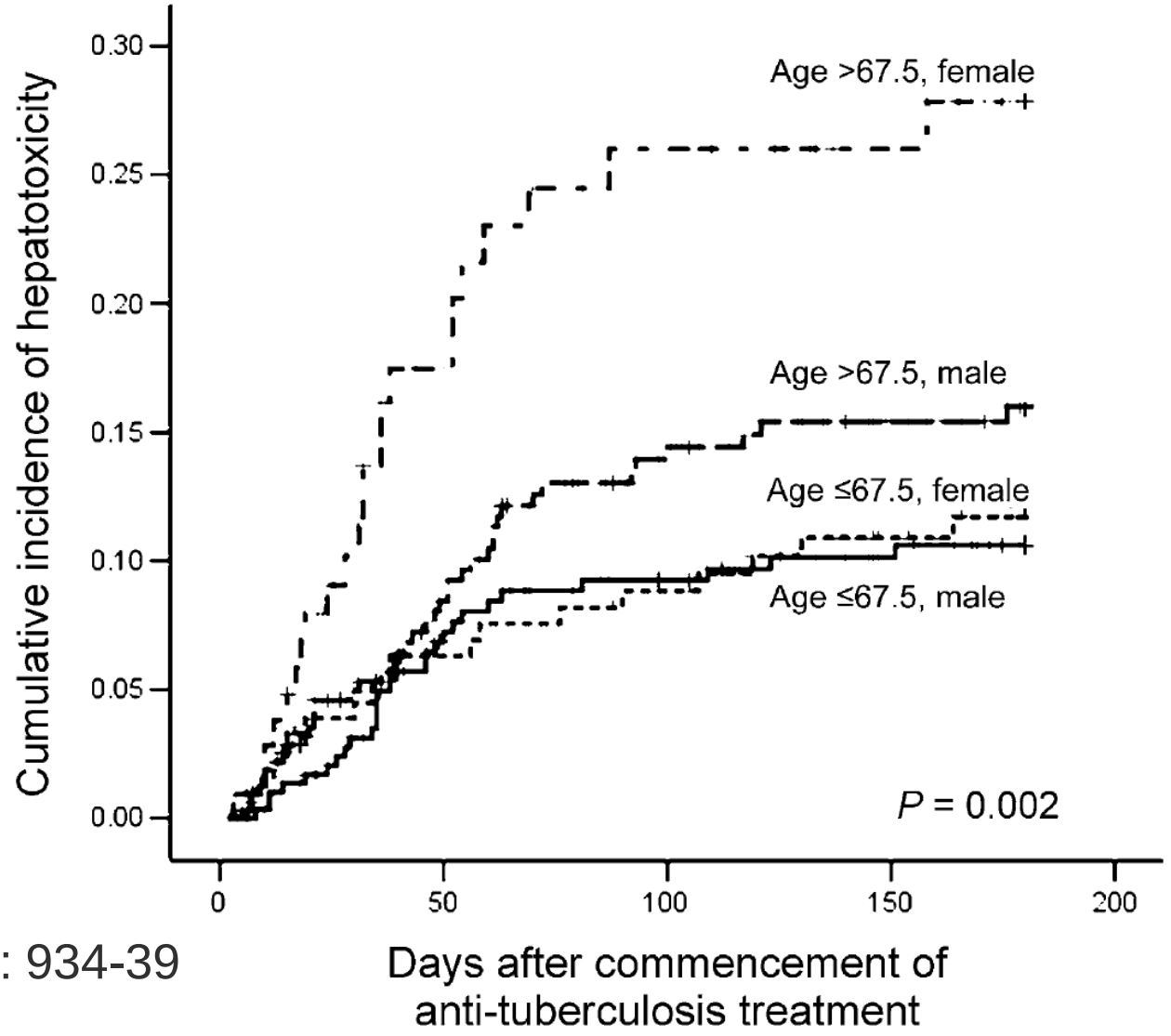
Effets indésirables: fréquence et facteurs de risque

Table 2. – Number of side-effects due to isoniazid, rifampin or pyrazinamide followed by final termination of one of the drugs (n=519)

Side-effect	Isoniazid	Rifampin	Pyrazinamide	Total
Hepatotoxicity	19 (4)	8 (1.5)	28 (5)	55 (11)
Arthralgia	1 (0.2)		12 (2)	13 (2)
Exanthema	6 (1.2)		27 (5)	33 (6)
CNS toxicity*	8 (1.5)			8 (1.5)
Nausea			5 (0.9)	5 (0.9)
Others#			7 (1.4)	7 (1.4)
Total	34 (7)	8 (1.5)	79 (15)	121 (23)

Schaberg T, Eur Respir J 1996;9:2026-30

Hépatotoxicité des antituberculeux, par sexe et classe d'âge



Shu CC, IJTLD 2013; 17(7): 934-39

Hépatotoxicité de l'isoniazide

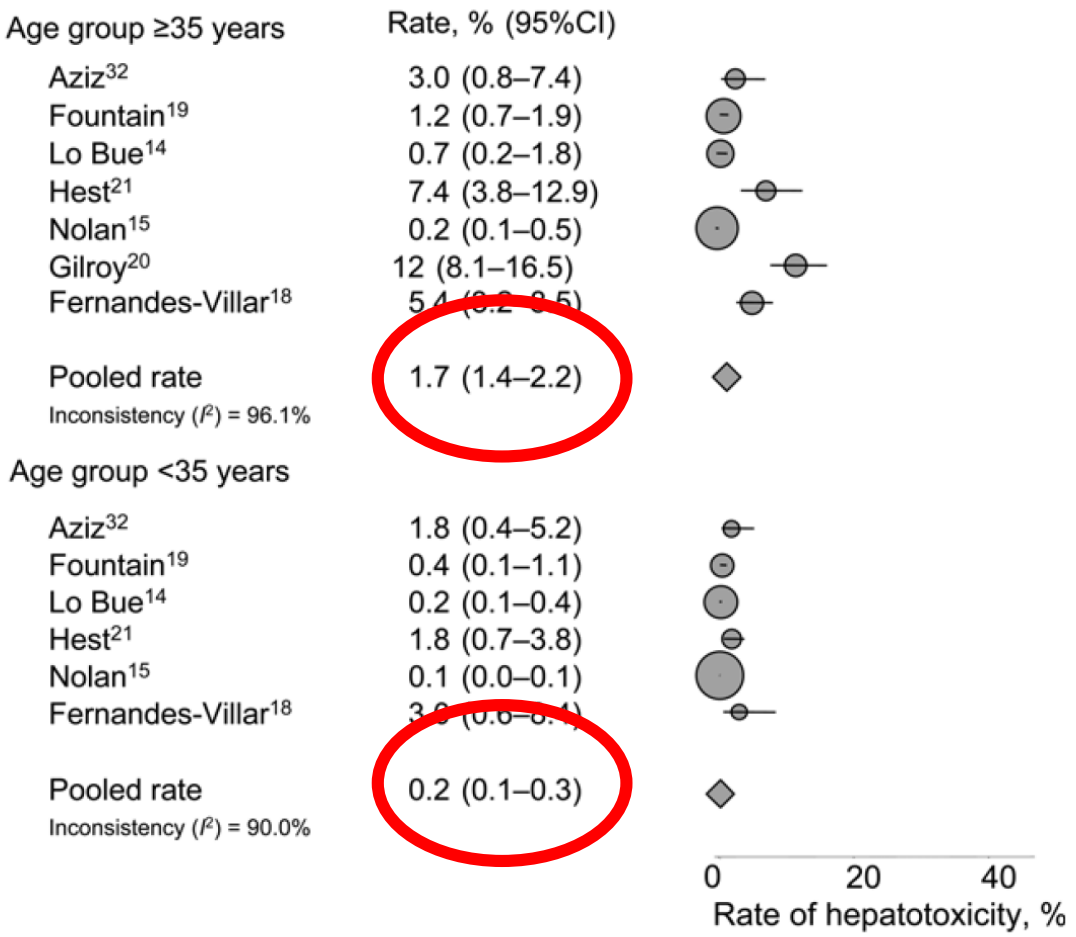
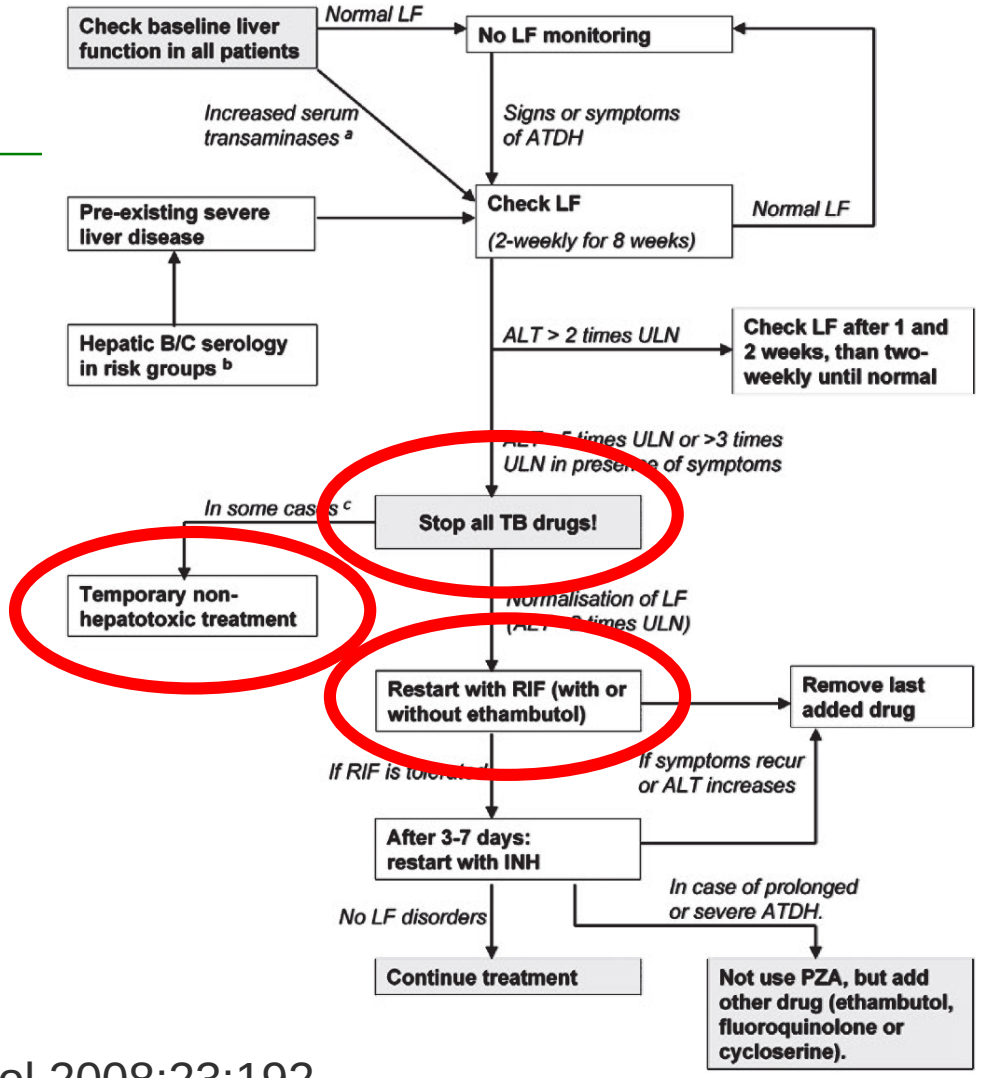


Figure 3 Age-related rates of hepatotoxicity in treatment for latent tuberculosis infection. Data for individual studies pre-

Kunst H, IJTLD 2010;14(11):1374-81

Attitude face à l'hépatotoxicité



Tostman A, J Gastroentorol and Hepatol 2008;23:192

Effets indésirables: fréquence et facteurs de risque

Table 4. – Multivariate analysis* of risk factors for severe side-effects of standard antituberculosis therapy

Risk factor	OR	95% CI	Likelihood	p-value
History of hepatitis	3.4	1.6–7.6	8.0	0.0026
Age ≥60 yrs	1.9	1.2–3.2	5.6	0.017
Female gender	1.6	1.0–2.5	3.5	0.06
Diabetes mellitus	1.2	0.45–2.6	0.1	0.75
Previous TB therapy	1.3	0.3–2.1	0.3	0.56

Une nouvelle menace: prolongation de l'intervalle QTc

Plusieurs antituberculeux utilisés pour le traitement de la TB multirésistante (ou en remplacement des antituberculeux de base) peuvent prolonger l'intervalle QTc (risque d'arythmie léthale)

Les médicaments les plus souvent incriminés sont les fluoroquinolones, la clofazimine, la bedaquiline et le delamanid.

Les facteurs associés qui augmentent le risque de prolongation de l'espace QTc sont l'hypokaliémie, l'hypomagnésiémie et l'hypocalcémie ainsi que l'infection VIH ainsi que les variantes génétiques (QTc long)

INT J TUBERC LUNG DIS 22(12):1411–1421
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http://dx.doi.org/10.5588/ijtld.18.0423

QTc and anti-tuberculosis drugs: a perfect storm or a tempest in a teacup? Review of evidence and a risk assessment

I. Monedero-Recuero,* L. Hernando-Marrupe,† A. Sánchez-Montalvá,‡ V. Cox,§ M. Tommasi,¶ J. Furin,# C-Y. Chiang,*,**†† M. Quelapio,¶ K. G. Koura,*‡‡ A. Trébucq,* X. Padanilam,§§ G. Dravniece,¶ A. Piubello*

Table A.2 QTc-prolonging drugs commonly used during TB management

Type of drug	Specific drug	Observations
Anti-tuberculosis drugs		
	Moxifloxacin	Considered the most QTc-prolonging drug among the fluoroquinolones. Estimated QTc increased by 10–20 msec
	Gatifloxacin	QTc prolongation potential. Considered safer than moxifloxacin
	Levofloxacin	QTc prolongation potential. Considered safer than moxifloxacin
	Clofazimine	Few studies and lack of sufficient evidence. Estimated QTc increased by 10–20 msec
	Bedaquiline	Peak in QTc prolongation thought to occur 8 weeks after starting the drug. Estimated QTc increased by 10–15 msec
	Delamanid	Peak in QTc prolongation thought to occur 8 weeks after starting the drug. Estimated QTc increased by 5–15 msec
	Capreomycin	May prolong QTc due to hypopotassaemia and renal function deterioration
	Amikacin, kanamycin	May prolong QTc due to renal function deterioration

Risque de troubles du rythme sévères

Severe drug-related cardiac adverse events have rarely been reported in DR-TB patients and are largely associated with other additive risk factors. The combination of risk factors is likely far more important in the development of arrhythmia than the use of QTc-prolonging drugs alone. According to the evidence reviewed here, the benefits of using QTc-prolonging drugs outweigh the risks in DR-TB patients.

Attitude avant le début du traitement

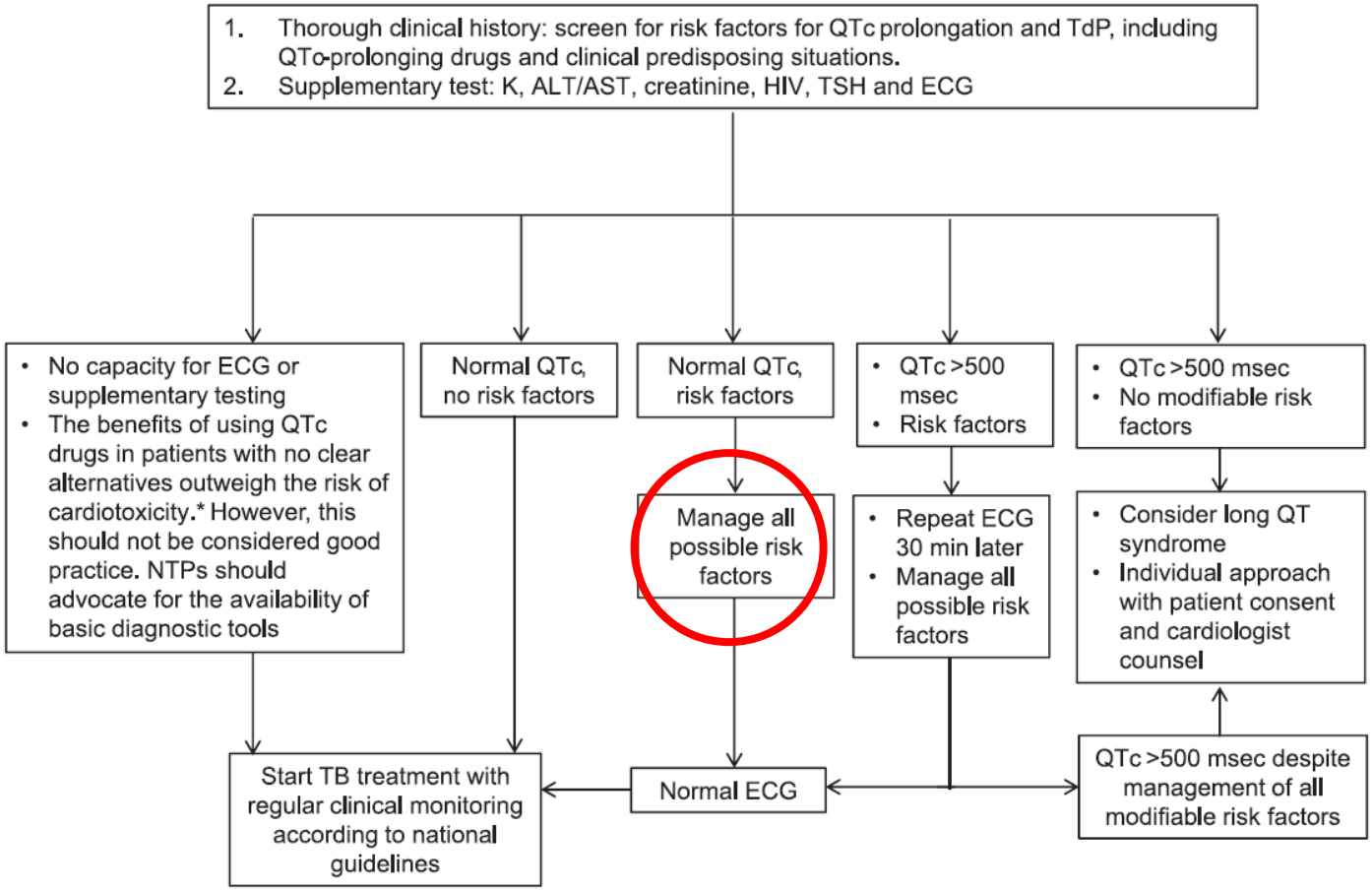


Figure A.1 Algorithm for action and baseline assessment according to the current evidence in TB patients who are candidates to receive multiple QTc-prolonging drugs. QTc = corrected QT interval; TdP = torsade de pointes; K = potassium; ALT = alanine transaminase; AST = aspartate transaminase; HIV = human immunodeficiency virus; TSH = thyroid stimulating hormone; ECG = electrocardiogram; NTP = National TB Control Programme.

Attitude en cours de traitement

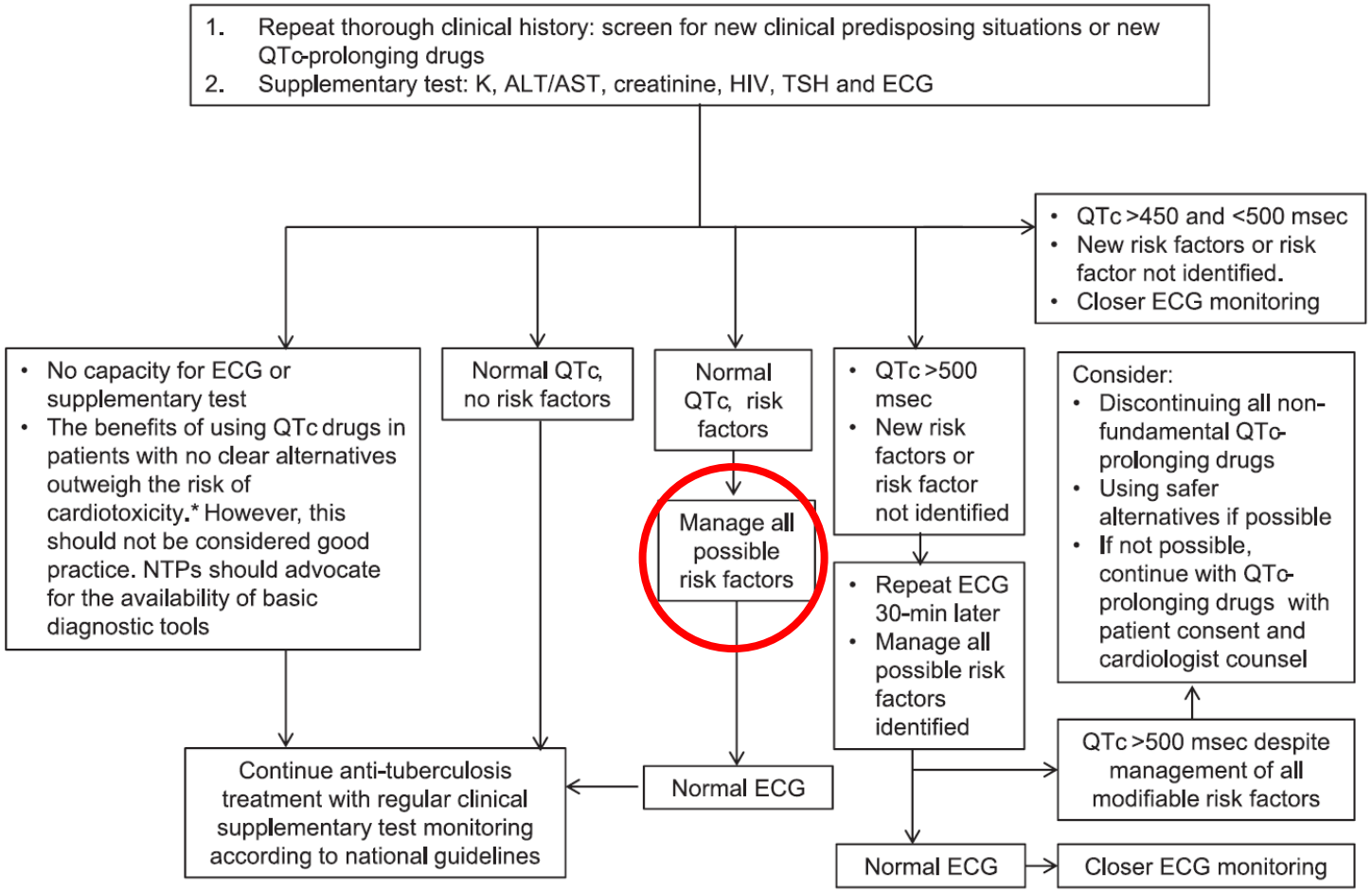


Figure A.2 Periodic assessment for TB patients using multiple QTc-prolonging drugs. Algorithm for action and monitoring assessment according to the current evidence in TB patients who are candidates to receive multiple QTc-prolonging drugs. QTc = corrected QT interval; K = potassium; ALT = alanine transaminase; AST = aspartate transaminase; HIV = human immunodeficiency virus; TSH = thyroid-stimulating hormone; ECG = electrocardiogram; NTP = National TB Control Programme.

Suivi du traitement et interruptions

La tendance naturelle de l'être humain est d'interrompre le traitement médical dès que les symptômes de maladie s'atténuent.

La difficulté est donc de maintenir le traitement jusqu'au terme prévu

Le taux de succès du traitement attendu par l'OMS (85%) n'est souvent pas atteint.

Le taux de succès du traitement avant 1990 ne dépassait pas 70% dans le canton de Vaud, 71% à Zürich et 79% en Suisse

Issue du traitement chez 178 patients tuberculeux licenciés de l'hôpital (NY 1991)

COMPLIANCE AND OUTCOME OF 178 PATIENTS DISCHARGED ON TUBERCULOSIS TREATMENT

	No.	(%)
Compliant		
Cured	7	(4)
In treatment	10	(6)
Died of AIDS	2	(1)
Total	19	(11)
Noncompliant		
No follow-up treatment	99	(56)
Lost to follow-up		
< 3 months treatment	49	(28)
> 3 months treatment	11	(6)
Total	159	(89)

TABLE 5

OUTCOME OF 48 PATIENTS LOST TO FOLLOW-UP AND READMITTED WITH ACTIVE TUBERCULOSIS*

Outcome	No.
Died in hospital	7
Remain in hospital	1
Discharged	40
Again lost to follow-up	35†
Placed in TB homeless shelter	1
Follow-up < 30 days	4

* Culture positive.

† Of these patients eight were admitted a third time with active TB.

Brudney, K and Dobkin, J., Am Rev Respir J 1991;144:745

TABLE 2

DEMOGRAPHIC FEATURES OF 224 CONSECUTIVE TUBERCULOSIS INPATIENTS

Feature	%	No.
Male	79	177/224
Alcoholic	53	103/196*
Homeless	45	85/189*
Unstably housed	23	43/189*
Stably housed	32	61/189*
Unemployed	82	171/208*
AIDS/ARC	40	89/224
Age, mean yr ± SD	42.5	12.4

* These denominators include only those patients on whom the information was obtained and are therefore less than the total 224.

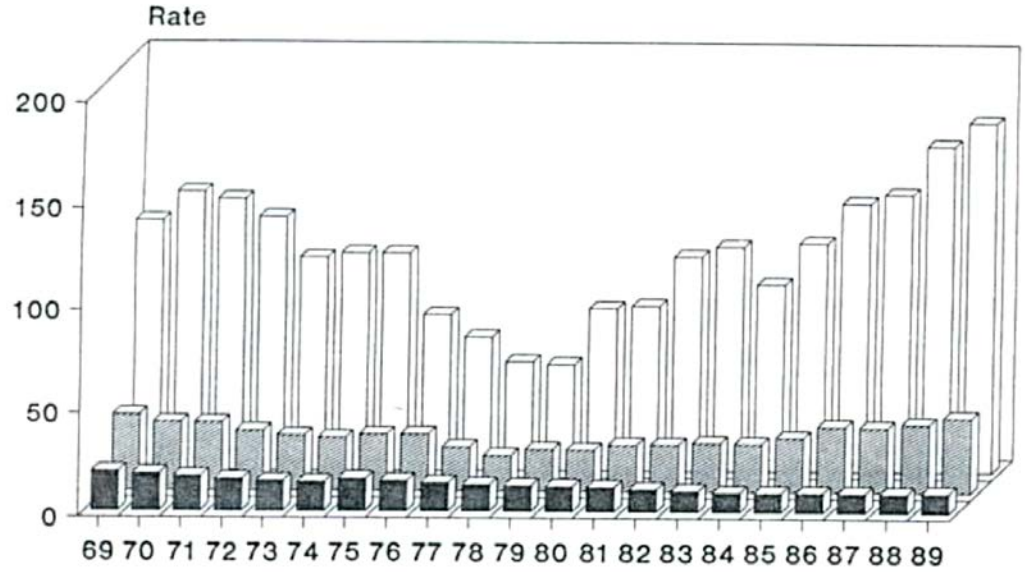


Fig. 1. Tuberculosis case rates for the United States, New York City, and central Harlem from 1969 to 1989 per 100,000 population. Closed bars = United States; hatched bars = New York City; shaded bars = Harlem.

Traitement supervisé ou non?

La supervision du traitement antituberculeux diminue le risque de rechutes et de création de résistances

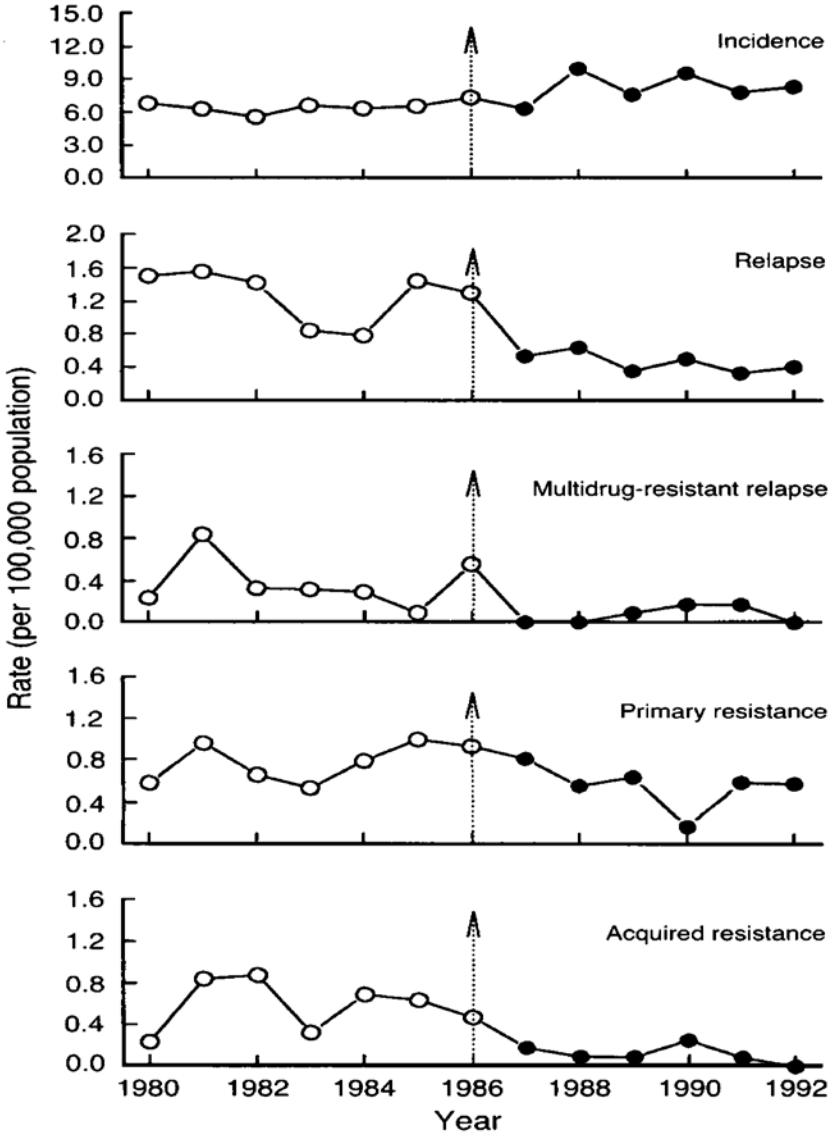


Figure 1. Incidence of *M. tuberculosis* and Rates of Relapse, Relapse with Multidrug-Resistant Tuberculosis (Multidrug-Resistant Relapse), Primary Resistance, and Acquired Resistance from 1980 through 1992.

The rates have been adjusted for increases in the population of Tarrant County, Texas. The arrow indicates the change from traditional to directly observed drug therapy.

Weis S., NEJM 1994;330;1179-84

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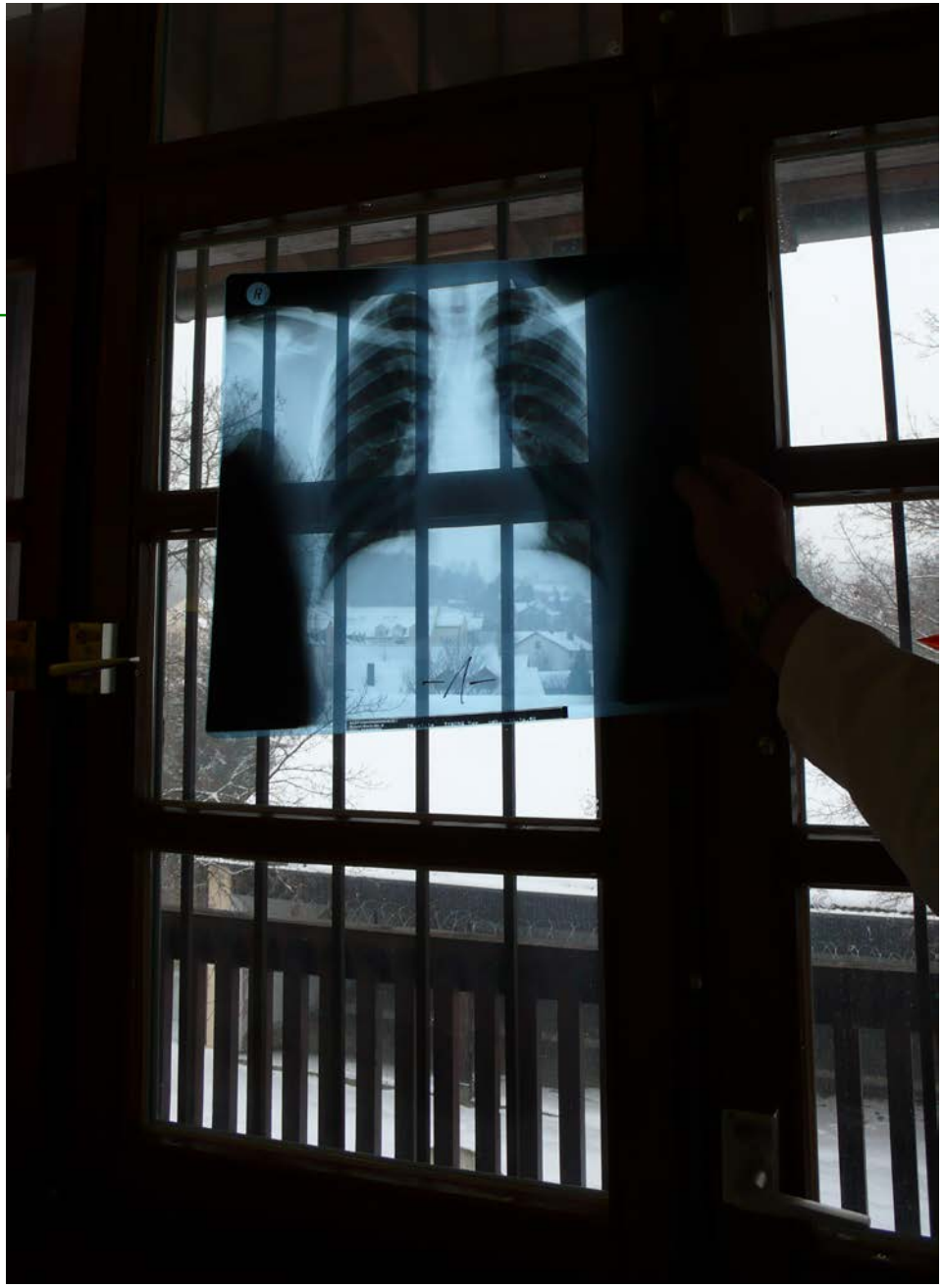
Inclusion du traitement supervisé dans la stratégie OMS

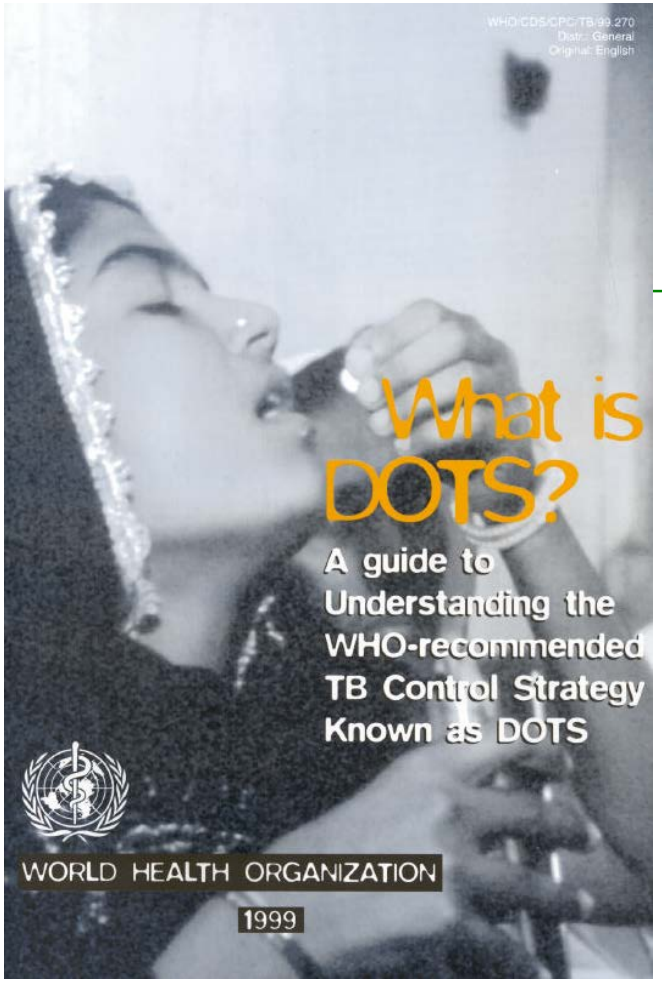
Vu la proportion élevée d'abandons et de rechutes dans les groupes marginalisés ou à risque et l'effet apparemment favorable de la supervision, le traitement supervisé (DOT) a été inclus dans la stratégie globale de lutte antituberculeuse de l'OMS (DOTS).

Dans certains programmes, la non-adhérence a mené à l'hospitalisation forcée, voire à l'incarcération des patients récalcitrants.

Hôpital pénitentiaire pour patients tuberculeux récalcitrants







· Government commitment to sustained TB control activities.

· Case detection by sputum smear microscopy.

· Standardized treatment regimen of six to eight months …with directly observed treatment(DOT) for at least the initial two months.

· A regular, uninterrupted supply of all essential anti-TB drugs.

· A standardized recording and reporting system that allows assessment of treatment results.

Directly observed treatment (DOT)—watching patients taking their medications—is essential at least during the intensive phase of treatment (the first two months)



DOT à Lausanne

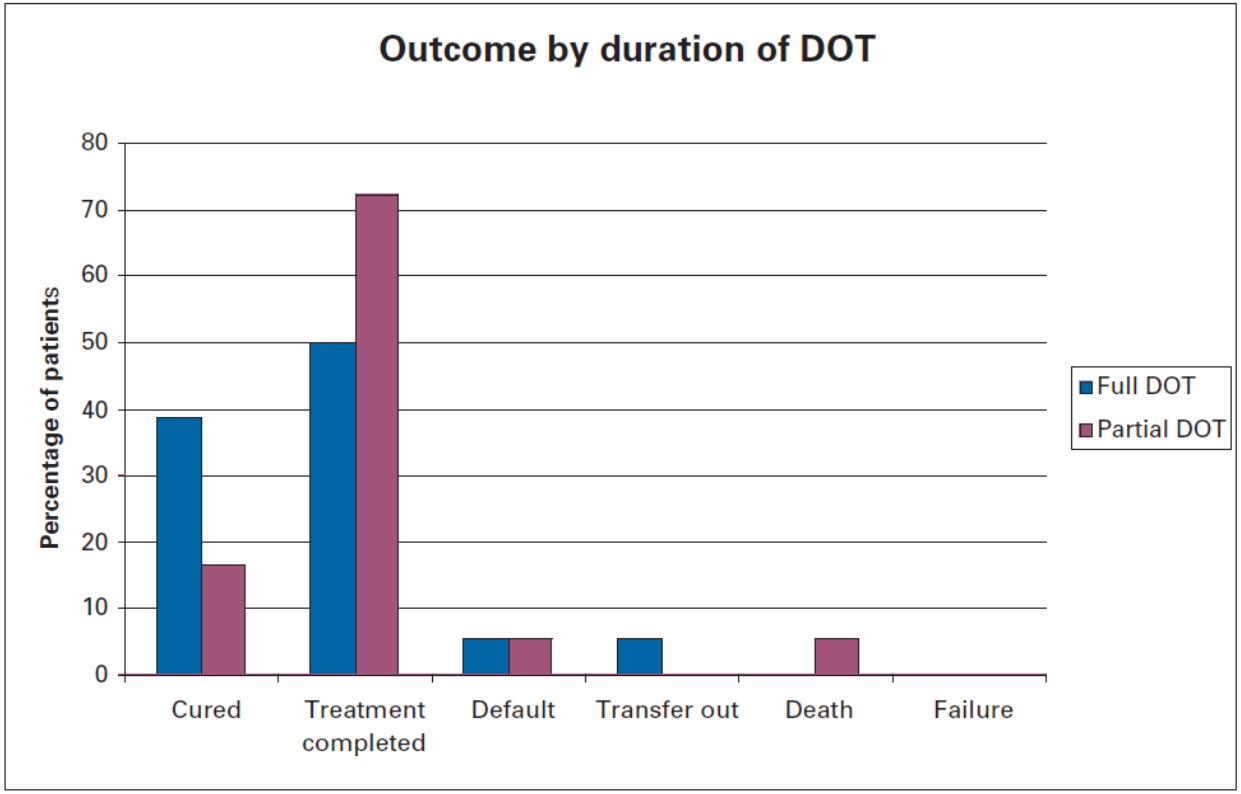
et à Cotonou



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Résultats du traitement antituberculeux après la mise en place de la supervision (dispensaire antituberculeux Lausanne)

Figure 2
Outcome of treatment by duration of DOT.
Full DOT = whole duration of treatment. Partial DOT = intensive phase only. Favourable outcome (cured and treatment completed) is similar for both groups (88.9%), with no statistical difference (p = 1.00).



Deruaz J et Zellweger JP, Swiss Med Wkly 2004;134:552

Controverses sur le DOT

Plusieurs études randomisées n’ont pas montré d’avantages du traitement supervisé sur le traitement non supervisé

D’autres études concluent à une diminution du risque de résistance acquise

Le DOT est en général plus coûteux que le traitement individuel, surtout si le patient doit se déplacer

Le DOT est parfois vue comme une intrusion intolérable et une limitation de la liberté du patient

Cochrane review (2015)

Directly observed therapy (DOT) versus self-administered TB treatment

Patient or population: Patients on TB treatment
Settings: Low-, middle- or high-income countries
Intervention: DOT
Comparison: Self-administered therapy

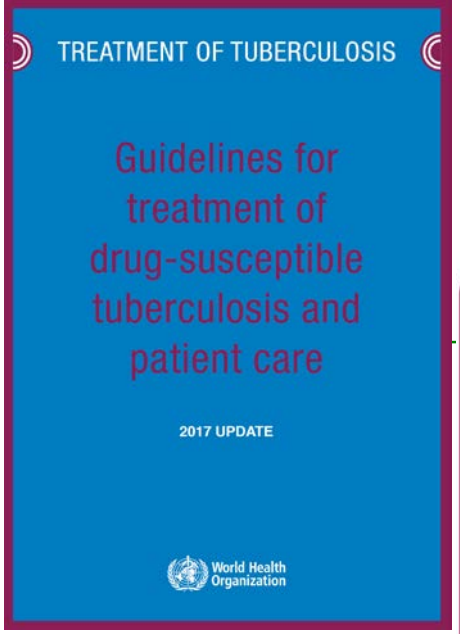
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)
	Assumed risk	Corresponding risk	
	Self-administered therapy	DOT	
Cure Follow-up: up to 6 months	617 per 1000	666 per 1000 (561 to 784)	RR 1.08 (0.91 to 1.27)
Treatment completion Follow-up: 2 to 8 months[5]	709 per 1000	751 per 1000 (680 to 829)	RR 1.07 (0.96 to 1.19)

Cochrane systematic review of directly observed therapy for treating tuberculosis: good analysis of the wrong outcome

Le bénéfice principal de la supervision est la diminution des rechutes et du risque de création de résistances (et non du taux de guérison)

La non-adhérence existe aussi avec la DOT

La DOT à elle seule ne résout pas le problème de la non adhérence



Position actuelle de l'OMS

Recommendations

2.1.1 Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment (Strong recommendation, moderate certainty in the evidence)

2.1.2 A package of treatment adherence interventions[25] may be offered to patients on TB treatment in conjunction with the selection of a suitable treatment administration option[26] (Conditional recommendation, low certainty in the evidence)

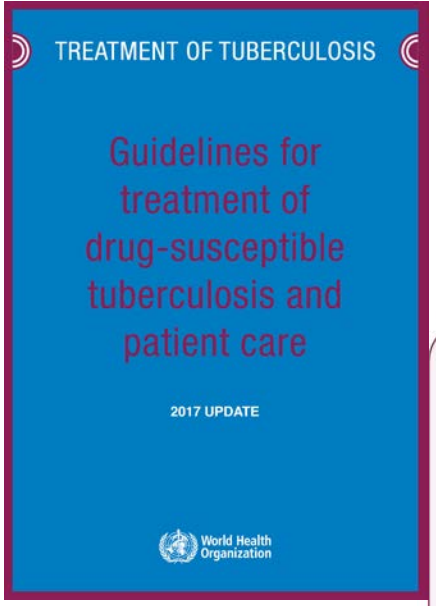
2.1.3 One or more of the following treatment adherence interventions (complementary and not mutually exclusive) may be offered to patients on TB treatment or to health-care providers:

a) tracers[27] and/or digital medication monitor[28] (Conditional recommendation, very low certainty in the evidence)

b) material support[29] to patient (Conditional recommendation, moderate certainty in the evidence)

c) psychological support[30] to patient (Conditional recommendation, low certainty in the evidence)

d) staff education[31] (Conditional recommendation, low certainty in the evidence).



Recommendations

2.1.4 The following treatment administration options may be offered to patients on TB treatment:

a) Community- or home-based DOT is recommended over health facility-based DOT or unsupervised treatment (Conditional recommendation, moderate certainty in the evidence).

b) DOT administered by trained lay providers or health-care workers is recommended over DOT administered by family members or unsupervised treatment (Conditional recommendation, very low certainty in the evidence).

c) Video observed treatment (VOT) may replace DOT when the video communication technology is available and it can be appropriately organized and operated by health-care providers and patients (Conditional recommendation, very low certainty in the evidence).

Recommandations actuelles (Manuel TB 2019)

Pour ces raisons, la surveillance directe est recommandée dans certaines situations, en particulier:

- chez les patients avec qui il est difficile de communiquer,
- chez les patients aux conditions sociales instables ou présentant des troubles mentaux ou cognitifs,
- chez les patients qui ont déjà eu un ou plusieurs traitements ou qui reçoivent un traitement contre la tuberculose multirésistante.

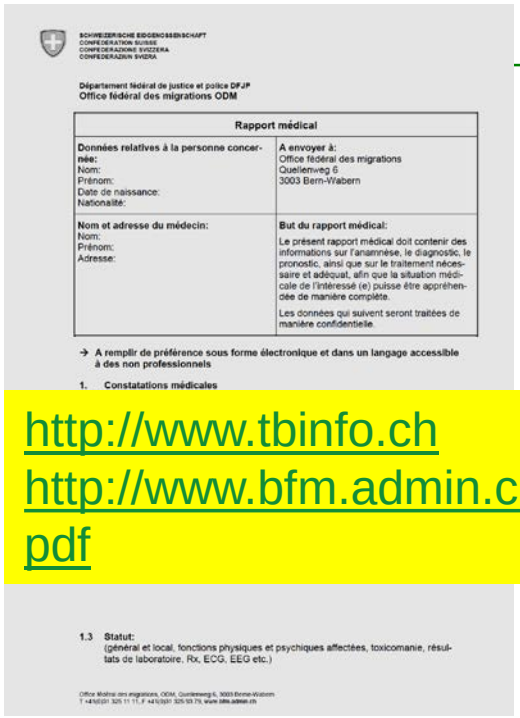
Prise en charge de la TB chez les migrants

Les migrants atteints de TB doivent recevoir un traitement adéquat, quel que soit leur statut juridique

Le traitement doit être mené jusqu'à son terme, si nécessaire de manière supervisée

- Déclaration à la santé publique
- Transmission des informations en cas de déplacement
- Gestion des obstacles financiers, légaux, personnels et culturels
- Demande de suspension de renvoi à adresser au Secrétariat pour les Migrations

Rapport médical au Secrétariat pour les Migrations



SCHWEIZERISCHE EIDGENOSSENSCHAFT
CONFÉDÉRATION SUISSE
CONFEDERAZIONE SVIZZERA
CONFEDERAZIUN SVIZRA

Département fédéral de justice et police DFJP
Office fédéral des migrations ODM

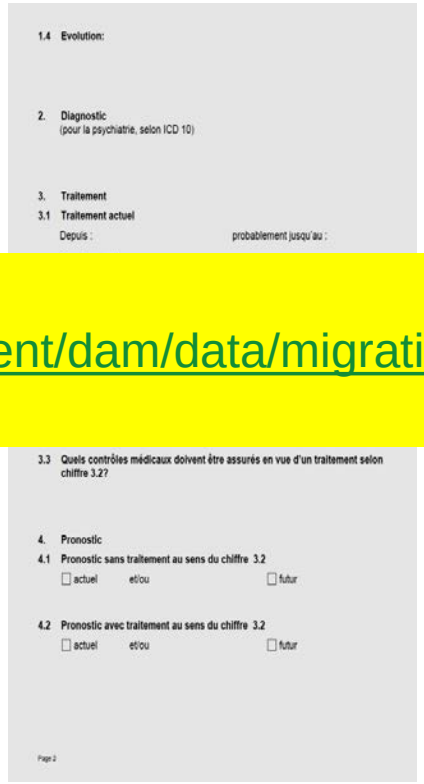
Rapport médical

Données relatives à la personne concernée: Nom: Prénom: Date de naissance: Nationalité:	**A envoyer à:** Office fédéral des migrations Quellenweg 6 3003 Bern-Wabern
Nom et adresse du médecin: Nom: Prénom: Adresse:	**But du rapport médical:** Le présent rapport médical doit contenir des informations sur l'anamnèse, le diagnostic, le pronostic, ainsi que sur le traitement nécessaire et adéquat, afin que la situation médicale de l'intéressé (e) puisse être appréhendée de manière complète. Les données qui suivent seront traitées de manière confidentielle.

→ **A remplir de préférence sous forme électronique et dans un langage accessible à des non professionnels**

1. Constatations médicales

1.3 Statut:
(général et local, fonctions physiques et psychiques affectées, toxicomanie, résultats de laboratoire, Rx, ECG, EEG etc.)



1.4 Evolution:

2. Diagnostic
(pour la psychiatrie, selon ICD 10)

3. Traitement
3.1 Traitement actuel
Depuis : probablement jusqu'au :

3.3 Quels contrôles médicaux doivent être assurés en vue d'un traitement selon chiffre 3.2?

4. Pronostic
4.1 Pronostic sans traitement au sens du chiffre 3.2
☐ actuel et/ou ☐ futur

4.2 Pronostic avec traitement au sens du chiffre 3.2
☐ actuel et/ou ☐ futur

Page 2



5. Possibilités de traitement dans les pays d'origine
Dans le cadre de la procédure, l'Office fédéral des migrations examine d'office la question des possibilités de traitement dans le pays d'origine qui peuvent être complétées par des mesures d'aide médicale au retour.

5.1 Connaissez-vous éventuellement un médecin ou une structure médicale qui

6. Remarques éventuelles du médecin

L'Office fédéral des migrations vous prie de bien vouloir désigner avec précision les éventuels rapports médicaux établis par des hôpitaux ou des médecins-spécialistes, afin qu'ils puissent être, en cas de nécessité, demandés par un expert médical.

Annexes:

(Lieu et date) (Timbre et signature du médecin)

Envoyez svp ce formulaire par la poste! Meilleures salutations

Page 3

http://www.tbinfo.ch
http://www.bfm.admin.ch/content/dam/data/migration/downloads/aerztlicher_berichtf.pdf

Conclusions (1)

Le traitement de la tuberculose est long, difficile, cher et ennuyeux!

Les erreurs et les problèmes sont fréquents en cours de traitement

La supervision peut aider à diminuer les risques d’interruption, de rechute et de résistance acquise

La supervision en soi ne suffit pas mais doit être accompagnée d’une série de mesures pratiques destinées à soutenir le patient et à faciliter l’adhérence thérapeutique

Ce que voit le patient:




Ce qu’il devrait recevoir:



28. Tuberkulose-Symposium Magglingen

Patientenbetreuung und Erhebung von Therapieresultaten

Tanja Schneider, Lungenliga St.Gallen-Appenzell
Bea Začek, LUNGE ZÜRICH

LUNGE ZÜRICH
Hilft. Informiert. Wirkt.

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ST.GALLEN – APPENZELL

Administrative monitoring of tuberculosis treatment in Switzerland

S. Guglielmi,* J. Barben,† L. Horn,† O. D. Schoch*†

* Pulmonary Division, Kantonsspital, St Gallen, † Cantonal Lung Association, St Gallen, Switzerland

Hintergrund: Der Erfolg der TB-Behandlung wird bestimmt durch die Adhärenz, die durch Directly observed treatment (DOT) gewährleistet werden kann.

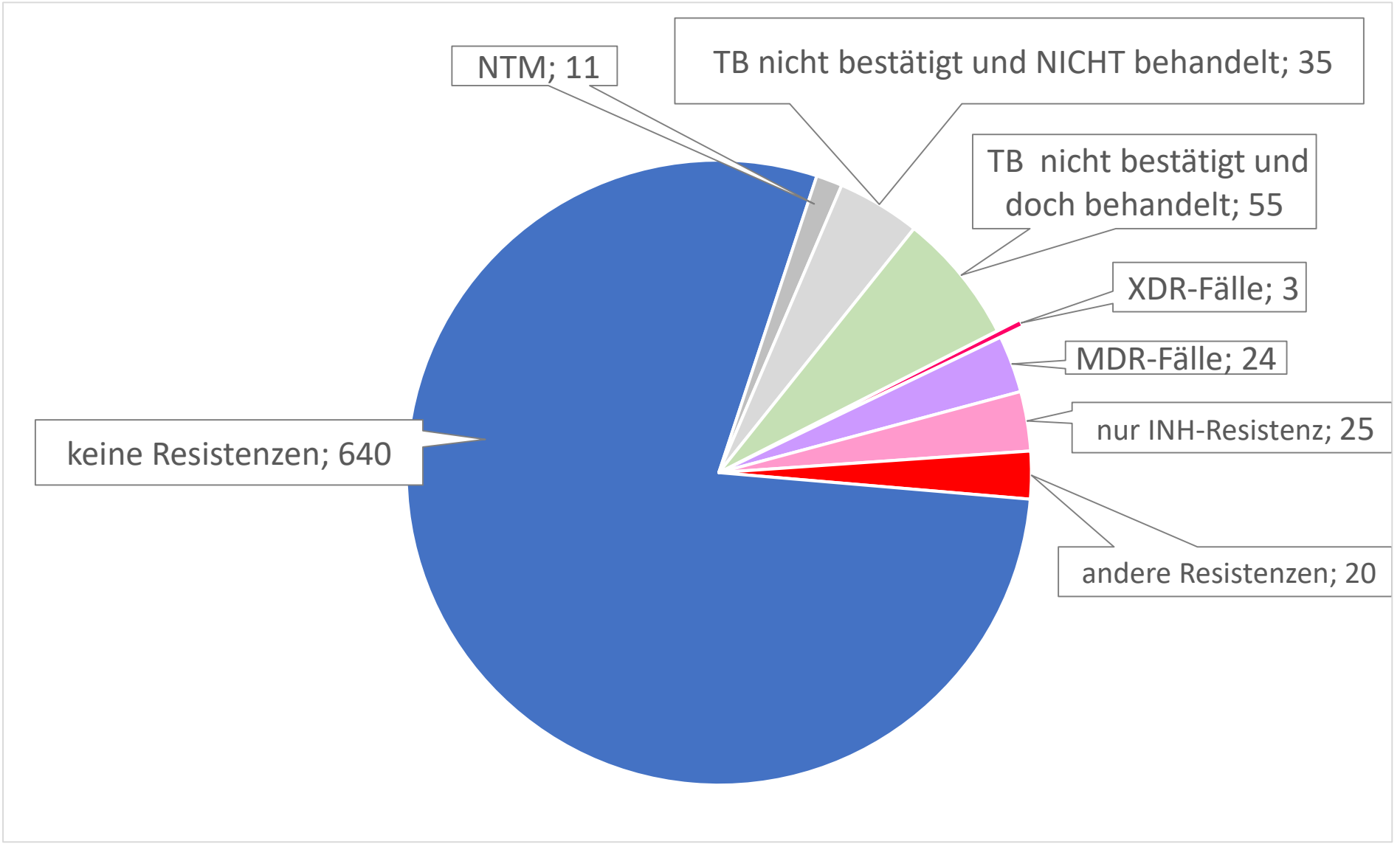
Fragestellung: Brauchen wir in der LL St.Gallen-Appenzell mehr DOT?

Analyse: Hausarzt-Anfrage alle 2 Monate wurde in der Ostschweiz eingeführt. HA, welche nicht antworten werden telefonisch kontaktiert. Was bringt das?

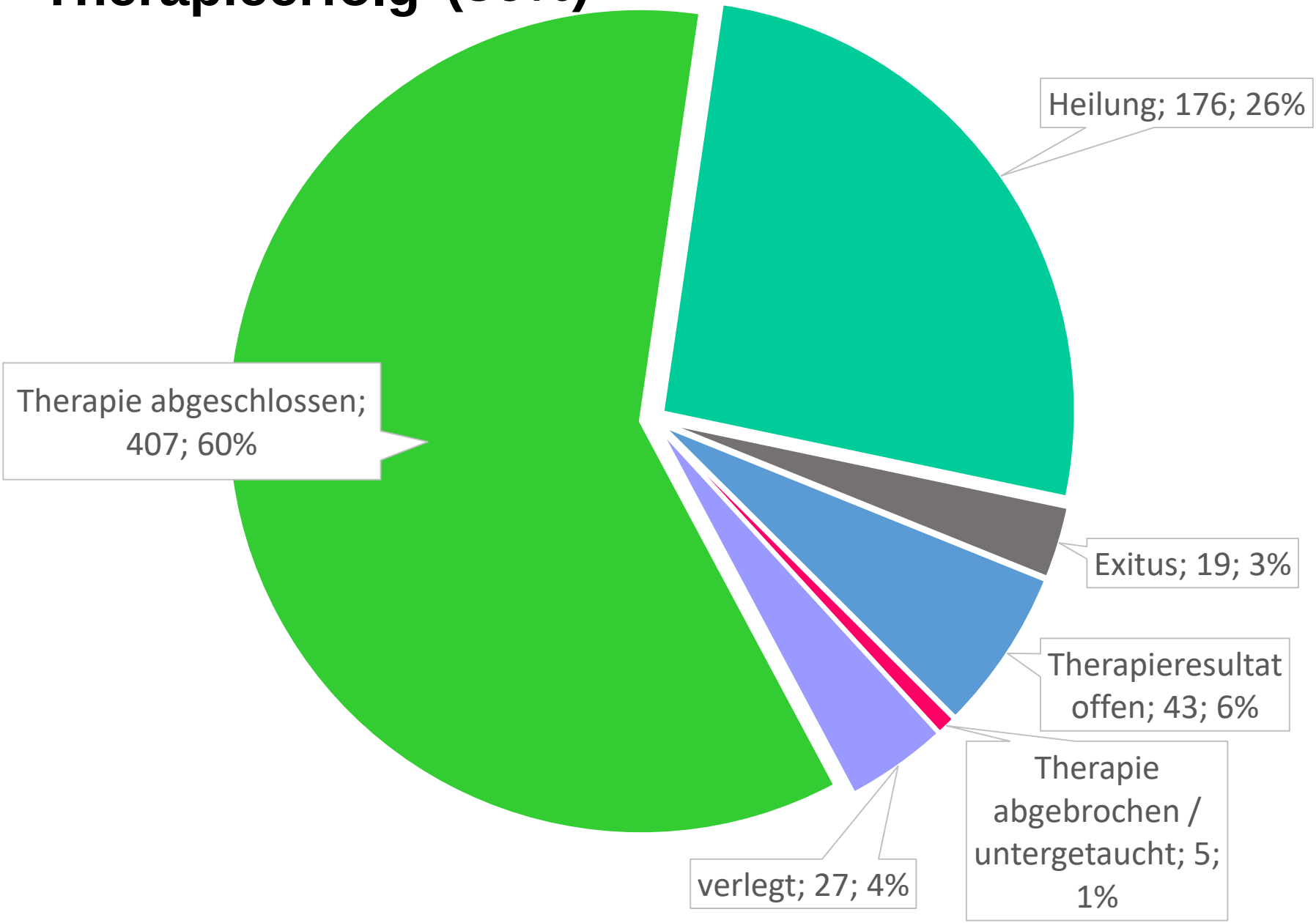
Resultat: 2002 – 2004 haben 98 (87.5%) von 112 TB Patienten 6 Monate Therapie beendet, 8 Patienten verstarben (nicht wegen TB), 4 wurden übergeben und 2 konnten nicht mehr gefunden werden. Eine DOT wurde 7x durchgeführt.

Fazit:
Mit 87.5% Erfolg ist die Hausarzt-Anfrage-Methode bei uns meist ausreichend. Die universelle DOT für Alle ist nicht notwendig.

TB Fälle 2013-2018 im Kanton Zürich



Therapieerfolg (86%)



Therapieerfolg, was heisst das?



Zusammenarbeit!

- Meldung kommt
- Telefon
  - Station und / oder Ärztin (Standardisierter Fragebogen)
  - Herkunft, Sprache?
- Erstgespräch vor Ort –falls nötig mit Dolmetschdienst
  - Komplexität abschätzen (Ressourcenplanung)
  - Angehörige ins Spiel bringen / Kontaktpersonen
  - Therapieweitführung / DOT
    - Asylzentrum, Apotheke, Hausärztliche Praxis, LL, Gemeinde, Arbeitgeber, Spitex
  - Ziel: Genesung und Geduld für Heilungsprozess, Verständnis für weiteres Vorgehen →UU!

Therapieerfolg, was heisst das?



Indikation für DOT

- Flüchtlingsstatus und/oder keinen festen Wohnsitz
- Suchtproblematik
- Nebenwirkungen
- Sicherheit

Konkrete Schritte

- Idealer Zeitpunkt, zentraler, gut erreichbarer Ort
- Kontakt mit Apotheke, Hausärztliche Praxis, Arbeitgebende, Spitex, Asylzentrum, Gemeinde
- Schriftlicher Auftrag an Abgabestelle
- Überwachungsblatt wird immer anfangs Monat kontrolliert

  → Umstellung / Nebenwirkungen / Compliance

DOT: Überwachungstabelle für die direkt überwachte Medikamenteneinnahme zur Behandlung der Tuberkulose

LUNGENLIGA ST.GALLEN – APPENZELL

Bitte dieses Formular am Monatsende oder bei Transfer an die Lungenliga ST. GALLEN-APPENZELL zurücksenden.

Name, Vorname:
Therapiebeginn:
Behandelnder Arzt:

Geburtsdatum:

Adresse:
Telefon:

Medikamente	Datum	Dosis	Morgen	Mittag	Abend	Stopdatum
			☐	☐	☐	
			☐	☐	☐	
			☐	☐	☐	
			☐	☐	☐	

Überwachungstabelle **Monat:**

Datum	Medikamente Abgegeben, Visum	Befinden / Spezielles	Datum	Medikamente Abgegeben, Visum	Befinden / Spezielles
1.			16.		
2.			17.		
3.			18.		
4.			19.		
5.			20.		
6.			21.		
7.			22.		
8.			23.		
9.			24.		
10.			25.		
11.			26.		
12.			27.		
13.			28.		
14.			29.		
15.			30.		
			31.		

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LUNGENLIGA ST.GALLEN – APPENZELL

Therapieerfolg, was heisst das?

Falls keine DOT

Zwischenkontrolle des Therapieverlaufes, 2-monatlich

→ Brief an behandelnde Ärztin

Behandlungserfolg nach Therapieabschluss



LUNGENLIGA
ST.GALLEN – APPENZELL

St. Gallen Kantonsspital
Rorschacherstrasse 95
CH 9007 St. Gallen

St. Gallen, 4. Februar 2019

Zwischenkontrolle zum Tuberkulose-Therapieverlauf bei
(Name Patient)

Sehr geehrte Frau Dr.

Im Auftrag des Kantonsarztes führt die Lungenliga in regelmässigen Abständen Therapiekontrollen durch. Die Ergebnisse werden dem Kantonsarzt gemeldet.

Datum Therapiestart: 19.01.2018

Ist der/die Patient/in noch in ihrer Behandlung? ☐ Ja ☐ Nein

Wenn Nein: Wer behandelt sie/ihn jetzt? .....

Ist die Einnahme der Medikamente gewährleistet? ☐ Ja ☐ Nein

Datum der letzten Konsultation: .....

Bitte retournieren Sie das ausgefüllte Formular mit beiliegendem Rückantwortumschlag an untenstehende Adresse uns zurück.

Wir danken für Ihre Mithilfe.

Freundliche Grüsse

LUNGENLIGA ST. GALLEN-APPENZELL

Tanja Schneider
Fachstelle Tuberkulose

Datum: .....

Stempel/Unterschrift:



Tanja Schneider
schneider@lungenliga-sg.ch
071/ 228 47 40

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LUNGENLIGA
ST.GALLEN – APPENZELL

LUNGENLIGA
ST.GALLEN – APPENZELL

Adresse
Behandelnder Arzt

St. Gallen 25. März 2019

Erhebungsformular für das Behandlungsresultat von
(Name Indexpatient)

Sehr geehrte Frau Dr.

Im Auftrag des kantonsärztlichen Dienstes bitten wir Sie, uns das Behandlungsresultat gemäss den WHO-Kategorien für (Name Indexpat.) mitzuteilen.
Bitte senden Sie das ausgefüllte Formular mit beiliegendem Rückantwortumschlag an unten stehende Adresse zurück.

Besten Dank und freundliche Grüsse

LUNGENLIGA ST. GALLEN-APPENZELL

Tanja Schneider
Fachstelle Tuberkulose

Behandlungsresultat nach WHO-Kategorien

Behandlungsabschluss am: ..... (Datum)

- ☐ **Heilung:** Dokumentierte, vollständig durchgeführte Behandlung mit kultureller Konversion
- ☐ **Therapie abgeschlossen:** Dokumentierte, vollständig durchgeführte Behandlung ohne Dokumentation einer kulturellen Konversion
- ☐ **Therapieunterbruch:** Unterbrechung der Behandlung für mindestens zwei Monate
- ☐ **Therapieversagen:** Nach ≥ 5 Monaten Behandlung andauernd oder erneut positive *M.tuberculosis*-Kulturen
- ☐ **Exitus aufgrund der Tuberkulose:** Tod an Tuberkulose vor Beginn oder während der Tuberkulosebehandlung
- ☐ **Exitus aus anderen Gründen:** Tod an einer anderen Erkrankung (als TB) vor Beginn oder während der Tuberkulosebehandlung
- ☐ **Verlegung:** Überweisung an eine andere Stelle und kein Therapieresultat vorhanden
- ☐ **Anderes Resultat:** z.B. weitere Behandlung eines MDR-Falles

Datum:.....

Stempel und Unterschrift:.....

Tanja Schneider
071 228 47 40
schneider@lungenliga-sg.ch



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LUNGENLIGA
ST.GALLEN – APPENZELL

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Eidgenössisches Departement des Innern EDI
Bundesamt für Gesundheit BAG
Direktionsbereich Öffentliche Gesundheit

2019 (nur bisher)

Bitte ausgefüllt innerhalb 1 Woche an Kantonsärztin/-arzt senden (nicht direkt ans BAG).*

Tuberkulose (TB) Ergänzungsmeldung

TB ohne Multiresistenz: Stamm sensibel auf Isoniazid und Rifampicin

Die Informationen zum Behandlungsresultat werden 12 Monate nach Behandlungsbeginn eingeholt.

Patient/in

Name/Vorname: _____ Geburtsdatum: __/__/____ Geschlecht: ☐ w ☐ m

Verlauf

Datum des Behandlungsbeginns: __/__/____

Datum des ursprünglich geplanten Behandlungsendes: __/__/____

Datum des effektiven Behandlungsendes (letzte Dosis Antituberkulotika): __/__/____

Behandlungsresultat

Bitte nur das erste eingetroffene Ereignis ankreuzen:

☐ **Patient geheilt**: Dokumentierte, über die vorgesehene Therapiedauer durchgeführte Behandlung mit Negativierung der Kulturen

☐ **Therapie abgeschlossen**: Dokumentierte, über die vorgesehene Therapiedauer durchgeführte Behandlung, aber ohne Nachweis einer Negativierung der Kulturen

☐ **Therapieunterbruch oder -abbruch**: Unterbrechung der Behandlung durch den Patienten für mindestens zwei aufeinander folgende Monate, bzw. Abbruch

Grund: _____

☐ **Therapieversagen**: Nach ≥5 Monaten Behandlung andauernd oder erneut positive Kulturen

☐ **Patient verstorben** vor Beginn oder während der Tuberkulose-Behandlung,

Todesursache: ☐ TB ☐ andere Ursache

☐ **Überweisung** an eine andere Stelle zur Behandlung / Weiterbehandlung *und* es liegt kein Therapieresultat vor:

Name Arzt/Ärztin: _____ Telefon: _____

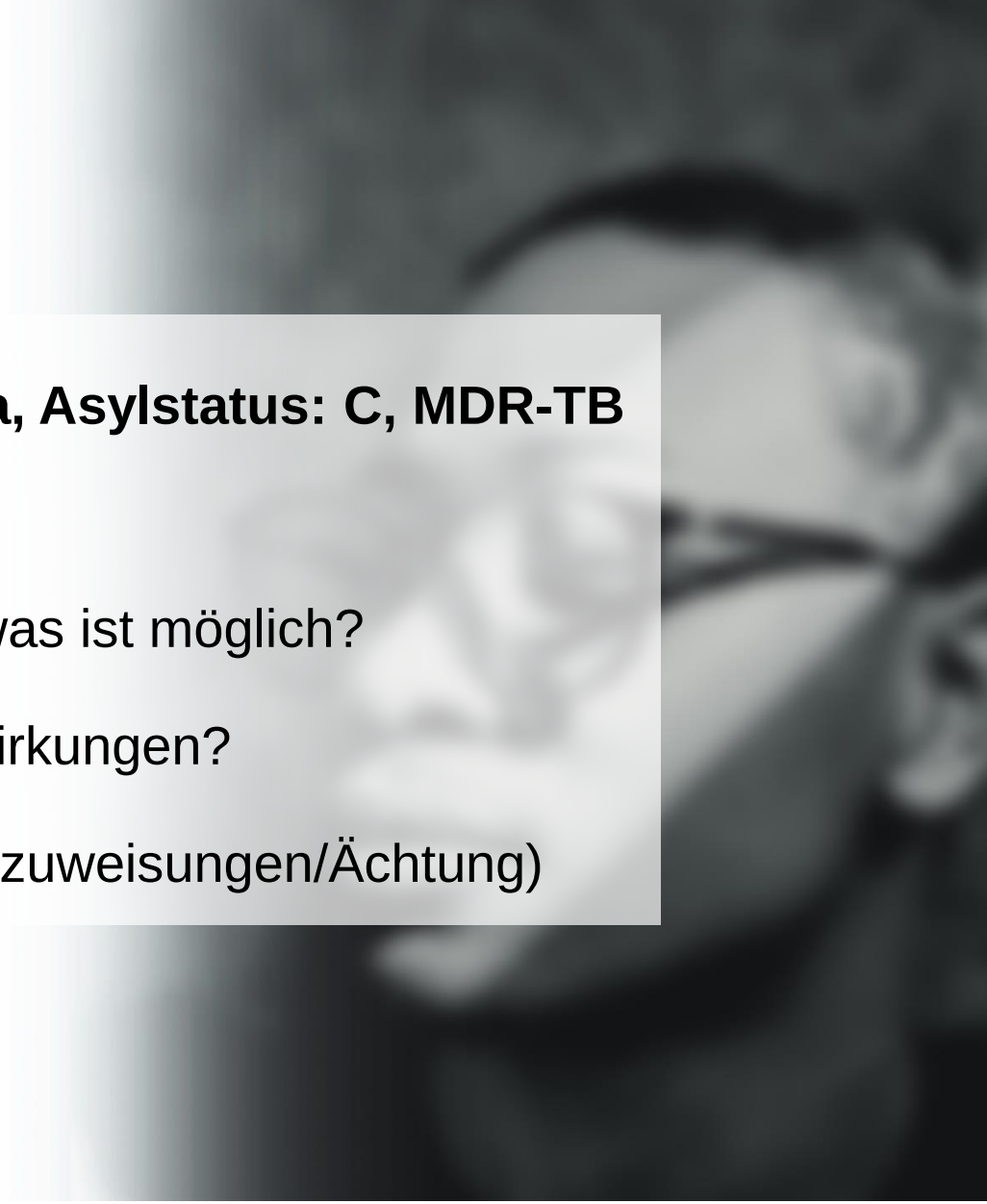
Adresse der Praxis / des Spitals: _____ E-Mail: _____



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ST.GALLEN – APPENZELL

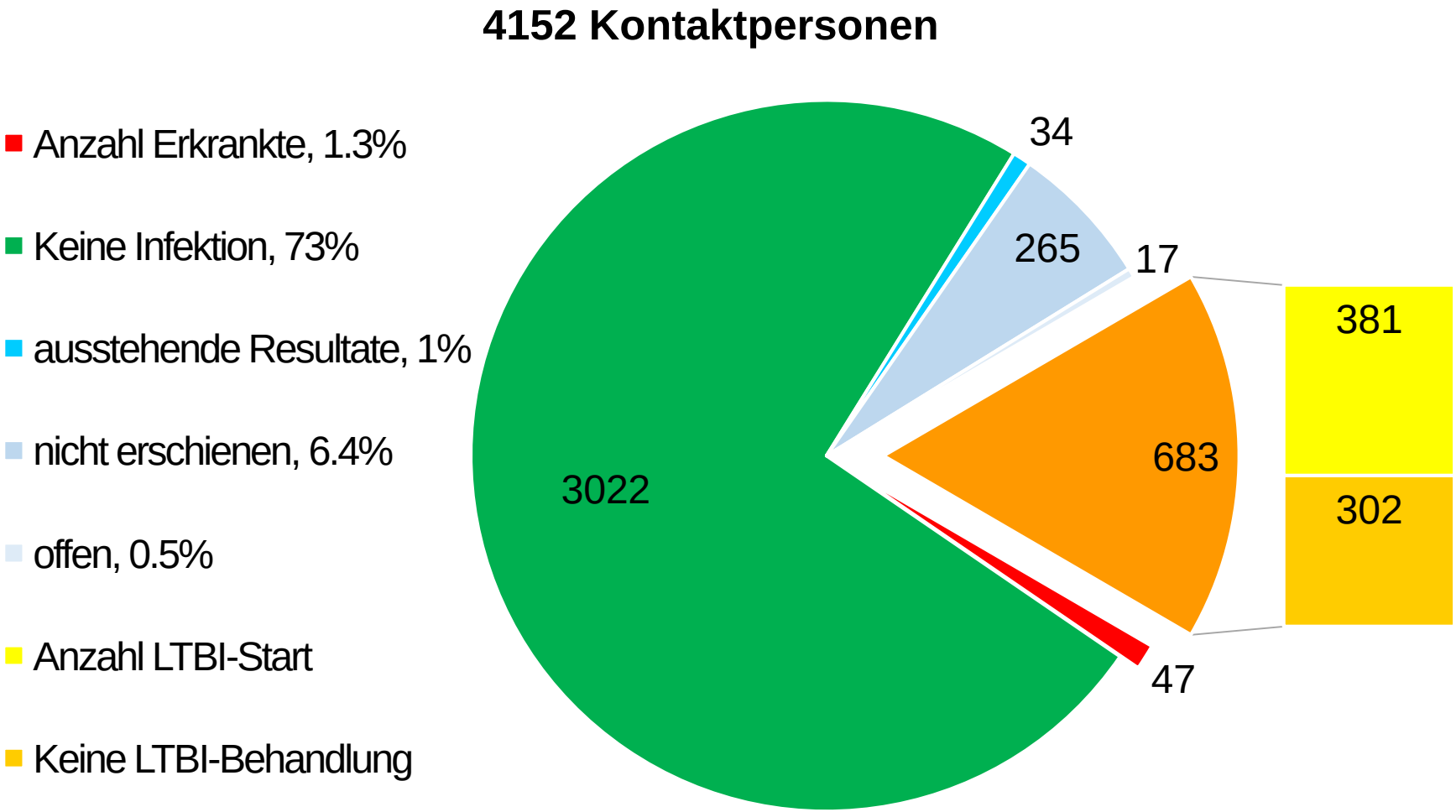
Fallbeispiel



Herr A., 35-jährig aus Eritrea, Asylstatus: C, MDR-TB

- Spricht deutsch
- Berufstätig (Schichtarbeit): was ist möglich?
- DOT: wann, wo? → Nebenwirkungen?
- UU: Angst um Stelle (Schuldzuweisungen/Ächtung)

Erhebung von Therapieergebnissen bei LTBI – Behandlung, 2013-2018, Kanton ZH





Vielen Dank für Ihre Aufmerksamkeit!

Bea Začek & Tanja Schneider

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Schweizerische Eidgenossenschaft
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Confederazione Svizzera
Confederaziun svizra

Federal Department of Home Affairs FDHA
Federal Office of Public Health FOPH
Public Health Directorate

Tuberculosis in Switzerland

Treatment outcome monitoring 2016 and 2017

March 27th, 2019

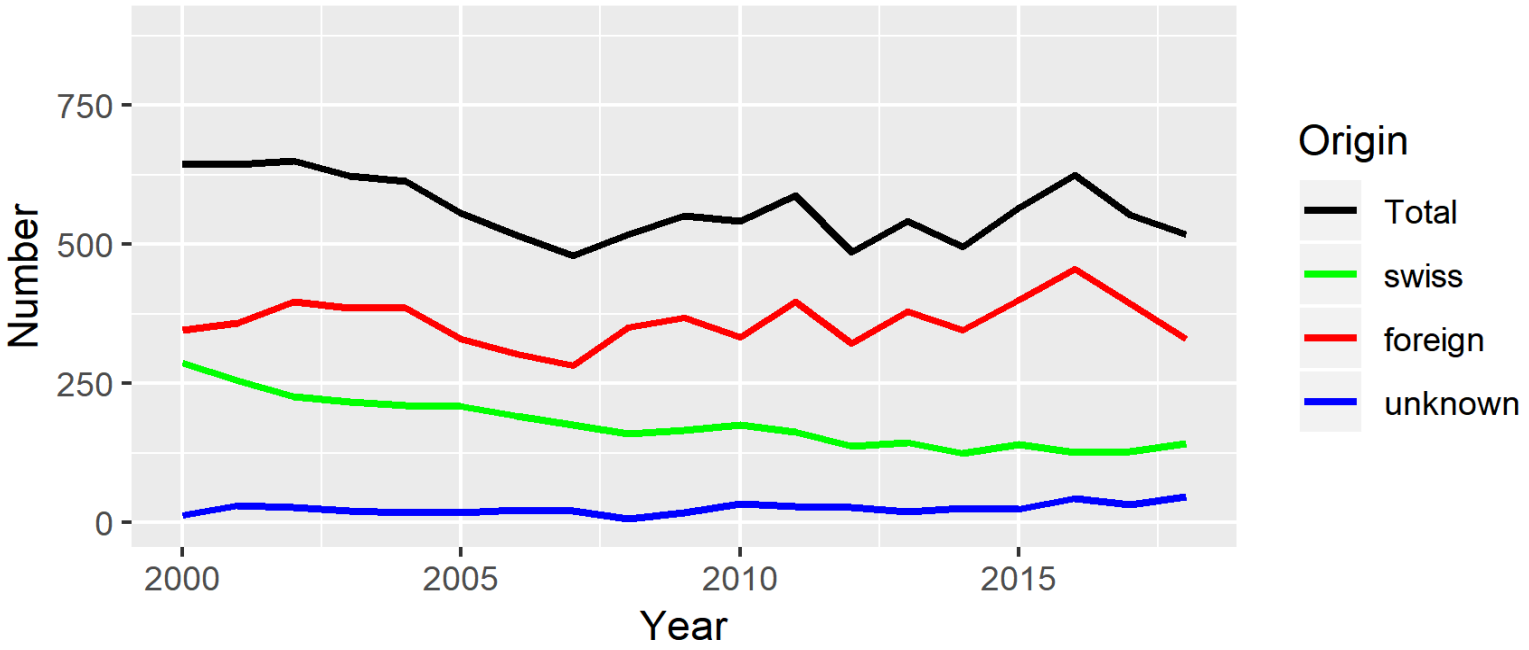
Outline

- Introduction
- Epidemiology of tuberculosis in Switzerland
- Treatment outcomes
  - Surveillance system
  - Definitions
  - Results
- Discussion and open questions
- Acknowledgements

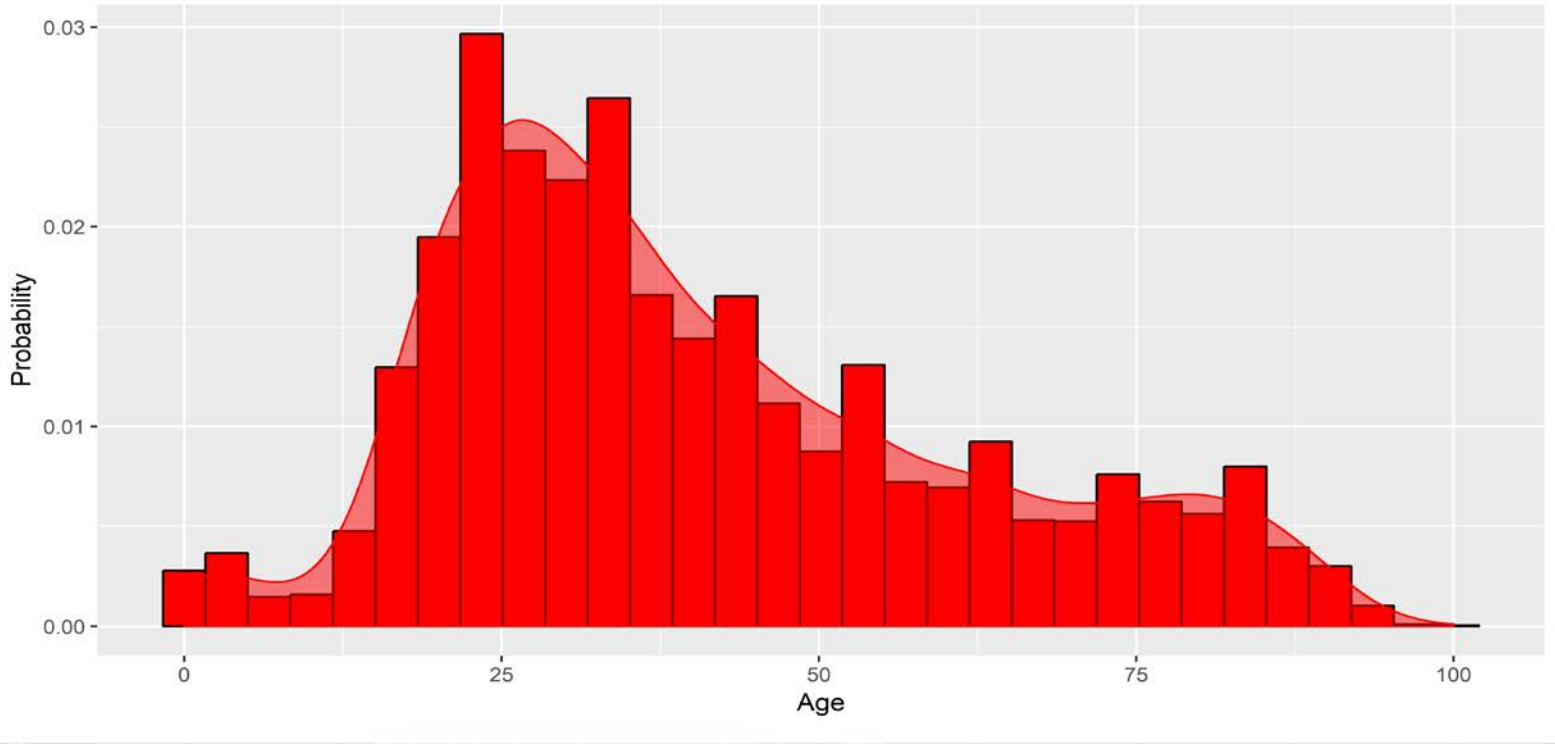
Introduction:
Why do we monitor treatment outcome?

- Do we successfully treat TB in Switzerland?
- Do we treat patients correctly in order to prevent resistance?
- Do we control TB in Switzerland?
- Do we have potential to improve TB control?
- Do we reach the WHO target of 85% treatment success?

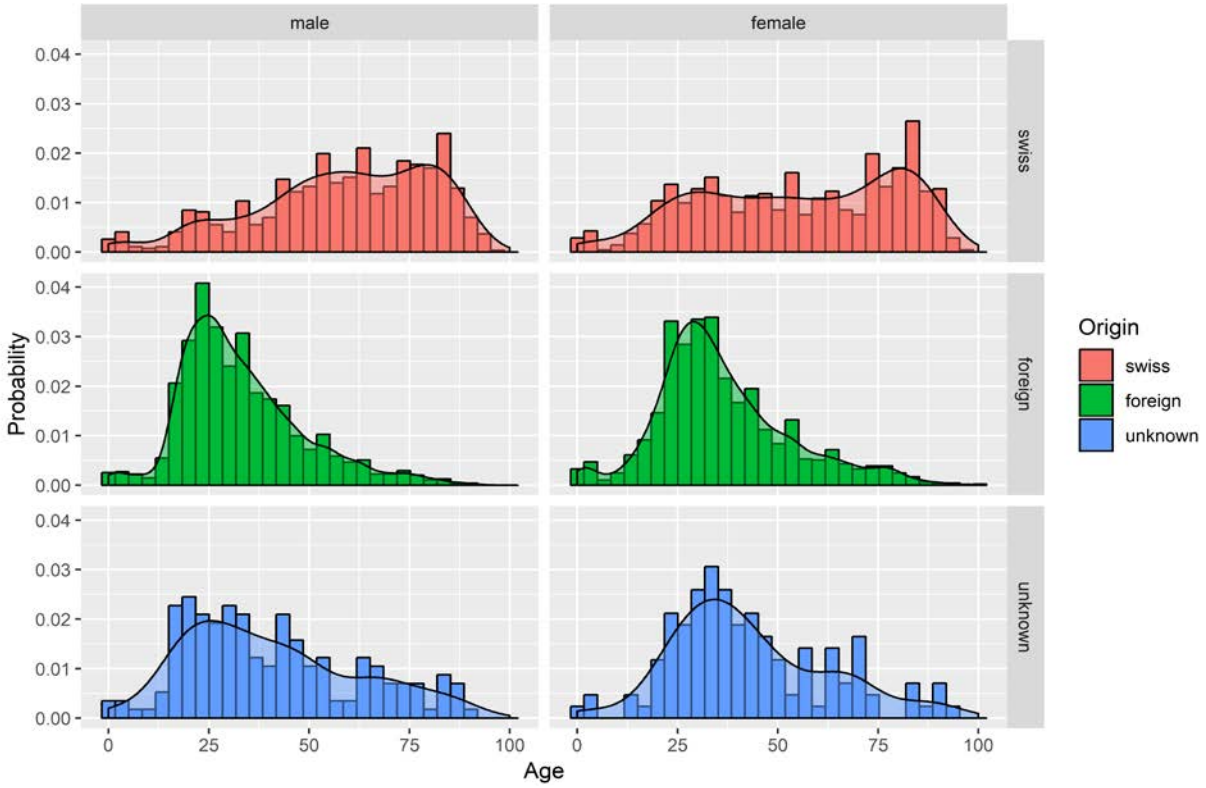
Number of notified TB cases, 2000-2018



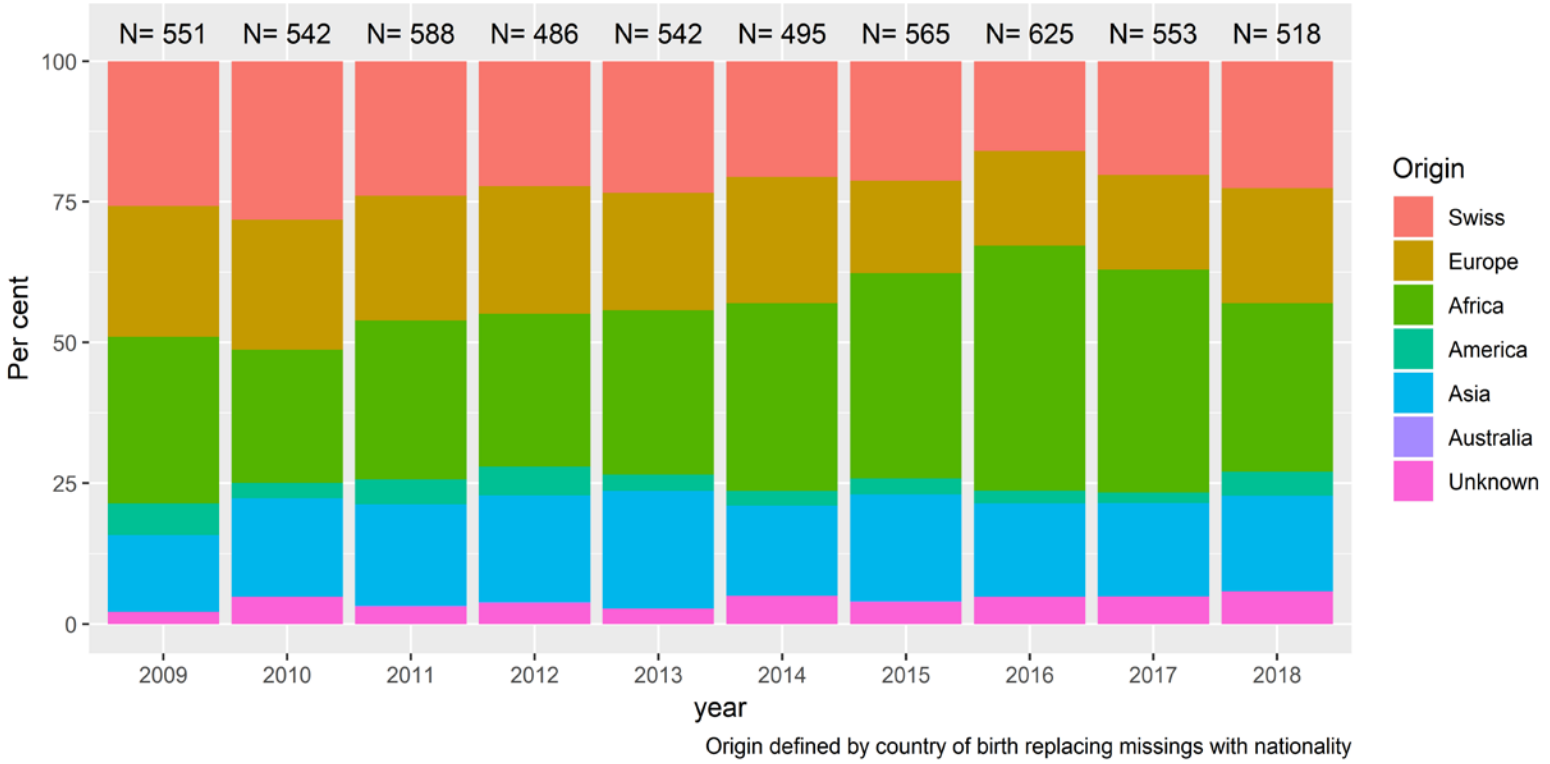
Age distribution of TB cases 2009-2018



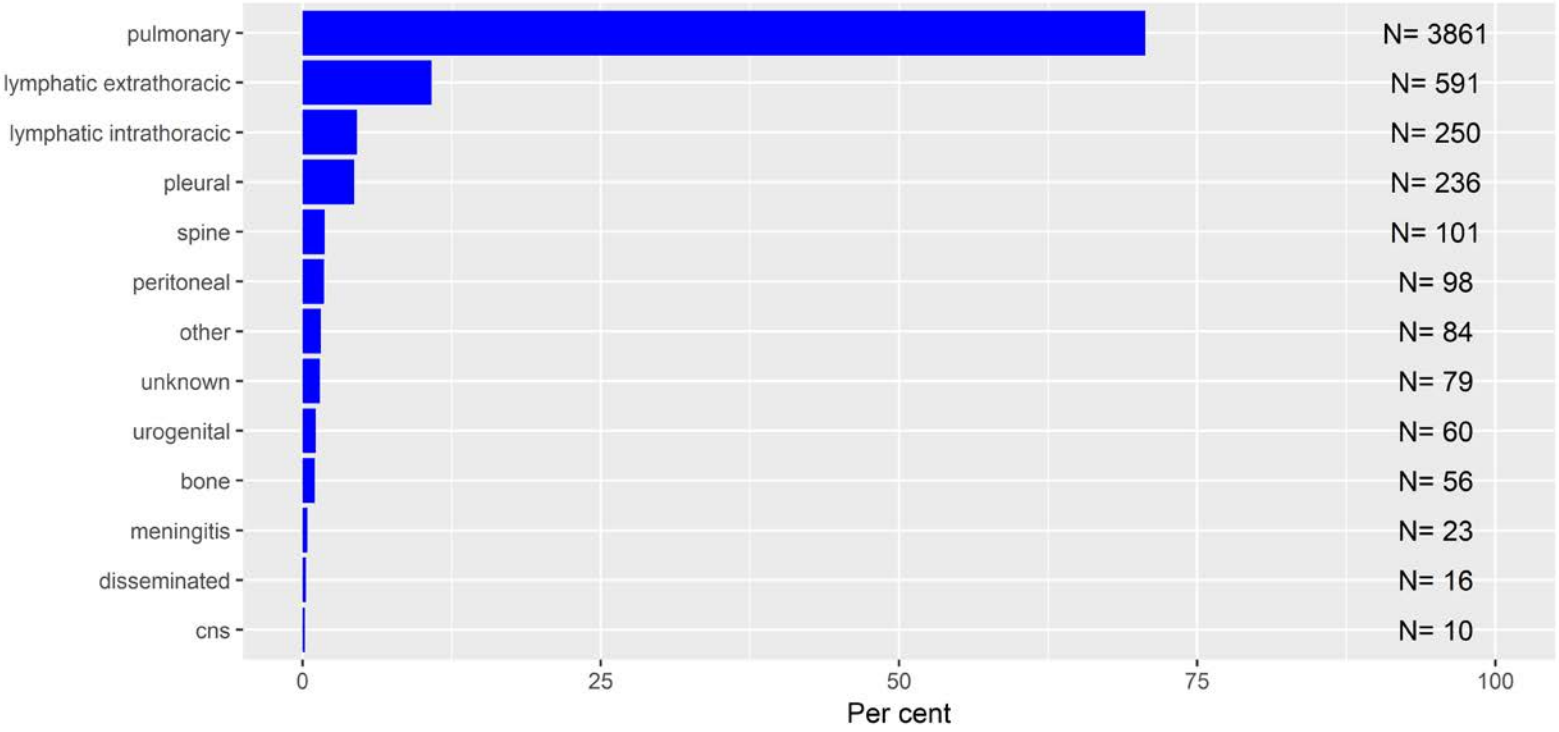
Age distribution of TB cases by gender and origin 2009-2018



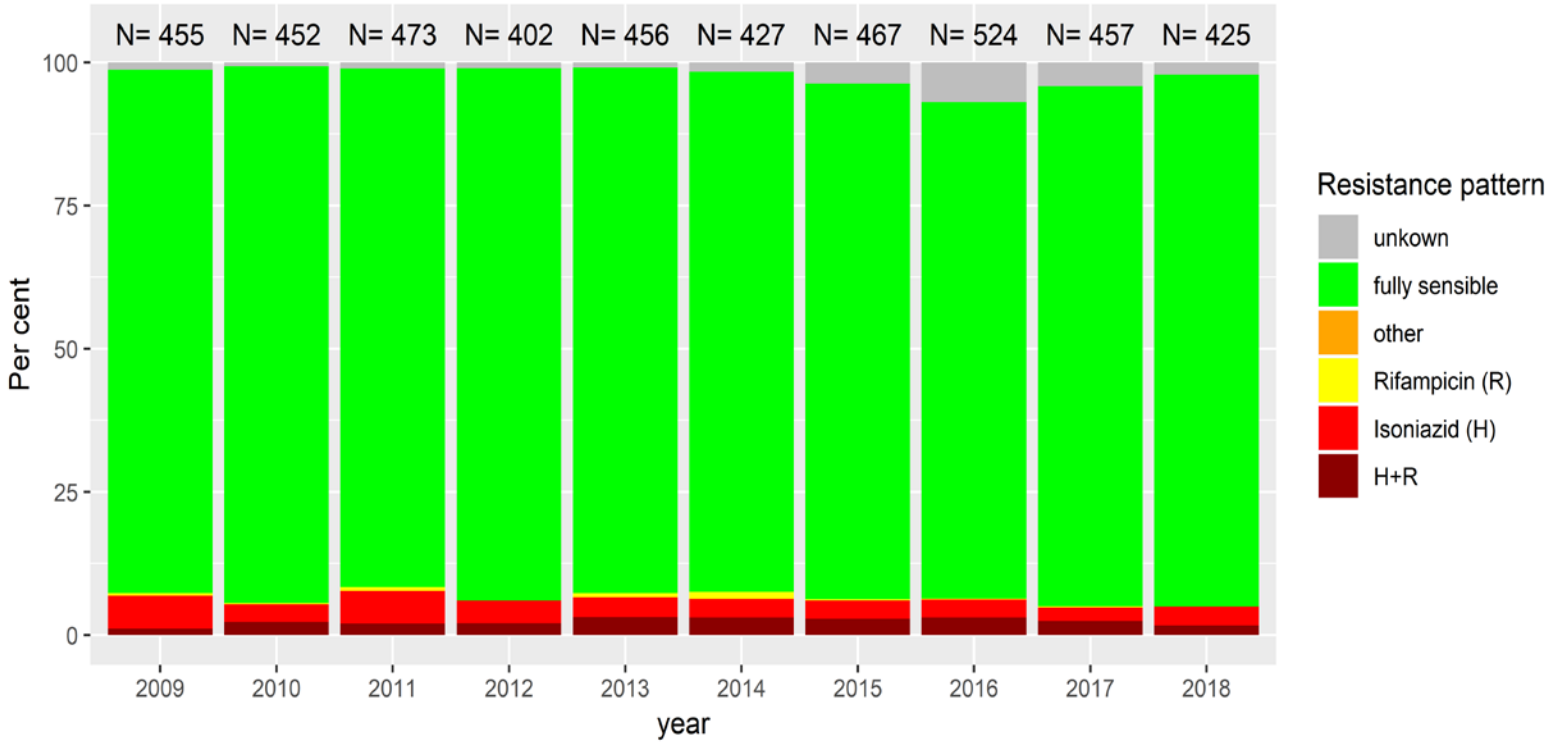
TB cases by origin (Switzerland vs. other countries by continent) 2009-2018



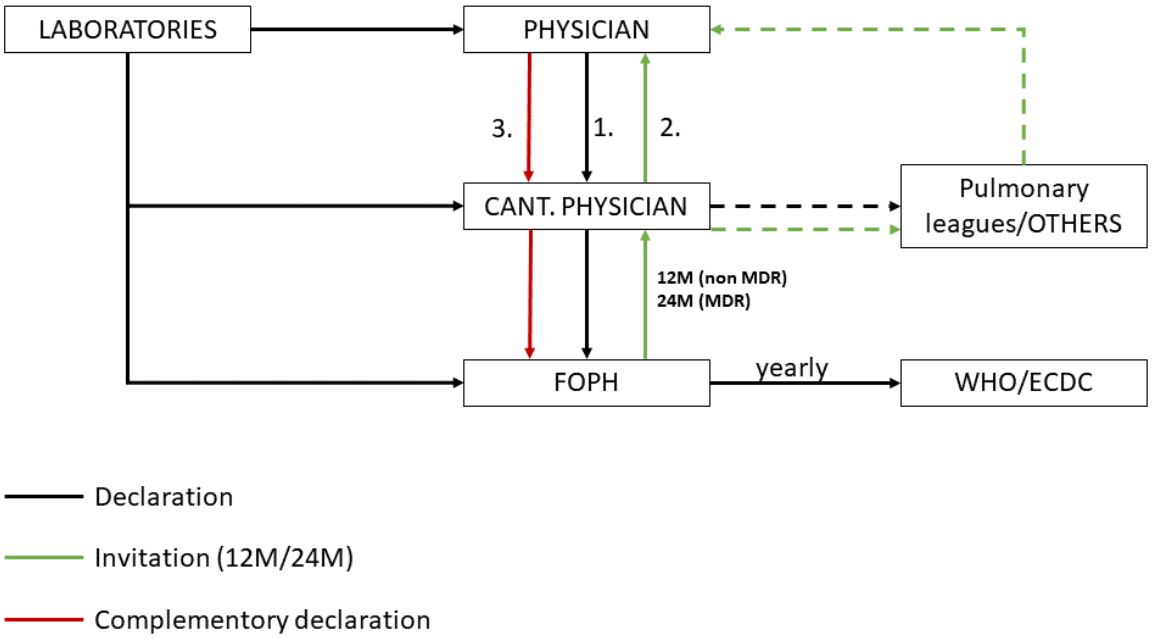
Clinical picture of TB cases 2009-2018



TB: Resistance against Isoniazid and Rifampicin (2009-2018)

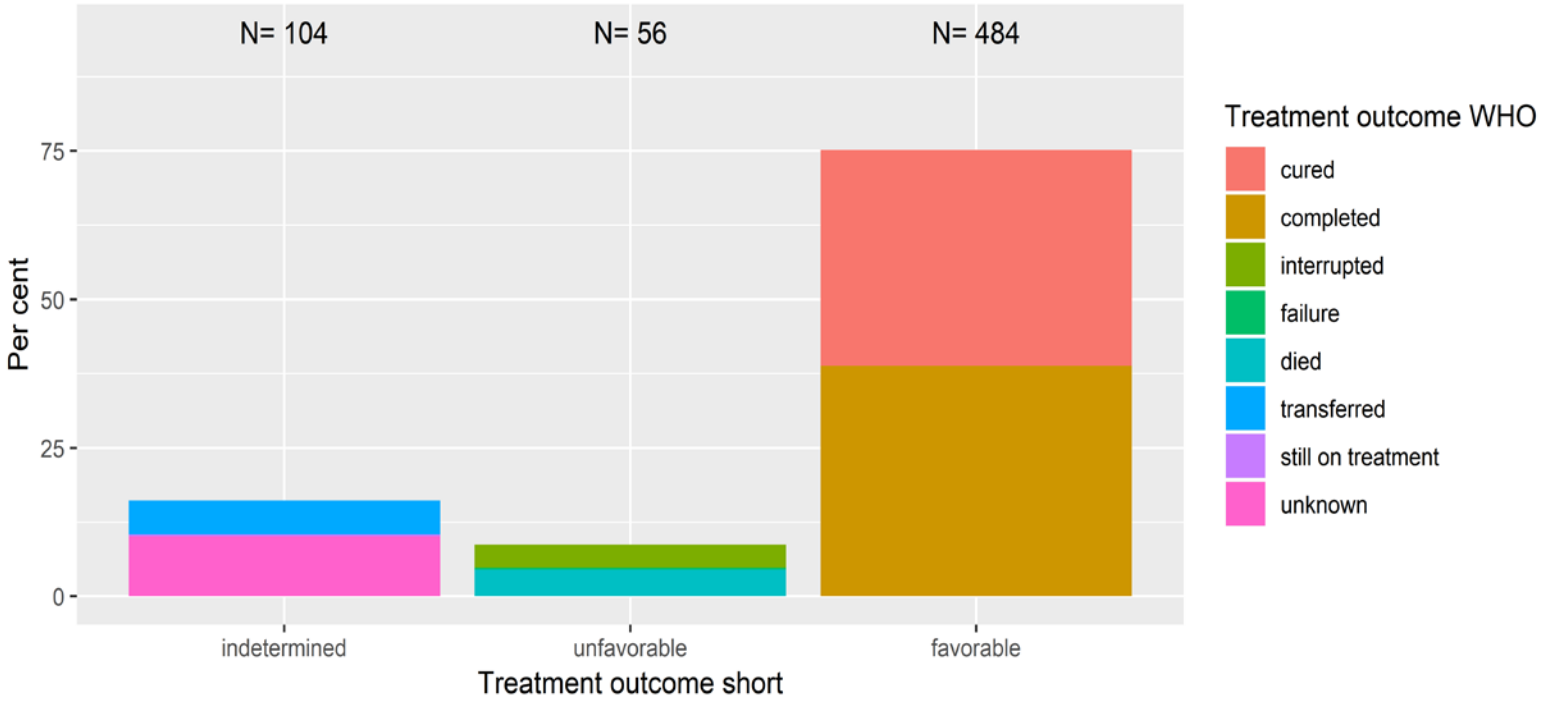


National Surveillance System for TB

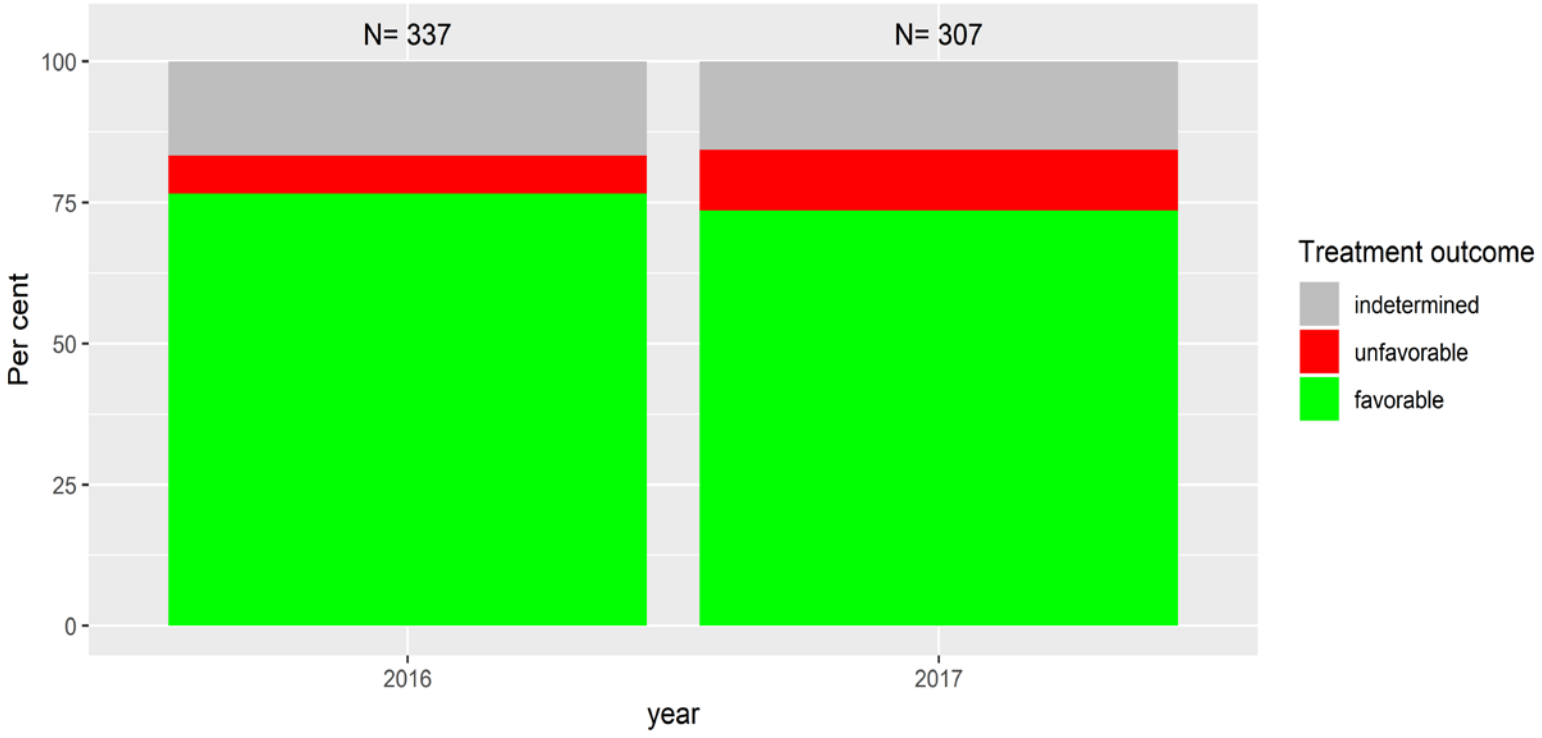


Treatment outcome monitoring became mandatory in 2016

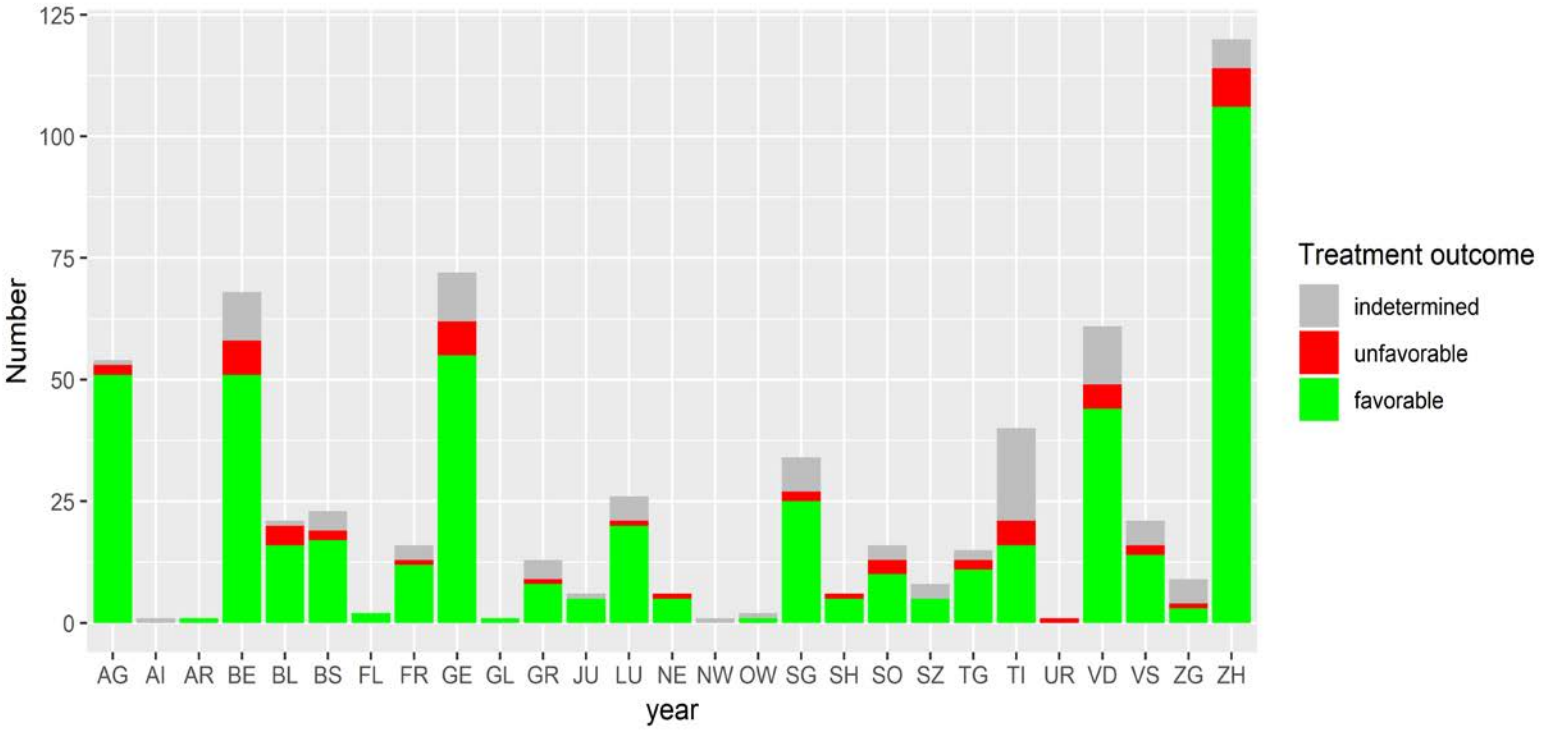
Treatment outcome monitoring of culture positive pulmonary TB (cPTB) cases 2016/2017



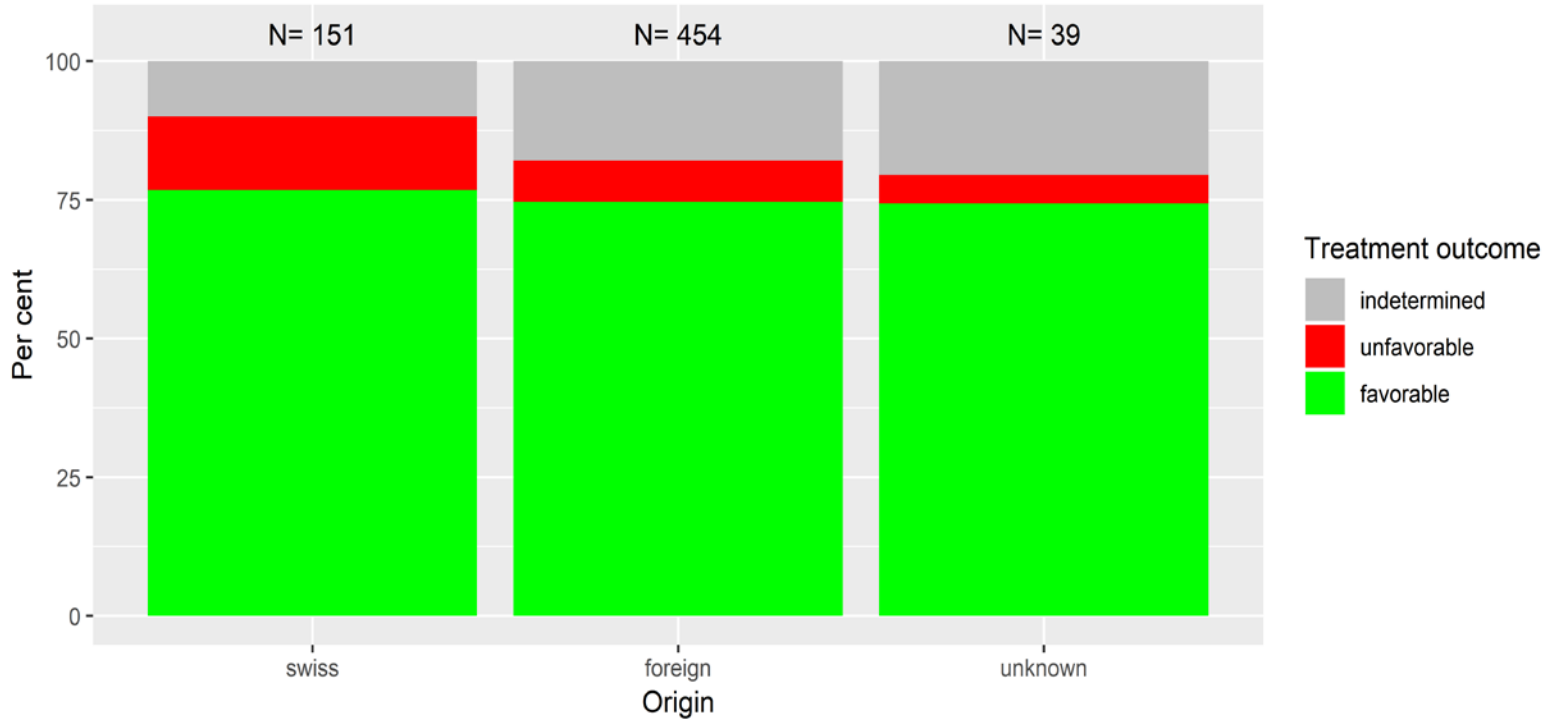
Treatment outcome monitoring of cPTB cases 2016/2017 by year



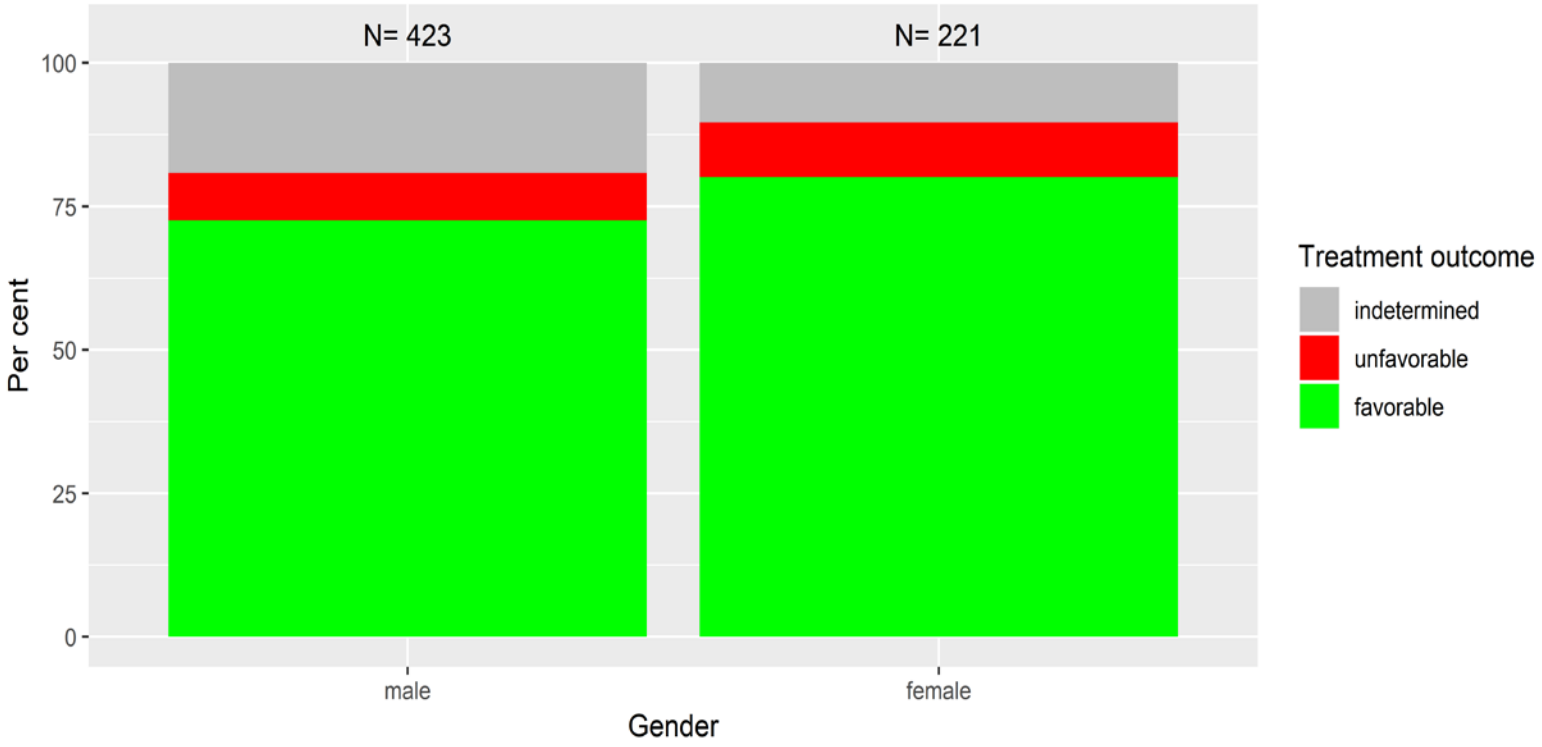
Treatment outcome monitoring of cPTB cases 2016/2017 by canton



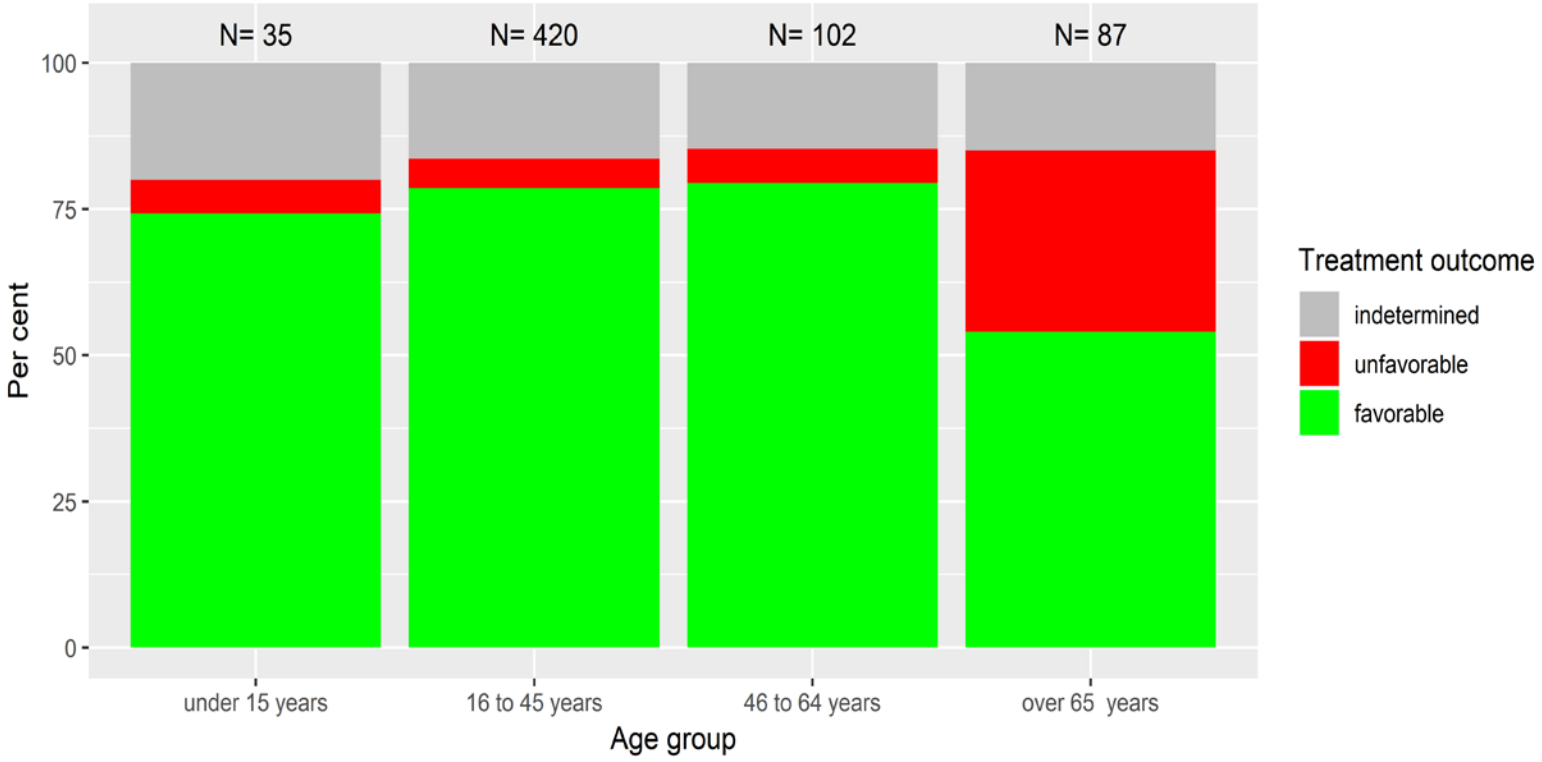
Treatment outcome monitoring of cPTB cases 2016/2017 by origin



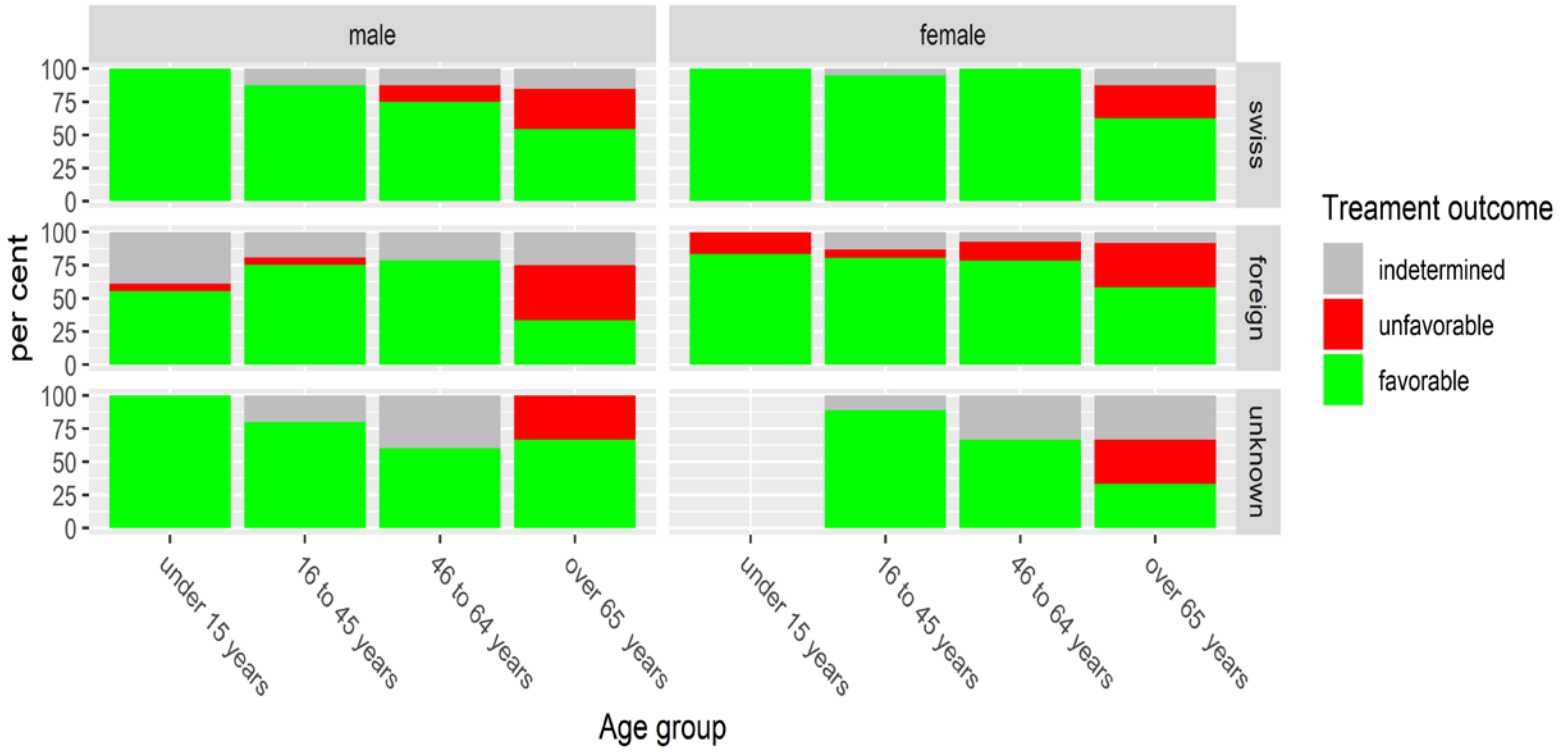
Treatment outcome monitoring of cPTB cases 2016/2017 by gender



Treatment outcome monitoring of cPTB cases 2016/2017 by age

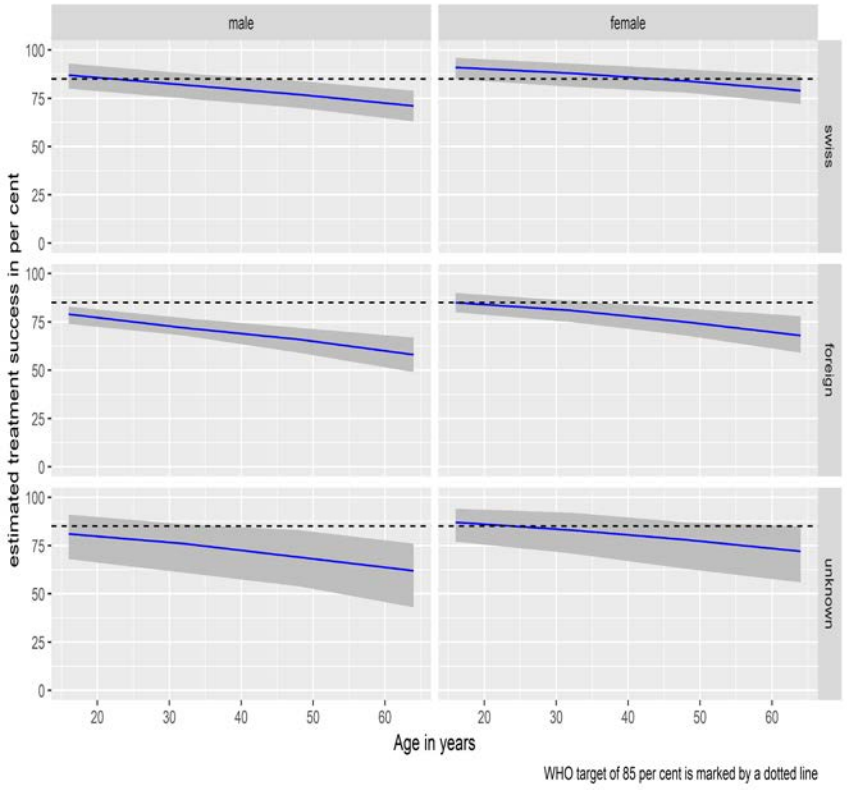


Treatment outcome monitoring of cPTB cases 2016/2017 by age, gender and origin

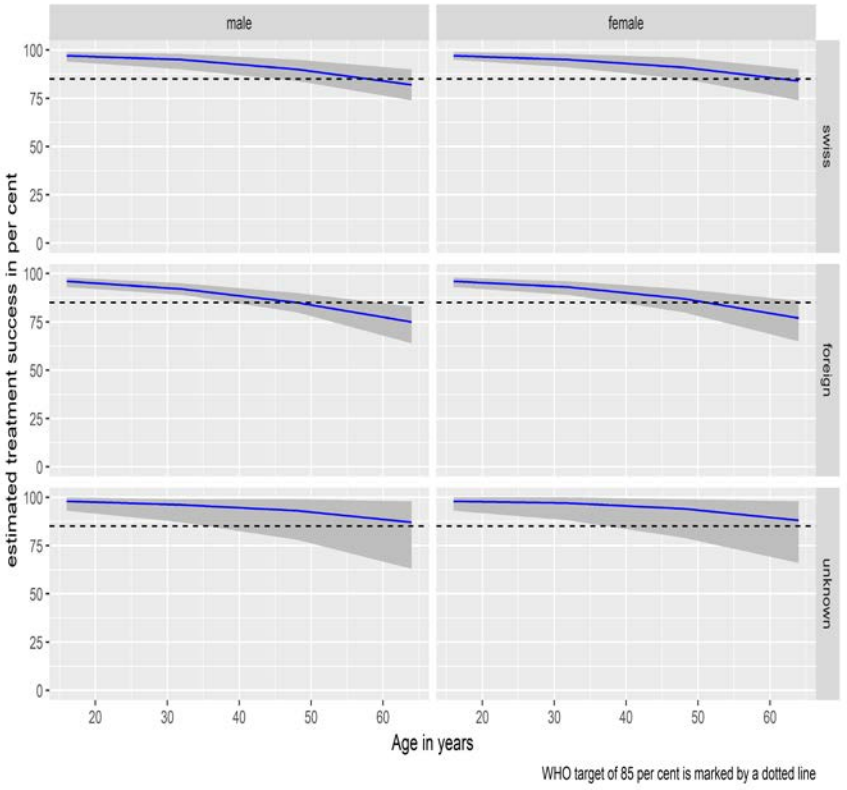


Treatment outcome monitoring of cPTB: favorable outcomes by age, gender and origin

including «indetermined» outcomes



excluding «indetermined» outcomes



Summary I

- Overall the number of TB cases has remained stable in Switzerland since the year 2000.
- TB mostly affects young adult men of foreign origin
- The number of TB cases is declining in persons of Swiss origin.
- TB is a pulmonary disease in about 75% of the cases. CAVE: extrapulmonary TB in 25%!

Summary II

- Overall treatment outcome of culture confirmed pulmonary TB is successful in 75%, however regional differences do exist.
- There is no change between 2016 and 2017.
- It is less likely to be favorable in patients of foreign or unknown origin
- It is more likely to be favorable in women than in men.
- It is less likely to be favorable in elderly patients.
- Switzerland does not (yet) reach the WHO target of an overall 85% treatment success.

Discussion and open questions

- Monitoring is important and shows that treatment is successful in about 75%.
- There are cantonal/regional differences. We hypothesize that
  - improving transmission of information between cantons and within the same canton improves treatment outcome.
  - use of tools like «*Informationssystem Meldungen (ISM)*» that are readily available facilitate information transfer and treatment outcome monitoring
  - collaboration with or mandating partner organisations will improve the monitoring.

Acknowledgements

- physicians in Switzerland
- cantonal physicians
- Swiss Lung Association and the cantonal pulmonary leagues
- My colleagues at the FOPH for their support

Digital technologies to support tuberculosis patients

Dennis FALZON
Global TB Programme, WHO/HQ, Geneva

28e Symposium Tuberculose
Macolin - Suisse

27 mars 2019

Objective

- Outline how digital technologies are supporting the different elements of the WHO End TB Strategy

Key definitions

Digital health (previously eHealth or electronic health) is the cost-effective and secure use of information and communication technologies (ICTs) for health and health-related fields.

mHealth (mobile health) is a component of digital health, and involves the provision of health services and information via mobile technologies such as mobile phones and Personal Digital Assistants (PDAs)

The global TB situation (1)

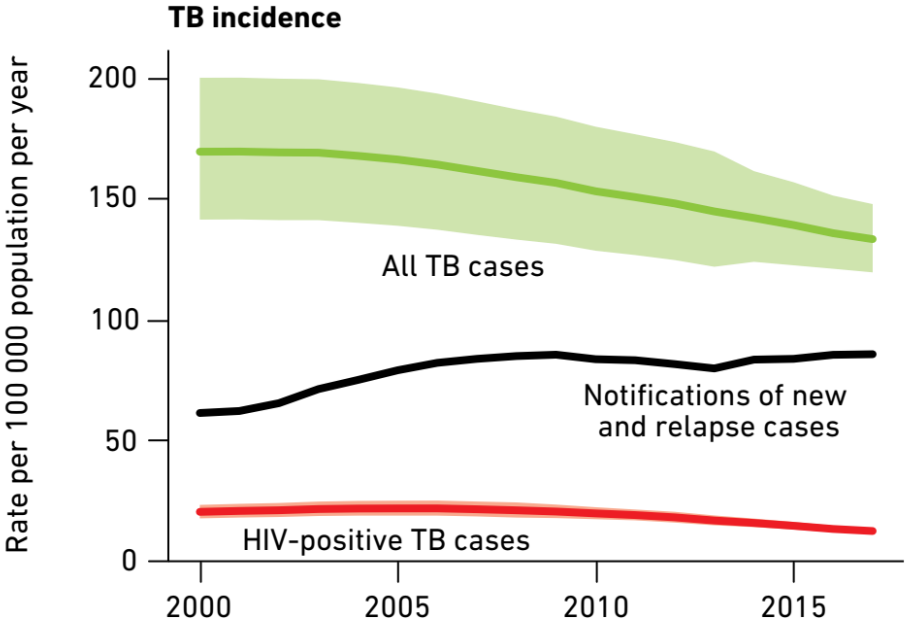
	Estimated incidence, 2017	Estimated number of deaths, 2017
All forms of TB	**10.0 million** (9.0–11.1 million)	**1.3 million*** (1.2–1.4 million)
HIV-associated TB	**0.9 million** (0.8–1.0 million)	**300,000** (266,000–335,000)
Multidrug- / rifampicin-resistant TB (MDR/RR-TB)	**558,000** (483,000–639,000)	**230,000** (140,000–340,000)

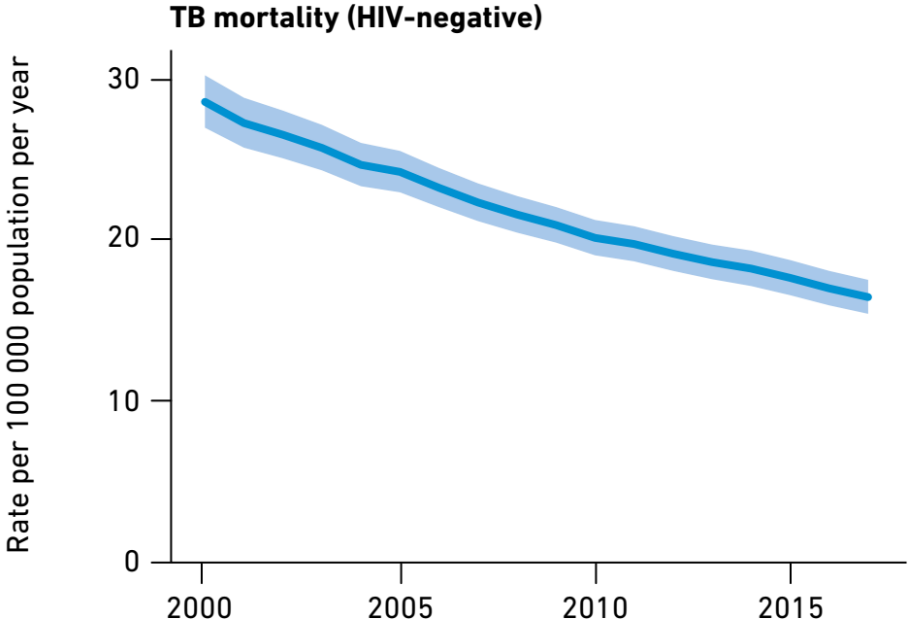
***Source*: WHO Global Tuberculosis Report 2018**

* Excluding deaths attributed to HIV/TB

The global TB situation (2)

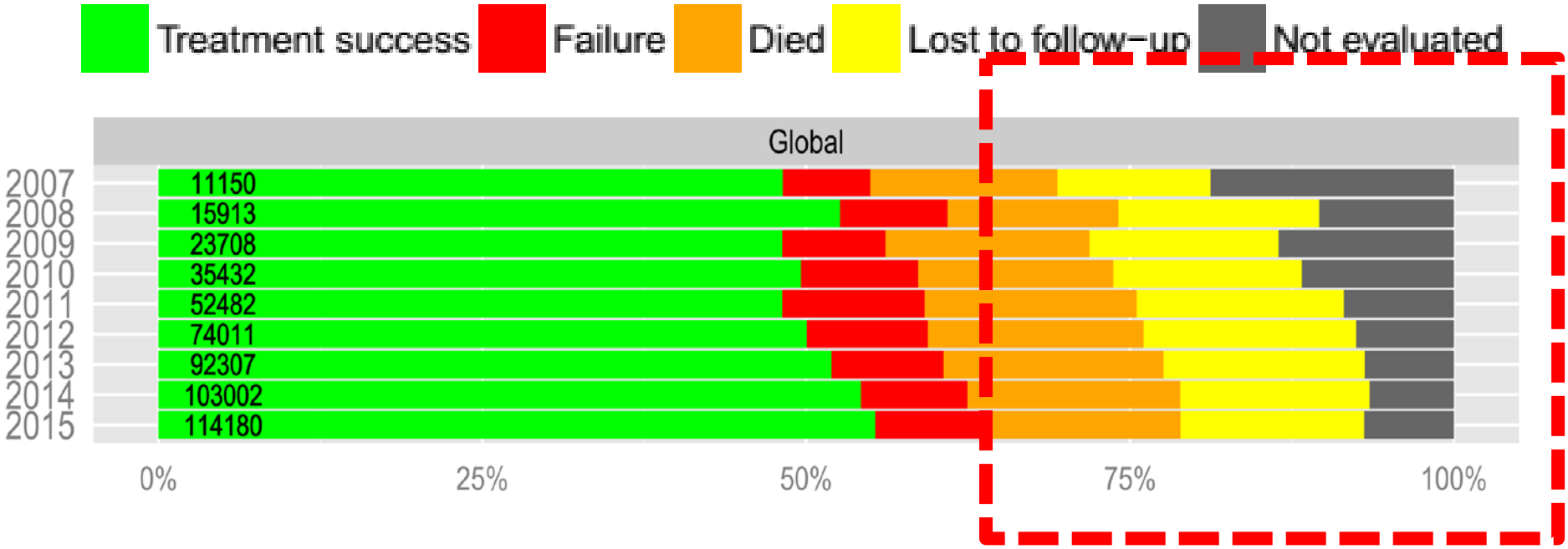
Estimated TB incidence and mortality, 2000-2017

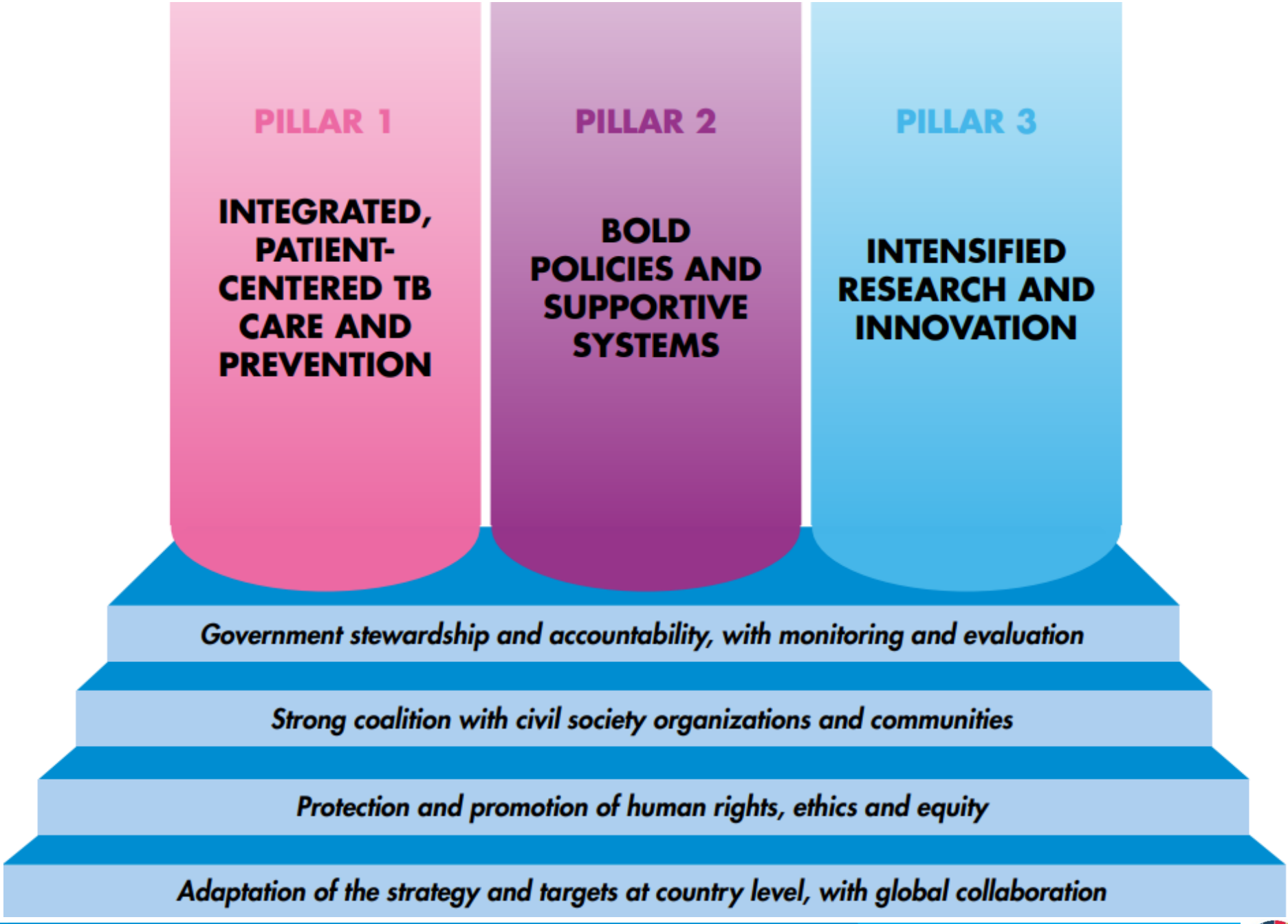




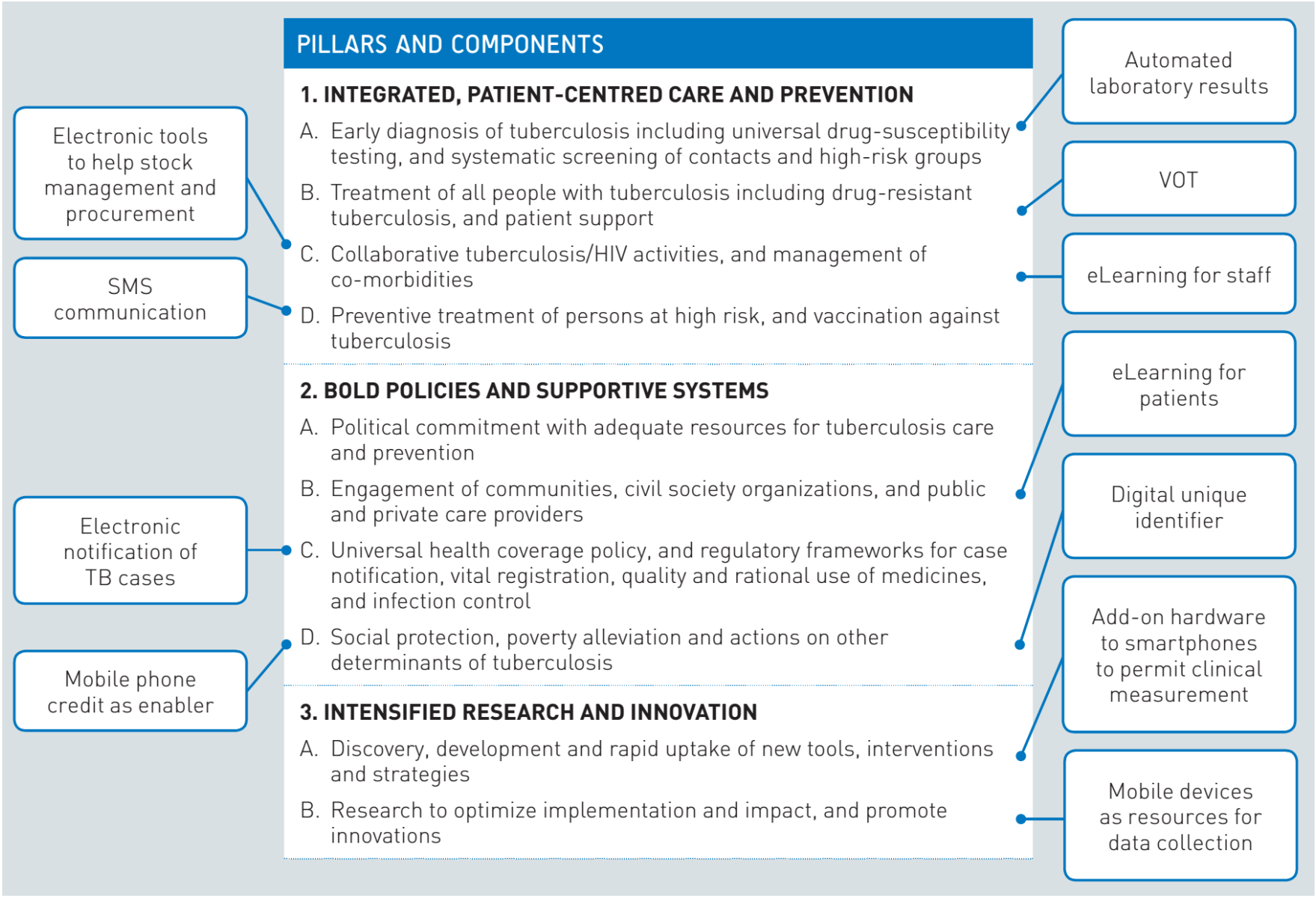
Outcomes of MDR/RR-TB treatment

Annual cohorts, by WHO region and global, 2007-2015




PILLAR 1
INTEGRATED, PATIENT-CENTERED TB CARE AND PREVENTION
PILLAR 2
BOLD POLICIES AND SUPPORTIVE SYSTEMS
PILLAR 3
INTENSIFIED RESEARCH AND INNOVATION
Government stewardship and accountability, with monitoring and evaluation
Strong coalition with civil society organizations and communities
Protection and promotion of human rights, ethics and equity
Adaptation of the strategy and targets at country level, with global collaboration

The End TB Strategy and digital technologies



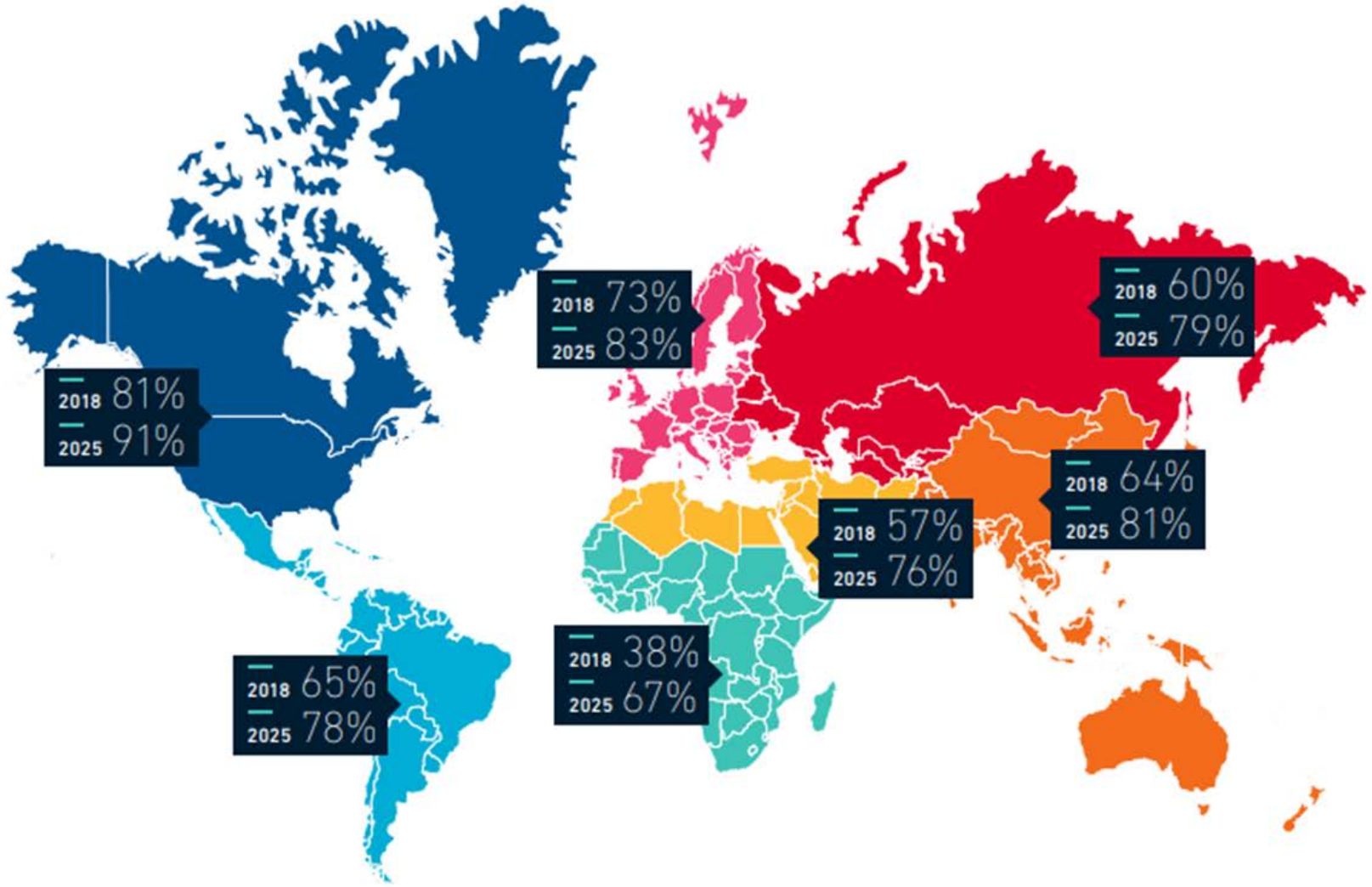
Sustainable Development Goals

& digital technologies



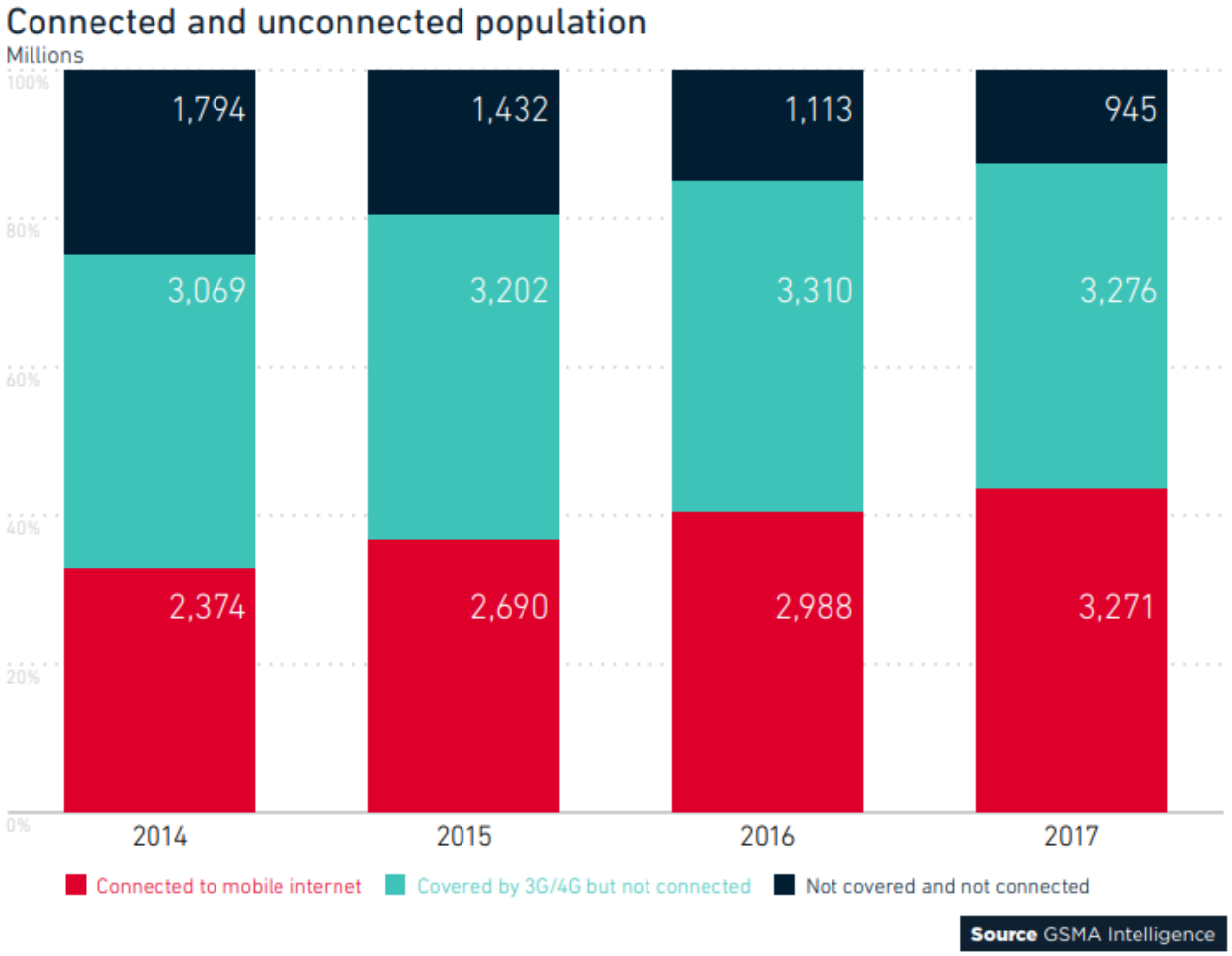
Global smartphone adoption will reach 80% by 2025

Smartphone connections as a percentage of total mobile connections



https://www.gsmaintelligence.com/ ***(October 2018)***

80% of people without internet are covered by 3G/4G – what's the problem?

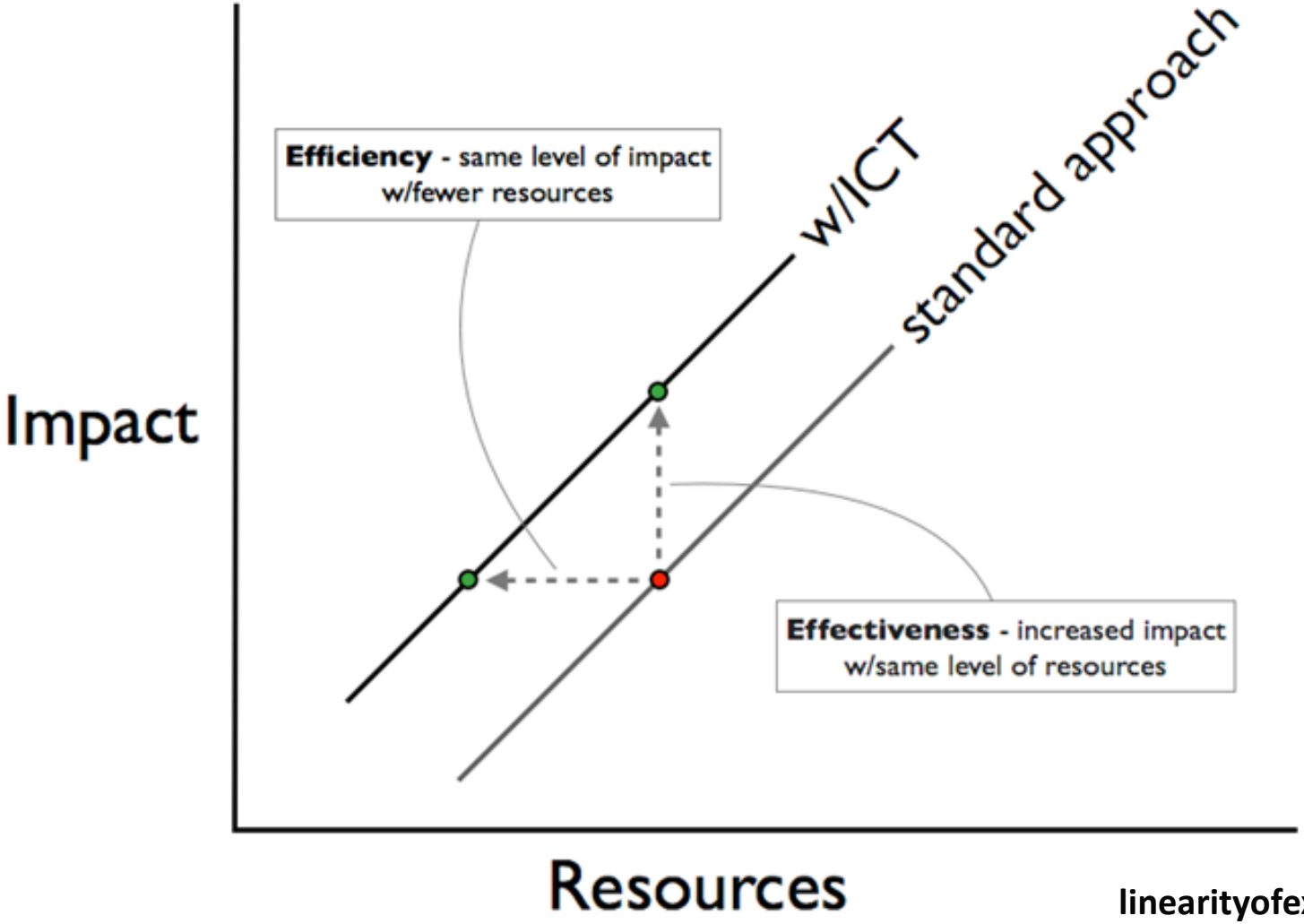


- At the end of 2017, 3.3 billion people (44% of the population) were connected to mobile internet. Some 4 billion people in the world remain offline.
- The lack of infrastructure availability is often cited as a problem – and it is, but not nearly as much as would be thought.
- Of the unconnected, 80% live within range of a 3G or 4G signal. The trickiest problems now lie with 'hidden' factors; for example, in low-income countries:
  - 40% of adults are illiterate
  - 500 MB of data costs almost 10% of monthly GDP per capita
  - only 0.2% of all active mobile applications were developed in low income countries in 2017.

For further information see:
www.mobileconnectivityindex.com

https://www.gsmaintelligence.com/research/?file=8535289e1005eb248a54069d82ceb824&download ***(October 2018)***

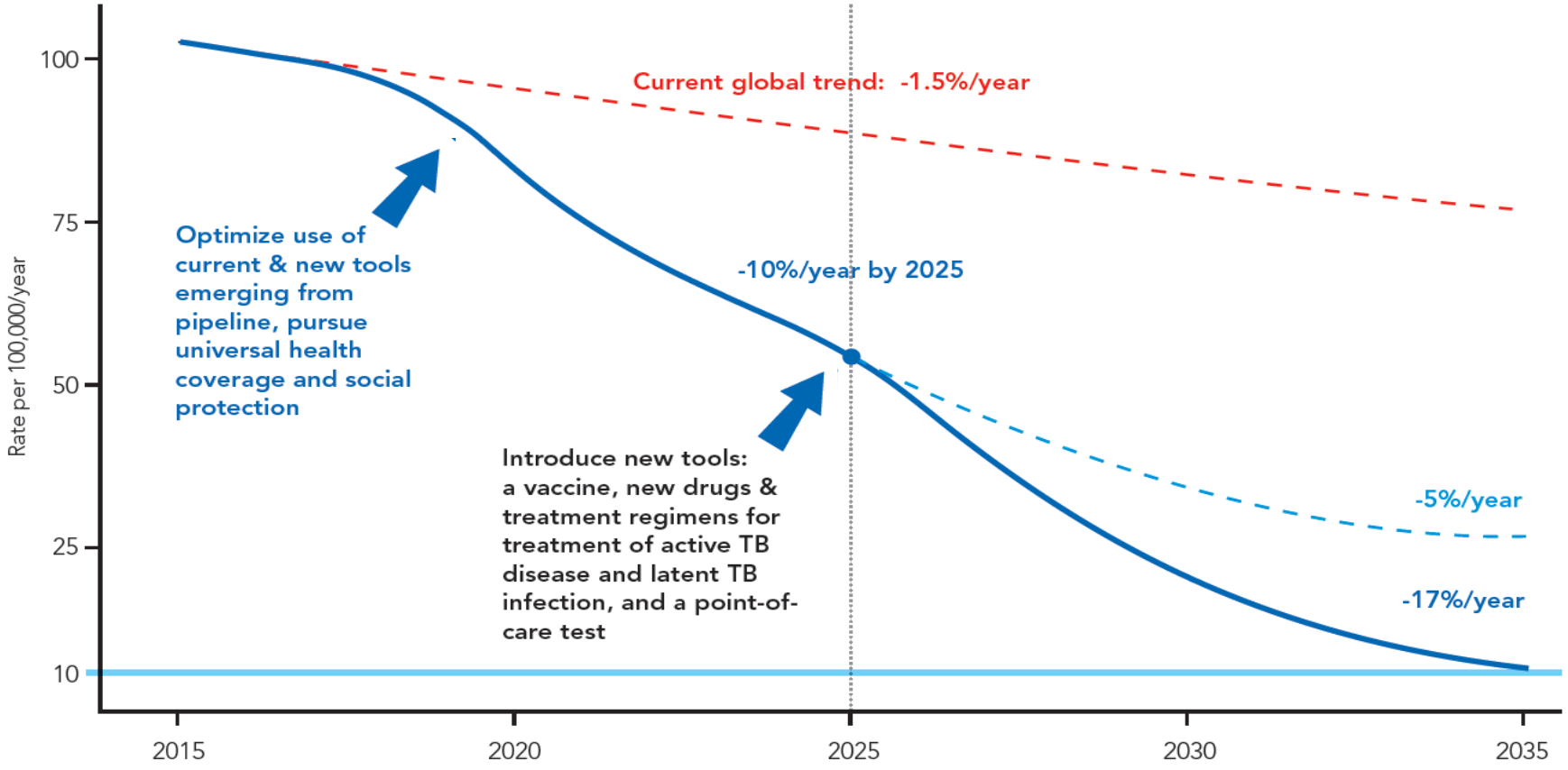
"… if your initiative isn't increasing effectiveness or efficiency (or both) then you shouldn't be doing it."



John BONTEMPO
linearityofexpectation.blogspot.ch

How scalable?

the ability to handle a growing amount of work in a capable manner or its ability to be enlarged to accommodate that growth



What evidence?

CONCEPT

↓

PILOT PROJECT

↓

STUDIES

↓

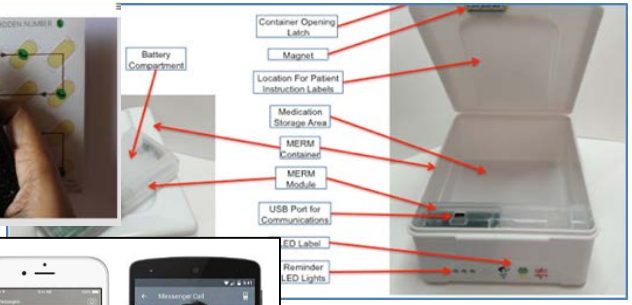
EVIDENCE REVIEW

↓

POLICY CHANGE

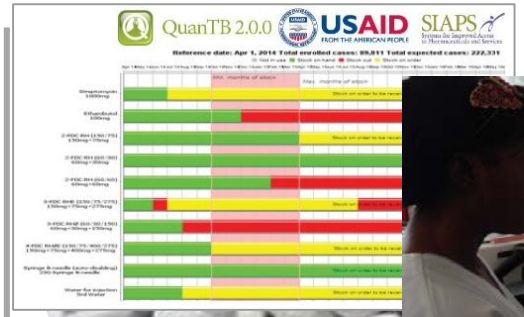
Diversification of the application of digital technologies in TB control







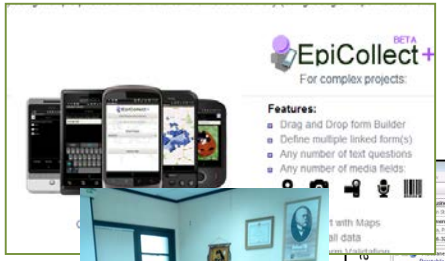
Patient care



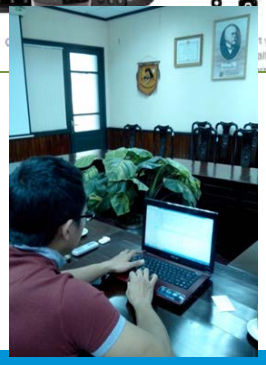


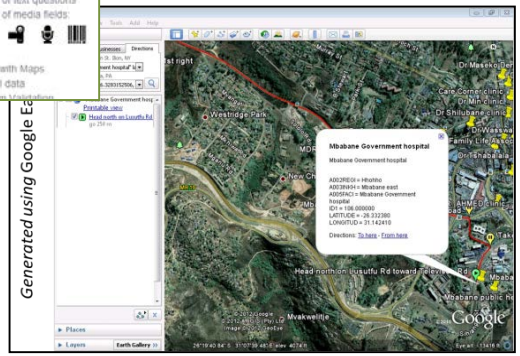


Programme management

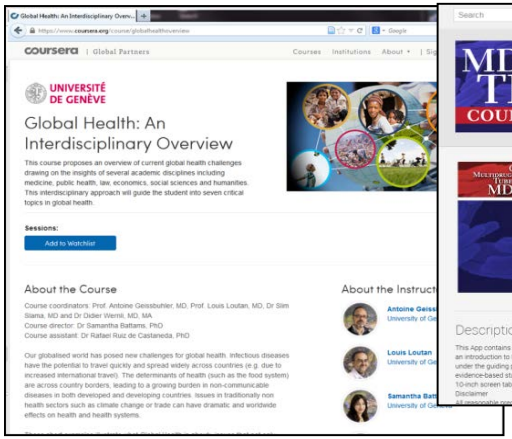


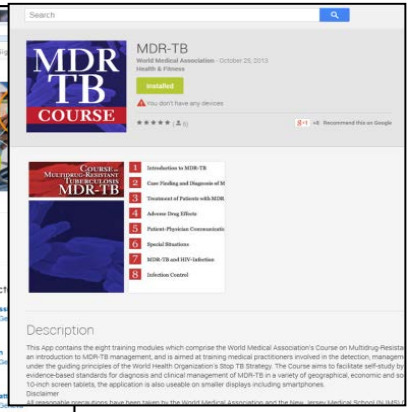
Surveillance



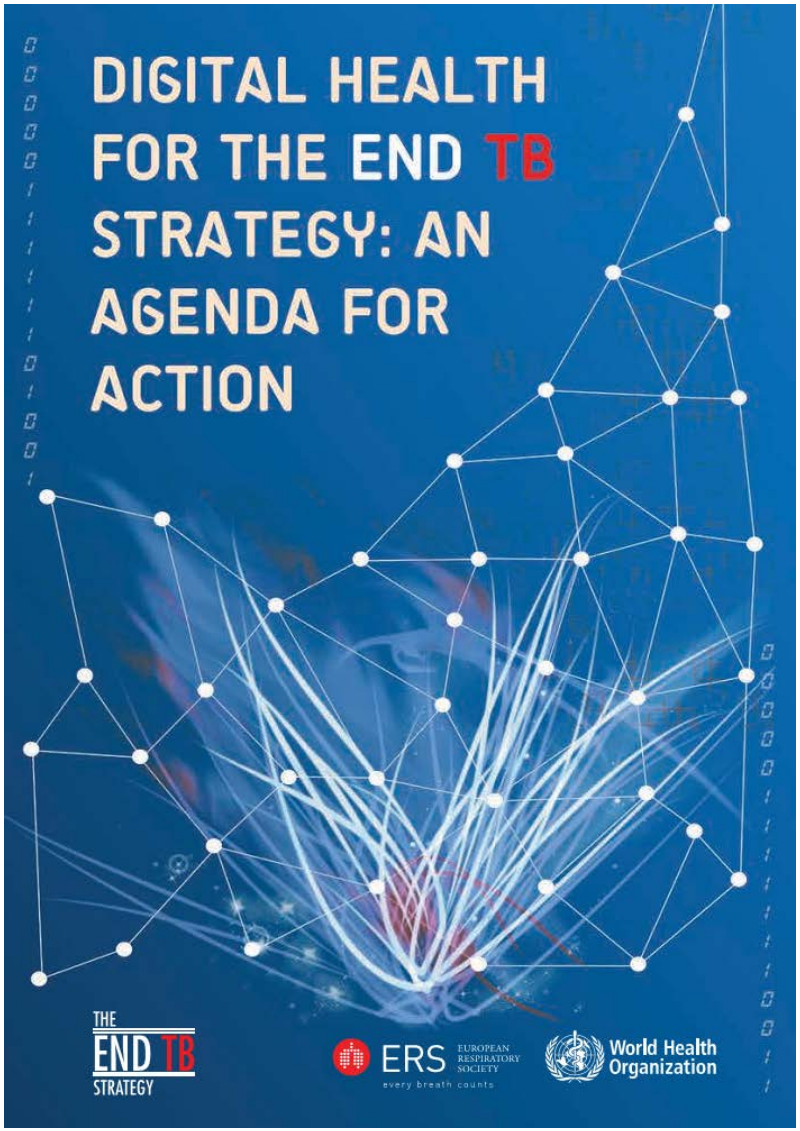


eLearning





“Agenda for action”



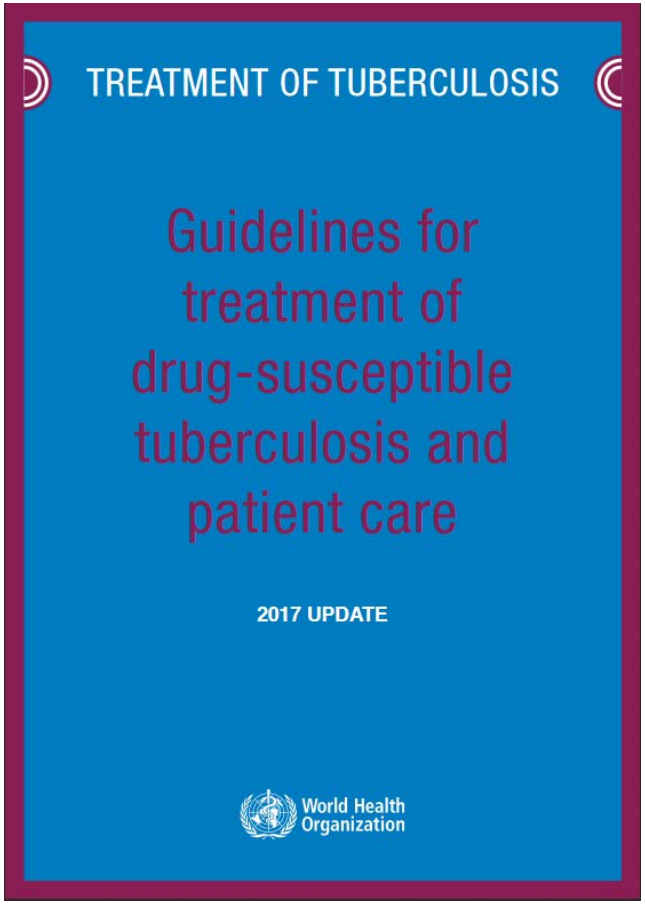
The strategic direction that WHO is mapping out to integrate digital health into preventive and care activities for the different components of the End TB strategy

Comments on the evidence and an outline of the target product profiles

Sep 2015

evidence -> WHO policy, 2016/2017

administration option



"The following treatment administration options may be offered to patients on TB treatment:

…

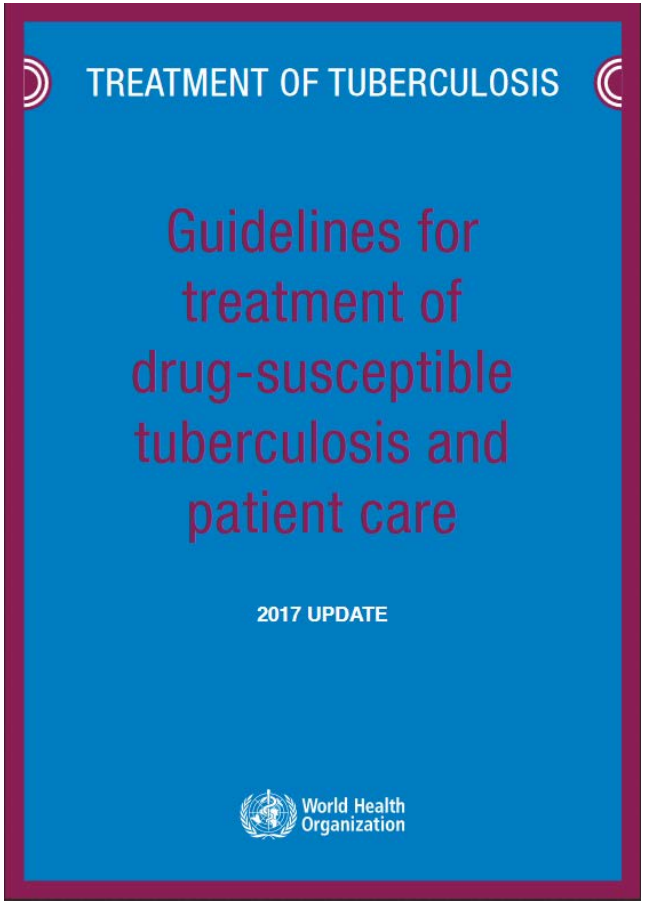
c) Video observed treatment (VOT) can replace DOT when the video communication technology is available and can be appropriately organized and operated by health-care providers and patients"

[Conditional recommendation, low certainty in the evidence]

apps.who.int/iris/bitstream/10665/255052/1/9789241550000-eng.pdf

evidence -> WHO policy, 2016/2017

adherence interventions



Treatment adherence interventions - including SMS, voice, and electronic medication monitors - may be offered to patients on TB treatment

[Conditional recommendation, low certainty in the evidence]

apps.who.int/iris/bitstream/10665/255052/1/9789241550000-eng.pdf

VOT for TB

Countrywide expansion of VOT, Belarus

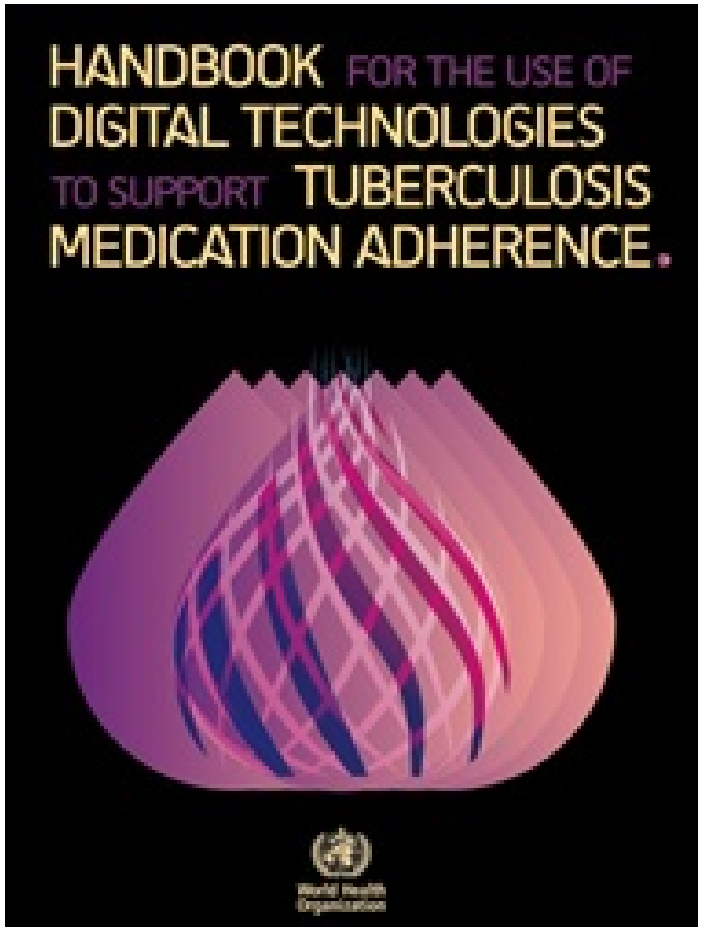


Minsk City	**71**
Minsk region	40
Gomel region	52
Mogilev region	21
Vitebsk region	24
Brest region	5
Grodno region	18

Update:
> 360 patients by Oct 2018

Source: Alena Skrahina, NTP Belarus

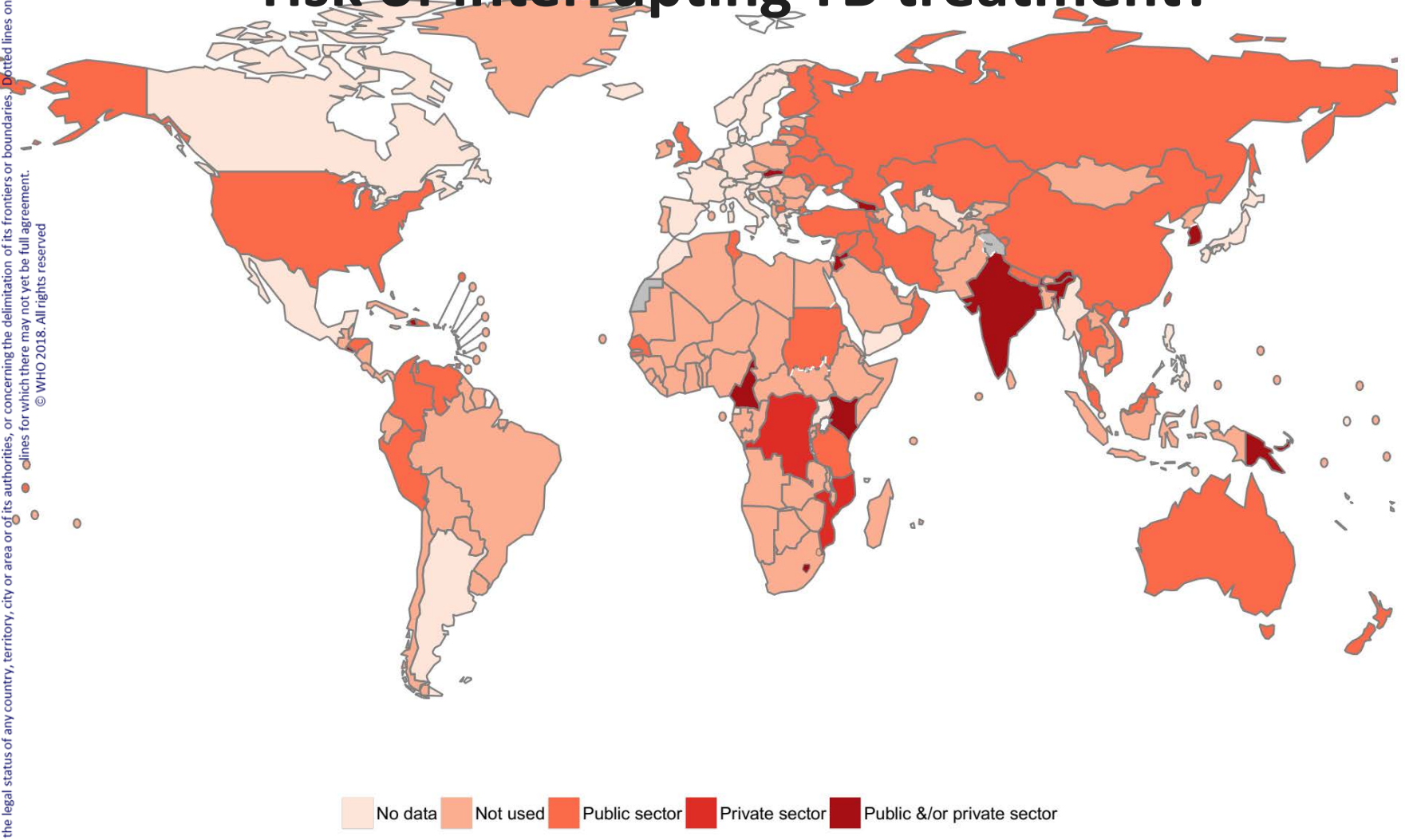
“How to” for adherence support



- Focuses on three technologies that are being widely used to help TB patients complete their treatment
- Addresses common questions the implementer has for emerging technologies

www.who.int/tb/publications/2018/TB_medication_adherence_handbook_2018/en/

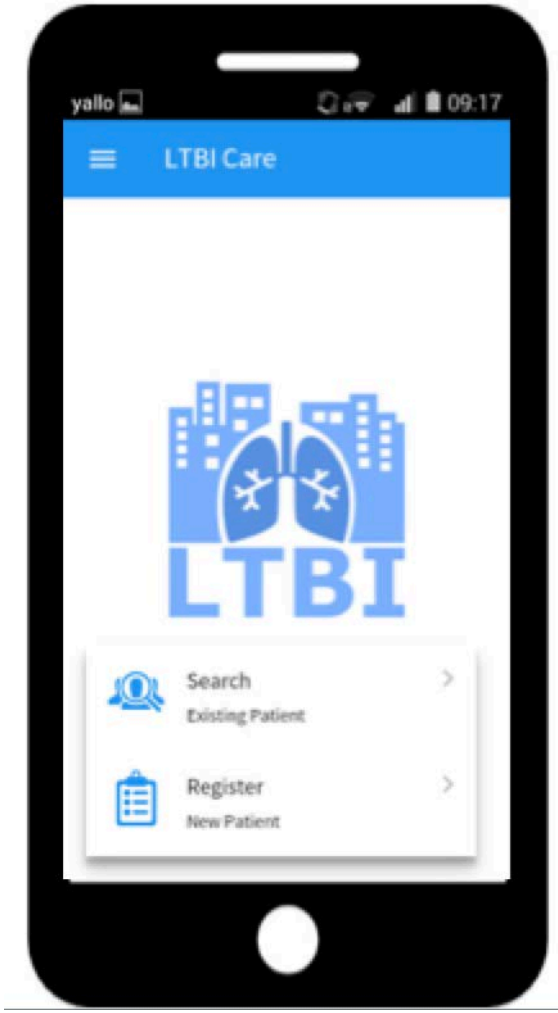
In 2017, were text, VOT, MEMS or other digital technologies being used to support patients at risk of interrupting TB treatment?



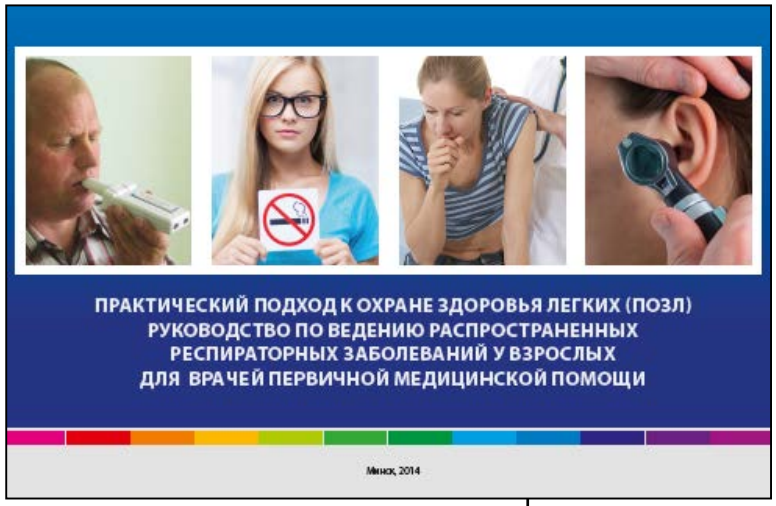
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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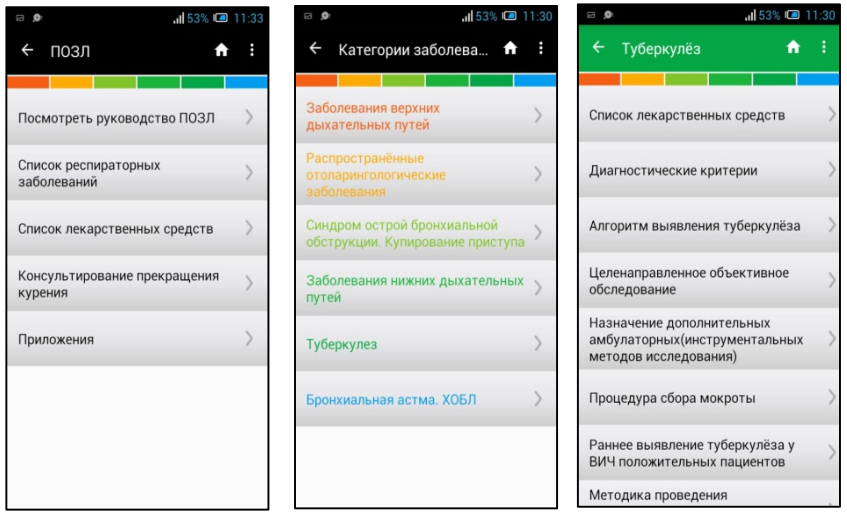
LTBI digital tool key characteristics

- Free – downloadable from WHO website
- Adaptable- to country specific context and needs
- Functional- on mobile devices
- Flexible- record data off line and synchronise later and use local server

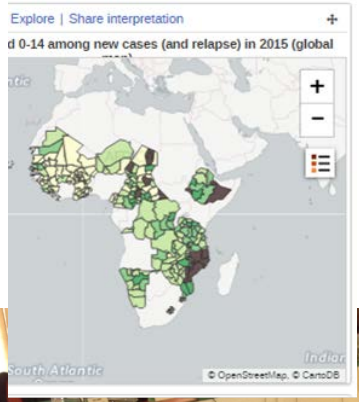


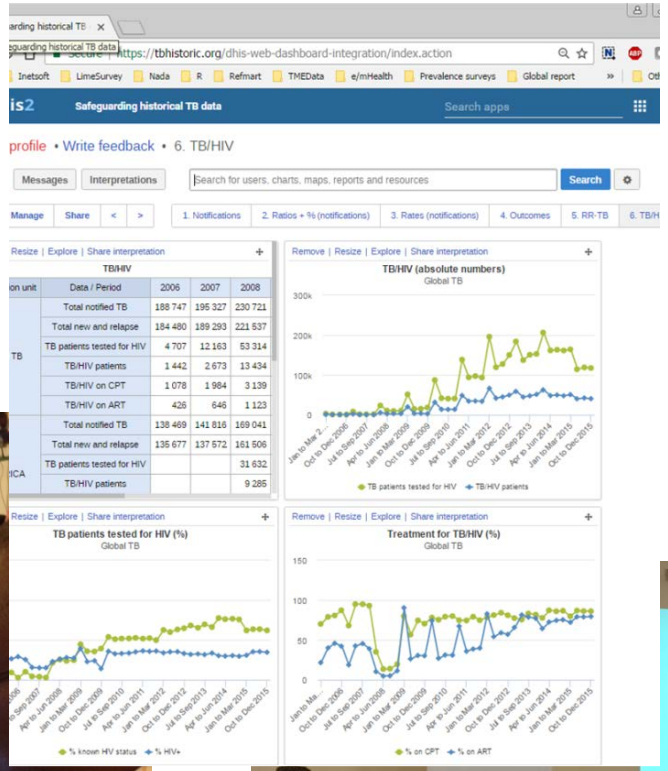
eLearning apps

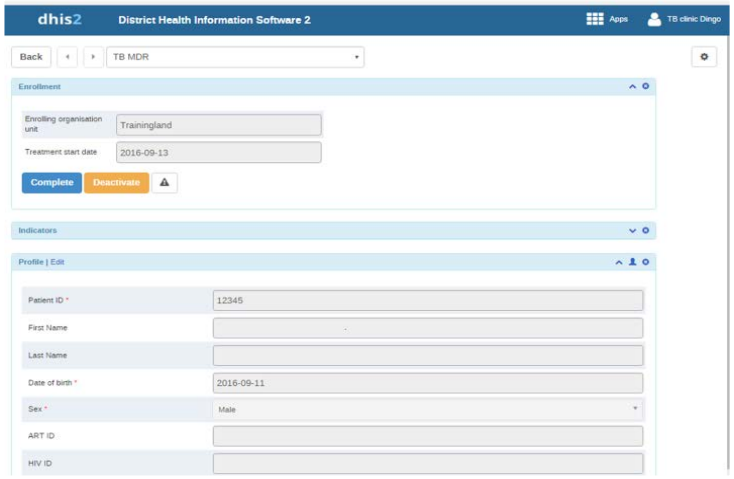


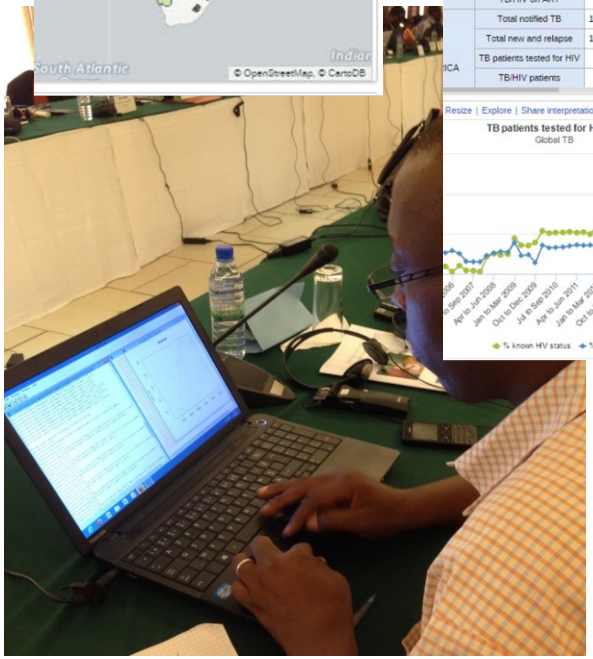


Electronic case-based surveillance

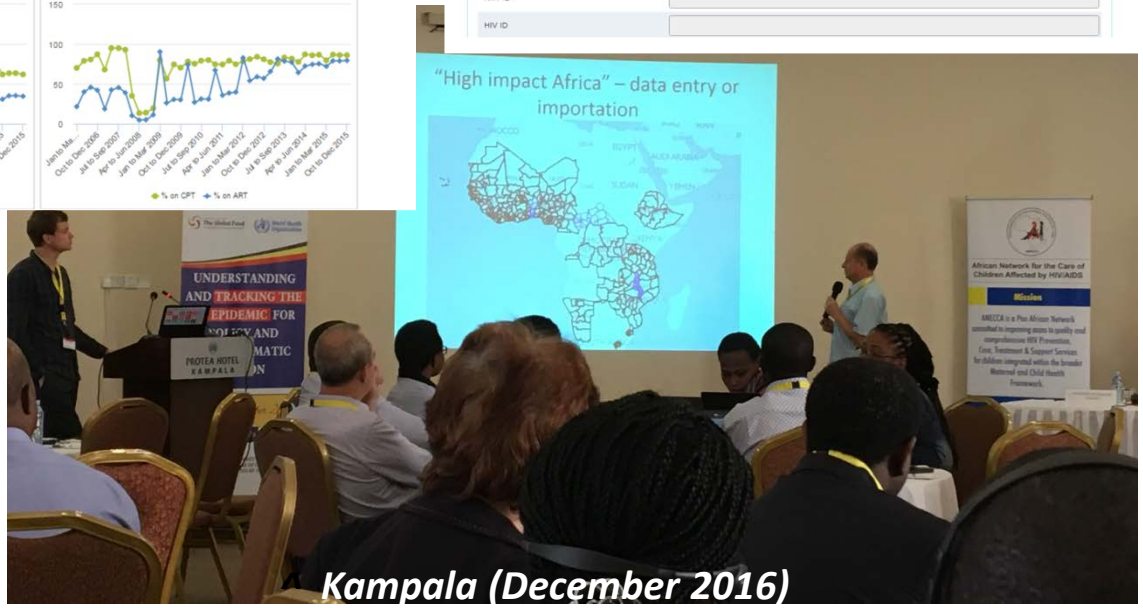








Benin (October 2015; May & October 2016)



Kampala (December 2016)

Integrating ICT solutions (India)



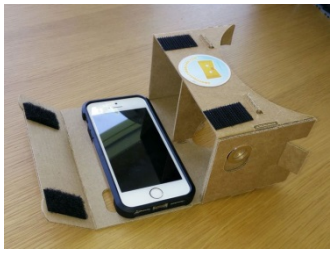
Future perspectives (1)

- New approaches to adherence support
- Artificial intelligence to extend the reach of today's products
- Personalized care and public health
- Implementation research

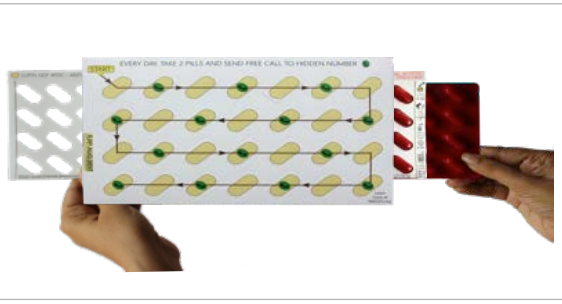


Future perspectives (2)



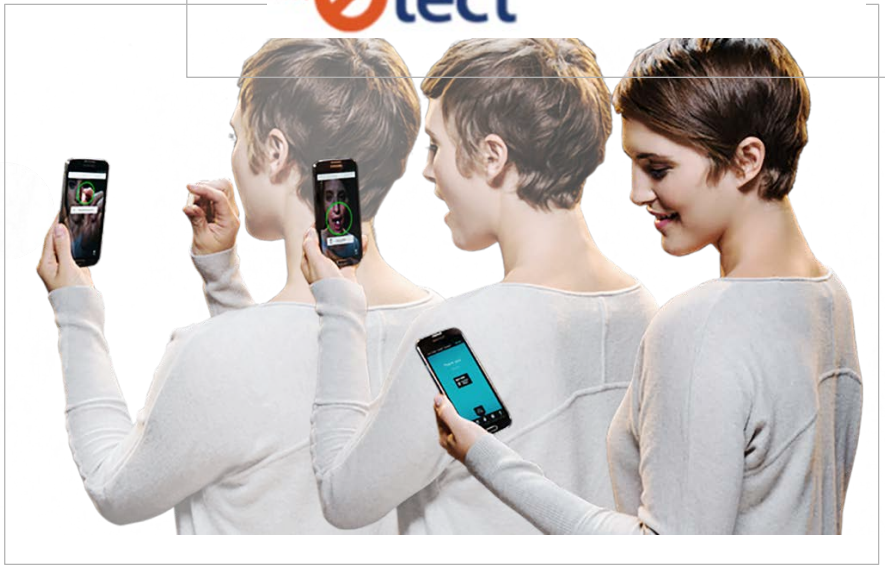






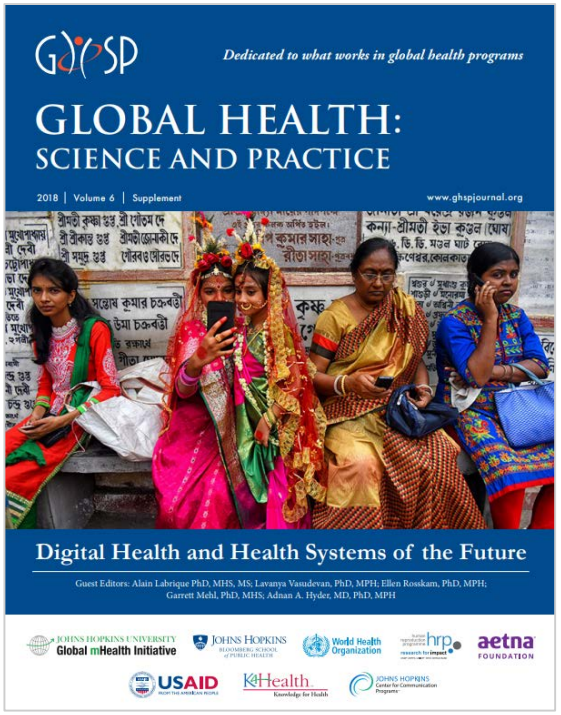


etect proteus DIGITAL HEALTH



What does it take to be an effective national steward of digital health ?

- strategic direction
- policies and procedures
- roles and responsibilities
- health service delivery



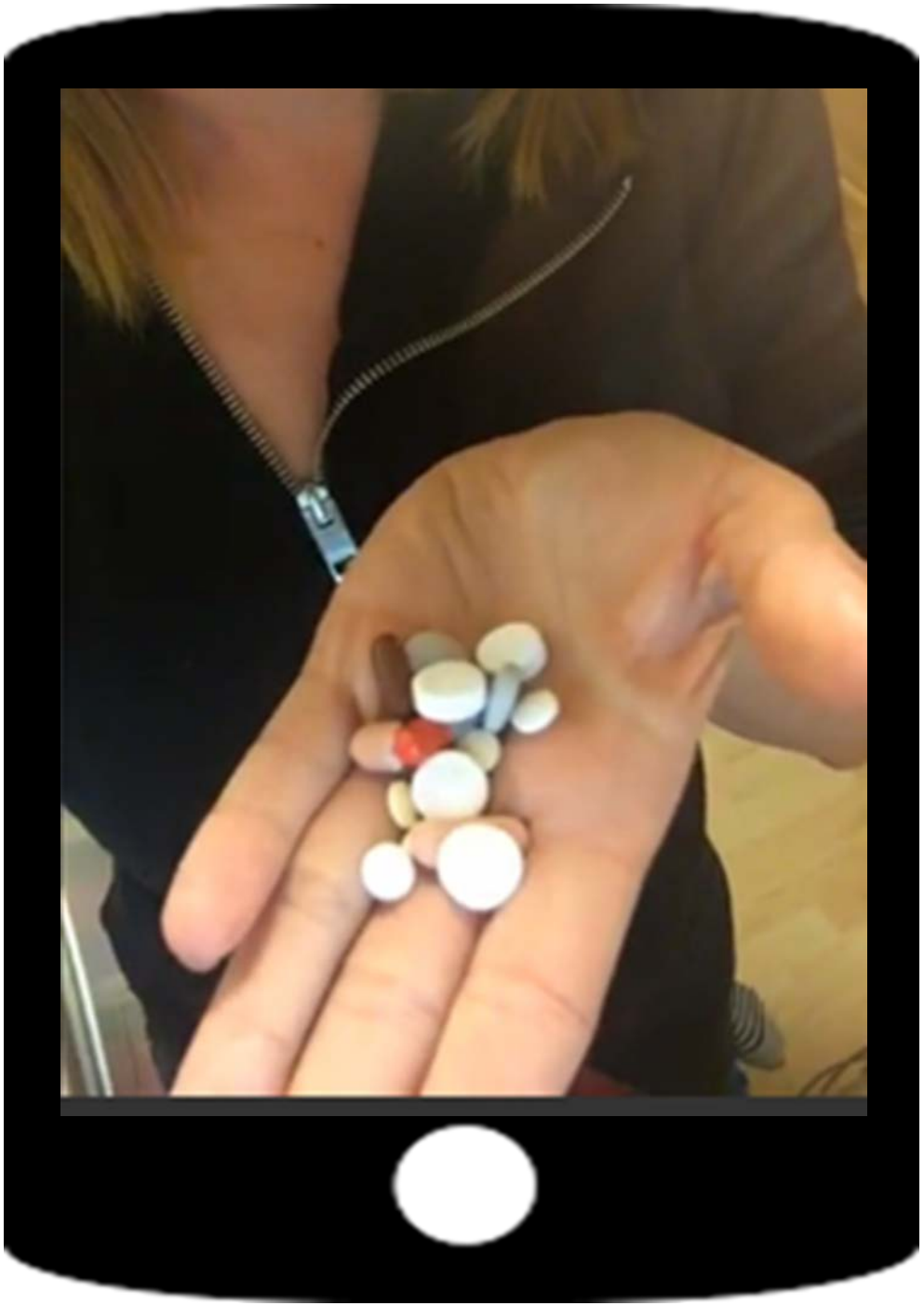
Frost MJ, et al. Global Health: Science and Practice. 2018 Oct 10;6(Supplement 1):S18–28.

Acknowledgements

- Ligue Pulmonaire Suisse
- European Respiratory Society
- *Global task force on digital health for TB*
- National TB programmes
- Technical and funding partners
- WHO/GTB & many other WHO colleagues

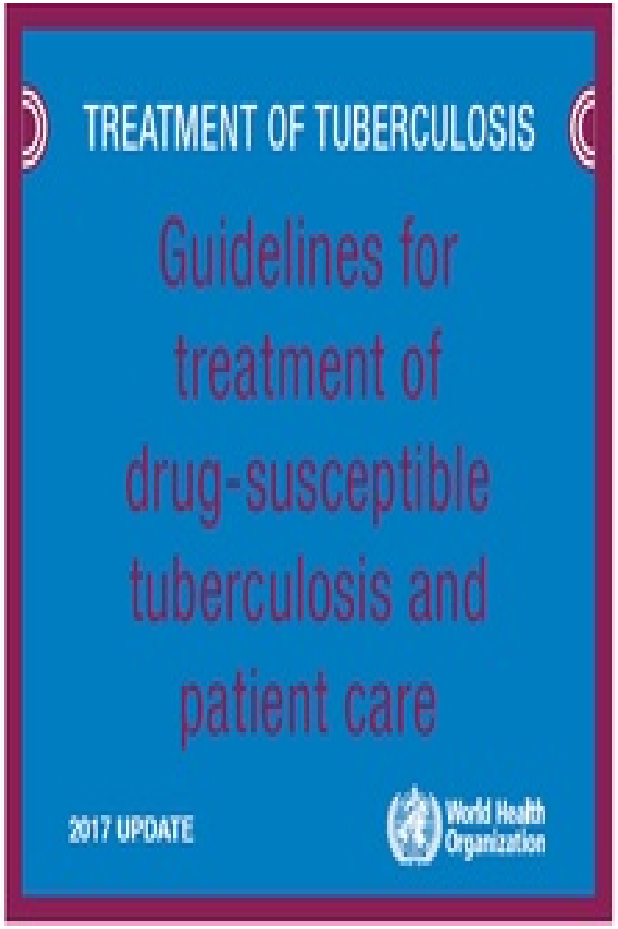
Video Observed Treatment (VOT)

Professor Andrew Hayward
Director UCL Institute of Epidemiology and Healthcare



2017 WHO TB guidance recommends

- Community or home-based DOT over health facility-based DOT or unsupervised treatment
- DOT administered by trained lay providers or health care workers over DOT administered by family members or unsupervised treatment
- the use of thrice-weekly dosing is not recommended…and daily dosing remains the recommended dosing frequency



Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO

In England DOT is recommended as part of Enhanced Case Management

for those with History of homelessness, imprisonment, mental health problems, drug use, previous TB, previous poor adherence, MDRTB

*NICE TB Guideline NG33;

Case Management & Cohort Review Toolkit;

Collaborative TB Strategy for England;

NICE Quality Standards for TB (QS141)

Pan-London DOT survey
2008 & 2014

- Only two-thirds of patients who need DOT get DOT
- Main reasons:
  - Lack of resources
  - No out of hours service
  - Complex drug regimens (bd, tds & qds)

And…

- It’s expensive and time consuming
- It usually amounts to max 71% of doses observed – 5-x-week
- Limited to once daily dosing
- Patients don’t like it
  - High rate of refusal
  - High rate of self administered doses
  - High rate of drop out

"...I'd rather not go every morning to my pharmacy...if I can do it from home...that's better for me."

"...but to the clinic I have to go everyday far away...so to me it's better to be the phone"

"At the pharmacy I had to take them [the tablets] in front of everyone...Now I do it in my own personal time...I can do that without no issue"

From interviews conducted at UCL as part of VOT RCT. Awaiting publication

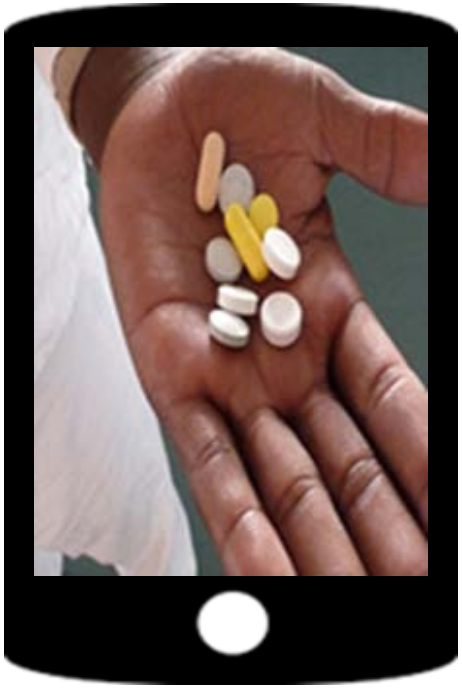
VOT in 3 easy steps

1



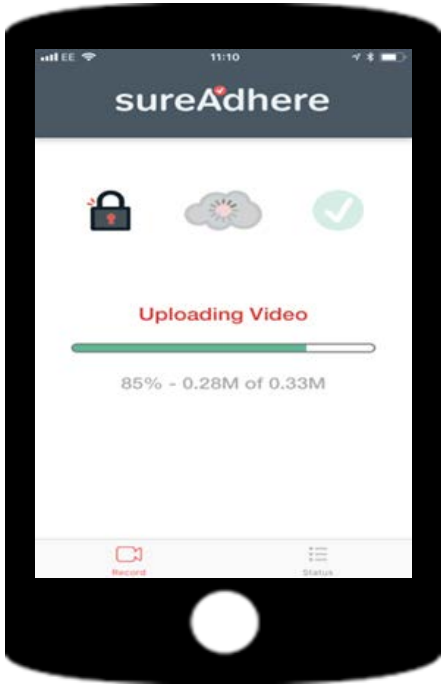
Enter unique pin code

2



Film tablets and ingestion, report side effects

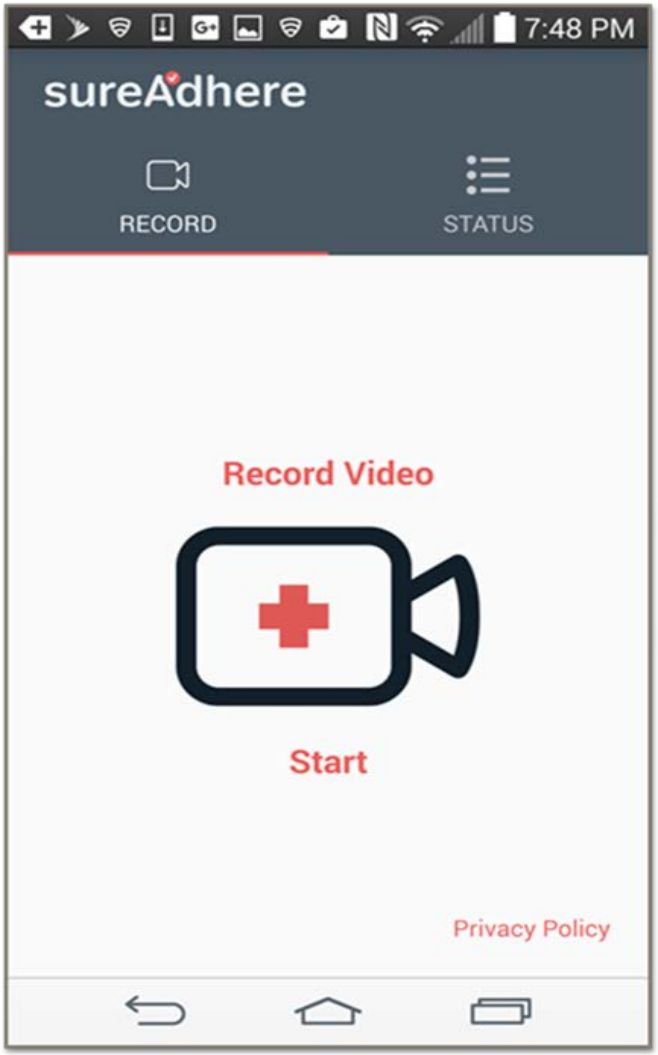
3



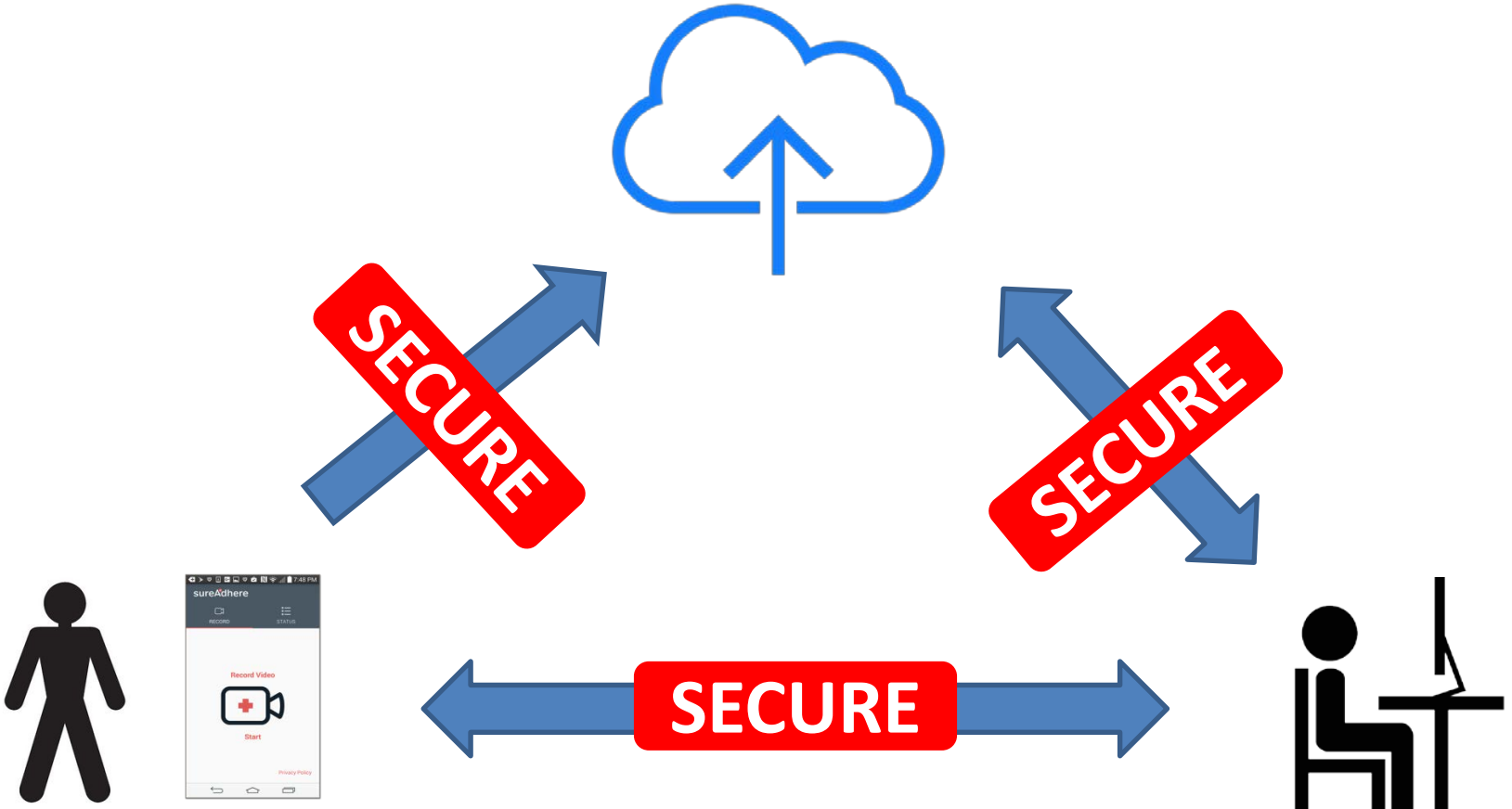
Films uploaded automatically

Governance and data protection issues covered by F&T

- Fully GDPR compliant ✓
- Easy, safe & secure filming ✓
- End-to-end encryption ✓
- Password protection on app & CMS ✓
- No patient identifiable information ✓
  - unique username and pin code
- Films do not get stored on patient's phone ✓
  - films automatically uploaded using WiFi or mobile data
- Films date & time stamped ✓
  - patients decide where/what time to film
- Phones/data can be provided ✓



Client Management System



THE LANCET

Smartphone-enabled video-observed versus directly observed treatment for tuberculosis: a multicentre, analyst-blinded, randomised, controlled superiority trial

Alistair Story, Robert W Aldridge, Catherine M Smith, Elizabeth Garber, Joe Hall, Gloria Ferenando, Lucia Possas, Sara Hemming, Fatima Wurie, Serena Luchenski, Ibrahim Abubakar, Timothy D McHugh, Peter J White, John M Watson, Marc Lipman, Richard Garfein, Andrew C Hayward

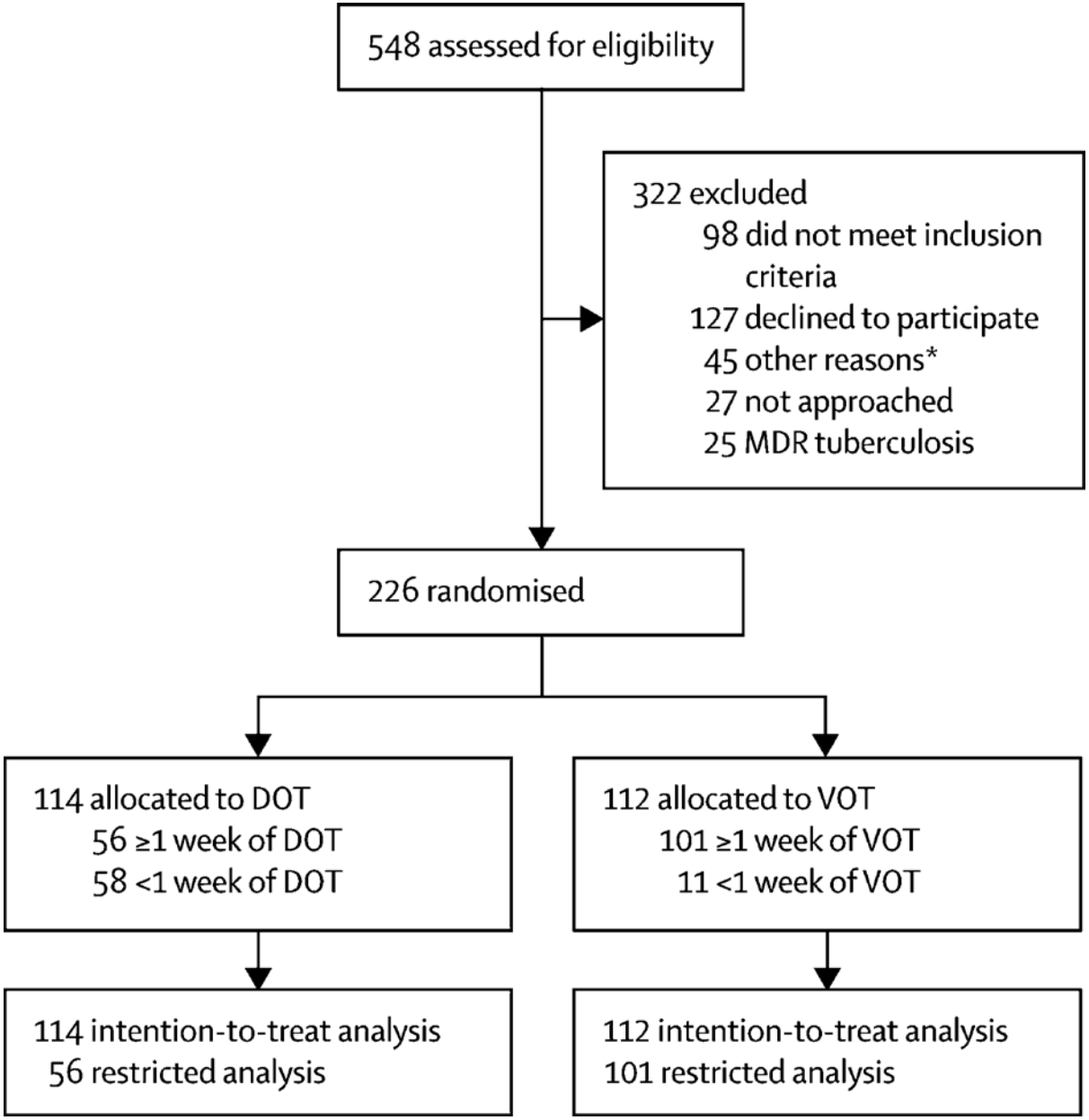
DOI: 10.1016/S0140-6736(18)32993-3

Inclusion / Exclusion Criteria

- Inclusion
  - Eligible for DOT under national or local guidance
  - Age > 16 years
- Exclusion
  - No place to charge a smart phone*
  - <2 months treatment left
  - MDRTB (non randomised arm)

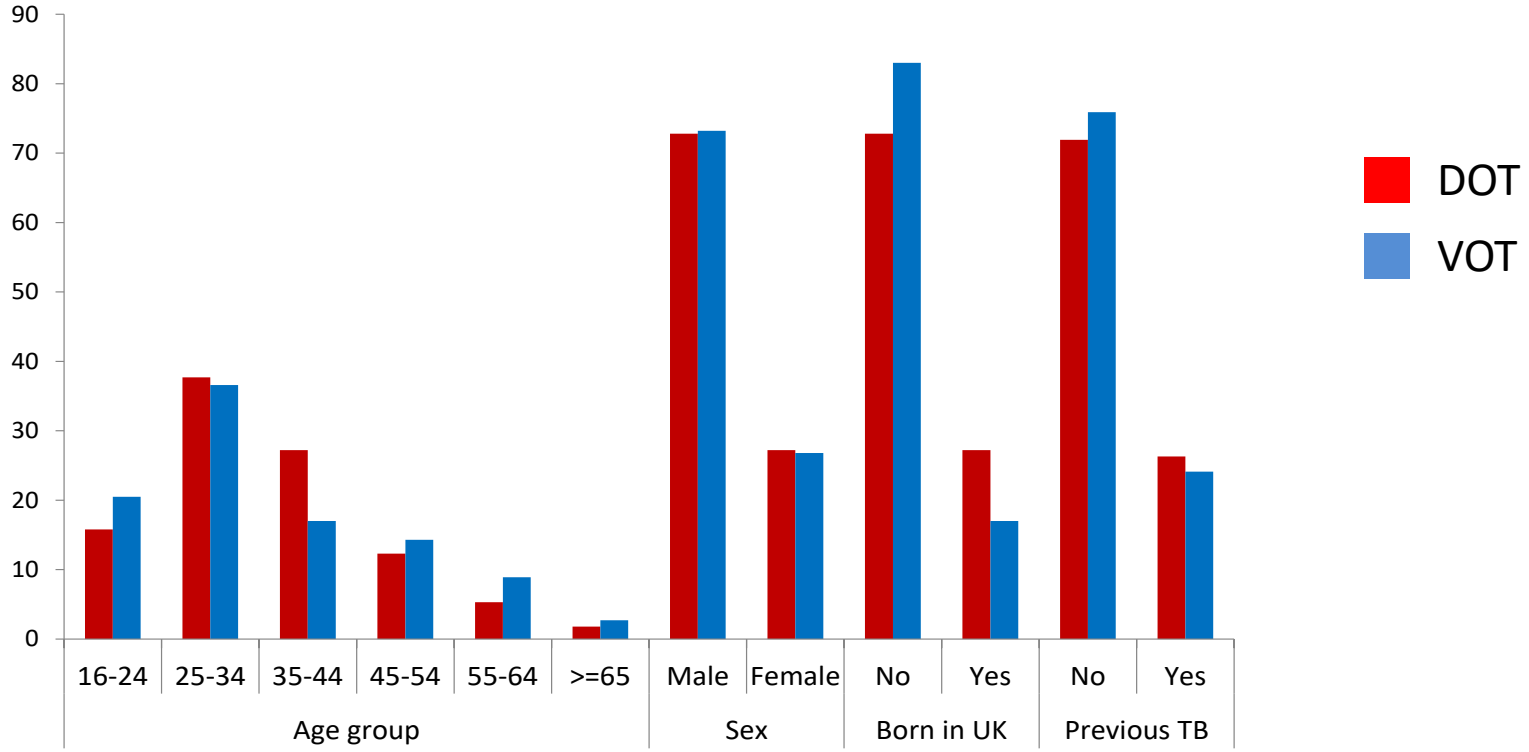
  - 22 clinics in England (UK; London [17 sites], Birmingham [three], Coventry [one], and Leicester [one])

  - * if street homeless the VOT started once accommodation found

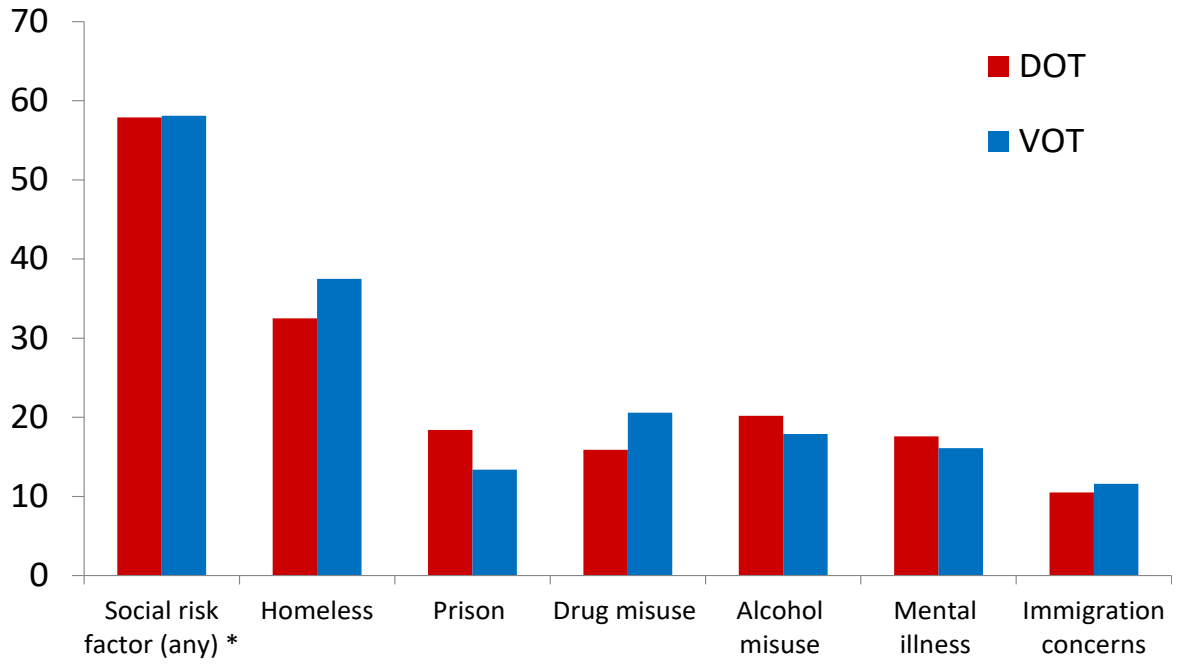

548 assessed for eligibility
322 excluded
98 did not meet inclusion criteria
127 declined to participate
45 other reasons*
27 not approached
25 MDR tuberculosis
226 randomised
114 allocated to DOT
56 ≥1 week of DOT
58 <1 week of DOT
112 allocated to VOT
101 ≥1 week of VOT
11 <1 week of VOT
114 intention-to-treat analysis
56 restricted analysis
112 intention-to-treat analysis
101 restricted analysis

Baseline characteristics

Balanced randomisation



Socially complex cases



* Any current social risk factor = Homeless, problem drug use, alcohol, prison

Interventions

VOT

- 7 days a week - Initial training by main VOT observer
- All videos acknowledged via personalised e-mail or text
- Telephone contact if no video sent
- Weekend videos read on Mondays
- Standard smartphone and App + unlimited UK calls and texts
- No further incentives

DOT

- 3 or 5 in-person clinic or community observations per week
- Incentives and enablers as per local protocols - usually £5 per dose observed + Travel card payments

- 58% had history of homelessness, drug use, imprisonment, alcohol problems, mental health problems.

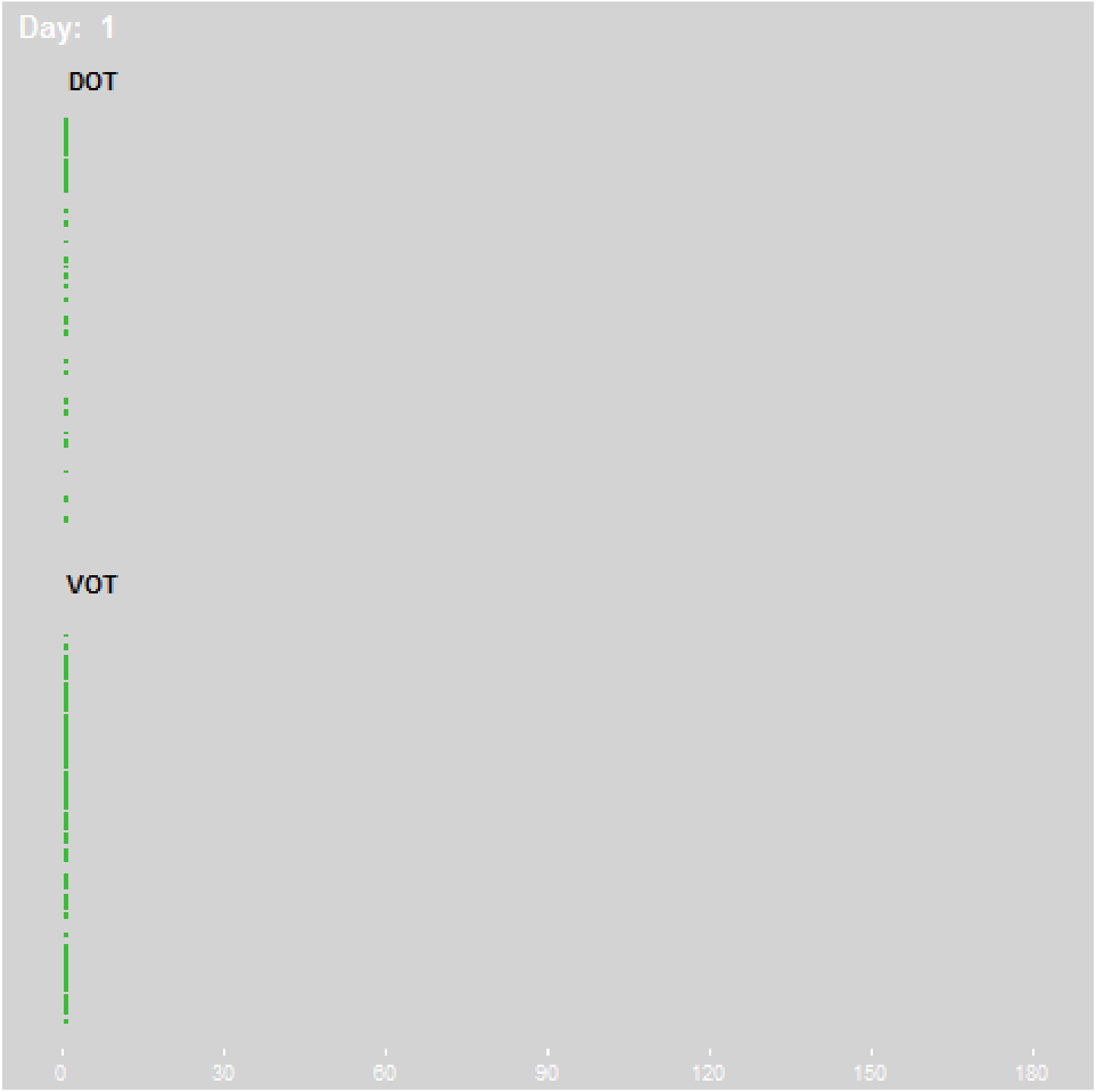
- The primary outcome was completion of 80% or more scheduled treatment observations over the first 2 months following enrolment.

- Intention-to-treat (ITT) and restricted (including only patients completing at least 1 week of observation on allocated arm) analyses were done.

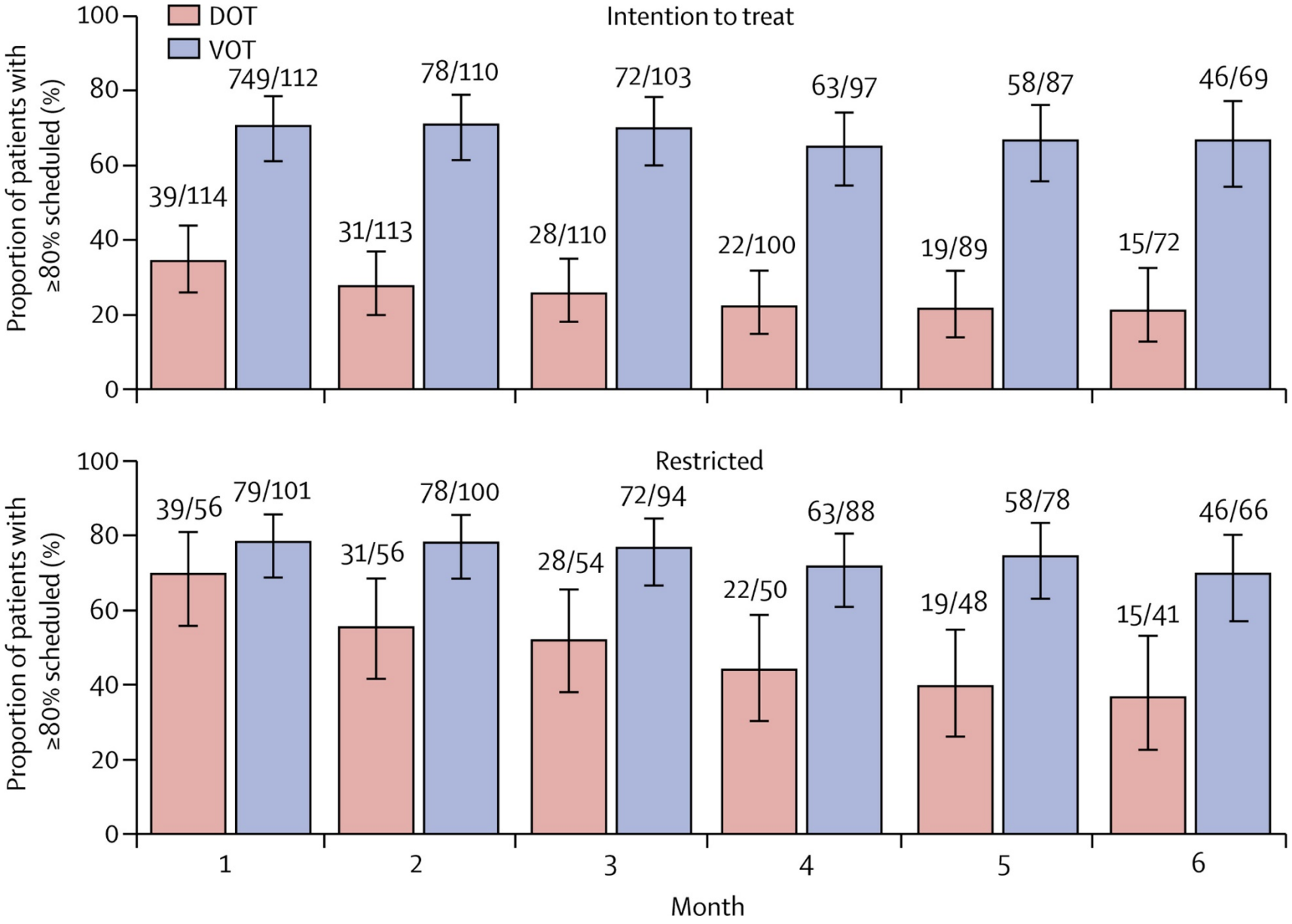
Initial engagement with VOT and DOT

- Overal levels of initial engagement with VOT were 90% and exceeded 70% in all subgroups,

- Overal levels of initial engagement with DOT were 50% and were particularly low (<50%) in younger adults, foreign-born patients and those without social risk factors or mental health problems



DOT Vs VOT


DOT
VOT
Intention to treat
Proportion of patients with ≥80% scheduled (%)
100
80
60
40
20
0
39/114
749/112
31/113
78/110
28/110
72/103
22/100
63/97
19/89
58/87
15/72
46/69
Restricted
Proportion of patients with ≥80% scheduled (%)
39/56
79/101
31/56
78/100
28/54
72/94
22/50
63/88
19/48
58/78
15/41
46/66
1
2
3
4
5
6
Month

ITT analysis

- % Achieving ≥ 80% of scheduled observations during 1st 2 months
- VOT 70% (78/112)
- DOT 31% (35/114)
- adjusted OR 5·48, 95% CI 3·10–9·68; p<0·0001).

- % of scheduled observations completed over first 2 months
- VOT 79% (5091/6474)
- DOT 45% (1774/3922)

- % of scheduled observations completed up to 6 months
- VOT 77% (12422/16230)
- DOT 39% (3884/9882)
- p<0·0001.

Restricted analysis

- % Achieving ≥ 80% of scheduled observations during 1st 2 months
- VOT 77% (78/101)
- DOT 63% (35/56)
- adjusted OR 2·52; 95% CI 1·17–5·54; p=0·017.

- % of scheduled observations completed over first 2 months
- VOT 86% (5091/5893)
- DOT 73% (1774/2418)

- % of scheduled observations completed up to 6 months
- VOT 83% (12422/14907)
- DOT 61% (3884/6351)
- p<0·0001.

Costs

- Average staff time per dose observed
- 56 min for community based DOT (including travel time);
- 15 min for clinic-based DOT,
- 3·2 min for VOT.

- Cost over 6 months
- 5 times weekly DOT £5700 per patient
- 3 times weekly DOT £3420 per patient
- Daily VOT £1645 per patient

"I've been down with some of my medication...stopping my medication for no reason...this gave me an opportunity to take my medication whenever I had to take it...I felt good"
(From VOT RCT)

"I also had a very bad addiction to substances and stuff...I think it's probably not a very good idea to just give it [medication]... I think VOT did a really good job. It's a really good programme"
(from VOT RCT)

"...the process was very quick. All I had to do was wake up in the morning...and record the patient video...that's all"
(from VOT RCT)

"I enjoy doing my films and managing my medication myself...It's good and really easy to use. I'm happy with it"

"I don't think I would've taken the medications regularly...I wasn't going to be compliant" (from VOT RCT)

VOT is Recommended by World Health Organisation (WHO)

Video observed treatment (VOT) can replace DOT when the video communication technology is available and it can be appropriately organised and operated by health care providers and patients

Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO

VOT vs DOT

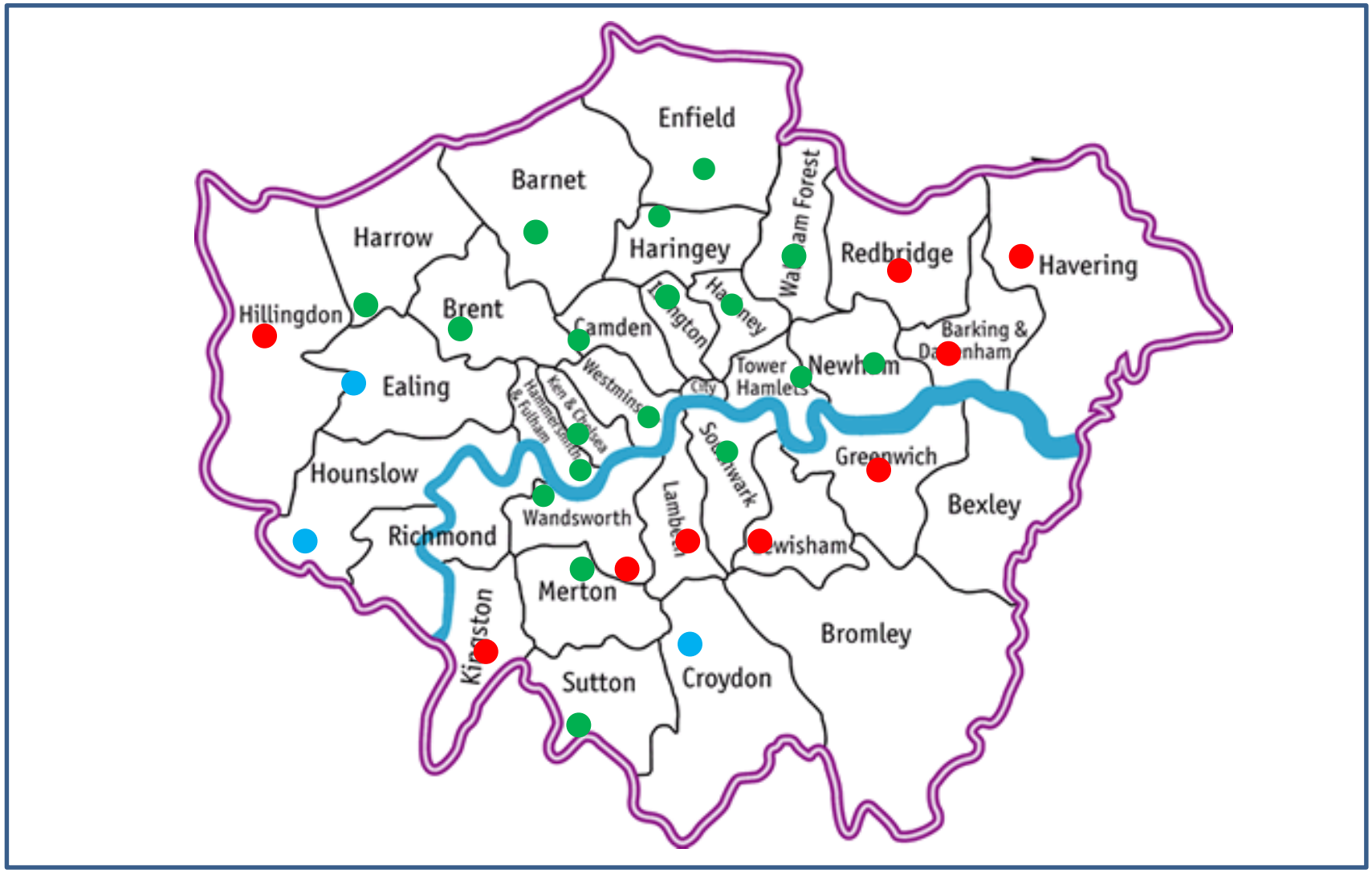
- More effective
- Cheaper
- Preferred by patients

- Video observed treatment (VOT) ~~can~~ should replace DOT

VOT is rapidly expanding nationally

- > 120 + referrals in last 18 months (350 + patients since 2009)
  - Nearly 40% of these in last 6 months
  - 17% are out of London referrals
- 54 of these have completed Rx on VOT
- 8 (6%) have crossed-over to DOT (VOT unsuccessful)
- 60 + patients currently on VOT (or waiting to start)
- One-third of patients on VOT have MDR/XDR TB
  - VOT is standard Rx option for MDR patients

VOT in London



● = new services referring patients for VOT (since 01/04/17)

● = Services previously using VOT (prior to 01/04/17)

● = referrals for VOT (since 01/04/17)

Find&Treat National VOT Service

- Available nationwide
- Easy to use VOT app (developed by SureAdhere)
  - Available for iOS & Android phones
- Patient uses own phone or F&T provided VOT phone
- Easy referral process
  - Contact F&T to discuss referral
  - Complete out of London VOT agreement form
- Quick set-up
  - Same day set up if patient using own phone
- Cheap daily costs (tariff basis)

VOT Tariff costs

Fully sensitive TB (with VOT phone)	£6.99 per film	£48.93 p/w
Fully sensitive TB (with patient's own device)	£6.23 per film	£43.61 p/w
MDR TB (with VOT phone)	£5.99 per film	From £41.93 p/w
MDR TB (with patient's own device)	£5.23 per film	From £36.61 p/w

Tariff cost covers app rental, phone/data charges (if applicable), server rental/maintenance costs & VOT observer/admin time

13 year old male multi-organ MDRTB

Breakfast

Linezolid - Cycloserine - Delaminid - Prothionamide - Pyrazinamide



flowplayer

00:04 01:13 flowplayer

Thank you



Andrew Hayward
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Find&Treat National VOT Service

Alistair Story
Al.story@nhs.net



28 Tuberkulose-Symposium

Magglingen

27. März 2019



Video observed treatment for tuberculosis patients in Belarus

Alena Skrahina, Minsk, Belarus



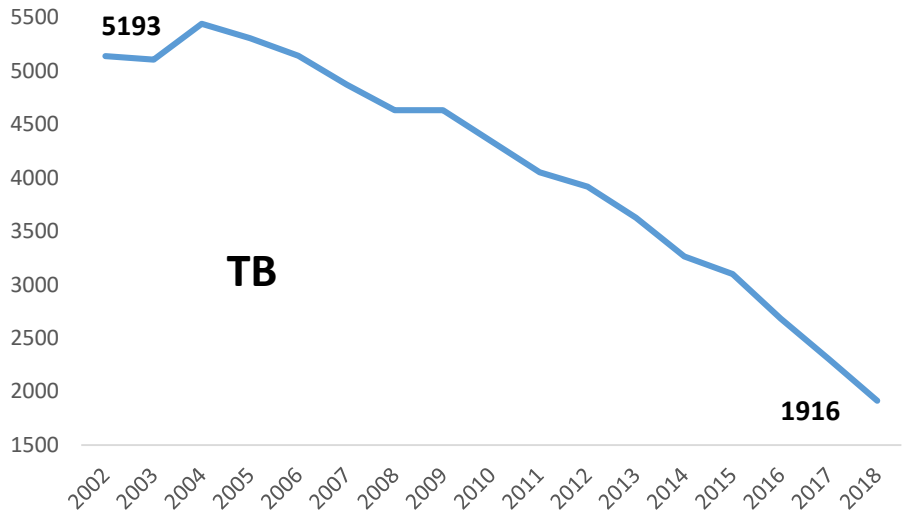




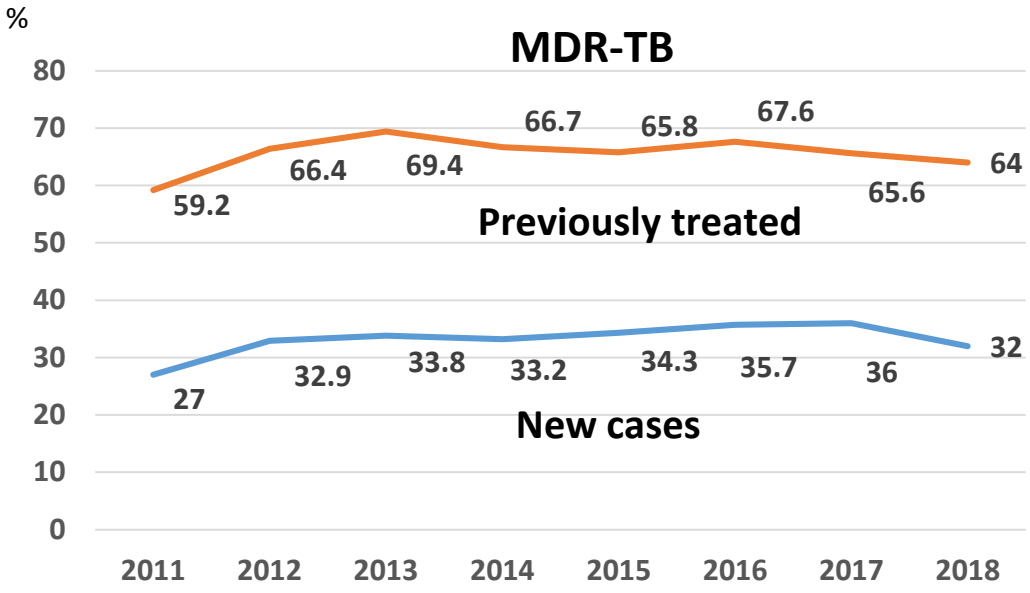
Conflict of interest disclosure

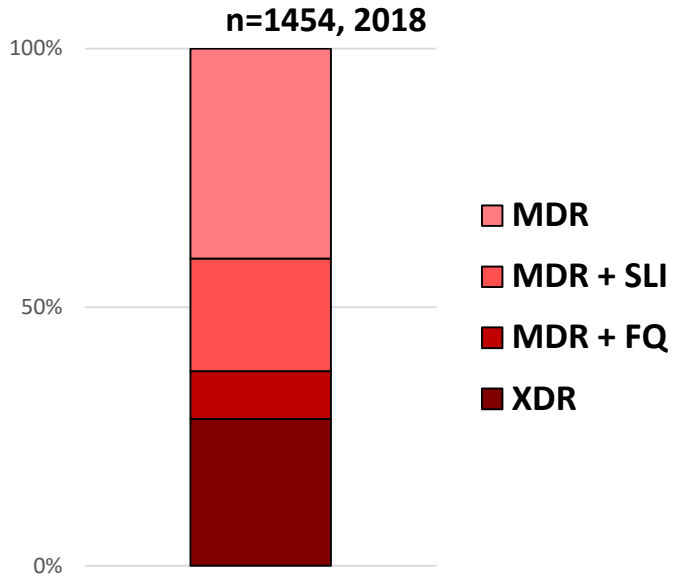
- ☑ I have **no**, real or perceived, direct or indirect conflicts of interest that relate to this presentation.

Belarus challenges *M/XDR-TB*



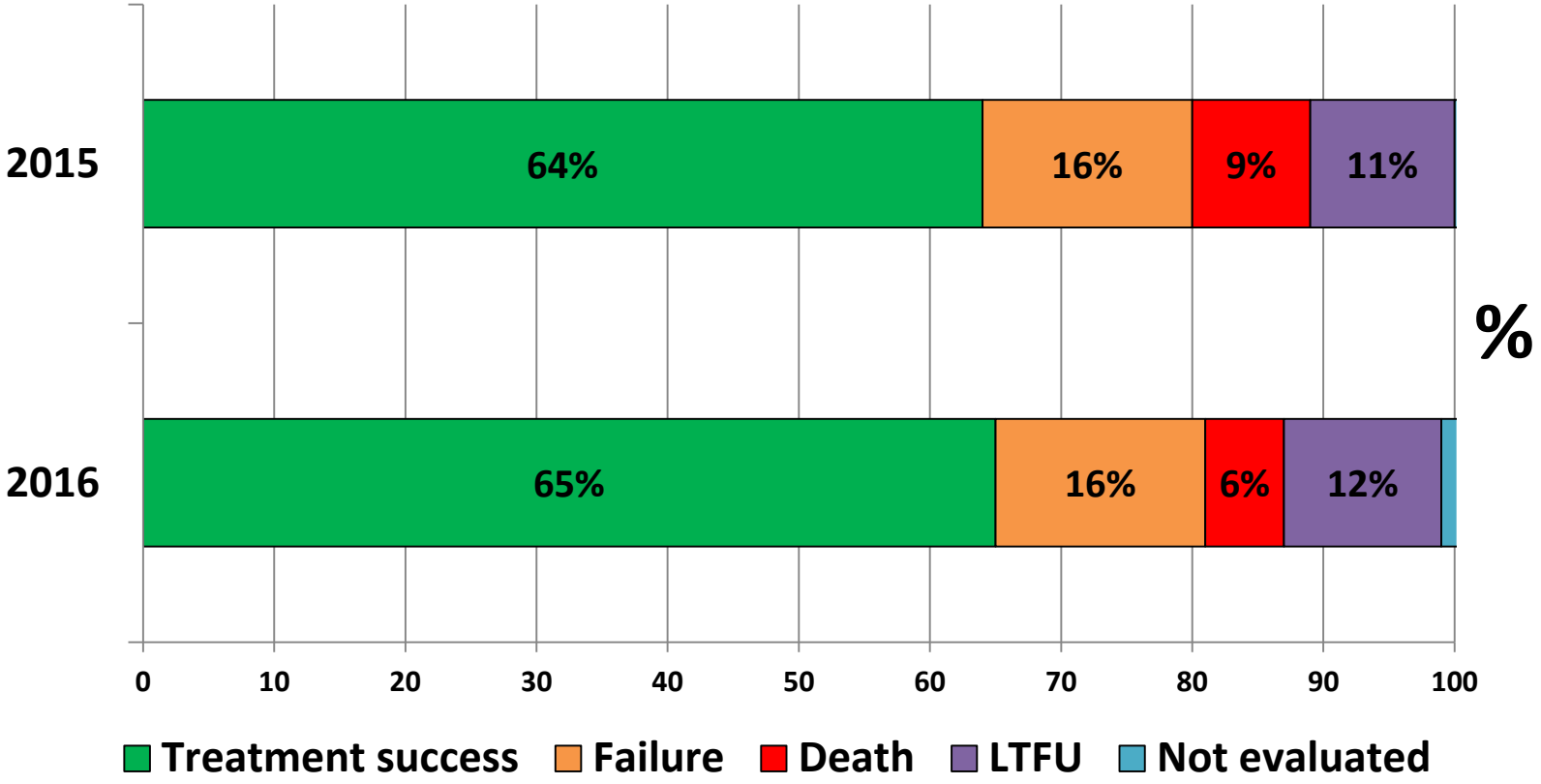
TB indicator	No. of patients	Per 100 000
Incidence	1916	20,2
Prevalence	4035	42,5
Mortality	242	2,6





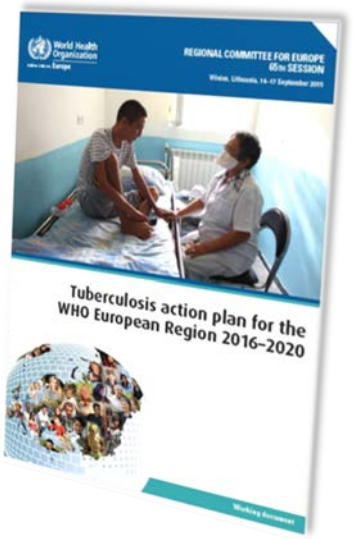
M/XDR-TB Treatment outcomes

Belarus country cohort



Key strategic directions of NSP

1. Scale up of case finding and prophylaxis
2. Full scale-up of rapid molecular diagnostics
3. Rapid uptake of new drugs and regimens
4. Expanding patients-centered models of care
5. Scale up TB research





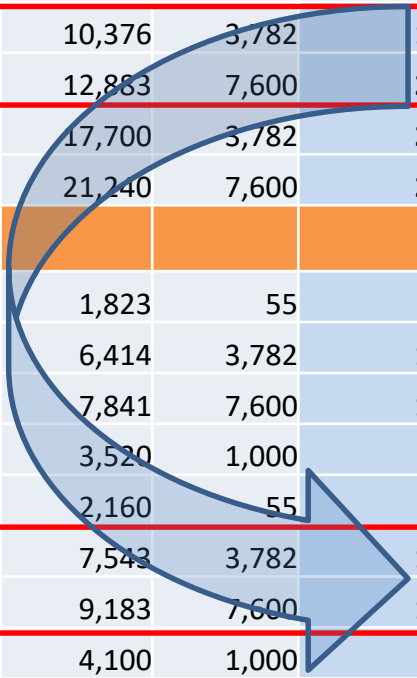
Bedaquiline (June 2015)
Delamanid (June 2016)

Linezolid Clofazimine
Carbapenems,
Amoxicilline/clavulonat

Transition to ambulatory based TB care

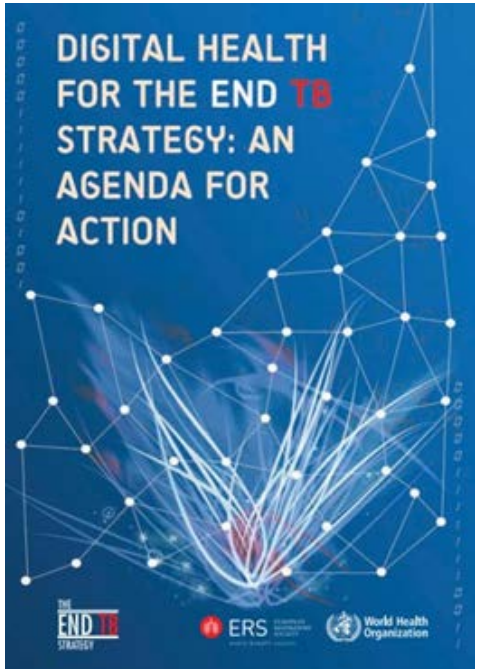
Treatment cost components (in USD)

		Costs of care	Other costs		Total non-drug costs	Drug costs	Total costs	
Modality	**Treatment regimen group**	**Total**	**Food packages**	**Incentives**		**Full course**	**Full course**	**Annualized**
Current practice								
Hospital-based	DS treatment	2491.52	63		2,555	55	**2,610**	2609.7
Hospital-based	**MDR**	10170.43	205		10,376	3,782	**14,158**	8612.8
Hospital-based	**XDR**	12646.19	237		12,883	7,600	**20,483**	10383.8
Involuntary isolation	MDR	17700.00	0		17,700	3,782	**21,482**	13068.4
Involuntary isolation	XDR	21240.00	0		21,240	7,600	**28,840**	14620.3
Alternative modalities								
Standard ambulatory	DS treatment	1735.40	87		1,823	55	**1,878**	1877.8
Standard ambulatory	MDR	6121.77	292		6,414	3,782	**10,196**	6202.7
Standard ambulatory	XDR	7493.35	348		7,841	7,600	**15,441**	7827.7
Standard ambulatory	MDR - short	3370.36	150		3,520	1,000	**4,520**	4520.5
Incentivized ambulatory	DS treatment	1735.40	87	338	2,160	55	**2,215**	2215.4
Incentivized ambulatory	**MDR**	6121.77	292	1129	7,543	3,782	**11,325**	6889.2
Incentivized ambulatory	**XDR**	7493.35	348	1342	9,183	7,600	**16,783**	8508.0
Incentivized ambulatory	MDR - short	3370.36	150	580	4,100	1,000	**5,100**	5100.0



VOT in Belarus

Project milestones



- 2015 WHO/ERS digital health TPP
- Jan 2015 : feasibility assessment of VOT (WHO)
- Feb 2015: VOT included in GF project proposal; MoH VOT working group
- May 2015 : technical specifications for VOT app; software finished by Jan 2016
- Jan 2016 : pilot single center VOT project
- Oct 2016: programmatic expansion of VOT with GF support

Pilot study of VOT for TB, Minsk, 2016

Eligibility Criteria

- Patient informed consent
- Older than 18 years
- Completed in-person DOT for at least 2 weeks
- Practical test (2 consecutive successful uploads of VOT video) in the presence of the nurse
- Treatment scheme without injectable agents
- No alcohol or drug problems
- Android smartphone



Pilot study of VOT for TB, Minsk, 2016 (1)

Patient characteristics

- 10 TB patients enrolled (5 males, 5 females)
- Age 19-50 years
- 4 MDR-TB, 6 non-MDR-TB
- 6 employed, 1 unemployed, 3 students





Video-observed treatment for tuberculosis patients in Belarus: findings from the first programmatic experience

To the Editor:

The treatment of tuberculosis requires daily intake of multiple medications for between 6 months and 2 years, or more [1, 2]. This long duration predisposes to the interruption of medications with the risk of the emergence of drug resistance, death, disease persistence and continued transmission of tuberculosis in the community. Directly observed treatment, together with patient support, has been recommended to improve adherence [3]. However, daily treatment observation presents challenges for both patients and observers, which have limited its implementation [4]. Digital technologies, like video (or virtually)-observed treatment (VOT) can help bridge the gap between patients and health services and promote adherence [5]. VOT usually requires patients to film themselves taking medications on a computer or mobile device and then transmit these images to a remote observer *via* the internet [6–9].

TABLE 1 Profile of tuberculosis patients in the pilot video-observed therapy (VOT) programme in Minsk, Belarus (2016)

Age-group years	Sex	Tuberculosis resistance pattern	VOT episodes (by May 12, 2016)	Video recording of insufficient quality
20–29	Male	MDR-TB	99	7 (7)
30–39	Male	Isoniazid-monoresistant	102	5 (5)
20–29	Female	Drug-susceptible	99	1 (1)
<20	Female	MDR-TB	91	1 (1)
40–49	Male	Drug-susceptible	82	1 (1)
20–29	Male	Drug-susceptible	43	1 (2)
30–39	Male	MDR-TB	28	2 (7)
30–39	Female	MDR-TB	22	0 (0)
20–29	Female	MDR-TB	14	0 (0)
30–39	Female	Drug-susceptible	15	0 (0)

Data are presented as n or n (%). MDR-TB: multidrug-resistant tuberculosis.

Pilot study of VOT for TB, Minsk, 2016 (3)

- DOT – 1-3 hours to travel to and from the TB dispensary, patients on VOT saved from 1 to 3 hours daily
- VOT treatment was not interrupted at the weekends
- 8 of 10 patients reported spending less money for internet than for travel to TB facility (~1 USD per day)
- 8 of 10 patients confirmed that VOT is easer than visiting the TB facility daily
- All respondents confirmed acceptability of VOT and would recommend it to other TB patients



Programmatic expansion of VOT in Belarus (1)

from October 2016

- The GF-supported project
- All country regions
- 150 patients per year – planned recruitment
- Belarusian Red Cross is a country partner
- Smartphones (60 USD each) are provided
- cellular service (9 USD per month) is provided



Programmatic expansion of VOT in Belarus (2)

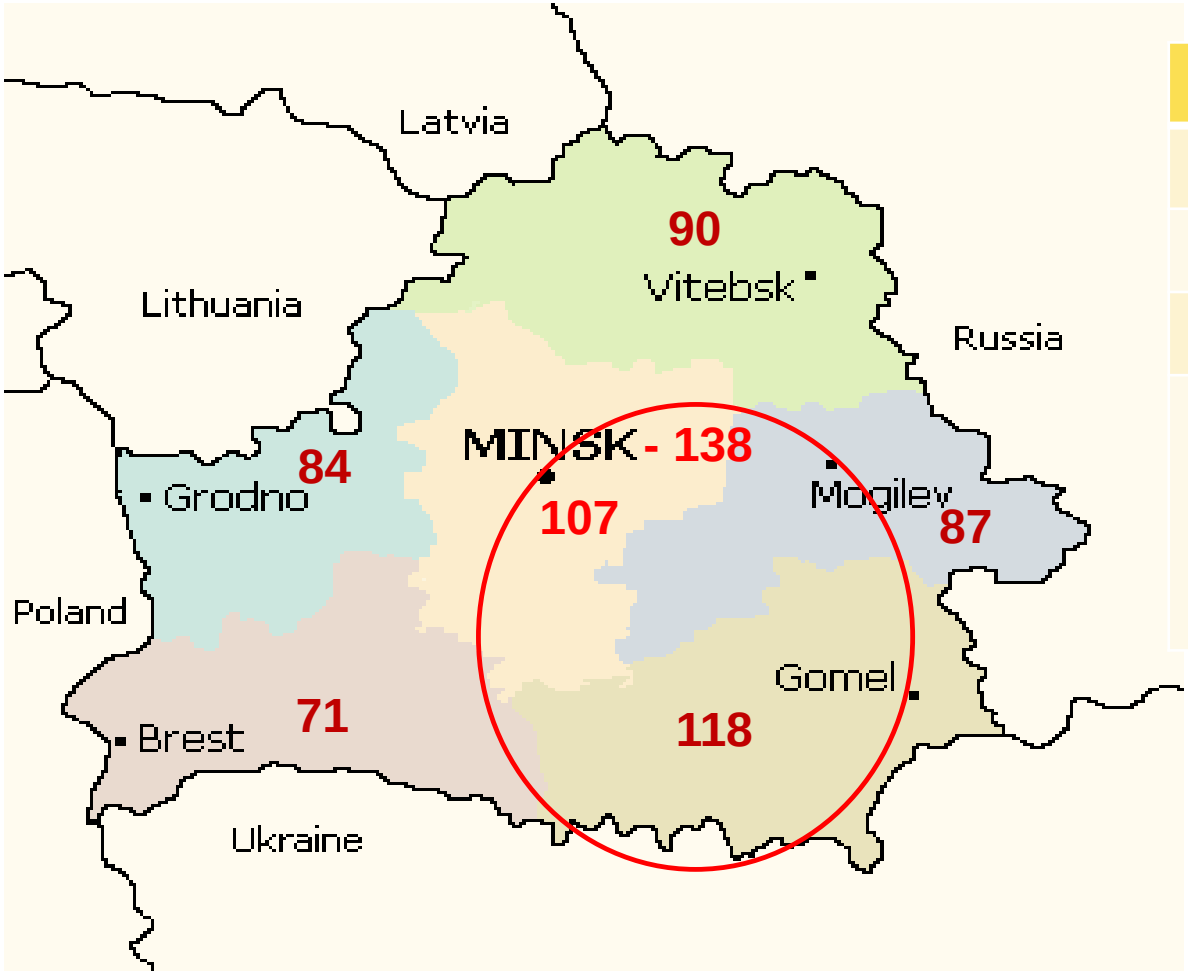
Patients

n=695 (by March 1, 2019)					
Gender m/f	431/264 (62%/38%)				
Age		**Social data**		**DR profile**	
18-25	75 (11%)	**employed**	**372 (53%)**	Drug susceptible	313 (45%)
26-35	**236 (34%)**	**student**	**32 (5%)**	Monoresistance (R)	28 (4%)
36-45	**195 (28%)**	unemployed	254 (36%)	**M/XDR**	**354 (51%)**
46-55	**100 (14%)**	maternity leave	33 (5%)	incl.	
56-65	76 (11%)	military service	4 (1%)	Pre-XDR	119 (17%)
>65	13 (2%)			XDR	96 (14%)

n=695 (by March 1, 2019)

Programmatic expansion of VOT in Belarus (3)

Patients regional distribution



Minsk City	**138**
Minsk region	107
Gomel region	118
Mogilev region	87
Vitebsk region	90
Brest region	71
Grodno region	84

Programmatic expansion of VOT in Belarus (4)

Video sessions quality

good quality	insufficient quality to confirm intake of medication	No data/ not received	total
83713	1077	255	85045
98.4%	1.3%	0.3%	100%

1) 0 phones were lost

2) 6 phones were returned for repair under warranty

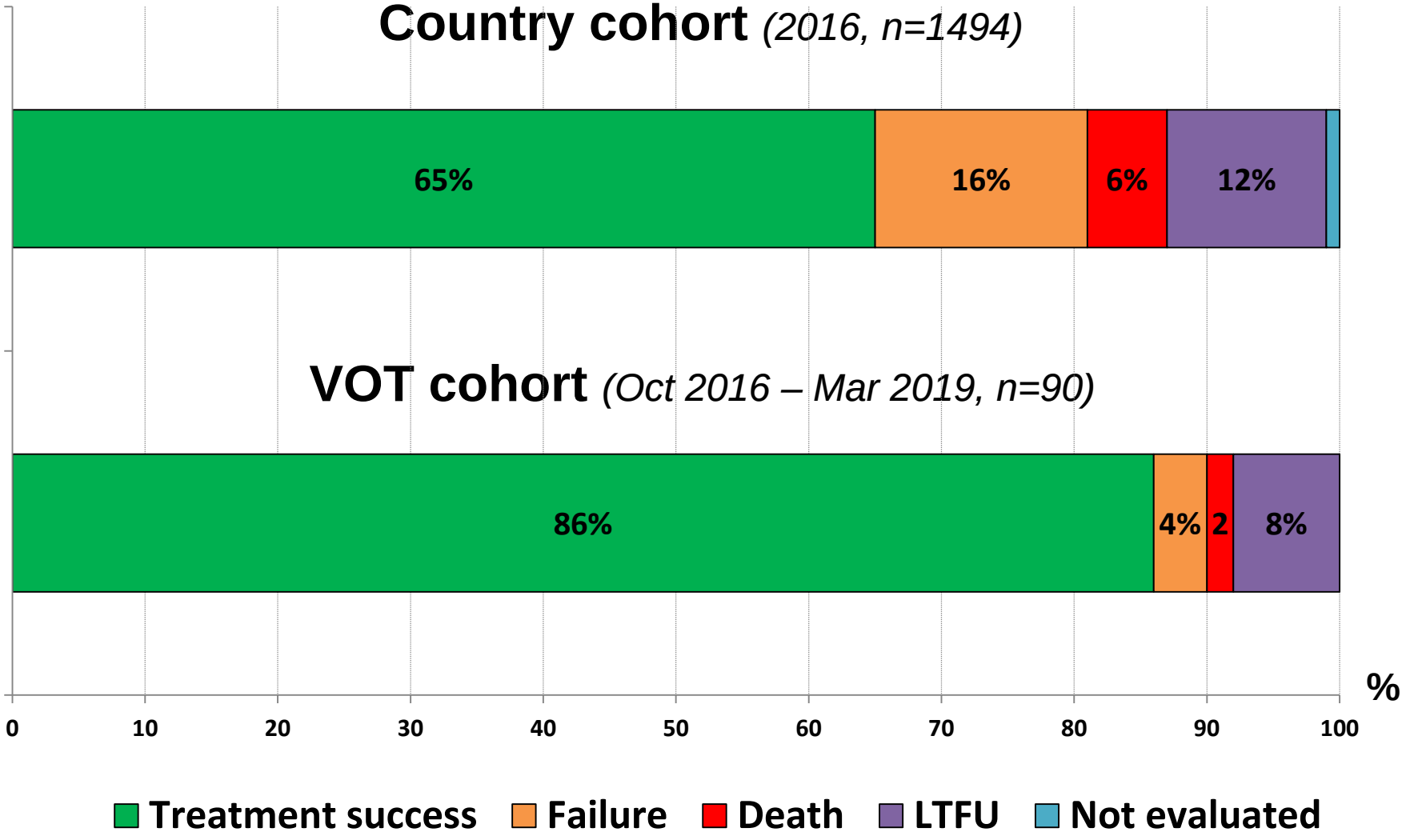
Treatment outcomes

Final treatment outcomes were notified in 317 TB patients on VOT:

- treatment success – 303 (95.65%)
- treatment failure – 4 (1.25%)
- death (XDR-TB) – 2 (0.65%)
- LTFU (MDR-TB) – 8 (2.45%)

- 378 patients are still on treatment

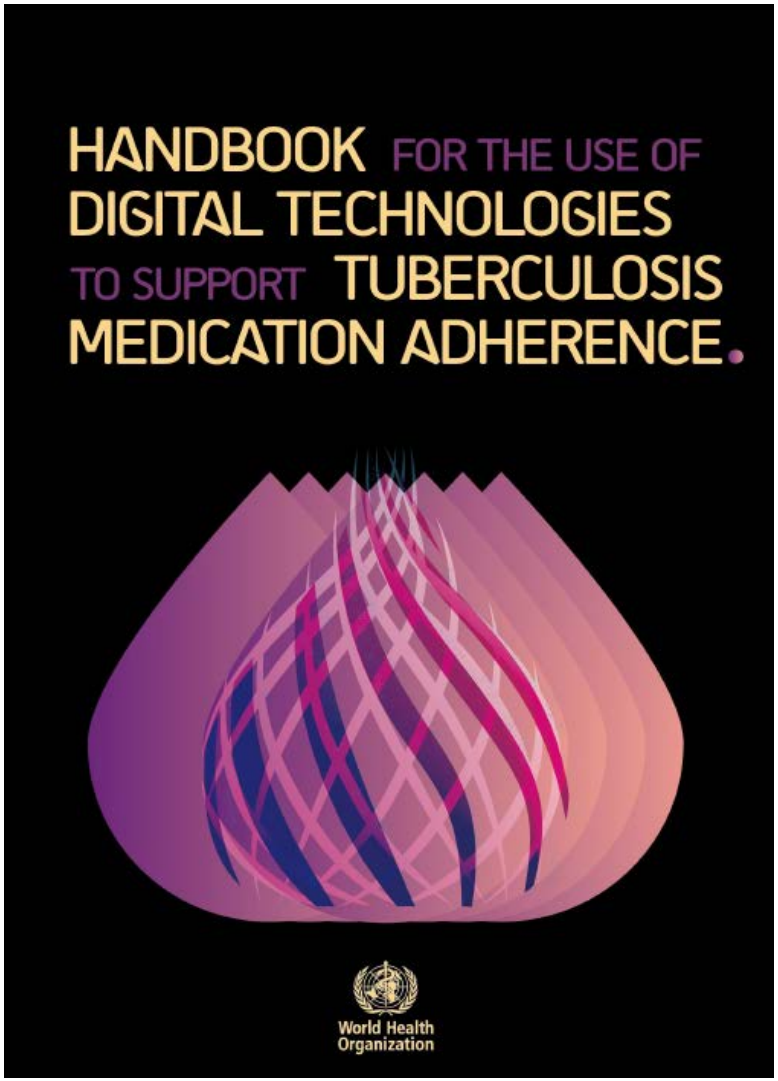
M/XDR-TB treatment outcomes



Lessons learned

- VOT works better on smartphones procured for the project purpose rather than relying on a patient's device
- Clear written instruction to patients is needed
- Feedback to the patient on the quality of the videos is important
- The comments and additional instructions to patient during his/her visiting TB facility are also practical
- A drug container with at least 2 weeks' drug supply is practical

Belarus VOT experience



ANNEX V. PROGRAMMATIC IMPLEMENTATION OF VOT IN BELARUS

Example of a 5-year timeline[10]

Objective(s). To develop and implement a national VOT programme in Belarus in support of treatment adherence and supervision during the ambulatory phase of treatment, and to improve TB treatment outcomes
Phase 1. Planning (Year 1 – 2015) • *Conduct a feasibility assessment* – conducted by WHO in January 2015 with support of the European Respiratory Society (ERS) • *Engage stakeholders to provide input on solution* – WHO survey of public views on priority areas in early 2015, WHO/ERS joint technical consultation to develop detailed technical TPP for VOT in February 2015 • *Develop a costed project proposal* – developed by the Global Fund in February 2015 • *Establish a working group to provide oversight and guidance* – established by the Ministry of Health of Belarus in February 2015 • *Draft detailed technical specifications* – drafted by local Belarusian company "BelPromProject" for VOT app in May 2015 • *Secure in-country ethics committee approval for pilot project* – secured through Ministry of Health in September 2015
Phase 2. Development/adaptation (Year 2 – 2016) • *Finalize the software* – development finalized by BelPromProject in January 2016 • *Link solution to current national digital health systems* – "VOT module" added to the Ministry of Health of Belarus' national electronic tuberculosis patient registers in February 2016 • *Train staff* – trained dispensary nurses in January 2016 • *Distribute hardware and train patients* – distributed smartphones and trained patients in January 2016
Phase 3. Roll-out (Years 2 & 3 – 2016-2017) • *Initiate patient enrolment* – initiated single-site preliminary pilot in Minsk in January and February 2016 • *Monitoring and evaluation of pilot study results* – monitoring by NTP, Ministry of Health of Belarus from January to October 2016 • *Publication of preliminary results* – pilot findings published in European Respiratory Journal in March 2017 *(58)*
Phase 4. Maintenance/scale up (Years 2–5 – late 2016–2019) • *Expansion of solution nationwide* – expansion to all seven country regions with planned recruitment of 450 patients (150/year) with Belarus Red Cross and the Global Fund from October 2016 to 2019; 231 patients from all regions of the country were on VOT by 1 September 2017

10 Adapted from Box 4.1 *(67)*

Conclusions

Preliminary data of using VOT, among a diverse mix of TB patients in all 7 regions of Belarus demonstrate

- high levels of patient acceptability and treatment adherence
- excellent treatment outcomes
- the experience gained can promote this approach for TB patients with
  - comorbidities (e.g. HIV, substance abuse) and
  - complex social issues

Thank You!





Management (treatment) of TB in migrant populations in Europe

G. B. Migliori

WHO Collaborating Centre for TB and Lung Disease,
Maugeri Institute, IRCCS Tradate, Italy
GTN (Global Tuberculosis Network)

Conflict of interest disclosure

☑ **I have no real or perceived conflicts of interest that relate to this presentation.**

❑ **I have the following real or perceived conflicts of interest that relate to this presentation:**

Bibliography search

Key words:

((tuberculosis[Title/abstract]) AND treatment[Title/abstract]) AND (migrant*[Title/abstract] OR migration[Title/abstract] OR migrat*[Title/abstract])

No time limits: 6,185 documents

2015-2019: 373 documents

- Few with relevant information on *treatment results*
- Majority focused on *screening*

Introduction

Objectives

to discuss treatment issues with special focus on:

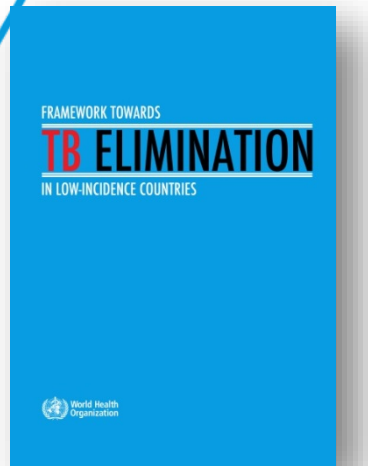
- Migration: ‘myths’ and reality
- History of migration and screening
- Screening options for TB and LTBI
- Migration and health
- Research priorities

• Conclusions

ACTION FRAMEWORK

8 priority actions for elimination in low-incidence countries



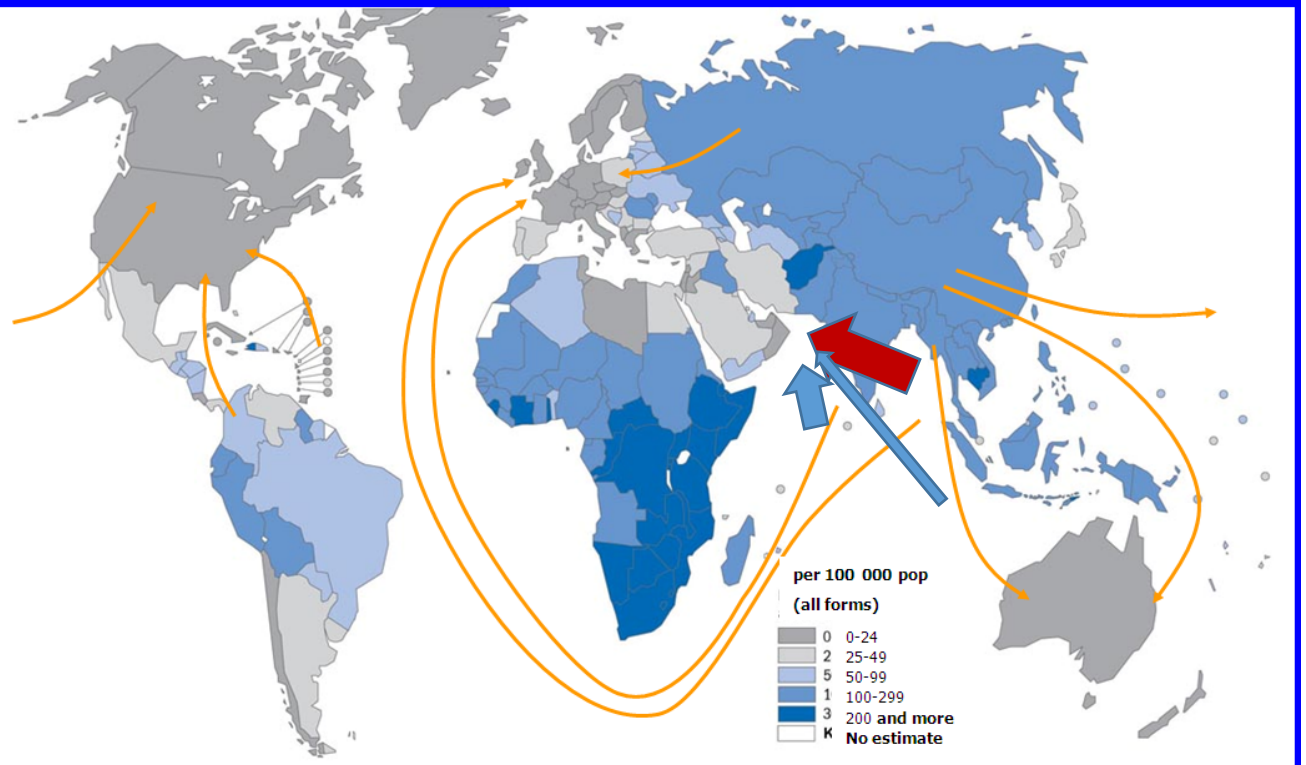


TB is poverty-related: the two faces of San Paulo



Migration

Re-import of TB into industrialized countries



Accord. WHO Report 2006





Migration Language
Migrant

- Any person who *is moving* or *has moved* across an *international* border or *within a state* (IDP) away from his/her habitual place of residence, regardless of:
  - The person's legal status;
  - Whether the movement is voluntary or involuntary;
  - What the causes for the movement are
  - What the length of the stay is.

Migration Language
Asylum-seeker & Refugee

Asylum-seeker*: individual seeking international protection.

In countries with individualized procedures, is someone whose claim has not yet been finally decided

Refugee*: a person who meets the eligibility criteria under the applicable definition (UNHCR's mandate or national legislation)

- **Every refugee is *initially* an asylum-seeker**
- **…but** not every asylum-seeker will *ultimately be recognized* as a refugee

**Master Glossary of Terms, UNHCR, June 2006*

Migrants: myths and realities

MYTH	REALITY
Migrants keep increasing	Not true: peak in 2015/16
TB increases in Europe due to migration	TB declining in Europe, MDR increasing
	Foreign-born majority of cases in some countries (not all)
	Rates of TB x 100,000 stable in migrants
Foreign-born non adherent to treatment	In some countries: the opposite
Migrants transmit to local population	No evidence

Recent evidence on migrants' movements to Europe

(available at: https://data2.unhcr.org/en/situations/mediterranean)

Last updated 25 Feb 2019



Total arrivals .CSV JSON

10,958

Last updated 25 Feb 2019

Sea arrivals in 2019 JSON

Includes refugees and migrants arriving by sea to Italy, Greece, Spain, Cyprus and Malta

8,573

Last updated 25 Feb 2019

Land arrivals in 2019 JSON

Includes refugees and migrants arrivi

2,385

Last updated 24 Feb 2019

Dead and missing in 2019

207

Most common nationalities of Mediterranean sea and land arrivals from January 2018 .CSV JSON

Country of origin	Source	Data date	Population

Most common nationalities of Mediterranean sea and land arrivals from January 2018 .CSV JSON

Country of origin	Source	Data date	Population	
Guinea		31 Jan 2019	11.3%	13,068
Morocco		31 Jan 2019	11.0%	12,747
Syrian Arab Rep.		31 Jan 2019	9.0%	10,382
Mali		31 Jan 2019	8.9%	10,347
Afghanistan		31 Jan 2019	8.4%	9,788
Iraq		31 Jan 2019	6.7%	7,800
Algeria		31 Jan 2019	5.4%	6,205
Côte d'Ivoire		31 Jan 2019	5.2%	6,055
Tunisia		31 Jan 2019	5.0%	5,756
Others		31 Jan 2019	4.7%	5,443

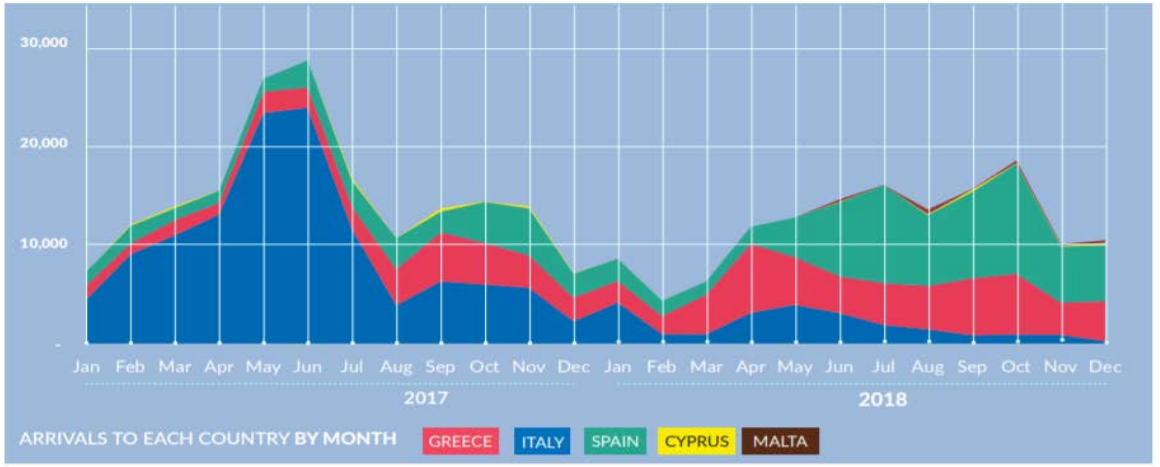
UNHCR The UN Refugee Agency

JAN – DEC 2018

REFUGEES & MIGRANTS ARRIVALS TO EUROPE IN 2018 (MEDITERRANEAN)

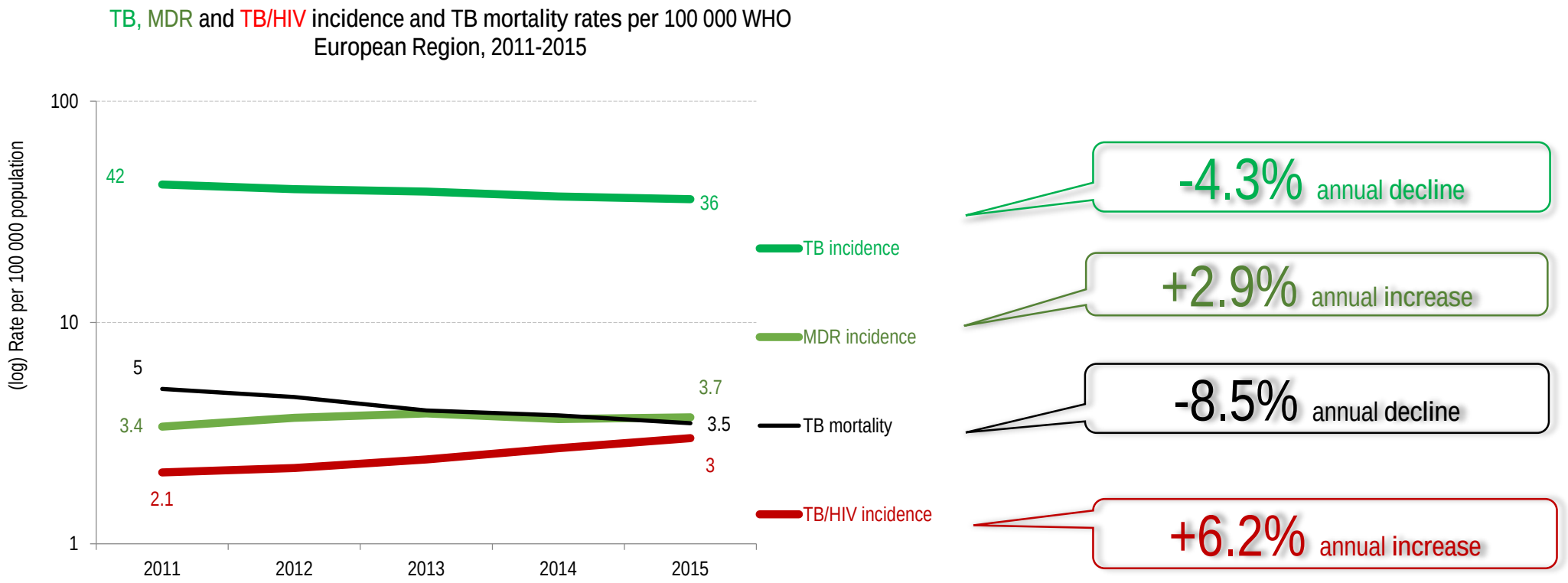
TOTAL ARRIVALS [1] (January -December 2018)

2018	141,500
2017	185,100
2016	373,700
2015	1,032,400



Myth: Migrants keep increasing

Myth: TB increases in Europe due to migration

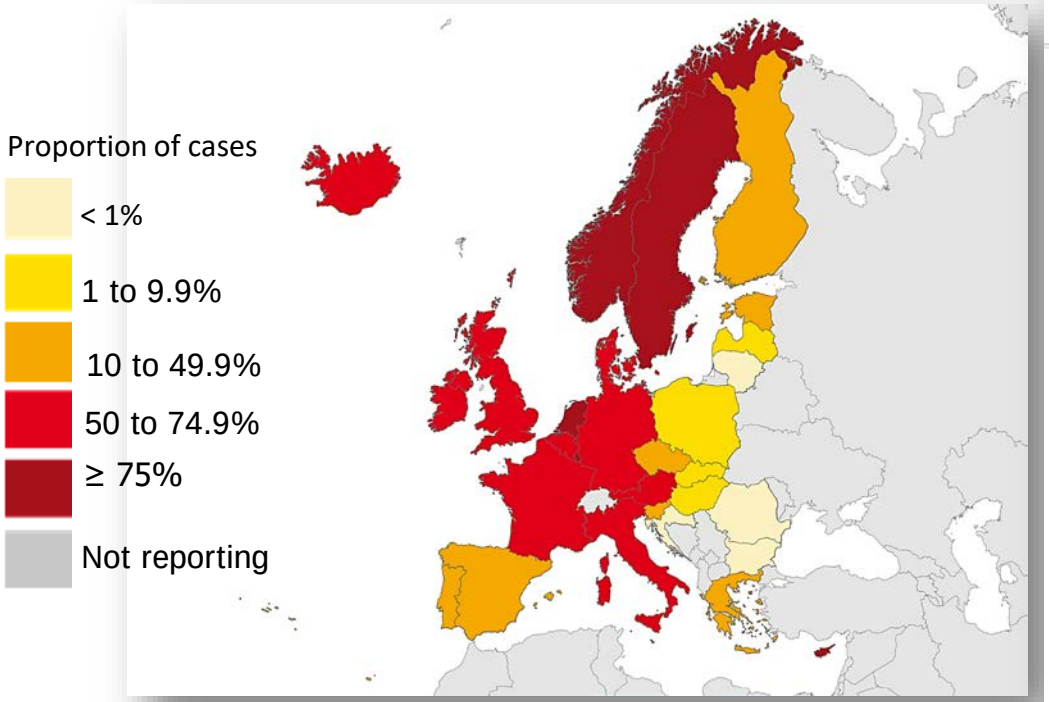


Source: WHO Europe / ECDC. Tuberculosis surveillance and monitoring in Europe 2017

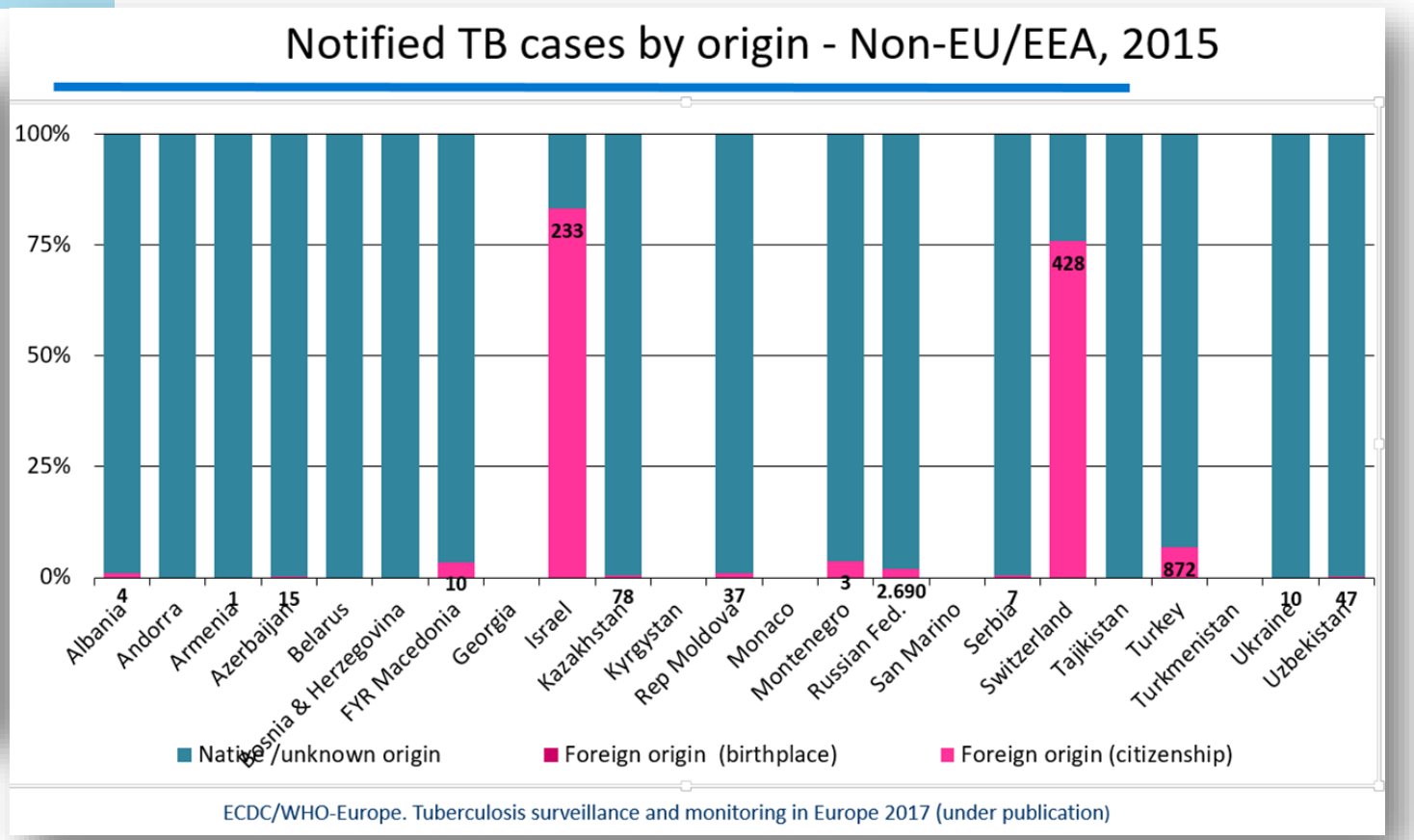
Courtesy Dr. A. Dadu, WHO/EURO

TB in persons of foreign origin in and beyond EU/EEA, 2016

- **19 312** TB cases were notified in persons originating from other countries than the reporting country
- **32.7%** of all TB cases (range 0.2–96.0%)

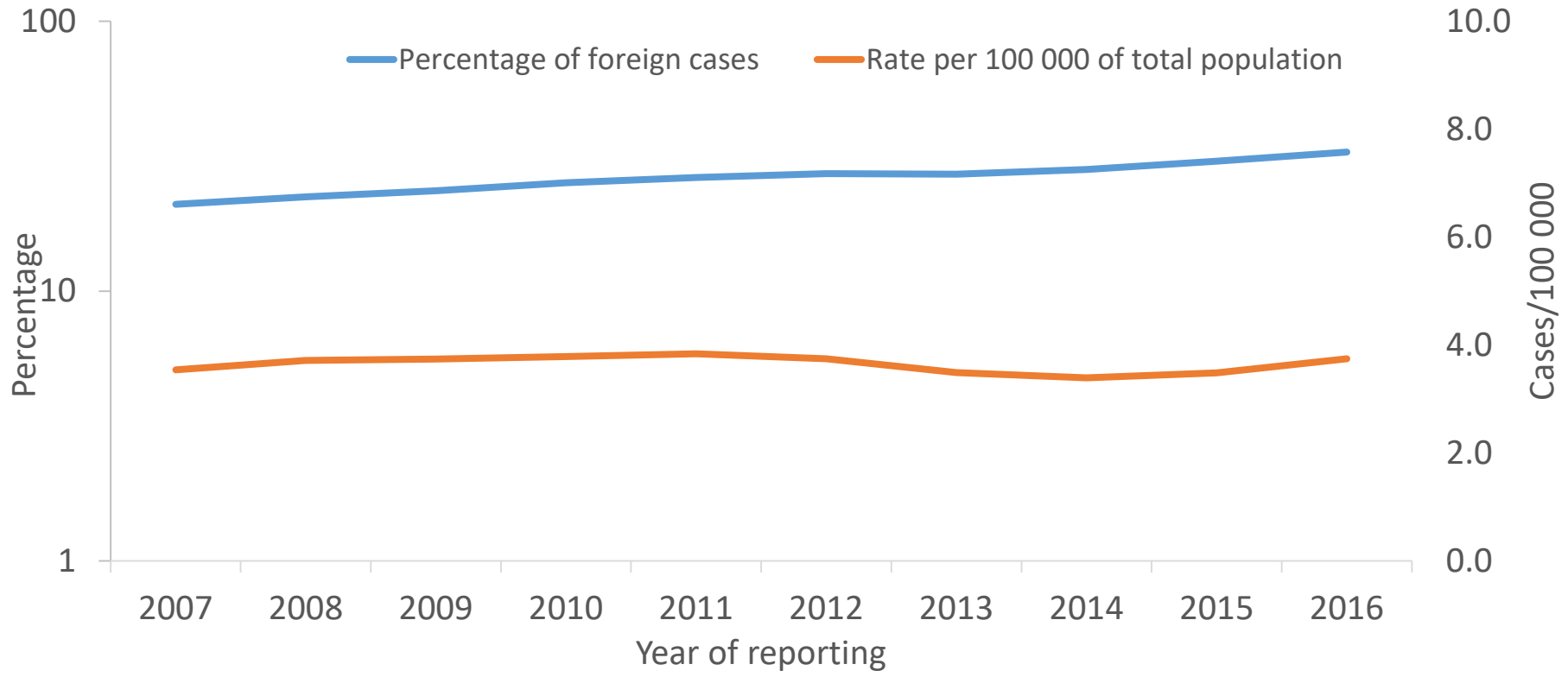


Source: ECDC/WHO (2018). Tuberculosis surveillance and monitoring in Europe 2018–2016 data



TB cases in persons of foreign origin, EU/EEA, 2007–2016

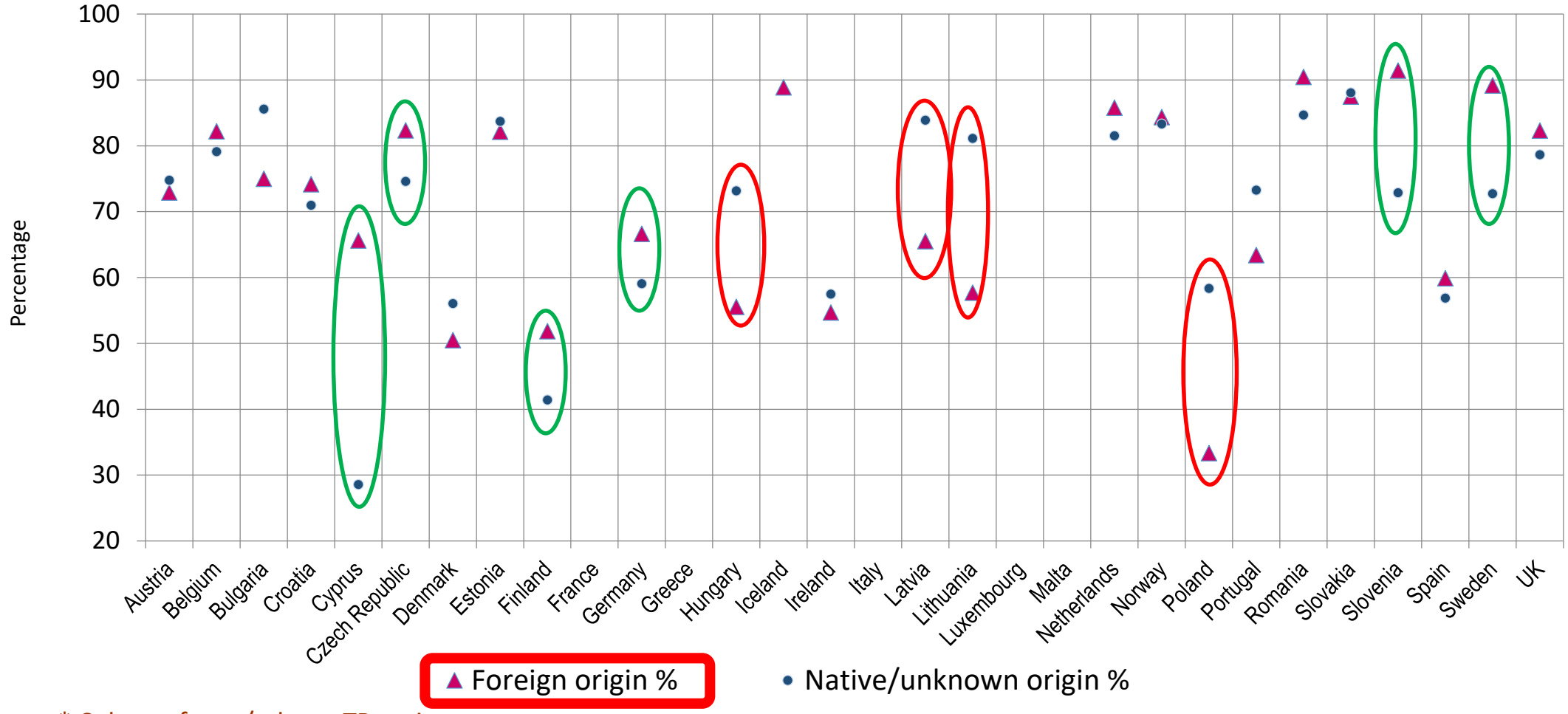
The percentage of cases in persons of foreign origin increased from **21.0%** in 2007 to **32.7%** in 2016
Rate per 100 000 total population was stable between **3.4** and **3.7**



Source: ECDC/WHO (2018). Tuberculosis surveillance and monitoring in Europe 2018–2016 data

Myth: foreign born not adherent

*TB treatment success** by origin; EU/EEA, 2014



* Cohort of new/relapse TB patients

Tuberculosis surveillance and monitoring in Europe 2017. WHO/ECDC joined report

Nellums *et al. BMC Medicine* (2018) 16:27
DOI 10.1186/s12916-017-1001-7

BMC Medicine

RESEARCH ARTICLE Open Access

Multidrug-resistant tuberculosis treatment adherence in migrants: a systematic review and meta-analysis

Laura B. Nellums[†], Kieran Rustage[†], Sally Hargreaves[†] and Jon S. Friedland[*]

Abstract

Background: Multidrug-resistant tuberculosis (MDR-TB) is a growing concern in meeting global targets for TB control. In high-income low-TB-incidence countries, a disproportionate number of MDR-TB cases occur in migrant (foreign-born) populations, with concerns about low adherence rates in these patients compared to the host non-migrant population. Tackling MDR-TB in this context may, therefore, require unique approaches. We conducted a systematic review and meta-analysis to identify and synthesise data on MDR-TB treatment adherence in migrant patients to inform evidence-based strategies to improve care pathways and health outcomes in this group.

Methods: This systematic review and meta-analysis was conducted in line with PRISMA guidelines (PROSPERO 42017070756). The databases Embase, MEDLINE, Global Health and PubMed were searched to 24 May 2017 for primary research reporting MDR-TB treatment adherence and outcomes in migrant populations, with no restrictions on dates or language. A meta-analysis was conducted using random-effects models.

Results: From 413 papers identified in the database search, 15 studies reporting on MDR-TB treatment outcomes for 258 migrants and 174 non-migrants were included in the systematic review and meta-analysis. The estimated rate of adherence to MDR-TB treatment across migrant patients was 71% [95% confidence interval (CI) = 58–84%], with non-adherence reported among 20% (95% CI = 4–37%) of migrant patients. A key finding was that there were no differences in estimated rates of adherence [risk ratio (RR) = 1.05; 95% CI = 0.82–1.34] or non-adherence (RR = 0.97; 95% CI = 0.79–1.36) between migrants and non-migrants.

Conclusions: MDR-TB treatment adherence rates among migrants in high-income low-TB-incidence countries are approaching global targets for treatment success (75%), and are comparable to rates in non-migrants. The findings highlight that only just over 70% of migrant and non-migrant patients adhere to MDR-TB treatment. The results point to the importance of increasing adherence in all patient groups, including migrants, with an emphasis on tailoring care based on social risk factors for poor adherence. We believe that MDR-TB treatment targets are not ambitious enough.

Keywords: Tuberculosis, Drug resistance, Migration, Treatment adherence

15/413 studies included

- MDR outcomes: **258 migrants vs 171 non-migrants**
- **Estimated rate of adherence**: 71%
- **No difference between migrants and non-migrants**



Although there are standardized recommendations for treatment regimens, variation in access to treatment and treatment adherence impact on the effectiveness of care, and there is evidence in migrant populations of loss to follow-up at every stage of the screening and treatment pathway, plus challenges in linking screening with secondary care (43,108).

Pulmonol. 2018;24(2):99–105



PULMONOLOGY
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REVIEW

Migration, TB control and elimination: Whom to screen and treat☆

A. Rendon[a,1], R. Centis[b], J.-P. Zellweger[c,1], I. Solovic[d], C.A. Torres-Duque[e], C. Robalo Cordeiro[f], F.C. de Queiroz Mello[g], D. Manissero[h,1], G. Sotgiu[i,*,1]

Abstract Tuberculosis (TB) in migrants represents an important clinical and public health threat, particularly in low TB incidence countries. The current review is aimed to assess issues related to screening and treatment of migrants with latent TB infection or TB disease.

RESEARCH ARTICLE

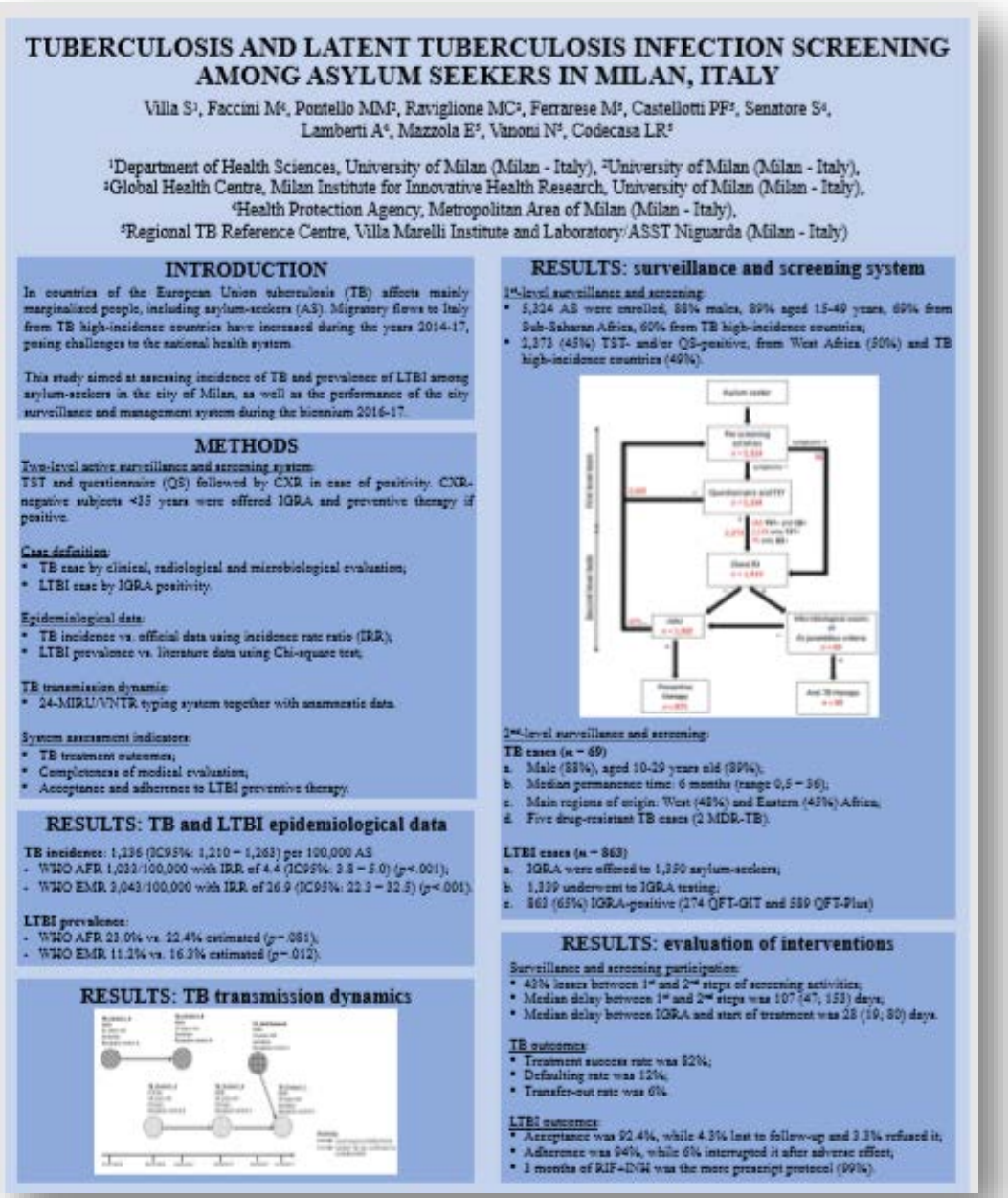
Find and treat or find and lose? Tuberculosis treatment outcomes among screened newly arrived asylum seekers in Germany, 2002 to 2014

Anna Kuehne[1,2], Barbara Hauer[1], Bonita Brodhun[1], Walter Haas[1], Lena Fiebig[1]
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2. Postgraduate Training for Applied Epidemiology, Robert Koch Institute, Berlin, Germany affiliated to the European Programme for Intervention Epidemiology Training, ECDC, Stockholm, Sweden

Correspondence: Lena Fiebig (FiebigL@rki.de)

to follow-up. **Results:** TB treatment success was highest among cases identified by contact tracing (87%; 3,139/3,591), followed by passive case finding (74%; 28,804/39,019) and by screening asylum seekers (60%; 884/1,474). Cases identified by screening asylum seekers had 2.4 times higher odds of not having a successful treatment outcome as opposed to all other

While specific reasons for the higher odds of non-successful treatment among asylum seekers in Germany need to be studied further, available research suggests that patients need to be better linked to treatment facilities and structural barriers to treatment completion need to be addressed to secure screening benefits for asylum seekers and the communities.



TUBERCULOSIS AND LATENT TUBERCULOSIS INFECTION SCREENING AMONG ASYLUM SEEKERS IN MILAN, ITALY

Villa S[1], Faccini M[4], Pontello MM[2], Raviglione MC[3], Ferrarese M[2], Castellotti PF[2], Senatore S[4], Lamberti A[4], Mazzola E[5], Vanoni N[5], Codecasa LR[5]

[1]Department of Health Sciences, University of Milan (Milan - Italy), [2]University of Milan (Milan - Italy), [3]Global Health Centre, Milan Institute for Innovative Health Research, University of Milan (Milan - Italy), [4]Health Protection Agency, Metropolitan Area of Milan (Milan - Italy), [5]Regional TB Reference Centre, Villa Marelli Institute and Laboratory/ASST Niguarda (Milan - Italy)

INTRODUCTION

In countries of the European Union tuberculosis (TB) affects mainly marginalized people, including asylum-seekers (AS). Migratory flows to Italy from TB high-incidence countries have increased during the years 2014-17, posing challenges to the national health system.

This study aimed at assessing incidence of TB and prevalence of LTBI among asylum-seekers in the city of Milan, as well as the performance of the city surveillance and management system during the biennium 2016-17.

METHODS

Two-level active surveillance and screening system:
TST and questionnaire (QS) followed by CXR in case of positivity. CXR-negative subjects <35 years were offered IGRA and preventive therapy if positive.

Case definition:
- TB case by clinical, radiological and microbiological evaluation;
- LTBI case by IGRA positivity.

Epidemiological data:
- TB incidence vs. official data using incidence rate ratio (IRR);
- LTBI prevalence vs. literature data using Chi-square test;

TB transmission dynamic:
- 24-MIRU/VNTR typing system together with anamnestic data.

System assessment indicators:
- TB treatment outcomes;
- Completeness of medical evaluation;
- Acceptance and adherence to LTBI preventive therapy.

RESULTS: TB and LTBI epidemiological data

TB incidence: 1,236 (IC95%: 1,210 – 1,263) per 100,000 AS
- WHO AFR 1,032/100,000 with IRR of 4.4 (IC95%: 3.8 – 5.0) ($p<.001$);
- WHO EMR 3,043/100,000 with IRR of 26.9 (IC95%: 22.3 – 32.5) ($p<.001$).

LTBI prevalence:
- WHO AFR 23.0% vs. 22.4% estimated ($p=.081$);
- WHO EMR 11.2% vs. 16.3% estimated ($p=.012$).

RESULTS: TB transmission dynamics

RESULTS: surveillance and screening system

1st-level surveillance and screening:
- 5,324 AS were enrolled, 88% males, 89% aged 15-49 years, 60% from Sub-Saharan Africa, 60% from TB high-incidence countries;
- 2,373 (45%) TST- and/or QS-positive, from West Africa (50%) and TB high-incidence countries (49%).

2nd-level surveillance and screening:
TB cases (n = 69)
a. Male (88%), aged 10-29 years old (39%);
b. Median permanence time: 6 months (range 0,5 – 36);
c. Main regions of origin: West (48%) and Eastern (45%) Africa;
d. Five drug-resistant TB cases (2 MDR-TB).

LTBI cases (n = 863)
a. IGRA were offered to 1,350 asylum-seekers;
b. 1,139 underwent to IGRA testing;
c. 863 (65%) IGRA-positive (274 QFT-GIT and 589 QFT-Plus)

RESULTS: evaluation of interventions

Surveillance and screening participation:
- 42% losses between 1st and 2nd steps of screening activities;
- Median delay between 1st and 2nd steps was 107 (47; 153) days;
- Median delay between IGRA and start of treatment was 28 (19; 80) days.

TB outcomes:
- Treatment success rate was 82%;
- Defaulting rate was 12%;
- Transfer-out rate was 6%.

LTBI outcomes:
- Acceptance was 92.4%, while 4.3% lost to follow-up and 3.3% refused it;
- Adherence was 94%, while 6% interrupted it after adverse effect;
- 3 months of RIF-INH was the more prescript protocol (99%).

Asylum seekers in Milan

- TB incidence is high among asylum seekers in Milan
- Transmission within reception centres is rare
- Within the system, attrition may occur frequently when different screening sites are involved
- TB treatment success (82%) is high although improvement is possible by reducing defaulting (12%) and transfer-out (6%)
- LTBI treatment acceptance (92.4%) and adherence (94% with 6% interrupting for AE) are high

If you really care, good results are guaranteed

Courtesy Dr Simone Villa & Mario Raviglione, Milano 2018

Myth: migrants transmit TB to the native population

Assessing transmission dynamics from foreign-born to native European populations

Tuberculosis transmission between foreign- and native-born populations in the EU/EEA: a systematic review

Andreas Sandgren[1,6], Monica Sañé Schepisi[2,6], Giovanni Sotgiu[3], Emma Huitric[1], Giovanni Battista Migliori[4], Davide Manissero[1,5], Marieke J. van der Werf[1] and Enrico Girardi[2]

Eur Respir J 2014; 43: 1159–1171

- Molecular epidemiology studies 1990-2012 (IS6110 RFLP and MIRU-VNTR (12&15 loci)
- **15 studies** (1992-2007) covering 12,366 cases, median 49% foreign born
- Countries: B, D, DK, F, I, E, S, N, UK
- Clustered isolates (=recent transmission) 8.5-49% of all TB case genotypes
- **Foreign-born cases were equally or more likely to have unique isolates**, but % of clustered cases not negligible, esp. in foreign clusters
- 1/3 of clusters were mixed (foreign/native) with 0-34% of all genotyped cases
- **Cross-transmission was bi-directional**
- **TB in foreigners has no significant influence on TB in native populations in Europe**

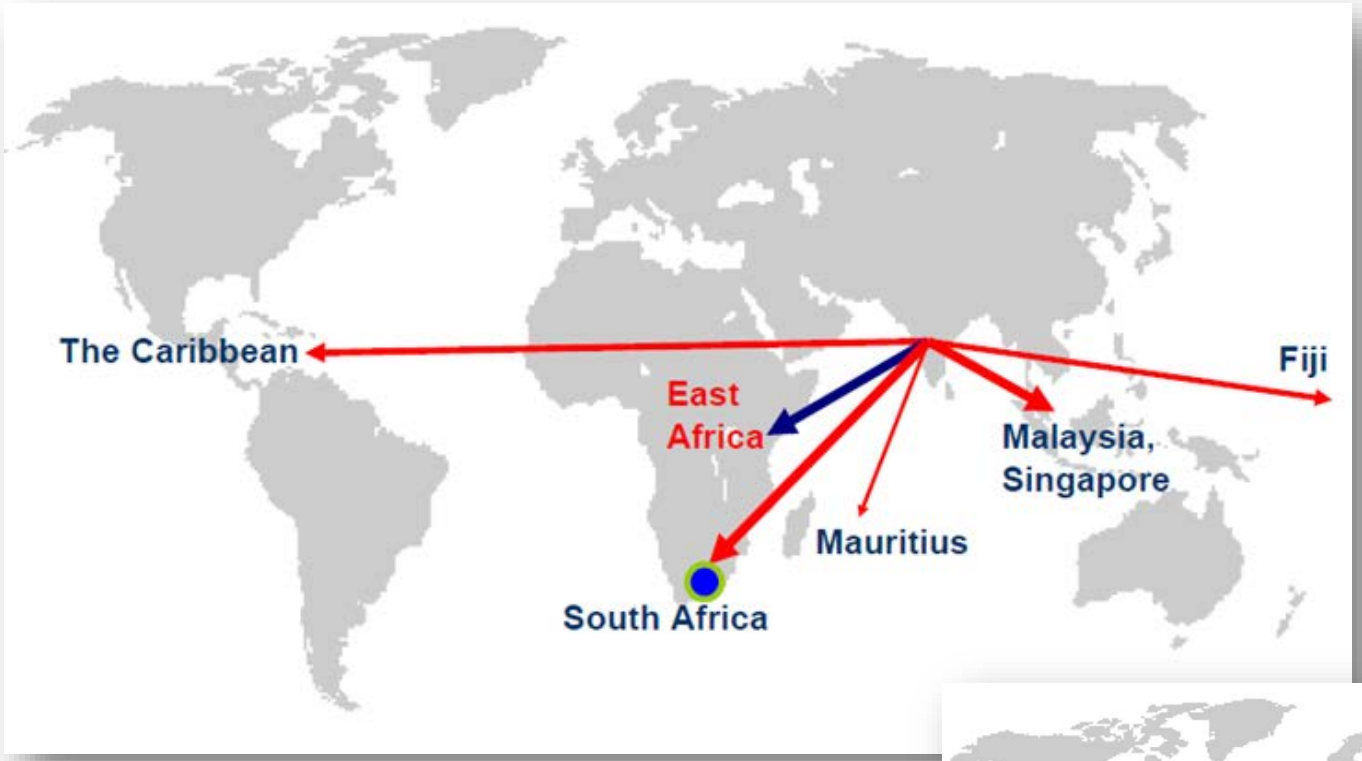
History of migration

History of migration
120 years ago, 70 million to overseas



Source: Rainer Münz-Erste group

1870-1940 South-South Emigration





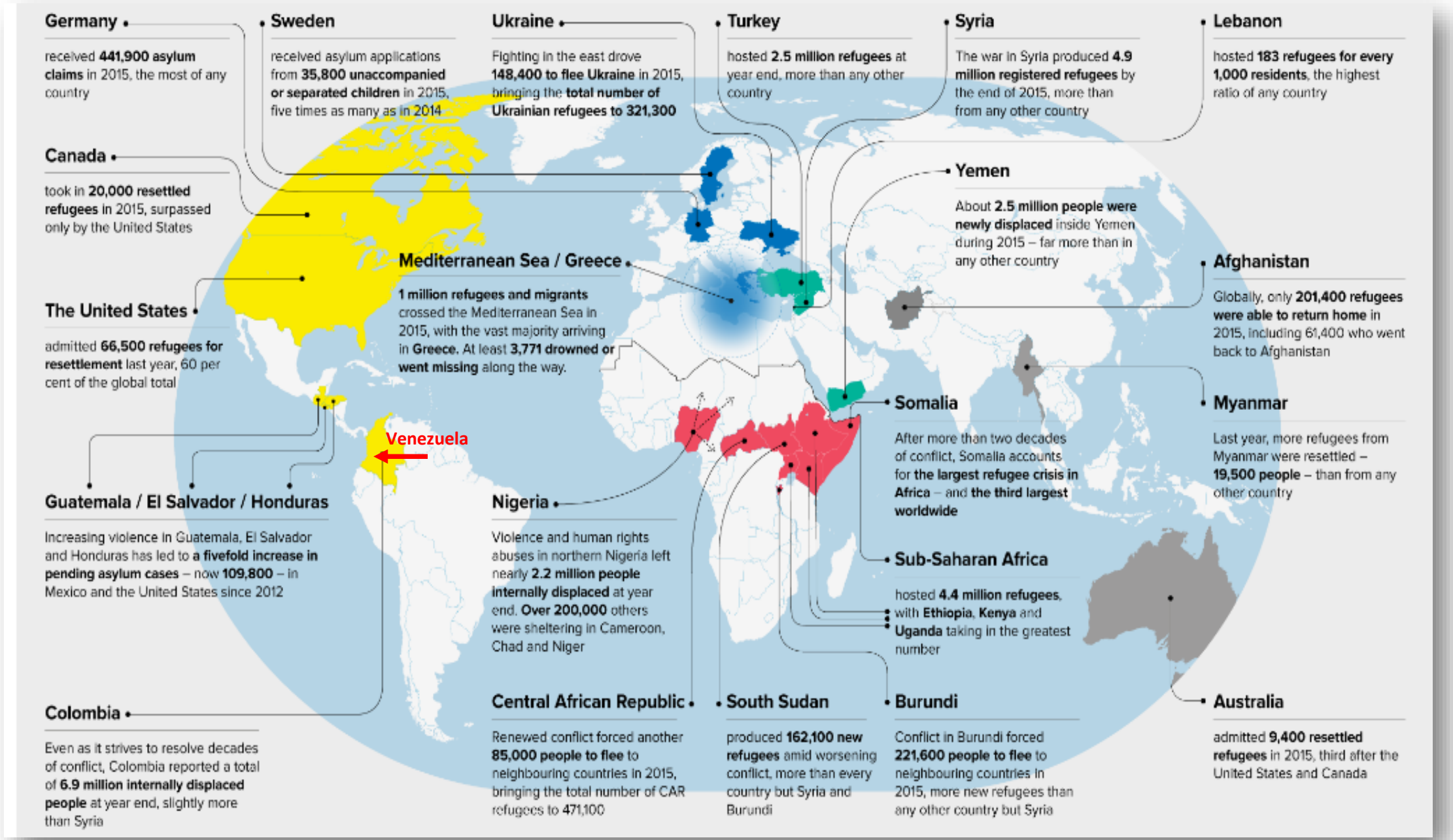
Source: Rainer Münz-Erste group

1945-1950: World Migration

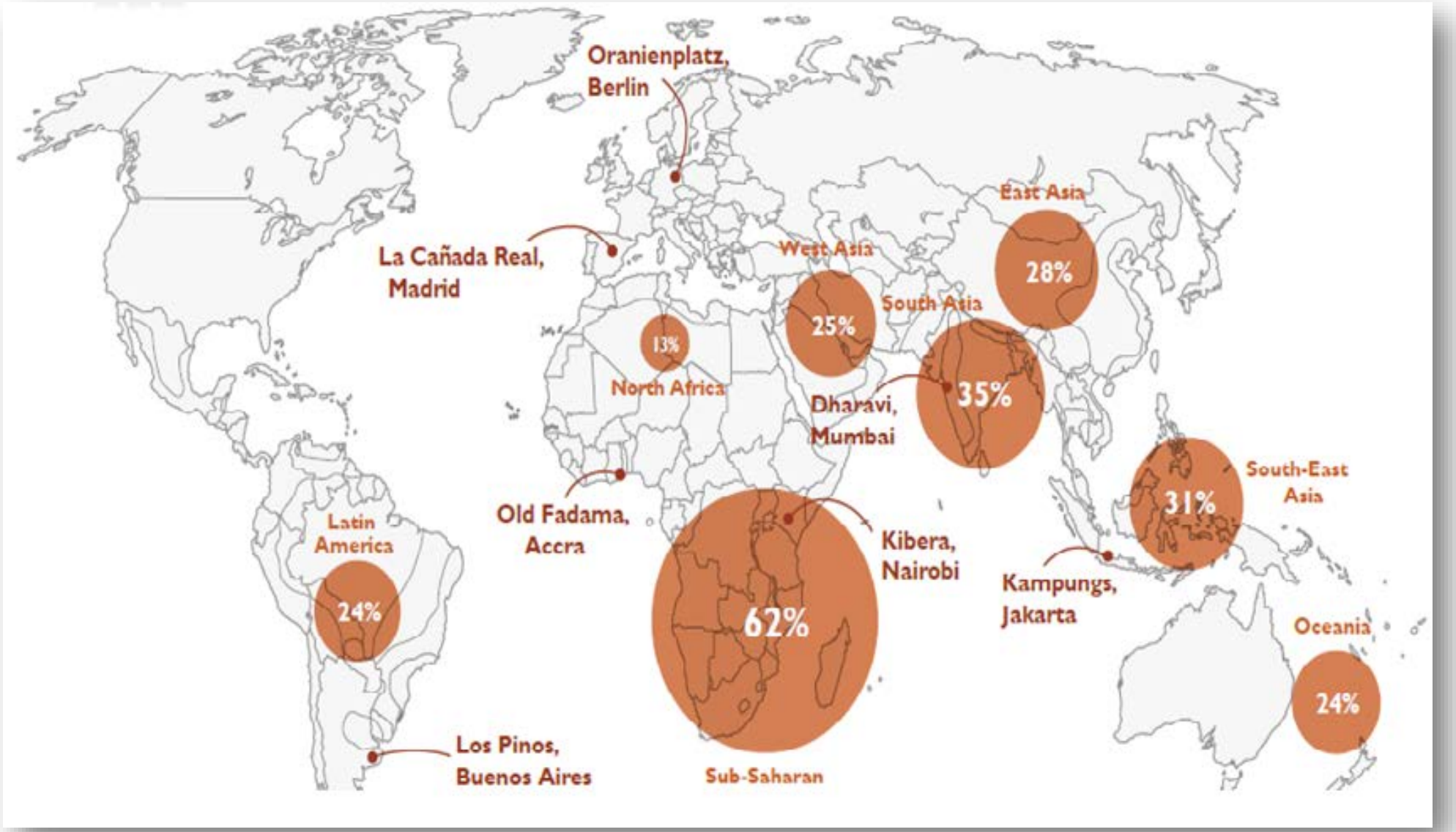


Source: Rainer Münz-Erste group

Highest record for Forced Displacement



Informal Settlement and Slums

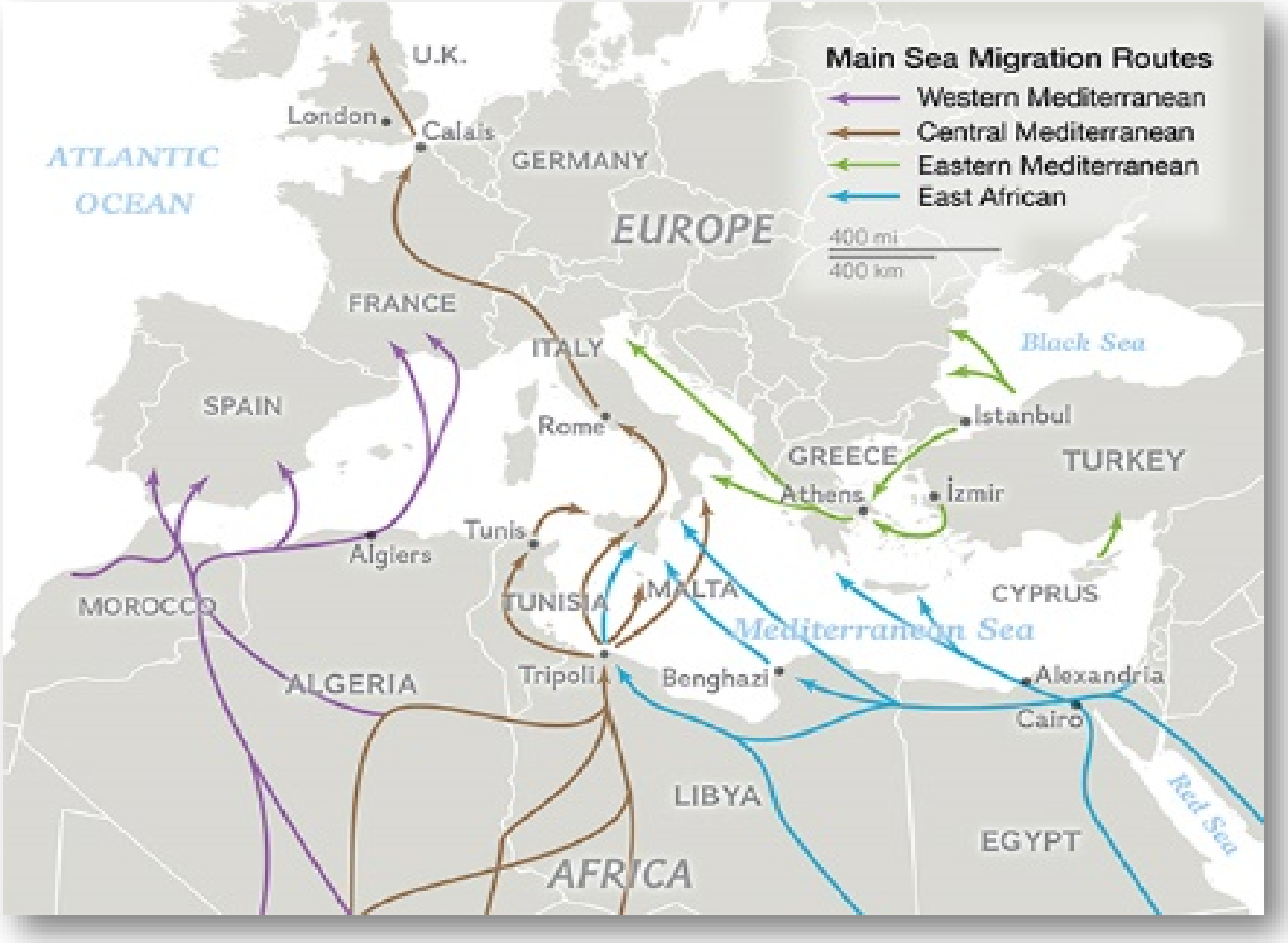


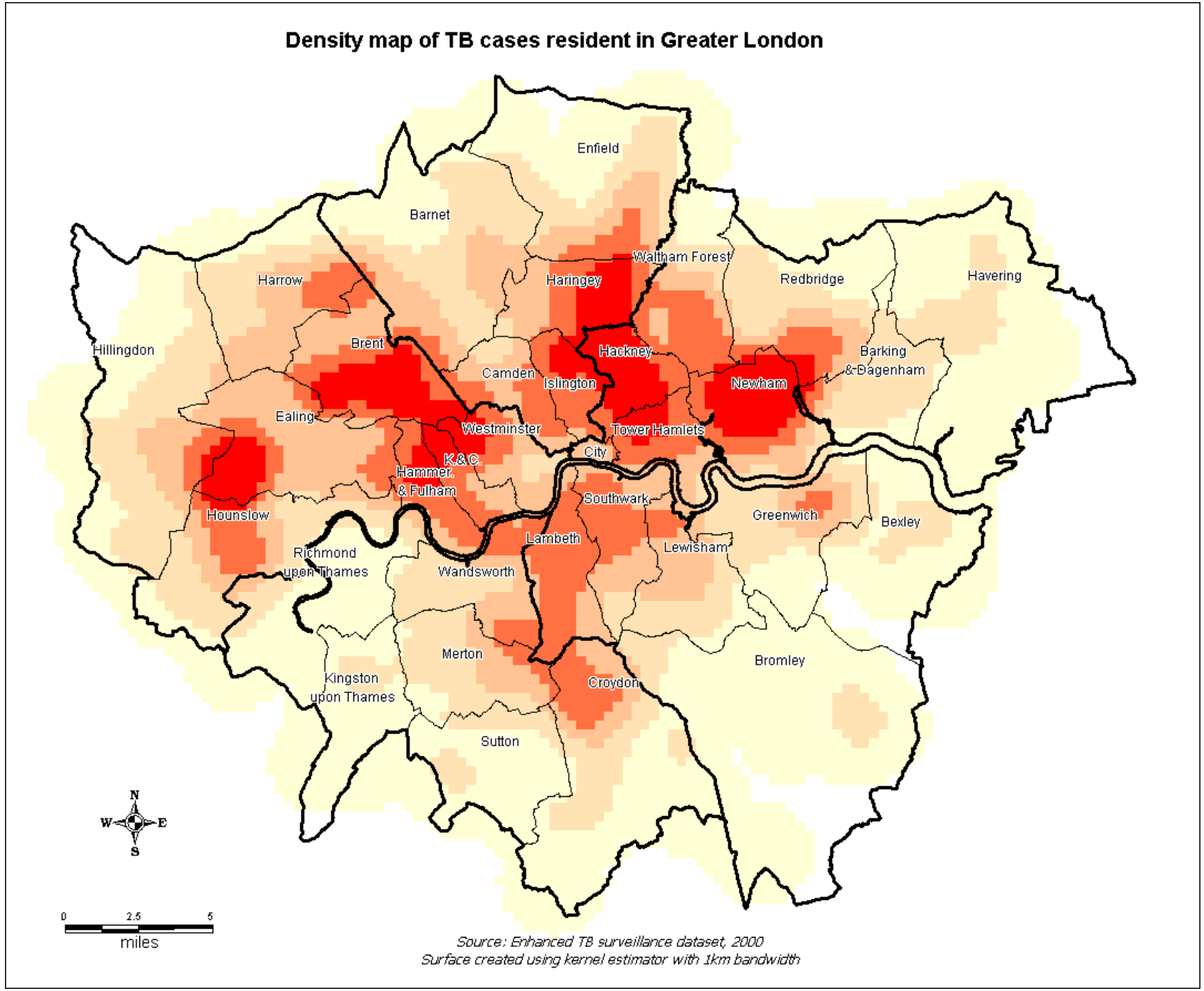
Transit cities: Africa



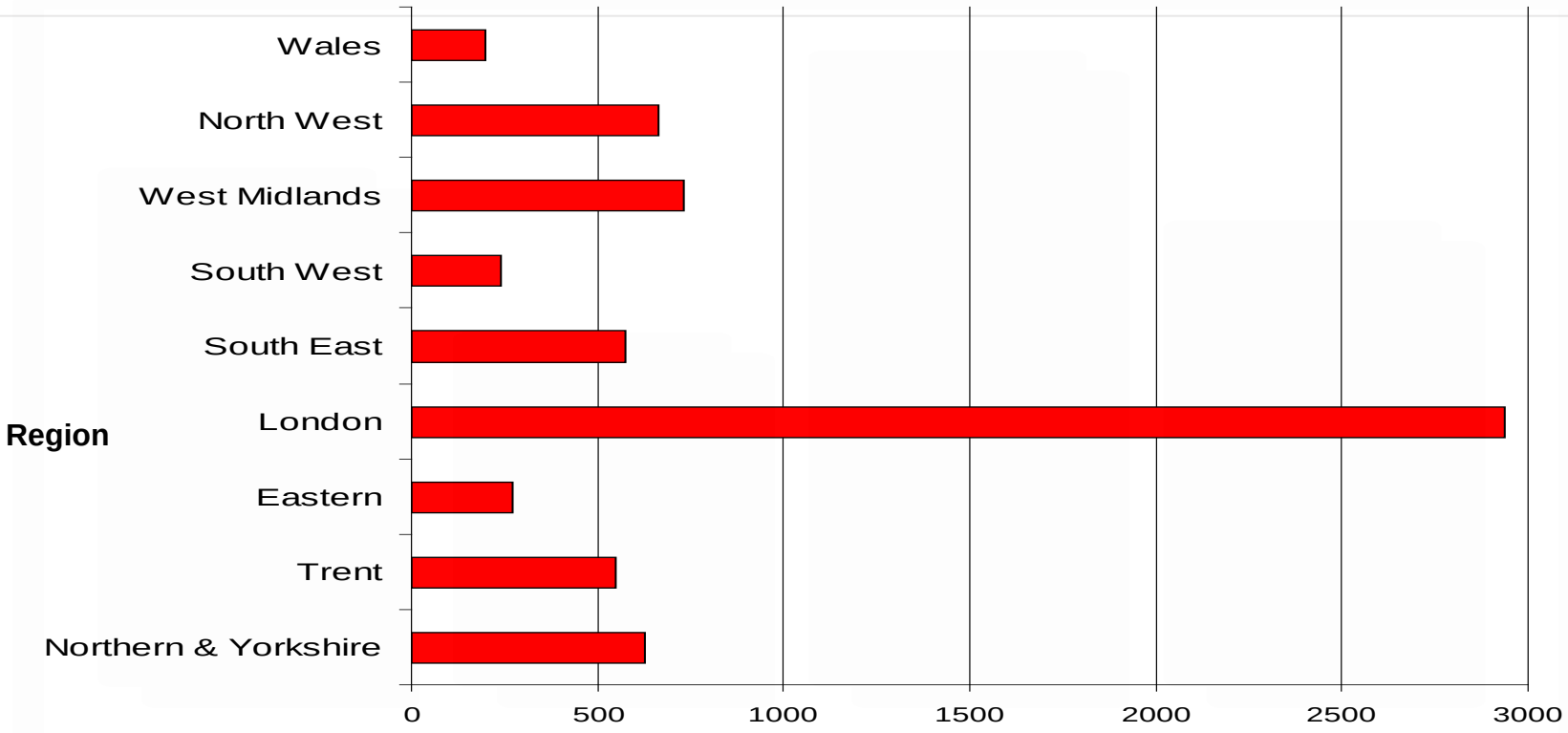
Source: Adapted from the 2014 Mediterranean Transit Migration (MTM) Map on Mixed Migration Routes in the MTM Region (i-Map).

Migration routes through the Mediterranean Sea




Density map of TB cases resident in Greater London
Enfield
Barnet
Waltham Forest
Harrow
Haringey
Redbridge
Havering
Hillingdon
Brent
Hackney
Barking
& Dagenham
Camden
Islington
Newham
Ealing
Westminster
Tower Hamlets
City
K&C.
Hammer.
& Fulham
Southwark
Greenwich
Bexley
Hounslow
Lambeth
Lewisham
Richmond
upon Thames
Wandsworth
Merton
Bromley
Kingston
upon Thames
Croydon
Sutton
N
W
E
S
0
2.5
5
miles
Source: Enhanced TB surveillance dataset, 2000
Surface created using kernel estimator with 1km bandwidth

Tuberculosis notifications - England and Wales by region



Data excludes chemoprophylaxis and Port Health Authorities
RHO boundaries as at April 1999
Source: Statutory notifications to the Communicable Disease Surveillance Centre
2000 data provisional

PHLS COMMUNICABLE DISEASE SURVEILLANCE CENTRE

History of screening

Quarantine in the Dubrovnik Republic



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EXPERT REVIEWS

The history and evolution of immigration medical screening for tuberculosis

Expert Rev. Anti Infect. Ther. 11(2), 137–146 (2013)

Masoud Dara[1], Brian D Gushulak[2], Drew L Posey[3], Jean-Pierre Zellweger[4] and Giovanni B Migliori*[5]

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Identifying and managing TB in immigrating populations has been an important aspect of immigration health for over a century, with the primary aim being protecting the host population by preventing the import of communicable diseases carried by the arriving migrants. This review describes the history and development of screening for TB and latent TB infection in the immigration context (describing both screening strategies and diagnostic tests used over the last century), outlining current practices and considering the future impact of new advances in screening. The recent focus of the WHO, regarding their elimination strategy, is further increasing the importance of diagnosing and treating latent TB infection. The last section of this review discusses the latest public health developments in the context of TB screening in immigrant populations.

KEYWORDS: chest radiography • control • elimination • immigrants • screening • tuberculosis

The identification and management of diseases of public health importance in new arrivals is a relevant component of immigration health programs [1]. These programs were originally focused on protecting the health of the host population by excluding the arrival of those with communicable diseases.

Lazarettos were created in Europe since the 16th century to control prevalent epidemics

considers the future impact of new advances in screening.

The history of immigration medical screening

Evolving with quarantine and border health practices, immigration medical screening was a clinical process where new arrivals were assessed, inspected and examined by border or quarantine



Figure 1. Screening for tuberculosis, mental illness and syphilis, Ellis Island (USA), 1917. Upon arrival, migrants were asked to climb the steep stairs carrying with them their heavy luggage. On the top of the stairs, those coughing were examined for TB, while those smiling or looking happy were examined for mental illness and/or syphilis (which being often localized in the brain, was clinically diagnosed through psychiatric disturbances). The pictures were kindly provided by JP Zellweger.

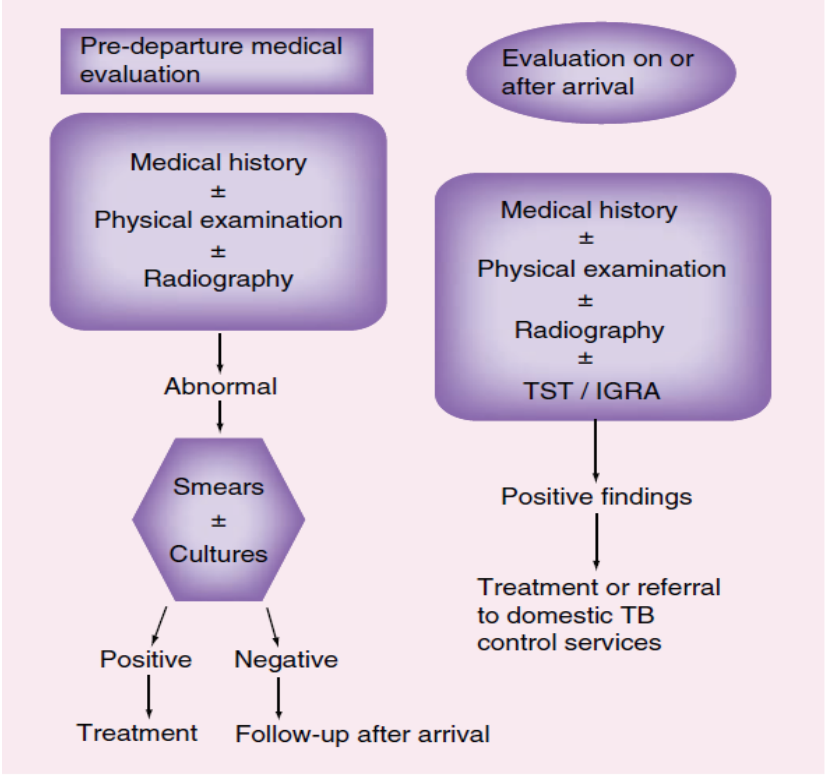


Figure 3. Examples of national practices.

At the same time, the improved understanding of the factors behind the reactivation of LTBI will allow better and more specific targeting of new diagnostic methodologies. Integrating immigration screening with programs to specifically identify LTBI at risk of reactivation and coupling that with domestic short course preventive therapy can be expected to be elements of widely applied best practices for managing TB in the foreign born in the future.

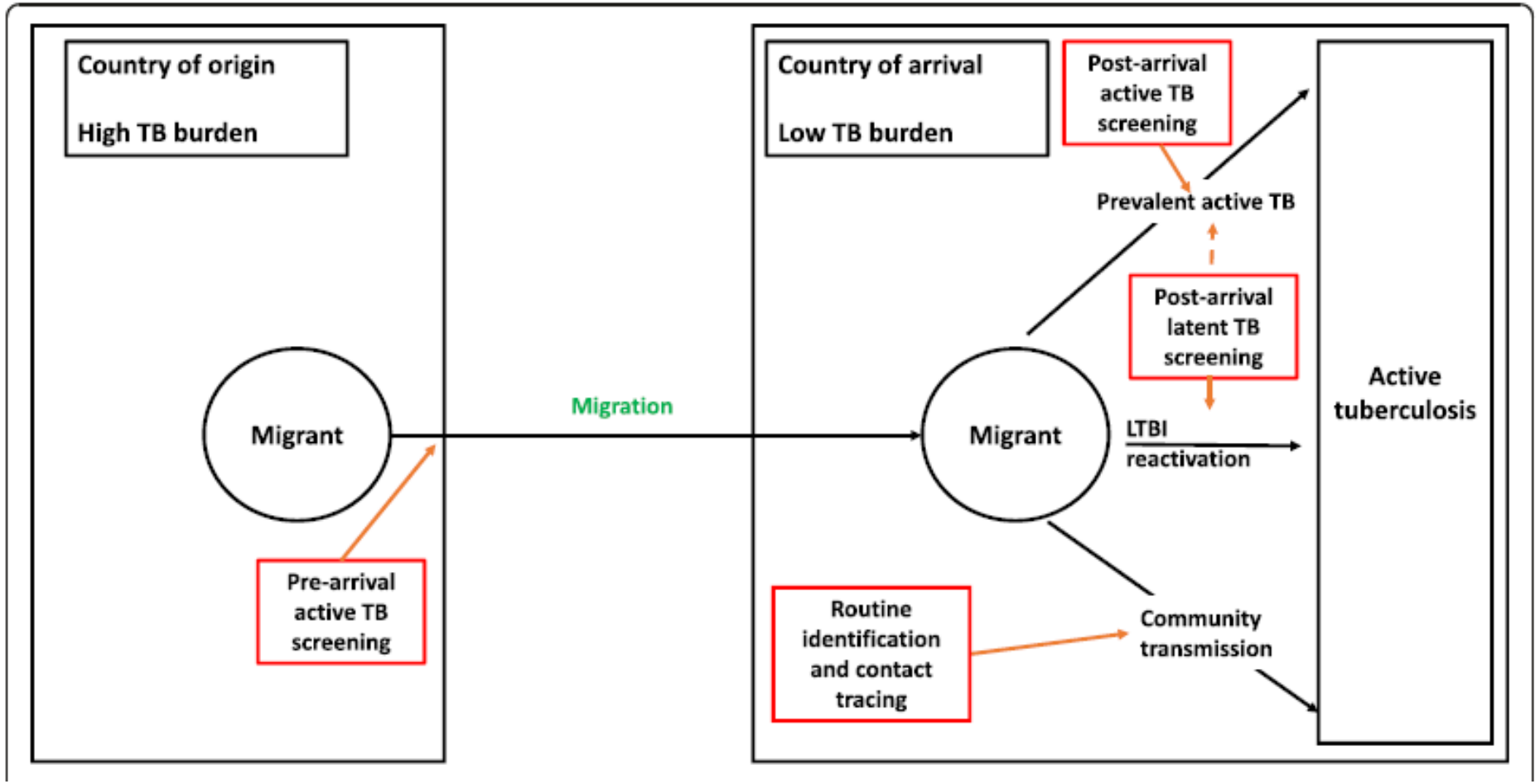
There is also a growing discussion about how screening programs can benefit broader control efforts. A recent analysis suggested that investments in TB infrastructure within a country will in the long run reduce the TB burden entering a receiving country greater than improvements in screening algorithms [70].

Key issues

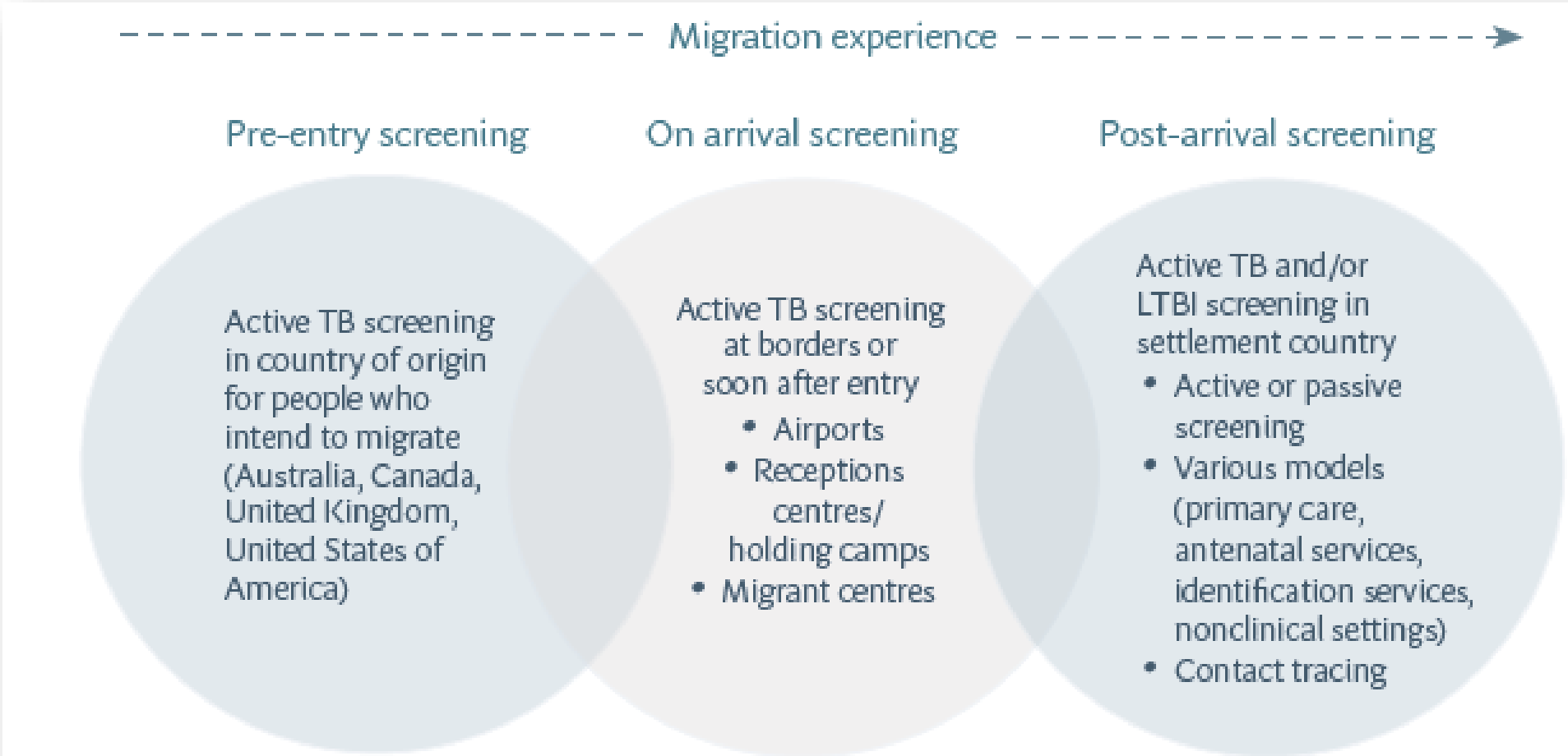
- Quarantine health practices and screening aimed at identifying transmissible diseases to protect host populations started before the 18th century.
- As the science and understanding of TB developed, programs and practices began to focus on the identification and management of diseases in a manner that supported organized immigration.
- While initially organized at the port of entry, screening practices were gradually integrated with predeparture investigations as requested by legislation in force in some countries.
- Initial immigration medical screening for TB is commonly undertaken through a combination of clinical and radiological methods. Individuals applying for permanent residence, temporary workers and long-staying visitors are often required to undergo a medical evaluation.
- The possibility to identify individuals in need of further investigation through scores and thresholds tuned on the country of origin of the migrants demonstrated significant advantages in terms of flexibility, cost and burden of medical procedures on the screened population, while maintaining approximately the same yield in terms of infectious TB cases detected.
- In the perspective of eliminating TB from low incidence countries, identification and treatment of latent infection is gaining more and more interest.

Screening practices for TB and LTBI

Schematic diagram of migration, factors determining how incident active tuberculosis occurs and methods of screening migrants



Pareek et al. BMC Medicine, 2016



Source: Modified from Pareek et al., 2016 (3).

Different approaches for the migrant screening process methods

Table 3 Potential strengths and weaknesses of different migrant screening methods

	Screening methodology	
	Screening for active tuberculosis	Screening for latent tuberculosis infection
Screening tool used	Chest x-ray	Tuberculin skin test
		Interferon gamma release assay
Screening location	Pre-arrival	Post-arrival
	At arrival	
	Post-arrival	
Strengths	Able to identify active TB	Identifies latent TB before reactivation occurs
	Able to identify infectious individuals	Can be built into community programmes
	Can be integrated into immigration processes	Targeted screening likely to be cost-effective
Weaknesses	Low yields for active TB	Programmatically difficult to implement
	Uncertain cost-effectiveness (unless screening targeted)	Numbers accepting and completing treatment may be suboptimal
	Does not identify patients with latent TB who can go on to reactivate	

Table 1. Immigration medical examination options.

Screening option	Location	Examples
Predeparture screening	Prior to the migrants' departure for the destination country	Australia, Canada, New Zealand and the USA
Immediate on-arrival screening	Examination at port of entry	UK and Switzerland
Postarrival screening	Screening after arrival and transit through the port of entry	Several European nations and Israel

Pareek et al. BMC Medicine, 2016
Dara M et al, Expert Review Anti Infect Therapy 2013

Yields for active tuberculosis from previous meta-analyses

Author	Year	Yield for active tuberculosis (%)		
		Overall	Pre-arrival	At/post-arrival
Klinkenberg [19]	2009	0.35	1.21	0.31
		0.51		
Arshad [18]	2010	0.35	-	0.35
Aldridge [71]	2014	0.22	0.22	-

Pareek et al. BMC Medicine, 2016

Yield of TB screening: Switzerland

INT J TUBERC LUNG DIS 14(11):1388–1394
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Screening for tuberculosis in asylum seekers: comparison of chest radiography with an interview-based system

S. Schneeberger Geisler,* P. Helbling,* J. P. Zellweger,† E. S. Altpeter*

*Division of Communicable Diseases, Federal Office of Public Health, Berne, †Swiss Lung Association, Berne, Switzerland

SUMMARY

SETTING: Mandatory initial screening of asylum seekers for tuberculosis (TB) in Switzerland, 2004–2005 and 2007–2008.

OBJECTIVE: To compare the yield of screening by chest radiography with an individual assessment based on geographic origin, personal history and symptoms.

DESIGN: Cross-sectional retrospective comparison of two 2-year periods.

RESULTS: The prevalence of detected TB cases was defined as the proportion of screenees starting anti-tuberculosis treatment for culture-confirmed pulmonary TB within 90 days. TB prevalence was 14.3 per 10 000 asylum seekers screened (31/21 727) using chest radiography and 12.4 (29/23 402) using individual assessment. The sensitivity of radiography was 100% vs. 55% for individual assessment, but its specificity was lower (89.9% vs. 96.0%, respectively). The higher sensitivity of radiography meant shorter delays between screening and start of treatment (median 6 vs. 25 days). Its lower specificity led to a larger proportion of screenees needing further investigations for suspicion of TB (12% vs. 4%).

CONCLUSION: The interview-based system initially missed more cases, but the ultimate 90-day yield was comparable for the two periods. The main difference is the delay until start of treatment, which potentially increases transmission and secondary cases. The radiograph system was more burdensome to both the health care system and the screenees, as more suspects required further investigations.

KEY WORDS: tuberculosis; screening; immigrants; asylum seekers

Yield of screening for LTBI: Switzerland

Sarivalasis *et al. BMC Infectious Diseases* 2012, **12**:285
http://www.biomedcentral.com/1471-2334/12/285

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Factors associated with latent tuberculosis among asylum seekers in Switzerland: a cross-sectional study in Vaud County

Apostolos Sarivalasis[1*], Jean - Pierre Zellweger[2], Mohamed Faouzi[3], Oscar Daher[4], Charlotte Deslarzes[5] and Patrick Bodenmann[1]

Abstract

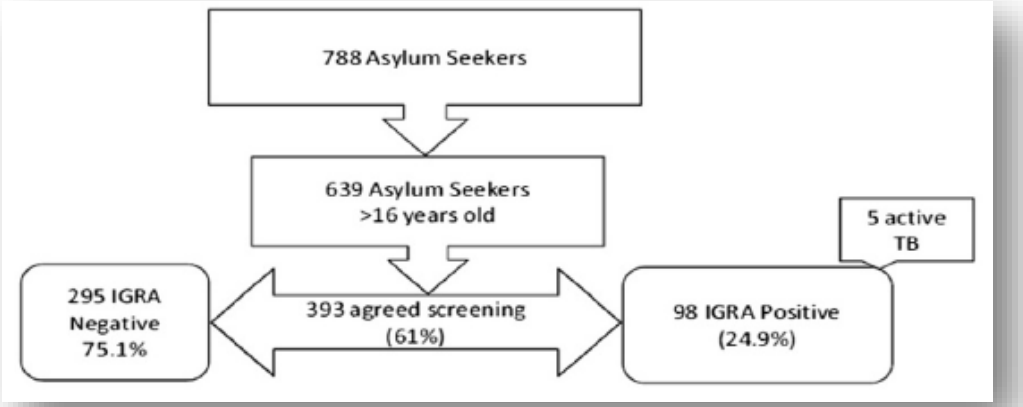
Background: Screening and treatment of latent tuberculosis infection (LTBI) in asylum seekers (AS) may prevent future cases of tuberculosis. As the screening with Interferon Gamma Release Assay (IGRA) is costly, the objective of this study was to assess which factors were associated with LTBI and to define a score allowing the selection of AS with the highest risk of LTBI.

Methods: In across-sectional study, AS seekers recently arrived in Vaud County, after screening for tuberculosis at the border were offered screening for LTBI with T-SPOT.TB and questionnaire on potentially risk factors. The factors associated with LTBI were analyzed by univariate and multivariate regression.

Results: Among 393 adult AS, 98 (24.93%) had a positive IGRA response, five of them with active tuberculosis previously undetected. Six factors associated with LTBI were identified in multivariate analysis: origin, travel conditions, marital status, cough, age and prior TB exposure. Their combination leads to a robust LTBI predictive score.

Conclusions: The prevalence of LTBI and active tuberculosis in AS is high. A predictive score integrating six factors could identify the asylum seekers with the highest risk for LTBI.

Keywords: Asylum seeker, Latent tuberculosis infection, Tuberculosis, Risk factors, Predictive score, Interferon gamma release assay



Conclusions

This study highlights the factors associated with LTBI among asylum seekers entering Vaud County, Switzerland. The observed prevalence of LTBI (24.9%) matches with the prevalence from the literature. The prevalence of TB previously undetected at the border in asylum seekers with LTBI was also high (5.1%). The factors associated with LTBI identified in this population (age, origin from FSU, Asian and African countries, ground transportation; married status; prior TB exposure and cough) were combined to create a predictive score of LTBI for asylum seekers which could be used at border screening. The application of this score to an asylum seeker population could help discriminating those most at risk for LTBI permitting a limitation of the number of IGRA to be performed in a border screening setting.

Migrants and health

Cross-border migration and tuberculosis care: the settings

- Migrants crossing borders have health problems, which may be pre-existing or discovered after arrival
- In case of further migration, some chronic or long-term diseases may need a further treatment in another country
- Continuity of care needs (ideally)
  - understanding the migrant's history, needs and priorities
  - search for prior medical documents
  - addressing the legal problems with local authorities
  - contacts with foreign structures in charge of further treatment
  - comprehensive information of the migrants

Infectious diseases to consider according to country of origin

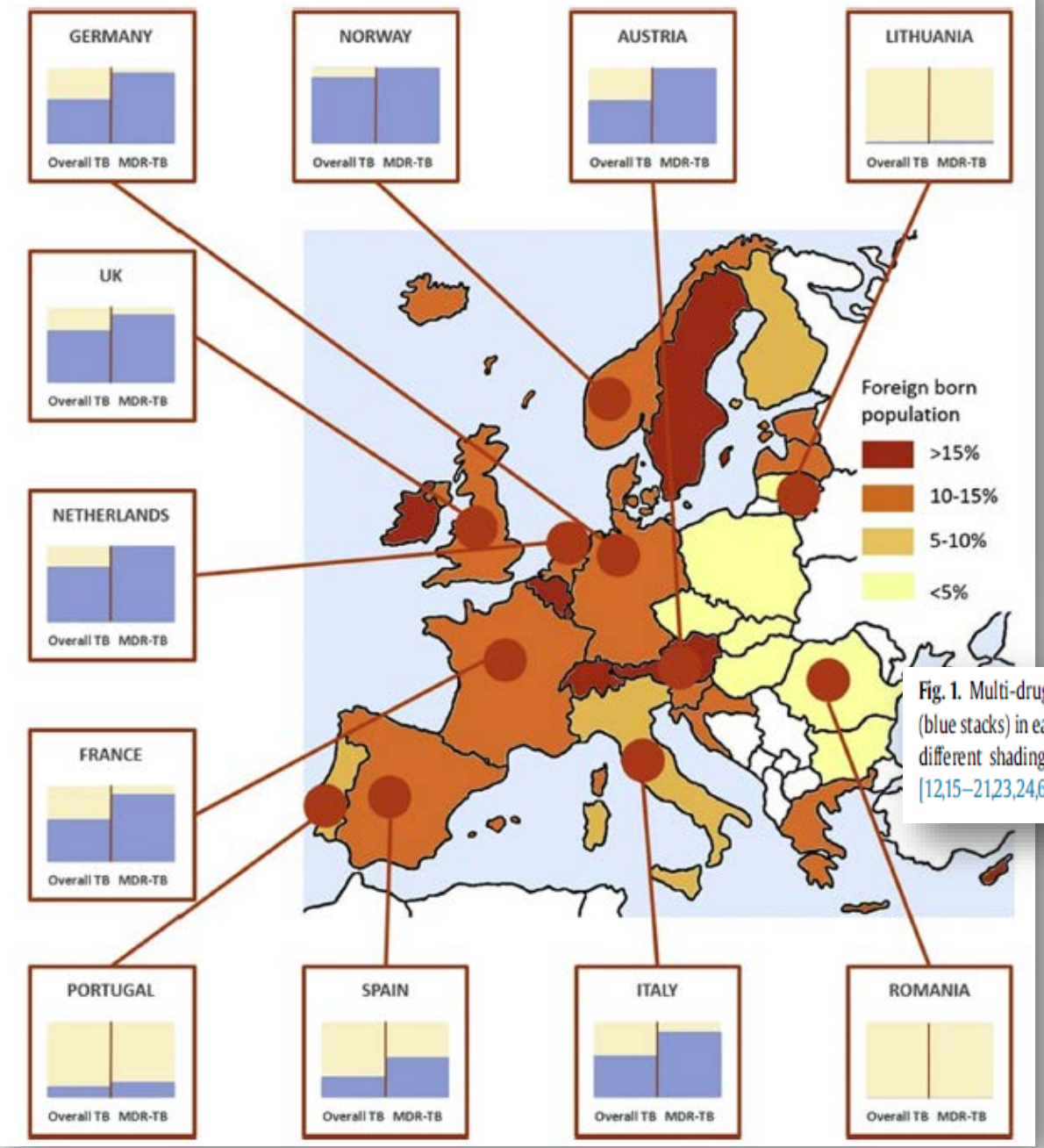
Disease	Indicator	Syria	Afghanistan	Iraq	Eritrea	Somalia
Diphtheria [3]	Cases reported to WHO in 2012, 2013, 2014	0, 0, and NA	0, 0, 0	3, 4, and 5	8, 0 and NA	65, 7 and NA
Typhoid fever	Risk of typhoid	✓	✓	✓	✓	✓
Cholera*	Risk	No recent outbreak	Recurrent outbreaks	On-going outbreak in Baghdad Babylon, Najaf, Qadisiyyah, and Muthanna.	NA	Recurrent outbreaks
Hepatitis A†	Risk	High endemicity	NA	High endemicity	High endemicity	High endemicity
Hepatitis E‡	Risk	NA	NA	High endemicity	NA	High endemicity
Helminthiasis§	Risk of soil transmitted helminthiasis (ascaris, whipworm, hookworm)	+	++	+	++	++
	Risk of urinary schistosomiasis	✓	Non-endemic country	✓	✓	✓
Leishmaniasis**	Risk of cutaneous leishmaniasis	✓	✓	✓	✓	✓
	Risk of visceral leishmaniasis	✓	✓	✓	✓	✓
Hepatitis B††	Prevalence of chronic hepatitis B	Intermediate prevalence: 5.6%	High prevalence: 10.5%	Low prevalence: 1.3%	High prevalence: 15.5%	High prevalence: 12.4%
Hepatitis C‡‡	Prevalence	High prevalence: 3.1%	High prevalence: 1.1%	High prevalence: 3.2%	High prevalence: 1%	NA
HIV	Prevalence	Low	NA	Low	Low	Low
Malaria§§	Risk of malaria	Malaria-free	Risk of *P. vivax* >> *P. falciparum*	Malaria-free	Risk *of P. falciparum* >> *P. vivax*	Risk *of P. falciparum*
Measles*	Incidence per 100 000 in 2013 and 2014	1.84 and 2.68	1.41 and 1.75	2.09 and 3.02	0.77 and 0.02	2.17 and 9.12
Polio***	Cases reported to WHO in 2012, 2013 and 2014	0, 35 and NA	46, 17, and 28	0, 0, and 2	0, 0, and 0	1, 195 and 5
Tuberculosis†††	Incidence/100 000	Low: 17	High: 189	Low: 25	High: 40 to 499	High: 285
Antimicrobial resistance	Risk of carriage of multidrug-resistance Gram-negative bacteria	NA	NA	NA	NA	NA
Rabies	Risk level for humans contracting rabies	High	High	High	High	High

ECDC 2015. Infectious diseases of specific relevance to newly-arrived migrants in the EU/EEA

Differential diagnosis among newly arrivad migrants

Clinical presentation	Differential diagnosis to consider
Fever	Typhoid fever Malaria Louse-borne diseases Visceral leishmaniasis Amoebic abscess Arboviruses
Respiratory symptoms	Tuberculosis Influenza
Gastrointestinal symptoms	Cholera Typhoid fever Shigellosis Amoebic colitis Helminthiasis: ascaris, whipworm, hookworm
Sores	Scabies Cutaneous leishmaniasis Cutaneous diphtheria
Skin rash	Measles Rubella Louse-borne diseases
Meningitis or other neurological symptoms	Rabies Invasive bacterial diseases (*Neisseria meningitidis, Haemophilus influenza type b and Streptococci pneumoniae*) Polio Dengue and other arboviruses

ECDC 2015. Infectious diseases of specific relevance to newly-arrived migrants in the EU/EEA



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journal homepage: www.clinicalmicrobiologyandinfection.com

Review

Multidrug-resistant tuberculosis and migration to Europe

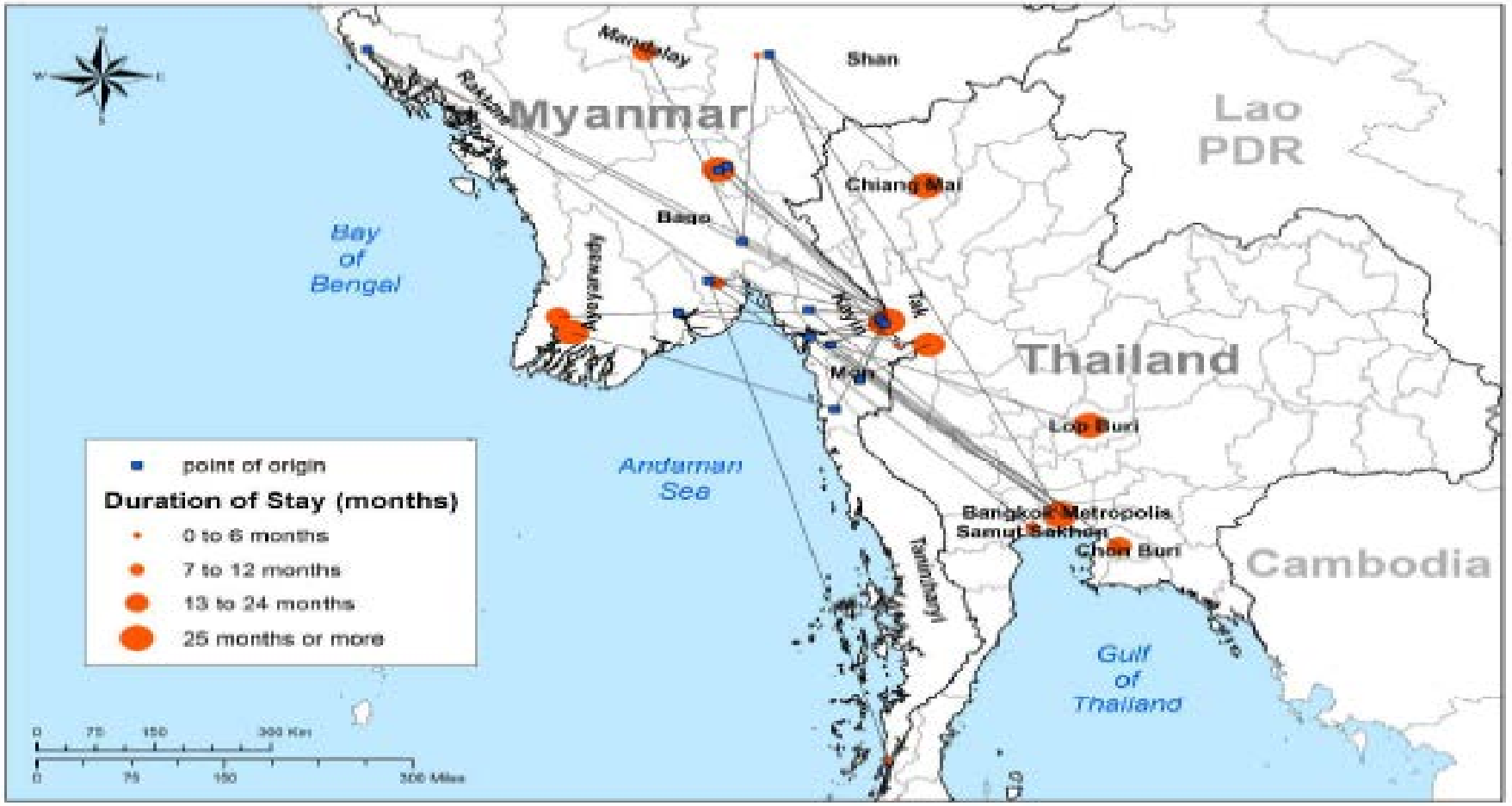
S. Hargreaves [1], K. Lönnroth [2, 3], L.B. Nellums [1], I.D. Olaru [4, 5], R.R. Nathavitharana [1, 6], M. Norredam [7, 8], J.S. Friedland [1, *]

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Fig. 1. Multi-drug-resistant tuberculosis (MDR-TB) and migration in Europe. The boxes in this figure illustrate the proportion of TB cases and MDR-TB cases that occur in migrants (blue stacks) in each country. Columns in the boxes represent the percentage of foreign-born overall, among the total TB and MDR-TB cases reported in that country. On the map, the different shadings of the countries represent the proportions of foreign-born individuals living in that country that are comprised by migrants. Data taken from references [12,15–21,23,24,61].

MDR-TB and migration in Europe

Migration from Myanmar to Thailand



Sein Sein Thi et al., Int J Tuberc Lung Dis. 2017

A cluster of multidrug-resistant *Mycobacterium tuberculosis* among patients arriving in Europe from the Horn of Africa: a molecular epidemiological study

Timothy M Walker, Matthias Merker*, Astrid M Knoblauch*, Peter Helbling, Otto D Schoch, Marieke J van der Werf, Katharina Kranzer, Lena Fiebig, Stefan Kröger, Walter Haas, Harald Hoffmann, Alexander Indra, Adrian Egli, Daniela M Cirillo, Jérôme Robert, Thomas R Rogers, Ramona Groenheit, Anne T Mengshoel, Vanessa Mathys, Marjo Haanperä, Dick van Soolingen, Stefan Niemann†, Erik C Böttger†, Peter M Keller†, and the MDR-TB Cluster Consortium‡*

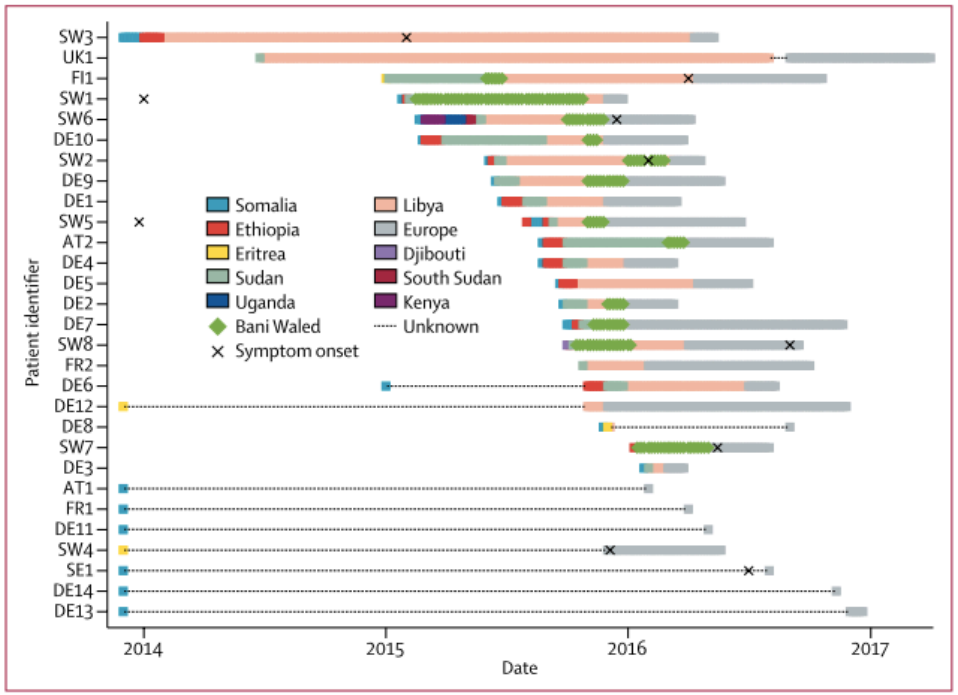


Figure 2: **Timeline of patient journeys until diagnosis**
The 1st of each month is shown as the country entry date. Subsequent countries visited in the same month are presented at 5-day intervals.

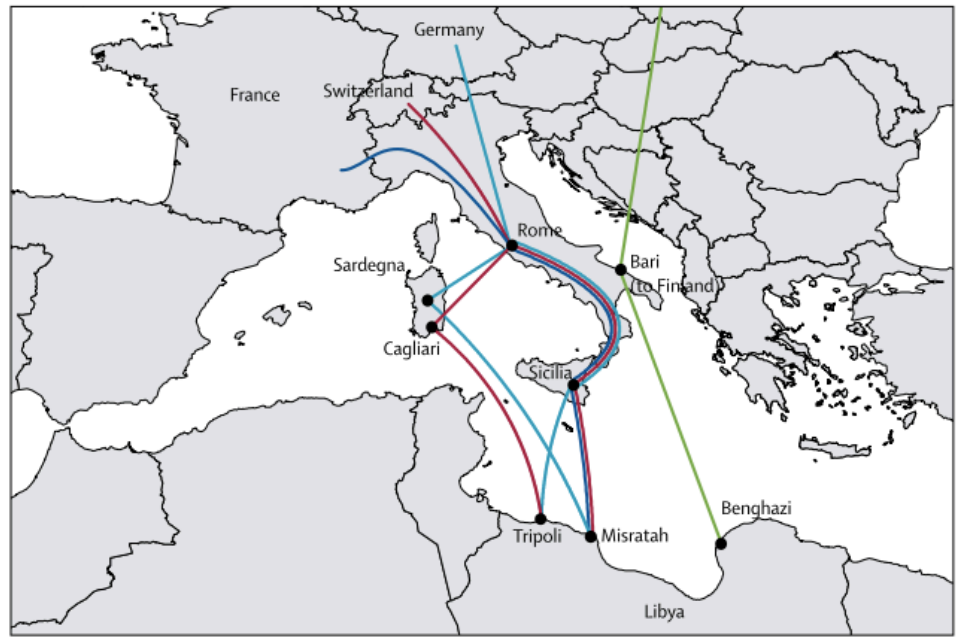
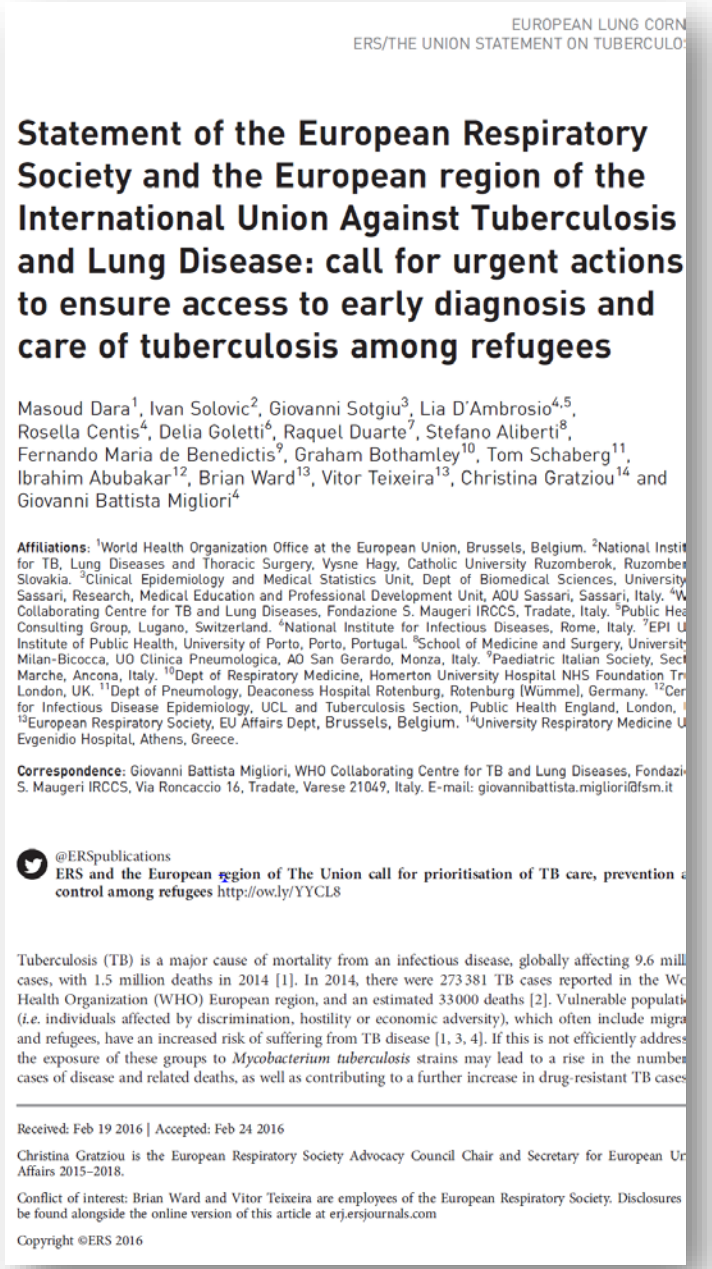


Figure 3: **Reported migration routes through Italy of 29 outbreak patients with a documented migration route, August, 2014, to February, 2017**



EUROPEAN LUNG CORN
ERS/THE UNION STATEMENT ON TUBERCULO

Statement of the European Respiratory Society and the European region of the International Union Against Tuberculosis and Lung Disease: call for urgent actions to ensure access to early diagnosis and care of tuberculosis among refugees

Masoud Dara[1], Ivan Solovic[2], Giovanni Sotgiu[3], Lia D'Ambrosio[4,5], Rosella Centis[4], Delia Goletti[6], Raquel Duarte[7], Stefano Aliberti[8], Fernando Maria de Benedictis[9], Graham Bothamley[10], Tom Schaberg[11], Ibrahim Abubakar[12], Brian Ward[13], Vitor Teixeira[13], Christina Gratziou[14] and Giovanni Battista Migliori[4]

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@ERSpublications
ERS and the European region of The Union call for prioritisation of TB care, prevention control among refugees http://ow.ly/YYCL8

Tuberculosis (TB) is a major cause of mortality from an infectious disease, globally affecting 9.6 mill cases, with 1.5 million deaths in 2014 [1]. In 2014, there were 273 381 TB cases reported in the Wo Health Organization (WHO) European region, and an estimated 33 000 deaths [2]. Vulnerable populati (*i.e.* individuals affected by discrimination, hostility or economic adversity), which often include migra and refugees, have an increased risk of suffering from TB disease [1, 3, 4]. If this is not efficiently address the exposure of these groups to *Mycobacterium tuberculosis* strains may lead to a rise in the number cases of disease and related deaths, as well as contributing to a further increase in drug-resistant TB cases

Received: Feb 19 2016 | Accepted: Feb 24 2016

Christina Gratziou is the European Respiratory Society Advocacy Council Chair and Secretary for European Ur Affairs 2015–2018.

Conflict of interest: Brian Ward and Vitor Teixeira are employees of the European Respiratory Society. Disclosures be found alongside the online version of this article at erj.ersjournals.com

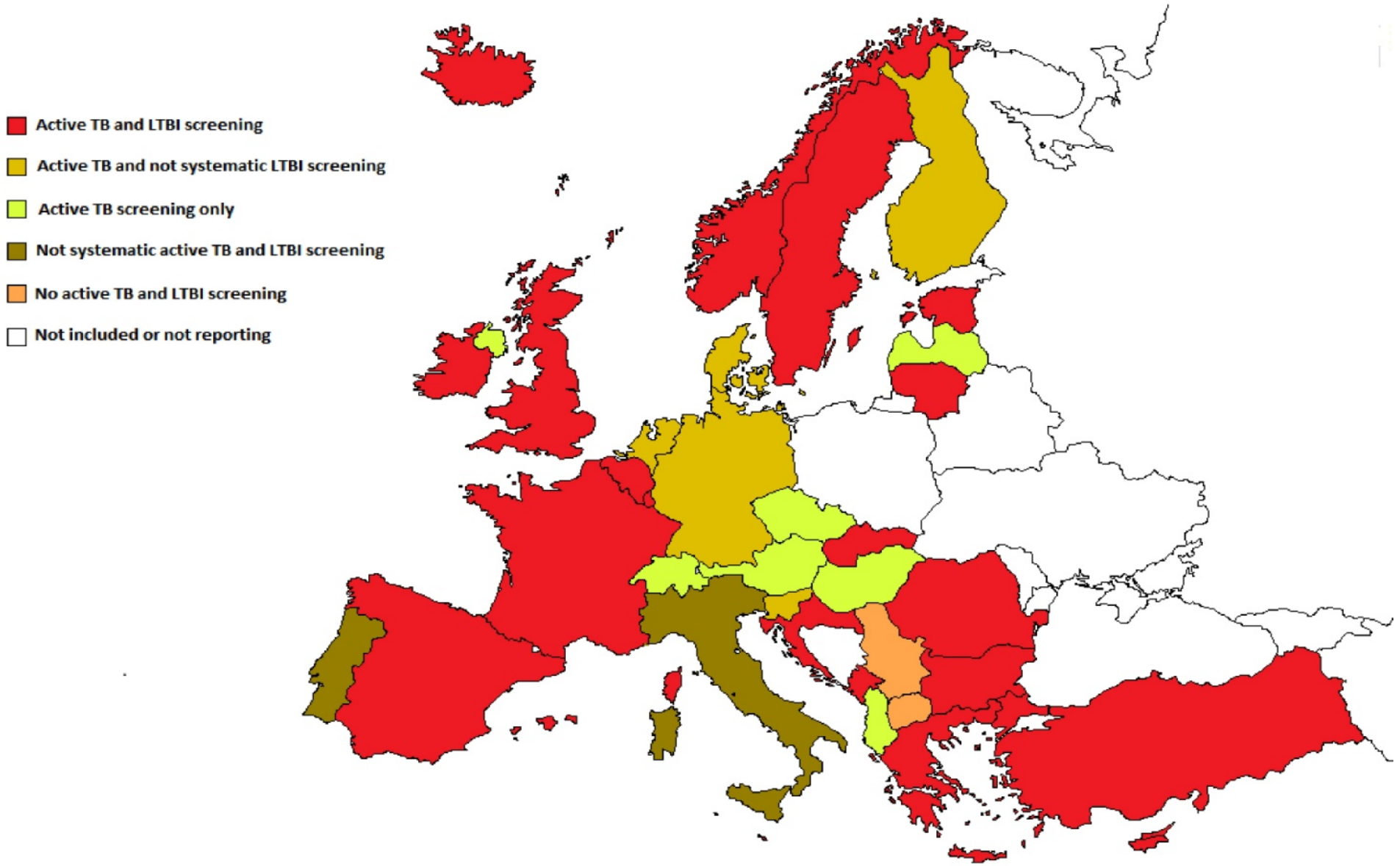
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Recommendations ERS, UNION-ER (+WHO Euro)

- **Refugees to benefit from End TB Strategy principles**
- **Improve surveillance M&E, research on TB/LTBI**
- **Timely screening**
- **Avoid stigma & steroetypes**
- **Universal access TB/LTBI services**
- **Infection control**

The European Respiratory Society and the European region of the International Union Against TB and Lung Disease urge health authorities, national and international technical agencies and civil society organisations, as well as donor agencies, to prioritise TB care, prevention and control. They strongly recommend: 1) adapting and implementing the principles of the WHO End TB Strategy to ensure adequate prevention, diagnosis and treatment of TB (and of LTBI in the countries where these are offered) among refugees [1, 5]; 2) providing quality surveillance, monitoring and evaluation, and operational research to enhance TB prevention, control and care among refugees; 3) ensuring timely screening for active TB among refugees coming from middle or high TB incidence countries; 4) avoiding stigmatisation and stereotypes of both TB-infected people and vulnerable groups; 5) promoting universal access to prevention, diagnosis and treatment services for LTBI (in the countries where these are offered) and TB, as well as to the necessary care of existing comorbidities [1, 5]; and 6) ensuring quality infection control, including protective measures for staff, and providing HIV testing and counselling to detect HIV and TB/HIV co-infected individuals [18, 19].

SUMMARY OF TB AND LTBI SCREENING



Conclusions 1

- High response rate; TB screening considered important public health intervention
- Country-specific algorithms (questionnaire/CXR +bacteriology)
- Lack of analysis on yield of screening (workload?)
- >TB <LTBI: implications for TB Elimination?
- 11/36 countries ‘equipped’ to collect info on LTBI, but 3 do collect (Finland, Norway, UK)

Minimum package for cross border TB control and care

Eur Respir J 2012; 40: 1081–1090
DOI: 10.1183/09031936.00053012
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PERSPECTIVE

Minimum package for cross-border TB control and care in the WHO European region: a Wolfheze consensus statement

Masoud Dara, Pierpaolo de Colombani, Roumyana Petrova-Benedict, Rosella Centis, Jean-Pierre Zellweger, Andreas Sandgren, Einar Heldal, Giovanni Sotgiu, Niesje Jansen, Rankica Bahtijarevic and Giovanni Battista Migliori on behalf of the members of the Wolfheze Transborder Migration Task Force

ABSTRACT: The World Health Organization (WHO) European region estimates that more than 400,000 tuberculosis (TB) cases occur in Europe, a large proportion of them among migrants.

A coordinated public health mechanism to guarantee TB prevention, diagnosis, treatment and care across borders is not in place. A consensus paper describing the minimum package of cross-border TB control and care was prepared by a task force following a literature review, and with input from the national TB control programme managers of the WHO European region and the Wolfheze 2011 conference. A literature review focused on the subject of TB in migrants was carried out, selecting documents published during the 11-yr period 2001–2011.

Several issues were identified in cross-border TB control and care, varying from the limited access to early TB diagnosis, to the lack of continuity of care and information during migration, and the availability of, and access to, health services in the new country.

The recommended minimum package addresses the current shortcomings and intends to improve the situation by covering several areas: political commitment (including the implementation of a legal framework for TB cross-border collaboration), financial mechanisms and adequate health service delivery (prevention, infection control, contact management, diagnosis and treatment, and psychosocial support).

KEYWORDS: Control, Europe, human rights, immigration, multidrug-resistant tuberculosis, tuberculosis

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Received:
March 30 2012
Accepted after revision:
May 04 2012
First published online:
May 31 2012

Management, human rights and finance	Governance	Legal framework	Commitment to cross-border TB control and care Ensure legal basis for cross-border TB control and care within EU and non-EU, and between EU and non-EU
		Funding	Ensure funding from government resources, health insurance and/or bilateral and multilateral funding mechanisms
		Intercountry correspondence	Create and maintain a live list of TB service providers in the region
	Service delivery	Prevention	Diagnosis and treatment of LTBI
		TB infection control	Administrative measures, environmental measures and personal protection
		Diagnosis	Early diagnosis including drug-resistant TB
		Treatment	Prompt and effective treatment
		Continuity of care	No deportation before the end of treatment or at least until the end of intensive phase and ensuring continuation phase treatment will be followed
	Surveillance and monitoring	Individual patient data	Effective transfer of patient's record
			Feedback to the centre sending patients
		Programme performance	Relevant indicators at country and regional level measure progress
	Supportive environment	Enablers and incentives	Counselling Psychosocial support to patients
		Advocacy communication and social mobilisation	Empower communities for providing migrant-sensitive services Improve communication with migrant communities Advocate for full engagement of health authorities and stakeholders

Defining a migrant-inclusive tuberculosis research agenda to end TB

Operational and implementation research	
Prevention and screening	Evaluate feasibility of LTBI targeted testing and treatment algorithms on migrants at key points along the migration pathway
	Assess the use of mobile health (mHealth) and digital health technologies to support linkage to care and treatment adherence in migrant populations
	Evaluate the operational impact of LTBI screening tools (both pre- and post-arrival)
Diagnostics	Evaluate specific evidence-based diagnostic guidelines in migrant populations compared to native populations
	Identify health systems and patient barriers to implementation of diagnostic testing strategies in migrants
Treatment	Establish the comparative effectiveness of treatment strategies (e.g., DOT vs. SAT)
	Evaluate the impact of novel treatment regimens, including short-course treatment, in migrants when implemented in programmatic settings
	Identify core components of interventions needed to maximize treatment adherence
	Pilot mechanisms to ensure that culture and drug susceptibility results are communicated to providers treating a patient along the migration pathway
Health systems and health economics research	Evaluate the cost and cost-effectiveness of migrant-focused TB interventions
	Analyze gaps in health system access specific to documented and undocumented migrants along the migration pathway
	Establish critical components necessary for operationalizing cross-border collaborations
Social protection research	Identify context-specific social and economic vulnerabilities in migrants
	Identify targetable socio-economic barriers to TB care for migrants
	Evaluate the effectiveness and impact of social protection strategies on reducing vulnerabilities and improving public health and TB outcomes in migrants
	Understand the contextual requirements for including migrants in social protection schemes
	Identify and evaluate TB-sensitive and TB-specific interventions on migrant health
Health and human rights research	Document infringements on human rights by TB programs
	Develop TB-specific interventions that support the human rights of migrants

TB = tuberculosis; LTBI = latent tuberculous infection; MDR-TB = multidrug-resistant TB; DOT = directly observed therapy; SAT = self-administered therapy.

Shete P.B et al. Int J Tuberc L Dis 2018

Factsheets for World TB Day 2019

E DETECT TB: a research consortium for the early detection and integrated management of tuberculosis in Europe (Link: https://e-detecttb.eu/)

EUROPEAN MIGRANT TB SCREENING DATABASE PUBLISHED IN IJID
(MARCH 2019)



International Journal of Infectious Diseases 80 (2019) 545–549

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

ELSEVIER

Building a European database to gather multi-country evidence on active and latent TB screening for migrants

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ARTICLE INFO

Article history:
Received 9 January 2019
Received in revised form 22 February 2019
Accepted 23 February 2019
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

ABSTRACT

Background and aim: Screening for active and latent TB among migrants in low TB incidence countries may constitute an important contribution to TB elimination. E-DETECT TB, a European multi-county collaboration, aims to address the present lack of evidence on effectiveness of migrant TB screening by collating data in an international database and perform cross-country pooled and comparative analyses of screening coverage, results and linkage to care.
Method: A database was established using migrant TB screening data from participating countries'

E-DETECT TB's projects

Outreach for early diagnosis (work package 4): WHO recommends systematic screening for active TB in subpopulations that have poor access to healthcare. Romania and Bulgaria are countries in transition from a high to intermediate incidence and are experiencing high TB rates among certain populations. In this work package we're using a mobile diagnostic unit equipped with digital radiography and molecular point of care tests to improve early diagnosis in these populations. (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/7b29ec18-23c3-4b06-98cc-f9362a082c04/fact_sheet_WP4_WTBD_2019.pdf)



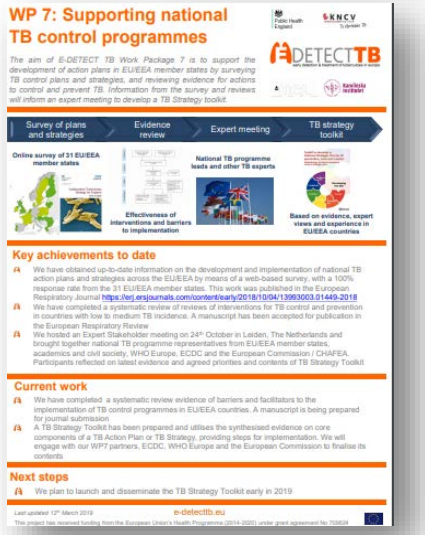
Migrant TB detection, prevention and treatment (work package 5): In Italy, we are actively screening new and settled migrants for active and latent TB respectively, ensuring that those testing positive are appropriately managed and generating the evidence to support future European policy (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/63b2d415-3ce0-4008-80ea-fb707dfbfdce/fact_sheet_WP5_WTBD_2019.pdf.)



Establishing a database on migrant TB screening in Europe (work package 6): Many low-incidence EU countries have a high TB burden in migrants from endemic countries. Migrant TB screening policies vary widely across EU countries. This work package is establishing a multi-country database on migrant TB screening that will be used to inform the identification and harmonisation of cost-effective screening strategies in the EU. (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/810d65f4-45a4-49ee-84d8-f10a6d83466d/fact_sheet_WP6_WTBD_2019.pdf.)



Supporting national TB control programmes (work package 7): The aim of E-DETECT TB work package 7 is to support the development of action plans in EU/EEA member states by surveying TB control plans and strategies, and reviewing evidence for actions to control and prevent TB. Information from the survey and reviews will inform an expert meeting to develop a TB Strategy toolkit. (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/989c1ae6-f29e-4329-b59c-6d3504417add/Fact_sheet_WP7_WTBD_2019.pdf.)



Conclusions (2)

- We have discussed some of the ‘myths’ (migrants keep increasing and increase TB rates; *are not adherent to treatment* and transmit to local populations)
- We have briefly discussed pre- and post-entry screening options for TB and LTBI, their yield as well as the existing policies in Europe
- Migrants have several health issues beyond TB
- Among research *priorities related to treatment*, continuity of care is one of the core ones
- Free access, sensitivity of services, trans-border collaborations are some of the ingredients necessary to improve *adherence to treatment and treatment outcomes*

Thank you!! Merci!! Danke!! Grazie!!



Concluding remarks and take home messages

Macolin TB meeting, 2019

Jean-Paul Janssens

Geneva



Welcome: Jörg Spieldenner

- LPS: founded in 1903
- 1/3 TB asylum seekers or refugees
- Importance of preserving collaboration between all structures involved
- Importance of training and maintaining a good level of competence

LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Delay in TB diagnosis in TB

- Patient delay and health system delay
- Focus on PTB > 18 yrs; n=162
- Median patient delay 5.2 weeks (25% > 13 weeks)
- Median health system delay: 2 weeks (25% > 7 weeks)

Christian Auer, SMW 2018

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Diagnosis of ETTB; JP Janssens

- ET TB : ca 30% of TB
- Low to moderate Se of smear and cultures. Lowest levels for pleura
- Major contribution of Xpert and UltraXpert systems for all ET TB
- Clinicial suspicion remains mandatory

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TB in elderly; Jesica Mazza-Stalder

- Increased mortality
- Difficult diagnosis
- Increased incidence in most countries; substantial proportion of TB cases; prone to increase in developing countries
- Lesser tolerance to drugs
- Importance of comorbidities: COPD, diabetes, and anti-TNF

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Difficulties in the treatment of TB

- Errors: voluntary or involuntary selection of drugs.
- Poor absorption of drugs (10% for RIF!)
- Drug interactions (aged!)
- Undesired effects: PYR > INH> RIF, may lead to interruption
- Toxicity increased in older women

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Difficulties in the treatment of TB

- 0.2 % hepatotoxicity of INH if > 35 yrs vs 1.7% > 35 yrs
- Known risk factors: F, age, hepatitis, diabetes
- Increased QTc: FQ, CLO, BED, DEL
- Cardiac toxicity: Combination of risk factors is most important (K, Mg, Ca, HIV, genetics)
- ECG 1x/mois

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Difficulties in the treatment of TB

- «U shaped curve of concern» of TB in NYC
- Importance of DOT, essential for 2 first months
- CHUV: 89% cure & treatment completed with DOT (2004, JPZ)
- Cochrane (2015): RR of tt completion or cure n.s. with DOT
- WHO: package of treatment adherence interventions

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Follow-up of TB: St Gall / Zurich

- St Gall: DOT not necessary for all; follow-up by GP, and follow-up tel every 2 months
- Zurich: 86%: treatment completed or cured, low % of LTFU or transfer. Close contact with GP and physicians implicated in FU of migrants. Questionnaire for GPs

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OFSP data; Ekkehardt Altpeter

- Welcome data
- Rather stable numbers
- Fluctuations related to foreigners
- 20-25% of undetermined outcome in foreigners and subjects of unknown origin
- Outcome less favorable in foreigners, women, and elderly

Swiss-TB award

- Comparing resistance profile obtained by PCR in field genotypic resistance profile vs reference data from reference lab in Zurich
- 50% HIV
- 19% of discordant results with severe clinical consequences on mortality (resistance under treatment)
- Zurcher & Ballif, Lancet ID, 2019

Management of TB in migrants

- TB is poverty-related
- Migrants are not continuously increasing (peak 2015/6)
- TB is not increasing in the EU due to migrants
- In WHO European region: 33% of all cases foreign born
- Myth: foreign born are not adherent: highyl variable, community dependant

Management of TB in migrants

- No difference in adherence between migrants and non-migrants
- Myth: migrants transmit TB to the native population: in fact impact is minor, but clusters reported; recent report of MDR cluster over several european countries, from Africa
- Importance of informal settlement and slums
- Low yield of TB screening for incoming migrants

Management of TB in migrants

- Very little understanding on the yield of screening
- Importance of networking at a European level
- Migrants have several health issues other than TB
- Continuity of care, free access to care are mandatory

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Digital technologies to support TB patients

- Global smartphone adoption will reach 80% by 2025
- Presently 38-81%
- 3.3 billion people connected to internet (44%)
- DT in TB: 4 main topics:
- Patient care; Surveillance; Program mangement; eLearning

Dennis Falzon, Global TB program, WHO, Geneva

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Digital technologies to support TB patients

- Video observed treatment may replace DOT when available
- Treatment adherence interventions: SMS, Voice, electronic medication monitors.. may be offered
- Handbook of DT for TB edited by WHO, 2018
- Techniques already in use worldwide (Skype, WhatsApp)
- eLearning Apps

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LIA PULMUNARA SVIZRA

Dennis Falzon, Global TB program, WHO, Geneva

VOT: Andrew Hayward

- For DOT: are recommended
  - Community or home-based DOT
  - DOT administered by trained lay providers or HCW
  - Daily treatment vs thrice-weekly
- Target population
- Underused, expensive, time consuming

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VOT: Andrew Hayward

- sureAdhere App: PIN, Film upload, report of UE
- Lancet 2016; RCT, 22 clinics in UK; n=226 DOT «face to face» with incentives vs VOT (daily messages acknowledged; tel if no contact, smartphone provided)
- Difference in acceptance at 1 week
- Outcome: > 80% of observations completed. VOT>>DOT
- Major impact on time and costs

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VOT: Alena Skrahina, Minsk, Belarus

- High prevalence of MDR and XDR TB; 65% tt success
- Transition to incentivized ambulatory care
- VOT implemented in 2016 (pilot study) +
- GF supported project as of Oct 2016: 317 patients; 95.6% success rate
- Smartphones & 2 week drug supply provided

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LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Have a safe trip home; thank you for your participation

