ISS-Rome Workshop

Migrant screening for tuberculosis

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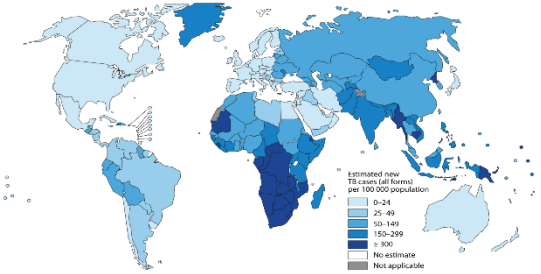
NHS
National Institute for Health Research

Conflict of interest statement

- I have no financial conflicts of interest

Areas to cover today…



Epidemiology

Future directions

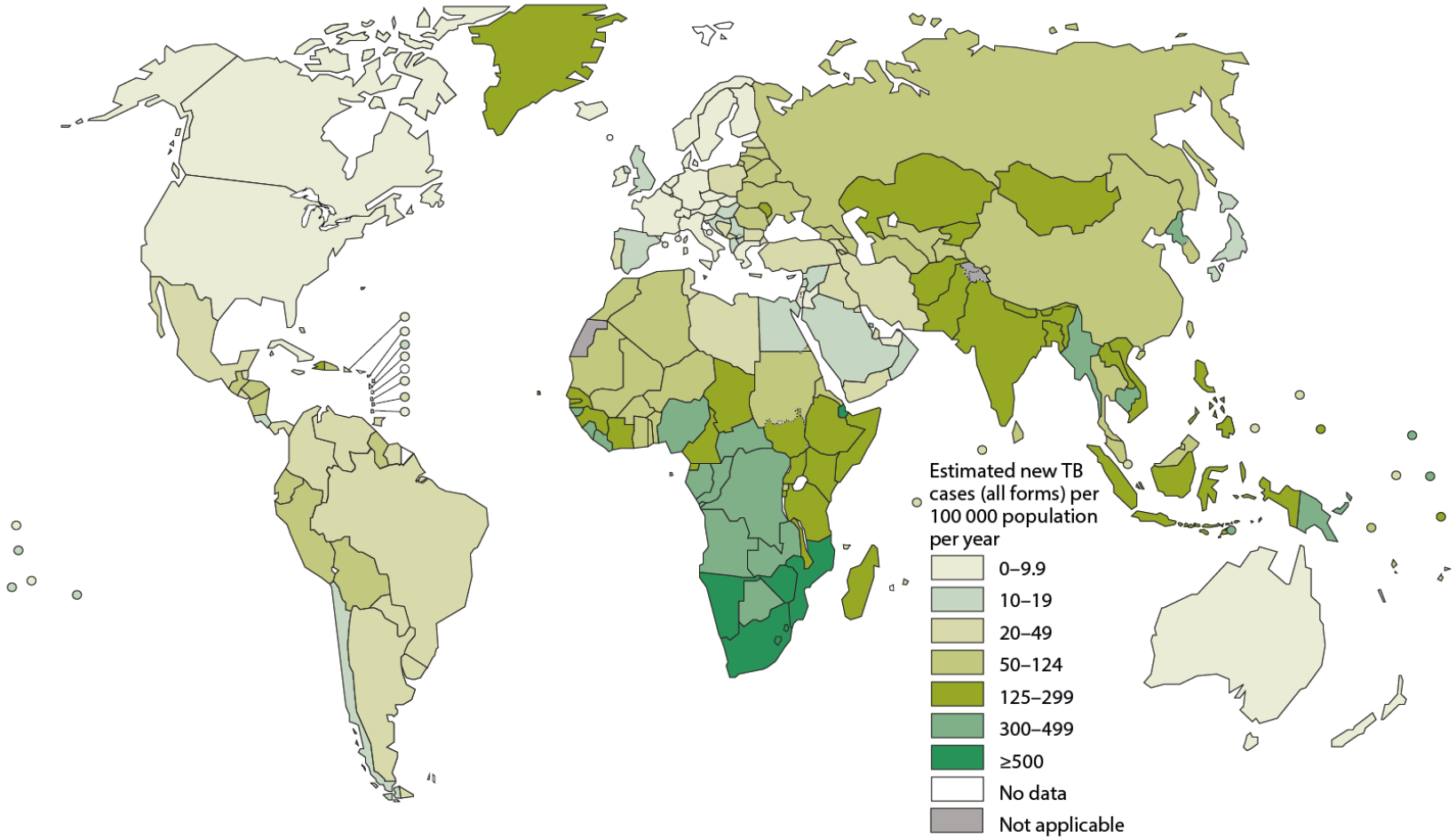
TB in migrants

Screening for latent TB

Screening for active TB

Epidemiology

22 high burden countries account for over 80% of cases



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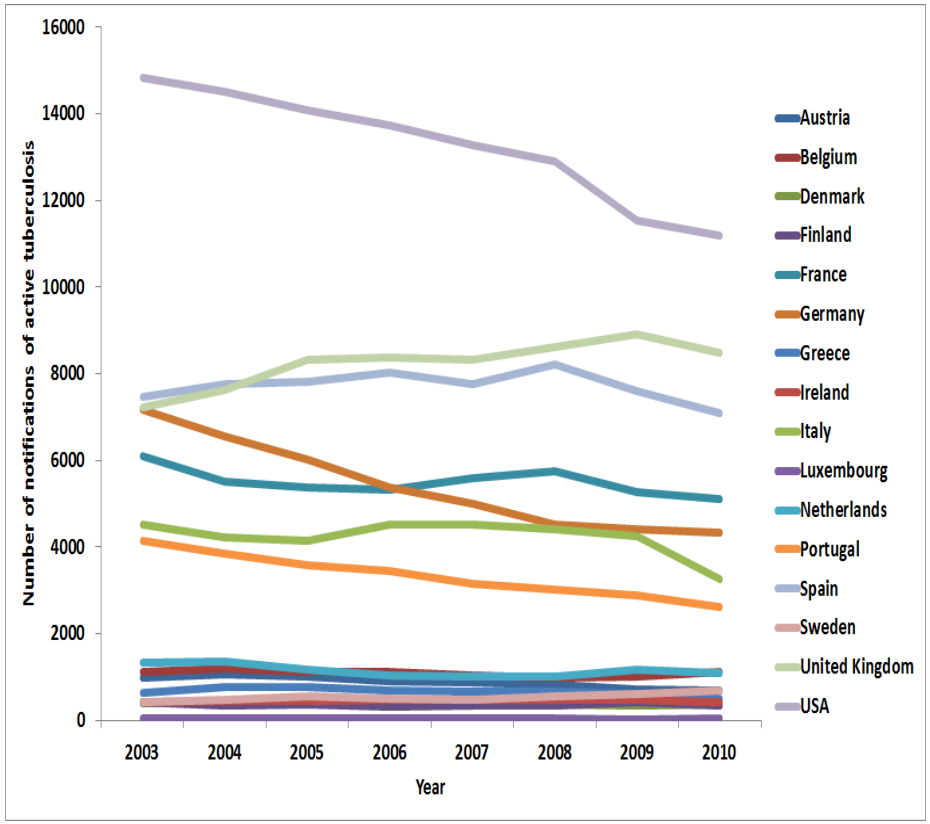
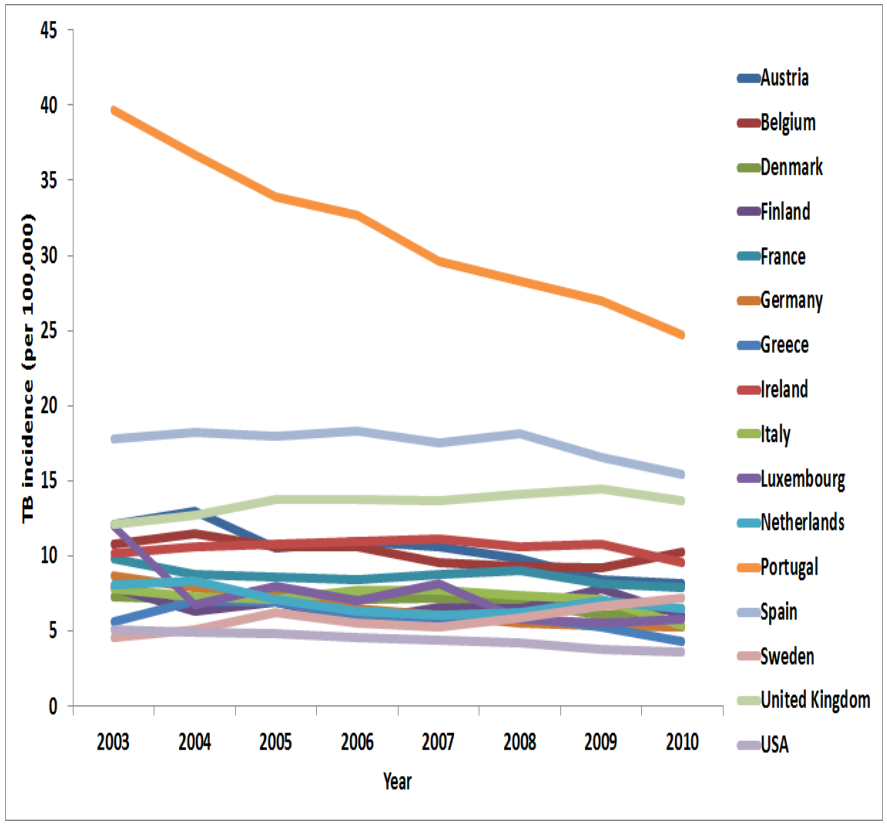
Source: WHO 2013

TB remains a problem in high-income countries





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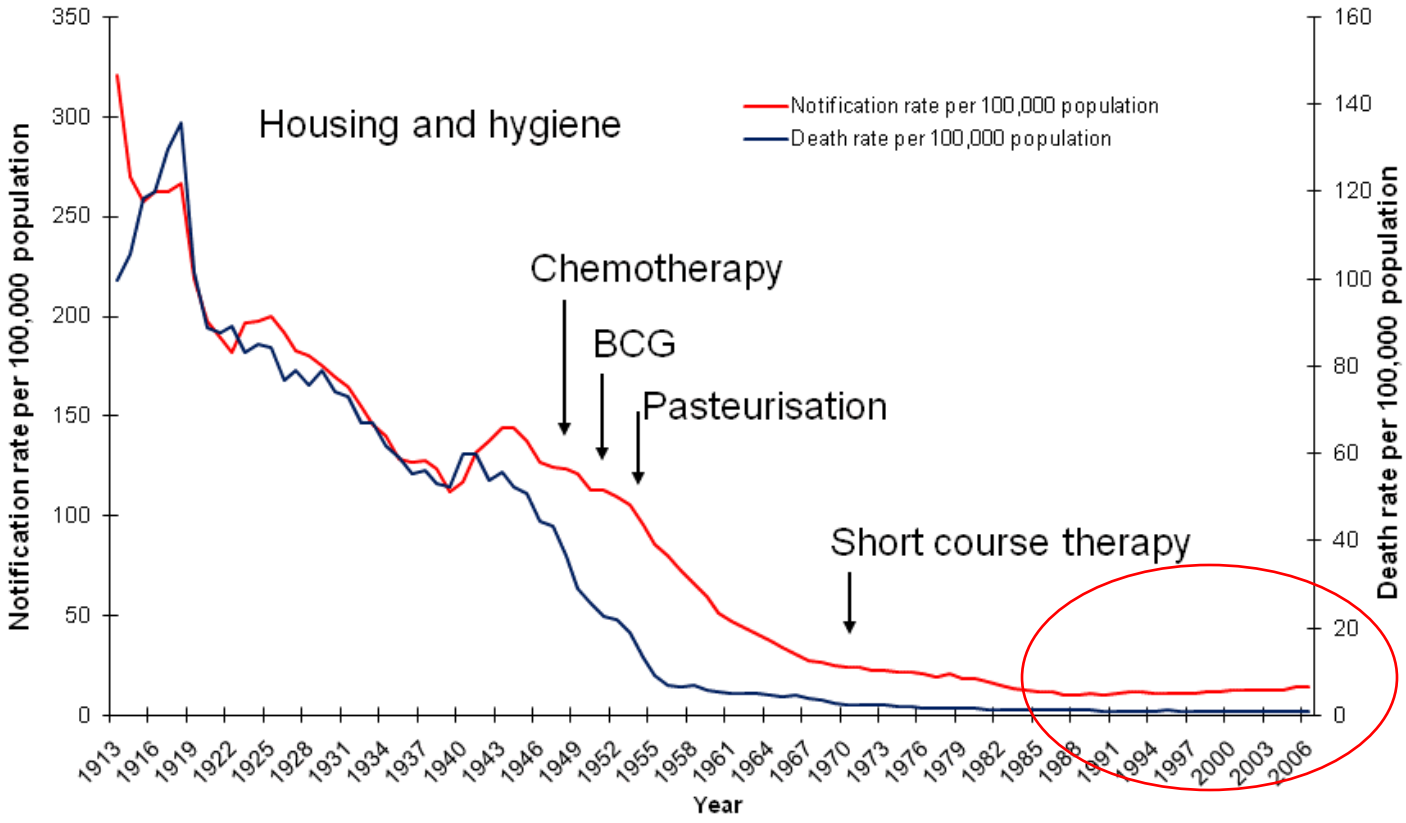
Source: ECDC 2012, CDC 2011

TB in high-income countries: UK as an example



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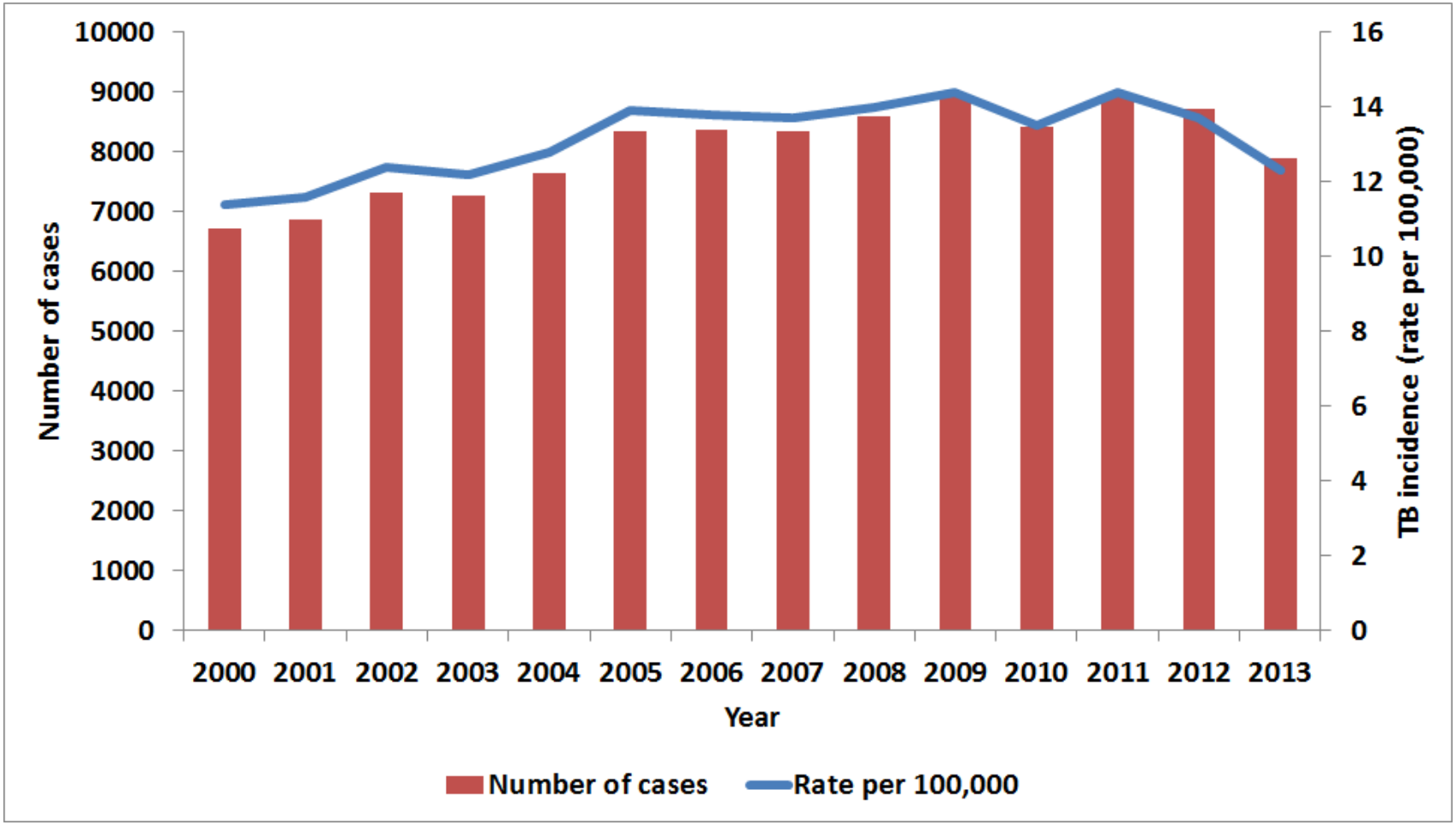
Source: HPA 2009

TB incidence in the UK is increasing…



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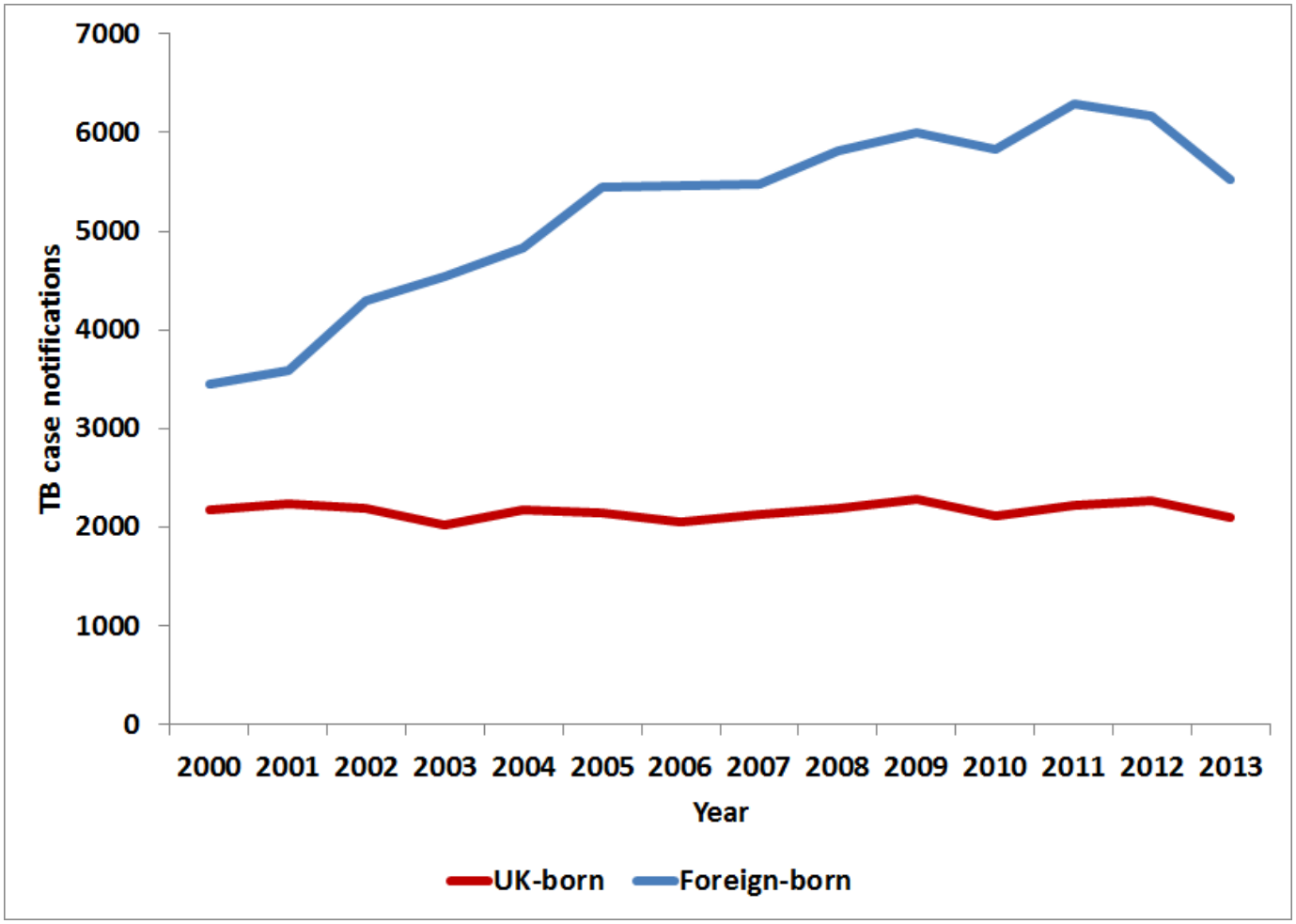
Source: PHE 2014

…but mainly in the foreign-born



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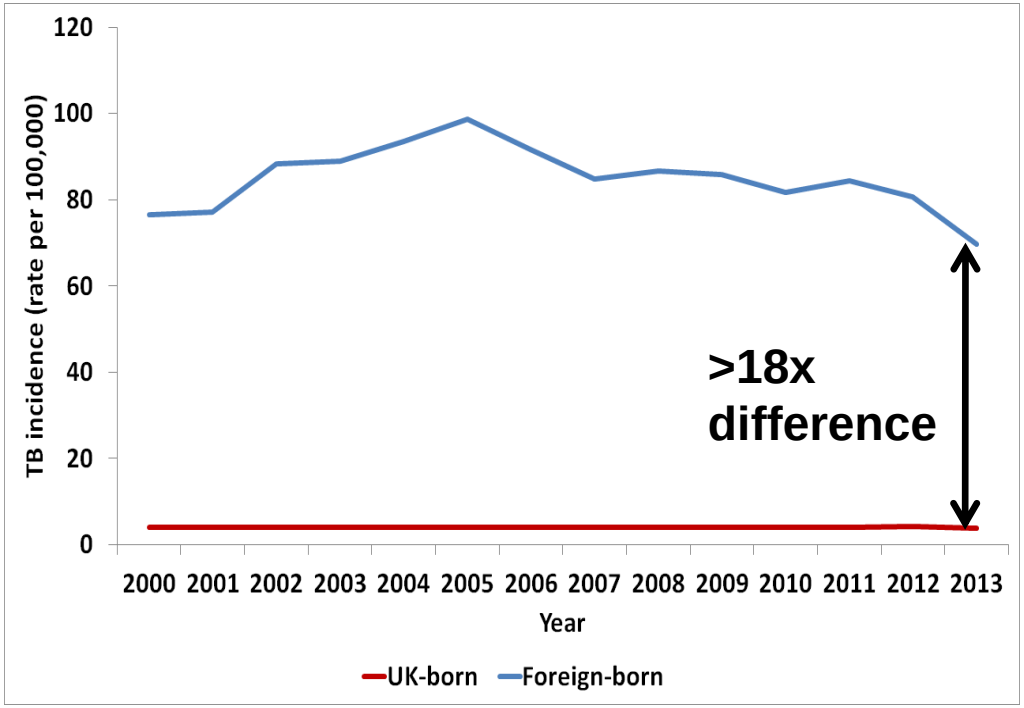
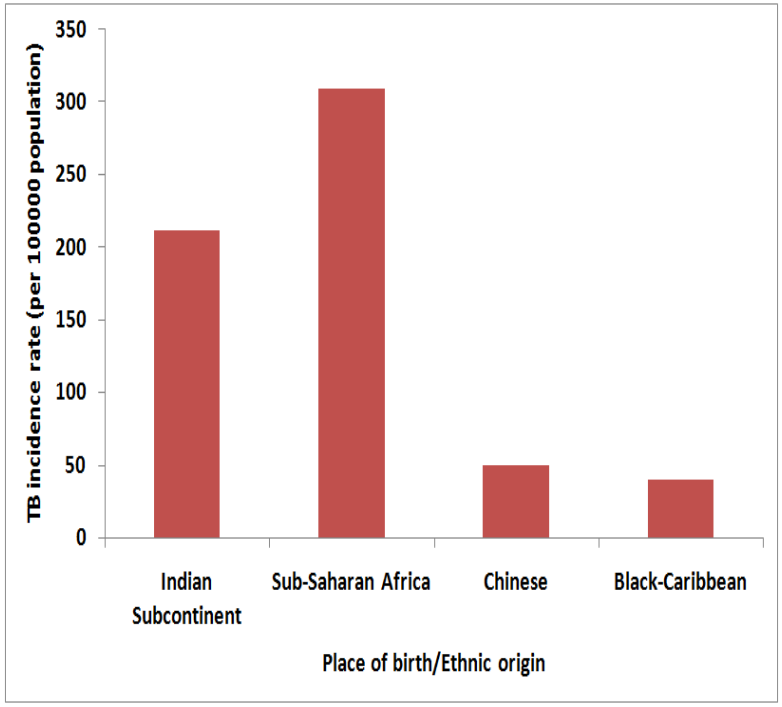
Source: HPA 2012

TB mainly a disease of foreign-born in the UK





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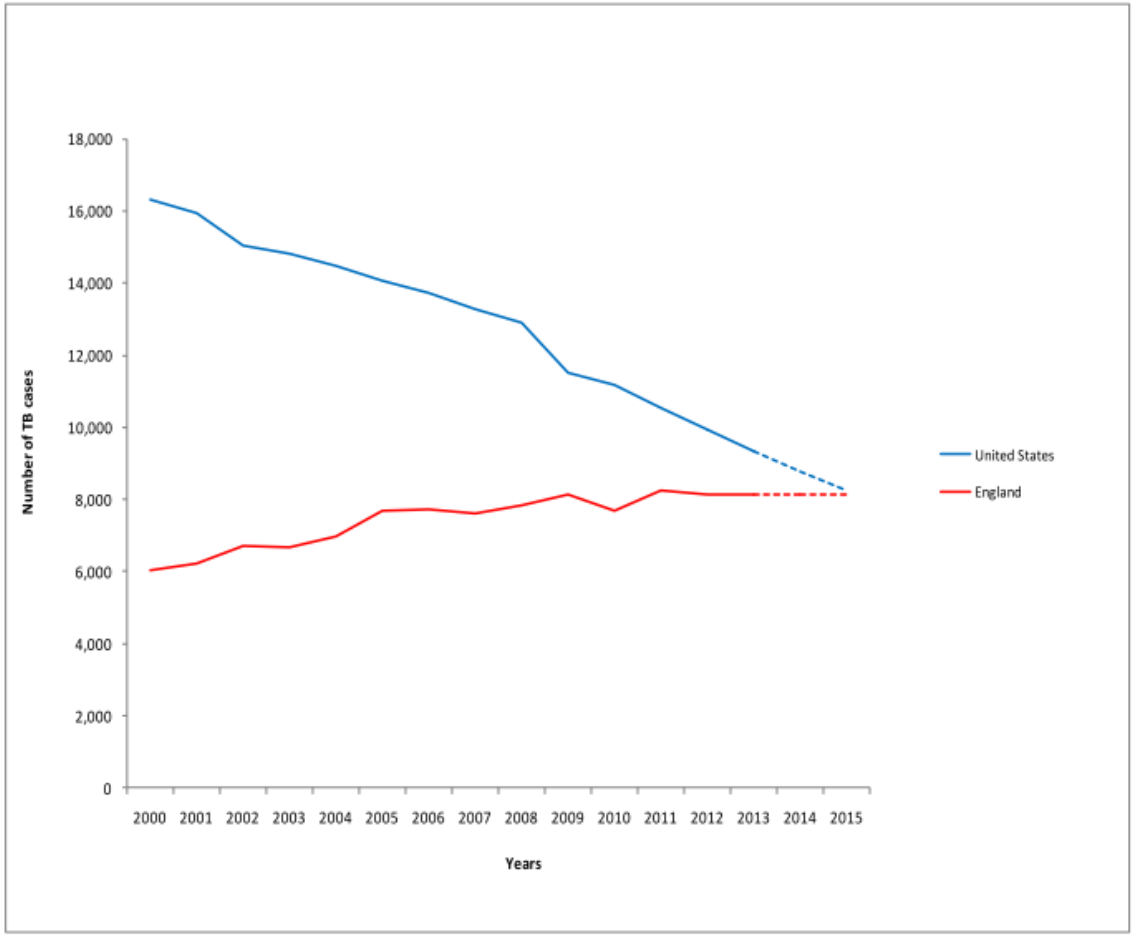
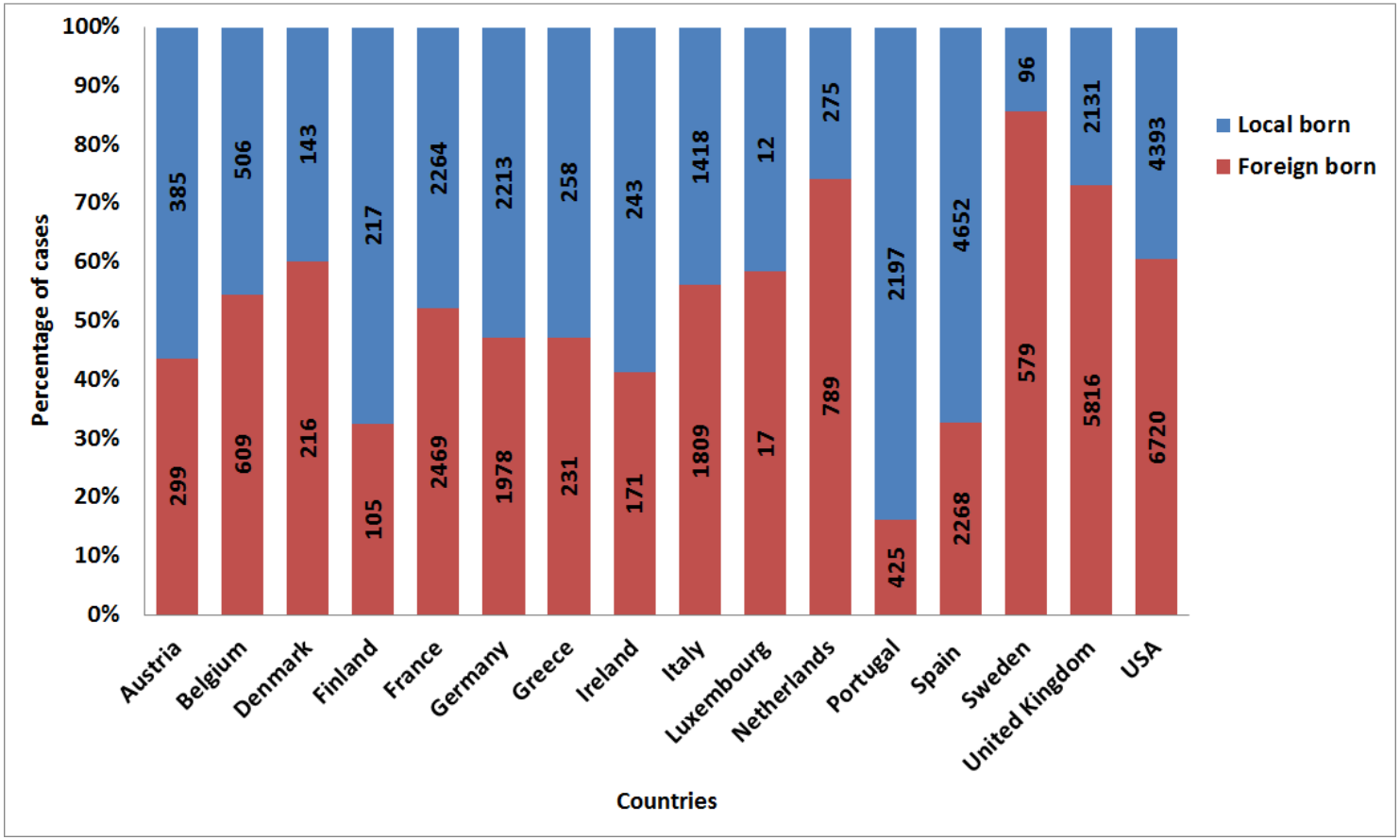
Source: PHE 2014

UK predicted to have more cases of TB than the US within the next two years



Foreign-born TB: a significant proportion of the TB burden in high-income countries



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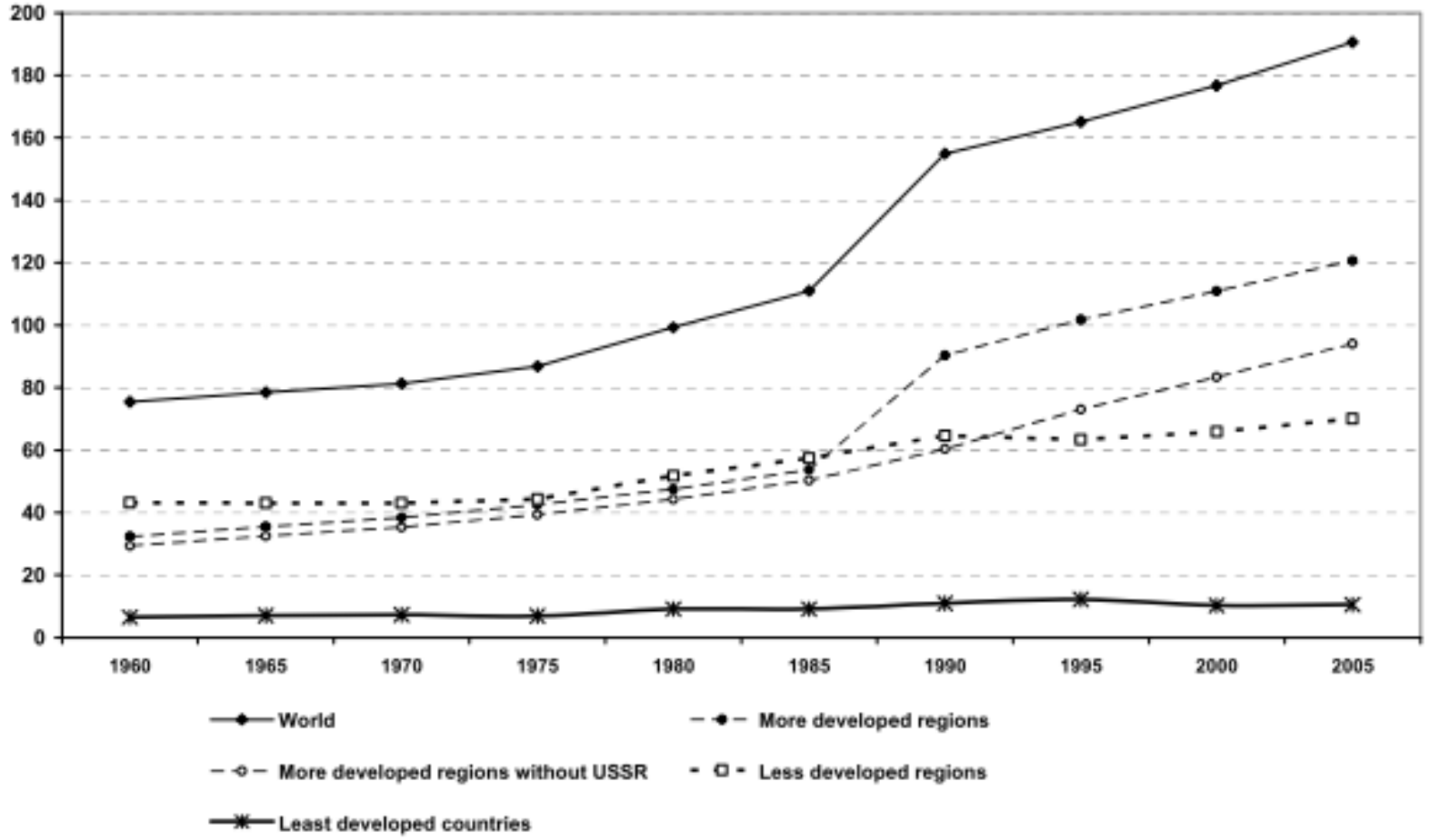
But why?

Reason: Synergistic impact of migration and reactivating latent tuberculosis infection

Evolving migration patterns during the 20th/21st century



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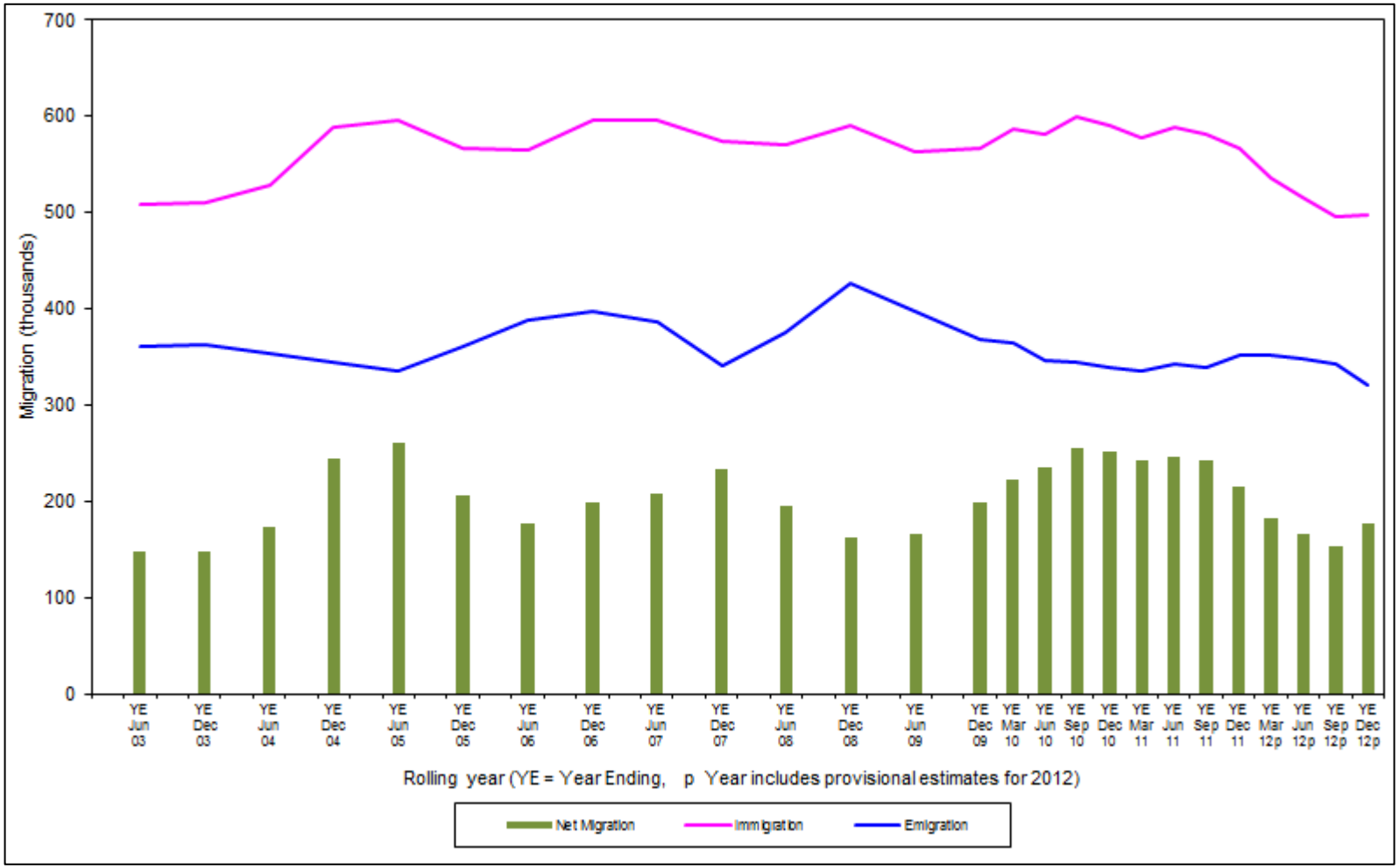
Source: IOM 2005

Migration to the UK



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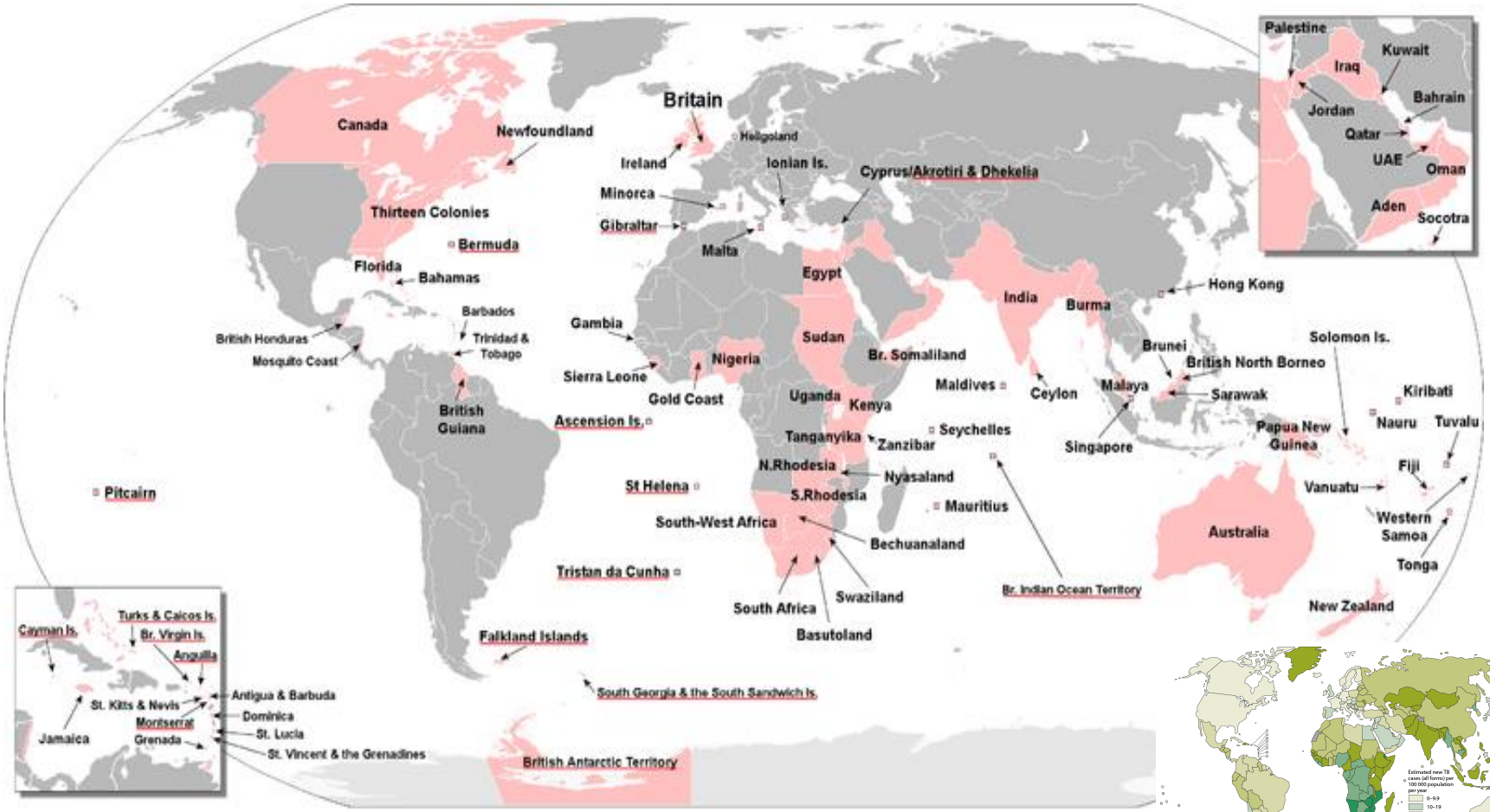
Source: ONS 2013

Migration to UK influenced by its past



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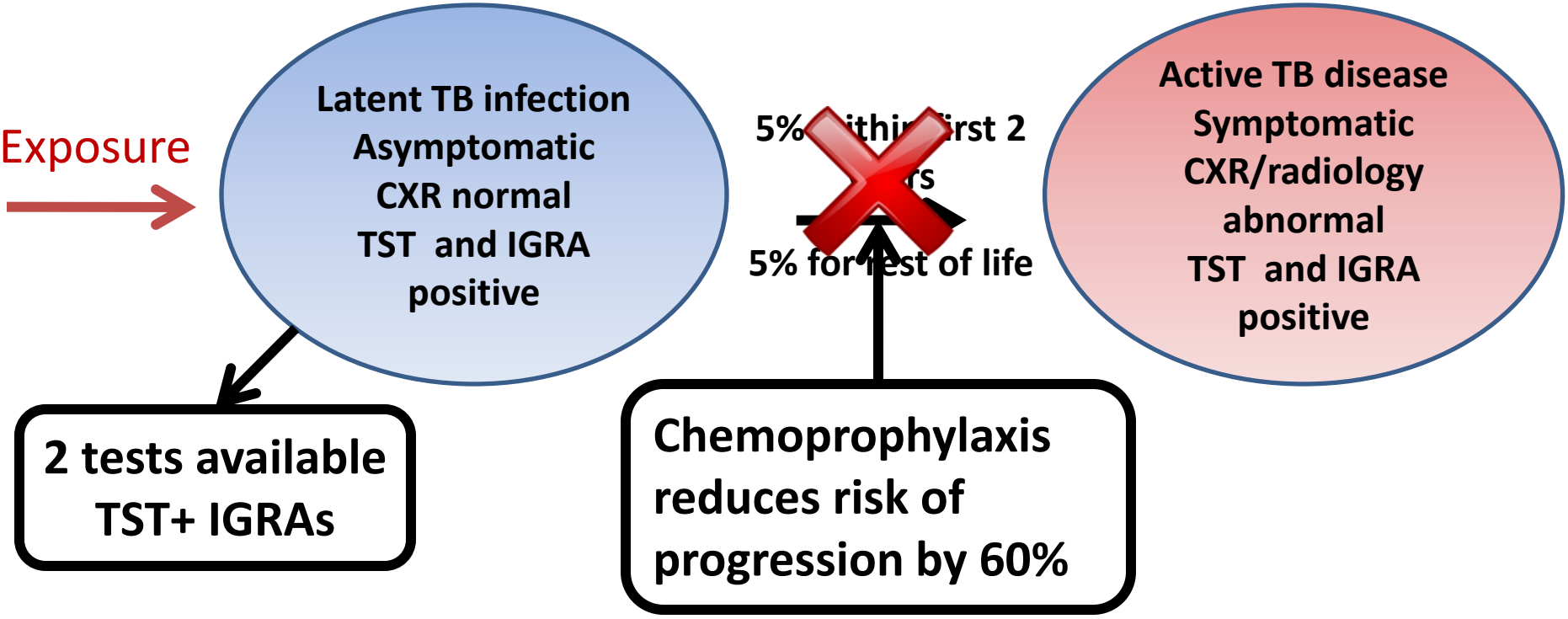
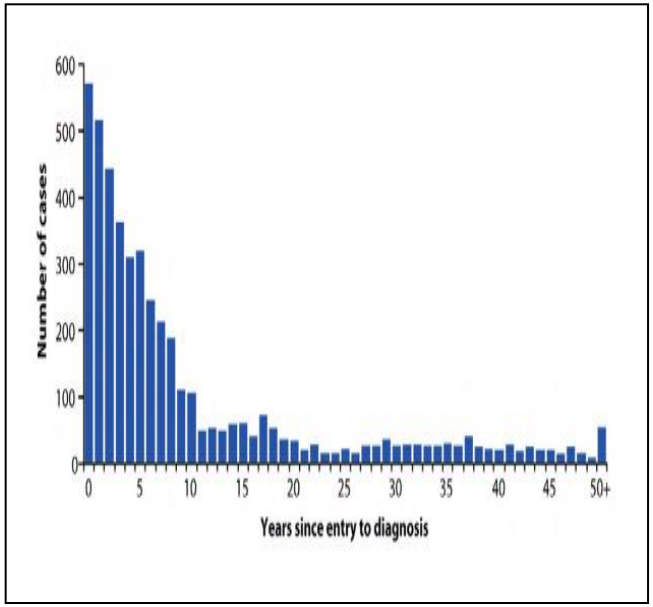
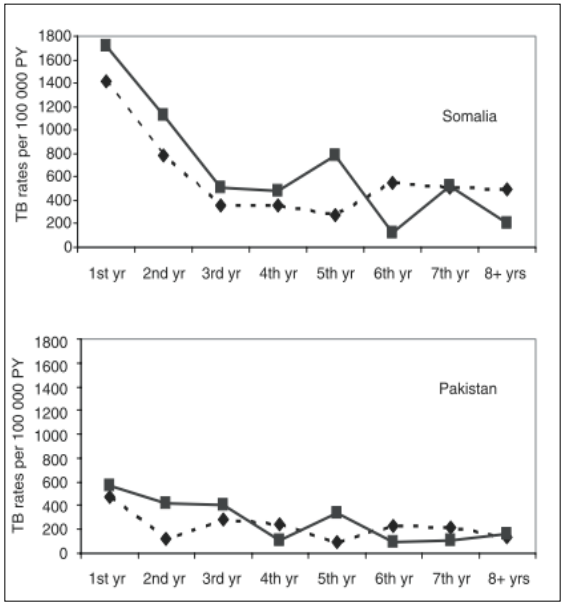
Migration alone not enough…
Need to consider TB natural history

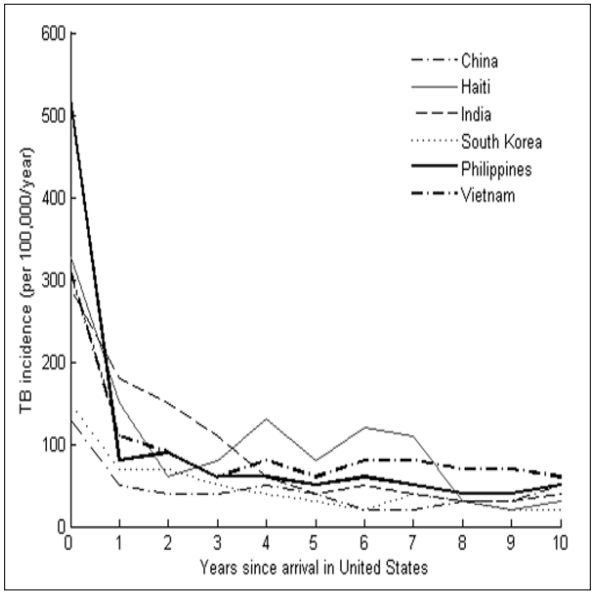


Reactivation of LTBI plays critical role

- Data suggests little active TB at time of migration
- High rates in initial years after migration (new-entrants)







Molecular studies: limited community transmission

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Sources: HPA 2011, Ormerod 1998, Cohen 2001

To recap…

- TB cases in the foreign-born make up a significant proportion of TB burden
- Combined impact of migration and reactivation of pre-existing latent TB infection
- High rates within the first 5 years after entry

So how do high-income countries screen migrants?

Screening practices in high-income countries

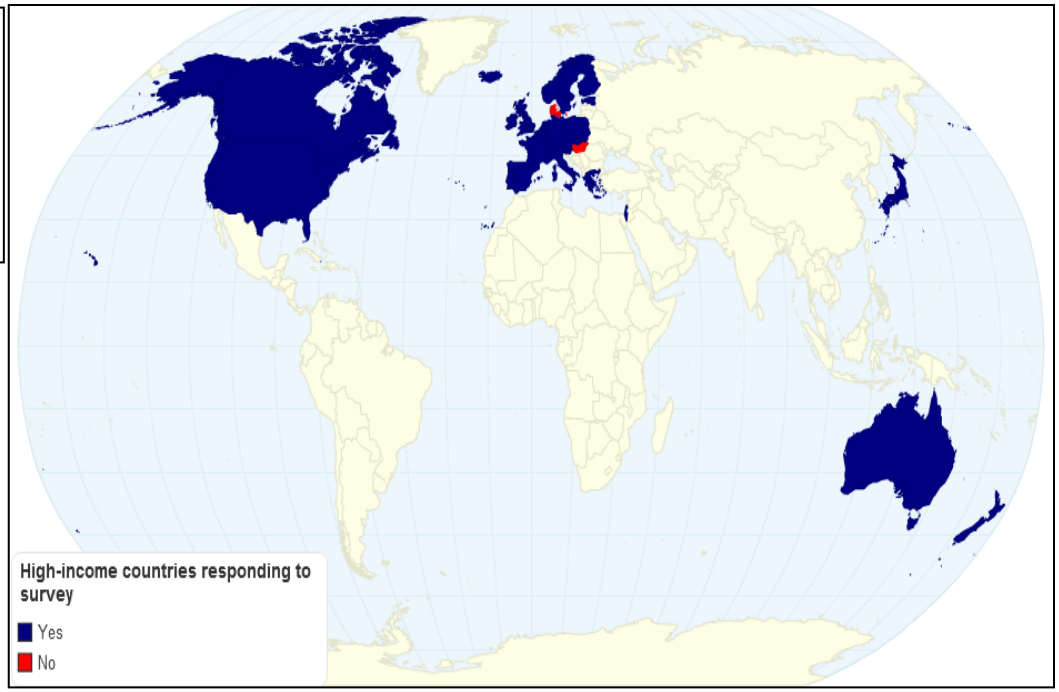
Evaluation of Immigrant Tuberculosis Screening in Industrialized Countries

Manish Pareek, Iacopo Baussano, Ibrahim Abubakar, Christopher Dye, and Ajit Lalvani

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 18, No. 9, September 2012

- International survey of 31 OECD high-income countries

- Evaluated screening practices for active and latent TB
  - Where do they screen?
  - Which groups are screened?
  - How do they screen?



- 29/31 countries responded

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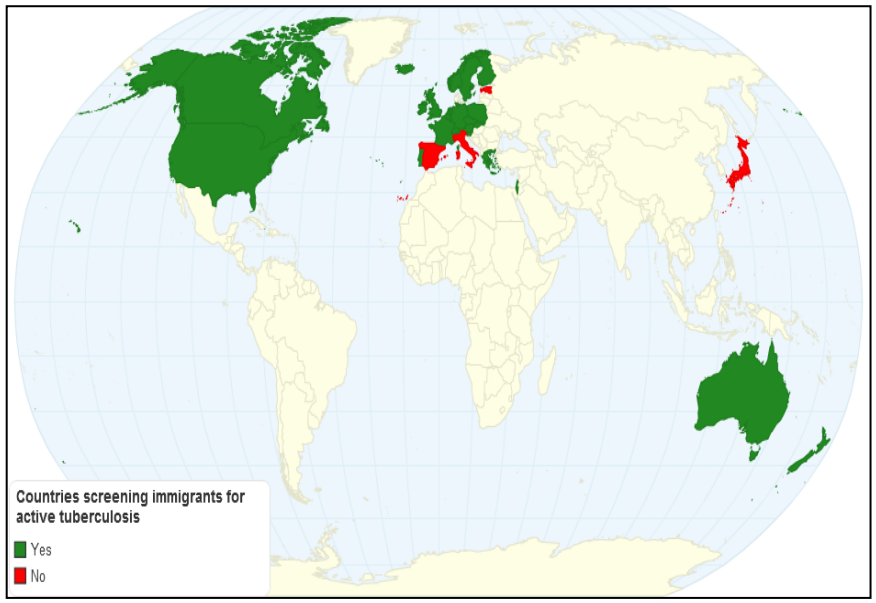
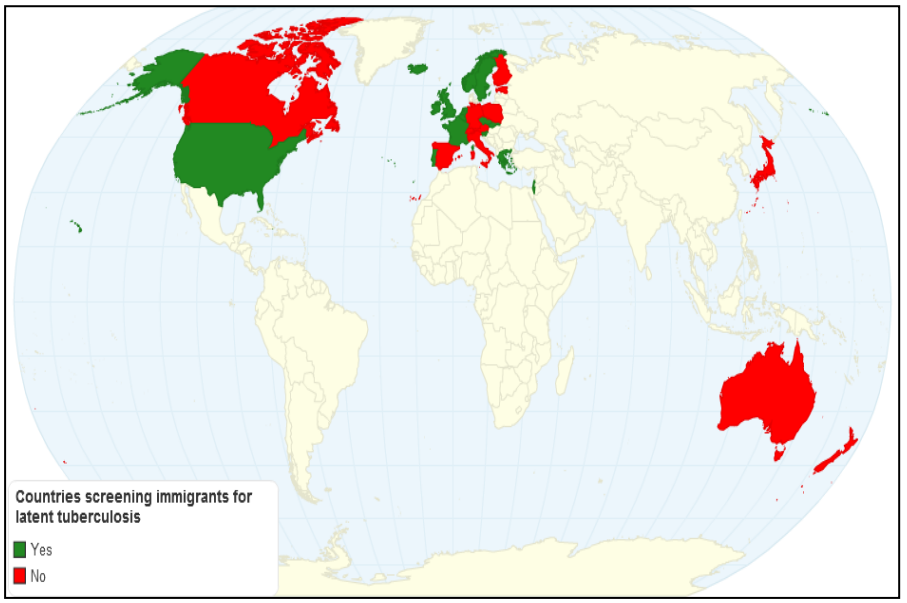
Source: Pareek M 2012

High-income countries prioritise screening for active TB rather than latent TB





25/29 (86.2%) - active TB

16/29 (55.1%) - latent TB

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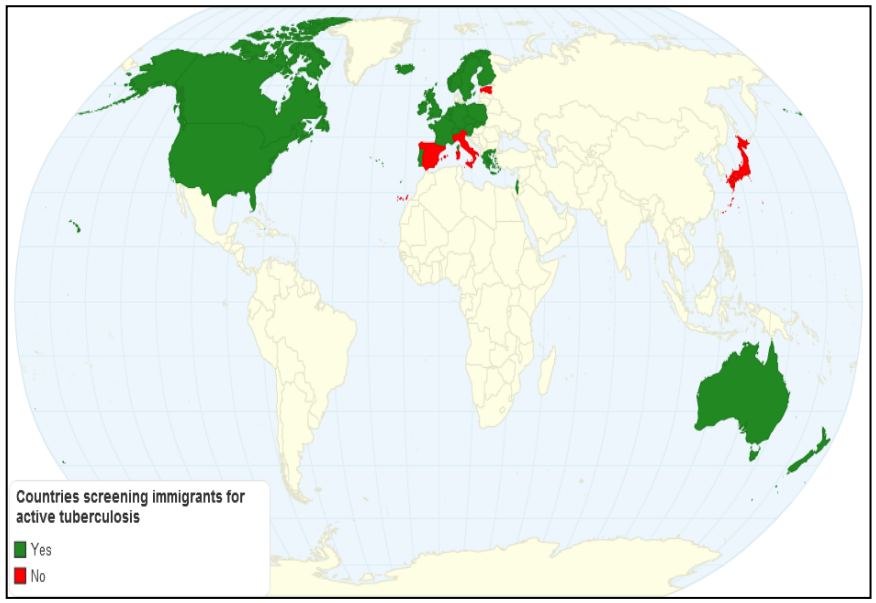
Source: Pareek M 2012

High-income countries prioritise screening for active TB rather than latent TB



Pre-arrival	At-arrival	Post-arrival
8/25 (32.0%)	5/25 (25.0%)	23/25 (92.0%)

25/29 (86.2%) - active TB

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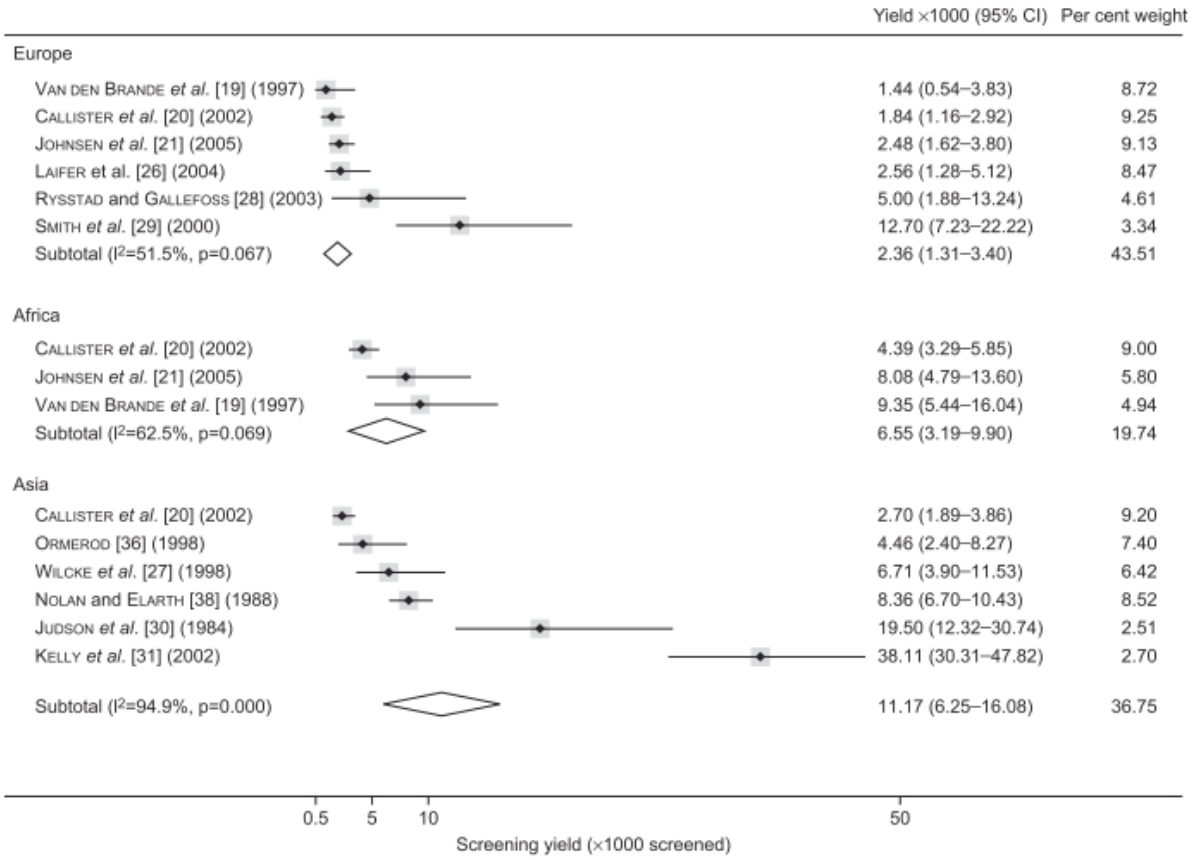
Source: Pareek M 2012

…But screening yields for active tuberculosis are highly variable



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Source: Arshad et al 2010

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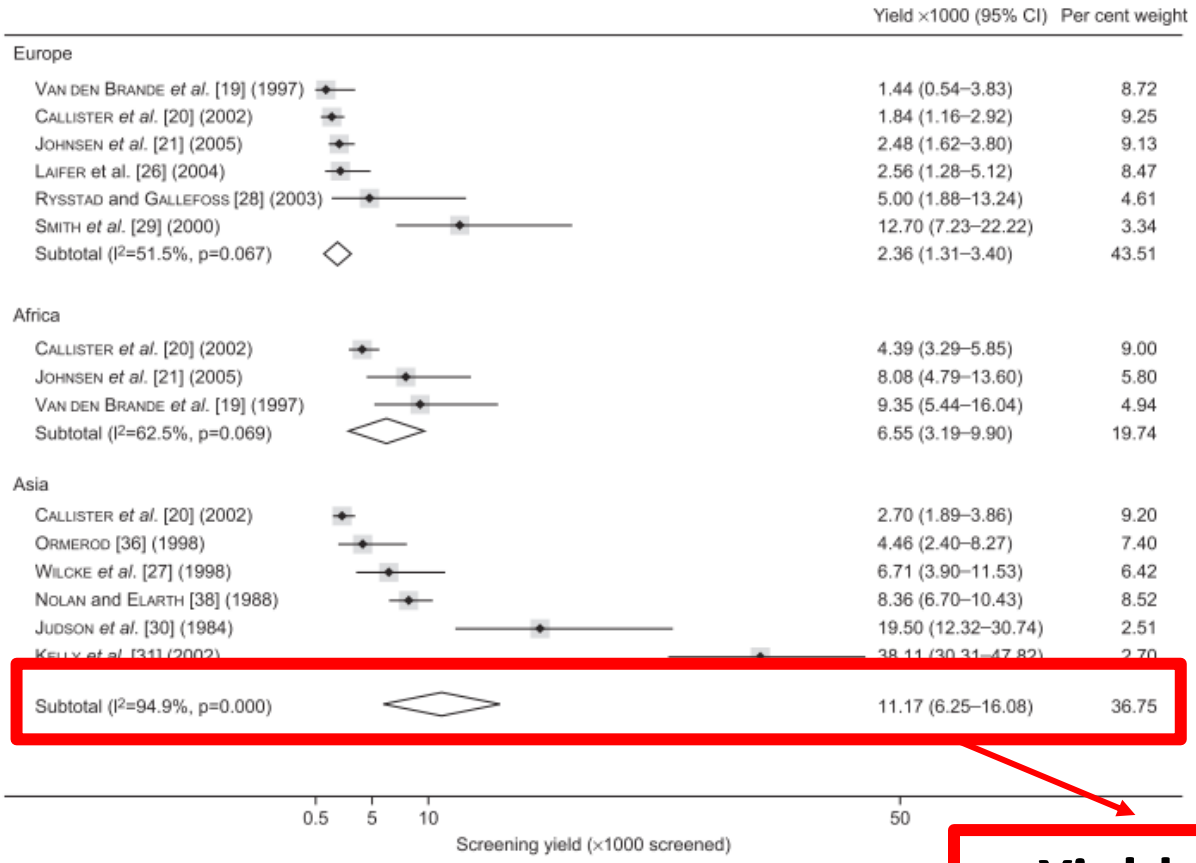

Yield 0.11%

Source: Arshad et al 2010

UK port of entry screening has a low yield and may not be cost-effective

Heathrow

- **Total referrals** **175,039**
- **Have X ray** **71,000**
- **Abnormal** **173**
- **TB diagnosed** **92 (0.12%)**

Imperial College London

Source: HPA 2007

Pre-arrival screening yields for active tuberculosis may be higher

Table 1. Prevalences of Smear-Negative and Inactive Tuberculosis among U.S.-Bound Immigrants, 1999–2005.

Variable	All Immigrants	Immigrants with Smear-Negative Tuberculosis		Immigrants with Inactive Tuberculosis	
	no. (%)	*no. (%)*	*no./100,000 persons (95% CI)*	*no. (%)*	*no./100,000 persons (95% CI)*
Total	2,714,223 (100.0)	26,075 (100.0)	961 (949–973)	22,716 (100.0)	837 (826–848)
Sex					
Male	1,203,271 (44.3)	13,175 (50.5)	1095 (1076–1114)	11,146 (49.1)	926 (909–943)
Female	1,510,952 (55.7)	12,900 (49.5)	854 (839–869)	11,570 (50.9)	766 (752–780)
Age					
0–14 yr	676,821 (24.9)	2,024 (7.8)	299 (286–312)	412 (1.8)	61 (55–67)
15–24 yr	535,218 (19.7)	1,077 (4.1)	201 (189–213)	1,183 (5.2)	221 (208–234)
25–44 yr	821,394 (30.3)	5,422 (20.8)	660 (642–678)	4,881 (21.5)	594 (577–611)
45–64 yr	500,072 (18.4)	10,643 (40.8)	2128 (2088–2168)	9,683 (42.6)	1936 (1898–1974)
≥65 yr	180,718 (6.7)	6,909 (26.5)	3823 (3734–3912)	6,557 (28.9)	3628 (3542–3714)
World Health Organization region of birth					
African	148,095 (5.5)	41 (0.2)	28 (19–37)	159 (0.7)	107 (90–124)
The Americas	1,029,503 (37.9)	1,491 (5.7)	145 (138–152)	3,249 (14.3)	316 (305–327)
Eastern Mediterranean	220,672 (8.1)	41 (0.2)	19 (13–25)	268 (1.2)	121 (106–136)
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Western Pacific	694,894 (25.6)	23,760 (91.1)	3419 (3376–3462)	15,986 (70.4)	2300 (2265–2335)
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Vietnam	114,764 (4.2)	6,980 (26.8)	6082 (5943–6221)	1,721 (7.6)	1500 (1429–1571)
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Other	1,609,413 (59.3)	1,258 (4.8)	78 (74–82)	7,411 (32.6)	460 (450–470)
Prevalence of tuberculosis in birth country‡					
0–9 cases/100,000	170,727 (6.3)	17 (0.1)	10 (5–15)	97 (0.4)	57 (45–69)
10–19 cases/100,000	110,148 (4.1)	10 (<0.1)	9 (3–15)	148 (0.7)	134 (112–156)
20–49 cases/100,000	629,895 (23.2)	1,029 (3.9)	163 (153–173)	1,665 (7.3)	264 (251–277)
50–99 cases/100,000	229,260 (8.4)	103 (0.4)	45 (36–54)	1,843 (8.1)	804 (767–841)
100–149 cases/100,000	334,288 (12.3)	460 (1.8)	138 (125–151)	2,085 (9.2)	624 (597–651)
≥150 cases/100,000	1,207,380 (44.5)	24,385 (93.5)	2020 (1995–2045)	16,165 (71.2)	1339 (1318–1360)
No estimate	32,525 (1.2)	71 (0.3)	218 (166–270)	713 (3.1)	2192 (2031–2353)

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Source: Liu et al 2009

Pre-arrival screening yields for active tuberculosis may be higher

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Prevalence of tuberculosis in birth country‡					
0–9 cases/100,000	170,727 (6.3)	17 (0.1)	10 (5–15)	97 (0.4)	57 (45–69)
10–19 cases/100,000	110,148 (4.1)	10 (<0.1)	9 (3–15)	148 (0.7)	134 (112–156)
20–49 cases/100,000	629,895 (23.2)	1,029 (3.9)	163 (153–173)	1,665 (7.3)	264 (251–277)
50–99 cases/100,000	229,260 (8.4)	103 (0.4)	45 (36–54)	1,843 (8.1)	804 (767–841)
100–149 cases/100,000	334,288 (12.3)	460 (1.8)	138 (125–151)	2,085 (9.2)	624 (597–651)
≥150 cases/100,000	1,207,380 (44.5)	24,385 (93.5)	2020 (1995–2045)	16,165 (71.2)	1339 (1318–1360)
No estimate	32,525 (1.2)	71 (0.3)	218 (166–270)	713 (3.1)	2192 (2031–2353)

Yield 0.96%

Yield 0.019%-3.4%

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Source: Liu et al 2009

Data from UK pilot of pre-arrival screening also highlights variable yields for active tuberculosis

	2005*	2006	2007	2008	2009	2010*	Total
Bangladesh	0	19,711	22,185	23,457	58,996	15,024	139,373
Burkina Faso	0	0	6	32	22	6	66
Cambodia	0	64	76	80	127	83	430
Côte d'Ivoire	0	0	116	339	263	145	863
Eritrea	0	0	58	45	30	25	158
Ghana	0	0	10,896	8,446	4,065	2,809	26,216
Kenya	0	0	2,859	2,981	2,529	1,676	10,045
Laos	1	16	25	22	25	19	108
Niger	0	0	5	34	18	4	61
Pakistan	0	0	50,251	61,896	55,944	42,142	210,233
Somalia	0	0	316	458	519	429	1,722
Sudan	5	817	819	1,020	1,006	659	4,326
Tanzania	354	1,934	1,906	2,054	1,362	751	8,361
Thailand	634	8,731	8,314	8,690	7,866	6,122	40,357
Togo	0	0	17	86	55	33	191
Total	**994**	**31,273**	**97,849**	**109,640**	**132,827**	**69,927**	**442,510**

Total positive cases, overall = 294 TB cases or 66 per 100,000 population

The scheme is now self-financing, applicants paying a fee of between $50 and $77 US (up to £50). However, the cost of culture diagnostics is free for the applicants.

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Source: UKBA FOI request

Cost-effectiveness of migrant screening for active tuberculosis

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Studies/documents which have examined migrant screening for tuberculosis

Author	Year	Location	Aim of study/analysis	Tools assessed	Empirical data	Model type (Decision-analysis (DA) or Markov (M))	Assessment of cost-effectiveness
Dasgupta	2000	Canada	Compare CXR and TST in screening migrants	CXR and TST	Yes	DA and M	$/ active TB case averted
Schwartzman	2000	Canada	Compare CXR and TST in screening migrants from hypothetical high, medium and low TB burden settings	CXR and TST	No	DA and M	$/ active TB case averted
Khan	2002	USA	Compare TST versus no screening for latent TB in recent migrants from different world regions	TST vs No screening	No	DA	$/ active TB case averted
NICE	2006	UK	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants	TST, IGRA, TST+IGRA	No	DA	£/QALY loss averted
Oxlade	2007	Canada	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants	CXR, TST, IGRA, TST+IGRA	No	DA	$/ active TB case averted
NICE	2011	UK	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants	TST, IGRA, TST+IGRA	No	DA	£/QALY loss averted
Pareek	2011	UK	Compare no screening versus IGRA screening at different incidence thresholds	IGRA	Yes	DA	£/ active TB case averted
Linas	2011	USA	Compare no screening vs TST, IGRA or TST+IGRA as screening tools for latent TB in migrants	TST vs IGRA	No	M	$/Life year gained
Pareek	2012	UK	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants. Assessment of screening threshold and where to screen also.	TST, IGRA, TST+IGRA	Yes	DA	$/ active TB case averted

Is it cost-effective to screen migrants for active tuberculosis?

Author	Year	Location	Aim of study/analysis	Tools assessed	Empirical data	Model type (Decision-analysis (DA) or Markov (M))	Assessment of cost-effectiveness
Dasgupta	2000	Canada	Compare CXR and TST in screening migrants	CXR and TST	Yes	DA and M	$/ active TB case averted
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Unclear whether it is cost-effective to screen migrants for active tuberculosis

Author	Year	Location	Aim of study/analysis	Tools assessed	Empirical data	Model type (Decision-analysis (DA) or Markov (M))	Assessment of cost-effectiveness
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Comparison of Cost-Effectiveness of Tuberculosis Screening of Close Contacts and Foreign-Born Populations

KABERI DASGUPTA, KEVIN SCHWARTZMAN, ROBERT MARCHAND, TERRY NAN TENNENBAUM, PAUL BRASSARD, and DICK MENZIES

Conclusion: Not cost-effective to screen migrants for active TB using chest radiographs

Tuberculosis Screening of Immigrants to Low-Prevalence Countries

A Cost-effectiveness Analysis

KEVIN SCHWARTZMAN and DICK MENZIES

AM J RESPIR CRIT CARE MED 2000;161:780–789.

NHS National Institute for Health Research

Conclusion: Cost-effective to screen migrants from high prevalence countries for active TB using chest radiographs

Unclear whether it is cost-effective to screen migrants for active tuberculosis

Author	Year	Location	Aim of study/analysis	Tools	Empirical	Model type (Decision-analysis	Assessment of

Limited data but differences in conclusions relate to differences in parameters and model structure

PAUL BRASSARD, and DICK MENZIES

TB using chest radiographs

Tuberculosis Screening of Immigrants to Low-Prevalence Countries

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Screening migrants for latent tuberculosis

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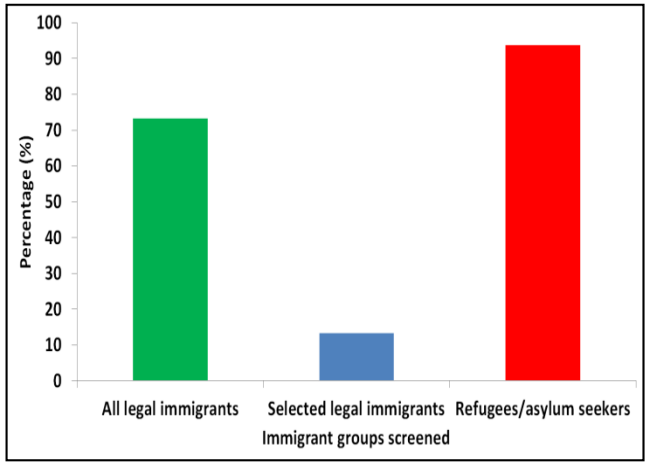
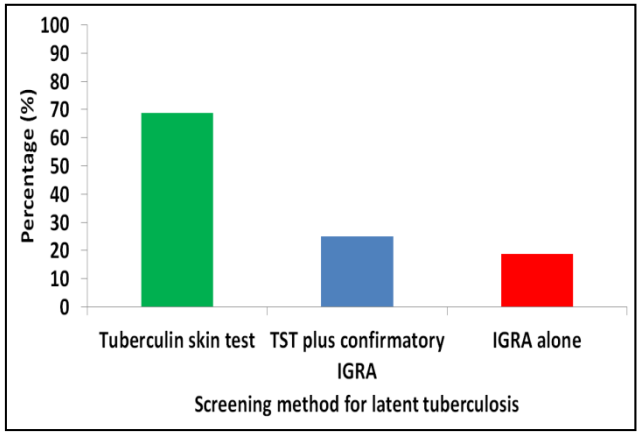
High-income countries display heterogeneity in screening for latent TB

Where?	Pre-arrival	At-arrival	Post-arrival
	2/16 (12.5%)	2/16 (12.5%)	16/16 (100.0%)



Who is screened?



How is screening undertaken?

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Source: Pareek M 2012

UK: Screening practices for latent TB in migrants are also highly variable

Tuberculosis screening of migrants to low-burden nations: insights from evaluation of UK practice

M. Pareek*,#, I. Abubakar¶,+, P.J. White§,/, G.P. Garnett/ and A. Lalvani*

EUROPEAN RESPIRATORY JOURNAL

Sequence of tests used	Low TB burden PCOs	High TB burden PCOs
New entrants aged <16 yrs#		
Total PCOs n	91	14
TST+CXR	23 (25.3)	5 (35.7)
TST+CXR+IGRA	66 (72.5)	9 (64.3)
IGRA+CXR	5 (5.5)	1 (7.1)
Other	2 (2.2)	0 (0.0)
IGRA	66 (72.5)	9 (64.3)
New entrants aged 16–35 yrs¶		
Total PCOs n	90	14
CXR+TST	5 (5.6)	0 (0.0)
CXR+TST+IGRA	27 (30.0)	1 (7.1)
CXR+IGRA	3 (3.3)	0 (0.0)
TST+CXR	18 (20.0)	6 (42.9)
TST+ IGRA+CXR	39 (43.3)	6 (42.9)
IGRA+CXR	2 (2.2)	1 (7.1)
IGRA	67 (74.4)	8 (57.1)

	Low TB burden PCOs
Total PCOs n	92
New entrants aged <16 yrs	
>40 cases per 100,000 *p.a.*	84 (91.3)
>500 cases per 100,000 *p.a.*	91 (98.9)
Sub-Saharan Africa	91 (98.9)
Other countries	4 (4.3)
New entrants aged 16–35 yrs	
>40 cases per 100,000 *p.a.*	37# (41.1)
>500 cases per 100,000 *p.a.*	90 (97.8)
Sub-Saharan Africa	90 (97.8)
Other countries	4 (4.3)

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Pareek M et al Eur Resp J 2011

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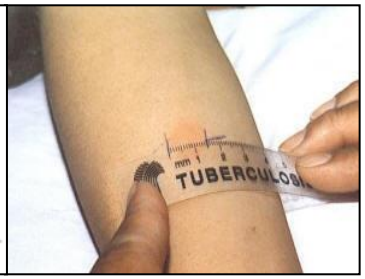
Heterogeneity in who to screen and how to screen

National Institute for Health Research

Pareek M et al Eur Resp J 2011

Inconsistency and heterogeneity in practice highlight need for more data

QuantiFERON Gold in-tube



Tuberculin skin test

T-SPOT.TB

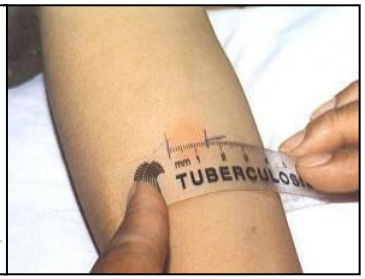
Who to screen?

How and where to screen?

Inconsistency and heterogeneity in practice highlight need for more data

Who to screen?

QuantiFERON Gold in-tube

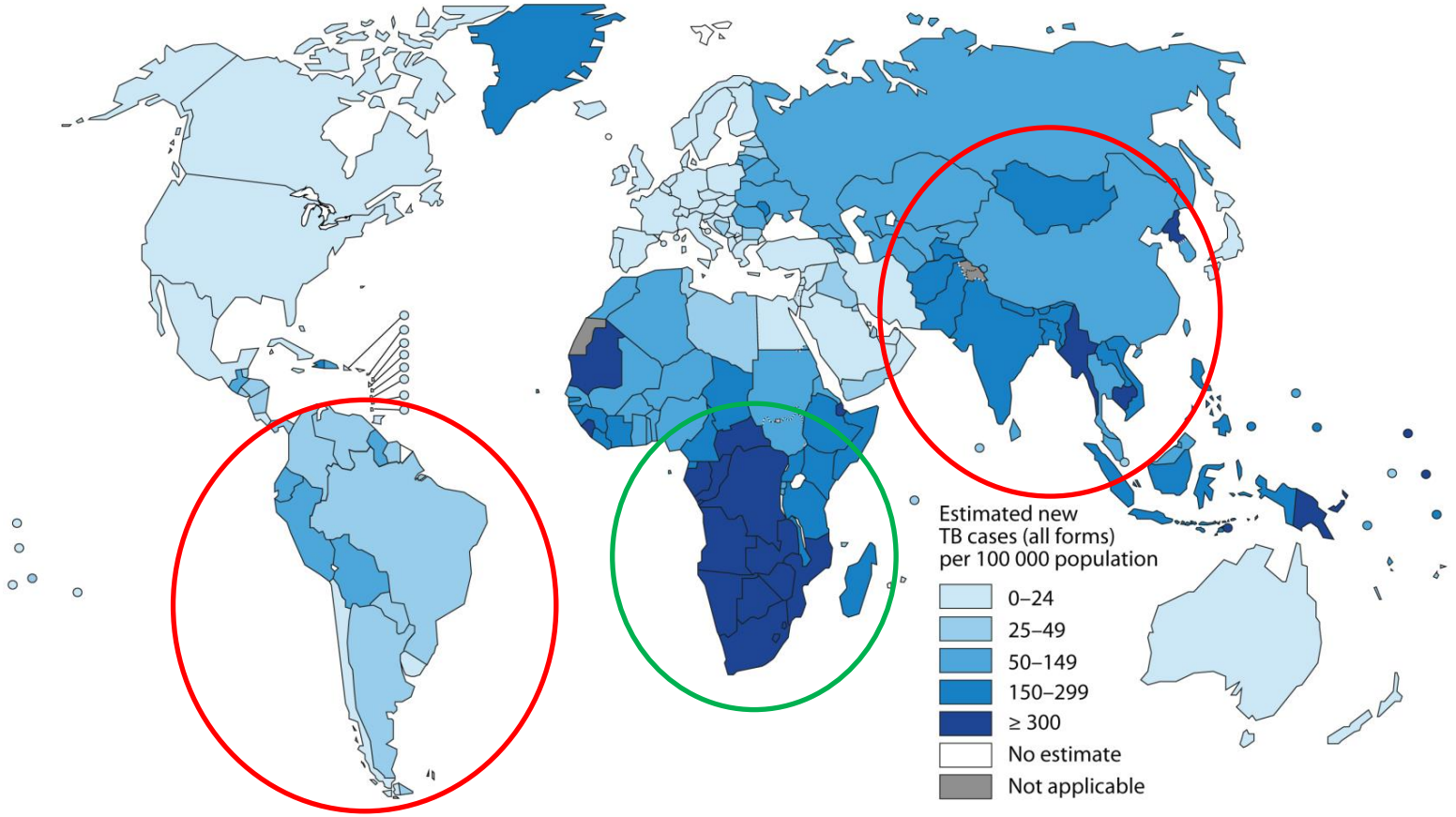


Tuberculin skin test

T-SPOT.TB

How and where to screen?

Augmenting the evidence base: who to screen?



Which migrant groups to screen: evidence from the United Kingdom

Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis

Manish Pareek, John P Watson, L Peter Ormerod, Onn Min Kon, Gerrit Woltmann, Peter J White, Ibrahim Abubakar, Ajit Lalvani

THE LANCET Infectious Diseases *Lancet Infect Dis* 2011; 11: 435–44

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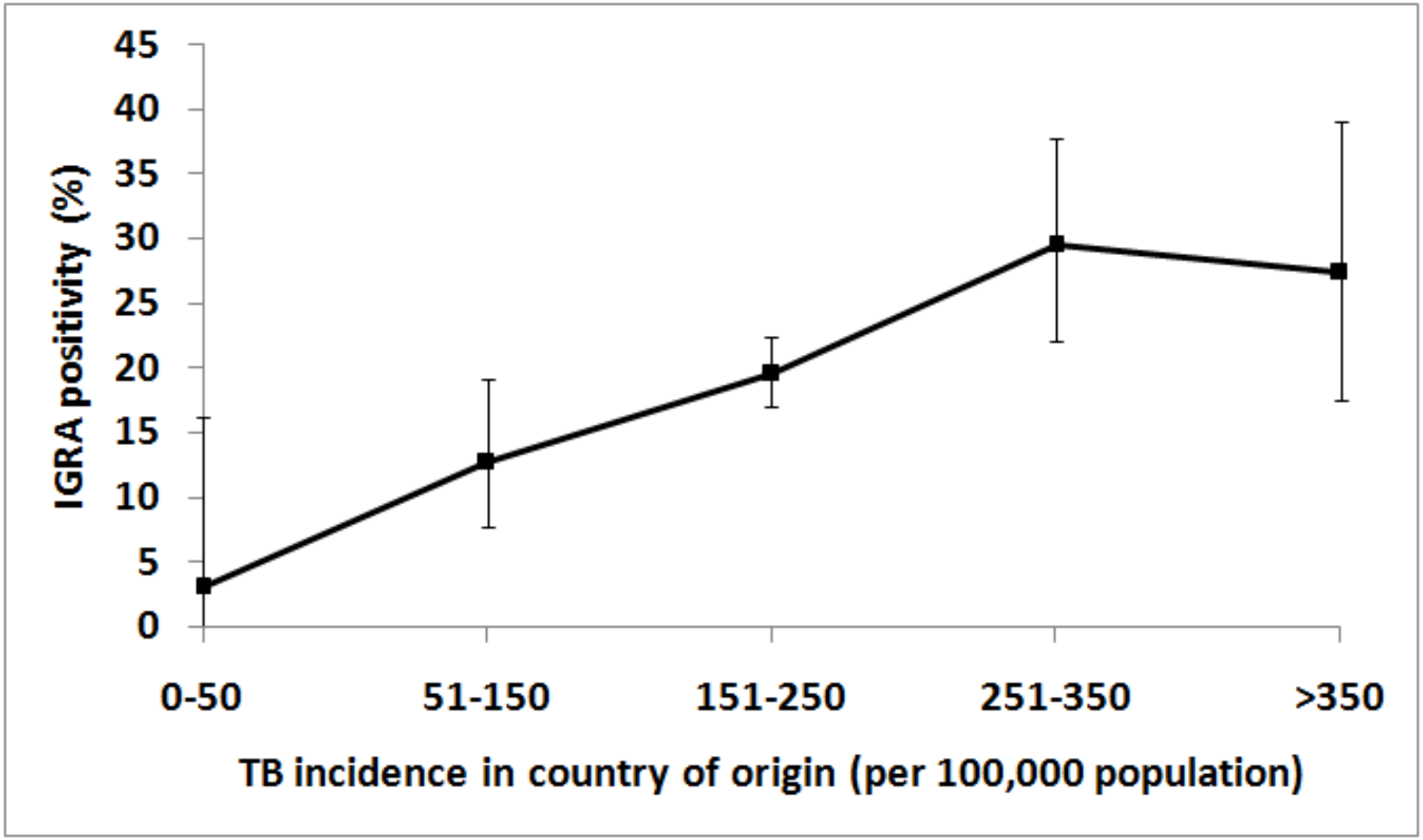
	Number in total cohort (n=1229)	Number of IGRA-positive individuals/total number tested (n=245)	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Age (years)						
<16*	36 (3%)	7/36 (19%)	1	0·0051†	1‡	<0·0001§
16–25	589 (48%)	86/589 (15%)	0·7 (0·3–1·7)	..	0·9 (0·4–2·1)	..
26–35	604 (49%)	152/604 (25%)	1·4 (0·6–3·2)	..	1·7 (0·7–4·1)	..
Sex						
Female	629 (51%)	109/629(17%)	1	0·02	1¶	0·046
Male	600 (49%)	136/600 (23%)	1·4 (1·1–1·9)	..	1·3 (1·0–1 8)	..
Origin‖						
Europe, Americas	50 (4%)	2/50 (4%)	1	0·0011	..	..
Middle East, North Africa	26 (2%)	1/26 (4%)	1·0 (0·1–11·1)	..	..	..
Other Asia	162 (13%)	29/162 (18%)	5·2 (1·2–22·8)	..	..	..
Indian subcontinent	740 (60%)	144/740 (20%)	5·8 (1·4–24·1)	..	..	..
Sub-Saharan Africa	251 (20%)	69/251 (28%)	9·1 (2·2–38·5)	..	..	..
Incidence of tuberculosis in country of origin (cases per 100 000 population per year)‖						
0–50	32 (3%)	1/32 (3%)	1	<0·0001†	1**	0·0006
51–150	150 (12%)	19/150 (13%)	4·5 (0·60–34·9)	..	4·5 (0·60–35·3)	..
151–250	835 (68%)	164/835 (20%)	7·6 (1·0–55·9)	..	7·9 (1·1–58·3)	..
251–350	139 (11%)	41/139 (30%)	13·0 (1·7–98·2)	..	13·3 (1·8–101·5)	..
>350	73 (6%)	20/73 (27%)	11·7 (1·5–91·5)	..	13·1 (1·7–102·7)	..
BCG vaccinated?						
No	113 (17%)	16/113 (14%)	1	0·17	..	..
Yes	544 (83%)	107/544 (20%)	1·5 (0·8–2·6)	..	..	..

IGRA=interferon-γ release assay. OR=odds ratio. *Of the 36 individuals aged <16 years, one (2·8%) was aged ≤4 years, one (2·8%) was 5–9 years, and 34 (94·4%) were 10–15 years. †χ^2 p for trend. ‡Mutually adjusted for sex and incidence of tuberculosis in country of origin. §p value denotes overall effect of age in the model. ¶Mutually adjusted for age and tuberculosis incidence in country of origin. ‖Region of origin and tuberculosis incidence in country of origin were strongly correlated; therefore, in the multivariate analysis, region of origin was left out. **Mutually adjusted for age and sex.

Table 1: Demographics of cohort and risk factors associated with IGRA positivity in immigrants

IGRA positivity independently associated with TB incidence in country of origin



Yields for latent TB: UK guidance missed majority of imported latent TB

Age group and TB incidence screening threshold (per 100,000)	Number tested	Number positive	Yield at incidence level, ie. proportion of those tested giving a positive result (%)	% of all LTBI identified if threshold set at this level
Screen ≥500 and SSA	235	65	27.7	27.3
Screen ≥500	46	12	26.1	5.0
Screen ≥450	54	13	24.1	5.5
Screen ≥350	66	18	27.3	7.6
Screen ≥250	197	58	29.4	24.4
Screen ≥150	1013	219	21.6	92.0
Screen ≥40	1180	238	20.2	100

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Screen ≥250	197	58	29.4	24.4
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Screen ≥40	1180	238	20.2	100

Health-economic analyses: screening at lower thresholds averts more cases of TB but with increased total costs

Screening threshold for immigrants (annual incidence per 100,000)		Cases of active TB (over 20 years)	Costs over 20 years (2010 GB pounds)	ICER (GBP per TB case averted)
Under 16	16-35 years			
None	None	95.4	608,370.0	Baseline
40	500	91.9	678,586.5	Extended dominance
40	400	91.8	683,710.0	Strict dominance
40	450	91.7	683,267.9	Extended dominance
40	350	90.8	697,208.7	Extended dominance
40	300	87.1	761,431.6	Extended dominance
40	250	83.4	823,312.8	17,956.0
40	500 +SSA	82.2	850,103.1	Extended dominance
40	200	71.1	1,121,093.2	Extended dominance
40	150	54.2	1,431,928.5	20,818.8
40	100	53.7	1,456,820.1	Extended dominance
40	40	50.9	1,527,478.5	29,403.1
All	All	50.9	1,532,256.6	101,938.3

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Source: Pareek M et al Lancet Infectious Diseases 2011

Cost-effectiveness of migrant screening for latent tuberculosis: who to screen?

Author	Year	Location	Type of data	Migrants to target for screening			Conclusion on cost-effectiveness
				Regions/Countries of origin	Age	Time since arrival	
Schwartzman	2000	Canada	Model and literature	High/intermediate and low prevalence of active TB, latent TB and HIV	Only 20 year olds	Not stated	Screen migrants from high prevalence settings
Khan	2002	USA	Model and literature	Different countries and world regions	>18 years	Not stated	Screen migrants from high TB burden countries and regions
Oxlade	2007	Canada	Model and literature	Low, intermediate and high incidence of smear positive pulmonary tuberculosis	Not stated	Not stated	Screen migrants from high TB incidence settings
Pareek	2011	UK	Empirical data, model simulation and literature	Screening thresholds determined by TB incidence in country of origin (increments of 50/100,000)	<16 and 16-35 years	≤5 years	Screen all migrants <35 years arriving from countries with TB incidence ≥250 or ≥150/100,000 resident ≤5 years
Linas	2011	USA	Model and literature	Not stated	Various age groups considered: 6-14, 15-24, 25-44, 45-64, 65+ years	<5 years and >5 years	Screen foreign-born <65 years irrespective of time since arrival in the US
Pareek	2012	UK	Empirical data, model simulation and literature	Screening thresholds determined by TB incidence in country of origin (increments of 50/100,000)	16-35 years	≤5 years	Screen migrants from countries with TB incidence ≥250 or ≥150/100,000 resident ≤5 years

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Cost-effectiveness of migrant screening for latent tuberculosis: who to screen?

Author	Year	Location	Type of data	Migrants to target for screening			Conclusion on cost-effectiveness
				Regions/Countries of origin	Age	Time since arrival	
			Model and literature	High/intermediate and low			Screen migrants from high
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Screen (recent) migrants from high TB burden settings but which age-groups to screen is less clear

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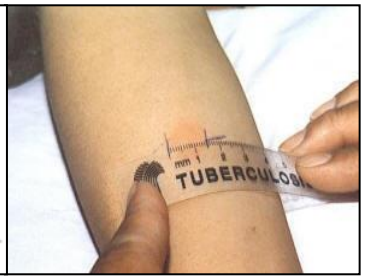
Inconsistency and heterogeneity in practice highlight need for more data

Who to screen?

QuantiFERON Gold in-tube

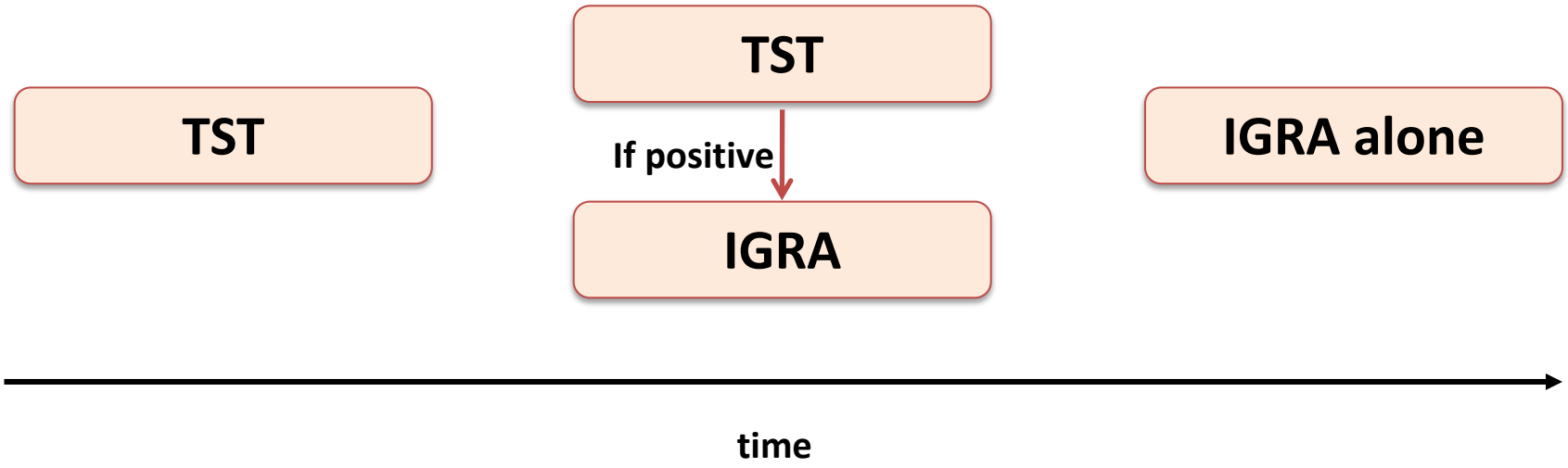


Tuberculin skin test

T-SPOT.TB

How and where to screen?

Methods of screening migrants are evolving but certain questions unanswered



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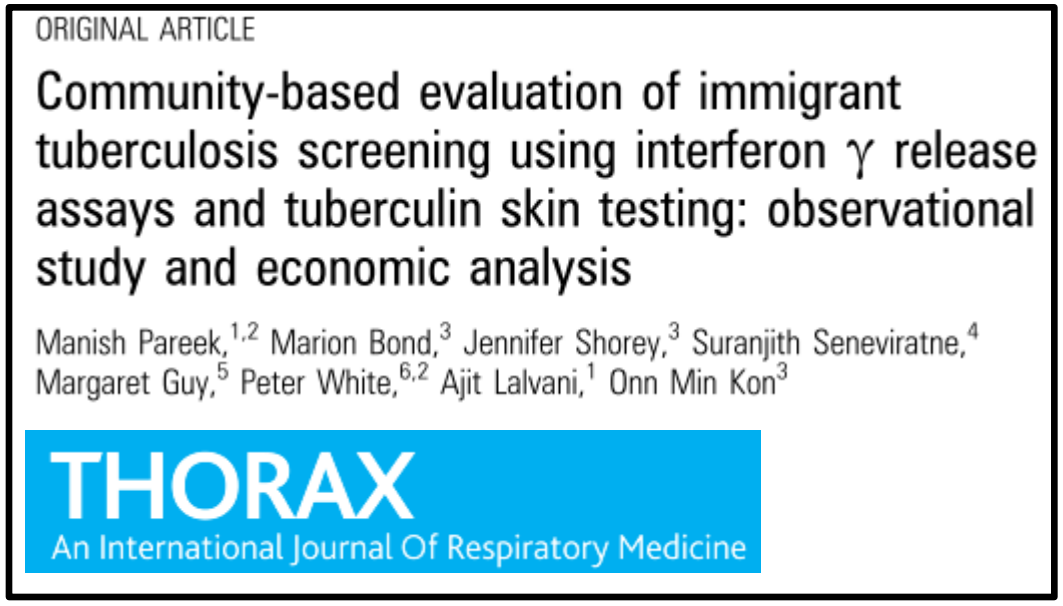
Source: NICE 2006

Community-based LTBI screening with single-step IGRA practicable and cost-effective



ORIGINAL ARTICLE

Community-based evaluation of immigrant tuberculosis screening using interferon γ release assays and tuberculin skin testing: observational study and economic analysis

Manish Pareek,[1,2] Marion Bond,[3] Jennifer Shorey,[3] Suranjith Seneviratne,[4] Margaret Guy,[5] Peter White,[6,2] Ajit Lalvani,[1] Onn Min Kon[3]

THORAX
An International Journal Of Respiratory Medicine

- **Community-based comparison of different screening methods in Westminster, London**

Source: Pareek M et al Thorax 2012

Health-economics: Screening at intermediate threshold with single-step QuantiFERON Gold in-tube but without port-of-entry chest radiography most cost-effective

Table 4 Projected cases of active tuberculosis (TB) and associated costs arising from undertaking immigrant screening using different screening tools at different screening thresholds (arranged in order of increasing effectiveness—ie, fewer cases of active TB) for a hypothetical cohort of 10 000 immigrants over a 20-year time horizon

CXR at port of arrival	Screening for LTBI: Screening tool	Screening threshold for immigrants (cases of TB/ 100 000 per year)	Cases of active TB (over 20 years)	Costs (£, 2010)	Incremental cases of active TB	Incremental costs (£, 2010)	ICER
No	None	None	100.5	659 609.4	Baseline	Baseline	Baseline
No	TST plus QFN	350	100.4	690 521.6	Extended dominance	Extended dominance	Extended dominance
No	TST plus T-SPOT.TB	350	100.3	696 433.4	Extended dominance	Extended dominance	Extended dominance
No	TST	350	100.1	706 478.7	Strict dominance	Strict dominance	Strict dominance
No	TST plus QFN	300	100.0	707 756.2	Strict dominance	Strict dominance	Strict dominance
No	TST plus T-SPOT.TB	300	99.8	715 317.0	Strict dominance	Strict dominance	Strict dominance
No	QFN	350	99.4	701 675.9	Extended dominance	Extended dominance	Extended dominance
No	TST	300	99.4	721 759.0	Extended dominance	Extended dominance	Extended dominance
No	T-SPOT.TB	350	99.3	728 560.7	Strict dominance	Strict dominance	Strict dominance
Yes	None	None	98.9	754 339.9	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus QFN	350	98.8	785 252.0	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus T-SPOT.TB	350	98.7	791 163.9	Strict dominance	Strict dominance	Strict dominance
Yes	TST	350	98.5	801 209.1	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus QFN	300	98.4	802 486.6	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus T-SPOT.TB	300	98.2	810 047.5	Strict dominance	Strict dominance	Strict dominance
No	QFN	300	98.0	723 513.2	Extended dominance	Extended dominance	Extended dominance
Yes	QFN	350	97.8	796 406.3	Strict dominance	Strict dominance	Strict dominance
Yes	TST	300	97.8	816 489.4	Strict dominance	Strict dominance	Strict dominance
No	TST plus QFN	250	97.8	793 192.7	Strict dominance	Strict dominance	Strict dominance
No	T-SPOT.TB	300	97.7	751 926.8	Extended dominance	Extended dominance	Extended dominance
Yes	T-SPOT.TB	350	97.7	823 291.1	Strict dominance	Strict dominance	Strict dominance
No	TST plus T-SPOT.TB	250	97.3	813 690.1	Extended dominance	Extended dominance	Extended dominance
Yes	QFN	300	96.4	818 243.7	Extended dominance	Extended dominance	Extended dominance
Yes	TST plus QFN	250	96.2	887 923.2	Strict dominance	Strict dominance	Strict dominance
No	TST	250	96.2	823 749.7	Extended dominance	Extended dominance	Extended dominance
Yes	T-SPOT.TB	300	96.1	846 657.3	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus T-SPOT.TB	250	95.7	908 420.5	Strict dominance	Strict dominance	Strict dominance
No	TST plus QFN	200	95.6	867 394.4	Strict dominance	Strict dominance	Strict dominance
No	TST plus T-SPOT.TB	200	95.0	913 943.4	Strict dominance	Strict dominance	Strict dominance
Yes	TST	250	94.6	918 480.1	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus QFN	200	94.0	962 124.9	Strict dominance	Strict dominance	Strict dominance
No	TST	200	93.8	995 462.9	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus T-SPOT.TB	200	93.4	1 008 673.9	Strict dominance	Strict dominance	Strict dominance
No	TST plus QFN	150	93.0	954 636.7	Strict dominance	Strict dominance	Strict dominance
No	TST plus T-SPOT.TB	150	92.3	1 023 409.3	Strict dominance	Strict dominance	Strict dominance
Yes	TST	200	92.2	1 090 193.4	Strict dominance	Strict dominance	Strict dominance
No	QFN	250	92.1	839 713.7	8.4	180 104.3	21 565.3
No	TST plus QFN	100	91.5	1 018 843.7	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus QFN	150	91.4	1 049 367.2	Strict dominance	Strict dominance	Strict dominance
No	T-SPOT.TB	250	91.3	909 426.7	Extended dominance	Extended dominance	Extended dominance
No	TST plus T-SPOT.TB	100	90.7	1 113 644.2	Strict dominance	Strict dominance	Strict dominance
Yes	TST plus T-SPOT.TB	150	90.7	1 118 139.7	Strict dominance	Strict dominance	Strict dominance
No	TST	150	90.6	1 149 671.8	Strict dominance	Strict dominance	Strict dominance
Yes	QFN	250	90.6	934 444.2	Extended dominance	Extended dominance	Extended dominance
Yes	TST plus QFN	100	89.9	1 113 574.1	Strict dominance	Strict dominance	Strict dominance
Yes	T-SPOT.TB	250	89.7	1 004 157.2	Strict dominance	Strict dominance	Strict dominance
No	QFN	200	89.1	959 014.5	Extended dominance	Extended dominance	Extended dominance
Yes	TST plus T-SPOT.TB	100	89.1	1 208 374.6	Strict dominance	Strict dominance	Strict dominance
No	TST	100	89.0	1 319 841.4	Strict dominance	Strict dominance	Strict dominance
Yes	TST	150	89.0	1 244 402.3	Strict dominance	Strict dominance	Strict dominance
No	T-SPOT.TB	200	88.2	1 171 931.5	Strict dominance	Strict dominance	Strict dominance
Yes	QFN	200	87.6	1 053 744.9	Extended dominance	Extended dominance	Extended dominance
Yes	TST	100	87.4	1 414 571.9	Strict dominance	Strict dominance	Strict dominance
Yes	T-SPOT.TB	200	86.6	1 266 562.0	Strict dominance	Strict dominance	Strict dominance
No	TST plus QFN	40	86.5	1 159 835.9	Strict dominance	Strict dominance	Strict dominance
No	TST plus T-SPOT.TB	40	85.5	1 296 089.2	Strict dominance	Strict dominance	Strict dominance
Yes	**TST plus QFN**	**40**	**84.9**	**1 254 566.3**	**Strict dominance**	**Strict dominance**	**Strict dominance**

Table 4 Continued

CXR at port of arrival	Screening for LTBI: Screening tool	Screening threshold for immigrants (cases of TB/ 100 000 per year)	Cases of active TB (over 20 years)	Costs (£, 2010)	Incremental cases of active TB	Incremental costs (£, 2010)	ICER
No	QFN	150	84.3	1 089 176.5	7.8	249 462.8	31 867.1
Yes	**TST plus T-SPOT.TB**	**40**	**83.9**	**1 390 819.6**	**Strict dominance**	**Strict dominance**	**Strict dominance**
No	TST	40	83.3	1 597 273.1	Strict dominance	Strict dominance	Strict dominance
No	T-SPOT.TB	150	83.0	1 408 873.0	Strict dominance	Strict dominance	Strict dominance
No	QFN	100	82.8	1 195 634.0	Strict dominance	Strict dominance	Strict dominance
Yes	QFN	150	82.7	1 183 906.9	Extended dominance	Extended dominance	Extended dominance
Yes	TST	40	81.7	1 692 003.5	Strict dominance	Strict dominance	Strict dominance
No	T-SPOT.TB	100	81.5	1 666 546.8	Strict dominance	Strict dominance	Strict dominance
Yes	T-SPOT.TB	150	81.4	1 503 603.4	Strict dominance	Strict dominance	Strict dominance
Yes	QFN	100	81.2	1 290 364.5	Extended dominance	Extended dominance	Extended dominance
Yes	T-SPOT.TB	100	79.9	1 761 277.3	Strict dominance	Strict dominance	Strict dominance
No	QFN	40	74.9	1 414 623.3	9.4	325 446.8	34 753.5
Yes	**QFN**	**40**	**73.4**	**1 509 353.7**	**1.6**	**94 730.4**	**59 489.1**
No	T-SPOT.TB	40	73.3	2 095 182.0	Extended dominance	Extended dominance	Extended dominance
Yes	**T-SPOT.TB**	**40**	**71.7**	**2 189 912.4**	**1.7**	**680 558.7**	**402 421.8**

- Health-economic model evaluated 70 different combinations of screening
  - CXR at port of entry
  - LTBI screening tool
  - LTBI screening threshold

→ Results…

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Source: Pareek M et al Thorax 2012

Screening at intermediate threshold with single-step QuantiFERON Gold in-tube but without port-of-entry chest radiography most cost-effective

Chest radiography	Screening tool(s)	Screening threshold (per 100,000)	Cases of active TB (over 20 years)	Costs over 20 years (2010 GB pounds)	ICER (GBP per TB case averted)
No	None	None	100.5	659,609.4	Baseline
No	QFN-GIT	250	92.1	839,713.7	21,565.3
No	QFN-GIT	150	84.3	1,089,176.5	31,867.1
No	QFN-GIT	40	74.9	1,414,623.3	34,753.5
Yes	QFN-GIT	40	73.4	1,509,353.7	59,489.1
Yes	T-SPOT.TB	40	71.7	2,189,912.4	402,421.8

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Source: Pareek M et al Thorax 2012

Cost-effectiveness of migrant screening for latent tuberculosis: how to screen?

Author	Year	Location	Tools assessed	Incidence threshold assessed	Empirical data	Model type (Decision-analysis (DA) or Markov (M))	Assessment of cost-effectiveness	Conclusion on cost-effectiveness
Schwartzman	2000	Canada	CXR and TST	No	No	DA and M	$/ active TB case averted	CXR
NICE	2006	UK	TST, IGRA, TST+IGRA	Yes	No	DA	£/QALY loss averted	TST+IGRA
Oxlade	2007	Canada	CXR, TST, IGRA	No	No	DA	$/ active TB case averted	CXR
NICE	2011	UK	TST, IGRA, TST+IGRA	No	No	DA	£/QALY loss averted	TST+IGRA or IGRA
Pareek	2011	UK	IGRA	Yes	Yes	DA	$/ active TB case averted	IGRA
Linas	2011	USA	TST vs IGRA	No	No	M	$/Life year gained	IGRA
Pareek	2012	UK	TST, IGRA, TST+IGRA	Yes	Yes	DA	$/ active TB case averted	IGRA

Cost-effectiveness of migrant screening for latent tuberculosis: how to screen?

Author	Year	Location	Tools assessed	Incidence threshold assessed	Empirical data	Model type (Decision-analysis (DA) or Markov (M))	Assessment of cost-effectiveness	Conclusion on cost-effectiveness

Use single-step IGRA
Little data on which IGRA to use

Pareek	2011	UK	IGRA	Yes	Yes	DA	$/ active TB case averted	IGRA
Linas	2011	USA	TST vs IGRA	No	No	M	$/Life year gained	IGRA
Pareek	2012	UK	TST, IGRA, TST+IGRA	Yes	Yes	DA	$/ active TB case averted	IGRA

Cost-effectiveness of migrant screening for latent tuberculosis: where to screen?

Author	Year	Location	Aim of study/analysis	Tools assessed	Empirical data	Model type (Decision-analysis (DA) or Markov (M))	Assessment of cost-effectiveness
Dasgupta	2000	Canada	Compare CXR and TST in screening migrants	CXR and TST	Yes	DA and M	$/ active TB case averted
Schwartzman	2000	Canada	Compare CXR and TST in screening migrants from hypothetical high, medium and low TB burden settings	CXR and TST	No	DA and M	$/ active TB case averted
Khan	2002	USA	Compare TST versus no screening for latent TB in recent migrants from different world regions	TST vs No screening	No	DA	$/ active TB case averted
NICE	2006	UK	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants	TST, IGRA, TST+IGRA	No	DA	£/QALY loss averted
Oxlade	2007	Canada	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants	CXR, TST, IGRA, TST+IGRA	No	DA	$/ active TB case averted
NICE	2011	UK	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants	TST, IGRA, TST+IGRA	No	DA	£/QALY loss averted
Pareek	2011	UK	Compare no screening versus IGRA screening at different incidence thresholds	IGRA	Yes	DA	£/ active TB case averted
Linas	2011	USA	Compare no screening vs TST, IGRA or TST+IGRA as screening tools for latent TB in migrants	TST vs IGRA	No	M	$/Life year gained
Pareek	2012	UK	Compare no screening versus TST, IGRA or TST+IGRA as screening tools for latent TB in recent migrants. Assessment of screening threshold and where to screen also.	TST, IGRA, TST+IGRA	Yes	DA	$/ active TB case averted

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Cost-effectiveness of migrant screening for latent tuberculosis: where to screen?

Author	Year	Location	Type of data	Screening locational assessed	Conclusion

Screen post-arrival
Community-based setting

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Sensitivity analysis: cost-effectiveness highly determined by certain parameters

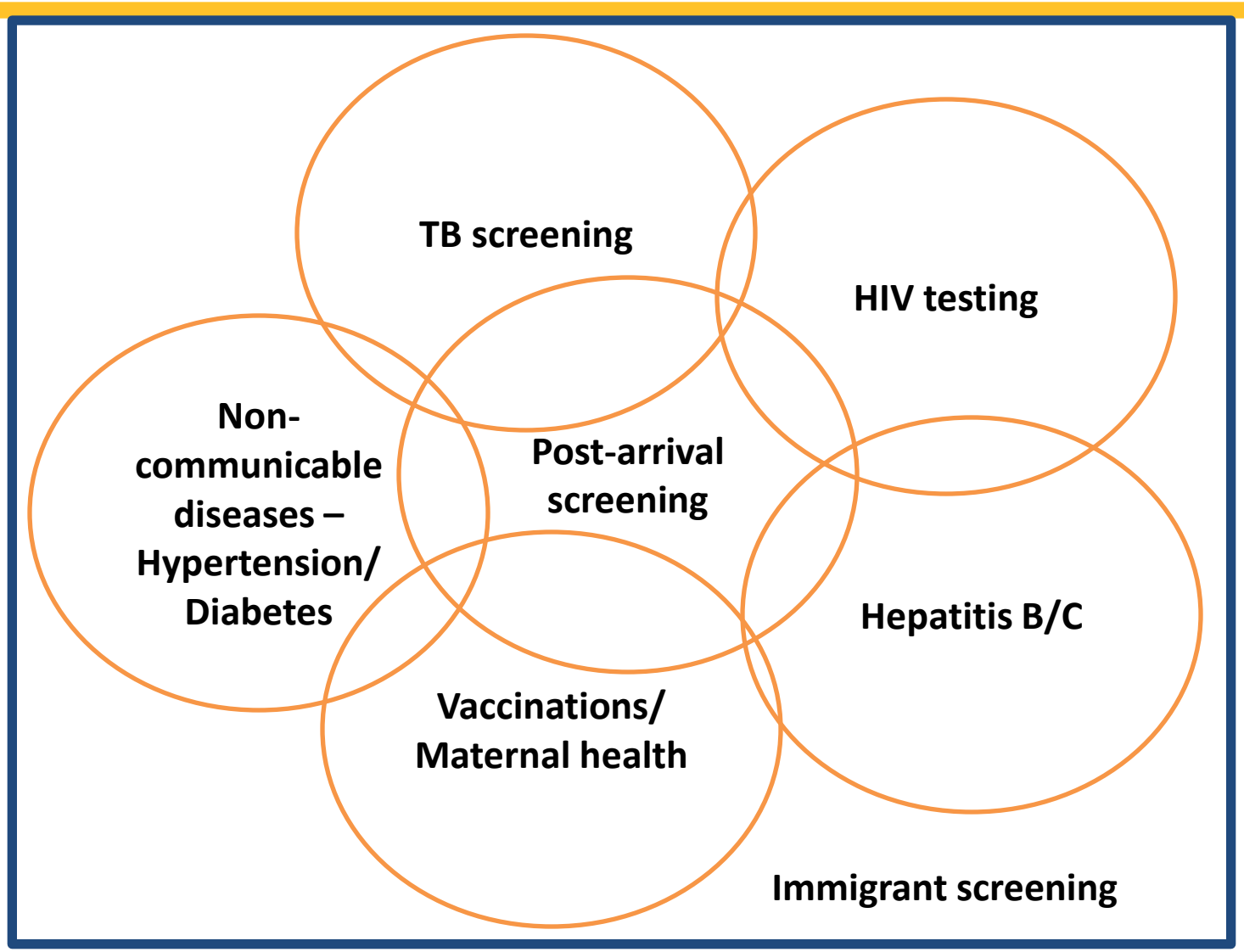
Author	Year	Location	Parameters which make migrant screening more cost-effective
Dasgupta	2000	Canada	Increased risk of future disease, higher levels of compliance with medication
Schwartzman	2000	Canada	Higher prevalence of latent TB and HIV, prescription and completion of chemoprophylaxis
Khan	2002	USA	Incidence of tuberculosis
NICE	2006	UK	Prevalence of latent TB and rate of reactivation
Oxlade	2007	Canada	Rate of reactivation and completion of chemoprophylaxis
NICE	2011	UK	Prevalence of latent TB and rate of reactivation
Pareek	2011	UK	Prevalence of latent TB and rate of reactivation
Linas	2011	USA	Rate of reactivation
Pareek	2012	UK	Prevalence of latent TB and rate of reactivation

Sensitivity analysis: cost-effectiveness highly determined by certain parameters

Author	Year	Location	Parameters which make migrant screening more cost-effective
Dasgupta	2009	Canada	Increased risk of future disease, higher levels of compliance with medication
Pareek	2011	UK	Prevalence of latent TB and rate of reactivation
Linas	2011	USA	Rate of reactivation
Pareek	2012	UK	Prevalence of latent TB and rate of reactivation

Prevalence of latent TB, reactivation rate and operational factors affect cost-effectiveness most significantly

Post-arrival, community-based screening facilitates wider migrant health programmes



Areas for further research

- Data on prevalence of latent TB in wide range of migrants
- Data on the natural history of TB in migrants
  - Reactivation rates
- Age cut-offs for screening
- How to operationalise screening
- Acceptability of screening to migrants
- Completion rates for chemoprophylaxis

Concluding statements

- Foreign-born individuals disproportionately bear the TB burden in high-income countries
- Reactivation of latent TB important
- Migrant screening likely to comprise multiple elements
  - Pre-arrival screening for active TB
  - Targeted post arrival screening for LTBI
    - Migrants from intermediate/high burden settings
    - Single-step IGRA
- Further research required in this area

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Thank you

Any questions/comments?

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