

Title. Active screening at entry for tuberculosis among new immigrants: a systematic review and meta-analysis

Authors. Shazia Arshad^{1*}; Luckshman Bavan^{1*}; Kataryna Gajari^{1*}; Sophia N. J. Paget^{1*}; Iacopo Baussano^{1,2}

*Those authors have contributed equally to the work and should be considered first authors.

Affiliations.

¹Imperial College of Science, Technology and Medicine. Division of Epidemiology, Public Health and Primary Care. Faculty of Medicine, London.

²Unit of Medical Statistics – Università ‘A.Avogadro’ and CPO-Piemonte, Novara, Italy

Short title. Tuberculosis among new immigrants

Keywords. tuberculosis, screening, migrants.

Words count, text: 3703.

Words count, abstract: 199.

Number of tables: 2.

Number of figures: 4.

Principal Degrees and current positions of the authors

Shazia Arshad, B.Sc. Current position: medical student.

Luckshman Bavan, B.Sc. Current position: medical student

Kataryna Gajari, B.Sc. Current position: medical student

Sophia Paget, B.Sc. Current position: medical student

Iacopo Baussano, see below (corresponding authors details)

Full address

Imperial College of Science, Technology and Medicine. Division of Epidemiology, Public Health and Primary Care. Faculty of Medicine. St Mary's Campus, Norfolk Place, London W2 1PG.

Corresponding author.

Iacopo Baussano, MD, MSc., M.Phil., Specialist in Infectious Diseases.

Current position: researcher

Imperial College of Science, Technology and Medicine. Division of Epidemiology, Public Health and Primary Care. Faculty of Medicine, room 512 (fifth floor). St Mary's Campus, Norfolk Place, London W2 1PG.	SCDU di Epidemiologia dei Tumori Servizio di Statistica Medica CPO Piemonte Via Solaroli, 17 28100 - NOVARA Italy
---	--

Abstract.

Background. Although there is no evidence that imported tuberculosis increases the incidence of the disease in the host countries, the rise in migration worldwide raises concerns regarding the adequacy of surveillance and control of immigrant-associated tuberculosis in low incidence countries. Assessing the performance of screening of immigrants for tuberculosis is key to rationalize the control policies to detect and manage immigrant-associated tuberculosis.

Methods. We performed a systematic review and meta-analysis to determine the yield of active screening for tuberculosis among new immigrants at the point of entry.

Results. The yield for pulmonary tuberculosis was 3.5 cases per thousand screened (95% CI 2.9– 4.1, $I^2= 94\%$), for refugees, asylum seekers and regular immigrants the estimates were 11.9 (95% CI 6.7 – 17.2, $I^2= 92\%$), 2.8 (95% CI 2.0 – 3.7, $I^2= 96\%$) and 2.7 (95% CI 2.0 – 3.4, $I^2= 81\%$), respectively. The yield estimates for immigrants from Europe, Africa and Asia were 2.4 (95% CI 1.3 – 3.4, $I^2= 51.5\%$), 6.5 (95% CI 3.2 – 10.0, $I^2= 62\%$) and 11.2 (95% CI 6.2 – 16.1, $I^2= 95\%$), respectively.

Conclusions. These results provide useful data to inform the development of coherent policies and rational screening services to detect immigrant-associated tuberculosis.

Introduction

In 2007, according to the World Health Organization (WHO), there were an estimated 13.7 million prevalent cases of tuberculosis and an estimated 0.5 million cases of multidrug-resistant tuberculosis worldwide. In the same year, the number of new cases increased from 9.24 million cases in 2006 to 9.27 due to population growth, while there were 1,756,000 deaths from tuberculosis, 456,000 of which occurred in HIV-positive people. The African, South-East Asia and Western Pacific regions accounted for around 80% of total case notifications.[1] As with other infections, the movements of populations across countries can be critically important in shaping the global epidemiology of tuberculosis.[2] The displacement of people from areas characterized by a high burden of tuberculosis and poor implementation of control strategies may hinder the tuberculosis control in areas with unprepared or overstretched control programmes. Contact patterns both within and outside the migrant communities, immigration patterns and tuberculosis control measures are likely to affect the effective contact between infectious and susceptible individuals.[3] Thus, migrants from countries with a high prevalence of tuberculosis may play a role as a source of tuberculosis infection particularly within migrant communities.[4,5] The dramatic rise in migration to Europe and the potential consequences of this in terms of infectious diseases circulation, has recently been addressed at the second Conference on Applied Infectious Disease Epidemiology (ESCAIDE) supported by the European Centre for Disease Prevention and Control (ECDC).[6] The issues of surveillance of communicable diseases and screening of migrants for tuberculosis are politically sensitive topics that need robust evidence about the burden of immigrant-associated tuberculosis and about the efficacy of screening services to be adequately addressed.[7,8,9] Very recently, overseas screening has been reported as a high-yield intervention for identifying tuberculosis in regular immigrants and refugees in their countries of origin[10]. Similarly, contact tracing among migrants and the foreign-born population has been recently reviewed as a potentially effective, though poorly standardized, strategy to identify cases in a high-prevalence population.[11]

We review the current literature in order to provide a measure of performance of screening at entry in settings of low tuberculosis prevalence. Specifically looking at evidence on the yield (defined as the ratio between number of cases detected and individuals screened) of active case finding or active screening programmes targeted to migrants moving from areas of high tuberculosis incidence to areas of low incidence.

Methods

Search strategy

We initially searched the available literature for systematic reviews or meta-analyses reporting tuberculosis prevalence amongst migrants. In 2005 Dasgupta and Menzies published a systematic review aimed at assessing the cost-effectiveness of tuberculosis control strategies among immigrants and refugees.[7] In order to optimize the sensitivity of the search the focus was not specifically on active screening yield. We aimed our search strategy to identify all the studies that assessed the prevalence of tuberculosis amongst immigrants moving from high incidence, i.e. >49 new TB cases/100,000 persons-year, to medium or low incidence, i.e. <50 new TB cases/100,000 persons-year. We searched three electronic databases for primary studies: PubMed, EMBASE and Web of Knowledge. The search included published reports through July 2008, using the following combination of terms: 'tuberculosis' and 'prevalence' or 'screening' and 'emigrants' or 'refugees' or 'foreign born' or 'immigrants'. We restricted the language of the publications to English, French, Spanish and Italian. To identify relevant articles not found in the electronic databases we supplemented the search strategy as follows: a) we hand-searched the indices of the *International Journal of Tuberculosis and Lung Disease* (1997-2004), b) we reviewed the reference lists of primary studies.

Study selection

Studies were eligible for inclusion if they reported the proportion of active pulmonary tuberculosis among screened immigrants, including the number of migrants investigated and number of cases found, and if they assessed through active case finding or an active screening programme, that is screening targeting all immigrants, irrespective of symptoms. For the purpose of this review we considered studies performing both radiological and microbiological tests to identify cases of active tuberculosis.[12] We excluded the following studies: (1) studies only reporting prevalence of latent tuberculosis infection; (2) studies only reporting tuberculosis cases in children (reported as such in the paper or younger than 16 years of age); (3) studies only identifying cases through passive case finding; (4) studies only reporting tuberculosis prevalence among migrants moving from areas of low incidence; (5) studies only reporting cases of multi-drug resistant tuberculosis; (6) studies only including migrants who had undergone screening prior to leaving the country of origin and (7) studies only reporting tuberculosis incidence data among immigrants.

All duplicate citations were eliminated from the initial database. Four reviewers (SA, SP, KG, LB) screened these citations by reviewing titles and abstracts to identify potentially

relevant studies. Disagreements between the reviewers were resolved by consensus. The database was then screened again to include only primary articles, and the full text of each citation was obtained and reviewed.

Data extraction

A data extraction form was designed and pilot tested by four reviewers (SA, SP, KG, LB), then a subset of five studies were independently reviewed to extract the relevant data. The inter-rater agreement obtained for the data from these studies was 100%. Subsequently, the papers were independently reviewed by the reviewers (SA, SP, KG, LB) and data extraction cross-checked. The study period, the number of migrants screened and cases of active tuberculosis were recorded. The pattern of screening has been classified as 'routine' or 'on purpose' to differentiate information collected through ongoing and settled programmes from those obtained from programmes developed *ad hoc*. If reported, we also collected data on the country or geographic area of origin of the migrants, their age and gender distribution. We considered as 'migrants' those reported as such in the original study. Since migrants were differently reported in different studies, we grouped the migration patterns according to the following classification: regular immigrant (including immigrant workers and students), asylum seekers (including individuals who went through asylum centres or state registration centres at the border; individuals arriving through transit centres and reporting to ports and border health divisions) and refugees (reported as such in the papers). Only studies that identified pulmonary tuberculosis using chest X-rays and/or sputum smear and/or microbiological culture were included.

As estimates of tuberculosis prevalence among the general populations in the host countries, we considered estimates provided by the WHO for the corresponding study period.[13]

Finally, we assessed the quality of each study, adapting the Newcastle-Ottawa scoring scale for cohort studies.[14] In brief, the quality of the studies has been assessed considering the definition and representativeness of the cohort of migrants, the diagnostic criteria for cases of active tuberculosis and the comparability of the cohorts on the basis of the study design or analysis.

Data collation and meta-analysis

For each study the yield of active screening for pulmonary tuberculosis has been calculated. The yield was defined as the number of cases detected per 1,000 individuals screened. We performed a random-effects meta-analysis in order to account for the expected between-study variability for each study, that is we drew pooled estimates under the assumption that each study had different characteristics and measured different, though related, underlying

yields[15]. We used the software for statistical analysis STATA version 9.2 (StataCorp., College Station, TX, USA). The studies included in the meta-analysis were weighted by the inverse variance of their effect-size estimate.[16] In order to assess the magnitude of the disproportion of the risk of pulmonary tuberculosis among screened immigrants and the general population of the host country, we also compared the yield of active screening for pulmonary tuberculosis with the estimated prevalence of tuberculosis in the general population of the host country. The latter estimates are usually drawn from passive case finding programmes, we therefore considered active screening yield as a proxy measure of the pulmonary tuberculosis prevalence among immigrants.

The presence of heterogeneity across studies was assessed by the conventional chi-squared test for heterogeneity and by calculating the I^2 statistic, which accounts for the number of studies included in the meta-analysis and provide a direct measure of the variability not explained by the information included in the analysis.[17]

To investigate possible sources of heterogeneity, we stratified the analysis by patterns of migration, geographic area of destination and patterns of screening. To account for the effect of continuous variables, such as the study period and quality scoring of the study, we performed univariate meta-regression analyses. Using some studies, it was possible to estimate a pooled pulmonary tuberculosis prevalence among screened migrants according to their geographic origin and to assess the relative risk of tuberculosis between men and women. There were insufficient studies reporting the distribution of the migrants by age, gender and country of origin to warrant analysis. Finally, we qualitatively assessed the publication bias by drawing a funnel plot.

Results

The study selection process is shown in figure 1. We identified 468 potentially relevant unique citations from all literature searches, and 22 of these publications were eligible for inclusion, accounting for 5,446 cases of pulmonary tuberculosis out of 2,620,739 screened immigrants.[18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39] No publication has been excluded from the analysis on the basis of the quality assessment. The median number of cases of pulmonary tuberculosis among immigrants was 31 (inter-quartile range [IQR]: 10–76), while the median number of immigrants screened in each study was 6526 (IQR: 945–19912). Of the 22 studies, seven reported pulmonary tuberculosis cases among refugees,[26,27,28,29,30,31,38] seven reported cases among regular immigrants,[32,33,34,35,36,37,39] seven reported cases among asylum

seekers,[18,19,20,21,22,23,24] one did not report any pulmonary tuberculosis case.[25] Twelve studies reported information about the geographic origin of the migrants,[19,20,21,26,27,28,29,30,31,36,38,39] while only three studies reported a gender distribution of pulmonary tuberculosis cases.[22,29,31] Among the studies reporting the geographic origin of immigrants, six reported cases from Europe (median number of cases: 10 [IQR: 4 – 8]; median number of immigrants: 2,950 [IQR:945 – 8,462]),[19,20,21,26,28,29] six reported cases from Asia (median number of cases: 24 [IQR: 13 – 71]; median number of immigrants: 2,089 [IQR: 1,863– 9,328]),[20,27,30,31,36,38] three reported cases from Africa (median number of cases: 14 [IQR: 13–46]; median number of immigrants: 1,732 [IQR:1,390–10,490])[19,20,21], one reported cases from the Middle East[20] and finally one paper reported cases from Haiti.[39] Table 1 summarizes the findings of the 22 studies that reported cases of active pulmonary tuberculosis among migrants and the prevalence of tuberculosis among the general population in the host countries. Figure 2 shows the pooled and study specific estimates, stratified by patterns of migration, of the yield of active screened programmes. These estimates ranged between a minimum of one every thousand screened to a maximum of 38.1 per thousand, while the pooled estimate was 3.5 per thousand (95% confidence interval [CI]: 2.9–4.1)). The study reported by Denburg et al. did not identify any pulmonary tuberculosis cases out of the 68 refugees investigated and therefore did not contribute to the estimate of the pooled relative risk.[25] Interestingly, the stratified pooled estimates allowed us to identify a fourfold increase of the yield for refugees (yield = 11.9 per thousand; 95%CI: 6.7–17.2, $I^2 = 92\%$) compared to the other group of migrants: namely, regular immigrants (yield = 2.8 per thousand; 95%CI: 2.0–3.6, $I^2 = 96\%$) and asylum seekers (yield = 2.7 per thousand; 95%CI: 2.0– 3.4, $I^2 = 81\%$). Since different geographic area of destination may experience different patterns of immigration and implement different screening services, we performed a sensitivity analysis considering estimates exclusively from European countries (figure 3). The active screening yield for refugees decreased to 5.8 per thousand (95% CI: 2.0–9.5, $I^2 = 68\%$), while the yield for regular immigrants (yield = 2.2 per thousand; 95%CI: 1.3–3.2, $I^2 = 89\%$) and for asylum seekers (yield = 2.7 per thousand; 95%CI: 1.9–3.4, $I^2 = 84\%$) virtually did not change.

In order to account for the possible differences between routine and *ad hoc* screening programmes, we conducted an analysis restricted to the routine screening programmes. Also in this case the yields for both regular immigrants (yield = 2.0 per thousand; 95%CI: 1.3–2.8, $I^2 = 96\%$) and asylum seekers (yield = 2.1 per thousand; 95%CI: 1.8–2.5, $I^2 = 30\%$) remained

substantially unchanged, while the heterogeneity between studies targeted to asylum seekers decreased significantly.

We investigated the role of the study period and quality scoring of the study for other sources of heterogeneity, neither appeared to significantly influence the meta-analysis estimates.

The prevalence estimated in host countries ranged between 0.03 and 0.3 per thousand (table 1), while the overall pooled estimate of the active pulmonary tuberculosis prevalence ratio between screened new immigrants and autochthonous population was 48.2 (95% CI:23.3–99.6 $I^2 = 99\%$). The stratification by migration patterns of the prevalence ratio (figure 4), mirrored the stratification of the screening yield, namely: refugees prevalence ratio for tuberculosis was 130.6 (95% CI: 58.8–290.2, $I^2 = 96\%$), for regular immigrants was 29.4 (95% CI:9.7–88.9, $I^2 = 99\%$), and for asylum seekers it was 30.1 (95% CI:19.3–47.1, $I^2 = 93\%$).

Since some studies also reported pulmonary tuberculosis cases according to their geographic origin, we tentatively estimated the pooled yield of active tuberculosis among migrants from some continents (figure 5): the pooled yield for immigrants from European countries was 2.4 per thousand (95%CI: 1.3–3.4, $I^2=51,5\%$), from Africa it was 6.5 (95%CI: 3.1–9.9, $I^2=62.5\%$), while from Asia the yield was 11.2 (95%CI: 6.2–16.1, $I^2=94.9\%$).

Finally, using the data reported by four studies, we estimated the prevalence ratio for pulmonary active tuberculosis between migrant men and women (table 2). Men were at a higher risk of active pulmonary tuberculosis than women, RR = 1.39, however, this difference was not statistically significant (95%CI: 0.94–2.04, $I^2=49.4\%$).

The possible distortion of the estimates due to publication bias could be reasonably excluded by visual inspection of the funnel plot, although the method has been designed for meta-analysis of randomised controlled trials.[40]

Discussion

Population mobility across the world is rapidly becoming a key determinant of the infectious diseases epidemiology.[41] The relationship existing between international migration and tuberculosis control has been extensively addressed by a report of a European Task Force from the International Union Against Tuberculosis and Lung Disease (IUATLD) and WHO in 1994,[2] while Dasgupta and Menzies compared the cost-effectiveness of different tuberculosis control strategies.[7] In the present study we attempt to summarize the evidence on the yield of active screening of immigrants for pulmonary tuberculosis from countries with high incidence of tuberculosis migrating to low incidence countries. Overall, the

proportion of screened immigrants with active pulmonary tuberculosis ranged between 1 and 38 per thousand, that is between ten to one hundred times greater than the prevalence measured in the general population of the host country. The overall stratified analysis has shown that the patterns of migration are indicators of the risk of tuberculosis: namely refugees have been shown to be four times more likely to be diagnosed with active pulmonary tuberculosis than the other immigrants. The sensitivity analysis restricted to the European host countries has shown a similar pattern, although the screening yield for refugees halved and the confidence intervals between groups overlapped. These differences in screening yield may reflect a different risk of pulmonary tuberculosis infection associated with each pattern of migration. Refugees usually leave their own countries as consequence of critical and relatively rapid events, therefore they might be less subject to a process of selection based on their health status, the so called 'healthy immigrant effect'.^[42] Furthermore, refugees may spend some time in overcrowded camps before moving to the host country; in these settings the living conditions may favour both the transmission and the occurrence of tuberculosis. Our findings are consistent with the estimates reported from the overseas screening for U.S.-bound immigrants and refugees. The reported analyses shows that prevalence (per thousand screened) among refugees is larger (10.4; 95%CI 10.0-10.7) than among other immigrants (9.6; 95%CI 9.5-9.7)^[10]. Unfortunately, those values are not readily comparable with our estimates since they refer exclusively to smear negative tuberculosis cases, whereas our analysis accounts also for smear positive cases. However, the consistency of the findings highlights the need for recommendations on screening of refugees as a high risk group for active tuberculosis. To be fully effective screening should be part of an integrated preventive strategy focused on improving housing conditions to decrease the risk of tuberculosis transmission, on enhancing tuberculosis case finding^[11] and on setting case management within the framework of directly-observed treatment programme.^[43]

It has been observed, among regular immigrants, that the prevalence at entry was higher than expected from the WHO estimated prevalence of tuberculosis in the country of origin, possibly because migrants are a selected group with a higher risk for active tuberculosis, as are young adults and lower socioeconomic status groups.^[34] Interestingly, an analysis of the data (not shown) from those studies reporting the country of origin of migrants suggested a similar pattern. Unfortunately however, data were too limited to draw any convincing conclusion.

Immigrants from Asia and Africa have been found to be about five and three times, respectively, more likely to be affected by pulmonary tuberculosis at their entry, than their

European counterparts. These differences grossly reflect the worldwide distribution of tuberculosis. Unexpectedly, the pooled yield for immigrants from Africa was lower than for immigrants from Asia. This could be explained by the fact that about 51% of immigrants from Asia were refugees, whereas all immigrants from Africa were asylum seekers. Furthermore, according to a restricted analysis, the pooled yield for asylum seekers from European countries[19,20,21] was 2.00 per thousand (95%CI: 1.36–2.63, $I^2=0.0\%$). This finding suggests that a finer definition of the risk groups might result in a reduction of heterogeneity of the estimates, possibly supporting more specific indications about which immigrant groups should be targeted for screening. Unfortunately, the available data were not sufficient to further stratify the whole analysis by geographic origin and migration patterns.

The comparison of prevalence of active tuberculosis among screened immigrants at entry with the prevalence estimated for the autochthonous general population, has shown that overall immigrants at entry into the country are a 40 times more at risk of having active tuberculosis than the local general population. Also, as expected, the comparison between patterns of migration confirmed that refugees are four to fivefold as much at risk of pulmonary tuberculosis than the other groups. These comparisons should be however considered cautiously, since a) tuberculosis prevalence, in absence of specifically designed surveys, is usually derived from the incidence and duration estimates obtained from the notification systems based on a passive case finding approach,[44] b) active screening anticipate diagnosis of asymptomatic cases of tuberculosis, for example Monney et al. found that 49% of actively screened cases were asymptomatic compared to 18% of those detected through passive case finding,[24] and c) some prevalent cases may be missed by screening at entry, for example Erkens et al. detected 97% of prevalent cases through screening, the remaining cases were detected passively during the first five months of immigration.

Further limitation should be considered when interpreting the findings of this study. Firstly, the pooled analysis of all studies showed substantial heterogeneity. Similar levels of heterogeneity have been observed in other systematic reviews focusing on tuberculosis transmission control issues and analysing observational studies.[45,46] Such heterogeneity can be due to differences in methodological quality, study design, sampling variability, and study populations across studies. In particular, we accounted for the patterns of migration and we restricted the analysis to the European and to the routine screening programmes, under the assumption of a greater homogeneity within each subgroup. In fact, some reduction of the heterogeneity has been observed, possibly due to a more consistent organization of routine screening programmes and more consistent migration patterns within Europe. The variations

in the study quality and in the study period, did not significantly affect the heterogeneity between study estimates. The high level of heterogeneity limits the ability to interpret the pooled estimates and to compare estimates among subgroups. However the yield of active screening of new immigrants and the prevalence ratios for active tuberculosis between migrants and the general population in the host country were so high to warrant serious consideration. Secondly, it was not possible to account for the level of coverage of screening services, furthermore, it is uncertain whether and how our estimates, drawn for refugees, asylum seekers or regular immigrants, can be projected on to illegal immigrants, who are likely to be those bearing the greatest share of imported tuberculosis burden. Finally, some misclassification between migration patterns could not be excluded, in particular between refugees and asylum seekers. However when the analysis has been restricted to the data from routine screening programmes, the heterogeneity between studies investigating asylum seekers decreased by about 50%, while the screening yield remained virtually unchanged.

It is noteworthy that currently there is no evidence that imported tuberculosis has significantly increased the incidence of tuberculosis among the autochthonous population.[7] On the contrary, overall the number of notifications from the local population is decreasing every year in most industrialized countries, whereas the proportion of foreign-born tuberculosis cases is increasing.[47,48] However, imported tuberculosis has been shown to be transmitted within population subgroups with poor living conditions and poor access to health care provision.[5,8,49,50] Therefore, favouring the detection of tuberculosis cases by active screening and by promoting the access of immigrants to health care facilities may shorten the infectious periods, interfere with the transmission network, and improve the control of potential tuberculosis reservoirs.

The assessment of effectiveness of active screening of immigrants at entry is beyond the scope of this paper. However, our yield estimates, in particular for refugees from countries with high incidence of tuberculosis, support the recommendation of the introduction of screening at entry as an element of an integrated preventive strategy for tuberculosis control.

In particular, screening programmes targeting high-risk groups within the framework of coordinated activities of control and management of tuberculosis, such as contact tracing investigations and tailored directly-observed treatment programmes can be successful in reducing the burden among migrants.[4,8] **The early identification and management of tuberculosis among immigrants before they are dispersed within the host country is expected to prevent unnecessary transmission between recent immigrants. Furthermore, it would guarantee a more equitable access to health care provision and, possibly, eventually result**

into higher treatment success rates. In conclusion, the presented findings provide useful data to inform the development of coherent policies and rational screening services to detect immigrant-associated tuberculosis.

Figures and Tables

Figure 1: Flow diagram for study selection.

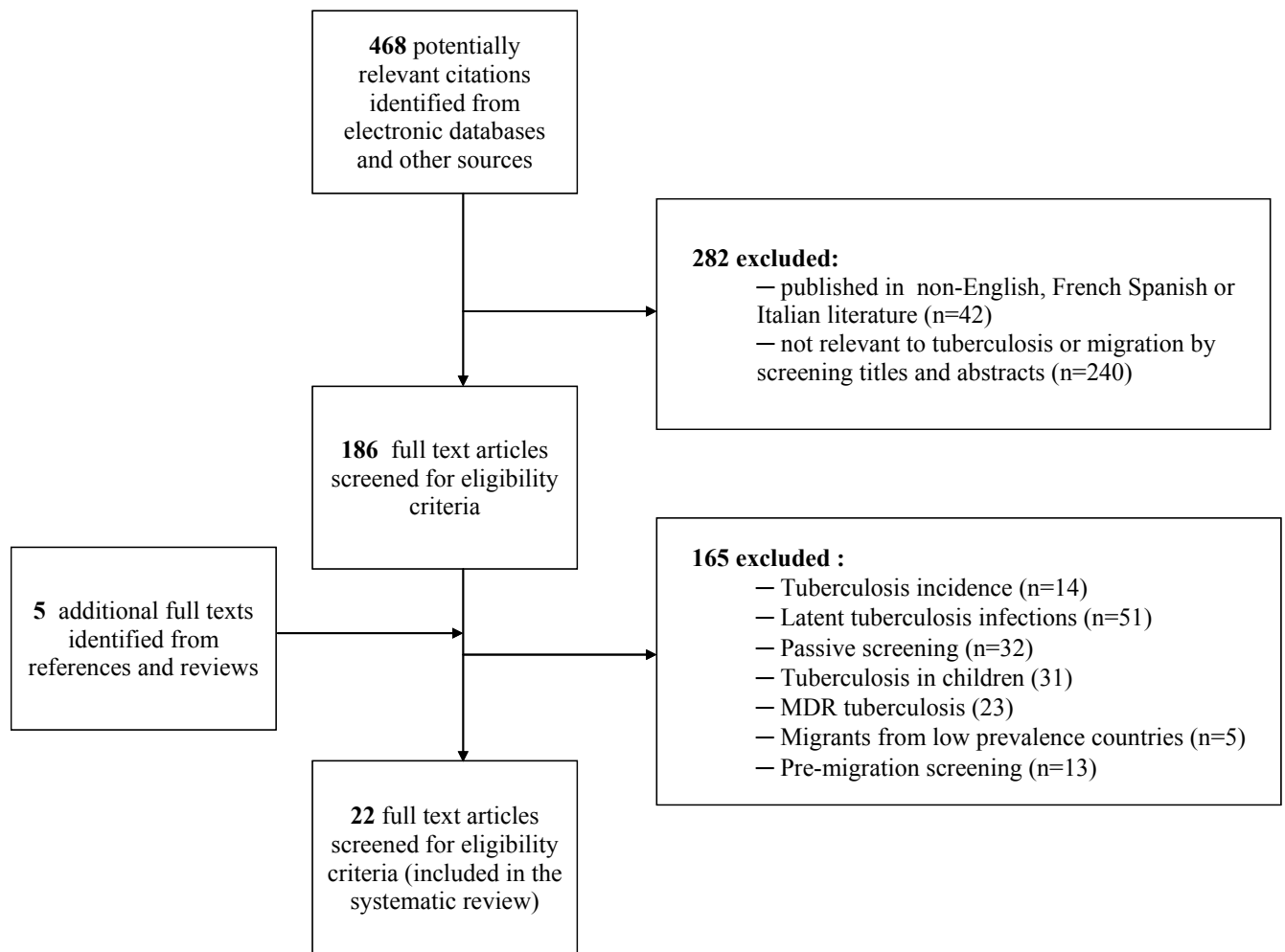


Table 1: Prevalence of tuberculosis among migrants.

Study Author, year of publication	Study Period	Pattern of Migration	Host country	TB cases among migrants	Migrants screened for TB	TB prevalence in the host country (per 100 000)[13]	Method of screening at entry [†]	Study Quality Scoring*
Harling et al., 2007[18]	2002-03	Asylum Seekers	UK	11	8258	12	Routine	5
Van den Brande et al., 1997[19]	1993	Asylum Seekers	Belgium	19	4794	15	On purpose	8
Callister et al., 2001[20]	1995-1999	Asylum Seekers	UK	100	41470	9	Routine	8
Johnsen et al., 2005[21]	1987-1995	Asylum Seekers	Norway	43	19912	8	Routine	10
van Burg et al., 2003[22]	1994-1997	Asylum Seekers	Netherlands	103	46424	8	Routine	9
Hobbs et al., 2002[23]	1999-2000	Asylum Seekers	New Zealand	4	900	11	Routine	8
Monney et al., 2005[24]	2001-2002	Asylum Seekers	Switzerland	71	13507	6	On purpose	11
Pitchenik et al., 1982[39]	1980	Regular immigrants	USA	101	15544	7	On purpose	7
Nolan et al., 1988[38]	1980	Refugees	USA	78	9328	7	On purpose	9
Denburg et al., 2007[25]	2006	Refugees	Canada	0	68	4	On purpose	8
Laifer et al., 2004[26]	1999	Refugees	Switzerland	8	3119	8	On purpose	8
Wilcke et al., 1997[27]	1995	Refugees	Denmark	13	1936	9	On purpose	5
Rysstad et al., 2002[28]	1999	Refugees	Norway	4	800	5	On purpose	8
Smith et al., 2000[29]	1999-2000	Refugees	Ireland	12	945	12	On purpose	5

Judson et al., 1984[30]	1981-1982	Refugees	USA	18	923	7	On purpose	8
Kelly et al., 2002[31]	1999	Refugees	Australia	71	1863	6	On purpose	8
Akhtar et al., 2008[32]	1997-2006	Regular Immigrants	Kuwait	4608	2328582	31	Routine	7
Laifer et al., 2007[33]	1997-2004	Regular Immigrants	Switzerland	43	42601	7	Routine	11
Erkens et al., 2008[34]	1998-2002	Regular Immigrants	Netherlands	76	68122	6	Routine	10
Salinas Solano et al., 2002[35]	1998	Regular Immigrants	Spain	3	406	27	On purpose	7
Ormerod et al., 1998[36]	1990-1994	Regular Immigrants	UK	10	2242	10	Routine	7
Mathez et al., 2007[37]	2004	Regular Immigrants	Switzerland	50	8995	6	Routine	8

^fRoutine: standard screening protocol adopted by the local authorities. On purpose: screening protocol specifically adopted to face a specific situation or for the study purposes. *Adapted from the Newcastle-Ottawa scoring scale for cohort studies[14].

Figure 2: Forest plot, yield(X 1000 individuals tested) of active screening of immigrants at entry, by pattern of migration (all studies included).

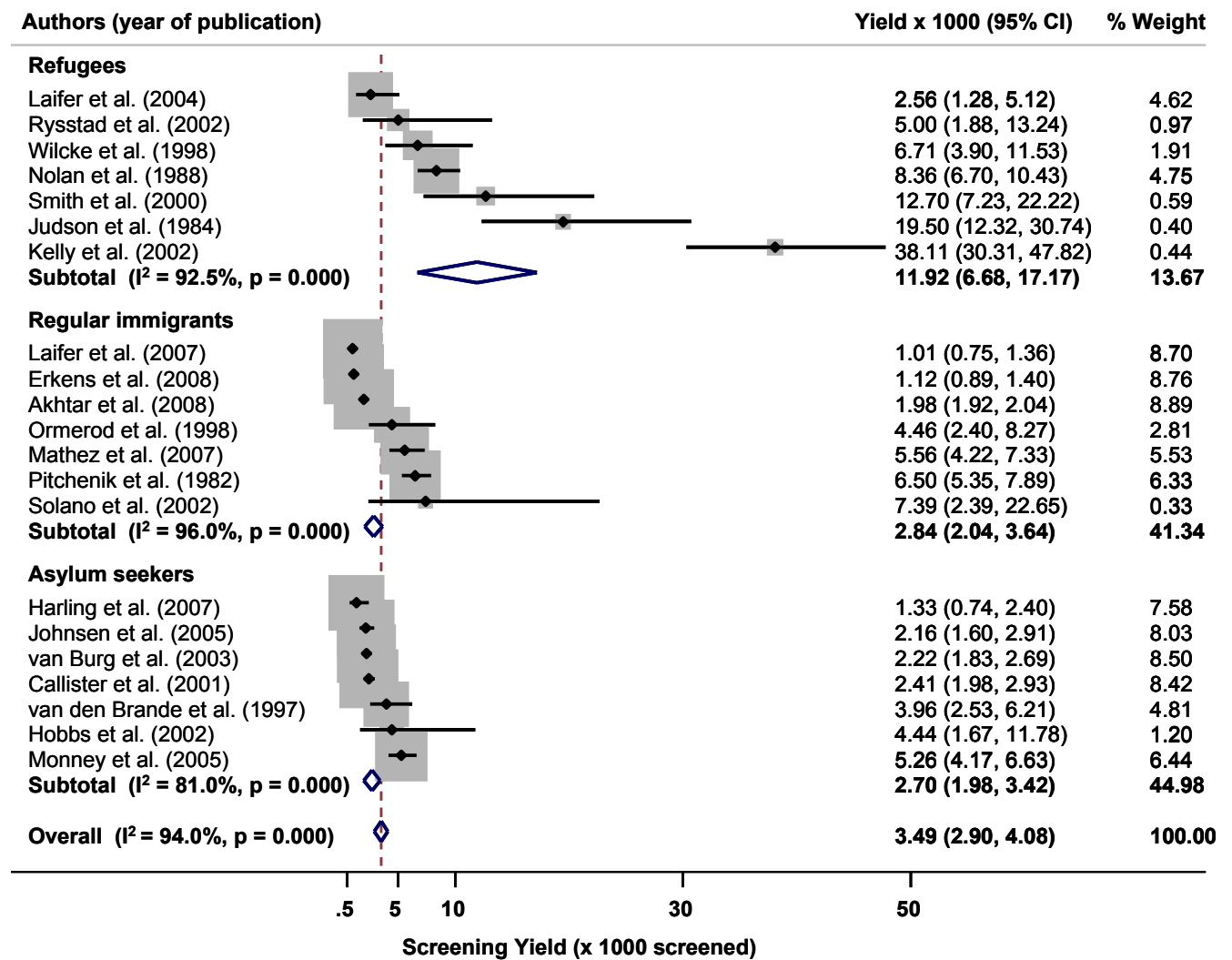


Figure 3: Forest plot, yield(X 1000 individuals tested) of active screening of immigrants at entry, by pattern of migration (only studies from European countries included).

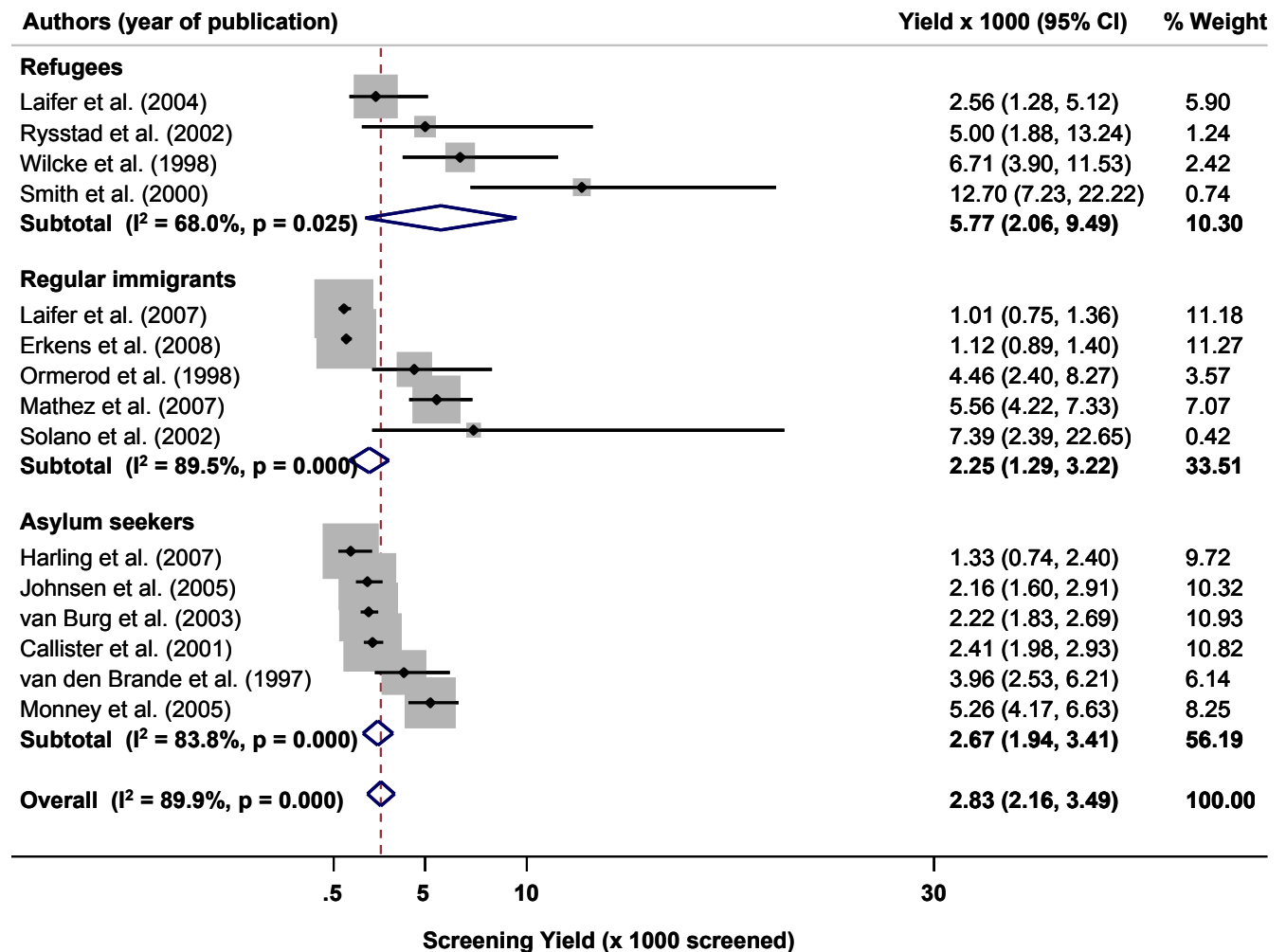


Figure 4: Forest plot, prevalence ratio for pulmonary tuberculosis among immigrants actively screened at entry compared to general population in the host country, by pattern of migration.

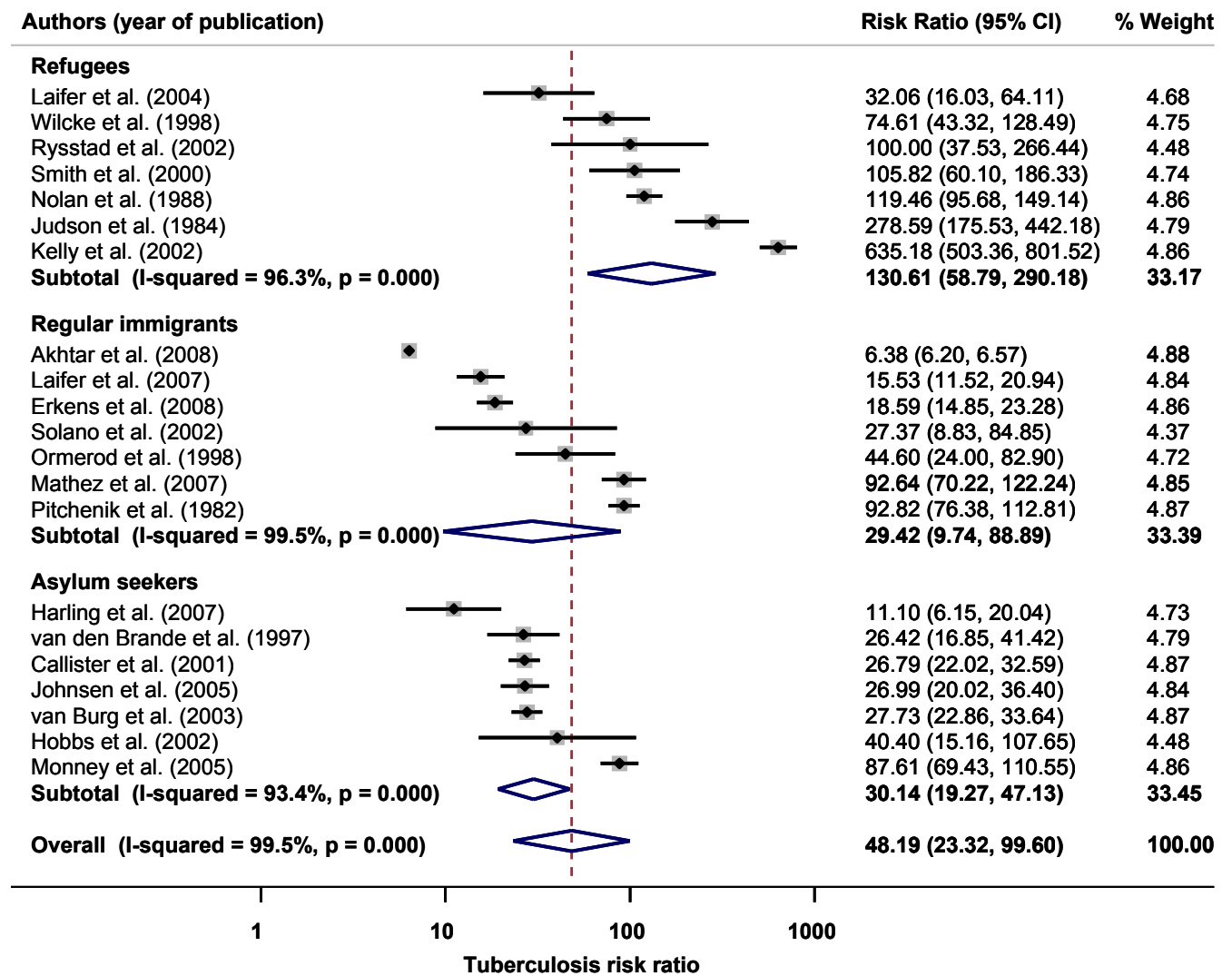


Figure 5: Forest plot, yield(X 1000 individuals tested) of active screening of immigrants at entry, by geographic origin of the immigrants.

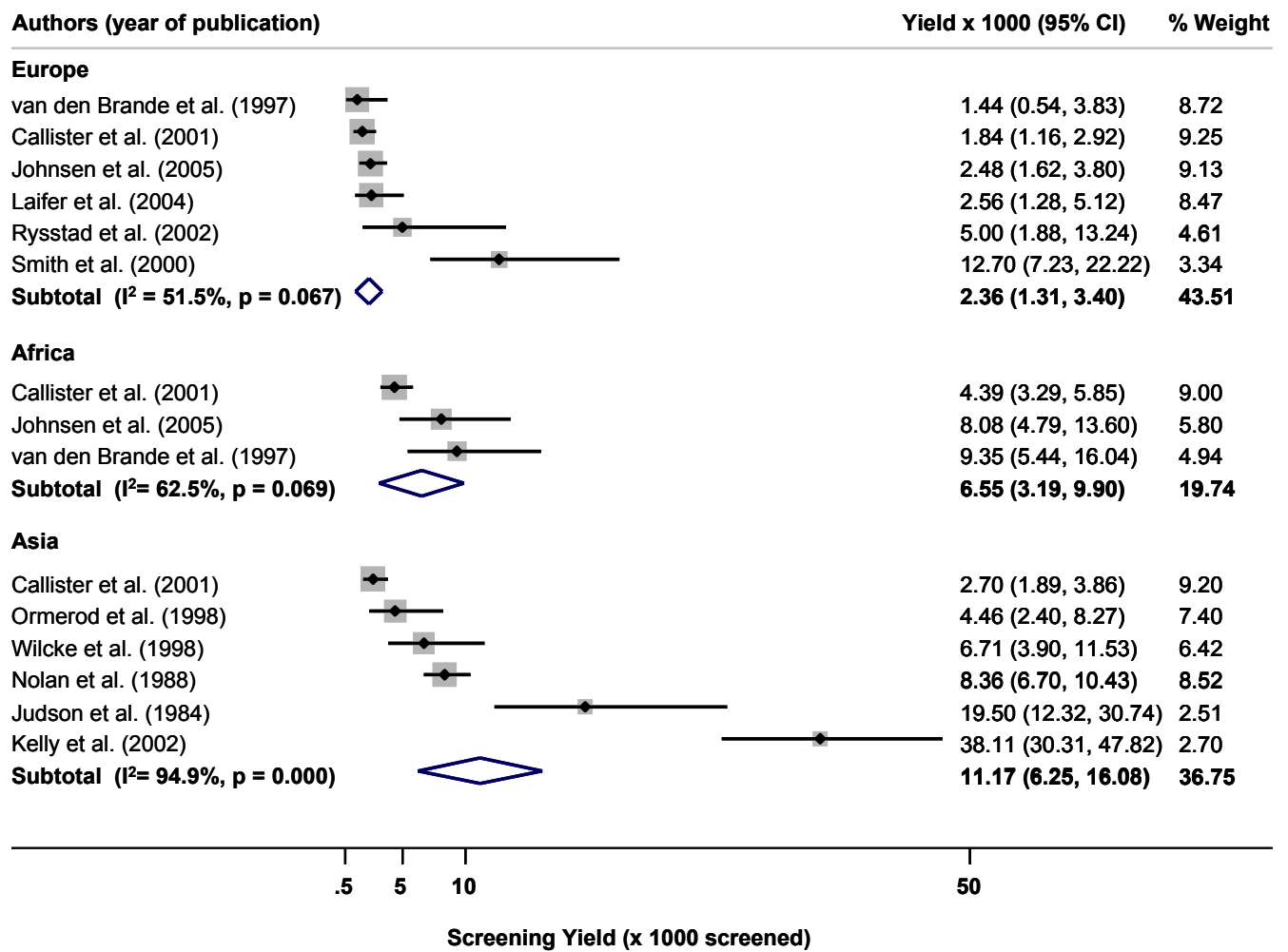


Table 2: Risk of pulmonary tuberculosis among migrants, by gender

Study Author, year of publication	Study Period	Pattern of Migration	Men with TB	Men	Women with TB	Women	Relative risk – 95%CIs (men vs. women)
Kelly et al., 2002[31]	1999	Refugees	42	958	29	905	1.35 (0.85–2.15)
Van Burg et al., 2003[22]	1994-1997	Asylum Seekers	78	28875	25	17509	1.89 (1.21–2.96)
Erkens et al., 2008[34]	1998-2002	Regular Immigrants	30	28566	46	38415	0.90 (0.57–1.42)
Smith et al., 2000[29]	1999-2000	Refugees	8	435	4	510	2.32 (0.70–7.65)
Pooled Relative risk – 95%CIs (men vs. women)				1.39 (0.94–2.04)		I²=49.4%	

Acknowledgments

The authors would like to thank Massimiliano Bugiani, Ugo Fedeli, Edwin Michael, Gabriela Gomez and Fabio Scano for their thoughtful comments. The paper has been conceived and prepared within the framework of a BSc. module in Global Health held by the Faculty of Medicine of the Imperial College of Science, Technology and Medicine in London, UK. The authors would like to thank the course directors, Helen Ward and Paolo Vineis. IB has been supported by the “Regione Piemonte” Italy, Assessorato Sanità, Progetti di Ricerca Sanitaria Finalizzata, 2008.

Conflict of interest statement

The authors do not have any conflict of interest to disclose.

References

1. WHO-Report (2009) Global Tuberculosis Control: Epidemiology, Strategy, Financing. WHO Report 2009. Geneva, Switzerland: World Health Organization.
2. Riley S (2007) Large-scale spatial-transmission models of infectious disease. *Science* 316: 1298-1301.
3. Verver S, Venn J (2006) Tuberculosis control and migration. In: Raviglione MC, editor. Reichman and Hershfield's Tuberculosis: a comprehensive, intrantional approach. New York: Informa HealthCare. pp. 869-906.
4. Rieder HL, Zellweger JP, Raviglione MC, Keizer ST, Migliori GB (1994) Tuberculosis control in Europe and international migration. *Eur Respir J* 7: 1545-1553.
5. Lillebaek T, Andersen AB, Dirksen A, Smith E, Skovgaard LT, et al. (2002) Persistent high incidence of tuberculosis in immigrants in a low-incidence country. *Emerg Infect Dis* 8: 679-684.
6. Hargreaves S (2009) Migration high on the agenda at ESCAIDE 2008. *Lancet Infect Dis* 9: 11.
7. Dasgupta K, Menzies D (2005) Cost-effectiveness of tuberculosis control strategies among immigrants and refugees. *Eur Respir J* 25: 1107-1116.
8. Coker R, Bell A, Pitman R, Zellweger JP, Heldal E, et al. (2006) Tuberculosis screening in migrants in selected European countries shows wide disparities. *Eur Respir J* 27: 801-807.
9. Hargreaves S, Carballo M, Friedland JS (2009) Screening migrants for tuberculosis: where next? *Lancet Infect Dis* 9: 139-140.
10. Liu Y, Weinberg MS, Ortega LS, Painter JA, Maloney SA (2009) Overseas screening for tuberculosis in U.S.-bound immigrants and refugees. *N Engl J Med* 360: 2406-2415.
11. Mulder C, Klinkenberg E, Manissero D (2009) Effectiveness of tuberculosis contact tracing among migrants and the foreign-born population. *Euro Surveill* 14.
12. Broekmans JF, Migliori GB, Rieder HL, Lees J, Ruutu P, et al. (2002) European framework for tuberculosis control and elimination in countries with a low incidence. Recommendations of the World Health Organization (WHO), International Union Against Tuberculosis and Lung Disease (IUATLD) and Royal Netherlands Tuberculosis Association (KNCV) Working Group. *Eur Respir J* 19: 765-775.
13. World Health Organization Global Health Atlas.
14. Wells G, Shea B, O'Connell D, Peterson J, Welch V, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses.

15. Normand SL (1999) Meta-analysis: formulating, evaluating, combining, and reporting. *Stat Med* 18: 321-359.
16. Sterne JAC, Bradburn MJ, Egger M (2001) Meta-analysis in Stata. In: Egger M, Davey-Smith G, Altman DG, editors. *Systematic reviews in health care: meta-analysis in context*. London: BMJ publishing group. pp. 347-369.
17. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. *Bmj* 327: 557-560.
18. Harling R, Pearce M, Chandrakumar M, Mueller K, Hayward A (2007) Tuberculosis screening of asylum seekers: 1 years' experience at the Dover Induction Centres. *Public Health* 121: 822-827.
19. Van den Brande P, Uydebrouck M, Vermeire P, Demedts M (1997) Tuberculosis in asylum seekers in Belgium. VRGT (Flemish Lung and Tuberculosis Association). *Eur Respir J* 10: 610-614.
20. Callister ME, Barringer J, Thanabalasingam ST, Gair R, Davidson RN (2002) Pulmonary tuberculosis among political asylum seekers screened at Heathrow Airport, London, 1995-9. *Thorax* 57: 152-156.
21. Johnsen NL, Steen TW, Meyer H, Heldal E, Skarpaas IJ, et al. (2005) Cohort analysis of asylum seekers in Oslo, Norway, 1987-1995: effectiveness of screening at entry and TB incidence in subsequent years. *Int J Tuberc Lung Dis* 9: 37-42.
22. van Burg JL, Verver S, Borgdorff MW (2003) The epidemiology of tuberculosis among asylum seekers in The Netherlands: implications for screening. *Int J Tuberc Lung Dis* 7: 139-144.
23. Hobbs M, Moor C, Wansbrough T, Calder L (2002) The health status of asylum seekers screened by Auckland Public Health in 1999 and 2000. *N Z Med J* 115: U152.
24. Monney M, Zellweger JP (2005) Active and passive screening for tuberculosis in Vaud Canton, Switzerland. *Swiss Med Wkly* 135: 469-474.
25. Denburg A, Rashid M, Brophy J, Curtis T, Malloy P, et al. (2007) Initial health screening results for Karen refugees: a retrospective review. *Can Commun Dis Rep* 33: 16-22.
26. Laifer G, Widmer AF, Frei R, Zimmerli W, Fluckiger U (2004) Polymerase chain reaction for *Mycobacterium tuberculosis*: impact on clinical management of refugees with pulmonary infiltrates. *Chest* 125: 981-986.
27. Wilcke JT, Poulsen S, Askgaard DS, Enevoldsen HK, Ronne T, et al. (1998) Tuberculosis in a cohort of Vietnamese refugees after arrival in Denmark 1979-1982. *Int J Tuberc Lung Dis* 2: 219-224.
28. Rysstad OG, Gallefoss F (2003) TB status among Kosovar refugees. *Int J Tuberc Lung Dis* 7: 458-463.

29. Smith A, O'Flanagan D, Igoe D, Cronin J, Forde D, et al. (2000) Outcome of medical screening of Kosovan refugees in Ireland: 1999. *Commun Dis Public Health* 3: 291-294.
30. Judson FN, Lince DM, Anders BJ, Tapy JM, Le Van D, et al. (1984) Health status of Southeast Asian refugees. *West J Med* 141: 183-188.
31. Kelly PM, Scott L, Krause VL (2002) Tuberculosis in east timorese refugees: implications for health care needs in East Timor. *Int J Tuberc Lung Dis* 6: 980-987.
32. Akhtar S, Mohammad HG (2008) Nonlinear pattern of pulmonary tuberculosis among migrants at entry in Kuwait: 1997-2006. *BMC Public Health* 8: 264.
33. Laifer G, Widmer AF, Simcock M, Bassetti S, Trampuz A, et al. (2007) TB in a low-incidence country: differences between new immigrants, foreign-born residents and native residents. *Am J Med* 120: 350-356.
34. Erkens C, Slump E, Kamphorst M, Keizer S, van Gerven PJ, et al. (2008) Coverage and yield of entry and follow-up screening for tuberculosis among new immigrants. *Eur Respir J* 32: 153-161.
35. Salinas Solano C, Altube Urrengoetxea L, Espana Yandiola PP, Capelastegui Saiz A, Quintana Lopez JM (2002) [Tuberculosis among immigrants in Bilbao (Spain)]. *Arch Bronconeumol* 38: 506-510.
36. Ormerod LP (1998) Is new immigrant screening for tuberculosis still worthwhile? *J Infect* 37: 39-40.
37. Mathez C, Bangala Y, Bady P, Zellweger JP (2007) Active screening for pulmonary tuberculosis among immigrants by chest x-ray at the Swiss border. *Swiss Med Wkly* 137: 649-654.
38. Nolan CM, Elarth AM (1988) Tuberculosis in a cohort of Southeast Asian Refugees. A five-year surveillance study. *Am Rev Respir Dis* 137: 805-809.
39. Pitchenik AE, Russell BW, Cleary T, Pejovic I, Cole C, et al. (1982) The prevalence of tuberculosis and drug resistance among Haitians. *N Engl J Med* 307: 162-165.
40. Tatsioni A, Zarin DA, Aronson N, Samson DJ, Flamm CR, et al. (2005) Challenges in systematic reviews of diagnostic technologies. *Ann Intern Med* 142: 1048-1055.
41. Cliff A, Haggett P (2004) Time, travel and infection. *Br Med Bull* 69: 87-99.
42. McDonald JT, Kennedy S (2004) Insights into the 'healthy immigrant effect': health status and health service use of immigrants to Canada. *Soc Sci Med* 59: 1613-1627.
43. Macq JC, Theobald S, Dick J, Dembele M (2003) An exploration of the concept of directly observed treatment (DOT) for tuberculosis patients: from a uniform to a customised approach. *Int J Tuberc Lung Dis* 7: 103-109.

44. Dye C, Bassili A, Bierrenbach AL, Broekmans JF, Chadha VK, et al. (2008) Measuring tuberculosis burden, trends, and the impact of control programmes. *Lancet Infect Dis* 8: 233-243.
45. Joshi R, Reingold AL, Menzies D, Pai M (2006) Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. *PLoS Med* 3: e494.
46. Morrison J, Pai M, Hopewell PC (2008) Tuberculosis and latent tuberculosis infection in close contacts of people with pulmonary tuberculosis in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Infect Dis* 8: 359-368.
47. Murray MB (2002) Molecular epidemiology and the dynamics of tuberculosis transmission among foreign-born people. *CMAJ* 167: 355-356.
48. Bloom BR (2002) Tuberculosis--the global view. *N Engl J Med* 346: 1434-1435.
49. Hernandez-Garduno E, Kunimoto D, Wang L, Rodrigues M, Elwood RK, et al. (2002) Predictors of clustering of tuberculosis in Greater Vancouver: a molecular epidemiologic study. *CMAJ* 167: 349-352.
50. Kulaga S, Behr M, Musana K, Brinkman J, Menzies D, et al. (2002) Molecular epidemiology of tuberculosis in Montreal. *CMAJ* 167: 353-354.