THE LANCET Infectious Diseases

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Aldridge RW, Yates TA, Zenner D, White PJ, Abubakar I, Hayward AC. Pre-entry screening programmes for tuberculosis in migrants to low-incidence countries: a systematic review and meta-analysis. *Lancet Infect Dis* 2014; published online Nov 7. http://dx.doi.org/10.1016/S1473-3099(14)70966-1.

Supplementary Appendix

Figures

Figure 1. Forrest plot of yield for principal outcome of active tuberculosis cases found by each study (case definition varies between studies, sorted by year of publication) stratified by prevalence in the country of origin, population screened, screening method and receiving country (Freeman-Tukey transformed data).

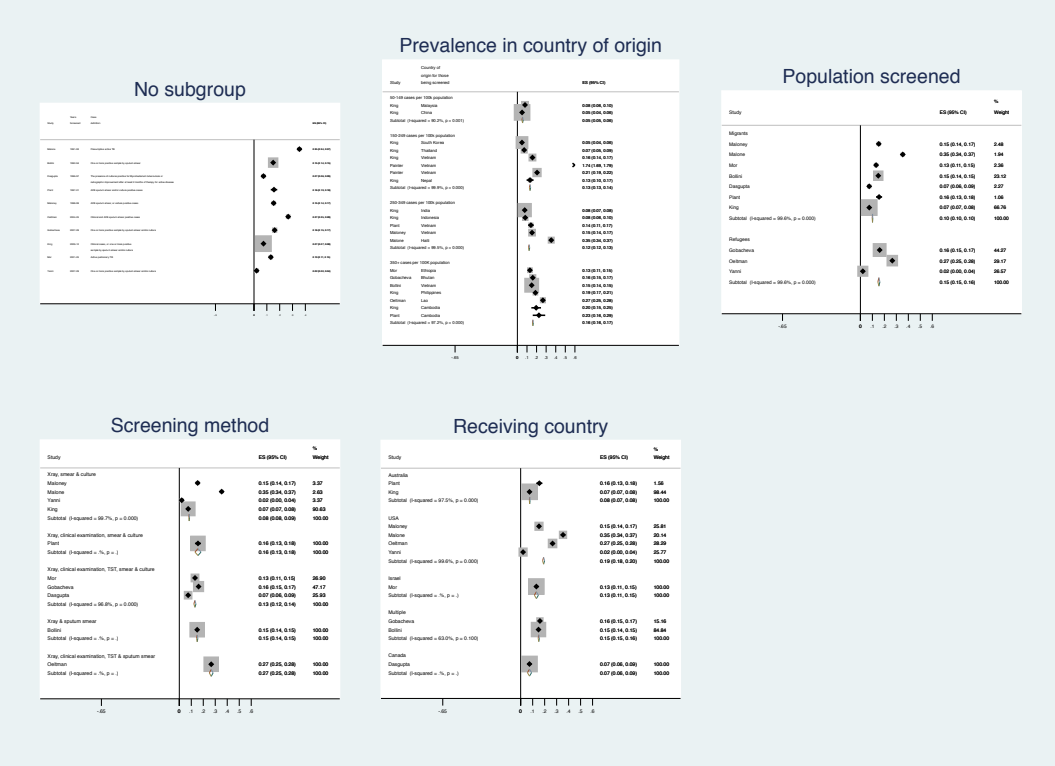


Figure 2. Forrest plot of yield for culture confirmed cases found by each study, stratified by prevalence in the country of origin, population screened, screening method and receiving country (Freeman-Tukey transformed data).

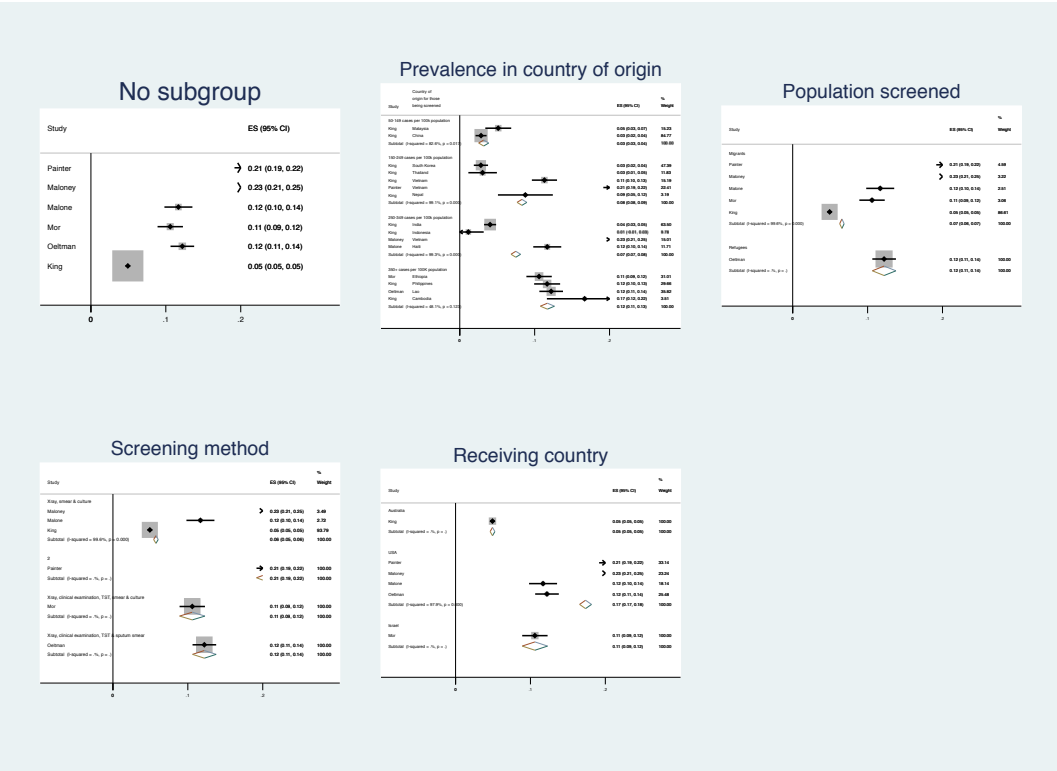


Figure 3. Forrest plot of yield for AFB confirmed cases found by each study, stratified by prevalence in the country of origin, population screened, screening method and receiving country(Freeman-Tukey transformed data).

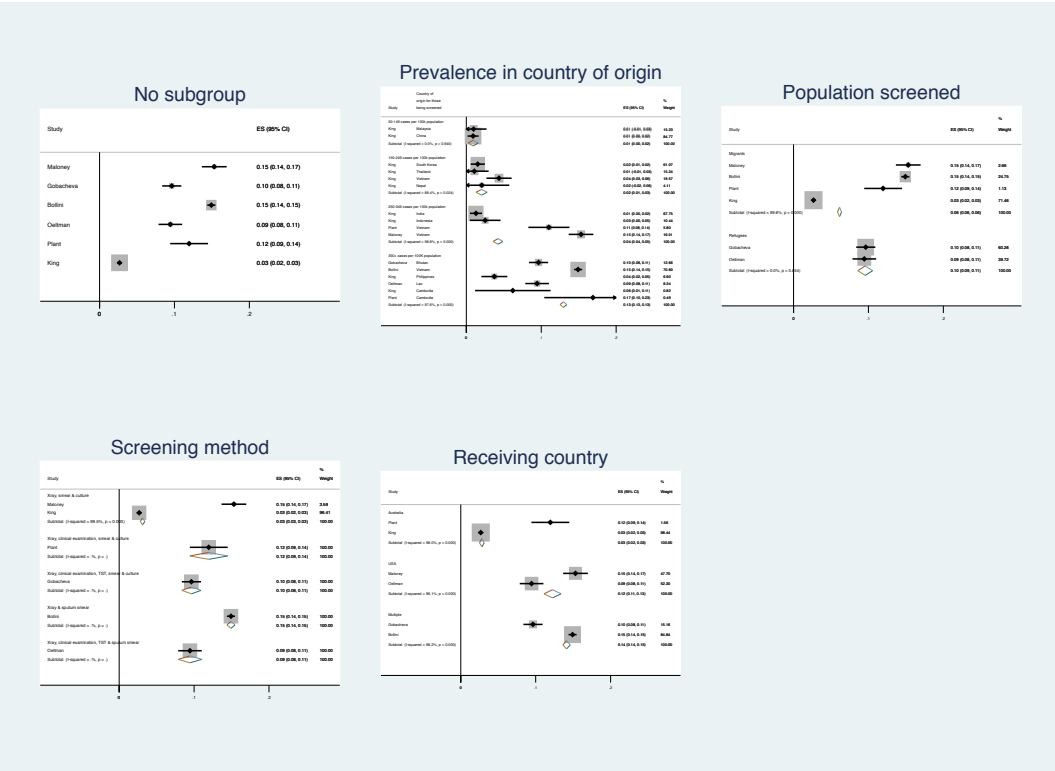
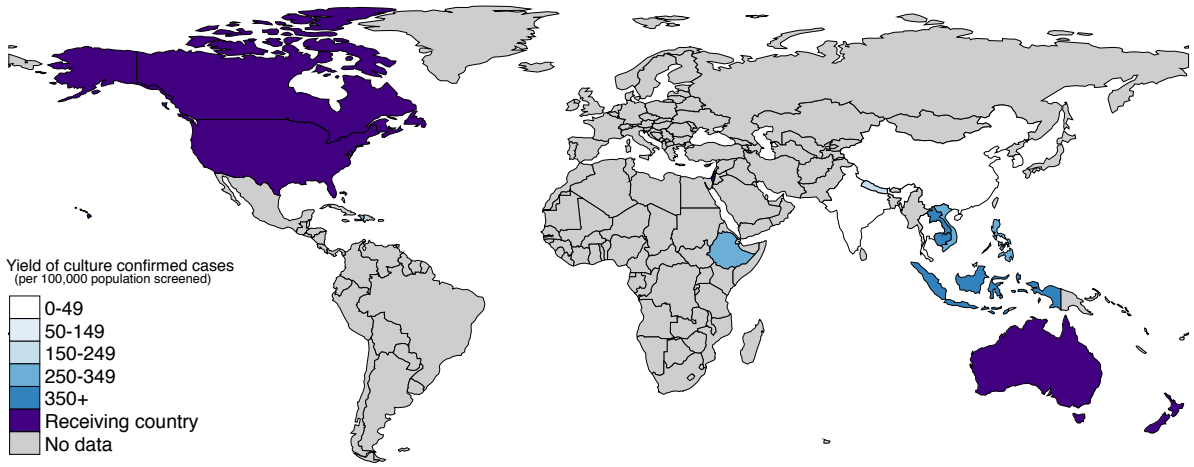


Figure 4. Map of countries conducting pre-entry screening of migrants (receiving countries) and the yield of culture confirmed cases for migrants by country of origin.



Note: For countries with yield for culture confirmed cases in more than one study, data from the most recent study is presented.

Detailed search terms used

1. Migrant$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
2. exp migration/
3. "Transients and Migrants"/
4. Expatriate$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
5. Refugee$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
6. exp Refugees/
7. Departee$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
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9. exp immigrant/
10. Immigrant$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
11. "Emigrants and Immigrants"/
12. Asylum seeker$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
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14. Asylum.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
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17. exp foreign student/
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47. exp Tuberculosis/
48. exp Mycobacterium tuberculosis/
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51. TB.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
52. 46 or 47 or 48 or 49 or 50 or 51
53. 19 and 45 and 52

Detailed characteristics of the included studies

Study	Bollini(1)
Population Screened	Migrants
Method of screening	X-ray. If compatible with tuberculosis, sputum smear samples were taken on three consecutive days
Principal case definition	One or more positive sample by sputum smear.
Country of Origin	Vietnam
Country where screening took place	Vietnam
Years screened	1992-94
Notes	Case definition extrapolated from study by Keane, which reports data from same IOM screening locations. Single smear positive finding considered positive.

Study	Das Gupta(2)
Population Screened	Migrants
Method of screening	Initially a chest radiograph for active TB. If radiographic abnormalities are detected, the affected individual is referred, usually to a chest specialist, for further evaluation, including additional radiographic, microbiologic (e.g., sputum acid-fast bacilli), and tuberculin tests when judged appropriate.
Principal case definition	The presence of cultures positive for *Mycobacterium tuberculosis* or radiographic improvement after at least 2 months of therapy for active disease.
Country of Origin	Multiple
Country where screening took place	Multiple
Years screened	1996-97
Notes	Primary aim of the study was to examine “the efficiency and cost-effectiveness of immigrant applicant screening and of surveillance of newly arrived immigrants were compared with investigation of close contacts active cases of TB, and all three methods were com- pared with a policy of passive case detection”. Immigrant applicant screening was a pre-entry screening programme.

Study	Gobacheva(3)
Population Screened	Refugees
Method of screening	X-ray, clinical examination, history and TST. Three sputum specimens in those with findings suggestive of tuberculosis
Principal case definition	One or more positive sample by sputum smear and/or culture.
Country of Origin	Bhutan
Country where screening took place	Nepal
Years screened	2007-09
Notes	Data on cases found were calculated from prevalence rates as raw numbers not provided. Exact criteria for selecting patients for microbiological investigation not specified “Suspected cases were referred for microbiological examination of three sputum sample by both acid-fast bacilli and liquid culture for TB". Screening was conducted for several receiving countries (USA, Canada, Australia, New Zeland, Denmark and Norway) and exact protocol is therefore likely to vary as per the country technical instructions.

Study	King(4)
Population Screened	Migrants
Method of screening	X-ray. If compatible with tuberculosis, sputum smear and culture testing.
Principal case definition	Clinical cases, or one or more positive sample by sputum smear and/or culture.
Country of Origin	Multiple
Country where screening took place	Multiple
Years screened	2009-10
Notes	A positive case was defined on the basis of one or more sputum smear or culture results. Limitations with culture testing data were acknowledged by study authors as this was not uniformly performed across all sites for all cases and not available for all individuals.

Study	Lange(5)
Population Screened	Adoptees aged between 2.5 months and 12 years, with median age of 4 months.
Method of screening	Intradermal injection of 5 tuberculin units of purified protein derivative.
Principal case definition	Latent infection defined as those with 10mm induration after PPD.
Country of Origin	South Korea
Country where screening took place	South Korea
Years screened	1985-88
Notes	Analysis based on data from a case note review, not prospective collection.

Study	Lui(6)
Population Screened	Refugees and Migrants
Method of screening	Based on 1991 Technical Instructions for Panel Physicians: X-ray, clinical examination, and if compatible with tuberculosis, sputum smear samples taken on three consecutive days.
Principal case definition	The principal case definitions for this study were smear-negative and inactive tuberculosis. Smear-negative tuberculosis was defined as: "if the chest radiograph was suggestive of active tuberculosis and sputum smears were negative for acid-fast bacilli on 3 consecutive days". Inactive tuberculosis was defined as: "if the chest radiograph was suggestive of tuberculosis that was not clinically active (e.g., showing fibro- sis, scarring, pleural thickening, diaphragmatic tenting, or blunting of costophrenic angles)". For this systematic review we considered smear-negative tuberculosis as the principal outcome.
Country of Origin	Multiple
Country where screening took place	Multiple
Years screened	1999-2005
Notes	No mycobacterial cultures were obtained during the study period and data for smear positive tuberculosis cases were not presented in the manuscript.

Study	Malone(7)

Population Screened	Migrants
Method of screening	X-ray and physical examination. If compatible with tuberculosis, sputum smear and culture testing on three consecutive samples
Principal case definition	Presumptive active tuberculosis (definition not provided and authors not contactable)
Country of Origin	Haiti
Country where screening took place	U.S. Naval Base in Guantanamo Bay, Cuba
Years screened	1991-93
Notes	Authors report that denominator data for population screened is approximate. Three consecutive sputum specimens were obtained in the morning; these specimens were treated with Kinyoun carbolfuchsin stain and sent to the laboratory at the Naval Hospital in Portsmouth, Virginia. At this laboratory the specimens were digested with sodium hydroxide and then inoculated onto Lowenstein-Jensen culture media and Middlebrook 7HIO agar.

Study	Maloney(8)
Population Screened	Migrants
Method of screening	X-ray. If compatible with tuberculosis, sputum smear and culture testing on three consecutive samples
Principal case definition	"Participants with 1 or more AFB-positive smear results were designated as AFB smear positive, and those with 3 AFB-negative smear results were designated as AFB smear negative. Any participant with at least 1 M tuberculosis–positive culture result was designated as M tuberculosis culture positive and was therefore determined to have PTB. Participants with no M tuberculosis–positive culture results were divided into 4 separate categories: (1) those with 3 negative culture results were desig- nated as being M tuberculosis culture negative; (2) those with 3 contaminated culture results were designated as having contami- nated cultures; (3) those with 3 M avium-intracellulare complex– positive results were designated as being M avium-intracellulare complex culture positive; and (4) those with at least 1 but fewer than 3 negative culture results were designated as being M tuber- culosis culture indeterminate (ie, the 2 additional culture results were some combination of negative, contaminated, or M avium- intracellulare complex)."
Country of Origin	Vietnam
Country where screening took place	Vietnam
Years screened	1998-99
Notes	Cases only reported for individuals over the age of 18 whereas all individuals over the age of 15 screened by X-ray. Screening was compulsory, but participation in this study (with reporting of

	outcomes) was voluntary, with a 95.3% participation rate.

Study	Mor(9)
Population Screened	Migrants
Method of screening	X-ray, clinical examination, history and TST. Three sputum specimens in those with findings suggestive of tuberculosis.
Principal case definition	Active pulmonary TB (Symptomatic patient with pulmonary disease and confirmed Mycobacterium tuberculosis complex culture)
Country of Origin	Ethiopia
Country where screening took place	Ethiopia
Years screened	2001-05
Notes	The primary aim of this study was: “to determine the validity of CXR screening in detecting radiological findings compatible with active PTB or with old healed tuberculosis”.

Study	Oeltman(10)
Population Screened	Refugees
Method of screening	X-ray, clinical examination, history. Three sputum specimens in those with findings suggestive of tuberculosis
Principal case definition	Clinical and, or AFB sputum smear positive cases.
Country of Origin	Lao People's Democratic Republic
Country where screening took place	Thailand
Years screened	2004-05
Notes	The primary aim of this study was to present data from an outbreak of MDR TB among US-bound Hmong Refugees and the results of enhanced screening and treatment protocol among this population after initial detection of the outbreak. Latent TB detected using tuberculin skin tests (TSTs) with induration >5 mm considered a positive test result.

Study	Painter(11)
Population Screened	Migrants
Method of screening	Migrants were screened according to 2009 technical instructions published by CDC: X-ray, clinical examination, and if compatible with tuberculosis, sputum smear samples taken on three consecutive days. “Following the results of chest radiograph applicants were invited to participate in a study of TST and QFT for which they would be provided the results, but the result of which would not affect their visa application.”
Principal case definition	QuantiFERON ®-TB Gold In-Tube Assay (QFT) and TST (varying size) positive cases.
Country of Origin	Vietnam
Country where screening took place	Vietnam
Years screened	2008-10
Notes	The primary aims of this study were to: 1. Compare the sensitivity of QuantiFERON ®-TB Gold In-Tube Assay (QFT) and TST for culture- positive pulmonary TB. 2. Compare the age-specific and overall prevalence of positive TST and QFT among applicants with normal and abnormal CXR. The study also reports data on 20,100 visa applicants screened over the age of 15 as part of their visa medical exam and that 211 had culture-confirmed pulmonary tuberculosis.

Study	Plant(12)
Population Screened	Migrants
Method of screening	X-ray, clinical examination and history. Three sputum specimens in those with findings suggestive of tuberculosis
Case definition	AFB sputum smear and/or culture positive cases.
Country of Origin	Vietnam
Country where screening took place	Vietnam
Years screened	1997-01
Notes	Screening was compulsory but participation in this study was voluntary (with reporting of outcomes).

Study	Wang(13)
Population Screened	Migrants
Method of screening	X-ray followed by three sputum cultures in those with findings suggestive of tuberculosis
Case definition	Inactive tuberculosis defined by authors as: “radiograph shows evidence of tuberculosis, it is repeated at a minimum interval of 3 months to confirm stability of the lesion. In addition, 3 sputum cultures, incubated for 7-8 weeks, taken at least 24h apart, are required to be negative.”
Country of Origin	Multiple
Country where screening took place	Multiple
Years screened	1982-85
Notes	Data reported for migrants from China, Hong Kong, Taiwan, Korea, India, Philippines and Japan.

Study	Watkins(14)
Population Screened	Migrants
Method of screening	X-ray
Principal case definition	X-ray positive cases
Country of Origin	Vietnam
Country where screening took place	Vietnam
Years screened	Not stated
Notes	Primary focus of study was on subjective and clinical indicators of health status, not tuberculosis screening, therefore data were extracted from secondary analyses within the study.

Study	Yanni(15)
Population Screened	Refugees
Method of screening	Corresponding author confirmed that the study used CDC Division of Global Migration and Quarantine 2007 TB Screening guidance: X-ray, clinical examination, history and sputum testing for M. tuberculosis.
Principal case definition	One or more positive sample by sputum smear and/or culture.
Country of Origin	Iraq
Country where screening took place	Jordan
Years screened	2007-09
Notes	Primary aim of study was to provide a health profile of Iraqi refugees therefore data were extracted from secondary analyses presented in this study. Latent TB cases were defined as: "Positive TST C 10 mm with normal chest X-ray, and negative smears and culture"

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