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Cost-effectiveness of tuberculosis control strategies among immigrants and refugees

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ABSTRACT: Today, in Western Europe, Canada and the USA, more than half of all new active tuberculosis (TB) cases occur among foreign-born migrants. This article examines the impact of migration from high TB-incidence to low TB-incidence countries, and compares the cost-effectiveness of different TB control strategies.

A Medline search was conducted to identify relevant English language publications prior to December 2003. Additional articles were identified from the reference lists from these publications.

Despite the high proportion of active cases in low-incidence countries attributable to foreign-born residents, the public health impact is relatively low. Current chest radiograph screening programmes have little impact and are not cost-effective. Screening with sputum culture would improve cost-effectiveness marginally. Treatment of latent infection detected through screening with tuberculin skin testing or chest radiographs may require coercive measures to maximise impact and cost-effectiveness. In contrast, contact tracing, particularly within ethnic communities, appears to be more cost-efficient and less intrusive.

In low-incidence countries, screening of migrants at entry has little overall impact and is not a very cost-effective tuberculosis control strategy. More effective alternatives include contact tracing delivered through primary care and increased investment in global tuberculosis control.

KEYWORDS: Cost-effectiveness, migration, screening, tuberculosis control, tuberculosis diagnosis, tuberculosis prevention

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Historically, human migration has had a major impact on the spread of tuberculosis (TB) [1–4]. Early in the nineteenth century, 25% of deaths in Western Europe were attributable to TB [5]. Western Europeans subsequently carried this disease to central Africa, south and Southeast Asia, and the Americas, resulting in major TB epidemics in these regions [5]. Since the 1950s, the incidence of active TB has fallen dramatically in Western European and North American countries with established market economies [1–4]. However, TB incidence remains high in most low-income countries and, in some, has even increased since the 1980s [6]. Migrants from these low-income countries continue to have relatively high rates of active TB for years after they migrate to high-income, low-incidence countries [7–9].

METHODS

A Medline search was conducted to identify English language publications prior to December 2003. The search strategy included the keyword tuberculosis, together with any of the following: migration, immigration, refugees, screening, chest radiograph, serology, seroassay, serological tests, cell-mediated immunity, tuberculin skin test, purified protein antigen, purified protein derivative, sputum culture, sputum smear, DNA amplification, PCR, cost-effectiveness, effectiveness, and

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economic analysis. Articles relevant to the topics of interest were then searched for additional references.

RESULTS

Current levels of migration

Since the 1980s, human migration has reached an unprecedented scale [10]. In 1990, the International Organization for Migration estimated that 120 million people were long-term residents of a country other than their country of birth. Just over 10 yrs later, this has increased to >150 million [11]. Short-term travellers are even more numerous. For example, >50 million foreign residents entered the USA in 2002 as short-term visitors [12] compared with 1.1 million who entered seeking permanent-resident status [13].

Migration and TB in low-incidence countries

Most migrants and many visitors travel from countries where the incidence of active TB is >40 per 100,000 (high incidence) to countries where the incidence is <25 per 100,000 (low incidence) [14]. The incidence of active TB is higher among foreign-born populations than among native-born populations. In the UK, for example, the crude incidence of active TB in the native-born population in 1998 was 4.4 per 100,000 compared with 121–210 per 100,000 in certain foreign-born populations. The increased risk among foreign-born individuals may continue for 20 yrs after migration [7–9]. As a result, in low-incidence countries, the foreign-born population account for a large proportion of reported cases of active TB, ranging from 35–70% of all cases [1–4, 15].

IMPACT OF TB AMONG THE FOREIGN-BORN WITHIN LOW-INCIDENCE COUNTRIES

Public health impact on the native-born population

Nowadays, in most low-incidence countries, the majority of cases of active TB arise among the foreign-born; this can result in significant transmission within certain foreign-born communities in these countries [16]. However, restriction fragment length polymorphism studies have detected relatively little TB transmission from foreign-born residents to the general population [3, 17]. The estimated proportion of active TB cases among the native-born that can be attributed to transmission from the foreign-born may be as low as 2% [18] or 11% [19], or as much as 17% [16, 20–22]. In one USA study, foreign-born TB patients were more likely to have acquired TB from USA-born individuals than *vice versa* [20]! A recent study indicated that 17% of active TB cases among Dutch patients were acquired from foreign-born cases, but the absolute risk in Dutch-born persons of developing active TB following transmission from a foreign-born patient was less than one in 100,000 [16]. At present, it appears that, in low-incidence countries, the overall public health impact of TB among foreign-born persons is modest.

TB transmission within ethnic communities

Many active TB cases among the foreign-born are attributable to the reactivation of latent TB infection. Reactivation rates are highest during the first 2–5 yrs following migration [1, 2, 23]. In some cases, however, active TB cases are the result of new infection acquired after migration, as demonstrated in an analysis conducted in the Netherlands of TB cases among Moroccan-origin residents [3]. In another Dutch molecular epidemiological study, isolates from all new active TB cases reported over 5 yrs demonstrated that 20–30% of all TB within several foreign-born populations was attributable to transmission within the Netherlands [16]. In the UK, even the children of foreign-born residents have higher active TB rates than the general population [24], particularly if regular visits are made to the country of origin [24, 25].

Economic impact

Although active TB incidence is higher among the foreign-born than within the general population, absolute rates are low, as are transmission rates. Nonetheless, the economic impact of TB among the foreign-born is substantial in low-incidence countries. In the early 1990s, total annual healthcare expenditures for TB exceeded $700 million in the USA [26]. Given that the foreign-born now account for close to 50% of all TB cases in the USA, TB among the foreign-born accounts for more than $350 million in healthcare expenditures annually in that country. Levels of expenditure are probably comparable in other industrialised countries, such as Canada, the UK and in Western Europe, where more than half of all cases arise among the foreign-born [2, 27].

SCREENING FOR ACTIVE TB AMONG PERMANENT-RESIDENT APPLICANTS

Previous and existing chest radiography screening programmes

Screening for TB was implemented in a number of industrialised countries shortly after World War II, when refugees from Europe had high rates of active TB. These early screening programmes employed chest radiographs, which were popular in that era as a method of active detection of TB disease [15]. However, mass screening of the general population has since been abandoned, not only because the incidence in the general populations of these countries has declined, but also because it was demonstrated repeatedly that such screening had no appreciable impact on the incidence of smear-positive cases, overall morbidity or mortality [28, 29].

However, almost all high-income industrialised countries, with the exception of Italy, continue to utilise chest radiography screening for the detection of active TB among applicants for permanent residence [30]. In the UK, applicants undergo radiography at international ports upon arrival, and are subsequently referred to the health authority of the district of intended residence [31]. In the Netherlands, applicants undergo a screening chest radiograph within 1 week of arrival and at 6-month intervals for 2 yrs thereafter [3]. For applicants to Canada, screening chest radiographs are performed where the application is made, either overseas or within Canada [32]. Applicants with latent TB and an abnormal radiograph consistent with a prior TB infection (so-called ''inactive TB'') are referred to Canadian health authorities for follow-up after immigration [32].

General considerations concerning utility of screening programmes

Screening for a disease is justified if that disease is relatively common and treatable. The ideal screening test should be inexpensive, easy to administer, cause no discomfort to the patient, and offer both high sensitivity and specificity [33].

TABLE 1 Prevalence of tuberculosis (TB) among migrants to low-incidence countries

Authors [ref.]	Year	Population	Prevalence %		
			Active TB	Latent TB infection	
				With abnormalities#	Without abnormalities#
Blum *et al*. [34]	1993	Amnesty programme adjustments for illegal migrants from Mexico in the USA	0.08	5	42
Markey *et al*. [35]	1986	Port of entry screening of all immigrants to the UK	0.04	0.1	NA
Pitchenik *et al*. [36]	1982	Haitian refugees in the USA	0.65		
Nolan *et al*. [37]	1987	Southeast-Asian refugees in the USA	0.8	5.6	35.7
Dasgupta *et al*. [29]	2000	Permanent-resident applicants in Canada	0.15	2.6	NA

NA: not available. #: on the chest radiograph.

As shown in table 1, only a small proportion of permanent-resident applicants evaluated through TB screening programmes are found to have active pulmonary TB at the time of evaluation [29, 34–37]. The prevalence is higher among refugees from high-incidence countries, although still <1% [34, 36, 37]. Conversely, the prevalence of latent infection with chest radiograph abnormalities (inactive TB and/or apical fibronodular disease) is substantially higher, with estimates ranging from 3–5% [36, 37]. Latent infection without chest radiograph abnormalities is even more common, with prevalence estimates between 35% and 42%.

Effective treatments exist for both active TB and latent infection. While the risk of reactivation of latent TB without chest radiograph abnormalities is ~0.1%·yr^{-1} [37, 38], the reactivation risk rises to 0.2%·yr^{-1} in the presence of a granuloma [39, 40] and 0.6%·yr^{-1} in the presence of apical fibronodular disease [37, 41].

Two widely used screening tests for TB are the chest radiograph to detect active disease and the tuberculin skin test to detect latent infection. Sputum cultures, acid-fast staining and nucleic amplification tests are alternative tools for active TB screening. Seroassays and tests of cell-mediated immunity may have a role in the future for the identification of TB infection or disease, but these tests are still under development, and their potential utilities are unknown. The properties of these tests are reviewed below.

Screening tests to detect active TB

Chest radiograph

In the studies summarised in table 2, chest radiography had a sensitivity of 59–82% and a specificity of 52–63% for the detection of active pulmonary TB [35, 40, 42–44]. The differences in these estimates may be attributed to variations in the gold standard used (*e.g.* number of sputum cultures), as well as the frequency of TB and other pulmonary diseases in the populations studied. Chest radiography is less sensitive and less specific among HIV-infected individuals with advanced immunosuppression [43, 44]. If chest radiography has an overall sensitivity of 70% and specificity of 60%, then,

TABLE 2 Sensitivity and specificity of chest radiography for the diagnosis of active pulmonary tuberculosis (TB)

	Barnes *et al*. [42]	Tattevin *et al*. [43]	Cohen *et al*. [44]	Markey *et al*. [35]	Grzybowski *et al*. [40]
Population	Patients hospitalised with suspicion of active TB	Patients hospitalised with suspicion of active TB	Patients hospitalised with suspicion of active TB	Individuals suspected to have active TB on entry to England (UK)	Voluntary participants, inner-city TB screening initiative
Gold standard	Sputum cultures (number unspecified)	Three spontaneous sputum cultures	Up to six sputum cultures, some induced	Three sputum cultures and gastric aspirate cultures	One or two spontaneous sputum cultures
Patients n	392	214	100	196	1333
Active TB cases n	188	47	44	47	8
Smear positive %	82	66	75	59	60
HIV positive %	No data	11	29	No data	No data
Sensitivity of radiography %	80	71	73	64	75
Specificity of radiography %	Insufficient data	52	63	63	99

with a prevalence of active disease of 1%, chest radiography would have a positive predictive value <1%. This means that when chest radiography is used for screening for active TB in a foreign-born population, the vast majority of positive results will be falsely positive.

Sputum culture

Microbiological culture of three to six sputum samples is highly sensitive for active pulmonary TB and often serves as the gold standard for TB detection [45, 46]. However, as shown in table 3, the sensitivity of a single culture is comparable with that of a chest radiograph [28]. The specificity of mycobacterial culture is very high as there are very few false positives (1–2%) resulting from cross-contamination during laboratory handling [47]. Culture results are available ⩾2 weeks after sputum sampling. Sputum may be obtained by asking the subject to cough or by inducing cough with saline aerosol, a technique termed sputum induction. In one study, culture of a single induced sputum sample was found to have greater sensitivity (96%) than the culture of three spontaneous sputum samples (81%) [48].

Acid-fast staining

Acid-fast staining of a sputum sample will reveal mycobacteria at a threshold of 5,000–10,000 bacilli·mL^{-1} of sputum [45, 46]. Sensitivity may be improved through changing the concentration of sputum samples and/or the use of fluorescent microscopy [45, 46]. Specificity depends on the relative prevalence of active pulmonary disease from *Mycobacterium tuberculosis* compared with that caused by nontuberculous mycobacteria. As indicated in table 3, acid-fast staining is more specific but less sensitive than chest radiography.

Amplification tests

These tests selectively replicate mycobacterial DNA segments. Among smear-positive cases, these tests are 95% sensitive [49–51]. However, among smear-negative, culture-positive cases, the sensitivity is lower (50–70%) [49–52]. PCR test results are highly specific (>98%) [49–52] and may be available within hours of sputum sampling.

Immunological tests

Most existing seroassays for TB measure immunoglobulin G responses to single antigens, such as the 38-kDa antigen. Seroassays are more sensitive for smear-positive disease than smear-negative disease, and are poorly sensitive among the immunocompromised [62]. Sensitivity (21–90%) varies with the antigen used and the burden of disease in the population examined. No single antigen is recognised by serum antibodies from all patients [59, 63]. Specificity is high when the control population tested includes only normal healthy volunteers, but lower when the controls have latent infection with TB. Assays that involve cocktails of antigens are presently in development [64]. Tests of cell-mediated immunity measure cytokines and interleukins or their messenger RNA precursors. One commercialised test kit is available (Quantiferon©; Cellestis International, Carnegie, Australia), but, to date, published results are somewhat disappointing [55], although ongoing work may improve sensitivity and specificity. Results from research laboratories have demonstrated better sensitivity and specificity, which is comparable or superior to the chest

TABLE 3 Sensitivity, specificity and positive predictive values of commonly used tests for the diagnosis of tuberculosis (TB) disease

Test	Chest radiography	Microbiological			Amplification	Immunological		
		Smear	Single culture	Three cultures	PCR	TST	Serology	Cell-mediated immunity test
Sensitivity % [ref.]								
Pulmonary TB overall	59–82 [35, 40, 42–44]	50–80 [28, 46]	80–85 [28, 46]	80–100 [28, 46]	50–95 [49–52]	53–90 [53]	21–90 [54]	53–77 [55, 56]
Smear positive	80 [35, 40, 42–44]	100 [28, 46]	85–96 [28, 46]	90–100 [28, 46]	95 [49–51]	53–73 [57, 58]	45–96 [52, 59–61]	
Smear negative	60 [35, 40, 42–44]	0	50 [28, 46]	80 [28, 46]	48–53 [49–52]	90 [52]	16–97 [52, 59–61]	
Specificity % [ref.]	52–99 [35, 40, 42–44]	95 [28, 46]	98 [47]	98 [47]	98 [49–52]	5[¶] [53]	80–100 [54]	64–100 [55, 56]
Positive predictive value[#] %	2.9	11.6	29.3	31.3	26.9	<1	5.2	3.5

TST: tuberculin skin test. [#]: calculated for 1% prevalence of active TB, using the mid-point of the range of sensitivity and specificity for each test; [¶]: the specificity of positive TST is to distinguish active TB disease from latent TB infection.

radiograph [54], but these laboratories utilise highly complex procedures with lymphocyte separation, *in vitro* culture and stimulation, and detection of cytokines using real-time PCR. Nevertheless, results from these laboratories suggest that these tests may be promising for the diagnosis of disease and may be able to identify, among all those with latent TB infection, those individuals who are at a particularly high risk of disease [65].

Predictive values of tests for active TB

Using average estimates of sensitivity and specificity, and a disease prevalence of 1%, the positive predictive values for chest radiography, tuberculin skin test (TST), acid-fast bacilli smear, single sputum culture, multiple sputum cultures, and seroassays are shown in table 3. The negative predictive value of all these tests is >99%. Most of these tests, including the chest radiograph, have a positive predictive value (PPV) of <10%. Sputum culture has a higher PPV, which is attributable to its greater specificity. A single sputum culture was estimated to have a PPV of 25%, and three sputum cultures would result in a PPV of 33%.

Cost-effectiveness of a chest radiography screening programme for active TB

Permanent-resident applicants residing in Canada at the time of application (*e.g.* visitors, students) undergo chest radiography screening at Canadian centres. A cost-effectiveness evaluation of chest radiography screening was conducted, using a cohort of all immigration applicants screened in the province of Quebec. During the 1-yr period examined (June 1996–June 1997), 12,898 screening chest radiographs were performed, and 722 were considered to be compatible with active TB. Seventeen applicants were confirmed to have active pulmonary TB through the chest radiography screening programme. Using chart review and micro-costing techniques, the cost of detection and treatment of active TB through the programme was $31,418 (Canadian) per active case detected and treated. Conservatively estimating the cost of passive diagnosis and treatment to be $11,090, the incremental cost of the chest radiography screening programme was $20,328 per active case. This analysis was conducted from the perspective of the Canadian government, as Canada has a publicly funded healthcare system. Direct and indirect costs incurred by individual patients were not included [32].

Cost-effectiveness of alternative tools for active TB screening

The costs of alternative screening tests, as outlined in table 4, were derived from published sources and estimates provided by the laboratories of the McGill University Health Centre (Montréal, Canada). The material costs of nucleic acid amplification assays are six-fold higher than the other tests that were considered. Labour costs for both amplification tests and sputum culture are considerable, particularly if sputum is induced. Using these cost figures and cohort data from a previous study [32], rough estimates of the cost to detect each active case from screening using different tests are shown in table 5. Although the cost of the screening test itself would be higher using sputum culture, the cost per active case of TB disease detected would be lower with a single sputum culture than with chest radiography. Similarly, despite the low cost for

TABLE 4 Costs of potential screening tests for active tuberculosis (TB)[#]

Cost components	Radiological	Microbiological			Amplification	Immunological		
	Chest radiograph	Induction	Smear	Culture	PCR	TST	Cell-mediated immune tests[¶]	Serology
Capital costs	$500000 for radiography unit	Room $15000 or booth $5000; nebuliser $1200	$5000 for light microscope	$65000 for Bactec unit (Becton, Dickinson and Co., Franklin Lakes, NJ, USA)	$5000–10000 for PCR unit	None	$149000	$50000–100000 for light reader
Materials	$5	$1	$5	$5	$35–50	$1.25	$25–120	$3–5
Labour	$10	$24	$15	$30	$15–30	$6	$10–150	$5
Overall cost per test[+]	$22	$25	$13	$25	$75	$7	$35–270	$8–10
Complexity[§]	3	1	1	3	4	2	5	2
Time to result	1 h	15 min	1 h	3–8 weeks	4 h	2–3 days	1–2 days	1 h

TST: tuberculin skin test. [#]: all costs in Canadian dollars; [¶]: tests of cell-mediated immunity range from Quantiferon© (Cellestis International, Carnegie, Australia), the simplest and only commercially available test, to tests performed in research laboratories, which performed lymphocyte separation, *in vitro* culture with stimulation, and detection using RT-PCR; [+]: overall cost includes material and labour, but does not incorporate depreciation on capital or other overhead costs; [§]: complexity scored from 1) very simple, requires little training to 5) very complex, requires sophisticated equipment and highly trained technicians.

TABLE 5 Total cost per active tuberculosis (TB) case detected using different screening tests, in a hypothetical cohort of 1,000 immigrants, with 1% prevalence of active TB[#]

	TST	Chest radiograph	Sputum TB culture[¶]		Sputum TB PCR (one sample)	Serology	*In vitro* tests of CMI
			One specimen	Three specimens			
Cost to screen 1000 persons $	7000	22000	50000	150000	75000	19000[§]	45000[§]
Cases of active TB detected n	8	7	8.2	9	7.3	5.5	6.5
False-positive tests n	470[f]	238	19.8	19.8	19.8	99	178
Costs of work-up after positive test[+] $	92254	47285	5404	5558	5230	20169	35609
Total cost for screening $	99254	69285	55404	155558	80230	39169	80609
Total cost per active case detected $	12407	9898	6757	17284	10990	7122	12401

TST: tuberculin skin test; CMI: cell-mediated immunity. [#]: all costs in Canadian dollars; [¶]: sputum TB culture includes cost of sputum induction, but does not include acid-fast bacilli smear; [+]: average costs were $193 for the evaluation of persons with positive screening test in a chest specialist clinic [32], and costs do not include overhead, administration or patient costs; [§]: serology and CMI include the cost of drawing blood samples ($10); [f]: assume that the prevalence of positive TST would be 50%.

initial screening with TSTs or serology, overall costs to detect each active case would be higher because of their poor specificity. This is because screening with a more specific test, such as sputum culture, would result in a much smaller number of false-positive tests. This would result in much lower costs for the further evaluation of individuals with false-positive tests. This is important because the second step of medical evaluation and further investigation is more expensive than all screening tests.

SCREENING FOR LATENT TB INFECTION

The TST involves the intradermal injection of purified protein antigen, with measurement of the resulting induration within 48–72 h. Development of induration requires a cell-mediated immune response. The TST is the diagnostic test used to define latent infection and is considered to be the most sensitive test for this condition. However, when the TST is used in patients with active TB, 10–47% will have a falsely negative TST [52, 57, 58], and the size of the TST reaction is not useful for distinguishing between prevalent active disease and latent infection [66].

The use of the TST as the primary screening test in the USA is consistent with a shift in emphasis from the detection of prevalent active TB to the detection of latent infection. The US Institute of Medicine has recommended TST testing among all immigrants from countries with high TB incidence [67]. The prevalence of latent infection among permanent-resident applicants is 30–75% [67]. Future risk of TB may be reduced through preventive treatment with agents such as isoniazid [42, 68]. The specificity of the TST for latent infection can range 60–90% [53] with false-positive tests due to previous bacillus Calmette–Guérin vaccination or exposure to environmental, nontuberculous mycobacteria, both of which are common among applicants from developing countries [69].

A recent cost-effectiveness analysis concluded that tuberculin screening of all immigrants and refugees to the USA would result in net cost savings to the American society. In this analysis, a hypothetical cohort of immigrants entering the USA during 2000 was constructed. The analytical horizon was the expected lifetime of the cohort. Using a decision analysis model, the investigators calculated that, without TST screening, 13,933 active TB cases would occur, but, with screening and isoniazid treatment, 4,342 cases would occur. The net cost without TST screening would be $338 million, while the cost with TST screening would be $258 million. There would, therefore, be a net saving of $8,320 per case prevented. Patient-incurred costs (transportation, time) were included in this analysis, increasing costs associated with active disease because of the loss of time attributable to hospitalisation. However, administrative costs and the costs that would be incurred to institute a TB screening programme were not included in the analysis. Such costs would substantially increase the cost of a TST screening programme. In addition, the completion rates for latent TB infection (LTBI) did not take into account the following: refusal to undergo tuberculin testing; failure of those with positive TST to report for medical evaluation; physician noncompliance with guidelines for the prescription of therapy; and refusal of patients to start the therapy. In several reports from large-scale screening programmes, these problems resulted in a very substantial reduction in overall programme effectiveness, as only 11–30% of individuals with a positive TST completed an adequate course of LTBI therapy [34, 70–74].

The TST should be more sensitive in detecting latent infection, because chest radiographs will be abnormal in only 10–20% of those with latent infection. However, the subgroup of individuals with latent TB infection who have abnormal chest radiographs are at an increased risk of reactivation. Therefore,

chest radiography screening, followed by TST screening, may be more cost-effective if this results in the treatment of fewer individuals with latent infection but who have a much higher risk of reactivation.

This approach has been examined in a study of the cost per active TB case prevented through chest radiography screening in Canada. Among 722 permanent-resident applicants with chest radiograph abnormalities identified over a 1-yr period, 353 were diagnosed as having latent infection: that is, TST was positive, chest radiograph abnormalities were stable, and sputum cultures were negative. A Markov model was used to examine the number of active TB cases prevented through treatment of these patients. In this model, the yearly probability of reactivation among TST reactors varied with chest radiograph abnormalities (no TB-compatible changes 0.1%, granuloma 0.2%, fibronodular disease 0.6%). Among these 353 patients, 145 actually completed preventive therapy, resulting in the prevention of 7.85 cases of active TB. The incremental cost per active TB case prevented was $39,409. All programme costs, including administrative costs, were included in this calculation. Had 90% of eligible patients been prescribed preventive treatment and 80% been compliant, the incremental cost per case prevented would have decreased to $21,240. The analysis was conducted from the perspective of the government. Patient-incurred costs were not included [32].

An alternative scenario compared the chest radiograph *versus* TST as the primary screening tool among immigrants to Canada, a low-incidence country. This study relied on Markov modelling and was conducted from the perspective of the Canadian government. The costs borne by patients were not included. In this analysis, the annual risk of TST reactors was set at 0.1% for those without chest radiograph abnormalities and 0.66% for those with TB-compatible abnormalities. If the prevalence of latent TB infection was 50%, chest radiography screening was projected to prevent 1.2 active cases per 1,000 individuals screened, whereas TST screening would prevent 2.9 cases per 1,000 individuals screened. The incremental cost per case prevented was $10,627 for chest radiography screening compared with $66,750 for TST screening. Higher costs of the TST screening strategy were attributed to the identification of a larger number of low-risk, as well as false-positive, reactors as candidates for chemoprophylaxis.

ALTERNATIVE APPROACHES TO SCREENING AT ENTRY

The evaluation of close contacts of active pulmonary TB cases has been established as a cost-effective method for detecting as well as preventing active TB. Studies in the UK have estimated that 1% of all contacts had active disease at the time of initial screening, and that 10% of all active TB cases were identified through contact screening [75–77]. A contact-tracing programme in Quebec resulted in an incremental $815 saving per active case detected, because of the relatively high number of active cases detected (six cases among 103 infected contacts of 244 identified) and the reduced need for hospitalisation compared with a passive detection strategy [32]. Contact tracing also resulted in incremental savings of $600 per active case prevented, because of the detection of a large number of individuals with LTBI and the high rate of completion of LTBI therapy among these individuals [32].

A recent study conducted in an economically deprived area of the UK with a large proportion of Bangladeshi immigrants demonstrated that contact tracing was more effective than new-entrant screening. Among 263 contacts of smear-positive index cases, 13 cases of active TB were diagnosed compared with no cases detected among 322 new entrants screened. Interestingly, when 227 contacts of nonpulmonary index active TB cases were evaluated, two active TB cases were identified. The investigators suggested that, although nonpulmonary TB is not transmissible, it may identify communities or families at an increased risk (*e.g.* high-density housing, frequent return trips to country of origin) [78].

LIMITATIONS OF SCREENING OF IMMIGRANTS AND REFUGEES

One of the greatest limitations of screening new immigrants and refugees is that screening is performed only once at the time of initial entry, and only for individuals who seek permanent-resident status. However, permanent residents make frequent return visits, and there are far more foreign-born migrants entering industrialised countries under other legal statuses. Of all foreign-born entrants to the USA, only 2% seek permanent residence. The remainders are students, migrant labourers, individuals visiting friends and family in the USA, other categories of visitor, and persons who enter illegally. All of these may stay for many years, but they are not screened at entry. Permanent residents may also return to their country of origin, often doing so repeatedly. In two studies conducted in England, it was estimated that 20–30% of all TB cases among foreign-born permanent residents were due to re-exposure during these return visits [24, 25]. Such cases will not be prevented by screening programmes.

CONCLUSIONS

The magnitude of human migration from high TB-incidence regions to low-incidence regions has reached an unprecedented scale. Foreign-born individuals currently account for the majority of active TB cases in most low-incidence countries. The costs of treating these individuals are substantial. While rates of transmission to the general population are low, transmission within specific ethnic communities of low-incidence countries may be higher.

When considering the most cost-effective approach for the control of TB in foreign-born migrants, it is important to remember that cost-effectiveness is affected by the perspective of the analysis (government, private payer, patient, society), costs of services (evaluations, tests, hospitalisation, transportation), and the effectiveness of available interventions. Existing TB screening programmes for migrants to low TB-incidence countries have used chest radiography to detect active TB in permanent-resident applicants. Due to the very low prevalence of active TB in this population and the low PPV of the chest radiograph, radiographic screening for active TB at entry has minimal impact and is not cost-effective. The major potential benefit of screening at entry is the detection of individuals with LTBI and abnormal chest radiographs, but only if they receive preventive therapy. This means that the screening programme must have the capacity to provide treatment for LTBI. Given the current recommended standard of isoniazid treatment for 9 months, a substantial infrastructure is necessary to ensure

adequate compliance, and to ensure that adverse events, which can rarely be fatal, are detected and managed promptly. This increases the expense and complexity of any screening programme. Nevertheless, the detection and treatment of inactive TB through chest radiography will be more cost-effective than the detection of latent infection through TST, but neither is highly cost-efficient.

The replacement of chest radiography screening with sputum culture would offer a small improvement in cost-effectiveness, but would not detect latent infection. Tests of cell-mediated immunity and seroassays involving cocktails of antigens are emerging technologies that offer the potential to both detect and differentiate active and LTBI. However, these new technologies have not been evaluated for screening purposes and, at the present time, are generally more costly than chest radiograph or TST, so their utility and cost-effectiveness remain unclear at this time.

Effective TB screening strategies are also needed for all other entrants, as well as for permanent residents who return home to their high-incidence countries. Designing screening programmes that address all of these potential sources of TB infection is likely to be complex and expensive. A more effective use of resources may be comprehensive contact tracing within foreign-born communities through local primary care networks.

The ideal long-term tuberculosis control strategy would be global investment to improve tuberculosis control in high-incidence countries. If successful, this could result in a global reduction in tuberculosis incidence, which would reduce the risk of tuberculosis among human migrants travelling from high tuberculosis-incidence to low tuberculosis-incidence regions. Such a strategy would be more humanitarian and may be more cost-effective than the current approaches to tuberculosis control among these migrants.

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