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PRE-IMMIGRATION SCREENING PROCESS AND PULMONARY TUBERCULOSIS AMONG ETHIOPIAN MIGRANTS IN ISRAEL

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SHORT TITLE:

Pre-immigration screening to migrants to low-TB country

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ABSTRACT

Israel absorbs displaced immigrants from Ethiopia, in which tuberculosis incidence is 44 times higher than in Israel (344 *vs*. 8 per 100,000, respectively). The aims of this retrospective cohort study were to evaluate the pre-immigration screening process initiated in 2001 on pulmonary tuberculosis (PTB) morbidity and to assess its cost-effectiveness.

Ethiopian immigrants who were screened before departure (study group) were compared to those who were screened after arrival (comparison group).

Between 1998 and 2005, 24,051 Ethiopian immigrants arrived in Israel. PTB was diagnosed in 332 (1.4%), demonstrating incidence density of 325 patients: 100,000 persons-years. PTB cumulative incidence was lower in the study than in the comparison group, demonstrating 711 and 1,746 patients: 100,000 immigrants, respectively (RR= 0.4). PTB was detected earlier in the study than in the comparison group (193 *vs.* 487 days from entry, respectively, $p<0.01$). Disease incidence declined significantly during the first two years following immigration. A five-year predictive model indicated that 98 individuals would be free of PTB, saving US $91,055 annual treatment cost, due to screening.

Pre-immigration screening process reduced PTB incidence in subsequent years following immigration. PTB was diagnosed earlier in the screened group than in the comparison group and the process was found cost-benefit and cost-effective.

KEY WORDS

Cost-effectiveness**,** immigration**,** Israel**,** latent tuberculosis infection, screening, tuberculosis

INTRODUCTION

The flux of international immigration from developing to industrialized countries[a] has increased by 17% between 1990 and 2005, and it is estimated that more than 190 million immigrants[b] are living outside of their home countries [1]. This global movement is accompanied by public health concerns of the host countries to the threat of disseminating communicable infections from the immigrants to indigenous population [2].

Israel has encouraged immigration of people of Jewish descent. This special trend of homecoming to Israel is distinctive in comparison to labour migration or immigration elsewhere, as Jewish immigrants are never refused, regardless of her/his health status, age, education or sex. Thus, there exist a possibility that the composition of newcomers to Israel may not meet the requirement for work force, and potentially may include a larger proportion of older and sick people, more women and children and un-educated individuals. These sub-populations at risk possibly may be less prepared medically, mentally and socially to the stresses involved in immigration.

Tuberculosis incidence in Ethiopia is 344 per 100,000 populations (2005 data [3]). Following a few events of detecting retrospectively immigrants who were clinically infected with communicable diseases such as pulmonary tuberculosis (PTB), meningococcal meningitis and rubella, even during the flight to Israel, the Israeli Public Health Services decided to change the process of medical absorption of the Ethiopian immigrants. Therefore, a pre-immigration screening process of the eligible immigrants was initiated by establishing a "health station" in the Israeli embassy compound in Addis Ababa in April 2001. The targets of the new screening program were to minimize the arrival of infected immigrants, to speed the

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[a] "Established market economies" as defined by the World Bank. Source: World Bank. World Development Report 2006: Equity and development. New York: Oxford University Press, 2005.

[b] Defined as a foreign born person legally admitted and expected to settle in the host country.

medical screening procedures by providing the immigrants "health clearance" within the first days in Israel and to contain health expenses, as the immigrants are granted health insurance upon arrival. Whereas previously it had taken approximately a month to perform similar screening procedures, while the immigrants were already in Israel. Only following "health clearance" could the immigrants take part in educational, social and labour activities. Additionally, the screening procedure in Ethiopia reduces the cost of PTB treatment in Israel, while benefiting from the lower cost of health commodities in Ethiopia, and from the high quality of Israeli health providers.

The pre-immigration screening procedure in Ethiopia included medical evaluation, vaccinations against infectious diseases and TB screening: first step for tuberculin skin tests (TST), which were read 48-72 hours following intra dermal injection, and chest radiographs (CXR), which were performed for each immigrant older than six months, and were then sent to Israel for reading. Individuals complaining cough, weight loss, fever and those who CXR showed changes suggestive of PTB were asked to provide sputum in three consecutive days for microscopy. PTB cases diagnosed were treated in Ethiopia in the directly observed therapy approach for two weeks or until sputum smears were negative, ensuring that the patients were no longer infectious. All other immigrants were airlifted and housed in absorption centres in Israel, which are hostels in the community guided by professionals who are in the assisting immigration process. A public health nurse visited the absorption centre within the first two weeks, gathered the medical documents, collected blood samples for HIV and performed a second-step TST to all individuals whose first step showed indurations lesser than 10mm. A positive reaction to the second test represents a boosted reaction indicating that infection most likely occurred in the past. Patients with positive findings were referred to the regional TB clinic. Individuals identified with latent TB infection (LTBI) were recommended preventive therapy and directly observed therapy was initiated for LTBI individuals younger than 18 years of age or HIV infected.

The aims of the study were to evaluate the impact of the pre-immigration screening process on PTB morbidity rates among Ethiopian immigrants in Israel and to assess its cost-effectiveness as compared to the post-immigration screening process.

MATERIALS AND METHODS

A retrospective cohort analysis of surveillance data for all Ethiopian immigrants developing PTB in Israel between January 1998 and December 2005 was performed. In conjunction with the inauguration of the health station in Addis Ababa and the establishment of the pre-immigration process in April 2001, the *study group* contained immigrants in whom pre-immigration screening was performed and arrived in Israel between June 2001 and December 2005. The *comparison group* composed of immigrants in whom post-immigration screening was performed and arrived in Israel between January 1998 and May 2001 (historical comparison).

The TB national registry has been the primary source for the reporting of PTB. HIV status was obtained by cross-matching PTB cases individually with the national name-based HIV/AIDS registry. The figures of Ethiopian immigrants to Israel were obtained from the Ministry of Absorption and from the Jewish Agency. Dates of arrival in Israel and mortality data were obtained by linking each of the PTB cases with the national civil registry. Those figures enabled an accurate calculation of the time elapsed from the date of arrival to disease diagnosis for each patient and for death dates verified at the end of the follow-up period. Laboratory results were compared separately for each PTB case with the national TB laboratory. TST results, when available, were obtained from the patients' medical records.

A definite case of TB was a patient with culture confirmed disease due to *M. tuberculosis* complex or two consecutive sputum smear examinations positive for acid-fast bacilli. The latter was practiced more commonly in Ethiopia. PTB was also defined when clinical judgments led to decision to treat the patient with a full course of antituberculous therapy after a therapy failure to broad-spectrum antibiotics [4,5].

Cost of operations of the pre-immigration infrastructure in Addis Ababa were obtained from decision makers and liaison professionals supervising the operation of the health station in Ethiopia, and include salaries, rent, drugs and equipment used for diagnosis and treatment, charge of the CXR performed in Ethiopia and the readings costs which were performed in Israel. Costs of treatment in Israel were determined by the Ministry of Health tariff.

Morbidity trends were described using incidence, prevalence and central tendency features. Comparison of categorical attributes between the study and the comparison group were performed using chi-square tests and the Fisher approach. Comparisons of continuous attributes were performed using a Student t-test for independent samples. Comparison of patients' survival periods from date of arrival in Israel to either disease date or death between the study and the comparison group were calculated using the Log Rank test for survival analysis. Mortality and disease incidence were available only for the PTB cases. Thus, the same assumption of "no additional deaths" for both groups, to compare the net influence of the pre-immigration screening process was employed.

Statistical analyses were performed by SPSS, version 13 (College Station, TX, USA).

RESULTS

Between 1998 and 2005, 24,051 Ethiopian of Jewish descent immigrated to Israel, in an average flux of 3,006 immigrants annually (range: 2,228 – 3,791, Sd = 571). Pre-immigration screening was performed in 9,283 immigrants; while in 14,768, post-immigration screening was performed. The average age at immigration was 22 years (range 0-98), and nearly 80% were younger than 35 years of age.

A total of 332 (1.4%) Ethiopian immigrants *both* immigrated and were diagnosed with PTB between 1998 and 2005. In order to associate the influence of the time elapsed from immigration date to disease diagnosis, 65 patients from either the comparison (19 patients) or the study group (46 patients) who were diagnosed within the fortnight following immigration were identified and were excluded from the analyses (figure 1). It is assumed that they arrived in Israel already with an active disease, and the first two weeks between immigration dates to registration represent the delay in the reporting process by local health personnel. Thus, these patients should be considered as point prevalent (270 PTB patients: 100,000 immigrants) upon entry rather than incident cases.

Those 267 immigrants who both immigrated and were diagnosed with PTB after 1998, excluding those diagnosed during the first 14 days following immigration, were further divided into a study group, which included 105 individuals who were screened in Ethiopia and developed PTB in Israel, and a comparison group, which included 162 individuals who immigrated to Israel, were screened following arrival and developed PTB in Israel. No major differences were detected in demographic determinants between the two groups (table 1). PTB incidence density in the study and the comparison groups were 267 and 324 cases per 100,000 person-years, respectively. Disease odds ratio between the study and comparison group is equal to 0.4.

Both the number of PTB cases and the disease rates (table 2) were lower in the study group than the comparison group for each of the years following immigration (RR=0.82,

p<0.01) and in decreasing rates throughout the follow-up period. The most significant effect was noticed during the first year after arrival in Israel (figure 2).

Time elapsed from entry to disease date was significantly shorter in the study group (average of 193 days, Sd = 260) than in the comparison group (average 487 days, Sd = 640), p<0.01. Survival analysis demonstrated a continuous and increasing gap in detection period (from immigration to disease diagnosis date) during the entire follow-up period (OR=0.72, log rank test = 0.002) (figure 3).

HIV rates among PTB patients from the study group were not statistically different than that in the comparison group (12.3% and 12.4%, respectively, p=0.99).

Based on the promising findings in morbidity trends following the initiation of the pre-immigration screening process, a five-year predictive model indicated that nearly 98 individuals would be free of PTB as a result of the screening process, if the immigration rate continues to be 3,000 individuals per year (table 3). Any PTB case diagnosed in Ethiopia is treated before departure in a lower cost than in Israel. In addition, individuals diagnosed with LTBI are recommended preventive therapy. Expenses pertaining to the diagnosis, treatment and follow up of each individual PTB case in Israel amount to US $7,619[c]. On the other hand, the annual cost for maintaining the health station in Addis Ababa for the screening process is US $60,100. Thus, the net direct saving costs for the pre-immigration screening process come to US $449,817[d] for five years, which is the sum of 98 PTB cases saved per year deducted by the annual cost of the maintenance of the health station.

[c] Based on the Israeli Ministry of Health tariff, January 2005.
[d] Due to the differences in the health services cost index between 2001 and 2005, sensitivity analysis may allow a 2.7% range.

DISCUSSION

PTB incidence among the pre-immigration screened Ethiopian immigrants was lower than immigrants who were screened post-immigration (267 and 324 for 100,000 person-years, respectively). Cumulative incidence was highest in the first year of residence in Israel, and declined in an exponential manner, particularly within the first two years following immigration.

Annual PTB incidence in Ethiopian immigrants during their first year in Israel was higher than the published Ethiopian national rate for PTB, which is 102 patients per 100,000 populations (both smear positive and negative patients, 2005 data [3]), and also higher than that recorded among south-east Asians immigrants to Australia [5] and asylum seekers to the Netherlands [6] (74.9 and 284 patients per 100,000 immigrants, respectively). Incidence in our study decreased significantly during the first years following immigration and became as low as 50 per 100,000 immigrants[e] in the study group after three years, despite the relatively high HIV prevalence among Ethiopian in Israel (~2% in 2004. Mor Z, personal communication). It is worth noticing that the decline in PTB incidence reported from the Netherlands on immigrants from Somalia, which borders Ethiopia at the horn of Africa, was more gradual, showing sustainable annual TB incidence as high as 9.5% seven years after arrival [7] and even after a decade [8]. The same phenomenon was recorded in the USA, where TB rates remain high for years in the older age groups of immigrants [9]. The variations between the studies cited above and our findings can be partially explained by differences in the social status of the immigrants in the absorbing country. Somali refugees to the Western Europe and migrant workers to the USA may be undocumented, discriminated against, under the threat of deportation and lacking access to medical facilities. On the contrary, Ethiopian newcomers to

[e] As a general rule, immigrants from countries with incidence rates higher than this level are eligible for screening.

Israel are naturalized upon arrival, are eligible for health and social insurance, governmental lodging, financial benefits, opportunities in the labour market, free educational and nutritional support during the initial phase of acculturating in Israel. Additionally, Ethiopian immigrants in Israel are examined periodically by medical staff at the absorption centres. Those efforts are encouraged by government, social and health authorities, and are regarded as core values in the Israeli moral ethos.

The health status of the Ethiopian immigrants may be worse than average migrant labourers, as they lived in rural area in the country of origin, belong to lowest social class, are uneducated, illiterate and displaced population. Thus, the Ethiopian immigrants in Israel are not enjoying the "healthy migrant effect" as typical labour migrants. Nevertheless, most of the PTB cases were diagnosed early due to screening efforts and to the effective medical vigilance of the index case and his/her contacts thereafter by the district health departments and by the TB regional clinics throughout the country. For this reason, expanding the screening process among immigrants during subsequent years in the host country, as suggested in the Netherlands [5] and Belgium [10] may be unnecessary in the Israeli setting.

The PTB point prevalence on arrival in our study was 270 per 100,000 immigrants, which is lower than in documented among asylum seekers at Heathrow Airport, London [11] and in Belgium [12], but is higher than in Somalis screened in Norway [13] or in Switzerland [14] (415, 252, 248 and 198 cases per 100,000 immigrants, respectively). The gap in TB prevalence between Ethiopia and Somalia may be related to the relatively higher TB prevalence in Ethiopia, to the age composition and the basic health status of the immigrants to Israel, and to the active case finding process of all immigrants in our process.

PTB was diagnosed an average of 294 days earlier in the study than in the comparison group. Several explanations can elucidate the shorter diagnosis period in the study group: first, detection of LTBI individuals by TST while in Ethiopia allowed a better follow up in Israel and early detection and treatment of PTB and their contacts. Second, the establishment of a

database of all the immigrants in the study group, which included pre-immigration performance of CXR, TST and physical examination allowed for easier and a more rapid access and follow-up of PTB patients and their contacts while performing epidemiological investigations. Lastly, time differences in immigration between the two groups allowed for greater experience gained among TB health professionals in Israel and for better preparedness of the entire TB infrastructure in Israel in diagnosis, treatment and follow-up of the immigrants.

The pre-immigration screening process was found to be cost-beneficial in our study, sparing 98 possible cases in five years from contracting PTB, and also cost-effective, saving direct expenses of US $90,000 per annum. The screening process takes advantage of the low cost of CXRs and of staff there relative to those paid in Israel for similar services, and the advantage of size once the procedure is operated by a single provider. This calculation is conservative, as it does not capture the entire expected savings of the faster health clearance of the immigrants in the study group in a presumptive period of one month in comparison to the post-immigration procedures practiced in the comparison group. As those medically non-cleared immigrants were unable to work or attend language classes during the time of the post immigration screening, all 45% of the immigrants who were at working age were paid an unemployment fee of US $343 per month by the Israeli government, which sums US $2,083,500 for the study period paid by the national budget. Thus, the faster health clearance, as a consequence of the pre-immigration screening process, allowed the immigrants to take part in absorption in the Israeli society and in the labour market sooner, thus saving governmental funds.

The pre-immigration screening process in Ethiopia further emphasizes the value of the centralized fashion of TB control performed by a single provider. Whereas the post-immigration screening was performed in a decentralized manner and was operated by multiple district health departments in Israel. Due to the variability of the capabilities and experience

between the health departments, each office responded differently in terms of timeliness to screen the immigrants. As *M. tuberculosis* has the potential to spread in the community, control measures should begin in the earliest stage possible, preferably before departure. The study demonstrated the advantage of a national organization, which is capable of funding and maintaining TB clinics, is responsible for a reliable inter-organizational data flow and is able to establish a feedback mechanism.

As TB screening in immigrants is a fundamental activity performed by developed countries, the Israeli experience may demonstrate the benefits of centralized screening process, which is supported by a national organization and provides incentive for both immigrants and for the experts in diagnosing and treating TB.

This study is subject to several limitations: 1) Limited follow up period: 4.5 years for the study group and up to seven years for the comparison group. Yet, due to the intensity and the quality of the screening process, the majority of PTB cases were detected in first year following immigration. 2) Incomplete data available regarding TST results among the immigrants. More complete data would have allowed us to associate between CXRs and TSTs. 3) The study group followed the comparison group, rather than being studied concomitantly. This sampling (selection) bias may have represented different immigration groups in time and better treatment in the latter group, as a result of the learning curve of the staff treating the immigrants. Yet, interviewing key professionals involved in Ethiopian immigration to Israel, it is unlikely that there are ethnical or demographic differences between the two groups. 4) Over-diagnosis (selection) bias in the study group may be differential in the direction of higher detection rates in that group. Yet, our findings of actual lower morbidity rates founding this study in the study group make this bias even more conservative, lowering the relative risk.

The strengths of this study include the close follow up of the entire cohort of all Ethiopian immigrants and of every TB patient, the high sensitivity and specificity of case ascertainment in the unique data base performed, and the numerous total person-years of follow up. This study includes the entire immigrant population, thus it is far less subject to both selection and information bias.

In conclusion, the pre-immigration screening process for PTB is centralistic in nature, allows for unification of medical procedures, and reduces the burden on local health departments and on medical providers. It has proven to be effective among Ethiopian immigrants arriving in Israel. Following the process, PTB disease incidence reduced and the infection was detected in earlier stages. The screening process was proven both cost-beneficial and cost-effective, and may be performed by other developed countries in order to ensure better TB detection in immigrants from high-TB prevalence areas.

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DISCLOSER

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TABLES

Table 1: Demographic characteristics of pulmonary tuberculosis of Ethiopians in Israel, who immigrated and were diagnosed between 1998-2005, by a screening procedure*

Determinant	Post immigration screened individuals N=9,282	Pre immigration screened individuals N=14,768	Pv
Age in immigration	27.4±20.1	28.8±22.4	0.58
Age in diagnosis	28.7±20.3	29.4±22.5	0.81
Male: Female ratio	1.04	1.14	0.82
HIV rates	13.8%	14.2%	0.93

* Excluding those who were reported within 14 days following immigration to Israel

Table 2: Pulmonary tuberculosis morbidity rates in Ethiopian immigrants arrived in Israel before or after the initiation of the pre-immigration screening, by length of follow-up from immigration.

	Person years		Pulmonary tuberculosis cases, N		Rate of pulmonary tuberculosis/100,000 person years			
	Post-immigration screened individuals	Pre-immigration screened individuals	Post-immigration screened individuals	Pre-immigration screened individuals	Post-immigration screened individuals	Pre-immigration screened individuals	RR*	AR[§]
During first year[∞]	9,268	14,783	100	87	1,079	588	0.55	0.49
During second year	18,536	22,366	18	12	97	54	0.56	0.43
During third year	27,849	22,176	15	4	54	18	0.34	0.36
During fourth year	37,072	17,328	9	2	24	11.5	0.47	0.125
During fifth year	46,340	8,225	8	0	17	0	0.0	0.17
During the entire five years	46,340	39,334	150	105	324	267	0.82	0.57

* Rate ratio
[§] Attributable risk
[∞] excluding those who were reported within 14 days following immigration to Israel

Table 3: A predicted model comparing probable pulmonary tuberculosis cases from a presumed annual influx of 3,000 screened immigrants

Years after immigration	If post-immigration screening is performed (estimated number of patients)	If pre-immigration screening is performed (estimated number of patients)	Disease prevented (estimated number of cases)
1	32.4	17.7	14.7
2	37.9	20.8	17.1
3	42.6	22.3	20.3
4	44.1	22.6	21.5
5	46.1	22.3	23.9
Total	**203.1**	**105.5**	**97.6**

FIGURES

Figure 1: Study flow chart

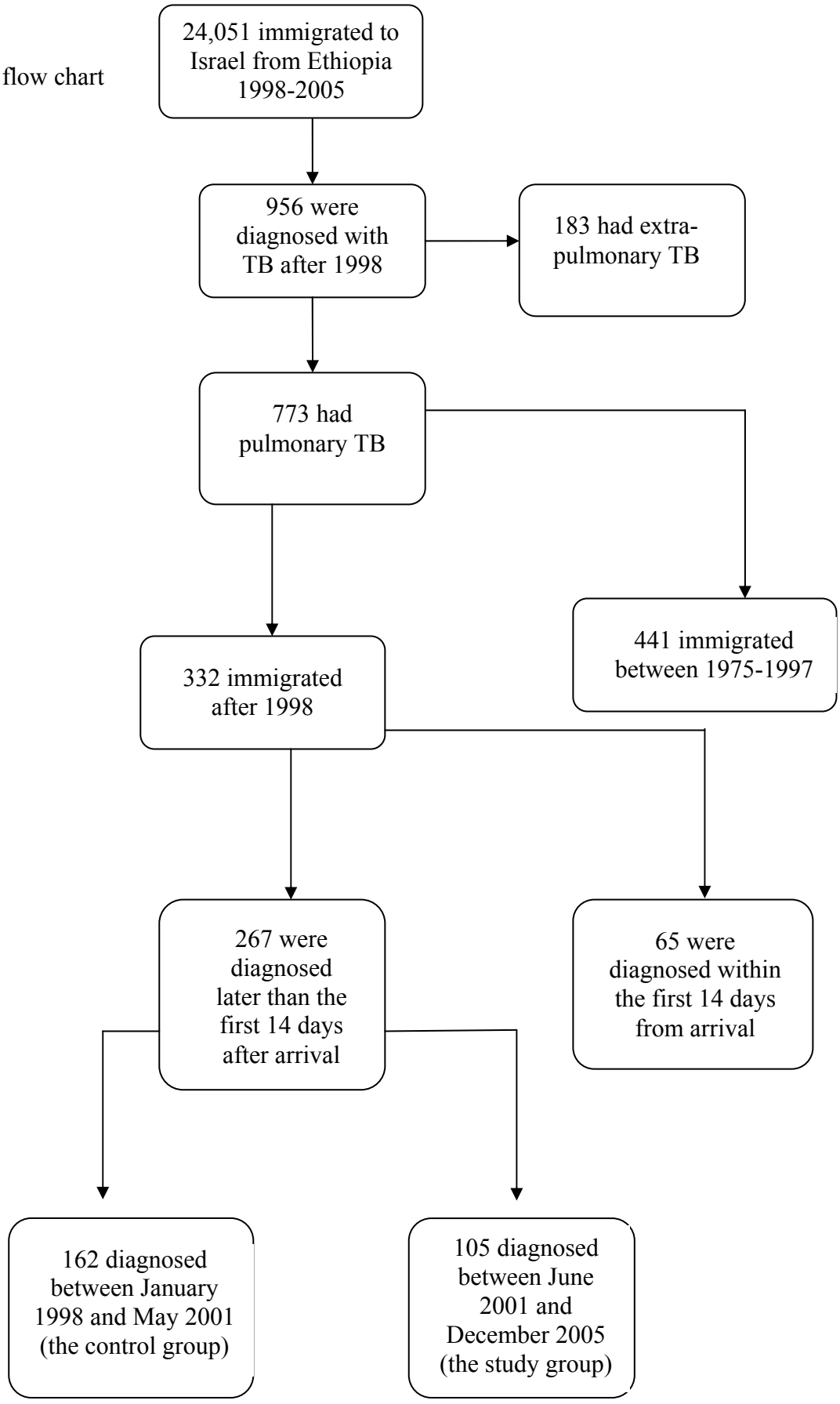

Figure 2: Cumulative incidence of PTB in Ethiopian immigrants, by duration in Israel and screening procedure.

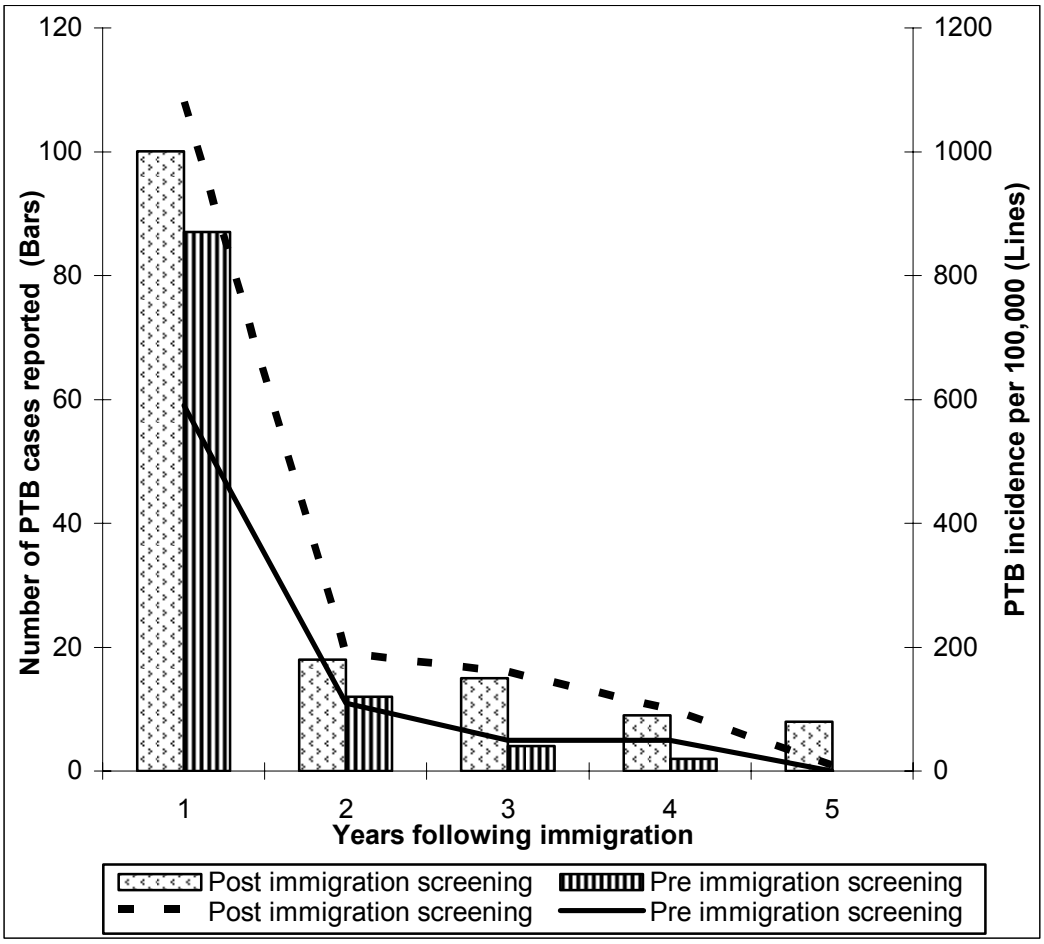

Figure 3: Survival function for the cohort immigrated before and after screening process