

Coverage and yield of entry and follow-up screening for tuberculosis among new immigrants

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ABSTRACT

Objective: Determine the effectiveness of entry screening for tuberculosis and bi-annual follow-up screening among new immigrants in the Netherlands.

Methods: Analysis of screening, prevalence and incidence data on 68,122 immigrants, followed-up for 29 months. Patients diagnosed within 5 months and 6-29 months after entry screening were considered to be detected at entry and follow-up period, respectively.

Results: Coverage of the second to fifth screening round was 59, 46, 36 and 34%, respectively. Yield of entry screening was 119 /100,000 persons, and prevalence at entry 131/100,000. Average yield of follow-up screening was highest among immigrants with abnormalities on the chest X-ray (CXR) at entry (902/100,000). When excluding these, yield of follow-up screening was 9/100,000, 37/100,000 and 97/100,000 screenings, for immigrants from countries with TB incidences of <100, 100-200, and >200 /100,000 respectively. The incidence during follow-up in persons with a normal CXR was 11, 58 and 145/100,000 persons years follow-up in these groups. The proportion of cases detected through screening declined per screening round from 91% to 31%.

Conclusions: Yield of entry screening was high. Overall coverage and yield of follow-up screening was low. Follow-up screening of immigrants with a normal CXR from countries with an incidence of <200/100,000 was therefore discontinued.

INTRODUCTION

In Western-Europe, about half the tuberculosis (TB) patients are of foreign origin [1]. In the Netherlands, approximately 1000 to 1400 patients with active tuberculosis are diagnosed yearly, of whom 68% are foreign-born persons [2]. In 2004 the incidence of all forms of tuberculosis among foreign born persons was 52.4 per 100,000, 17 times the incidence of Dutch born persons (3.1 per 100,000 populations).

Active case finding in risk groups is an important strategy for TB control in low-prevalence countries in the elimination phase [3]. In 1995 a risk group policy was formulated in the Netherlands. The Committee for Practical TB Control and the National Health Council defined a risk group for tuberculosis as a (sub)population with an incidence of more than 50/100,000, approximately 10 times the rate in the general Dutch population [4]. Screening for active tuberculosis is mandatory for all immigrants from non-western countries, intending to stay longer than three months in the Netherlands [5]. At the time of the study this included all countries except the European Union, Australia, Canada, Iceland, Israel, Japan, Monaco, New Zealand, Norway, Surinam, Switzerland and the USA. Immigrants applying for a residence permit in the Netherlands are referred by the Immigration Department to the Municipal Health Services for tuberculosis screening. Screening is performed by chest X-ray (CXR) in persons older than 12 years. Asymptomatic children below 12 years, if not vaccinated with BCG, are tested with a tuberculin skin test (TST) [6,7]. In some Municipal Health Services (MHS) non-BCG vaccinated individuals up to 25 years are screened with TST. Immigrants older than 12 years are offered voluntary follow-up screening by CXR every six months for a period of one or two years, depending on the MHS. Chest X-rays are read within two working days by trained TB-specialists or pulmonologists. All persons with any abnormalities in the CXR or with positive TST are subjected to medical examination. In any TB-suspect further diagnosis with sputum microscopy and culture is performed. Persons with suspected extra pulmonary tuberculosis are usually referred to hospital services for further diagnosis.

Tuberculosis screening of asylum seekers and other immigrants at entry is common practice in many other low-incidence countries [8-15]. Apart from the Netherlands, few other countries perform follow-up screening among immigrants with a normal CXR [11, 16, 17]. The effectiveness of tuberculosis screening of immigrants has been disputed [12,18].

The objective of this study was to assess the effectiveness of the Dutch immigrant screening policy by determining prevalence and incidence of tuberculosis disease among immigrants and the yield and coverage of entry and follow-up screening in subgroups of immigrants, in order to identify risk groups to which screening can be targeted.

METHODS

We used data from the Monitoring System for Screening of Immigrants (MSI) [19, 20]. The MSI-system registers individual data on the results of entry and follow-up screening of documented immigrants. It does not include asylum seekers, since they move frequently during their stay. Due to privacy regulations they are not registered by a unique identification number, and are therefore difficult to follow over time. Municipal Health Services (MHSs) register year of birth, gender, nationality, date and result of CXR and TST and final result of screening in a special database in Microsoft Excel or in an electronic client register. Data from electronic client registers were extracted for MSI through a query of the database. KNCV Tuberculosis Foundation collects the data in a central Excel database. This study utilized the data of cohorts entering in 1998-2002 including the follow-up period of 29 months after entry until mid 2005. Data were standardized and checked for inconsistencies. To validate the data on tuberculosis patients in the MSI-system, the data were compared with the Netherlands Tuberculosis Register (NTR) [2], using year of diagnosis, year of birth, gender and nationality to match cases. If patients were registered in the MSI-system and not in the NTR or vice versa, the MHS was asked for clarification to improve completeness of the database.

Definitions

Cohort was defined by date of entry screening. Coverage was defined as the number of persons screened divided by the number of persons in the target population per screening round. The yield was defined as the number of patients detected per screening round. Prevalence was defined as the total number of patients diagnosed (either through screening or through passive case finding) per 100,000 persons screened on entry. The incidence rate was defined as the total

number of patients diagnosed (either through screening or through passive case finding) per 100,000 person years follow-up in the target population. Patients detected at entry screening or passively until 5 months after entry were considered to be prevalent cases. All patients diagnosed between 6-29 months after entry were considered to be incident cases.

The target population per screening was calculated for every screening semester (6-11, 12-17, 18-23, 24-29 months) from the number of immigrants screened at entry minus the number of immigrants who were detected with active tuberculosis, completed the screening according to the MHS or were known to have left the country. Immigrants not known to have left the country were assumed to be still present. In cases where the result of the screening was not coded by the MHS, a completed screening was defined as: more than 704 days (23 months) between the first (entry) and the last screening (regardless of the attendance to previous screenings).

The result of the initial CXR was classified as 'suspect active TB', 'abnormality, possibly old TB', 'abnormality, no TB', 'no abnormalities' and 'unknown'. For the purpose of this analysis the CXR result was aggregated in three groups: 'any abnormalities', 'no abnormalities' and 'unknown'.

Active TB cases were classified by site of disease according to the revised international definitions in tuberculosis control [21].

Patients were defined as detected passively when the reason for medical examination leading to the diagnosis of active tuberculosis was not immigrant screening. The majority of these patients were diagnosed through presentation of symptoms suspect for tuberculosis in the health care system.

Analysis

Data were analyzed using SPSS 14.0.1 for Windows (United Kingdom). Stratified risk analysis was done for age, gender, nationality grouped in countries or continents, incidence groups according to WHO estimated incidence in the country of origin in 2002, and abnormalities on the initial CXR. For sake of brevity, countries of origin with an incidence of <100/100,000, 100-200/100,000, and >200/100,000 are classified as low, medium and high incidence countries.

Patient data are presented for all TB and pulmonary TB (PTB) cases, since CXR is performed to detect PTB, but also frequently detects other forms of TB. Follow-up screening and incidence is only presented for persons >12 years of age (n=61,237), since no follow-up screening is offered to children ≤12 years.

RESULTS

Study groups

Data on 70,173 new immigrants entering the Netherlands from 27 MHSs were available (figure 1). In total 68,122 records were complete (97%). The number of immigrants per MHS varied from 105 to 4,456 per cohort year. We identified 187 TB patients in the study group, of whom 74% were bacteriologically confirmed (smear and/or culture positive) among PTB cases and 28% among ETB cases (table 1). There were 89 prevalent cases and 98 incident cases 6-29 months after entering the country, of which one case was younger than 12 years.

Coverage

The coverage of the second to fifth screening was 59, 46, 36 and 34% respectively (figure 2). The coverage in the four screening rounds varied considerably between MHSs ranging from as low as 31, 23, 6 and 17% in one MHS to as high as 87, 77, 67, and 75% in another. The coverage among persons from Turkey and Morocco was 8-18% higher than persons from other countries. No relevant differences were found between men and women, and between other groups of nationalities.

Entry yield & prevalence

In total 1,620 persons with an abnormal CXR at entry requiring further examination were recorded. In 81 patients active TB was detected. The yield of screening at entry was 119/100,000 persons screened for all forms of tuberculosis and 112/100,000 for PTB. A further eight patients, were detected passively within five months after entering the country. Adding up passively and actively detected patients, the prevalence of TB at entry was 131/100,000 (table 2).

The yield of entry screening was highest in age groups 25-34 and 45+, and hardly differed between males and females. The yield of the entry screening for all subgroups varied from 56 to 271 TB cases per 100.000 persons screened.

Follow-up yield & incidence

Forty-seven (47) patients >12 years were detected during follow-up screening and 50 patients were detected passively 6-29 months after entering the country. Of the 47 patients detected through follow-up screening, 30 had a normal initial CXR. Among the 20 PTB patients detected passively, 2 had abnormalities in the initial CXR (figure 1). In 19/50 TB patients detected passively, the interval between the last screening and diagnosis was more than 7 months.

The yield of follow-up screening was highest among persons with an abnormality on the initial X-ray and who were not diagnosed with TB in the first semester (table 3). In 1,412 immigrants with abnormalities in the CXR on entry, follow-up screening detected 17 cases (902/100,000 screenings). Even in the low incidence nationalities group a high number of cases was detected (411/100,000 screenings). The yield of follow-up screening among persons with a normal CXR was 36/100,000 screenings and the incidence 6-29 months after entry was 53/100,000 person years (pyrs) follow-up. Among subgroups of immigrants from low, medium and high incidence countries the yield was 9/100,000, 37/100,000 and 98/100,000 screenings respectively (9, 28 and 89/100,000 for PTB cases) and the incidence was 11, 58 and 145/100,000 pyrs follow-up respectively (7, 35 and 77/100,000 pyrs for PTB cases).

The yield and incidence during the follow-up period were associated with the incidence in the country of origin. Yield and incidence among persons with a normal CXR were higher in females than males. Yield and incidence were highest in the age group of 25-44 years. The yield and incidence was high when the nationality was "unknown", but the absolute number of patients with an unknown nationality was very low, and therefore the confidence intervals are wide.

The yield of screening for all forms of tuberculosis for the second, third, fourth and fifth screening rounds was respectively 48, 67, 66 and 30/100.000 persons screened and for pulmonary cases 45, 67, 40 and 23/100.000 persons screened. In all incidence groups the yield of screening declined in the last two rounds, even in the high incidence group, despite a continued high incidence (figure 3). The proportion of patients detected through screening declined with consecutive screening rounds (figure 4). There were no significant differences in age, sex and estimated incidence in country of origin between patients found through screening or detected otherwise (data not shown).

DISCUSSION

We found that the yield of entry screening was 56-271/100,000 persons screened depending on the subgroup analyzed. Furthermore we showed that in persons from low, medium and high incidence countries and with a normal CXR at entry, the yield of follow-up screening during follow-up was 9, 37 and 98/100,000 screenings respectively. Of the prevalent cases 91% were detected through screening. Of the incident cases during follow-up 48% were found through screening (67% of PTB cases). The proportion detected through screening was low in the last two rounds.

Abnormalities on the chest X-ray at entry were the most important predictor to develop TB, irrespective of the incidence in the country of origin. Among those with any abnormalities in the CXR 1.6% were diagnosed with active TB during follow-up. Abnormalities in the CXR are often fibrotic lesions due to healed TB, and a known risk factor for TB activation [22, 23]. Immigrants with abnormalities on the CXR at entry are usually either targeted for more frequent follow-up screening and additional diagnostics or offered preventive therapy.

Our results suggest that, when accepting a cut-off for the yield of 50/100,000 persons screened, entry screening is useful to detect TB for all immigrants that are currently targeted. Entry screening is also useful to identify an important risk group for intervention, being persons with abnormalities on the CXR. Follow-up screening can be targeted towards persons from high incidence countries. However, the choice in the Netherlands for a cut-off value for 50/100,000 for the definition of a target group for screening is arbitrary. It may not be cost-effective to screen all immigrants belonging to such groups with a relatively low risk [14, 24]. To study cost-effectiveness was not the objective of this study, but consideration of cost-effectiveness may lead to a more effective use of resources. Limiting follow-up screening to persons from high endemic

countries will reduce the number of CXR's performed for screening of immigrants and asylum seekers with 40-45%, an estimated 35,000 CXR's in 2007.

It can be argued that entry screening could also be restricted to persons from high incidence countries, but our results suggest that migrants are not representative for the total population in the country of origin. For two nationalities we could compare our results with WHO estimates. We found that among Moroccan and Turkish nationals the prevalence at entry (170/100,000 and 101/100,000) was higher than expected from the WHO-estimated prevalence of TB in the country of origin (86/100,000 vs. 44/100,000) [25]. However, incidence during follow-up in these groups (68/100,000 and 13/100,000), was lower than the estimated incidence in the countries of origin. This suggests that immigrants from these countries are a selected group with a higher risk for active TB at entry, such as young adult age-groups or lower socio-economic groups. In our study population 38% of the population was 25-34 year, the group with the highest prevalence of active TB. The lower incidence during follow-up can be explained by a lower risk of infection in the Netherlands. Early case-finding through screening on entry in these groups is likely to contribute to a lower risk of infection among immigrants in the Netherlands.

Other studies in low incidence countries have reported a persistent high incidence of tuberculosis in immigrants, although some found a decline over time [10, 13, 26, 27, 28]. The incidences that we found were similar to those in another study in the Netherlands where both regular immigrants and asylum seekers were included [29]. In that study it was found that incidence remained high many years after immigration. In our study we found that despite a high incidence throughout the follow-up period in the high incidence group, the proportion of patients detected through screening per consecutive screening round declined and the yield in the last two rounds was low. The duration of follow-up screening of two years is therefore debatable for two reasons: the prolonged higher incidence after entry into the country and the reduced effectiveness of the follow-up screening in the second year. About half of the patients with PTB detected passively, could have been detected earlier, since the last screening was more than 7 months before diagnosis. So the yield of follow-up screening could be improved with a better coverage.

Our yield of screening may have been affected by a selection bias since persons with symptoms may be more likely to report for screening. On the other hand it is also likely that patients detected passively belong to risk groups that are less likely to report for screening. Not all eligible immigrants undergo entry screening [30]. It was estimated from routine surveillance and population data that in 2002 [31] approximately 70% of the target immigrant population was screened at entry in the Netherlands. Furthermore, in the NTR 35 patients 6-29 months after entry were detected in the participating MHSs, who were eligible for screening in the study period, but never screened, and therefore could not be included in this study. These patients may represent an immigrant population group with a different risk profile. Therefore, when the coverage of follow-up screening will improve, the absolute number of cases detected through screening will increase, but the yield per 100,000 persons screened may decrease. Interventions to increase the coverage should therefore address specific subgroups within the target population with the highest risk such as the younger age groups and will need to be low-cost to maintain the effectiveness of the screening. It may also be more effective to ensure passive case-finding among high-incidence groups. The duration of the follow-up period could then be limited to a maximum of one year. Alternatively, if it would be possible to reduce the pool of latent infected persons among immigrants, the incidence caused by reactivation would be reduced and follow-up screening could be abolished for all groups.

There are some other limitations concerning the coverage of screening and the representativeness of the data in this study. The low coverage of the follow-up screening rounds was comparable to earlier studies [6, 24, 32]. We have underestimated coverage and therefore incidence since we assumed all immigrants were still in the Netherlands during the follow-up period, while some may have left. The number of persons who left the country amounted to at least 15% in 20 MHSs that registered intended length of stay in this study and 26% in the first 2 years in a pilot study at one MHS in 1996 [6]. Marriage and labor are the most important immigration motives for migrants coming to the Netherlands. During the period 1995-2003 more than a third of the migrants came for marriage, 31% for labor, 13% for study and 9% for family unification. Other reasons (14%) for migration were: family member of migrant, au pair, internship and medical treatment [33]. We think the data are representative for immigrants, other than asylum seekers, screened by MHSs in the Netherlands, although the data did not cover all MHSs in the country. The participating MHSs are distributed evenly over the country, giving a fairly even geographic coverage and urban and rural distribution. In 2001 and 2002 the data covered 55-66% of the

total immigrants screened in the Netherlands. Furthermore, trends in coverage and yield are largely comparable between cohorts (table 2 and 3). However, the results may not be generalisable to asylum seekers. Firstly, the prevalence among immigrants at entry was lower than that found in asylum seekers in earlier studies [23, 34]. This can be explained by the differences in incidence in countries of origin between immigrants and asylum seekers. Another explanation is that asylum seekers had social circumstances that involve a higher risk of infection or breakdown. This may be related to the process of asylum seeking [35]. Our study is also not generalisable to undocumented immigrants, since by definition they are not a target group for screening.

Conclusions and recommendations

The yield of entry screening was high. Entry screening should be continued for all immigrants groups that are currently screened. Follow-up screening for persons from countries with a low or medium incidence and with no abnormalities on their CXR at entry has been abolished as a result of this study. The proportion of cases detected through screening declined per screening round and the coverage and yield of follow-up screening was low after the third round even in groups from high incidence countries. This suggests follow-up screening may be limited to a period of one year. Coverage of follow-up screening needs to be increased especially in subgroups with the highest risk.

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Table 1: number of bacteriological confirmed cases and percentage of total

PTB	0-5 months			6-29 months			total		
	bacterio-logical confirmed cases	total cases	%	bacterio-logical confirmed cases	total cases	%	bacterio-logical confirmed cases	total cases	%
detected through screening	61	76	80%	28	41	68%	89	117	76%
passively detected	2	3	67%	13	20	65%	15	23	65%
total PTB cases	63	79	80%	41	61	67%	104	140	74%
ETB									
detected through screening	0	5	0%	1	6	17%	1	11	9%
passively detected	2	5	40%	10	30	33%	12	35	34%
total ETB cases	2	10	20%	11	36	31%	13	46	28%

Table 2: Yield of screening and prevalence on entry (0-5 months) 1998-2002

	Number screened	Number TB patients detected by screening	Number TB patients found passively	Yield per 100,000 screened	95% CI	Prevalence per 100,000 screened#	95% CI
Age							
< 13	6,885	8	1	116	50-229	131	60-248
13-24	25,163	20	3	79	49-123	91	58-137
25-34	25,009	41	3	164	114-214	176	124-228
35-44	8,176	6	0	73	27-160	73	27-160
45+	2,883	6	1	208	76-453	243	98-500
unknown	6	0	0	-	-	-	-
Gender							
Male	28,566	33	2	116	76-155	123	82-163
Female	39,415	48	6	122	87-156	137	101-174
Unknown	141	0	0	-	-	-	-
Nationality							
Morocco	11,154	17	2	152	89-244	170	103-266
Turkey	9,910	9	1	91	42-172	101	48-186
Africa (except Morocco)	7,603	11	0	144	72-258	144	72-258
Asia (except Turkey)	19,354	31	4	160	104-217	181	121-241
Central&East Europe	12,554	7	1	56	22-115	64	28-125
Other	5,425	6	0	111	41-241	111	41-241
Unknown	2,122	0	0	-	-	-	-
Incidence country of origin per 100,000*							
< 100	26,687	17	2	64	37-102	71	44-111
100-200	27,865	33	5	118	78-159	136	93-180
> 200	11,435	31	1	271	176-366	280	183-377
Unknown	2,125	0	0	-	-	-	-
Entry cohort							
1998	5,608	9	0	160	73-305	160	73-305
1999	9,417	11	2	117	58-209	138	74-236
2000	12,055	10	4	83	40-153	116	63-195
2001	17,930	24	1	134	80-187	139	85-194
2002	23,112	27	1	117	73-161	121	76-166
Result chest X-ray (CXR)							
Normal CXR	66,502	0	5	0	-	8	2-18
Any abnormalities	1,620	81	3	4,883	3,911-6,089	5,185	4,076-6,294
Total	68,122	81	8	119	93-145	131	104-158

* estimated incidence total TB WHO 2002

prevalence= (number of cases detected through screening plus number of cases detected passively) divided by number of persons screened

Table 3: Yield of screening and incidence of all TB cases during follow-up period (6-29 months), stratified by results chest x-ray at entry.

Normal Chest X-Ray at entry (n=58,529)									
	Person years follow-up	Number of screenings in round 2-5	Number TB patients detected	Number TB patients found passively	Total TB cases	Yield per 100,000 screened	95% CI	Incidence per 100,000 pyrs follow-up#	95% CI
Age									
13-24	57,059	33,237	7	16	23	21	8-43	40	26-60
25-34	57,500	34,693	14	21	35	40	22-68	61	41-81
35-44	18,296	11,910	8	5	13	67	29-132	71	38-122
45+	6,160	3,811	1	2	3	26	1-146	49	10-142
Unknown	10	-	-	-	-	-	-	-	-
Gender									
Male	56,549	33,232	10	19	29	30	14-55	51	34-74
Female	82,194	50,340	20	25	45	40	24-61	55	39-71
Unknown	283	79	0	0	0	-	-	-	-
Nationality									
Morocco	23,355	17,365	5	10	15	29	9-67	64	36-106
Turkey	21,575	15,808	1	0	1	6	0-35	5	0-26
Africa (except Morocco)	15,187	7,998	5	8	13	63	20-146	86	46-146
Asia (except Turkey)	38,097	21,854	15	20	35	69	38-113	92	61-122
Central&East Europe	25,973	12,821	2	4	6	16	2-56	23	8-50
Other	10,603	5,810	0	1	1	-	-	9	0-53
Unknown	4,236	1,995	2	1	3	100	12-362	71	15-207
Incidence country of origin per 100,000*									
< 100	56,079	33,798	3	3	6	9	2-26	11	4-23
100-200	56,702	35,549	13	20	33	37	19-63	58	38-78
> 200	22,003	12,300	12	20	32	98	50-170	145	95-196
Unknown	4,242	2,004	2	1	3	100	12-360	71	15-207
Cohort									
1998	11,369	7,340	3	4	7	41	8-119	62	25-127
1999	18,455	12,156	6	6	12	49	18-107	65	34-114
2000	24,732	15,663	6	8	14	38	14-83	57	31-95
2001	36,664	21,886	5	11	16	23	7-53	44	25-71
2002	47,806	26,606	10	15	25	38	18-69	52	34-77
Total	139,026	83,651	30	44	74	36	23-49	53	41-65
Abnormal chest X-ray at entry (n=1,412)									
Incidence country of origin per 100,000*									
< 100	1,236	730	3	1	4	411	85-1,201	324	88-828
100-200	1,328	791	9	3	11	1,138	520-2,160	828	414-1,482
> 200	677	363	5	2	7	1,377	447-3,215	1,034	416-2,130
Total	3,241	1,884	17	6	23	902	526-1,445	710	450-1,064

*estimated incidence total TB WHO 2002

incidence= (number of cases detected through screening plus number of cases detected passively) divided by number of screenings

Figure 1. Results of entry and follow-up (f-up) screening (6-29 months)

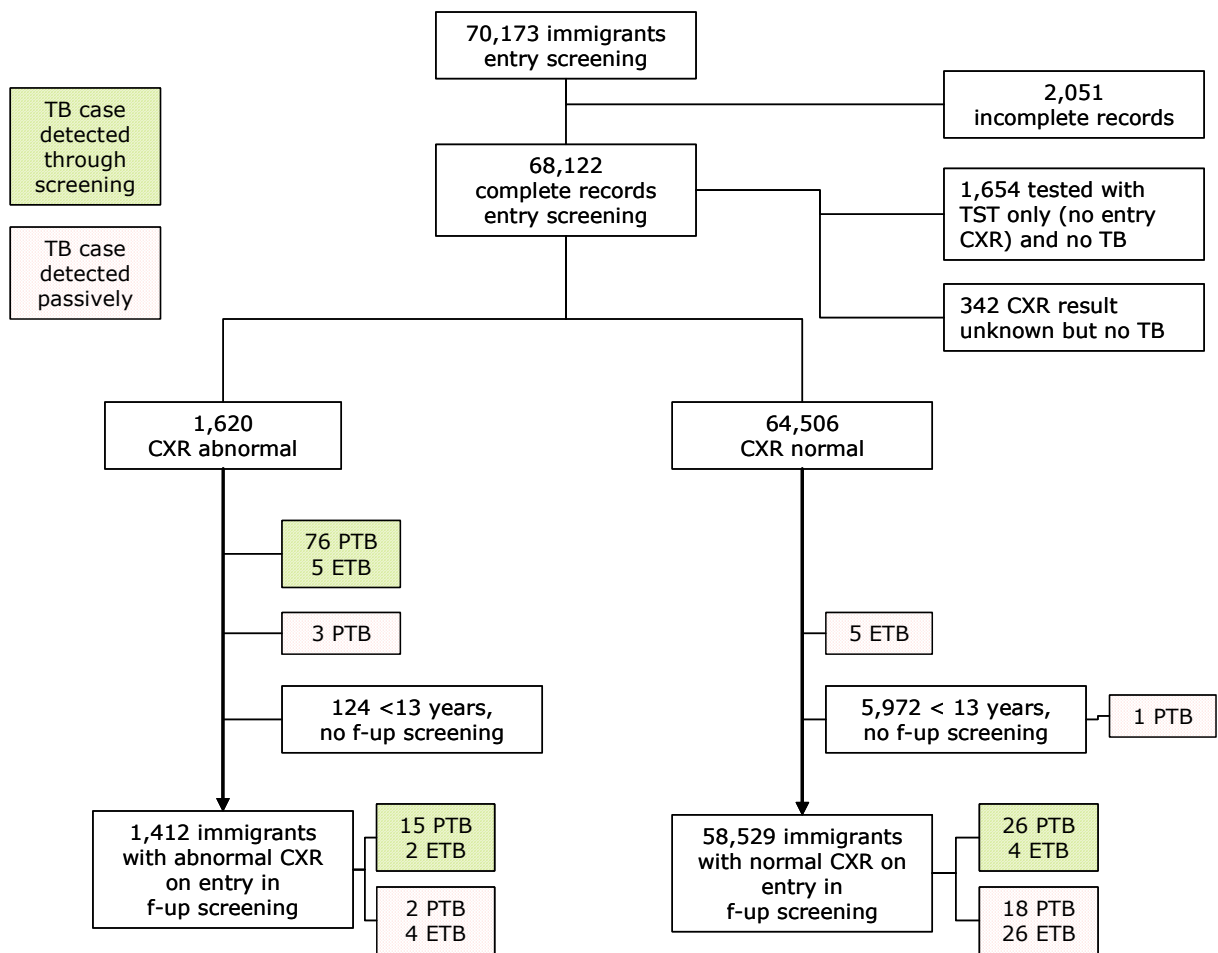
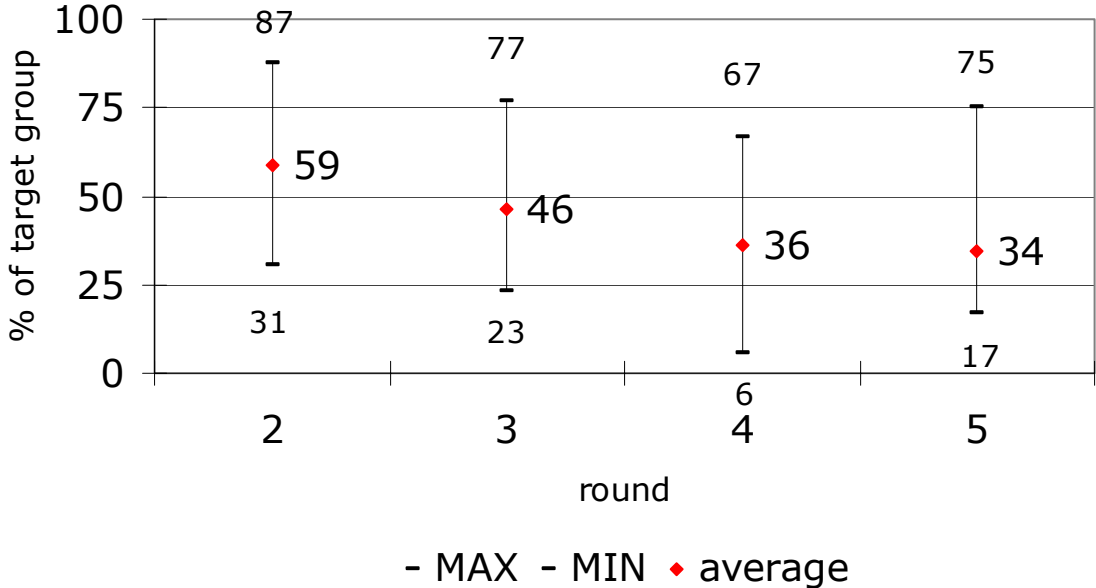


Figure 2: Coverage per screening round in 68,122 immigrants screened at entry as percentage of target group screened *



*Lines indicate range of minimum and maximum observed coverage in MHSs

Figure 3: Yield and incidence of TB, all cases, and PTB by screening round in persons from countries with an estimated TB-incidence of > 200/100.000 and normal CXR at entry (error bars represent 95% CI).

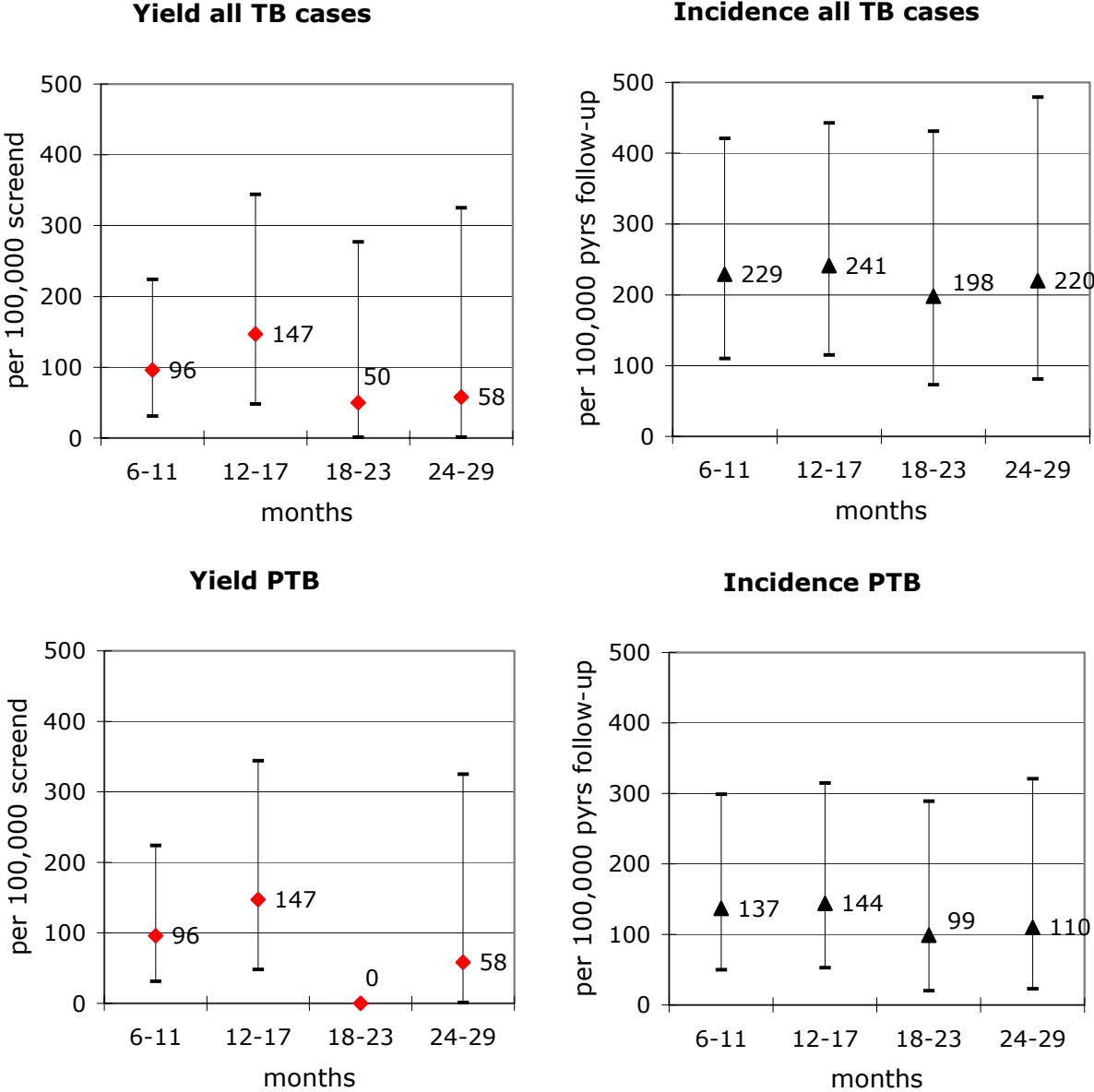
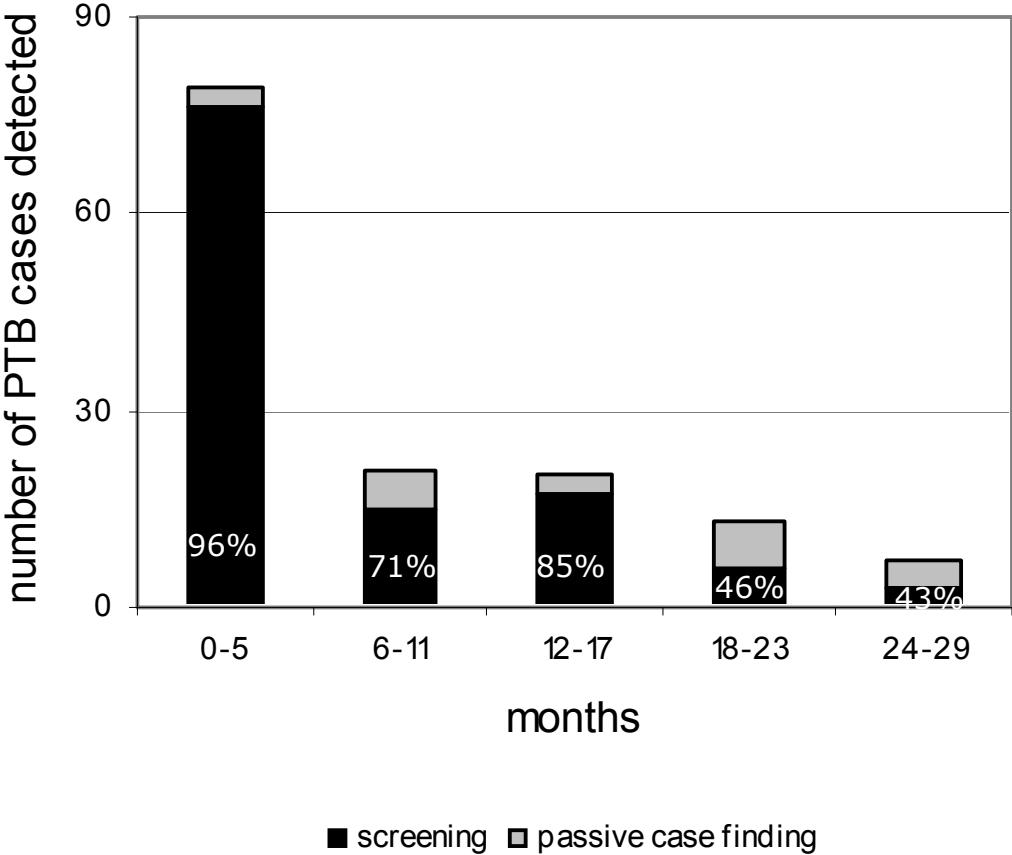


Figure 4: number of PTB cases per screening semester, by type of case detection.



In columns: percentage of total cases detected by screening.