



Early View

Research letter

Tailored approaches facilitate high completion of tuberculosis infection treatment among migrants

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Tailored approaches facilitate high completion of tuberculosis infection treatment among migrants

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Tuberculosis (TB) prevention is an essential component of the End TB Strategy to work towards elimination (1). Currently, the guidelines of the World Health Organization recommend TB preventive treatment (TPT) in populations at risk for TB (2). In low TB incidence countries, the foreign born are a population of interest for TB prevention as they constitute >50% of TB patients (3, 4). Previous studies showed that TB infection (TBI) screening and TPT among specific migrant populations can be organized and executed in practice (5-9), with TPT initiation (23-97%) and completion (7-83%) proportions varying considerably between countries (10). Identifying factors that contribute to these differences may aid the successful implementation of TPT in high TB risk migrants. We therefore compiled and analyzed data from three recent Dutch TBI screening and TPT implementation studies (5-7) among various migrant populations to assess factors facilitating TPT uptake and completion.

The implementation of TBI screening and TPT was studied among three different migrant groups, of which two are currently targeted for TB disease screening by CXR: newly arriving immigrants from countries with a TB incidence >50/100,000 (5); and asylum seekers from countries with a TB incidence >200/100,000 (7). During the study period, participating Public Health Services (PHSs), responsible for TB care and prevention activities in the Netherlands, replaced current CXR screening at specific time points for immigrants (mandatory CXR entry-screening: i.e., under the Dutch law immigrants are mandatory to participate and complete TB screening to obtain their residence permit) and asylum seekers (voluntary biannual CXR follow-up screening for a period of two years) with TBI screening. The third group were settled migrants with a high (>500 per 100,000) TB incidence despite TB disease screening upon entry: settled Eritrean migrants living in The Netherlands for up to 10 years reached, invited, and motivated to participate in the TBI screening through a community-engaged approach (6).

Twelve (out of 25) regional participated in at least one of the studies. Prior to screening, immigrants received an information brochure and asylum seekers and settled Eritreans received verbal group education on the purpose of TBI screening. TBI screening consisted of a health questionnaire and TBI test (tuberculin skin test followed by interferon gamma release assay (IGRA) or IGRA alone). Clients reporting symptoms indicative of TB were also screened by CXR. Persons with a positive IGRA received TBI diagnosis after exclusion of TB disease by the TB physician. Clients eligible for TPT were

offered 3 months of daily rifampicin and isoniazid combination therapy. Clients who did not initiate TPT were offered two-year bi-annual follow-up screening. All clients on TPT were counselled by a PHS nurse on how their TPT would be supported. PHSs followed Dutch guidelines on TBI screening and TPT (11, 12).

In total, 1541 clients were screened for TBI (566 immigrants; 718 asylum seekers; and 257 settled Eritreans), of whom eight (0.5%) were diagnosed with TB disease, 302 (20%) were diagnosed with TBI, and 20 (all asylum seekers) with a positive IGRA were lost to follow-up. Of 302 clients with TBI, 227 (75%) initiated TPT. TPT initiation varied between immigrants ($n=49/94$ (52%)), asylum seekers ($n=149/178$ (84%)) and settled Eritreans ($n=29/30$ (97%)). Of all clients on TPT, 191 (84%) completed treatment, 29 (13%) discontinued treatment, and seven (3%) were lost to follow-up. TPT completion differed between immigrants ($n=34/49$ (69%)), asylum seekers ($n=129/149$ (87%)) and settled Eritrean migrants ($n=28/29$ (97%)). Overall, these TPT completion proportions fall in the higher range when compared to those in other studies (7-83% TPT completion among immigrants) (10). (Table 1)

One possible explanation for the lower TPT uptake among immigrants is the lower a-priori motivation due to the mandatory nature of the TBI screening for this group. This is reflected by the most frequently reported reasons for TPT refusal: low perceived chance of developing TB disease (36%) and planned return to the country of origin within a few years (27%). Indeed, immigrants with an intended duration of stay in the Netherlands of more than five years were more likely to initiate TPT than those with a shorter intended duration (RR: 1.2; 95%CI: 1.0-1.4) (5). Another factor possibly influencing the difference in TPT uptake is the type of information and education received. Immigrants received an information brochure before screening; asylum seekers and settled Eritreans received more extensive verbal education in their mother tongue. The interactive education may have facilitated TPT uptake of screened asylum seekers and settled Eritreans with TBI.

TPT completion was lowest among immigrants (69%) compared to asylum seekers (87%) and Eritrean migrants (97%). Patient-centered TPT support, provided by PHS nurses, was least given to immigrants (67%) compared to asylum seekers (87%) and settled Eritreans (100%). Furthermore,

compared to immigrants, TPT support to asylum seekers and settled Eritreans involved more frequent and longer contact (6, 7). Hence, patient centered TPT support is a facilitator for TPT completion. Additionally, asylum seekers and settled Eritreans more often missed appointments than immigrants because of barriers related to travelling to the PHS and competing priorities (6, 7). As expected, this could have resulted in lower completion of TPT among asylum seekers and settled Eritreans. However, the efforts of PHS staff to track down asylum seeking and Eritrean clients for appointments seem to have resulted in retention of those clients on TPT (6, 7).

Another explanatory factor for the lower TPT completion among immigrants was side effects (i.e., occurrence of predicted, but undesirable events on correctly dosed TPT). Considerably larger proportion of immigrants reported one or more side effects and discontinued TPT because of side effects: 47% and 18% of the immigrants, respectively, compared to 34% and 2% of asylum seekers, and 24% and 3% of settled Eritreans, respectively. (Table 1) As a result of lower self-perceived severity and chance of developing TB disease, immigrants may have been less acceptant of side effects and have had lower intrinsic motivation to continue TPT when experiencing side effects. The proportion of reported side effects among all three migrant populations is high compared to that reported nationally (10%) (13). This may be due to the study setting: we asked TB physicians to report any type of adverse event, whereas in the surveillance system only adverse events (i.e., occurrence of unintended and harmful events on correctly dosed TPT regimen) are reported.

Language can be an important barrier to TPT uptake and completion. Professional interpreters were less frequently used in consultations with immigrants (19%) than with asylum seekers (65%) and settled Eritreans (91%). (Table 1) Because of time constraints, PHS staff asked more proficient family members to interpret for 17 out of 19 immigrant clients, compared with 6 out of 121 asylum seeking clients with limited English proficiency (7). No family members acted as interpreters among settled Eritreans. Using informal interpreters, such as family members, is undesirable because of unfamiliarity with medical terminology, confidentiality issues, and personal agendas, which can lead to misunderstandings and errors in interpretation (14).

TPT initiation and completion are crucial to avert TB disease, reduce TB transmission, and therewith stimulate the decline in TB incidence to work towards TB elimination (4, 15). To reach those goals, motivation among healthcare workers and TBI diagnosed individuals is important to initiate and complete TPT among those eligible for TPT. However, evidence on effective interventions to stimulate TPT initiation, adherence, and completion is limited (16). In this letter, we demonstrated differences in TPT uptake and completion among three different migrant groups and showed that TPT uptake and completion was lowest and most challenging among newly arriving immigrants. A verbal education session about TB, TBI, TPT, and the risk of TB development, in combination with committed and supportive TB care staff and the use of professional interpreters were important facilitators for TPT initiation and completion among asylum seekers and settled Eritrean refugees and should also be applied among immigrants eligible for TPT.

Table 1. Evaluation of treatment of tuberculosis infection by TB physician and nurse stratified for type of migrant population

	Immigrants	Asylum seekers	Settled Eritrean migrants
	n (%)	n (%)	n (%)
Characteristics of persons screened for TBI			
Total persons screened for TBI	566	718	257
Age			
0-17 years	85 (15%)	60 (8%)	48 (19%)
18-24 years	64 (11%)	219 (31%)	63 (25%)
25-34 years	286 (51%)	269 (37%)	103 (40%)
≥35 years	131 (23%)	171 (24%)	43 (17%)
Sex			
Female	329 (58%)	305 (42%)	129 (50%)
Male	237 (42%)	414 (58%)	128 (50%)

Level of education¹			
No formal / lower education	38 (7%)	238 (33%)	116 (45%)
Secondary education	51 (9%)	312 (43%)	108 (42%)
Tertiary education	456 (81%)	132 (18%)	28 (11%)
TBI screening outcomes			
Persons with a positive IGRA	101 (21%) ²	205 (29%) ³	33 (13%) ⁴
Persons with a TBI diagnosis	94 (17%)	178 (25%)	30 (12%)
Consultation by TB physician of persons with a positive IGRA			
Yes	101 (100%)	185 (90%)	33 (100%)
Was an interpreter used during those consultations?			
Yes	19 (19%)	121 (65%)	27 (82%)
A professional interpreter was used	2	110	13
A family member was used	17	6	0
Other	0	5	14
TPT initiation among clients with a TBI diagnosis			
TPT started	49 (52%)	149 (84%)	29 (97%)
TPT not started	45 (48%)	29 (16%)	1 (3%)
Reasons for not starting TPT (reported by TB physician)⁵			
▪ Contraindication ⁶	8	14	0
▪ Client perceived small chance of TB development	16	5	0
▪ Afraid of (severe) side effects / Objection against duration of therapy and large amount of tablets	6	2	0
▪ Borderline IGRA values ⁷	6	0	1
▪ Client expects to return / frequent travelling to country of origin	12	2	0
▪ Other / unknown	5	7	0
Characteristics of clients on TPT			

Age			
0-18 years	3 (6%)	8 (5%)	1 (3%)
18-24 years	5 (10%)	37 (25%)	5 (17%)
25-34 years	27 (55%)	58 (39%)	12 (41%)
≥35 years	14 (29%)	46 (31%)	11 (38%)
Gender			
Male	25 (51%)	101 (68%)	19 (66%)
Female	24 (49%)	48 (32%)	10 (35%)
Level of education¹			
No formal / primary education	11 (22%)	58 (39%)	11 (41%)
Secondary education	7 (14%)	57 (38%)	13 (48%)
Tertiary education	28 (57%)	26 (17%)	2 (7%)
Any type of side effects among clients on TPT, reported by PHS staff¹			
Yes	23 (47%)	50 (34%)	7 (24%)
Client-related problems among clients on TPT during TPT reported by PHS staff¹			
Yes	15 (31%)	50 (34%)	8 (28%)
Most frequent reported problems during TPT⁵			
Compliance / Adherence	3 (20%)	6 (12%)	1 (13%)
Difficulties follow-up appointments	6 (40%)	23 (46%)	1 (13%)
Difficulties duration of TPT / amount of pills	2 (13%)	7 (14%)	1 (13%)
TPT support among clients on TPT given by a PHS nurse¹			
Yes	33 (67%)	129 (87%)	29 (100%)
Completion of TPT			
Yes	34 (69%)	129 (87%)	28 (97%)
No	15 (31%)	20 (13%)	1 (3%)
Reasons reported for discontinuing TPT			
Side-effects ⁸	9 (18%)	3 (2%)	1 (3%)
Pregnancy	2 (4%)	2 (1%)	0 (0%)

Withdrawn for unknown reasons	4 (8%)	4 (3%)	0 (0%)
Lost to follow-up	0 (0%)	7 (5%)	0 (0%)
Other / Unknown	0 (0%)	4 (3%)	0 (0%)

PHS: Public Health Service; TB: tuberculosis; TBI: tuberculosis infection; TPT: tuberculosis preventive treatment

¹ Data missing for immigrants, asylum seekers, and settled Eritreans for the following variables: level of education of population screening: 21 (4%), 37 (5%), 5 (2%); interpreter used: 3 (3%), 6 (3%), 1 (3%); level of education of clients on TPT: 3 (6%), 8 (5%), 1 (4%); reported side effects: 0 (0%), 6 (4%), 2 (7%); reported problems: 2 (4%), 7 (5%), 3 (10%); TPT support: 2 (4%), 8 (5%), 0 (0%).

² Of 101 immigrants with a positive IGRA, 94 were diagnosed with TBI; 3 with TB disease; 3 had treated TB disease in the past; 1 had received TB preventive treatment for fibrotic lesions.

³ Of 205 asylum seekers with a positive IGRA, 178 were diagnosed with TBI; 4 with TB disease; 3 had treated TB disease in the past; 20 persons were lost to follow-up (Reasons: 8 left with unknown destination / were deported; 11 did not response to invitation letters of the PHS; 1 PHS failed to transfer one person to another PHS).

⁴ Of 33 persons with a positive IGRA, 30 were diagnosed with TBI; 1 with TB disease; 2 had treated TB disease in the past.

⁵ Multiple reasons / problems can be reported for one client.

⁶ Contra-indications reported (multiple can be reported per client): medication use (n=6), psychosocial complaints (n=6), Alcohol abuse (n=2), Cancer (n=1), Other (n=2), Pregnancy (n=5).

⁷ TB care staff can consider IGRA values 0.35-0.70 as borderline or low-positive, respectively.

⁸ Side effects reported among immigrants: 5 had gastrointestinal and/or fatigue/dizziness, 2 had hepatotoxicity, 1 fever and shivering, 1 low back pain; asylum seekers: 2 had gastrointestinal and/or dizziness, 1 oedema of extremities; and one settled Eritrean had psychosis.

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AUTHORS CONTRIBUTIONS

In collaboration with the other authors, CJ and IS wrote the study's plan of analysis. CJ performed data management. CJ and IS conducted statistical analysis and wrote the manuscript. IS, CE, SH supervised the statistical analysis. All authors read, commented on, and approved the final manuscript.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

DATA AVAILABILITY

The data supporting the results of this study are obtained from the TB ENDPoint project. Anonymous data supporting the study results can be made available upon request, and upon approval by the Dutch National Tuberculosis Registration Committee.

ETHICS

Research involving population health screening subjected to licensing as stated in the Population Screening Act (WBO), is not subjected to the Dutch Medical Research Involving Human Subjects Act (WMO). The Public Health Services, who were responsible for the TBI screening part of involved studies, are licensed under the WBO act to perform screening for tuberculosis, including latent tuberculosis infection. (see <https://english.ccmo.nl/investigators/legal-framework-for-medical-scientific-research/laws/population-screening-act>). Consequently, the Medical Ethical Committee (METC) of University Medical Centre Amsterdam (UMC-AMC) waived the need for ethical approval of the three implementation studies (5-7) which are part of the larger TB ENDPoint project. We obtained permission of the registration committee of the National TB register (NTR) to collect and analyse data

from the NTR database. We followed the ethical principles of the Declaration of Helsinki, adopted by the World Medical Association (WMA Declaration of Helsinki 2000).

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