

Table 1 Study characteristics and main findings from RCTs and controlled studies

a) Different drug regimens and treatment lengths

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Juarez-Reyes 2015, US ¹	Latent	Single arm (prospective) compared with historical control	Both groups: inmates of Santa Clara Jail (California). Large proportion also with history of alcoholism and/or drug use (in the prospective group).	3HP by DOT (prospective group, n=91)	9H by DOT (historical control, n=154)	3HP: 77/91 (85%) completed versus 9H: 28/154 (18%) completed, p<0.001 (unadjusted comparison). Complete AEs reported only for 3HP arm.	Main reason for non-completion was transfer out of jail; other reasons included discontinuation due to rash, unrelated illness/declined further treatment, no identifiable reason.
Wheeler & Mohle-Boetani 2019, US ²	Latent	Single arm prospective and single arm retrospective (NB not designed as comparative study)	Patients entering California state prisons (prospective group); patients from the California Correctional Health Care Services registry (retrospective group). Additional risk factors not reported.	3HP by DOT (prospective group, n=122)	9H by DOT (retrospective group, n=92)	3HP:110/122 (90%) versus 9H: 39/92 (42%). Higher completion rate in 3HP prospective cohort compared with 9H retrospective cohort but not designed as comparative study.	Main reason was parole, discharge or transfer out of system, discontinuation by providers or refusal to complete treatment.
Villa 2019, Italy ³	Latent	Retrospective cohort study	General population, with sub-group analysis for homeless people, "irregular" migrants and asylum seekers and refugees.	3HP or 4R (not stated if DOT, n=4065)	6H (not stated if DOT, n=15,605)	Overall: 85.6% (3HP or 4R) completed versus 77.8% (6H), p<0.0001 (unadjusted comparison). Based on those without treatment changes only (n=17,859): Homeless people: 55.6% (6H) versus 76.8% (3HP or 4R), p<0.0001; "irregular" migrants: 73.0% (6H) versus 70.8% (3HP or 4R), p=0.54; asylum seekers or refugees: 100% (6H) versus 93.3% (3HP or 4R), p=1. More frequent AEs in 6H vs 3HP/4R.	Main reason was loss to follow-up (did not return for follow-up visits), other reasons were patient default, suspension, unknown or death. Not reported separately for sub-groups.
Chevrier 2022, Canada ⁴	Latent	Before and after study - part of mixed methods study	Government assisted refugees from a TB endemic country.	3HP or 4R (post 2015, n with DOT not stated, n=115)	9H (pre 2015, n with DOT not stated, n=74)	3HP or 4R: 104/115 (90.4%) completed versus 9H: 61/74 (82.4%), p=0.170. No differences in adherence reported by staff between clients receiving 3HP (DOT) versus SAT with 4R (no numerical data presented).	Multinomial regression models found that the short treatment regimen, and female sex tended to positively affect the treatment completion proportion.

DOT: directly observed therapy; SAT: self-administered therapy; 3HP: three months of once-weekly isoniazid plus rifapentine; 4R: four months of daily rifampin; 3HR: three months of daily isoniazid plus rifampin; 6H: isoniazid for 6 months; 9H: isoniazid for 9 months.

b) Different types of treatment administration (DOT/VOT/SAT)

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Bishara 2023, Israel ⁵	Latent	Retrospective cohort study	Ethiopian immigrants living in reception centres	semi-DOT provided once weekly by nurse with second dose self-administered (n=231)	SAT with medication provided during monthly follow-up visits (n=224)	Slightly lower treatment completion rate with SAT compared with DOT (87.9% vs 93%) but no statistically significant difference (non-adjusted OR 0.54 (95% CI 0.28, 1.04)).	Treatment completion rate significantly lower in those with side effects; no statistically significant difference for sex or age group (though slightly higher completion rate in males).
Story 2019, UK ⁶	Active	Randomised controlled trial	58% with social risk factor (history of homelessness, imprisonment, drug use, alcohol problems, or mental health problems).	DOT provided 3-5 times/week (n=114)	VOT provided by a centralised service and patients trained to send videos using a smartphone app (n=112)	VOT significantly improved odds of successful completion of 80% or more scheduled treatment observations over 2 months compared with DOT (ITT analysis). Partially adjusted OR (95% CI) 5.48 (3.10, 9.68), p<0.0001 (ITT analysis). Fully adjusted OR (95% CI) 2.52 (1.17, 5.47), p=0.019 (restricted analysis which excluded patients with <1 week in observation arm).	Less initial engagement with DOT compared with VOT –particularly among younger adults, foreign-born patients and those without social risk factors or mental health problems. Similar rates of engagement with VOT across all subgroups.
Onwubiko 2019, US ⁷	Latent	Retrospective cohort study	Homeless people who were current residents of an emergency shelter at time of treatment initiation. Higher proportions of current alcohol use (25% vs 8%), illicit drug use (11% vs 3%) and a mental health disorder (12% vs 2%) in the DOT group.	4R DOT provided 5 days/week (n=181)	4R SAT - pill box with 30 doses provided each month (n=93)	DOT significantly improved the odds of treatment completion compared with SAT. Adjusted OR (parsimonious weighted model): OR: 1.30 (1.01, 1.67), p = 0.045. Adjusted OR (fully weighted and adjusted model): OR: 1.40 (1.07, 1.82), p = 0.014.	Male sex, Black/African American, age (50–59, 60 years and older) and positive HIV status significantly associated with increased odds of treatment completion while alcohol use was associated with decreased odds of completing treatment (fully adjusted analysis).

DOT: directly observed therapy; VOT: video observed therapy; SAT: self-administered therapy; 4R: four months of daily rifampin

c) Screening or test focussed approaches

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Lim 2021, Canada ⁸	Latent	Retrospective cohort study	Privately sponsored refugees, government-assisted refugees or refugee claimants.	IGRA only screening (QuantiFERON-TB Gold Plus (QFT)). Positive QFT triggered chest x-ray and referral for Treatment* at the local TB clinic (n=41 with LTBI).	Sequential screening: initial TST, followed by confirmatory IGRA if the TST was positive. Positive QFT triggered a chest x-ray and referral for LTBI treatment* at the local TB clinic (n=20 with LTBI).	IGRA: 29/33 (87.9%) who started treatment completed. Sequential: 14/16 (87.5%) who started treatment completed. Screening completion rates (85% IGRA vs 54% sequential). Adjusted OR (95% CI) 3.74 (2.30, 6.09) < 0.001.	Not reported for completion rates. In the adjusted analysis, IGRA only screening and privately sponsored refugees were predictors of screening completion (adjusted analysis).
Walters 2016, US ⁹	Latent	Before and after study	Newly arrived refugees	Post 2011: widespread introduction of IGRA (QuantiFERON-TB Gold Plus (QFT)), n=287 with LTBI	Pre 2011: mainly TST, n=393 with LTBI	Post-QFT: 215/287 (75%) candidate for treatment; 160/215 (74%) started treatment; 107/160 (67%) completed treatment. Pre-QFT: 333/393 (85%) candidate for treatment; 221/333 (66%) started treatment; 154/221 (70%) completed treatment. Significantly greater proportion of refugees diagnosed with LTBI pre-2011, and a significantly greater proportion initiated treatment post 2011.	Reasons for non-completion mostly loss to follow-up and patients stopping treatment (both time periods). 4R or 6R was significantly associated with greater completion rate compared with 6H or 9H; refugees from South Asia had higher odds of treatment completion than refugees from sub-Saharan Africa (bivariate analyses). Age group was not found to be a significant predictor of treatment completion.
Spruijt 2020a, The Netherlands ¹⁰	Latent	Prospective comparison of six strategies - part of mixed methods study.	Eritrean migrants	Six community strategies ^b to encourage screening and treatment, developed with Eritreans from the community. All strategies included 1-3 education sessions in a community setting followed by screening sessions*; n=410 (participation in community strategies), n=30 (with LTBI). Screening and treatment offered free of charge. LTBI treatment support by TB nurse and interpreters where necessary.		Completion rate: 28 of 29 (97%) of those initiating LTBI treatment after diagnosis. Not reported by community strategy arm. Uptake of LTBI education differed between strategies from 13% to 75% (overall 44%). Uptake of screening of those who participated in education session was 64%.	Includes: participants prioritising only compulsory appointments, lack of motivation due to competing priorities, lack of understanding of LTBI and scepticism about the project's purpose. <i>See qualitative studies in supplementary material for further detail.</i>

IGRA: Interferon-Gamma Release Assays; TST: tuberculin skin test; * treatment with 3HP, 4R or 9H according to local practice and patient factors; a standard treatment 6H or 9H or 4R or 6R depending on age and risk factors. b Strategy 1: invitation by email, Facebook group and WhatsApp church group (education session at community centres); strategy 2: face-to-face promotion through PHS staff (Dutch language classes, libraries, the church, and the gym), education at local community centre; strategy 3: Dutch language classes for promotion by teacher or key community figures, flyers and displaying posters, education session at the PHS; strategy 4: education session in community space of group housing (education session at the house); strategy 5: Education after sports club (football), education session at sports club; strategy 6: promotion of education/screening after church service.

d) Strategies tailored to people experiencing homelessness, social risk factors or substance abuse

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Crosby 2023, UK ¹¹	Active	Comparative cross-sectional	Homeless TB patients with complex social needs; proportion with history of drug use, prison, alcohol use or need for DOT.	Residential respite service for homeless TB patients (facilitates timely/safe discharge from hospital, provides accommodation, DOT, psychological help and support for drug and alcohol dependency and support for finding work, living independently and reconciling with families or communities), n=89	Standard community treatment, n=24,092	Greater odds of treatment completion with residential; respite service, adjusted OR 2.97 (95% CI 1.44, 6.96). Adjusted for demographic, social and clinical variables, including drug resistance, history of homelessness, drug or alcohol use and need for DOT.	Strong association between missing data and treatment failure - covariate data may be less likely to be recorded in non-completers.
Nyamathi 2021, US ¹²	Latent	Single arm (prospective) compared with historical control	Homeless person defined as anyone who spent the previous night in a public or private shelter or on the streets, proportion with history of drug or problematic alcohol use.	Tailored nurse-led, community health worker (RN/CHW) program across the LTBI pathway (screening, diagnosis, treatment); CHWs were formerly homeless adults; each RN/CHW assigned 7-8 participants; weekly meetings and provision of DOT; weekly one-on-one case management sessions (coaching support, education, support for drug/alcohol use and mental health issues); health and social service referrals; tracking of participants who missed a dose; n=50	3HP LTBI treatment in historical control (no RN/CHW program), n=56	Greater proportion of people completed in the intervention group compared with the historical control group: 91.8% (95% CI 80.8, 96.8)) in intervention group versus 66% (CI not reported) in historical control group.	Younger age (<50) significantly associated with non-completion in intervention group; men less likely to complete than women (not statistically significant). No association found with drug or alcohol use or anxiety/depression.
Izzard 2021, UK ¹³	Active	Retrospective cohort study	Social risk factors, mainly homelessness. Also included a proportion on benefits, immigrants, people with financial issues or drug/alcohol misuse.	North Central London TB network re-configured to include a social care team (SCT). Provision of (additional) dedicated specialist support; intensive individualised casework support for homelessness, housing, benefits, employment, immigration and financial issues such as debt, referrals to other services including drug and alcohol and mental health. Can include regular phone calls, administrative support, and accompanying patients to appointments (e.g. Job Centre, Council, Citizens Advice Bureau, solicitors, or for GP registration); 48% DOT/VOT; n=170	Standard care without access to SCT (i.e. patients who had not been referred); 12% DOT/VOT; n=734	Patients referred to SCT significantly more likely to complete planned treatment. 88.2% (SCT) versus 77.7% (comparison cohort) completed. Adjusted OR 2.35 (1.41, 3.91), p=0.001 (in favour of social care team).	Increased completion rate remained when patients stratified by DOT/VOT or no DOT/VOT, with a stronger association in those not receiving DOT/VOT.
Ricks 2015, US ¹⁴	Active	Randomised controlled trial	Substance users (illicit drug use and/or daily consumption of at least 2 alcoholic drinks during the 6 months before enrolment). Proportion with history of incarceration or unstable housing.	Enhanced arm: use of trained and experienced community (HIV prevention) outreach staff who were former substance users to perform DOT; two-person mixed-sex team to provide DOT.	Standard arm: standard DOT provided by trained and experienced communicable disease investigators.	Patients in standard treatment arm at significantly greater risk of failing to complete treatment (RR 2.5 (95% CI 1.2, 5.1)).	Nine covariates significantly associated with failure to complete treatment: Hispanic ethnicity, primary residence not own or partner's, shelter stay in past 6 months, ≥1 night in rented room, ≥1 night in shelter, ≥1 night in abandoned building, non-cavitary TB, previous TB diagnosis, HIV positive (multivariate model using imputed data).

e) Refugee specific clinics (integrated care)

Study	Type of TB	Design	Population/ risk factors	Intervention (n=) and comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non- completion
Subedi 2015, US ¹⁵	Latent	Retrospective cohort study	Newly arrived refugees	<p><u>Intervention:</u> Philadelphia Refugee Health Collaborative (PRHC) clinics. Collaborative working between refugee resettlement agencies and refugee health clinics; includes outpatient paediatric, internal medicine, and family medicine programmes; led by physicians with expertise in primary care for new immigrants; services reimbursed during first 8 months; refugees reminded of appointments; bilingual services and pre-set visit schedule; provision of regular, culturally appropriate refugee orientation meetings, follow-up patient education meetings and educational materials. Multidisciplinary approach by doctors, nurses, social workers and case workers from volunteer agencies and Department of Public Health; n=38.</p> <p><u>Comparator:</u> non-PRHC clinics. Health screening and follow-up appointments left to patient. No cross-clinic referral system or logistical support from resettlement agencies; n=19.</p>	<p>Significantly greater proportion completed in the PRHC clinic group (89.5%) compared with the non-PRHC clinic group (47.4%). Unadjusted OR (95% CI) 9.44 (2.39, 37.30).</p> <p>Time to initial screening shorter, and greater proportion of follow-up appointments completed in PRHC group compared with non-PRHC-group.</p>	Not reported.
Kunin 2022, Australia ¹⁶	Latent	Prospective cohort study - part of mixed methods study	Asylum seekers and refugees	<p><u>Intervention:</u> Monash Health Refugee Health and Wellbeing (MHRHW) service. Integrated primary care and specialist services; intensive transitional care to asylum seekers/refugees experiencing high levels of vulnerability, complex health needs and restricted access to Medicare. Includes refugee health assessments; use of interpreting services; delivery of capacity building and community development strategies. Multi-disciplinary team, including GPs, GP refugee health fellows, refugee health nurses, infectious diseases physicians, paediatricians, bicultural workers, community development workers, psychiatrists, counsellors and pharmacists. Development of comprehensive training module for primary care providers, GPs, and nurses, and a Patient Education Resource Pack; n=15..</p> <p><u>Comparator:</u> universal primary care clinic. Includes onsite pharmacy; consultations subsidised through Medicare; multi-lingual staff; n=16.</p>	Significantly higher completion rate at MHRHW compared with universal care: 93% (MHRHW) versus 56% (universal care), p=0.0373 (unadjusted analysis).	MHRHW: 1 opted out; Universal care: 1 opted out, 3 adverse reactions, 1 relocated, 2 discontinued collecting medication at less than 6 months (also AEs).

f) Other strategies tailored to migrants, refugees and asylum seekers

Study	Type of TB	Design	Population/ risk factors	Intervention (n=)	Comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Bishara, 2015, Israel ¹⁷	Latent	Retrospective cohort study	'Hard-to-reach' Ethiopian immigrants	<u>Intervention:</u> Nurse-managed semi-DOT and TB clinic at migrant centre. Semi-DOT was two weekly doses, one supervised, one self-administered; team outreach programme consisted of physician and nursing outreach at the migrant reception centre (onsite) TB clinic. Professional interpreter (veteran Ethiopian immigrant) available throughout study. All services free of charge, n=297. <u>Comparator:</u> Nurse-managed semi-DOT and regional TB clinic. No team outreach programme, evaluation and follow-up provided at regional TB clinic to which transport was provided free of charge, n=366.		Similar completion rates. On-site clinic: 96.0% versus regional clinic: 93.7%. Similar number of physician follow-up visits in both groups.	Age < 5 years and side effects were each significantly associated with treatment non-completion (p = 0.03 and p< 0.001, respectively).
Olsson 2018, Sweden ¹⁸	Latent	Before-and-after study	Asylum seekers with or without residence permits	<u>Intervention:</u> Standard care + change of strategy introduced in June 2013. Since then, all subjects were given pre-scheduled appointments for nurse visits, assisted by interpreters; n=297. <u>Comparator:</u> standard care -specialised nurses responsible for distribution of drugs and follow-up during treatment; drugs dispensed at outpatient clinic every 1–2 months where nurses inquire about adherence and side effects and register the number of tablets dispensed; people who fail to show up for the collection of medication are contacted by telephone and mail; n=not stated.		Completion rate significantly higher in those initiating treatment after June 2013 (90%) compared with those initiating therapy earlier (69%), p<0.01 (unadjusted analysis).	Factors significantly associated with completion (multivariate analysis): starting treatment after 30th June 2013; isoniazid treatment for 6 months as compared to 9 months; and receiving LTBI treatment in connection to treatment with immunosuppressive treatment as compared to contacts.

g) Conditional cash transfer

Study	Type of TB	Design	Population/ risk factors	Intervention (n=)	Comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Klein 2019, Argentina ¹⁹	Active	Prospective cohort	Socio- economically disadvantaged patients. Between 45%- 55% with current/past drug use and between 21%- 23% with current/recent alcohol use.	Registration for conditional cash transfer (CCT). Payment of a monthly amount to eligible patients identified and incorporated into the Provincial TB Control Program (PTP); recipients have to adhere to health checks, treatments, and other conditions established by the PTP; failure to do so may result in the loss of the benefit. Process initiated by a health professional; a social worker and a physician evaluate each case, taking into account the severity, the socioeconomic situation, the community risks, and the most susceptible age groups. Registration into the program was considered present if the administrative procedures to get the cash transfer were started during treatment (intention to treat) and absent otherwise; n=337.	Standard care (not registered for CCT); n=564	83% treatment success (completed 6 months of treatment or cure) with CCT versus 69% (control). Crude OR (95% CI) for treatment success 2.08 (1.49, 2.92); adjusted OR (95% CI) 2.91 (1.97, 4.28, p=0.001)	Variables associated with a higher risk of incomplete treatment were self-administered treatment, younger age, lack of insurance, lower income, and use of alcohol and illicit drugs.

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