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Testing and treatment for latent tuberculosis infection in people living with HIV and substance dependence: a prospective cohort study

Tessa Runels,[1] Elizabeth J Ragan ,[1] Alicia S Ventura,[2,3] Michael R Winter,[4] Laura F White,[5] C Robert Horsburgh,[1,5,6] Jeffrey H Samet,[2,3] Richard Saitz,[2,3] Karen R Jacobson[1]

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Dr. RS deceased

TR and EJR are joint first authors.

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For numbered affiliations see end of article.

Correspondence to
Dr Karen R Jacobson;
kjacobso@bu.edu

ABSTRACT

Objective To quantify the proportion of people living with HIV (PLWH) with other tuberculosis (TB) risk factors that completed the latent tuberculosis infection (LTBI) care cascade and describe factors associated with attrition. The care cascade was defined as follows: (1) receipt of an LTBI test and result, (2) initiation of LTBI treatment and (3) completion of LTBI treatment.

Design Prospective cohort study.

Setting Reactivation of LTBI remains a large source of active TB disease in the USA. PLWH and those who use substances are at greater risk and are harder to engage and retain in care.

Participants Participants enrolled in a Boston cohort of PLWH from 2012 to 2014.

Primary and secondary outcome measures Our primary outcome was the number and proportion of participants who completed each stage of the cascade and the factors associated with completing each stage. Our secondary outcomes were differences between participants tested with an interferon gamma release assay (IGRA) versus tuberculin skin test and differences between participants who tested positive versus negative for LTBI.

Results Only 189 of 219 (86.3%) participants completed testing. Five of the 11 with LTBI initiated and three completed treatment. Participants tested with an IGRA were more likely to complete testing (OR 3.87, 95% CI 1.05 to 14.30) while among participants successfully tested, being foreign-born was associated with a positive test result (OR 3.95; 95% CI 1.13 to 13.77).

Conclusions Although the majority completed LTBI testing, our findings warrant further investigation in a larger cohort to better understand factors that lead to suboptimal treatment initiation and completion in a low-burden country.

Strengths and limitations of the study

- While other studies have investigated predictors of latent tuberculosis infection (LTBI) care cascade completion in the USA, our analysis uses predictors derived from validated biobehavioural instruments (eg, Mini-International Neuropsychiatric Interview V.6.0, Addiction Severity Index and 30-day Timeline Followback), especially capturing substance use and dependence, reducing misclassification bias of these risk factors.
- A unique element of our study is that we looked at individuals engaged in HIV care, that is, a group that, per guidelines, should be receiving LTBI testing in the clinical setting and therefore provides an opportunity to understand how well testing is done under these conditions.
- Our study is limited by its small sample size, preventing us from further assessing risk factors for non-completion along the entire cascade of LTBI care.
- Our study is limited in its generalisability: our participants were all engaged in HIV care at the time of enrolment, potentially increasing the likelihood that they received LTBI testing compared with the broader population of people living with HIV.
- Our study was not randomised, which may lead to unmeasured confounding and impact validity of findings.

INTRODUCTION

Reactivation of tuberculosis (TB) infection remains a source of active TB disease in the USA. An estimated 13 million people in the USA have latent TB infection (LTBI).[1] To reduce TB disease incidence and mortality, TB testing and treatment is prioritised for individuals at increased risk for progression to active disease, including persons living with HIV (PLWH) and people who inject drugs (PWID).[1 2]

In PLWH, TB preventive therapy has been shown to reduce the risk of progression to active disease by up to 62%.[3] HIV is one of the greatest risk factors for active TB development; PLWH are 20–30 times more likely to develop TB than individuals without HIV.[4] Injection drug use (IDU) has also

been associated with higher LTBI risk, with an estimated 10%–59% of PWID to be infected with TB.[5] Alcohol use is also a risk factor for TB disease, with individuals who consume ≥40 g of alcohol daily having a nearly threefold increased risk.[6] For these reasons, PLWH and individuals who use drugs and alcohol have been prioritised for LTBI testing and TB preventive therapy.

PLWH are a particularly high priority group for TB testing because for those with LTBI, TB preventive therapy decreases their risk of progressing to active TB, development of immune reactivation inflammatory syndrome and overall HIV-associated morbidity and mortality.[3 7 8] The reduced risk of TB disease and mortality attributable to TB preventive therapy among PLWH is independent of whether an individual is on antiretroviral therapy (ART).[9]

The two main diagnostic tests for LTBI are the Mantoux tuberculin skin test (TST) and the interferon-gamma release assay (IGRA), the former an intradermal hypersensitivity test and the latter a whole blood immune assay.[2] The care cascade for TB testing includes: (1) being successfully tested for TB (ie, receiving a result), (2) initiating TB preventive therapy and (3) completing treatment. Currently, 3 months of weekly isoniazid (INH) plus rifapentine, 4 months of daily rifampin or 3 months of daily INH plus rifampin are standard regimens in the USA. Six or 9 months of daily INH can also be offered, the latter which was standard at the time of this study.[1] A meta-analysis on the LTBI cascade found that among individuals intended for screening in high-income countries, 76% received a test result, 65% accepted and started treatment and 23% completed treatment.[10] Another meta-analysis of the LTBI cascade among PLWH found treatment completion to be 37.9% in high-income countries.[11] Populations at higher risk for LTBI and HIV, including people who are foreign-born, homeless, have a history of incarceration and who use substances,[2] are often harder to engage and retain in care. US-based studies report that between 54% and 79% of eligible PLWH receive TB testing which, although greater than the general population, falls short of the 100% goal.[12 13] One US-based study found that individuals who reported consuming ≥3 alcoholic drinks daily were half as likely to initiate treatment than those who did not use alcohol.[14] Treatment completion rates are also lower than desired among PLWH, people with substance dependence, who are foreign-born and who are homeless.[15–24] Increased understanding of the drivers of failure to complete each stage of the LTBI cascade could improve interventions for these priority populations.

In this prospective study of a well-characterised US-based cohort of PLWH with substance dependence (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)) history, we aimed to quantify the percentage that completed each stage of the LTBI care cascade and to describe factors associated with failure to complete each stage.

METHODS

Study setting and population

We conducted a secondary analysis of the prospective Boston Alcohol Research Collaboration on HIV/AIDS (ARCH) cohort, a study of individuals with multiple risk factors for both LTBI and poor completion of the LTBI cascade of care.[25] All cohort participants were recruited from the Boston Medical Center infectious disease and HIV clinic or the Boston Healthcare for the Homeless Programme's HIV primary care clinic between September 2012 and November 2014. All participants were actively receiving HIV care at the time of cohort enrolment, enabling us to identify dropout from the LTBI cascade among those already engaged in care. Eligibility criteria for the cohort have been described previously.[25] Additionally for our analysis, participants were excluded if they had past active TB disease or documentation of previous TB preventive therapy, as these individuals would no longer be eligible for repeat testing or treatment. TB testing and treatment were conducted by participants' routine care providers and were not done as part of ARCH cohort participation. Those who test positive were offered 9 months INH with vitamin B_6 and, if they agreed to start treatment, were seen monthly by clinical nurses to confirm medication tolerance. One participant received experimental LTBI treatment as part of a trial. TB testing was either by TST or QuantiFERON TB-Gold In-Tube.

Data collection

Demographic characteristics of study participants were obtained through research assistant administered interviews and medical record review. Alcohol and other drug use were assessed using validated questionnaires by Boston ARCH study personnel. Information on TB testing and treatment and history of active TB was abstracted from the electronic medical record.

Definitions

The Mini-International Neuropsychiatric Interview V.6.0 was used to assess current alcohol use disorder (past 12 months) as well as current alcohol and drug dependence using DSM-IV criteria. History of IDU, current use of ART, time on ART, country of birth and smoking status were ascertained via self-report. Past 30-day IDU was measured using questions from the Addiction Severity Index (ASI) while current prescription of methadone or buprenorphine (treatment for opioid addiction) was measured using the ASI in conjunction with the medical record. Current alcohol use was measured using a 30-day Timeline Followback assessment with drinking behaviour categorised as abstinent, not heavy (not exceeding the National Institute on Alcohol Abuse and Alcoholism (NIAAA) daily or weekly limits by gender), heavy (exceeding NIAAA daily or weekly limits by gender, but <5 heavy days in past month) or frequent heavy (≥5 heavy days in past month). Lifetime alcohol consumption was ascertained using the lifetime drinking history instrument.

Homelessness was defined as self-reported one or more nights on the street or in a shelter in the past 6 months. History of incarceration was abstracted from the medical record. Diabetes without chronic complications was measured according to the Charlson Comorbidity Index. Being foreign-born was defined as being born outside of the USA. Each participant's medical record was reviewed at the time of enrolment and, if available, within the past 3 months for HIV viral load. An undetectable viral load was defined as ≤50 copies/mL. If the medical record lacked documentation, HIV viral load was tested at the time of enrolment. Adherence to ART was defined as self-reported adherence of ≥95% of doses in the last month using a Visual Analogue Scale. Viral hepatitis was defined as having either a positive hepatitis C virus (HCV) antibody result, an HCV viral load of greater than zero, or a positive hepatitis B virus antigen test. Variables collected as part of this study, as defined above, that were comparable to US Centers for Disease Control and Prevention (CDC)-defined risk factors for LTBI were summed to create a final cumulative count, and included: being foreign born; ever IDU; alcohol or drug dependence in the past 12 months; HIV; homelessness; ever incarceration; diabetes; and liver disease. All study participants had a minimum of two risk factors (ie, HIV infection and substance dependence).

The LTBI care cascade included the following: (1) completed TB testing in the 10 years prior to enrolment in the Boston ARCH cohort or up to 12 months thereafter; (2) initiation of TB preventive therapy; and (3) treatment completion (figure 1). TST was interpreted as negative if induration was <5 mm and positive if ≥5 mm, per guidelines.[26] IGRA was recorded as positive, negative or unsuccessful based on standard cut-off of Nil ≥0.35 IU/mL.[27] TB testing completion was defined as receiving a valid TST or IGRA result. Initiation of TB preventive therapy was defined as having a physician visit where TB preventive therapy was prescribed. Information on adherence was not available. Treatment completion was defined as documented completion of a TB preventive therapy regimen in the medical record.

Data analysis

We quantified participants who completed each stage of the cascade, and, when sample size allowed, compared factors associated with completing each stage. We assessed differences in demographics, including number of CDC-defined risk factors, cascade completion and test positivity

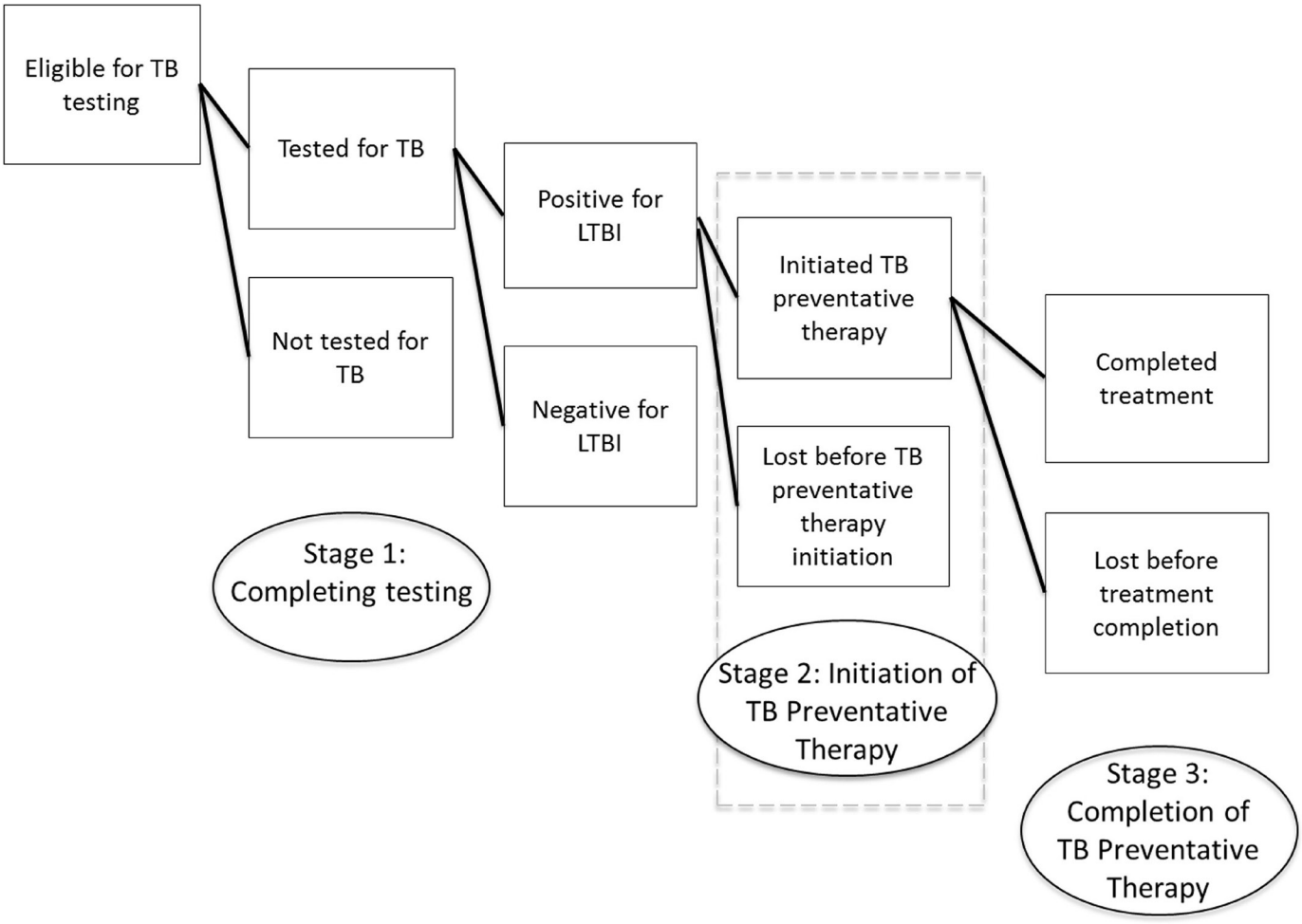

Figure 1 Flowchart of the latent tuberculosis infection (LTBI) cascade of care: (1) completion of tuberculosis (TB) testing; (2) initiation of TB preventive therapy; and (3) completion of TB preventive therapy.

between participants tested with an IGRA versus TST. Lastly, we looking at differences between participants who tested positive versus negative for LTBI. Measures of central tendency were used to describe the distribution of continuous variables. We employed χ^2 and Fisher's exact tests for categorical variables and t-tests for continuous variables to assess the association between cohort characteristics and completion of each stage of the cascade. Wilcoxon rank-sum tests were used for non-normal data. SAS University Edition was used for all statistical analyses with two-tailed significance defined at p<0.05. We report ORs with 95% CIs.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Cohort characteristics

Of the 250 Boston ARCH cohort participants, 1 had a previous history of active TB and 30 had already been treated with TB preventive therapy, leaving 219 eligible for TB testing (table 1). More than half (51.6%) reported concurrent alcohol and drug dependence in the past 12 months, with 11.4% reporting IDU and 53% reporting heavy or frequent heavy alcohol drinking in the 30 days prior to assessment. Including HIV-infection and substance use, half (50.7%) had four or more CDC-defined risk factors for LTBI.

Completion of the cascade of care

Of the 219 participants eligible for this analysis, 203 (92.7%) were tested for LTBI and 189 (86.3%) completed testing (figure 2). Participants tested with IGRA (n=100, 49.3%) were four times more likely to complete testing than those tested with TST (OR=3.87, 95% CI 1.05 to 14.30). Of those who completed testing, more of those tested with TST compared with those tested with IGRA required more than one test (8.8% vs 1.0%, p=0.02). Cumulative number of CDC-defined TB risk factors was not associated with whether a participant was tested for LTBI (table 2), nor was it associated with which test was used (online supplemental additional file 1). Substance dependence was also not associated with lack of TB test completion (OR=1.11, 0.37–3.31). Individuals with alcohol dependence were more likely to be tested with TST (OR=2.15, 1.16–4.00) (online supplemental additional file 1).

Eleven (5.8%) individuals tested positive for LTBI. Among participants successfully tested (n=189), being foreign-born (OR=3.95; 1.13–13.77) was associated with having a positive test result (table 3). Of the 11 participants who tested positive for LTBI, 5 received a TST and 6 received an IGRA. Of those who received a TST, three had information on their induration ranging from 10 mm to 30 mm while one participant originally tested with IGRA

Table 1 Characteristics of study participants eligible for TB testing (n=219)

Demographics	n (%) or mean (SD)	
Mean age, years	48.7	(9.5)
Female	82	(37.4)
Race/ethnicity		
White	44	(20.1)
Black	108	(49.3)
Hispanic/other	67	(30.6)
Employed	35	(16.0)
Foreign-born	38	(17.4)
Completed high school	140	(63.9)
Married/live with partner	56	(25.6)
Ever incarceration	106	(48.4)
Homeless*	58	(26.5)
Number of CDC-defined TB risk factors		
2 risk factors	47	(21.5)
3 risk factors	61	(27.9)
4 or more	111	(50.7)
Substance use		
Current smoking, n=217	175	(80.7)
Lifetime alcohol use, n=215		
<150 kg of alcohol	68	(31.6)
150–600 kg of alcohol	66	(30.7)
>600 kg of alcohol	81	(37.7)
Lifetime IDU, n=218	122	(56.0)
Current IDU†	25	(11.4)
Currently prescribed methadone or buprenorphine, n=199	47	(23.6)
Current alcohol and drug dependence‡		
No dependence	37	(16.9)
Alcohol dependence only	21	(9.6)
Drug dependence only	48	(21.9)
Both alcohol and drug dependence	113	(51.6)
Current alcohol use disorder§		
Neither	76	(34.7)
Alcohol abuse	9	(4.1)
Alcohol dependence	134	(61.2)
Current alcohol use†		
Abstinent	71	(32.4)
Low risk	32	(14.6)
Heavy	55	(25.1)
Frequent heavy	61	(27.9)
Health characteristics		
Health insurance¶	218	(99.5)
Medicaid/Masshealth	211	(96.4)
Medicare	99	(45.2)

Continued

Table 1 Continued

Demographics	n (%) or mean (SD)	
Diabetes mellitus	49	(22.4)
Undetectable HIV viral load**, n=218	139	(63.8)
Mean length of HIV infection, years n=214	15.7	(8.3)
Viral hepatitis (B and/or C)	125	(57.1)
Median CD4 count, n=218 (IQR)	549	(328-769)
Time using ART, years n=206	11.7	(8.2)
Current use of ART, n=218	191	(87.6)
ART adherence 95% or greater††, n=190	111	(58.4)

*1+nights on street or in shelter past 6 months.
†In past 30 days.
‡From MINI combined alcohol and drug DSM-IV 12-month dependence.
§From MINI 12-month DSM-IV alcohol dependence/abuse.
¶Non-cumulative.
**50 copies/mL or less.
††Self-report on Visual Analogue Scale.
ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention ; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition ; IDU, injection drug use; MINI, Mini-International Neuropsychiatric Interview ; TB, tuberculosis.

was retested with TST and had a recorded TST induration of 25 mm. Five individuals initiated TB preventive therapy even though two patient records detailed a history of liver disease or the need to abstain from drinking. Four participants initiated the standard 9-month INH regimen and one initiated a 1 month short course of a rifamycin and INH as part of a clinical trial. Three individuals completed treatment. Of those that discontinued treatment, one participant cited abdomen cramping and seizures while the other did not have details other than the provider noting that stopping treatment was safest in light of chronic liver disease.

DISCUSSION

For this cohort of PLWH and substance dependence engaged in clinical care, we found a high proportion were successfully tested for LTBI, higher than previously reported by two studies of HIV-infected populations with lower levels of substance use, which may reflect that our cohort was more engaged in HIV care (ie, all on ART, median CD4 count >500).[28 29] Substance dependence was not predictive of whether an individual successfully completed testing. However, our findings show that even with successful engagement in the beginning of the cascade, retention through the treatment phase of the LTBI cascade was poor. All participants should have been tested for LTBI, and all those who tested positive should have initiated and completed TB preventive therapy.[1 2] Only a quarter of participants eligible completed the full cascade. No known risk factors nor the cumulative number of risk factors were associated with attrition from TB testing. Trends in LTBI and TB disease in the USA continue to support the prioritisation of the testing and treatment of populations such as our cohort. A review of TB outbreaks in the USA from 2002 to 2011 reported that substance use disorder, homelessness and incarceration were significant drivers in outbreak development.[30]

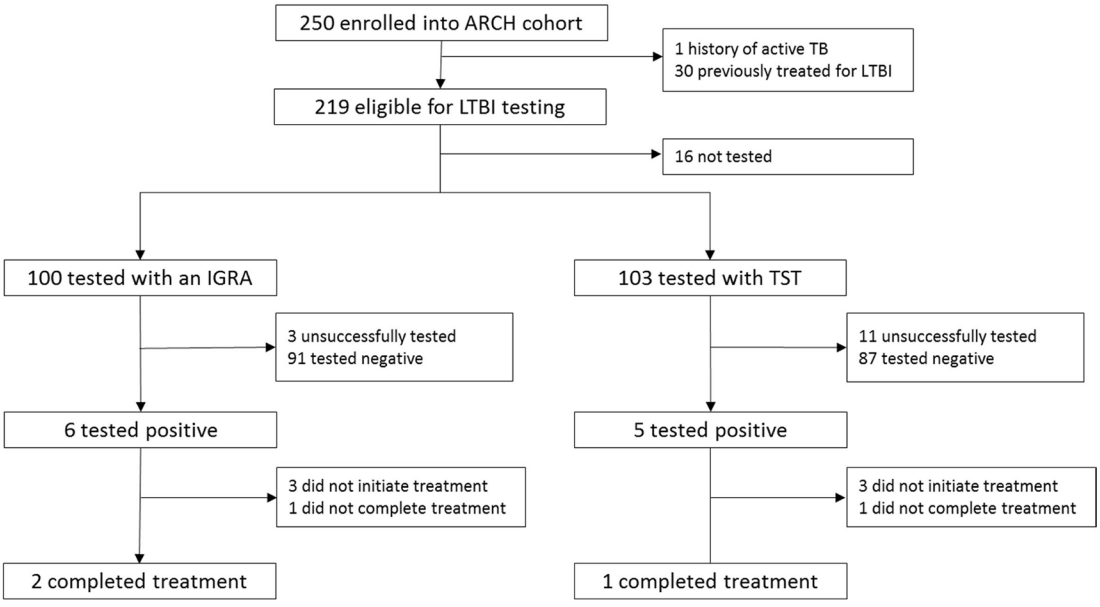

Figure 2 Flowchart of study participants who were eligible for TB testing, received a test (IGRA or TST), were successfully tested (ie, received a valid result), tested positive for TB infection, initiated treatment and completed treatment (N=250). ARCH, Alcohol Research Collaboration on HIV; IGRA, interferon-gamma release assay; LTBI, latent TB infection; TB, tuberculosis; TST, tuberculin skin test.

Table 2 Comparison of participants who completed testing* versus those who did not (n=219)

	Completed testing (n=189) n (%) or mean(SD)		Did not complete testing (n=30) n (%) or mean(SD)		OR	(95% CI)
Demographics						
Mean age, years†‡	48.5	(9.4)	49.9	(9.9)	0.86	(0.56 to 1.30)
Received TST, n=203	92	(48.7)	11	(78.6)	0.26	(0.07 to 0.96)‡
Female	69	(36.5)	13	(43.3)	0.75	(0.34 to 1.64)
Race/ethnicity						
White	38	(20.1)	6	(20.0)	ref	—
Black	89	(47.1)	19	(63.3)	0.74	(0.27 to 2.00)
Hispanic/other	62	(32.8)	5	(16.7)	1.96	(0.56 to 6.86)
Employed	33	(17.5)	2	(6.7)	2.96	(0.67 to 13.05)
Foreign-born	36	(19.1)	2	(6.7)	3.29	(0.75 to 14.47)¶
Completed high school	125	(66.1)	15	(50.0)	1.95	(0.90 to 4.25)§
Ever incarceration	93	(49.2)	13	(43.3)	1.27	(0.58 to 2.75)
Homeless**	52	(27.5)	6	(20.0)	1.52	(0.59 to 3.93)
Number of CDC-defined TB risk factors						
2 risk factors	38	(20.1)	9	(30.0)	ref	—
3 risk factors	55	(29.1)	6	(20.0)	2.17	(0.71 to 6.61)
4 or more	96	(50.8)	15	(50.0)	1.52	(0.61 to 3.76)
Substance use						
Current smoking, n=217	153	(81.8)	22	(73.3)	1.64	(0.67 to 3.99)
Lifetime IDU, n=218	107	(56.9)	15	(50.0)	1.32	(0.61 to 2.86)
Current IDU††	19	(10.1)	6	(20.0)	0.45	(0.16 to 1.23)
Current alcohol and drug dependence§§						
No dependence	32	(16.9)	5	(16.7)	ref	—
Alcohol dependence only	15	(7.9)	6	(20.0)	0.39	(0.10 to 1.49)
Drug dependence only	43	(22.8)	5	(16.7)	1.34	(0.36 to 5.04)
Both	99	(52.4)	14	(46.7)	1.11	(0.37 to 3.31)
Current alcohol use disorder††						
Neither	67	(35.5)	9	(30.0)	ref	—
Alcohol abuse	8	(4.2)	1	(3.3)	0.80	(0.11 to 5.62)
Alcohol dependence	114	(60.3)	20	(66.7)	0.79	(0.34 to 1.80)
Current alcohol use**						
Abstinent	64	(33.9)	7	(23.3)	ref	—
Low risk	28	(14.8)	4	(13.3)	0.77	(0.21 to 2.83)
Heavy	46	(24.3)	9	(30.0)	0.56	(0.19 to 1.61)
Frequent heavy	51	(27.0)	10	(33.3)	0.56	(0.20 to 1.57)
Health characteristics						
Health insurance¶¶	188	(99.5)	30	(100)	—	—
Medicaid/Masshealth	181	(95.8)	30	(100)	—	—
Medicare	90	(47.6)	9	(30.0)	2.12	(0.92 to 4.87)§
Diabetes mellitus	40	(21.2)	9	(30.0)	0.63	(0.27 to 1.47)
Undetectable HIV viral load††††, n=218	119	(63.3)	20	(66.7)	0.86	(0.38 to 1.95)
Mean length of HIV infection, years†*** n=214	15.6	(8.4)	16.3	(7.5)	0.95	(0.75 to 1.20)
Median CD4 count†‡‡‡, n=218 (IQR)	544	(331.5–777.5)	565	(258-684)	1.05	(0.92 to 1.20)

Continued

Table 2 Continued

	Completed testing (n=189) n (%) or mean(SD)		Did not complete testing (n=30) n (%) or mean(SD)		OR	(95% CI)
ART adherence 95% or greater§§§, n=190	98	(59.8)	13	(50.0)	1.48	(0.65 to 3.40)

*Completing testing was defined as having a valid result, including having been tested more than once before receiving a valid result, versus those who were never tested or who did not have a valid result.
†Due to non-normal data, Wilcoxon rank-sum test was used.
‡OR per 10 years change.
§Test statistic is statistically significant at the 0.05 significance level.
¶Test statistic is statistically significant at the 0.10 significance level.
**1+ nights on street or in shelter past 6 months.
††In past 30 days.
‡‡From MINI combined alcohol and drug DSM-IV 12-month dependence.
§§From MINI 12-month DSM-IV alcohol dependence/abuse.
¶¶Non-cumulative.
***50 copies/mL or less.
†††OR per 5 years change.
‡‡‡OR per 100 copies change.
§§§Self-report on Visual Analogue Scale.
ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention ; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition ; IDU, injection drug use; MINI, Mini-International Neuropsychiatric Interview; TST, tuberculin skin test .

Among the study participants, 5.8% of those successfully tested had a positive result. A 2010–2012 analysis of a representative nationwide US database of PLWH showed 6.9% had evidence of LTBI.[31] Consistent with both national and state trends and a well-recognised risk factor for LTBI,[2 32] foreign-born participants were more likely to test positive. Substance dependence did not increase individual risk for LTBI in our study population.

LTBI diagnostics may have an impact on cascade retention. Participants tested with TST were less likely to be successfully tested, reflecting the challenges associated with this test. TST is susceptible to operator performance variability and requires a second visit to obtain a result.[2 33] IGRAs are more specific and require only one visit, but are costly and discordance with TST and higher frequency of positive results raises concerns about interpretation.[33] Current guidelines suggest the two tests can be used interchangeably, but that IGRA is preferentially used for individuals unlikely to return for TST reading.[2] A previous study found that patients at an urban HIV clinic were 1.5 times more likely to receive care adherent to TB treatment guidelines after the clinic transitioned to using an IGRA.[29] Another study found being tested with an IGRA to be significantly associated with treatment completion.[34] Findings such as ours highlight the potential benefit of IGRAs for patients at-risk of not returning for TST reading. Interpretation of LTBI test results can be challenging and may ultimately impact likelihood of providers recommending and patients subsequently initiating treatment.

The length of the standard regimen for treating LTBI in PLWH is another barrier to retention. New shorter rifapentine-containing regimens have shown similar efficacy to and higher completion rates than 9 months of INH,[19 35 36] providing a treatment alternative for groups difficult to retain in care. However, rifamycin-containing regimens require coordination with HIV medications to avoid drug interactions and recent studies may suggest needs for alternate dosing for PLWH.[37] Directly observed therapy, patient incentives and social interventions during treatment, such as education, adherence coaching and peer counselling, have been shown to improve adherence and could also improve completion rates.[38 39] The overwhelming summary is that successful interventions depend on the target population, and further research is required to inform strategies for high-risk populations.

Our study has limitations. First, the sample size was too small to assess risk factors along the entire cascade of LTBI care. This limited our ability to draw conclusions about who begins and completes treatment for LTBI. Second, our study is limited in its generalisability: our participants were all engaged in care at the time of enrolment, potentially increasing the likelihood that they received LTBI testing compared with the broader population of PLWH. However, even with our smaller sample size and focus on those engaged in care, we did not find 100% LTBI testing and our low treatment initiation and completion numbers demonstrate a persistent gap.

CONCLUSIONS

Our study demonstrates that high testing coverage for LTBI is possible among PLWH with numerous other TB risk factors, including high rates of substance use, incarceration and homelessness. However, we also demonstrate persistent challenges in retaining patients through treatment completion. Our findings reaffirm that high-risk populations, such as PLWH and PWID, can be successfully tested, but reasons for attrition from

Table 3 Participants with a positive result on TST/IGRA compared with participants with a negative test result (n=189)

	Positive (n=11) n (%) or mean (SD)		Negative (n=178) n (%) or mean (SD)		OR	95% CI
Participant characteristics						
Mean age at time of TB test, years*	44.4	(12.4)	47.1	(9.4)	0.75	(0.41 to 1.38)
Received TST	5	(45.5)	87	(48.8)	0.87	(0.26 to 2.96)
Female	4	(36.4)	65	(36.5)	0.99	(0.28 to 3.52)
Mean time between test and ARCH enrolment††, months	14.9	(34.1)	12.9	(22.4)	1.04	(0.78 to 1.40)
Race/ethnicity						
White	2	(18.2)	36	(20.3)	ref	—
Black	3	(27.3)	86	(48.3)	0.63	(0.10 to 3.92)
Hispanic/other	6	(54.6)	56	(31.5)	1.93	(0.37 to 10.08)
Employed	0	(0.0)	33	(18.5)	—	—
Foreign-born	5	(45.5)	31	(17.4)	3.95	(1.13 to 13.77)§
Ever incarceration	4	(36.4)	89	(50.0)	0.57	(0.16 to 2.02)
Homeless¶	4	(36.4)	48	(27.0)	1.55	(0.43 to 5.52)
Number of CDC-defined TB risk factors						
2 risk factors	3	(27.3)	35	(19.7)	ref	—
3 risk factors	1	(9.1)	54	(30.3)	0.22	(0.02 to 2.16)
4 or more	7	(63.6)	89	(50.0)	0.92	(0.22 to 3.75)
Substance use						
Current smoking, n=187	11	(100)	142	(80.7)	—	—
Lifetime IDU, n=188	8	(72.7)	99	(55.9)	2.10	(0.54 to 8.18)
Current IDU**	2	(18.2)	17	(9.6)	2.10	(0.42 to 10.55)
Current alcohol and drug dependence††						
No dependence	3	(27.3)	29	(16.3)	ref	—
Alcohol dependence only	0	(0.0)	15	(8.4)	0.27	(0.01 to 6.15)
Drug dependence only	1	(9.1)	42	(23.6)	0.30	(0.04 to 2.19)
Both	7	(63.6)	92	(51.7)	0.68	(0.18 to 2.64)
Current alcohol use disorder‡‡						
Neither	3	(27.3)	64	(36.0)	ref	—
Alcohol abuse	1	(9.1)	7	(3.9)	3.05	(0.28 to 33.4)
Alcohol dependence	7	(63.6)	107	(60.1)	1.40	(0.35 to 5.59)
Current alcohol use§§						
Abstinent	3	(27.3)	61	(34.3)	ref	—
Low risk	2	(18.2)	26	(14.6)	1.56	(0.25 to 9.92)
Heavy	2	(18.2)	44	(24.7)	0.92	(0.15 to 5.77)
Frequent heavy	4	(36.4)	47	(26.4)	1.73	(0.37 to 8.11)
Health characteristics						
Health insurance¶¶	11	(100)	177	(99.4)	—	—
Medicaid/Masshealth	10	(90.9)	171	(96.1)	0.41	(0.05 to 3.66)
Medicare	5	(45.5)	85	(47.8)	0.91	(0.27 to 3.10)
Diabetes mellitus	2	(18.2)	38	(21.4)	0.82	(0.17 to 3.95)
Undetectable HIV viral load***, n=188	10	(90.9)	109	(61.6)	6.24	(0.78 to 49.83)§§
Mean length of HIV infection, years†††† n=185	14.5	(7.0)	15.6	(8.5)	0.93	(0.65 to 1.33)
Median CD4 count‡‡‡, n=188 (IQR)	389	(274–570)	552	(343–780)	0.85	(0.68 to 1.07)

Continued

Table 3 Continued

	Positive (n=11) n (%) or mean (SD)		Negative (n=178) n (%) or mean (SD)		OR	95% CI
Current use of ART, n=188	11	(100)	153	(86.4)	—	—

*OR per 10 years change.
†Due to non-normal data, Wilcoxon rank-sum test was used.
‡OR per 12 month change.
§Test statistic is statistically significant at the 0.05 significance level.
¶1+ nights on street or in shelter past 6 months.
**In past 30 days.
††From MINI combined alcohol and drug DSM-IV 12-month dependence.
‡‡From MINI 12-month DSM-IV alcohol dependence/abuse.
§§Non-cumulative.
¶¶Non-cumulative.
***50 copies/mL or less.
†††OR per 5 years change.
‡‡‡OR per 100 copies change.
ARCH, Alcohol Research Collaboration on HIV; ART, antiretroviral therapy; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition ; IDU, injection drug use; MINI, Mini-International Neuropsychiatric Interview ; TB, tuberculosis; TST, tuberculin skin test .

initiation and completion of preventive therapy need further investigation.

Author affiliations
[1]Section of Infectious Diseases, Boston Medical Center, Boston, Massachusetts, USA
[2]Section of General Internal Medicine, Boston Medical Center, Boston, Massachusetts, USA
[3]Clinical Addiction Research and Education Unit, Boston University School of Medicine, Boston, Massachusetts, USA
[4]Data Coordinating Center, Boston University School of Public Health, Boston, Massachusetts, USA
[5]Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts, USA
[6]Department of Global Health, Boston University School of Public Health, Boston, Massachusetts, USA

Twitter Alicia S Ventura @AliciaSVentura

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Competing interests RS reports that Alkermes provides medication for a comparative effectiveness study funded by NIAAA/NIH for which he is the principal investigator. Authors report no other conflicts.

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Ethics approval The study protocol was approved by the Boston University Medical Campus' Institutional Review Board (application #H-31295) and written informed consent was obtained from all individual participants included in the study. The NIAAA provided a Certificate of Confidentiality to further protect participants. All data collection methods were done in conformance with Good Clinical Practice (GCP) standards, including automated validation and quality control checks in the electronic database. Participants gave informed consent to participate in the study before taking part.

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ORCID iD
Elizabeth J Ragan http://orcid.org/0000-0001-6062-0058

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