HHS Public Access

Author manuscript

J Pediatr. Author manuscript; available in PMC 2023 July 11.

Published in final edited form as:

J Pediatr. 2023 February ; 253: 181–188.e5. doi:10.1016/j.jpeds.2022.09.038.

Multicenter analysis of attrition from the pediatric TB infection care cascade in Boston

Jeffrey I. Campbell, MD,
Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts, USA

Mary Tabatneck, MD,
Department of Pediatrics, Boston Children's Hospital, Boston, Massachusetts

Mingwei Sun, BA,
Center for Research Information Technology, Boston Children's Hospital, Boston, Massachusetts, USA

Wei He, BA,
Center for Research Information Science and Computing, Massachusetts General Hospital, Boston, Massachusetts, USA

Nicholas Musinguzi, MS,
Global Health Collaborative, Mbarara University of Science and Technology, Mbarara, Uganda

Bethany Hedt-Gauthier, PhD,
Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts, USA

Gabriella S. Lamb, MD MPH,
Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts, USA

Kezia Domond, BA,
Center for Global Health, Massachusetts General Hospital, Boston, Massachusetts, USA

Don Goldmann, MD,
Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts, USA

Vishakha Sabharwal, MD,
Division of Pediatric Infectious Diseases, Boston Medical Center, Boston, Massachusetts, USA

Thomas J. Sandora, MD MPH,
Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts, USA

Jessica E. Haberer, MD MSc
Center for Global Health, Massachusetts General Hospital, Boston, Massachusetts, USA

Corresponding author: Jeffrey Campbell, MD, Boston Children's Hospital, Division of Infectious Diseases, 333 Longwood Avenue, 6th Floor, Boston, MA 02115, Jeffrey.campbell@childrens.harvard.edu, phone: 617-355-6832, fax: 617-730-0254.

Conflict of interest disclosures: Dr. Haberer is a consultant for Merck. The other authors have no conflicts of interest to disclose.

Prior presentation of data: Results from this study were previously presented at The Union North America Region annual conference, Vancouver, BC, Canada, March 2022.

Abstract

Objectives: Characterizing losses from the pediatric tuberculosis (TB) infection care cascade is important to identify ways to improve TB infection care delivery.

Study design: We conducted a retrospective cohort study of children (<18 years old) screened for TB within 2 Boston-area health systems between January 2017-May 2019. Patients who received a tuberculin skin test (TST) and/or interferon gamma release assay (IGRA) were included.

Results: We included 13,353 tests among 11,622 patients; 93.9% of tests were completed. Of 199 patients with positive tests for whom TB infection evaluation was clinically appropriate, 59.3% completed treatment or were recommended not to start treatment. Age 12–17 (vs <5 years; aOR 1.59 [95%CI 1.32–1.92]), non-English/non-Spanish language preference (vs English; aOR 1.34 [95%CI 1.02–1.76]), and receiving an IGRA (vs TST, aOR 30.82 [95%CI 21.92–43.34]) were associated with increased odds testing completion. Odds of testing completion decreased as census tract social vulnerability index quartile increased (i.e., social vulnerability worsened; most vulnerable quartile vs least vulnerable quartile, aOR 0.77 [95%CI 0.60–0.99]). Odds of completing treatment after starting treatment were higher among females (vs males, aOR 2.35 [95%CI 1.14–4.85]) and were lower among patients starting treatment in a primary care clinic (vs TB/infectious diseases clinic, aOR 0.44 [95%CI 0.27–0.71]).

Conclusions: Among children with a high proportion of negative TB infection tests, completion of testing was high, but completion of evaluation and treatment was moderate. Transitions towards IGRA testing will improve testing completion; interventions addressing social determinants of health are important to improve treatment completion.

Keywords

latent tuberculosis; pediatric; care cascade; interferon gamma release assay; tuberculin

Introduction:

Approximately one-quarter of the world's population, including >1 million children and adolescents in the US, is estimated to have latent tuberculosis (TB) infection.[1, 2] In the US, TB remains an infection predominantly affecting socially marginalized groups, such as immigrants,[2] who often face social and structural barriers to accessing TB care.[3] Diagnosis and treatment of TB infection is a cornerstone of global efforts to eradicate TB[4] and is especially critical for children and adolescents, given their increased risk of progression to TB disease.[5]

Identification and treatment of TB infection require completion of multiple steps collectively termed the TB infection care cascade. The TB infection care cascade typically begins with identification of individuals at risk for TB infection and concludes with completion of treatment[6]. In our analysis, we assessed five steps of the care cascade: 1) completion of testing, 2) completion of medical evaluation (with physical exam and chest radiograph) after a positive test to exclude TB disease, 3) documentation of a recommendation to start treatment, 4) treatment initiation, and 5) treatment completion. Prior studies have shown

attrition between each of these steps.[6, 7] Children who do not appropriately complete the care cascade remain susceptible to missed diagnosis or progression to TB disease. Reducing attrition from the cascade is thus critical to TB eradication.

Understanding factors that predict cascade completion can guide improvement of TB infection care delivery. Prior studies have focused primarily on the final step of the cascade—from treatment initiation to treatment completion.[7] However, there is an ongoing knowledge gap for how to identify, diagnose, and engage at risk children and adolescents before they begin therapy. In addition, most pediatric TB infection care cascade studies have examined cascade completion within a single clinical setting, such as a TB clinic or primary care practice.[7] These studies provide rich insights into patient-specific factors that may affect retention, but they are not designed to examine broader health system factors that may affect retention, such as transitions between care settings or variation in practice. Identifying community and health-system factors associated with cascade completion is particularly important to strengthen care for underserved and immigrant populations who already experience challenges accessing routine care in the US.[8]

Our objectives were to understand completion of each step in the TB infection care cascade and to identify individual/community-level (pertaining to patient and family characteristics) and health system-level (pertaining to clinicians and their care decisions and clinical environments) predictors of testing and treatment completion within two large health networks in Boston, Massachusetts. We aimed to compare different care practices and trace children and families as they navigated between clinics and clinicians.

Methods

Setting and subject selection

We conducted a retrospective cohort study of patients ages 0–17 years old who had a TB infection test obtained between January 1, 2017 and May 31, 2019 within two health systems in a low TB-prevalence setting (Boston, USA). The end date was selected to allow patients who were diagnosed with TB infection to complete 9 months of treatment prior to the COVID-19 pandemic. Tests were identified using automated searches of these health systems' electronic data warehouses; searches were designed to capture all tuberculin skin tests (TSTs) and interferon gamma release assays (IGRAs) that were recorded in medication administration records and laboratory records. Because some patients received multiple TB tests during our study period, and because each test could be followed by completion or non-completion of the cascade, the unit of analysis in our study was the individual test. For patients with a positive test, subsequent tests were excluded.

One hospital system includes a 475-bed quaternary care pediatric hospital; affiliated primary care clinics within the hospital, elsewhere in Boston, and in Boston suburbs; and multiple subspecialty clinics located in the main hospital and in Boston suburbs. The second health system includes five hospitals, including an approximately 100-bed pediatric hospital-within-a-hospital; a network of pediatric, internal medicine-pediatric, and family medicine primary care community-based clinics; and multiple subspecialty clinics located in Boston and its suburbs in Massachusetts.

Outcomes

The primary outcome was completion of individual steps of the care cascade. Because of the limitations of the electronic health record for determining all individuals at risk for TB infection, our cascade starts with a TB infection test being ordered. At each cascade step, patients could appropriately exit the cascade (e.g., if the test was negative), appropriately complete the step and move to the next step, or inappropriately exit the cascade at that step. Ways in which patients could appropriately complete the cascade are summarized in Table 1, online. Optimal follow-up after an indeterminate/borderline/invalid IGRA has not been defined;[9] the CDC recommends repeat testing when concern for TB persists.[10] We considered these tests to be complete if they were followed by a repeat test within 60 days of the initial test, because it was often difficult to determine suspected pretest suspicion of TB and because 60 days approximates the window period for IGRA conversion after an exposure.[11] Patients who were diagnosed with mycobacterial disease were considered to have completed the testing step because subsequent diagnostics and treatment for TB disease follow a distinct cascade.[12] Because pharmacy records were not available, treatment completion was determined by review of clinical documentation in the medical record. We determined completion and non-completion of specific steps by electronic chart review and clinician documentation. Patients who interrupted care after a positive test could complete the care cascade if care was subsequently re-established and treatment was completed within the study period within the two healthcare systems.

To understand predictors of completion of key steps of the cascade, secondary outcomes were 1) completion of testing, and 2) completion of treatment after it was initiated. These secondary outcomes were selected because they represented the points in the cascade with clinical importance, potentially distinct factors affecting losses, and the most losses numerically.

Predictors of completion of cascade steps

Hypothesized predictors were based on the socioecological model.[13] Specifically, we selected predictors that could be ascertained from the electronic health record and that reflected individual- and community-level factors (age, sex, Social Vulnerability Index [SVI][14], preferred language, insurance type) and health system-level factors (testing location type, testing modality) that could be associated with completion of cascade steps. In analyses of treatment completion, we included additional health system-level factors (treatment prescriber type, rifamycin-based initial therapy).

Sex at birth, as recorded in the electronic health record, was reported as a binary variable (male or female). We recorded preferred language as English, Spanish, or other language, because 90% of families reported English or Spanish as their preferred language. We defined insurance type as public insurance (Medicaid), private insurance, other insurance (including Medicare), and no listed insurance. The Centers for Disease Control and Prevention (CDC)/ Agency for Toxic Substances and Disease Registry (ATSDR) SVI is a standardized rating of census tract-level vulnerability, comprised of 15 indicators measured in the American Community Survey and reported as a ranking of census tracts in the state in relation to each other.[14] To compute SVI, we geocoded patients' addresses using ArcGIS Pro v10.3,

using a match score ≥80 as an indicator of an acceptable match.[15] We then measured each address's census tract to determine SVI percentile, based on the 2018 five-year estimates from the American Community Survey. Location of testing was defined as primary care clinic versus other (i.e., subspecialty clinic or inpatient). We defined testing type as TST or IGRA. For patients who started treatment, we defined initial treatment location as primary care versus TB/infectious diseases clinic (including inpatient settings under the auspices of TB/infectious diseases clinicians), based on the location of the initial treatment prescription. We categorized initial treatment type as either containing or excluding rifamycins.

Inclusion and exclusion

For our primary analysis, we excluded tests that were obtained to confirm previous positive test results, to prevent duplicate inclusion of patients with positive results. Patients who were found to have false positive results or who were diagnosed with mycobacterial disease exited the cascade at the diagnostic evaluation step; we retained these patients in the initial steps of the cascade because the disposition of these initial tests was relevant to our understanding of the cascade. From our analysis of secondary outcomes, we excluded all patients with addresses outside of Massachusetts (to enable SVI comparisons using census tract data benchmarked to the Massachusetts population), patients with missing demographic information, and patients for whom SVI could not be computed.

Missing data

Because testing location type was missing for approximately 24% of tests, we employed multiple imputation to estimate this variable in analysis of testing completion. To perform multiple imputation, we used a logit model and test completion (the outcome variable), testing modality, age, month of testing, insurance, language, SVI quartile, and sex as predictors to create 30 imputation datasets, which were analyzed with Rubin's combination rules. In analysis of treatment completion, patients who moved away from the Boston area after starting TB infection treatment were considered to have completed therapy, because documentation of their move in the medical record suggested a high degree of engagement with their treating teams. Sensitivity analysis explored this assumption, and these patients are specifically demarcated throughout the cascade and predictor analyses.

Statistical analyses

We used proportions and 95% confidence intervals to describe completion of each step of the cascade. Because patients could receive multiple TB tests during our time frame, to identify predictors of test completion while accounting for within-patient auto-correlation, we used bivariable and multivariable generalized estimating equations with a logit link, exchangeable correlation structure, and robust standard errors to measure associations. We first determined bivariable associations between predictors and outcomes using generalized estimating equations and a joint Wald test. Predictors that were significant at a level of $P<0.2$ in univariable analysis were included in a multivariable model. This analysis was conducted using the multiply imputed testing location type. We also conducted sensitivity analyses with complete cases (i.e., only analyzing individuals with a known testing location type) using mixed effects logistic regression, accounting for clustering within clinics and within patients who were nested within clinics and had multiple tests.

To analyze predictors of treatment completion, we used bivariable and multivariable mixed effects logistic regression, accounting for clustering within the clinic where initial treatment was prescribed. Variables that were significant in univariable regression using a joint Wald test and level of $P<0.2$ were included in multivariable models. We did not account for within-patient autocorrelation in analysis of treatment completion because patients could only have a single positive TB test in our study. Finally, we conducted a sensitivity analysis in which patients who moved out of catchment during therapy were considered not to have completed therapy.

Analyses were conducted using Stata v17.0.

Ethical review

The Boston Children's Hospital (Protocol P00037273) and MassGeneral Brigham (Protocol 2020P003660) institutional review boards approved this study. Informed consent was waived.

Results

Patient characteristics

We identified 13,378 tests obtained within our study timeframe. After excluding 25 confirmatory positive tests, a total of 13,353 tests among 11,622 patients were included in the primary analysis of the care cascade (Figure 1). Patient characteristics, reported for each test, are presented in Table 2. Tests were obtained in 161 settings, including 49 primary care clinics and 112 outpatient subspecialty clinics or inpatient settings (including emergency departments). Treatment was initiated in 28 settings, including 20 primary care clinics, 6 TB/infectious disease clinics, and 2 inpatient settings (under auspices of TB/infectious disease clinicians).

Testing completion and results (Step 1)

Figure 2 shows completion of care cascade steps relevant for testing. Of 13,353 included tests (5,302 TST and 8,051 IGRA), 12,537 (93.9% [95%CI 93.5–94.3%]) were completed, while 816 (6.1% [95%CI 5.7–6.5%]) were not completed. Among completed tests, 12,170 tests (91.1%) were negative, 89 (0.7%) were borderline/indeterminate/invalid IGRAs and were followed within 60 days by a negative TB infection test, and 278 tests (2.1%) were positive. Of the 816 tests that were not completed, 774 (94.9%) were TSTs, and 42 (5.1%) were IGRAs that were borderline/indeterminate/invalid and were not followed by a subsequent test. Of the 5,302 TSTs obtained, 14.6% were not read, while 0.7% of the 8,051 IGRAs did not produce a valid result and were not followed with a second TB test.

Of the 278 positive tests obtained, 72 were determined to be false positives by the ordering clinicians (56 had subsequent negative testing; 8 were deemed to have low likelihood of TB infection with no subsequent testing; and 8 were found to have previously completed treatment for TB disease or infection). An additional 6 patients were diagnosed with TB disease, and 1 was diagnosed with non-tuberculous mycobacterial disease.

TB infection evaluation and diagnosis (Step 2)

A total of 199 patients with positive TB infection tests were eligible for subsequent evaluation for TB infection. Of these 186 (93.5% [95%CI 89.0–96.2%]) completed evaluation, while 13 (6.5% [95%CI 3.8–11.0%]) did not.

Treatment recommendation, initiation, and completion (Step 3–5)

Of the 186 patients who completed evaluation, 167 (89.8% [95%CI 84.5–93.4%]) had a treatment recommendation documented, while 19 (10.2% [95%CI 6.6–15.5%]) did not. Among the 19 patients for whom no treatment recommendation was documented, none were prescribed TB infection therapy. Of the 167 patients with a treatment recommendation, 166 were recommended to start treatment, and 1 was recommended to delay treatment due to pregnancy.

Of the 166 patients recommended to start treatment, 161 started (97.0% [95%CI 92.9–98.7%]), while 5 did not start (3.0% [95%CI 1.3–7.1%]).

Among the 161 patients who started therapy, 106 (65.8% [95%CI 51.8–72.8%]) had documented treatment completion, 44 (27.3% [95%CI 21.0–34.8%]) did not complete treatment, and 11 (6.8% [95%CI 3.8–12.0%]) moved away while treatment was ongoing. Most patients (107, 66.5%) were prescribed an initial regimen of 9 months of isoniazid, while 46 (28.6%) patients were initially prescribed 4 months of rifampin, and 8 (5.0%) were prescribed 3 months of isoniazid plus rifapentine. Table 3 online shows treatment completion by initial regimen. Most patients (123, 76.4%) received an initial treatment prescription in primary care clinics, compared to 28 (17.4%) in dedicated TB or infectious diseases clinics, and 10 (6.2%) in other settings.

Overall, among the 199 patients eligible for TB infection evaluation, 118 (59.3% [95%CI 52.3–65.9%]) completed treatment or were recommended to not start treatment.

Predictors of testing completion and treatment completion

Because potential factors affecting testing completion were likely distinct from factors affecting treatment completion, we first analyzed predictors of test completion. Table 4 summarizes characteristics for the 12,150 tests (among 10,667 patients) with complete demographic information included in the predictor analysis (comprising 91.0% of the cascade cohort). In multivariable analysis, age 12–17 years (vs 0-<5 years; aOR 1.59 [95% CI 1.32–1.92]), preferring a language that was not English or Spanish (vs English; aOR 1.34 [95%CI 1.02–1.76]), and receiving an IGRA (vs TST, aOR 30.82 [95% CI 21.92–43.34]) were associated with increased odds of test completion (Table 4). Odds of test completion decreased in a dose-dependent fashion as census tract SVI quartile increased (i.e., social vulnerability worsened), but the association was only significant for the most vulnerable SVI quartile (vs. least vulnerable quartile, aOR 0.77 [95% CI 0.60–0.99]). In a complete case analysis accounting for within-clinic clustering, SVI quartile and language were no longer significantly associated with testing completion (table 5, online). In the sensitivity analysis, the within-clinic intra-class correlation coefficient (ICC) was 0.09 (95%CI 0.03–0.24).

A total of 156 patients were included in analysis of predictors of treatment completion after treatment initiation. Female sex (aOR 2.35 [95%CI 1.11–4.98]) was independently associated with increased odds of treatment completion, while treatment initiation in a primary care clinic (versus TB/infectious diseases clinic) was associated with decreased odds of completion (aOR 0.44 [95%CI 0.27–0.71]) in the multivariable model (Table 6, online). The ICC for treatment initiation clinic was <0.001 (95%CI <0.001-<0.001). In a sensitivity analysis in which patients who moved out of catchment were considered not to have completed treatment, sex was no longer significantly associated with treatment completion (Table 7, online).

Discussion

In this large cohort study of the pediatric TB infection care cascade in two health systems in Massachusetts, losses occurred at each cascade step, with most attrition occurring at the initial diagnostic step. Age, language, social vulnerability, and testing modality were associated with testing (non)completion, and sex and clinic type were associated with treatment (non)completion.

Attrition in the diagnostic step occurred primarily among children who did not return for a TST read: 14.6% of TSTs were not read. Previously-identified factors associated with failure to return for a TST read include age,[16, 17] race/ethnicity,[17] parent language and citizenship,[18] forgetfulness,[19] and transportation barriers.[19] Non-completion of TST has contributed to others' recommendation to discontinue the use of TSTs when IGRAs are available.[20] Furthermore, 25.9% of positive tests were assessed to be falsely positive by treating clinicians, commonly in patients with a positive TST and negative IGRA. In contrast, invalid, indeterminate, or borderline IGRAs accounted for only 131/8,051 (1.6%) IGRA results in our study, though only 89/131 (67.9%) of these tests were followed by a subsequent positive or negative test. Taken together, our findings lend support to shifting away from TST-based screening when IGRAs are available and a high proportion of at-risk children have been BCG-vaccinated.[21]

In contrast to a recent multicenter study of the TB infection care cascade among adults and children in the US,[22] we found that a relatively high proportion of eligible children started treatment. Our finding was potentially related to greater promotion of treatment for children (vs adults) with TB infection because of higher rates of progression to TB disease. Similar to prior studies among adults and children,[6, 7, 23] we found that a high proportion of patients who started treatment did not complete it, highlighting the need for evaluation and implementation of strategies to improve adherence and treatment engagement for children.

Our finding that age 12–17 years old was associated with testing completion could be due to factors such as ability to independently return to clinic or incentive to receive test results (e.g. as required for schools, jobs or volunteer opportunities). Prior studies have found conflicting effects of age on completion of multiple steps of the care cascade.[16, 17, 24–26] In our study, age did not significantly predict completion after starting treatment. Heterogeneous results among studies likely reflect varying effects of caregiver influence,

child development and emerging autonomy, and social and environmental influences on children and their caregivers.

We used the CDC/ATSDR SVI—initially designed to identify areas with high vulnerability during natural disasters[14]—as a proxy for social and structural barriers to TB care and found social vulnerability to correlate with lower completion of testing. The SVI has been used to study disparities in access to and utilization of care,[27–29] and its components conceptually relate to multiple pathways relevant for the TB infection care cascade, including transportation, poverty and economic strain, and language barrier and minority status. Our use of SVI at the census tract level enabled categorization of social vulnerability among our population, which largely resided in the Boston area and itself has a high degree of socioeconomic heterogeneity. TB is known to highlight health disparities in the US,[30–32] and TB is typically viewed through a lens of inequitable disease incidence by race, ethnicity, and nativity. Yet our findings indicate that social disparities in access to care may layer on top of the inequities that lead to disparities in TB incidence. Our study also suggests that area-based markers of deprivation may aid in targeting interventions to promote cascade retention. The finding that non-English/non-Spanish language preference was associated with increased odds of testing completion suggests that social and economic factors related to access to care are complex and likely affect diverse populations—and particularly immigrant groups—differently.

We found that patients who started treatment in primary care clinics had lower odds of treatment completion compared with patients who started treatment in TB/infectious diseases clinics. Two studies from Canada have yielded conflicting results on whether prescriber type (primary care clinicians or family medicine physicians versus other clinicians) is associated with treatment completion.[33, 34] While our findings indicate that TB/infectious diseases clinics may more optimally retain patients in care than primary care clinics, our results must also be considered in light of potential selection biases, whereby patients who were able to attend a referral visit to a TB/infectious diseases clinic may have had higher propensity to engage in care in the first place. The question of whether decentralized TB treatment care leads to improved retention for children could be addressed though larger studies that control for factors that may be associated with treatment initiation in primary care vs dedicated TB/infectious disease clinics.

We found no association between rifamycin-based treatment and treatment completion, contrary to a large body of high-quality evidence.[35, 36] Lack of association in our study may have been due to small numbers of patients receiving rifamycin-based treatment. Notably, we did not determine medication adherence or changes to treatment regimen after initiation, which may have masked the effects of rifamycin-based treatment. We also did not find that testing modality affected treatment completion, in contrast to a recent claims-based study suggesting higher treatment completion among patients tested with IGRA.[37] Additional strategies that have been shown to improve cascade retention, such as patient incentives, protocolized reminder systems, and home visits,[38] were not routinely used in our clinical settings. While other evidence-based strategies, such as patient and clinician education,[38] were likely employed in some settings, our study highlights the need to understand practice

variation and identify opportunities for care improvement that can be implemented across the whole system of TB infection care.

Our findings also suggest a need to improve targeted TB testing. After removing confirmatory positive tests, the overall test positivity rate in our study was 2.1%. This rate is approximately the same as the estimated state-wide prevalence of TB infection in Massachusetts.[39] Targeted TB testing is recommended to limit testing and treatment to those individuals most likely to benefit from TB infection treatment.[9, 11] Despite these recommendations, our findings suggest need for improvements in use of screening algorithms, or in the algorithms themselves, to increase the pre-test probability of infection among populations who receive testing. We were not able to determine indications for testing, which limits our ability to determine if positivity rates varied among sub-populations. We were also unable to determine the population at risk for TB infection; development of strategies to characterize this risk group in large populations like ours would be valuable for understanding gaps in the cascade that occur before testing.

Our study has limitations. First, entry into our cohort was determined by receiving a TB test; patients who were at risk for TB but not tested were not included in our cascade, though missed opportunities to identify at-risk patients or obtain testing likely constitutes a large portion of attrition from the TB infection care cascade overall.[6] Second, our inability to determine indications for testing along with the lack of known TB risk factors in our cohort prevented us from determining if specific risk groups were more or less likely to complete the cascade. Additionally, we were unable to distinguish testing for TB infection from testing for TB disease, though the initial steps of the care cascade (starting with TST and/or IGRA) are typically the same for both forms of TB. Third, we relied on clinician documentation of completion of care cascade steps. It is possible that patients completed specific steps of the cascade without adequate documentation, leading to bias through outcome misclassification. Fourth, as a retrospective cohort study based on electronic health record data, there is risk for selection bias (in which patients with risks for attrition from the cascade may not have been tested in the first place, and thus would not have been included in our cohort), and misclassification of exposures arising from our use of retrospective data recorded for administrative rather than research purposes (e.g. address, insurance status, language). Fifth, access to and engagement in healthcare activity is a complex phenomenon involving multiple levels of individual and societal characteristics.[13] Yet we were not able to capture data on many possible factors related to cascade completion, such as family and other social support, immigration status, income, education, and health beliefs, which may have contributed to residual confounding or have been independent predictors of completion of specific cascade steps. Sixth, we restricted our analysis to completion of the care cascade prior to onset of the COVID-19 pandemic. COVID-19 has disrupted TB testing and diagnosis,[40] though health systems designed to improve care access during the pandemic may facilitate retention in care for children with TB infection. Finally, Boston is a medium-sized urban center with a large immigrant population, extensive healthcare infrastructure (including multiple state-sponsored TB clinics within the city and suburbs), and a state-sponsored public health insurance program. Our results may be generalizable to other similar urban settings, but may be less generalizable to communities with different

levels of access to primary and subspecialty care, different health insurance access, and different population composition.

Our study also has key strengths. We measured completion of the care cascade among more than 11,000 patients within two large health systems serving a population at risk of disparities in care access: 32% of tests were obtained in patients living in census tracts with highest quartile of social vulnerability in Massachusetts; 64% of tests were obtained among patients using public insurance; and 38% of tests were obtained among families who preferred a language other than English. Our design enabled us to compare testing and treatment delivery across multiple clinical settings. Our use of SVI enabled a quantitative assessment of social determinants of health, and demonstrates how address can be used to evaluate adversity through the electronic health record. The size of our cohort also powered our assessment of multiple risk factors for completion of key steps of the cascade.

In conclusion, we identified attrition at all steps of the pediatric TB infection care cascade. Interventions to improve retention in the care cascade should improve return after TST reads (or transition to IGRA-based testing), address mechanisms by which social and demographic factors contribute to testing and treatment attrition, and further examine clinical variability in practice and accessibility to understand differences in completion by care setting. Taken together, interventions should aim to eliminate inequitable care for children with this already inequitable disease.

Funding/Support:

Dr. Campbell was supported by Agency for Healthcare Research and Quality grant number T32 HS000063 as part of the Harvard-wide Pediatric Health Services Research Fellowship Program. Dr. Haberer was supported by K24MH114732.

Role of Funder/Sponsor:

The funders/sponsors did not participate in the work.

Data statement:

Data are available upon request.

Abbreviations:

aOR	adjusted odds ratio
BCG	Bacille Calmette-Guérin
ATSDR	Agency for Toxic Substances and Disease Registry
CDC	US Centers for Disease Control and Prevention
IGRA	interferon gamma release assay
PCP	primary care provider
SVI	Social Vulnerability Index

TB	tuberculosis
TST	tuberculin skin test

References

[1]. Cohen A, Mathiasen VD, Schon T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. The European respiratory journal. 2019;54.

[2]. Mancuso JD, Diffenderfer JM, Ghassemieh BJ, Horne DJ, Kao TC. The Prevalence of Latent Tuberculosis Infection in the United States. American journal of respiratory and critical care medicine. 2016;194:501–9. [PubMed: 26866439]

[3]. Dhavan P, Dias HM, Creswell J, Weil D. An overview of tuberculosis and migration. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2017;21:610–23. [PubMed: 28482955]

[4]. WHO. Implementing the end TB strategy: the essentials. WHO Press 2015.

[5]. Thomas TA. Tuberculosis in Children. Pediatr Clin North Am. 2017;64:893–909. [PubMed: 28734517]

[6]. Alsdurf H, Hill PC, Matteelli A, Getahun H, Menzies D. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. The Lancet Infectious diseases. 2016;16:1269–78. [PubMed: 27522233]

[7]. Campbell JI, Sandora TJ, Haberer JE. A scoping review of paediatric latent tuberculosis infection care cascades: initial steps are lacking. BMJ Glob Health. 2021;6.

[8]. Khullar D, Chokshi DA. Challenges for immigrant health in the USA-the road to crisis. Lancet. 2019;393:2168–74. [PubMed: 30981536]

[9]. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2017;64:111–5. [PubMed: 28052967]

[10]. Prevention CfDCa. Interferon-Gamma Release Assays (IGRAs) – Blood Tests for TB Infection. Accessed online at: https://wwwcdcgov/tb/publications/factsheets/testing/igrahtm Last accessed February 16, 2022 2016.

[11]. American Academy of Pediatrics. Red Book: 2021–2024 Report of the Committee on Infectious Diseases, 32 ed, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH (Eds), American Academy of Pediatrics, Itasca, IL 2021.

[12]. Subbaraman R, Nathavitharana RR, Mayer KH, Satyanarayana S, Chadha VK, Arinaminpathy N, et al. Constructing care cascades for active tuberculosis: A strategy for program monitoring and identifying gaps in quality of care. PLoS medicine. 2019;16:e1002754. [PubMed: 30811385]

[13]. McLeroy KR, Bibeau D, Steckler A, Glanz K. An ecological perspective on health promotion programs. Health Educ Q. 1988;15:351–77. [PubMed: 3068205]

[14]. Flanagan BE, Hallisey EJ, Adams E, Lavery A. Measuring Community Vulnerability to Natural and Anthropogenic Hazards: The Centers for Disease Control and Prevention's Social Vulnerability Index. J Environ Health. 2018;80:34–6.

[15]. Duncan DT, Castro MC, Blossom JC, Bennett GG, Gortmaker SL. Evaluation of the positional difference between two common geocoding methods. Geospat Health. 2011;5:265–73. [PubMed: 21590677]

[16]. Saunders MJ, Koh GC, Small AD, Dedicoat M. Predictors of contact tracing completion and outcomes in tuberculosis: a 21-year retrospective cohort study. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2014;18:640–6. [PubMed: 24903932]

[17]. van der Heijden YF, Heerman WJ, McFadden S, Zhu Y, Patterson BL. Missed opportunities for tuberculosis screening in primary care. Journal of Pediatrics. 2015;166:1240–5.e1. [PubMed: 25720366]

[18]. Vivier PM, O'Haire C, Alario AJ, Simon P, Leddy T, Peter G. A statewide assessment of tuberculin skin testing of preschool children enrolled in Medicaid managed care. Maternal & Child Health Journal. 2006;10:171–6. [PubMed: 16496221]

[19]. Cheng TL, Ottolini MC, Baumhaft K, Brasseux C, Wolf MD, Scheidt PC. Strategies to increase adherence with tuberculosis test reading in a high-risk population. Pediatrics. 1997;100:210–3. [PubMed: 9240801]

[20]. Cruz AT, Reichman LB. The Case for Retiring the Tuberculin Skin Test. Pediatrics. 2019;143.

[21]. Starke JR. Tuberculin Skin Test Versus the Interferon-gamma Release Assays: Out With the Old, In With the New. Pediatrics. 2020;145.

[22]. Holzman SB, Perry A, Saleeb P, Pyan A, Keh C, Salcedo K, et al. Evaluation of the latent tuberculosis care cascade among public health clinics in the United States. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2022.

[23]. Szkwarko D, Hirsch-Moverman Y, Du Plessis L, Du Preez K, Carr C, Mandalakas AM. Child contact management in high tuberculosis burden countries: A mixed-methods systematic review. PloS one. 2017;12:e0182185. [PubMed: 28763500]

[24]. Al Mekaini LA, Al Jabri ON, Narchi H, Kamal SM, Mabrook A, Al Kuwaiti MM, et al. The use of an interferon-gamma release assay to screen for pediatric latent tuberculosis infection in the eastern region of the Emirate of Abu Dhabi. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2014;23:4–7. [PubMed: 24657274]

[25]. Bishara H, Ore L, Vinitsky O, Bshara H, Armaly N, Weiler-Ravell D. Cost of nurse-managed latent tuberculous infection treatment among hard-to-reach immigrants in Israel. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2015;19:799–804. [PubMed: 26056104]

[26]. Minodier P, Lamarre V, Carle ME, Blais D, Ovetchkine P, Tapiero B. Evaluation of a school-based program for diagnosis and treatment of latent tuberculosis infection in immigrant children. Journal of infection and public health. 2010;3:67–75. [PubMed: 20701894]

[27]. Diaz A, Hyer JM, Azap R, Tsilimigras D, Pawlik TM. Association of social vulnerability with the use of high-volume and Magnet recognition hospitals for hepatopancreatic cancer surgery. Surgery. 2021;170:571–8. [PubMed: 33775393]

[28]. Carmichael H, Moore A, Steward L, Velopulos CG. Using the Social Vulnerability Index to Examine Local Disparities in Emergent and Elective Cholecystectomy. J Surg Res. 2019;243:160–4. [PubMed: 31177035]

[29]. Abbas A, Madison Hyer J, Pawlik TM. Race/Ethnicity and County-Level Social Vulnerability Impact Hospice Utilization Among Patients Undergoing Cancer Surgery. Annals of surgical oncology. 2021;28:1918–26. [PubMed: 33057860]

[30]. Noppert GA, Wilson ML, Clarke P, Ye W, Davidson P, Yang Z. Race and nativity are major determinants of tuberculosis in the U.S.: evidence of health disparities in tuberculosis incidence in Michigan, 2004–2012. BMC public health. 2017;17:538. [PubMed: 28578689]

[31]. Katrak S, Flood J. Latent Tuberculosis and Current Health Disparities in California: Making the Invisible Visible. Am J Public Health. 2018;108:S242–S5. [PubMed: 30383424]

[32]. Asabor EN, Vermund SH. Confronting Structural Racism in the Prevention and Control of Tuberculosis in the United States. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2021;73:e3531–e5. [PubMed: 33242078]

[33]. Rubinowicz A, Bartlett G, MacGibbon B, Greenaway C, Ronald L, Munoz M, et al. Evaluating the role of primary care physicians in the treatment of latent tuberculosis: a population study. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2014;18:1449–54. [PubMed: 25517810]

[34]. Ronald LA, FitzGerald JM, Bartlett-Esquilant G, Schwartzman K, Benedetti A, Boivin JF, et al. Treatment with isoniazid or rifampin for latent tuberculosis infection: Population-based study of hepatotoxicity, completion and costs. European Respiratory Journal. 2020;55.

[35]. Sterling TR, Njie G, Zenner D, Cohn DL, Reves R, Ahmed A, et al. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers

Association and CDC, 2020. MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control. 2020;69:1–11.

[36]. Assefa Y, Assefa Y, Woldeyohannes S, Hamada Y, Getahun H. 3-month daily rifampicin and isoniazid compared to 6- or 9-month isoniazid for treating latent tuberculosis infection in children and adolescents less than 15 years of age: an updated systematic review. The European respiratory journal. 2018;52.

[37]. Stockbridge EL, Loethen AD, Annan E, Miller TL. Interferon gamma release assay tests are associated with persistence and completion of latent tuberculosis infection treatment in the United States: Evidence from commercial insurance data. PloS one. 2020;15:e0243102. [PubMed: 33270737]

[38]. Barss L, Obeng J, Fregonese F, Oxlade O, Adomako B, Afriyie AO, et al. Solutions to improve the latent tuberculosis Cascade of Care in Ghana: a longitudinal impact assessment. BMC Infect Dis. 2020;20:352. [PubMed: 32423422]

[39]. Mirzazadeh A, Kahn JG, Haddad MB, Hill AN, Marks SM, Readhead A, et al. State-level prevalence estimates of latent tuberculosis infection in the United States by medical risk factors, demographic characteristics and nativity. PloS one. 2021;16:e0249012. [PubMed: 33793612]

[40]. Malik AA, Safdar N, Chandir S, Khan U, Khowaja S, Riaz N, et al. Tuberculosis control and care in the era of COVID-19. Health Policy Plan. 2020;35:1130–2. [PubMed: 32832996]

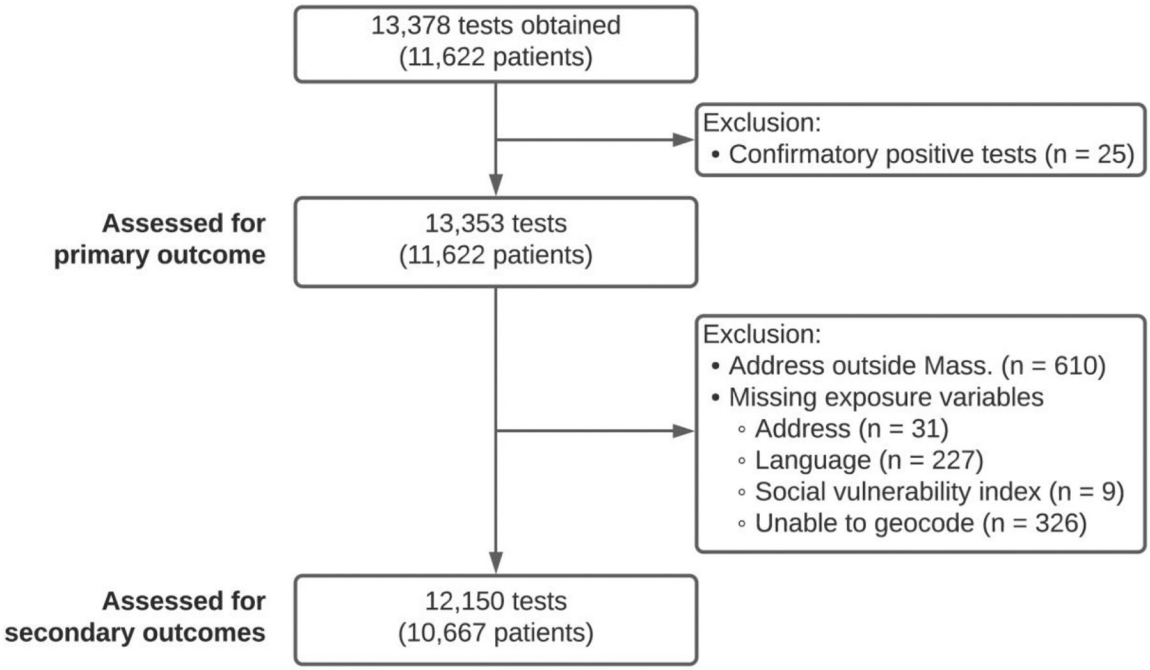

Figure 1.
Summary of analyzed tests and patients.

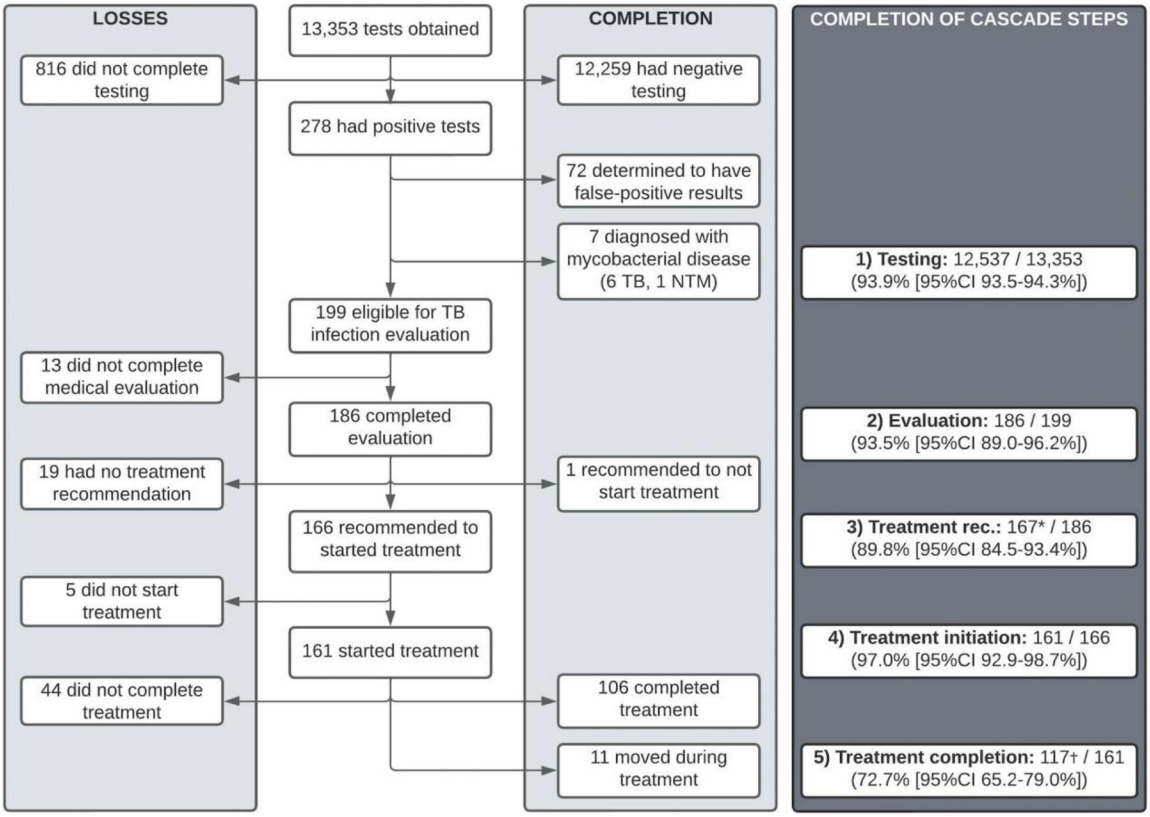

Figure 2.

Attrition from and completion of the TB infection care cascade.

*Includes the 1 patient who was recommended to not start treatment.

†Includes 11 patients who moved away during treatment

J Pediatr. Author manuscript; available in PMC 2023 July 11.

Table 1, online.

Definitions of appropriate continuation through and exit from the care cascade.

	Appropriate continuation to the next step		Exit from the cascade
Step	**TST**	**IGRA**	
Step 1: Testing	TST planted **AND** TST result recorded[1]	IGRA obtained **AND** valid result reported. Repeat test (IGRA or TST) obtained within 60 days for invalid/ indeterminate/borderline results.[2]	Testing negative **OR** positive test deemed to be falsely positive**OR** diagnosed with mycobacterial disease
Step 2: Evaluation	Chest imaging **AND** medical exam completed		
Step 3: Treatment recommended	Documented TB infection treatment recommendation		Documented clinician decision to not treat
Step 4: Treatment initiation	TB infection treatment prescribed		
Step 5: Treatment completion			Treatment completion documented by clinician[3]

[1] To successfully receive a TST result, the test was read within 48–72 hours of placement.

[2] 60 days was selected as the interval for repeating an invalid/indeterminate/borderline IGRA because 60 days approximates the window period for IGRA conversion after an exposure.

[3] In cases of treatment interruption, patients could be labeled as completing treatment if treatment was subsequently re-initiated and completed, per documentation of treating clinicians.

Table 2.

Description of patient characteristics associated with each test included in the care cascade.

	Total tests (N = 13,353)
Age, years	
0 - <5	3,516 (26.3%)
5 - <12	4,113 (30.8%)
12 – 17	5,724 (42.9%)
Sex	
Male	6,367 (47.7%)
Female	6,986 (52.3%)
Social Vulnerability Index (n, %)	
Quartile 1 (least vulnerable)	2,625 (19.7%)
Quartile 2	2,474 (18.5%)
Quartile 3	3,106 (23.3%)
Quartile 4 (most vulnerable)	3,985 (29.8%)
Missing	1,163 (8.71%)
Preferred language	
English	8,181 (61.3%)
Spanish	3,591 (26.9%)
Other	1,343 (10.1%)
Missing	238 (1.8%)
Insurance type	
Public	8,193 (61.4%)
Private	4,911 (36.8%)
Other	175 (1.3%)
None listed	74 (0.6%)
Testing type	
TST	5,302 (39.7%)
IGRA	8,051 (60.3%)
Testing location type	
Primary care	8,262 (61.9%)
Subspecialty/inpatient	2,439 (18.3%)
Missing	2,652 (19.9%)

Online table 3.

Treatment completion status by initial treatment regimen.

Treatment regimen	Complete	Moved away[1]	Did not complete	Total
9H	69 (64.5%)	9 (8.4%)	29 (27.1%)	107
4R	32 (69.6%)	1 (2.2%)	13 (28.3%)	46
3HP	5 (62.5%)	1 (12.5%)	2 (25.0%)	8
Total	106 (65.8%)	11 (6.8%)	44 (27.3%)	161

Abbreviations: 9H – 9 months isoniazid; 4R – 4 months of rifampin; 3HP – 3 months of isoniazid plus rifapentine

[1] In the primary analysis, patients who moved out of catchment while on treatment were considered to have completed therapy.

Table 4.

Individual-, community-, and health system-level factors and associations with testing completion.

	Completed testing (n = 11,371)	Did not complete testing (n = 779)	Bivariable Analysis		Multivariable Analysis[1]	
			Odds ratio (95%CI)	P value[2]	Adjusted odds ratio (95%CI)	P value
Individual/community-level factors						
Age, years				**<0.001**		
0 - <5	2,811 (87.8%)	391 (12.2%)	Ref		Ref	-
5 - <12	3,572 (95.3%)	178 (4.8%)	2.77 (2.29–3.34)		1.14 (0.93–1.39)	0.20
12 – 17	4,988 (96.0%)	210 (4.0%)	3.27 (2.74–3.91)		1.59 (1.32–1.92)	**<0.001**
Sex				0.52		
Male	5,408 (93.7%)	361 (6.3%)	Ref			
Female	5,963 (93.5%)	418 (6.6%)	0.95 (0.82–1.11)			
Social Vulnerability Index (n, %)				**0.017**		
Quartile 1 (least vulnerable)	2,467 (94.8%)	136 (5.2%)	Ref		Ref	-
Quartile 2	2,325 (94.2%)	142 (5.8%)	0.93 (0.72–1.19)		1.04 (0.80–1.35)	0.78
Quartile 3	2,881 (92.9%)	222 (7.2%)	0.74 (0.59–0.93)		0.91 (0.71–1.17)	0.47
Quartile 4 (most vulnerable)	3,698 (93.0%)	279 (7.0%)	0.76 (0.61–0.94)		0.77 (0.60–0.99)	**0.046**
Preferred language				0.08		
English	6,990 (93.3%)	503 (6.7%)	Ref		Ref	-
Spanish	3,272 (94.2%)	202 (5.8%)	1.22 (1.02–1.45)		0.94 (0.78–1.15)	0.56
Other	1,109 (93.7%)	74 (6.3%)	1.12 (0.86–1.45)		1.34 (1.02–1.76)	**0.037**
Insurance type				**0.013**		
Public	7,260 (93.0%)	547 (7.0%)	Ref		Ref	-
Private	4,046 (94.6%)	231 (5.4%)	1.28 (1.08–1.51)		1.15 (0.95–1.40)	0.16
Other	46 (100.0%)	0 (0.0%)	-[3]		-[3]	-[3]
None listed	19 (95.0%)	1 (5.0%)	1.46 (0.19–11.49)		0.87 (0.11–6.80)	0.89
Health system factors						
Testing type				**<0.001**		
TST	4,249 (85.2%)	739 (14.8%)	Ref		Ref	-

	Completed testing (n = 11,371)	Did not complete testing (n = 779)	Bivariable Analysis		Multivariable Analysis[1]	
			Odds ratio (95%CI)	P value[2]	Adjusted odds ratio (95%CI)	P value
IGRA	7,122 (99.4%)	40 (0.6%)	31.3 (22.6–43.6)		30.82 (21.92–43.34)	**<0.001**
Testing location type (n = 9,736)				**<0.001**		
Primary care	7,296 (92.4%)	598 (7.6%)	Ref		Ref	-
Subspecialty/inpatient	1,800 (97.7%)	42 (2.3%)	3.32 (2.40–4.61)		0.83 (0.58–1.20)	0.32

Percentages refer to the proportion of tests followed by cascade completion or non-completion.

[1] Multiple imputation was used to estimate missing testing location type in the multivariable model.

[2] P values represent global tests of significance using a composite Wald test.

[3] Unable to calculate odds ratio due to zero cells

J Pediatr. Author manuscript; available in PMC 2023 July 11.

Online table 5.

Results from complete case analysis of predictors of test completion.

	Completed testing (n = 9,096)	Did not complete testing (n = 640)	Bivariable Analysis		Multivariable Analysis	
			Odds ratio (95%CI)	P value[1]	Adjusted odds ratio (95%CI)	P value
Individual/community-level factors						
Age, years				**<0.001**		
0 - <5	2,417 (87.1%)	358 (12.9%)	Ref		Ref	-
5 - <12	3,011 (95.2%)	152 (4.8%)	2.92 (1.55–5.50)		1.08 (0.76–1.53)	0.68
12 – 17	3,668 (96.6%)	130 (3.4%)	3.88 (2.05–7.33)		1.65 (1.24–2.20)	**0.001**
Sex				0.82		
Male	4,411 (93.4%)	310 (6.6%)	Ref			
Female	4,685 (93.4%)	330 (6.6%)	0.97 (0.78–1.22)			
Social Vulnerability Index (n, %)				0.38		
Quartile 1 (least vulnerable)	1,640 (95.8%)	72 (4.2%)	Ref			
Quartile 2	1,656 (94.2%)	102 (5.8%)	0.97 (0.66–1.42)			
Quartile 3	2,532 (92.2%)	215 (7.8%)	0.79 (0.50–1.23)			
Quartile 4 (most vulnerable)	3,268 (92.9%)	251 (7.1%)	0.82 (0.55–1.22)			
Preferred language				0.15		
English	5,250 (93.2%)	383 (6.8%)	Ref		Ref	-
Spanish	2,855 (93.9%)	185 (6.1%)	1.23 (0.95–1.57)		1.04 (0.77–1.40)	0.82
Other	991 (93.2%)	72 (6.8%)	1.23 (0.88–1.70)		1.13 (0.82–1.55)	0.46
Insurance type				0.65		
Public	6,246 (92.7%)	491 (7.3%)	Ref			
Private	2,788 (95.0%)	148 (5.0%)	1.15 (0.82–1.61)			
Other	43 (100.0%)	0 (0.0%)	-[2]			
None listed	19 (95.0%)	1 (5.0%)	1.03 (0.24–4.38)			
Health system factors						
Testing type				**<0.001**		
TST	3,389 (84.9%)	605 (15.2%)	Ref		Ref	-

	Completed testing (n = 9,096)	Did not complete testing (n = 640)	Bivariable Analysis		Multivariable Analysis	
			Odds ratio (95% CI)	P value[1]	Adjusted odds ratio (95% CI)	P value
IGRA	5,707 (99.4%)	35 (0.6%)	40.8 (20.3–82.3)		33.19 (16.59–64.41)	**<0.001**
Testing location type (n = 9,736)				**<0.001**		
Primary care	7,296 (92.4%)	598 (7.6%)	Ref		Ref	-
Subspecialty/inpatient	1,800 (97.7%)	42 (2.3%)	3.78 (2.03–7.06)		1.08 (0.61–1.92)	0.78

[1] P values represent global tests of significance using a composite Wald test.

[2] Unable to calculate odds ratio due to zero cells

J Pediatr. Author manuscript; available in PMC 2023 July 11.

Table 6, online.

Individual-, community-, and health system-level factors and associations with treatment completion among individuals who started treatment.

	Completed treatment (n = 114)	Did not complete treatment (n = 42)	Bivariable analysis[3]		Multivariable analysis[3]	
			Odds ratio (95%CI)	P value[2]	Adjusted odds ratio (95%CI)	P value
Individual/community-level						
Age, years				**0.001**		
0 - <5	24 (77%)[1]	7 (23%)	Ref		Ref	-
5 - <12	47 (81%)	11 (19%)	1.25 (0.44 – 3.54)		1.21 (0.46 – 3.18)	0.69
12 – 17	43 (64%)	24 (36%)	0.52 (0.19 – 1.41)		0.45 (0.17 – 1.18)	0.10
Sex				**0.04**		
Male	47 (65%)	25 (35%)	Ref		Ref	-
Female	67 (80%)	17 (20%)	2.10 (1.04 – 4.24)		**2.35 (1.14 – 4.85)**	**0.02**
Social Vulnerability Index (n, %)				0.51		
Quartile 1 (least vulnerable)	13 (87%)	2 (13%)	Ref			
Quartile 2	16 (80%)	4 (20%)	0.62 (0.09–4.26)			
Quartile 3	42 (74%)	15 (26%)	0.43 (0.08 – 2.22)			
Quartile 4 (most vulnerable)	43 (67%)	21 (33%)	0.32 (0.06 – 1.58)			
Language				0.59		
English	41 (73%)	15 (27%)	Ref			
Spanish	53 (70%)	23 (30%)	0.84 (0.34 – 2.06)			
Other	20 (83%)	4 (17%)	1.83 (0.34 – 9.92)			
Insurance type				0.44		
Public	95 (72%)	37 (28%)	Ref			
Private	19 (79%)	5 (21%)	1.48 (0.55 – 3.98)			
Other	None	None	-	-		
None listed	None	None	-	-		
Health system-level						
Testing type				0.68		
TST	53 (75%)	18 (25%)	Ref			

	Completed treatment (n = 114)	Did not complete treatment (n = 42)	Bivariable analysis[3]		Multivariable analysis[3]	
			Odds ratio (95%CI)	P value[2]	Adjusted odds ratio (95%CI)	P value
IGRA	61 (72%)	24 (28%)	0.86 (0.43 – 1.73)			
Testing location type (n = 137)				0.59		
Primary care clinic	101 (75%)	33 (25%)	Ref			
Subspecialty/inpatient	2 (67%)	1 (33%)	0.65 (0.14 – 3.01)			
Rifamycin-based treatment (initial)				0.66		
No	76 (74%)	27 (26%)	Ref			
Yes	38 (72%)	15 (28%)	0.86 (0.45 – 1.67)			
Treatment started in primary care clinic				**0.005**		
No	29 (83%)	6 (17%)	Ref		Ref	-
Yes	85 (70%)	36 (30%)	0.49 (0.30 – 0.80)		**0.44 (0.27 – 0.71)**	**0.001**

[1] Percentages refer to the proportion of patients who completed or did not complete treatment.

[2] P values represent global tests of significance using a composite Wald test.

[3] Regression analysis accounts for clustering at the level of the clinic where treatment was initially prescribed.

J Pediatr. Author manuscript; available in PMC 2023 July 11.

Table 7, online.

Individual-, community-, and health system-level factors and associations with treatment completion among individuals who started treatment, assigning 10 patients[1] who moved away during treatment to the non-completion group.

	Completed treatment (n = 104)	Did not complete treatment (n = 52)	Bivariable analysis[4]		Multivariable analysis+4	
			Odds ratio (95%CI)	P value[3]	Adjusted odds ratio (95%CI)	P value
Individual/community-level						
Age, years				**0.07**		
0 - <5	22 (71%)[2]	9 (29%)	Ref		Ref	-
5 - <12	42 (72%)	16 (28%)	1.07 (0.41–2.82)		1.05 (0.42–2.60)	0.92
12 – 17	43 (64%)	24 (36%)	0.61 (0.23–1.58)		0.54 (0.20–1.43)	0.21
Sex				**0.15**		
Male	43 (60%)	29 (40%)	Ref		Ref	-
Female	61 (73%)	23 (27%)	1.79 (0.82–3.92)		1.94 (0.87–4.32)	0.11
Social Vulnerability Index (n, %)				0.77		
Quartile 1 (least vulnerable)	12 (80%)	3 (20%)	Ref			
Quartile 2	14 (70%)	6 (30%)	0.58 (0.11–3.08)			
Quartile 3	37 (65%)	20 (35%)	0.46 (0.10–2.21)			
Quartile 4 (most vulnerable)	41 (64%)	23 (36%)	0.45 (0.10–2.04)			
Language				0.81		
English	39 (70%)	17 (30%)	Ref			
Spanish	49 (64%)	27 (36%)	0.79 (0.39–1.61)			
Other	16 (67%)	8 (33%)	0.87 (0.27–2.85)			
Insurance type				0.33		
Public	86 (65%)	46 (35%)	Ref			
Private	18 (75%)	6 (25%)	1.60 (0.62–4.15)			
Other	None	None	-	-		
None listed	None	None	-	-		
Health system-level						
Testing type				0.90		

	Completed treatment (n = 104)	Did not complete treatment (n = 52)	Bivariable analysis[4]		Multivariable analysis+4	
			Odds ratio (95%CI)	P value[3]	Adjusted odds ratio (95%CI)	P value
TST	47 (66%)	24 (34%)	Ref			
IGRA	57 (67%)	28 (33%)	1.04 (0.57–1.88)			
Testing location type (n = 137)				0.33		
Primary care clinic	92 (69%)	42 (31%)	Ref			
Subspecialty/inpatient	1 (33%)	2 (67%)	0.23 (0.01–4.34)			
Rifamycin-based treatment (initial)				0.87		
No	69 (66%)	35 (34%)	Ref			
Yes	35 (67%)	17 (33%)	1.04 (0.62–1.76)			
Treatment started in primary care clinic				**0.02**		
No	27 (77%)	8 (23%)	Ref		Ref	-
Yes	77 (63%)	44 (36%)	0.52 (0.30–0.90)		**0.48 (0.28–0.81)**	**0.006**

[1] 1 patient who moved away from catchment during treatment is excluded from this analysis due to incomplete information.

[2] Percentages refer to the proportion of patients who completed or did not complete treatment.

[3] P values represent global tests of significance using a composite Wald test.

[4] Regression analysis accounts for clustering at the level of the clinic where treatment was initially prescribed.