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The Health-System Benefits and Cost-effectiveness of Using *Mycobacterium Tuberculosis* Direct Nucleic Acid Amplification Testing to Diagnose Tuberculosis Disease in the United States

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Abstract

Background—The utility of Mycobacterium tuberculosis direct nucleic acid amplification testing (MTD) for pulmonary tuberculosis disease diagnosis in the United States has not been well described.

Methods—We analyzed a retrospective cohort of reported patients with suspected active pulmonary tuberculosis in 2008–2010 from Georgia, Hawaii, Maryland, and Massachusetts to assess MTD use, effectiveness, health-system benefits, and cost-effectiveness.

Results—Among 2140 patients in whom pulmonary tuberculosis was suspected, 799 (37%) were *M. tuberculosis*-culture-positive. Eighty percent (680/848) of patients having acid-fast-bacilli-smear-positive specimens had MTD performed; MTD positive-predictive value (PPV) was 98% and negative-predictive value (NPV) was 94%. Nineteen percent (240/1292) of patients having smear-negative specimens had MTD; MTD PPV was 90% and NPV was 88%. Among patients suspected of tuberculosis but not having MTD, smear PPV for lab-confirmed tuberculosis was 77% and NPV 78%. Compared with no MTD, MTD significantly decreased time to diagnosis in patients with smear-positive/MTD-positive specimens, decreased respiratory isolation for patients having smear-positive/MTD-negative/culture-negative specimens, decreased outpatient days of unnecessary tuberculosis medications, and reduced resources expended on contact investigation.

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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While MTD generally cost more than no MTD, incremental cost savings occurred in patients with human immunodeficiency virus (HIV) or homelessness to diagnose or to exclude tuberculosis, and in patients with substance abuse having smear-negative specimens to exclude tuberculosis.

Conclusions—MTD improved diagnostic accuracy and timeliness and reduced unnecessary respiratory isolation, treatment, and contact investigations. It was cost saving in patients with HIV, homelessness, or substance abuse, but not in others.

Keywords

tuberculosis; diagnosis; molecular; cost; nucleic acid amplification

Improvements in diagnosis of tuberculosis disease are needed. Sputum-smear microscopy for acid-fast-bacilli (AFB) is simple and inexpensive to perform but generally detects less than half of patients with culture-confirmed pulmonary *Mycobacterium tuberculosis* complex disease (culture-positivity) [1, 2] and has a poor positive predictive value (PPV) in persons with human immunodeficiency virus (HIV) infection [3, 4]. While culture is the gold standard for active tuberculosis diagnosis, it takes 2–8 weeks for results [1]. Nucleic acid amplification testing for *M. tuberculosis* can provide information within 24–48 hours. A meta-analysis of *M. tuberculosis* direct nucleic acid amplification testing (MTD, Gen-Probe, San Diego, California) studies found sensitivity of 97% and specificity of 96% among smear-positive respiratory specimens, and sensitivity of 76% and specificity of 97% among smear-negative specimens [5].

The US Food and Drug Administration (FDA) approved the MTD in 1995 for smear-positive specimens and an enhanced MTD in 1999 for both smear-positive and smear-negative specimens. The Centers for Disease Control and Prevention (CDC) recommended in 1996 and 2000 that nucleic acid amplification testing be performed on at least one (preferably the first) respiratory specimen if smear-positive, and beginning in 2009 on smear-negative specimens from patients for whom the test result would alter tuberculosis case management [6].

Despite these recommendations, the request for MTD by individual providers, hospitals, and laboratories determines its use, which is not universal. Moreover, there are limited US data demonstrating the cost-effectiveness of the MTD, which might influence its use. D. W. Dowdy evaluated the MTD in smear-positive patients having 31.4% tuberculosis prevalence at a US urban hospital and found it not cost-effective for early tuberculosis exclusion in that setting [7].

The purpose of this study is to evaluate the use, effectiveness, health-system benefits, and cost-effectiveness of MTD in a retrospective cohort of patients reported to have suspected pulmonary tuberculosis in 2008–2010 from Georgia, Hawaii, Maryland, and Massachusetts. Study results will help guide future decisions about efficient MTD and provide a baseline for newer molecular tuberculosis disease diagnostics, such as Xpert INH/RIF (Cepheid, Sunnyvale, California).

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METHODS

This study evaluated MTD already in use by study sites for comparison with no MTD for pulmonary tuberculosis diagnosis, using culture positivity as the gold standard, at 4 independent US sites: metropolitan Atlanta, Georgia, 4 areas of Maryland, and the states of Hawaii and Massachusetts. Sites were evaluated on MTD use following existing CDC recommendations available to all US jurisdictions. We conducted retrospective reviews of inpatient and outpatient medical records of a 2008–2010 cohort reported to local tuberculosis jurisdictions with suspected pulmonary tuberculosis (see Supplementary data online Appendix for details). According to US standard of practice, all patients suspected of tuberculosis were to have ≥1 specimen from any respiratory source tested by smear and cultured for *M. tuberculosis*; any patients lacking smear/culture results were excluded. Data were collected from initial tuberculosis suspicion through final tuberculosis determination (either disease confirmation or definitive exclusion as defined by each clinician). We defined the date of initial tuberculosis suspicion uniformly as the earliest of respiratory isolation, smear positivity, tuberculosis treatment start, suspect report, or tuberculosis disease diagnosis as noted by the provider. We defined smear-positive as having ≥1 positive-AFB smear and smear-negative as never having a positive-AFB smear. Similarly, MTD positive was defined as having ≥1 MTD-positive result and MTD-negative as never having a positive MTD result. CDC's and local Institutional Review Boards waived the need for patient informed consent and approved the study, because it posed minimal risk to human subjects and involved an FDA-approved diagnostic device already in use by participating sites.

Person-days to event were measured from the date of initial tuberculosis suspicion to date of: tuberculosis-related hospitalization, inpatient respiratory isolation, tuberculosis treatment start, final tuberculosis determination, and contact investigation initiation. Duration of person-days was measured for hospitalization, respiratory isolation, intensive care, mechanical ventilation, outpatient treatment, and contact investigation. Person-days were calculated by multiplying the number of persons receiving a service by the average service days while the patient was suspected of having tuberculosis.

To assess associations with dichotomous outcomes, we used multivariable log-binomial regression (SAS version 9.2,9.3) to estimate relative risks, including in the final model all variables (eg, patient demographics, sites) statistically significant at the 95% confidence interval (CI); we report adjusted relative risks (aRR). All analyses of practices were stratified by smear. We used multi-variable Cox proportional hazards models to assess days to event and report adjusted hazard ratios (aHR) at the 95% confidence interval. A propensity score for use of MTD was included to adjust the model of days to final tuberculosis determination.

We ascribed standard costs in 2010 US dollars, updated from original sources using changes in the medical-care component of the US Consumer Price Index [8] or in Average Hourly Earnings [9], to each person-day of outcome to compute health-system costs. Unit costs per person per day were as follows: MTD $50 [10]; tuberculosis hospitalization $1,355 (a comprehensive average cost for tuberculosis-related hospitalization) [11]; physician/

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provider costs of respiratory isolation $36 [10], intensive care $114 [10], mechanical ventilation $65 [10]; outpatient management and medication $33 [12]; and contact investigation/management $2 [13]. From the health-system perspective, by smear, we calculated the average costs per patient evaluated with MTD versus no MTD and incremental cost-effectiveness (compared with no MTD) per true positive MTD and per true negative MTD based on culture result.

RESULTS

The cohort consisted of 2150 reported patients suspected of having pulmonary tuberculosis, minus 10 excluded because of missing smear or culture (N = 2140). Compared with patients with tuberculosis disease in 2009 reported to the US National Tuberculosis Surveillance System, study patients were significantly older; more likely to be non-Hispanic, of nonwhite race/ethnicity, or foreign-born; have HIV infection, homelessness, or injection-drug use; or to be employed (Table 1). One third of study patients had unknown HIV status, including 24% of those who started tuberculosis medications.

An average of 3.6 specimens were collected and recorded per study patient. Forty percent (848/2140) of patients had ≥1 smear-positive specimen, and 60% (1292/2140) had all smear-negative specimens.

Of the 2140 patients, 799 (37%) had culture-positivity (2.7 suspected patients/case). Foreign-born patients were 1.3 times (CI, 1.1–1.5) more likely to have culture-positivity than US-born patients. Patients less likely to have culture-positivity were HIV-infected (aRR = 0.6, CI, .5–.7), aged 25–44 (aRR = 0.9, CI, .8–1.0), or aged 45–64 (aRR = 0.8, CI, .7–.9) versus patients without those characteristics, controlling for site.

Fifteen percent of patients received a diagnosis of nontuberculous mycobacterial disease (not solely a culture of nontuberculosis mycobacterium), including 52% of patients with HIV infection. Patients with HIV infection (aRR = 2.3, CI, 1.7–3.2) were more likely to have received a diagnosis of nontuberculous mycobacterial disease than HIV-uninfected patients. Foreign-born patients were significantly less likely to have received a nontuberculous mycobacteria disease diagnosis (aRR = 0.6, CI, .4–.9), compared with other patients, controlling for site.

Among eventual culture-positive patients, there were fewer days from initiation of patient tuberculosis symptoms to clinician tuberculosis suspicion in Massachusetts (aHR = 1.4, CI, 1.1–1.7) and Georgia (aHR = 1.5, CI, 1.1–1.9), compared with remaining sites. There were differences in patient composition (Table 1) and management by site.

Forty-three percent (920/2140) of the cohort was evaluated using MTD. Overall, 59% of hospitalized patients received MTD, versus 25% of those not hospitalized. MTD for those hospitalized varied by site: at Massachusetts, 35% of hospitalized received MTD versus 18% of those not hospitalized; at Maryland, 47% versus 55%; at Hawaii, 81% versus 8%; and at Georgia, 98% versus 100%.

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Eighty percent (680/848) of patients having smear-positive specimens and 19% (240/1292) having smear-negative specimens received MTD (17% before 2009, 20% after 2009). Sixty-one percent (418/680) of patients having ≥1 smear-positive specimen had MTD on the first specimen; 73% (176/240) of patients having all smear-negative specimens had MTD on the first specimen. Twelve percent (259/2140) of patients and 21% (73/353) with discordant smear/MTD results had multiple (range 2–5) MTDs documented on the same specimen (Table 2). Two percent (53) of patients had 3–5 MTDs on a specimen, for which results were sometimes reported on the same day. Among 206 (10%) patients having 2 MTDs on a specimen, 96% of subsequent MTDs agreed with the initial result (Table 2). Turn-around time from specimen collection to reported MTD result averaged 4.0 days for clinic specimens and 2.6 days for hospital specimens. Three percent (26/920) of patients whose specimens had MTD had no MTD report date recorded. MTD was conducted for 32% (7/22) of children < 15 years (all smear-negative); 5 were MTD- negative/culture-negative, one was MTD-negative/culture-positive, and one was MTD-positive/culture-positive. Figure 1 shows MTD by population and site. From a smear-positive multivariable model, the only predictor of MTD was Georgia (aRR = 1.4, CI, 1.4–1.5). From a smear-negative multivariable model, MTD was used more often on specimens from patients who were in Georgia (aRR = 7.4, CI, 5.0–11.1) or in Maryland (aRR = 4.4, CI, 3.2–6.4), and less often on specimens from patients who were foreign-born (aRR = 0.8, CI, .6–.9) or in Hawaii (aRR = 0.3, CI, .2–.6) than on smear-negative specimens from other patients. Hospitalization was not found to be a significant predictor of MTD, controlling for site.

Fifty-four percent of patients started treatment (1161/2140), 14% after culture results were reported. Nearly all (355/367 smear-positive/MTD-positive, 40/40 smear-negative/MTD-positive) patients having MTD-positive specimens were started on treatment, compared with 23% (73/313) of smear-positive/MTD-negative and 54% (107/200) of smear-negative/MTD-negative. The differences in days to treatment start were not statistically significant.

MTD Performance and Health-System Benefits

In patients having smear-positive specimens, MTD PPV was 98%, compared to smear PPV of 77% for patients who did not have MTD (ie, no MTD); in patients having smear-negative specimens, MTD NPV was 88% compared to smear NPV of 78% for no MTD. Among all subpopulations examined (HIV-infected, homeless, substance abuser, foreign born), MTD PPV, sensitivity, and NPV were higher than that of no MTD (Table 3). MTD was also more specific in all subpopulations, except those with homelessness. MTD NPV in foreign-born patients having smear-positive specimens was significantly lower than that in other subpopulations (ie, there were proportionally more false-negative MTD results in foreign-born patients having smear-positive specimens).

For culture-negative patients having MTD-negative results compared with no MTD, there were significant reductions in respiratory isolation, computed tomography (CT) exams, bronchoscopies, and biopsies (Figure 2). There were also significantly fewer contact investigations initiated. Patients who had smear-negative specimens but had MTD-positive results and ultimately were culture-positive were significantly more likely to have received a bronchoscopy or a biopsy, compared to patients whose specimens had no MTD. There were

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significantly fewer average days on outpatient medications taken while tuberculosis was suspected for culture-negative patients having MTD-negative specimens versus those having no MTD (53 fewer days for patients having smear-positive/culture-negative specimens and 42 fewer days for smear-negative/culture-negative; Figure 3). In unadjusted analysis, MTD significantly decreased average time to final tuberculosis determination for all patients, except for those having smear-negative/MTD-positive/culture-negative specimens versus patients with smear-negative/no MTD/culture-negative (Figure 4). Multivariable analysis of time to determination of smear-positive/culture-positive found that a MTD-positive result speeded time to tuberculosis determination (aHR = 2.3, CI, 1.4–3.7), controlling for age 45–64, and being at the Georgia or Maryland sites. For culture-negative patients, MTD did not significantly decrease time to tuberculosis exclusion in multivariable analysis.

There were some drawbacks to MTD, particularly for 4 patients having smear-negative/MTD-positive/culture-negative results (ie, false positives) who averaged 100 days on outpatient tuberculosis medications and 3 of whom were placed in respiratory isolation. There were 18 patients having smear-positive/MTD-negative/culture-positive results (ie, false negatives), particularly among foreign-born patients; 19% of MTD-negative foreign-born patients had false negative results versus 6% of all patients.

Cost-effectiveness of MTD

Hospitalization costs from initial suspicion through final tuberculosis determination accounted for 95% of all costs among patients suspected of pulmonary tuberculosis who received MTD, but outpatient management costs were greater and hospitalization costs less (59% of total) for patients whose specimens had no MTD. This was true for all study sites.

Among patients having smear-positive specimens, health-system costs per patient whose specimen received MTD averaged $17 300, versus $15 200 for those without MTD (Table 4). For all patients, MTD cost $10 300 more per additional (incremental) smear-positive patient diagnosed accurately (ie, true positive) and $32 700 more per additional smear-negative patient (ie, true negative) in health-system costs. However, there were substantial incremental cost savings in patients with HIV or homelessness to diagnose or to exclude tuberculosis, and in patients with substance abuse having smear-negative specimens to exclude tuberculosis. There were also incremental cost savings for smear-positive patients in Maryland and for smear-negative patients in Georgia (Table 4).

LIMITATIONS

We were limited to available data in medical records or lab reports. We were unable to assess repeat MTD resulting from inhibitor detection because of lack of documentation. Data were limited in Hawaii from private outpatient-care providers of patients without tuberculosis disease and in Massachusetts from hospitalized low-suspicion patients ruled out quickly. Practices in managing patients suspected of tuberculosis differed at each site, as they do across the US. Study findings might not be generalizable to all US settings.

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DISCUSSION

This study, conducted at 4 independent sites, comprised the largest known cohort of patients suspected of pulmonary tuberculosis from multiple US sites that evaluated the use, effectiveness, health-system benefits, and cost-effectiveness of MTD to diagnose tuberculosis disease. We found:

1. MTD most often for patients whose specimens were smear-positive, especially those in Georgia, and for Georgia/Maryland patients whose specimens were smear-negative; MTD less often for foreign-born and Hawaii patients whose specimens were smear-negative,
2. significant health-system benefits in improved diagnostic accuracy, reduced time to tuberculosis diagnosis in smear-positive/MTD-positive, reductions in medical procedures and respiratory isolation for patients having smear-positive/MTD-negative/culture-negative specimens, less time (average 1.5 months) taking unnecessary tuberculosis medications, and fewer resources expended on contact investigation for patients whose specimens were smear-positive/MTD-negative/culture-negative compared with no MTD, and
3. incremental cost savings for patients with HIV or homelessness to either diagnose or exclude tuberculosis, and in patients with a history of substance abuse whose specimens were smear-negative to exclude tuberculosis.

The study documents detailed US practices and the diverse activities (eg, hospitalization, tuberculosis clinic management, and contact investigation) of multiple entities, which impact tuberculosis diagnostic health-system resource use. Time to initial tuberculosis suspicion was significantly less in Georgia and Massachusetts, which had high hospitalization rates. Most patients suspected of pulmonary tuberculosis were hospitalized prior to or on the same day that tuberculosis was initially suspected for isolation and evaluation, or because patients sought hospital care for other reasons. While more hospitalized patients received MTD, hospitalization was not an independent predictor of MTD, controlling for site.

We compared practices found at study sites with CDC recommendations [6]. We found a high percentage (80%) of ≥1 MTD in patients having ≥1 smear-positive and 20% use after 2009 for patients having all smear-negative specimens, well over half on the first specimen collected. If smear and MTD results differ, additional MTD tests are recommended. Among 353 patients having discordant smear and MTD results, only 73 (21%) had documentation of an additional MTD. Also recommended for smear-positive/MTD-negative specimens is inhibitor testing, which was rarely documented in laboratory records. MTD results appeared to influence providers' decisions to start treatment but did not significantly decrease days to treatment start. Turn-around times (average 4.0 days for clinic specimens, 2.6 days for hospital specimens) were greater than the recommended 2 days. We also identified a need for standard lab reporting of results. Routine HIV testing is recommended for all patients starting tuberculosis treatment [14]. However, 33% of patients had unknown HIV status, including 24% of patients who started tuberculosis medications. We found that MTD was

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highly beneficial for some groups, especially patients with HIV infection, but providers must test for HIV to realize these benefits.

Of the 2140 patients, a relatively high proportion (37%) had culture-positivity. Most at risk for tuberculosis were foreign-born patients suspected of tuberculosis, who were 3 times as likely as US-born patients to have culture-positivity. We found that foreign-born patients were significantly less likely than others suspected of tuberculosis to have received a diagnosis of nontuberculous mycobacterial disease. While greater MTD would benefit foreign-born patients suspected of tuberculosis, their significantly higher proportion of false-negatives as a percentage of MTD-negative results (19% vs 6%) resulted in incremental costs rather than savings. Reasons for these false-negative MTD results, including assessment of specimen inhibitors, should be investigated. Compared with Greco [5], our study found similar MTD sensitivity in smear-positive patients and specificity in both smear-positive and smear-negative patients but much lower sensitivity (59% vs 76%) in smear-negative patients.

Hospitalization costs accounted for 95% of health-system costs among patients suspected of tuberculosis who received MTD and 59% of the total for no MTD. Although incremental cost effectiveness was higher for all patients using MTD, MTD was cost saving over no MTD in patients with HIV infection or homelessness to either diagnose or exclude tuberculosis. Targeting these populations (who often have false-positive or false-negative smears, are hospitalized at tuberculosis diagnosis, and are more likely to have tuberculosis-associated deaths) for rapid tuberculosis diagnosis might reduce transmission and be life-saving, as well as cost-saving over later diagnosis. Since a large proportion of patients suspected to have tuberculosis had public insurance (44%) or had no health insurance (29%), these cost savings to the public sector, along with added diagnostic accuracy, provide incentives for greater MTD in these populations. To reduce health-system costs of tuberculosis diagnosis, US tuberculosis providers either need to diagnose patients suspected of tuberculosis prior to hospitalization, which could occur with increased patient access to care, or to conduct critical diagnostic procedures early after hospital admission. We plan to assess these scenarios in a modeling study. Primary tuberculosis prevention through treatment of latent tuberculosis infection is also important.

CONCLUSIONS

MTD has significant health-system benefits for evaluation of patients suspected of pulmonary tuberculosis. MTD in both smear-positive and smear-negative specimens was more accurate and timely in diagnosing or ruling out tuberculosis compared with no MTD. MTD conserved hospital and clinic resources expended on diagnostic procedures, respiratory isolation, and contact investigation. MTD also reduced the burden on patients of unnecessary and potentially toxic tuberculosis medications. Moreover, MTD can be cost saving in patients with HIV, homelessness, or substance abuse. Our analysis suggests similar or greater health-system benefits are likely with newer molecular diagnostics that are as accurate, less technically complex, and less expensive to implement than MTD.

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Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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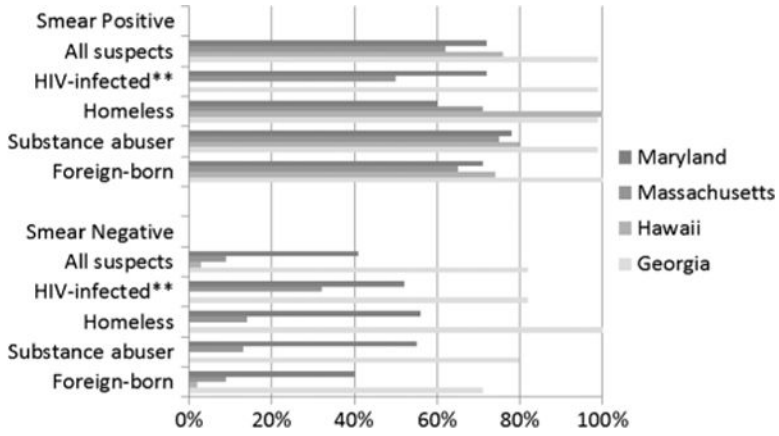

Figure 1.

Mycobacterium tuberculosis direct nucleic acid amplification testing (MTD) by population* and study site. *There was overlap among populations: Of human immunodeficiency virus (HIV)–infected patients, 20% were homeless, 45% were substance abusers, and 21% were foreign-born. Of homeless, 41% were HIV-infected, 64% were substance abusers, and 22% were foreign-born. Of substance abusers, 45% were HIV-infected, 31% were homeless, and 25% were foreign-born. Of foreign born, 5% were HIV-infected, 3% were homeless, and 6% were substance abusers. **One-third of suspected patients had unknown HIV status. Hawaii had <5 known HIV-infected suspected patients.

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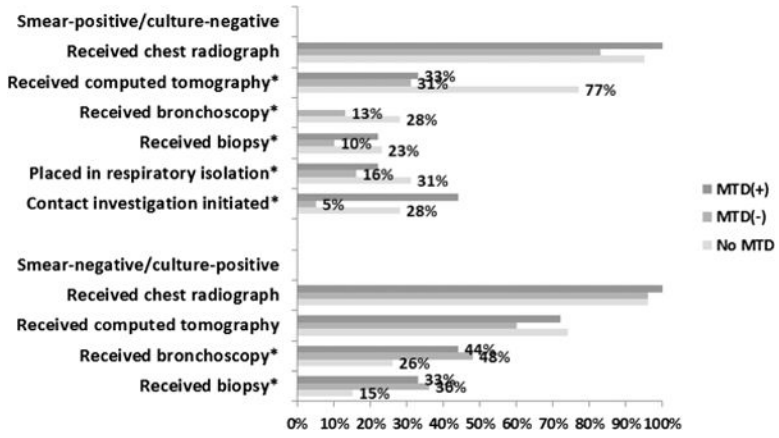

Figure 2.

Differences in procedures, respiratory isolation, and contact investigation initiation by *Mycobacterium tuberculosis* direct nucleic acid amplification testing (MTD) result versus no MTD, cases in which the smear was not predictive of tuberculosis disease. *Significant differences between MTD percentage and no MTD percentage at $P < .05$. For smear-positive/culture-negative, n = 39 for no MTD, n = 295 for MTD-negative, n = 9 for MTD-positive. For smear-negative/culture-positive, n = 233 for no MTD, n = 25 for MTD-negative, n = 36 for MTD-positive. Abbreviation: MTD, *Mycobacterium tuberculosis* direct nucleic acid amplification testing.

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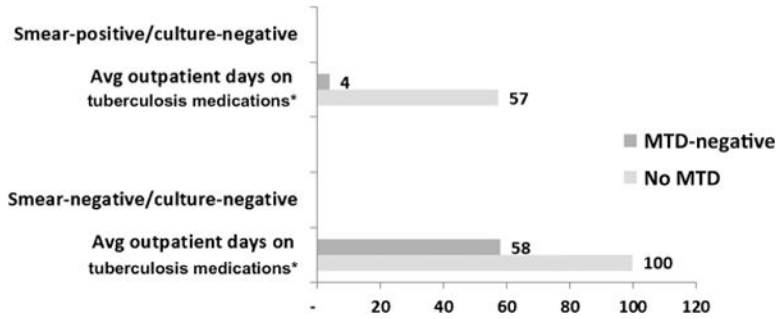

Figure 3.

Differences in outpatient days on tuberculosis medications by *Mycobacterium tuberculosis* direct nucleic acid amplification testing (MTD)–negative result versus no MTD.

*Significant differences between no MTD days and MTD-negative days at $P < .05$.

Abbreviation: MTD, *Mycobacterium tuberculosis* direct nucleic acid amplification testing.

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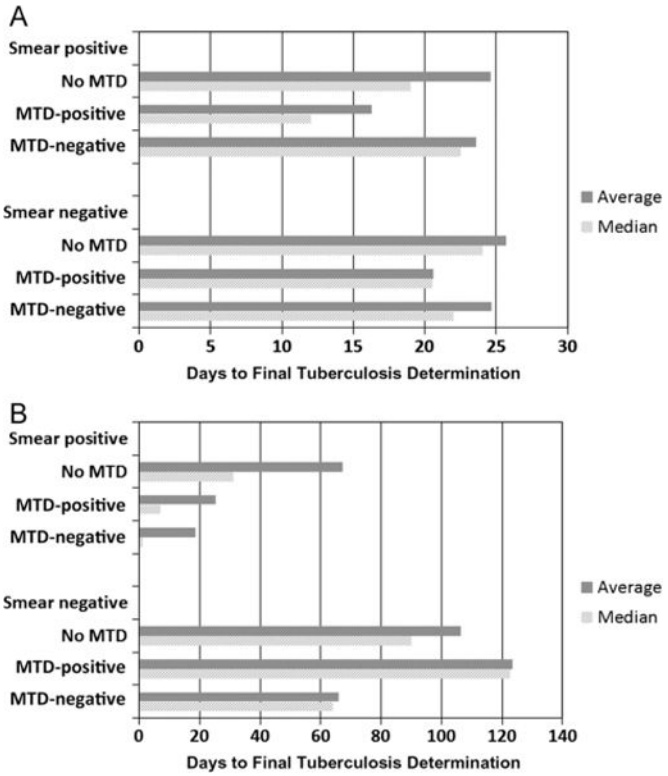

Figure 4.

Days to final tuberculosis determination by tuberculosis disease status. *A*, Patients with tuberculosis disease. Significantly fewer average days to tuberculosis disease determination at $P < .05$ for smear-positive/*Mycobacterium tuberculosis* direct nucleic acid amplification testing (MTD)–positive versus smear-positive/no MTD. *B*, Patients without tuberculosis disease. Significantly fewer average days to exclude tuberculosis at $P < .05$ for: smear-positive/MTD-positive versus smear-positive/no MTD; smear-positive/MTD-negative versus smear-positive/no MTD; smear-negative/MTD-negative versus smear-negative/no MTD. Abbreviation: MTD, *Mycobacterium tuberculosis* direct nucleic acid amplification testing.

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Table 1

Demographics of Study Suspects 2008–2010 Versus Tuberculosis Patients in 2009

Characteristic	No.	% of Study Suspects	% of GA	% of HI	%of MA	%of MD	% of Tuberculosis Patients in 2009
No.		2140	347	617	585	591	11 545
Gender							
Male	1258	59%	73%	49%	61%	59%	61%
Female	880	41%	27%	51%	39%	41%	39%
Transgender (MTF)	2	0%	0%	0%	0%	0%	NA
Age							
0–14 y[a]	22	1%	0%	0%	2%	2%	6%
15–24 y[a]	168	8%	4%	5%	12%	9%	11%
25–44 y[a]	626	29%	42%	19%	28%	34%	34%
45–64 y[a]	847	40%	48%	46%	34%	34%	30%
≥ 65 y[a]	477	22%	5%	30%	25%	21%	20%
Race/ethnicity							
Hispanic[a]	220	10%	6%	0%	16%	17%	29%
White[a]	263	12%	6%	2%	30%	9%	16%
Black[a]	694	32%	85%	1%	23%	44%	25%
American Indian/Alaska Native	4	0%	0%	0%	1%	0%	1%
Asian[a]	842	39%	1%	87%	28%	23%	28%
Native Hawaiian/other Pacific Islander[a]	67	3%	0%	10%	0%	1%	1%
Unknown	50	2%	1%	0%	3%	5%	1%
Origin							
US-born	664	32%	89%	8%	28%	28%	40%
Foreign-born[a]	1397	68%	11%	92%	72%	72%	59%
Unknown	79						
HIV-infected[a]	353	25%	73%	1%	10%	22%	10%
HIV-uninfected	1075	75%	27%	99%	90%	78%	90%

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Characteristic	No.	% of Study Suspects	% of GA	% of HI	%of MA	%of MD	% of Tuberculosis Patients in 2009
HIV status unknown	712						
Correctional resident[a]	41	2%	6%	1%	2%	1%	4%
Homeless[a]	174	8%	26%	2%	7%	6%	5%
Long-term care resident	50	2%	2%	1%	4%	2%	2%
Injecting drug user[a]	48	2%	3%	0%	2%	4%	1%
Non-injecting drug user	191	9%	33%	0%	6%	6%	8%
Excess alcohol user	270	13%	33%	4%	10%	12%	13%
Any substance abuse	355	17%	46%	5%	13%	15%	NA
Employed[a,b]	1015	47%	19%	58%	44%	57%	43%
Insurance at clinic intake[c]	1136						
Private	302	27%	5%	35%	29%	45%	NA
Public	505	44%	55%	31%	53%	35%	NA
Jail/prison	25	2%	4%	0%	4%	0%	NA
Other	7	1%	1%	0%	2%	0%	NA
None	327	29%	35%	37%	16%	25%	NA
Unknown	1004						
Hospitalized	1159	54%	91%	11%	72%	60%	NA

Abbreviations: GA, Georgia; HI, Hawaii; HIV, human immunodeficiency virus; MA, Massachusetts; MD, Maryland; MTF, male to female; NA, not available.

[a] Percentages of study patients significantly differed from those of tuberculosis disease patients in 2009 at $P < .05$.

[b] Those not unemployed, retired, or not seeking work.

[c] Multiple categories were possible.

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Table 2

Mycobacterium tuberculosis Direct Nucleic Acid Amplification Testing Results for Patients Having Specimens Tested ≥1 Time, N = 259

	All Negative		All Positive		Mixed Results		
Total No. of MTDs	**No.**	**%**	**No.**	**%**	**No.**	**%**	**Total**
Smear positive							
2	32	30%	70	66%	4	4%	106
3	4	20%	8	40%	8	40%	20
4	1	25%	0	0%	3	75%	4
5	1	100%	0	0%	0	0%	1
Smear negative							
2	88	88%	8	8%	4	4%	100
3	18	75%	0	0%	6	25%	24
4	2	100%	0	0%	0	0%	2
5	0	0%	0	0%	2	100%	2
Total							259

Abbreviation: MTD, *Mycobacterium tuberculosis* direct nucleic acid amplification testing.

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Table 3

Positive-Predictive Value, Negative-Predictive Value, Sensitivity, and Specificity of *Mycobacterium tuberculosis* Direct Nucleic Acid Amplification Testing (MTD) Versus No MTD, by Population

Suspect Category	MTD PPV[a]	NoMTD PPV[a]	MTD Sensitivity[b]	NoMTD Sensitivity[b]	MTD NPV[c]	No MTD NPV[c]	MTD Specificity[d]	NoMTD Specificity[d]
Smear positive								
All suspects	358/367 (98%)	129/168 (77%)	358/376 (95%)	129/362 (36%)	295/313 (94%)		295/304 (97%)	
HIV-infected	52/58 (90%)	12/19 (63%)	52/58 (90%)	12/24 (50%)	182/188 (97%)		182/188 (97%)	
Homeless	54/55 (98%)	11/12 (92%)	54/57 (95%)	11/22 (50%)	52/55 (95%)		52/53 (98%)	
Substance abuser	75/78 (96%)	14/19 (74%)	75/79 (95%)	14/35 (40%)	122/126 (97%)		122/125 (98%)	
Foreign-born	235/238 (99%)	101/114 (89%)	235/244 (96%)	101/282 (36%)	39/48 (81%)		39/42 (93%)	
Smear negative								
All suspects	36/40 (90%)		36/61 (59%)		175/200 (88%)	819/1052 (78%)	175/179 (98%)	819/858 (95%)
HIV-infected	8/9 (89%)		8/8 (100%)		35/35 (100%)	32/44 (73%)	35/36 (97%)	32/39 (82%)
Homeless	3/5 (60%)		3/3 (100%)		14/14 (100%)	22/33 (67%)	14/16 (88%)	22/23 (96%)
Substance abuser	3/5 (60%)		3/6 (50%)		38/41 (93%)	65/86 (76%)	38/40 (95%)	65/70 (93%)
Foreign-born	27/29 (93%)		27/46 (59%)		97/116 (84%)	671/852 (79%)	97/99 (98%)	671/684 (98%)

Abbreviations: HIV, human immunodeficiency virus; MTD, *Mycobacterium tuberculosis* direct nucleic acid amplification testing; NPV, negative-predictive value; PPV, positive-predictive value.

[a] PPV = true positive/(true positive + false positive). PPV of "No MTD" is the proportion of smear-positive who were culture-positive.

[b] Sensitivity = true positive/(true positive + false negative).

[c] NPV = true negative/(true negative + false negative). NPV of "No MTD" is the proportion of smear-negative who were culture-negative.

[d] Specificity = true negative/(true negative + false positive).

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Table 4

Incremental Health-System Cost-effectiveness, By Patient Characteristics

	Average Cost per Suspect	Cost per 1000 Suspects	MTD Net Cost	TP or TN Suspects	Additional TP Using MTD	Additional TN Using MTD	Incremental Cost per TP	Incremental Cost per TN
All SP suspects								
No MTD	$15181	$ 15 181 396		768				
MTD	$17316	$ 17 316 401	$ 2 135 005	975	208		$ 10283	
HIV-infected SP suspects								
No MTD	$18710	$ 18 710 372		632				
MTD	$5313	$ 5312 791	$ (13 397 581)	897	265		$ (50 562)	
Homeless SP suspects								
No MTD	$23414	$ 23 414 159		917				
MTD	$14057	$ 14 057 343	$ (9356 816)	982	65		$ (143 616)	
Substance abuser SP suspects								
No MTD	$7777	$ 7776 807		737				
MTD	$13303	$ 13 302 661	$ 5 525 854	962	225		$ 24593	
Foreign-born SP suspects								
No MTD	$17378	$ 17 378 086		886				
MTD	$20079	$ 20 078 854	$ 2 700 768	987	101		$ 26627	
Georgia SP suspects								
No MTD	$6181	$ 6181 333		333				
MTD	$6474	$ 6473 845	$ 292 512	943	609		$ 480	
Hawaii SP suspects								
No MTD	$2320	$ 2319 644		750				
MTD	$13426	$ 13 426 217	$ 11 106 572	1000	250		$ 44426	
Massachusetts SP suspects								
No MTD	$20348	$ 20 348 288		727				
MTD	$23686	$ 23 686 331	$ 3 338 043	992	264		$ 12632	
Maryland SP suspects								
No MTD	$13633	$ 13 633 116		878				
MTD	$10179	$ 10 178 611	$ (3454 505)	970	92		$ (37 489)	
All SN Suspects								

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	Average Cost per Suspect	Cost per 1000 Suspects	MTD Net Cost	TP or TN Suspects	Additional TP Using MTD	Additional TN Using MTD	Incremental Cost per TP	Incremental Cost per TN
No MTD	$5132	$ 5132 381		779				
MTD	$8288	$ 8288 000	$ 3 155 619	875		96		$ 32707
HIV-infected SN Suspects								
No MTD	$21693	$ 21 692 511		727				
MTD	$13747	$ 13 747 162	$ (7945 349)	1000		273		$ (29 133)
Homeless SN Suspects								
No MTD	$27761	$ 27 760 545		667				
MTD	$13998	$ 13 998 158	$ (13 762 388)	1000		333		$ (41 287)
Substance abuser SN suspects								
No MTD	$16106	$ 16 106 488		756				
MTD	$11908	$ 11 907 500	$ (4198 988)	927		171		$ (24 553)
Foreign-born SN suspects								
No MTD	$4507	$ 4506 828		788				
MTD	$9034	$ 9034 310	$ 4 527 482	836		49		$ 93066
Georgia SN suspects								
No MTD	$27610	$ 27 610 472		500				
MTD	$11597	$ 11 597 399	$ (16 013 074)	1,000		500		$ (32 026)
Hawaii SN suspects								
No MTD	$4275	$ 4274 814		912				
MTD	$5972	$ 5972 420	$ 1 697 606	545		less effective		…
Massachusetts SN suspects								
No MTD	$8898	$ 8897 565		538				
MTD	$21767	$ 21 766 738	$ 12 869 173	950		412		$ 31 216
Maryland SN suspects								
No MTD	$2187	$ 2187 070		832				
MTD	$3850	$ 3849 879	$ 1 662 810	876		44		$ 37921

Negative cost figures indicate cost savings.

Abbreviations: HIV, human immunodeficiency virus; MTD, *Mycobacterium tuberculosis* direct nucleic acid amplification testing; SN, smear negative; SP, smear positive; TN, true negative; TP, true positive.