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MAJOR ARTICLE

Use of Nucleic Acid Amplification Testing for Rapid Detection of *Mycobacterium tuberculosis* Complex Among US Tuberculosis Patients, 2011–2017

Varsha Kumar,[1,a] Tracy L. Dalton,[1] Lori R. Armstrong,[1,b] Amy Whitesell,[1,c] Rongxia Li,[1] and Angela M. Starks[1]

[1]Division of Tuberculosis Elimination, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Background. Nucleic acid amplification (NAA) tests rapidly detect *Mycobacterium tuberculosis* complex directly from clinical specimens, providing valuable results for those evaluated for tuberculosis.

Methods. We analyzed characteristics of cases with NAA testing performed, compared cases with positive and negative NAA test results, and calculated turnaround time and time to treatment for all verified cases reported to the National Tuberculosis Surveillance System in the United States during 2011–2017.

Results. Among 67 082 verified tuberculosis cases with NAA testing information, 30 820 (45.9%) were reported as not having an NAA test performed; the proportion without NAA testing declined annually, from 60.5% in 2011 to 33.6% in 2017. Of 67 082 verified cases, 27 912 (41.6%) had positive, 8215 (12.2%) had negative, and 135 (0.2%) had indeterminate NAA test results. Among the 33 937 cases with an acid-fast bacilli (AFB) smear-positive result, 24 093 (70.9%) had an NAA test performed; 11 490 of the 30 244 (38.0%) with an AFB smear-negative result had an NAA test performed. Although sputum was the most common specimen type tested, 79.8% (7023/8804) of nonsputum specimen types had a positive NAA test result. Overall, 63.7% of cases with laboratory testing had NAA test results reported <6 days following specimen collection; for 13 891 cases not yet on treatment, median time to treatment after the laboratory report date was 2 days.

Conclusions. Our analyses demonstrate increased NAA test utilization between 2011 and 2017. However, a large proportion of cases did not have an NAA test performed, reflecting challenges in broader uptake, suggesting an opportunity to expand use of this diagnostic methodology.

Keywords. nucleic acid amplification testing; NAA; tuberculosis.

Tuberculosis (TB), a disease caused by *Mycobacterium tuberculosis* complex (MTBC), remains a global public health challenge. With 8916 new cases reported to the National Tuberculosis Surveillance System (NTSS) in 2019, TB in the United States (US) has steadily declined to a rate of 2.7 cases per 100 000 persons [1], due to a national strategic focus on preventing MTBC transmission, improving case management [2], and treating latent TB infection [3]. The rate of TB is consistently higher among non-US-born persons than those born in the US [4].

Effective control of MTBC transmission hinges upon early diagnosis of infectious TB cases and rapid public health response [5, 6]. Microbiologically, the standard of practice is the testing of 3 sputum specimens collected at least 8–24 hours apart [6, 7]. Acid-fast bacilli (AFB) smear microscopy is typically the first laboratory test performed, followed by culture and drug susceptibility testing [6, 7]. However, AFB smear results can be nonspecific (ie, are also positive for other mycobacteria), and, due to MTBC's slow growth, culture and susceptibility results can take weeks. In contrast, nucleic acid amplification (NAA) testing can rapidly identify MTBC directly from clinical specimens and, with some assays, simultaneously detect drug resistance (eg, Cepheid Xpert MTB/RIF, hereafter "Xpert MTB/RIF") [8].

In recent years, NAA testing has become an increasingly valuable tool. NAA test results can help release patients from airborne infection isolation, prevent delays in treatment, and minimize inappropriate treatment [9–14]. Compared to traditional reliance on serial AFB smear results, alternative decision-making strategies can reduce duration of isolation from a median of 68 hours using smear microscopy to a median of 20.8 or 41.2 hours based on Xpert MTB/RIF testing of 1 or 2 sputum specimens, respectively [11], and potentially save an estimated $2278 per admission [12].

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[a]Present affiliation: Division of Global Health Protection, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

[b]Retired.

[c]Present affiliation: Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

Correspondence: Angela M. Starks, PhD, Centers for Disease Control and Prevention, Division of Tuberculosis Elimination, 1600 Clifton Rd NE, Bldg. 17, Rm 4040, M/S H17-4, Atlanta, GA 30329, USA (astarks@cdc.gov).

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In 2009, the US Centers for Disease Control and Prevention (CDC) updated NAA test guidelines to recommend routine NAA testing for any patient being evaluated for pulmonary TB, for whom a diagnosis has not been established and an NAA test result would affect case management [15]. The objective of this analysis was to examine subsequent NAA testing among US TB cases, including the demographic and microbiological factors associated with use of this diagnostic methodology.

METHODS

We conducted a retrospective cohort analysis of verified US TB cases reported to the CDC NTSS during 2011–2017. NTSS collects data from all US states and the District of Columbia on individual cases of TB using a standardized form, the Report of a Verified Case of Tuberculosis (RVCT). The RVCT collects data regarding risk and clinical factors, laboratory information, and demographics [16]. A case is considered verified if it meets the 2009 national TB surveillance case definition [17] or is determined to be a verified TB case by a healthcare provider.

For inclusion, the reported case's NAA test result had to be recorded as positive, negative, indeterminate, or not done. The RVCT form used during this study period (ie, before an RVCT update to allow serial results starting in 2020) allowed 1 NAA test result per case report. Jurisdictions were instructed to report NAA testing of only specimens collected before TB treatment began and that any positive result superseded all other available results; a negative NAA test result means there were no positive results on that patient. Cases either missing (n = 63) or with unknown (n = 158) NAA test results were excluded from analysis.

To analyze NAA test results by specimen type, we dichotomized sputum from nonsputum (ie, any other respiratory or nonrespiratory specimens). Turnaround time (TAT) was defined as number of days between specimen collection date and laboratory report date. We focused on <6 or ≥6 days to explore alignment with the CDC National Tuberculosis Indicators Project objective that aims to increase the proportion of NAA test results reported within 6 days of specimen collection [18]. We included cases with NAA test results reported both before and after treatment began. For those with results reported before treatment began, time to treatment (TTT) was the time interval between laboratory report date and treatment start date. Cases with >365-day TAT were presumed to be misreported and excluded from analysis (n = 74).

To assess NAA test utilization patterns, we stratified cases by whether an NAA test was performed (if positive, negative, and indeterminate results) or not performed (if NAA test reported as not done). Among TB cases where an NAA test was performed, we excluded those with indeterminate results and compared those with a positive result to those with a negative result. For comparisons, data were stratified by clinical characteristics, patient demographics, and risk factors associated with TB. Nativity was categorized based on US Census Bureau definitions: US-born for persons eligible for US citizenship at birth and non-US-born for all other persons, regardless of current immigration or citizenship status. NTSS defines homelessness and substance use on the basis of the 12 months before diagnosis. Contact with an infectious TB case was defined as a known exposure within the 2 years before diagnosis. Except for recent contact, any variables that were missing or reported as "unknown" were excluded from analysis.

We calculated odds ratios (ORs) with 95% confidence intervals (CIs) using logistic regression models to evaluate the associations between case characteristics and odds of having an NAA test performed, of a positive test result, and of TAT in <6 days. SAS version 9.4 software was used for all analyses, and Microsoft Excel was used to generate graphs.

Because these data were collected and analyzed as part of routine public health surveillance, CDC determined that this analysis did not constitute human subjects research and thus did not require approval by an institutional review board.

RESULTS

The 67 082 TB cases reported in the US during 2011–2017 that had any reported value for the NAA test variable were included in this analysis: 27 912 (41.6%) positive, 8215 (12.2%) negative, 135 (0.2%) indeterminate, and 30 820 (45.9%) as NAA test not done. Overall, NAA testing increased during this time frame (Figure 1). The proportion of cases without a positive or negative NAA test result declined a mean of 4.5 percentage points annually, from 60.5% in 2011 to 33.6% in 2017.

Sputum was the most frequently reported specimen type to undergo NAA testing (ie, 26 352 of 36 262 [72.7%] with results). When we further stratified data by anatomic code to examine testing for specimen types other than sputum, we determined that of the remaining 8710 nonsputum samples, 5079 (58.3%) were reflective of testing performed on lymph node (1091 [12.5%]), bronchial fluid (3105 [35.6%]), and lung tissue (883 [10.1%]) combined (data not shown). In our analysis, 4442 of 13 781 (32.2%) of extrapulmonary only cases had NAA performed. Additionally, 1136 of 67 082 (1.7%) of all verified cases had a positive NAA test result only (no culture confirmation) for laboratory criteria for diagnosis and the site of disease available. Of these, 344 of 1136 (30.3%), or 0.5% of our overall dataset, had extrapulmonary disease only.

Having an NAA test performed was associated with a positive AFB smear (OR, 4.0 [95% CI, 3.87–4.13]) and culture (OR, 2.39 [95% CI, 2.30–2.49]) result (Table 1). However, we noted a steady increase in NAA testing among AFB smear-negative specimens over time. Among the 33 937 cases with an AFB smear-positive result, 70.9% (24 093) had an NAA test performed, whereas 11 490 of the 30 244 (38.0%) cases with an

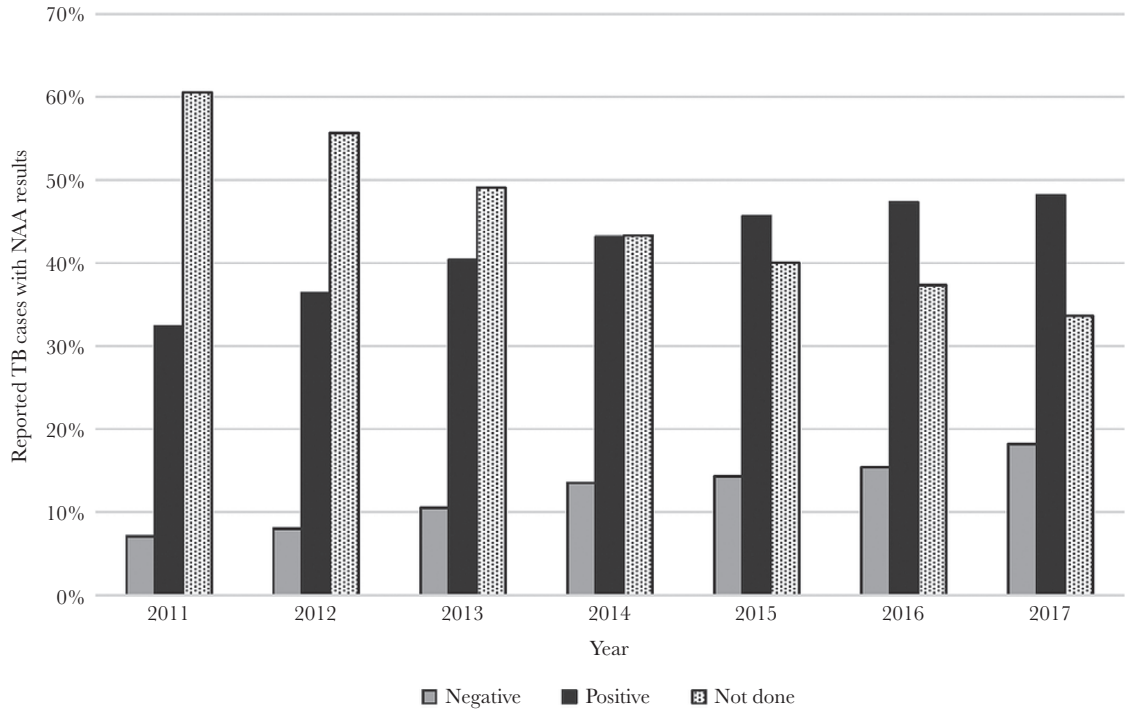

Figure 1. Nucleic acid amplification (NAA) test results among reported tuberculosis (TB) cases by year, United States (US), 2011–2017. Data displayed are percentages of verified cases of TB in the US reported to the National Tuberculosis Surveillance System with a positive, negative, or not done value for NAA testing during 2011–2017 (N = 66 947). Indeterminate results are excluded due to the low number (n = 135 over the 7-year study period).

AFB smear-negative result had an NAA test performed. Among the 51 909 culture-positive cases, 59.8% (31 028) had a reported NAA test performed, whereas 4851 of the 12 657 (38.3%) culture-negative cases had an NAA test performed.

The odds of having an NAA test performed were higher for cases with an abnormal chest radiograph (OR, 2.46 [95% CI, 2.36–2.57]). Other characteristics associated with NAA testing were being non-US-born (OR, 1.12 [95% CI, 1.08–1.16]), male sex (OR, 1.21 [95% CI, 1.17–1.25]), and age ≥15 years (ORs, 3.08–3.91 [95% CIs, 2.83–4.28]) (Table 1). Only 27.0% (876 of 3249) of TB cases in children aged <15 years were reported as having NAA testing performed. Recent contact with an infectious TB case was associated with not having an NAA test performed (OR, 0.81 [95% CI, .77–.86]).

We next examined factors associated with having a positive NAA test result among cases with NAA testing performed. Although sputum was the most common specimen type tested, that specimen type was less likely to have a positive NAA test result: 76.9% (20 200/26 269) of sputum specimens, compared with 79.8% (7023/8804) of nonsputum specimen types, had a positive result (OR, 0.84 [95% CI, .80–.90]) (Table 2). A positive AFB smear was strongly associated with a positive NAA test result (OR, 13.17 [95% CI, 12.41–13.98]); however, 47.0% (5358 of 11 409) of AFB smear-negative cases tested by NAA had a positive NAA test result.

We then examined the concordance between NAA test and other laboratory test results. Culture-positive cases were much more likely to have a report of positive NAA result (OR, 27.75 [95% CI, 25.65–30.03]) (Table 2). Among culture-positive cases, 84.5% (26 775/31 679) were NAA positive, whereas only 19.1% (920/4824) of culture-negative cases were NAA positive (Table 2). Among the 35 138 cases with complete positive or negative NAA test, AFB smear, and culture results, 27 305 (77.7%) had a positive and 7833 (22.3%) had a negative NAA test result (Figure 2). Among the 22 002 NAA test-positive cases that were also AFB smear positive; 1.8% (n = 392) were reported as culture negative. Among the 5303 NAA test-positive cases that were AFB smear negative, 9.7% (n = 515) were reported as culture negative. Among the 1855 NAA test-negative cases that were AFB smear positive, 64.4% (n = 1194) were reported as culture-positive and accounted for 15.2% (1194/7833) of NAA test-negative cases. Among the 5978 of cases that were both NAA test negative and AFB smear negative, 46.6% (n = 2786) were reported as culture positive (Figure 2). The sensitivity of NAA tests in smear-negative, culture-positive cases in this sample set was 63.2% (4788/7574), compared to 94.8% (21 610/22 804) in smear-positive, culture-positive cases. Among NAA test-negative, culture-positive cases, 27.3% (1117/4089) had extrapulmonary disease only. For cases with NAA test positivity, 13.4% (284/2118) of those with extrapulmonary disease only had a negative culture result in comparison to 2.5% (565/22 750) of those with pulmonary disease only having a negative culture result (data not shown). For those aged <15 years, 87.6% (332/379) of cases with a positive NAA test result

Table 1. Characteristics of Tuberculosis Cases With and Without Nucleic Acid Amplification Tests Performed, US National Tuberculosis Surveillance System, 2011–2017 (N = 67 082)

Characteristic	NAA Test Performed, No.	NAA Test Performed, %	No NAA Test Performed, No.	No NAA Test Performed, %	Unadjusted OR, Performed vs Not Performed	95% CI
AFB smear						
Negative[a]	11 490	32.3%	18 754	65.6%	…	…
Positive	24 093	67.7%	9844	34.4%	4.00	3.87–4.13
Culture						
Negative[a]	4851	13.5%	7806	27.2%	…	…
Positive	31 028	86.5%	20 881	72.8%	2.39	2.30–2.49
CXR						
Normal[a]	4001	11.4%	7056	24.1%	…	…
Abnormal	30 989	88.6%	22 186	75.9%	2.46	2.36–2.57
HIV status						
Negative[a]	30 685	93.5%	24 300	93.8%	…	…
Positive	2134	6.5%	1587	6.2%	1.07	1.00–1.14
Nativity						
US-born[a]	11 748	32.4%	10 736	34.9%	…	…
Non-US-born	24 549	67.6%	20 063	65.1%	1.12	1.08–1.16
Sex						
Female[a]	13 429	37.0%	12 801	41.5%	…	…
Male	22 893	63.0%	18 016	58.5%	1.21	1.17–1.25
Age, y						
0–14[a]	876	2.4%	2373	7.7%	…	…
15–24	3945	10.9%	2736	8.9%	3.91	3.56–4.28
25–44	11 451	31.5%	9216	29.9%	3.37	3.10–3.65
45–64	11 720	32.3%	9168	29.7%	3.46	3.19–3.76
≥65	8328	22.9%	7325	23.8%	3.08	2.83–3.35
Homelessness						
No[a]	33 881	93.9%	29 275	95.6%	…	…
Yes	2196	6.1%	1333	4.4%	1.42	1.33–1.53
Injection drug use						
No[a]	35 325	98.4%	30 069	98.8%	…	…
Yes	558	1.6%	371	1.2%	1.28	1.12–1.46
Noninjection drug use						
No[a]	33 071	92.2%	28 624	94.1%	…	…
Yes	2807	7.8%	1808	5.9%	1.34	1.26–1.43
Excess alcohol use						
No[a]	31 562	88.0%	27 697	91.1%	…	…
Yes	4291	12.0%	2721	8.9%	1.38	1.32–1.46
Previous episode of TB						
No[a]	34 276	94.8%	29 262	95.4%	…	…
Yes	1870	5.2%	1396	4.6%	1.14	1.07–1.23
Recent contact to infectious TB case						
Unknown[a]	33 557	92.4%	27 976	90.8%	…	…
Yes	2768	7.6%	2844	9.2%	0.81	.77–.86

Denominators for each percentage exclude missing data points for that variable.

Abbreviations: AFB, acid-fast bacilli; CI, confidence interval; CXR, chest radiograph; HIV, human immunodeficiency virus; NAA, nucleic acid amplification; OR, odds ratio; TB, tuberculosis; US, United States.

[a]Reference group used for OR calculations.

also had a positive culture vs 96.8% (26 439/27 312) of those in older age groups (data not shown).

Of the 34 774 cases with an evaluable NAA test result TAT, 63.7% (n = 22 160) had laboratory test results reported in <6 days and 36.3% (n = 12 614) in ≥6 days, including 2648 with a TAT of ≥30 days. During 2011–2017, the proportion of NAA test results reported in <6 days increased a mean of 2.5 percentage points annually (data not shown). In this analysis, sputum specimens and AFB smear-positive cases were more likely to have TAT of <6 days (Table 3). The mean reported TAT for all NAA test results was 8.7 days, with a median of 4 days. For cases with sputum specimens tested by NAA, the mean TAT was 7.4 days with a median of 4.0 days compared to a mean of 14.5 days with a median of 6 days for nonsputum specimens.

Table 2. Characteristics of Tuberculosis Cases With Positive and Negative Nucleic Acid Amplification Test Results, US National Tuberculosis Surveillance System, 2011–2017 (N = 36 127)

Characteristic	Positive NAA Test Result, No.	Positive NAA Test Result, %	Negative NAA Test Result, No.	Negative NAA Test Result, %	Unadjusted OR, Positive vs Negative	95% CI
Specimen type						
Nonsputum[a]	7023	25.8%	1781	22.7%	…	…
Sputum	20 200	74.2%	6069	77.3%	0.84	.80–.90
AFB smear						
Negative[a]	5358	19.5%	6051	76.1%	…	…
Positive	22 109	80.5%	1896	23.9%	13.17	12.41–13.98
Culture						
Negative[a]	920	3.3%	3904	44.3%	…	…
Positive	26 775	96.7%	4904	55.7%	27.75	25.65–30.03
CXR						
Normal[a]	2381	8.5%	1593	20.0%	…	…
Abnormal	25 531	91.5%	6340	80.0%	2.59	2.41–2.77
HIV status						
Negative[a]	23 526	93.4%	7005	93.8%	…	…
Positive	1655	6.6%	466	6.2%	1.06	.95–1.18
Nativity						
US-born[a]	9231	33.1%	2444	29.8%	…	…
Non-US-born	18 660	66.9%	5765	70.2%	0.86	.81–.90
Age, y						
0–14[a]	392	1.4%	469	5.7%	…	…
15–24	2915	10.4%	1004	12.2%	3.47	2.98–4.04
25–44	8679	31.1%	2705	32.9%	3.84	3.33–4.42
45–64	9150	32.8%	2518	30.7%	4.35	3.78–5.01
≥65	6772	24.3%	1518	18.5%	5.34	4.62–6.17
Sex						
Female[a]	9926	35.6%	3426	41.7%	…	…
Male	17 984	64.4%	4789	58.3%	1.30	1.23–1.36
Homelessness						
No[a]	25 972	93.7%	7730	94.7%	…	…
Yes	1756	6.3%	432	5.3%	1.21	1.09–1.35
Injection drug use						
No[a]	27 142	98.4%	8004	98.5%	…	…
Yes	433	1.6%	121	1.5%	1.06	.86–1.29
Noninjection drug use						
No[a]	25 239	91.5%	7661	94.3%	…	…
Yes	2335	8.5%	462	5.7%	1.53	1.38–1.70
Excess alcohol use						
No[a]	23 920	86.9%	7476	91.9%	…	…
Yes	3619	13.1%	656	8.1%	1.72	1.58–1.88
Previous episode of TB						
No[a]	26 327	94.8%	7762	94.8%	…	…
Yes	1436	5.2%	427	5.2%	0.99	.89–1.11
Recent contact to infectious TB case						
Unknown[a]	25 988	93.1%	7394	90.0%	…	…
Yes	1924	6.9%	821	10.0%	0.67	.61–.73

Denominators for each percentage exclude missing data points for that variable.

Abbreviations: AFB, acid-fast bacilli; CI, confidence interval; CXR, chest radiograph; HIV, human immunodeficiency virus; NAA, nucleic acid amplification; OR, odds ratio; TB, tuberculosis; US, United States.

[a]Reference group used for OR calculations.

For sputum specimens, 25% of NAA test results were reported in 2 days after specimen collection. The mean NAA test TAT for AFB-positive cases was 7.3 days with a median of 4.0 days while AFB-negative cases had a mean TAT of 13.2 days with a median of 5.0 days.

To assess how NAA testing affected TTT, we stratified NAA test results by those reported before and after treatment initiation. Of the 34 166 cases with an evaluable TTT, 59.3% (n = 20 275) began treatment before an NAA test result was reported by the laboratory (data not shown); 80.4% of these

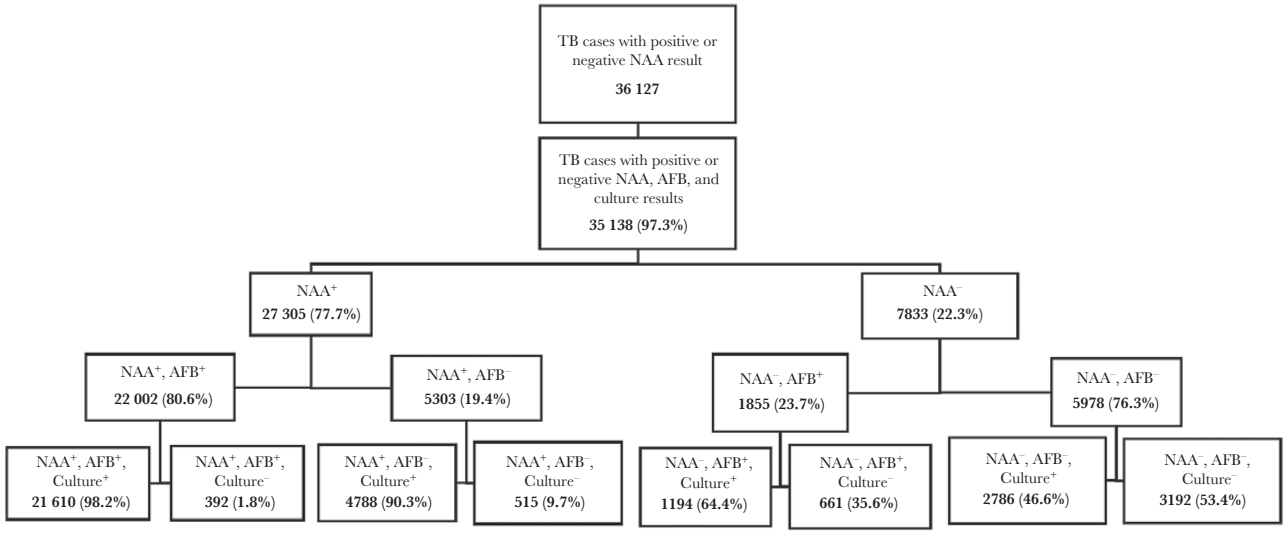

Figure 2. Distribution of tuberculosis (TB) nucleic acid amplification (NAA), acid-fast bacilli (AFB), and culture results. Stratified data include verified US cases from the National Tuberculosis Surveillance System that had completeness of reporting for all 3 laboratory tests: a reported positive or negative NAA test result, AFB smear microscopy result, and *Mycobacterium tuberculosis* complex culture result (N = 35 138 during 2011–2017).

(n = 16 296) later had a positive NAA test result. When treatment was initiated beforehand, the median TTT was 5 days before the NAA test result report date. Among the 40.7% (n = 13 891) whose treatment began afterward, median TTT after the NAA test result report date was 2 days, and 77.2% (n = 10 721) of those had a positive NAA test result.

DISCUSSION

Our analysis shows a clear increase in NAA test utilization among TB cases in the US during 2011–2017. Several factors potentially contributed to this observed increase. In 2009, updated CDC guidance recommended NAA testing as standard practice, [15] and CDC targeted funding support to public health laboratories to increase access to NAA testing. Additionally, in 2013, the US Food and Drug Administration authorized a novel type of NAA test, the Xpert MTB/RIF, that also assesses for mutations associated with rifampin resistance [8, 19, 20]. However, a large proportion of cases overall (45.9%) did not have an NAA test performed, reflecting challenges in broader uptake. Barriers include few commercially available options, resource limitations prohibiting universal testing, and empiric treatment that could limit the utility of NAA testing (eg, some methods are validated only for cases on treatment for ≤3 days).

As expected, we found that sputum was the specimen type most likely to be used for NAA testing. In 2019, 79% of US TB cases had pulmonary involvement [1]. Laboratories may be reluctant or unable to validate nonsputum specimen types for commercially available or laboratory-developed tests [21]. Interestingly, we found that nonsputum specimens, compared to sputum specimens, were more likely to have positive NAA test results, suggesting value of NAA testing with these specimen types. Additionally, we observed that a third of cases with positive NAA test results as the sole laboratory criteria for diagnosis had extrapulmonary disease only, indicating the potential

Table 3. Nucleic Acid Amplification Test Result Turnaround Time by Specimen Type, US National Tuberculosis Surveillance System, 2011–2017 (N = 34 774)

Characteristic	<6-day TAT, No.	<6-day TAT, %	≥6-day TAT, No.	≥6-day TAT, %	Unadjusted OR ≥6 day vs <6-day TAT	95% CI
Specimen type						
Nonsputum[a]	4051	18.7%	4410	36.2%	…	…
Sputum	17 662	81.3%	7771	63.8%	0.40	.38–.43
AFB smear						
Negative[a]	5778	26.6%	4853	39.2%	…	…
Positive	15 955	72.4%	7525	60.8%	0.56	.54–.59
Culture						
Negative[a]	2810	12.8%	1495	12.0%	…	…
Positive	19 094	87.2%	10 973	88.0%	1.08	1.01–1.16

Denominators for each percentage exclude missing data points for that variable.

Abbreviations: AFB, acid-fast bacilli; CI, confidence interval; OR, odds ratio; TAT, turnaround time.

[a]Reference group used for OR calculations.

importance of testing other tissue types, including fixed tissue samples, when additional microbiological testing may not be possible.

As in other studies, we found a greater association between AFB smear-positive results and any reported NAA result [14, 22]. A common testing algorithm among US laboratories is to perform an NAA test for every newly AFB smear-positive specimen but only for AFB smear-negative specimens on request [23]. However, we noted a steady increase in NAA testing among AFB smear-negative specimens over time. Given the sensitivity of NAA testing among smear negatives in this study (63.2%), use of NAA testing may well be considered including for patients who may not have a classic presentation of TB.

A small number (n = 1194) of the overall TB cases in this analysis were AFB smear positive and culture positive yet NAA test negative; yet, these represented 15.2% of all NAA test-negative samples. This is a notable finding given the smear and culture positivity and the high percentage of NAA test positivity observed for these samples in our analysis. However, specimens from these individuals could have contained inhibitory substances impacting NAA testing or included nontuberculous mycobacteria (ie, AFB positive) with few MTBC. We also noted that almost 10% of AFB smear-negative, NAA test-positive cases were culture negative, underscoring the benefit of NAA testing in AFB smear-negative cases. The potential lack of culture positivity in these cases could have been due to testing of different specimens by each method or empiric treatment of patients prior to laboratory evaluation, therefore impacting MTBC viability.

While our findings suggest an increase in NAA testing over time, at least 2 limitations should be acknowledged. First, the NTSS dataset comprise only verified TB cases; we lack information about the broader context of NAA testing among persons who were evaluated for TB but ultimately determined not to have a verified case of TB to report. Without that other group, we cannot assess overall NAA test utilization nationwide. Second, the NTSS allowed for only 1 NAA test result, 1 AFB smear result, and 1 culture result to be reported per TB case during 2011–2017 (with instructions to report the first positive result for each test if there were positive results on any of the specimens). Therefore, when our analysis compared NAA test, AFB smear, and culture results, we were not necessarily comparing results from the same specimen. The 2020 RVCT will allow reporting of multiple results for these laboratory tests [24]. Nevertheless, this analysis advances our understanding of the use of NAA testing in the US in recent years.

During 2011–2017, TB cases among non-US-born individuals ranged from 63% to 71% of all US TB cases [1], correlating with the higher proportion of NAA testing within this group (Table 1). A study by Marks et al that included individuals being evaluated for pulmonary TB, not just reported TB cases, found that NAA testing was also common for non-US-born individuals but was used more often for those with smear-positive vs smear-negative disease [14]. NAA testing may be used more often for non-US-born individuals due to a higher index of clinical suspicion for TB due to country of birth or other factors including travel history to areas with higher rates of TB than the US.

Compared with other age groups, those aged <15 years had the lowest proportion of NAA testing performed, even though nearly half (392/861) had positive results (Table 2). NAA tests generally have a lower sensitivity in children compared to adults [25, 26] due to difficulties in obtaining specimens from children and the paucibacillary nature of TB in this population. These challenges may limit use of NAA tests for pediatric cases. However, 12.4% of those aged <15 years who had positive NAA test results were culture negative, highlighting the value of NAA testing in this group for laboratory diagnosis of TB.

Improvement in TAT <6 days from 2011 to 2017 could be due to changes in NAA test algorithms, improved understanding of the surveillance variable, and some standardizing of laboratory report formats. During the timeframe of this surveillance analysis, educational efforts by CDC focused on timely NAA testing and reporting. Given the need for rapid detection of pulmonary TB to prevent ongoing transmission, it was reassuring that cases with sputum specimen tested, AFB-positive disease, and abnormal chest radiograph were less likely to have long TAT (≥6 days) for NAA testing. Longer TAT for nonsputum specimen types could be due to limited onsite laboratory validation of NAA testing for other specimen types and delays associated with transport to another laboratory for testing. Treatment was frequently initiated before an NAA test result was reported, suggesting a high clinical suspicion of TB that the subsequent NAA test result generally supported. However, it should be noted in our analysis that among cases where the positive or negative NAA, AFB smear, and culture results were available, more than half of cases with a negative NAA test result were culture positive for MTBC, highlighting the continued need for specimen culture. Because AFB smear status is often the first laboratory result available, treatment could have been initiated based on smear positivity before NAA test results are received, in accordance with treatment guidelines [6].

To summarize, NAA testing was increasingly used in the diagnostic evaluation of TB cases in the US between 2011 and 2017. However, nearly half of cases did not have an NAA test performed, suggesting an opportunity to continue to expand use of this valuable diagnostic methodology for nonsputum specimens and for cases with AFB smear-negative TB.

Notes

Author contributions. A. M. S. and T. L. D. conceived of the study concept. A. M. S. oversaw overall direction and writing. A. W. developed the analytic plan and performed initial analyses. T. L. D., R. L., and L. R. A.

provided guidance on analytic approaches and provided critical feedback. V. K. performed analyses and wrote the manuscript. All authors discussed the results and commented on the manuscript.

Patient consent statement. Patient consent was not required because these data were collected and analyzed as part of routine public health surveillance.

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