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Characteristics of TB cases without documented sputum culture in the United States, 2011–2021

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SUMMARY

BACKGROUND: Culture-based diagnostics are the gold standard for diagnosing pulmonary TB (PTB). We characterized culture practices by comparing cases with documented sputum culture to those without.

METHODS: Using multivariable logistic regression, we examined associations between PTB case characteristics and no documented sputum culture reported to the U.S. National TB Surveillance System during 2011–2021.

RESULTS: Among 69,538 PTB cases analyzed, no sputum culture attempt was documented for 5,869 (8%). Non-sputum culture specimens were documented for 54%, 80%, and 89% of cases without documented sputum culture attempts among persons aged <15 years, 15–64, and 65+ years, respectively; bronchial fluid and lung tissue were common non-sputum specimens among cases in persons >15 years old. Having no documented sputum culture was associated with age <15 years (aOR 23.84, 99% CI 20.09–28.27) or ≥65 years (aOR 1.22, 99% CI 1.07–1.39), culture of a non-sputum specimen (aOR 6.57, 99% CI 5.93–7.28), residence in a long-term care facility (aOR 1.58, 99% CI 1.23–2.01), and receiving TB care outside of a health department (aOR 1.79, 99% CI 1.61–1.98).

CONCLUSIONS: Inability to obtain sputum from children and higher diagnostic suspicion for disease processes that require tissue-based diagnostics could explain these findings.

RÉSUMÉ

Les diagnostics basés sur la culture sont considérés comme la méthode de référence pour diagnostiquer la TB pulmonaire (TBP). Nous avons étudié les pratiques de culture en comparant les cas avec une culture d'expectoration documentée à ceux sans culture.

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En utilisant une régression logistique multivariable, nous avons analysé les liens entre les caractéristiques des cas de TBP et l'absence de culture d'expectoration documentée signalée au système national de surveillance de la TB des États-Unis entre 2011 et 2021.

Parmi les 69 538 cas de PTB, aucune tentative de culture des expectorations n'a été enregistrée pour 5 869 (8%) d'entre eux. Nous avons documenté des échantillons non liés à la culture de l'expectoration pour 54%, 80% et 89% des cas sans tentative de culture de l'expectoration chez les personnes âgées de moins de 15 ans, de 15 à 64 ans et de 65 ans et plus, respectivement. Le liquide bronchique et le tissu pulmonaire étaient des échantillons non liés à la culture de l'expectoration fréquemment observés parmi les cas chez les personnes âgées de plus de 15 ans. L'absence de documentation de l'expectoration était liée à l'âge <15 ans (aOR 23,84; IC à 99% 20,09–28,27) ou 65 ans (aOR 1,22; IC à 99% 1,07–1,39), à la culture d'un échantillon différent de l'expectoration (aOR 6,57; IC à 99% 5,93–7,28), à la résidence dans un établissement de soins de longue durée (aOR 1,58; IC à 99% 1,23–2,01), et au fait de recevoir des soins contre la TB en dehors d'un service de santé (aOR 1,79; IC à 99% 1,61–1,98).

L'incapacité de recueillir des expectorations chez les enfants et une suspicion diagnostique accrue pour les processus pathologiques nécessitant un diagnostic à partir des tissus pourraient expliquer ces résultats.

Keywords

Mycobacterium tuberculosis ; TB diagnostics; long-term care

Even with one of the lowest TB incidence rates in the world at 2.4 cases/100,000 persons, there were 7,882 TB cases reported in the United States in 2021.¹ In this low-incidence context, clinicians might not initially consider TB in their differential diagnoses and perform appropriate diagnostic evaluations for patients with risk factors for and clinical presentations compatible with TB.² Culture is the most sensitive diagnostic test for pulmonary TB (PTB) disease, a key component of a diagnostic evaluation, and recommended by current clinical practice guidelines.^{2,3} In addition to confirming diagnoses, culture facilitates drug susceptibility testing to inform treatment regimens and genotyping to assist in public health surveillance and investigations. Collection of spontaneous or induced sputa for culture is non-invasive and facilitates culture-based testing for *Mycobacterium tuberculosis* without the need for anesthesia or specialized equipment.³

Despite the benefits of sputum culturing and clinical practice guidelines that recommend collection of sputum cultures during PTB diagnostic evaluations, factors associated with the lack of a sputum culture among PTB cases are not well characterized. We analyzed data from the U.S. National Tuberculosis Surveillance System (NTSS) to investigate demographic, clinical, and laboratory characteristics associated with lack of sputum culture documentation in NTSS among PTB cases diagnosed by other means.

METHODS

We analyzed NTSS data for PTB cases reported by the 50 U.S. states and the District of Columbia (DC) during 2011–2021 among persons alive at diagnosis.⁴ TB cases are verified

based on the following hierarchy: positive culture, positive nucleic-acid amplification test (NAAT; when culture results are unavailable or negative), positive acid-fast bacilli smear (when culture results are unavailable), meeting the clinical case definition, or provider diagnosis.⁴ Demographic, clinical, and laboratory characteristics are reported for all TB cases. Race and ethnicity were combined as described in Office of Management and Budget's Policy Directive 15.⁵ Hispanic or Latino persons were considered Hispanic/Latino regardless of race.

We described characteristics of PTB cases stratified by whether a sputum culture result was documented (reported as a positive or negative result) or not documented (i.e., reported as 'not done') in NTSS. No data were available to explain the reason that a sputum culture result was not done, but gaps at any step in the process (e.g., test ordering, specimen collection, processing, shipping, and reporting of results) could result in a non-documented sputum culture in NTSS. Patients with missing or unknown values for sputum culture were included for frequency tables but excluded from regression models.

We used χ^2 tests or Fisher's exact tests with expected cell counts, 5 cases to compare the frequency distributions of case characteristics, including missing and unknown values as an analytic category. For regression analyses, cases with missing or unknown values were excluded, except for race/ethnicity, for which 'multiple' and unknown were grouped together, and provider type. We used logistic regression to conduct bivariate analyses between each characteristic and sputum culture documentation and calculated crude odds ratios (ORs) and 99% confidence intervals (CIs). We selected a high level of confidence to ensure that the true population value was within the interval for each assessed covariate in the study. For the multivariable analysis, we performed backward selection procedures with Schwarz Bayesian information criterion for model selection and used $\alpha = 0.01$ to determine inclusion in the model. We compared demographic characteristics of cases included and excluded from regression models to assess for bias. After assessing for effect modification and multicollinearity, we calculated adjusted odds ratios (aORs) and 99% CIs and examined the estimate for the area under the ROC curve to assess the predictive power of the final model.

All analyses were performed using SAS software v9.4 (SAS Institute Inc, Cary, NC, USA). This project was determined not to be human subjects research by the U.S. Centers for Disease Control and Prevention (CDC) and did not require approval by an institutional review board because NTSS data are collected and analyzed as part of a routine public health surveillance activity.

RESULTS

During 2011–2021, 100,114 TB cases were reported in the 50 U.S. states and DC (Figure). Pulmonary involvement was documented for 79,490 (79%) cases; of these, 77,662 (98%) occurred among persons alive at diagnosis and were included in the analyses. Patients' median age was 49 years (interquartile range [IQR] 31–64); 63% were male and 67% were non-U.S.-born. Among the 6,616 cases without sputum culture documentation, 5,817 (88%) also had no sputum smear documented.

A total of 8,124 cases (10%) were excluded from bivariate and multivariable analyses because of missing values for one or more covariates or the model outcome. Of the 69,538 cases included in the analyses, no sputum culture was documented for 5,869 (8%) cases. There were statistically significant associations ($\alpha = 0.01$) between each of the variables examined and sputum culture documentation. A final model selected for the multivariable analysis included 15 main effects (Table 1). No multicollinearity was detected and no effect modification terms were included in the final model. The area under the ROC curve was 0.88. Pediatric patients (age, 15 years) comprised 36% ($n = 2,117$) of cases with no documented sputum culture compared with 2% ($n = 1,150$) of cases with a documented sputum culture ($P < 0.001$). The median age of pediatric patients was 3 years (IQR 1–9). Among those patients with no documented sputum culture, 56% ($n = 3,292$) of patients were U.S.-born compared with 31% ($n = 19,730$) of persons with a documented sputum culture ($P < 0.001$).

Among cases without documented sputum cultures, 73% had documented culture obtained from another anatomic site; the frequency of non-sputum cultures varied by age (54% of pediatric patients, 80% of patients 15–64 years, and 89% of patients ≥ 65 years) (Table 2). Among pediatric patients, most non-sputum specimens were gastric aspirates (74%). Bronchial fluid was the most common non-sputum specimen documented for patients aged 15–64 years (46%) and patients aged ≥ 65 years (55%), followed by lung tissue biopsy (16% and 18%, respectively). Odds of no documented sputum culture were higher for patients with a reported culture result from another specimen type (aOR 6.48, 99% CI 5.86–7.17) compared with patients without a documented culture from another specimen. The reason for TB evaluation was reported as ‘incidental’ for 12% ($n/N = 269/2,188$) of patients with a culture from a lung tissue or bronchial fluid specimen, compared to 6% ($n/N = 3,772/63,669$) of patients with a sputum culture completed.

Patients who resided in long-term care facilities (LTCFs) at the time of diagnosis had higher odds of no documented sputum culture (aOR 1.62, 99% CI 1.27–2.06) compared with non-residents (Table 1). In LTCFs, 89% ($n/N = 176/197$) of patients without documented sputum culture had a culture from a non-sputum specimen done; bronchial fluid was the most frequent specimen source (63%, $n/N = 110/176$).

Lower odds of having no sputum culture documentation were observed among some demographic groups (sputum culture non-documentation: aOR 0.42, 99% CI 0.27–0.66 among non-Hispanic American Indian/Alaska Native patients and aOR 0.85, 99% CI 0.74–0.98 non-Hispanic Black patients compared to White patients), and among patients reporting homelessness (aOR 0.66, 99% CI 0.51–0.85) and substance use (aOR 0.67, 99% CI 0.57–0.79) (Table 1). Patients who received TB care outside of the health department had higher odds of having no documented sputum culture result (aOR 1.82, 99% CI 1.64–2.01) compared to those receiving TB care exclusively through a health department.

Patients who were not offered an HIV test had higher odds of not having sputum culture documented compared with those who were offered an HIV test (aOR 2.50, 99% CI 2.19–2.85). Higher odds of no documented sputum culture were also associated with lack of tuberculin skin test (TST; aOR 1.10, 99% CI 1.00–1.22), interferon-gamma release assay

(IGRA; aOR 1.30, 99% CI 1.19–1.43), and NAAT completion (aOR 2.55, 99% CI 2.34–2.78).

DISCUSSION

For this study, we describe demographic, laboratory, and clinical data associated with sputum culture non-documentation to identify potential gaps in TB evaluation and opportunities for improving TB care. In this analysis of PTB cases reported for national surveillance, we found higher odds of no documented sputum culture for patients aged <15 or ≥65 years, patients who had a documented non-sputum culture result, and LTCF residents. We also found that having no documented sputum culture was associated with a lack of other non-culture diagnostic tests and receipt of TB care outside of the health department. These findings suggest that efforts to increase implementation of TB clinical practice guidance are warranted, particularly for certain groups at higher risk for TB. Guidance from CDC and American Thoracic Society (ATS) recommends that TB diagnostic evaluation include both sputum smear and culture to exclude PTB disease;² sputum induction, which has similar diagnostic sensitivity and can be performed without sedation, should also be considered to diagnose TB disease in patients unable to produce an expectorated sputum sample. While bronchoscopy facilitates collection of specimens that can be used to diagnose TB, lung cancer, and other pulmonary diseases, collection of sputum (induced or not) facilitates TB diagnoses without the sedation and infection control risks associated with bronchoscopy.^{2,3} Among patients without documented sputum culture attempts, most did not have a sputum smear, which is valuable for identifying highly contagious TB cases.⁶ High diagnostic suspicion for processes, such as lung cancer, requiring tissue diagnoses might have influenced biopsies of lung tissue and collection bronchoscopy specimens. Though these patients ultimately had culture-based testing for *M. tuberculosis*, sputum smear still contributes to TB care and prevention since current guidance for contact investigations prioritizes sputum smear-positive cases relative to smear-negative cases.⁷ In some jurisdictions, contact investigations around sputum smear-negative cases are considered lower priority.

Sputum culture was documented more reliably for some groups, including some racial and ethnic groups, patients with reported substance use, and those experiencing homelessness. Since many of these groups have increased TB incidence,⁸ this finding might represent early consideration of TB during these patients' diagnostic evaluations and implementation of guideline-based care plans that include sputum culture.⁷

Documentation of both sputum and non-sputum cultures was less common in individuals aged <15 years compared with adults aged 15–64 years. Challenges in diagnosing pediatric TB are widely recognized, which is why pediatric TB diagnoses rely heavily on epidemiologic and clinical findings.^{3,9,10} According to Infectious Diseases Society of America guidelines, microbiological confirmation may not be necessary for some children if the source case of drug-susceptible TB can be identified.² Consistent with pediatric TB clinical practice guidelines, gastric aspirate specimens were the non-sputum specimen most frequently collected from children without a sputum culture.^{2,3,11}

Lower prevalence of sputum culture documentation in patients ≥ 65 years has been reported elsewhere.¹² Among adult cases without a documented sputum culture result, the prevalence of non-sputum specimen culturing was 89% for patients ≥ 65 years and 80% for patients 15–64 years. The most common specimens were lung tissue and bronchial fluid. There are at least two possibilities for these findings. Some patients with TB cannot produce sputum. Bronchoscopy or lung biopsy can be necessary to make culture-confirmed diagnoses in these cases. However, we suspect that diagnostic suspicion for other processes requiring tissue diagnoses, such as lung cancers, interstitial lung diseases, and pulmonary sarcoidosis, might explain a larger proportion of diagnoses using these specimen types in adults. TB cases diagnosed via these methods might also have been unanticipated, as supported by the higher prevalence of ‘incidental’ TB evaluations among patients with lung tissue and bronchial fluid cultures compared to patients with sputum cultures.

Documentation of sputum culture was less common among people residing in LTCFs, including rehabilitation facilities, hospitals, nursing and residential homes, and mental healthcare facilities. Most cases without a sputum culture had a non-sputum culture documented, and cultures of bronchial fluid and lung biopsies were most frequently reported, suggesting challenges with specimen collection or low suspicion for TB. An outbreak of TB in an LTCF is especially serious because transmission in a congregate setting within a population with a higher prevalence of medical risk factors can lead to increased risk for TB disease progression.¹³ Some patients, especially those in a congregate setting, might have been empirically treated for TB after a known exposure.¹⁴

Our results suggest that clinicians affiliated with health departments might have a higher suspicion for TB. If patients who initially presented to a public health department have more TB risk factors, this could result in increased suspicion for TB and better experience with clinical recognition of TB.^{15,16} Differences between TB care provided by a public health department and other types of healthcare providers have been reported elsewhere,¹⁶ suggesting further investigation of provider type and use of diagnostic tools are warranted.

The use of NAAT is recommended when TB is presumed due to fast turnaround time, but culture must be performed even if NAAT is used. NAAT alone is not sensitive enough to replace mycobacterial culture for diagnosis and provides limited information about TB drug susceptibility.² Our finding of an association between use of sputum culture and use of NAAT, HIV testing, TST, and IGRA as well as association with unanticipated TB diagnoses from lung tissue and bronchial fluid could indicate suboptimal use of diagnostic methods, reflecting low awareness in the differential diagnosis.⁶ This emphasizes the need for continued vigilance for established TB risk factors and consideration of TB for patients presenting with symptoms consistent with TB.

These analyses are subject to several limitations. Some testing for TB and HIV might not be reported to surveillance systems. Excluding missing data can cause bias in the estimation of parameters where distributions across variables differ, for example in the distribution of patients across Census regions. As analysis of large data sets can result in spuriously small *P*-values, we addressed this by increasing the alpha for statistical analyses and considering the practical or clinical relevance in our interpretation of these findings. Finally, lack of

documented sputum culture can occur at many points in the diagnostic and record-keeping process, and the specific reason cannot always be identified based on analysis of surveillance data.

CONCLUSION

Culture is the most sensitive diagnostic test for TB and should be considered during diagnostic evaluation for any patient with compatible signs or symptoms, especially if any epidemiologic and social risk factors for TB are present. Among PTB cases, we found that sputum culture non-documentation was associated with ages <15 and ≥65 years, LTCF residency, receiving care outside of a health department, and non-sputum culture documentation, suggesting age-based inability to gather sputum specimen for mycobacterial culture in children and higher diagnostic suspicion for other disease processes in adults. Nonetheless, most (73%) PTB cases were confirmed by culture of a non-sputum specimen, and bronchoscopy specimens and lung biopsy tissue were the two most common specimens among adults. Though useful for confirming TB diagnoses, bronchoscopy and lung biopsy are invasive, require sedation, and can facilitate transmission of *M. tuberculosis* through aerosols. Culture has been the gold standard for laboratory confirmation of PTB and continues to play an important role in clinical and public health efforts to treat and prevent TB.

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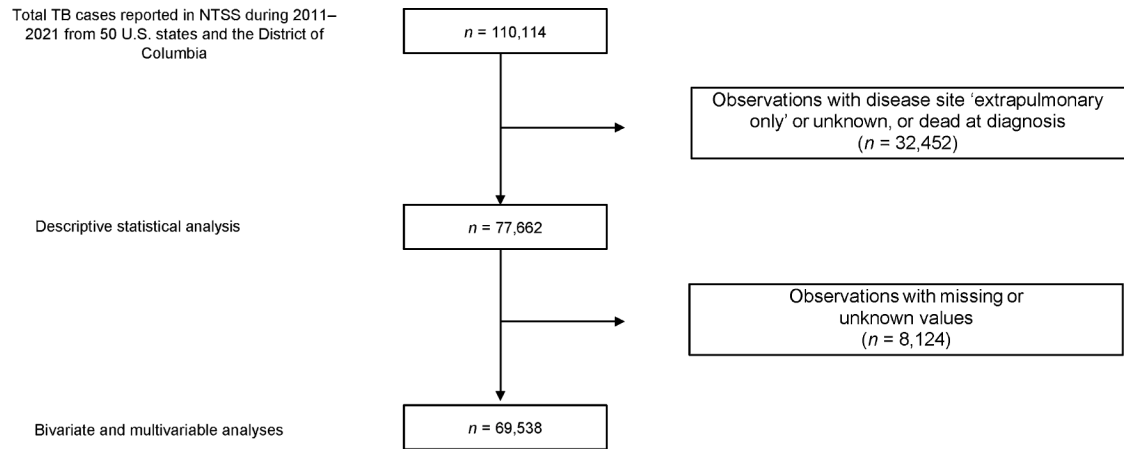
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National Tuberculosis Surveillance System data are currently available through a pilot project with the Research Data Center National Center for Health Statistics, <https://www.cdc.gov/rdc/b1datatype/tuberculosis.htm>.

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**Figure.**

STROBE diagram for inclusion of cases into the study. NTSS = National Tuberculosis Surveillance System; STROBE = Strengthening the Reporting of Observational Studies in Epidemiology.

Table 1.

Frequencies, crude ORs, and aORs for lack of sputum culture documentation by patient characteristic, 2011–2021 ($n = 69,538$).

	Sputum culture not documented n (%)	Sputum culture documented n (%)	Bivariate analysis		Multivariable analysis	
			OR (99%CI)	P value	aOR (99%CI)	P value
Total	5,869 (8.4)	63,669 (91.6)				
Sex						
Female	2,632 (44.8)	22,855 (35.9)	1.45 (1.35–1.56)	<0.001	1.23 (1.13–1.34)	<0.001
Male	3,237 (55.2)	40,814 (64.1)	Reference	—	Reference	—
Age, years						
0–14	2,117 (36.1)	1,150 (1.8)	39.48 (35.37–44.06)	<0.001	27.36 (23.59–31.74)	<0.001
15–64	2,200 (37.5)	47,177 (74.1)	Reference	—	Reference	—
>65	1,552 (26.4)	15,342 (24.1)	2.17 (1.99–2.37)	<0.001	1.34 (1.21–1.48)	<0.001
Origin						
Non-U.S.-born	2,577 (43.9)	43,939 (69.0)	0.35 (0.33–0.38)	<0.001	0.63 (0.56–0.70)	<0.001
U.S.-born	3,292 (56.1)	19,730 (31.0)	Reference	—	Reference	—
Race/ethnicity						
NH American Indian/Alaska Native	62 (1.1)	861 (1.4)	0.63 (0.45–0.90)	<0.001	0.42 (0.27–0.66)	<0.001
NH Asian	1,601 (27.3)	21,561 (33.9)	0.65 (0.58–0.73)	<0.001	1.01 (0.87–1.18)	0.877
NH Black	1,270 (21.6)	12,718 (20.0)	0.88 (0.78–0.99)	0.004	0.85 (0.74–0.98)	0.003
Hispanic or Latino	1,801 (30.7)	19,049 (29.9)	0.83 (0.75–0.93)	<0.001	1.03 (0.89–1.19)	0.579
NH Native Hawaiian/other Pacific Islander	127 (2.2)	592 (0.9)	1.88 (1.44–2.46)	<0.001	1.54 (1.04–2.27)	0.004
NH White	953 (16.2)	8,367 (13.1)	Reference	—	Reference	—
Multiple races or unknown	55 (0.9)	521 (0.8)	0.93 (0.64–1.35)	0.602	0.94 (0.59–1.51)	0.744
U.S. Census region						
Midwest	992 (16.9)	6,876 (10.8)	2.17 (1.94–2.43)	<0.001	2.12 (1.84–2.45)	<0.001
Northeast	995 (17.0)	10,288 (16.2)	1.46 (1.30–1.63)	<0.001	1.52 (1.32–1.73)	<0.001
South	2,485 (42.3)	25,464 (40.0)	1.47 (1.34–1.61)	<0.001	1.61 (1.43–1.81)	<0.001
West	1,397 (23.8)	21,041 (33.0)	Reference	—	Reference	—
Diagnosis in a long-term care facility						
No	5,672 (96.6)	62,732 (98.5)	Reference	—	Reference	—
Yes	197 (3.4)	937 (1.5)	2.33 (1.90–2.86)	<0.001	1.62 (1.27–2.06)	<0.001

	Sputum culture not documented <i>n</i> (%)	Sputum culture documented <i>n</i> (%)	Bivariate analysis		Multivariable analysis	
			OR (99%CI)	<i>P</i> value	aOR (99%CI)	<i>P</i> value
Diagnosis in a correctional facility						
No	5,757 (98.1)	61,096 (96.0)	Reference	—		
Yes	112 (1.9)	2,573 (4.0)	0.46 (0.36–0.59)	<0.001		
Substance use *						
None	5,498 (93.7)	10,611 (16.6)	Reference	—	Reference	—
Any	371 (6.3)	53,058 (83.3)	0.34 (0.29–0.39)	<0.001	0.67 (0.57–0.79)	<0.001
Experiencing homelessness						
No	5,734 (97.7)	59,855 (94.0)	Reference	—	Reference	—
Yes	135 (2.3)	3,814 (6.0)	0.37 (0.29–0.47)	<0.001	0.66 (0.51–0.85)	<0.001
HIV test offered						
Offered	4,617 (78.7)	61,164 (96.1)	Reference	—	Reference	—
Not offered	1,252 (21.3)	2,505 (3.9)	6.62 (6.01–7.30)	<0.001	2.50 (2.19–2.85)	<0.001
Previous TB						
No	5,697 (97.1)	60,286 (94.7)	Reference	—		
Yes	172 (2.9)	3,383 (5.3)	0.54 (0.44–0.66)	<0.001		
Disease site						
Pulmonary only	4,776 (81.3)	55,460 (87.1)	Reference	—		
Both pulmonary and extrapulmonary	1,096 (18.7)	8,209 (12.9)	1.55 (1.42–1.70)	<0.001		
Provider type						
Health department	3,277 (55.8)	41,313 (64.9)	Reference	—	Reference	—
Non-health department †	1,668 (28.4)	12,766 (20.1)	1.65 (1.52–1.79)	<0.001	1.82 (1.64–2.01)	<0.001
Both	607 (10.3)	6,320 (9.9)	1.21 (1.08–1.36)	<0.001	1.09 (0.94–1.26)	0.138
Missing	317 (5.4)	3,270 (5.1)	1.22 (1.04–1.43)	0.001	1.41 (1.16–1.70)	<0.001
Chest radiograph						
Abnormal with no cavitation	4,548 (77.5)	40,644 (63.8)	0.94 (0.82–1.07)	0.226	1.02 (0.87–1.20)	0.701
Abnormal with cavitation	617 (10.5)	16,683 (26.2)	0.31 (0.26–0.37)	<0.001	0.73 (0.60–0.88)	<0.001
Normal	469 (8.0)	3,939 (6.2)	Reference	—	Reference	—
Not done	235 (4.0)	2,403 (3.8)	0.82 (0.66–1.02)	0.019	0.95 (0.74–1.21)	0.561
Non-sputum culture documentation						

	Bivariate analysis		Multivariable analysis	
	OR (99%CI)	P value	aOR (99%CI)	P value
Sputum culture not documented <i>n</i> (%)				
No result documented	1,592 (27.1)			
Result documented	4,277 (72.9)			
Tuberculin skin test documentation				
No result documented	3,189 (54.3)			
Result documented	2,680 (45.7)			
Interferon-gamma release assay documentation				
No result documented	3,148 (53.6)			
Result documented	2,721 (46.4)			
Nucleic-acid amplification test documentation				
No result documented	3,721 (63.4)			
Result documented	2,148 (36.6)			

* Any reported alcohol use, injection drug use or non-injection drug use in the 12 months prior to diagnostic evaluation for TB.

[†] Comprises nursing homes, assisted living facilities, all types of correctional facilities, Indian Health Services, inpatient hospital care, a private healthcare provider, or other care provider that is not a public health department.

OR = odds ratio; CI = confidence interval; aOR = adjusted OR; NH = non-Hispanic.

Type of non-sputum specimen cultured among pulmonary TB patients without documented sputum culture, 2011–2021 (*n* = 5,869).

Table 2.

Non-sputum culture type	Age group, years				Overall (<i>n</i> = 5,869) <i>n</i> (%)
	0–14 (<i>n</i> = 2,117) <i>n</i> (%)	15–64 (<i>n</i> = 2,200) <i>n</i> (%)	65 (<i>n</i> = 1,552) <i>n</i> (%)		
No non-sputum culture documented	972 (45.9)	445 (20.2)	175 (11.3)		1,592 (27.1)
Any non-sputum culture documented	1,145 (54.1)	1,755 (79.8)	1,377 (88.7)		4,277 (72.9)
Bronchial fluid	69 (6.0)	805 (45.9)	755 (54.8)		1,629 (38.1)
Gastric aspirate	850 (74.2)	15 (0.9)	4 (0.3)		869 (20.3)
Lung tissue	21 (1.8)	289 (16.4)	249 (18.1)		559 (13.1)
Pleural fluid	12 (1.1)	96 (5.4)	71 (5.2)		179 (4.2)
Lymph node	17 (1.5)	83 (4.7)	24 (1.7)		124 (2.9)
Cerebrospinal fluid	54 (4.7)	36 (2.1)	13 (0.9)		103 (2.4)
Other type of non-sputum culture	122 (10.7)	431 (24.6)	261 (19.0)		814 (19.0)