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## Robustness of NHANES Estimates of the U.S. Prevalence of a Positive Tuberculin Skin Test

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### Abstract

**Background:** A single 2-year National Health and Nutrition Examination Survey (NHANES) cycle is designed to provide accurate and stable estimates of conditions with prevalence of at least 10%. Recent NHANES-based estimates of a tuberculin skin test 10 mm in the noninstitutionalized U.S. civilian population are at most 6.3%.

**Methods:** NHANES included a tuberculin skin test in 1971–1972, 1999–2000, and 2011–2012. We examined the robustness of NHANES-based estimates of the U.S. population prevalence of a skin test 10 mm with a bias analysis that considered the influence of non-U.S. birth distributions and within-household skin test results, reclassified borderline-positive results, and adjusted for tuberculin skin test item nonresponse.

**Results:** The weighted non-U.S. birth distribution among NHANES participants was similar to that in the overall U.S. population; further adjustment was unnecessary. We found no evidence of bias due to sampling multiple participants per household. Prevalence estimates changed 0.3% with reclassification of borderline-positive tuberculin skin test results and 0.2%–0.3% with adjustment for item nonresponse.

**Conclusions:** For estimating the national prevalence of a tuberculin skin test 10 mm during these three survey cycles, a conventional NHANES analysis using the standard participant weights and masked design parameters that are provided in the public-use datasets appears robust.

### Keywords

latent tuberculosis infection; National Health and Nutrition Examination Survey; survey methodology; systematic bias; tuberculin; United States

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The authors report no conflicts of interest.

Replication:

The eAppendix for this article includes the SAS and SUDAAN code for executing this analysis, which is based on public-use data available from <https://www.cdc.gov/nchs/nhanes/>.

Supplemental digital content: 3 eTables, 1 eFigure, and eAppendix with replication code

## Introduction

Although it is fundamentally a general health and nutrition survey, the National Health and Nutrition Examination Survey (NHANES) can add infectious disease components, such as tuberculosis (TB), to a 2-year survey cycle. A tuberculin skin test was part of the 1971–1972, 1999–2000, and 2011–2012 NHANES cycles,<sup>1–5</sup> leading to estimates that between 3.1% and 6.3% of the noninstitutionalized U.S. civilian population were latently infected with *Mycobacterium tuberculosis* in 1999–2000 and 2011–2012.<sup>2–5</sup> Detecting and treating infection in high-risk populations is an increasingly important strategy to achieve the Institutes of Medicine’s call to eliminate TB from the United States.<sup>6</sup> Because there is no ongoing population-based surveillance for latent TB infection, NHANES provides the only nationwide prevalence estimates to monitor progress toward elimination. The U.S. Preventive Services Task Force, the Centers for Disease Control and Prevention, the American Thoracic Society, and the Infectious Diseases Society of America all cite NHANES data in their latent TB infection guidelines.<sup>7,8</sup> However, a single 2-year NHANES cycle is designed to provide accurate and stable estimates of conditions with 10% prevalence.<sup>9,10</sup>

NHANES participants are selected at established rates to ensure target sample sizes for analytic subdomains based on sex, age, and race/ethnicity. To enable more precise estimates within subpopulations, NHANES 1999–2000 oversampled persons of Mexican heritage (i.e., “Mexican-Americans”),<sup>9,11</sup> when approximately half the Mexican-Americans in the United States were non-U.S.-born.<sup>12–14</sup> In NHANES 2011–2012, the broader “Hispanic” category was used, when approximately 60% were non-U.S.-born.<sup>15</sup> NHANES 2011–2012 also oversampled persons of Asian heritage (i.e., “Asians”),<sup>16–19</sup> when approximately two-thirds of Asians in the United States were non-U.S.-born.<sup>15</sup> A person from an oversampled subpopulation typically represents fewer people in the overall population (i.e., has a lower sample weight). The sample weights provided in the NHANES public-use datasets account for the participant’s sex, age, and race/ethnicity, but do not account for birth outside the United States, which is an established risk factor for TB infection.<sup>2–11,16–19</sup>

Starting in 1999, NHANES aimed to maximize the number of sampled participants per household. A conventional NHANES analysis accounts for correlations of health outcomes within primary sampling units (i.e., typically single counties), but does not account for correlations within later sampling stages, such as households.<sup>17–19</sup> Because most NHANES analyses are thought to be done within subdomains, within-household clustering at the subdomain level is considered generally small.<sup>11,16</sup> However, this might not be the case for an infectious disease like TB, where same-household NHANES participants might have correlated tuberculin skin test results.

A third analytic challenge for the 2011–2012 cycle is the digit preference for tuberculin skin test results to be recorded as borderline-positive 8 or 9 mm readings, suggesting some degree of systematic under-measurement. Digit preference for positive 10 mm measurements is more typical.<sup>2–4,20,21</sup>

A fourth analytic challenge is item nonresponse. Across all three NHANES cycles, tuberculin skin test results were not recorded for approximately one in five examined participants within the age groups eligible for the test. Some previous analysts have addressed this challenge by excluding participants without tuberculin skin test results and then creating higher weights for participants with results.<sup>3–5</sup> That reweighting approach assumes that tuberculin skin test results are missing at random. To be missing at random, item nonresponse must not have been influenced by what the (unobserved) tuberculin skin test results would have been, conditional on measured covariates.<sup>22–26</sup>

Given these four plausible sources of bias, we sought to evaluate the extent to which NHANES-based estimates for the national prevalence of a positive tuberculin skin test<sup>1–5</sup> might change with an analysis that considers the influence of non-U.S. birth distributions and within-household test results, reclassifies borderline-positive test results, and adjusts for tuberculin skin test item nonresponse.

## METHODS

### Data sources and target populations

Each 2-year NHANES cycle is designed to be nationally representative of the noninstitutionalized U.S. civilian population. Most of the data used for this analysis are publicly available at <https://www.cdc.gov/nchs/nhanes/>. Examination dates and design parameters beyond the primary sampling unit (e.g., household) are restricted variables that are not released publicly. However, the National Center for Health Statistics, subject to proposal approval, can allow a researcher to access restricted variables through the Research Data Center (<https://www.cdc.gov/rdc/>).

NHANES examinations included a tuberculin skin test component in 1971–1972, 1999–2000, and 2011–2012, and an interferon-gamma release assay blood test for TB infection in 2011–2012. The age groups eligible for tests of TB infection changed in each cycle: participants aged 25–74 in 1971–1972, when NHANES represented 103 million adults, aged 1 year in 1999–2000 to represent 268 million, and aged 6 years in 2011–2012 to represent 282 million.<sup>1–5,11,16–19,27</sup>

### Outcome of interest and frequency of item nonresponse

We defined our outcome of interest as a tuberculin skin test measurement in the public-use NHANES dataset of 10 mm.<sup>1–5,7,20,27</sup> Tuberculin skin test results were missing for 397 (21%) of the 1,891 age-eligible examined participants in 1971–1972, for 1,466 (16%) of the 8,832 in 1999–2000, and for 1,693 (22%) of the 7,821 in 2011–2012.

### Statistical approach

NHANES public-use datasets include masked design variables and participant weights to account for the complex, multistage, probability sampling design when generating national estimates.<sup>9,17–19,27,28</sup> We used the PROC DESCRIPT procedure in SAS-callable SUDAAN (Research Triangle Institute, Research Triangle Park, NC) to estimate the population prevalence of a tuberculin skin test 10 mm. By default, SUDAAN uses Taylor linearization

methods to estimate standard errors.<sup>29–31</sup> We specified a with-replacement design and used SUDAAN's SUBPOPX option to subset to age-eligible participants with non-missing tuberculin skin test results.<sup>29–31</sup> First, we conducted a conventional NHANES analysis using only variables in the public-use datasets — that is, with the standard 2-year examination weights and the masked major stratum and primary sampling units as the only levels of nesting.<sup>9,17–19,27,28</sup> Then within the Research Data Center, we replicated the conventional analysis after replacing the public-use masked variables with the unmasked (true) major stratum and primary sampling unit variables. Next we sequentially added Census tract, block group, block, and household. Doing so allowed us to examine the effect of multilevel clustering on the estimated population prevalence of a tuberculin skin test  $\geq 10$  mm. Because we specified more than two levels of nesting, we used SUDAAN's /PSULEV = and /MISSUNIT options.<sup>30,31</sup>

### **Non-U.S. birth distributions**

We used the March 2000 Current Population Survey and March 2010 American Community Survey to compare the weighted U.S.- vs. non-U.S. birth distributions of Hispanic and Asian participants to their corresponding relative proportions in the general U.S. population.<sup>12–15</sup> If they differed, our plan was to create an additional post-stratification adjustment to the 2-year examination weights.

### **Households with multiple participants**

We also examined the influence of the preferential selection of households that had multiple eligible participants. Household types were partitioned into those with only U.S.-born, with only non-U.S.-born, or with both U.S.-born and non-U.S.-born participants aged  $\geq 6$  years with tuberculin skin test results. We determined within-household concurrence of skin test results and whether results differed between persons from households with  $\geq 2$  examined participants and persons who were their household's only examined participant.

### **Record-level reclassification of borderline-positive tuberculin skin test results**

We reclassified 40 NHANES 2011–2012 participants with positive interferon-gamma release assay blood test results and 8 mm or 9 mm tuberculin skin test results as having positive tuberculin skin tests. This record-level reclassification remained in place for all subsequent analyses.

### **Tuberculin skin test item nonresponse**

We observed that 124 (31%) of the 397 missing tuberculin skin test results during 1971–1972 occurred among participants examined during the final 2–3 days that NHANES examinations were scheduled in that county. Their skin test results presumably were not recorded because of logistical difficulties in scheduling the test reading after the examination center in that county had closed. However, our analysis within the Research Data Center demonstrated that being scheduled for a later examination date did not influence the likelihood of having a recorded tuberculin skin test result in 1999–2000 or 2011–2012. Excluding that possibility allowed us to focus on other potential predictors of tuberculin skin test item nonresponse.

Among the NHANES participants with tuberculin skin test item nonresponse in 1999–2000 and 2011–2012, we used responses to the question, “Have you ever had a severe reaction to a TB skin test?” (TBQ070), which was asked just before the tuberculin skin test was administered during the examination, to discriminate between the small number who did not have the test placed due to an affirmative response, the moderate number who had the test placed but did not return for it to be measured, and the large number of examined participants with tuberculin skin test item nonresponse who did not receive the test (Table 1).

Previous NHANES analyses had noted that tuberculin skin test item nonresponse was more common among younger participants and among non-U.S.-born persons.<sup>3,4</sup> To better understand the associations of age, race/ethnicity, and U.S. vs. non-U.S. birth with tuberculin skin test results, we divided participants into four age-based groupings, then into the three major race/ethnicity categories used in NHANES 1999–2000 and the four used in NHANES 2011–2012, and then by U.S. vs. non-U.S. birth, yielding a total of 24 distinct participant profiles in 1999–2000 (Table 2) and 32 in 2011–2012 (Table 3).

Our analysis of the subset of participants with complete results had shown that a personal TB history was associated with a positive tuberculin skin test and positive interferon-gamma release assay blood test during the NHANES examination (eTable 1). Therefore, to address tuberculin skin test item nonresponse within each participant profile, we invoked a missing-at-random assumption that was conditional on the participant’s self-reported TB history (i.e., whether or not the participant reported a previous positive test or previous treatment for either active or latent TB). We created 30 replicates of each NHANES dataset, replacing missing tuberculin skin test results with an imputed positive or negative result based on a Bernoulli trial, where the individual participant’s probability of a positive tuberculin skin test was the weighted proportion of a positive skin test among persons who were in the same participant profile and had self-reported a similar TB history. We used SUDAAN’s MI\_FILES statement so that the estimated variance would incorporate the additional uncertainty added by the imputations.<sup>24–26,29–33</sup>

## RESULTS

Both the conventional analysis using the masked variables from the NHANES 1999–2000 and 2011–2012 public-use datasets and the unmasked analysis with their true counterparts in the Research Data Center yielded the same estimated population prevalence of a tuberculin skin test result  $\geq 10$  mm. Incorporation of additional sample design parameters (i.e., Census tract, Census block group, Census block, and household) improved precision but did not change point estimates (eTable 2).

A weighted 46% of Mexican-American participants in NHANES 1999–2000 were non-U.S.-born. A weighted 53% of Hispanic and 74% of Asian participants in NHANES 2011–2012 were non-U.S.-born. These proportions were similar to that seen in the U.S. population at large.<sup>12–15</sup> Therefore, no further adjustments were made to the examination weights provided in the public-use datasets.

Similar proportions of NHANES 1999–2000 and 2011–2012 participants shared a household with other examined participants (eFigure). Within-household concordance of tuberculin skin test results was 94% in households with only U.S.-born participants and 65% in households with any non-U.S.-born participants. The weighted prevalence of a positive skin test between households represented by a single or by multiple participants did not differ, except for higher prevalence among U.S.-born participants who lived in households with non-U.S.-born participants. In these shared households, a weighted 7.8% (95% confidence interval = 4.9%–12.2%) of U.S.-born persons in 1999–2000 and 6.0% (95% confidence interval = 3.6%–9.8%) in 2011–2012 had positive tuberculin skin test results (eTable 3). However, because these persons with positive results represented approximately 1 million (<1%) of the total U.S.-born population in each NHANES cycle, their influence on national prevalence estimates was negligible.

The 40 reclassified borderline-positive tuberculin skin test results in 2011–2012 occurred within 16 of the 32 participant profiles (Table 3). The pooled effect of these record-level reclassifications on the estimate of the overall noninstitutionalized U.S. civilian population being tuberculin skin test-positive was a modest 0.3% change from the conventional NHANES analysis estimate of 4.3% (95% confidence interval = 3.0%–5.9%) to 4.6% (95% confidence interval = 3.3%–6.3%) (Figure).

We observed differences between NHANES participants with complete tuberculin skin test results and those with skin test item nonresponse. A self-reported previous positive test for TB infection or previous treatment for either active or latent TB was associated with tuberculin skin test item nonresponse (1971–1972 not shown, 1999–2000 and 2011–2012 shown in Table 1). Among persons with complete results, this history was associated with a positive test for *Mycobacterium tuberculosis* infection (eTable 1). Persons aged 60 years were oversampled in NHANES 1999–2000 and had some of the most complete tuberculin skin test results in that cycle. Mexican-Americans were also oversampled and had a level of participation in the TB component of the examination like that of non-Hispanic persons (Table 1). In contrast, Asians, who were oversampled in NHANES 2011–2012, had some of the lowest participation in the TB component of the examination (Table 1), with missing tuberculin skin test results most pronounced among Asians aged 60 years (Table 3).

Table 2 and Table 3 show how weighted prevalence estimates would change if missing tuberculin skin test results were replaced under the missing-at-random assumption (i.e., where the individual participant's probability of a positive skin test was the weighted proportion of a positive skin test among persons in the same profile who had self-reported a similar TB history). Within most participant profiles, the estimated population prevalence of a positive tuberculin skin test increased slightly. However, the new prevalence estimates were only markedly different among black non-Hispanic non-U.S.-born participants aged 40–59 years, and there were relatively few of them, so these estimates were unstable.

The pooled effects of all these adjustments are shown as the final set of estimates for 1999–2000 and 2011–2012 in the Figure. With these imputations for the missing tuberculin skin test results, the estimated point prevalence of a positive test in the population decreased by 0.2% for 1999–2000 and increased by 0.3% for 2011–2012. However, the 95% confidence

intervals (i.e., 3.3%–5.2% and 3.6%–6.6%, respectively) remained similar to estimates without any adjustment for tuberculin skin test item nonresponse. Confidence intervals also overlapped across both cycles.

## DISCUSSION

We evaluated whether past NHANES-based estimates for the national prevalence of a positive tuberculin skin test might change with an analysis that considered four plausible sources of bias. Conditional on our having accurately identified and adequately addressed the four most likely sources of uncertainty, this bias analysis reinforces our confidence in the validity of estimates based on a conventional analysis of the public-use NHANES datasets for 1971–1972, 1999–2000, and 2011–2012.<sup>1–5,9,10,33,34</sup> The estimated U.S. population prevalence of a positive tuberculin skin test was robust to a variety of different bias adjustments. Consistent with the intent when masked design parameters are created for the public-use datasets, none of the restricted variables that we accessed within the Research Data Center proved to have any substantial influence on results.<sup>9,17–19</sup> Incorporation of additional NHANES design parameters beyond the primary sampling unit simply improved precision, which is consistent with the NHANES design (i.e., based on sampling from strata that are “homogeneous within” and “heterogeneous between”).<sup>29, p. 32</sup>

Despite lower participation in the tuberculin skin test component of the medical examination by Asian adults in NHANES 2011–2012 (Table 1), their skin test results remained similar after our missing-at-random adjustment based on self-reported TB history (Table 3). Although the estimated population prevalence of a positive tuberculin skin test increased across most age groups and most race/ethnic subdomain groupings following adjustment for tuberculin skin test item nonresponse, the pooled effect on overall population prevalence estimates was negligible (Figure).

We could not examine all potential sources of systematic error with respect to TB in NHANES. A limitation of this analysis, for example, is that we do not know whether questions were systematically asked differently between the two most recent cycles, despite the use of nearly identical TB protocols. One finding that remains inexplicable is the different responses to the TBQ070 question, “Have you ever had a *severe* reaction to a tuberculosis skin test?” When asked of 7,613 respondents during the NHANES 1999–2000 examinations, just prior to the tuberculin skin test placement, the recorded response was always “no.” When in 2011–2012 the same question was asked of 6,437 respondents, 87 participants said “yes,” even though only 45 of those 87 had reported a previous positive tuberculin skin test during the NHANES interview some days beforehand (Table 1).

Following precedent, we defined our outcome of interest as a tuberculin skin test measurement in the public-use NHANES dataset of  $\geq 10$  mm.<sup>1–5,7,8</sup> As a proxy measure for latent TB infection, Comstock called this cutoff, put forward by the American Thoracic Society in 1971, an “arbitrary definition [that] has worked surprisingly well for most of us.”<sup>20, p. 467</sup> The tuberculin skin test is 1912 technology known to produce false-negative results with incorrect administration, immunosuppression, or timing (i.e., very early or very late in the course of infection), and false-positive results with bacille Calmette-Guérin

vaccination.<sup>7,20,35</sup> With no gold standard for diagnosing latent TB infection, measuring the concordance of tuberculin skin test results with exposure risk, active TB disease incidence, and, more recently, interferon-gamma release assay blood test results has been the only way to assess their validity.<sup>35,36</sup> We used IGRA results to inform our reclassification of borderline-positive tuberculin skin test results in the 2011–2012 dataset. Ideally, misclassification and other sources of potential error such as digit preference would be prevented in the study design, rather than addressed in the analysis phase.<sup>25,33</sup> The tuberculin skin test reader, for example, could use calipers that demarcate the skin test induration but do not reveal the measurement (i.e., blind the reader to the measurement in mm units) until after the caliper jaws have been locked.<sup>20</sup>

Epidemiologists often work with data collected by other entities that did not have their specific research topic in mind. Although none of the additional variables that we considered proved to be influential on NHANES-based prevalence estimates for TB infection, some aspects of our approach might have relevance for other health conditions. Any researcher working with publicly available survey data should carefully read all provided documentation,<sup>9,11,16–19,28,29</sup> not only to understand how participants were recruited and data were collected but also to consider, for example, whether a survey that often selects multiple persons from the same household might skew results for the health condition of interest. NHANES is primarily a general health and nutrition survey, and each individual participant represents thousands of other persons. A single 2-year cycle is designed to estimate conditions with 10% prevalence with a relative standard error of 30%.<sup>9,10</sup> Nevertheless, Curtin et al. have pointed out that NHANES collects so many detailed measures that a “rare event” is not uncommon.<sup>10</sup> Having TB components implemented for 4 consecutive years in future NHANES cycles would help achieve more stable prevalence estimates.<sup>9,10,17,18</sup>

Threatening to thwart the national goal to eliminate TB,<sup>6</sup> the estimated U.S. population prevalence of a positive tuberculin skin test remained essentially the same between 1999–2000 and 2011–2012 (Figure). Given concomitant U.S. population growth, stable prevalence means that a growing number of persons residing in the United States are infected with *Mycobacterium tuberculosis*. Being able to accurately measure the prevalence of latent TB infection is arguably more important now than ever.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position or views of the Research Data Center, the National Center for Health Statistics, or the Centers for Disease Control and Prevention.

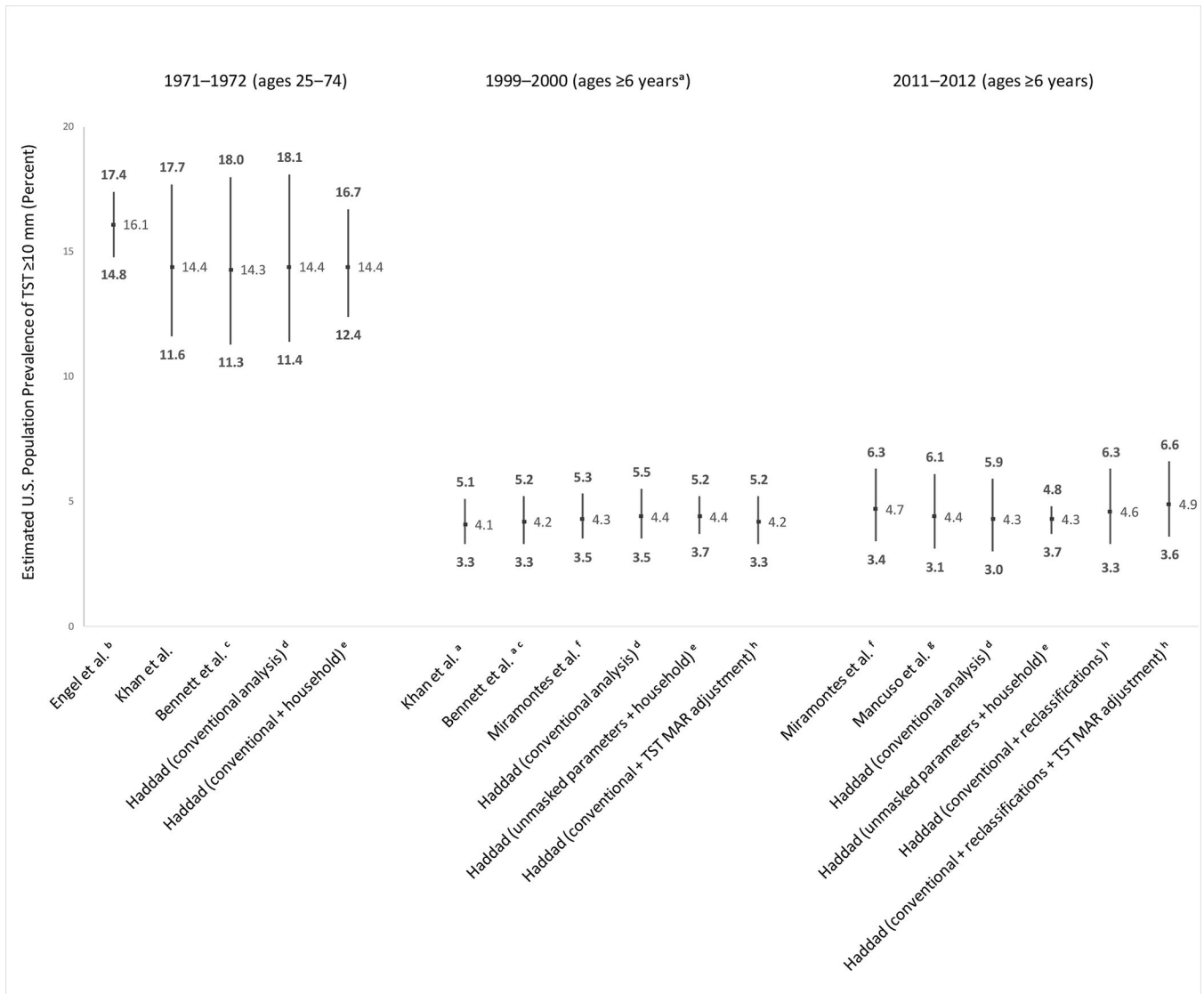


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**FIGURE.** Pooled 95% Confidence Intervals and Point Estimates for Prevalence of Tuberculin Skin Test (TST) 10 mm in Overall U.S. Noninstitutionalized, Civilian Population — Previous and These Analyses of National Health and Nutrition Examination Survey (NHANES), 1971–1972, 1999–2000, and 2011–2012

Abbreviations: NHANES, National Health and Nutrition Examination Survey; TB, tuberculosis; TST, tuberculin skin test; MAR, missing at random.

<sup>a</sup> The Khan et al.<sup>2</sup> and Bennett et al.<sup>3</sup> 1999–2000 estimates were for participants aged 1 year.

<sup>b</sup> The Engel et al.<sup>1</sup> 1971–1972 “tuberculin positive” estimates for participants aged 25–74 years apparently included examinees not given a TST because they reported a “history of a positive reaction, tuberculosis, or isoniazid prophylaxis.”

<sup>c</sup> Bennett et al.<sup>3</sup> addressed missing TST results in 1971–1972 and 1999–2000 by excluding participants without TST results and then creating higher weights for participants with

results by multiplying the NHANES-provided 2-year examination weight by the inverse of the probability of having a result. In 1971–1972; this inverse probability reweighting approach was based on the 73% of examined participants aged 25–34 and 80% of those aged 35–74 with TST results. In 1999–2000, it was 75% of U.S.-born and 66% of the non-U.S.-born examined participants aged 1–14 years, and 88% of the U.S.-born and 83% of the non-U.S.-born aged 15 years.

<sup>d</sup> These 1971–1972, 1999–2000, and 2011–2012 “conventional analysis” estimates are based entirely on NHANES data publicly available at <https://www.cdc.gov/nchs/nhanes/>, including the masked major strata and primary sampling units, and no changes to the standard NHANES-provided 2-year examination weights. Instead of addressing TST item nonresponse with a reweighting approach, this analysis used SUDAAN’s SUBPOPX option within PROC DESCRIPT to subset to age-eligible participants with complete TST results. For the SAS-callable SUDAAN code used, see eAppendix.

<sup>e</sup> This 1971–1972 “conventional + household” estimate was possible using the masked household ID that is available in the public-use NHANES dataset for 1971–1972. In addition to nesting participants by masked major strata and primary sampling unit, household was added as a third level of nesting to account for the possibility of within-household clustering of TST results. However, in 1971–1972, only 49 (3%) of 1,842 households with TST results had >1 participant with TST results, in contrast to over half of participants in the later cycles. The 1999–2000 and 2011–2012 “unmasked parameters + household” estimates required access to restricted variables not in the public-use datasets. These replicated the conventional analysis but used the unmasked major strata and primary sampling units while also accounting for the possibility of within-household clustering of TST results. For more detailed results of what happened when the other restricted variables of Census tract, block group, and block were added, as well as the results stratified between participants who shared households and participants who were the only household representative, see eTable 3.

<sup>f</sup> The Miramontes et al.<sup>4</sup> estimates for 1999–2000 used the same Bennett et al.<sup>3</sup> inverse probability reweighting approach for missing TST results, except that Miramontes et al. subsetted the 1999–2000 participants to those aged 6 years (i.e., excluding those aged 1–5 years), to enable better comparison to 2011–2012, when only participants aged 6 years were offered a TST. For 2011–2012, Miramontes et al. increased the NHANES-provided 2-year examination weights based on the 73% of the U.S.-born and 69% of the non-U.S.-born aged 6–14 years, and 83% of the U.S.-born and 74% of the non-U.S.-born aged 15 years, with TST results. The Miramontes et al. estimates also employed smoothing techniques to address the digit preferences for 10 mm measurements in 1999–2000 and 8 and 9 mm measurements in 2011–2012.

<sup>g</sup> Mancuso et al. 2011–2012<sup>5</sup> report that the standard NHANES-provided 2-year examination “weights were further adjusted for nonparticipation in TB testing so that it would represent the applicable study population” but do not provide further detail.

<sup>h</sup> These 1999–2000 and 2011–2012 “conventional + TST MAR adjustment” analyses employed the conventional analysis of masked public-use NHANES datasets with further adjustment for TST item nonresponse (i.e., summarizing the overall population effect of the stratified results presented in Table 2). The missing TST result was replaced with 30 imputed positive or negative TST results based on a Bernoulli trial, where the individual

participant's probability of a positive TST was the weighted proportion of a positive TST among persons in the same participant profile who had self-reported a similar TB history. Additionally for 2011–2012, the "+ reclassifications" analysis addressed the digit preference for 8 and 9 mm rather than 10 mm TST measurements in that cycle. Any participant whose interferon-gamma release assay blood test result was positive and whose TST result in the public-use NHANES dataset was 8 mm or 9 mm was reclassified as having a positive TST. For the SAS and SAS-callable SUDAAN code used, see the eAppendix.

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TABLE 1.

Unweighted Participation in Tuberculin Skin Test (TST) Component of the National Health and Nutrition Examination Survey (NHANES) Examination, by Response to Interview Questions — 1999–2000 and 2011–2012

	8,832 Examined Participants Aged 1 Year, 1999–2000				7,821 Examined Participants Aged 6 Years, 2011–2012									
	Complete TST Results		TST Item Nonresponse ( <i>n</i> = 1,446)		Complete TST Results		TST Item Nonresponse ( <i>n</i> = 1,693)							
	No.	Row %	No TST Placed But Reason Unknown ( <i>n</i> = 1,219)	TST Placed But No Result Recorded ( <i>n</i> = 227)	No.	Row %	No TST Placed But Reason Unknown ( <i>n</i> = 1,384)	No TST Placed Due to Past Severe Reaction <sup>a</sup> ( <i>n</i> = 87)	No.	Row %	No.	Row %		
Participant's Self-Reported Tuberculosis (TB) History and Other Response to NHANES Interview Questions	( <i>n</i> = 7,386)				( <i>n</i> = 6,128)									
No history to suggest previously diagnosed TB infection or active disease	6,898	84.1	1,088	13.3	212	2.6	5,720	78.9	1,288	17.8	34	0.5	208	2.9
Reported any previous TST	4,922	83.8	806	13.7	146	2.5	3,748	78.6	806	16.9	79	1.1	137	2.9
Reported previous positive TST	275	72.9	93	24.7	<i>b</i>	<i>b</i>	203	65.1	57	18.3	45	14.4	<i>b</i>	<i>b</i>
Self-reported history of active TB	23	67.6	10	29.4	<i>b</i>	<i>b</i>	32	76.2	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
No personal history of either positive TST or active TB but was in household with active TB	190	85.2	28	12.6	<i>b</i>	<i>b</i>	144	80.4	22	12.3	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
Self-reported race/ethnicity/birthplace														
White non-Hispanic U.S.-born	2,366	85.1	380	13.7	33	1.2	1,960	81.3	374	15.5	16	0.7	62	2.6
Black non-Hispanic U.S.-born	1,600	84.8	244	12.9	42	2.2	1,567	79.9	324	16.5	16	0.8	53	2.7
Hispanic U.S.-born	1,773	81.7	197	13.7	100	4.6	748	81.5	143	15.6	<i>b</i>	<i>b</i>	26	2.8
Hispanic non-U.S.-born	1,134	83.8	176	13.0	43	3.2	720	81.0	134	15.1	11	1.2	24	2.7

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	Asian race not a category during 1999–2000 NHANES	221	67.4	94	28.7	<i>b</i>	11	3.4			
Asian U.S.-born											
Asian non-U.S.-born	Asian race not a category during 1999–2000 NHANES	496	67.9	181	24.8	24	3.3	4.1			
Other U.S.-born	200	81.0	41	16.6	<i>b</i>	188	77.4	44	18.1	<i>b</i>	<i>b</i>
Other non-U.S.-born	313	78.8	81	20.4	<i>b</i>	228	68.1	90	26.9	<i>b</i>	<i>b</i>
Age group											
<1 year	TST offered to only participants aged 1 year in 1999–2000										
1–5 years	707	69.8	291	28.7	15	1.5	TST offered to only participants aged 6 years in 2011–2012				
6–11 years	853	80.4	191	18.0	17	1.6	TST offered to only participants aged 6 years in 2011–2012				
12–15 years	1,025	84.8	142	11.7	42	3.5					
16–19 years	958	86.7	93	8.4	54	4.9					
20–29 years	679	85.1	88	11.0	31	3.9					
30–39 years	664	86.1	94	12.2	13	1.7					
40–49 years	622	86.5	84	11.7	13	1.8					
50–59 years	480	87.3	61	11.1	<i>b</i>						
60–69 years	649	85.6	89	11.7	20	2.6					
70–79 years	459	87.3	56	10.6	11	2.1					
80 years	290	90.1	30	9.3	<i>b</i>						

Abbreviations: NHANES, National Health and Nutrition Examination Survey; TB, tuberculosis; TST, tuberculin skin test.

<sup>a</sup> According to the survey protocol, which did not change between 1999–2000 and 2011–2012, affirmative responses to any of the TB-related questions during the NHANES interview were not exclusion criteria for being offered a TST as part of the NHANES examination. However, an affirmative response to the question, “Have you ever had a severe reaction to a TB skin test?” (TBQ070), which was asked just before the TST was placed during the NHANES medical examination, was a contraindication to offering the TST. In 1999–2000, the same question was asked just before the TST was placed, but no participant was recorded as answering it affirmatively.

<sup>b</sup> Some cell contents suppressed due to small numbers.

Twenty-four Stratified Participant Profiles Created for this National Health and Nutrition Examination Survey (NHANES) 1999–2000 Analysis, Showing Weighted Tuberculin Skin Test (TST) Results, Including Adjustments for TST Item Nonresponse

TABLE 2.

	Black non-Hispanic participants aged 6–19 yrs		Mexican-American participants <sup>a</sup> aged 6–19 yrs		White/other participants <sup>a</sup> aged 6–19 yrs	
Unweighted No participants	934 U.S.-born	40 non-U.S.-born	1,072 U.S.-born	362 non-U.S.-born	869 U.S.-born	96 non-U.S.-born
Average participant weight <sup>b</sup>	9,000	8,000	4,000	3,000	44,000	37,000
Percent with TST result <sup>c</sup>	85.1	90.5	82.2	86.1	79.8	78.0
Unadjusted positive TST percent <sup>d</sup>	0.6	11.5 <sup>a</sup>	1.6	11.8	0.2	6.3
Adjusted positive TST percent <sup>e</sup>	0.6	11.5 <sup>a</sup>	1.7	11.8	0.2	6.1
	Black non-Hispanic participants aged 20–39 yrs		Mexican-American participants <sup>a</sup> aged 20–39 yrs		White/other participants <sup>a</sup> aged 20–39 yrs	
Unweighted No participants	262 U.S.-born	42 non-U.S.-born	161 U.S.-born	277 non-U.S.-born	674 U.S.-born	153 non-U.S.-born
Average participant weight <sup>b</sup>	35,000	33,000	18,000	16,000	83,000	69,000
Percent with TST result <sup>c</sup>	86.4	90.4	86.3	84.4	89.1	81.1
Unadjusted positive TST percent <sup>d</sup>	5.1	18.9 <sup>a</sup>	4.4	17.3	0.3	19.7
Adjusted positive TST percent <sup>e</sup>	5.5	18.7 <sup>a</sup>	4.4	17.6	0.3	19.6
	Black non-Hispanic participants aged 40–59 yrs		Mexican-American participants <sup>a</sup> aged 40–59 yrs		White/other participants <sup>a</sup> aged 40–59 yrs	
Unweighted No participants	227 U.S.-born	49 non-U.S.-born	146 U.S.-born	211 non-U.S.-born	526 U.S.-born	109 non-U.S.-born
Average participant weight <sup>b</sup>	26,000	23,000	11,000	10,000	90,000	69,000
Percent with TST result <sup>c</sup>	85.0	73.0	86.3	87.8	90.0	84.9
Unadjusted positive TST percent <sup>d</sup>	10.7	22.9 <sup>a</sup>	2.0	27.0	1.6	25.3
Adjusted positive TST percent <sup>e</sup>	11.6	30.8 <sup>a</sup>	1.9	27.9	1.9	25.2
	Black non-Hispanic participants aged 60 yrs <sup>a</sup>		Mexican-American participants <sup>a</sup> aged 60 yrs <sup>a</sup>		White/other participants <sup>a</sup> aged 60 yrs <sup>a</sup>	
Unweighted No participants	257 U.S.-born	24 non-U.S.-born	195 U.S.-born	209 non-U.S.-born	774 U.S.-born	144 non-U.S.-born



Average participant weight <sup>b</sup>	12,000	11,000	3,000	3,000	42,000	34,000
Percent with TST result <sup>c</sup>	85.9	72.0	87.1	86.1	90.5	76.8
Unadjusted positive TST percent <sup>d</sup>	16.6	25.1 <sup>a</sup>	13.3	21.9	3.4	10.9
Adjusted positive TST percent <sup>e</sup>	17.0	28.0 <sup>a</sup>	13.9	22.1	3.6	11.5

Abbreviations: NHANES, National Health and Nutrition Examination Survey; TB, tuberculosis; TST, tuberculin skin test.

<sup>a</sup>To enable more precise prevalence estimates within subpopulations, elderly persons and persons either born in Mexico or of Mexican heritage (i.e., “Mexican-Americans”) were deliberately oversampled in NHANES 1999–2000; oversampled subpopulations have lower average sample weights. The white/other person category in 1999–2000 included Hispanic persons not of Mexican heritage (i.e., 287 U.S.-born and 301 non-U.S.-born). In addition, the 1999–2000 participant profiles exclude 6 examined participants aged 6 years whose birthplace was not recorded. Prevalence estimates for non-U.S.-born black non-Hispanic persons are imprecise owing to the small number of NHANES 1999–2000 participants in this subpopulation.

<sup>b</sup>Average 2-year examination sample weight per participant (i.e., how many noninstitutionalized U.S. civilians in 1999–2000 represented by that participant), rounded to the thousands for this table. NHANES selection probabilities were not directly influenced by birthplace, but non-U.S.-born persons could, for example, be more likely to reside in densely populated counties having a higher probability of selection during the first NHANES sampling stage, which would contribute downstream to a lower sample weight.

<sup>c</sup>Weighted percent of examined NHANES participants in that participant profile with complete TST results, using the 2-year examination sample weights provided in the NHANES public-use datasets.

<sup>d</sup>Weighted percent of examined NHANES participants with complete TST results who had a positive TST, without any adjustment for TST item nonresponse.

<sup>e</sup>Weighted percent of examined NHANES participants with complete TST results who had a positive TST, after adjustment for TST item nonresponse based on self-reported TB history and the missing-at-random assumption. For the missing-at-random adjustment, the individual participant’s probability of a positive TST was the weighted proportion of a positive TST among persons in the same participant profile who had self-reported a similar TB history. Self-reported personal TB history was defined as a previous positive TST or any previous treatment for either active or latent TB.

**TABLE 3.**

Thirty-two Stratified Participant Profiles Created for this National Health and Nutrition Examination Survey (NHANES) 2011–2012 Analysis, Showing Weighted Tuberculin Skin Test (TST) Results, Including Effects of Reclassification of Borderline-Positive TST Results and Adjustments for TST Item Nonresponse

	Black non-Hispanic participants aged 6–19 yrs		Hispanic participants aged 6–19 yrs		Asian participants <sup>a</sup> aged 6–19 yrs		White/other participants aged 6–19 yrs		
Unweighted No participants	716 U.S.-born	26 non-U.S.-born	12,000	595 U.S.-born	156 non-U.S.-born	212 U.S.-born	93 non-U.S.-born	683 U.S.-born	21 non-U.S.-born
Average participant weight <sup>b</sup>	12,000			17,000	19,000	9,000	9,000	48,000	44,000
Percent with TST result <sup>c</sup>	79.1	48.9	81.1	81.1	79.5	64.3	72.7	71.3	76.9
Unadjusted positive TST percent <sup>d</sup>	1.1	47.1 <sup>a</sup>	0.5	0.5	7.4	1.4	11.5	0.0	4.6 <sup>a</sup>
Positive percent when reclassify <sup>e</sup>	not applicable	not applicable	0.6	not applicable	not applicable	not applicable	not applicable	not applicable	not applicable
Adjusted positive TST percent <sup>f</sup>	1.1	49.0 <sup>a</sup>	0.6	0.6	7.2	1.4	11.7	0.0	4.6 <sup>a</sup>

	Black non-Hispanic participants aged 20–39 yrs		Hispanic participants aged 20–39 yrs		Asian participants <sup>a</sup> aged 20–39 yrs		White/other participants aged 20–39 yrs		
Unweighted No participants	397 U.S.-born	48 non-U.S.-born	22,000	155 U.S.-born	239 non-U.S.-born	82 U.S.-born 2	231 non-U.S.-born	671 U.S.-born	55 non-U.S.-born
Average participant weight <sup>b</sup>	24,000			45,000	40,000	16,000	17,000	68,000	67,000
Percent with TST result <sup>c</sup>	82.8	62.1	84.4	84.4	83.1	75.5	69.9	81.2	63.9
Unadjusted positive TST percent <sup>d</sup>	2.8	22.1	4.8	4.8	15.5	3.8	26.3	0.8	4.8 <sup>a</sup>
Positive percent when reclassify <sup>e</sup>	3.0	24.2	not applicable	not applicable	16.4	not applicable	28.4	not applicable	not applicable
Adjusted positive TST percent <sup>f</sup>	3.1	28.3	5.1	5.1	16.2	3.7	28.0	0.9	5.9 <sup>a</sup>

	Black non-Hispanic participants aged 40–59 yrs		Hispanic participants aged 40–59 yrs		Asian participants <sup>a</sup> aged 40–59 yrs		White/other participants aged 40–59 yrs		
Unweighted No participants	430 U.S.-born	68 non-U.S.-born	83 U.S.-born	83 U.S.-born	268 non-U.S.-born	15 U.S.-born	254 non-U.S.-born	598 U.S.-born	35 non-U.S.-born

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Average participant weight <sup>b</sup>	21,000	19,000	35,000	30,000	18,000	16,000	96,000	60,000
Percent with TST result <sup>c</sup>	80.6	71.7	92.0	83.0	78.6	67.3	87.3	81.0
Unadjusted positive TST percent <sup>d</sup>	6.7	23.8	3.6	25.7	0.0 <sup>a</sup>	34.1	0.6	13.0 <sup>a</sup>
Positive percent when reclassified <sup>e</sup>	6.9	25.3	not applicable	28.4	not applicable	37.4	0.6	not applicable
Adjusted positive TST percent <sup>f</sup>	7.2	30.1	3.6	28.5	0.0 <sup>a</sup>	37.8	0.7	13.0 <sup>a</sup>
	Black non-Hispanic participants aged 60 yrs							
	Black non-Hispanic participants aged 60 yrs		Hispanic participants aged 60 yrs		Asian participants <sup>a</sup> aged 60 yrs		White/other participants aged 60 yrs	
Unweighted No participants	417 U.S.-born	45 non-U.S.-born	85 U.S.-born	226 non-U.S.-born	19 U.S.-born	153 non-U.S.-born	703 U.S.-born	37 non-U.S.-born
Average participant weight <sup>b</sup>	11,000	10,000	15,000	14,000	14,000	13,000	64,000	37,000
Percent with TST result <sup>c</sup>	80.5	62.5	78.0	80.0	72.5	61.1	83.2	77.7
Unadjusted positive TST percent <sup>d</sup>	12.1	29.8	11.0	25.9	0.0 <sup>a</sup>	26.0	1.2	13.9 <sup>a</sup>
Positive percent when reclassified <sup>e</sup>	13.0	34.5	12.1	30.1	not applicable	30.0	1.3	not applicable
Adjusted positive TST percent <sup>f</sup>	13.6	35.3	12.8	30.9	0.0 <sup>a</sup>	30.1	1.4	13.1 <sup>a</sup>

Abbreviations: NHANES, National Health and Nutrition Examination Survey; TB, tuberculosis; TST, tuberculin skin test.

<sup>a</sup>To enable more precise prevalence estimates within subpopulations, persons of Asian heritage were deliberately oversampled in NHANES 2011–2012; oversampled subpopulations have lower average sample weights. In addition, the 2011–2012 participant profiles exclude 6 years whose birthplace was not recorded. Prevalence estimates for non-U.S.-born black non-Hispanic persons aged 6–19, U.S.-born Asian persons aged 40, and non-U.S.-born white/other persons of all ages are imprecise owing to the small numbers of NHANES 2011–2012 participants in these subpopulations.

<sup>b</sup>Average 2-year examination sample weight per participant (i.e., how many noninstitutionalized U.S. civilians in 2011–2012 represented by that participant), rounded to the thousands for this table. NHANES selection probabilities were not directly influenced by birthplace, but non-U.S.-born persons could, for example, be more likely to reside in densely populated counties having a higher probability of selection during the first NHANES sampling stage, which would contribute downstream to a lower sample weight.

<sup>c</sup>Weighted percent of examined NHANES participants in that participant profile with complete TST results, using the 2-year examination sample weights provided in the NHANES public-use datasets.

<sup>d</sup>Weighted percent of examined NHANES participants with complete TST results who had a positive TST, without any reclassification or adjustment for TST item nonresponse.

<sup>e</sup>The 2011–2012 NHANES cycle was marked by a digit preference for TST measurements being recorded as borderline-positive 8 and 9 mm readings.<sup>4</sup> We used interferon-gamma release assay (IGRA) blood test results to address this potential misclassification. Any participant whose IGRA result was positive and whose TST result in the public-use NHANES dataset was 8 mm or 9 mm was reclassified as having a positive TST. Eight of these 40 reclassified participants also had some element of self-reported TB history. This record-level reclassification remained in place for all subsequent analyses.

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Weighted percent of examined NHANES participants with complete TST results who had a positive TST, after borderline-positive TST reclassification and adjustment for TST item nonresponse based on self-reported TB history and the missing-at-random assumption. For the missing-at-random assumption, the individual participant's probability of a positive TST was the weighted proportion of a positive TST among persons in the same participant profile who had self-reported a similar TB history. Self-reported personal TB history was defined as a previous positive TST or interferon-gamma release assay blood test, or any previous treatment for either active or latent TB.