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## Influence of County Sampling on Past Estimates of Latent Tuberculosis Infection Prevalence

To the Editor:

The National Health and Nutrition Examination Survey (NHANES) has tested for *Mycobacterium tuberculosis* infection three times: in 1971–1972, 1999–2000, and 2011–2012. Based on tuberculin skin test results, the estimated national prevalence of latent tuberculosis infection (LTBI) among adults was 11–18% in 1971–1972 but has remained less than or equal to 6% in subsequent NHANES cycles (1–4). A single 2-year NHANES cycle is designed to produce accurate and stable estimates for

conditions with at least 10% prevalence in the noninstitutionalized civilian U.S. population (5–7), suggesting that NHANES might no longer be as nationally representative for LTBI as it is for more common health conditions. Approximately 30 counties were selected for each 2-year cycle (5). We wished to examine whether persons in selected counties might have been systematically more or less likely to have a positive tuberculin skin test result than their counterparts in the approximately 3,100 counties that were not selected for NHANES participation.

### Methods

We created a non-NHANES dataset with demographic profiles and tuberculosis data for all 3,143 U.S. county equivalents (Table 1). The U.S. Census Bureau and Department of Agriculture websites provided each county's population size and racial/ethnic composition, rural versus urban classification, and poverty prevalence for 1970 through 2013. The National Tuberculosis Surveillance System provided annual tuberculosis disease incidence, with the U.S. Census Bureau's Current Population Survey providing county population denominators.

We also used genotyping results to derive an estimate of LTBI prevalence for each county. Briefly, this simple back-calculation method assumed that tuberculosis cases not attributed to recent transmission (i.e., based on genotyping results) instead arose from preexisting LTBI. Then a 0.1% annual risk of reactivation was used to derive an estimated number of county residents with untreated longstanding LTBI (8). This county-level LTBI estimation method has not been

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**Author Contributions:** M.B.H. conceptualized the analysis, and all of the authors contributed to its design. M.B.H. and K.M.R. created the non-National Health and Nutrition Examination Survey county-level dataset. M.B.H. executed the analysis and prepared the first draft of the article within the National Center for Health Statistics Research Data Center. All of the authors provided critical revisions and approved the final version of the manuscript.

**Table 1.** Demographic profiles and characteristics pertinent to tuberculosis, by county or county equivalent (*N* = 3,143)

	Counties ( <i>n</i> [%])		
	1971–1972	1999–2000	2011–2012
County size			
≤10,000 population at time of NHANES cycle	876 (28)	697 (22)	698 (22)
10,001–24,999	1,016 (32)	886 (28)	845 (27)
25,000–99,999	902 (29)	1,036 (33)	1,022 (33)
≥100,000	349 (11)	524 (17)	578 (18)
Non-U.S.-born population*			
<2% of county's total population	—*	1,702 (54)	1,683 (54)
2.0–4.9% of county's total population		832 (26)	788 (25)
5.0–9.9% of county's total population		376 (12)	410 (13)
≥10% of county's total population		233 (7)	262 (8)
Metropolitan/urban <sup>†</sup>	2,495 (79) <sup>†</sup>	2,053 (65)	1,976 (63)
Nonmetropolitan/rural <sup>†</sup>	648 (21) <sup>†</sup>	1,090 (35)	1,167 (37)
Poverty level			
<10% of population in poverty	322 (10) <sup>‡</sup>	851 (27)	310 (9)
10–15.5% in poverty	1,407 (45) <sup>‡</sup>	1,362 (43)	1,092 (35)
15.6–19.9% in poverty	518 (16) <sup>‡</sup>	558 (17)	825 (26)
≥20% in poverty	896 (29) <sup>‡</sup>	372 (12)	916 (29)
Historical tuberculosis disease incidence (1963–1972) based on state's total population <sup>‡</sup>			
Low (in state averaging <15 annual cases per 100,000)	631 (20)	—	—
Medium (15–20 cases per 100,000)	488 (16)	—	—
High (≥20 cases per 100,000)	2,024 (64)	—	—
Recent tuberculosis disease incidence (1996–2003)			
Among county's U.S.-born population			
None (county with 0 cases among U.S.-born)	—	622 (20)	—
Low/medium (averaging <10 annual cases per 100,000)	—	2,339 (74)	—
High (county with ≥10 annual cases per 100,000)	—	182 (6)	—
Among county's non-U.S.-born population*	—	—	—
None (county with 0 cases among non-U.S.-born)	—	1,641 (52)	—
Low/medium (averaging <10 annual cases per 100,000)	—	173 (6)	—
High (county with ≥10 annual cases per 100,000)	—	1,329 (42)	—
Modern tuberculosis disease incidence (2008–2015)			
Among county's U.S.-born population			
None (county with 0 cases among U.S.-born)	—	—	1,041 (33)
Low/medium (averaging <10 annual cases per 100,000)	—	—	2,076 (66)
High (county with ≥10 annual cases per 100,000)	—	—	26 (1)
Among county's non-U.S.-born population*	—	—	—
None (county with 0 cases among non-U.S.-born)	—	—	1,607 (51)
Low/medium (averaging <10 annual cases per 100,000)	—	—	275 (9)
High (county with ≥10 annual cases per 100,000)	—	—	1,261 (40)

*Definition of abbreviation:* NHANES = National Health and Nutrition Examination Survey.

Included as county equivalents are the Alaska boroughs, the District of Columbia, Louisiana parishes, and Virginia independent cities.

\*When the county's non-U.S.-born proportion was provided by the U.S. Census Bureau's Current Population Survey, that proportion was applied to the total county population size to derive a non-U.S.-born count. In 2000, the Current Population Survey provided an estimate of the proportion of the county's population that was born outside the United States; in later years, that proportion is only consistently available at the state level. In 2010, it was provided for 801 counties only; for the other 2,342 counties, the non-U.S.-born population size was imputed on the basis of the county's non-U.S.-born proportion in 2000 and the state's total non-U.S.-born population in 2010.

<sup>†</sup>Rural-Urban Continuum Codes from the U.S. Department of Agriculture for 1974, 2003, and 2013 were dichotomized into these two categories (i.e., codes 4–9 considered rural and codes 0–3 considered metropolitan). Note that owing to changes to the criteria that were implemented after the 2000 census, the 1974 Rural-Urban Continuum Codes are not directly comparable with those in 2003 and 2013.

<sup>‡</sup>Measures of poverty in 1970 and tuberculosis disease incidence in 1963–1972 only available at the state level; later measures from the Current Population Survey and National Tuberculosis Surveillance System are at the county level.

validated; the only potential comparison in the literature is based on 1958–1965 data (9). However, median estimated LTBI prevalence by county among the U.S.-born population was 0.7% (lower and upper quartiles, 0.4%, 1.3%), and among the non-U.S.-born population it was 13.1% (lower and upper quartiles, 8.8%, 18.5%), both of which were similar to previous national NHANES-based estimates (1, 3, 4).

Because of disclosure risk, county of residence is not included in the NHANES public-use datasets and cannot be released (10). Following Research Data Center procedures ([www.cdc.gov/rdc/](http://www.cdc.gov/rdc/)), the National Center for Health Statistics merged masked NHANES 1971–1972, 1999–2000, and 2011–2012 data with our non-NHANES county dataset and allowed us to conduct this geographic analysis without access to county identifiers.

## Results

The demographics of the counties selected for NHANES participation in 1971–1972, 1999–2000, and 2011–2012 were similar across time, except that the counties selected for NHANES 2011–2012 had higher proportions of residents living in poverty, consistent with the recent national trend (Table 1). We compared the selected counties with nonselected counties within strata of counties of similar population size, racial/ethnic composition, rural versus urban classification, and poverty prevalence. Within those strata, mean tuberculosis disease incidence and estimated LTBI prevalence were similar ( $P > 0.05$  for each test of equivalence) when we compared the selected counties with the nonselected counties in NHANES 1971–1972, 1999–2000, and 2011–2012. In 90% of the counties selected for NHANES 2011–2012, the unweighted prevalence of a tuberculin skin test result of at least 10 mm of induration was within 1% of the genotyping-derived LTBI prevalence estimate for that county (8).

## Discussion

Because of strict confidentiality protections that include the geographic locations of NHANES participants, the results of this masked analysis cannot be shown in more detail (10). However, our findings reinforce confidence in national LTBI prevalence estimates based on past NHANES cycles (1–4). We found no evidence that the selected counties had different tuberculosis disease incidence or different LTBI prevalence from the counties not selected for NHANES participation in 1971–1972, 1999–2000, and 2011–2012.

Despite these reassuring findings, both the low prevalence and the geographic heterogeneity of this condition in the United States suggest that incorporating tuberculosis components (e.g., interferon- $\gamma$  release assays) into future NHANES cycles for more than two consecutive years would help achieve more stable population estimates (4–7). Our findings also imply that genotyping-derived estimates of LTBI prevalence that do not rely on NHANES data could continue to prove useful in the future (8).

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