Epidemiology of tuberculosis among children and adolescents in the USA, 2007–17: an analysis of national surveillance data

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Summary

Background Understanding tuberculosis epidemiology among children and adolescents informs treatment and prevention efforts, and efforts to eliminate disparities in tuberculosis incidence and mortality. We sought to describe the epidemiology of children and adolescents with tuberculosis disease in the USA, including tuberculosis incidence rates by parental country of birth and for US territories and freely associated states, which have not been previously described.

Methods We analysed data for children aged younger than 15 years and adolescents aged 15–17 years with tuberculosis disease reported to the National Tuberculosis Surveillance System during 2007–17, and calculated tuberculosis incidence rates using population estimates from the US Census Bureau.

Findings During 2010–17, 6072 tuberculosis cases occurred among children and adolescents; of these, 5175 (85%) of 6072 occurred in the 50 US states or the District of Columbia and 897 (15%) of 6072 in US-affiliated islands. In US states, 3520 (68%) of 5175 cases occurred among US-born people overall, including 2977 (76%) of 3896 children and 543 (42%) of 1279 adolescents. The incidence rate among children and adolescents was 1·0 per 100 000 person-years during 2007–17 and declined 47·8% (95% CI −51·4 to −44·1) during this period. We observed disproportionately high tuberculosis rates among children and adolescents of all non-white racial or ethnic groups, people living in US-affiliated islands, and children born in or with parents from tuberculosis-endemic countries.

Interpretation Overall, tuberculosis incidence among children and adolescents in the USA is low and steadily declining, but additional efforts are needed to eliminate disparities in incidence and mortality.

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Introduction

Globally, approximately 1 million cases of tuberculosis disease and 233 000 tuberculosis-related deaths occurred among children aged younger than 15 years during 2018.[1] Tuberculosis in children and adolescents is clinically and epidemiologically heterogeneous, making care and prevention challenging. In children, tuberculosis is often difficult to diagnose because of non-specific symptoms and limited sensitivity and specificity of laboratory tests for both latent tuberculosis infection and tuberculosis disease. Children aged younger than 5 years are also more likely to progress to tuberculosis disease after infection, and have the highest rates of severe, disseminated forms of tuberculosis such as meningitis, compared with older age groups.[2–7] Adolescents aged 15–17 years are more likely to develop infectious forms of pulmonary tuberculosis than younger children.[3,8] Understanding heterogeneity in tuberculosis burden and clinical presentation in children and adolescents is crucial to inform tuberculosis care and prevention efforts.

Although tuberculosis rates in the USA are the lowest ever recorded, it continues to affect many communities unequally, especially communities of colour, Indigenous peoples, people born outside the USA, and people who are experiencing homelessness.[9–13] In children and adolescents, current practice guidelines recommend tuberculosis testing for people who are in contact with people with tuberculosis and people who were born or travelled outside of the USA.[14] Although rates are ten to 20 times higher among children and adolescents born outside of the USA than among those born in the USA, more than two-thirds of children and adolescents with tuberculosis are US born, and therefore it is important to identify determinants other than origin of birth in these groups.[15,16]

Previous studies[16,17] suggest that US-born children with non-US-born parents might be at increased risk of tuberculosis. Approximately two-thirds of US-born children with tuberculosis reported during 2009–10 had at least one non-US-born parent.[15,16] Additionally, several large tuberculosis clusters with a high proportion of children have been reported in the freely associated states of the Marshall Islands and the Federated States of Micronesia, and among Marshallese people living in the USA.[18,19] However, rates of tuberculosis among US-born children by parental country of birth and among children and adolescents in US territories and freely associated states have not been systematically reported. Additionally,

Research in context

Evidence before this study

Although tuberculosis rates in the USA are the lowest ever recorded, tuberculosis continues to affect many communities unequally, especially communities of colour, Indigenous peoples, those born outside the USA, and people experiencing homelessness. Although we did not do a formal systematic review, we reviewed national surveillance reports and journal articles published between Jan 1, 1994, and Dec 31, 2014, for those that used data from the National Tuberculosis Surveillance System and reported national estimates of tuberculosis burden among children or adolescents in the USA. Among children and adolescents, previous national estimates suggest that although tuberculosis incidence rates among people born outside of the USA are ten to 20 times higher than those who are US born, more than two-thirds of children and adolescents with tuberculosis are US born. Therefore, it is important to identify and address determinants other than origin of birth in these groups. Additionally, national rates of tuberculosis among US-born children stratified by parental country of birth and rates among children and adolescents in the US territories and freely associated states have not been systematically reported. Finally, national estimates of tuberculosis disease counts and incidence rates among children and adolescents were last reported in 2010 and 2007, respectively.

Added value of this study

Using data from the National Tuberculosis Surveillance System and US Census Bureau, this study reinforces understanding of the epidemiology and clinical characteristics of tuberculosis disease occurring in children and adolescents in the USA. We report updated national estimates of tuberculosis burden and trends among children and adolescents including incidence rates by country of birth for both children and their parents, and for US territories and freely associated states, which have not been previously described. Overall tuberculosis incidence rate among children and adolescents was low (1·0 case per 100 000 person-years) and decreased substantially (–48%) during 2007–17; however, consistent with previous reports, substantial heterogeneity exists in burden and trends across geographies and sociodemographic groups. We observed disproportionately high rates of tuberculosis among children and adolescents of all non-white racial or ethnic groups, children and adolescents living in US territories and freely associated states, and children born in or with parents from tuberculosis-endemic countries. Finally, compared with US states, we observed disproportionately high mortality among children and adolescents with tuberculosis in the freely associated states of the Marshall Islands and Federated States of Micronesia.

Implications of all the available evidence

Although our results show that overall tuberculosis incidence among children and adolescents in the USA is low and steadily declining, additional attention and possibly new approaches are needed to address the stark disparities we report in tuberculosis incidence and mortality. Given limited sensitivity and specificity of tuberculosis diagnostics in children and current strategies for targeted tuberculosis testing in low-incidence areas, variations in tuberculosis epidemiology among children and adolescents could be used to optimise the predictive value of tuberculosis testing by prioritising groups with the highest rates. Furthermore, strategies to eliminate tuberculosis in the USA should account for the contextual factors that markedly increase risk in particular populations so that disparities in tuberculosis-associated morbidity and mortality among children and adolescents do not persist or worsen, even as overall tuberculosis burden declines.

detailed analyses of national estimates of tuberculosis disease counts and incidence rates among children and adolescents were last published in 2010 and 2007, respectively.[15,20]

We describe the clinical characteristics and epidemiology of tuberculosis among children and adolescents reported to the US National Tuberculosis Surveillance System (NTSS) during 2007–17, including overall burden and trends in tuberculosis incidence rates by sociodemographic groups, country of birth for children and their parents, and reporting jurisdiction, including US territories and freely associated states.

Methods

Study design and data collection

We considered all verified cases of tuberculosis disease reported to the NTSS among children aged younger than 15 years and adolescents aged 15–17 years between Jan 1, 2007, and Dec 31, 2017, excluding cases with missing information for sex or country of birth. The NTSS defines a verified tuberculosis case as one that had been reviewed at the local level (eg, state or county) by a tuberculosis control official who was familiar with the NTSS surveillance definitions and had verified that the NTSS criteria for a tuberculosis case are met. Verified cases included both laboratory-confirmed tuberculosis and clinically diagnosed tuberculosis without laboratory confirmation. The NTSS captures demographic, clinical, and laboratory characteristics of all tuberculosis cases reported in the 50 US states and District of Columbia (hereafter referred to as US states), and in US-affiliated islands which include five US territories (American Samoa, Guam, Northern Mariana Islands, Puerto Rico, and the Virgin Islands) and three freely associated states (Federated States of Micronesia, Marshall Islands, and Palau).[13,21] Under the Compacts of Free Association, the USA provides economic assistance to the sovereign nations of Marshall Islands, Federated States of Micronesia, and Palau.[22,23] The US Centers for Disease Control and Prevention (CDC) provides financial and technical support to public health programmes in these jurisdictions. In this Article, the phrase reported to the NTSS

	Reported in US states*				Reported in US-affiliated islands† (n=897)	Total reported to the NTSS (n=6072)
	US born‡ (n=3520)	Non-US born (n=1655)	Total (n=5175)	p value§		
Age, years						
<15	2977 (85%)	919 (56%)	3896 (75%)	<0·0001	754 (84%)	4650 (77%)
<1	448 (13%)	26 (2%)	474 (9%)	<0·0001	55 (6%)	529 (9%)
1–4	1503 (43%)	253 (15%)	1756 (34%)	<0·0001	293 (33%)	2049 (34%)
5–14	1026 (29%)	640 (39%)	1666 (32%)	<0·0001	406 (45%)	2072 (34%)
15–17	543 (15%)	736 (45%)	1279 (25%)	<0·0001	143 (16%)	1422 (23%)
Sex at birth						
Female	1725 (49%)	784 (47%)	2509 (48%)	0·2727	424 (47%)	2933 (48%)
Male	1795 (51%)	871 (53%)	2666 (52%)	0·2727	473 (53%)	3139 (52%)
Race or ethnicity¶						
Asian	468 (13%)	591 (36%)	1059 (20%)	<0·0001	46 (5%)	1105 (18%)
Black	861 (25%)	489 (30%)	1350 (26%)	<0·0001	0	1350 (22%)
Hispanic	1659 (47%)	444 (27%)	2103 (41%)	<0·0001	7 (1%)	2110 (35%)
Native American or Alaska Native	107 (3%)	0	107 (2%)	<0·0001	0	107 (2%)
Native Hawaiian or other Pacific Islander	100 (3%)	47 (3%)	147 (3%)	0·9896	834 (93%)	981 (16%)
Two or more races	36 (1%)	9 (1%)	45 (1%)	0·0849	1 (<1%)	46 (1%)
White	277 (8%)	65 (4%)	342 (7%)	<0·0001	0	342 (6%)
Nativity of parents or primary guardians‖						
Both US born	604 (20%)	40 (4%)	644 (17%)	<0·0001	25 (3%)	669 (14%)
Both non-US born	1205 (41%)	526 (57%)	1731 (44%)	<0·0001	372 (49%)	2103 (45%)
Non-US born and US born	284 (10%)	19 (2%)	303 (8%)	<0·0001	9 (1%)	312 (7%)
US born and unknown	280 (9%)	15 (2%)	295 (8%)	<0·0001	3 (<1%)	298 (6%)
Non-US born and unknown	355 (12%)	224 (24%)	579 (15%)	<0·0001	137 (18%)	716 (15%)
Both unknown	249 (8%)	95 (10%)	344 (9%)	0·0654	208 (28%)	552 (12%)
Patient lived outside USA for ≥2 months‖						
Yes	346 (12%)	668 (73%)	1014 (26%)	<0·0001	55 (7%)	1069 (23%)
No	2383 (80%)	143 (16%)	2526 (65%)	<0·0001	384 (51%)	2910 (63%)
Unknown	248 (8%)	108 (12%)	356 (9%)	0·0017	315 (42%)	671 (14%)
Primary reason evaluated for tuberculosis**						
Tuberculosis symptoms	1220 (35%)	698 (42%)	1918 (37%)	<0·0001	457 (51%)	2375 (39%)
Contact investigation	1456 (41%)	159 (10%)	1615 (31%)	<0·0001	306 (34%)	1921 (32%)
Abnormal chest x-ray	550 (16%)	360 (22%)	910 (18%)	<0·0001	108 (12%)	1018 (17%)
Immigration medical exam	0	208 (13%)	208 (4%)	<0·0001	6 (1%)	214 (4%)
Incidental laboratory result	152 (4%)	72 (4%)	224 (4%)	0·9576	14 (2%)	238 (4%)
Targeted testing	95 (3%)	104 (6%)	199 (4%)	<0·0001	2 (<1%)	201 (3%)
Other††	16 (1%)	22 (1%)	38 (1%)	0·0006	0	38 (1%)
Tuberculosis disease verification criteria‡‡						
Positive culture	1266 (36%)	766 (46%)	2032 (39%)	<0·0001	187 (21%)	2219 (37%)
Nucleic acid amplification test	63 (2%)	26 (2%)	89 (2%)	0·5723	6 (1%)	95 (2%)
Positive smear, absent culture	22 (1%)	2 (<1%)	24 (<1%)	0·0137	6 (1%)	30 (1%)
Clinical case definition	1759 (50%)	756 (46%)	2515 (49%)	0·004	355 (40%)	2870 (47%)
Provider diagnosis	410 (12%)	105 (6%)	515 (10%)	<0·0001	343 (38%)	858 (14%)
Initial chest x-ray§§						
Abnormal	2806 (80%)	1317 (80%)	4123 (80%)	0·82	804 (90%)	4927 (81%)
Normal	640 (18%)	311 (19%)	951 (18%)	0·616	59 (7%)	1010 (17%)
Not done	66 (2%)	26 (2%)	92 (2%)	0·4359	22 (3%)	114 (2%)

(Table 1 continues on next page)

	Reported in US states*				Reported in US-affiliated islands† (n=897)	Total reported to the NTSS (n=6072)
	US born‡ (n=3520)	Non-US born (n=1655)	Total (n=5175)	p value§		
(Continued from previous page)						
HIV status at diagnosis						
Positive	4 (<1%)	14 (1%)	18 (<1%)	<0·0001	1 (<1%)	19 (<1%)
Negative	2135 (61%)	1319 (80%)	3454 (67%)	<0·0001	479 (53%)	3933 (65%)
Unknown	1381 (39%)	322 (20%)	1703 (33%)	<0·0001	417 (47%)	2120 (35%)
Site of disease¶¶						
Pulmonary only	2406 (68%)	1135 (69%)	3541 (68%)	0·879	679 (76%)	4220 (70%)
Extrapulmonary only	772 (22%)	382 (23%)	1154 (22%)	0·3563	167 (19%)	1321 (22%)
Both pulmonary and extrapulmonary	339 (10%)	137 (8%)	476 (9%)	0·1157	51 (6%)	527 (9%)
Drug resistance||||						
DST done	1240 (98%)	750 (98%)	1990 (98%)	0·7652	176 (94%)	2166 (98%)
INH resistance	114 (9%)	59 (8%)	173 (9%)	0·3009	5 (3%)	178 (8%)
RIF resistance	14 (1%)	16 (2%)	30 (2%)	0·076	3 (2%)	33 (2%)
Any first-line resistance (INH, RIF, PZA, EMB)	198 (16%)	102 (14%)	300 (15%)	0·1527	6 (3%)	306 (14%)
MDR***	11 (1%)	14 (2%)	25 (1%)	0·0642	2 (1%)	27 (1%)
XDR†††	1 (<1%)	0	1 (<1%)	>0·999	0	1 (<1%)
Tuberculosis treatment outcome						
Completed	3256 (93%)	1544 (93%)	4800 (93%)	0·3048	721 (80%)	5521 (91%)
Died	14 (<1%)	0	14 (<1%)	0·0073	18 (2%)	32 (1%)
Other outcome‡‡‡	32 (1%)	24 (1%)	56 (1%)	0·0794	19 (2%)	75 (1%)
Missing	218 (6%)	87 (5%)	305 (6%)	0·1822	139 (16%)	444 (7%)

Data are n (%), unless otherwise indicated. Percentages might not add to 100% because of rounding. DST=drug susceptibility testing. EMB=ethambutol. INH=isoniazid. MDR=multidrug-resistant tuberculosis. NTSS=National Tuberculosis Surveillance System. PZA=pyrazinamide. RIF=rifampicin. XDR=extensively drug-resistant tuberculosis. *US states reporting areas include 50 US states, New York City, and the District of Columbia. †US-affiliated island reporting areas include US territories: American Samoa, Guam, Northern Mariana Islands, Puerto Rico, and Virgin Islands; and freely associated states: Federated States of Micronesia, Marshall Islands, and Palau. ‡Consistent with US Census Bureau definitions, anyone who was a US citizen at birth (ie, born in the US or a US territory, or born abroad to at least one parent who is a US citizen) were considered to be US born; all others were considered non-US born, including those born in the freely associated states, Federated States of Micronesia, Marshall Islands, and Palau.[24] §For the statistical test for differences between US-born and non-US-born children and adolescents. ¶Self-reported or reported by parent or guardian. Hispanic individuals might be of any race, including two or more races. Excludes 13 people missing information on race or ethnicity. ||Among 4650 children aged younger than 15 years; NTSS does not collect this information for people aged 15 years or older. **"Situation or reason that led to the initial suspicion that the patient might have tuberculosis disease";[21] excludes 67 people with missing or unknown reason for evaluation. ††Other reasons evaluated include employment or administrative testing (eg, testing at schools), testing for health-care workers. ‡‡Disease verification criteria categories are hierarchical in the order listed. For definitions see the US Centers for Disease Control and Prevention report of verified case of tuberculosis manual.[21] §§Excludes 21 people with missing or unknown chest x-ray results. ¶¶Excludes four people missing site of tuberculosis disease. ||||Among 2219 people with a positive culture for *Mycobacterium tuberculosis* and drug susceptibility results. ***Resistant to at least isoniazid and rifampin. †††Resistant to at least isoniazid and rifampin plus any fluoroquinolone and at least one second-line injectable (ie, amikacin, kanamycin, or capreomycin). ‡‡‡Other outcomes include adverse treatment event (n=3), lost to follow-up (n=16), refused (n=14), or other (n=42).

Table 1: **Demographic and clinical characteristics of people aged younger than 18 years with tuberculosis in US states and US-affiliated islands, 2010–17**

refers to aggregate tuberculosis case data from all reporting jurisdictions, unless otherwise specified. In 2009, the NTSS implemented new variables, including how tuberculosis was initially identified (eg, contact investigations, targeted testing of people with risk factors, and evaluation for tuberculosis symptoms), country of birth for parents or primary guardians of children aged younger than 15 years, and whether the child lived outside the USA for at least 2 months (appendix p 2).

See Online for appendix

Consistent with US Census Bureau definitions, we considered people who were US citizens at birth to be US born (ie, anyone born in a US state or territory, or born abroad to at least one US citizen parent). All others were considered non-US born, including people born in the freely associated states (ie, Federated States of Micronesia, Marshall Islands, and Palau).[24]

Statistical analysis

To avoid gaps or overlaps with previous paediatric reports using NTSS data, we reported rates starting in 2007 and tuberculosis case counts starting in 2010.[15,16] We used Poisson models offset with log population size to obtain point estimates and 95% CIs of overall and stratum-specific incidence rates, incidence rate ratios, and 10-year trends in incidence rates. We obtained population estimates from the US Census Bureau's American Community Survey public use microsample 1-year data files for

2007–17 compiled by the Integrated Public Use Microdata Series,[25,26] or US Census Bureau modelled estimates when American Community Survey data were unavailable (ie, for US-affiliated islands;[27,28] appendix p 2). We did all analyses using SAS, version 9·3, and reported results from US-affiliated islands separately from US states, unless otherwise specified. These data were collected as part of routine public health surveillance and therefore did not require institutional board review at the US CDC.

Role of the funding source

Authors were paid salaries by the US CDC and did not receive specific funding for this study. The data in this study are collected and managed by the US CDC; however, authors were responsible for study design, analysis, interpretation, and writing of this Article.

Results

During 2007–17, 121582 tuberculosis cases were reported to the NTSS. We excluded 373 with missing age, sex, or country of birth. Of the remaining 121209 tuberculosis cases, 9276 (8%) occurred among children and adolescents aged younger than 18 years. Both annual tuberculosis counts and proportion of tuberculosis that occurred among children and adolescents decreased from 2007 (n=1125, 8%) to 2017 (n=701, 7%).

During 2010–17, 6072 cases of tuberculosis were reported to the NTSS among children and adolescents; of these, 5175 (85%) of 6072 were reported from US states and 897 (15%) of 6072 from US-affiliated islands (table 1). In US-affiliated islands, the majority (747 [83%] of 897) of tuberculosis was reported from either Marshall Islands (378 [42%] of 897) or Federated States of Micronesia (369 [41%] of 897). Among children and adolescents with tuberculosis in US states, 3520 (68%) of 5175 occurred among US-born people; among children aged younger than 15 years, 2977 (76%) of 3896 were US born and among adolescents aged 15–17 years, 543 (42%) of 1279 were US born. Nearly half (1659 [47%] of 3520) of US-born children and adolescents with tuberculosis were Hispanic compared with more than a quarter (444 [27%] of 1655) of non-US-born people. Non-US-born children and adolescents with tuberculosis were most commonly Asian (591 [36%] of 1655) or black (489 [30%] of 1655).

Many of the tuberculosis diagnoses among children and adolescents in US states were prompted by the presence of tuberculosis symptoms (1918 [37%] of 5175); however, diagnoses were more likely to be made following contact investigations among the US born than non-US born (1456 [41%] of 3520 *vs* 159 [10%] of 1655, respectively; table 1). Culture confirmation of disease among children and adolescents was uncommon (2032 [39%] of 5175) in US states, but adolescents were more likely to have culture confirmation than children (880 [69%] of 1279 *vs* 1152 [30%] of 3896, respectively).

In total, 5521 (91%) of 6072 children and adolescents with tuberculosis reported to the NTSS completed treatment. 32 deaths occurred: 18 among children and adolescents diagnosed in the US-affiliated islands and 14 among the US born diagnosed in US states.

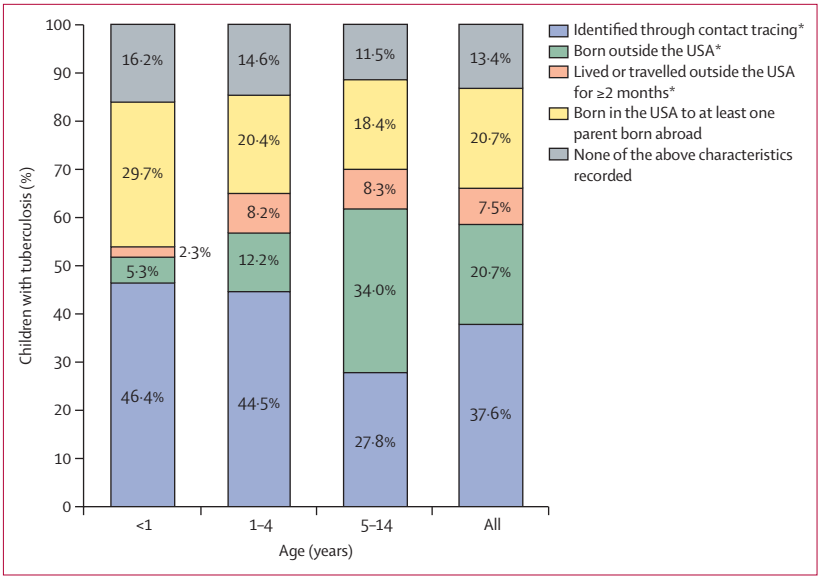

Figure 1: **Percentage of children younger than 15 years with tuberculosis in US states, 2010–17**
474 children aged younger than 1 year, 1756 children aged 1–4 years, and 1666 children aged 5–14 years were included. Categories are hierarchical in the order listed in the legend above (ie, category lived or travelled outside the USA for at least 2 months does not include children and adolescents identified through contact tracing or those born outside the USA). *Categories currently covered under US-targeted testing guidelines. The category none of the above characteristics recorded includes 136 (3·5%) children for whom nativity of both parents was unknown or missing, and 119 (3·1%) children who had one US-born parent and one parent of unknown or missing nativity status.

Approximately two-thirds (2565 [66%] of 3896) of children aged younger than 15 years with tuberculosis in US states from 2010 to 2017 would have been recommended for tuberculosis testing under current targeted testing guidelines—1465 (38%) of 3896 were identified through contact tracing, and 807 (21%) of 3896 and 294 (8%) of 3896 were born or travelled outside the USA for at least 2 months, respectively (figure 1). An additional 806 (21%) of 3896 did not meet guidelines for testing but did have at least one parent born abroad. The remaining 524 (13%) of 3896 had none of these characteristics reported.

Next, we assessed tuberculosis incidence rates during 2007–17 among children and adolescents living in US states, and found that overall, the tuberculosis incidence rate was 1·0 per 100000 person-years (8030 tuberculosis cases reported among an estimated 73·6 million children and adolescents; table 2). Tuberculosis incidence rates were highest in children aged 1 year or younger (1·9 per 100000 person-years; table 2), lowest among children aged 7–12 years (0·5 per 100000 person-years; appendix p 3) and intermediate among adolescents aged 15–17 years (1·4 per 100000 person-years; table 2). Although age-specific incidence rates were at least ten times higher among non-US-born children and adolescents than among US-born children and adolescents, age-related trends in rates were consistent (appendix p 3).

	Overall (2007–17)				2007 incidence rate† (95% CI)	2017 incidence rate† (95% CI)	Percent change, 2017 *vs* 2007 (95% CI)§
	Population aged <18 years* (2012)	Number with tuberculosis	Incidence rate† (95% CI)	Incidence rate ratio‡ (95% CI)			
Total aged <18 years	73 632 197	8030	1·0 (1·0 to 1·0)	NA	1·4 (1·3 to 1·5)	0·8 (0·7 to 0·8)	–47·8% (–51·4 to –44·1)
Age, years							
<1	3 675 358	798	1·9 (1·8 to 2·0)	3·4 (3·2 to 3·7)	2·8 (2·3 to 3·4)	1·4 (1·1 to 1·9)	–57·9% (–66·3 to –47·3)
1–4	16 136 463	2797	1·6 (1·5 to 1·6)	2·8 (2·7 to 3·0)	2·1 (1·9 to 2·4)	1·1 (0·9 to 1·3)	–52·9% (–58·2 to –46·9)
5–14	41 339 646	2508	0·6 (0·5 to 0·6)	1 (ref)	0·8 (0·7 to 0·9)	0·5 (0·4 to 0·6)	–44·2% (–50·8 to –36·8)
15–17	12 480 730	1927	1·4 (1·3 to 1·4)	2·5 (2·3 to 2·6)	1·8 (1·6 to 2·1)	1·2 (1·0 to 1·4)	–33·8% (–42·5 to –23·7)
Sex at birth							
Female	35 961 951	3905	1·0 (1·0 to 1·0)	1 (ref)	1·4 (1·3 to 1·6)	0·8 (0·7 to 0·9)	–47·7% (–52·7 to –42·1)
Male	37 670 246	4125	1·0 (1·0 to 1·0)	1·0 (1·0 to 1·1)	1·3 (1·2 to 1·4)	0·8 (0·7 to 0·9)	–48·0% (–52·8 to –42·7)
Race or ethnicity¶							
Asian	3 255 938	1555	4·4 (4·2 to 4·6)	34·8 (31·6 to 38·4)	5·4 (4·7 to 6·4)	1·3 (1·1 to 1·5)	–44·7% (–52·8 to –35·2)
Black	10 137 456	2145	1·9 (1·8 to 2·0)	15·2 (13·9 to 16·8)	2·9 (2·6 to 3·3)	1·4 (1·2 to 1·7)	–52·4% (–58·5 to –45·4)
Hispanic	17 544 826	3380	1·8 (1·7 to 1·8)	14·1 (12·9 to 15·4)	2·8 (2·6 to 3·1)	1·3 (1·1 to 1·5)	–62·1% (–66·1 to –57·8)
Native American or Native Alaskan	568 812	133	2·2 (1·8 to 2·6)	17·1 (14·2 to 20·7)	1·6 (0·8 to 3·1)	2·7 (1·6 to 4·5)	39·8% (–18·8 to 140·4)
Native Hawaiian or Pacific Islander	127 473	191	14·4 (12·5 to 16·6)	114·0 (96·6 to 134·4)	16·4 (10·2 to 26·3)	24·8 (17·4 to 35·3)	50·3% (–5·3 to 138·5)
Two or more races	3 030 887	56	0·2 (0·1 to 0·2)	1·3 (1·0 to 1·8)	0·2 (0·1 to 0·5)	0·1 (0·1 to 0·3)	22·4% (–47·6 to 185·7)
White	38 765 384	543	0·1 (0·1 to 0·1)	1 (ref)	0·2 (0·2 to 0·2)	0·1 (0·0 to 0·1)	–55·8% (–66·3 to –41·9)
Nativity‖							
US born	71 061 556	5424	0·7 (0·7 to 0·7)	1 (ref)	0·9 (0·9 to 1·0)	0·6 (0·5 to 0·6)	–47·9% (–52·2 to –43·3)
Non-US born	2 570 641	2606	9·0 (8·6 to 9·3)	12·9 (12·3 to 13·5)	12·1 (10·9 to 13·4)	7·0 (6·1 to 8·1)	–39·3% (–46·2 to –31·4)
Nativity and world area of birth**							
US born							
US state	70 332 800	5380	0·7 (0·7 to 0·7)	1 (ref)	0·9 (0·9 to 1·0)	0·6 (0·5 to 0·6)	–48·3% (–52·6 to –43·7)
US island area or Oceania††	188 416	24	1·1 (0·7 to 1·6)	1·6 (1·1 to 2·4)	3·2 (1·5 to 7·2)	1·3 (0·4 to 4·0)	–33·9% (–81·2 to 132·0)
Non-US born							
Latin America	1 322 256	893	6·0 (5·6 to 6·4)	8·6 (8·0 to 9·2)	8·6 (7·3 to 10·1)	5·5 (4·3 to 7·0)	–36·2% (–48·3 to –21·2)
Asia	781 065	938	10·8 (10·1 to 11·5)	15·5 (14·5 to 16·6)	13·9 (11·4 to 16·9)	6·8 (5·3 to 8·8)	–51·2% (–60·2 to –40·2)
Europe	227 336	51	1·9 (1·4 to 2·5)	2·7 (2·0 to 3·5)	4·0 (2·3 to 6·8)	0·0 (0·0 to 0·0)	–88·7% (–96·0 to –67·9)
Africa	178 612	641	32·3 (29·9 to 34·9)	46·4 (42·8 to 50·4)	59·7 (48·7 to 73·3)	19·9 (15·1 to 26·4)	–61·0% (–69·4 to –50·2)
Oceania	17 535	67	30·3 (23·9 to 38·6)	43·7 (34·3 to 55·6)	36·3 (18·2 to 72·6)	37·8 (18·0 to 79·4)	–10·5% (–57·6 to 89·3)

NA=not applicable. *Population estimates are from the US Census Bureau American Community Survey Public Use Microdata Sample 1-year estimates, 2007–17. Population estimate at midpoint (2012) displayed for each demographic group. †All incidence rates are reported per 100 000 person-years. ‡Incidence rate ratio for relative differences between demographic groups overall (2007–17). §10-year percent change in rate for 2017 compared with 2007 estimated from Poisson model (percent change is 1-incidence rate ratio). ¶Self-reported or reported by parent or guardian. Hispanic might be of any race, including two or more races. n=27 cases aged younger than 18 years occurred among those with unknown race or ethnicity. ‖Consistent with US Census Bureau definition.[24] **n=36 children and adolescents with tuberculosis not shown (n=20 US born, born abroad to parents who are US citizens; n=3 non-US born, born in North America; n=13 non-US born, with unknown world area of birth). ††Combined based on collapsed US Census Bureau data categories; US island areas: American Samoa, Guam, Northern Mariana Islands, Virgin Islands, Puerto Rico, Marshall Islands, Federated States of Micronesia, Palau; Oceania: Fiji, New Zealand, Australia, Tonga, Samoa, Oceania not specified, or at sea.

Table 2: **Incidence rates of tuberculosis among children and adolescents aged younger than 18 years in US states, 2007–17**

Incidence varied substantially between racial and ethnic groups; rates were 14·4 per 100 000 person-years among Native Hawaiian and Pacific Islander children and adolescents—more than three times as high as any other racial or ethnic group and 114·0 times higher (95% CI 96·6–134·4) than non-Hispanic white children and adolescents. Rates among all other single race or ethnicity groups were at least 14 times higher than among non-Hispanic white children and adolescents (table 2).

Incidence was 12·9 times higher (95% CI 12·3–13·5) among children and adolescents born outside the USA compared with US born; nonetheless, incidence among non-US-born children varied substantially according to their birth region. The highest rates (>30 per 100 000 person-years) occurred among children born in Africa or Oceania (table 2).

Tuberculosis incidence rates among children and adolescents in US states declined 47·8% (95% CI –51·4 to –44·1) from 1·4 per 100 000 person-years in 2007

to 0·8 per 100 000 person-years in 2017. Although rates decreased across all age categories, the greatest declines occurred among children aged younger than 5 years (table 2). Rates also decreased among all racial or ethnic groups, except Native Americans or Alaska Natives, Native Hawaiian or Pacific Islanders, and children and adolescents of two or more races. The greatest decreases were observed among Hispanic people (62·1%, 95% CI −66·1 to −57·8), followed by black people (52·4%, −58·5 to −45·4).

Although consistent decreases in incidence rates occurred among both US-born (−47·9%, 95% CI −52·2 to −43·3) and non-US-born (−39·3%, −46·2 to −31·4) children and adolescents, the most precipitous occurred among children and adolescents born in Africa (−61·0%, −69·4 to −50·2) and Europe (−88·7%, −96·0 to −67·9). Smaller, but significant decreases occurred among children and adolescents born in Latin America (−36·2%, −48·3 to −21·1) and Asia (−51·2%, −60·2 to −40·2). No significant changes occurred among children and adolescents born in Oceania (−10·5%, −57·6 to 89·3).

Incidence rates of tuberculosis were substantially higher in US-affiliated islands than US states (11·7 *vs* 1·0 per 100 000 person-years, respectively), but varied widely by reporting jurisdiction (table 3; appendix p 4). Incidence rates in Marshall Islands and Federated States of Micronesia exceeded 150 per 100 000 person-years, while rates in Puerto Rico and American Samoa were lower than in the US states (<1·0 per 100 000 person-years). Despite having small populations, the Federated States of Micronesia (n=526) and Marshall Islands (n=469) ranked third and sixth, respectively, in absolute number of tuberculosis cases reported among children and adolescents, whereas the US states with the greatest numbers of cases were California (n=1483), Texas (n=1227), New York (n=516), and Florida (n=490) (appendix p 4). Tuberculosis incidence rates among children and adolescents in US states ranged from 0·1 per 100 000 person-years in Wyoming to 3·9 per 100 000 person-years in Alaska (table 3).

During 2010–17, tuberculosis rates varied both by birthplace of the child and that of their parents. Although incidence rates were highest among children born outside the USA (6·5 per 100 000 person-years), rates among US-born children with at least one parent born outside the USA were substantially higher than among children without (1·7 per 100 000 person-years *vs* 0·3 per 100 000 person-years, respectively; table 4, figure 2). US-born children with two parents born outside the USA had higher incidence (2·4 per 100 000 person-years) than children with only one parent born outside the USA (1·0 per 100 000 person-years); these rates were 8·5 (95% CI 7·7–9·3) and 3·5 (3·0–4·0) times higher than among children with two US-born parents (table 4).

Among children born outside the USA, tuberculosis burden varied by country of birth (figure 2). Although children born in Mexico (n=99), Ethiopia (n=78), Philippines (n=61), Myanmar (n=60), and Haiti (n=42) accounted for the largest absolute number of tuberculosis cases, incidence rates were highest among children born in Marshall Islands (149·4 per 100 000 person-years), Somalia (139·4 per 100 000 person-years), Myanmar (79·0 per 100 000 person-years), Malaysia (66·0 per

	Population aged <18 years (2012)*	Number with tuberculosis	Incidence rate† (95% CI)
US-affiliated islands	1 022 536	1246	11·7 (11·1–12·4)
American Samoa	21 656	1	0·6 (0·1–4·3)
Northern Mariana Islands	18 034	23	16·3 (10·8–24·5)
Federated States of Micronesia	42 508	526	159·7 (146·6–173·9)
Guam	55 572	201	45·3 (39·5–52·1)
Palau	5684	11	24·8 (13·8–44·9)
Puerto Rico	836 637	15	0·2 (0·1–0·3)
Marshall Islands	29 819	469	195·3 (178·4–213·8)
US states and DC‡	73 632 197	8030	1·0 (1·0–1·0)
Distribution by number of tuberculosis cases			
California (maximum)	9 229 544	1483	1·5 (1·4–1·5)
Virginia (3rd quartile)	1 855 004	164	0·8 (0·7–0·9)
Alaska (median)	184 564	79	3·9 (3·1–4·8)
Iowa (1st quartile)	721 858	26	0·3 (0·2–0·5)
Wyoming (minimum)	136 250	1	0·1 (0·0–0·5)
Distribution by tuberculosis incidence rate			
Alaska (maximum)	184 564	79	3·9 (3·1–4·8)
Arizona (3rd quartile)	1 619 974	207	1·1 (1·0–1·3)
Alabama (median)	1 125 653	94	0·8 (0·6–0·9)
Vermont (1st quartile)	122 488	6	0·4 (0·2–1·0)
Wyoming (minimum)	136 250	1	0·1 (0·0–0·5)

*Population estimates for Puerto Rico and US states come from the US Census Bureau's American Community Survey, Public Use Microsample Data 1-year estimates. Population estimates for American Samoa, Guam, and Northern Mariana Islands obtained from the US Census Bureau[27] and Federated States of Micronesia, Marshall Islands, and Palau also obtained from the US Census Bureau.[29] †Tuberculosis incidence rate per 100 000 person-years. ‡Total for all 50 US states and DC combined. Selected states shown below for comparison to US-affiliated islands. States were selected based on the distribution of number of reported tuberculosis cases and tuberculosis incidence rates among children and adolescents. Data for all reporting jurisdictions are shown in the appendix (p 4).

Table 3: **Incidence rates of tuberculosis among children and adolescents aged younger than 18 years in US-affiliated islands and selected US states, 2007–17**

	Nativity of parents or primary guardians†	Number with tuberculosis	Population aged <15 years‡	Incidence rate (95% CI)§	Incidence rate ratio (95% CI)
Non-US-born child	All nativities	919	1 765 819	6·5 (6·1–6·9)	23·1 (20·9–25·6)
US-born child	Both non-US born	1205	6 310 790	2·4 (2·3–2·5)	8·5 (7·7–9·3)
US-born child	One US born, one non-US born	284	3 629 607	1·0 (0·9–1·1)	3·5 (3·0–4·0)
US-born child	Both US born	604	26 819 512	0·3 (0·3–0·3)	1 (ref)

*The nativity of parents or primary guardians variable was introduced in 2009 and only collected for children with tuberculosis aged younger than 15 years. Data are shown for children aged younger than 15 years from 2010 to 2017 when the variable was collected regularly. †Only children with known nativity for two parents or guardians are shown. Children with at least one unknown or missing nativity for parent or guardian not shown to prevent misclassification between National Tuberculosis Surveillance System numerators and US Census Bureau population estimates. ‡Annualised (average) population estimate, 2010–17. §Tuberculosis incidence rate per 100 000 person-years.

Table 4: **Incidence rates of tuberculosis by nativity of child and nativity of parents for children with tuberculosis aged younger than 15 years in US states, 2010–17***

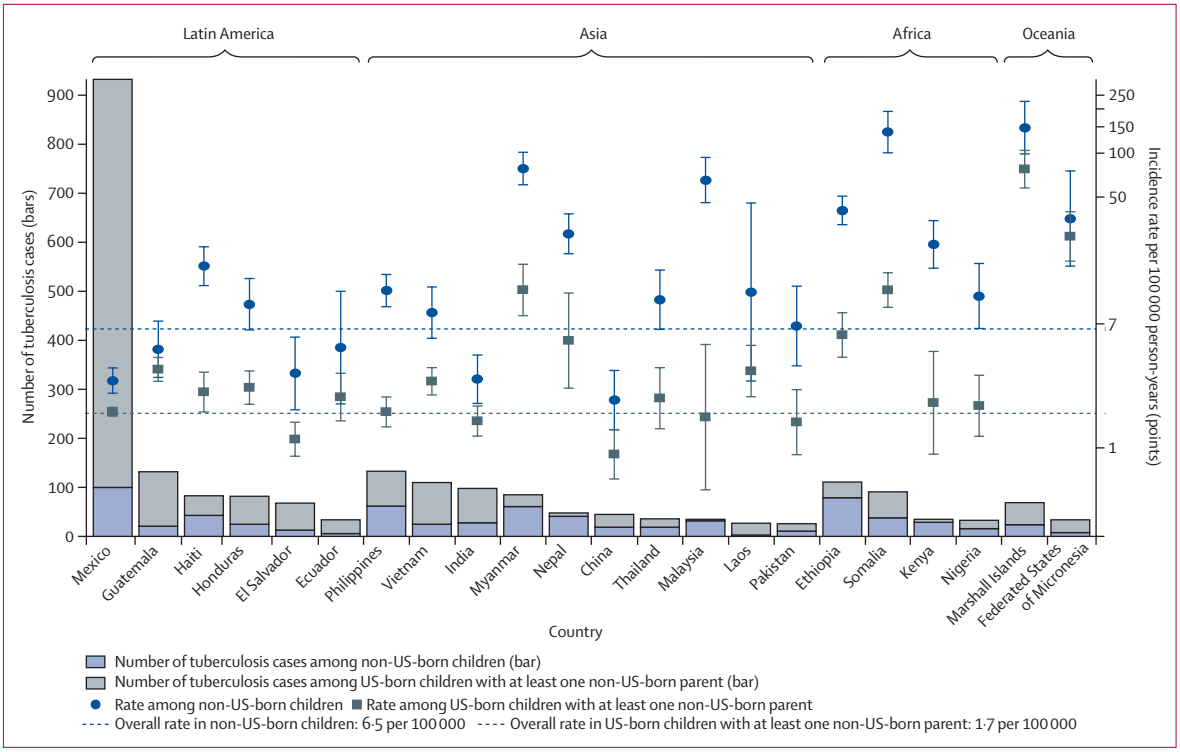

Figure 2: **Number of tuberculosis cases and tuberculosis incidence rates by country of birth among non-US-born children aged younger than 15 years and by parental country of birth among US-born children with at least one non-US-born parent in US states, 2010–17**

Countries are shown by descending case count (bars) within US Census Bureau world regions (Latin America, Asia, Africa, and Oceania). All countries with at least 25 children who were non-US born or had non-US-born parents from that country (total bar height) are shown. For US-born children with at least one non-US-born parent, includes children who have two non-US-born parents, children with one non-US-born and one US-born parent, and children with one non-US-born parent and one parent with unknown nativity. For the 100 children with two non-US-born parents from different countries, children are counted twice for each country of birth for their parents (eg, for a child with one parent born in El Salvador and one parent born in Ecuador, the child will appear in the calculations and totals for both El Salvador and Ecuador).

100 000 person-years), and Ethiopia (41·2 per 100 000 person-years).

Similarly, tuberculosis incidence among US-born children with non-US-born parents varied substantially by parents' birth country (figure 2). Although the most common birth countries for non-US-born parents of US-born children were Mexico (n=832), Guatemala (n=111), Vietnam (n=85), Philippines (n=71), and India (n=70), rates were highest among children with parents from Marshall Islands (78·2 per 100 000 person-years), Federated States of Micronesia (27·5 per 100 000 person-years), Myanmar (11·9 per 100 000 person-years), and Somalia (11·9 per 100 000 person-years), for whom rates exceeded those among non-US-born children.

Discussion

Although overall tuberculosis incidence among children and adolescents during 2007–17 was low, at 1·0 case per 100 000 person-years, and tuberculosis rates in these age groups decreased substantially (48%) during this period, substantial heterogeneity in burden exists. During this examination of national surveillance data, we observed disproportionately high rates of tuberculosis among children and adolescents of all non-white racial or ethnic groups, children and adolescents living in US-affiliated islands, and children born in or with parents from tuberculosis-endemic countries. In addition, we observed disproportionately high mortality among children and adolescents with tuberculosis in US-affiliated islands compared with US states. These wide-ranging and pervasive disparities probably reflect structural inequalities that give rise to disproportionate exposure, vulnerability to infection and disease, and unequal access to prompt diagnosis and treatment. Our findings suggest that tuberculosis care and prevention strategies in the USA are succeeding in reducing overall tuberculosis burden among children and adolescents, but that more attention and possibly new approaches are needed to address the disparities in tuberculosis incidence and mortality in these age groups.

Tuberculosis in children and adolescents is preventable and curable. In the context of historically low tuberculosis incidence in the USA and limited sensitivity and specificity of available diagnostic tests for tuberculosis infection and disease, epidemiological information might be useful in ascertaining risk to inform tuberculosis testing decisions.[14] In addition to people with compatible signs or symptoms and people with medical conditions that convey higher

risk for progression to tuberculosis, current clinical practice guidelines recommend tuberculosis testing for people in contact with individuals with tuberculosis, as well as children and adolescents immigrating from, or who have travelled to, tuberculosis-endemic countries.[14] Our findings are consistent with previous studies in the USA and Canada, and reinforce these characteristics as potential markers of increased tuberculosis risk and indicators for targeted testing.[15,20,30] 31% of children and adolescents with tuberculosis in US states were diagnosed through contact tracing. 32% were non-US born, for whom rates of tuberculosis were about 13 times higher than among US-born children and adolescents; and more than a quarter (26%) of children with tuberculosis lived outside the USA for at least 2 months. Taken together, targeted testing characteristics accounted for 66% of children with tuberculosis in US states. Nevertheless, a third of tuberculosis in children occurred outside of these groups, highlighting the opportunity to improve tuberculosis care and prevention efforts through consideration of additional characteristics, such as parental place of birth.

In our analysis, 21% of children with tuberculosis in US states had at least one non-US-born parent, but were not known contacts of people with tuberculosis, and had neither been born nor lived outside the USA. For children aged younger than 1 year, this figure was 30%. We observed increasing tuberculosis rates with increasing numbers of non-US-born parents for US-born children; rates were 8·5 and 3·5 times higher among children with two and one non-US-born parent, respectively, compared with children with two US-born parents. These findings are consistent with previous evidence of tuberculosis rates among US-born children with at least one non-US-born parent being six times higher than those with two US-born parents.[17]

Tuberculosis burden in children varied widely by their country of birth and that of their parents. Rates in US-born children with parents from Marshall Islands, Federated States of Micronesia, Somalia, and Myanmar exceeded the overall rate in non-US-born children. By contrast, children born in or with parents from several countries, including Mexico and Guatemala, contributed a large number of cases, but had low rates of tuberculosis. Variation in tuberculosis burden by country of birth of children and their parents underscores the importance of local context, as the epidemiology, demography, and determinants of health might vary widely between settings. In addition to approaches already recommended to reduce tuberculosis burden, including overseas screening of US-bound immigrants and current guidelines for targeted testing for latent tuberculosis infection, clinicians and public health professionals might find these data helpful to identify and reach children at highest risk for tuberculosis and optimise the predictive value of tuberculosis testing in the context of the populations they serve. For example, the California Department of Public Health and California TB Controllers Association have developed a Pediatric TB Risk Assessment Tool and User Guide[31] to help providers in California identify asymptomatic children and adolescents who might benefit from tuberculosis testing. In addition to characteristics covered under current targeted testing guidelines, the guide also notes that tuberculosis testing can be considered in children and adolescents "with frequent exposure to adults at high risk of tuberculosis infection", which, in some contexts, might include consideration of parental birthplace or extensive parental travel to areas with high tuberculosis rates. The user guide also encourages local tuberculosis control programmes and clinics to further customise the paediatric tuberculosis risk assessment tool according to local recommendations. Our findings support the role of local epidemiology in devising tuberculosis risk assessments for children and adolescents.

We observed pervasive racial or ethnic and geographical disparities in tuberculosis incidence and mortality among children and adolescents. Every racial or ethnic group examined had significantly increased tuberculosis incidence rates compared with non-Hispanic white children and adolescents, suggesting potentially broad influences of structural and social determinants of health that drive increased risk of tuberculosis exposure, infection, or disease progression among historically marginalised children and adolescents. Despite small population sizes, Native Hawaiians or Pacific Islanders living in US states and people in US-affiliated islands arguably bear the most disproportionate burden of tuberculosis among children and adolescents. In US states, tuberculosis rates among Native Hawaiian or Pacific Islander children and adolescents were more than 100 times higher than their non-Hispanic white counterparts. Additionally, incidence among children living in the USA with parents from Marshall Islands and Federated States of Micronesia were higher than any other country. In Marshall Islands and Federated States of Micronesia, tuberculosis incidence rates among children and adolescents were at epidemic levels, exceeding 150 per 100 000 person-years. Children and adolescents living in Marshall Islands and Federated States of Micronesia accounted for 11% of tuberculosis disease during 2007–17, and more than half of all tuberculosis deaths during 2010–17, despite representing less than 0·1% of the estimated population.

Although we highlight heterogeneity in tuberculosis burden by race or ethnicity, geography, and place of birth, we note that this heterogeneity is probably attributable to underlying social, policy, and environmental conditions. We lack data to determine causes of the stark disparities in tuberculosis burden among children and adolescents. However, tuberculosis occurrence is widely recognised to be inextricably linked with social deprivation and living conditions. Previous work suggests that coarse, area-level socioeconomic status explained more than half of racial

disparities in adult tuberculosis, and a 1994 study of children in New York showed tuberculosis rates were closely tied to neighbourhood crowding.[32,33] In addition, research on a diverse array of health outcomes has identified additional factors that contribute to population-level health disparities.[12,32,34–37] These factors might include food security and nutrition, access to economic and material resources, residential segregation, exposure to second-hand smoke, indoor and outdoor air quality, lasting effects of historical trauma (eg, slavery, colonisation, displacement), and health-care policy, access, and infrastructure (eg, insurance coverage, availability of providers, absence of translation services).[9,36,38–41] Additionally, physiological responses to acute and chronic stress attributable to poverty, racism, stigma, and other forms of social trauma and deprivation can affect immune function and might shape population distribution of disease.[34,41–45] In addition to efforts to prevent and treat tuberculosis among children and adolescents at highest risk, efforts to elucidate and ameliorate the underlying social and structural drivers of increased risk should be explored.

Our analysis has limitations. Variables capturing parental nativity and international travel were introduced in 2009 only for children aged younger than 15 years, limiting our ability to draw conclusions about trends for these variables. Second, information about other potential tuberculosis exposures, such as international travel or tuberculosis contacts who are not parents or primary guardians are not systematically captured. The NTSS does not collect information on health insurance, household crowding, nutrition, or individual or household socioeconomic indicators such as income or education. Consequently, we could not examine whether observed disparities might be explained by these factors. Finally, for approximately 31% of children, nativity of one or both parents was unknown; therefore, incidence rates based on parental nativity probably underestimate rates among children with at least one non-US-born parent.

Although overall tuberculosis rates among children and adolescents are low and steadily declining, sub stantial heterogeneity exists in burden and trends across geo-graphies and sociodemographic groups. Given limited sensitivity and specificity of tuberculosis diagnostics in children and current strategies for targeted tuberculosis testing in low-incidence areas, variations in tuberculosis epidemiology among children and adolescents could be used to optimise the predictive value of tuberculosis testing by prioritising groups with the highest rates. Furthermore, strategies to eliminate tuberculosis in the USA should account for the contextual factors that markedly increase tuberculosis risk in particular populations so that disparities in tuberculosis-associated morbidity and mortality among children and adolescents do not persist or worsen, even as overall tuberculosis burden declines.

Contributors

TLC conceptualised and designed the study, did the initial analyses, drafted the initial Article, and reviewed and revised the Article. DCB and JMW conceptualised and designed the study, drafted the initial Article, and reviewed and revised the Article. All authors approved the final Article as submitted and agree to be accountable for all aspects of the work.

Declaration of interests

We declare no competing interests. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US CDC.

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