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Global impact of COVID-19 on childhood tuberculosis: an analysis of notification data

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Summary

Background There is concern that the COVID-19 pandemic has damaged global childhood tuberculosis management. Quantifying changes in childhood tuberculosis notifications could support more targeted interventions to restore childhood tuberculosis services. We aimed to use time-series modelling to evaluate the impact of COVID-19 on child tuberculosis notifications.

Methods Annual tuberculosis case notification data reported to WHO by 215 countries were used to calculate annual notification counts for the years 2014–20, stratified by age groups (0–4, 5–14, and ≥15 years) and sex. We used time-series modelling to predict notification counts for 2020, and calculated differences between these predictions and observed notifications in 2020 for each of the six WHO regions and at the country level for 30 countries with high tuberculosis burden. We assessed associations between these differences and the COVID-19 stringency index, a measure of COVID-19 social impact.

Findings From 2014 to 2019, annual tuberculosis notification counts increased across all age groups and WHO regions. More males than females in the 0–4 years age group and ≥15 years age group had notifications in all years from 2014 to 2020 and in all WHO regions. In the 5–14 years age group, more females than males were notified globally in all years, although some WHO regions had higher notifications from males than females. In 2020, global notifications were 35·4% lower than predicted (95% prediction interval −30·3 to −39·9; 142 525 observed *vs* 220 794 predicted notifications [95% prediction interval 204 509 to 237 078]) for children aged 0–4 years, 27·7% lower (−23·4 to −31·5; 256 398 *vs* 354 578 [334 724 to 374 431]) in children aged 5–14 years, and 18·8% lower (−15·4 to −21·9; 5 391 753 *vs* 6 639 547 [6 375 086 to 6 904 007]) for people aged 15 years or older. Among those aged 5–14 years, the reduction in observed relative to predicted notifications for 2020 was greater in males (−30·9% [−24·8 to −36·1]) than females (−24·5% [−18·1 to −29·9]). Among 28 countries with high tuberculosis burden, no association was observed between the stringency of COVID-19 restrictions and the relative difference in observed versus predicted notifications.

Interpretation Our findings suggest that COVID-19 has substantially affected childhood tuberculosis services, with the youngest children most affected. Although children have mostly had fewer severe health consequences from COVID-19 than have adults, they have been disproportionately affected by the effects of the pandemic on tuberculosis care. Observed sex differences suggest that targeted interventions might be required. As countries rebuild health systems following the COVID-19 pandemic, it is crucial that childhood tuberculosis services are placed centrally within national strategic plans.

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Introduction

COVID-19, caused by SARS-CoV-2, was first detected in Wuhan, China in December, 2019, and rapidly spread throughout the world. National responses were highly varied but, by early 2020, most countries sought to reduce transmission through public health policies and restrictions to the activities of individuals. By the end of May, 2022, over 500 million confirmed cases of SARS-CoV-2 infection had been reported globally, with over 6 million deaths.[1] Despite early concerns that COVID-19 would cause substantial mortality in young children, particularly in low-resource settings,[2] it rapidly became apparent that children were mostly unaffected by the most severe form of the disease and that death in children with COVID-19 was very rare.[3]

Despite years of neglect, the field of childhood tuberculosis had shown progress in the 10 years before the start of the COVID-19 pandemic.[4] Estimates of disease burden had been generated, molecular diagnostic testing had become widespread, training and education for the diagnosis of tuberculosis in children was increasingly prioritised and funded, and child-friendly drug formulations had been developed. Despite this progress, in 2019, an estimated 1·2 million children aged 0–14 years developed incident tuberculosis, yet only 520 000 were diagnosed by national programmes and reported to WHO.[5] In the same year, tuberculosis killed an estimated 220 000 children and represented one of the top ten causes of death in children younger than 5 years.[6]

Research in context

Evidence before this study

We searched PubMed using the search terms ("children" OR "childhood" OR "paediatric" OR "pediatric") AND ("tuberculosis") AND ("COVID" or "coronavirus") to identify primary research studies published in any language between March 11, 2020 (the date on which WHO declared COVID-19 a pandemic) and June 8, 2022. Multiple analyses of regional and national data, as well as several modelling studies, reported substantial delays and reductions in tuberculosis diagnosis and treatment due to the focus on COVID-19. One study evaluated the increase in tuberculosis deaths if global case detection decreased by an average of 25% over 3 months compared with pre-pandemic, and another predicted a 20% reduction in case detection over the 5 years since the pandemic. A study that evaluated the impact of COVID-19 on childhood tuberculosis notifications in India found a substantial reduction in notifications that persisted beyond lockdown measures.

Added value of this study

In this analysis of WHO-collated notification data, we used time-series prediction modelling to quantify the effect of the COVID-19 pandemic on tuberculosis notifications. We found that notifications in 2020 were substantially lower than predicted, with the greatest effect seen in the youngest children (aged 0–4 years). We also found a disparity by sex in tuberculosis notifications in each year from 2014 to 2020 in the 0–4 years age group, with more boys notified than girls; this sex difference was not present in the 5–14 years age group.

Implications of all the available evidence

These findings indicate a potential shortfall in case detection for childhood tuberculosis, with an effect more pronounced in the youngest children. As health systems recover from the COVID-19 pandemic it will be vital that efforts focus on enhanced screening and case finding, particularly in the 0–4 years age group. The sex discrepancies seen in the 0–4 years age group warrant further investigation to ascertain whether social or biological factors are primarily responsible for this difference.

There are several reasons to suspect that the COVID-19 pandemic has had a damaging effect on global childhood tuberculosis control. It is likely that infection with SARS-CoV-2 affects the human host immune response to *Mycobacterium tuberculosis* and that it could increase the risk of progression from *M tuberculosis* infection to tuberculosis disease and negatively affect disease outcome.[7] Given the overlap in symptoms, there is a concern that children with tuberculosis presenting to health facilities have been diagnosed with COVID-19 without appropriate evaluation for tuberculosis disease. Delayed adult pulmonary tuberculosis presentations are likely to have led to prolonged exposure of other household members to the infected person, and an associated increase in infection and disease, particularly in younger children.[8] In addition, in some contexts, GeneXpert PCR testing platforms being used for tuberculosis diagnostic evaluations were co-opted for SARS-CoV-2 testing, and some staff from tuberculosis clinics were redeployed to care for patients with COVID-19. Public health responses to COVID-19, particularly social and travel restrictions, are likely to have restricted access to childhood tuberculosis diagnostic services, and some caregivers might have been hesitant to take their children to health facilities because of concerns about exposing them to SARS-CoV-2. Finally, the economic impact of COVID-19 has impoverished many families, further affecting their ability to prioritise seeking diagnostic services for children with symptoms.[9]

Quantifying the magnitude of effect of COVID-19 and the public health response to the pandemic on childhood tuberculosis services will allow prioritisation of efforts to restore childhood tuberculosis services and help to justify the allocation of additional resources. Estimating the true incidence of childhood tuberculosis is challenging.[10] National notifications, however, are collated by WHO and are available for almost all countries in the world, stratified by sex and into age groups of 0–4 and 5–14 years. We aimed to use routinely available global data on notifications for tuberculosis in children from 2014 to 2020 to describe the effect of COVID-19 on the number of children notified as having tuberculosis.

Methods

Study design and data source

We conducted a time-series modelling study to evaluate the effect of COVID-19 on childhood tuberculosis notifications. Annual case notification data reported to WHO by 215 countries were used.[11] New and relapse case notification counts were extracted by country, sex, and age group from 2014 to 2020. Three age groups were used in this analysis: 0–4 years, 5–14 years, and 15 years or older. Data from all 215 reporting countries were used to estimate annual WHO regional and global notification counts.

Construction of time-series models

Autoregressive integrated moving average (ARIMA) time-series modelling was used to predict 2020 case notifications on the basis of data from 2014 to 2019, with the aim of estimating counterfactual notification counts if there had been no effect of the global COVID-19 pandemic. Notification counts were predicted for groups defined by sex, age group, and location (by each of

30 countries with high tuberculosis burden[12] or by WHO region) then aggregated for each analysis. WHO regions comprised the European region, African region, region of the Americas, Eastern Mediterranean region, South-East Asia region, and the Western Pacific region. Point estimates and variance of predictions were assumed to be independent. Given the low proportion of missing data, linear interpolation was used for simplicity to impute missing counts in data from countries with a high tuberculosis burden. We used data from 2014 to 2018, stratified by sex, age group, and location, to develop 216 independent time series for training. We fitted ARIMA models to these training time series, and the ten combinations of pdq parameters (where p is the number of lagged values included in the autoregressive dependence, d is the order of differencing applied to the data, and q is the number of terms in the moving-average dependence) with the lowest average corrected Akaike's Information Criterion were taken forward for assessment of predictive accuracy. The predictive accuracy of these models was evaluated by comparing the total absolute difference between their predicted 2019 values and the observed 2019 values. The model specification with the lowest total absolute difference and that fitted all time series was chosen to generate all time-series predictions. Further details are provided in the appendix (p 3).

Statistical analysis

Individual country counts were summed to generate WHO regional estimates and global estimates. Aggregated point estimates and variances were calculated through addition and used to calculate 95% CIs. Comparisons across study years by age group, sex, and WHO region are presented. Absolute and relative differences between groups are reported. Comparisons between observed and predicted 2020 notification counts are also reported. We compared predicted 2020 notification counts with observed counts from the 30 countries with high tuberculosis burden,[12] by age and sex, and age and WHO region. Where predicted counts are reported, point estimates and 95% prediction intervals (PIs) are included. Further information is available in the appendix (p 3).

To assess sex differences in notifications, we generated summary estimates of the proportion of notifications that were from males for age groups 0–4 years, 5–14 years, and 15 years or older, using random-effects meta-analyses for the 30 countries with a high tuberculosis burden, considering years nested within countries.

We used linear regression to examine whether there was a correlation between estimated percentage reductions in tuberculosis notifications in 2020 and magnitude of government-imposed restrictions on mixing to mitigate COVID-19, quantified as the mean of a COVID-19 stringency index for 2020 for the 30 high-burden countries (appendix pp 3–4).[13] Scatter plots and correlation coefficients were calculated for each age group separately.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

From 2014 to 2020, 73 (34%) of 215 countries had at least one missing annual count in at least one age group and sex. Of 9030 observations disaggregated by country, age group, sex, and year, 853 (9%) were missing. All countries that reported missing counts and their contributions to global notification figures are shown in the appendix (pp 2–3). From the 30 countries with a high tuberculosis burden,[12] eight included at least one missing annual count for at least one age group and sex. In total, 76 (6%) of 1260 annual counts by high tuberculosis-burden country, age group, and sex were missing.

See Online for appendix

From 2014 to 2019, global tuberculosis notifications increased in all age groups (table 1; appendix p 11). The relative increase in notifications was greatest in the 0–4 years age group, which showed a 70·3% increase (from 115 979 notifications in 2014 to 197 526 notifications in 2019), compared with a 38·3% increase (from 233 886 to 323 475) in the 5–14 years age group and a 25·0% increase (from 5 114 990 to 6 391 329) in those aged 15 years or older. The two regions with the fewest childhood tuberculosis

	Age 0–4 years				Age 5–14 years				Age ≥15 years			
	Male	Female	Difference*	Male:female ratio	Male	Female	Difference*	Male:female ratio	Male	Female	Difference*	Male:female ratio
2014	63 706	52 273	11 433	1·219	113 040	120 846	−7806	0·935	3 255 905	1 859 085	1 396 820	1·751
2015	73 319	57 900	15 419	1·266	121 347	129 457	−8110	0·937	3 426 488	1 939 862	1 486 626	1·766
2016	82 590	65 916	16 674	1·253	137 812	146 025	−8213	0·944	3 693 715	2 094 826	1 598 889	1·763
2017	89 789	70 895	18 894	1·267	141 237	144 385	−3148	0·978	3 641 494	2 094 775	1 546 719	1·738
2018	109 305	86 792	22 513	1·259	156 977	161 444	−4467	0·972	3 930 278	2 330 710	1 599 568	1·686
2019	110 224	87 302	22 922	1·263	158 996	164 479	−5483	0·967	3 998 138	2 393 191	1 604 947	1·671
2020	79 151	63 374	15 777	1·249	123 317	133 081	−9764	0·927	3 349 079	2 042 674	1 306 405	1·640

Data are n or ratio of males to females. *Number of notifications in males minus that in females.

Table 1: **Total number of notifications globally by age and sex from 2014 to 2020**

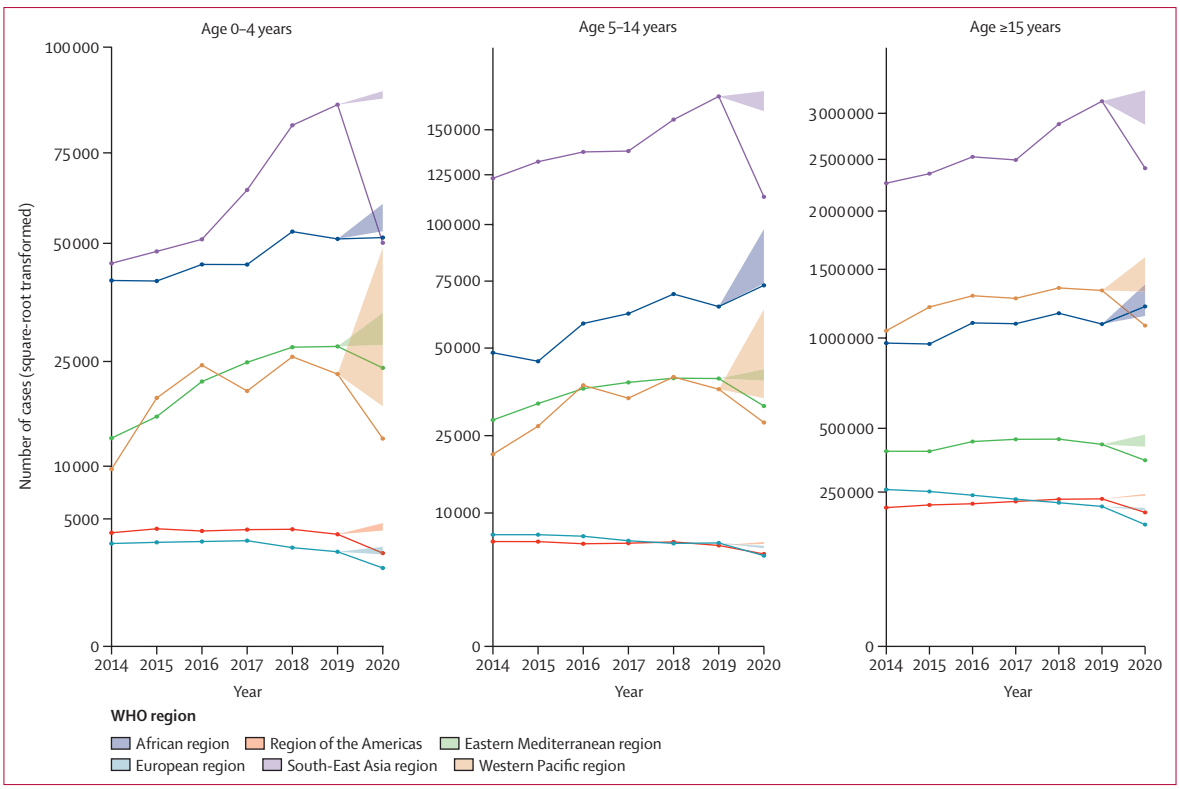

Figure 1: **Age-stratified notifications from 2014 to 2020 by WHO region**
Using data from 2014 to 2019, our model predicts notification data for 2020 with 95% prediction intervals (shaded triangles) originating from the 2019 value. Data on case numbers were square-root transformed for the purpose of visualisation.

notifications (European and American regions) had a slight decline in notifications in both the 0–4 years and 5–14 years age groups (figure 1).

Across all recorded years, more males than females were notified in the groups aged 0–4 years and 15 years or older, and more females than males in the group aged 5–14 years (table 1; appendix p 5). In the 30 countries with high tuberculosis burden, the meta-analytic summary proportions of notifications from males among all notifications in 2014–19 were 55·4% (95% CI 54·2–56·6) for those aged 0–4 years, 49·9% (48·7–51·1) for those aged 5–14 years, and 61·6% (59·6–63·5) for those aged 15 years or older (appendix p 12).

There was a notable decline in observed tuberculosis notifications in 2020 compared with 2019 in all age groups and in all regions except the African region (figure 1; appendix pp 6–7). The largest relative reduction was in the 0–4 years age group (–27·84% [from 197 526 notifications in 2019 to 142 525 notifications in 2020]) followed by the 5–14 years age group (–20·74% [from 323 475 to 256 398]) and the 15 years or older age group (–15·64% [from 6 391 329 to 5 391 753]; appendix pp 6–7). The relative decrease in notifications among males was greater than that among females across all three age groups (appendix p 6). In the 0–4 years and 5–14 years age groups, the South-East Asia and Western Pacific regions showed the greatest absolute and relative decreases in notifications among all regions (appendix pp 7, 13). Notifications increased with each consecutive year for all age groups until 2019, with a substantial decrease in 2020 (appendix p 14).

The ARIMA (2, 0, 0) with drift model was selected to generate predictions for the year 2020 (figure 1). Observed notifications in 2020 were lower than predicted notifications in all age groups and regions (table 2; appendix p 8). The 0–4 years age group showed the greatest relative reduction between observed and predicted notifications (–35·4% [95% PI –30·2 to –39·9]; 142 525 observed *vs* 220 794 [204 509 to 237 078] predicted notifications) followed by the 5–14 years age group (–27·7% [–23·4 to –31·5]; 256 398 *vs* 354 578 [334 724 to 374 431]) and the 15 years or older age group (–18·8% [–15·4 to –21·9]; 5 391 753 *vs* 6 639 547 [6 375 086 to 6 904 007]). This trend was also seen in the analysis of the 30 countries with high tuberculosis burden (figure 2; appendix p 10). On a regional basis, the Western Pacific and South-East Asia regions showed the greatest relative difference in the 0–4 years and 5–14 years age groups between observed and predicted notifications. Similar differences between predicted and observed notifications for 2020 were seen between males and females in the 0–4 years and 15 years or older age groups, whereas for the 5–14 years age group,

	Observed notifications	Predicted notifications	Difference, observed *vs* predicted	
			n	%
Age 0–4 years				
Male	79 151	122 371 (110 665 to 134 076)	−43 220 (−31 514 to −54 925)	−35·3% (−28·5 to −41)
Female	63 374	98 423 (87 101 to 109 744)	−35 049 (−23 727 to −46 370)	−35·6% (−27·2 to −42·3)
All	142 525	220 794 (204 509 to 237 078)	−78 269 (−61 984 to −94 553)	−35·4% (−30·3 to −39·9)
Age 5–14 years				
Male	123 317	178 403 (163 963 to 192 842)	−55 086 (−40 646 to −69 525)	−30·9% (−24·8 to −36·1)
Female	133 081	176 175 (162 548 to 189 801)	−43 094 (−29 467 to −56 720)	−24·5% (−18·1 to −29·9)
All	256 398	354 578 (334 724 to 374 431)	−98 180 (−78 326 to −118 033)	−27·7% (−23·4 to −31·5)
Age ≥15 years				
Male	3 349 079	4 119 747 (3 906 774 to 4 332 719)	−770 668 (−557 695 to −983 640)	−18·7% (−14·3 to −22·7)
Female	2 042 674	2 519 800 (2 363 013 to 2 676 586)	−477 126 (−320 339 to −633 912)	−18·9% (−13·6 to −23·7)
All	5 391 753	6 639 547 (6 375 086 to 6 904 007)	−1 247 794 (−983 333 to −1 512 254)	−18·8% (−15·4 to −21·9)

Data are n, n (95% PI), or % (95% PI). PI=prediction interval.

Table 2: **Global time-series predictions for 2020 generated using data from 2014–19 compared with observed notifications for 2020, by sex and age**

the difference was greater in males (–30·9% [–24·8 to –36·1]) than in females (24·5% [–18·1 to –29·9]; table 2), with variability in the direction and magnitude of sex differences across WHO regions (appendix p 9).

Across 28 countries with high tuberculosis burden (excluding North Korea and Liberia from the analysis), no correlation was observed between the COVID-19 stringency index and the percentage difference in notifications between time-series predictions and observed notifications in 2020; r^2=0·00088, p=0·88 [0–4 years]; r^2=0·036, p=0·34 [5–14 years]; and r^2=0·093, p=0·11 [≥15 years]; figure 3).

Discussion

We examined childhood tuberculosis notification data for the period from 2014 to 2020 and observed increasing notifications in the years leading up to the COVID-19 pandemic in almost all areas of the world and in all age groups. We noted more notifications among boys than girls under the age of 5 years over that period, but this discrepancy disappeared among those aged 5–14 years. In 2020, notification numbers decreased substantially compared with notifications in 2019 in all regions except for the African region. Differences between predicted notifications for 2020 and observed notifications were greatest in children aged 0–4 years.

Recent WHO statements and several modelling studies have suggested an effect of the COVID-19 pandemic on tuberculosis incidence and mortality.[14–18] WHO's provisional analysis of routine data from 84 countries indicated that an estimated 1·4 million fewer people were diagnosed with and treated for tuberculosis because of COVID-19, leading to an estimated additional half a million deaths.[19] Modelling studies have estimated substantial increases in the number of individuals who would develop tuberculosis and the number dying of tuberculosis over both short and long time intervals. Most of these increases were primarily driven by disruptions to diagnostic and treatment services leading to an increase in the number of individuals with undetected tuberculosis driving future transmission. One study evaluating the effect of COVID-19 on childhood tuberculosis notifications in India noted dramatic and sustained reductions in notifications, even after the end of restrictions.[20] However, it is important to note that from the studies conducted to date, it is not possible to quantify the relative contributions of reduced tuberculosis transmission, reduced access to diagnostic services, and the potential increased mortality in people with tuberculosis contracting COVID-19 to reductions in tuberculosis notifications.

Interpreting the reduction in notifications found in our study is complex. Because notifications are a result of both true incidence and case detection, it is plausible that at least some of this decrease in notifications is due to a real drop in childhood tuberculosis incidence. Mask wearing and reduced social interaction might have resulted in reduced transmission. Given that more than 80% of children who progress to tuberculosis disease do so within a year of exposure,[21] reductions in tuberculosis transmission could be seen as reductions in childhood tuberculosis incidence, even within a relatively short time frame. However, this reduction could also be due to reductions in health-care use.[22] Children with tuberculosis might have been less frequently taken to health-care centres, or, if they did present, been less likely to be diagnosed. During lockdown periods, many clinics were closed because of COVID-19 and when open were commonly affected by extensive staffing shortages resulting from staff being ill, caring for family members, or having to isolate following COVID-19 diagnosis. Because the diagnosis of childhood tuberculosis is more dependent on well trained staff than is the diagnosis of adult tuberculosis, it is possible that the redeployment of staff away from tuberculosis

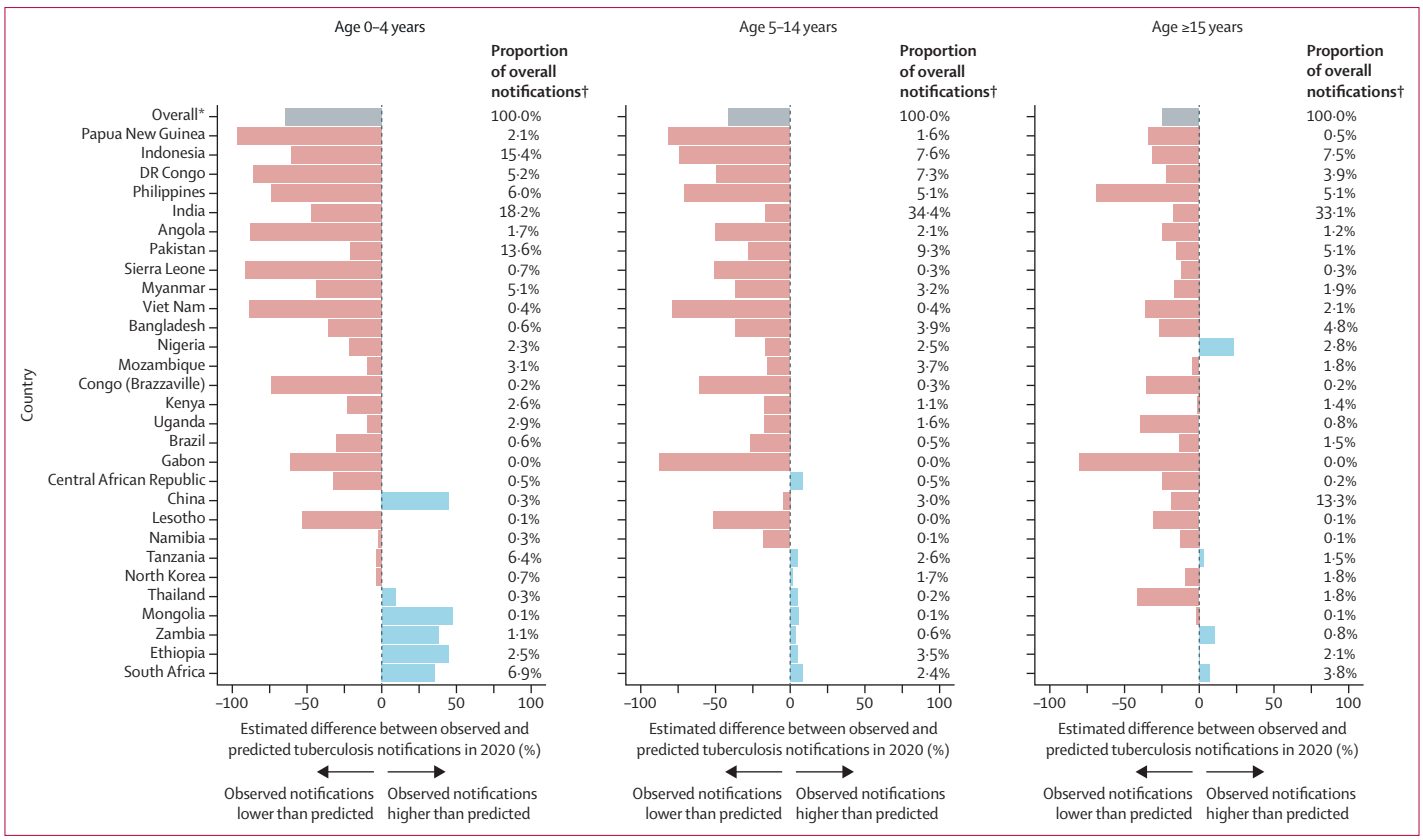

Figure 2: **Proportional difference between the number of predicted and number of observed notifications for 2020 for 29 countries with high tuberculosis burden**
Predicted notifications were from time-series modelling using data from 2014 to 2019. Liberia was excluded because of very high relative but low absolute changes in notifications. Countries are ordered by the total difference between observed and predicted values across all age groups. *Aggregates across the 29 included high-burden countries. †Proportion of overall notifications in the 29 reported high-burden countries in each age group accounted for by each country.

services affected evaluations of children more than adults. Many children presenting with cough and fever might not have been investigated appropriately for tuberculosis because of health-care workers' fears about COVID-19. In addition, parents might have been hesitant to attend health-care settings because of a fear that either they or their children might contract COVID-19. In many contexts, transport options were severely disrupted during lockdown periods, making access to health-care facilities even harder.

The finding that the WHO African region had the smallest reduction in notifications is noteworthy, yet the reasons for this finding are unclear. Because of generally younger population demographics, it is possible that fewer severe cases of COVID-19 developed per capita, placing fewer constraints on health services and allowing tuberculosis services to continue with less disruption. It is also possible that less severe government restrictions permitted ongoing transmission of tuberculosis, as well as leaving tuberculosis diagnostic services less affected.

The sex differences in tuberculosis notifications before COVID-19 are also notable. Although extensively studied in adults,[23] only a few studies have evaluated these sex differences in children.[24] For overall respiratory morbidity, male sex in childhood has been associated with increased hospital admission for respiratory illnesses;[25] however, it has generally been assumed that before puberty, tuberculosis in boys and girls was similar from epidemiological and immunological perspectives. Yet, consistently, in all WHO regions, we found that substantially more boys aged 0–4 years were notified for tuberculosis each year. This disparity could reflect genuine differences in tuberculosis incidence, potentially driven by differences in exposure, differences in immunological response to *M tuberculosis*,[26] or differential protection from the BCG vaccine.[27] However, it could also reflect gender-driven differences in care-seeking behaviour, with caregivers more willing to expend the necessary time and resources to access health-care for boys as opposed to girls. The disparity might also reflect attitudes of clinical staff evaluating children. The disappearance of this imbalance in the 5–14 years age group could reflect the onset of puberty being earlier in girls than boys, leading to increased female susceptibility to progression from *M tuberculosis* infection to tuberculosis disease,[28] or gender-related differences in other risk factors for tuberculosis (eg, HIV, nutrition, or social mixing patterns) and care-seeking behaviour. A surprising finding from

this study is that the difference between observed and predicted notifications for 2020 was greater for boys aged 5–14 years than for girls. This might reflect a greater reduction in tuberculosis incidence in boys than girls in this age group or could indicate that fewer boys than girls with tuberculosis in this age group were identified because of the pandemic. Differential decreases in incidence might be a consequence of greater protection of boys of this age from tuberculosis exposure, sex differences in the effect of SARS-CoV-2 infection on tuberculosis disease progression, or variations in socioeconomic consequences of COVID-19 affecting tuberculosis risk. Differential case detection might relate to gender differences in health-care access or willingness of caregivers to seek care. As this age group is largely in education, the role of school attendance on both tuberculosis and COVID-19 risk might be highly relevant. Given the importance of these sex and gender differences in tuberculosis notifications and the substantial implications for health-care delivery, far more work in this area is merited to better understand the mechanisms driving this disparity.

Our analysis has limitations. We used routine data reported by the public health sector in all countries across the world. Therefore, variations in reporting standards or missing data could have created artifactual trends. In addition, we were only able to look at the crude age cutoffs of 0–4 years and 5–14 years; more granular age disaggregation might help us to better understand the differences in the sex ratios of notifications. Our analysis shows a decrease in observed notifications in 2020 compared with predicted notifications for 2020 based on a time-series model using data from 2014–19, but does not in itself provide a causal link between COVID-19 and tuberculosis notifications. In addition, the COVID-19 stringency index used here does not capture all the effects of COVID-19. Our hypothesised relationship between health-care access and movement restrictions used a stringency index that was calculated using daily data from 2020 and compared this with an estimated deficit in 2020 notifications. It might be that notifications for 2021 will better reflect the stringency index for 2020. However, such ecological analyses are susceptible to confounding,

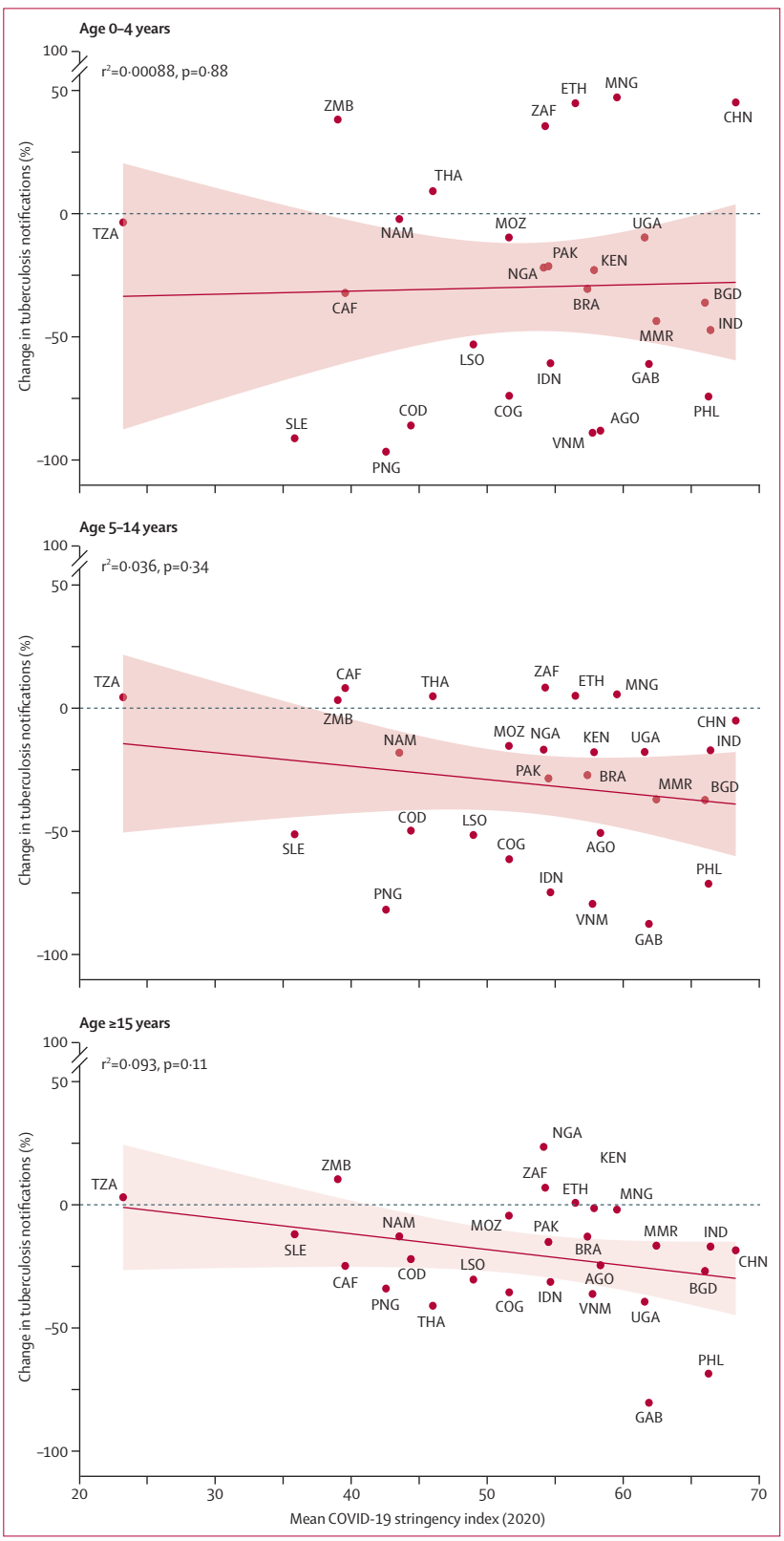

Figure 3: **Age-stratified correlations between mean COVID-19 stringency index and percentage difference in tuberculosis notifications between time-series predictions and observed notifications in 2020 for 28 countries with high tuberculosis burden**

Liberia was excluded because of very high relative but low absolute changes in notifications, and North Korea was excluded because of the lack of a stringency index. Countries are indicated by their three-letter ISO 3166 codes. AGO=Angola. BGD=Bangladesh. BRA=Brazil. CAF=Central African Republic. CHN=China. COD=Democratic Republic of the Congo. COG=Congo. ETH=Ethiopia. GAB=Gabon. IDN=Indonesia. IND=India. KEN=Kenya. LSO=Lesotho. MMR=Myanmar. MNG=Mongolia. MOZ=Mozambique. NAM=Namibia. NGA=Nigeria. PAK=Pakistan. PHL=Philippines. PNG=Papua New Guinea. SLE=Sierra Leone. THA=Thailand. TZA=Tanzania. UGA=Uganda. VNM=Viet Nam. ZAF=South Africa. ZMB=Zambia. *Negative values indicate number of observed notifications was lower than predicted; positive values indicate number of observed notifications was higher than predicted.

and the stringency index only included government-directed restrictions on mixing.

Our analysis suggests that childhood tuberculosis notifications decreased substantially in 2020 compared with the number predicted, and that children aged 0–4 years had the greatest shortfall in notifications, probably representing, at least in part, missed cases. Many of these cases will have resulted in death from tuberculosis or led to more severe disease, leading to long-term morbidity. Although children largely escaped many of the damaging direct effects of COVID-19, it is likely that they have been substantially affected by the consequences of the pandemic on tuberculosis care. Delineating the groups that have been particularly affected by the COVID-19-related disruptions to tuberculosis care should motivate targeted interventions to mitigate any detrimental effects that the pandemic has had on the path towards ending tuberculosis. As health programmes seek to rebuild in the aftermath of COVID-19, substantial investment will be required to make up the deficits that have been seen in the field of childhood tuberculosis.

Contributors

LR and JAS conceived the study. LR, JA, and PJD did the data analysis. LR, JA, MG, EW, PJD, and JAS contributed to designing the methods, critiquing the results, writing the first draft of the article, and revising and editing the submitted article. LR, JA, PJD, and JAS accessed and verified the data underlying the study. All authors had final responsibility for the decision to submit for publication and all authors approved the final version.

Declaration of interests

We declare no competing interests.

Data sharing

To **access the code used in this study** see https://github.com/JayAchar/tb-covid-child-notifications

Code used in this study can be accessed through GitHub. All analyses used publicly available data.

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