

Tuberculosis Incidence Trends from 1990 to 2017 Highlight Impact of Drug Resistance: Results from the Global Burden of Disease Study

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Abstract

Objectives This study aimed to determine the global incidence trends of tuberculosis (TB) from 1990 to 2017.

Methods Data was obtained from the Global Burden of Disease (GBD) study. The estimated annual percentage changes (EAPCs) were calculated with the age-standardised incidence rate (ASIR) to estimate trends in incidence of TB, including multidrug-resistant TB (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).

Results Globally, the number of TB cases was 8965.81×10^3 in 2017, with a 9.42% increase since 1990. The ASIR for TB showed a decreasing trend from 1990 to 2017 (EAPC = -1.19 , 95% confidence interval [CI]: -1.32 to -1.07). Meanwhile, decreasing trends were observed in 162 countries/territories, particularly in Ethiopia and China where EAPCs were -4.51 (95%CI: -5.22 to -3.80) and -4.21 (95%CI: -4.98 to -3.44), respectively. However, obvious increasing trends of MDR-TB cases occurred in areas with low and low-middle sociodemographic indexes (SDI), with EAPCs of 7.97 (95%CI: 2.47 to 13.75) and 6.30 (95%CI: 1.17 to 11.68), respectively. The ASIR for XDR-TB showed pronounced increasing trends globally from 1991 to 2017, with an EAPC of 11.74 (95%CI: 7.50 to 16.16). The largest rising trends of XDR-TB were observed in Kyrgyzstan (EAPC = 31.06 , 95%CI: 23.07 to 39.57), followed by Azerbaijan and Uzbekistan.

Conclusions There was a decreasing trend for TB incidence worldwide, although it was more pronounced in specific countries and regions. However, the rapidly rising trends of MDR-TB and XDR-TB cases in low and low-middle SDI areas and countries may have an adverse impact on the global control of TB.

Introduction

Tuberculosis (TB) is one of the most important infectious diseases worldwide, and significant success in controlling the transmission of the infection has been achieved. However, antituberculosis drug resistance has become an important health concern in recent years (1).

Over the past decades, epidemiological patterns of TB have changed dramatically. In 2008, over 9 million new cases of TB were diagnosed worldwide, and more than one million individuals died (2). In recent years, there has been a declining trend in the global incidence and mortality rates of TB (3). The 2018 Global Tuberculosis Report reported that the incidence of TB fell by about 2% per year during 2000–2017 (4). However, global control of TB is strongly influenced by antituberculosis drug resistant bacteria (5). Multidrug-resistant tuberculosis (MDR-TB) is caused by *Mycobacterium tuberculosis* strains, which are resistant to at least isoniazid (INH) and rifampin (6). In 1994, the World Health Organization (WHO) launched a global program on surveillance of drug-resistant tuberculosis, and the results showed that the occurrence of MDR-TB had increased dramatically worldwide (7). Globally, MDR-TB was estimated to be approximately 460,000 cases in 2017, which accounted for 3.6% of all new cases and 17% of previously treated cases (4). China, India, Russia, and South Africa experienced the highest burden of MDR-TB,

accounting for as much as > 60% of all cases globally (8). Furthermore, an estimated 6.7% of MDR-TB patients were also resistant to fluoroquinolones and second-line injectable drugs, and these cases are defined as extensively drug-resistant tuberculosis (XDR-TB) (4, 9). Furthermore, this scenario worsened following an inundation of drug use and human immunodeficiency virus (HIV) infection, which accelerated the development of drug resistance (10).

Antituberculosis drug resistance has become an increasing threat to global public health. Therefore, it is necessary to track trends in TB burden including MDR-TB and XDR-TB with the latest data from the Global Burden of Disease (GBD) study. In this study, we investigated the incident trends of TB from 1990 to 2017 to facilitate improvement of TB control strategies.

Methods

Data source

Data sources for the TB burden were explored using the Global Health Data Exchange (GHDx) query tool (<http://ghdx.healthdata.org/gbd-results-tool>). We obtained data on the incidence of TB and MDR-TB from 1990 to 2017 stratified by sex, age, subtype, sociodemographic index (SDI) area, geographic region, and country, whereas data relative to XDR-TB were available from 1991 to 2017. The SDI was classified into 5 categories: low, low-middle, middle, high-middle, and high. Data was available for 21 geographic regions and 195 countries/territories worldwide. The methodologies for estimation of disease burden have been described in detail in previous studies (11). Data on the Human Development Index (HDI) were obtained from the United Nations Development Program (<http://hdr.undp.org/en/data>).

Statistical analysis

The age-standardised rate (ASR) is a necessary and representative index when considering differences in the age structure of multiple populations, and is calculated using the following formula:

$$ASR = \frac{\sum_{i=1}^A a_i w_i}{\sum_{i=1}^A w_i} \times 100,000$$

where a_i is the age-specific rate in the i^{th} age group, w is the number of people (or the weight) in the corresponding i^{th} age group from among the selected reference standard population, and A is the number of age groups.

The estimated annual percentage changes (EAPCs) is a reliable method for describing the magnitude of the trends in ASR (12). A regression line is fitted to the natural logarithm of the rates, for example, $y = \alpha + \beta x + \epsilon$, where $y = \ln(ASR)$ and $x = \text{calendar year}$. The EAPC was estimated as $100 \times (\exp(\beta) - 1)$, and its 95% confidence interval was calculated using the linear regression model. Based on the above calculations, trends were assessed as follows: the EAPC value and respective 95%CI > 0 was used to define an

increasing trend in ASR; and the EAPC value and respective 95% CI < 0 defined a decreasing trend in ASR; other values indicated that ASR was stable over time. Pearson's correlation analysis was used to detect factors influencing EAPCs at a national level, including ASR and HDI in 1990 and 2017. Data were analysed using the Statistical Package for Social Sciences (SPSS; version 25.0; SPSS Inc., Chicago, IL, USA). Choropleth maps were drawn using an R program (version 3.6.2).

Results

Trends in incidence of TB

Globally, the incidence of TB was 8965.81×10^3 (95%UI: 8191.85×10^3 to 9820.79×10^3) in 2017, corresponding to an increase of 9.42% from 1990 (Table 1). The overall ASIR decreased by an annual average of 1.19% during 1990–2017 (EAPC = - 1.19, 95%CI: -1.25 to - 1.13). The decreasing trend in ASIR of TB was more obvious in females, with the EAPC of - 1.28 (95%CI: -1.35 to - 1.21). When comparing different age groups, the highest increase in number of TB cases was observed in age groups above 70 years, and a decrease in the number of TB cases occurred in age groups under 14 globally (see web-only Supplementary Table S1). Decreasing trends of TB were observed in most SDI areas and geographic regions. All SDI areas showed a decreasing trend of ASIR, particularly in high-middle SDI areas (EAPC = - 2.83, 95%CI: -3.07 to - 2.59). In terms of geographic regions, the largest increase in incidence was found in Central Sub-Saharan Africa (81.66%), followed by Oceania (64.78%) and Eastern Sub-Saharan Africa (62.39%), while the largest decrease was in East Asia (- 49.05%) (Table 1). The decreasing trends in ASIR of TB occurred in 19 geographic regions, and those with the largest decrease were in East Asia (EAPC = - 4.05, 95%CI: -4.38 to - 3.72), followed by Andean Latin America and high-income North America (Table 1, Figs. 1 and 2). Among the 195 countries/territories, the highest increased change in the incidence of TB cases occurred in the United Arab Emirates (257.45% increase), while the strongest decrease (- 58.62%) was seen in Estonia (see web-only Supplementary Table S2, Fig. 3). The ASIR of TB showed decreasing trends in 168 countries/territories, particularly in Ethiopia and China, in which the EAPCs were - 4.51 (95%CI: -5.00 to - 4.02) and - 4.21 (95%CI: -4.56 to - 3.87), respectively (see web-only Supplementary Table S2, Fig. 3). However, increasing trends occurred in 17 countries/territories, and the largest increase occurred in Kenya (EAPC = 2.10, 95% CI: 1.71 to 2.49), followed by Lesotho and Ukraine (see web-only Supplementary Table S2, Fig. 3). The EAPCs (2000–2017) showed a positive correlation with the ASIR in 1990, and a negative association with the HDI in 2017 at a national level ($\rho = 0.23$, $p = 0.01$, Fig. 10A; $\rho = -0.26$, $p < 0.001$, Fig. 10B, respectively).

Table 1

The number and age-standardised rate of tuberculosis incidence globally and stratified by sex, SDI areas and geographic regions in 1990 and 2017, and the percentage change in the absolute number of cases and the EAPCs from 1990 to 2017

	1990		2017		1990–2017	
Characteristics	Number	ASR per 100 k	Number	ASR per 100 k	Percentage change in absolute number (%)	EAPCs No. (95%CI)
	No.×10 ³ (95% UI)	No. (95% UI)	No.×10 ³ (95% UI)	No. (95% UI)		
Overall	8194.03 (7476.18–9014.58)	156.59 (143.02–171.37)	8965.81 (8191.85–9820.79)	115.78 (105.79–126.95)	9.42	-1.19 (- 1.25 to - 1.13)
Sex						
Male	4213.78 (3845.21–4609.42)	167.53 (153.86–182.49)	4913.77 (4499.26–5375.83)	126.57 (116.25–137.97)	16.61	-1.13 (- 1.20 to - 1.07)
Female	3980.25 (3616.03–4389.58)	148.16 (135.07–163.1)	4052.04 (3689.23–4447.33)	106.17 (96.62–116.67)	1.80	-1.28 (- 1.35 to - 1.21)
SDI						
Low	2147.49 (1964.12–2354.29)	377.33 (346.05–410.62)	3081.85 (2809.34–3392.95)	277.77 (255.4–302.38)	43.51	-1.18 (- 1.25 to - 1.12)
Low-middle	2403.69 (2198.44–2639.18)	268.08 (247.07–290.59)	2940.34 (2684.15–3229.73)	185.65 (170.59–201.77)	22.33	-1.38 (- 1.45 to - 1.31)
Middle	2431.81 (2205.75–2688.37)	169.49 (154.83–185.08)	2123.69 (1941.70–2325.71)	98.20 (89.85–107.32)	-12.67	-2.02 (- 2.06 to - 1.99)
High-middle	963.52 (873.52–1065.25)	86.77 (79.00–95.58)	666.03 (608.42–729.37)	43.78 (39.97–47.72)	-30.88	-2.83 (- 3.07 to - 2.59)

EAPC: estimated annual percentage change; ASR, age-standardised rate; CI, confidence interval; UI: uncertainty interval; SDI: socio-demographic index. Percentage change in absolute number was calculated based on the crude data.

	1990		2017		1990–2017	
High	214.91 (191.96– 241.01)	20.64 (18.42– 23.3)	135.65 (125.09– 146.93)	9.98 (9.13– 10.90)	-36.88	-2.71 (- 2.82 to - 2.60)
Regions						
East Asia	1770.77 (1610.58– 1954.82)	144.88 (132.56– 158.41)	902.29 (823.24– 987.73)	55.94 (51.06– 61.02)	-49.05	-4.05 (- 4.38 to - 3.72)
South Asia	2734.76 (2493.13– 3018.24)	294.27 (269.81– 320.92)	3432.76 (3132.77– 3765.86)	205.34 (188.55– 224.02)	25.52	-1.29 (- 1.35 to - 1.23)
Southeast Asia	1023.97 (929.33– 1138.69)	251.89 (230.31– 275.82)	964.54 (878.85– 1056.06)	149.42 (136.93– 162.47)	-5.80	-1.90 (- 2.07 to - 1.74)
Central Asia	63.38 (56.91– 70.58)	94.63 (85.28– 104.85)	73.65 (67.25– 80.66)	79.05 (72.39– 85.96)	16.20	-0.86 (- 1.32 to - 0.40)
High-income Asia Pacific	91.05 (80.64– 102.64)	47.90 (42.49– 54.13)	56.77 (52.33– 61.3)	20.91 (19.21– 22.73)	-37.65	-2.73 (- 3.06 to - 2.40)
Oceania	9.88 (8.96– 10.97)	176.37 (161.53– 192.86)	16.28 (14.69– 18.16)	138.76 (126.33– 152.26)	64.78	-1.10 (- 1.29 to - 0.91)
Australasia	1.57 (1.38– 1.79)	7.55 (6.64– 8.6)	1.65 (1.50– 1.79)	5.68 (5.15– 6.22)	5.10	-0.81 (- 1.05 to - 0.56)
Eastern Europe	144.22 (128.78– 161.67)	61.11 (54.60– 68.50)	141.27 (126.67– 157.05)	60.32 (54.23– 66.78)	-2.05	0.21 (- 0.32– 0.75)
Western Europe	51.51 (45.21– 59.13)	13.17 (11.52– 15.21)	31.81 (28.91– 34.97)	7.89 (7.06– 8.79)	-38.25	-1.66 (- 1.78 to - 1.54)

EAPC: estimated annual percentage change; ASR, age-standardised rate; CI, confidence interval; UI: uncertainty interval; SDI: socio-demographic index. Percentage change in absolute number was calculated based on the crude data.

	1990		2017		1990–2017	
Central Europe	39.77 (35.64–43.91)	30.27 (27.18–33.54)	26.62 (24.63–28.67)	19.94 (18.38–21.51)	-33.07	-2.03 (- 2.34 to - 1.72)
High-income North America	15.65 (13.84–17.64)	5.18 (4.59–5.87)	9.69 (8.73–10.84)	2.51 (2.25–2.81)	-38.08	-3.11 (- 3.4 to - 2.82)
Andean Latin America	54.17 (49.36–59.64)	158.70 (146.05–172.85)	40.43 (36.97–44.36)	66.55 (61.03–72.81)	-25.36	-3.69 (- 4.01 to - 3.38)
Central Latin America	37.17 (33.69–41.14)	29.06 (26.62–31.77)	47.37 (43.28–52.2)	18.65 (17.09–20.49)	27.44	-2.13 (- 2.34 to - 1.93)
Caribbean	15.93 (14.58–17.5)	45.75 (41.97–50.06)	15.71 (14.31–17.28)	33.41 (30.34–36.68)	-1.38	-1.23 (- 1.42 to - 1.05)
Tropical Latin America	58.35 (51.97–65.98)	42.48 (38.07–47.71)	70.87 (63.5–79.84)	30.03 (26.89–33.7)	21.46	-1.65 (- 1.79 to - 1.50)
Southern Latin America	10.64 (9.59–11.88)	21.72 (19.62–24.21)	8.48 (7.85–9.15)	12.53 (11.57–13.54)	-20.30	-2.31 (- 2.54 to - 2.08)
Eastern Sub-Saharan Africa	691.34 (631.29–757.06)	442.10 (404.97–483.88)	1122.69 (1021.94–1238.74)	315.86 (289.27–346.1)	62.39	-1.34 (- 1.55 to - 1.13)
Southern Sub-Saharan Africa	272.85 (246.01–301.34)	528.83 (480.24–580.35)	345.38 (308.85–386.87)	430.09 (388.77–477.49)	26.58	0.52 (0.09–0.95)
Western Sub-Saharan Africa	615.49 (565.31–671.29)	393.42 (362.79–426.17)	912.74 (836.25–999.91)	258.94 (238.85–282.09)	48.29	-1.70 (- 1.79 to - 1.62)

EAPC: estimated annual percentage change; ASR, age-standardised rate; CI, confidence interval; UI: uncertainty interval; SDI: socio-demographic index. Percentage change in absolute number was calculated based on the crude data.

	1990		2017		1990–2017	
North Africa and Middle East	221.10 (200.94–243.18)	71.41 (65.35–78.11)	253.52 (228.39–281.59)	43.44 (39.48–47.93)	14.66	-1.99 (- 2.05 to - 1.93)
Central Sub-Saharan Africa	270.45 (245.85–296.71)	615.27 (562.23–672.39)	491.30 (443.99–544.68)	504.77 (459.88–551)	81.66	-0.73 (- 0.82 to - 0.65)
EAPC: estimated annual percentage change; ASR, age-standardised rate; CI, confidence interval; UI: uncertainty interval; SDI: socio-demographic index. Percentage change in absolute number was calculated based on the crude data.						

Trends in incidence of MDR-TB

Globally, the number of incident MRD-TB cases increased 642.57% from 1990 to 2017, and was 432.77×10^3 (95% UI: 254.61×10^3 – 726.95×10^3) in 2017 (see web-only Supplementary Table S3, Fig. 1). The trend in ASIR of MDR-TB showed an increasing trend globally from 1990 to 2017, with an EAPC of 2.59 (95% CI: 1.01 to 4.20) (see web-only Supplementary Table S3). The largest increase in the number of incident cases of MDR-TB occurred in low SDI areas (4447.76%) (see web-only Supplementary Table S3, see web-only Supplementary Figure S1). The ASIR of MDR-TB showed increasing trends in low-middle SDI areas, and particularly in low SDI areas (EAPC = 7.97, 95% CI: 5.52 to 10.46). For 21 geographic regions, the number of incident cases of MDR-TB decreased in East Asia and high-income North America, and conversely, increased in other regions, particularly in Central Asia (16566.67%) (see web-only Supplementary Table S3 and Supplementary Figure S1). The increasing trends in ASIR were found in 10 geographic regions, especially in Central Asia (EAPC = 14.19, 95%CI: 10.2 to 18.33), followed by Oceania and South Asia. Among the 195 countries/territories, the highest increase in the number of incident cases was observed in Azerbaijan (60486.61%), whereas the highest decrease was observed in Slovenia (-78.01%) (see web-only Supplementary Table S6, Supplementary Figure S5). The ASIR for MDR-TB showed rising trends in 133 countries/territories, particularly Kyrgyzstan, Azerbaijan, and Uzbekistan, in which the EAPCs were 19.95 (95%CI: 15.54 to 24.52), 18.86 (95%CI: 14.5 to 23.39), and 18.84 (95%CI: 14.31 to 23.56), respectively. However, trends in the ASIR for MDR-TB decreased in 33 countries/territories, and the most pronounced decreases occurred in Slovenia and Japan, in which the EAPCs were -7.81 (95%CI: -9.77 to -5.79) and -6.77 (95%CI: -8.51 to -4.99), respectively (see web-only Supplementary Table S5 and Supplementary Figure S3). The EAPCs had a positive association with the HDI in 2017 at the national level ($\rho = -0.20$, $p = 0.01$, see web-only Supplementary Figure S5), but not with the ASIR in 1990.

Incidence trends of XDR-TB

Globally, the incident cases of XDR-TB increased 5726.19% from 1991, and was 24.47×10^3 (95% UI: $17.68-35 \times 10^3$) in 2017 (see web-only Supplementary Table S4). The ASIR of XDR-TB showed an increasing trend (EAPC = 11.74, 95% CI: 9.05 to 14.50) (see web-only Supplementary Table S4, Fig. 1). Increasing changes in the number of incident cases of XDR-TB were found across all age groups globally, especially in individuals aged between 50 and 69 years (Table S1, see web-only Supplementary Figure S2). Increasing trends in the ASIR for XDR-TB were observed stratifying cases by sex, SDI area, and geographic region from 1991 to 2017, and were particularly evident for the low and low-middle SDI areas, in which EAPCs were 20.30 (95%CI: 16.08 to 24.67) and 13.85 (95%CI: 11.12 to 16.65), respectively (see web-only Supplementary Table S4 and Supplementary Figure S2). Central Asia and Oceania had the most pronounced increasing trends, with the EAPCs of 25.46 (95%CI: 20.16 to 30.99) and 24.75 (95%CI: 21.57 to 28.02), respectively. Furthermore, the pronounced increasing trends in ASIR of XDR-TB were observed in 192 countries/territories, particularly Kyrgyzstan, Azerbaijan, and Uzbekistan, in which the EAPCs were 31.06 (95%CI: 25.44 to 36.93), 29.97 (95%CI: 24.53 to 35.66), and 29.96 (95%CI: 24.15 to 36.06), respectively (see web-only Supplementary Tables S4 and S5, and Supplementary Figure S4). No association was found between EAPCs and the ASIR in 1990, and the HDI in 2017 at a national level.

Discussion

In this study, a decreasing trend in the global incidence of TB was observed from 1990 to 2017, likely due to effective strategies of disease prevention and control established in previous decades, such as poverty reduction, improvement in health infrastructure, vaccination programmes, and international cooperation (13). Differences in the incidence of TB existed in countries and regions based on demographic and socioeconomic status. The fastest decrease in ASR for TB occurred in high-middle and high SDI areas. This might also be associated with economic status and health-related behaviour (14). For example, East Asia had the fastest decline in the number of TB cases, which might be explained by a reduction in poverty and under-nutrition combined with increased funding for TB control activities (15). Meanwhile, the largest decrease in trend in ASIR of TB cases was observed in China. The Chinese government had achieved great success in the control of TB due to the revitalization of anti-TB programs in the 1990s. Meanwhile, national initiatives associated with anti-TB strategies were also endorsed, including reducing poverty, improving health infrastructure, and infectious disease management (16). However, an increasing trend still existed in several countries across Eastern Europe and Sub-Saharan Africa, characterised by population expansion, poverty, and poor health infrastructure (17). Several practical strategies, such as extensive scale-up of the availability of health extension workers and the adoption of the Directly Observed Treatment Short-Course strategy (18), probably explain why Ethiopia had the highest decline in ASIR of TB. However, increasing trends in DS-TB also occurred in some countries, such as Norway, a country with a previously low incidence of TB, which was probably attributed to the ageing population (19).

Targets were established for the End TB Strategy, for example, to reduce tuberculosis incidence by 80% in 2030 compared to 2015 (20). However, the rapid development of antituberculosis drug resistance has

threatened the targeted strategies for TB control. The numbers of incident cases and ASIR for MDR-TB and XDR-TB have dramatically increased in areas of low and low-middle SDI areas and countries. In these areas and countries, poverty, malnutrition, and overloaded health systems were still the main social factors associated with the incidence of TB (21). The highest increased change in ASIR of MDR-TB and XDR-TB cases occurred in the former Soviet countries of Kyrgyzstan, Azerbaijan, and Uzbekistan, and was associated with TB patients having a higher risk of developing antituberculosis drug resistance (22), and in countries where there had been a lack of proper implementation of the DOTS strategy (23). Furthermore, the situation deteriorated further with the spread of drug use and increased incidence of HIV infection (24, 25). In contrast, only seven countries/territories showed a decrease in the trend of ASIR for MDR-TB cases, with the largest decrease being observed in Slovenia, where rigorous TB prevention and treatment programs had been established (26).

The limitations of this study should be considered. The GBD study incidence estimates depended on the quality and quantity of the collected data and on the potential biases from misclassification and/or miscoding of disease by different countries, which may have affected the accuracy and robustness of the results. The diagnosis and detection of drug resistance also varied across countries and over time, which may have caused a potential bias. Although age is an important factor, due to the limitations of the ASR formula, this study estimated trends using the percentage change in the incident number across age groups only.

Conclusion

This study found that there was a global decrease in the incidence of TB between 1990 and 2017 across most areas with different SDI and across different geographic regions. However, the rapidly increasing trend in resistance to antituberculosis drugs has had a significant impact on the control of TB worldwide. There remains a huge challenge in the global control of TB, and more efficient prevention and diagnostic strategies and increasing investment to health infrastructure are urgently needed.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Conflict of interests

The authors declare that they have no competing interests.

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Authors' contributions

ZJO, WQH: Project administration and drafting.

DFY, YHL: Data analysis and validation.

YZL, YHG: Data analysis and visualization.

MYZ, HH, FW: Data collection and collation.

QC: supervision and drafting and editing.

All authors read and approved the final manuscript.

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Figures

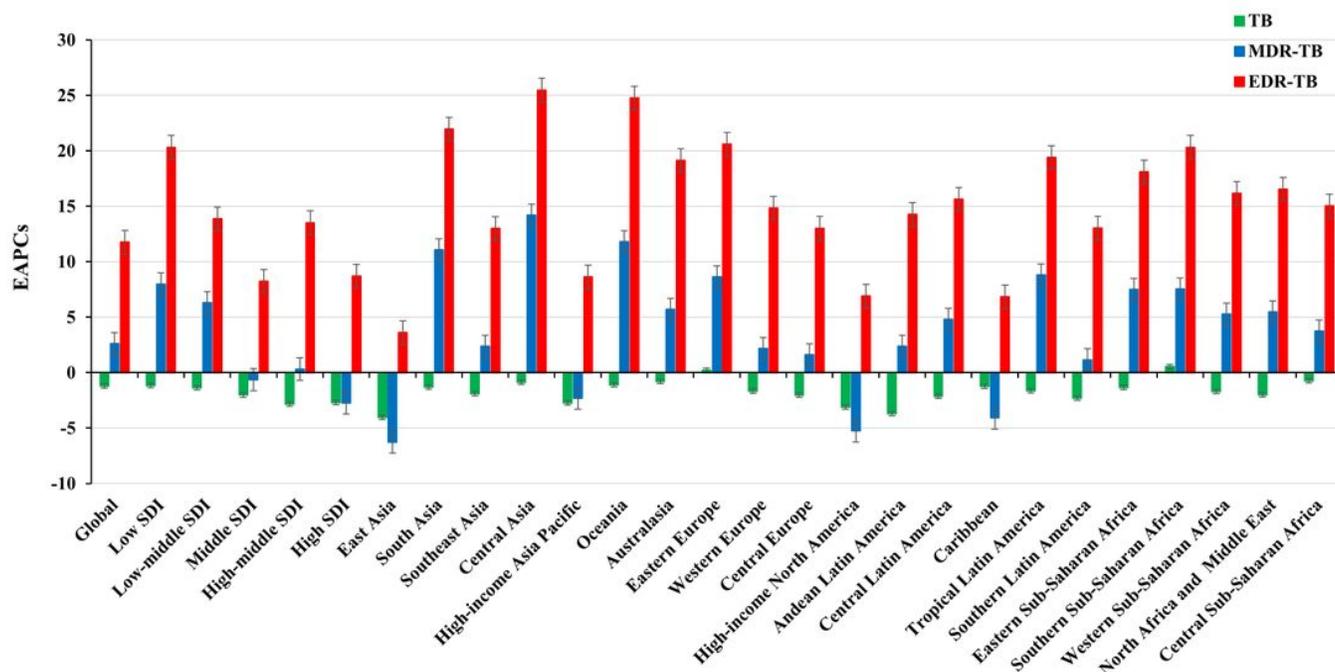


Figure 1

Trends in TB burden including TB, MDR-TB, and XDR-TB, globally and stratified by SDI areas and geographic regions from 1990 to 2017.

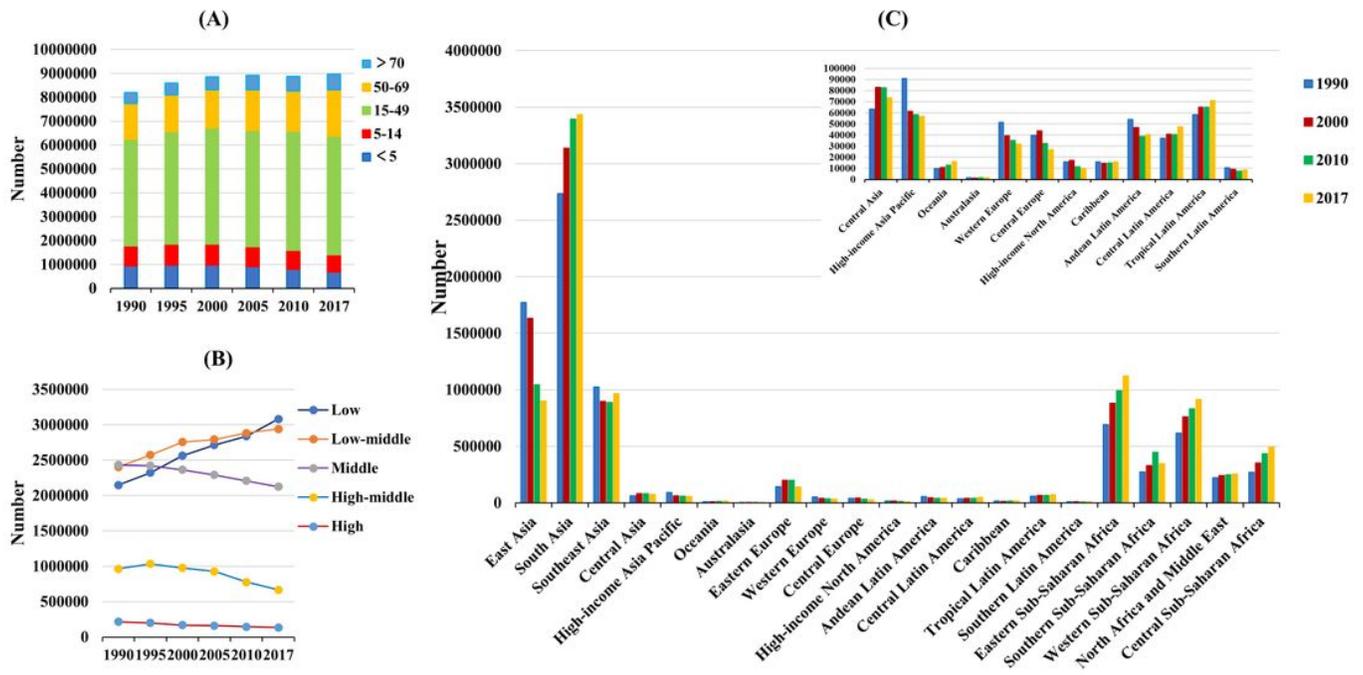


Figure 2

The distribution in the global incidence of TB, and in SDI areas and geographical regions from 1990 to 2017. (A) The incidence of TB across age groups; (B) Change in incidence of TB in SDI areas; (C) Incidence of TB in geographical regions.

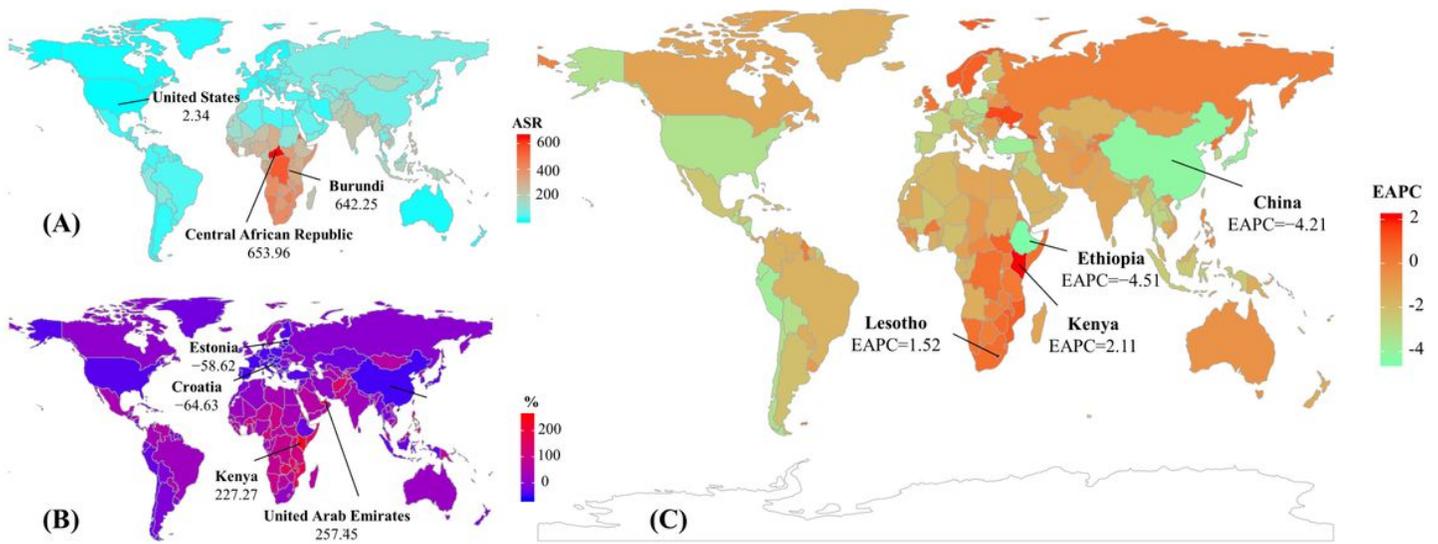


Figure 3

The distribution of ASR, percentage changes in absolute number, and EAPCs of TB incidence at national levels from 2000 to 2017, including (A) the ASIR of TB in 2017, (B) the percentage change in the absolute number of TB cases between 1990 and 2017, and (C) the EAPCs of TB. Countries/territories with extreme values were annotated. ASIR, age-standardised incident rate; EAPC, estimated annual percentage change. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

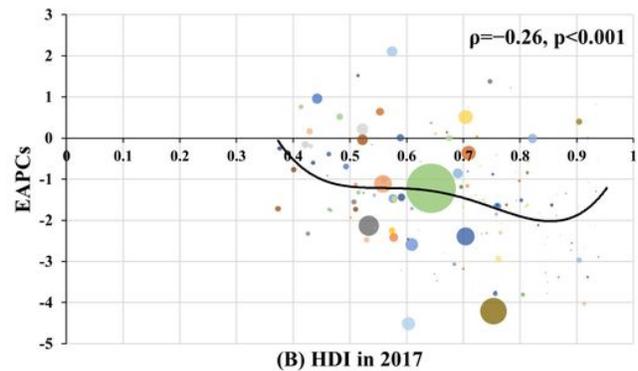
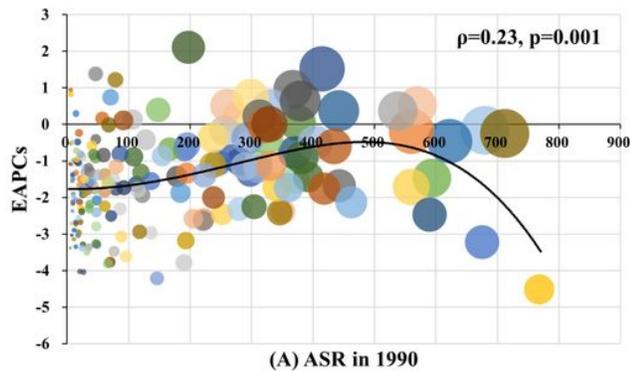


Figure 4

The correlation between EAPCs and ASIR in 1990, and HDI in 2017 at national levels. The EAPCs of TB were positively associated with the ASIR in 1990 (A), and negatively associated with the HDI in 2017 (B). ASIR, age-standardised incident rate; EAPC, estimated annual percentage change; HDI, human development index.

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