Yang et al. BMC Public Health (2024) 24:3111
https://doi.org/10.1186/s12889-024-20664-w

BMC Public Health

DATABASE

Open Access

Global, regional, and national burden of tuberculosis and attributable risk factors for 204 countries and territories, 1990–2021: a systematic analysis for the Global Burden of Diseases 2021 study

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Abstract

Background Tuberculosis (TB) remains a major global health threat. Despite ongoing efforts to control and eradicate TB, various factors including socioeconomic issues, policy modifications, and unexpected public health crises like COVID-19 pandemic have posed new obstacles to achieving TB elimination. This study aims to analyze the changes in global tuberculosis burden over the past 32 years, and provide scientific support for global initiatives targeting the eradication of TB in the post-pandemic period.

Methods The data for this study were obtained from the Global Burden of Disease (GBD) 2021 database, with age-standardized incidence rate (ASIR), prevalence rate (ASPR), mortality rate (ASDR), and disability-adjusted life years (DALYs) as the primary assessment indicators. Dynamic changes in the TB burden were analyzed by estimating the annual percentage changes (EAPCs). The attributable ratios of six main risk factors to TB burden were calculated, and the correlation between the Socio-Demographic Index (SDI) and the TB burden was analyzed using Pearson correlation tests.

Results The global TB incidence decreased from 8.6 million cases in 1990 to 8.4 million cases in 2021, with a corresponding decline in deaths. However, the TB burden remains higher among men than women. The highest incidence and mortality rates were observed in the age group of 15–69 years, with a notable gender disparity, especially in Eastern Europe. These rates were generally elevated in low-income and lower-middle-income regions, with significantly higher Age-Standardized Incidence Rates and Age-Standardized Death Rates in males compared to females. A significant negative correlation was found between SDI values and TB burden. Analyzing risk factors from the Global Burden of Disease study, it was determined that globally, dietary risks, high body-mass index, high fasting plasma glucose, low physical activity, tobacco, and alcohol use were the main contributors to TB age-standardized

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Disability-Adjusted Life Years, with tobacco and alcohol use having the most significant impact. Analysis of risk factors suggests that tailored public health interventions for specific genders and regions can effectively lessen the TB burden.

Keywords Tuberculosis, Disease burden, Systematic analysis, Post-pandemic period, Preventive strategies, Socio-demographic factor

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* (MTB), primarily transmitted via airborne particles. It remains a significant global public health issue and is one of the leading causes of death from infectious disease worldwide [1]. According to the World Health Organization (WHO), in 2022, there were 10.6 million new cases of TB. Approximately 1.3 million deaths were attributed to TB, which include 167,000 cases of TB/HIV co-infection. This positions TB as the second largest infectious disease killer globally, after COVID-19 [2].

In recent years, substantial efforts have been made globally to prevent and control TB. There has been a general decline in global TB prevalence and mortality rates from 2000 to 2022, while the ongoing global COVID-19 pandemic posed huge risks to the global TB elimination efforts. Recent figures show an increase in TB incidence, with an additional 1.1 million cases recorded between 2021 and 2022 [3]. This surge likely reflected a backlog of TB cases that did not receive timely diagnosis and treatment due to disruptions in healthcare services caused by the pandemic.

With the advancement of socio-economic development and urbanization, population mobility has notably increased, This shift has influenced TB transmission dynamics, together with the continued presence of risk factors such as HIV infection, diabetes, smoking, and malnutrition [4, 5]. These factors collectively contribute to the growing complexity of TB prevention.

The socioeconomic impact of TB is particularly severe in resource-limited low-income and lower-middle-income countries. Although the global burden of TB has decreased overall, disparities across countries and regions persist. High-income countries have lower rates of tuberculosis morbidity and mortality due to well-established health systems and effective preventive measures. In contrast, low-income and lower-middle-income countries continue to struggle with a high burden of TB. This disparity not only highlights differences in economic development and healthcare resources, but also underscores the influence of sociodemographic factors on TB prevalence.

In 2022, the World Health Organization (WHO) released *'Implementing the End TB Strategy: The Essentials*, 2022 Update,' which provides the recently updated resources for guiding TB control efforts globally [6]. This publication is crucial for analyzing the current condition of the global TB epidemic and understanding the disease burden in the post-epidemic era.

Since its establishment in 1990, the Global Burden of Disease (GBD) research program has provided an analytical framework and comprehensive data to assess global and regional disease burdens [7]. Through the utilization of extensive epidemiological data and systematic modeling, the GBD program has examined the occurrence, prevalence, mortality, and disability-adjusted life years (DALYs) associated with various diseases, including TB. Furthermore, the GBD divides the world into seven super-regions based on epidemiological similarities and geographic proximity, further subdividing them into 21 specific regions which include Andean Latin America, Australasia, Caribbean, Central Asia, Central Europe, Central Latin America, Central Sub-Saharan Africa, East Asia, Eastern Europe, Eastern Sub-Saharan Africa, High-income Asia Pacific, High-income North America, North Africa and Middle East, Oceania, South Asia, Southeast Asia, Southern Latin America, Southern Sub-Saharan Africa, Tropical Latin America, Western Europe, and Western Sub-Saharan Africa. This categorization is used to study the epidemiological patterns and the geographic distribution of diseases, serving as a scientific foundation for countries to develop disease prevention strategies and public health policies.

This study, utilizing data from the GBD 2021 database, aims to evaluate the current status and changes in the TB burden globally and regionally by analyzing its incidence, prevalence, and mortality rates over time. By examining the 21 regions defined by GBD, the study also explores the influence of gender, age, and socioeconomic development on the TB burden. The study aspires to serve as a valuable resource for global TB control efforts, and its findings aim to inform more effective strategies for TB prevention, contributing to the global goal of eliminating the TB epidemic by 2030.

Methods

The data acquisition and calculation methods for the relevant indicators in this study were based on existing literature [8], with modifications and adjustments made to meet the specific needs of this research.

Data acquisition

The Global Burden of Disease (GBD 2021) database includes the disease burden of 371 diseases around the world, across different geographical regions and 204 countries and regions [9], with subnational level analysis conducted for 21 regions. The concepts and analytical framework of GBD, the cause hierarchy, and detailed methods have been extensively introduced in other literature [7, 10]. Data on the incidence, prevalence, mortality, DALYs, and their corresponding age-standardized rates (ASRs) for tuberculosis were downloaded from the Global Health Data Exchange (GHDx) [11]. Gender and age distribution information was also collected, which reflects social development based on total fertility rates, per capita income, and years of education. According to previous research records, the level of social development is an important factor affecting the incidence, prevalence, and mortality of pulmonary tuberculosis [8]. We obtained the Socio-Demographic Index (SDI) values to investigate the correlation between the burden of Tuberculosis in different countries and the level of social development.

Statistical analysis

Incidence, prevalence, mortality, and DALYs are key parameters used to evaluate the burden of tuberculosis. To account for changes in population size and age distribution, we also used age-standardized rates for incidence, prevalence, mortality (referred to as ASIR, ASPR, and ASDR, respectively), and DALY rates. To monitor the evolving disease burden, a statistical model was utilized to estimate the EAPCs, which is calculated based on ASRs using the formula: $y=\alpha+\beta x$. Here, x represents the year, and y represents log10(ASRs). The EAPC value is derived from $\text{EAPC}=100 * (10^{\beta} - 1)$. If the EAPCs value and its 95% CI are above zero, it indicates an increasing trend, and vice versa. Furthermore, we conducted a Pearson correlation analysis to assess the relationship between SDI values and ASRs [11].

Data visualization

Data visualization was conducted using R software (version 4.3.2) to illustrate the burden of tuberculosis in various countries or regions via a world map. In this study, software packages such as map, ggplot2, and dplyr were used.

Results

Tuberculosis incidence, prevalence, and annual percentage change

The global number of incident cases of tuberculosis decreased from 8.6 million in 1990 (95% CI: 7.5 million to 9.9 million) to 8.4 million in 2021 (95% CI: 7.5 million to 9.4 million) (Table 1). When examining gender differences, the total number of incident cases for males in 2021 was 4.7 million (95% CI: 4.2 million to 5.2 million), while for females it was 3.7 million (95% CI: 3.3 million to 4.2 million). Despite variations in population size and age distribution, males consistently showed a higher TB incidence rate than females. In 2021, ASIR for males was 115.34 per 100,000 population (95% CI: 103.71-128.58), while ASIR for females was 91.96 per 100,000 population (95% CI: 81.49-102.62). Additionally, the decline of incidence rate in females is slightly faster than that in males (EAPC: males, -1.86, 95% CI: -1.96 to -1.76; females, -2.01, 95% CI: -2.11 to -1.92).

From a geographical perspective, South Asia had the greatest the number of incident cases in the whole of Asia (3.5 million in 1990 and 3.6 million in 2021), whereas Eastern Europe had the highest ASIR among Europe (98.97 in 1990 and 57.89 per 100,000 population in 2021). As for Asia continent, all regions experienced a significant decrease in ASIR. Among them, East Asia has the greatest decline over the past three decades (EAPC: -2.68, 95% CI -3.09 to -2.27), while the reduction of ASIR in Southeast Asia was relatively the smallest one (EAPC: -1.22, 95% CI: -1.41 to -1.03). In Eastern Sub-Saharan Africa, the number of incident cases rose from 731,640 in 1990 to 860,550 in 2021 (Fig. 1a), accompanied by a considerable change in ASIR (574.71 in 1990 and 282.94 per 100,000 population in 2021, EAPC: -2.25, 95% CI: -2.36 to -2.13). In most of the regions except for Southern Sub-Saharan Africa, there has been a significant decline in incidence rates. Specifically, the EAPC for Southern Sub-Saharan Africa was 0.09 (95% CI: -0.21 to 0.37).

In terms of social development levels, all SDI countries showed a declining trend in ASIR (Figure S1), and high SDI countries had significantly lower number of incident cases and ASIR for TB (21.51 in 1990, 9.19 per 100,000 population in 2021; EAPC: -2.28, 95% CI: -2.68 to -1.88). Regarding the changes over the entire period, the most rapid decrease in ASIR can be seen in High-middle SDI countries (EAPC: -2.02, 95% CI: -2.10 to -1.94), while the data of middle SDI countries shows the lowest change over years (EAPC: -1.30, 95% CI: -1.45 to -1.15).

Tuberculosis death and annual percentage change

Global tuberculosis deaths have decreased from 1.8 million in 1990 to 1.2 million in 2021 (Table 2). Gender subgroup analysis for 2021 indicated higher deaths and age-standardized death rate (ASDR) in males compared to females (deaths: male, 725,385, female, 437,411; ASDR: male, 18.19 per 100,000 population, female, 10.22 per 100,000 population). Females showed a slightly greater decline in tuberculosis-related mortality compared to males (male EAPC: -3.03, 95% CI -3.21 to -2.84; female EAPC: -3.29, 95% CI -3.43 to -3.16). Analysis by Socio-Demographic Index (SDI) value revealed that all SDI

Table 1 The number of incident cases and incidence rates of tuberculosis in 1990 / 2021 and temporal trends

	1990	1990	2021	2021	1990–2021
	Incident cases No. *10^3(95%CI)	**ASIR/100,000 No. (95%CI)**	**Incident cases No. *10^3(95%CI)**	**ASIR/100,000 No. (95%CI)**	**EAPC No. (95%CI)**
Overall	8598.52(7528.23-9854.79)	173.03(152.89-198.71)	8407.13(7519.79-9393.77)	103.00(92.21-114.91)	-1.57(-1.71–1.43)
Sex					
Male	4467.13(3942.67-5108.72)	190.24(168.06-217.32)	4684.70(4183.37-5243.43)	115.34(103.71-128.58)	-1.86(-1.96–1.76)
Female	4131.39(3588.42-4748.72)	159.87(139.83-183.66)	3722.43(3313.15-4158.32)	91.96(81.49-102.62)	-2.01(-2.11–1.92)
Socio-demographic factor					
High SDI	209.88(186.48-235.64)	21.51(19.23–24.07)	128.65(112.44-145.76)	9.19(8.04–10.61)	-2.28(-2.68–1.88)
High-middle SDI	863.67(764.94-985.28)	80.25(71.28–90.99)	543.00(479.14-613.32)	35.45(31.54–40.33)	-2.58(-3.22–1.94)
Middle SDI	2503.57(2196.59-2876.20)	173.03(152.89-198.71)	2525.80(2270.80-2798.41)	97.92(88.07-107.77)	-1.30(-1.45–1.15)
Low-middle SDI	3382.96(2910.05-3954.65)	372.83(322.07-432.47)	3231.46(2883.99-3665.30)	184.63(164.33-208.36)	-2.02(-2.10–1.94)
Low SDI	1634.24(1455.70-1832.95)	446.33(399.31-499.36)	1974.06(1753.39-2214.87)	240.81(214.02-269.43)	-2.15(-2.25–2.06)
Region					
Andean Latin America	67.21(58.04–76.85)	199.71(175.82-225.08)	40.74(35.28–47.86)	61.56(53.60-71.69)	-3.90(-4.18–3.62)
Australasia	1840.63(1547.13-2203.41)	8.54(7.21–10.19)	1.69(1.45–1.98)	5.13(4.37–6.02)	-1.35(-1.55–1.14)
Caribbean	17.29(15.53–19.36)	50.00(45.41–55.52)	16.55(14.62–18.62)	34.13(30.04–38.28)	-1.06(-1.23–0.90)
Central Asia	62.07(54.00-70.47)	96.50(85.29-108.97)	50.92(44.32–58.50)	53.28(46.65–60.59)	-1.79(-2.22–1.35)
Central Europe	47.45(41.77–53.58)	35.17(31.26–39.51)	19.96(17.07–23.03)	13.65(11.86–15.67)	-2.81(-3.44–2.17)
Central Latin America	53.38(48.03–59.69)	42.76(38.40-47.46)	50.15(44.04–57.51)	19.25(16.93–21.93)	-1.84(-2.15–1.53)
Central Sub-Saharan Africa	232.48(206.33-257.99)	545.66(491.34–602.20)	400.10(356.01–448.00)	392.31(352.37-437.48)	-1.06(-1.22–0.90)
East Asia	1242.81(1072.33-1439.98)	112.27(97.95-127.84)	707.42(630.58-786.49)	40.28(36.25–44.72)	-2.68(-3.09–2.27)
Eastern Europe	239.72(206.95–279.30)	98.97(85.92-114.92)	136.68(113.80-165.44)	57.89(48.95–70.52)	-2.00(-3.18–0.81)
Eastern Sub-Saharan Africa	731.64(657.33-816.91)	574.71(515.67-636.78)	860.55(755.46-974.84)	282.94(250.78-314.99)	-2.25(-2.36–2.13)
High-income Asia Pacific	87.67(78.62–97.60)	45.65(41.13–50.53)	47.26(40.22–54.41)	15.44(13.33–17.83)	-1.92(-2.34–1.50)
High-income North America	13.08(11.20-15.35)	4.15(3.56–4.87)	10.05(8.61–11.74)	2.31(1.99–2.73)	-2.36(-2.78–1.95)
North Africa and Middle East	200.12(177.81-224.84)	73.05(66.44–80.54)	163.76(143.32-188.97)	28.94(25.47–32.99)	-2.68(-2.91–2.45)
Oceania	7.72(6.91–8.60)	161.13(147.22-177.15)	13.74(12.45–15.19)	122.03(111.69-133.54)	-0.59(-0.68–0.49)
South Asia	3494.30(2922.17-4234.28)	408.70(342.56-488.64)	3569.83(3155.74-4088.87)	204.05(180.62-231.66)	-2.03(-2.13–1.94)
Southeast Asia	1166.40(1050.84-1289.09)	314.14(285.20-345.81)	1264.29(1148.25-1395.42)	181.42(164.65–198.80)	-1.22(-1.41–1.03)
Southern Latin America	13.39(11.71–15.36)	27.60(24.24–31.53)	9.82(8.55–11.49)	13.63(11.79–15.97)	-1.92(-2.13–1.71)
Southern Sub-Saharan Africa	268.05(237.16-302.37)	544.24(490.50-608.71)	344.14(300.92-393.27)	417.09(370.36–470.40)	0.09(-0.21-0.37)
Tropical Latin America	72.82(63.26–84.15)	55.11(48.44–62.97)	72.89(62.72–85.11)	29.53(25.53–34.40)	-1.33(-1.96–0.70)
Western Europe	54.72(47.20-64.61)	13.01(11.07–15.41)	24.82(21.59–28.63)	5.69(4.79–6.76)	-2.79(-3.10–2.47)
Western Sub-Saharan Africa	524.36(476.28-579.52)	363.61(330.80–399.00)	601.76(533.19-676.84)	177.75(155.88-200.89)	-2.57(-2.78–2.36)

countries showed a declining trend in ASDR (Figure S2), and tuberculosis deaths are predominantly concentrated in low-middle SDI countries (deaths: 753,220 in 1990, 505,640 in 2021; ASDR: 103.17 in 1990, 33.81 per 100,000 population in 2021). Notably, in 2021, the ASDR in low SDI countries (60.16 per 100,000 population) is significantly higher than in low-middle SDI countries (33.81 per 100,000 population), despite the latter having higher absolute numbers of fatalities (low SDI: 352,026, low-middle SDI: 505,642). The ASDR in high SDI countries had seen a substantial decrease (ASDR: 3.06 in 1990 and 0.61 per 100,000 population in 2021; EAPC: -5.47, 95% CI: -5.58 to -5.35) (Fig. 1b, accurate data was included in Table S1). Geographically, South Asia recorded the highest number of tuberculosis-related deaths (772,826 in 1990, 500,932 in 2021), Eastern Sub-Saharan Africa had the highest ASDR in 1990 (219.15 per 100,000 population, 95% CI: 177.37-270.33), and Central Sub-Saharan

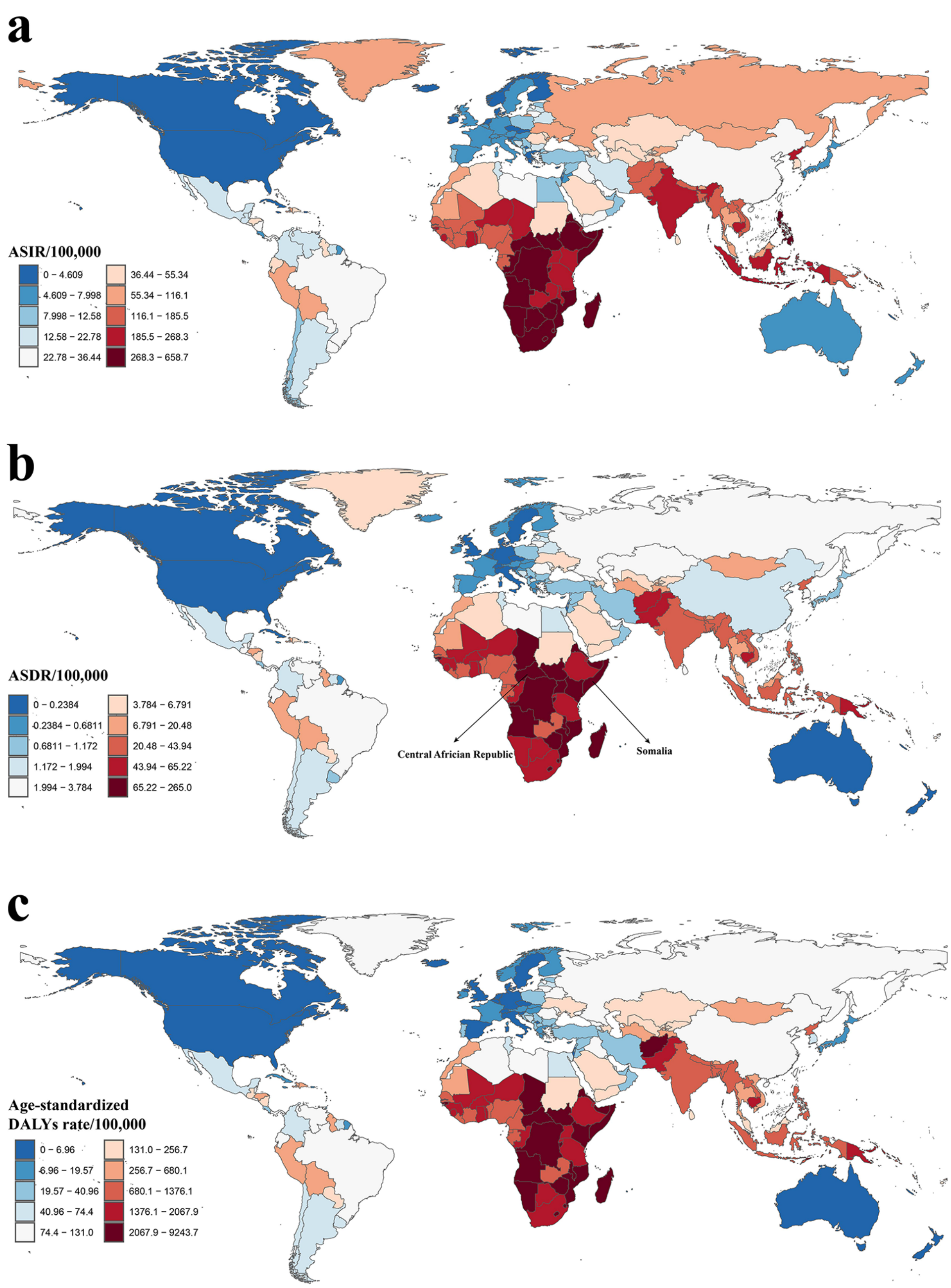

Fig. 1 The global burden of tuberculosis in 204 countries or territories in 2021. **a** The ASIR of 204 countries; **b** the ASDR of 204 countries; **c** the age-standardized DALYs rate of 204 countries. Notes: ASIR = age-standardized incidence rate; ASDR = age-standardized death rate. Accurate ASRs was contained in Additional file 1 (Table S1). Global tuberculosis disease burden among different age groups

Africa had the highest ASDR in 2021 (102.62 per 100,000 population, 95% CI: 73.09-148.92).

Additionally, the tuberculosis deaths have been declined from 1990 to 2021 in nearly all 21 regions. The East Asia region (EAPC: -6.48, 95% CI -6.72 to -6.22) and the High-income Asia Pacific region (EAPC: -6.46, 95% CI: -6.59 to -6.31) showed a rapid decline in ASDR. At the national or regional level, the Central African Republic and Somalia had a relatively high ASDR for tuberculosis in 2021 (Central African Republic: 264.97 per 100,000 population, Somalia: 264.82 per 100,000 population) (Fig. 2b, accurate data was included in Table S2). Furthermore, China and Kazakhstan have seen a significant decrease ASDR from tuberculosis (China: EAPC: -7.79; Kazakhstan: EAPC: -7.08).

Age distribution is a critical parameter in the epidemiology of tuberculosis. Globally, in 2021, significant differences in the epidemiological parameters of tuberculosis were observed across different age groups and genders (Fig. 3a).

Table 2 The number of deaths and death rates of tuberculosis in 1990 / 2021 and temporal trends

	1990	1990	2021	2021	1990–2021
	Death cases No. *10^3(95%CI)	**ASDR/100,000 No. (95%CI)**	**Death cases No. *10^3(95%CI)**	**ASDR/100,000 No. (95%CI)**	**EAPC No.(95%CI)**
Overall	1778.87(1532.82-1980.8)	39.99(34.16–44.76)	1162.80(1050.01-1313.99)	13.96(12.61–15.72)	-3.09(-3.25–2.93)
sex					
Male	1051.72(810.02-1227.16)	51.79(39.84–61.09)	725.38(646.28-868.62)	18.19(16.16–21.80)	-3.03(-3.21–2.84)
Female	727.15(660.77-815.16)	30.49(27.66–34.05)	437.41(396.77–482.6)	10.22(9.28–11.33)	-3.29(-3.43–3.16)
Socio-demographic factor					
High SDI	32.86(30.76–34.64)	3.06(2.86–3.23)	13.21(11.41–14.69)	0.61(0.54–0.68)	-5.47(-5.58–5.35)
High-middle SDI	97.95(83.26-112.02)	9.76(8.30-11.17)	37.19(33.14–42.71)	2.07(1.85–2.37)	-4.47(-4.84–4.09)
Low SDI	460.61(396.2-539.73)	155.35(130.24-183.69)	352.03(302.73-415.76)	60.16(52.67–70.85)	-2.67(-2.87–2.46)
Low-middle SDI	753.22(648.04-842.94)	103.17(87.11-117.11)	505.64(445.26-580.69)	33.81(29.83–38.66)	-3.28(-3.43–3.12)
Middle SDI	433.29(372.44-475.75)	37.92(32.19–41.76)	254.08(227.48-300.42)	9.85(8.81–11.63)	-4.05(-4.19–3.91)
Region					
Andean Latin America	13.98(12.02–16.21)	51.31(43.79–59.65)	4.33(3.48–5.47)	7.05(5.66–8.92)	-6.33(-6.59–6.06)
Australasia	0.14(0.13–0.15)	0.59(0.55–0.63)	0.08(0.07–0.09)	0.14(0.13–0.16)	-4.53(-4.78–4.27)
Caribbean	4.00(3.20–8.32)	12.69(10.04–27.66)	2.53(1.69–6.20)	5.07(3.37–12.21)	-2.97(-3.14–2.80)
Central Asia	7.30(6.90–7.78)	12.29(11.62–13.18)	4.42(3.88–5.01)	4.67(4.12–5.27)	-2.45(-3.28–1.61)
Central Europe	6.58(6.33–6.80)	4.64(4.45–4.79)	1.86(1.72-2.00)	0.99(0.91–1.07)	-4.5(-4.85–4.13)
Central Latin America	13.57(13.16–13.93)	13.73(13.23–14.12)	6.09(5.38–6.96)	2.41(2.13–2.75)	-6.15(-6.43–5.86)
Central Sub-Saharan Africa	64.11(45.30-82.27)	190.86(126.63-252.52)	70.26(49.30-101.23)	102.62(73.09-148.92)	-1.57(-1.78–1.35)
East Asia	184.41(152.31-218.41)	20.91(17.37–24.55)	49.03(40.01–61.65)	2.43(1.99–3.04)	-6.48(-6.72–6.22)
Eastern Europe	14.86(14.56–15.15)	5.57(5.46–5.67)	8.45(7.60–9.49)	2.96(2.67–3.31)	-0.98(-2.01–0.055)
Eastern Sub-Saharan Africa	220.49(186.98-264.77)	219.15(177.37-270.33)	159.77(129.45-195.01)	81.60(67.28–98.09)	-2.75(-2.97–2.52)
High-income Asia Pacific	13.57(12.44–15.11)	7.04(6.45–7.82)	6.65(5.43–7.55)	1.10(0.93–1.23)	-6.46(-6.59–6.31)
High-income North America	2.48(2.33–2.56)	0.72(0.68–0.74)	0.92(0.83–0.97)	0.15(0.14–0.16)	-5.51(-5.85–5.15)
North Africa and Middle East	36.43(29.34–56.45)	17.99(14.01–30.34)	20.89(16.35–29.85)	4.37(3.44–6.33)	-4.51(-4.61–4.40)
Oceania	2.25(1.69–3.11)	65.69(49.39–89.41)	3.04(2.47–3.76)	36.51(29.41–45.06)	-1.88(-1.91–1.83)
South Asia	772.83(666.72-861.44)	113.31(96.24-128.39)	500.93(442.26-588.28)	33.11(29.19–39.07)	-3.65(-3.82–3.47)
Southeast Asia	252.32(201.82-288.29)	87.28(68.30-100.45)	170.55(147.94-199.98)	27.25(23.53–31.56)	-3.38(-3.52–3.22)
Southern Latin America	2.78(2.65–2.92)	5.97(5.69–6.27)	1.25(1.16–1.34)	1.50(1.40–1.60)	-4.79(-5.01–4.57)
Southern Sub-Saharan Africa	29.63(25.48–36.23)	82.08(69.58-100.72)	39.36(34.35–45.83)	60.44(53.28–69.99)	-0.85(-1.32–0.37)
Tropical Latin America	8.79(8.56–9.03)	7.89(7.63–8.11)	5.83(5.55–6.07)	2.29(2.18–2.38)	-4.23(-4.34–4.11)
Western Europe	8.89(8.35–9.24)	1.55(1.46–1.61)	2.85(2.48–3.06)	0.27(0.24–0.29)	-5.73(-5.85–5.59)
Western Sub-Saharan Africa	119.45(99.77-145.55)	106.06(89.09-129.95)	103.68(79.41-130.73)	45.01(36.28–54.17)	-2.2(-2.43–1.95)

The incidence rate of tuberculosis in the 5–9 age group is the lowest among all age groups (19.01 in males and 28.38 per 100,000 population in females). The incidence rate in the 85 and older age group is the highest across all age groups (298.84 in males and 142.99 per 100,000 population in females), however the number of incident cases is comparatively low due to the smaller base population of elderly individuals. Conversely, in the 15–69 age group, which comprises the prime working-age population, had the highest incidence rate, number of incident cases and considerable gender disparities of tuberculosis. Globally, in 2021, prevalence of tuberculosis is most common in the 15–44 age range, particularly in the 30–34 age group. Specifically, 370,318 males and 281,555 females in this age range were infected, with incidence rates of 121.20 and 94.19 per 100,000 population respectively. The number of prevalent cases began to decrease starting from the

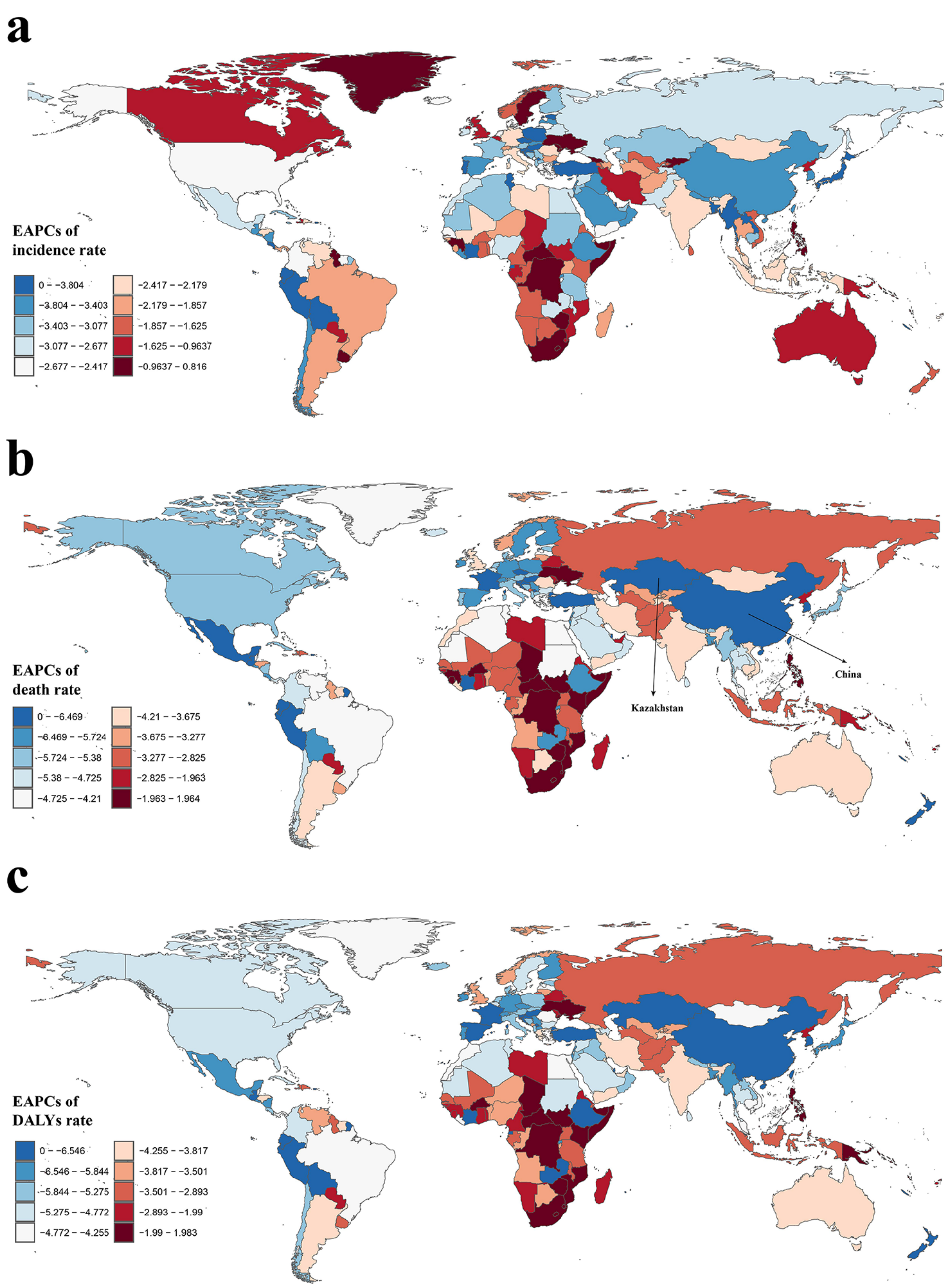

Fig. 2 The EAPCs of incidence rate (**a**), mortality rate (**b**), and DALYs rate (**c**) caused by tuberculosis in 204 countries or territories from 1990 to 2021. Note: EAPCs = Estimate the annual percentage change. Accurate EAPCs was contained in Additional file 1 (Table S2)

35–39 age group and prevalence rate began to decrease from the 55–59 age group.

Disparities in age distribution were also observed in both mortality and disability-adjusted life years (DALYs) related to tuberculosis. Among individuals aged 20 and above, the tuberculosis deaths and DALYs of males are higher than that of female in the same age group. Among the various age periods under 19, the age group of 5 years old and below had the highest number of deaths, DALYs, and corresponding rates. In 2021, within the 15–70 age groups, the number of tuberculosis-related deaths increased with age (Fig. 1c), and there was a significant difference between males and females. For instance, the number of male deaths from tuberculosis in the 50–70 age group was approximately twice that of females in the same age range. It is noteworthy that although the number of deaths continues to decline with increasing age in individuals over 70, the death rate per 100,000 people shows a sharp upward trend for males. Specifically, In the 90–94 age range, mortality of males is almost three times

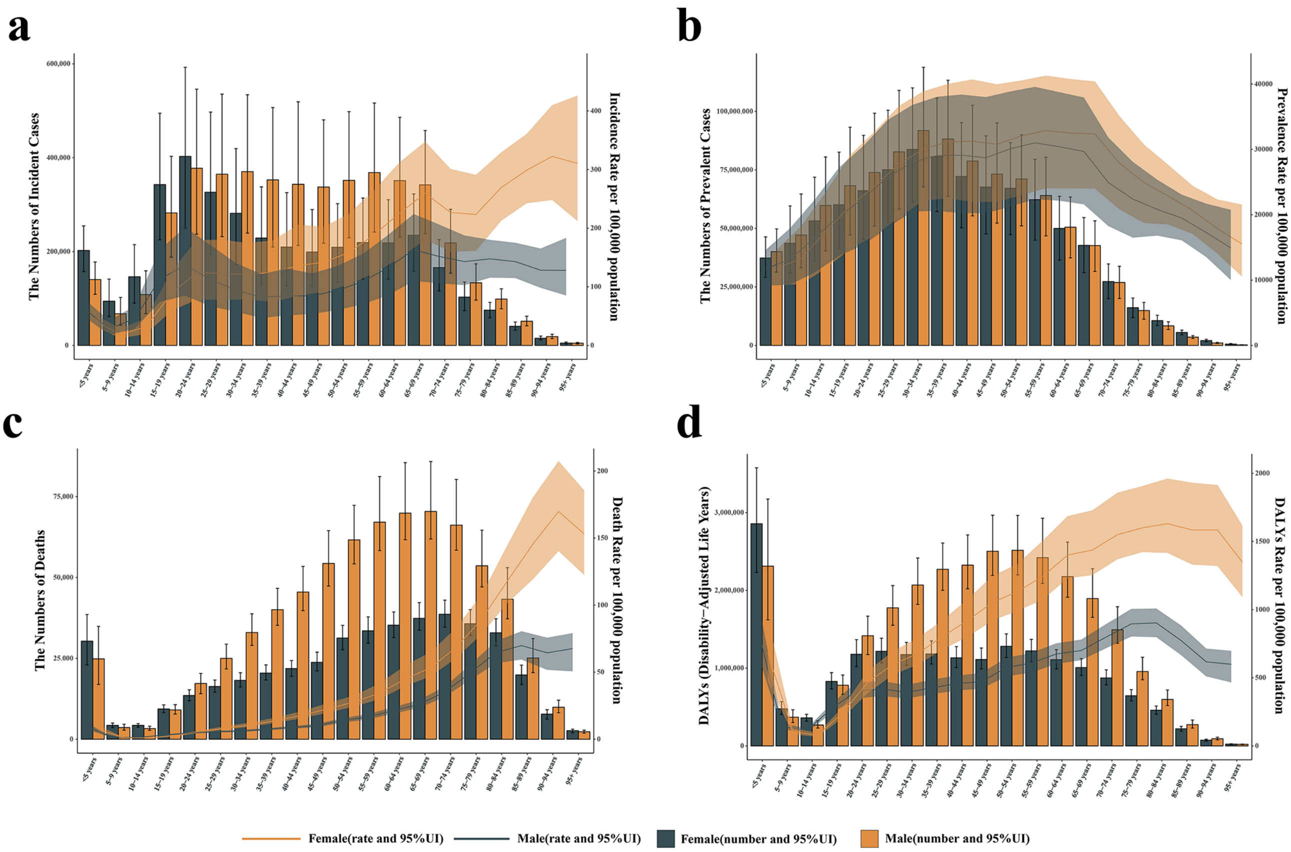

Fig. 3 The Global Burden of TB by Age Group and Gender in 2021. **a** The number of incident cases and incidence rate among different age groups. **b** the number of prevalent cases and prevalence rate among different age groups; **c** the number of deaths and death rate among different age groups; **d** the number and rate of DALYs caused by tuberculosis among different age groups. Note Accurate figures were contained in Additional file 1 (Table S3 and S4)

more than that of females (males: 168.82 per 100,000 population, females: 64.44 per 100,000 population). Besides, the trends for DALYs, deaths, and their corresponding rates all showed a pattern of initially increasing and then decreasing with age. Unlike death cases, the peak of DALYs occurred in the age group of 50–54 years. Additionally, within the age group of 20–50 years, there was a brief period where the DALYs of females showed a slight decline as age increased.

Global tuberculosis burden in different genders and regions

Pyramid charts were generated using GBD 2021 data to delve deeper into the disease burden of tuberculosis across various genders. These graphs show ASIR, ASPR, ASDR, and AS-DALYs rate across different genders and 21 global regions (Fig. 4, data see in Table S5).

The analysis of the age-standardized incidence rates across the 21 regions found that among these regions, Southern Sub-Saharan Africa had the highest female ASIR, while Central Sub-Saharan Africa had the highest male ASIR. Moreover, there were notable gender disparities in tuberculosis burden in Eastern Europe and Tropical Latin America (Eastern Europe: males vs. females = 85.73 vs. 32.95; Tropical Latin America: males vs. females = 41.39 vs. 18.73).

The prevalence rate is an important indicator reflecting the current condition of infectious disease epidemics. Oceania had the highest ASPR (Fig. 4b), with 40,606 per 100,000 population of males and 39,885 per 100,000 population of females. Corresponding to the region's high incidence rate, the East Asia region also had a considerably high ASPR (31,714 in male and 29,464 per 100,000 population in female). In contrast, Western Europe had the lowest ASPR (6,826 in male and 6,488 per 100,000 population in female). In most regions, males had a greater ASPR than females. This gender disparity was evident even in developed regions like Western Europe and high-income North America, where overall ASPRs were lower.

Comparing with the age-standardized incidence rates, prevalence rates, death rates, and DALYs rate, ASDR and age- standardized DALYs showed more pronounced gender differences than incidence and prevalence rates (Fig. 4). Overall, tuberculosis ASDR (Table 1) and age-standardized DALY rate (males: 220.05 per 100,000

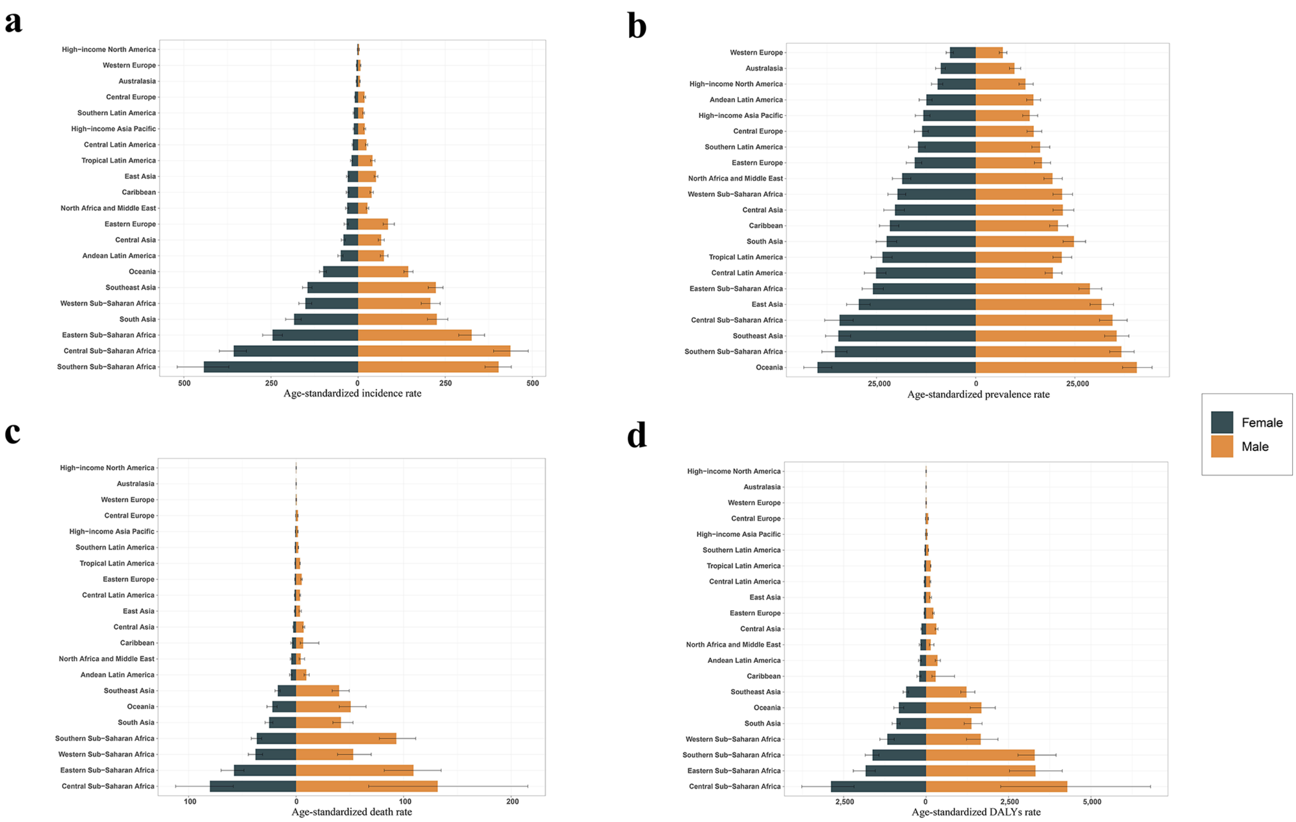

Fig. 4 Gender-specific ASIR (**a**), ASPR (**b**), ASDR (**c**), DALYs rate (**d**) of 21 regions in 2021. Note Accurate rate was contained in Additional file 1 (Table S5)

populations, females: 58.95 per 100,000 population) were significantly higher in males than in females. Compared to other Sub-Saharan Africa regions, Southern Sub-Saharan Africa had a relatively higher male-to-female ASDR ratio (Southern Sub-Saharan Africa: 2.11; Eastern Sub-Saharan Africa: 1.73; Central Sub-Saharan Africa: 1.36; Western Sub-Saharan Africa: 1.33). Four regions of Sub-Saharan Africa had the high age-standardized DALYs due to their severe tuberculosis burden, and both males and females in Central Sub-Saharan Africa had extremely high age-standardized DALYs (Fig. 4d). The high-income Asia Pacific region and Western Europe had relatively lower age-standardized DALY rates (33.83 in males and 14.49 per 100,000 population in female).

The correlation analysis between SDI value and the tuberculosis burden

To explore the potential correlation between the level of social development and the burden of tuberculosis, we conducted a correlation analysis between SDI values and ASRs in 21 different geographical regions from 1990 to 2021. The results indicated that ASRs are significantly negatively correlated with SDI values (ASIR-SDI coefficient: -0.77, ASDR-SDI coefficient: -0.74, age-standardized DALY rate-SDI coefficient: -0.76; all P values are <0.001).

Attributable risk factors

In the GBD database, we searched for risk factors associated with tuberculosis-related disability and death, which show a similar result with WHO tuberculosis report 2023 [2]. To enhance clarity and conciseness, ultimately, we have selected second-level risk factors for our final classification, which includes low physical activity, tobacco use, high fasting plasma glucose, alcohol consumption, dietary risks, and high body mass index. Tobacco and alcohol use are two major risk factors, both globally and within different SDI countries (Fig. 6). However, the attributable risk of tobacco has shown a gradual decline over time, both globally and in regions with different SDI levels, while the other risk factors related to DALYs have gradually increased over time. At the same time, according to the subgroup analysis based on different SDI levels, the proportion of tuberculosis-related DALYs attributable to tobacco use in 2021 in high-middle SDI (23%) and middle SDI (19%) countries was higher than the global level (11%) (see in Table S11). The attributable risk of alcohol use in high-middle and high SDI countries has declined in the past decade, while regions with lower SDI levels have shown a more significant upward trend. Moreover, in low SDI countries, over the past decade, high fasting plasma glucose and alcohol use have surpassed tobacco as the two most significant contributors.

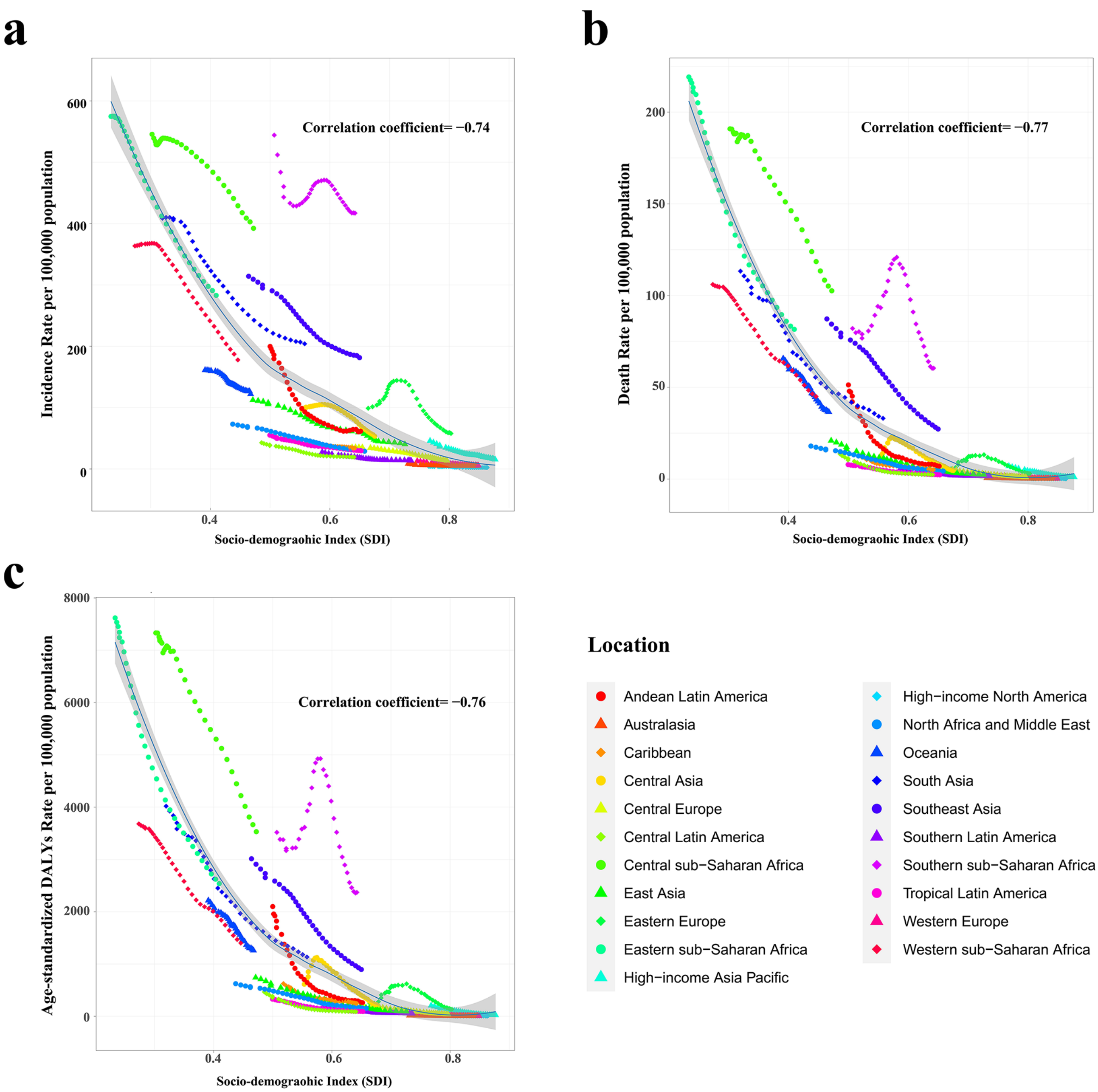

Fig. 5 Correlation Between Socio-demographic Index (SDI) and Tuberculosis Burden in 2021. **a** The incidence rate per 100,000 population; **b** the mortality rate per 100,000 population; **c** the DALYs rate per 100,000 population. Note Accurate SDI from 1990 to 2021 was contained in Additional file 1 (Table S6)

A gender and SDI regional subgroup analysis of the global age-standardized DALYs (Fig. 7) revealed that, excluding high body-mass index, the proportion of other risk factors in global females in 2021 was not higher than among males. In males, tobacco is the main attributable risk factor, while in females, it is high fasting plasma glucose. Besides, in high-middle and high SDI regions, the high body-mass index had a relatively great influence on females, accounted for 15% and 9% respectively. Compared to those from lower SDI countries and regions, the proportion of the tobacco factor among people in higher SDI areas was higher, and that in middle-high SDI countries was the highest one, approximately made up 31% of total. In low SDI countries, alcohol use was the top attributable risk for tuberculosis DALYs in males, accounted for with approximately 14%; however, it was still lower than in high-middle and high SDI countries, accounted for approximately 22% and 21% respectively (see in Table S8).

The differences in the main risk factors for tuberculosis were visually processed among different genders in the 21 global regions (Fig. 8). Males and females showed

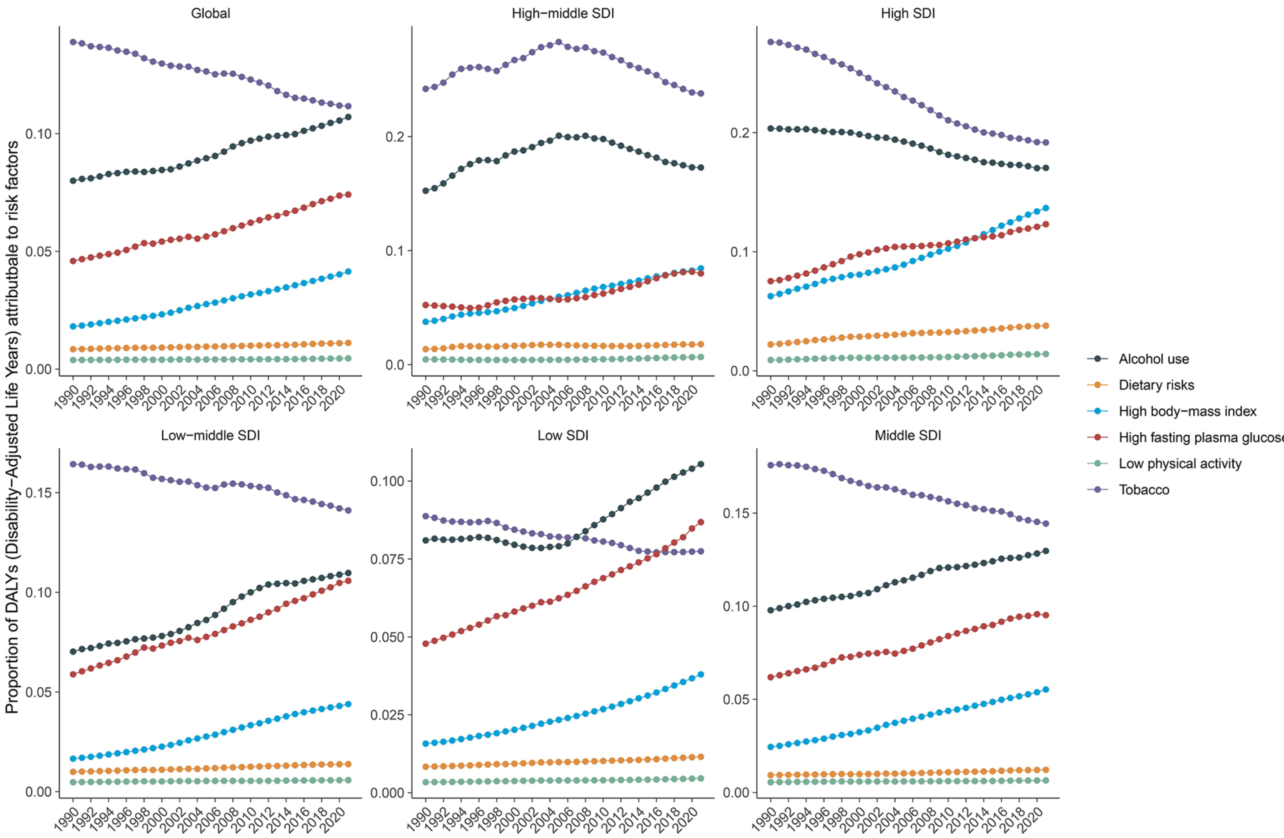

Fig. 6 Trends of the proportion of age-standardized DALYs attributable to 6 main risk factors from 1990 to 2021, grouping by different SDI quintiles. Note: the proportions in the figure are displayed in decimal format for better accuracy. Trends of DALYs for TB from 1990 to 2021 varied from SDI regions can be seen in Additional file 1 (Table S7)

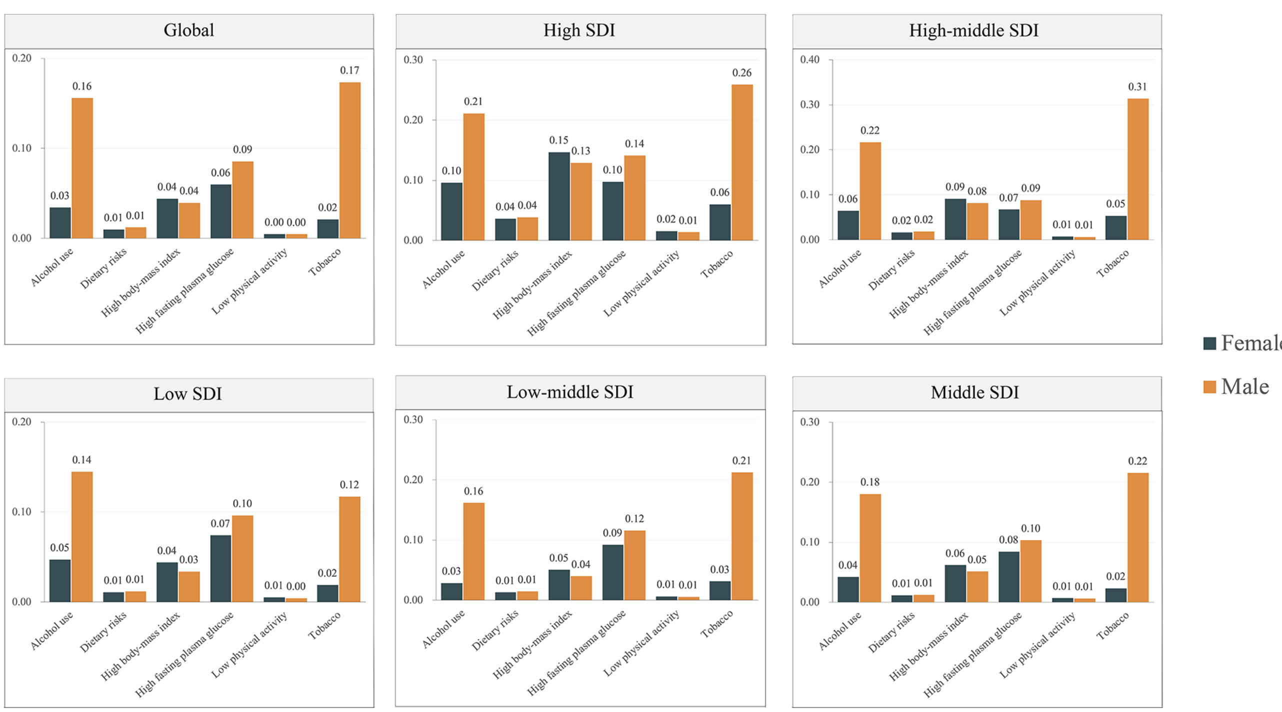

Fig. 7 Contributions of 6 main risk factors to the proportion of age-standardized DALYs due to Tuberculosis by different SDI quintiles and sex in 2021. Note: The proportions in the figure are displayed in decimal format for better accuracy. Accurate proportions were contained in Additional file 1 (Table S8)

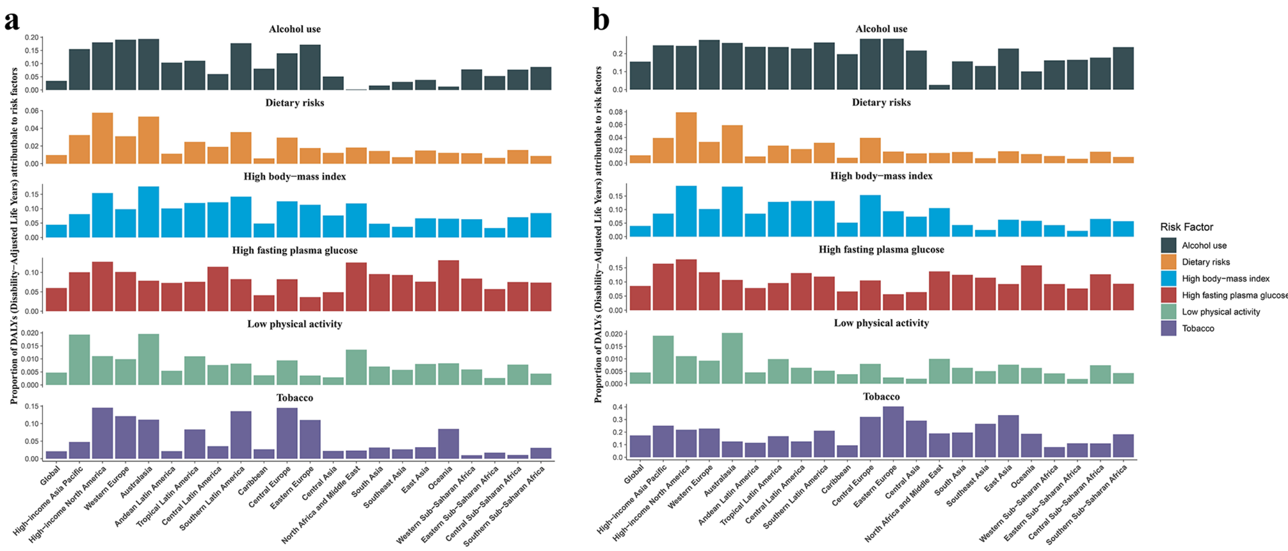

Fig. 8 Proportion of TB Disability-Adjusted Life Years (DALYs) Attributable to Risk Factors Across 21 Regions in 2021. Note: The proportions in the figure are displayed in decimal format for better accuracy, which was shown in Additional file 1 (Table S9 and S10)

disparities in the main risk factors across various regions. In males, alcohol use is almost the main risk factor in every region, except for North Africa and the Middle East. Tobacco use is also a major factor affecting the DALYs of tuberculosis in many regions, such as in Eastern Europe and East Asia, where its attributable risk proportion is extremely high, with approximately 40% and 33% respectively. Slightly different from the situation in males, high fasting plasma glucose is the highest proportional risk factor in global females (Fig. 8b), and its attributable risk is higher in economically developed areas than in economically backward areas. Showing the same trend, alcohol use and tobacco are also important risk factors for tuberculosis in females. Overall, low physical activity and dietary risks had the lowest attributable risk, but upon further analysis, we found that in economically developed areas such as Western Europe and high-income North America, their impact on DALYs was more pronounced compared to low-income areas. These findings underscore the significant gender disparities in main risk factors of TB across regions, emphasizing the need for gender- and region-specific public health policies to effectively reduce the TB burden of DALYs.

Discussion

Overall global tb burden trends

This study provides a comprehensive overview and summary of the tuberculosis burden using data from the GBD 2021 database, which shows a global decline in tuberculosis incidence, prevalence, and mortality from 1990 to 2021. Despite this overall trend, notable variations persist across different regions and genders.

Males consistently bear a greater burden of tuberculosis compared to females, evident in higher rates of incidence, prevalence, and mortality. Evidences from World Health Organization and other pertinent studies indicate that, both globally and in specific nations and areas, there were notable disparities in the incidence of tuberculosis between men and women before to and including 2021 [12–15]. Gender disparities are especially prominent in regions like East Asia, Andean Latin America, and sub-Saharan Africa. Additionally, this disparity may be attributed to factors such as occupational exposure, social habits, and higher prevalence of smoking and alcohol consumption among men. Relevant studies have demonstrated, for example, that men prefer to believe their bodies are superior to those of women and may, on a worldwide scale, intentionally or unconsciously repress their illnesses in order to avoid being viewed as weak or feminine. In addition, men are more likely than women to work in sectors like construction and mining, which raises their risk of tuberculosis [16, 17]. Furthermore, according to our research data and other studies concerned [18, 19], smoking and drinking are risk factors that influence the incidence of tuberculosis, and the higher rates of smoking and drinking among men compared to women may be one of the reasons for the greater disease burden in men.

Given the observed gender differences in TB burden, it is crucial to propose more targeted interventions. For instance, tailored health education and support programs for men should be developed, as they may be at higher risk due to occupational or behavioral factors. Additionally, establishing stricter safety exposure limits in high-risk occupations could help reduce the incidence of TB in environments where men are more likely to face occupational hazards.

Differences between regions

The data indicates that the burden of tuberculosis varies significantly across geographic regions. Sub-Saharan Africa stands out as having the highest global rates of TB incidence, prevalence, mortality, and age-standardized disability-adjusted life years (DALYs). In contrast, Western Europe and high-income North America exhibit much lower TB burdens. These disparities may be attributed to factors such as economic development, healthcare infrastructure, public health awareness, and TB control measures specific to each region. For example, a study conducted in Kenya [20] found that unequal distribution of healthcare resources between urban and rural areas led to lower tuberculosis diagnosis rates and limited access to health treatment in rural areas, which may contribute to a higher tuberculosis burden. Additionally, the overburdened public healthcare system in the region has made it difficult for low-income populations to access standardized treatment, which often leads to impoverishment as a consequence of the disease. Besides, the region's social and cultural context, such as beliefs favoring traditional treatment methods and tuberculosis-related stigma, influences the proper understanding of the disease, thereby compounding the burden of illness. These factors contribute to an increased risk of TB-related mortality and have a significant impact on DALYs [9, 21].

Our analysis sends evidence to a result of significant negative correlations between Social Development Index (SDI) values and tuberculosis burden, including incidence, mortality, and age-standardized Disability-Adjusted Life Years (DALY) rates. This indicates that higher levels of social development are associated with lower tuberculosis burden, underscoring the importance of socio-economic development in tuberculosis control. Two Chinese studies, supporting our speculations, show that factors related to economic and cultural development, such as rising per capita GDP, rising urban and rural populations, falling unemployment rates, and an increase in the number of people receiving higher education, can reduce tuberculosis incidence. In terms of healthcare, the steady rise in health resources has resulted in a dramatic decrease in tuberculosis incidence. Economic development may also lead to higher per capita daily living and healthcare costs, which could lower the prevalence of tuberculosis by enhancing daily healthcare services, enhancing nutrition, and improving living conditions [22, 23].

These findings send us valuable insights, suggesting that improving education levels, increasing per capita income, and enhancing healthcare conditions are crucial strategies for reducing the burden of tuberculosis.

Risk factors

Analyzing the current major risk factors for TB is crucial for countries to effectively prevent and control this disease. Globally, factors such as dietary risks, high body-mass index, high fasting plasma glucose, low physical activity, tobacco use, and alcohol consumption have been identified as significant contributors to TB disability-adjusted life years (DALYs).

Among these factors, tobacco use ranked first and alcohol use ranked second. However, the attributable risk of tobacco has gradually declined from 1990 to 2021, potentially due to the emergence of epidemiological evidence, increased individual health awareness, and the implementation of tobacco control regulations in various countries. Unhealthy lifestyle choices, particularly smoking and alcohol abuse, have been consistently linked to an increased risk of TB. Tobacco contains harmful substances like nicotine, leading to lung tissue damage and decreased resistance to MTB [24]. Chronic alcohol consumption weakens the immune system, making individuals more susceptible to MTB infection and impairing the response of alveolar macrophages to pathogens [25]. Studies have also shown an association and interaction between TB and diabetes, making diabetic patients facing a higher risk of developing TB [4]. Elevated blood glucose levels that promote the growth and reproduction of MTB and weaken immune function [26]. In high-income countries, higher rates of tobacco and alcohol consumption, along with the prevalence of high body-mass index linked to overnutrition, contribute to a significant burden of related health risks. In contrast, in low SDI countries, the attributable risk of alcohol use has been rising over the past decade, likely as a result of economic development. Men, who exhibit higher rates of smoking and alcohol use, often have a higher attributable risk for TB DALYs. These behavioral risk factors, however, do not exist in isolation. They often interact with broader socioeconomic determinants like poverty, education, and healthcare access, which exacerbate their effects on TB burden. For instance, malnutrition, which is more prevalent in low-income regions, weakens the immune system, increasing susceptibility to TB. Poverty also restricts access to healthcare services, delaying diagnosis and treatment, which allows TB to spread more easily. Research has shown that socioeconomic factors such as housing conditions, employment status, and education levels strongly influence both exposure to Mycobacterium tuberculosis and the progression of the disease [27]. Thus, the coexistence of these risk factors with unfavorable socioeconomic conditions creates a complex web of influences that heightens the overall TB burden.

Tuberculosis control

Researchers worldwide have devoted substantial efforts to improving the diagnosis and treatment of TB. Shorter treatment regimens using rifapentine have been shown to enhance availability and scale-up. Swift diagnosis and targeted treatment play a vital role in preventing adverse disease outcomes and transmission. A study conducted in Germany revealed an increasing use of Interferon-Gamma Release Assays (IGRAs) for detecting latent TB infection (LTBI), enabling these patients to receive preventive treatment [28].

Despite the availability of effective treatment regimens and preventive measures, TB continues to be a leading cause of death in low- and middle-income countries, as they may face a multitude of severe social problems and diseases while having limited resources [29]. WHO statistics reveal that only 36% of patients worldwide receive standardized treatment, underscoring a significant imbalance between TB detection and treatment, and a funding gap still persists. The Lancet TB Commission's 2023 report recommends that funding for TB in middle-income countries should be tied to these countries increasing their mobilization of domestic resources [30].

Suggestions for strategies

Regarding all these data and former researches [31], we found out that social determinants can influence population behaviors, lifestyles, and healthcare accessibility, thereby affecting the spatial, temporal, and demographic distribution of risk factors across different populations. In terms of this, we suggest that several practical strategies can be implemented, including strengthening health systems, improving surveillance, and integrating TB services with other public health efforts.

Targeted screening and diagnosis

Rather than universal screening, focusing on high-risk populations, such as those in crowded settings, migrants, and individuals with HIV, is essential to maximize resources. Mobile clinics or community health workers (CHWs) can support early diagnosis in underserved regions, thus improving access to care and preventing TB transmission. WHO advocates for research into new TB diagnostic tools, which further strengthens this targeted approach.

Task-shifting in healthcare

Training CHWs to handle essential TB tasks, including case detection and treatment monitoring, can relieve pressure on healthcare systems. This approach uses local resources more effectively and promotes patient adherence to treatment. Additionally, international exchange programs, where healthcare workers from high TB-burden countries train in more advanced healthcare systems, could enhance expertise and improve TB care.

Leveraging technology for diagnosis

In regions with limited healthcare access, digital health tools can significantly improve TB management. Mobile apps for symptom tracking and remote consultations enable early diagnosis and continuous treatment monitoring. These tools also facilitate real-time data collection, which strengthens TB surveillance and control.

International cooperation and funding

Addressing TB in low-SDI countries requires strong international cooperation to bridge funding gaps. While financial sustainability remains a challenge, collaborations among governments, NGOs, and other stakeholders are essential. However, specific and viable funding strategies need further development due to the complexity of international financing.

Limitations of the study

While this study provides a detailed analysis of the global burden of tuberculosis, it is not without its limitations. The analysis relies on an established GBD model, and the assumptions and parameter choices made within this model have the potential to influence the results. Furthermore, the accuracy and completeness of the data are heavily reliant on the quality of reporting and the standard of care in each country. For instance, in low-income countries, data may be delayed or missing, which could affect the reliability of our findings. Additionally, there is a lack of systematic monitoring data on TB treatment adherence and outcomes across different regions, which restricts our ability to offer a comprehensive overview of the current condition and effectiveness of global TB treatment.

Socioeconomic factors, policy changes, and emergencies, such as the COVID-19 pandemic, also pose challenges to our anticipated analyses of the tuberculosis burden from the current period to 2030 [32]. The COVID-19 pandemic had a strong impact on TB prevention efforts globally, which caused a huge disruption to healthcare services, lockdowns, and reduced access to diagnostic and treatment facilities. This have led to delays in TB diagnoses and treatments, which in turn resulted in an increase in TB cases and deaths during and after the pandemic. For instance, in several high-burden countries, treatment success rates declined, while failure and loss-to-follow-up rates increased [33]. Additionally, global TB incidence dropped during the pandemic due to restricted health service access, but this led to an increase in undiagnosed cases, exacerbating future outbreaks [34]. Future changes in the burden of tuberculosis are expected to be shaped by various factors, highlighting the needs for enhanced epidemiologic data and continuous surveillance and examination of these trends.

Abbreviations

TB	Tuberculosis
MTB	Mycobacterium tuberculosis
SDI	Socio-demographic Index
DALYs	Disability-adjusted life years
ASRs	Age-standardized rates
ASIR	Age-standardized incidence rates
ASPR	Age-standardized prevalence rates
ASDR	Age-standardized death rates
EAPCs	Estimate the annual percentage change

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20664-w.

Supplementary Material 1

Acknowledgements

We are grateful for the GBD research team for data support and all researchers and institutions involved in this study for their contributions.

Author contributions

HY and XR contributed equally to this work. HY, XR and WL contributed to study design, data analysis, and manuscript writing. JX and YZ contributed to study design and manuscript editing. All authors reviewed the manuscript.

Funding

This study received no external funding.

Data availability

The datasets generated and analyzed during the current study are available in the Global Burden of Disease (GBD) 2021 database, https://vizhub.healthdata.org/gbd-results/. The related data was contained in our articles and Additional files.

Declarations

Ethics approval and consent to participate

This article does not contain individual data.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 9 June 2024 / Accepted: 7 November 2024

Published online: 11 November 2024

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