Global, regional, and national burden of preterm birth, 1990–2021: a systematic analysis from the global burden of disease study 2021

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Summary

Background Preterm birth and its complications are leading causes of mortality among children under five years of age. Given the increasing burden of preterm birth on neonatal mortality and long-term health outcomes worldwide, a comprehensive global analysis is essential to guide effective public health interventions and policies. This study aims to assess the burden of preterm birth at the global, regional, and national levels.

Methods Using data from the Global Burden of Disease (GBD) 2021 database, this study analysed trends in age-standardized incidence rates (ASIR), age-standardized mortality rates (ASMR), and disability-adjusted life-years (DALYs) as primary outcomes for preterm birth from 1990 to 2021 at global, regional, and national levels. Data were assessed using joinpoint regression analysis, decomposition analysis, and the health inequality concentration index.

Findings Globally, the incidence, mortality and DALYs due to preterm birth have shown a declining trend, but ASIR started to increase in 2016. Males were more commonly born preterm than females (12329075.82, 95% uncertainty interval [UI]: 12192632.55–12464605.4 vs. 9224694.94, 95% UI: 9113876.1–9330107.89). Changes in DALYs were primarily due to epidemiological change (111.97%) and population (−21.59%). Low Socio-demographic Index (SDI) regions increased in annual incidence cases (43.1%, 95% UI: 40.17–46.09), while high SDI regions decreased in annual incidence cases (−9.6%, 95% UI: −11.45 to −7.79). The highest annual mortality and DALYs respectively occurred in sub-Saharan Africa (295490.66, 95% UI: 241762.78–353624.41) and South Asia (32760273.93, 95% UI: 27295547.76–39070225.69). Western sub-Saharan Africa showed the largest increase in annual incidence (98.95%, 95% UI: 94.77 to 103.09), and Australasia had the lowest annual mortality (287.18, 95% UI: 244.26–339.42) and DALYs (61081.4, 95% UI: 50897.33–73069.96). Western sub-Saharan Africa also had the highest ASMR (21.57, 95% confidence interval [CI]: 17.9–25.89). The highest ASIR (543.78, 95% CI: 535.11–553.21) and age-standardized DALYs (2064.65, 95% CI: 1717.27–2473.36) both occurred in South Asia, while the lowest ASIR and age-standardized DALYs were seen in East Asia (147.31, 95% CI: 144.22–150.85) and High-income Asia Pacific (143.32, 95% CI: 117.9–167.25). India, Nigeria, and Pakistan ranked highest globally in terms of annual incidence cases, mortality, and DALYs, while the lowest annual incidence, mortality and DALYs respectively occurred in Tokelau (2.34, 95% UI: 2.12–2.56), San Marino (0.04, 95% UI: 0.02–0.07) and Tokelau (17.22, 95% UI: 11.11–24.95).

Interpretation While the global burden of preterm birth has decreased, significant disparities persist, especially in low SDI regions. There is a need for more refined policies and preventive measures to effectively address preterm birth.

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Keywords: Preterm birth; Incidence; Mortality; Disability-adjusted life-years

Introduction

As an urgent global public health issue, preterm birth is defined as birth before 37 weeks of gestation. Annually, about 13.4 million newborns are delivered prematurely, accounting for approximately 1 in 10 of all live births. Alarmingly, nearly one million of these preterm infants

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Research in context

Evidence before this study

To provide a comprehensive overview of the existing evidence on the burden of preterm births, we conducted a thorough literature review using multiple databases including PubMed, Scopus, and Web of Science. The search terms included "preterm birth," "incidence," "mortality," "disability-adjusted life-years (DALYs)," and "Global Burden of Disease (GBD)." Our search included publications up to June 2024 and was not restricted to English language articles. Previous studies have examined the burden of preterm births using national databases, registry data, or single-centre cohort data. Many of these studies were conducted in high-income countries, with fewer reports from low- and middle-income regions. Moreover, there is a lack of comprehensive analyses covering the global, regional, and national burden of preterm births over an extended period, especially from 1990 to 2021. No previous studies have systematically evaluated trends in preterm birth incidence, mortality, and DALYs using the latest GBD 2021 data, nor have they incorporated decomposition analyses to understand the drivers of changes in these metrics.

Added value of this study

Our study provides an updated and systematic analysis of the global, regional, and national burden of preterm births from 1990 to 2021 using the latest GBD 2021 data. It fills a critical gap in the literature by offering a detailed examination of trends in age-standardized incidence rates (ASIR), age-standardized mortality rates (ASMR), and DALYs across different socio-demographic index (SDI) levels. This study is the first to employ decomposition analyses to explore the factors contributing to changes in DALYs, highlighting the roles of epidemiological shifts and population dynamics. Despite an overall decline in the global burden of preterm births, significant disparities persist, particularly in low SDI countries. Our findings provide valuable insights into the regional variations and temporal trends in preterm birth burdens, informing targeted policy and intervention strategies.

Implications of all the available evidence

Despite global reductions in preterm birth incidence, mortality, and DALYs, substantial disparities remain, particularly in low SDI countries. The increasing trends observed in certain regions since 2016 suggest that socio-economic and environmental factors, including conflicts and climate change, may be reversing previous gains. Policymakers need to prioritize interventions that address these disparities, focusing on improving maternal and neonatal care in low-resource settings. Additionally, our findings highlight the need for continued surveillance and research to monitor trends and assess the effectiveness of public health interventions. Future research should explore subnational variations and the impact of specific policies and programs to better understand and mitigate the burden of preterm births globally.

die each year.[1,2] Research indicated that preterm birth mortality accounted for 40% of neonatal deaths, which was recognized as the leading cause of death of children under five years old worldwide and the most common cause of perinatal death.[1,3,4] The Sustainable Development Goal 3.2 target less than 12 neonatal deaths per 1000 live births by 2030.[5] Continued and enhanced efforts are required to achieve this target.

Infants born preterm carry a higher risk of complications than infants born at full-term, leading to a range of short-term health issues such as respiratory distress syndrome, hypoglycaemia, hypothermia, jaundice, feeding difficulties, and infections, as well as long-term health problems such as cerebral palsy, epilepsy, blindness, etc.[6] According to a system analysis, the annual global preterm birth rate between 2010 and 2020 was 0.14%.[7] India had the highest incidence in 2020, which accounted for more than 20% of all preterm birth worldwide.[7] Higher preterm birth incidence was observed not only in middle-income and low-income countries and regions, but also in high-income countries like the United States.[7] An analysis of data based in the United States showed that the preterm birth mortality rates rose sharply with decreasing gestational age, and declined about 10% from 1995 to 2020.[8] This demonstrates that the incidence of preterm birth varies significantly among nations. Examining the global and regional trends in preterm birth incidence, mortality, and DALYs is crucial to understanding the full impact of preterm birth on public health, identifying regional disparities, and informing targeted strategies to enhance neonatal survival and long-term health.

Despite the development of various measures to reduce the incidence and mortality of preterm birth, it remains a significant societal challenge that demands continued attention. Global Burden of Disease (GBD) 2021 highlights new and existing health threats that need to be prioritized on the international public health agenda, with estimates for 204 countries and territories.[9] A previous study primarily presented data from the GBD 2019, showing the incidence and mortality of preterm birth.[10] To further fill the gap in data on the global burden of preterm birth, we have utilized the updated GBD2021 data and extended their work by employing multiple analytical methods. Specifically, we have identified and discussed key join points, performed decomposition analysis, and conducted a cross-country health inequality analysis considering the Socio-demographic Index (SDI) to get an in-depth understanding of the global burden of preterm births. The aim is to support efforts to reduce global burden of preterm birth, narrow health disparities worldwide, and promote the development of public health policies.

Methods

Data source and framework

Data in this study were obtained from the GBD 2021 results (available from https://vizhub.healthdata.org/gbd-results/), which is the largest and most recent comparative assessment of the burdens of 371 diseases and injuries at the global, regional, and national levels. GBD 2021 produced estimates for 204 countries and territories, grouped into 21 regions (Supplementary Table S1, Supplementary Fig. S1).[9] In the GBD study, according to the World Health Organization (WHO), preterm birth is defined as infant born alive before 37 weeks of pregnancy.[11] We extracted the annual incidence, mortality and DALYs data of preterm birth from 1990 to 2021. Bayesian meta-regression disease Modelling-Meta Regression (DisMod-MR, version 2.1) is a Bayesian meta-regression framework applied to GBD data modelling, which generates internally consistent estimates of prevalence, incidence, remission and mortality based on sex, location, year and age group, and can also be used to analyse the estimates based on a linear regression model of the age-standardized rates (ASR) (Details are in Supplementary file).[9,12] DisMod-MR provides these measures for locations with missing raw epidemiological data by estimating prevalence across a cascade down the five levels of the GBD geographical hierarchy, and it can also use location-level covariates to provide prevalence and incidence for locations with missing data.[9] DALYs were obtained by calculating the sum of the years of life lost (YLLs) and years lived with disability (YLDs).[13] YLDs were calculated by multiplying cause-age-sex-location-year-specific prevalence of sequelae by their respective disability weights, for each disease and injury.[9] YLLs were calculated by multiplying cause-age-sex-location-year-specific deaths by the standard life expectancy at the age that death occurred.[9]

Data were grouped by SDI (Supplementary Table S1) and sex. The SDI is estimated by composite of income per capita, average years of schooling, and fertility rate in females under 25 years old.[14] The SDI divides regions into five levels with higher values indicating a higher economic level.[14]

Decomposition analysis

Decomposition analyses can provide insights into the specific causes that influence changes in DALYs over the defined time periods at the global, regional and national levels.[15] This study further explored the impact of underlying factors on the epidemiology of DALYs through decomposition analyses. Changes in DALYs due to preterm birth were decomposed into aging, population and epidemiological change, thus quantifying the impact of these factors on overall DALYs.[13,16]

Cross-country health inequality analysis

The distribution inequality of preterm birth burden across countries was measured by the slope index of inequality and the health inequality concentration index.[17] The slope index of inequality was calculated by regressing the incidence, mortality and DALYs of preterm birth on the income-related relative social position scale, defined as the midpoint of the cumulative class interval of the population sorted by gross domestic product per capita.[17] Heteroskedasticity was calculated using a weighted regression model. The health inequality concentration index was calculated by fitting the observed cumulative relative distribution of the population sorted by income to the Lorenz concentration curve for the burden of preterm birth and numerically integrating the area under the curve.[18]

Statistics

Temporal trends in the global burden of preterm birth were analysed by Joinpoint regression (Version 5.1.0.0), and then the simplest possible model was fitted to the data by joining several different line segments on a logarithmic scale.[19] Joinpoint software used a structured approach to appreciate time trends and identified the most suitable joins for trend changes that were statistically significant.[20,21] The annual percentage change (APC) and its 95% confidence interval (CI) were calculated using the geometrically weighted average of the various annual percentage change values in the regression analysis and used to estimate the temporal trend in incidence, mortality and DALYs.[22] Average annual percentage change (AAPC) is a summary of trends over a predetermined fixed time interval and a weighted average of APC to describe the average APC over a multiple year period. In addition, the estimated annual percentage change (EAPC) is also an important indicator to assess the trends of changes.[23] All rates were reported per 100,000 population and presented with 95% uncertainty interval (UI), which are the 25th and 975th ordered values on the 1000 draws of the posterior distribution.[13,22] All data analysis and visualization were used R software (Version 4.3.0), and two-sided $P < 0.05$ was considered statistically significant.

Ethics statement

For GBD studies, the Institutional Review Board of the University of Washington reviewed and approved a waiver of informed consent (https://ghdx.healthdata.org/gbd-2021).[9]

Role of the funding source

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

Results

The incidence and changes of preterm birth

The global annual incidence cases of preterm birth declined by −6.29% (95% UI: −7.37 to −5.2, Table 1), from 23000790.05 (95% UI: 22827689.49–23186894.79) in 1990–21553770.76 (95% UI: 21378909.71–21730108.45) in 2021 (Table 1). Moreover, ASIR decreased from 358.94 (95% UI: 356.24–361.84) in 1990–348.41 (95% UI: 345.58–351.26) in 2021, with an EAPC of −0.27 (95% CI: −0.34 to −0.2) and an AAPC of −0.09 (Table 1, Fig. 1). The ASIR began to decline in 1997, with a more moderate downward trend until 2006 (APC: −0.15, 95% CI: −0.178 to −0.12, Fig. 1, Supplementary Table S2) and steeper downward trends from 2006 to 2009 (APC: −1.02, 95% CI: −1.27 to −0.76, Fig. 1, Supplementary Table S2) and from 2009 to 2016 (APC: −0.67, 95% CI: −0.71 to −0.62, Fig. 1, Supplementary Table S2). Global ASIR showed an increasing trend after 2016 (APC: 0.56, 95% CI: 0.5–0.62, Fig. 1, Supplementary Table S1). Even though the EAPC for ASIR decreased by −0.33 (95% CI: −0.39 to −0.26) in males, the annual incidence cases were higher in males than in females (Table 1). The AAPC for ASIR was −0.15 in males, while there was no change in females (Supplementary Fig. S2). There was a significant upward trend in 2016 for both, as with the global trend (Table 1, Supplementary Fig. S2).

In contrast to the global, the annual incidence cases in low SDI regions increased by 43.1% (Table 1). ASIR decreased in each region except high SDI regions (EAPC: 0.23, 95% CI: 0.16–0.31, Table 1). Low-middle and low SDI regions had an obvious EAPC of −0.66 (95% CI: −0.73 to −0.6) and −0.47 (95% CI: −0.5 to −0.43), and AAPC were also reduced substantially at −0.52 and −0.41 respectively, but ASIR was always above the global level (Table 1, Fig. 1). The ASIR for middle, high-middle and high SDI regions were consistently lower than the global level. The ASIR for high and high-middle SDI regions overlapped around 1996, and since then the ASIR for high SDI regions have been higher than high-middle SDI regions (Fig. 1). Similar to the global trend, ASIR in middle (APC: 1.08, 95% CI: 0.95–1.22, Fig. 1, Supplementary Table S2) and high-middle SDI regions (APC: 1.09, 95% CI: 0.96–1.23, Fig. 1, Supplementary Table S2) exhibited an upward trend from 2016, with high SDI regions also exhibited an upward trend from 2017 (APC: 0.52, 95% CI: 0.47–0.57, Fig. 1, Supplementary Table S2). In 2021, males were more commonly born preterm than females in each region (Supplementary Table S3). At the regions level, North Africa and Middle East (APC: 0.23, Supplementary Fig. S4) and Central Asia (APC: 0.22, Supplementary Fig. S19) also showed similar trends. Southern Latin America has been on an upward trend in ASIR except from 2016 to 2019 (APC: −0.35), with an inflection point in 2019 (Supplementary Fig. S21). Over the past 31 years, the annual incidence cases increased nearly 100 times in Western sub-Saharan Africa (98.95%, 95% UI: 94.77%–103.09%, Table 1) and Oceania (96.64%, 95% UI: 79.84–114.33%, Table 1), with the sharpest decline in East Asia (−67.05%, 95% UI: −68.09 to −65.93, Table 1). In both 1990 and 2021, the highest ASIR was consistently in South Asia with an EAPC of −0.53 (95% CI: −0.6 to −0.46, Table 1). The lowest ASIR in 2021 with a sharp decrease was seen in East Asia (EAPC: −1.45, 95% CI: −1.6 to −1.31, AAPC: −1.22, Table 1, Supplementary Fig. S7). The most significant increase in EAPC (0.78, 95% CI: 0.74–0.81) and AAPC (0.68%) was seen in Southern Latin America (Table 1, Supplementary Fig. S21).

Among 204 countries and territories, India, Nigeria, Pakistan and China were the top four countries with the highest annual incidence cases in 2021 (Fig. 2A, Supplementary Table S4). India accounted for 29.55% of the global annual incidence cases. The lowest annual incidence cases in 2021 occurred in Tokelau (2.34, 95% UI: 2.12–2.56, Supplementary Table S4). Compared to 1990, the annual incidence cases of Qatar increased more than two hundred-fold, Chad, Greece, Niger, Afghanistan, Papua New Guinea and 11 other countries more than one hundred-fold, and the most speed decline was in Albania (Supplementary Table S4). The highest and lowest ASIR were observed in Mauritania (644.6, 95% UI: 599.31–692.39) and China (146.46, 95% UI: 143.24–150.14, Supplementary Table S4, Supplementary Fig. S72). ASIR of Greece showed an incredible increased trend with an EAPC of 4.36 (95% CI: 3.37–5, Supplementary Table S4, Supplementary Fig. S73). Nepal experienced a substantial decreasing with an EAPC of −1.66 (95% CI: −1.78 to −1.55, Supplementary Table S4, Supplementary Fig. S72). Mali, Gabon and United States of America did not change in the last 31 years with an EAPC of 0% (Supplementary Table S4, Supplementary Fig. S72).

The mortality and changes of preterm birth

The global annual mortality in 2021 was −42.86% (95% UI: −52.63 to −32.34, Table 1) lower than in 1990, but as high as 739,670.71 (95% UI: 622745.54–877043.08, Table 1). The global ASMR declined with an EAPC of −1.67 (95% CI: −1.71 to −1.62) from 20.27 (95% UI: 18.65–21.9) in 1990 to 11.94 (95% UI: 10.05–14.16) in 2021. It has shown a downward trend (AAPC: −1.68), with a flattening decline from 1990 to 1993 (APC: −0.72, 95% CI: −1.06 to −0.37, Fig. 3, Supplementary Table S2) and the fastest decline from 2012 to 20,021 (APC: −2.21, 95% CI: −2.32 to −2.11, Fig. 3, Supplementary Table S2). Annual mortality was lower in females (320312.29, 95% UI: 265844.63–372893.42)) compared with males (419358.42, 95% UI: 339646.3–506667.59). Additionally, the decrease in EAPC was greater for ASMR for females (−1.77, 95% UI: −1.84 to −1.71) compared with males (Table 1). The largest reduction in ASMR was seen in high-middle SDI regions (EAPC: −4.31, 95% CI: −4.49 to −4.12), followed by high

Location	Incidence						Mortality						DALYs					
	Number (95% UI)		Percentage change (95% UI)	ASIR (95% UI)		EAPC (95% CI)	Number (95% UI)		Percentage change (95% UI)	ASMR (95% UI)		EAPC (95% CI)	DALYs (95% UI)		Percentage change (95% UI)	Age-standardized DALYs (95% UI)		EAPC (95% CI)
	1990	2021		1990	2021		1990	2021		1990	2021		1990	2021		1990	2021	
Global	23000790.05 (22827689.49, 23186894.79)	21553770.76 (21378909.71, 21730108.45)	−6.29 (−7.37, −5.2)	358.94 (356.24, 361.84)	348.41 (345.58, 351.26)	−0.27 (−0.34, −0.2)	1294528.79 (1190588.75, 1399065.7)	739670.71 (622745.54, 877043.08)	−42.86 (−52.63, −32.24)	20.27 (18.65, 21.9)	11.94 (10.05, 14.16)	−1.67 (−1.71, −1.62)	124349683.84 (114962460.28, 133879960.64)	80335171.21 (69875880.73, 93716788.97)	−35.4 (−45.51, −25.26)	1962.26 (1814.42, 2111.62)	1254.24 (1088.18, 1465.54)	−1.4 (−1.44, −1.36)
Sex																		
Female	9550078.22 (9436355.26, 9656370.19)	9224694.94 (9113876.1, 9330107.89)	−3.41 (−1.75, −5.11)	309.26 (305.58, 312.71)	308.84 (305.13, 312.37)	−0.19 (−0.26, −0.12)	553117.62 (498109.14, 609762.03)	320312.29 (265844.63, 372893.42)	−42.09 (−30.36, −51.76)	17.96 (16.18, 19.8)	10.7 (8.88, 12.46)	−1.77 (−1.84, −1.71)	53248516.68 (48106241.24, 58594625.79)	35196273.07 (30065534.75, 40303138.22)	−33.9 (−43.45, −22.67)	1741.83 (1573.76, 1916.22)	1131.58 (960.47, 1292.87)	−1.34 (−1.39, −1.29)
Male	13450711.83 (13321036.42, 13580416.07)	12329075.82 (12192632.55, 12464605.4)	−8.34 (−6.91, −9.49)	405.15 (401.24, 409.05)	385.35 (381.09, 389.59)	−0.33 (−0.39, −0.26)	741411.17 (670716.93, 819273.66)	419358.42 (339646.3, 506667.59)	−43.44 (−31.05, −53.68)	22.41 (20.28, 24.77)	13.09 (10.6, 15.82)	−1.13 (−1.21, −1.06)	71101167.16 (64912847.08, 77866276.66)	45138898.13 (38481998.29, 53297215.99)	−36.51 (−47.05, −24.06)	2167.68 (1979.59, 2370.97)	1368.86 (1156.13, 1624.64)	−1.45 (−1.48, −1.41)
Low SDI	4816490.13 (4748046.07, 4893397.95)	6892457.61 (6801448.36, 6983754.06)	43.1 (40.17, 46.09)	453.55 (447.1, 460.79)	398.92 (393.65, 404.21)	−0.47 (−0.5, −0.43)	263919.54 (236090.43, 295462.14)	286116.8 (235161.87, 343865.25)	8.41 (−10.45, 32.34)	25.23 (22.54, 28.21)	16.62 (13.66, 19.98)	−2.43 (−2.54, −2.32)	24531562.16 (21999806.41, 27379346.39)	27888156.27 (23625702.46, 33171116.61)	13.68 (−4.87, 37.26)	2400.57 (2156.43, 2670.67)	1667.11 (1421.01, 1982.42)	−0.96 (−1.04, −0.89)
Low-middle SDI	9075073.98 (8933627.46, 9231453.98)	7762338.07 (7637894.47, 7895512.05)	−14.47 (−16.41, −12.45)	488.27 (480.66, 496.69)	416.03 (409.36, 423.17)	−0.66 (−0.73, −0.6)	535555.47 (481479.76, 586400.28)	299790.7 (244911.88, 356,282)	−44.02 (−54.42, −31.18)	28.96 (26.04, 31.71)	16.07 (13.13, 19.1)	−4.31 (−4.49, −4.12)	51073851.4 (46358312.7, 55809318.78)	32461035.93 (27390271.51, 38091866.39)	−36.44 (−47.58, −24.68)	2820.9 (2565.57, 3093.96)	1718.94 (1449.88, 2019.09)	−1.48 (−1.54, −1.42)
Middle SDI	5717900.7 (5648218.13, 5785963.25)	4455140.24 (4409831.31, 4498695.86)	−22.08 (−23.31, −20.8)	285.4 (281.93, 288.8)	291.08 (288.12, 293.93)	−0.06 (−0.1, −0.02)	355057.21 (327137.16, 386016.3)	123712.66 (103522.47, 143864.46)	−65.16 (−71.21, −58.84)	17.75 (16.35, 19.29)	8.06 (6.75, 9.37)	−2.67 (−2.78, −2.55)	34124620.99 (31412367.12, 37158355.63)	14940730.78 (12931455.75, 17073763.97)	−56.22 (−62.83, −49.81)	1713.08 (1577.07, 1866.34)	887.08 (763.42, 1022.9)	−2.02 (−2.11, −1.94)
High-middle SDI	2038426.34 (1999354.58, 2078757.96)	1218508.17 (1197443.06, 1242861.63)	−40.22 (−41.83, −38.68)	232.23 (227.78, 236.83)	216.68 (212.93, 221.01)	−0.42 (−0.49, −0.35)	102783.36 (93710.96, 114497.56)	17749.13 (15531.8, 20095.47)	−82.73 (−85.52, −79.94)	11.68 (10.65, 13.02)	3.14 (2.74, 3.55)	−0.6 (−0.87, −0.34)	10264766.06 (9298450.73, 11390300.78)	2780884.58 (2406882.07, 3171279.57)	−72.91 (−76.71, −68.75)	1146.86 (1043.38, 1273.1)	383.41 (342.02, 431.67)	−3.64 (−3.77, −3.51)
High SDI	1337379.05 (1317970.01, 1359009.01)	1209005.4 (1190994.36, 1226195.86)	−9.6 (−11.45, −7.79)	222.49 (219.26, 226.09)	244.32 (240.68, 247.79)	0.23 (0.16, 0.31)	36442.62 (34887.51, 38209.36)	11861.04 (10593.73, 12936.66)	−67.45 (−70.56, −64.58)	6.05 (5.79, 6.34)	2.39 (2.13, 2.61)	−4.5 (−4.68, −4.32)	4278445.12 (3980591.83, 4617511.27)	2216635.35 (1883535.23, 2557046.16)	−48.19 (−53.35, −43.66)	663.41 (625.26, 706.01)	334.94 (296.63, 374.55)	−1.96 (−2.06, −1.87)
Central Asia	180116.4 (172873.47, 187393.01)	181507.19 (173160.59, 190584.54)	0.77 (−5.14, 6.87)	190.85 (183.18, 198.56)	184.81 (176.31, 194.05)	−0.21 (−0.24, −0.18)	8667.92 (7923.72, 9475.12)	7000.5 (5860.83, 8272.74)	−19.24 (−32.81, −1.73)	9.19 (8.4, 10.04)	7.12 (5.96, 8.41)	−4.12 (−4.46, −3.78)	849475.2 (778158.67, 925236.92)	711364.64 (607218.63, 825605.38)	−16.26 (−29.04, −0.39)	919.48 (842.97, 1001.98)	723.84 (618.02, 840.05)	−0.56 (−0.8, −0.33)
Central Europe	170002.3 (165482.12, 174666.05)	111895.11 (109062.8, 114943.34)	−34.18 (−36.55, −31.63)	205.97 (200.49, 211.62)	222.41 (216.78, 228.47)	0.22 (0.2, 0.25)	9636.4 (9187.4, 10131.52)	1435.35 (1208.08, 1666.62)	−85.1 (−87.75, −82.57)	11.64 (11.1, 12.24)	2.84 (2.39, 3.3)	−2.26 (−2.37, −2.14)	998902.86 (946068.03, 1063249.35)	234290.21 (200067.57, 269806.23)	−76.55 (−79.7, −73.52)	1157.15 (1102.06, 1220.67)	361.59 (315.07, 411.38)	−3.75 (−3.93, −3.57)
Eastern Europe	238467.07 (233169.31, 243840.58)	156145.23 (153154.79, 159293.64)	−34.52 (−36.36, −32.69)	166.14 (162.45, 169.89)	181.07 (177.6, 184.72)	0.33 (0.3, 0.35)	11370.35 (10807.79, 11967.24)	1965.85 (1753.23, 2180.67)	−82.71 (−84.48, −80.83)	7.9 (7.51, 8.31)	2.27 (2.03, 2.52)	−2.34 (−2.8, −1.87)	1170679.51 (1108802.28, 1246001.63)	309334.27 (272429.12, 348574.4)	−73.58 (−76.39, −70.84)	780.21 (739.77, 824.73)	279.1 (253, 309.06)	−3.47 (−3.73, −3.21)
High-income	1339513.32 (1320791.78, 1359506.17)	1244314.9 (1225957.45, 1262041.68)	−7.11 (−8.96, −5.17)	222.11 (219.01, 225.43)	247.07 (243.43, 250.59)	0.31 (0.23, 0.38)	35129.03 (34507.71, 35705.85)	12787.47 (11334.87, 14150.12)	−63.6 (−67.84, −59.63)	5.81 (5.71, 5.91)	2.53 (2.24, 2.8)	−4.36 (−4.53, −4.19)	4,168,926 (3879385.9, 4499474.58)	2291502.19 (1955920.27, 2634409.49)	−45.03 (−50, −40.22)	640.35 (607.36, 679.7)	347.94 (307.5, 389.7)	−1.65 (−1.74, −1.55)
Australasia	27883.68 (26393.29, 29405.08)	35210.9 (32471.73, 37943.11)	26.28 (15.33, 39.96)	182.74 (172.97, 192.71)	204.7 (188.78, 220.59)	0.42 (0.37, 0.47)	745.03 (708.87, 787.69)	287.18 (244.26, 339.42)	−61.45 (−67.97, −54.01)	4.88 (4.64, 5.16)	1.67 (1.42, 1.97)	−1.39 (−1.55, −1.22)	95512.44 (86073.84, 106287.33)	61081.4 (50897.33, 73069.96)	−36.05 (−44.24, −26.72)	583.17 (533.23, 639.79)	273.81 (232.18, 322.08)	−1.7 (−2.04, −1.37)
High-income Asia Pacific	152521.23 (146587.54, 158848.72)	99783.47 (96987.48, 103,004)	−34.58 (−37.66, −31.09)	160.62 (154.37, 167.28)	174.62 (169.73, 180.26)	0.33 (0.27, 0.4)	3040.58 (2711.09, 3407.09)	397.76 (356.29, 444.04)	−86.92 (−88.66, −84.59)	3.19 (2.85, 3.57)	0.69 (0.62, 0.77)	−3.18 (−3.29, −3.06)	405278.66 (360058.37, 457181.79)	164585.02 (127979.24, 202984.31)	−59.39 (−66.61, −53.32)	365.53 (329, 408.24)	143.32 (117.9, 167.25)	−2.66 (−2.83, −2.5)
High-income North America	570528.73 (559604.16, 582073.98)	536186.45 (527210.57, 545915.63)	−6.02 (−8.43, −3.46)	259.74 (254.77, 264.99)	275.06 (270.45, 280.05)	0.06 (−0.09, 0.21)	13305.22 (12,985, 13633.7)	6535.04 (5819.71, 7268.23)	−50.88 (−56.1, −45.17)	6.05 (5.9, 6.2)	3.34 (2.98, 3.72)	−2.8 (−2.96, −2.64)	1610388.83 (1484924.02, 1737629.66)	1074544.97 (930615.13, 1229268.05)	−33.27 (−39.28, −27.61)	698.66 (651.18, 747.48)	450.21 (398.6, 502.58)	−1.04 (−1.18, −0.91)
Southern Latin America	101451.42 (94207.03, 108527.02)	92394.15 (86844.22, 98558.57)	−8.93 (−17.15, 0.75)	200.04 (185.76, 213.99)	248.22 (233.31, 264.78)	0.78 (0.74, 0.81)	7421.12 (7083.38, 7762.9)	1891.74 (1494.9, 2359.35)	−74.51 (−79.94, −67.99)	14.63 (13.97, 15.3)	5.07 (4, 6.32)	−3.59 (−3.8, −3.39)	727968.76 (695384.13, 764826.58)	253169.48 (212726.3, 296964.18)	−65.22 (−70.49, −58.91)	1436.37 (1371.95, 1509.18)	584.99 (487.46, 694.16)	−2.69 (−2.81, −2.58)
Western Europe	487128.25 (473725.27, 501602.03)	480739.92 (466192.8, 493835.72)	−1.31 (−5.38, 2.59)	218.94 (212.91, 225.44)	243.88 (236.5, 250.52)	0.34 (0.32, 0.37)	10617.07 (10385.81, 10858.58)	3675.76 (3242.32, 4087.7)	−65.38 (−69.8, −61.31)	4.76 (4.66, 4.87)	1.86 (1.64, 2.07)	−1.26 (−1.37, −1.15)	1329777.3 (1221710.33, 1450175.74)	738121.31 (616257.24, 858873.31)	−44.49 (−50.19, −39.14)	532.32 (500.38, 567.39)	272.73 (236.48, 308.19)	−1.96 (−2.11, −1.82)
Andean Latin America	147798.96 (140158.06, 155720.39)	131176.88 (124241.89, 138643.58)	−11.25 (−17.8, −4.14)	262.52 (248.95, 276.59)	220.67 (209, 233.23)	−0.63 (−0.75, −0.52)	9041.71 (7772.52, 10598.01)	2986.56 (2292.62, 3772.14)	−66.97 (−76.06, −57)	16.11 (13.85, 18.89)	5.01 (3.85, 6.33)	−3.07 (−3.21, −2.93)	869726.51 (757100.94, 1017761.58)	339843.67 (276541.74, 409022.98)	−60.93 (−69.72, −51.42)	1583.36 (1381.71, 1842.75)	557.68 (453.33, 672.95)	−3.24 (−3.41, −3.07)
Caribbean	156649.64 (150811.47, 162396.27)	147715.99 (141284.57, 153440.01)	−5.7 (−10.89, −0.5)	362.64 (349.13, 375.95)	387.28 (370.42, 402.29)	0.18 (0.13, 0.24)	6903.15 (6104.86, 7876.45)	4044.49 (3173.79, 5192.68)	−41.41 (−54.38, −22.6)	16 (14.16, 18.26)	10.6 (8.32, 13.61)	−4.92 (−5.03, −4.8)	698296.56 (623154.91, 789303.32)	441834.89 (356230.84, 547679.95)	−36.73 (−49.04, −19.94)	1645.23 (1467.26, 1858.8)	1124.83 (900.5, 1401.62)	−1.14 (−1.24, −1.03)
Central Latin America	515241.71 (502766.59, 527557.73)	441695.38 (431018.28, 452944.19)	−14.27 (−17.27, −11.38)	215.06 (209.85, 220.2)	235.71 (230.02, 241.72)	0.4 (0.35, 0.44)	39591.66 (37201.94, 42203.15)	11466.33 (9003.26, 14513.35)	−71.04 (−77.47, −63.37)	16.55 (15.55, 17.64)	6.1 (4.79, 7.72)	−3.8 (−3.99, −3.6)	3744487.31 (3524863.24, 3983896.96)	1309814.36 (1073637.83, 1584532.46)	−65.02 (−71.09, −57.52)	1587.8 (1495.08, 1689.65)	660.29 (541.61, 804.47)	−2.7 (−2.83, −2.58)
Tropical Latin America	421156.89 (410696.35, 431548.93)	470460.58 (462004.64, 479914.01)	11.71 (8.08, 15.64)	261.37 (254.87, 267.82)	284.62 (279.51, 290.34)	0.3 (0.19, 0.4)	36944.11 (33083.06, 40778.14)	8187.23 (6601.98, 10066.48)	−77.84 (−82.78, −72.09)	22.94 (20.54, 25.32)	4.94 (3.98, 6.07)	−4.59 (−4.91, −4.26)	3464283.65 (3116224.49, 3808557.8)	1074378.4 (903714.88, 1260069.52)	−68.99 (−74.53, −62.64)	2149.12 (1933.01, 2363.24)	599.13 (501.58, 709.91)	−4.12 (−4.17, −4.07)

(Table 1 continues on next page)

Location	Incidence						Mortality						DALYs					
	Number (95% UI)		Percentage change (95% UI)	ASIR (95% UI)		EAPC (95% CI)	Number (95% UI)		Percentage change (95% UI)	ASMR (95% UI)		EAPC (95% CI)	DALYs (95% UI)		Percentage change (95% UI)	Age-standardized DALYs (95% UI)		EAPC (95% CI)
	1990	2021		1990	2021		1990	2021		1990	2021		1990	2021		1990	2021	
(Continued from previous page)																		
North Africa and Middle East	1814182.36 (1770777.37, 1858896.29)	2042855.68 (1984150.29, 2094880.93)	12.6 (8.26, 16.69)	345.26 (337, 353.77)	357.05 (346.79, 366.15)	0.09 (0.07, 0.11)	171189.76 (153179.39, 194058.24)	52628.57 (44268.56, 61917.67)	−69.26 (−74.58, −63.14)	32.71 (29.26, 37.08)	9.17 (7.71, 10.79)	−0.18 (−0.33, −0.03)	16040584.9 (14403546.89, 18192621.15)	5715722.11 (4924995.26, 6619896.43)	−64.37 (−69.95, −58.38)	3111.51 (2792.65, 3528.48)	977.35 (841.33, 1135.46)	−3.48 (−3.63, −3.33)
East Asia	2466916.59 (2409970.78, 2520598.71)	812742.38 (795675.16, 832278.47)	−67.05 (−68.09, −65.93)	215.08 (210.11, 219.76)	147.31 (144.22, 150.85)	−1.45 (−1.6, −1.31)	125550.81 (101486.33, 156945.11)	15037.48 (12593.17, 17942.04)	−88.02 (−90.98, −84.73)	10.95 (8.85, 13.69)	2.69 (2.25, 3.21)	−1.55 (−1.66, −1.45)	12154929.83 (9967045.75, 15030633.65)	2223325.71 (1882580.21, 2595761.4)	−81.71 (−85.82, −76.93)	1052.95 (861.49, 1304.16)	305.77 (263.36, 356.47)	−4.11 (−4.38, −3.83)
Oceania	37821.7 (35524.89, 40249.16)	74373.51 (68858.79, 79556.01)	96.64 (79.84, 114.33)	350.92 (329.61, 373.44)	362.23 (335.37, 387.47)	0.11 (0.08, 0.14)	1229.5 (998.3, 1474.8)	2199.27 (1688.42, 2798.87)	78.87 (32.43, 141.73)	11.44 (9.29, 13.72)	10.73 (8.24, 13.65)	−2.26 (−2.31, −2.2)	122272.81 (100412.04, 145237.04)	219317.23 (172126.89, 272100.14)	79.37 (37.42, 135.76)	1182.8 (973.61, 1399.28)	1103.83 (870.46, 1366.46)	−0.18 (−0.32, −0.05)
South Asia	10067203.78 (9926260.49, 10221069.92)	8232352.64 (8101110.23, 8375185.87)	−18.23 (−20.16, −16.26)	610.71 (602.16, 620.04)	543.78 (535.11, 553.21)	−0.53 (−0.6, −0.46)	521280.04 (452500.3, 583146.28)	280575.62 (223512.92, 345598.45)	−46.18 (−57.06, −32.48)	31.76 (27.57, 35.52)	18.54 (14.77, 22.83)	−0.56 (−0.65, −0.48)	50484356.68 (44349018.64, 56166300.56)	32760273.93 (27295547.76, 39070225.69)	−35.11 (−46.91, −22.06)	3141.9 (2770.52, 3493.99)	2064.65 (1717.27, 2473.36)	−1.19 (−1.29, −1.09)
Southeast Asia	1703067.74 (1669173.98, 1736631.74)	1408128.31 (1382216.7, 1435053.16)	−17.32 (−19.48, −15.14)	287.35 (281.63, 293.01)	261.11 (256.31, 266.1)	−0.29 (−0.32, −0.26)	96349.67 (86868.14, 106181.25)	43865.35 (35809.4, 51847.81)	−54.47 (−62.8, −45.99)	16.28 (14.68, 17.95)	8.13 (6.64, 9.61)	−0.65 (−0.88, −0.43)	9253903.81 (8375372.63, 10180636.03)	4779508.81 (4057968.29, 5568026.53)	−48.35 (−56.59, −40.11)	1579.17 (1429.09, 1739.15)	851.59 (719.82, 993.2)	−2 (−2.04, −1.96)
sub-Saharan Africa	3742651.6 (3693898.46, 3791588.39)	6,098,407 (6024338.27, 6179575.73)	62.94 (60.05, 65.69)	353.12 (348.52, 357.74)	338.78 (334.67, 343.29)	−0.15 (−0.19, −0.12)	221644.68 (195721.53, 263228.25)	295490.66 (241762.78, 353624.41)	33.32 (7.32, 67.2)	21.31 (18.86, 25.28)	16.48 (13.48, 19.73)	−1.38 (−1.44, −1.33)	20328858.21 (17972063.14, 24058244.19)	27924660.79 (23413677.78, 33171188.44)	37.36 (11.74, 70.73)	1981.82 (1758.4, 2338.6)	1583.89 (1334.5, 1878.88)	−0.46 (−0.54, −0.37)
Central sub-Saharan Africa	376559.31 (354970.58, 398748.24)	548475.18 (519375.21, 578495.2)	45.65 (34.63, 58.63)	305.6 (288.08, 323.61)	256.58 (242.96, 270.62)	−0.63 (−0.67, −0.59)	18281.81 (13969.12, 24724.41)	22596.51 (17425.92, 28660.66)	23.6 (−14.11, 69.79)	15.01 (11.49, 20.28)	10.59 (8.17, 13.44)	−0.29 (−0.39, −0.19)	1682513.62 (1290976.04, 2257752.99)	2158245.02 (1700552.48, 2711770.93)	28.28 (−9.14, 73.23)	1403.22 (1085.29, 1876.33)	1028.86 (818.16, 1290.82)	−0.54 (−0.75, −0.34)
Eastern sub-Saharan Africa	1623650.28 (1588837.09, 1662511.36)	2313001.05 (2262491.15, 2367855.3)	42.46 (38.12, 46.95)	377.5 (369.4, 386.53)	352.54 (344.84, 360.9)	−0.24 (−0.28, −0.21)	81577.49 (72233.18, 94200.37)	78150.78 (61890.82, 97877.08)	−4.2 (−24.42, 23.37)	19.25 (17.04, 22.27)	11.94 (9.45, 14.95)	−0.3 (−0.4, −0.2)	7507791.06 (6680559.02, 8632488.24)	7630926.94 (6,224,695, 9395284.03)	1.64 (−18.16, 29.08)	1801.72 (1606.51, 2070.1)	1193.44 (981.08, 1464.23)	−1.16 (−1.22, −1.1)
Southern sub-Saharan Africa	248313.5 (240592.91, 256047.82)	264337.76 (255618.78, 272199.42)	6.45 (1.52, 11.11)	319.59 (309.65, 329.54)	338.18 (327.02, 348.24)	0.16 (0.07, 0.25)	13140.57 (11165.23, 15153.47)	12198.62 (9781.65, 15152.07)	−7.17 (−26.29, 18.03)	16.94 (14.4, 19.54)	15.61 (12.51, 19.38)	−1.13 (−1.21, −1.06)	1239129.32 (1058726.45, 1420481.34)	1198771.14 (989506.78, 1460362.12)	−3.26 (−21.57, 20.79)	1616.08 (1383.83, 1848.21)	1523.43 (1255.22, 1858.51)	−0.19 (−0.29, −0.1)
Western sub-Saharan Africa	1494128.51 (1473835.08, 1514950.33)	2,972,593 (2925271.6, 3020761.96)	98.95 (94.77, 103.09)	348.41 (343.68, 353.27)	348.87 (343.32, 354.52)	0.01 (−0.03, 0.05)	108644.82 (93965.36, 130967.9)	182544.75 (151726.37, 218905.03)	68.02 (31.01, 117.03)	26.04 (22.46, 31.25)	21.57 (17.9, 25.89)	−1.77 (−1.84, −1.71)	9899424.21 (8579586.68, 11905676.5)	16936717.68 (14228840.27, 20162346.84)	71.09 (34.69, 119.75)	2398.31 (2079.5, 2866.26)	2031.27 (1702.32, 2416.97)	−0.23 (−0.33, −0.14)

UI, uncertainty interval; CI, confidence interval; EAPC, estimated annual percentage change; ASIR, age-standardized incidence rates; ASMR, age-standardized mortality rates; DALYs, disability-adjusted life-years; SDI, Socio-demographic Index.

***Table 1:* The incidence, mortality and DALYs of preterm births in 1990 and 2021, and changes from 1990 to 2021 at the global level and different regions.**

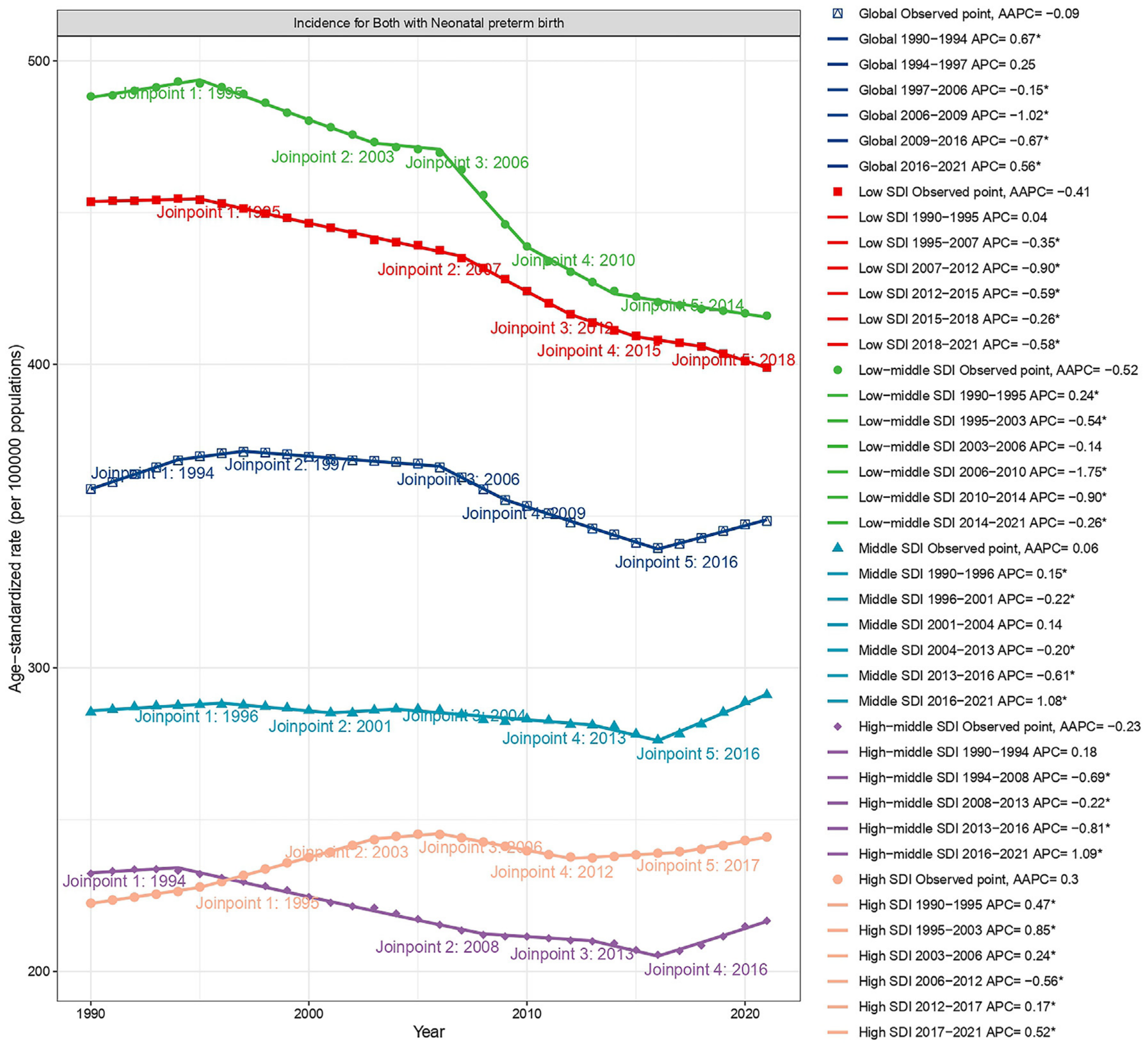

Fig. 1: Global and 5 SDI regions changes of age-standardized incidence rate per 100,000 population of preterm birth from 1990 to 2021. APC, annual percentage change; AAPC, average annual percentage change; SDI, Socio-demographic Index, *$P < 0.05$.

SDI regions (EAPC: −2.67, 95% CI: −2.78 to −2.55) (Table 1). The highest ASMR was seen in low SDI regions (16.62, 95% UI: 13.66–19.98), followed by low-middle SDI regions (16.07, 95% UI: 13.13–19.1) (Table 1). All SDI regions have observed a clear downward trend in ASMR (Fig. 3). ASMR in middle, high-middle and high SDI regions were lower than the global level. Low and low-middle SDI regions had higher ASMR than the global level. Until 2014, the ASMR of low-middle SDI regions were consistently higher than low SDI regions, after which low SDI regions were higher than low-middle SDI regions (Fig. 3). In each region, males had higher annual mortality and ASMR compared to females (Supplementary Table S3). The highest annual mortality was in sub-Saharan Africa and South Asia, and the lowest annual mortality was in Australasia and High-income Asia Pacific in 2021 (Table 1). Western sub-Saharan Africa increased by 68.02% (95% UI: 31.01–117.03) in annual mortality with the highest ASMR (21.57, 95% UI: 17.9–25.89) in 2021 (Table 1). The annual mortality in East Asia and High-income Asia Pacific decreased distinctly by −88.02% (95% UI: −90.98 to −84.73, Table 1) and −86.92% (−88.66 to −84.59, Table 1), respectively. High-income Asia Pacific also had the lowest ASMR in 2021 (0.69, 95% UI: 0.62–0.77) with a sharp EAPC of −4.36 (95% CI: −4.53 to −4.19) (Table 1). The AAPC of ASMR was negative in all regions (Supplementary Fig. S26–S48), with the most pronounced decline in Tropical Latin America (AAPC: −4.81, Supplementary Fig. S29). The ASMR of Oceania (APC: 0.02, Supplementary Fig. S28) and Southern sub-Saharan Africa (APC: 5.63, Supplementary Fig. S30) increased in 2019.

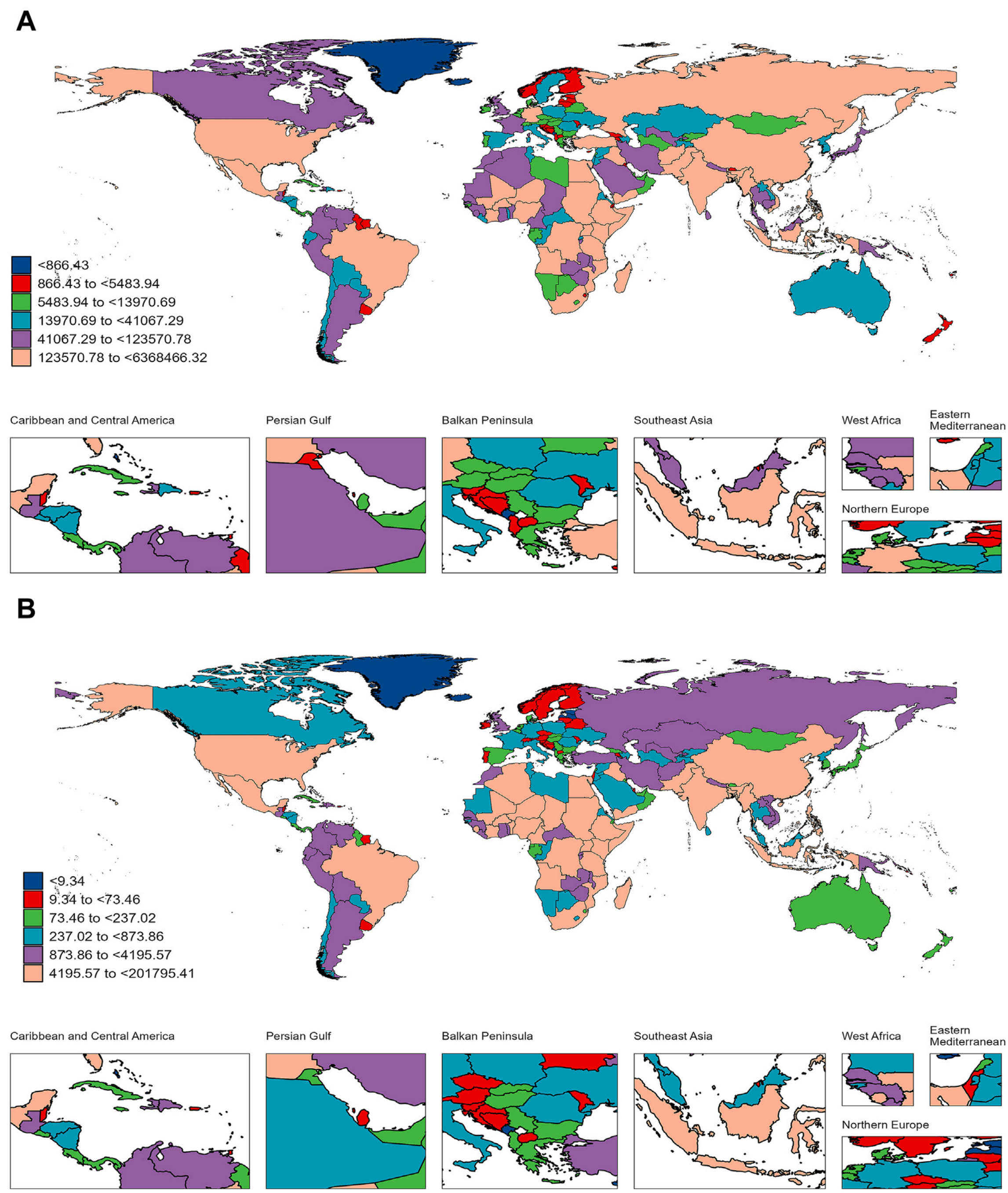

Fig. 2: Global map of annual incidence cases (A) and mortality (B) of preterm birth for both sexes by 204 countries and territories in 2021.

India, Nigeria, Pakistan and Ethiopia ranked the top four countries with the highest annual preterm birth mortality in 2021 (Fig. 2B, Supplementary Table S4). India had the highest annual mortality in both 1990 (7852111.99, 95% UI: 7741026.37–7973421.52) and 2021 (201795.41, 95% UI: 151331.04–255955.66) with an EAPC of −1.18 (95% CI: −1.31 to −1.06) (Supplementary Table S4). The annual mortality for San Marino 2021 was only 0.04 (95% UI: 0.02–0.07, Supplementary Table S4) and the ASMR was the lowest (0.37, 95% UI: 0.2–0.54, Supplementary Table S4, Supplementary Fig. S74) with an EAPC of −2.61 (95% CI: −2.89 to −2.32, Supplementary Table S4, Supplementary Fig. S75). This indicated significant

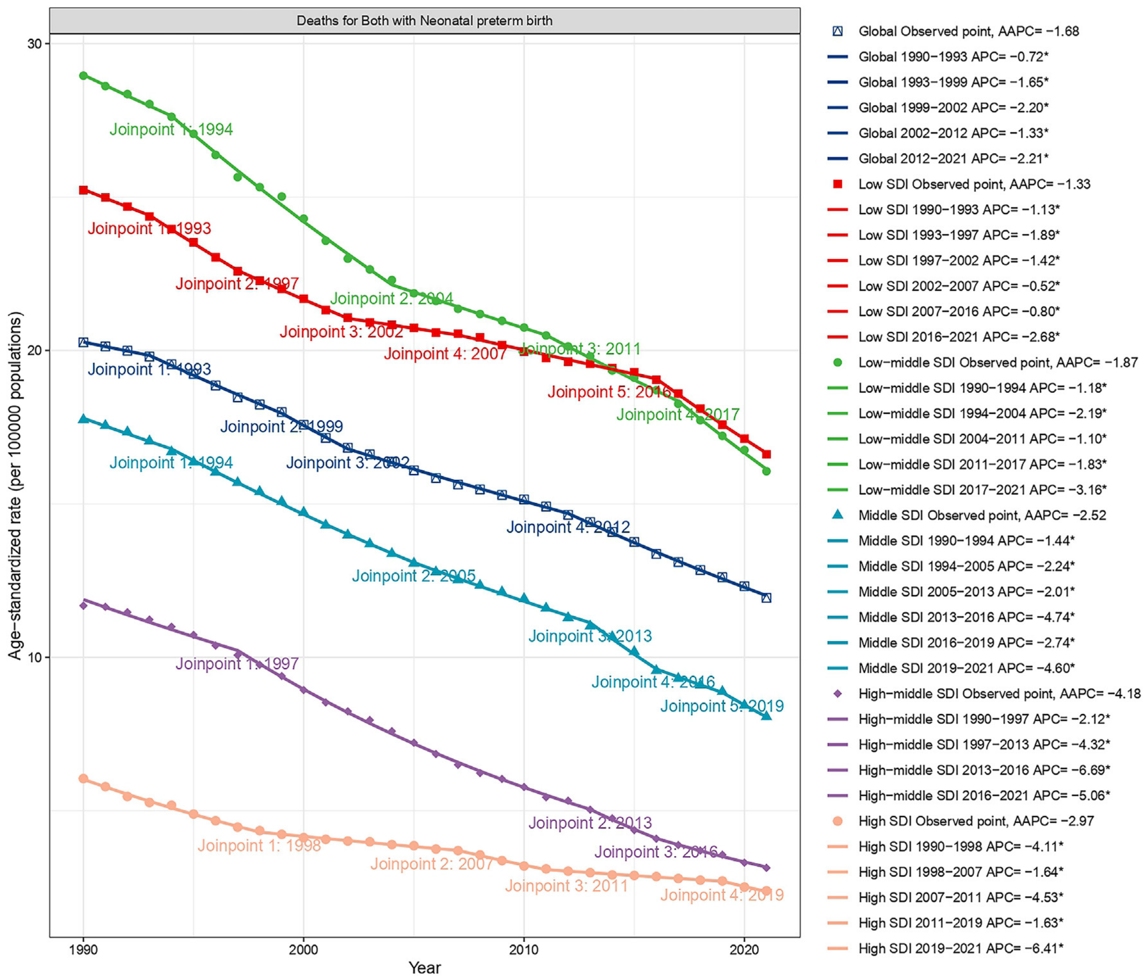

Fig. 3: Global and 5 SDI countried changed of age-standardized mortality rate per 100,000 population of preterm birth from 1990 to 2021. APC, annual percentage change; AAPC, average annual percentage change; SDI, Socio-demographic Index, **P* < 0.05.

differences between nations. There were 44 nations with higher ASMR than the global level (Supplementary Table S4). Mali (ASMR: 39.46, 95% UI: 31.45–48.43), Sierra Leone (ASMR: 31.97, 95% UI: 24.07–41.09), Nigeria (ASMR: 24.9, 95% UI: 19.06–31.75), Yemen (ASMR: 24.73, 95% UI: 19.65–31.6), and South Sudan (ASMR: 22.78, 95% UI: 15.17–33.96) were the top five nations with higher ASMR (Supplementary Table S4). The highest increase in ASMR was Uzbekistan, from 3.92 (95% UI: 3.2–4.99) to 7.65 (95% UI: 6.2–9.44) with an EAPC of 3.13 (95% CI: 2.67–3.6) (Supplementary Table S4). The dramatic decrease in ASMR was Estonia, from 3.79 (95% UI: 3.28–4.3) to 0.39 (95% UI: 0.335–0.45) with an EAPC of −7.87 (95% CI: −8.28 to −7.46) (Supplementary Table S4).

The DALYs and changes of preterm birth

The global DALYs decreased by −35.4% (95% UI: −45.51 to −25.26, Table 1) from 124349683.84 (95% UI: 114962460.28–133879960.64) in 1990–80335171.21 (95% UI: 69875880.73–93716788.97) in 2021 (Table 1). The global age-standardized DALYs showed a download trend from 1990 to 2021 (EAPC: −1.4, Table 1), decreasing from 1962.26 (95% CI: 1814.42–2111.62, Table 1) to 1254.24 (95% UI: 1088.18–1465.54, Table 1), with a slow decline in the first three years (APC: −0.66, 95% CI: −1.01 to −0.32, Fig. 4, Supplementary Table S2) and a rapid decrease after 2021 (APC: −1.88, 95% CI: −2 to −1.77, Fig. 4, Supplementary Table S2). Although the downward trend in DALYs was more obvious in males, it remains higher than in females with an EAPC of −1.45 (95% CI: −1.48 to −1.41) of age-standardized DALYs (Table 1).

The age-standardized DALYs in low SDI decreased by −0.96 (95% UI: −1.04 to −0.89, Table 1) and were lower than the global level. The most pronounced decline was in high-middle SDI regions (−72.91%, 95% UI: −76.71 to −68.75, Table 1), followed by middle SDI

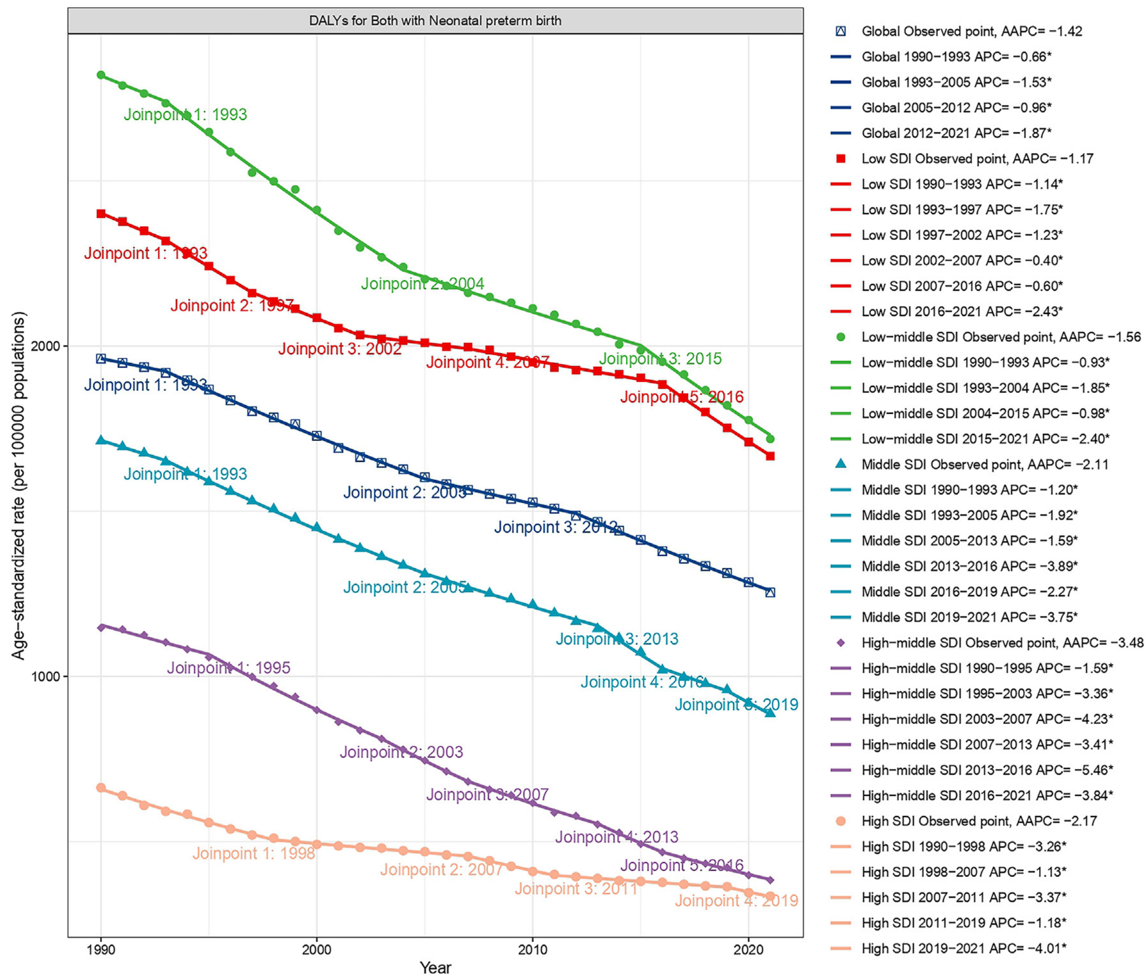

Fig. 4: Global and 5 SDI countried changed of age-standardized DALYs per 100,000 population of preterm birth from 1990 to 2021. APC, annual percentage change; AAPC, average annual percentage change; SDI, Socio-demographic Index; DALYs, disability-adjusted life-years, *$P < 0.05$.

regions (–56.22%, 95% UI: –62.83 to –49.81, Table 1). The trend of age-standardized DALYs for all SDI regions was similar to ASMR (Fig. 4, Supplementary Table S2). The difference was that age-standardized DALYs in low-middle SDI regions were consistently higher than those in low SDI regions, and both began to decline at an accelerated rate between 2015 and 2016 (Fig. 4). Similarly with the annual incidence cases and mortality in 2021, males had higher DALYs and age-standardized DALYs compared to females in each region (Supplementary Table S3). The highest DALYs and age-standardized DALYs were in South Asia, and the lowest DALYs and age-standardized DALYs were in Australasia and High-income Asia Pacific in 2021 (Table 1). EAPCs in all regions showed a downward trend, with the steepest decline in Tropical Latin America (EAPC: –4.12, 95% CI: –4.17 to –4.07, Table 1). Age-standardized DALYs were decreased in all regions (Supplementary Fig. S49–S71), particularly in Tropical Latin America (APC: –4.04, Supplementary Fig. S52). As with ASMR, the age-standardized DALYs of Oceania (APC: 0.1, Supplementary Fig. S51) and Southern sub-Saharan Africa (APC: 4.99, Supplementary Fig. 55) also increased after 2019.

Similar to the annual incidence cases, India, Nigeria, Pakistan and China also were the top four countries with highest DALYs in 2021 (Supplementary Table S4) and Tokelau had the lowest DALYs in 2021 (17.22, 95% UI: 11.11–24.95, Supplementary Table S4). Nine nations with more than 2000 age-standardized DALYs (Mail, Sierra Leone, Yemen, Nigeria, Pakistan, India, Sudan, South Sudan and Niue, Supplementary Table S4). Mail had the highest age-standardized DALYs (3640.04, 95% UI: 2940.35–4462.03, Supplementary Table S4) in 2021. The most dramatic increasing and decreasing in EAPC were Saudi Arabia (–6.79, 95% CI: –6.95 to –6.63), and Uzbekistan (3.14, 95% CI: 2.44–3.86) (Supplementary Table S4).

Decomposition analysis of change in DALYs

Fig. 5 and Supplementary Table S5 presented the decomposition analysis results of DALYs changes attributable to the three population-level determinants (aging, population and epidemiologic change) at the global level, across five SDI strata and GBD super regions. The decomposition analyses indicated that, globally, 111.97% of the changes in DALYs were contributable to epidemiologic change, followed by population (−21.59%) and aging (9.62%) (Fig. 5, Supplementary Table S5). Among the different SDI regions, those most affected by the three population-level determinants were in low SDI regions, with −576.52% of epidemiological change, −731.34% of population, and −54.82% of aging (Fig. 5, Supplementary Table S5). Epidemiological change was least affected by high-middle SDI regions (81.08%), population was least affected by middle SDI regions (5.57%), and aging was least affected by high SDI regions (3.49%) (Fig. 5, Supplementary Table S5). Seen in this light, there was a great difference in the contribution of the three determinants to DALYs. The contribution of epidemiological change to DALYs was positive for all SDI regions except low SDI regions (−576.52%, Fig. 5, Supplementary Table S5). The contribution of population to DALYs was positive in all but low-middle SDI regions (−27.78%), while the contribution of aging to DALYs was positive in all but low SDI regions (−54.82%) (Fig. 5, Supplementary Table S5). It is striking that the contributions of epidemiologic change (2865.63%), population (−3063.82%) and aging (298.19%) to the change in overall DALYs were all the largest in Eastern sub-Saharan Africa (Fig. 5, Supplementary Table S5). Among the different regions, those least affected by epidemiological change, population and ageing were Oceania (−13.52%), High-income North America (−0.69%), and Central Europe (−1.04%), respectively (Fig. 5, Supplementary Table S5).

Cross-country health inequality analysis

The results of the study showed significant absolute and relative income inequality in incidence, mortality and DALYs burden due to preterm birth (Fig. 6). The burden of preterm birth was concentrated in poor regions. Comparison of 1990 and 2019 data showed a reduction in health inequality. The concentration index of incidence did not change significantly in 2021 (Fig. 6A), and the slope index of inequality indicated that the gap in incidence between low and high SDI regions decreased from 778 in 1990 to 448 in 2021 (Fig. 6B). The

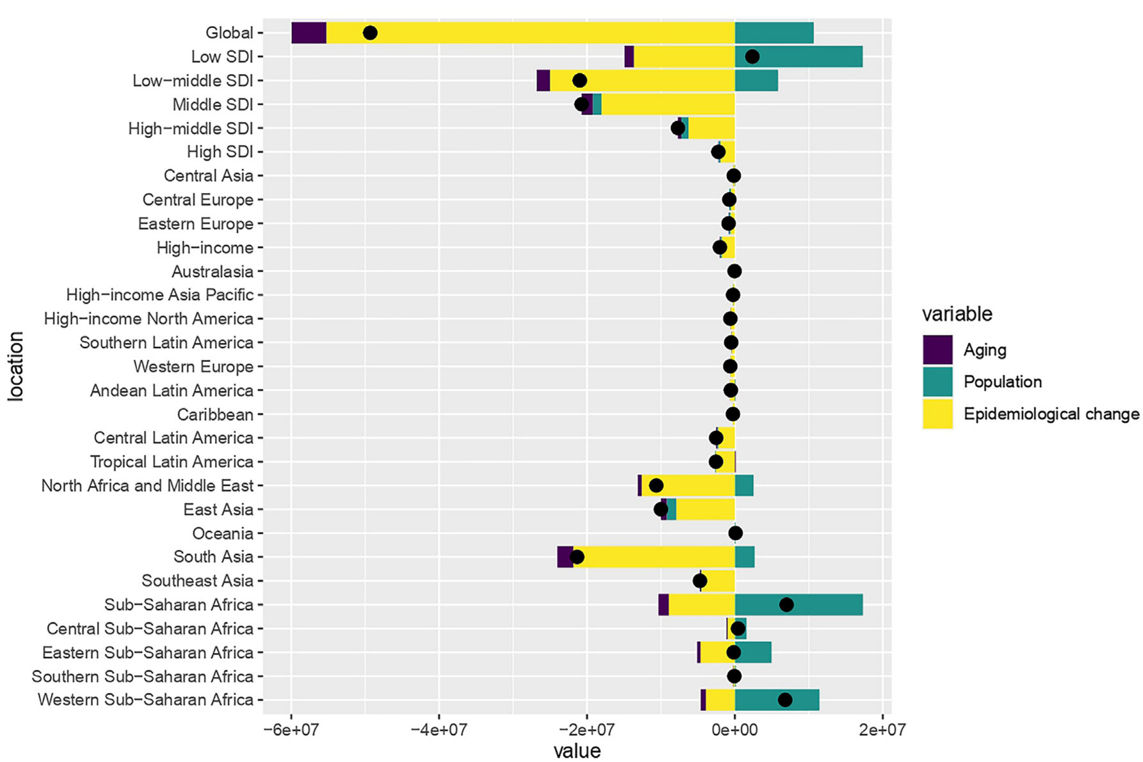

Fig. 5: Change in disability-adjusted life-years of preterm birth decomposed by three population-level determinants: aging, population and epidemiological change at the global level and various regions. The black dots indicate the total value of change attributable to all three components. SDI, Socio-demographic Index.

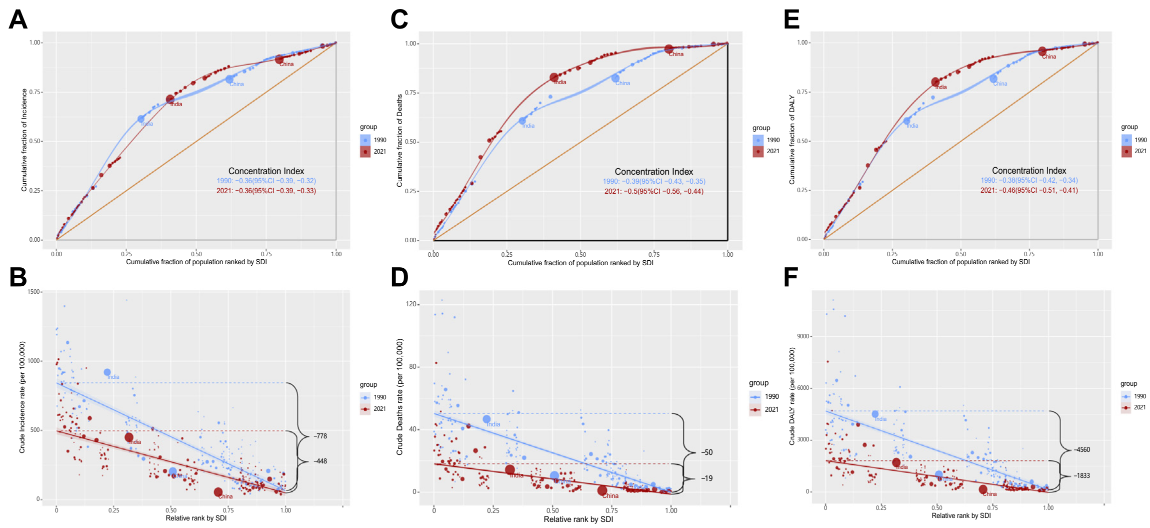

Fig. 6: Health inequality regression curves and concentration curves for the incidence (A and B), mortality (C and D) and disability-adjusted life-years (E and F) of preterm birth. SDI, Socio-demographic Index.

concentration index of mortality changed from −0.39 (95% CI: −0.43 to −0.35) in 1990 to −0.5 (95% CI: −0.56 to −0.44) in 2021 (Fig. 6C), and the slope index of inequality was −50 in 1990 and −19 in 2021 (Fig. 6D). The concentration index of DALYs ranged from −0.38 (95% CI: −0.42 to −0.34) in 1990 to −0.46 (95% CI: −0.51 to −0.41) in 2021 (Fig. 6E). The slope index of inequality of DALYs decreased from −4560 in 1990 to −1833 in 2021 (Fig. 6F). All these results demonstrated a reduction in the unequal burden of preterm birth.

Discussion

Preterm birth is the leading cause of neonatal morbidity and mortality.[24] In addition to the high risk of adverse health outcomes, preterm birth also imposes substantial economic burdens.[25–27] Globally, more than one in ten newborns are preterm infants, with the preterm birth rates ranging from 4% to 16% across different countries.[7,28] It has been estimated that a total of 900,000 cases of infant deaths were attributed to preterm birth per year.[2] Using the latest GBD 2021 data, our study comprehensively analysed the burden of preterm birth. The results identified a decline in the global burden of preterm birth, with males experiencing a higher burden than females. The burden of preterm birth varied significantly in regions with different income levels and was inversely associated with income. Health inequality decreased in all regions. Epidemiological change and population were the two major drivers of changes in DALYs. India, Nigeria, and Pakistan were top 3 nations globally in terms of annual incidence cases, annual mortality and DALYs. This study highlights the impact of prematurity on global health and provides a scientific basis for the development of prevention and management strategies.

The results of our study indicated a downward trend in the global incidence, mortality, and DALYs related to preterm birth, which reflected significant strides in maternal and neonatal health over recent decades. Central to these improvements have been initiatives like the Every Newborn Action Plan (ENAP), which was launched in 2014 and aims to end preventable newborn and maternal deaths by 2030, emphasizing the importance of improving care around the time of birth and reducing complications associated with preterm birth.[29] The success of ENAP and similar global efforts has led to substantial reductions in neonatal mortality and morbidity, particularly in low-resource regions with heavy burden of preterm birth.[5,30]

Despite these positive outcomes, our analysis indicated a troubling shift in preterm birth rates around 2016, where the previously declining incidence rates began to rise. This shift may reflect regional differences in socioeconomic conditions, environmental factors. In regions such as North Africa, the Middle East, and Eastern Europe, ongoing conflicts and resulting displacement of populations have had profound impacts on maternal and child health.[31] Political instability and armed conflicts have disrupted healthcare systems, leading to inadequate prenatal care and increased stress levels among pregnant women. Refugee populations often face severe healthcare access barriers, leading to higher rates of untreated maternal conditions and preterm birth.[32] Furthermore, economic instability and austerity measures in various countries can lead to reduced funding for public health programs, affecting maternal health services and increasing preterm birth rates.[33]

Moreover, in the 2010s, marked significant changes occurred in global climate and environmental conditions, which have been linked to adverse pregnancy outcomes, including preterm birth.[34] Increased exposure to pollution and environmental degradation in rapidly urbanizing areas might contribute to the observed rise in preterm birth. For instance, regions like North Africa and the Middle East have experienced extreme heatwaves and air quality deterioration, which may have contributed to the observed rise in preterm birth rates in these areas.[35] Additionally, natural disasters, such as hurricanes in Caribbean and drought in Eastern Africa, disrupted healthcare services and increased stress and physical demands on pregnant women.[36]

Western Europe, despite having well-developed healthcare systems, experienced a rise in preterm birth rates around 2016. Factors such as increased migration, economic austerity measures and healthcare funding cuts could have contributed to this trend.[37] Several studies suggested that an increase in migrants, often coming from areas with poor access to prenatal care, may have put pressure on healthcare services and contributed to the rise in preterm birth rates.[37] Furthermore, austerity policies and reductions in public healthcare funding in recent years have likely exacerbated these challenges by limiting access to essential maternal health services.[38] These economic and social pressures may have disproportionately affected vulnerable populations, further contributing to the observed rise in preterm births.[39] The stress from the refugee crisis and economic austerity measures may have impacted prenatal care services, leading to higher preterm birth rates.[40] Additionally, rising levels of maternal age and associated health complications might play a role.[41]

Global ASIR has increased after 2016 and remained on an upward trend especially after 2019, most likely related to Coronavirus disease 2019 (COVID-19). The greatest change was the rise of ASIR in Southern Latin America after 2019. Some studies have shown that Latin America had one of the highest COVID-19 mortality rates in the world and the second highest ASMR due to COVID-19,[42,43] suggesting that the increased burden of preterm birth in Latin America was highly likely to be influenced by the COVID-19. Latin America faced a humanitarian crisis during COVID-19, rooting in political instability, poor health systems, and inequities in health care.[43] Oceania and Southern sub-Saharan Africa of ASMR and age-standardized DALYs also saw an inflection point in 2019. During the COVID-19 pandemic, some regions were faced with the challenge of inadequate medical resources as they were redirected to the treatment of COVID-19 patients. Consequently, maternal and preterm infants had reduced access to healthcare services.[44] Additionally, maternal mental health was also affected by the epidemic, increasing the burden of preterm births.[45]

Although the burden of preterm births was generally on a downward trend, the burden of preterm births among males was consistently high, and there was an urgent need for the health service to increase its attention to preterm births among males. Earlier studies have pointed out that the risk of preterm birth was greater in males than in females, and was related to the fact that males are more prone to produce pro-inflammatory factors.[46] In addition, hormonal differences between males and females, and faster growth rates in males may also contribute to the increased burden of preterm birth in males.

Low or low-middle SDI regions had a higher burden of preterm birth, with an increasing trend. The burden of preterm birth in Western sub-Saharan Africa and South Asia was higher and continues to increase, such as Nigeria and Sierra Leone, which were consistent with previous studies.[7] United Nations reported that about 65% of preterm birth in 2020 would occur in sub-Saharan Africa and South Asia, where more than 13% of infants were born prematurely.[47] Western sub-Saharan Africa was prone to epidemics-prone infectious diseases, which can cause large numbers of deaths in the population.[48] Studies have shown that lower maternal education, maternal unemployment and lower household wealth index were the most common socio-economic status factors associated with adverse birth outcomes and infant malnutrition in sub-Saharan Africa.[49] A previous study[50] indicated that a significant proportion of birth in sub-Saharan Africa were not supervised by skilled workers, and there was a lack of nurses and midwives, in addition to lack of antenatal care and lack of quality care, significantly increasing the risk of preterm birth and deaths.

Southeast Asia and sub-Saharan Africa were prone to seasonal influenza-associated respiratory diseases with high mortality.[51] Simultaneously, Southeast Asia was vulnerable to natural disasters, which were major contributors to mortality and also added to the burden of preterm birth.[48] In South Asia, intrauterine hypoxia and congenital infections were the leading causes of preterm infant mortality. Fetal vascular malperfusion and placental abruption also increased the risk of adverse outcomes.[52] This may be due to poor quality and availability of medical care resources in low and middle-income nations.[53] In addition, poor nutrition for pregnant women and preterm infants increased susceptibility to infections, further increasing preterm birth incidence and mortality.[54]

It was shown that pregnancy complications are closely associated with the occurrence of preterm birth.[55] Implementing prenatal care policies is crucial in reducing preterm birth incidence.[56] For example, in Nigeria, the 2015 G-8 and African Union summits, along with the UN's Global Strategy for Women's and Children's Health,[57] were followed by a substantial decline in preterm births from 2017 to 2021, as shown by our join point analysis. Similarly, Tanzania's 2011 National Road Map Strategic Plan led to a significant reduction in preterm birth rates from 2011 to 2021.[58] These examples align with our join point analysis results, emphasizing the importance of structured prenatal care protocols in improving maternal and child health outcomes.

A previous study analysed data on preterm birth from 103 countries and territories between 2010 and 2020, noting that India had the highest number of preterm births globally, followed by Pakistan, Nigeria, and China.[7] Our findings generally correspond with the study, with some differences in country rankings. Specifically, Nigeria has moved up in rank. In our analysis, India has the highest number of preterm births, followed by Nigeria, Pakistan, and China, differing from previous results where Pakistan was listed before Nigeria.

India, the second most populous country in the world, exhibited significant subnational disparities in healthcare access and quality.[59] These disparities mean that some populations cannot receive the healthcare services and care they need. A previous study[60] showed that in India, less than a quarter of eligible females received quality antenatal care, with the majority of this care concentrated among females in high-income regions. In contrast, the coverage of quality antenatal care in rural areas was less than 10%. Anaemia and iron deficiency are highly prevalent in the first trimester and are associated with an increased risk of adverse pregnancy and infant outcomes.[61] Additionally, high HIV prevalence in India contributes to the increased number of preterm birth.[62] Studies have shown that affluent pregnant women are more likely to give preterm birth than poor pregnant women.[63] These findings highlight the need for further efforts are needs to narrow the socioeconomic gap, enhance the health care delivery system, and strengthen prenatal, perinatal and postnatal care.

Approximately 11% of neonatal deaths in India and Pakistan are attributed to preterm birth.[52] In Pakistan, the top five factors contributing to the occurrence of preterm birth include placenta previa, maternal thyroid disease, being a minority, fetal distress and maternal asthma,[64] all of which require comprehensive attention. Household air pollution from cooking with unclean fuels and indoor smoking has emerged as a significant contributor to mortality and morbidity globally, especially in low- and middle-income countries. For example, in Nigeria, mothers using unclean cooking fuels were facing a higher risk of stillbirths.[65] The increased burden of preterm birth in China is associated with an increase in maternal age at delivery, the proportion of mothers with complications, in the number of multiple pregnancies, and the implementation of the universal two child policy.[66] However, the decrease in caesarean sections and the increase in antenatal visits have slowed this upward trend.[66]

Countries with a low burden of preterm births were also found in high SDI regions, such as Australia, largely due to improved maternal, individual woman and newborn health care,[67] good nutritional status and effective medical interventions that also reduced the incidence and mortality of infants.[68] The establishment of the Institute for Urban Indigenous Health in Australia has fueled the development of health care services.[69] High SDI regions ensured adequate neonatal care and skilled staff at all deliveries,[10] thereby improving the survival rates and reducing the mortality rates of preterm birth. However, the burden of preterm birth was rising in some high and high-middle SDI regions, such as Qatar and Greece, indicating potential gaps in care and implementation of health interventions. In the USA, the ASIR has remain unchanged, possibly related to the limited midwifery availability, and the relevant authorities should increase the coverage of midwifery.[70]

This study provided a comprehensive analysis of the global burden of preterm birth from 1990 to 2021 using the latest GBD 2021 data. The insights provided by this study are important for reducing neonatal mortality, developing health policies and improving healthcare, thereby contributing to public health improvement. However, there are some limitations. First, lack of raw data for some countries, which were estimated through the DisMod-MR tool. Although the model helps fill data gaps, its reliance on indirect data and assumptions may result in the findings not fully reflecting the true situation in these countries, increasing the potential for inaccuracy. Second, High-quality data on preterm birth in several low and middle SDI regions and countries are limited, leading to underestimation of the true values. Third, the study analysed data at the national level and did not analyse specific differences at the subnational level, and the results of the current study are not necessarily applicable at the subnational level. In addition, the lack of subnational data analyses may lead to ignoring some important local factors. To enhance the accuracy of the results and the relevance of policy recommendations, future researches should consider including subnational data to explore the specific differences across various regions. Finally, this study relied on the GBD database and did not include data from other global databases, leading to a relatively narrow data source. Including data from other databases could potentially reduce errors caused by differences in data collection methods, thereby improving the accuracy and comprehensiveness of the results.

In summary, preterm birth incidence, mortality and DALYs have declined globally. Males bear a heavier burden of preterm births. The level of health inequality has decreased over time. High income countries had the lowest burden of preterm birth, while the greatest burden was seen in low and low-middle SDI regions. Despite decreasing health inequality, targeted institutional strategies and interventions are urgently needed to further reduce the burden of preterm birth in low SDI regions and specific high-income countries where the burden remains high.

Contributors
Cheng Chi: conceptualisation, data curation, formal analysis, supervision, visualisation, writing–review & editing, verified the underlying data; Xifeng Liang: data curation, formal analysis, visualisation, writing–original draft, writing–review & editing, verified the underlying data; Yaning Lyu: formal analysis, writing–review & editing; Jing Li: writing–review & editing; Yu Li: writing–review & editing. All authors read and approved the final version of the manuscript, and ensure it is the case.

Data sharing statement
All data used in this study can be freely accessed at the Global Health Data Exchange GBD 2021 website (https://ghdx.healthdata.org/gbd-2021).

Editor note
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Declaration of interests
The authors declare that there is no conflict of interest regarding the publication of this article.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102840.

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