DOI Link: https://doi.org/10.61586/MmzzD
Vol.50, Issue.7, Part.1, July 2025, PP.81-116

Global Burden of Type 2 Diabetes Mellitus in Reproductive-Age Women: Systematic Analysis of 1990-2021 Trends and 2040 Projections Using Nordpred and BAPC Models

Lin Hu[1], Jiahui Deng[1], Shiying Di[2], Jing Yang[3*]
1 Radiology Department of Chengdu Xindu District Second People's Hospital, Chengdu, 610501, China.
2 Department of Radiology,Second People's Hospital of Gansu Province, Lanzhou, 730000, China.
3 Demonstration Center for Experimental Teaching in Biomedicine, Chengdu Medical College, Chengdu, 610500, China.
* Corresponding author.
E-mail addresses: 18030433667@163.com (Lin Hu), 18030432667@163.com (Jiahui Deng), dsying1618@163.com (Shiying Di), jingyang@cmc.edu.cn (Jing Yang)

Received May 2025 Accepted June 2025 Published July 2025

Abstract

Background: Type 2 diabetes mellitus (T2DM) is a metabolic disorder that significantly impacts women's reproductive health. Therefore, this study utilizes the latest Global Burden of Disease (GBD) data to comprehensively assess the burden of T2DM among women of reproductive age (WRA) worldwide from 1990 to 2021.

Methods: Data on T2DM incidence, prevalence, disability-adjusted life years (DALYs), and mortality among WRA were extracted from the GBD database for 1990–2021. Global, regional, and age-specific trends were analyzed using percentage changes and estimated annual percentage changes. The Spearman correlation test examined the relationship between the Social Development Index (SDI) and disease burden indicators. Future trends were projected using Bayesian Age-Period-Cohort and Nordpred models.

Results: From 1990 to 2021, the global burden of T2DM among WRA rose substantially, with incidence, prevalence, DALYs, and deaths increasing by 201%, 251%, 181%, and 90%, respectively. Age-standardized incidence rates (ASIR), prevalence rates (ASPR), and mortality rates (ASDR) also exhibited significant upward trends. Low-SDI regions experienced the highest growth in absolute numbers, while high-SDI regions saw the greatest increases in ASIR, ASPR, and ASDR. Age-stratified analysis indicated a pronounced rise in burden with advancing age. Projections suggest a continued increase in the global T2DM burden among WRA by 2040.

Conclusions: The global burden of T2DM among WRA has increased significantly from 1990 to 2021, with this trend expected to further worsen in the coming years. It is imperative to strengthen relevant management measures to address this severe health challenge.

Keywords: women of reproductive age, type 2 diabetes, disease burden, Global Burden of Disease

Introduction

Diabetes has become one of the most prevalent chronic diseases globally. In 2021, approximately 526 million individuals were diagnosed with diabetes worldwide [1], with related healthcare expenditures estimated to reach a staggering $966 billion USD [2], placing a significant economic burden on global public health systems. Diabetes refers to a group of metabolic disorders characterized by chronic hyperglycemia, with type 2 diabetes mellitus (T2DM) being the most common form, accounting for 90–95% of cases [3]. The primary pathophysiological features of T2DM are insulin resistance and β-cell dysfunction [4]. Currently, there is no definitive cure for T2DM, and patients rely on long-term pharmacological treatments to manage disease progression. This dependence imposes a considerable economic strain on individuals [5]. Moreover, T2DM may lead to a range of complications, including cardiovascular disease [6], cognitive impairment [7], chronic kidney disease [8], and retinopathy [9]. These complications not only exacerbate the burden of diabetes but also play a critical role in significantly reducing patients' quality of life, leading to disability and, in severe cases, premature death [6].

Women with diabetes often experience more severe clinical symptoms compared to men [10]. Research has shown that the risk of coronary heart disease in female patients with diabetes is over 40% higher than in their male counterparts [11]. Similarly, women with diabetes face a 19% greater risk of vascular dementia [12] and a 38% higher relative risk of developing end-stage renal disease compared to men [13]. Additionally, after developing T2DM, women experience a faster deterioration in cardiovascular risk factors, such as blood pressure and lipid profiles, than men [14]. For women of reproductive age (WRA), the burden of T2DM is particularly pronounced. T2DM can lead to irregular menstruation, reproductive dysfunction, and early menopause [15]]. Pre-existing T2DM before pregnancy may also induce severe adverse maternal and neonatal outcomes, including preeclampsia, preterm birth, congenital malformations, and other conditions, which have a profound impact on the long-term health of offspring[17].

The global prevalence of T2DM has emerged as a significant public health challenge, while WRA face unique health risks due to their special physiological, reproductive, and social roles. From the perspective of disease burden, studying the epidemiological characteristics, health impacts, and social costs of T2DM in this population is not only relevant to individual health but also holds profound significance for population quality, medical resource allocation, and public health policy-making. Although previous studies have conducted macro-level analyses of the global diabetes burden in WRA[18], there remains a lack of in-depth exploration of the specific disease burden characteristics of T2DM within this demographic. To address this gap, this study systematically analyzed the spatiotemporal distribution characteristics and trends of the disease burden of T2DM among WRA at the global

and regional levels from 1990 to 2021, and further compared the disease burden differences across different age groups. Additionally, this research deeply explored the potential causes of high disease burden formation and proposed targeted prevention and control recommendations based on the research results, aiming to provide a scientific basis for optimizing prevention, screening, and clinical management strategies for T2DM in WRA.

Methods

Data Sources and Study Design

This study utilized data from the GBD 2021 database (https://ghdx.healthdata.org/gbd-2021), which provides comprehensive estimates for 204 countries and territories, 371 diseases and injuries, and 88 risk factors. We selected "Cause of death or injury" under GBD Estimate, "Incidence," "Prevalence," "DALYs," and "Deaths" under Measure, and both "Number" and "Rate" under Metric. "Number" represents the absolute count of corresponding incidents, prevalence, DALYs, and deaths in the population, while "Rate" denotes these measures per 100,000 population. T2DM was chosen under Cause, focusing on WRA. The study period spanned from 1990 to 2021[],[]-[21].

Disease Definition and Classification

According to the GBD 2021, diseases and injuries are typically categorized into four main levels. T2DM is classified under the first level of non-communicable diseases, the second level of diabetes and kidney diseases, the third level of diabetes, and as a fourth-level disease. In the International Classification of Diseases (ICD)-10, T2DM is primarily coded as E11. In ICD-11, it is classified under 5A []-[19].

EAPC Model Construction

The Estimated Annual Percentage Change (EAPC) was calculated to describe long-term trends in the age-standardized rates (ASR) of disease burden. This was achieved by fitting a simple linear regression model of the natural logarithm of ASR against year. The slope of the regression equation represents the EAPC, indicating the annual percentage change. The EAPC and its 95% confidence interval were derived from the regression coefficient and its standard error.

Decomposition Analysis

To further explore factors contributing to global disparities in disease burden, we employed decomposition analysis. This method allows for the disaggregation of overall health differences into contributions from various factors, such as population growth, population aging, and epidemiological changes.

Socio-demographic Index

The Socio-demographic Index (SDI), developed by GBD researchers, is a composite indicator of development status closely related to health outcomes. It is calculated as the geometric mean of indices of total fertility rate under age 25 (TFU25), mean education for those aged 15 and older (EDU15+), and lag distributed income (LDI) per capita, scaled from 0 to 1. An SDI of 0 represents the theoretical minimum level of development relevant to health, while an SDI of 1 represents the maximum level. We applied LOESS smoothing to visualize trends and conducted Spearman correlation tests to quantify the relationship between SDI and disease burden indicators.

BAPC Model Construction

The Bayesian Age-Period-Cohort (BAPC) prediction model is a statistical method based on a Bayesian framework that combines age, period, and birth cohort effects to forecast future trends in disease incidence, mortality, or other health indicators. We utilized the INLA framework within the BAPC package to project disease burden from 2022 to 2040.

Nordpred Model Construction

The Nordpred model was employed to assess and predict future trends in disease burden. We used the Nordpred package in R to forecast disease burden from 2022 to 2040.

Statistical Analysis

All data processing, statistical analyses, and visualizations were performed using R version 4.4.1. Descriptive statistics were used to summarize the characteristics of the study population and disease burden indicators. Trends in age-standardized rates were analyzed using joinpoint regression, which identifies statistically significant trend change points and calculates the annual percent change (APC) for each segment.

Results

Global Burden of Type 2 Diabetes Mellitus Among Women of Reproductive Age

From 1990 to 2021, the global burden of T2DM among WRA increased substantially. During this period, the numbers of incidence, prevalence, DALYs, and deaths rose by 201%, 251%, 181%, and 90%, respectively. By 2021, these metrics reached 5,317,767 (95% UI: 3,951,143–6,923,346) incident cases, 73,858,922 (95% UI: 63,433,476–85,320,524) prevalent cases, 6,895,581 (95% UI: 5,237,271–8,947,854) DALYs, and 42,106 (95% UI: 37,840–46,438) deaths. These undoubtedly highlights the huge burden of type 2 diabetes in WRA. Over the same

period, ASRs for incidence, prevalence, DALYs, and deaths also increased, with respective growth rates of 88%, 112%, 64%, and 6%. The EAPC values were 1.95 (95% CI: 1.91, 1.99), 2.43 (95% CI: 2.35, 2.52), 1.51 (95% CI: 1.44, 1.58), and 0.01 (95% CI: -0.1, 0.12), respectively. Notably, the EAPC for the age-standardized mortality rate (ASMR) suggests that the increase in mortality was not statistically significant (Figure 1, Figure 2; table 1, Table S1-S3).

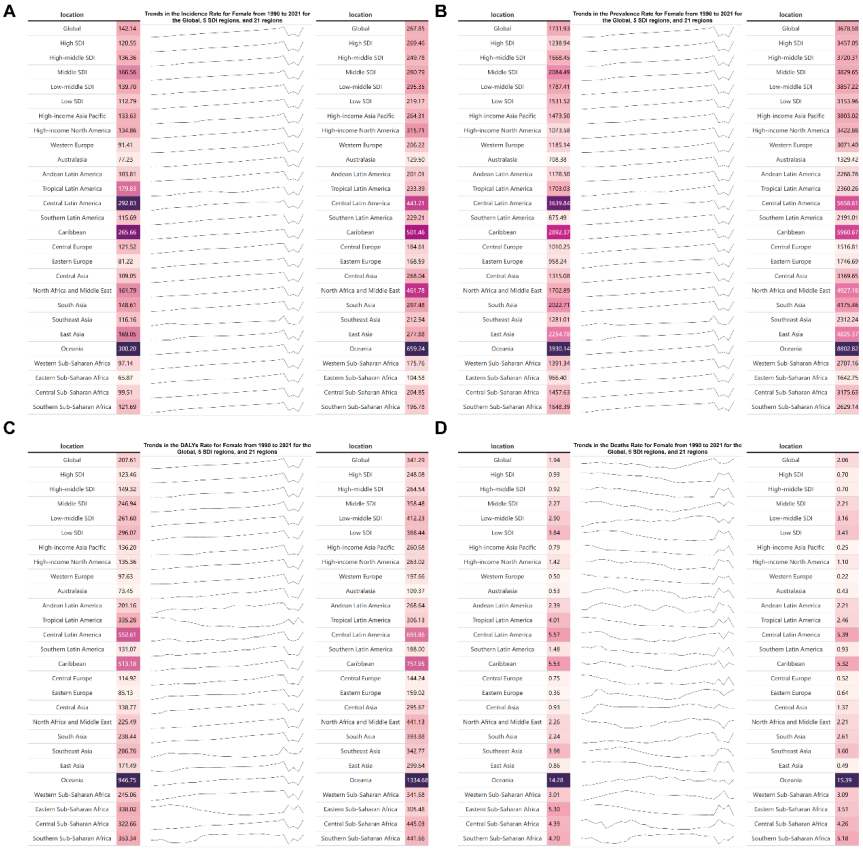


Figure 1 . Trends in Age-Standardized Rates of Type 2 Diabetes Mellitus Among Women of Reproductive Age, 1990-2021
A: Global, SDI-specific, and regional trends in age-standardized incidence rates
B: Global, SDI-specific, and regional trends in age-standardized prevalence rates
C: Global, SDI-specific, and regional trends in age-standardized DALY rates
D: Global, SDI-specific, and regional trends in age-standardized mortality rates

ISSN: 0378-1844

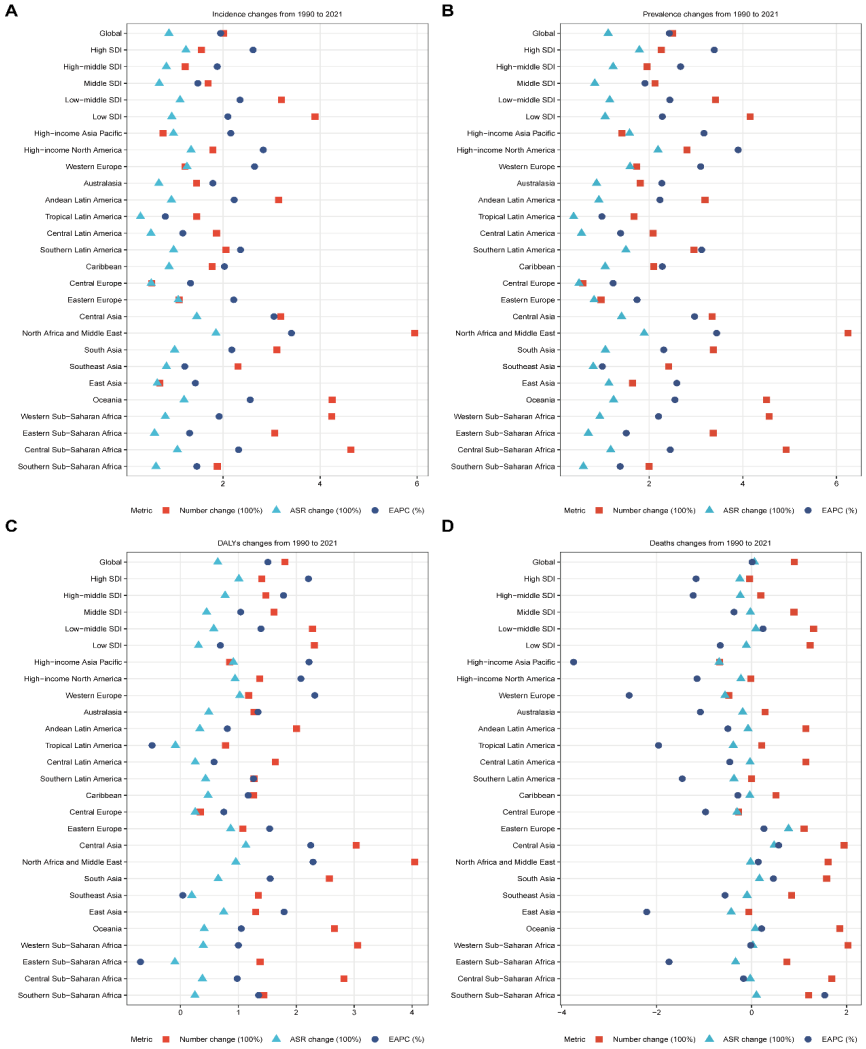


Figure 2. Percentage Changes and EAPC in Type 2 Diabetes Mellitus Burden Among Women of Reproductive Age, 1990-2021

A: Global, SDI-specific, and regional changes in incidence numbers, rates, and EAPC

B: Global, SDI-specific, and regional changes in prevalence numbers, rates, and EAPC

C: Global, SDI-specific, and regional changes in DALY numbers, rates, and EAPC

D: Global, SDI-specific, and regional changes in death numbers, rates, and EAPC

Table 1. Global Incidence of Type 2 Diabetes Mellitus Among Women of Reproductive Age in 1990 and 2021, with Trends from 1990 to 2021.

Location	Incidence cases			Incidence rates			
	1990_numbers (95% UI)	2021_numbers (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Global	1767577 (1256520, 2392378)	5317767 (3951143, 6923346)	2.01	142.14 (101.61,192.05)	267.85 (198.9,348.61)	0.88	1.95 (1.91 to 1.99)
Low SDI	112350 (79525, 150066)	550209 (398701, 721306)	3.90	112.79 (80.52,149.91)	219.17 (159.14,287.26)	0.94	2.1 (2.07 to 2.13)
Low-middle SDI	343558 (247752, 455157)	1443665 (1066090, 1871389)	3.20	139.7 (101.62,184.41)	295.35 (218.74,382.4)	1.11	2.35 (2.32 to 2.39)
Middle SDI	669286 (467424, 913787)	1802786 (1331666, 2351922)	1.69	166.56 (117.07,227.12)	280.79 (207.35,365.97)	0.69	1.48 (1.42 to 1.54)
High-middle SDI	359960 (245536, 501392)	799263 (574762, 1064590)	1.22	136.36 (93.41,189.4)	249.78 (179.81,331.74)	0.83	1.88 (1.81 to 1.95)
High SDI	280448 (205173, 370643)	716378 (543293, 918305)	1.55	120.55 (87.94,159.65)	269.46 (203.17,346.03)	1.24	2.62 (2.55 to 2.68)
High-income Asia Pacific	64236 (47456, 84331)	113156 (82260, 151222)	0.76	133.63 (98.24,175.92)	264.31 (190.73,352.27)	0.98	2.16 (2.04 to 2.28)
High-income North America	103152 (73413, 137640)	288060 (218474, 367467)	1.79	134.86 (95.6,180.53)	315.71 (238.45,403.53)	1.34	2.83 (2.79 to 2.87)
Western Europe	89139 (61713, 121837)	197214 (138206, 265085)	1.21	91.41 (63.04,125.07)	206.22 (144.18,276.37)	1.26	2.65 (2.58 to 2.73)
Australasia	4209 (2971, 5641)	10323 (7137, 13981)	1.45	77.23 (54.34,103.73)	129.5 (88.9,176.37)	0.68	1.79 (1.75 to 1.84)
Andean Latin America	8403 (6202, 10887)	34834 (26251, 44074)	3.15	103.81 (77.76,133.06)	201.01 (151.54,254.25)	0.94	2.23 (2.14 to 2.32)
Tropical Latin America	61901 (44046, 83406)	152097 (108868, 204186)	1.46	179.83 (129.07,241.72)	233.39 (166.31,314.15)	0.30	0.81 (0.71 to 0.91)
Central Latin America	106873 (78928, 139581)	306276 (229384, 393048)	1.87	292.83 (218.49,380.83)	443.21 (331.63,569.07)	0.51	1.17 (1.08 to 1.27)
Southern Latin America	13815 (10327, 18033)	42271 (30913, 54481)	2.06	115.69 (86.62,150.93)	229.21 (167.17,295.96)	0.98	2.36 (2.28 to 2.45)
Caribbean	22129 (16810, 27677)	61408 (45873, 78058)	1.78	265.66 (203.9,329.65)	501.46 (374.41,637.34)	0.89	2.03 (2 to 2.06)
Central Europe	39209 (29657, 49696)	59957 (45485, 76560)	0.53	121.52 (91.7,154.33)	184.61 (138.8,237.25)	0.52	1.33 (1.29 to 1.37)
Eastern Europe	46204 (31981, 62708)	96791 (68578, 129928)	1.09	81.22 (56.05,110.6)	168.59 (118.56,227.04)	1.08	2.22 (2.13 to 2.3)
Central Asia	15984 (11425, 20985)	66947 (50357, 85256)	3.19	109.05 (79.2,142.37)	268.04 (201.29,341.53)	1.46	3.05 (2.92 to 3.17)
North Africa and Middle East	105948 (78369, 137733)	736526 (563818, 923290)	5.95	161.79 (121.48,208.74)	461.78 (353.64,578.99)	1.85	3.41 (3.37 to 3.46)
South Asia	350411 (247330, 474810)	1439968 (1030069, 1909162)	3.11	148.61 (105.43,201.29)	297.48 (213.09,394.38)	1.00	2.18 (2.12 to 2.24)
Southeast Asia	122274 (85870, 162918)	404778 (303090, 517030)	2.31	116.16 (82.58,153.91)	212.94 (159.06,272.34)	0.83	1.21 (0.96 to 1.46)
East Asia	521495 (339992, 745046)	883695 (606233, 1214883)	0.69	169.05 (109.99,241.7)	277.88 (195.01,374.77)	0.64	1.43 (1.31 to 1.56)
Oceania	4200 (3127, 5368)	22047 (16448, 27931)	4.25	300.2 (224.99,381.48)	659.24 (492.7,833.65)	1.20	2.56 (2.53 to 2.59)
Western Sub-Saharan Africa	36902 (25461, 50248)	193297 (137233, 259214)	4.24	97.14 (67.86,131.99)	175.76 (125.21,235.84)	0.81	1.92 (1.88 to 1.95)
Eastern Sub-Saharan Africa	25635 (17738, 34716)	104249 (73209, 139825)	3.07	65.87 (45.9,88.93)	104.58 (73.61,140.13)	0.59	1.31 (1.23 to 1.39)
Central Sub-Saharan Africa	11077 (7747, 14974)	62425 (44189, 82647)	4.64	99.51 (70.02,133.82)	204.85 (145.46,270.45)	1.06	2.32 (2.29 to 2.35)
Southern Sub-Saharan Africa	14381 (9917, 19669)	41448 (28726, 56353)	1.88	121.69 (84.43,166.44)	196.78 (136.45,267.62)	0.62	1.46 (1.39 to 1.52)

Disparities in Type 2 Diabetes Mellitus Burden Among Reproductive-Age Women Across Sociodemographic Index Regions

From 1990 to 2021, regions with higher SDI levels showed smaller percentage increases in the incidence and prevalence of T2DM among WRA, with the smallest changes observed in high-middle SDI regions. Despite these relatively modest percentage changes, the ASRs in high-middle SDI regions experienced the largest increases, with EAPCs of 2.62 (95% CI: 2.55, 2.68) for incidence and 3.39 (95% CI: 3.32, 3.46) for prevalence. For DALYs and deaths, the percentage increases diminished progressively with higher SDI levels, with high SDI regions showing the smallest growth. In fact, high SDI regions experienced negative growth in death counts. While the increase in DALYs counts was smallest in high SDI regions, the age-standardized DALY rate (ASDR) in these areas showed the largest rise across 5 SDI regions, with an EAPC of 2.21 (95% CI: 2.12, 2.30). In terms of ASMR, most regions experienced declines, except for low-middle SDI regions, where ASMR showed positive growth. The largest reduction in ASMR was observed in high-middle SDI regions, with an EAPC of -1.23 (95% CI: -1.38, -1.08) (Figure 1, Figure 2; table 1, Table S1-S3).

Global Disparities in Type 2 Diabetes Mellitus Among Reproductive-Age Women

Compared to 1990, the incidence, prevalence, and DALYs of T2DM increased across all 21 geographical regions worldwide in 2021. The most dramatic percentage increases were observed in North Africa and the Middle East, with rises of 595%, 624%, and 405%, respectively. This region also registered the greatest increase in the age-standardized incidence rate (ASIR), with an EAPC of 3.41 (95% CI: 3.37, 3.46). For the age-standardized prevalence rate (ASPR), the largest increase occurred in High-Income North America, with an EAPC of 3.90 (95% CI: 3.80–4.01). Western Europe recorded the largest rise in the ASDR, with an EAPC of 2.32 (95% CI: 2.22, 2.42). North Africa and the Middle East ranked second in ASPR and ASDR increases, with EAPCs of 3.44 (95% CI: 3.40, 3.49) and 2.29 (95% CI: 2.19, 2.39), respectively. Among the 21 regions, only Tropical Latin America and Western Sub-Saharan Africa showed decreases in ASDR, with EAPCs of -0.49 (95% CI: -0.60, -0.34) and -0.69 (95% CI: -0.82, -0.55), respectively. While the number of deaths increased in most regions, the largest percentage rise was observed in Western Sub-Saharan Africa, reaching 203%. In contrast, the ASMR displayed a declining trend across most regions, with the greatest decrease occurring in High-Income Asia Pacific, where the EAPC was -3.75 (95% CI: -3.98, -3.52) (Figure 1, Figure 2; table 1, Table S1-S3).

Age-Specific Patterns in the Global Burden of Type 2 Diabetes Mellitus Among Reproductive-Age Women

In 2021, the incidence, prevalence, DALYs, and deaths numbers related to T2DM among WRA all increased with age. Compared to 1990, the percentage change of these indicators also grew with age by 2021. However, it is noteworthy that the ASIR showed a higher growth trend in younger age groups. Overall, the 45-49 age group exhibited the highest burden of T2DM. Interestingly, while this age group had the highest ASIR, both the ASPR and the ASDR showed the smallest increases. Additionally, the ASMR decreased only in the 30-34 age group. Regarding EAPC trends, most age groups exhibited a downward pattern, although these changes were not statistically significant (Figure 3, Figure4; Table 2, Table S4-S6).

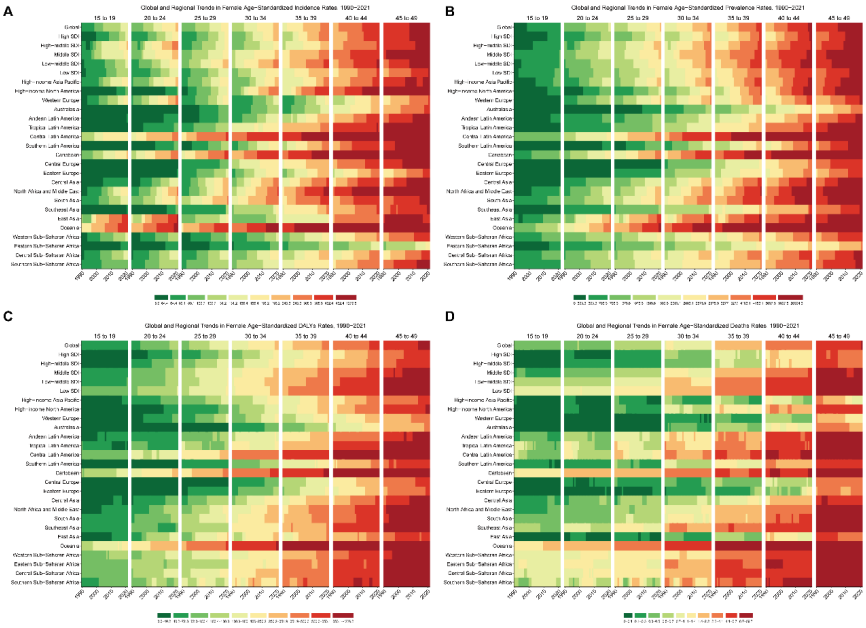


Figure 3 . Age-Specific Trends in Type 2 Diabetes Mellitus Burden Among Women of Reproductive Age, 1990-2021

A: Global, SDI-specific, and regional trends in age-specific incidence rates

B: Global, SDI-specific, and regional trends in age-specific prevalence rates

C: Global, SDI-specific, and regional trends in age-specific DALY rates

D: Global, SDI-specific, and regional trends in age-specific mortality rates

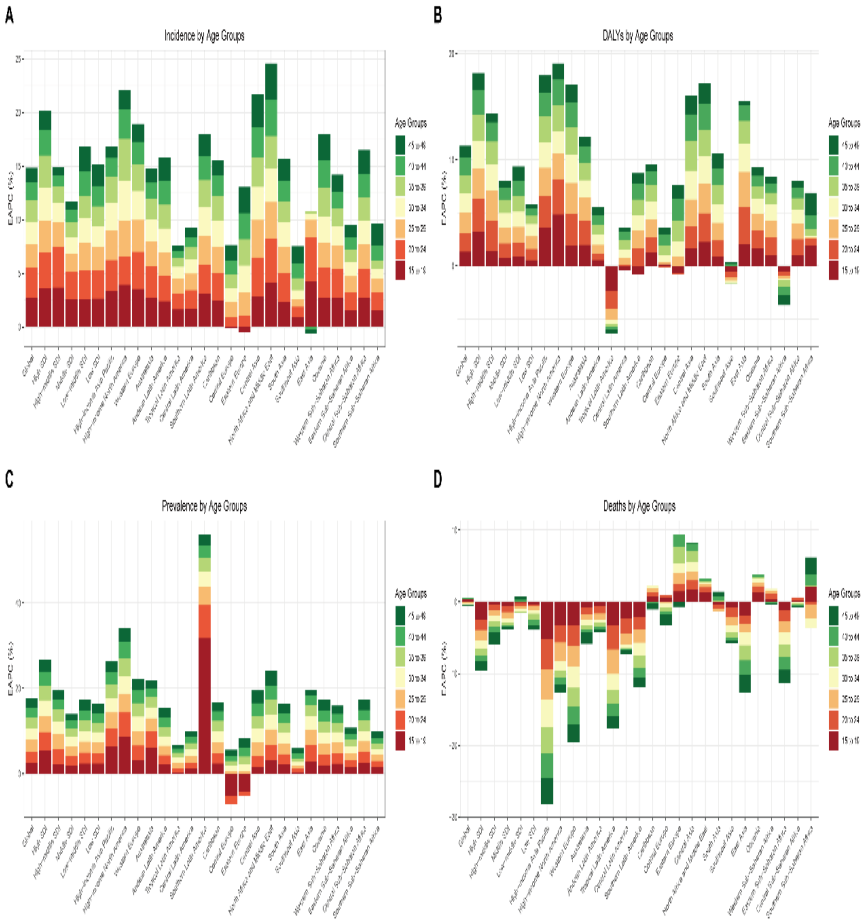


Figure 4 . Trends in Type 2 Diabetes Mellitus Among Women of Reproductive Age from 1990 to 2021

A: EAPC in incidence rates globally, in 5 SDI regions, and 21 world regions, stratified by age group

B: EAPC in prevalence rates globally, in 5 SDI regions, and 21 world regions, stratified by age group

C: EAPC in DALY rates globally, in 5 SDI regions, and 21 world regions, stratified by age group

D: EAPC in mortality rates globally, in 5 SDI regions, and 21 world regions, stratified by age group

Table 2. Age-specific Incidence of Type 2 Diabetes Mellitus Among Women of Reproductive Age in 1990 and 2021, with Trends in Age Patterns from 1990 to 2021.

		Incidence cases			Incidence rates			
Location	**Age (years)**	1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Global	15 to 19	182543.51 (120169.03-248385.64)	470749.17 (345364.62-604282.16)	1.58	71.43 (47.03-97.2)	155.03 (113.74-199.01)	1.17	2.76 (2.51 to 3)
Global	20 to 24	224174.85 (157821.35-309075.1)	585491.25 (435713.4-761868.87)	1.61	91.82 (64.65-126.6)	199.31 (148.33-259.36)	1.17	2.76 (2.61 to 2.9)
Global	25 to 29	199076.69 (131396.49-278619.65)	539886.29 (365481.99-732247.25)	1.71	90.45 (59.7-126.59)	185.54 (125.6-251.64)	1.05	2.25 (2.17 to 2.32)
Global	30 to 34	212806.16 (146590.51-283171.1)	650067.28 (466931.05-845773.34)	2.05	111.94 (77.11-148.95)	217.46 (156.2-282.93)	0.94	2.07 (2.04 to 2.11)
Global	35 to 39	256387.04 (178710.61-360825.78)	783230.17 (567536.03-1037491.72)	2.05	147.81 (103.03-208.02)	281.94 (204.29-373.46)	0.91	1.98 (1.94 to 2.02)
Global	40 to 44	313124.19 (247652-390342.08)	992639.28 (803063.49-1208894.15)	2.17	223.3 (176.61-278.37)	400.11 (323.7-487.28)	0.79	1.66 (1.59 to 1.72)
Global	45 to 49	379464.56 (274180.24-521959.07)	1295703.44 (967052.29-1732788.66)	2.41	333.45 (240.93-458.66)	549.86 (410.39-735.35)	0.65	1.36 (1.29 to 1.42)
High SDI	15 to 19	14877.81 (9266.19-20664.45)	40487.11 (28751.91-52280.18)	1.72	46.68 (29.08-64.84)	139.17 (98.83-179.71)	1.98	3.63 (3.54 to 3.72)
High SDI	20 to 24	22100.66 (15590.66-30440.98)	58030.68 (43314.06-75561.83)	1.63	65.82 (46.43-90.66)	184.09 (137.4-239.7)	1.80	3.3 (3.22 to 3.37)
High SDI	25 to 29	24728.14 (16236.83-34110.12)	59974.1 (41197.53-81290.23)	1.43	68.98 (45.3-95.16)	173.54 (119.21-235.22)	1.52	2.94 (2.85 to 3.02)
High SDI	30 to 34	32093.39 (22364.05-42253.05)	83126.17 (62201.9-106619.21)	1.59	90.44 (63.02-119.07)	222.07 (166.17-284.83)	1.46	3.08 (2.99 to 3.17)
High SDI	35 to 39	41020.74 (28199.22-55984.29)	112411.53 (82465.42-145057.4)	1.74	122.67 (84.33-167.42)	296.35 (217.4-382.41)	1.42	3.05 (2.96 to 3.15)
High SDI	40 to 44	63284.44 (51027.12-77158.81)	155555.55 (127296.57-187227.96)	1.46	202.68 (163.43-247.12)	423.72 (346.75-510)	1.09	2.37 (2.3 to 2.44)
High SDI	45 to 49	82342.65 (62488.99-110031.03)	206792.79 (158065.54-270267.85)	1.51	325.89 (247.32-435.48)	575.93 (440.22-752.71)	0.77	1.75 (1.68 to 1.82)
High-middle SDI	15 to 19	36560.24 (23775.09-50630.02)	68814.83 (50079.28-89793.88)	0.88	77.2 (50.2-106.9)	199.85 (145.44-260.77)	1.59	3.68 (3.19 to 4.18)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
High-middle SDI	20 to 24	49214.28 (33894.11-68577.41)	97784.38 (75162.32-122309.39)	0.99	102.23 (70.41-142.45)	274.71 (211.16-343.61)	1.69	3.77 (3.46 to 4.09)
High-middle SDI	25 to 29	40002.48 (24652.34-58529.48)	72159.02 (45030.44-103058.06)	0.80	87.45 (53.89-127.95)	179.01 (111.71-255.67)	1.05	2.32 (2.18 to 2.47)
High-middle SDI	30 to 34	41085.51 (26524.77-57744.16)	89854.17 (60039.07-124821)	1.19	98.41 (63.53-138.31)	174.51 (116.6-242.41)	0.77	1.76 (1.69 to 1.83)
High-middle SDI	35 to 39	49677.69 (32922.45-74308.01)	105646.34 (73315.5-147107.01)	1.13	125.78 (83.35-188.14)	213.21 (147.96-296.88)	0.70	1.55 (1.47 to 1.62)
High-middle SDI	40 to 44	62739.33 (47810.04-80426.03)	143701.04 (113483.79-181056.67)	1.29	204.07 (155.51-261.6)	315.69 (249.31-397.76)	0.55	1.09 (1 to 1.18)
High-middle SDI	45 to 49	80680.22 (55957.22-111177.08)	221303.65 (157651.44-296444.03)	1.74	329.07 (228.23-453.46)	458.87 (326.89-614.67)	0.39	0.77 (0.67 to 0.88)
Middle SDI	15 to 19	79742.41 (52907.5-108270.9)	158025.36 (117400-203222.46)	0.98	86.48 (57.38-117.43)	179.91 (133.66-231.36)	1.08	2.62 (2.26 to 2.98)
Middle SDI	20 to 24	96529.05 (66977.32-132297.31)	189546.25 (142736.07-242664.43)	0.96	109.28 (75.82-149.77)	218.71 (164.69-279.99)	1.00	2.5 (2.27 to 2.72)
Middle SDI	25 to 29	76750.24 (50302.16-107779.71)	165209.24 (110630.39-224248.77)	1.15	102.46 (67.15-143.88)	182.35 (122.11-247.52)	0.78	1.71 (1.61 to 1.81)
Middle SDI	30 to 34	76709.14 (52939.24-103568.58)	210983.22 (149724.84-275904.03)	1.75	127.77 (88.17-172.5)	213.65 (151.62-279.39)	0.67	1.51 (1.45 to 1.57)
Middle SDI	35 to 39	93984.93 (64133.52-134181.01)	262853.24 (189337.09-355004.68)	1.80	169.55 (115.7-242.07)	286.81 (206.59-387.36)	0.69	1.43 (1.33 to 1.53)
Middle SDI	40 to 44	111268.67 (86641.59-139163.57)	343873.01 (274263.38-418682.72)	2.09	263.32 (205.04-329.33)	420.12 (335.08-511.52)	0.60	1.13 (1.02 to 1.24)
Middle SDI	45 to 49	134301.22 (93522.41-188526.07)	472295.89 (347574.32-632194.83)	2.52	396.25 (275.93-556.24)	582.28 (428.52-779.42)	0.47	0.84 (0.72 to 0.95)
Low-middle SDI	15 to 19	36468.96 (23980.34-48999.01)	122367.87 (85897.61-162287.72)	2.36	62.07 (40.82-83.4)	135.36 (95.02-179.52)	1.18	2.58 (2.51 to 2.65)
Low-middle SDI	20 to 24	41576.56 (29347.86-57727.39)	159556.98 (113325.18-214802.31)	2.84	79.72 (56.27-110.69)	183.38 (130.25-246.87)	1.30	2.74 (2.67 to 2.81)
Low-middle SDI	25 to 29	43387.31 (29607.37-59295.77)	173534.35 (118496.97-230804.79)	3.00	96.67 (65.97-132.11)	213.59 (145.85-284.08)	1.21	2.53 (2.48 to 2.58)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Low-middle SDI	30 to 34	47663.9 (33950.16-61498.21)	195403.79 (144390.87-249833.16)	3.10	127.29 (90.67-164.24)	264.39 (195.37-338.03)	1.08	2.28 (2.25 to 2.32)
Low-middle SDI	35 to 39	54101.22 (38788.96-71820.96)	224784 (162403.59-292681.52)	3.15	168.89 (121.09-224.2)	337.58 (243.9-439.55)	1.00	2.13 (2.08 to 2.18)
Low-middle SDI	40 to 44	57781.46 (45625.61-71357.04)	264913.8 (211620.15-324100.11)	3.58	222.71 (175.86-275.04)	459.27 (366.88-561.88)	1.06	2.22 (2.16 to 2.27)
Low-middle SDI	45 to 49	62579.02 (46451.29-84458.62)	303104.01 (229956.07-396879.32)	3.84	288.31 (214.01-389.12)	613.11 (465.15-802.8)	1.13	2.36 (2.31 to 2.41)
Low SDI	15 to 19	14770.45 (9964.58-19777.05)	80717.38 (59170.98-103243.33)	4.46	58.78 (39.65-78.7)	130.91 (95.97-167.44)	1.23	2.65 (2.59 to 2.7)
Low SDI	20 to 24	14595.12 (10149.29-20526.27)	80116.14 (57906.2-107448.03)	4.49	67.19 (46.73-94.5)	151.93 (109.81-203.76)	1.26	2.6 (2.54 to 2.67)
Low SDI	25 to 29	14012.33 (9319.85-19544.27)	68521.37 (46221.41-92853.78)	3.89	75.65 (50.31-105.51)	155.56 (104.93-210.8)	1.06	2.19 (2.14 to 2.24)
Low SDI	30 to 34	14990.1 (10593.55-19504.75)	70034.64 (50229.44-90724.68)	3.67	98.55 (69.64-128.23)	188.68 (135.32-244.42)	0.91	1.96 (1.9 to 2.01)
Low SDI	35 to 39	17279.57 (12140.24-22973.07)	76663.7 (55082.08-101460.13)	3.44	134.11 (94.22-178.3)	240.58 (172.86-318.4)	0.79	1.85 (1.79 to 1.91)
Low SDI	40 to 44	17639.56 (13617.32-22127.29)	83433.54 (65438.54-103576.92)	3.73	177.9 (137.34-223.17)	319.42 (250.53-396.54)	0.80	1.93 (1.88 to 1.97)
Low SDI	45 to 49	19063.28 (13739.99-25613.35)	90722.06 (64652.72-121999.53)	3.76	229.63 (165.51-308.53)	436.85 (311.32-587.46)	0.90	2.01 (1.9 to 2.12)
High-income Asia Pacific	15 to 19	4864.51 (3323.68-6546.58)	6883.6 (4902.47-8967)	0.42	65.93 (45.05-88.73)	169.92 (121.02-221.35)	1.58	3.37 (3.19 to 3.55)
High-income Asia Pacific	20 to 24	5907.33 (4315.34-7827.98)	9518.39 (6822.53-12644.87)	0.61	87.16 (63.67-115.5)	204.36 (146.48-271.48)	1.34	2.88 (2.75 to 3.01)
High-income Asia Pacific	25 to 29	5345.91 (3564.03-7268.46)	9510.47 (6342.29-13203.89)	0.78	82.62 (55.08-112.33)	190.8 (127.24-264.9)	1.31	2.72 (2.58 to 2.86)
High-income Asia Pacific	30 to 34	6190.88 (4446.13-8170.73)	11269.96 (8112.61-15096.83)	0.82	99.49 (71.45-131.31)	221.55 (159.48-296.78)	1.23	2.61 (2.41 to 2.81)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
High-income Asia Pacific	35 to 39	8302.34 (5907.37-11519.89)	16213.79 (11234.41-21556.53)	0.95	131.63 (93.66-182.64)	284.48 (197.11-378.22)	1.16	2.49 (2.24 to 2.73)
High-income Asia Pacific	40 to 44	14148.85 (11348.06-17408.3)	24361.67 (18955.64-30222.51)	0.72	208.63 (167.33-256.69)	381.48 (296.83-473.25)	0.83	1.69 (1.55 to 1.82)
High-income Asia Pacific	45 to 49	19476.59 (14551.87-25588.87)	35398.57 (25889.76-49530.71)	0.82	335.71 (250.83-441.07)	493.5 (360.94-690.53)	0.47	1.08 (0.93 to 1.23)
High-income North America	15 to 19	2672.15 (1154.82-4144.2)	11050.57 (7780.47-14528.9)	3.14	27.37 (11.83-42.44)	94.52 (66.55-124.27)	2.45	3.94 (3.81 to 4.07)
High-income North America	20 to 24	3896.61 (2123.7-6291.86)	10591.68 (6437.98-15818.2)	1.72	36.67 (19.98-59.21)	89.77 (54.57-134.07)	1.45	2.64 (2.42 to 2.86)
High-income North America	25 to 29	6883.73 (4082.27-9892.66)	19559.69 (13189.35-26409.7)	1.84	57.11 (33.87-82.07)	158.42 (106.82-213.9)	1.77	3.28 (3.11 to 3.44)
High-income North America	30 to 34	11583.12 (8100.37-15346.48)	36411.56 (28259.58-44961.56)	2.14	93.11 (65.11-123.36)	285.38 (221.48-352.39)	2.06	3.82 (3.56 to 4.08)
High-income North America	35 to 39	15446.33 (9881.42-21401.52)	50771.31 (37167.86-65241.96)	2.29	135.52 (86.7-187.77)	409.53 (299.8-526.25)	2.02	3.87 (3.62 to 4.13)
High-income North America	40 to 44	26352.41 (21236.79-32229.13)	69655.67 (57992.47-81903.58)	1.64	259.29 (208.95-317.11)	587.45 (489.09-690.75)	1.27	2.78 (2.72 to 2.84)
High-income North America	45 to 49	36317.54 (26834.08-48333.97)	90019.35 (67646.28-118603.37)	1.48	458.53 (338.79-610.24)	805.82 (605.55-1061.7)	0.76	1.79 (1.67 to 1.92)
Western Europe	15 to 19	7616.82 (4639.28-10554.96)	19758.17 (13184.42-26278.97)	1.59	57.06 (34.76-79.07)	172.67 (115.22-229.66)	2.03	3.55 (3.45 to 3.65)
Western Europe	20 to 24	13074.33 (9583.69-17286.09)	31533.73 (24139.47-39709.82)	1.41	87.69 (64.28-115.94)	265.38 (203.15-334.18)	2.03	3.46 (3.38 to 3.54)
Western Europe	25 to 29	11043.17 (6829.67-15694.3)	23105.97 (14503.3-31903.69)	1.09	71.92 (44.48-102.22)	182.81 (114.75-252.42)	1.54	2.98 (2.85 to 3.11)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Western Europe	30 to 34	9713.94 (6134.24-13987.56)	20352.97 (13151.09-28555.5)	1.10	68.64 (43.35-98.84)	148.16 (95.74-207.88)	1.16	2.68 (2.56 to 2.79)
Western Europe	35 to 39	10882.06 (7203.49-15379.25)	23263.84 (15888.11-32510.42)	1.14	81.79 (54.14-115.6)	165.41 (112.96-231.15)	1.02	2.52 (2.43 to 2.62)
Western Europe	40 to 44	15946.21 (12207.02-20425.55)	32296.99 (24495.19-42019.42)	1.03	121.34 (92.88-155.42)	222.8 (168.98-289.87)	0.84	2.09 (2.02 to 2.15)
Western Europe	45 to 49	20862.21 (15116.03-28508.82)	46902.79 (32844.47-64107.04)	1.25	183.98 (133.3-251.41)	314.42 (220.17-429.75)	0.71	1.66 (1.61 to 1.72)
Australasia	15 to 19	97.23 (43.12-168.2)	196.56 (73.12-357.98)	1.02	11.76 (5.21-20.34)	22.36 (8.32-40.73)	0.90	2.77 (2.16 to 3.39)
Australasia	20 to 24	222.11 (127.17-346.47)	590.28 (354.39-874.71)	1.66	27.87 (15.96-43.47)	61.64 (37.01-91.34)	1.21	2.93 (2.8 to 3.06)
Australasia	25 to 29	435.22 (287.35-596.41)	1095.76 (745.8-1483.44)	1.52	52.1 (34.4-71.39)	100.63 (68.49-136.23)	0.93	2.33 (2.23 to 2.43)
Australasia	30 to 34	579.07 (398.83-768.54)	1446.01 (1009.48-1947.49)	1.50	69.87 (48.12-92.73)	124.84 (87.15-168.14)	0.79	2.05 (1.97 to 2.13)
Australasia	35 to 39	665.22 (459.5-912.29)	1650.45 (1134.76-2303.36)	1.48	85.43 (59.01-117.15)	146.93 (101.02-205.05)	0.72	1.85 (1.8 to 1.9)
Australasia	40 to 44	987.75 (773.62-1232.48)	2135.06 (1614.8-2715.61)	1.16	134.5 (105.34-167.83)	212.6 (160.79-270.4)	0.58	1.52 (1.46 to 1.59)
Australasia	45 to 49	1222.64 (881.11-1616.3)	3208.73 (2204.65-4298.79)	1.62	215.95 (155.63-285.49)	318.39 (218.76-426.56)	0.47	1.31 (1.23 to 1.39)
Andean Latin America	15 to 19	652.58 (407.1-900.49)	1730.65 (1166.68-2373.48)	1.65	31.6 (19.72-43.61)	64.42 (43.43-88.35)	1.04	2.4 (2.3 to 2.5)
Andean Latin America	20 to 24	772.34 (521.22-1115.47)	2411.27 (1713.12-3286.74)	2.12	42.16 (28.45-60.89)	84.51 (60.04-115.19)	1.00	2.35 (2.24 to 2.47)
Andean Latin America	25 to 29	889.81 (588.58-1204.77)	3032.7 (2093.72-4040.28)	2.41	56.66 (37.48-76.72)	106.2 (73.32-141.48)	0.87	2.23 (2.11 to 2.35)
Andean Latin America	30 to 34	1128.42 (828.41-1485.28)	4169.24 (3123.8-5279.54)	2.69	85.89 (63.05-113.05)	158.84 (119.01-201.14)	0.85	2.22 (2.06 to 2.38)
Andean Latin America	35 to 39	1387.17 (1010.24-1814.86)	5647.07 (4200.6-7219.09)	3.07	125.98 (91.75-164.82)	234.88 (174.71-300.26)	0.86	2.2 (2.02 to 2.37)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Andean Latin America	40 to 44	1666 (1358.89-2007.1)	7817.76 (6273.52-9319.63)	3.69	186.91 (152.45-225.18)	362.43 (290.84-432.06)	0.94	2.2 (2.11 to 2.3)
Andean Latin America	45 to 49	1906.83 (1487.27-2359)	10025.58 (7679.23-12555.19)	4.26	268.25 (209.23-331.87)	535.93 (410.5-671.15)	1.00	2.21 (2.13 to 2.3)
Tropical Latin America	15 to 19	2862.9 (1516.37-4246.35)	4830.46 (2778.39-7052.64)	0.69	36.34 (19.25-53.9)	59.84 (34.42-87.37)	0.65	1.64 (1.58 to 1.69)
Tropical Latin America	20 to 24	4248.32 (2823.22-6118.06)	8268.3 (5510.84-11967.81)	0.95	58.35 (38.78-84.03)	93.03 (62.01-134.66)	0.59	1.5 (1.46 to 1.55)
Tropical Latin America	25 to 29	5421.13 (3555.17-7568.75)	11217.65 (7448.07-15651.07)	1.07	80.54 (52.82-112.45)	124.59 (82.72-173.83)	0.55	1.4 (1.36 to 1.45)
Tropical Latin America	30 to 34	7638.99 (5477.97-9925.08)	16789 (12255.16-21880.4)	1.20	131.18 (94.07-170.43)	184.84 (134.93-240.9)	0.41	1.08 (0.99 to 1.17)
Tropical Latin America	35 to 39	10251.02 (6924.98-14208.67)	25310.2 (17602.32-34614.36)	1.47	206.19 (139.29-285.79)	270.75 (188.29-370.28)	0.31	0.84 (0.71 to 0.97)
Tropical Latin America	40 to 44	13977.78 (11090.43-17035.01)	37165.02 (29333.9-45902.85)	1.66	348.01 (276.12-424.13)	427.57 (337.47-528.09)	0.23	0.62 (0.49 to 0.74)
Tropical Latin America	45 to 49	17500.83 (12658.32-24304.43)	48515.89 (33939.77-67116.59)	1.77	548.78 (396.93-762.13)	644.61 (450.94-891.75)	0.17	0.47 (0.35 to 0.59)
Central Latin America	15 to 19	10401.18 (7053.72-14135.05)	20307.65 (14214.52-26862.11)	0.95	112.45 (76.26-152.82)	188 (131.59-248.68)	0.67	1.67 (1.5 to 1.84)
Central Latin America	20 to 24	12607.41 (9011.74-17010.84)	28651.16 (20652-37787.73)	1.27	154.21 (110.23-208.07)	266.62 (192.18-351.64)	0.73	1.76 (1.59 to 1.93)
Central Latin America	25 to 29	13477.5 (9366.06-18273.28)	32979.52 (22903.71-43137)	1.45	192.55 (133.81-261.06)	312.87 (217.28-409.23)	0.62	1.55 (1.36 to 1.74)
Central Latin America	30 to 34	15446.48 (11360.8-19628.07)	39187.6 (29073.41-50497.54)	1.54	263.36 (193.7-334.66)	392.93 (291.52-506.34)	0.49	1.3 (1.15 to 1.45)
Central Latin America	35 to 39	17198.37 (12596.76-22574.91)	47861.29 (34907.45-63516.68)	1.78	356.27 (260.94-467.64)	506.61 (369.5-672.32)	0.42	1.14 (1.01 to 1.27)
Central Latin America	40 to 44	18447.4 (14834.28-22160.01)	61278.17 (49336.48-73812.64)	2.32	485.21 (390.18-582.87)	699.95 (563.55-843.12)	0.44	1 (0.87 to 1.12)
Central Latin America	45 to 49	19295.08 (14705.13-25799.26)	76011.01 (58296.39-97433.96)	2.94	644.46 (491.15-861.7)	958.44 (735.07-1228.56)	0.49	0.79 (0.62 to 0.96)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Southern Latin America	15 to 19	471.36 (286.97-677.13)	1331.1 (836.88-1862.97)	1.82	21.19 (12.9-30.44)	53.98 (33.94-75.55)	1.55	3.11 (3.05 to 3.18)
Southern Latin America	20 to 24	852.92 (593.74-1122.91)	2515.44 (1784.99-3350.63)	1.95	42.21 (29.38-55.57)	96.54 (68.5-128.59)	1.29	2.71 (2.67 to 2.74)
Southern Latin America	25 to 29	1062.12 (726.52-1440.19)	3304.34 (2225.87-4451.87)	2.11	54.68 (37.4-74.14)	122.77 (82.7-165.4)	1.25	2.71 (2.66 to 2.76)
Southern Latin America	30 to 34	1507.66 (1136.69-1973.95)	4736.63 (3457.29-6201.17)	2.14	83.3 (62.8-109.06)	179.39 (130.94-234.86)	1.15	2.62 (2.56 to 2.68)
Southern Latin America	35 to 39	2078.15 (1458.87-2892.3)	6601.33 (4608.94-8870.43)	2.18	126.67 (88.92-176.3)	265.73 (185.53-357.07)	1.10	2.55 (2.49 to 2.61)
Southern Latin America	40 to 44	3232.85 (2616.31-3841.12)	9894.13 (7538-11971.96)	2.06	219.85 (177.92-261.21)	419.9 (319.91-508.09)	0.91	2.27 (2.17 to 2.36)
Southern Latin America	45 to 49	4609.77 (3507.81-6085.8)	13888 (10461.49-17772.17)	2.01	359.1 (273.26-474.08)	635.39 (478.62-813.09)	0.77	2.04 (1.91 to 2.18)
Caribbean	15 to 19	1654.4 (1104.66-2205.05)	3596.34 (2540.8-4670.88)	1.17	89.38 (59.68-119.13)	193.69 (136.84-251.56)	1.17	2.43 (2.39 to 2.48)
Caribbean	20 to 24	2152.49 (1501.56-2959.33)	5184.77 (3738.72-6866.04)	1.41	123.55 (86.18-169.86)	275.36 (198.56-364.65)	1.23	2.58 (2.5 to 2.66)
Caribbean	25 to 29	2412 (1694.02-3158.43)	6031.64 (4127.82-8028.85)	1.50	150.33 (105.58-196.85)	325.77 (222.94-433.64)	1.17	2.47 (2.39 to 2.56)
Caribbean	30 to 34	2672.18 (1962.68-3378.43)	7837.51 (5810.75-10132.98)	1.93	208.21 (152.93-263.24)	424.7 (314.88-549.09)	1.04	2.43 (2.38 to 2.48)
Caribbean	35 to 39	3205.68 (2357.48-4119.66)	9646 (6895.15-12515.72)	2.01	289.51 (212.91-372.06)	576.76 (412.28-748.35)	0.99	2.35 (2.3 to 2.41)
Caribbean	40 to 44	4353.17 (3592.24-5067.45)	12556.15 (10038.32-14884.45)	1.88	461.44 (380.78-537.15)	855.42 (683.89-1014.04)	0.85	1.87 (1.8 to 1.94)
Caribbean	45 to 49	5679.47 (4597.13-6788.89)	16555.18 (12721.54-20958.97)	1.91	719.17 (582.11-859.65)	1140.29 (876.24-1443.62)	0.59	1.39 (1.34 to 1.44)
Central Europe	15 to 19	303.64 (126.59-542.63)	175.53 (64-366.91)	-0.42	6.34 (2.65-11.34)	6.18 (2.25-12.92)	-0.03	-0.1 (-0.16 to -0.04)
Central Europe	20 to 24	721.46 (365.7-1178.63)	660.56 (314.91-1120.07)	-0.08	16.49 (8.36-26.95)	22.68 (10.81-38.46)	0.38	0.97 (0.92 to 1.01)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Central Europe	25 to 29	2699.77 (1828.24-3587.4)	3358.58 (2351.8-4473.52)	0.24	64.46 (43.65-85.65)	102.12 (71.51-136.02)	0.58	1.33 (1.28 to 1.39)
Central Europe	30 to 34	5880.43 (4480.29-7270.72)	7287.37 (5536.31-9055.97)	0.24	121.64 (92.68-150.4)	189.67 (144.1-235.7)	0.56	1.31 (1.27 to 1.35)
Central Europe	35 to 39	7602.4 (5452.45-9935.93)	9803.82 (7072.63-13109.14)	0.29	156 (111.88-203.88)	235.38 (169.81-314.73)	0.51	1.27 (1.22 to 1.31)
Central Europe	40 to 44	9998.79 (8072.2-12064.38)	15622.22 (12605.7-18859.13)	0.56	235.45 (190.08-284.09)	353.36 (285.13-426.58)	0.50	1.34 (1.28 to 1.39)
Central Europe	45 to 49	12002.79 (9331.74-15116.36)	23049.36 (17539.55-29575.58)	0.92	352.09 (273.74-443.42)	537.99 (409.38-690.31)	0.53	1.42 (1.35 to 1.48)
Eastern Europe	15 to 19	1747.35 (884.17-2639.22)	1070.15 (369.39-1798.38)	-0.39	22.57 (11.42-34.08)	20.51 (7.08-34.46)	-0.09	-0.5 (-0.71 to -0.29)
Eastern Europe	20 to 24	3175.67 (2048.28-4608.23)	3116.89 (1938.99-4633.24)	-0.02	43.12 (27.81-62.58)	64.84 (40.33-96.38)	0.50	1.08 (0.91 to 1.24)
Eastern Europe	25 to 29	5862.8 (3992.28-7961.64)	7812.08 (5599.1-10251.93)	0.33	65.54 (44.63-89.01)	137.56 (98.59-180.52)	1.10	2.15 (2.02 to 2.27)
Eastern Europe	30 to 34	8109.75 (5582.83-10765.46)	15688.7 (11494.74-20210.91)	0.93	84.23 (57.99-111.82)	192.38 (140.95-247.83)	1.28	2.5 (2.4 to 2.6)
Eastern Europe	35 to 39	9052.35 (6266.91-12177.55)	19932.93 (13974.19-26788.68)	1.20	101.41 (70.21-136.42)	225.9 (158.37-303.6)	1.23	2.45 (2.33 to 2.56)
Eastern Europe	40 to 44	9011.99 (6765.41-11666.06)	22404.88 (16774.43-28400.19)	1.49	127.89 (96.01-165.56)	280.4 (209.94-355.44)	1.19	2.43 (2.34 to 2.52)
Eastern Europe	45 to 49	9243.76 (6441.35-12890.14)	26764.92 (18427.02-37844.73)	1.90	163.85 (114.18-228.49)	353.63 (243.47-500.03)	1.16	2.44 (2.4 to 2.49)
Central Asia	15 to 19	1233.78 (712.38-1675.58)	2948.36 (1936.42-3911.88)	1.39	38.13 (22.02-51.79)	87.49 (57.46-116.08)	1.29	2.85 (2.66 to 3.05)
Central Asia	20 to 24	1513.71 (989.04-2171.44)	4924.14 (3481.01-6554.55)	2.25	50.12 (32.75-71.9)	145.2 (102.64-193.27)	1.90	3.64 (3.48 to 3.79)
Central Asia	25 to 29	2282.72 (1506.4-3096.61)	7986.75 (5832.69-10285.94)	2.50	71.75 (47.35-97.33)	203.7 (148.76-262.34)	1.84	3.5 (3.4 to 3.6)
Central Asia	30 to 34	2779.29 (2066.13-3587.49)	10735.07 (8074.75-13921.33)	2.86	102.62 (76.29-132.46)	257.44 (193.64-333.85)	1.51	3.07 (3 to 3.13)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Central Asia	35 to 39	2918.82 (2127.89-3696.24)	11207.08 (8352.82-14166.2)	2.84	136.21 (99.3-172.49)	309.72 (230.84-391.5)	1.27	2.73 (2.67 to 2.8)
Central Asia	40 to 44	2444.42 (1897.72-2946.04)	12916.61 (10332.87-15573.56)	4.28	185.41 (143.94-223.46)	423.79 (339.02-510.96)	1.29	2.82 (2.7 to 2.94)
Central Asia	45 to 49	2810.86 (2125.07-3811.8)	16228.77 (12346.86-20842.64)	4.77	240.22 (181.61-325.76)	590.84 (449.51-758.82)	1.46	3.08 (2.85 to 3.3)
North Africa and Middle East	15 to 19	9740.68 (6302.23-13137.33)	47752.11 (34527.36-62014.39)	3.90	55.02 (35.6-74.21)	185.84 (134.37-241.34)	2.38	4.1 (3.99 to 4.21)
North Africa and Middle East	20 to 24	10600.38 (7450.78-14686.76)	60716.12 (45002.48-79365.03)	4.73	69.84 (49.09-96.76)	249.26 (184.75-325.82)	2.57	4.13 (4.03 to 4.23)
North Africa and Middle East	25 to 29	9566.05 (6193.84-13455.94)	52715.56 (35440.62-72171.53)	4.51	74.41 (48.18-104.66)	220.44 (148.2-301.8)	1.96	3.43 (3.36 to 3.49)
North Africa and Middle East	30 to 34	12403.34 (9104-15790.29)	75661.66 (56143.36-96242.93)	5.10	116.15 (85.26-147.87)	312.42 (231.82-397.4)	1.69	3.09 (3.05 to 3.14)
North Africa and Middle East	35 to 39	16699.63 (11986.19-22098.81)	115069.56 (82346.77-149963.83)	5.89	187.67 (134.7-248.34)	484.59 (346.79-631.55)	1.58	3.06 (2.99 to 3.13)
North Africa and Middle East	40 to 44	21019.17 (17152.48-24904.46)	168555.95 (138657.95-196781.08)	7.02	298.9 (243.91-354.15)	821.08 (675.44-958.57)	1.75	3.34 (3.28 to 3.39)
North Africa and Middle East	45 to 49	25918.41 (20179.8-33659.75)	216055.4 (171699.55-266751.6)	7.34	448.56 (349.24-582.54)	1279.47 (1016.8-1579.69)	1.85	3.43 (3.34 to 3.53)
South Asia	15 to 19	37850.33 (24716.07-51393.67)	125775.26 (86592.41-168158.23)	2.32	71.87 (46.93-97.59)	147.74 (101.71-197.52)	1.06	2.39 (2.31 to 2.46)
South Asia	20 to 24	44526.66 (30984.86-62123.88)	171257.17 (119885.86-231871.04)	2.85	92.99 (64.71-129.74)	203.97 (142.78-276.16)	1.19	2.6 (2.52 to 2.67)
South Asia	25 to 29	48158.12 (33108.3-65873.32)	197663.72 (134895.64-262891.11)	3.10	114.85 (78.96-157.1)	249.99 (170.61-332.48)	1.18	2.52 (2.46 to 2.58)
South Asia	30 to 34	50947.46 (36044.13-66350.43)	214413.47 (155656.43-279263.88)	3.21	143.81 (101.74-187.29)	294.01 (213.44-382.94)	1.04	2.25 (2.18 to 2.31)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
South Asia	35 to 39	55730.13 (39273.28-76258.44)	228075.25 (160745.61-304590.75)	3.09	180.15 (126.95-246.51)	343.03 (241.76-458.11)	0.90	1.96 (1.84 to 2.09)
South Asia	40 to 44	56666.4 (42941.9-73178.11)	242132.97 (184966.18-305622.75)	3.27	223.75 (169.56-288.95)	422.67 (322.88-533.5)	0.89	1.94 (1.82 to 2.06)
South Asia	45 to 49	56531.41 (40261.51-79632.65)	260650.24 (187327.03-356763.85)	3.61	272.74 (194.25-384.2)	529.03 (380.21-724.11)	0.94	2.04 (1.94 to 2.15)
Southeast Asia	15 to 19	9445.32 (5341.81-13399.13)	18006.63 (11331.07-24556.19)	0.91	38.29 (21.65-54.31)	65.19 (41.02-88.9)	0.70	0.95 (0.61 to 1.3)
Southeast Asia	20 to 24	12147.78 (7984.11-17616.41)	26127.06 (18322.75-36375.05)	1.15	53.31 (35.04-77.31)	94.53 (66.3-131.61)	0.77	0.94 (0.63 to 1.26)
Southeast Asia	25 to 29	14754.87 (9523.85-20506.14)	33726.59 (22840.79-45566.45)	1.29	71.29 (46.01-99.07)	120.23 (81.43-162.44)	0.69	0.67 (0.36 to 0.98)
Southeast Asia	30 to 34	18419.87 (13452.35-23523.43)	49920.25 (37274.54-62382.08)	1.71	104.25 (76.14-133.14)	183.15 (136.75-228.87)	0.76	0.87 (0.56 to 1.17)
Southeast Asia	35 to 39	21168.99 (15063.43-27505.11)	71864.25 (53864.5-91320.74)	2.39	148.43 (105.62-192.86)	277.3 (207.85-352.38)	0.87	1.14 (0.84 to 1.45)
Southeast Asia	40 to 44	22066.84 (17135.83-27107.1)	93892.16 (75957.93-112237.73)	3.25	202.62 (157.35-248.91)	384.35 (310.93-459.44)	0.90	1.38 (1.14 to 1.62)
Southeast Asia	45 to 49	24270.7 (17368.66-33260.56)	111241.16 (83498.32-144592.04)	3.58	263.45 (188.53-361.03)	499.09 (374.62-648.72)	0.89	1.58 (1.43 to 1.73)
East Asia	15 to 19	76365.72 (51933.22-103459.55)	134255.46 (100902.2-169052.57)	0.76	120.21 (81.75-162.86)	372.82 (280.2-469.45)	2.10	4.27 (3.7 to 4.84)
East Asia	20 to 24	94581.86 (66005.6-129552.67)	156787.12 (122967.66-190913.75)	0.66	142.27 (99.28-194.87)	436.17 (342.08-531.1)	2.07	4.08 (3.58 to 4.59)
East Asia	25 to 29	56854.66 (33642.17-85599.04)	74745.8 (43296.89-114775.76)	0.31	102.67 (60.75-154.58)	175.13 (101.45-268.93)	0.71	1.64 (1.4 to 1.87)
East Asia	30 to 34	45641.18 (26875.59-69294.35)	82056.19 (46725.55-124640.05)	0.80	103.97 (61.22-157.86)	136.25 (77.59-206.96)	0.31	0.59 (0.44 to 0.73)
East Asia	35 to 39	60935.77 (35760.69-96999.7)	84727.57 (51657.89-130397.25)	0.39	133.71 (78.47-212.85)	158.62 (96.71-244.12)	0.19	0.22 (0.13 to 0.3)
East Asia	40 to 44	79750.28 (57764.41-105286.07)	118107.11 (87634.23-154616.64)	0.48	241.16 (174.67-318.37)	253.99 (188.46-332.51)	0.05	-0.22 (-0.33 to -0.12)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
East Asia	45 to 49	107366.02 (68009.84-154854.36)	233015.37 (153048.29-330487.36)	1.17	421.69 (267.12-608.21)	415.15 (272.67-588.8)	-0.02	-0.42 (-0.55 to -0.28)
Oceania	15 to 19	535.17 (392.38-678.41)	2435.99 (1795.37-3092.79)	3.55	161.55 (118.45-204.79)	392.76 (289.47-498.66)	1.43	2.7 (2.62 to 2.78)
Oceania	20 to 24	588.94 (432.73-784.58)	3027.12 (2314.24-3820.85)	4.14	195.69 (143.79-260.7)	503.59 (385-635.64)	1.57	2.86 (2.77 to 2.96)
Oceania	25 to 29	513.73 (352.77-691.99)	2343.02 (1581.34-3139.83)	3.56	192.71 (132.33-259.58)	410.52 (277.07-550.13)	1.13	2.32 (2.26 to 2.39)
Oceania	30 to 34	550.37 (406.97-700.93)	2721.52 (2045.68-3544.18)	3.94	251.48 (185.95-320.27)	528.25 (397.07-687.94)	1.10	2.44 (2.41 to 2.46)
Oceania	35 to 39	638.2 (473.2-829.94)	3558.9 (2532.04-4621.52)	4.58	359.58 (266.62-467.61)	788.24 (560.81-1023.59)	1.19	2.66 (2.61 to 2.71)
Oceania	40 to 44	683.52 (543.14-817.35)	3990.86 (3165.91-4786.66)	4.84	475.08 (377.51-568.09)	1026.3 (814.15-1230.95)	1.16	2.58 (2.51 to 2.66)
Oceania	45 to 49	690.06 (525.97-864.37)	3969.57 (3013.23-4925.58)	4.75	600.81 (457.95-752.58)	1227.73 (931.95-1523.41)	1.04	2.44 (2.31 to 2.57)
Western Sub-Saharan Africa	15 to 19	6136.87 (4166.46-8139.73)	36781.18 (26970.11-47522.41)	4.99	60.08 (40.79-79.69)	133.07 (97.58-171.93)	1.21	2.73 (2.61 to 2.84)
Western Sub-Saharan Africa	20 to 24	5171.39 (3427.6-7432.8)	29351.95 (20158.44-40769.53)	4.68	58.56 (38.81-84.17)	126.31 (86.75-175.45)	1.16	2.65 (2.55 to 2.74)
Western Sub-Saharan Africa	25 to 29	4409.46 (2781.88-6218.36)	22419.63 (14796-31061.97)	4.08	59.29 (37.4-83.61)	114.34 (75.46-158.41)	0.93	2.21 (2.15 to 2.26)
Western Sub-Saharan Africa	30 to 34	4538.79 (3129.17-5956.94)	21551.44 (14850.88-28521.35)	3.75	75.71 (52.2-99.37)	132.5 (91.31-175.36)	0.75	1.84 (1.79 to 1.88)
Western Sub-Saharan Africa	35 to 39	4749.83 (3181.61-6510.55)	22898.95 (15777.23-31315.58)	3.82	102.63 (68.75-140.67)	169.91 (117.07-232.36)	0.66	1.62 (1.58 to 1.67)
Western Sub-Saharan Africa	40 to 44	5362.42 (4143.12-6763.38)	27428.01 (21266.06-34509.8)	4.11	151.53 (117.08-191.12)	252.3 (195.62-317.44)	0.66	1.57 (1.54 to 1.61)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Western Sub-Saharan Africa	45 to 49	6533.22 (4631.13-9226.36)	32865.83 (23414.74-45513.12)	4.03	220.66 (156.41-311.61)	373.87 (266.36-517.75)	0.69	1.58 (1.54 to 1.61)
Eastern Sub-Saharan Africa	15 to 19	4313.11 (2877.46-5843.2)	17542.64 (12329.48-23284.58)	3.07	41.91 (27.96-56.78)	71.39 (50.18-94.76)	0.70	1.53 (1.46 to 1.59)
Eastern Sub-Saharan Africa	20 to 24	3883.79 (2659.62-5492.53)	16485.52 (11355.32-22960.4)	3.24	44.49 (30.47-62.92)	78.18 (53.85-108.88)	0.76	1.65 (1.6 to 1.71)
Eastern Sub-Saharan Africa	25 to 29	3585.6 (2367.17-5009.83)	14593.02 (9777.87-19833.3)	3.07	49.08 (32.4-68.58)	83.61 (56.02-113.63)	0.70	1.55 (1.49 to 1.61)
Eastern Sub-Saharan Africa	30 to 34	3624.75 (2534.5-4732.31)	14480.79 (10307-19207.21)	2.99	62.71 (43.85-81.88)	100.13 (71.27-132.81)	0.60	1.35 (1.27 to 1.42)
Eastern Sub-Saharan Africa	35 to 39	3848.42 (2760.05-5017.91)	14906.41 (10680.8-19585.36)	2.87	81.96 (58.78-106.86)	122.8 (87.99-161.35)	0.50	1.15 (1.03 to 1.26)
Eastern Sub-Saharan Africa	40 to 44	3303.97 (2454.89-4213.94)	14126.98 (10513.81-17973.94)	3.28	95.25 (70.78-121.49)	143.41 (106.73-182.46)	0.51	1.11 (0.99 to 1.23)
Eastern Sub-Saharan Africa	45 to 49	3075.03 (2084.66-4405.96)	12113.19 (8245.04-16980.53)	2.94	106.75 (72.37-152.95)	160.74 (109.41-225.33)	0.51	1.13 (1.04 to 1.23)
Central Sub-Saharan Africa	15 to 19	1670.23 (1149.49-2243.97)	10471.58 (7561.53-13651.86)	5.27	59.09 (40.67-79.39)	141.59 (102.24-184.59)	1.40	2.71 (2.62 to 2.79)
Central Sub-Saharan Africa	20 to 24	1565.51 (1077.1-2202.93)	9584.15 (6635.05-13278.73)	5.12	64.33 (44.26-90.52)	155.09 (107.37-214.88)	1.41	2.67 (2.62 to 2.72)
Central Sub-Saharan Africa	25 to 29	1492.82 (981.81-2119.08)	8138.26 (5379.67-11060.9)	4.45	71.54 (47.05-101.55)	154.8 (102.33-210.39)	1.16	2.36 (2.32 to 2.41)
Central Sub-Saharan Africa	30 to 34	1545.28 (1088.61-2043.69)	8164.01 (5793.16-10692.02)	4.28	91.16 (64.22-120.56)	181.28 (128.64-237.42)	0.99	2.2 (2.16 to 2.24)

Location	Age (years)	Incidence cases			Incidence rates			
		1990_cases (95% UI)	2021_cases (95% UI)	Percentage change in case (100%)	1990_per 100 000 (95% UI)	2021_per 100 000 (95% UI)	Percentage change in ASRs (100%)	EAPC (95% CI)
Central Sub-Saharan Africa	35 to 39	1634.19 (1165.61-2197.35)	8435.9 (5878.57-11209.27)	4.16	117.07 (83.5-157.42)	224.67 (156.56-298.53)	0.92	2.18 (2.13 to 2.22)
Central Sub-Saharan Africa	40 to 44	1517.39 (1146.81-1891.32)	8747.89 (6548.86-11011.48)	4.77	148.05 (111.89-184.53)	284.24 (212.79-357.79)	0.92	2.19 (2.14 to 2.24)
Central Sub-Saharan Africa	45 to 49	1651.67 (1137.79-2275.41)	8883.44 (6392.32-11742.31)	4.38	183.8 (126.61-253.21)	357.6 (257.32-472.68)	0.95	2.2 (2.15 to 2.26)
Southern Sub-Saharan Africa	15 to 19	1908.19 (1266.48-2559.64)	3849.19 (2616.37-5136.75)	1.02	64.44 (42.77-86.44)	107.47 (73.05-143.42)	0.67	1.61 (1.47 to 1.75)
Southern Sub-Saharan Africa	20 to 24	1963.82 (1335.17-2794.64)	4188.43 (2927-5732.4)	1.13	75.83 (51.56-107.92)	124.71 (87.15-170.68)	0.64	1.59 (1.5 to 1.68)
Southern Sub-Saharan Africa	25 to 29	1925.47 (1268.42-2659.65)	4545.56 (3059.85-6329.58)	1.36	84.98 (55.98-117.38)	130.14 (87.6-181.21)	0.53	1.27 (1.23 to 1.32)
Southern Sub-Saharan Africa	30 to 34	1904.91 (1348.24-2540.32)	5186.34 (3563.51-6972.36)	1.72	103.47 (73.24-137.99)	148.82 (102.25-200.07)	0.44	0.95 (0.87 to 1.04)
Southern Sub-Saharan Africa	35 to 39	1991.99 (1328.86-2734.84)	5784.27 (3895.14-8086.49)	1.90	131.98 (88.04-181.19)	182.64 (122.99-255.34)	0.38	0.77 (0.64 to 0.91)
Southern Sub-Saharan Africa	40 to 44	2186.59 (1662.55-2803.2)	7553.02 (5688.28-9489.79)	2.45	186.34 (141.68-238.88)	299.04 (225.21-375.72)	0.60	1.41 (1.33 to 1.5)
Southern Sub-Saharan Africa	45 to 49	2499.66 (1706.86-3577.16)	10341.1 (6975.82-14606.01)	3.14	262.64 (179.34-375.86)	492.09 (331.95-695.04)	0.87	2.06 (2 to 2.12)

Divergent Trends in Type 2 Diabetes Mellitus Burden Across Sociodemographic Index Regions

In 2021, with the exception of the low SDI region, where the incidence numbers showed no clear age dependence, the absolute numbers of all burden indicators across the five SDI regions increased with age. Despite the lack of age dependence in low SDI areas, the 45-49 age group still accounted for the highest absolute number of cases. Compared to 1990, the percentage increases in incidence, prevalence, DALYs, and deaths in the high-middle, middle, and low-middle SDI regions in 2021 rose consistently with age. However, no significant trends were observed in the percentage changes of these burden indicators across different age groups in the low SDI and high-SDI regions. Additionally, negative growth in the number of deaths was observed in specific age groups, including the 15-39 age group in the high-SDI region, the 15-34 age group in the high-middle SDI region, and the 15-24 age group in the middle-SDI region (Figure 3, Figure4; Table 2, Table S4-S6).

In 2021, with the exception of the high-SDI and high-middle-SDI regions where ASIR showed no clear age dependence, the ASRs of various burden indicators across the five SDI regions generally increased with age. Nevertheless, the ASIR in the high-SDI and high-middle-SDI regions remained highest in older age groups, particularly in the 45-49 age group. From the perspective of EAPC, between 1990 and 2021, the ASIR in younger age groups across all five SDI regions, as well as the ASPR and ASDR, exhibited higher growth rates. Meanwhile, the ASMR decreased in most age groups across the five regions, with the exception of the low-middle-SDI region, where positive EAPC values were observed for the 40-49 age group (Figure 3, Figure4; Table 2, Table S4-S6).

Global Trends in Disease Burden of Type 2 Diabetes Mellitus Among Women of Reproductive Age Across 21 GBD Regions

Overall, in most regions, the numbers for incidence, prevalence, DALYs, and deaths, along with their ASRs, tended to increase with age. However, a few regions demonstrated a higher disease burden among younger age groups. For instance, in Western Sub-Saharan Africa, the 15-19 age group recorded the highest number of cases and the largest percentage increase in 2021. From 1990 to 2021, a small number of regions experienced negative growth in the numbers for incidence, prevalence, and DALYs among younger age groups. For example, Central Europe showed negative growth in the 15-24 age group. Similarly, in terms of ASRs, a few regions exhibited a downward trend in ASIR, ASPR, and ASDR among younger age groups. Moreover, more than half of the regions reported negative growth in death counts across all age groups or younger age groups. In most regions, the ASMR also displayed a declining trend across all age groups or younger age groups (Figure 3, Figure4; Table 2, Table S4-S6).

ISSN: 0378-1844

Association Between Type 2 Diabetes Mellitus Burden and SDI from 1990 to 2021

As shown in Figure 5, there is no straightforward linear relationship between the SDI index and the burden of T2DM among WRA. However, overall, from 1990 to 2021, ASIR, ASPR, and ASDR increased with higher SDI values, while ASMR decreased as the SDI index rose. Notably, no significant association was observed between ASIR and the SDI index. It is also worth highlighting that the disease burden in Oceania was significantly higher than expected.

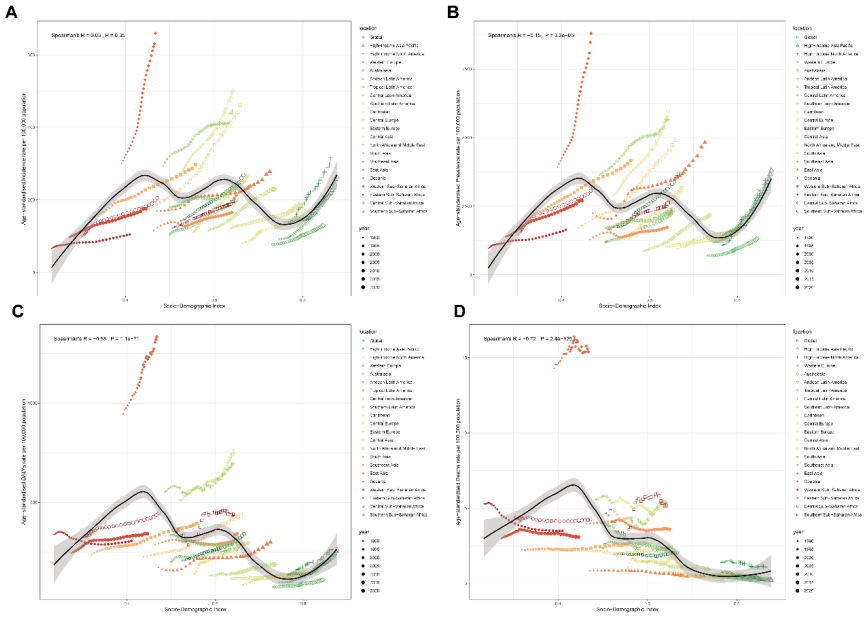


Figure 5 . Relationship between SDI and Type 2 Diabetes Mellitus Burden among Women of Reproductive Age

A: Association between SDI and incidence rates (per 100,000) of Type 2 Diabetes Mellitus among women of reproductive age in 21 GBD regions.

B: Association between SDI and prevalence rates (per 100,000) of Type 2 Diabetes Mellitus among women of reproductive age in 21 GBD regions.

C: Association between SDI and DALY rates (per 100,000) of Type 2 Diabetes Mellitus among women of reproductive age in 21 GBD regions.

D: Association between SDI and Death rates (per 100,000) of Type 2 Diabetes Mellitus among women of reproductive age in 21 GBD regions.

Decomposition Analysis of Type 2 Diabetes Mellitus Burden Among Women of Reproductive Age

From 1990 to 2021, the burden of T2DM among WRA increased significantly. Globally, the growth in the number of deaths was primarily driven by population (58.42%) and aging (31.78%), with only 9.81% attributed to epidemiological changes. In contrast, epidemiological changes contributed most significantly to the growth in DALYs (48.1%), prevalence (59.2%), and incidence (57.49%). Population was the second-largest contributor to these indicators, accounting for 36.63%, 30.66%, and 34.69%, respectively, while aging contributed 15.27%, 10.14%, and 7.83%, respectively (Figure 6; Table S7).

There were significant differences in the growth patterns of T2DM across different SDI regions. In high SDI regions, the burden of deaths decreased, with epidemiological changes making the largest contribution, accounting for 651.59%. In high-middle SDI regions, aging was the primary driver of death growth, contributing 208.61%. In middle SDI regions, aging and population contributed similarly to the increase in deaths, at 53.78% and 53.9%, respectively. In these three regions, epidemiological changes were the largest driving force behind the growth of DALYs, prevalence, and incidence. In low-middle SDI regions, population was the largest contributor to increases in deaths and DALYs, while epidemiological changes were the primary drivers of prevalence and incidence growth. In low SDI regions, population was the dominant driver of increases across all burden indicators (Figure 6; Table S7). Among the 21 geographic regions, most experienced an increase in the T2DM burden, with only a few regions showing a decrease in death burden. South Asia exhibited the most pronounced growth, with population growth being the primary contributor to increases in deaths and DALYs, while epidemiological changes were the largest contributors to the growth in prevalence and incidence (Figure 6; Table S7).

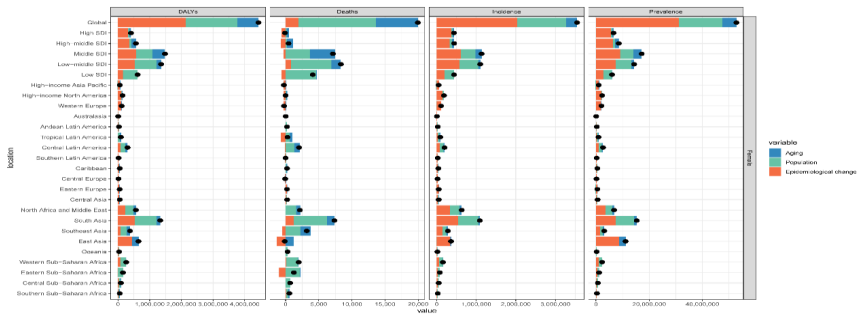


Figure 6. Decomposition Analysis of Type 2 Diabetes Mellitus Burden Among Women of Reproductive Age, 1990-2021

ISSN: 0378-1844

Projected Global Burden of Type 2 Diabetes Mellitus Among Women of Reproductive Age

We used the BAPC and Nordpred models to predict the burden of T2DM among WRA globally from 2022 to 2040. Predictions were also made specifically for China and India, given their status as the two major populous nations. Overall, both models demonstrated consistent trends. By 2040, ASIR, ASPR, and ASDR are projected to increase globally, as well as in China and India. However, the Nordpred model predicts that DALYs in India will peak in 2034 and then decline slightly, though remaining higher than in 2022. By 2040, global ASMR is expected to show an upward trend, while in contrast, ASMR in both China and India is projected to decrease (Figure 7; Table S8).

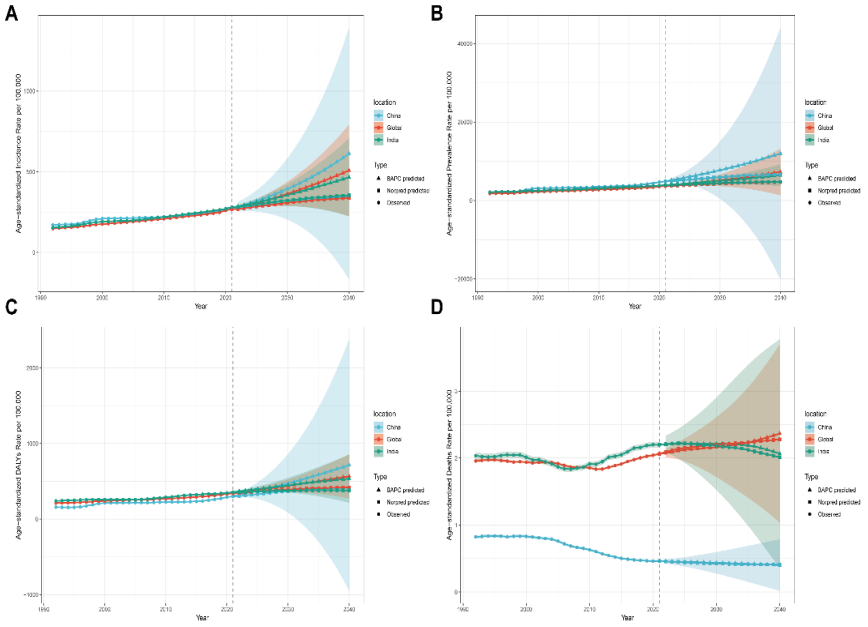


Figure 7. Projected Burden of Type 2 Diabetes Mellitus Among Women of Reproductive Age in 2040: Global, China, and India (Nordpred and BAPC Models)
A: Predicted age-standardized incidence rates per 100,000 population
B: Forecasted age-standardized prevalence rates per 100,000 population
C: Projected age-standardized DALY rates per 100,000 population
D: Estimated age-standardized mortality rates per 100,000 population

Discussion

WRA represent a key demographic in the fields of reproductive health and family planning, holding a critical position in global health strategies. The United Nations' Sustainable Development Goal 3 emphasizes reducing neonatal and maternal mortality and integrating reproductive health into national strategic planning frameworks [22]. However, the rising burden of type 2 diabetes and its adverse effects on reproductive health []-[18]] pose significant challenges to achieving these goals. In this context, the present study leverages the latest data from the GBD to comprehensively and deeply assess the burden of type 2 diabetes among WRA worldwide and its trends from 1990 to 2021. Through this research, we aim to elucidate its epidemiological characteristics, thereby establishing an evidence base for formulating tailored diabetes prevention and control measures aimed at enhancing health status and quality of life in this population.

Previously, multiple research data have all indicated a significant increase in the burden of T2DM in recent years [],[2]]. Our research data also reflect this situation. From 1990 to 2021, the burden of T2DM among WRA globally increased remarkably. The numbers of incidence, prevalence, DALYs, and deaths related to WRA increased by 201%, 251%, 181%, and 90% respectively, and their ASRs also exhibited an upward trend. Decomposition analysis reveals that the increase in global diabetes-related deaths is primarily influenced by population growth and aging, while epidemiological change is a key factor driving the rise in diabetes prevalence, incidence, and the number of DALYs. Existing evidence indicates that lifestyle factors are significant pathogenic factors for T2DM [23]. Among them, overweight and obesity caused by unhealthy lifestyles are core risk factors for the disease, a phenomenon potentially driven by social, economic, and environmental factors []-[26].Over the past few decades, numerous countries and regions around the world have entered the stage of the nutrition transition, characterized by a sharp increase in the consumption of ultra-processed foods and a significant reduction in physical activity. During this stage, the rates of overweight and obesity have climbed rapidly, and the prevalence rates of diseases such as diabetes have also shown a high growth trend [27]. Studies have shown that excessive intake of red meat and processed meats, along with insufficient fruit consumption, are major dietary contributors to diabetes [28]. Additionally, the current sedentary lifestyle has fueled the obesity epidemic and exacerbated diabetes progression [29]. In contrast, low-calorie, low-carbohydrate diets and moderate exercise can enhance insulin sensitivity, reduce the risk of T2DM, and improve long-term adverse outcomes in individuals with diabetes []-[33]. Furthermore, environmental factors such as tobacco smoke exposure and air pollution also increase the risk of T2DM [],[35]. Beyond lifestyle factors, genetic factors are equally significant determinants of T2DM [23]. Research indicates that differences in T2DM incidence across populations may be closely associated with their unique genetic susceptibility [],[37]. Meanwhile, people

with a family history of T2DM, especially first-degree relatives, are at higher risk of developing the disease, which is usually mediated by shared genetic risks as well as similar family environments and lifestyles [37]. For women, reproductive factors such as early or late menarche, a high number of childbirths, and a history of miscarriage can further exacerbate this genetic risk [38]. Therefore, priority should be given to strengthening early screening and targeted prevention for high-risk populations to effectively control disease progression.

The relationship between SDI and the burden of T2DM in WRA reflects a paradox between social development and disease risk. In regions with higher SDI, the absolute numbers of T2DM burden indicators have grown relatively slowly or even shown a downward trend, while ASIR, ASPR, and ASDR have significantly increased. Further attribution analysis shows that as SDI increases, the contribution of epidemiological transition to disease burden growth becomes greater.. This reflects the survival advantages brought by improved healthcare systems, including better disease screening, diagnosis, management, and survival rates [39], but also highlights the metabolic costs imposed by modern lifestyles, including the prevalence of risk factors caused by dietary structural changes, reduced physical activity, and other factors [],[29], to which healthcare systems have not fully adapted to. Current healthcare systems still lack sufficient capacity for long-term management of chronic metabolic diseases, and prevention systems have not effectively addressed the emerging risks from lifestyle transitions [40]. On the other hand, as SDI decreases, population growth contributes more to the increase in disease burden. However, the disease burden growth driven by epidemiological transition in these regions remains non-negligible, and the risk of rapid future disease burden escalation requires vigilance. Studies have indicated that in low- and middle-income regions, the rapid transition of dietary patterns from traditional to industrialized models has become a significant driver of the epidemic of metabolic diseases such as T2DM [41]. Meanwhile, the drastic shift in these regions from early-life malnutrition to adult nutritional transition may also enhance susceptibility to insulin resistance and metabolic diseases like diabetes [],[43]. Additionally, the higher ASDR and ASMR in low- and middle-income countries are closely associated with economic and sociopolitical factors. The coverage rate of diabetes medical care in these regions is generally low [44]. A study by Michael et al. pointed out that 80% of diabetes patients worldwide are in developing countries, yet they only account for 1% of the global medical expenditure on diabetes. This calls for the joint efforts of governments and various organizations to strengthen health systems and the improve diabetes care delivery in order to address such inequalities [44]. T2DM is regarded as an age-related metabolic disorder [45]. Previous studies have also demonstrated that prevalence increases with age [26]. Our results confirm this characteristic, showing that both the incidence and prevalence rates of T2DM among WRA globally increase with the increase in age. Besides genetic factors, the

cumulative impact of environmental factors must be taken into consideration. For example, in patients who develop T2DM due to obesity, the metabolic defects involve beta-cell dysfunction. Multiple studies have showen [])-[48]] that this phenomenon may be caused by the chronic low-grade inflammation associated with obesity. Over time, this inflammatory state impairs beta-cell function and progresses to insulin-resistant T2DM. As the duration of T2DM increases, the prevalence of its complications also increases [49]. Moreover, other types of diseases such as Parkinson's disease will also be aggravated along with T2DM [50], which may also be one of the reasons why higher age groups show a higher burden of DALYs and deaths. In addition, WRA in higher age groups are facing the situation of entering menopause, and suffering from T2DM may accelerate the progress of menopause. At this time, the risk of women suffering from cardiovascular diseases is further increased [51]. It is worth noting the population with early-onset T2DM, that is, those whose age at the onset of T2DM is less than 40 years old. Their prevalence rate has also increased significantly from 1990 to 2021. Multiple studies have shown that the lower the age at the diagnosis of T2DM, the higher the risk of developing subsequent complications, and at the same time, they also bear a higher risk of death [],[],[53]]. It is necessary to conduct risk stratification for such populations and strengthen preventive strategies and management guidelines in order to achieve a good prognosis.

Diabetes is the first non-communicable disease to be defined as an epidemic by the World Health Organization on a global scale [54]. Undoubtedly, its disease burden is enormous, and it is projected that the burden of T2DM will continue to intensify by 2040. Currently, many countries have already taken active measures. For instance, the Indian government has launched the Ayushman Bharat program, which aims to provide more robust basic medical security services for poor families [44]. China has introduced the "Implementation Plan for the Healthy China Initiative - Diabetes Prevention and Control Action (2024 - 2030)", which has continuously optimized the policy support system for chronic disease prevention and control and vigorously promoted the in-depth development of diabetes prevention and control work [55]. Fortunately, T2DM can be prevented through dietary interventions and physical exercise [27]. Studies have shown that weight management strategies through healthy diets and regular exercise can mitigate T2DM in a dose-dependent manner [56]. To achieve optimal intervention outcomes, it is recommended to develop localized intervention programs by integrating regional cultural characteristics (such as dietary structures and exercise habits), incorporate personalized dietary guidance into diabetes management systems, and advocate for individuals and communities to adopt healthy eating patterns and engage in physical activity, thereby alleviating the disease burden of T2DM. For WRA, drug treatment protocols for T2DM must emphasize individualization and patient-centered care, with particular attention to pregnancy status. Additionally, gender-sensitive

intervention strategies, such as community pre-pregnancy health programs, can be developed. For high-burden regions and high-risk age groups, population characteristic-based diabetes screening strategies should be promoted, incorporating reproductive health characteristics (such as a history of gestational diabetes mellitus or polycystic ovary syndrome) to improve individualized risk assessment models. Through multi-dimensional and tiered prevention and control strategies, the disease burden of T2DM in WRA can be effectively reduced while improving their reproductive health outcomes.

Limitation

This study has several limitations. First, the findings rely on the availability of GBD data, which are largely based on modeled estimates. This reliance may introduce inherent biases into the results. Secondly, in certain underdeveloped countries and regions with lower healthcare standards, there is a possibility of underdiagnosis of the condition. Thirdly, since many diabetes patients succumb to complications associated with the disease, the collection of diabetes-related mortality data may involve issues with data quality. Furthermore, in some underdeveloped areas, undiagnosed cases of diabetes leading to death at onset may occur [57], potentially contributing to assessment biases.

Conclusions

WRA represent a critical population group in the fields of reproductive health and family planning. Our study conducted a comprehensive analysis of the burden of T2DM among this demographic, revealing a significant increase in the global burden of T2DM from 1990 to 2021. Over this period, the incidence, prevalence, DALYs, and deaths rose substantially, with notable upward trends in ASIR, ASPR, and ASDR. Projections indicate that this burden will continue to intensify by 2040. In light of this escalating health challenge, it is imperative to enhance diagnostic and treatment management systems while actively promoting healthy dietary practices and regular physical activity. These measures are essential for effectively reducing the burden of T2DM and improving overall public health outcomes.

Data availability statement

The data used for the analyses in the study are publicly available at https://ghdx.healthdata.org/gbd-2021.

Funding: Not Applicable.

Competing interests

The authors declare no competing interests.

Acknowledgment

We gratefully acknowledge the Global Burden of Disease Study (GBD) for providing the comprehensive data that made this research possible.

References

[1] GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024 May 18;403(10440):2133-2161. doi: 10.1016/S0140-6736(24)00757-8.

[2] Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022 Jan;183:109119. doi: 10.1016/j.diabres.2021.109119.

[3] World Health Organization. Classification of diabetes mellitus 2019. Geneva: WHO; 2019.

[4] Ahmad E, Lim S, Lamptey R, et al. Type 2 diabetes. Lancet. 2022 Nov 19;400(10365):1803-1820. doi: 10.1016/S0140-6736(22)01655-5.

[5] Su J, Luo Y, Hu S, et al. Advances in Research on Type 2 Diabetes Mellitus Targets and Therapeutic Agents. Int J Mol Sci. 2023 Aug 29;24(17):13381. doi: 10.3390/ijms241713381.

[6] Dal Canto E, Ceriello A, Rydén L, et al. Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. Eur J Prev Cardiol. 2019 Dec;26(2_suppl):25-32. doi: 10.1177/2047487319878371.

[7] Luo A, Xie Z, Wang Y, et al. Type 2 diabetes mellitus-associated cognitive dysfunction: Advances in potential mechanisms and therapies. Neurosci Biobehav Rev. 2022 Jun;137:104642. doi: 10.1016/j.neubiorev.2022.104642.

[8] de Boer IH, Khunti K, Sadusky T, et al. Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 2022 Dec 1;45(12):3075-3090. doi: 10.2337/dci22-0027.

[9] Cioana M, Deng J, Nadarajah A, et al. Global Prevalence of Diabetic Retinopathy in Pediatric Type 2 Diabetes: A Systematic Review and Meta-analysis. JAMA Netw Open. 2023 Mar 1;6(3):e231887. doi: 10.1001/jamanetworkopen.2023.1887.

[10] de Ritter R, de Jong M, Vos RC, et al. Sex differences in the risk of vascular disease associated with diabetes. Biol Sex Differ. 2020 Jan 3;11(1):1. doi: 10.1186/s13293-019-0277-z.

[11] Peters SA, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014 Aug;57(8):1542-51. doi: 10.1007/s00125-014-3260-6.

[12] Chatterjee S, Peters SA, Woodward M, et al. Type 2 Diabetes as a Risk Factor

for Dementia in Women Compared With Men: A Pooled Analysis of 2.3 Million People Comprising More Than 100,000 Cases of Dementia. Diabetes Care. 2016 Feb;39(2):300-7. doi: 10.2337/dc15-1588.

[13] Shen Y, Cai R, Sun J, et al. Diabetes mellitus as a risk factor for incident chronic kidney disease and end-stage renal disease in women compared with men: a systematic review and meta-analysis. Endocrine. 2017 Jan;55(1):66-76. doi: 10.1007/s12020-016-1014-6.

[14] Bancks MP, Akhabue E, Rana JS, et al. Sex differences in cardiovascular risk factors before and after the development of type 2 diabetes and risk for incident cardiovascular disease. Diabetes Res Clin Pract. 2020 Aug;166:108334. doi: 10.1016/j.diabres.2020.108334.

[15] Thong EP, Codner E, Laven JSE, et al. Diabetes: a metabolic and reproductive disorder in women. Lancet Diabetes Endocrinol. 2020 Feb;8(2):134-149. doi: 10.1016/S2213-8587(19)30345-6.

[16] Mohile AA, Hedaoo RP, Jadhav SJ, et al. Unraveling the Link: A Comprehensive Literature Review of Type 2 Diabetes and Menopause Onset. Cureus. 2023 Dec 18;15(12):e50743. doi: 10.7759/cureus.50743.

[17] Ren Y, Hao L, Liu J, Wang P, Ding Q, Chen C, Song Y. Alterations in the Gut Microbiota in Pregnant Women with Pregestational Type 2 Diabetes Mellitus. mSystems. 2023 Apr 27;8(2):e0114622. doi: 10.1128/msystems.01146-22.

[18] Liu Y, Liu C, Liu J, Lei L, Tan L. Global, regional, and national burden of diabetes and its risk factors in women of child-bearing age, from 1990 to 2021. Public Health. 2025 Apr;241:99-106. doi: 10.1016/j.puhe.2025.02.004. Epub 2025 Feb 18. PMID: 39965323.

[19] GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2024 May 18;403(10440):2100-2132. doi: 10.1016/S0140-6736(24)00367-2.

[20] GBD 2021 Demographics Collaborators. Global age-sex-specific mortality, life expectancy, and population estimates in 204 countries and territories and 811 subnational locations, 1950-2021, and the impact of the COVID-19 pandemic: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. Lancet. 2024 May 18;403(10440):1989-2056. doi: 10.1016/S0140-6736(24)00476-8.

[21] GBD 2021 Forecasting Collaborators. Burden of disease scenarios for 204 countries and territories, 2022-2050: a forecasting analysis for the Global Burden of Disease Study 2021. Lancet. 2024 May 18;403(10440):2204-2256. doi: 10.1016/S0140-6736(24)00685-8.

[22] World Health Organization. Targets of Sustainable Development Goal 3. Available from: https://www.who.int/europe/about-us/our-work/sustainable-

development-goals/targets-of-sustainable-development-goal-3.
[23] Toi PL, Anothaisintawee T, Chaikledkaew U, et al. Preventive Role of Diet Interventions and Dietary Factors in Type 2 Diabetes Mellitus: An Umbrella Review. Nutrients. 2020 Sep 6;12(9):2722. doi: 10.3390/nu12092722.
[24] Malik VS, Hu FB. The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. Nat Rev Endocrinol. 2022 Apr;18(4):205-218. doi: 10.1038/s41574-021-00627-6.
[25] Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. Lancet Diabetes Endocrinol. 2021 Jun;9(6):373-392. doi: 10.1016/S2213-8587(21)00045-0. Erratum in: Lancet Diabetes Endocrinol. 2021 Jul;9(7):e2. doi: 10.1016/S2213-8587(21)00149-2.
[26] GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023 Jul 15;402(10397):203-234. doi: 10.1016/S0140-6736(23)01301-6.
[27] Popkin BM, Ng SW. The nutrition transition to a stage of high obesity and noncommunicable disease prevalence dominated by ultra-processed foods is not inevitable. Obes Rev. 2022 Jan;23(1):e13366. doi: 10.1111/obr.13366.
[28] Hong T, Sun F, Wang Q, et al. Global burden of diabetes mellitus from 1990 to 2019 attributable to dietary factors: An analysis of the Global Burden of Disease Study 2019. Diabetes Obes Metab. 2024 Jan;26(1):85-96. doi: 10.1111/dom.15290.
[29] Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care. 2010 Dec;33(12):e147-67. doi: 10.2337/dc10-9990.
[30] Juanola-Falgarona M, Salas-Salvad ó J, Ibarrola-Jurado N, et al. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: a randomized controlled trial. Am J Clin Nutr. 2014 Jul;100(1):27-35. doi: 10.3945/ajcn.113.081216.
[31] Robertson MD, Bickerton AS, Dennis AL, et al. Insulin-sensitizing effects of dietary resistant starch and effects on skeletal muscle and adipose tissue metabolism. Am J Clin Nutr. 2005 Sep;82(3):559-67. doi: 10.1093/ajcn.82.3.559.
[32] Sylow L, Tokarz VL, Richter EA, et al. The many actions of insulin in skeletal muscle, the paramount tissue determining glycemia. Cell Metab. 2021 Apr 6;33(4):758-780. doi: 10.1016/j.cmet.2021.03.020.
[33] Zhang Y, Pan XF, Chen J, et al. Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. Diabetologia. 2020 Jan;63(1):21-33. doi: 10.1007/s00125-019-04985-9.

[34] Ye Z, Li J, Gu P, et al. Early-life tobacco smoke exposure, genetic susceptibility and the risk of type 2 diabetes in adulthood: A large prospective cohort study. Sci Total Environ. 2023 Oct 1;893:164698. doi: 10.1016/j.scitotenv.2023.164698.
[35] GBD 2019 Diabetes and Air Pollution Collaborators. Estimates, trends, and drivers of the global burden of type 2 diabetes attributable to PM2·5 air pollution, 1990-2019: an analysis of data from the Global Burden of Disease Study 2019. Lancet Planet Health. 2022 Jul;6(7):e586-e600. doi: 10.1016/S2542-5196(22)00122-X.
[36] Weisman A, Fazli GS, Johns A, et al. Evolving Trends in the Epidemiology, Risk Factors, and Prevention of Type 2 Diabetes: A Review. Can J Cardiol. 2018 May;34(5):552-564. doi: 10.1016/j.cjca.2018.03.002.
[37] Misra S, Ke C, Srinivasan S, et al. Current insights and emerging trends in early-onset type 2 diabetes. Lancet Diabetes Endocrinol. 2023 Oct;11(10):768-782. doi: 10.1016/S2213-8587(23)00225-5.
[38] Flood D, Seiglie JA, Dunn M, et al. The state of diabetes treatment coverage in 55 low-income and middle-income countries: a cross-sectional study of nationally representative, individual-level data in 680 102 adults. Lancet Healthy Longev. 2021 Jun;2(6):e340-e351. doi: 10.1016/s2666-7568(21)00089-1.
[39] GBD 2019 Healthcare Access and Quality Collaborators. Assessing performance of the Healthcare Access and Quality Index, overall and by select age groups, for 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019. Lancet Glob Health. 2022 Dec;10(12):e1715-e1743. doi: 10.1016/S2214-109X(22)00429-6.
[40] Zhao S, Du R, He Y, et al. Elements of chronic disease management service system: an empirical study from large hospitals in China. Sci Rep. 2022 Apr 5;12(1):5693. doi: 10.1038/s41598-022-09784-8.
[41] Fahed AC, El-Hage-Sleiman AK, Farhat TI, et al. Diet, genetics, and disease: a focus on the middle East and north Africa region. J Nutr Metab. 2012;2012:109037. doi: 10.1155/2012/109037.
[42] Lopez-Jaramillo P, Lahera V, Lopez-Lopez J. Epidemic of cardiometabolic diseases: a Latin American point of view. Ther Adv Cardiovasc Dis. 2011 Apr;5(2):119-31. doi: 10.1177/1753944711403189.
[43] Lopez-Jaramillo P, Gomez-Arbelaez D, Sotomayor-Rubio A, et al. Maternal undernutrition and cardiometabolic disease: a Latin American perspective. BMC Med. 2015 Mar 2;13:41. doi: 10.1186/s12916-015-0293-8.
[44] Fralick M, Jenkins AJ, Khunti K, et al. Global accessibility of therapeutics for diabetes mellitus. Nat Rev Endocrinol. 2022 Apr;18(4):199-204. doi: 10.1038/s41574-021-00621-y.
[45] Sabbatinelli J, Giuliani A, Kwiatkowska KM, et al. DNA Methylation-derived

biological age and long-term mortality risk in subjects with type 2 diabetes. Cardiovasc Diabetol. 2024 Jul 13;23(1):250. doi: 10.1186/s12933-024-02351-7.

[46] Ying W, Fu W, Lee YS, et al. The role of macrophages in obesity-associated islet inflammation and β-cell abnormalities. Nat Rev Endocrinol. 2020 Feb;16(2):81-90. doi: 10.1038/s41574-019-0286-3.

[47] Lee YS, Olefsky J. Chronic tissue inflammation and metabolic disease. Genes Dev. 2021 Mar 1;35(5-6):307-328. doi: 10.1101/gad.346312.120.

[48] He F, Huang Y, Song Z, et al. Mitophagy-mediated adipose inflammation contributes to type 2 diabetes with hepatic insulin resistance. J Exp Med. 2021 Mar 1;218(3):e20201416. doi: 10.1084/jem.20201416.

[49] Antal B, McMahon LP, Sultan SF, et al. Type 2 diabetes mellitus accelerates brain aging and cognitive decline: Complementary findings from UK Biobank and meta-analyses. Elife. 2022 May 24;11:e73138. doi: 10.7554/eLife.73138.

[50] Athauda D, Evans J, Wernick A, et al. The Impact of Type 2 Diabetes in Parkinson's Disease. Mov Disord. 2022 Aug;37(8):1612-1623. doi: 10.1002/mds.29122.

[51] Lambrinoudaki I, Paschou SA, Armeni E, et al. The interplay between diabetes mellitus and menopause: clinical implications. Nat Rev Endocrinol. 2022 Oct;18(10):608-622. doi: 10.1038/s41574-022-00708-0.

[52] Bjornstad P, Chao LC, Cree-Green M, et al. Youth-onset type 2 diabetes mellitus: an urgent challenge. Nat Rev Nephrol. 2023 Mar;19(3):168-184. doi: 10.1038/s41581-022-00645-1.

[53] Nanayakkara N, Curtis AJ, Heritier S, et al. Impact of age at type 2 diabetes mellitus diagnosis on mortality and vascular complications: systematic review and meta-analyses. Diabetologia. 2021 Feb;64(2):275-287. doi: 10.1007/s00125-020-05319-w.

[54] Kotwas A, Karakiewicz B, Zabielska P, et al. Epidemiological factors for type 2 diabetes mellitus: evidence from the Global Burden of Disease. Arch Public Health. 2021 Jun 22;79(1):110. doi: 10.1186/s13690-021-00632-1.

[55] National Health Commission of the People's Republic of China. Health China Action - Implementation Plan of diabetes Prevention and Control Action (2024-2030). 2024.

[56] Magkos F, Hjorth MF, Astrup A. Diet and exercise in the prevention and treatment of type 2 diabetes mellitus. Nat Rev Endocrinol. 2020 Oct;16(10):545-555. doi: 10.1038/s41574-020-0381-5.

[57] GBD 2019 Diabetes Mortality Collaborators. Diabetes mortality and trends before 25 years of age: an analysis of the Global Burden of Disease Study 2019. Lancet Diabetes Endocrinol. 2022 Mar;10(3):177-192. doi: 10.1016/S2213-8587(21)00349-1.