• Investigation •

Vision loss and blindness due to type 2 diabetes mellitus among young adults: a global burden study from 1990 to 2021

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Abstract

● **AIM:** To assess the burden and temporal trends of blindness and vision loss attributable to type 2 diabetes mellitus (T2DM) in young adults aged 20–39y from 1990 to 2021.

● **METHODS:** Cross-sectional datasets were extracted from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. Prevalence and years lived with disability (YLDs) metrics were applied to quantify temporal changes in blindness and vision loss across 1990–2021. Data were stratified by global, regional, and socio-demographic index (SDI) tiers, and further split by age and sex for comprehensive subgroup analysis. Joinpoint regression was adopted to detect inflection points of trend shifts. A Bayesian age-period-cohort model was utilized to forecast disease burden projections for 2045.

● **RESULTS:** Globally, the prevalence of T2DM-related blindness and vision loss in young adults (20-39y) rose from 4.7 per 100 000 population in 1990 to 6.4 per 100 000 population in 2021 [average annual percentage change (AAPC)=1.03; *P*<0.001]. The YLD rate likewise increased from 0.5 per 100 000 in 1990 to 0.7 per 100 000 in 2021 (AAPC=1.02; *P*<0.001). Southeast Asia and Grenada bore the highest prevalence, whereas Central Latin America and Cambodia exhibited the highest YLD rates. Both prevalence and YLD rates increased markedly within the high-SDI quintile. Singapore was the only setting presenting declining prevalence and YLD trends. Females experienced steeper rises than males in prevalence (AAPC: 1.16 *vs* 0.88) and YLDs (AAPC: 1.16 *vs* 0.82).

● **CONCLUSION:** The global disease burden of early-onset T2DM-induced visual impairment has increased substantially among 20–39-year-old individuals, particularly in high-SDI regions, with females facing a greater rising prevalence burden. Targeted intervention measures are warranted to guide integrated population-level prevention and clinical management frameworks.

● **KEYWORDS:** vision loss; type 2 diabetes mellitus; global burden of disease; young adults
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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic disease that affects health and has reached alarming levels globally. More than 20y ago, the International Diabetes Federation (IDF) estimated that 151 million adults worldwide had diabetes. It will rise to over 783.2 million by 2045, with the global burden tripling over that period[1-2]. The incidence and prevalence of T2DM vary by geographic region, with more than 80% of patients living in low-to-middle-income countries. Since 1980, the overall trend in each country has been on the rise[3]. While the impact of diabetes is becoming more pronounced in older people, the rising prevalence of T2DM among younger

populations represents an emerging public health challenge requiring immediate attention.

Refractive errors, cataracts, age-related macular degeneration, glaucoma, and diabetic retinopathy (DR) can cause blindness. DR is the smallest cause of blindness in 2020, but it is the only contributor to blindness that has increased globally in age-standardized prevalence between 1990 and 2020. And it's particularly noticeable among people in the younger age group[4].

The long-term consequences of T2DM can lead to dysfunction and failure of various organs, particularly the eyes, kidneys, nerves, hearts, and blood vessels. Among these complications, DR stands out as a common microvascular disorder that is the leading cause of blindness and vision loss in working-age adults with T2DM[5]. Once diagnosed with DR, approximately 11% of T2DM patients will progress to the vision-threatening stage each year[6]. Moreover, the cost of diabetes care is at least 3.2 times greater than per capita healthcare expenditure, rising to 9.4 times in presence of complications, making DR a significant public health challenge[7].

There has been no comprehensive study specifically describing the global burden of disease and long-term trend of blindness and vision loss in young adults due to T2DM. In addition, the attributable risk factors for T2DM among young people in different countries remain unclear, which may hinder efforts to develop effective measures to deal with this issue at global, regional and national levels[8].

This study investigated T2DM associated prevalence, age-standardized rates (ASR) and years lived with disability (YLDs) of blindness and visual loss in young adults aged 20–39y at global, regional, and national level during 1990–2021 by social developmental level and sex.

PARTICIPANTS AND METHODS

Ethical Approval This study was conducted using secondary data obtained from the Global Burden of Disease (GBD) Study 2021, which is publicly available at https://ghdx.healthdata.org/gbd-results-tool. The GBD database provides aggregated health estimates at the population level and does not contain any personally identifiable information. As such, this research did not involve direct interaction with human participants nor the use of private or confidential data. Consequently, according to the policies of the Department of Ophthalmology, The Wenling Hospital, Wenzhou Medical University and the Department of Ophthalmology, Eye & ENT Hospital, Fudan University, and the International Committee of Medical Journal Editors (ICMJE), formal ethical review and approval were not required for this study.

Study Population and Data Collection for Trend Analysis We have successfully collected all pertinent cross-sectional data from the GBD 2021 database *via* the Global Health Data Exchange (GHDx) platform. This database encompasses the worldwide disease burden data for 371 diseases and injuries in 204 countries and territories and 811 subnational locations from the year 1990 to 2021[9]. The present study collected case number and ASR of blindness and vision loss caused by T2DM by sex, region, and country, from 1990 to 2021. And our study adopted the age range of 20–39y as the definition for young adults[10-11]. The prevalence estimates along with their 95% confidence intervals (CIs), as well as the YLDs estimates and their respective 95% uncertainty intervals (UIs), were identified and extracted from the data. The sociodemographic progress of a nation or territory was measured by socio-demographic index (SDI), representing a combination of the average income, educational level, and fertility rates. Subsequently, these 204 countries and regions were categorized into five distinct sociodemographic tiers, ranging from low to high, based on their SDI values, which including low, lower-middle, middle, upper-middle, and high[12].

Data Processing and Disease Model We examined the trends in prevalence and YLDs among young adults aged 20–39y of blindness and vision loss caused by T2DM using age-specific rates and their average annual percentage changes (AAPC). The AAPC was determined through linear regression, with the rates expressed on a logarithmic scale serving as the dependent variable and each year as the independent variable. A geometrically weighted average of the annual percentage change (APC) was used for the calculation in the regression analysis. In this study, the AAPC served as a key metric, allowing the use of a single figure to describe the average APCs over multiple years, to capture the observed underlying trend[13].

Statistical Analysis The Joinpoint Regression Program (version 5.2.0) was applied to identify years with significant changes by connecting line segments on a logarithmic scale[14]. When additional joinpoints were considered, the Monte Carlo permutation method was employed for testing[15]. The final model was selected using the Weighted Bayesian Information Criterion methods. A maximum number of four line segments (three join-points) were applied in the models[16].

To further understand global trends, we stratified the data by geographical regions and gender groups. We presented our findings with statistical tests, including effect size, CIs, UIs, and *P* values. All statistical analyses were conducted using RStudio (version 4.2.2) and the Joinpoint. Structured tables and descriptive charts were created to visually represent research features, utilizing Excel (Office 16, USA) and Adobe Illustrator (Version 2021, USA). A *P* value less than 0.05 was considered statistically significant.

The Bayesian age-period-cohort (BAPC) model, grounded in Bayesian statistical theory, was utilized to analyze and

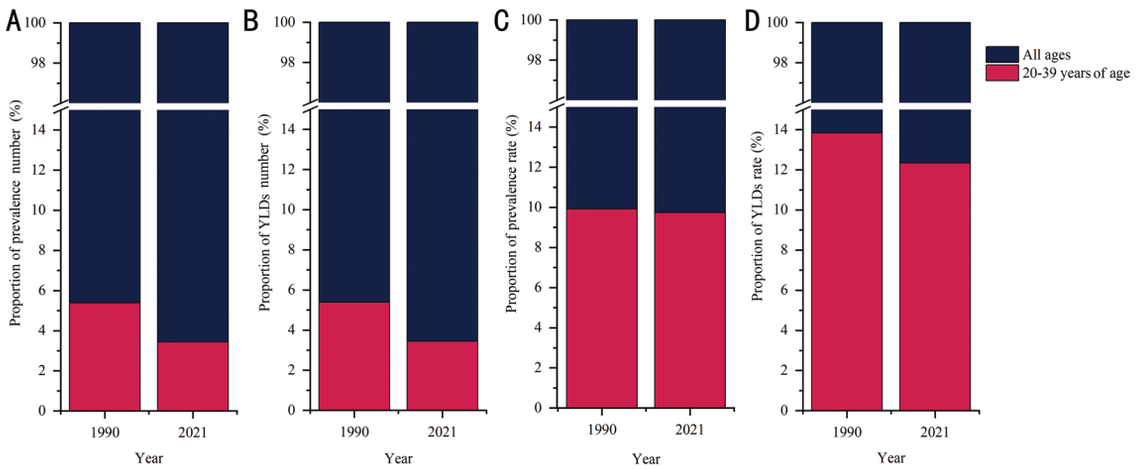

Figure 1 Trends between 1990 and 2021 A: The proportion of prevalence number in the 20–39y age group and all ages; B: The proportion of YLDs number in the 20–39y age group and all ages; C: The proportion of prevalence rate in the 20–39y age group and all ages; D: The proportion of YLDs rate in the 20–39y age group and all ages. YLDs: Years lived with disability.

elucidate the trends of individual attributes within a population. It took into account not only the effects of age and period but also incorporates birth cohort as a significant factor[17]. This comprehensive approach offered a more nuanced understanding and description of the impact of birth cohorts[18]. This model was used to predict the number and ASR of prevalence and YLDs by 2045.

RESULTS

Global Burden Trends Globally, the prevalence of blindness and vision loss caused by T2DM among young adults aged 20–39y increased approximately 210% between 1990 and 2021, from 73 thousand to 154 thousand. The ASR of prevalence (per 100 000 population) increased by 136% from 4.7 (95% UI 3.0 to 6.9) in 1990 to 6.4 per 100 000 population (95% UI 4.2 to 9.4) in 2021, with AAPCs of 1.03 (95%CI, 0.96 to 1.11, P<0.001; Table 1).

During the same period, the trend of YLDs also increased about 210% between 1990 and 2021, from 7.5 thousand to 15.8 thousand. The ASR of YLDs (per 100 000 population) increased 175% from 0.5 (95% UI 0.3 to 0.8) in 1990 to 0.7 (95% UI 0.4 to 1.1) in 2021, with AAPCs of 1.02 (95%CI, 0.83 to 1.21, P<0.001; Table 1). However, regardless of whether the count or the ASR, there has been a modest decline in the proportion of individuals aged 20–39y within the total population, as observed for both prevalence and YLDs (Figure 1).

Joinpoint regression analysis revealed substantial changes in the prevalence trends of blindness and vision loss caused by early-onset T2DM in 1995, 2000, and 2017. Notably, a significant increase was observed during two periods: from 1990 to 1995 (APC 1.46; 95%CI 1.24 to 1.69, P<0.001) and from 2000 to 2017 (APC 1.28; 95%CI 1.24 to 1.32, P<0.001). While, a slight increase was observed from 1995 to 2000 (APC 0.60; 95%CI 0.29 to 0.91, P=0.001; Figure 2A). A stable prevalence rate has been observed since 2017 (2017–2021 APC 0.0039, 95%CI 2.29 to 0.3, P=0.978), indicating no statistical significance in the change (Figure 2A).

A significant upward trend in the ASR of YLDs due to blindness and vision loss caused by T2DM was particularly evident among young adults aged 20–39y in the years 1995, 1999 and 2017. This increase spanned two distinct periods: from 1990 to 1995 (APC 1.72; 95%CI 1.18 to 2.25, P<0.001) and from 1999 to 2017 (APC 1.3; 95%CI 1.22 to 1.38; P<0.001). However, a minor decline was observed between 1995 and 1999 (APC -0.31; 95%CI -1.46 to 0.85, P=0.578). The period from 2017 to 2021 showed a slight increase in YLDs, although this was not statistically significant (Figure 2B).

The increase in prevalence and ASR of YLDs were more rapid among women than among men (prevalence: AAPC 1.16 *vs* 0.88; ASR of YLDs: AAPC 1.16 *vs* 0.82; Table 1). The joinpoint regression analysis revealed that both prevalence and YLDs showed a period of rapid growth for both women and men. For prevalence, the fastest period among women was observed from 1999 to 2017 with APC of 1.49 (P<0.001) and among men from 2010 to 2015 with APC of 1.48 (P<0.001; Figure 2C). In terms of YLDs, the longest period of growth for women was noted from 1999 to 2018 with an APC of 1.60 (P<0.001) and for men, the most rapid period is from 2011 to 2014 with an APC of 2.37 (P<0.001; Figure 2D).

Burden Trends by Region The prevalence (per 100 000 population) and YLDs (per 100 000 population) of blindness and vision loss attributed to early-onset T2DM from 1990 to 2021 based on the WHO region classification are presented in Table 1. The top three ASR of prevalence were observed in Southeast Asia (9.2, 95% UI 6.0 to 13.3), Southern Latin America (8.2, 95% UI 4.6 to 13.8) and Western Europe (7.4,

Table 1 The prevalence and YLDs for vision loss due to type 2 diabetes in 1990 and 2021 for different regions across the world

Parameters	Prevalence						YLDs					
	1990		2021		AAPC, 1990-2021	*P*	1990		2021		AAPC, 1990-2021	*P*
	Cases (95%CI)	Prevalence (per 100K)	Cases (95%CI)	Prevalence (per 100K)			Cases (95%CI)	YLDs (per 100K)	Cases (95%CI)	YLDs (per 100K)		
Global	72539.7 (45796.5, 107859.5)	4.7 (3.0, 6.9)	154487.3 (100859.4, 226412.2)	6.4 (4.2, 9.4)	1.03 (0.96, 1.11)	<0.001	7463.6 (4011.8, 11964.6)	0.5 (0.3, 0.8)	15803.5 (8496.9, 25462.5)	0.7 (0.4, 1.1)	1.02 (0.83, 1.21)	<0.001
Sex												
Male	33470.9 (21077.3, 49719.5)	4.2 (2.7, 6.3)	67787.3 (43497.9, 99935.8)	5.6 (3.6, 8.2)	0.88 (0.81, 0.96)	<0.001	3382.4 (1832.3, 5437.7)	0.4 (0.2, 0.7)	6699.2 (3637.4, 10724.8)	0.5 (0.3, 0.9)	0.82 (0.62, 1.01)	<0.001
Female	39068.9 (24800.2, 58061.1)	5.1 (3.2, 7.5)	86700.1 (56974.4, 126972.4)	7.3 (4.8, 10.6)	1.16 (1.05, 1.27)	<0.001	4081.2 (2183.1, 6609.3)	0.5 (0.3, 0.9)	9104.3 (4890.9, 14709.3)	0.8 (0.4, 1.2)	1.16 (0.95, 1.37)	<0.001
Sociodemographic index												
High	11287.5 (6418.1, 18318.8)	3.9 (2.2, 6.3)	21695.3 (13395.2, 33460.7)	6.7 (4.1, 10.4)	1.79 (1.74, 1.84)	<0.001	894.7 (464.9, 1471.4)	0.3 (0.2, 0.5)	1911 (1020.9, 3115.3)	0.6 (0.3, 1.0)	2.14 (2.04, 2.24)	<0.001
Middle-High	13909.8 (8888.6, 20666.1)	4 (2.6, 5.9)	22626.7 (14821.6, 33159.3)	5.3 (3.5, 7.9)	0.94 (0.8, 1.09)	<0.001	1525.1 (834.4, 2452)	0.4 (0.2, 0.7)	2420.9 (1320.2, 3890.4)	0.6 (0.3, 0.9)	0.84 (0.62, 1.06)	<0.001
Middle	30060.2 (19842.1, 43933.3)	6 (4.0, 8.7)	62122.5 (41773.8, 89854.5)	7.9 (5.3, 11.4)	0.9 (0.75, 1.04)	<0.001	3245 (1734.7, 5306.1)	0.6 (0.3, 1.0)	6584.2 (3592.1, 10765.6)	0.8 (0.5, 1.4)	0.91 (0.69, 1.13)	<0.001
Low-Middle	13191.7 (8197.5, 19683.9)	4.5 (2.8, 6.6)	34919.7 (22249.9, 51763.2)	5.9 (3.8, 8.8)	0.96 (0.85, 1.07)	<0.001	1377.1 (732.6, 2262)	0.5 (0.2, 0.8)	3601.5 (1925.8, 5868.7)	0.6 (0.3, 1.0)	0.85 (0.63, 1.06)	<0.001
Low	4031.8 (2385.1, 6164.9)	3.5 (2.1, 5.3)	12978.2 (7777.3, 20026.7)	4.6 (2.8, 7.0)	0.91 (0.88, 0.95)	<0.001	416 (222.3, 680.5)	0.4 (0.2, 0.6)	1269.9 (664.7, 2133.1)	0.4 (0.2, 0.7)	0.76 (0.63, 0.88)	<0.001
Region												
East Asia	12600.9 (8045.7, 18815)	3.1 (2.0, 4.7)	18500.6 (12273.9, 27136.9)	4 (2.6, 5.8)	0.72 (0.16, 1.29)	0.01	1541.9 (804.8, 2637.7)	0.4 (0.2, 0.7)	2351.9 (1236.6, 4010.3)	0.5 (0.3, 0.9)	0.76 (0.09, 1.44)	0.027
Southeast Asia	6907.9 (4266.7, 10501.9)	5.3 (3.3, 8)	20624.2 (13457.1, 30002.8)	9.2 (6.0, 13.3)	1.88 (1.62, 2.14)	<0.001	660.5 (349.3, 1134.9)	0.5 (0.3, 0.9)	2349.5 (1202.7, 4070.6)	1 (0.5, 1.8)	2.49 (2.03, 2.95)	<0.001
Oceania	52.7 (31.1, 83)	3.1 (1.9, 4.9)	226.5 (143.2, 332.3)	5.7 (3.6, 8.3)	1.91 (1.83, 1.99)	<0.001	6 (3.0, 10.4)	0.4 (0.2, 0.6)	29.3 (15.1, 49.3)	0.7 (0.4, 1.2)	2.35 (2.25, 2.45)	<0.001
Central Asia	501.6 (235.4, 894)	2.5 (1.2, 4.5)	1274 (645.1, 2187.8)	4 (2.0, 6.9)	1.43 (1.32, 1.55)	<0.001	38.5 (16.3, 76.9)	0.2 (0.1, 0.4)	93 (40.7, 173.6)	0.3 (0.1, 0.5)	1.3 (1.22, 1.38)	<0.001
Central Europe	765.2 (433, 1215.2)	1.9 (1.0, 3.0)	1072.6 (664.2, 1614.8)	3.1 (1.9, 4.7)	1.64 (1.46, 1.83)	<0.001	80.9 (40.0, 136.5)	0.2 (0.1, 0.3)	134.9 (67.9, 232)	0.4 (0.2, 0.7)	2.24 (1.94, 2.53)	<0.001
Eastern Europe	1273.8 (631.5, 2173.5)	1.7 (0.8, 2.9)	1323.5 (683, 2226)	1.9 (1.0, 3.2)	0.37 (0.34, 0.41)	<0.001	112.7 (49.1, 212)	0.1 (0.1, 0.3)	108.7 (48.2, 201.6)	0.2 (0.1, 0.3)	0.18 (0.05, 0.32)	<0.001
High-income Asia Pacific	2474.4 (1383.7, 3960.3)	4.6 (2.6, 7.4)	2303.4 (1269.2, 3793)	4.9 (2.7, 8.2)	0.19 (0.09, 0.29)	<0.001	198.6 (102.3, 335.3)	0.4 (0.2, 0.6)	169.3 (84.4, 289.5)	0.4 (0.2, 0.6)	-0.06 (-0.19, 0.06)	0.331
Australasia	133.7 (60.5, 240.2)	2.9 (1.3, 5.3)	267.8 (123.9, 493.6)	2.9 (1.3, 5.3)	1.07 (0.88, 1.26)	<0.001	7.1 (3, 14)	0.1 (0, 0.2)	13.8 (5.6, 27.6)	0.1 (0.1, 0.3)	0.97 (0.82, 1.12)	<0.001
Western Europe	5884.8 (3403.2, 9557.2)	5.1 (2.9, 8.2)	8592.4 (5288.5, 13283.2)	7.4 (4.5, 11.5)	1.28 (1.12, 1.44)	<0.001	528.6 (270.4, 897.1)	0.5 (0.2, 0.8)	785.7 (431, 1248.1)	0.7 (0.4, 1.1)	1.381.07, 1.69)	<0.001
Southern Latin America	786.4 (416.2, 1317.5)	5.6 (2.9, 9.3)	1742.1 (967.8, 2907.7)	8.2 (4.6, 13.8)	1.37 (1.2, 1.53)	<0.001	47 (22.9, 83.7)	0.3 (0.2, 0.6)	105.2 (50.8, 177.1)	0.5 (0.2, 0.8)	1.36 (1, 1.72)	<0.001
High-income North America	3983.9 (2088.4, 6616.5)	4.1 (2.1, 6.8)	7421.9 (4410.2, 11581.8)	7.1 (4.2, 11.1)	1.87 (1.55, 2.19)	<0.001	285.6 (139.4, 480.1)	0.3 (0.1, 0.5)	601.5 (325.9, 968.5)	0.6 (0.3, 0.9)	2.37 (2.14, 2.59)	<0.001
Caribbean	693.1 (424, 1061.3)	7.1 (4.4, 10.8)	1625.7 (1062.4, 2416.5)	11.3 (7.4, 16.8)	1.51 (1.43, 1.59)	<0.001	67.6 (33.9, 116.3)	0.7 (0.3, 1.2)	180.3 (82.1, 326.6)	1.3 (0.6, 2.3)	1.9 (1.65, 2.15)	<0.001
Andean Latin America	294.1 (140.3, 524.6)	3 (1.4, 5.3)	827.3 (398.8, 1435.3)	4 (1.9, 6.9)	1.01 (0.88, 1.14)	<0.001	18.2 (8.3, 35.3)	0.2 (0.1, 0.4)	50.5 (21.9, 95.2)	0.2 (0.1, 0.5)	0.9 (0.83, 0.98)	<0.001
Central Latin America	6759.4 (4485.6, 9826.9)	15.6 (10.4, 22.5)	14260.6 (9547.4, 20749.4)	18.2 (12.2, 26.4)	0.57 (0.46, 0.69)	<0.001	680.9 (372.8, 1118.8)	1.6 (0.9, 2.6)	1394.4 (781.7, 2265.8)	1.8 (1, 2.9)	0.53 (0.36, 0.7)	<0.001
Tropical Latin America	6951.1 (4710.7, 10067.5)	15.8 (10.7, 22.7)	12183.8 (8244.7, 17433)	16 (10.8, 22.9)	0.04 (-0.14, 0.21)	0.67	728.9 (370.1, 1216.8)	1.6 (0.8, 2.7)	1186 (619.6, 1978.6)	1.6 (0.8, 2.6)	-0.16 (-0.37, 0.06)	0.149
North Africa and Middle East	6466.9 (3545.1, 10689.1)	7.6 (4.2, 12.5)	24863.1 (14532.8, 39147.4)	11.7 (6.8, 18.5)	1.4 (1.36, 1.44)	<0.001	590.1 (267.9, 1047.6)	0.7 (0.3, 1.2)	2237.4 (1102.4, 3892.9)	1.1 (0.5, 1.8)	1.36 (1.31, 1.41)	<0.001
South Asia	12894.3 (8128.4, 18841.3)	4.5 (2.8, 6.5)	26281.1 (16335.8, 39031.5)	4.4 (2.8, 6.6)	0.04 (-0.1, 0.17)	0.58	1565.1 (831.3, 2555.9)	0.5 (0.3, 0.9)	2959.7 (1536.5, 4939.7)	0.5 (0.3, 0.9)	-0.19 (-0.37, 0.02)	0.033
Central Sub-Saharan Africa	136.4 (64.7, 247.5)	1.1 (0.5, 1.9)	515.2 (251, 911.8)	1.5 (0.7, 2.6)	1.17 (1.01, 1.32)	<0.001	8.9 (4.1, 16.8)	0.1 (0, 0.1)	34 (15.5, 62.8)	0.1 (0, 0.2)	1.21 (0.92, 1.49)	<0.001
Eastern Sub-Saharan Africa	1517.1 (910.1, 2304)	3.6 (2.2, 5.4)	5072 (3062.4, 7699.7)	4.7 (2.8, 7.1)	0.91 (0.82, 1)	<0.001	158.7 (85.6, 259.9)	0.4 (0.2, 0.6)	510.8 (275.8, 835.4)	0.5 (0.3, 0.8)	0.78 (0.7, 0.86)	<0.001
Southern Sub-Saharan Africa	673.6 (425.9, 1002.9)	4.9 (3.1, 7.3)	1934 (1274.8, 2827.5)	7.1 (4.7, 10.3)	1.18 (1.06, 1.3)	<0.001	72.6 (38.9, 120)	0.5 (0.3, 0.9)	208.7 (108.1, 353.8)	0.8 (0.4, 1.3)	1.2 (1.04, 1.36)	<0.001
Western Sub-Saharan Africa	788.3 (399.8, 1352.8)	1.8 (0.9, 3)	3575.5 (1863.8, 6073)	3 (1.6, 5.1)	1.76 (1.71, 1.82)	<0.001	65.1 (30.4, 116.8)	0.1 (0.1, 0.3)	298.7 (140.3, 548.2)	0.2 (0.1, 0.5)	1.8 (1.74, 1.86)	<0.001

YLDs: Years lived with disability; AAPC: Average annual percentage changes; CI: Confidence interval.

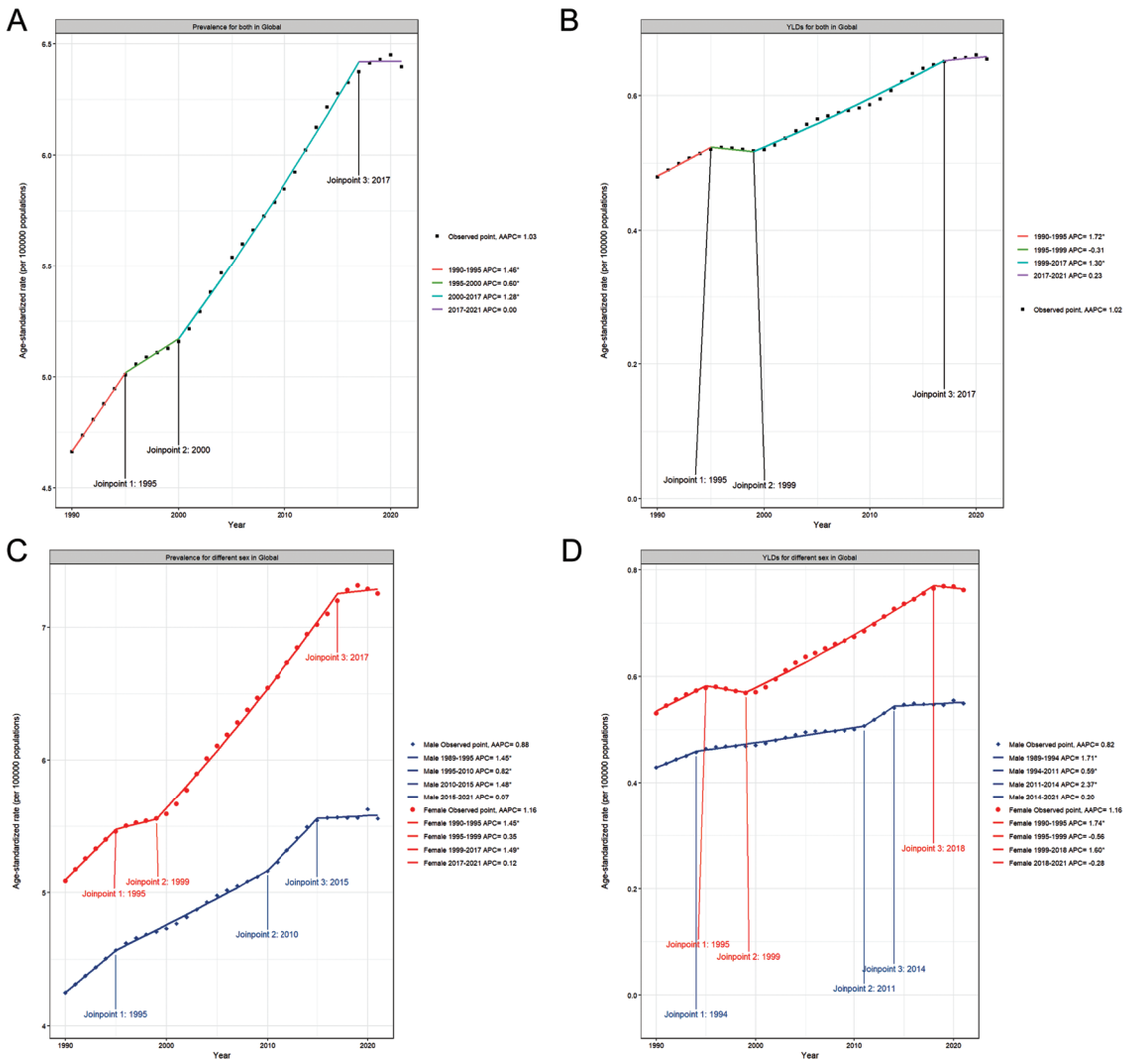

Figure 2 Trends from 1990 to 2021 A: Global changes of ASR of prevalence; B: Global changes of ASR of YLDs rate; C: Global changes of ASR of prevalence by sex; D: Global changes of ASR of YLDs rate by sex. ASR: Age-standardized rates; YLDs: Years lived with disability.

95% UI 4.5 to 11.5) per 100 000 population in 2021. Most of regions depicts the steepest increase in the ASR of prevalence, except East Asia, South Asia, and Tropical Latin America. However, ASR of East Asia showed a modest increase, rising from 3.1 per 100 000 population (95% UI 2 to 4.7) in 1990 to 4 (95% UI 2.6 to 5.8) in 2021, with an AAPC of 0.72 (95%CI 0.16 to 1.29, *P*=0.012; Table 1).

In 2021, the top three ASR of YLDs were observed in Central Latin America (1.8, 95% UI 1.0 to 2.9), Tropical Latin America (1.6, 95% UI 0.8 to 2.6) and Caribbean (1.3, 95% UI 0.6 to 2.3) per 100 000 population. Most regions reported a significant increase in the ASR of YLDs, however, a minor increase was observed in East Asia (AAPC 0.76; 95%CI 0.09 to 1.44, *P*=0.027), South Asia (AAPC -0.19; 95%CI -0.37 to 0.02, *P*=0.033), and Eastern Europe (AAPC 0.18; 95%CI 0.05 to 0.32, *P*=0.007). Nonetheless, YLDs did not demonstrate an increase in the High-income Asia Pacific region (AAPC -0.06; 95%CI -0.19 to 0.06, *P*=0.331) and Tropical Latin America (AAPC -0.16; 95%CI -0.37 to 0.06, *P*=0.149; Table 1).

Burden Trends by Country When analyzed at the individual country level, the ASR of prevalence has shown significant increase in most countries. The highest ASR of prevalence was noted in Syrian Arab Republic (9.6 per 100 000, 95% UI 5.1–15.9) in 1990, while in 2021 Grenada reported the highest ASR of prevalence (9.7 per 100 000, 95% UI 6–14.5). Furthermore, Greenland (AAPC 6.69, 95%CI 6.35–7.02), Cambodia (AAPC 5.14, 95%CI 4.77–5.51), Canada (AAPC 4.96, 95% CI 3.88–6.05), Seychelles (AAPC 4.83, 95%CI 4.59–5.07), and Federated States of Micronesia (AAPC 4.83, 95%CI 4.47–5.2) were identified as the top five countries with the most significant increasing trends in blindness and vision loss caused by early-onset T2DM over the past three decades. In contrast, a downward trend in the ASR of prevalence was observed in Singapore (AAPC -1.21, 95%CI -1.5–0.92), Cyprus (AAPC -0.67, 95%CI -0.8–0.53), Brunei Darussalam (AAPC -0.47, 95%CI -0.85–0.08), Ethiopia (AAPC -0.44, 95%CI -0.6–0.27), and India (AAPC -0.31, 95%CI -0.5–0.12; Table 1).

The Marshall Islands exhibited the highest ASR of YLDs at 4.1 per 100 000 population, followed by Cambodia with an ASR of 3.1 per 100 000 population, and Brunei Darussalam with an ASR of 3.1 per 100 000 population. The highest increase in the ASR of YLDs was shown in Cambodia with AAPC of 7.19, while the most significant decrease in the ASR of YLDs was observed in Singapore, with an AAPC of -1.98.

Burden Trends by SDI Since 1990, the ASR of prevalence and YLDs for blindness and vision loss caused by early-onset T2DM had exhibited significant increase across all SDI quintiles. The most substantial increase in prevalence was observed in the high-SDI quintile, rising from 3.9 per 100 000 in 1990 to 6.7 per 100 000 in 2021, with an AAPC of 1.79. Similarly, the most substantial increase in YLDs was also observed in the high-SDI quintile, increasing from 0.3 per 100 000 in 1990 to 0.6 per 100 000 in 2021, with an AAPC of 2.14 (Table 1).

In the high-SDI quintile, joinpoint regression analysis of prevalence data revealed significant increases in two distinct periods: from 1995 to 2005 (APC 2.16; 95%CI 2.08 to 2.23, P<0.001) and from 2005 to 2015 (APC 3.20; 95%CI 3.12 to 3.27, P<0.001). A modest increase was observed from 2015 to 2021 (APC 0.76; 95%CI 0.64 to 0.89; P<0.001), contrasting with a slight decrease from 1990 to 1995 (APC -0.49; 95%CI -0.67 to -0.3, P<0.001; Figure 3A). YLDs in the high-SDI quintile followed a similar trend, as observed through joinpoint regression analysis (Figure 3B).

Additionally, in the high-middle-SDI quintile, the prevalence exhibited a decline from 2014 to 2021 (APC -1.02; 95%CI -1.26 to -0.78, P<0.001), following three earlier phases of increase (Figure 3A). Concurrently, YLDs showed similar trend (Figure 3B).

Projections of the Prevalence Rates and YLDs of Vision Loss Projection analysis indicated a modest upward trend in both the prevalence and ASR of vision loss from 2021 to 2045 (Figure 4A). Gender-specific analysis revealed a contrasting pattern, with female patients demonstrating a slight decline in ASR during the same period, although their ASR values consistently exceeded those of male patients. Similarly, the number and ASR of YLDs showed a marginal increase from 2021 to 2045, following a transient decline phase (Figure 4B). Notably, the ASR of YLDs in female patients exhibited a decreasing trend throughout the projection period.

DISCUSSION

In this study, we conducted a comprehensive analysis of the global trends in the prevalence rates and YLDs of vision loss caused by T2DM among young adults aged 20 to 39y, spanning from 1990 to 2021. Our analysis encompassed regional, national, sex-based, and SDI quintile variations. These data had significantly advanced our understanding of vision impairment due to T2DM within the 20–39 age cohort, revealing not only a substantial increase in disease burden in high SDI countries but also a higher ASR of prevalence and YLDs among females compared to males. These findings could inform future intervention strategies targeted at this demographic group.

Globally, in 2021, blindness and vision loss caused by T2DM among young adults aged 20-39y accounted for 154.5 thousand cases and 15.8 thousand YLDs. Both prevalence and YLDs rates demonstrated an increase, with AAPCs of 1.03 and 1.02, respectively. T2DM is associated with a spectrum of ocular complications, including corneal ulceration due to neuropathy, elevated incidence of cataracts, and diabetic retinopathy, which is a leading cause of vision loss worldwide[19-20]. It also heightens the risk of retinal occlusions, optic neuropathies, and glaucoma[21]. Approximately 80% of global visual impairments are potentially avoidable, manageable, or curable through appropriate ocular health interventions[22]. Since 2017, we had observed a noticeable deceleration in the growth trend of incidence and YLDs at this age group, indicating that global policies are having a positive effect. Increased public interest in diabetes mellitus (DM) in Asia has spurred national policies for primary prevention and high-risk screening in countries such as Singapore, India, and China, potentially leading to earlier diagnosis and a reduction in related complications[23]. However, when compared to vision impairment caused by T2DM across all age groups, there had been a slight decrease in the proportion for the 20-39 age group from 1990 to 2021, indicating that the overall burden remains heavier for the broader age spectrum. Although some studies had shown that the effect of age on the prevalence of vision impairment was not statistically significant[23].

We observed that vision impairment caused by T2DM was more pronounced in women compared to men, which was consistent with previous study[24-27]. Many studies had indicated that women are at a higher risk of developing DR than men. Throughout their lifespan, women undergo more significant hormone fluctuations and physiological changes due to reproductive factors[28], which could contribute to a higher susceptibility to DR. DR was a predominant cause of vision impairment in women during their reproductive years[29]. It was estimated that 5% to 10% of women with gestational DM will continue to have diabetes post-pregnancy, and pregnancy itself had been identified as an independent risk factor for the exacerbation of DR[29]. This could accelerate the progression of retinopathy in women. In addition, psychosocial factors had a greater impact on diabetes risk in women than in men[28]. Meanwhile, women had limited access to medical resources for

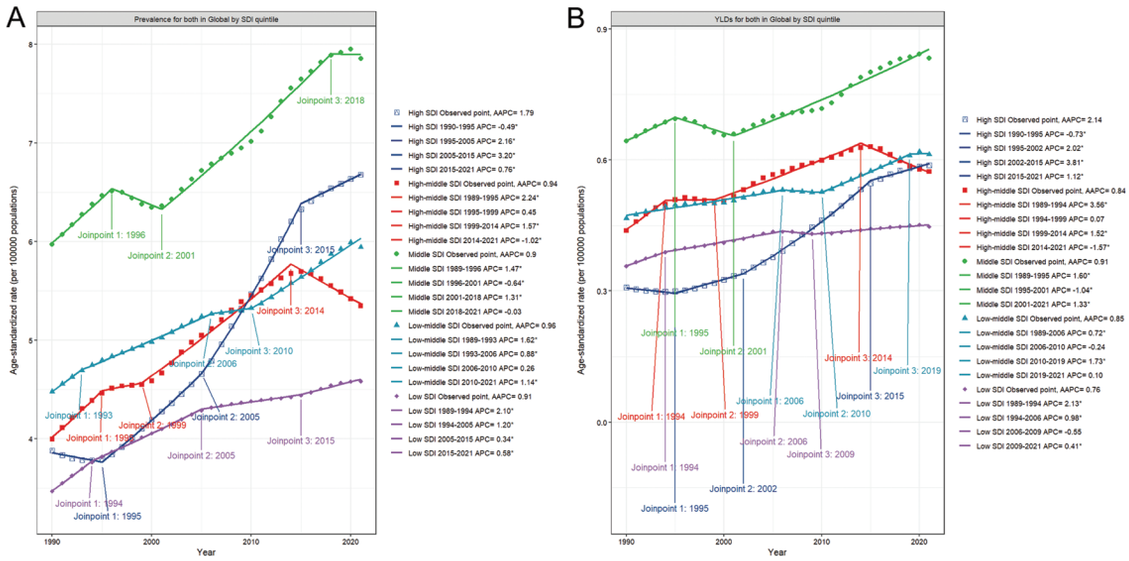

Figure 3 Trends from 1990–2021 A: Changes of ASR of prevalence by SDI; B: Changes of ASR of YLDs rates by SDI. ASR: Age-standardized rates; YLDs: Years lived with disability; SDI: Socio-demographic index.

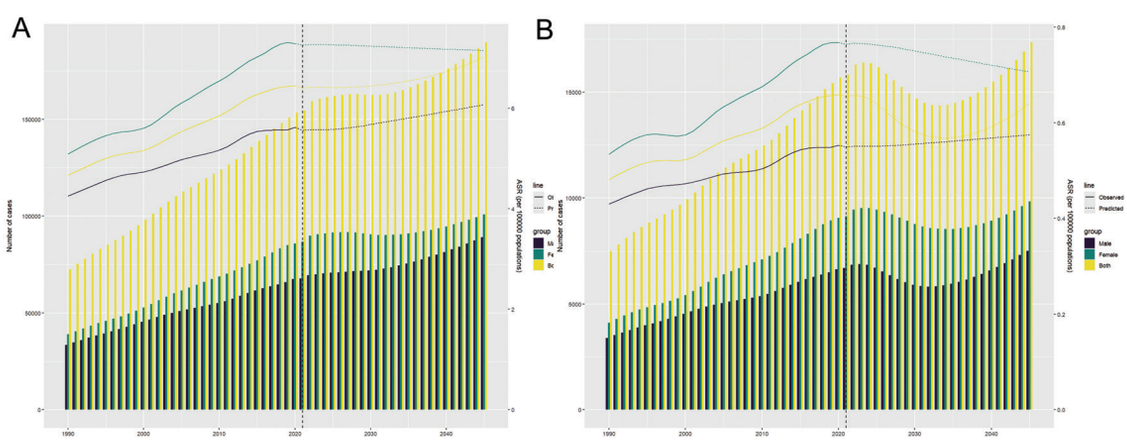

Figure 4 Prediction of vision loss and blindness by 2045 A: The number and ASR of prevalence by sex; B: The number and ASR of YLDs by sex. ASR: Age-standardized rates; YLDs: Years lived with disability.

eye care in some countries, which may exacerbate disparities in the management and outcomes of vision impairment related to T2DM.

Socioeconomic disparities and levels of care for persons with diabetes significantly influenced the global distribution of DR burden. Our findings demonstrated a disproportionately higher burden of DR-related vision loss in high SDI regions, particularly evident in the transition from high-middle to high SDI regions. This distribution pattern aligned with established evidence indicating a greater proportion of DR-attributable blindness in high-income versus low-income regions[30]. The observed disparities may be attributed to multiple factors: in low SDI regions, the predominance of uncorrected refractive, glaucoma and cataract-related blindness reduces the relative proportion of DR-related vision loss[30]. Furthermore, limited healthcare infrastructure in these regions resulted in reduced life expectancy among diabetes patients[24], thereby decreasing the likelihood of developing DR complications, given that diabetes duration was a critical risk factor for DR progression. On the contrary, high SDI regions with aging populations exhibited elevated DR burden, reflecting longer disease duration and improved survival rates. Understanding the epidemiology changes of DM is helpful to interpret socioeconomic distribution of DR burden. The epidemiological transition of diabetes mellitus, particularly in low- and middle-income countries, was further exacerbated by rapid urbanization and the adoption of Western dietary patterns and lifestyles[31]. Notably, our analysis revealed a significant decline in both prevalence and YLDs in high-middle SDI regions, potentially attributable to improved dietary practices characterized by increased fruit and vegetable consumption and reduced intake of processed foods[24].

Geospatial analysis revealed distinct regional patterns in the burden of young-onset T2DM and its complications. In 2021, the highest ASRs of prevalence were concentrated in Southeast Asia, Southern Latin America, and Western

Europe, with Grenada exhibiting particularly elevated rates. Longitudinal assessment identified Greenland, Cambodia, Canada, Seychelles, and Micronesia as the top five countries demonstrating the most significant increase in blindness and vision impairment caused by young-onset T2DM over the past three decades. The Marshall Islands recorded the highest ASR of YLDs, followed by Cambodia and Brunei Darussalam, while Cambodia and Singapore represented the extremes of ASR YLDs trends, showing the largest increase and decrease, respectively.

Southeast Asia's substantial disease burden reflected its demographic significance, encompassing 8% of the global population across 11 nations, including one of the world's most diabetes-prevalent countries (Indonesia). Southeast Asia faced substantial healthcare resource constraints, particularly in specialized ophthalmic care[1,32-33]. For instance, Cambodian ophthalmologist-to-population ratio significantly undershoot WHO recommendations, with fewer than one ophthalmologist and ophthalmic nurse serving 200 000 individuals[34]. Similarly, Latin America countries contend with elevated risk factors for diabetic retinopathy, including prevalent hypertension, cardiovascular disease, obesity and consumption of sugar- and fat-rich diets[35-37].

In contrast, Singapore exemplified effective public health intervention through its comprehensive diabetes prevention and management strategy. This multifaceted approach incorporates population-level initiatives (*e.g.*, the National Step Challenge promoting daily physical activity), regulatory measures (*e.g.*, incentivizing beverage manufacturers to reduce sugar content), and systematic screening programs for early diabetes detection[14]. The implementation of risk assessment tools and long-term management protocols had further enhanced diabetes care quality, contributing to improved population health outcomes and increased participation in physical activities[38].

This study provides critical insights for health policy formulation and clinical practice. The findings underscore the necessity for enhanced health resource allocation to address the escalating burden of T2DM, particularly in high SDI regions. From a clinical perspective, the results emphasize the importance of incorporating comprehensive blood glucose management and self-care skill development into clinical guidelines for young T2DM patients. Additionally, the study highlights the need for specialized training programs for healthcare professionals and caregivers to optimize diabetes management. The identified knowledge gaps call for innovative research initiatives focusing on novel therapeutic approaches and care strategies for T2DM and its complications.

This study has several limitations. First, the reliance on extrapolated data from countries with established epidemiological surveillance systems may introduce estimation biases, particularly in regions with limited or absent diabetes-related data. Second, some individuals might suffer from multiple diseases simultaneously, which makes it difficult to determine the main cause of vision loss. Third, the potential overestimation of DR prevalence due to the inclusion of self-reported diabetes cases without biochemical verification may affect data accuracy. Moreover, the heterogeneity in DR diagnostic methodologies across studies may influence the comparability of findings. Therefore, further large-scale global epidemiological studies are urgently needed in the future.

In conclusion, global epidemiological trends indicate a significant increase in both prevalence and YLDs related to early-onset T2DM in adults aged 20–39y, with particularly pronounced growth observed in high SDI regions. Gender-specific analysis reveals a consistently higher disease burden among women. However, the implementation of targeted public health interventions has yielded promising outcomes, with several nations demonstrating measurable reductions in both prevalence and YLDs. These findings provide robust evidence to inform the development of comprehensive strategies for early-onset T2DM management, with particular emphasis on preventing vision-related complications and mitigating the progressive health decline associated with this condition.

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