Postprint: Disease Burden Analysis and Future Trend Prediction of Type 1 Diabetes Mellitus in the Elderly in China and Worldwide, 1990-2021

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Abstract

Background Type 1 diabetes mellitus (T1DM) predominantly affects adolescents and young adults, which has led research to focus primarily on this population. Consequently, attention and research on T1DM in the elderly are relatively insufficient, resulting in a data gap regarding the disease burden in this group that urgently needs to be filled. Objective To analyze the disease burden and future trends of type 1 diabetes in the elderly from 1990 to 2021, providing a reference for public health decision-making. Methods Extracted and compiled data on the incidence and disability-adjusted life years (DALYs) burden of type 1 diabetes mellitus (T1DM) in the elderly (age $ $60 years) from 1990 to 2021 in the Global Burden of Disease (GBD) 2021 database, covering global, China, and five Socio-demographic Index (SDI) regions. Using the GBD2021 standard population as reference, the direct standardization method was employed to calculate age-standardized incidence rates and age-standardized DALYs rates for the elderly T1DM population. Joinpoint regression was used to analyze trends in disease burden changes, with results expressed as average annual percent change (AAPC). Subgroup analyses of disease burden were conducted based on patient age and sex, and a three-factor decomposition method was applied to analyze the relative impacts of three factors—population aging, population growth, and epidemiological changes—on disease burden changes. Bayesian models were used to forecast disease burden trends for elderly T1DM from 2022 to 2040. Results In 2021, the total number of new cases of elderly T1DM globally and in China was 42,330 and 3,049, respectively, representing increases of 199.47% and 427.50% compared with 1990. The total DALYs for elderly T1DM in 2021 were 659,117 person-years globally and 57,663 person-years in China, representing increases of 91.80% and 78.25% compared with 1990. The age-standardized DALYs rates for elderly T1DM patients globally and in China showed an overall decreasing trend from 1990 to 2021, with statistically significant differences (P<0.001). The 60-

64 years age group accounted for the highest proportion of incident cases among elderly T1DM patients globally, in China, and across the five SDI regions. The proportion of incident cases in the 60-64 years age group in China (27.91%) fell between that of the high-middle SDI region (26.01%) and the middle SDI region (30.26%); however, the proportion of DALYs for Chinese T1DM patients aged 60-64 years (24.06%) was lower than that in all other regions. Furthermore, incident cases among Chinese patients aged 60-69 years accounted for 53.51% of all elderly patients, and DALYs accounted for 55.25% of the total elderly patients. The primary factor contributing to the increase in incident cases of elderly T1DM in China was population growth, with a contribution of 58.34%. Population growth was also the decisive factor in the increase in DALYs among elderly T1DM patients in China, with a contribution as high as 178.96%. It is projected that from 2022 to 2040, the overall number of incident cases and DALYs for elderly T1DM patients globally and in China, as well as for males and females, will show an upward trend, and the trend of DALYs change for Chinese female T1DM patients will be more gradual than that for males. Conclusion The burden of incidence and DALYs of elderly T1DM globally and in China remains heavy, and there is an urgent need to further develop and implement more scientific and effective public health policies and clinical intervention strategies to actively address this serious health challenge.

Full Text

Analysis and Future Trend Prediction of Disease Burden of Elderly Type 1 Diabetes Mellitus in China and Globally from 1990 to 2021

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Abstract

Background Type 1 diabetes mellitus (T1DM) predominantly affects adolescents, which has concentrated research attention on this population. Consequently, older adults with T1DM have received relatively limited attention, resulting in a significant data gap regarding disease burden for this group that urgently needs to be filled.

Objective To analyze the disease burden and future trends of elderly T1DM from 1990 to 2021, providing evidence for public health decision-making.

Methods Data on incidence and disability-adjusted life years (DALYs) for elderly T1DM (age $\geq$ 60 years) were extracted from the Global Burden of Disease (GBD) 2021 database for the period 1990–2021, covering global, China, and five sociodemographic index (SDI) regions. Using the GBD 2021 standard population as reference, age-standardized incidence and DALY rates were calculated via direct standardization. Temporal trends were analyzed using Joinpoint regression, with results expressed as average annual percent change (AAPC). Subgroup analyses were conducted by age and sex, and a three-factor decomposition method was applied to quantify the relative contributions of population aging, population growth, and epidemiological changes to the burden shifts. Bayesian age-period-cohort modeling was employed to project disease burden trends from 2022 to 2040.

Results In 2021, the total incidence of elderly T1DM reached 42,330 cases globally and 3,049 cases in China, representing increases of 199.47% and 427.50% since 1990, respectively. Total DALYs amounted to 659,117 person-years globally and 57,663 person-years in China, marking increases of 91.80% and 78.25% over the same period. Age-standardized DALY rates declined significantly from 1990 to 2021 both globally and in China (P<0.001). The 60–64 age group accounted for the highest proportion of incident cases across all regions. In China, the 60–64 age group incidence proportion (27.91%) fell between the high-middle SDI region (26.01%) and middle SDI region (30.26%), yet its DALY proportion (24.06%) was lower than all other regions. Notably, Chinese patients aged 60–69 years comprised 53.51% of all elderly T1DM cases and 55.25% of total DALYs. Population growth was the primary driver of increased incidence in China, contributing 58.34%, and was the decisive factor for DALY increases, contributing 178.96%. Projections indicate that both incidence and DALYs for elderly T1DM will continue rising globally and in China from 2022 to 2040, with Chinese women showing a more gradual DALY trend than men.

Conclusion The incidence and DALY burden of elderly T1DM remain substantial globally and in China. Urgent formulation and implementation of sci-

entifically informed public health policies and clinical intervention strategies are needed to address this serious health challenge.

Keywords: Type 1 diabetes mellitus; The aged; Disease burden; Epidemiological study; Predictive analysis

Introduction

Type 1 diabetes mellitus (T1DM) is a chronic disease characterized by autoimmune destruction of pancreatic β-cells, resulting in lifelong insulin deficiency [1]. The disease progression involves a continuum from autoantibody formation to β-cell destruction, abnormal glucose metabolism, and ultimately hyperglycemia-related symptoms and complications [2]. T1DM is associated with numerous acute and chronic conditions, including diabetic ketoacidosis, drug-induced hypoglycemia, diabetic nephropathy, retinopathy, foot disease, neuropathy, coronary heart disease, autoimmune disorders, endocrine-metabolic diseases, and neurological damage [1]. Among autoimmune comorbidities, autoimmune thyroid disease is most common [3], followed by celiac disease [4] and pernicious anemia [5]. Research also indicates associations between T1DM and neurological conditions such as ADHD, tic disorders [6], epilepsy [7], and Alzheimer' s disease [8]. Both complications and early mortality rates are elevated, with patients' life expectancy reduced by approximately 10 years [1,7]. Lifelong continuous intervention is required to maintain glycemic stability and prevent complications [1], with lifetime treatment costs estimated to be $813 billion higher for T1DM patients compared to non-diabetic individuals [9].

China ranks fourth globally in T1DM incidence, following the United States, India, and Brazil. While the disease predominantly affects adolescents, approximately 19% of patients are elderly individuals over 60 years old [10]. The disease burden in elderly T1DM patients is influenced by multiple factors, with decreased immunity, increased care difficulty, and reduced income contributing to more severe outcomes [11].

The Global Burden of Disease (GBD) study is a comprehensive epidemiological research initiative involving multiple countries and regions worldwide, led by the Institute for Health Metrics and Evaluation at the University of Washington. The latest GBD database update in 2024 provides data through 2021 [12-13]. GBD data encompass health impact indicators for various diseases, injuries, and risk factors, and have been widely used to assess disease burden and inform health policy [14]. Previous research has demonstrated varying disease burdens across different sociodemographic index (SDI) regions [15]. SDI is a composite indicator of socioeconomic development recommended by the GBD collaborative group, classifying 204 countries/territories into five categories: low (<0.466), low-middle (0.466–0.619), middle (0.620–0.712), high-middle (0.713–0.810), and high (>0.810). China' s 2021 SDI was 0.722, placing it in the high-middle SDI region [12,16].

Because T1DM research has historically focused on adolescents, elderly T1DM remains understudied, creating a critical data gap [17]. This study aims to systematically analyze the disease burden of elderly T1DM from 1990 to 2021 using GBD 2021 data and project future incidence and DALY trends to support health resource allocation decisions.

Methods

1.1 Data Sources This study utilized data from the GBD 2021 database, released in May 2024, available at https://vizhub.healthdata.org/gbd-results/. We extracted incidence and DALY burden data for T1DM among individuals aged 60 years and older (defined as "elderly") in China, globally, and across five SDI regions from 1990 to 2021. The data extraction procedure [14] involved sequentially selecting: "Cause of death or injury"under GBD Estimate; "Incidence" and "DALYs (Disability-Adjusted Life Years)" under Measure; "Number" and "Rate" under Metric; "Diabetes mellitus type 1" under Cause; "Global," "China," and the five SDI regions under Location; age groups from "60-64 years" to "95+years" in 5-year intervals under Age; "Female," "Male," and "Both" under Sex; and all years from 1990 to 2021 under Year, followed by downloading the dataset.

1.2 Statistical Analysis Statistical analyses and visualizations were performed using R 4.4.0 and Excel 2021. First, using the GBD 2021 standard population [18] as reference, we calculated age-standardized incidence and DALY rates with 95% confidence intervals (CI) via direct standardization. Second, Joinpoint regression analysis was conducted with a maximum of five joinpoints to compute annual percent change (APC) and average annual percent change (AAPC) with 95% CI for age-standardized rates, assessing temporal trends [15]. APC reflects trend changes within specific time segments, while AAPC represents overall trend across the entire study period. A decreasing trend was defined when the 95% CI upper limit was below zero, an increasing trend when the lower limit exceeded zero, and a stable trend when the 95% CI included zero. Subgroup analyses were performed by sex (male and female) and eight age groups (60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, and 95 years).

Additionally, Gupta' s three-factor decomposition method [19] was applied to quantify the relative contributions of population aging, population growth, and epidemiological changes to burden shifts, with contributions summing to 100% within each region. Finally, a Bayesian age-period-cohort model [20-21] was used to forecast incidence and DALY counts for elderly T1DM from 2022 to 2040. This model is widely used for epidemiological burden projections. All statistical tests were two-sided, with statistical significance defined as 95% CI excluding zero or $P<0.05$.

Results

2.1 Trends in Incidence Burden of Elderly T1DM in China and Globally In 2021, global elderly T1DM incidence totaled 42,330 cases (24,929 females and 17,401 males), representing increases of 199.47%, 183.48%, and 225.80% since 1990, respectively. Age-standardized incidence rates increased significantly from 1990 to 2021, with AAPCs of 0.84% (95%CI=0.80%-0.88%), 0.75% (95%CI=0.72%-0.78%), and 1.02% (95%CI=0.99%-1.05%) for total, female, and male populations, respectively (all P<0.001). In 1990 and 2021, both incidence counts and age-standardized rates were higher in females than males globally [TABLE:1, FIGURE:1A].

In China, 2021 elderly T1DM incidence reached 3,049 cases (1,559 females and 1,490 males), marking increases of 427.50%, 432.08%, and 422.81% since 1990. Age-standardized incidence rates increased significantly, with AAPCs of 2.21% (95%CI=2.05%-2.38%), 2.21% (95%CI=2.04%-2.37%), and 2.19% (95%CI=2.06%-2.32%) for total, female, and male populations, respectively (all P<0.001) [TABLE:1, FIGURE:1B]. Across SDI regions, age-standardized incidence rates also increased, with the high SDI region showing the most pronounced growth (AAPC=1.35%, 95%CI=1.29%-1.41%; P<0.001).

2.2 Trends in DALY Burden of Elderly T1DM in China and Globally In 2021, global elderly T1DM DALYs totaled 659,117 person-years (350,303 female and 308,814 male), representing increases of 91.80%, 76.40%, and 112.88% since 1990. However, age-standardized DALY rates declined significantly from 1990 to 2021, with AAPCs of -0.49% (95%CI=-0.53% to -0.44%), -0.68% (95%CI=-0.74% to -0.62%), and -0.24% (95%CI=-0.35% to -0.13%) for total, female, and male populations, respectively (all P<0.001), with females showing steeper declines than males [TABLE:2, FIGURE:1C].

In China, 2021 elderly T1DM DALYs reached 57,663 person-years (30,776 female and 26,887 male), representing increases of 78.25%, 39.69%, and 160.58% since 1990. Age-standardized DALY rates declined significantly for total and female populations, with AAPCs of -1.28% (95%CI=-1.54% to -1.01%) and -2.01% (95%CI=-2.27% to -1.76%), respectively (both P<0.001), while male trends remained relatively stable [TABLE:2, FIGURE:1D]. Across SDI regions, age-standardized DALY rates declined significantly in all regions except low-middle SDI (all P<0.001), with the middle SDI region showing the most pronounced decrease (AAPC=-0.50%, 95%CI=-0.59% to -0.42%).

2.3 Age Group Analysis of Disease Burden In 2021, the 60–64 age group accounted for the highest proportion of incident cases globally, in China, and across all five SDI regions. China' s 60–64 age group incidence proportion (27.91%) fell between the high-middle SDI region (26.01%) and middle SDI region (30.26%), but its DALY proportion (24.06%) was lower than all other regions. Notably, Chinese patients aged 60–69 years comprised 53.51% of all elderly T1DM cases and 55.25% of total DALYs [Figure 2: see original paper].

2.4 Decomposition Analysis of Disease Burden Changes Decomposition analysis revealed that population growth was the primary driver of increased elderly T1DM incidence globally and across all SDI regions, contributing 87.43% in low SDI regions and 58.34% in China. Epidemiological change was the second major contributor, with its highest impact in China (40.56%) and lowest in low SDI regions (11.63%). For DALY increases, population growth was also the dominant factor, contributing 178.96% in China and 110.20% in high SDI regions. Epidemiological changes negatively affected DALYs in most regions, with the greatest negative impact in China (-78.98%). Aging had minimal influence on both incidence and DALY increases, likely due to T1DM' s clinical characteristics and our focus on an elderly population [Figure 3: see original paper].

2.5 Future Disease Burden Projections Bayesian age-period-cohort model projections for 2022–2040 indicate continued increases in incidence and DALYs for elderly T1DM patients globally and in China across total, male, and female populations. However, Chinese women are expected to experience a more gradual increase in DALYs compared to men [Figure 4: see original paper].

Discussion

This study found that both global and Chinese elderly T1DM incidence increased substantially in 2021 compared to 1990, with age-standardized incidence rates rising continuously from 1990 to 2021. Population growth emerged as a critical factor driving these increases. The disease burden remains severe, and with accelerating global population aging and rising incidence, this challenge will become increasingly prominent.

Chinese patients aged 60–69 years accounted for over half of all elderly T1DM cases and DALYs, with recent increases in both metrics. Projections indicate continued growth through 2040. Future policies should prioritize enhanced early screening and diagnostic capacity for elderly T1DM patients to reduce misdiagnosis and improve overall health management. Evidence suggests telemedicine and internet-based hospital services can support glycemic control in T1DM patients [37]. Beyond conventional insulin therapy, research and application of emerging treatments such as stem cell therapy and immunomodulation should be strengthened, alongside clinical research on traditional Chinese medicine interventions to explore effective diversified therapeutic approaches. As medical technology advances, more individuals diagnosed during adolescence will survive into old age. Therefore, promoting healthy lifestyle interventions and psychological support, establishing comprehensive chronic disease management systems, and improving healthcare accessibility and quality are essential.

Globally, elderly males had lower incidence counts and age-standardized rates than females in both 1990 and 2021. In China, male incidence counts were lower but age-standardized rates were higher than females. A meta-analysis found

higher T1DM incidence in young males [17], though evidence for sex differences in the elderly remains inconclusive. Postmenopausal hormonal changes may affect glycemic fluctuations in women [22], suggesting endocrine differences may contribute to sex-specific disease patterns. Additionally, visceral fat index correlates positively with diabetes risk [23], and lifestyle improvements significantly reduce diabetes risk in men [24]. These findings underscore the importance of considering sex differences in health policy development.

Although China' s 60–64 age group had the highest incidence proportion, its DALY proportion was lower than all other regions. DALYs represent the sum of years of life lost due to premature mortality and years lived with disability. Lower DALY proportions indicate a relatively lighter health burden [25]. China has made significant progress in diabetes management, particularly in pharmacotherapy, insulin therapy, and patient education, which may have effectively reduced complication rates and severity, thereby decreasing DALY proportions [26-28]. The "Healthy China 2030" blueprint has further optimized healthcare systems, expanding medical insurance coverage and chronic disease management programs for elderly patients, enabling timely treatment and care that alleviates diabetes burden [29].

Current T1DM treatment primarily relies on insulin therapy, glucose monitoring, and lifestyle interventions [30]. Emerging technologies such as islet transplantation, stem cell therapy, and immunomodulation are developing rapidly. For example, a Chinese research team recently achieved clinical functional cure of T1DM through chemically induced pluripotent stem cell-derived islet transplantation, published in *Cell* [31]. Novel strategies involving -cell replacement, cell delivery technologies, and localized targeted immunomodulation are being explored [32]. Anti-interleukin-21 antibody combined with liraglutide has shown -cell function preservation in newly diagnosed T1DM patients [33]. Matrix metalloproteinases (MMPs) such as MMP-1, MMP-2, and MMP-3 correlate independently with arteriosclerosis markers in T1DM patients and represent potential therapeutic targets [34]. Traditional Chinese medicine also shows promise: artesunate may improve insulin resistance in T1DM mouse models by inhibiting the PI3K/GSK3 pathway [35], and kaempferol may attenuate renal injury through HO-1/p38-mediated anti-inflammatory effects [36].

This study provides the first systematic analysis of global and Chinese elderly T1DM incidence and DALY burden from 1990 to 2021 based on GBD 2021 data, offering evidence for prevention, control, and health resource allocation decisions. However, limitations exist: GBD data are estimated through statistical modeling of diverse epidemiological sources, and their reliability depends heavily on primary data quality. Recent research suggests GBD estimates may overestimate real-world epidemiological data [38], necessitating cautious interpretation and application of secondary analyses. Future regional surveys across Chinese provinces are needed to comprehensively understand local disease burden patterns and disparities.

Author Contributions

ZHAO Xiaoxiao: data collection, figure preparation, initial draft writing, funding support. DING Yunhan: data collection, figure preparation, initial draft writing. CHEN Jiahui, WANG Haibo: data organization, manuscript revision. KE Lixin, WANG Ziyi, GAO Wulin, LU Xiaohui, WU Jibiao: data verification, manuscript revision. LU Cuncun: study conception, research guidance, statistical analysis, figure preparation, manuscript revision.

Conflict of Interest

The authors declare no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.