Received: 23 January 2025 | Revised: 31 March 2025 | Accepted: 29 April 2025

DOI: 10.1002/dad2.70126

Alzheimer's & Dementia
Diagnosis, Assessment & Disease Monitoring

RESEARCH ARTICLE

Alzheimer's and dementia: Diagnosis, assessment, and disease monitoring global, regional, and national burden of Alzheimer's disease and other dementias (ADODs) and their risk factors, 1990–2021: A systematic analysis for the Global Burden of Disease study 2021

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Abstract

INTRODUCTION: Aging populations globally lead to growing challenges in Alzheimer's disease and other dementias (ADODs). Tracking ADODs aids health strategies. To describe global, regional, and national incidence, prevalence, death, and disability-adjusted life years (DALYs) of ADODs in 2021, and analyze changes from 1990 to 2021.

METHODS: We analyzed ADODs using the 2021 Global Burden of Disease database, calculating estimated annual percentage change (EAPC), applying Joinpoint regression, and assessing risk factors.

RESULTS: Between 1990 and 2021, ADOD incidence, prevalence, deaths, and DALYs increased significantly. DALYs grew 295.45% and fatalities grew 167.72%. Age-standardized rates (ASRs) rose for both genders, with women generally higher but men showing steeper increases. ASRs correlated positively with Sociodemographic Index. Risk factor contribution to DALYs and death rose by 4.1%. In 2021, metabolic factors and high fasting plasma glucose most influenced ADODs.

DISCUSSION: The global ADOD burden has risen since 1990. Early screening, especially for elderly women, is crucial. Policymakers must act to reverse this trend.

KEYWORDS
ADODs, Alzheimer's disease, Global Burden of Disease, dementia, incidence, prevalence, Sociodemographic Index (SDI)

Highlights

- Based on Global Burden of Disease data 1990–2021, the incidence, prevalence, mortality, and disability-adjusted life years due to Alzheimer's and dementia are depicted globally, regionally, and nationally.

- The effects of gender and age were explored.
  The contribution of different risk factors to the disease was studied.

1 | INTRODUCTION

Alzheimer's disease (AD), alternatively referred to as senile dementia, represents an irreversible, chronic, and progressively degenerative condition of the central nervous system. Dementia is a syndrome caused by a brain disease. AD is the most common type of dementia, accounting for about 50% to 70% of all dementia cases. With the gradual aggravation of the disease, patients may have serious cognitive impairment and even lose the ability to take care of themselves, requiring long-term care and causing physical and mental harm to patients and their families.

Alzheimer's disease and other dementias (ADODs) are major public health challenges worldwide. The Global Burden of Disease (GBD) 2021 findings project that AD will rise from the 22nd leading cause of death in the global burden in 2022 to the 8th leading cause of death in 2050 (measured in disability-adjusted life years [DALYs]). It is projected that by 2050, the number of individuals with ADODs will reach 152 million.[1] The aging of the global population has led to an expected increase in the number of people with dementia from 55 million in 2019 to 139 million in 2050, and the associated costs will also increase significantly.[2] One study's projections suggest that ADODs will impose a staggering cost on the global economy of $14,513 billion (95% uncertainty level [UI] 12,106–17,778) over the period from 2020 to 2050, equivalent to total global health spending in 2020.[2] Understanding the prevalence and current situation of ADODs will inform the next steps of government policy.

2 | METHODS

2.1 | Data sources

The data analyzed in this study were retrieved from the most recently refreshed online Global Health Data Exchange Query Tool on May 16, 2024. The methodologies employed in this research adhered closely to those outlined in the GBD 2021 study.[3–5] The GBD 2021 approach to analyzing risk factors adhered to the comprehensive framework of comparative risk assessment (CRA), encompassing the identification of risk–outcome pairs, the estimation of relative risks, the ascertainment of exposure levels and distributions, the determination of counterfactual exposure levels, the calculation of population attribution scores and burdens, and the assessment of the intermediary effects of various risk factors through others.[6] Detailed procedural specifics have been documented in prior studies.[6] Our analysis focuses on trends in incidence, prevalence, death, and DALYs due to ADODs between 1990 and 2021. These trends were examined at global, regional, and national levels, with consideration given to differences across sexes and age ranges. To mitigate potential confounding effects related to age in our analysis and to ensure comparability among rates, age-standardized rates (ASRs) were utilized.

The Sociodemographic Index (SDI), a composite indicator ranging from 0 to 1, was calculated based on educational attainment, economic status, and total fertility rate of a country or region.[7] A higher SDI value signifies a more advanced level of social development. This study relied on data sourced from publicly accessible databases, thereby obviating the need for ethical approval.

2.2 | Statistical analysis

We characterized the figures (accompanied by their respective 95% UIs) and trends in incident cases, prevalent cases, deaths, and DALYs, along with their corresponding ASRs and associated 95% UIs, for ADODs. These analyses were stratified by sex, age, year, SDI subregion, GBD region, and across 204 countries and regions.

The temporal trends of ASRs over a specified period were captured using estimated annual percentage change (EAPC). Briefly, we employed the regression model $y = \alpha + \beta x + \varepsilon$ for these calculations, where y represents the natural logarithm of the ASR (ln(ASR)), x denotes the time variable, and ε signifies the error term. The assumption was made that ln(ASR) increases linearly with time; thus EAPC was computed as $100 \times [\exp(\beta) - 1]$. In addition, linear models were utilized to ascertain the 95% confidence intervals (95% CIs) for the EAPCs. An increasing trend in ASR was deemed present if both the EAPC and its lower 95% CI bound exceeded 0. Conversely, a decreasing trend was indicated when both the EAPC and its upper 95% CI limit were below 0.

To delineate the evolving trend over a defined period, Joinpoint regression analysis was conducted by fitting various periods using the simplest logarithmic model. This methodology enabled a granular examination of the distinct interval-specific variability characteristics of the disease on a global scale. The Joinpoint regression model primarily assessed the statistical significance of trends in disease rates across different segments by comparing the annual percent change (APC) and the average annual percent change (AAPC) with 0. The Joinpoint regression analysis was executed using Joinpoint version 5.2.0.0 software, developed by the National Cancer Institute. All remaining analyses and visualizations were performed utilizing GraphPad Prism 8 software, Excel 2019, and R software (version 4.4.1). A p-value $< .05$ was considered statistically significant.

3 | RESULTS

3.1 | Incidence trends from 1990 to 2021

Globally, from 1990 to 2021, there has been a significant increase in the incidence of ADODs, with a jump of 156.49%. In 1990, there were ≈3.83 million cases (95% UI: 3.37 to 4.36), whereas in 2021, this number surged to 9.84 million cases (95% UI: 8.62 to 11.16). When examining the incidence rates by sex, there has been a noticeable trend. Specifically, the age-standardized incidence rate (ASIR) of ADODs has increased among men during this period. The EAPC of men (0.02; 95% CI: 0 to 0.03) indicated a slight upward trend. In contrast, the ASIR for women (0;95% CI: −0.03 to 0.03) has remained relatively stable, suggesting no significant change over time. In summary, although the overall incidence of ADODs is rising globally, this increase is more pronounced among men, with women experiencing a more stable incidence rate (Table 1).

The ASIR of ADODs exhibited a positive correlation with SDI levels ($R = 0.392$, $p < .001$) (Figure 1). Specifically, in 2021, the ASIR demonstrated an upward trend in regions with high-middle SDI (132.4; 95% UI: 115.43 to 150.85), High SDI (122.61; 95% UI: 107.45 to 138.44), and middle SDI (123.79; 95% UI: 108.25 to 141.26). Conversely, a downward trend was observed in the other three SDI categories. Among these regions, the EAPC of ASIR for ADODs increased most notably in high-middle SDI areas (0.22; 95% CI: 0.18 to 0.26). In contrast, areas with a low SDI exhibited a decreasing trend (−0.19; 95% CI: −0.2 to −0.17). Similarly, regions with low-middle SDI (−0.17; 95% CI: −0.18 to −0.15) and middle SDI (−0.11; 95% CI: −0.12 to −0.10) also showed decreasing trends, respectively (Table 1). In the year 2021, the percentage of ASIR attributed to females surpassed that of males across all SDI regions and globally (Figure 2A). In regions characterized by a higher SDI, the prevalence of ADODs among individuals 60 years of age or older tended to be higher (Figure 3B).

In 2021, across 21 regions based on geographic location, the incidence rates of ADODs, as measured by ASIRs per 100,000 population, peaked in East Asia (149.61; 95% UI: 129.58–171.14), the North Africa and Middle East region (132.19; 95% UI: 115.75–150.35), and high-income North America (131.39; 95% UI: 114.67–149.04). Conversely, the lowest ASIRs were observed in Western Sub-Saharan Africa (73.18; 95% UI: 63.36–83.46), South Asia (79; 95% UI: 68.26–90.52), and Andean Latin America (79.55; 95% UI: 68.95–91.05). Between 1990 and 2021, East Asia exhibited the most pronounced increase in ADODs ASIR (EAPC: 0.4; 95% CI: 0.33–0.48), whereas Australasia reported the steepest decline (EAPC: −0.56; 95% CI: −0.6 to −0.52). For the majority of other regions, a downward trend in ASIR was prevalent (Table 2).

At the country level, among the 204 countries and regions analyzed, China, Germany, and Lebanon exhibited the highest ASIRs of ADODs. Conversely, Nigeria, Sao Tome and Principe, and Ghana reported the lowest ASIRs. Notably, China (including Taiwan) and Italy have experienced notable increases in their EAPCs of more than 20% between 1990 and 2021. Specifically, the EAPC of ASIR in China (including Taiwan) was 0.41 (95% CI: 0.34% to 0.49%), which represented the highest upward trend during this period, underscoring the urgent need for increased attention to ADODs prevention efforts. In contrast, the majority of countries and regions maintained relatively stable ASIRs per 100,000 population or even showed downward trends. Notably, Denmark (−0.73; 95% CI: −0.76 to −0.69), Norway (−0.64; 95% CI: −0.69 to −0.60), and Australia (−0.62; 95% CI: −0.67 to −0.58) experienced significant declines in their ASIRs (Table 2).

RESEARCH-IN-CONTEXT

1. **Systematic review**: Utilizing the Global Burden of Disease (GBD) database (1990–2021), this study analyzed global, regional, and national trends in Alzheimer's disease and other dementias, focusing on incidence, prevalence, death, disability-adjusted life years, and risk factors.
2. **Interpretation**: Findings reveal a persistent and significant burden of dementia despite health care advancements, underscoring the need for enhanced prevention, diagnosis, and management strategies.
3. **Future directions**: The study highlights disparities across populations and emphasizes the importance of global collaboration to improve access to care and develop innovative therapies. Leveraging GBD data, the research calls for refined diagnostic tools, biomarkers, and cross-country resource sharing to reduce dementia's impact and ensure equitable, high-quality care worldwide. By leveraging the wealth of data available in the GBD database and continuing to build upon existing knowledge, the global community can work towards reducing the impact of Alzheimer's disease and other dementias.

3.2 | Prevalence trends from 1990 to 2021

Globally, the number of ADODs patients increased significantly in 2021 compared to 1990, with a 160.83% rise, reaching 56.86 million (95% UI: 49.38 to 64.98 million). The age-standardized prevalence rate (ASPR) per 100,000 population in 2021 was 694.01 (95% UI: 602.88 to 794.08), showing a slight upward trend (EAPC: 0; 95% CI: −0.02 to 0.03) (Table 3).

The ASPR of ADODs exhibited a mixed trend of increases and decreases across all SDI regions. Specifically, the ASPR was highest in the high-middle SDI region, with an ASPR of 766.2 (95% UI: 659.8 to 879.64). Meanwhile, the EAPC of ASPR in the middle SDI region showed the fastest increase (0.21; 95% CI: 0.17 to 0.25). Both men and women demonstrated an upward trend in ASPR per 100,000 population, with women having a higher ASPR compared to men (769.94; 95% UI: 670.71 to 877.57) (Table 3). In addition, the prevalence rate increased with age (Figure 3A). Notably, younger patients were predominantly concentrated in lower SDI regions (Figure 3B).

TABLE 1 Incidence of Alzheimer's disease and other dementias in 1990 and 2021 for both sexes and all locations, with EAPC from 1990 and 2021.

	1990		2021		1990–2021
Characteristics	Incidence cases (*10^6) (95% UI)	ASIR per 100,000 (95% UI)	Incidence cases (*10^6) (95% UI)	ASIR per 100,000 (95% UI)	EAPC of ASIR (95% CI)
Global	3.83 [3.37–4.36]	116.97 [102.77–132.32]	9.84 [8.62–11.16]	119.76 [104.96–135.89]	−0.02 [−0.04 to 0]
Sex					
Female	2.48 [2.18–2.82]	127.82 [112.82–144.18]	6.19 [5.43–7.01]	132.29 [116.3–149.8]	0 [−0.03 to 0.03]
Male	1.35 [1.18-1.55]	100.69 [88.05–114.43]	3.65 [3.14–4.18]	103.4 [89.45–118.45]	0.02 [0 to 0.03]
Socio-demographic index					
High SDI	1.44 [1.26–1.62]	127.18 [112.55–142.92]	2.95 [2.59–3.34]	122.61 [107.45–138.44]	−0.11 [−0.12 to −0.1]
High-middle SDI	0.99 [0.86–1.14]	118.38 [103.82–134.11]	2.58 [2.25–2.94]	132.4 [115.43–150.85]	0.22 [0.18 to 0.26]
Middle SDI	0.84 [0.74–0.96]	113.27 [99.18–128.9]	2.9 [2.54–3.31]	123.79 [108.25–141.26]	0.09 [0.05 to 0.14]
Low-middle SDI	0.42 [0.36–0.47]	95.55 [83.27–108.9]	1.06 [0.93–1.21]	92.61 [80.79–105.71]	−0.17 [−0.18 to −0.15]
Low SDI	0.14 [0.13–0.16]	95.08 [82.74–108.32]	0.33 [0.29–0.37]	90.89 [79–103.12]	−0.19 [−0.2 to −0.17]
21 GBD Region					
Andean Latin America	0.01 [0.01–0.02]	80.6 [69.91–92.12]	0.04 [0.04–0.05]	79.55 [68.95–91.05]	−0.06 [−0.07 to −0.05]
Australasia	0.03 [0.02–0.03]	123.79 [108.48–139.61]	0.06 [0.06–0.07]	105.44 [92.56–118.63]	−0.56 [−0.6 to −0.52]
Caribbean	0.02 [0.02–0.03]	97.6 [85.15–110.9]	0.05 [0.05–0.06]	95.6 [83.53–108.64]	−0.16 [−0.19 to −0.13]
Central Asia	0.04 [0.04–0.05]	111.72 [97.73–127.69]	0.07 [0.06–0.08]	109.82 [95.87–125.3]	−0.06 [−0.07 to −0.04]
Central Europe	0.15 [0.13–0.18]	115.01 [100.69–131.62]	0.27 [0.23–0.31]	112.42 [97.97–128.46]	−0.08 [−0.09 to −0.07]
Central Latin America	0.07 [0.07–0.09]	111.25 [96.71–126.56]	0.25 [0.22–0.28]	106.12 [92.53–120.99]	−0.11 [−0.12 to −0.09]
Central Sub-Saharan Africa	0.02 [0.02–0.02]	126.9 [111.06–144.4]	0.04 [0.04–0.05]	126.14 [111.31–143.21]	−0.01 [−0.04 to 0.01]
East Asia	0.73 [0.62–0.83]	120.29 [104.75–137.02]	2.99 [2.57–3.43]	149.61 [129.58–171.14]	0.4 [0.33 to 0.48]
Eastern Europe	0.29 [0.25–0.34]	117.31 [102.49–133.78]	0.42 [0.36–0.48]	115.66 [100.94–131.87]	−0.08 [−0.11 to −0.04]
Eastern Sub-Saharan Africa	0.05 [0.05–0.06]	107.12 [93.44–121.63]	0.12 [0.11–0.14]	102.41 [89.7–116.09]	−0.13 [−0.14 to −0.12]
High-income Asia Pacific	0.21 [0.19–0.24]	116.94 [102.53–133.08]	0.7 [0.61–0.8]	118.62 [103.43–135]	0.19 [0.14 to 0.24]
High-income North America	0.52 [0.45–0.59]	139.57 [122.14–157.89]	0.93 [0.81–1.05]	131.39 [114.67–149.04]	−0.22 [−0.24 to −0.2]
North Africa and Middle East	0.17 [0.15–0.19]	138.06 [121.37–156.98]	0.47 [0.41–0.53]	132.19 [115.75–150.35]	−0.14 [−0.15 to −0.13]
Oceania	0 [0–0]	117.17 [102.35–133.78]	0.01 [0–0.01]	112.05 [96.98–128.81]	−0.18 [−0.21 to −0.16]
South Asia	0.32 [0.27–0.36]	80.57 [69.5–92.11]	0.92 [0.8–1.06]	79 [68.26–90.52]	−0.18 [−0.22 to −0.14]
Southeast Asia	0.22 [0.19–0.25]	114.85 [100.81–130.85]	0.58 [0.51–0.66]	110.07 [96.11–125.72]	−0.14 [−0.15 to −0.12]
Southern Latin America	0.05 [0.04–0.05]	111.77 [97.43–127.36]	0.1 [0.09–0.11]	107.09 [92.9–122.43]	−0.14 [−0.15 to −0.13]
Southern Sub-Saharan Africa	0.02 [0.02–0.03]	112.76 [98.34–128.64]	0.05 [0.04–0.05]	107.13 [93.16–122.19]	−0.14 [−0.15 to −0.12]
Tropical Latin America	0.09 [0.08–0.11]	129.14 [113.1–146.66]	0.31 [0.27–0.35]	126.83 [111.77–144.42]	−0.11 [−0.15 to −0.08]
Western Europe	0.76 [0.67–0.85]	122.45 [108.7–136.67]	1.35 [1.18–1.54]	118.56 [103.36–134.23]	−0.14 [−0.18 to −0.11]
Western Sub-Saharan Africa	0.05 [0.04–0.06]	78.42 [67.93–89.46]	0.1 [0.09–0.12]	73.18 [63.36–83.46]	−0.23 [−0.24 to −0.21]

Abbreviation: ASIR, age-standardized incidence rate; EAPC, estimated annual percent change; SDI, sociodemographic index; 95% CI, 95% confidence intervals; 95% UI, 95% uncertainty level.

In 2021, East Asia had the highest ASPRs of ADODs per 100,000 population, with an ASPR of 887.95 (95% UI: 759.95 to 1027.48). Conversely, Western Sub-Saharan Africa had the lowest ASPR per capita, at 406.02 (95% UI: 352.89 to 462.39). Across most territories, a downward trend in EAPC of ASPRs was observed, particularly in Australasia (−0.54; 95% CI: −0.58 to −0.5). However, slight upward trends were noted in East Asia (0.43; 95% CI: 0.35 to 0.51) and high-income Asia Pacific (0.28; 95% CI: 0.23 to 0.34) (Table 3). In addition, in 2021, a positive correlation was found between ASPRs and SDI values among the 21 regions analyzed ($R = 0.353$, $p < .001$) (Figure S1).

In 2021, the countries with the highest ASPR of ADODs were Somalia, the Central African Republic, and Niger. Conversely, the lowest ASPRs per capita were recorded in Singapore, Japan, and Canada. At the country level, a downward trend was observed in the EAPC of ASPRs across all countries. Notably, China (−0.14; 95% CI: −0.16 to −0.13), the Maldives (−0.13; 95% CI: −0.14 to −0.12), and Malaysia

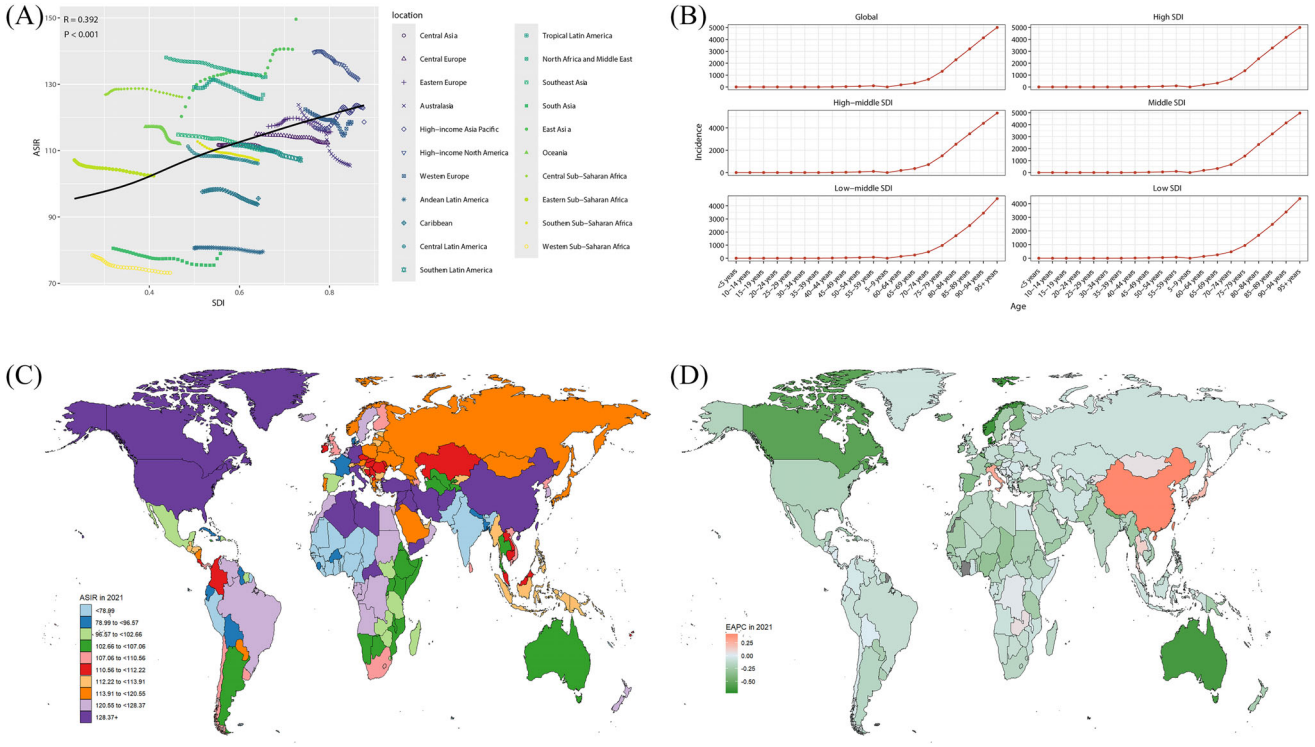

FIGURE 1 Delineates the incidence of ADODs across 204 countries and territories, stratified by age group and SDI region, from 1990 to 2021. (A) Explores the correlation between the ASIR of ADODs and SDI regions in 2021. These correlations were quantified using Pearson correlation analysis, with the black line indicating the expected values derived from the SDI and incidence rates of the diseases across all geographical locations. (B) Provides a comprehensive view of the incidence of ADODs in various age groups, both globally and within different SDI regions. (C) Displays the ASIR for each of the 204 countries and territories included in the study. Finally, (D) presents the EAPCs in the ASIR across these 204 countries and territories, offering valuable insights into the temporal trends in incidence associated with ADODs. ASIR, age-standardized incidence rate; EAPC, estimated annual percent change; SDI, sociodemographic index.

(−0.13; 95% CI: −0.14 to −0.12) exhibited the most rapid declines in ASPRs per 100,000 population (Table S1).

3.3 | Death trends from 1990 to 2021

Globally, the number of deaths attributed to ADODs rose significantly from 0.66 million (95% UI: of 0.16 to 1.76 million) in 1990 to 1.95 million (95% UI: 0.51 to 4.98 million) in 2021. In addition, the age-standardized death rate (ASDR) per 100,000 population also increased during this period (EAPC: 0.02; 95% CI: 0 to 0.03). From 1990 to 2021, the ASDR increased in both genders, with men experiencing an EAPC of 0.06 (95% CI: 0.04 to 0.07) and women experiencing an EAPC of 0.04 (95% CI: 0.02 to 0.06) (Table S2).

In 2021, the overall ASDR for women surpassed that of men across the globe, as well as in every SDI region (Figure S2A). Across all age brackets, death rates escalate with age (Figure 3A). Between 1990 and 2021, the age group of 95-year-olds experienced the most significant increase in deaths over time (Figure 3B).

In 2021, the ASDRs were notably elevated in regions categorized under high-middle SDI (26.42; 95% UI: 7.01 to 68.31) and high SDI (26.21; 95% UI: 7.05 to 64.83). Among the various SDI categories, the low-middle SDI regions exhibited the most pronounced increase in ASDRs per capita, with an EAPC of 0.43 (95% CI: 0.42 to 0.44) (Table S2). In 2021, a positive correlation was observed between the ASDRs and the SDI values across the 21 regions analyzed ($R = 0.2$, $p < .001$), indicating that regions with higher SDI values tended to have higher ASDRs (Figure S2). Figure S3 shows the Joinpoint regression analysis of the ASDRs for each SDI region from 1990 to 2021.

In 2021, the regions exhibiting the highest ASDRs per 100,000 population were Central Sub-Saharan Africa (34.89; 95% UI: 8.43 to 93.23), East Asia (30.41; 95% UI: 7.81 to 81.29), and high-income North America (28.25; 95% UI: 7.49 to 71.28). Conversely, the regions with the lowest ASDRs per capita were Andean Latin America (14.08; 95% UI: 3.49 to 37.9), the Caribbean (15.82; 95% UI: 3.87 to 43.17), and Central Latin America (16.84; 95% UI: 4.16 to 44.59). Notably, South Asia experienced the most significant increase in ASDRs per 100,000 population (EAPC: 0.68; 95% CI: 0.65 to 0.71). In contrast, the regions with the most substantial decreases in ASDRs per capita were North Africa and the Middle East (EAPC: −0.21; 95% CI: −0.26 to −0.17) and Oceania (EAPC: −0.21; 95% CI: −0.25 to −0.17) (Table S2).

In 2021, Gabon and the Democratic Republic of the Congo emerged as the nations with the highest ASDRs per 100,000 inhabitants, whereas Peru, Ecuador, and Mexico exhibited the lowest ASDRs per capita. On the other hand, India (EAPC: 0.89; 95% CI: 0.83 to 0.95) and Bhutan (EAPC: 0.85; 95% CI: 0.79 to 0.91) recorded the most

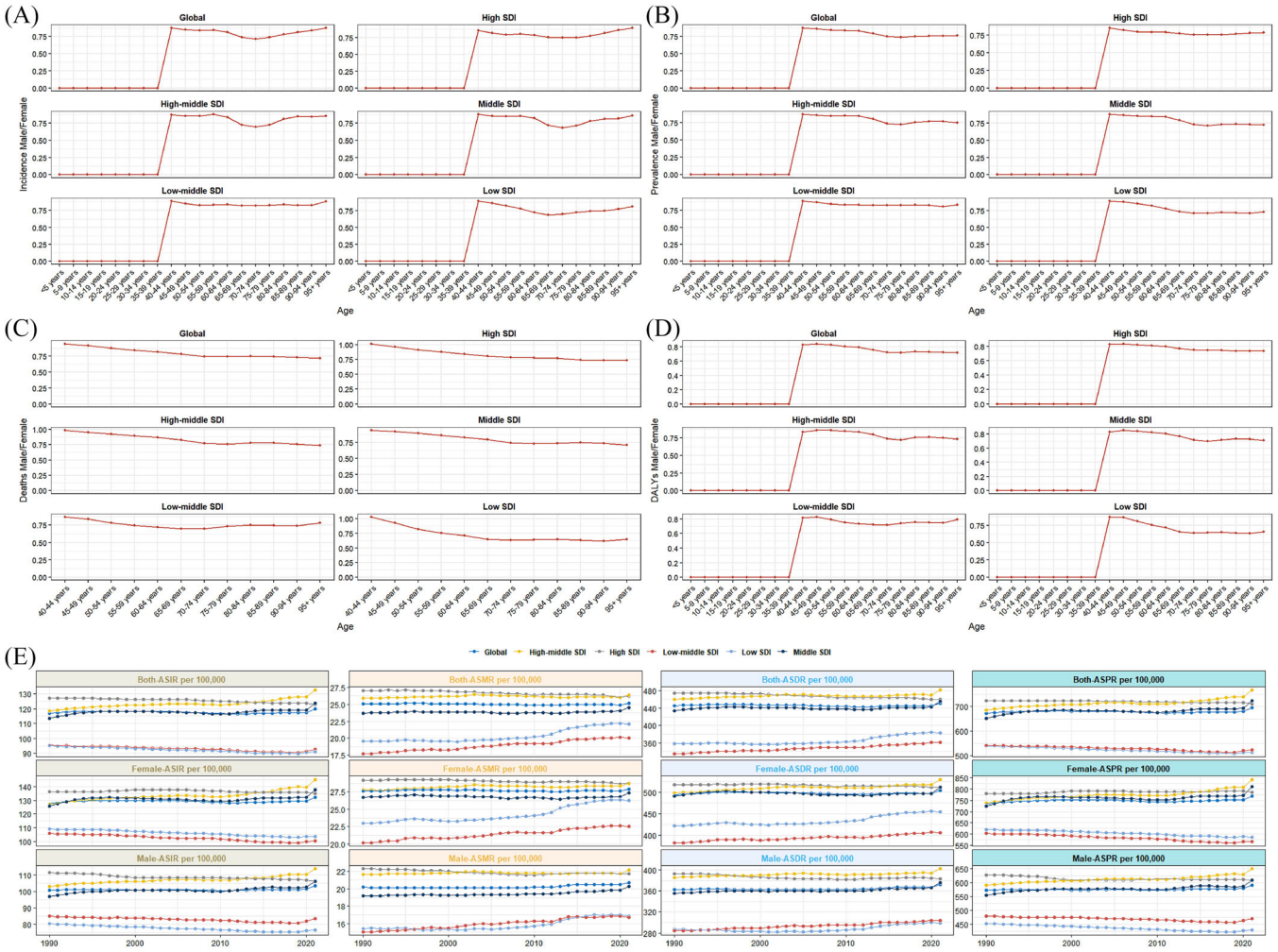

FIGURE 2 Illustrates the distribution patterns of ADODs across various age groups and SDI regions from 1990 to 2021. Specifically, the figure comprises the following components: (A) A comparative analysis of incidence rates between males and females within distinct age brackets. (B) A comparison of prevalence rates among men and women across different age groups. (C) A gender-based comparison of death rates within various age cohorts. (D) A comparative assessment of DALYs for males and females in different age groups. (E) Additionally, the figure presents annual variations in four pivotal gender-specific metrics: morbidity, prevalence, death, and disability-adjusted life expectancy, both globally and within the five SDI classifications, spanning the period from 1990 to 2021. ADODs, Alzheimer's disease and other dementias; DALYs, disability-adjusted life years; SDI, Sociodemographic Index. ASIR, age-standardized incidence rate; ASPR, age-standardized prevalence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life-years rate; SDI, sociodemographic index.

substantial increases in ASDRs per 100,000 population for ADODs. Conversely, ≈50% of the countries demonstrated a decline in their ASDRs per 100,000 population, with notable mentions including Guam (EAPC: −0.7; 95% CI: −0.76 to −0.64), South Korea (EAPC: −0.53; 95% CI: −0.59 to −0.47), and Bahrain (EAPC: −0.49; 95% CI: −0.56 to −0.41), which all displayed a downward trend in ADOD death rate (Table S3).

3.4 | DALYs trends from 1990 to 2021

Over the period spanning from 1990 to 2021, the global tally of DALYs attributed to ADODs escalated dramatically, from 13.57 million (95% UI: 6.44 to 29.59) to 450.98 million (95% UI: 212.69 to 950.16). In addition, the EAPC of ASRs of DALYs per 100,000 inhabitants witnessed a slight increase, albeit non-significant (−0.02; 95% CI: −0.03 to 0). Notably, in 2021, the disease burden associated with ADODs was consistently elevated among women compared to men, albeit the rate of increase was more pronounced in men (men: 0.05; 95% CI: 0.03 to 0.07, women: 0; 95% CI: −0.01 to 0.02) (Table S4).

Across all SDI regions, the ASRs of DALYs due to ADODs increased between 1990 and 2021, except for the high SDI region, which exhibited a downward trend (EAPC: −0.11; 95% CI: −0.12 to −0.1). In 2021, the high-medium SDI region emerged as having the highest ASR of DALYs per 100,000 inhabitants (ASR: 481.7; 95% UI: 228.79 to 1023.96). Furthermore, across all SDI and GBD territories in 2021, women consistently had a higher proportion of the ASR of DALYs compared to men (Table S4).

Central Sub-Saharan Africa had the highest ASR of DALYs per 100,000 inhabitants due to ADODs in 2021 (591.41; 95% UI: 255.67 to 1360.26), whereas Andean Latin America reported the lowest ASR

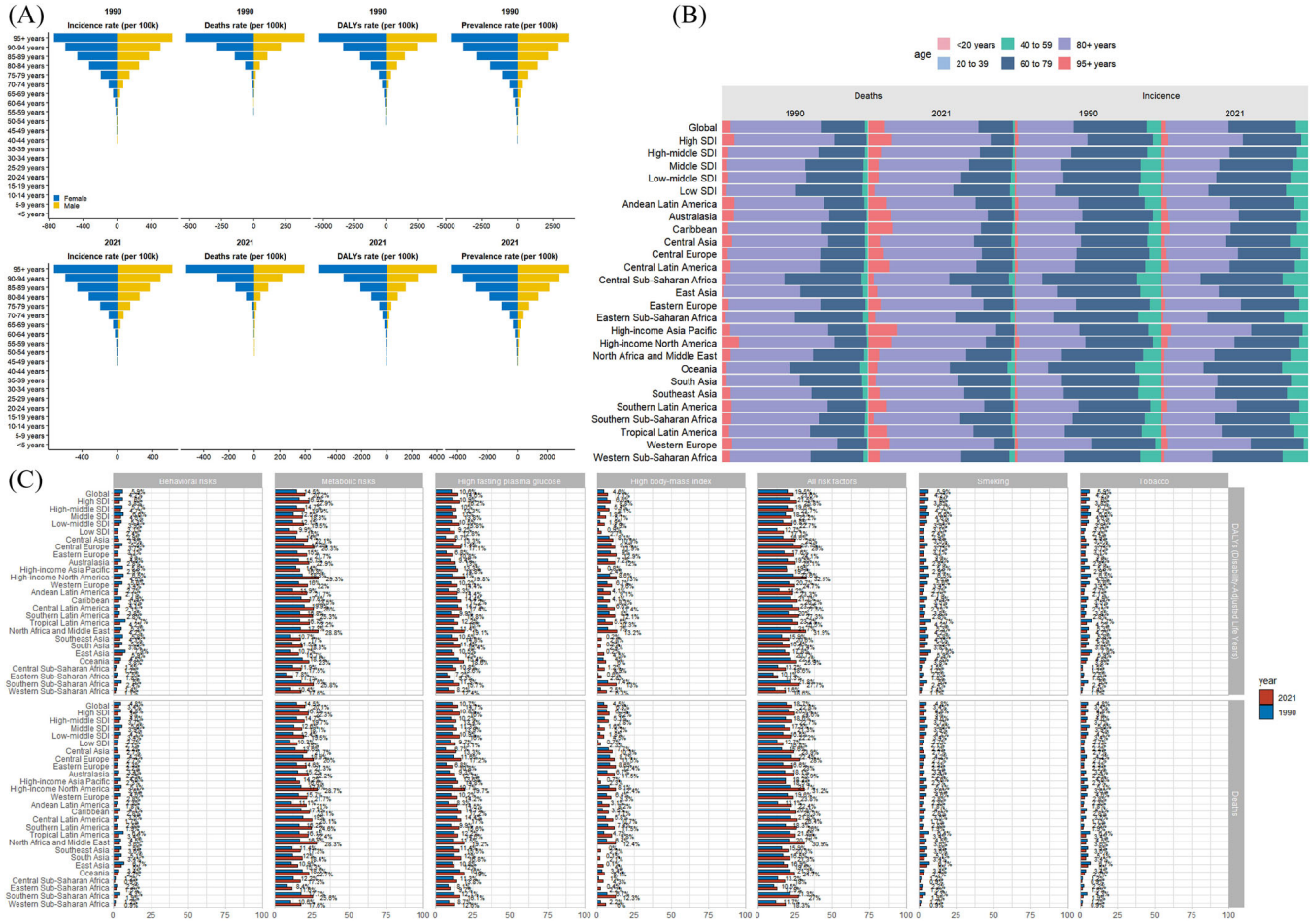

FIGURE 3 (A) Incidence, deaths, DALYs, and prevalence pyramid by age group, 1990 and 2021. (B) Age composition chart of death and morbidity in 1990 and 2021. (C) Death, disability-adjusted life year risk factor percentage chart. DALYs, disability-adjusted life-years; SDI, sociodemographic index.

(272.02; 95% UI: 131.15 to 573.64). Between 1990 and 2021, most regions witnessed an increase in the ASR of DALYs due to ADODs, with Australasia experiencing the most notable decrease (EAPC: −0.3; 95% CI: −0.32 to −0.29). Conversely, high-income North America observed a decline in the ASR of DALYs (EAPC: −0.3; 95% CI: −0.32 to −0.29) (Table S4). Notably, the ASR of DALYs in 2021 across regions were correlated positively with the SDI ($R = 0.212$, $p < .001$) (Figure S4).

Lesotho, Swaziland, and the Central African Republic reported the highest ASR of DALYs per 100,000 inhabitants at the country level in 2021. In contrast, India and Bangladesh had the lowest ASR. Since 1990, most nations have seen a decrease in the ASR of DALYs, particularly Rwanda, Ethiopia, and Burundi, which experienced substantial declines (Table S5).

3.5 | Risk factor

These factors accounted for 20.2% (95% UI: 43.0% to 0.3%) of DALYs due to metabolic risks, 14.60% (95% UI: 29.4% to 1.2%) due to high fasting plasma glucose, 7.10% (95% UI: 20.0% to 1.8%) due to high BMI, and 4.20% (95% UI: 5.5% to 3.0%) each for smoking, tobacco use, and behavioral risks. The influence of these risk factors exhibited regional variations. Notably, within the high SDI group, these risk factors had the most prominent effect on the burden of ADODs. Across five SDI regions and specifically in 21 regions worldwide, the total number of risk factors, particularly metabolic risks, high fasting glucose levels, and increased BMI, rose for ADODs in 2021 compared to 1990. In contrast, behavioral risks, smoking, and tobacco consumption demonstrated a reduction compared to 1990 levels (Figure 3C).

4 | DISCUSSION

Over the study period, there has been a significant surge in incidence (156.49%), prevalence (160.83%), death (195.45%), and DALYs (101.73%) associated with ADODs globally. Projections anticipate that by 2050, the number of ADOD cases worldwide will reach 153 million.[2] By 2050, the proportion of the population 60 years of age or older is expected to grow by 22%, marking the most rapid demographic expansion in this age group.[8] The incidence of ADODs has increased

TABLE 2 Incidence of Alzheimer's disease and other dementias in 1990 and 2021 for both sexes in 204 countries, with EAPC from 1990 and 2021.

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Afghanistan	6792 (5876 to 7741)	132.83 (116.86 to 152.07)	8764 (7688 to 10026)	130.94 (115.12 to 149.09)	0.29% (0.24 to 0.35)	−0.05% (−0.06 to −0.03)
Albania	1849 (1608 to 2107)	111.95 (97.18 to 127.9)	4828 (4174 to 5529)	112.62 (98 to 128.7)	1.61% (1.49 to 1.72)	0.04% (0.03 to 0.05)
Algeria	12123 (10341 to 14088)	134.08 (117.34 to 152.85)	37174 (32167 to 43066)	128.59 (112.65 to 146.91)	2.07% (1.88 to 2.27)	−0.14% (−0.15 to −0.14)
American Samoa	16 (14 to 19)	111.24 (95.84 to 128.11)	41 (35 to 47)	109.14 (93.39 to 125.47)	1.5% (1.41 to 1.61)	−0.08% (−0.09 to −0.07)
Andorra	61 (52 to 71)	121.55 (105.04 to 139.09)	190 (164 to 218)	114.28 (98.41 to 131.55)	2.11% (1.93 to 2.34)	−0.19% (−0.2 to −0.19)
Angola	2938 (2546 to 3329)	127.48 (111.77 to 145.28)	9171 (7979 to 10423)	124.21 (109.07 to 141.23)	2.12% (2.03 to 2.21)	−0.08% (−0.09 to −0.07)
Antigua and Barbuda	57 (50 to 66)	97.4 (85.27 to 111.61)	88 (76 to 101)	95.08 (82.7 to 109.64)	0.53% (0.46 to 0.61)	−0.07% (−0.08 to −0.06)
Argentina	32950 (28371 to 37756)	112.19 (97.11 to 128.39)	62825 (54326 to 72188)	106.73 (92.2 to 122.29)	0.91% (0.82 to 0.99)	−0.17% (−0.18 to −0.15)
Armenia	2555 (2228 to 2922)	114.41 (99.75 to 130.36)	4930 (4260 to 5655)	114 (99.56 to 130.25)	0.93% (0.83 to 1.02)	−0.02% (−0.02 to −0.01)
Australia	23451 (20535 to 26658)	122.93 (107.54 to 138.36)	52191 (45954 to 58772)	102.66 (90.27 to 115.36)	1.23% (1.06 to 1.39)	−0.62% (−0.67 to −0.58)
Austria	15981 (13685 to 18733)	123.67 (107.3 to 141.71)	25291 (21751 to 29369)	116.09 (99.55 to 133.87)	0.58% (0.51 to 0.67)	−0.25% (−0.27 to −0.22)
Azerbaijan	4662 (4083 to 5354)	113.74 (99.35 to 129.86)	8311 (7218 to 9441)	110.27 (96.65 to 126.18)	0.78% (0.7 to 0.88)	−0.13% (−0.15 to −0.11)
Bahrain	134 (115 to 153)	133.65 (117.28 to 152.36)	692 (594 to 788)	130.61 (114.78 to 148.7)	4.16% (3.9 to 4.42)	−0.05% (−0.06 to −0.04)
Bangladesh	30546 (26393 to 34911)	82.54 (71.13 to 94.38)	92254 (79987 to 105807)	79.47 (68.72 to 90.87)	2.02% (1.93 to 2.12)	−0.12% (−0.13 to −0.11)
Barbados	320 (276 to 374)	98.52 (86.53 to 112.22)	497 (433 to 573)	94.55 (82.58 to 109.16)	0.55% (0.47 to 0.64)	−0.14% (−0.16 to −0.12)
Belarus	14329 (12330 to 16547)	116.59 (101.35 to 133.27)	19115 (16467 to 21917)	116.35 (101.03 to 133.43)	0.33% (0.27 to 0.4)	0% (−0.01 to 0.02)
Belgium	22508 (19648 to 25797)	136.89 (120.08 to 155.5)	34245 (29719 to 39179)	121.59 (105.24 to 139.55)	0.52% (0.43 to 0.6)	−0.43% (−0.46 to −0.4)
Belize	91 (80 to 104)	101.05 (87.86 to 115)	244 (214 to 276)	97.17 (84.64 to 110.79)	1.67% (1.57 to 1.77)	−0.11% (−0.12 to −0.11)
Benin	1377 (1200 to 1579)	84.72 (73.95 to 97.15)	2909 (2552 to 3316)	75.85 (65.91 to 87.05)	1.11% (0.9 to 1.25)	−0.25% (−0.29 to −0.21)
Bermuda	56 (48 to 65)	99.8 (86.1 to 114.94)	150 (130 to 173)	98.24 (84.8 to 112.71)	1.66% (1.56 to 1.79)	−0.06% (−0.06 to −0.05)
Bhutan	129 (112 to 147)	83.88 (72.92 to 96.22)	415 (360 to 475)	77.45 (67.36 to 88.68)	2.22% (2.05 to 2.4)	−0.25% (−0.27 to −0.23)
Bolivia	2016 (1744 to 2305)	83.32 (72.16 to 95.49)	6052 (5222 to 6916)	82.05 (71.22 to 94.16)	2% (1.89 to 2.1)	−0.01% (−0.03 to 0.01)
Bosnia and Herzegovina	3521 (3015 to 4069)	111.71 (96.53 to 128.25)	7140 (6148 to 8275)	111.79 (96.79 to 127.27)	1.03% (0.94 to 1.13)	0.02% (−0.02 to 0.05)
Botswana	391 (337 to 448)	108.19 (93.86 to 123.77)	1062 (924 to 1218)	103.94 (90.71 to 119.61)	1.71% (1.58 to 1.83)	−0.1% (−0.12 to −0.08)
Brazil	90515 (79222 to 102650)	129.35 (113.26 to 146.89)	305421 (269292 to 345696)	127.08 (112.01 to 144.66)	2.37% (2.29 to 2.46)	−0.11% (−0.15 to −0.08)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Brunei	78 (67 to 91)	101.91 (88.2 to 118.19)	237 (205 to 273)	101.56 (88.37 to 116.86)	2.04% (1.88 to 2.2)	0.02% (−0.01 to 0.06)
Bulgaria	11721 (9853 to 13922)	114.97 (99.8 to 131.97)	17299 (14848 to 20198)	112.43 (97.8 to 128.73)	0.48% (0.38 to 0.58)	−0.08% (−0.11 to −0.06)
Burkina Faso	2570 (2214 to 2938)	85.31 (73.99 to 97.74)	5394 (4695 to 6140)	79.8 (69.33 to 91.77)	1.1% (1.02 to 1.18)	−0.23% (−0.24 to −0.23)
Burundi	1850 (1598 to 2124)	109.09 (95.51 to 124.1)	3237 (2823 to 3672)	100.5 (88.07 to 114.87)	0.75% (0.67 to 0.83)	−0.24% (−0.26 to −0.22)
Cambodia	3587 (3093 to 4101)	116.07 (101.32 to 132.03)	10162 (8838 to 11662)	112.21 (97.73 to 128.37)	1.83% (1.74 to 1.92)	−0.16% (−0.18 to −0.14)
Cameroon	2455 (2119 to 2795)	79.7 (69.02 to 91.36)	6433 (5588 to 7316)	75.45 (65.39 to 86.37)	1.62% (1.53 to 1.71)	−0.18% (−0.18 to −0.17)
Canada	48603 (43425 to 54209)	149.59 (134.39 to 165.87)	105264 (93819 to 117160)	132.4 (118.02 to 147.29)	1.17% (1.07 to 1.26)	−0.55% (−0.61 to −0.48)
Cape Verde	198 (170 to 230)	82.37 (70.98 to 94.3)	319 (276 to 363)	78.13 (67.85 to 89.4)	0.61% (0.52 to 0.71)	−0.18% (−0.18 to −0.17)
Central African Republic	865 (742 to 981)	132.85 (116.29 to 150.68)	1622 (1391 to 1837)	130.87 (114.21 to 148.33)	0.88% (0.79 to 1)	−0.1% (−0.11 to −0.08)
Chad	1872 (1620 to 2150)	84.07 (72.82 to 96.5)	3052 (2649 to 3472)	76.45 (66.54 to 87.28)	0.63% (0.57 to 0.7)	−0.32% (−0.33 to −0.31)
Chile	9601 (8388 to 10955)	109.85 (96.31 to 124.05)	28466 (24777 to 32535)	107.87 (93.91 to 123.11)	1.97% (1.82 to 2.13)	−0.03% (−0.05 to −0.01)
China	703178 (601506 to 808633)	121.11 (105.5 to 137.99)	2914112 (2504728 to 3350743)	151.47 (131.22 to 173.34)	3.14% (2.98 to 3.32)	0.41% (0.34 to 0.49)
Colombia	16113 (14111 to 18304)	113.71 (99.52 to 130.26)	63668 (55802 to 72058)	112.13 (97.75 to 127.51)	2.95% (2.79 to 3.12)	−0.03% (−0.05 to −0.01)
Comoros	138 (119 to 157)	105.26 (92.01 to 119.38)	381 (330 to 432)	100.96 (88.05 to 115.39)	1.76% (1.65 to 1.88)	−0.12% (−0.13 to −0.11)
Congo	857 (736 to 984)	124.97 (109.29 to 142.35)	2079 (1886 to 2269)	120.8 (109.94 to 132.53)	1.43% (1.22 to 1.68)	−0.08% (−0.11 to −0.06)
Cook Islands	11 (9 to 12)	111.54 (95.15 to 129.33)	28 (24 to 32)	109.53 (93.6 to 126.15)	1.61% (1.51 to 1.73)	−0.07% (−0.08 to −0.06)
Costa Rica	1812 (1578 to 2077)	113.52 (98.91 to 129.64)	6143 (5378 to 6985)	110.62 (95.96 to 126.87)	2.39% (2.27 to 2.52)	−0.07% (−0.09 to −0.06)
Cote d'Ivoire	1876 (1626 to 2132)	79.55 (69.19 to 91.73)	5598 (4850 to 6401)	76.63 (66.06 to 88.28)	1.98% (1.87 to 2.09)	−0.12% (−0.14 to −0.11)
Croatia	6091 (5281 to 7058)	116.47 (101.76 to 133.92)	11299 (9711 to 12993)	112.67 (98.23 to 128.39)	0.85% (0.77 to 0.94)	−0.08% (−0.1 to −0.07)
Cuba	9051 (7853 to 10346)	92.22 (80.31 to 104.84)	19278 (16865 to 21941)	91.41 (79.7 to 103.65)	1.13% (1 to 1.25)	−0.2% (−0.25 to −0.16)
Cyprus	831 (700 to 985)	122.06 (106.32 to 139.42)	2459 (2096 to 2871)	117.37 (101.52 to 134.87)	1.96% (1.77 to 2.2)	−0.09% (−0.11 to −0.07)
Czech Republic	15054 (12909 to 17515)	111.88 (97.48 to 128.14)	26327 (22779 to 30305)	111.23 (96.31 to 127.59)	0.75% (0.66 to 0.85)	−0.05% (−0.07 to −0.04)
Democratic Republic of the Congo	12092 (10446 to 13799)	126.38 (110.62 to 143.95)	29847 (26225 to 33722)	126.99 (111.77 to 144.57)	1.47% (1.36 to 1.59)	0.02% (−0.01 to 0.05)
Denmark	9292 (8124 to 10636)	102.88 (90.99 to 117.38)	11466 (9906 to 13148)	84.34 (72.78 to 96.21)	0.23% (0.16 to 0.3)	−0.73% (−0.76 to −0.69)
Djibouti	85 (74 to 96)	109.58 (95.81 to 124.89)	402 (347 to 454)	104.02 (90.57 to 118.65)	3.71% (3.56 to 3.86)	−0.13% (−0.14 to −0.11)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Dominica	58 (50 to 67)	99.5 (86.83 to 113.7)	74 (64 to 84)	96.57 (83.47 to 110.4)	0.27% (0.21 to 0.32)	−0.09% (−0.1 to −0.08)
Dominican Republic	2989 (2578 to 3425)	99.14 (86.33 to 112.62)	9479 (8275 to 10748)	99.53 (86.68 to 113.07)	2.17% (2.01 to 2.35)	−0.12% (−0.15 to −0.08)
Ecuador	3781 (3261 to 4331)	83.15 (71.74 to 95.91)	12517 (10756 to 14473)	81.16 (69.99 to 93.4)	2.31% (2.17 to 2.44)	−0.03% (−0.05 to −0.02)
Egypt	22678 (19874 to 25360)	130.73 (116.04 to 147.5)	50931 (44459 to 57309)	126.46 (111.45 to 144.07)	1.25% (1.16 to 1.33)	−0.04% (−0.07 to −0.02)
El Salvador	3066 (2698 to 3483)	111.03 (97.01 to 126.66)	7619 (6700 to 8708)	112.22 (98.14 to 128.45)	1.48% (1.38 to 1.57)	0.06% (0.05 to 0.08)
Equatorial Guinea	162 (141 to 184)	129.4 (113.39 to 147.34)	431 (377 to 490)	124.45 (108.79 to 141.57)	1.66% (1.56 to 1.76)	−0.15% (−0.16 to −0.14)
Eritrea	617 (528 to 702)	110.64 (96.26 to 126.77)	1735 (1503 to 1975)	104.21 (90.44 to 119.18)	1.81% (1.67 to 1.94)	−0.18% (−0.19 to −0.17)
Estonia	2268 (1946 to 2638)	113.98 (99.49 to 130.87)	3662 (3185 to 4204)	112.78 (98.89 to 128.28)	0.61% (0.53 to 0.7)	−0.01% (−0.05 to 0.04)
Ethiopia	13006 (11190 to 14826)	110.74 (96.77 to 126.37)	34226 (30050 to 38961)	102.87 (90.07 to 116.73)	1.63% (1.49 to 1.77)	−0.21% (−0.24 to −0.17)
Federated States of Micronesia	43 (37 to 50)	119.8 (102.66 to 137.56)	56 (48 to 64)	120.71 (104.84 to 139.46)	0.31% (0.24 to 0.38)	0.06% (0.05 to 0.07)
Fiji	255 (217 to 294)	112.73 (96.97 to 130.52)	582 (495 to 672)	110.65 (95.5 to 127.91)	1.28% (1.21 to 1.36)	−0.08% (−0.09 to −0.07)
Finland	9014 (7813 to 10306)	121.24 (105.54 to 137.41)	16662 (14213 to 19329)	108.45 (92.52 to 124.81)	0.85% (0.71 to 0.96)	−0.4% (−0.41 to −0.39)
France	91990 (82415 to 101758)	99.39 (89.46 to 109.62)	163141 (143062 to 184345)	93.63 (82.25 to 105.56)	0.77% (0.67 to 0.89)	−0.22% (−0.26 to −0.19)
Gabon	570 (494 to 652)	125.84 (109.61 to 143.75)	911 (794 to 1042)	123.01 (107.72 to 140.92)	0.6% (0.54 to 0.66)	−0.05% (−0.07 to −0.04)
Georgia	6399 (5542 to 7306)	113.74 (99.03 to 129.23)	7576 (6603 to 8611)	113.98 (99.53 to 129.49)	0.18% (0.13 to 0.24)	0.01% (0 to 0.02)
Germany	200149 (178695 to 222831)	145.12 (130.54 to 161.52)	339825 (299328 to 382749)	142.13 (124.57 to 159.72)	0.7% (0.58 to 0.82)	−0.1% (−0.13 to −0.07)
Ghana	3177 (2734 to 3631)	76.92 (66.34 to 88.65)	8608 (7446 to 9814)	75.09 (64.72 to 86.42)	1.71% (1.61 to 1.81)	−0.06% (−0.07 to −0.05)
Greece	18806 (16045 to 21942)	124.2 (107.47 to 142.66)	37087 (31838 to 42954)	119.17 (103.16 to 136.72)	0.97% (0.85 to 1.09)	−0.11% (−0.13 to −0.09)
Greenland	30 (26 to 35)	138.09 (119.55 to 159.13)	69 (60 to 79)	135.63 (117.63 to 156.11)	1.32% (1.22 to 1.43)	−0.07% (−0.1 to −0.05)
Grenada	83 (73 to 96)	99.53 (86.87 to 113.92)	92 (79 to 105)	98.02 (85.92 to 112.22)	0.1% (0.04 to 0.18)	−0.02% (−0.05 to 0.01)
Guam	54 (45 to 62)	109.67 (94.24 to 128.33)	242 (210 to 275)	108.97 (93.85 to 125.54)	3.52% (3.2 to 3.86)	−0.03% (−0.03 to −0.02)
Guatemala	2752 (2398 to 3134)	113.72 (99.12 to 129.64)	10938 (9620 to 12428)	112.54 (98.73 to 127.7)	2.97% (2.81 to 3.17)	−0.02% (−0.03 to 0)
Guinea	2174 (1893 to 2477)	83.16 (72.43 to 95.24)	3372 (2920 to 3850)	78.39 (67.86 to 90.01)	0.55% (0.5 to 0.6)	−0.19% (−0.21 to −0.18)
Guinea-Bissau	197 (169 to 224)	79.09 (68.36 to 91.21)	330 (283 to 376)	77.05 (66.66 to 89.04)	0.67% (0.62 to 0.73)	−0.07% (−0.08 to −0.06)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Guyana	289 (250 to 332)	97.11 (84.1 to 111.09)	481 (419 to 548)	96.25 (83.56 to 110.32)	0.67% (0.61 to 0.73)	−0.04% (−0.05 to −0.03)
Haiti	2210 (1904 to 2514)	102.3 (89.46 to 116.07)	4672 (4066 to 5354)	94.82 (82.42 to 108.66)	1.11% (1.04 to 1.18)	−0.26% (−0.28 to −0.25)
Honduras	1845 (1608 to 2107)	115.03 (100.77 to 131.35)	5675 (4919 to 6495)	113.19 (98.75 to 129.15)	2.08% (1.96 to 2.19)	−0.05% (−0.06 to −0.05)
Hungary	15685 (13499 to 18318)	112.52 (98.61 to 128.63)	24331 (21065 to 27869)	111.47 (96.69 to 127.63)	0.55% (0.47 to 0.64)	−0.02% (−0.05 to 0.02)
Iceland	416 (363 to 469)	135.01 (117.98 to 152.05)	799 (689 to 898)	122.36 (106.34 to 137.53)	0.92% (0.84 to 1)	−0.36% (−0.38 to −0.35)
India	241550 (209565 to 274946)	79.45 (68.69 to 90.82)	749490 (648646 to 856823)	78.92 (68.29 to 90.58)	2.1% (2.02 to 2.18)	−0.16% (−0.21 to −0.11)
Indonesia	78840 (68676 to 89397)	115.97 (101.07 to 132)	189722 (164142 to 216604)	113.31 (98.38 to 129.52)	1.41% (1.37 to 1.45)	−0.07% (−0.09 to −0.05)
Iran	23334 (20148 to 26479)	137.67 (120.79 to 156.35)	87937 (77508 to 99879)	133.73 (117.53 to 151.85)	2.77% (2.55 to 2.99)	−0.08% (−0.09 to −0.07)
Iraq	9439 (8246 to 10706)	135.28 (117.85 to 154.35)	22204 (19382 to 25184)	129.62 (113.05 to 148.98)	1.35% (1.26 to 1.45)	−0.17% (−0.19 to −0.16)
Ireland	4990 (4265 to 5795)	122.27 (105.91 to 140.72)	9579 (8205 to 11080)	111.99 (95.75 to 128.99)	0.92% (0.84 to 1.01)	−0.3% (−0.32 to −0.27)
Israel	5742 (4862 to 6706)	120.3 (103.78 to 138.38)	15408 (13247 to 17722)	113.13 (97.01 to 130.26)	1.68% (1.53 to 1.85)	−0.21% (−0.22 to −0.2)
Italy	106541 (89872 to 123112)	116.29 (98.96 to 133.09)	248809 (215069 to 285482)	134.76 (116.74 to 153.65)	1.34% (1.21 to 1.49)	0.28% (0.09 to 0.46)
Jamaica	2078 (1816 to 2383)	110.63 (96.95 to 126.27)	3490 (3046 to 3974)	104.77 (91.01 to 120.07)	0.68% (0.6 to 0.78)	−0.2% (−0.21 to −0.18)
Japan	184306 (160124 to 210886)	115.81 (101.01 to 131.94)	576270 (503457 to 662794)	117.23 (102.05 to 133.68)	2.13% (1.96 to 2.28)	0.2% (0.15 to 0.25)
Jordan	1219 (1065 to 1389)	133.38 (116.04 to 152.85)	7243 (6314 to 8274)	134.51 (116.99 to 153.81)	4.94% (4.74 to 5.14)	0.07% (0.03 to 0.1)
Kazakhstan	11926 (10449 to 13735)	113.75 (99.27 to 130.56)	15444 (13387 to 17642)	111.1 (96.76 to 126.81)	0.3% (0.23 to 0.36)	−0.08% (−0.1 to −0.05)
Kenya	6572 (5713 to 7457)	106.99 (93.29 to 121.75)	16494 (14435 to 18732)	105.14 (91.55 to 119.62)	1.51% (1.46 to 1.56)	−0.06% (−0.08 to −0.04)
Kiribati	28 (24 to 32)	121.16 (104.74 to 139.34)	54 (46 to 62)	121.84 (106.12 to 138.96)	0.92% (0.85 to 1)	0.01% (−0.02 to 0.04)
Kuwait	544 (478 to 612)	137.77 (120.63 to 157)	2814 (2484 to 3155)	131.46 (115.44 to 149.34)	4.17% (3.98 to 4.36)	−0.15% (−0.17 to −0.13)
Kyrgyzstan	2913 (2546 to 3333)	112.94 (98.41 to 128.4)	4134 (3622 to 4676)	113.88 (99.39 to 130.07)	0.42% (0.35 to 0.49)	0.05% (0.04 to 0.06)
Laos	1569 (1344 to 1800)	114.26 (100.61 to 130.8)	3764 (3280 to 4290)	111.82 (97.43 to 127.89)	1.4% (1.3 to 1.52)	−0.06% (−0.07 to −0.04)
Latvia	4055 (3487 to 4705)	114.61 (99.77 to 131.15)	5467 (4733 to 6277)	114.97 (99.97 to 131)	0.35% (0.29 to 0.42)	0.04% (0.02 to 0.06)
Lebanon	2401 (2107 to 2744)	139.66 (122.17 to 159.68)	9167 (8003 to 10453)	140.48 (122.53 to 159.62)	2.82% (2.61 to 2.99)	0% (−0.01 to 0.01)
Lesotho	738 (639 to 841)	110.5 (95.98 to 126.11)	791 (682 to 906)	108.92 (94.83 to 124.74)	0.07% (0.02 to 0.11)	−0.02% (−0.03 to −0.01)
Liberia	664 (570 to 761)	77.77 (67.19 to 89.07)	1101 (956 to 1253)	75.16 (64.95 to 86.14)	0.66% (0.58 to 0.74)	−0.11% (−0.12 to −0.1)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Libya	2154 (1898 to 2432)	137.01 (120.05 to 155.79)	5287 (4619 to 5998)	130.47 (114.04 to 148.13)	1.45% (1.38 to 1.52)	−0.16% (−0.18 to −0.14)
Lithuania	5085 (4375 to 5890)	113.06 (98.58 to 129.94)	7771 (6694 to 9018)	112.73 (98.22 to 129.2)	0.53% (0.47 to 0.59)	0.02% (−0.01 to 0.05)
Luxembourg	558 (475 to 655)	100.78 (86.37 to 116.34)	1033 (880 to 1191)	87.36 (74.31 to 101.13)	0.85% (0.66 to 1.01)	−0.51% (−0.57 to −0.45)
Macedonia	1754 (1525 to 2006)	111.85 (97.22 to 128.3)	3033 (2587 to 3532)	111.12 (96.41 to 127.65)	0.73% (0.63 to 0.83)	−0.01% (−0.02 to 0)
Madagascar	3781 (3272 to 4304)	105.1 (91.62 to 120.32)	6743 (5808 to 7654)	99.76 (86.8 to 114.13)	0.78% (0.71 to 0.87)	−0.15% (−0.17 to −0.14)
Malawi	2683 (2316 to 3057)	105.4 (91.35 to 120.59)	5280 (4599 to 6027)	104.71 (90.82 to 119.89)	0.97% (0.9 to 1.04)	−0.01% (−0.02 to 0.01)
Malaysia	9071 (7978 to 10274)	116.13 (101.28 to 132.46)	26046 (22443 to 29858)	111.29 (95.99 to 127.46)	1.87% (1.77 to 1.98)	−0.12% (−0.13 to −0.1)
Maldives	62 (54 to 71)	109.84 (95.49 to 126.07)	309 (269 to 355)	113.22 (98.24 to 129.67)	3.95% (3.67 to 4.26)	0.1% (0.07 to 0.13)
Mali	2125 (1833 to 2421)	81.91 (71.19 to 93.65)	4712 (4072 to 5355)	78.55 (68.4 to 89.84)	1.22% (1.14 to 1.29)	−0.13% (−0.14 to −0.12)
Malta	489 (421 to 568)	122.8 (106.32 to 141.45)	1295 (1113 to 1493)	113.91 (98.03 to 130.83)	1.65% (1.51 to 1.78)	−0.22% (−0.25 to −0.2)
Marshall Islands	12 (10 to 14)	107.43 (92.62 to 124.49)	21 (17 to 24)	103.94 (89.43 to 120.5)	0.76% (0.67 to 0.87)	−0.11% (−0.11 to −0.1)
Mauritania	627 (537 to 722)	83.53 (71.72 to 96.45)	1316 (1142 to 1500)	77.53 (67.33 to 88.83)	1.1% (1.03 to 1.18)	−0.24% (−0.25 to −0.23)
Mauritius	616 (532 to 710)	112.36 (97.71 to 130.05)	1883 (1629 to 2139)	111.73 (96.55 to 127.55)	2.06% (1.94 to 2.18)	0.01% (−0.01 to 0.04)
Mexico	36269 (31428 to 41673)	106.03 (91.84 to 120.63)	110467 (96168 to 125494)	97.19 (84.27 to 111.26)	2.05% (1.96 to 2.13)	−0.19% (−0.23 to −0.15)
Moldova	3862 (3317 to 4453)	110.64 (96.04 to 126.38)	6801 (5910 to 7736)	111.97 (97.12 to 128.21)	0.76% (0.67 to 0.86)	0.03% (0.01 to 0.05)
Mongolia	952 (823 to 1095)	114.4 (99.85 to 130.62)	1819 (1599 to 2051)	115.83 (101.21 to 132.52)	0.91% (0.83 to 0.99)	0.05% (0.04 to 0.06)
Montenegro	654 (571 to 754)	114.61 (100.1 to 131.64)	1006 (863 to 1163)	111.66 (97.13 to 128.15)	0.54% (0.47 to 0.6)	−0.12% (−0.16 to −0.08)
Morocco	16234 (14139 to 18419)	136.84 (120 to 155.37)	36514 (31637 to 41831)	127.85 (111.31 to 146.15)	1.25% (1.18 to 1.33)	−0.23% (−0.23 to −0.22)
Mozambique	4334 (3745 to 4930)	107.72 (94.15 to 122.63)	7516 (6505 to 8549)	104.33 (90.49 to 119.04)	0.73% (0.68 to 0.79)	−0.08% (−0.1 to −0.07)
Myanmar	19762 (17257 to 22522)	122.22 (107.45 to 139.08)	44028 (38392 to 49952)	113.09 (99.06 to 128.82)	1.23% (1.14 to 1.32)	−0.27% (−0.28 to −0.25)
Namibia	454 (393 to 517)	107.16 (93.53 to 121.95)	1012 (884 to 1148)	103.46 (89.84 to 117.7)	1.23% (1.13 to 1.33)	−0.11% (−0.12 to −0.09)
Nepal	5687 (4970 to 6481)	91.22 (79.31 to 104.24)	14856 (12919 to 16960)	81.31 (70.51 to 93.7)	1.61% (1.51 to 1.72)	−0.45% (−0.48 to −0.42)
Netherlands	26947 (23614 to 29768)	127.6 (112.23 to 140.58)	48272 (42168 to 54730)	121.79 (106.84 to 137.86)	0.79% (0.69 to 0.91)	−0.14% (−0.16 to −0.11)
New Zealand	4957 (4294 to 5705)	128.02 (110.92 to 146.45)	11097 (9639 to 12753)	120.84 (104.92 to 138.57)	1.24% (1.16 to 1.32)	−0.22% (−0.25 to −0.19)
Nicaragua	1443 (1268 to 1638)	115.45 (101.47 to 131.74)	4883 (4277 to 5562)	114.62 (100.58 to 131.05)	2.38% (2.26 to 2.5)	0% (−0.01 to 0.01)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Niger	1433 (1238 to 1632)	83.26 (72.29 to 95.94)	4296 (3712 to 4924)	78.36 (68.05 to 90.06)	2% (1.89 to 2.12)	−0.2% (−0.21 to −0.19)
Nigeria	24795 (21494 to 28164)	75.45 (65.4 to 86.12)	45312 (39635 to 51186)	68.83 (59.58 to 78.6)	0.83% (0.79 to 0.87)	−0.31% (−0.35 to −0.27)
North Korea	12410 (10608 to 14299)	110.89 (95.65 to 127.83)	31408 (26865 to 36668)	108.5 (93.89 to 125.37)	1.53% (1.38 to 1.68)	−0.09% (−0.11 to −0.07)
Northern Mariana Islands	10 (9 to 12)	109.52 (93.43 to 127.91)	38 (32 to 44)	107.94 (92.46 to 125.17)	2.78% (2.6 to 2.97)	−0.04% (−0.05 to −0.03)
Norway	10640 (9278 to 12217)	136.54 (119.38 to 155.02)	13149 (11352 to 15113)	114.3 (98.69 to 131.41)	0.24% (0.18 to 0.28)	−0.64% (−0.69 to −0.6)
Oman	636 (553 to 722)	132.92 (116.54 to 151.46)	1619 (1401 to 1863)	124.36 (108.14 to 143.21)	1.54% (1.44 to 1.64)	−0.2% (−0.24 to −0.15)
Pakistan	37269 (32344 to 42652)	84.44 (73.08 to 97.03)	67818 (58773 to 77287)	78.8 (67.99 to 90.38)	0.82% (0.77 to 0.87)	−0.25% (−0.26 to −0.24)
Palestine	961 (838 to 1094)	136.47 (119.22 to 154.4)	2402 (2103 to 2729)	131.55 (115.83 to 150.08)	1.5% (1.41 to 1.59)	−0.13% (−0.16 to −0.1)
Panama	1472 (1291 to 1676)	110.21 (95.8 to 125.86)	4943 (4336 to 5638)	108.64 (94.58 to 124.54)	2.36% (2.23 to 2.5)	−0.05% (−0.06 to −0.05)
Papua New Guinea	1229 (1051 to 1409)	120.02 (105.08 to 136.87)	3500 (3026 to 3981)	112.89 (97.86 to 129.7)	1.85% (1.73 to 1.97)	−0.25% (−0.28 to −0.22)
Paraguay	2431 (2118 to 2756)	123.19 (107.15 to 139.9)	6135 (5388 to 6970)	115.77 (101.31 to 132.33)	1.52% (1.45 to 1.6)	−0.22% (−0.23 to −0.21)
Peru	8297 (7192 to 9389)	78.97 (68.46 to 90.1)	25917 (22445 to 29526)	78.28 (67.57 to 89.77)	2.12% (1.99 to 2.24)	−0.09% (−0.11 to −0.06)
Philippines	25715 (22304 to 29465)	119.03 (104.7 to 135.62)	72092 (63052 to 81980)	113.91 (99.74 to 130)	1.8% (1.74 to 1.88)	−0.18% (−0.19 to −0.16)
Poland	48711 (41946 to 56293)	120.58 (105.09 to 137.37)	88407 (76685 to 101187)	114.27 (99.44 to 130.4)	0.81% (0.75 to 0.89)	−0.18% (−0.19 to −0.17)
Portugal	15775 (13603 to 18445)	118.74 (102.91 to 136.33)	35666 (30670 to 41514)	116.97 (100.45 to 134.76)	1.26% (1.11 to 1.42)	−0.02% (−0.04 to 0)
Principality of Monaco	104 (90 to 122)	123.3 (106.75 to 141.67)	136 (116 to 157)	113.72 (97.81 to 131.33)	0.3% (0.24 to 0.37)	−0.28% (−0.28 to −0.27)
Puerto Rico	3509 (3010 to 4024)	99.86 (86.41 to 113.62)	8775 (7670 to 10036)	97.8 (84.88 to 112.14)	1.5% (1.35 to 1.66)	−0.08% (−0.09 to −0.07)
Qatar	75 (66 to 85)	129.42 (112.13 to 147.88)	640 (553 to 721)	126.56 (110.1 to 145.4)	7.52% (7.22 to 7.84)	−0.01% (−0.05 to 0.02)
Republic of Nauru	3 (2 to 3)	110.81 (95.43 to 128.03)	4 (4 to 5)	113.97 (98.71 to 131.23)	0.42% (0.37 to 0.47)	0.06% (0.02 to 0.1)
Republic of Niue	3 (2 to 3)	110.25 (95.02 to 127.06)	2 (2 to 3)	107.28 (91.33 to 123.83)	−0.21% (−0.24 to −0.17)	−0.11% (−0.12 to −0.1)
Republic of Palau	8 (6 to 9)	107.16 (91.89 to 124.54)	16 (13 to 18)	103.98 (88.42 to 120.53)	1.08% (0.99 to 1.18)	−0.09% (−0.09 to −0.08)
Republic of San Marino	47 (41 to 54)	124.29 (108.62 to 141.54)	106 (92 to 122)	110.9 (96.02 to 127.71)	1.24% (1.13 to 1.38)	−0.38% (−0.4 to −0.36)
Romania	26480 (22582 to 30911)	111.56 (96.96 to 128.05)	46175 (39788 to 53464)	111.32 (96.82 to 127.73)	0.74% (0.64 to 0.86)	−0.03% (−0.05 to −0.02)
Russian Federation	183438 (158327 to 212154)	117.07 (102.29 to 133.67)	279806 (243531 to 319869)	115.89 (101.23 to 131.98)	0.53% (0.45 to 0.6)	−0.07% (−0.12 to −0.03)
Rwanda	1927 (1661 to 2194)	107.03 (93.96 to 122.04)	4609 (4024 to 5193)	106.57 (93.24 to 120.76)	1.39% (1.31 to 1.47)	0.04% (0.02 to 0.06)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Saint Kitts and Nevis	35 (30 to 41)	94.29 (82.57 to 107.74)	48 (42 to 56)	93.38 (80.85 to 107.47)	0.39% (0.3 to 0.49)	−0.04% (−0.05 to −0.03)
Saint Lucia	78 (66 to 90)	98.8 (85.78 to 113.56)	223 (192 to 255)	95.98 (82.99 to 109.74)	1.87% (1.73 to 2.02)	−0.12% (−0.14 to −0.1)
Saint Vincent and the Grenadines	67 (58 to 77)	101.6 (88.04 to 115.94)	128 (111 to 146)	96.56 (84.19 to 110.27)	0.9% (0.83 to 0.97)	−0.16% (−0.17 to −0.16)
Samoa	70 (60 to 81)	111.48 (96.61 to 128.63)	125 (107 to 144)	108.37 (93.13 to 125.19)	0.77% (0.71 to 0.84)	−0.11% (−0.12 to −0.1)
Sao Tome and Principe	42 (36 to 48)	78.52 (67.94 to 90.02)	60 (52 to 70)	73.4 (63.08 to 84.79)	0.43% (0.36 to 0.48)	−0.21% (−0.23 to −0.19)
Saudi Arabia	5403 (4676 to 6166)	127.34 (111.13 to 146.35)	13064 (11315 to 14779)	120.44 (104.42 to 138.45)	1.42% (1.28 to 1.56)	−0.19% (−0.2 to −0.17)
Senegal	1956 (1686 to 2231)	82.21 (71.27 to 94.43)	4513 (3919 to 5167)	76.64 (66.53 to 88.26)	1.31% (1.23 to 1.39)	−0.26% (−0.26 to −0.25)
Serbia	9635 (8166 to 11105)	111.13 (96.63 to 127.15)	19543 (16949 to 22543)	111.65 (96.91 to 128.06)	1.03% (0.9 to 1.17)	0% (−0.01 to 0.01)
Seychelles	63 (54 to 72)	113.14 (98.39 to 129.4)	108 (94 to 124)	109.25 (94.47 to 126.6)	0.72% (0.64 to 0.8)	−0.13% (−0.14 to −0.13)
Sierra Leone	1360 (1174 to 1557)	83.78 (72.77 to 95.51)	2201 (1908 to 2531)	79.15 (68.54 to 91.02)	0.62% (0.57 to 0.68)	−0.18% (−0.19 to −0.17)
Singapore	1572 (1364 to 1762)	91.55 (80.57 to 102.5)	7764 (6988 to 8584)	94.88 (85.54 to 104.85)	3.94% (3.64 to 4.27)	0.15% (0.12 to 0.17)
Slovakia	6379 (5512 to 7366)	112.67 (98.27 to 128.86)	10646 (9281 to 12234)	110.87 (97.08 to 127)	0.67% (0.6 to 0.74)	−0.05% (−0.06 to −0.04)
Slovenia	2666 (2305 to 3076)	110.1 (96.03 to 125.51)	5733 (4981 to 6582)	110.51 (96.63 to 126.67)	1.15% (1.05 to 1.27)	0.05% (0.02 to 0.08)
Solomon Islands	90 (77 to 104)	113.58 (98.83 to 130.2)	256 (219 to 295)	113.74 (98.07 to 131.08)	1.84% (1.72 to 1.97)	0.05% (0.02 to 0.07)
Somalia	1476 (1284 to 1670)	107.79 (94.2 to 122.85)	3590 (3086 to 4105)	106.72 (93.34 to 121.51)	1.43% (1.31 to 1.55)	−0.02% (−0.02 to −0.01)
South Africa	19443 (16975 to 21983)	114.18 (99.52 to 130.09)	39715 (34529 to 45264)	107.78 (93.63 to 122.59)	1.04% (1.01 to 1.07)	−0.16% (−0.17 to −0.14)
South Korea	26566 (23162 to 30284)	127.7 (112.52 to 145.12)	117489 (102910 to 133127)	124.63 (109.44 to 140.89)	3.42% (3.15 to 3.71)	0.01% (−0.04 to 0.06)
South Sudan	1980 (1716 to 2266)	105.62 (92.12 to 120.57)	2565 (2229 to 2899)	99.16 (85.85 to 113.38)	0.3% (0.24 to 0.35)	−0.19% (−0.21 to −0.16)
Spain	65155 (57005 to 72708)	117.06 (103.03 to 129.59)	123770 (107148 to 142152)	102.5 (88.99 to 116.45)	0.9% (0.72 to 1.1)	−0.37% (−0.44 to −0.3)
Sri Lanka	9121 (7923 to 10420)	111.29 (96.77 to 127.29)	25786 (22299 to 29882)	107.46 (93.3 to 123.54)	1.83% (1.73 to 1.93)	−0.13% (−0.14 to −0.12)
Sudan	9489 (8219 to 10856)	134.77 (118.25 to 154.07)	18538 (16236 to 21018)	125.81 (110.08 to 143.27)	0.95% (0.87 to 1.04)	−0.23% (−0.24 to −0.22)
Suriname	232 (203 to 263)	105.02 (91.54 to 120.14)	580 (506 to 663)	100.19 (87.41 to 115.47)	1.49% (1.4 to 1.57)	−0.16% (−0.18 to −0.15)
Swaziland	203 (176 to 231)	105.08 (91.43 to 120.24)	359 (310 to 411)	101.07 (88.65 to 115.8)	0.77% (0.7 to 0.84)	−0.13% (−0.14 to −0.12)
Sweden	24220 (21341 to 27345)	137.72 (121.98 to 154.24)	33511 (29061 to 38427)	126.32 (109.55 to 144.06)	0.38% (0.31 to 0.46)	−0.24% (−0.27 to −0.2)
Switzerland	14539 (12610 to 16716)	124.61 (108.66 to 142.14)	24776 (21498 to 28441)	113.27 (97.88 to 129.61)	0.7% (0.62 to 0.79)	−0.34% (−0.36 to −0.32)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Syria	5625 (4949 to 6361)	139.41 (122.36 to 159.02)	13051 (11335 to 14936)	129.77 (113.5 to 147.95)	1.32% (1.24 to 1.42)	−0.24% (−0.25 to −0.23)
Taiwan (Province of China)	10337 (8829 to 11878)	91.21 (78.72 to 104.55)	43204 (36980 to 48565)	98.1 (83.69 to 110.2)	3.18% (2.81 to 3.62)	0.38% (0.29 to 0.47)
Tajikistan	2619 (2301 to 2977)	111.93 (98.19 to 127.63)	4157 (3626 to 4715)	104.98 (92.03 to 120.4)	0.59% (0.51 to 0.67)	−0.23% (−0.23 to −0.22)
Tanzania	8091 (7036 to 9220)	107.04 (92.95 to 122.58)	18873 (16815 to 21095)	98.48 (87.78 to 110.14)	1.33% (1.2 to 1.47)	−0.25% (−0.26 to −0.23)
Thailand	27746 (24164 to 31442)	102.51 (89.15 to 116.4)	112595 (98738 to 127875)	103.27 (90.64 to 117.58)	3.06% (2.87 to 3.25)	0.12% (0.06 to 0.17)
The Bahamas	128 (111 to 145)	97.29 (84.85 to 110.7)	326 (285 to 372)	95.28 (82.97 to 109.64)	1.56% (1.47 to 1.64)	−0.07% (−0.08 to −0.07)
The Gambia	198 (171 to 226)	84.22 (73.25 to 96.89)	573 (493 to 658)	77.92 (67.57 to 89.88)	1.89% (1.77 to 2.02)	−0.26% (−0.27 to −0.25)
Timor-Leste	214 (187 to 241)	120.37 (105.37 to 137.35)	768 (666 to 888)	113.2 (98.46 to 129.74)	2.6% (2.4 to 2.83)	−0.18% (−0.2 to −0.16)
Togo	673 (587 to 768)	81.07 (70.07 to 92.89)	1900 (1634 to 2158)	78.26 (67.73 to 90)	1.82% (1.73 to 1.93)	−0.09% (−0.1 to −0.09)
Tokelau	1 (1 to 2)	111.36 (95.94 to 128.64)	2 (1 to 2)	109.37 (94.11 to 126.6)	0.24% (0.19 to 0.3)	−0.06% (−0.07 to −0.05)
Tonga	49 (42 to 56)	115.12 (99.63 to 133.62)	84 (73 to 97)	111.8 (97.12 to 128.75)	0.71% (0.63 to 0.79)	−0.11% (−0.12 to −0.09)
Trinidad and Tobago	735 (632 to 849)	100.82 (87.88 to 115.33)	1821 (1586 to 2070)	98.6 (85.73 to 112.51)	1.48% (1.36 to 1.62)	−0.06% (−0.07 to −0.05)
Tunisia	5480 (4747 to 6265)	142.94 (125.86 to 162.19)	15845 (13951 to 18011)	134.32 (117.99 to 153.04)	1.89% (1.77 to 2.02)	−0.19% (−0.2 to −0.18)
Turkey	40370 (35493 to 45675)	147.22 (129.54 to 166.99)	117991 (102838 to 133396)	139.1 (120.57 to 158.16)	1.92% (1.82 to 2.03)	−0.22% (−0.24 to −0.2)
Turkmenistan	1643 (1437 to 1865)	112.55 (98.74 to 128.5)	3296 (2869 to 3741)	107.05 (93.39 to 122.99)	1.01% (0.93 to 1.09)	−0.18% (−0.21 to −0.16)
Tuvalu	5 (4 to 6)	116.09 (100.33 to 134.46)	9 (8 to 11)	113.41 (97.97 to 130.03)	0.84% (0.75 to 0.92)	−0.07% (−0.08 to −0.06)
Uganda	4803 (4138 to 5478)	104.09 (91.02 to 118.56)	10731 (9352 to 12174)	102.68 (89.05 to 117.37)	1.23% (1.16 to 1.31)	−0.05% (−0.07 to −0.02)
Ukraine	77996 (66902 to 90222)	119.03 (103.58 to 135.93)	93467 (80738 to 107940)	115.57 (100.64 to 132.68)	0.2% (0.14 to 0.26)	−0.11% (−0.15 to −0.07)
United Arab Emirates	313 (269 to 359)	123.53 (107.13 to 142.63)	2324 (1963 to 2691)	113.49 (98.05 to 131.08)	6.42% (5.66 to 7.2)	−0.26% (−0.29 to −0.23)
United Kingdom	112869 (97201 to 130280)	114.58 (99.74 to 130.77)	164947 (142721 to 190062)	107.93 (93.37 to 123.89)	0.46% (0.43 to 0.5)	−0.17% (−0.2 to −0.13)
United States	471556 (410796 to 540646)	138.61 (120.85 to 157.59)	822911 (718803 to 935112)	131.29 (113.93 to 149.6)	0.75% (0.71 to 0.78)	−0.19% (−0.2 to −0.17)
Uruguay	4422 (3835 to 5070)	112.68 (98.67 to 128.38)	7017 (6124 to 8053)	107.09 (93.07 to 121.78)	0.59% (0.52 to 0.67)	−0.21% (−0.23 to −0.19)
Uzbekistan	11116 (9612 to 12821)	106.71 (92.5 to 122.44)	20088 (17467 to 22885)	106.19 (92.22 to 122.08)	0.81% (0.72 to 0.9)	−0.02% (−0.04 to −0.01)
Vanuatu	40 (34 to 47)	107.32 (92.84 to 124.06)	119 (101 to 138)	105.3 (90.64 to 121.61)	1.94% (1.84 to 2.06)	−0.08% (−0.1 to −0.06)
Venezuela	10207 (8939 to 11608)	127.09 (110.71 to 143.85)	34325 (30254 to 38771)	124.37 (108.4 to 141.62)	2.36% (2.21 to 2.51)	−0.08% (−0.12 to −0.05)

(Continues)

TABLE 2 (Continued)

location	Incidence cases_1990	ASIR_1990	Incidence cases _2021	ASIR_2021	Change of cases	EAPC_ASIR
Vietnam	39852 (34721 to 45600)	116.54 (102.61 to 133.79)	90172 (78824 to 102840)	110.09 (96.21 to 126.57)	1.26% (1.19 to 1.33)	−0.22% (−0.23 to −0.21)
Virgin Islands, U.S.	63 (55 to 73)	97.53 (84.95 to 111.49)	181 (156 to 212)	94.57 (82.02 to 109.17)	1.86% (1.72 to 2.01)	−0.11% (−0.12 to −0.11)
Yemen	4712 (4099 to 5383)	144.23 (127.32 to 163.56)	13410 (11724 to 15191)	133.11 (117.14 to 151.66)	1.85% (1.75 to 1.95)	−0.27% (−0.29 to −0.24)
Zambia	1986 (1720 to 2255)	102.35 (89.13 to 116.62)	4723 (4112 to 5326)	102.65 (89.99 to 117.22)	1.38% (1.31 to 1.45)	0.06% (0.04 to 0.08)
Zimbabwe	2998 (2580 to 3417)	106.36 (93.06 to 121.67)	4505 (3921 to 5133)	102.44 (89.41 to 116.93)	0.5% (0.45 to 0.56)	−0.11% (−0.12 to −0.1)

Abbreviation: ASIR, age-standardized incidence rate; EAPC, estimated annual percent change.

significantly around the world as life expectancy continues to rise.[9] Our analysis corroborates this observation, indicating that the disease burden of ADODs primarily impacts elderly individuals. The incidence, prevalence, death, and DALYs due to ADODs all rise with age. One report highlighted that the societal cost of ADODs is equivalent to that of cancer, heart disease, and stroke.[10] The global socioeconomic cost of ADODs is estimated at $957.56 billion.[11] ADODs have emerged as the seventh leading cause of death globally.[12] Over time, ADODs will pose a more severe burden on older families, societies, countries, and the world.

During this period, women consistently outperformed men in ASIR, ASPR, ASDR, and ASR of DALYs. Women bear a greater burden of disease than men. Differences in prevalence patterns between the sexes may be attributed to a variety of factors, including differences in reproductive ability, hormone levels, and the influence of mental states.[13] It is worth noting that despite the high proportion of women in the overall burden of disease, the EAPC for ASIR, ASPR, ASDR, and ASR of DALYs is higher for men than for women, meaning that the burden of disease is growing faster for men than for women.[14]

From 1990 to 2021, the incidence of ADODs in high-income Asia Pacific did not change much, but the prevalence increased. Japan,[15] South Korea,[16] and other countries[17] have entered an aging society. Benefiting from the popularization of early screening[18–20] and the relatively well-established medical system, the diagnosis rate of patients is high, and their survival duration is prolonged. Meanwhile, due to the rapid population aging,[21,22] unequal medical resources, insufficient statistics of new cases, and the high mortality rate of young males,[23] the incidence of Tropical Latin America decreased, but the prevalence still increased.

Compared with the reports in 2016[24] and 2019,[20] the EAPC changes of the three rates of global prevalence, mortality, and DALYs of ADODs in 1990–2021 were significantly lower than those in 1990–2016 and 1990–2019. Under the guidance of the WHO 's Global Action Plan for Public Health to Dementia 2017–2025,[25] countries around the world have increased awareness and attention to ADODs. The decline in the frequency of disease may be caused by the introduction of relevant policies, the improvement of medical service levels, the increase in the life expectancy, the increase in the number of casualties caused by war and hunger, and so on.

Inadequate health infrastructure in low SDI areas, poor delivery of health services, and poor management of health services with low levels of education will all contribute to a rapidly rising disease burden.[26] Our results show that in addition to the declining trend in high SDI areas, the death rate in other SDI areas showed an increasing trend between 2019 and 2021. In both 2020 and 2021, the coronavirus disease 2019 (COVID-19) –related death rate among individuals 60 years of age or older, across all income groups, exceeded 80% of the total COVID-19 death rate for the year 2019.[27] This may suggest that regions with higher SDIs had better medical support for ADODs during the COVID-19 pandemic, whereas those with lower SDIs experienced higher elderly mortality due to overwhelmed health care capacity.[28] From 1990 to 2021, the incidence, prevalence, mortality, and DALYs rose in high-middle and middle SDI regions, raising concerns.

To this day, no effective therapies exist to reverse ADODs, and pharmacological treatments face considerable constraints.[29] Consequently, targeting the risk factors of these diseases emerges as a feasible approach.[20] Risk factors for ADODs include type 2 diabetes,[30] smoking, air pollution, and so on.[31] Our DALY-benchmarked analysis shows that countries with a higher SDI have a higher prevalence of risk factors, elevated metabolic risks, and BMI. From 1990 to 2021, the burden of ADODs linked to high fasting blood glucose and BMI has generally increased globally.[32]

Because the disease burden of AD is intricately linked to age, early detection and intervention are of paramount importance for individuals and their families.[33] Currently, researchers are leveraging predictive models of AD to issue early warnings and identify high-risk populations.[34] Based on these findings, implementing intervention measures such as modifying unhealthy lifestyle habits and enhancing cognitive abilities[35] can significantly reduce or postpone the onset of AD.

This study is similar to, but not identical to, previous literature estimates of mortality and prevalence of ADODs in 1990. This may be

TABLE 3 Prevalence of Alzheimer's disease and other dementias in 1990 and 2021 for both sexes and all locations, with EAPC from 1990 and 2021.

	1990		2021		1990-2021
Characteristics	Prevalence cases (*10^6) (95% UI)	ASPR per 100,000 (95% UI)	Prevalence cases (*10^6) (95% UI)	ASPR per 100,000 (95% UI)	EAPC of ASPR (95% CI)
Global	21.8 [19.07–24.84]	672.22 [588.73–763.95]	56.86 [49.38–64.98]	694.01 [602.88–794.08]	0 [−0.02 to 0.03]
Sex					
Female	14.14 [12.36–16.11]	736.15 [646.05–834.27]	36.1 [31.47–41.12]	769.94 [670.71–877.57]	0.04 [0.01 to 0.06]
Male	7.66 [6.61–8.73]	571.47 [497.63–654.31]	20.75 [17.77–23.8]	589.47 [507.48-678.79]	0.03 [0.01 to 0.05]
Socio-demographic index					
High SDI	8.09 [7.09–9.19]	724.21 [637.6–815.94]	17.22 [15.03–19.55]	709.47 [619.94–807.4]	−0.05 [−0.06 to −0.04]
High-middle SDI	5.68 [4.93–6.52]	685.28 [598.24–781.65]	14.93 [12.86–17.16]	766.2 [659.8–879.64]	0.21 [0.17 to 0.25]
Middle SDI	4.83 [4.19–5.5]	651.47 [566.76–743.9]	16.8 [14.49–19.31]	723.42 [623.26–830.91]	0.12 [0.08 to 0.17]
Low-middle SDI	2.35 [2.03–2.68]	542.48 [473.62–616.16]	6.01 [5.21–6.84]	524.47 [455.82–596.8]	−0.17 [−0.19 to −0.15]
Low SDI	0.82 [0.7–0.93]	539.74 [471.27–612.06]	1.85 [1.6–2.1]	514.37 [447.22–584.18]	−0.19 [−0.21 to −0.18]
21 GBD Region					
Andean Latin America	0.08 [0.07–0.09]	450.85 [390.47–514.2]	0.25 [0.22–0.28]	444.09 [384.1–507.73]	−0.06 [−0.07 to −0.05]
Australasia	0.16 [0.14–0.18]	706.96 [614.59–802.27]	0.36 [0.32–0.41]	604.41 [526.77–679.94]	−0.54 [−0.58 to −0.5]
Caribbean	0.13 [0.11–0.15]	557.24 [485.64–629.27]	0.3 [0.26–0.34]	550.22 [476.89–624.84]	−0.15 [−0.18 to −0.12]
Central Asia	0.26 [0.22–0.29]	638.07 [553.08–725.58]	0.4 [0.35–0.45]	626.81 [541.85–713.52]	−0.06 [−0.08 to −0.04]
Central Europe	0.87 [0.75–1]	657.16 [565.4–750.94]	1.54 [1.33–1.77]	641.22 [554.05–732.31]	−0.09 [−0.09 to −0.08]
Central Latin America	0.42 [0.36–0.48]	625.86 [543.81–713.04]	1.4 [1.22–1.59]	596.48 [518.98–680.63]	−0.11 [−0.12 to −0.09]
Central Sub-Saharan Africa	0.1 [0.09–0.11]	752.86 [650.12–852.75]	0.25 [0.22–0.29]	750.54 [654.7–848.11]	0 [−0.02 to 0.03]
East Asia	4.15 [3.56–4.77]	697.26 [603.5–802.56]	17.41 [14.85–20.14]	887.95 [759.95–1027.48]	0.43 [0.35 to 0.51]
Eastern Europe	1.65 [1.43–1.9]	669.2 [578.77–768.96]	2.38 [2.06–2.73]	658.68 [571.31–752.67]	−0.08 [−0.12 to −0.04]
Eastern Sub-Saharan Africa	0.31 [0.26–0.35]	618.54 [538.17–701.19]	0.69 [0.6–0.78]	588.72 [513.88–667.2]	−0.14 [−0.15 to −0.14]
High-income Asia Pacific	1.18 [1.03–1.35]	658.06 [572.1–745.38]	4.11 [3.55–4.69]	684.82 [596.97–780.11]	0.28 [0.23 to 0.34]
High-income North America	3.02 [2.62–3.44]	815.9 [709.63–929.16]	5.51 [4.8–6.3]	775.11 [673.67–885.78]	−0.21 [−0.23 to −0.19]
North Africa and Middle East	0.98 [0.84–1.1]	812.51 [708.72–918.84]	2.68 [2.32–3.04]	772.66 [671.2–877.55]	−0.17 [−0.17 to −0.16]
Oceania	0.01 [0.01–0.01]	676.8 [584.15–778.03]	0.03 [0.03–0.03]	644.83 [554.28–737.37]	−0.2 [−0.22 to −0.18]
South Asia	1.76 [1.52–2.01]	446.47 [386.42–510.25]	5.15 [4.44–5.89]	437.07 [377–500.95]	−0.18 [−0.22 to −0.14]
Southeast Asia	1.27 [1.09–1.45]	675.02 [589.62–770.17]	3.39 [2.92–3.86]	644.38 [560.58–737.69]	−0.14 [−0.16 to −0.12]
Southern Latin America	0.26 [0.22–0.3]	622.39 [538.28–706.11]	0.55 [0.47–0.62]	595.26 [514.48–676.41]	−0.15 [−0.16 to −0.14]
Southern Sub-Saharan Africa	0.14 [0.12–0.16]	639.88 [554.13–730.43]	0.27 [0.23–0.31]	606.69 [524.69–692.07]	−0.14 [−0.16 to −0.13]
Tropical Latin America	0.54 [0.47–0.62]	758.68 [660.76–863.19]	1.86 [1.62–2.12]	759.83 [660–867.54]	−0.05 [−0.1 to −0.01]
Western Europe	4.23 [3.69–4.8]	691.03 [608.15–774.18]	7.75 [6.71–8.81]	670.36 [583.83–762.62]	−0.11 [−0.14 to −0.08]
Western Sub-Saharan Africa	0.28 [0.24–0.32]	436.85 [379.4–496.47]	0.57 [0.49–0.65]	406.02 [352.89–462.39]	−0.24 [−0.26 to −0.22]

Abbreviation: ASPR, age-standardized prevalence rate; EAPC, estimated annual percent change; SDI, sociodemographic index; 95% CI, 95% confidence intervals; 95% UI, 95% uncertainty level.

the continuous optimization of the statistical model and algorithm of the disease burden estimation by the GBD team. Update of data sources (new publication of historical statistical data, correction of original data), data cleaning, outlier processing, updating of new standard methods for missing value filling, and updating of covariates will all cause minor changes in estimated data. Based on the platform of GBD database, this research is to provide the latest results for ADOD policy research around the world and in various countries.

Previous articles[3,36] have documented the limitations of traditional methods, and so has this study. There are potential differences in data collection methods and accuracy between countries, but the GBD team's unified database construction standards, strict data review, and verification process provides us with reliable data. The inevitable deviations and gaps in modeling may lead to deviations between our findings and the actual disease burden. This study has some limitations. The GBD 2021 data used in this study is a secondary analysis. It is impossible to further explore the specific factors that cause the difference in regional disease burden. There are some limitations in using cross-sectional data to establish a causal relationship between risk factors and ADODs. Therefore, our analysis results need to be interpreted cautiously, which is worthy of further exploration and research.

5 | CONCLUSION

In summary, this study provides a comprehensive overview of the global epidemiological trends of ADODs spanning from 1990 to 2021. Notably, the risk of ADODs increases with age, making elderly individuals a critical population at risk. Despite widespread efforts, the disease burden remains significant across numerous countries and territories. Therefore, elders and females should be the primary focus of attention in ADOD prevention and management strategies.

ACKNOWLEDGMENTS

The authors thank all participants. This study was supported by the Shanxi Basic Research Project (grant number 20210302123317) and the Fund Program for the Scientific Activities of Selected Returned Overseas Professionals in Shanxi Province (grant number 20230023).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets analyzed during the current study are available.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Wang F, Li D, Gao X, Zhang X, Shi X, Guo Y. Alzheimer's and dementia: Diagnosis, assessment, and disease monitoring global, regional, and national burden of Alzheimer's disease and other dementias (ADODs) and their risk factors, 1990–2021: A systematic analysis for the Global Burden of Disease study 2021. *Alzheimer's Dement*. 2025;17:e70126. https://doi.org/10.1002/dad2.70126