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Original Article

The disease burden, risk factors and future predictions of Alzheimer's disease and other types of dementia in Asia from 1990 to 2021

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ABSTRACT

Background: There is a lack of analysis and prediction of the disease burden of Alzheimer's disease and other dementias (ADOD) in Asia.

Objectives: This study aims to explore the impact of ADOD on the Asian region during the period from 1990 to 2021.

Design: Data on ADOD in Asia from 1990 to 2021 were collected from the Global Burden of Disease (GBD) Study 2021. We analyzed the number and age-standardized rates (ASRs) of incidence, prevalence, mortality, and disability-adjusted life-years (DALYs) of ADOD from 1990 to 2021. Joinpoint regression analysis was performed, and the average annual percent changes (AAPCs) were calculated to evaluate the trends during this period. Subsequently, an auto - regressive integrated moving average (ARIMA) prediction model analysis was conducted to assess the trends in the next 30 years, aiming to report the epidemiology and disease burden of ADOD in Asia.

Results: According to the analysis of the GBD database in 2021, the deaths, DALYs, incidence, and prevalence of ADOD increased by 297.34 %, 249.54 %, 244.73 %, and 250.44 % in Asia from 1990 to 2021. The ASRs of incidence, prevalence, death, and DALYs in both males and females, which consistently increased over the study period, showed that the ASRs of all females were consistently higher than those of males in Asia from 1990 to 2021. During the period from 1990 to 2021, Qatar and the United Arab Emirates witnessed the greatest changes in the number of DALYs, incidence, and prevalence. Afghanistan and China had the highest age-standardized mortality rate (ASMR) in 2021. It is worth noting that high fasting blood glucose is the top risk factor for the onset of ADOD. Females are more susceptible to the risk factor of high body-mass index (BMI), while males are more likely to be affected by smoking. According to the analysis of the ARIMA prediction model, the disease burden of ADOD in Asia will continue to show an upward trend in the next 30 years.

Conclusions: We should pay attention to the issue of population aging, attach importance to the intervention measures targeting the risk factors of ADOD, and formulate action plans to address the rising incidence of ADOD.

Glossary

ADOD	Alzheimer's disease and other dementias
DALYs	disability-adjusted life-years
GBD	Global Burden of Disease
ASRs	age-standardized rates
ARIMA	auto-regressive integrated moving average
ASDR	Age-standardized DALY Rate
ASMR	Age-Standardized Mortality Rate
ASIR	Age-standardized Incidence Rate
ASPR	Age-standardized Prevalence Rate
AAPC	Average Annual Percent Change
APC	Annual Percent Change
YLL	years of life lost
YLD	years lived with disability
UI	uncertain interval
CI	Confidence Interval

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1. Introduction

Alzheimer's disease and related dementias (ADOD), typical degenerative neurological diseases [1], have become major causes of disability and death among the older adult. They have a profound impact on the quality of life and health of millions of people, and pose a severe global public health challenge. This health issue is becoming increasingly prominent and the situation is getting more critical in low - and middle - income countries. Regrettably, there is a severe scarcity, almost a complete lack, of epidemiological information in this area in these countries. Despite researchers' efforts, no effective preventive or curative measures have been found so far, hindering strategy formulation and complicating problem-solving [2,3]. According to the data retrieval results from the 2021 Global Burden of Disease (GBD) database, the number of global deaths due to ADOD was 1952,677.00 (95 % UI; 512,981.22–4984,737.48), and the number of deaths due to ADOD in Asia was 1026,938.69 (95 % UI, 267,220.27 - 2616,593.37), accounting for 52.60 % of the global deaths from ADOD. In addition, age-standardized disability-adjusted life-years (DALYs) rate (ASDR), age-standardized mortality rate (ASMR), age-standardized incidence rate (ASIR), and age-standardized prevalence rate (ASPR)in Asia showed a slow upward trend from 1990 to 2019, and a significant upward trend from 2019 to 2021. It was also reported that, affected by the Corona Virus Disease 2019 (COVID-19) pandemic, there has been a substantial increase in depression and anxiety [4]. Previous studies have confirmed that depression and anxiety are risk factors for Alzheimer's disease [5,6]. Therefore, the COVID - 19 pandemic may have an impact on the incidence and prevalence of Alzheimer's disease in Asia. Since the GBD database does not list depression and anxiety as risk factors for ADOD, we have not elaborated on this in this literature.

Given Alzheimer's incidence relates to age, its disease burden may rise with aging and longer life expectancy. Although there's no cure or prevention for dementia, more evidence shows over one-third of cases can be prevented/delayed by managing modifiable risk factors [7]. Long-term monitoring of the risk factors and prevalence trends of ADOD is crucial for global dementia prevention. The mortality rate of this disease is not determined by a single factor, but rather by the intricate interplay of numerous risk factors. Moreover, it exhibits distinct characteristics in different geographical regions [8]. According to research, long-term excessive alcohol consumption causes brain damage through multiple pathways. Thiamine deficiency is important. Meanwhile, ethanol and its metabolite acetaldehyde are toxic to the brain, eroding normal functions [9,10]. In addition, Long-term smoking is an important high-risk factor for the onset of dementia, some research indicates that quitting smoking in later life indeed has a positive impact on preventing dementia, which can reduce the number of dementia patients by 5 % [11]. Obesity is closely and complexly linked to Alzheimer's onset, interacting at multiple levels involving endocrine, inflammatory, and genetic factors. Specifically, obesity triggers metabolic disorders like insulin resistance, adiponectin resistance, and deficiency. It also activates inflammation, disrupts hormonal balance, and may change AD-related gene molecules. Through complex mechanisms, these factors are closely linked to Alzheimer's incidence and progression, forming an intricate pathological connection [12]. Some studies have shown that the Mediterranean diet is a healthy and sustainable dietary pattern, which is associated with a reduced risk of cognitive decline, dementia, and Alzheimer's disease [13]. In addition, in the field of Alzheimer's disease, the pathogenic mechanisms of genetic and environmental factors have not been fully elucidated [14]. It is projected that by 2050, the global economic burden borne by Alzheimer's disease will become even heavier. The geographical distribution of the economic burden and the health burden is severely uneven. The East Asia and Pacific region bears the brunt, suffering the most severe impact and the heaviest economic pressure. The regions of Europe, Central Asia, and North America follow closely behind [15]. However, research on Alzheimer's burden in Asia is limited. There's an urgent global need for more resources to curb its spread, especially with aging populations. This study aims to evaluate Alzheimer's incidence in Asia 1990–2021, analyze differences, assess risk factor burden, and predict related health. Deepening the understanding of the risk characteristics and pathogenesis of Alzheimer's disease and other types of dementia can help identify individuals at high risk of dementia at an early stage. Meanwhile, it also promotes the timely implementation of intervention measures to effectively reduce the disease burden imposed by dementia [16]. We hope it aids prevention, policy-making, health improvement, and resource allocation. Long-term monitoring of risk factors and trends is vital for global dementia prevention.

2. Methods

2.1. Data source

This study conducted a secondary analysis using the data from the 2021 GBD database. This research is a project of the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. The GBD applies a rules-based approach, integrating existing knowledge about the levels and patterns of various health outcomes, a large number of risk factors, and the responses of health systems. This study covers 204 countries and regions from 1990 to 2021, as well as data from the first - level administrative divisions of 22 countries [17]. At the same time, GBD provides data on incidence, prevalence, mortality, years of life lost (YLL), years lived with disability (YLD), and DALY related to 369 diseases and injuries. The data of GBD mainly come from censuses, surveys, hospital records, and administrative records. It follows the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) in a standardized and reproducible manner [17,18]. In terms of case definition, GBD adopts the definitions in the Diagnostic and Statistical Manual of Mental Disorders (DSM, including DSM-III, DSM-IV, or DSM-V) for surveys and cohort studies. Meanwhile, it uses the definitions in the International Classification of Diseases (ICD, including ICD-8, ICD-9, and ICD-10) for vital registration and claims data sources [19]. Dementia is defined as "a progressive, degenerative chronic neurological disease characterized by cognitive impairment that interferes with daily life [20]." In the 2021 GBD study, ADOD were identified based on ICD-10 codes F00-F03, G30, and G31, as well as ICD-9 codes 290, 2901.2, 291.8, 294, and 331 [21]. In this paper, according to the hierarchical structure of GBD, a three-level classification of causes was used [22]. The specific data analyzed in this study were obtained from the online Global Health Data. Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool), which was updated most recently on May 16, 2024. The detailed methods have been described elsewhere [23,24]. We analyzed the trends of incidence, prevalence, mortality, and DALYs for ADOD in Asia during 1990–2021, and predicted the dementia-related disease burden from 2021 to 2050. The prevalence denotes the number of existing cases, while the incidence represents the number of newly diagnosed cases. Both are estimated using population-representative data like scientific reports and health system surveys. DALYs, a comprehensive disease burden metric, is calculated by adding the years of life lost due to premature death to the years lived with disability, thus summarizing the impact of dementia on both the quantity and quality of life.

We also evaluated gender and age range differences. Age-standardized rates (ASRs) were used to avoid age-related confounding, ensuring rate consistency. As the study used public database data, ethical approval wasn't required.

2.2. Risk factors of ADOD

The 2021 GBD study estimated that the burden of dementia can be attributed to two modifiable risk factors, namely metabolic risk factors and behavioral risk factors. According to the 2021 GBD study, only two

metabolic risk factors associated with dementia mortality were evaluated, including high body-mass index (BMI) and high fasting plasma glucose (HFPG). At the same time, only one behavioral risk factor, smoking, was evaluated.

2.3. Data analysis

We detailed dementia trends in incident, prevalence, deaths, and DALYs, along with ASRs, by gender, age, year, and GBD region. Using ASRs and case numbers, we quantified the ADOD burden. Given the scarcity of dementia cases under 40, we excluded this age group, focusing only on those 40 and older.

Joinpoint regression analysis uses the simplest logarithmic model to fit time periods, describing trends within specific frames. Joinpoint divide the time series into sub-stages with different trends. The model assesses incidence trend significance by comparing annual percent change (APC) and average annual percent change (AAPC). It's done using Joinpoint 4.9.0.1 from the US National Cancer Institute. Other analyses and visualizations use R 4.1.2. A $p < 0.05$ is statistically significant.

2.4. Predict the disease burden related to ADOD from 2021 to 2050

The autoregressive integrated moving average (ARIMA) model, a go-to for time-series forecasting, combines the autoregressive (AR), integrated (I), and moving average (MA) components of time-series data. This allows it to deftly handle trends, seasonality, and irregular fluctuations. In our study, we used ARIMA to predict the 2021–2050 disease burden related to ADOD.

3. Results

3.1. The disease prevalence trends from 1990 to 2021 in Asia

Based on the analysis of the GDB Asian data, during the period from 1990 to 2021 in Asia, the ASMR of males increased by 10.71 % and that of females increased by 4.76 %. The ASDR of males increased by 9.62 % and that of females increased by 6.24 %. The ASPR of males increased by 12.56 % and that of females increased by 13.33 %. The ASIR of males increased by 11.70 % and that of females increased by 11.01 %.

In Fig. 1, ADOD ASDR of Afghanistan (577.72 per 100,000; 95 % UI, 26.16–1271.17), China (562.39; 95 % UI, 271.1–1238.81), Republic of Korea (500.05; 95 % UI, 234.92–1004.38), Turkey (491.99; 95 % UI, 236.53–1031.11), and Yemen (486.21; 95 % UI, 234.59–1103.25) are in highest level in 2021. Furthermore, the country with the lowest ASDR is India (305.73; 95 % UI,135.42–676.67), followed by Bangladesh (310.82; 95 % UI,138.97–735.74). The largest change in DALYs number is 649.91 % for Qatar between 1990 and 2021. The change for United Arab Emirates is 470.06 %, follow closely behind Qatar. At the same time, Afghanistan and Kazakhstan have seen minimal changes in DALYs number as 23.05 % and 23.89 %, respectively.

ADOD ASMR of Afghanistan (33.27 per 100,000; 95 % UI, 8.44–89.55), China (30.82; 95 % UI, 7.88–82.43), Republic of Korea (29.02; 95 % UI, 7.87–69.71), Viet Nam (27.29; 95 % UI, 6.67–75.83), and Qatar (26.54; 95 % UI, 6.57–73.95) are in highest level in 2021. Besides, India (16.98; 95 % UI,4.05–46.35) and Bangladesh (17.27; 95 % UI,4.04–50.94) also had the lowest ASMR. The largest change in mortality number of two countries is Maldives and Qatar between 1990 and 2021, which are 619.70 % and 572.73 %, respectively. Meanwhile, Kazakhstan and Afghanistan had the least change of 13.14 % and 28.24 % in Mortality number.

ADOD ASIR of China (151.47; 95 % UI, 131.22–173.34), Lebanese Republic (140.48; 95 % UI, 122.53–159.62), Turkey (139.10; 95 % UI, 120.57–158.16), Jordan (134.51; 95 % UI, 116.99–153.81), and Iran (133.73; 95 % UI, 117.53–151.85) are in highest level in 2021.In addition, Bhutan (77.45; 95 % UI, 67.36–88.68) had the lowest ASIR, followed by Pakistan (78.80; 95 % UI, 67.99–90.38). The largest change in incidence number is 751.51 % for Qatar between 1990 and 2021. The change for United Arab Emirates is 642.45 %, follow closely behind Qatar.

At the same time, Georgia and Afghanistan have seen minimal changes in incidence number as 18.40 % and 29.03 %, respectively ADOD ASPR of China (900.82; 95 % UI, 770.92–1043.22), Lebanese Republic (828.25; 95 % UI, 710.40–948.14), Turkey (819.36; 95 % UI, 706.20–936.59), Jordan (786.72; 95 % UI, 675.70–906.66), and Yemen (777.94; 95 % UI, 673.66–883.49) are in highest level in 2021. Moreover, Pakistan (433.58; 95 % UI, 374.32–499.28) and Bhutan (433.70; 95 % UI, 372.38–497.86) had the lowest ASPR. The largest change in prevalence number of two countries is Qatar and United Arab Emirates between 1990 and 2021, which are 740.31 % and 605.37 %, respectively. Meanwhile, Georgia and Afghanistan had the least change of 19.00 % and 26.72 % in prevalence number.

Based on the above study, we selected the China, Lebanese Republic, Turkey, and Jordan with the highest ADOD ASIR/ASPR and Afghanistan with the highest ADOD ASDR/ASMR for number analysis. Therefore, Table 1 presents number analysis of ADOD in the world, Asia, China, Lebanon, Turkey, and Jordan.

As shown in Table 1, the deaths of ADOD in Asia increased from 258,451.64 (95 % UI,62,057.89 −683,801.41)in 1990 to 1,026,938.69 (95 % UI,267,220.27–2,616,593.37) in 2021;the prevalence of ADOD in Asia increased from 9,090,622.20 (7,888,142.30–10,340,205.41) in 1990 to 31,857,009.27 (27,609,350.33–36,564,142.17) in 2021;the Incidence of ADOD in Asia increased from 1,597,920.57 (1,392,802.91–1,824,148.48)in 1990 to 5,508,584.66 (4,818,698.29–6,284,941.59) in 2021; the prevalence in males of ADOD in Asia increased from 3,518,228.43 (3,015,435.52–4,019,265.98)in 1990 to 11,844,941.80 (10,076,620.56 −13,577,622.09) in 2021; the prevalence in females of ADOD in Asia increased from 5,572,393.77 (4,845,238.08–6,355,122.10)in 1990 to 20,012,067.47 (17,369,975.97–22,900,588.65) in 2021.

In terms of age groups, overall ADOD burden is concentrated in the older age groups (>60 years old) in Asia. As shown in the Fig. 2, ASDR, ASMR, ASPR, and ASIR of ADOD increase with age as a unimodal distribution at different ages in Asia. The incidence and mortality of ADOD peak at the age group of 95+ years for both female and male. For both males and females, the peak of ADOD DALYs is located at 80–84 age group in Asia. Overall, Asian female have higher prevalence and DALYs than male. For DALYs, Mortality, incidence, and prevalence number, ADOD burden is concentrated in the age group of 80–89 for both female and male in Asia. The peaks of DALYs number are 2,588,517.17 (95 % UI, 1,197,655.59–5,520,538.82) and 1,404,233.48 (95 % UI, 632,049.18–3,243,414.27) for female and male. The peaks of mortality number are 170,862.78 (95 % UI, 44,246.67–438,197.21) and 78,526.50 (95 % UI, 18,869.18–223,795.28) for female and male in Asia. The peaks of incidence number are 684,263.92 (95 % UI, 471,669.40–907,221.02) and 399,970.61 (95 % UI, 272,188.08–533,207.89) for female and male. The peaks of prevalence number are 3,985,626.69 (95 % UI, 3,173,868.93–4,993,548.12) and 2,183,816.19 (95 % UI, 1,710,770.59–2,744,462.77) for female and male in Asia.

Based on the above study, we selected the China, Lebanese Republic, Turkey, and Jordan with the highest ADOD ASIR and ASPR together with Global and Asia for joinpoint regression analysis in Fig. 3. The findings show that ASDR in Asia has been showing a growing trend with AAPC of 0.2115 (95 % CI, 0.1570–0.2741) from 1990 to 2021. Similar growing trends were discovered with AAPC of 0.1782 (95 % CI, 0.1165–0.2400) and 0.2710 (95 % CI, 0.2102–0.3318) for female and male ASDR in Asia. China had the highest ASDR among the selected four countries in 2021, of which AAPC is 0.0831 (95 % CI, −0.0237–0.1900). For female and male ASDR in China, the variation trend is the analogous to both genders. And the AAPCs are 0.1474 (95 % CI, 0.0323–0.2626) and 0.1860 (95 % CI, 0.1120–0.2601) for female and male ASDR in China.

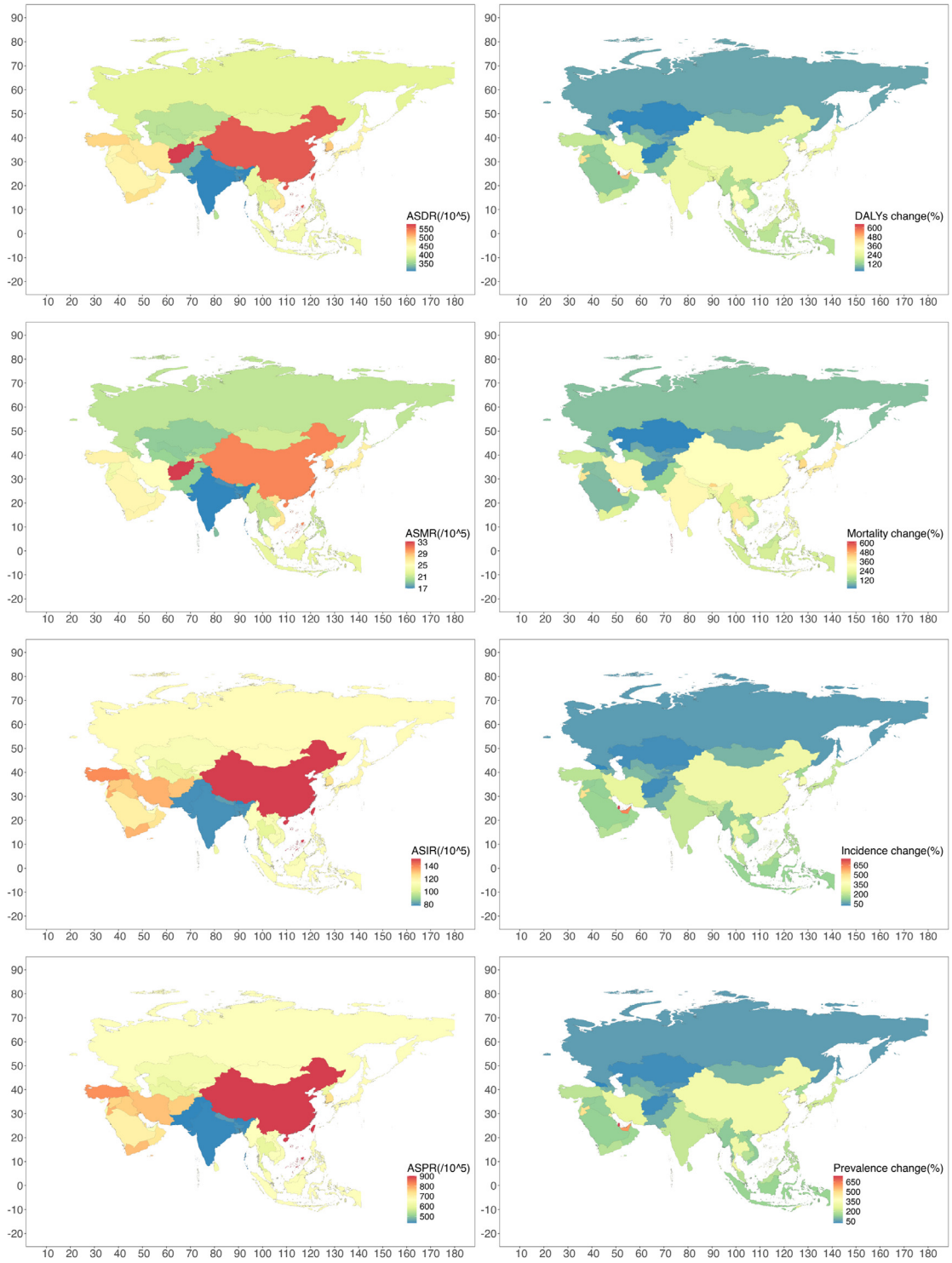

Fig. 1. Asian geographic distribution of 2021 ASRs and number changes between 1990 and 2021. (ASDR=Age-standardized DALY Rate; ASMR=Age-Standardized Mortality Rate; ASIR=Age-standardized Incidence Rate; ASPR=Age-standardized Prevalence Rate; ASRs=Age-standardized Rates).

The findings show that ASMR in Asia has been showing a growing trend with AAPC of 0.2000 (95 % CI, 0.1502–0.2498) from 1990 to 2021. Similar growing trends were discovered with AAPC of 0.1170 (95 % CI, 0.0681–0.1660) and 0.3254 (95 % CI, 0.2578–0.3930) for female and male ASDR in Asia. China had the highest ASMR among the selected four countries in 2021, of which AAPC is −0.0861 (95 % CI, −0.1716–−0.0005). In China, the variation trend is the analogous to both sexes for female ASMR but different to both sexes for male ASMR. And the AAPCs are −0.1006(95 % CI, −0.1989–−0.0022) and 0.0913 (95 % CI, 0.0126–0.1702) for female and male ASMR in China.

3.2. Risk factors in Asia

In Table 2, according to GBD 2021,the percentage of DALYs attributable to risk factors (per 100,000 people) due to high fasting plasma glucose were the highest in Asia, increasing from 11.04 (95 % UI,0.95–

Table 1
Deaths, DALYs, Prevalence, and Incidence of ADOD compared in 1990 and 2021.

Deaths, DALYs, Prevalence, and Incidence of ADOD in 2021			
Measure	Both sexes, number (95 % UI)	Males, number (95 % UI)	Females, number (95 % UI)
Global			
Deaths	1,952,677.00 (512,981.22 to 4,984,737.48)	626,872.13 (153,868.61 to 1,677,846.60)	1,325,804.87 (356,478.48 to 3,316,450.75)
DALYs	36,332,686.74 (17,237,624.04 to 76,873,276.22)	12,524,126.46 (5,871,758.06 to 27,158,682.55)	23,808,560.28 (11,368,142.66 to 49,746,523.96)
Prevalence	56,856,688.21 (49,382,064.01 to 64,977,511.92)	20,753,308.39 (17,769,420.13 to 23,796,797.51)	36,103,379.82 (31,468,184.99 to 41,117,469.75)
Incidence	9,837,055.84 (8,620,519.20 to 11,163,699.62)	3,645,491.67 (3,144,737.84 to 4,183,541.38)	6,191,564.17 (5,432,752.48 to 7,009,225.95)
Asia			
Deaths	1,026,938.69 (267,220.27 to 2,616,593.37)	336,041.56 (81,691.18 to 912,168.64)	690,897.12 (184,953.86 to 1,751,093.63)
DALYs	20,017,626.31 (9,585,678.52 to 42,792,471.30)	7,061,588.14 (3,318,365.87 to 15,605,520.05)	12,956,038.17 (6,192,375.14 to 27,341,593.00)
Prevalence	31,857,009.27 (27,609,350.33 to 36,564,142.17)	11,844,941.80 (10,076,620.56 to 13,577,622.09)	20,012,067.47 (17,369,975.97 to 22,900,588.65)
Incidence	5,508,584.66 (4,818,698.29 to 6,284,941.59)	2,077,499.32 (1,784,717.79 to 2,392,184.81)	3,431,085.34 (3,013,539.51 to 3,901,702.10)
China			
Deaths	491,773.96 (124,968.03 to 1,330,181.92)	163,343.35 (40,663.85 to 466,659.82)	328,430.61 (83,714.81 to 862,459.67)
DALYs	10,072,477.50 (4,947,154.11 to 22,219,153.71)	3,572,278.85 (1,694,715.53 to 8,148,477.56)	6,500,198.65 (3,171,764.56 to 13,681,028.96)
Prevalence	16,990,827.32 (14,488,494.04 to 19,672,741.19)	6,162,197.72 (5,142,286.06 to 7,141,800.17)	10,828,629.60 (9,315,735.20 to 12,515,957.37)
Incidence	2,914,112.02 (2,504,728.47 to 3,350,743.09)	1,077,297.18 (908,448.48 to 1,248,194.17)	1,836,814.84 (1,593,651.47 to 2,101,342.51)
Lebanon			
Deaths	1655.57 (422.37 to 4327.26)	639.08 (161.55 to 1717.81)	1016.49 (260.75 to 2580.45)
DALYs	30,711.10 (15,226.39 to 63,469.43)	11,755.24 (5772.47 to 25,781.75)	18,935.86 (9610.96 to 37,880.00)
Prevalence	54,345.82 (46,449.56 to 62,272.48)	21,497.78 (18,312.15 to 24,691.62)	32,848.03 (27,922.97 to 37,786.91)
Incidence	9166.70 (8003.26 to 10,453.15)	3731.97 (3239.93 to 4259.93)	5434.73 (4739.85 to 6191.39)
Türkiye			
Deaths	20,001.48 (5054.40 to 52,547.56)	7181.30 (1789.05 to 20,184.23)	12,820.19 (3270.27 to 33,348.38)
DALYs	401,906.16 (196,643.62 to 841,832.34)	148,095.71 (71,685.90 to 332,379.38)	253,810.44 (124,748.81 to 518,617.88)
Prevalence	688,425.25 (595,237.19 to 787,215.85)	261,604.06 (225,371.62 to 300,171.92)	426,821.19 (367,311.63 to 488,479.97)
Incidence	117,990.91 (102,837.51 to 133,396.24)	45,802.92 (39,809.30 to 52,403.51)	72,187.99 (62,727.92 to 82,126.02)
Jordan			
Deaths	914.37 (221.43 to 2489.29)	448.07 (110.70 to 1218.74)	466.30 (111.35 to 1260.85)
DALYs	21,644.38 (10,918.41 to 46,231.25)	10,197.67 (5032.05 to 21,931.81)	11,446.72 (5885.61 to 24,545.49)
Prevalence	41,147.49 (35,428.52 to 46,861.53)	19,466.19 (16,730.55 to 22,130.76)	21,681.30 (18,574.05 to 24,814.86)
Incidence	7242.94 (6314.13 to 8247.12)	3453.89 (3009.27 to 3937.58)	3789.05 (3287.10 to 4368.73)
Afghanistan			
Deaths	1621.70 (400.55 to 4285.84)	587.30 (140.78 to 1607.01)	1034.40 (254.46 to 2675.74)
DALYs	33,853.96 (15,203.78 to 74,090.50)	12,245.06 (5652.90 to 26,995.05)	21,608.90 (9366.76 to 47,648.49)
Prevalence	49,010.34 (42,192.18 to 56,057.24)	20,709.50 (17,749.11 to 23,790.68)	28,300.84 (24,397.05 to 32,409.87)
Incidence	8764.02 (7688.23 to 10,025.79)	3737.26 (3261.98 to 4290.75)	5026.76 (4381.61 to 5770.87)
Deaths, DALYs, Prevalence, and Incidence of ADOD in 1990			
Measure	Both sexes, number (95 % UI)	Males, number (95 % UI)	Females, number (95 % UI)
Global			
Deaths	663,294.44 (163,580.41 to 1,764,991.32)	200,382.91 (47,756.90 to 550,521.32)	462,911.53 (115,212.76 to 1,215,530.41)
DALYs	13,572,308.01 (6,439,340.75 to 29,586,865.34)	4,465,556.67 (2,092,517.14 to 9,971,767.69)	9,106,751.34 (4,330,350.39 to 19,615,097.65)
Prevalence	21,799,760.90 (19,067,087.20 to 24,837,693.05)	7,656,315.26 (6,611,275.56 to 8,728,099.19)	14,143,445.64 (12,361,842.01 to 16,105,291.71)
Incidence	3,834,525.86 (3,367,544.12 to 4,358,427.97)	1,352,318.94 (1,177,679.88 to 1,551,793.07)	2,482,206.92 (2,183,968.02 to 2,820,920.01)
Asia			
Deaths	258,451.64 (62,057.89 to 683,801.41)	87,914.96 (20,449.83 to 244,845.30)	170,536.69 (41,428.73 to 448,398.92)
DALYs	5,726,844.15 (2,671,160.54 to 12,706,695.43)	2,093,324.82 (965,365.48 to 4,756,646.55)	3,633,519.32 (1,708,520.87 to 7,928,193.17)
Prevalence	9,090,622.20 (7,888,142.30 to 10,340,205.41)	3,518,228.43 (3,015,435.52 to 4,019,265.98)	5,572,393.77 (4,845,238.08 to 6,355,122.10)
Incidence	1,597,920.57 (1,392,802.91 to 1,824,148.48)	616,057.96 (533,628.97 to 707,025.05)	981,862.61 (859,507.20 to 1,117,127.37)
China			
Deaths	119,808.81 (28,349.26 to 322,103.28)	39,596.64 (9246.58 to 113,674.51)	80,212.17 (19,176.26 to 212,442.40)
DALYs	2,702,484.11 (1,239,177.46 to 6,085,394.74)	972,799.22 (434,085.41 to 2,307,848.00)	1,729,684.89 (790,231.83 to 3,750,293.66)
Prevalence	4,024,535.83 (3,446,397.50 to 4,623,086.05)	1,511,602.03 (1,280,687.86 to 1,737,519.77)	2,512,933.80 (2,165,052.11 to 2,892,723.80)
Incidence	703,178.00 (601,505.73 to 808,633.19)	260,650.25 (222,339.29 to 301,788.28)	442,527.74 (381,566.69 to 507,193.91)
Lebanon			
Deaths	345.81 (85.06 to 944.77)	122.60 (29.90 to 341.04)	223.21 (55.59 to 602.21)
DALYs	7589.65 (3694.36 to 15,751.42)	2884.72 (1401.55 to 5909.44)	4744.93 (2317.82 to 9704.00)
Prevalence	13,979.20 (12,017.37 to 15,949.74)	5642.52 (4818.13 to 6452.37)	8336.69 (7199.73 to 9565.87)
Incidence	2400.57 (2106.67 to 2743.55)	987.38 (856.79 to 1125.94)	1413.18 (1233.20 to 1616.38)
Türkiye			
Deaths	6865.70 (1706.76 to 18,082.19)	2327.23 (558.41 to 6240.87)	4538.46 (1174.18 to 11,954.23)
DALYs	141,131.26 (68,913.83 to 297,639.33)	51,090.63 (24,462.84 to 111,470.84)	90,040.63 (44,367.25 to 189,323.56)
Prevalence	235,492.60 (203,402.00 to 268,352.11)	90,433.90 (77,985.92 to 102,877.88)	145,058.70 (125,030.23 to 165,101.07)
Incidence	40,370.06 (35,493.01 to 45,674.62)	15,909.97 (13,762.15 to 18,081.52)	24,460.09 (21,563.84 to 27,620.48)
Jordan			
Deaths	185.25 (47.41 to 492.92)	85.30 (21.53 to 221.77)	99.95 (25.91 to 273.46)
DALYs	4060.54 (2000.97 to 8589.84)	1829.61 (892.68 to 3765.28)	2230.93 (1101.57 to 4804.39)
Prevalence	6988.08 (6000.69 to 7974.96)	3208.69 (2761.00 to 3688.32)	3779.39 (3252.10 to 4310.78)
Incidence	1219.32 (1064.72 to 1388.76)	563.07 (491.58 to 640.73)	656.25 (568.75 to 748.91)
Afghanistan			
Deaths	1264.60 (300.76 to 3400.72)	535.70 (123.22 to 1459.74)	728.90 (179.13 to 1947.11)
DALYs	27,512.96 (12,139.80 to 63,092.10)	11,934.01 (5275.33 to 26,712.99)	15,578.95 (6657.37 to 36,401.37)
Prevalence	38,675.28 (33,029.14 to 44,211.81)	19,125.08 (16,326.81 to 22,079.32)	19,550.20 (16,685.38 to 22,276.83)
Incidence	6792.35 (5875.78 to 7741.37)	3362.94 (2895.47 to 3852.08)	3429.40 (2973.66 to 3899.23)

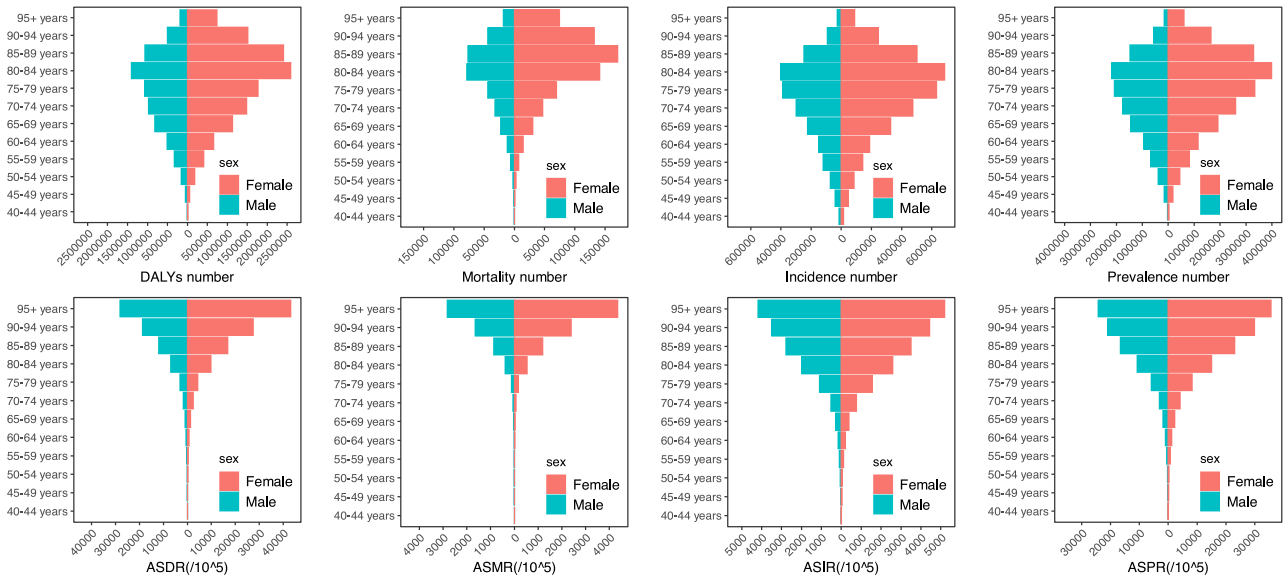

Fig. 2. ASRs and numbers of females and males in different age groups in Asia in 2021. (ASDR=Age-standardized DALY Rate; ASMR=Age-standardized Mortality Rate; ASIR=Age-standardized Incidence Rate; ASPR=Age-standardized Prevalence Rate; ASRs=Age-standardized Rates).

22.10) in 1990 to 13.71 (95 % UI,1.15- 27.37) in 2021, and smoking became the second major risk factor for ADOD, with percentage of DALYs attributable to risk factors attributable to risk factors due to smoking increasing from 6.64 (95 % UI,4.70–29.43) in 2019 in Asia; Smoking was the second major risk factor for ADOD in 1990 in Asia; BMI was the second major risk factor for ADOD in 2021 in Asia; Smoking was the second major risk factor for ADOD reduced from 6.64 (95 % UI,4.70–8.56) in 1990 to 4.79 (95 % UI,3.38–6.19) in 2021 in Asia. With smoking-induced percentage of DALYs attributable to risk factors (per 100,000 MY) of 11.00 (95 % UI,7.83–14.10) and 1.44 (0.96–1.94) for male and female, respectively; It is worth noting that, percentage of DALYs attributable to risk factors (per 100,000 people) due to high BMI have increased from 0.83 (95 % UI,−0.23–3.78) in 1990 to 4.06 (95 % UI,−0.44 to 11.55) in 2021 in the Asian region; Males are more vulnerable to the risks of behaviors such as smoking, and females are more likely to be affected by metabolic risk factors such as high body mass in Asia. High fasting plasma glucose, high BMI and smoking are the major risk factors for ADOD worldwide. Global high fasting plasma glucose caused the highest percentage of DALYs attributable to risk factors (per 100,000 people), increasing from 10.56 (95 % UI, 0.90–21.40) in 1990 to 14.64 (95 % UI, 1.21–29.43) in 2021; secondly, smoking was the second leading risk factor for ADOD in 1990; And in 2021, a high BMI becomes the second leading risk factor.

3.3. Future predictions of disease prevalence trends in Asia

According to the above analysis, it is expected that from 2021 to 2050, the burden of ADOD in Asia will change significantly, with all indicators showing an upward trend. The incidence of dementia is expected to increase among both Asian males and females. The ASDR for females is expected to increase from approximately 522.31 per 100,000 in 2021 to approximately 572.55 per 100,000 in 2050, representing an increase of about 9.62 % over 30 years (Fig. 4). For males, the ASDR will increase from approximately 372.44 per 100,000 in 2021 to approximately 403.02 per 100,000 in 2050, an increase of about 8.21 % over 30 years (Fig. 4). The ASDR for all genders will increase from approximately 460.48 per 100,000 in 2021 to approximately 490.30 per 100,000 in 2050, an increase of about 6.48 % over 30 years (Fig. 4) in Asia.

Regarding ASMR for females, it will increase from approximately 28.81 per 100,000 in 2021 to approximately 30.04 per 100,000 in 2050, an increase of about 4.27 % over 30 years (Fig. 4). For males, the ASMR will increase from approximately 20.57 per 100,000 in 2021 to approximately 24.21 per 100,000 in 2050, an increase of about 17.70 % over 30 years (Fig. 4). The ASMR for all genders will increase from approximately 25.67 per 100,000 in 2021 to approximately 27.21 per 100,000 in 2050, an increase of about 6.00 % over 30 years (Fig. 4) in Asia.

The ASIR for females is projected to increase from approximately 135.71 per 100,000 in 2021 to around 177.62 per 100,000 in 2050, representing an increase of approximately 30.88 % over a 30-year period (Fig. 4) in Asia. For males, the ASIR will rise from about 102.64 per 100,000 in 2021 to roughly 117.11 per 100,000 in 2050, a growth of approximately 14.10 % within 30 years (Fig. 4) in Asia. The ASIR for all genders will increase from approximately 121.12 per 100,000 in 2021 to about 179.70 per 100,000 in 2050, an increment of approximately 48.37 % in 30 years (Fig. 4) in Asia.

3.4. Research limitations

This study has certain limitations. Given that the GBD study relies on information from diagnosed cases, it is highly likely that the disease burden is underestimated. Therefore, this factor should be taken into account when interpreting the results [25]. The GBD study has another significant limitation. The category of "other dementias" is not further subdivided. This makes it impossible for us to determine the prevalence of causes such as frontotemporal dementia, Huntington's disease, and Wernicke-Korsakoff syndrome. Currently, over a hundred subtypes of dementia have been identified. Some of them are accompanied by cognitive impairment, while others are not, and their symptoms vary greatly. This undoubtedly significantly increases the difficulty of diagnosing dementia [26]. In addition, to date, 12 risk factors related to dementia have been reported [27]. However, GBD 2021 indicates that only metabolic and behavioral factors are associated with dementia, yet it provides no data on other risk factors [28].

4. Discussion

In summary, this study has illustrated the epidemiological trends of dementia in Asia from 1990 to 2021. During the period from 1990 to 2021, ASDR, ASMR, ASIR and ASPR in Asia all showed an upward trend, reaching 460.48, 25.66, 121.12, and 706.22 respectively in 2021. It

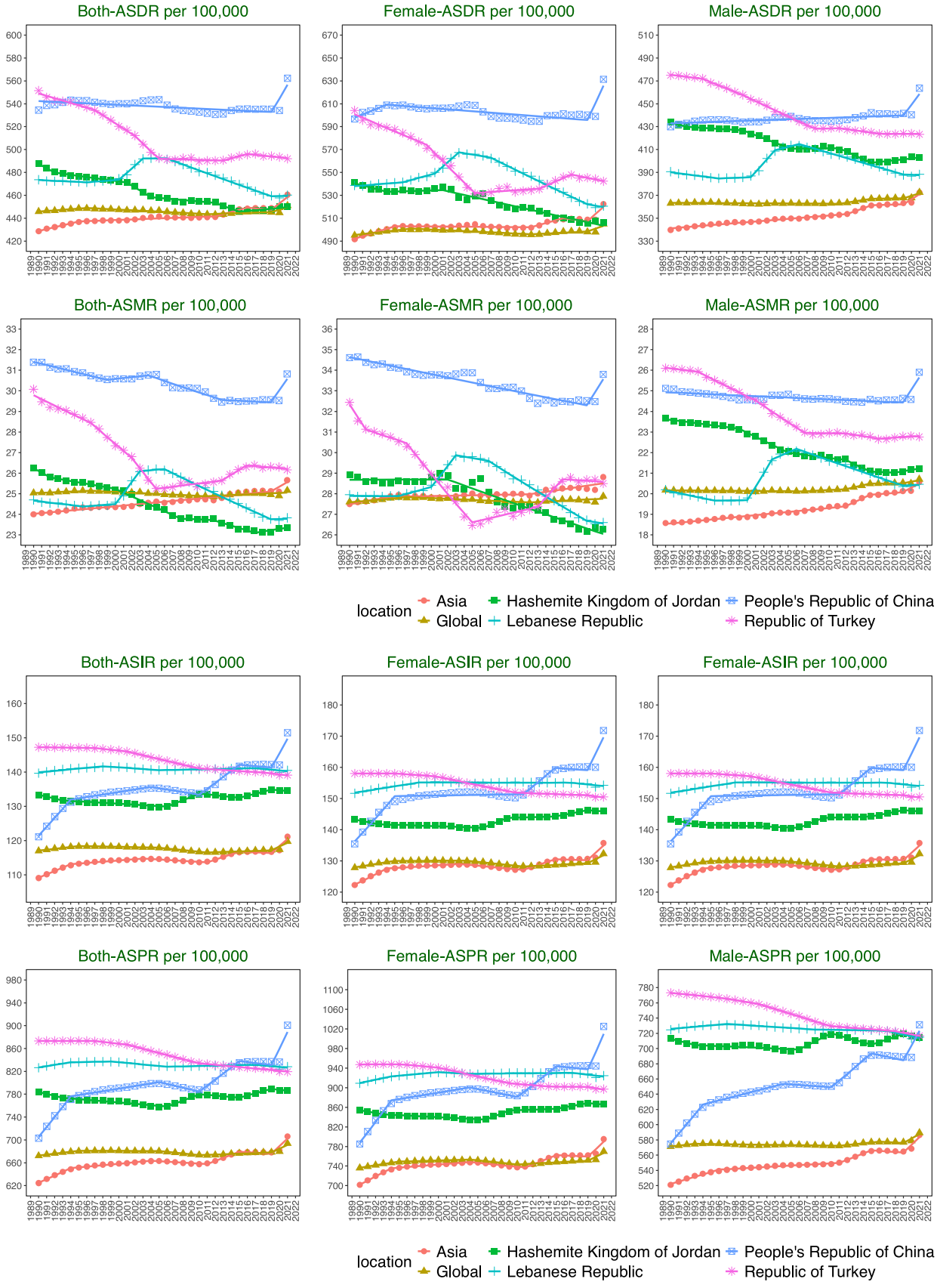

Fig. 3. Joinpoint analysis of ASRs for different gender groups in Asia, Global, Jordan, China, Lebanon and Turkey from 1990 to 2021 (ASDR=Age-standardized DALY Rate; ASMR=Age-Standardized Mortality Rate; ASIR=Age-standardized Incidence Rate; ASPR=Age-standardized Prevalence Rate; ASRs=Age-standardized Rates).

Table 2
Percentage of DALYs Attributable to Risk Factors of ADOD compared in 1990 and 2021.

Percentage of DALYs Attributable to Risk Factors of ADOD in 2021			
Risk factor	Both sexes, % (95 % UI)	Males, % (95 % UI)	Females, % (95 % UI)
Global			
Smoking	**4.23 (2.96 to 5.50)**	**8.91 (6.31 to 11.47)**	1.79 (1.24 to 2.35)
High fasting plasma glucose	**14.64 (1.21 to 29.43)**	**15.33 (1.28 to 31.03)**	14.28 (1.17 to 28.61)
High body-mass index	**7.12 (−1.75 to 19.97)**	**6.06 (−1.18 to 17.22)**	7.68 (−2.05 to 21.36)
Asia			
Smoking	**4.79 (3.38 to 6.19)**	**11.00 (7.83 to 14.10)**	1.44 (0.96 to 1.94)
High fasting plasma glucose	**13.71 (1.15 to 27.37)**	**14.22 (1.20 to 28.65)**	13.44 (1.13 to 26.69)
High body-mass index	**4.06 (−0.44 to 11.55)**	**3.09 (−0.13 to 8.92)**	4.59 (−0.61 to 13.08)
China			
Smoking	**5.97 (4.15 to 7.77)**	**13.89 (10.06 to 17.95)**	1.63 (1.01 to 2.35)
High fasting plasma glucose	**11.89 (1.02 to 23.70)**	**12.06 (1.05 to 24.30)**	11.80 (1.00 to 23.47)
High body-mass index	**4.43 (−0.45 to 12.79)**	**3.33 (−0.11 to 9.79)**	5.03 (−0.64 to 14.69)
Lebanon			
Smoking	**7.46 (4.97 to 10.38)**	**10.96 (7.44 to 15.05)**	5.31 (3.31 to 8.29)
High fasting plasma glucose	**20.65 (1.72 to 40.91)**	**20.99 (1.76 to 41.29)**	20.44 (1.70 to 40.74)
High body-mass index	**14.13 (−5.73 to 37.35)**	**12.45 (−4.31 to 33.40)**	15.16 (−6.75 to 39.12)
Türkiye			
Smoking	**3.79 (2.62 to 5.07)**	**8.58 (5.94 to 11.43)**	1.03 (0.64 to 1.50)
High fasting plasma glucose	**17.80 (1.45 to 35.69)**	**18.57 (1.45 to 37.91)**	17.35 (1.45 to 34.84)
High body-mass index	**14.22 (−5.53 to 37.05)**	**12.08 (−3.92 to 33.59)**	15.45 (−6.51 to 40.14)
Jordan			
Smoking	**6.92 (4.80 to 9.10)**	**12.06 (8.53 to 15.82)**	2.36 (1.52 to 3.32)
High fasting plasma glucose	**23.23 (2.09 to 44.40)**	**23.27 (2.17 to 43.94)**	23.20 (2.02 to 44.60)
High body-mass index	**17.71 (−9.04 to 43.37)**	**14.80 (−5.78 to 37.78)**	20.29 (−11.52 to 49.28)
Afghanistan			
Smoking	**2.11 (1.41 to 2.96)**	**4.84 (3.20 to 6.76)**	0.54 (0.33 to 0.78)
High fasting plasma glucose	**20.35 (1.74 to 39.76)**	**18.97 (1.56 to 39.32)**	21.14 (1.83 to 40.59)
High body-mass index	**6.20 (−1.23 to 17.20)**	**6.21 (−0.90 to 18.43)**	6.20 (−1.26 to 17.53)
Percentage of DALYs Attributable to Risk Factors of ADOD in 1990			
Risk factor	**Both sexes, % (95 % UI)**	**Males, % (95 % UI)**	Females, % (95 % UI)
Global			
Smoking	**5.87 (4.12 to 7.60)**	**11.96 (8.53 to 15.36)**	2.89 (2.01 to 3.80)
High fasting plasma glucose	**10.56 (0.90 to 21.40)**	**11.09 (0.95 to 22.29)**	10.30 (0.88 to 20.81)
High body-mass index	**4.57 (−0.44 to 13.37)**	**3.20 (−0.08 to 9.44)**	5.24 (−0.71 to 15.20)
Asia			
Smoking	**6.64 (4.70 to 8.56)**	**14.15 (10.14 to 17.99)**	2.33 (1.63 to 3.05)
High fasting plasma glucose	**11.04 (0.95 to 22.10)**	**11.20 (0.97 to 22.45)**	10.96 (0.94 to 22.08)
High body-mass index	**0.83 (−0.23 to 3.78)**	**0.37 (−0.53 to 2.80)**	1.09 (−0.17 to 4.24)
China			
Smoking	**7.96 (5.61 to 10.26)**	**17.22 (12.35 to 21.89)**	2.78 (1.94 to 3.74)
High fasting plasma glucose	**10.54 (0.92 to 21.23)**	**10.44 (0.92 to 21.10)**	10.60 (0.93 to 21.34)
High body-mass index	**0.21 (−0.88 to 2.97)**	**−0.02 (−1.10 to 2.43)**	0.33 (−0.80 to 3.10)
Lebanon			
Smoking	**7.36 (5.22 to 9.91)**	**11.48 (8.08 to 15.30)**	4.89 (3.20 to 7.12)
High fasting plasma glucose	**15.84 (1.27 to 32.71)**	**17.50 (1.37 to 36.20)**	14.85 (1.22 to 30.62)
High body-mass index	**8.48 (−2.05 to 23.86)**	**6.42 (−1.06 to 18.20)**	9.70 (−2.66 to 27.50)
Türkiye			
Smoking	**6.23 (4.34 to 8.18)**	**14.47 (10.13 to 18.96)**	1.57 (0.97 to 2.37)
High fasting plasma glucose	**10.10 (0.84 to 20.63)**	**9.85 (0.82 to 20.06)**	10.24 (0.84 to 20.71)
High body-mass index	**8.51 (−2.10 to 23.90)**	**5.12 (−0.66 to 15.01)**	10.42 (−2.95 to 28.69)
Jordan			
Smoking	**8.55 (5.99 to 11.28)**	**15.44 (10.84 to 20.13)**	2.92 (1.83 to 4.42)
High fasting plasma glucose	**17.84 (1.47 to 36.03)**	**16.86 (1.44 to 33.55)**	18.64 (1.50 to 36.88)
High body-mass index	**10.82 (−3.53 to 29.63)**	**8.16 (−1.97 to 23.32)**	13.00 (−4.80 to 34.23)
Afghanistan			
Smoking	**2.17 (1.42 to 3.07)**	**4.28 (2.85 to 6.12)**	0.53 (0.34 to 0.78)
High fasting plasma glucose	**13.83 (1.07 to 28.72)**	**12.06 (0.97 to 24.36)**	15.20 (1.14 to 32.34)
High body-mass index	**3.54 (−0.27 to 10.45)**	**1.86 (−0.18 to 6.34)**	4.83 (−0.64 to 13.64)

is predicted that by 2050, the ASDR, ASMR, ASIR, and ASPR will be 490.30, 27.21, 179.70, and 1149.55 respectively. Moreover, in terms of region, in Asia, China has relatively high levels of ASDR, ASMR, ASIR, and ASPR. In 2021, they reached 562.39, 30.82, 151.47, and 900.82 respectively. During the period from 1990 to 2021, Qatar and the United Arab Emirates witnessed the most significant changes in DALYs, incidence, and prevalence. Specifically, the change in DALYs in Qatar was 649.91 %, and in the United Arab Emirates it was 470.06 %. The change in incidence rate was 751.51 % in Qatar and 642.45 % in the United Arab Emirates. The change in prevalence rate was 740.31 % in Qatar and 605.37 % in the United Arab Emirates. Overall, among Asian countries with ADOD, China, Lebanon, Turkey, and Jordan had the highest ASIR/ASPR, while Afghanistan had the highest ASDR/ASMR. On the whole, the disease burden of ADOD in China is prominent. Driven by economic development, China has made comprehensive progress in medicine, steadily raising average life expectancy from a low past level. But with an aging society accelerating, geriatric diseases have become more severe and drawn high social attention. Neurodegenerative diseases, with Alzheimer's as an example, pose a major health challenge to the older adult due to high incidence, disability rates, and care demands, significantly reducing older adult quality of life and burdening families, society, and the medical system.

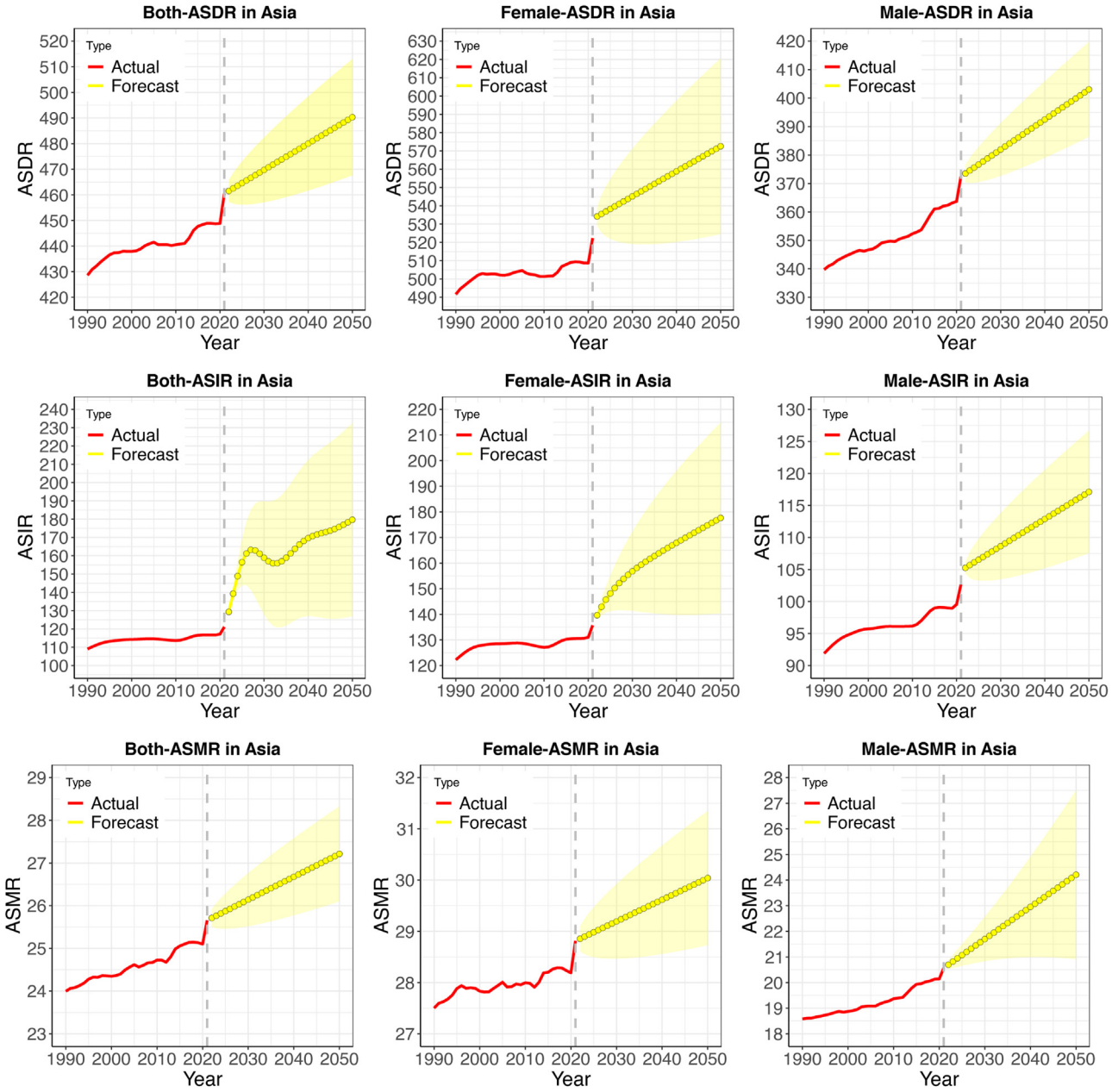

Fig. 4. Historical trends and future trajectories of ADOD ASDR, ASMR, ASIR, and ASPR in the Asia since1990 and up to 2050. (ASDR=Age-standardized DALY Rate; ASMR=Age-Standardized Mortality Rate; ASIR=Age-standardized Incidence Rate).

With the continuous increase in the average life expectancy, its incidence has risen significantly on a global scale [29]. Regarding the age -distribution characteristics, ASDR, ASMR, ASPR, and ASIR of ADOD all show an upward trend with the increase of age, presenting a unimodal distribution among different age groups. Specifically, for both females and males, the incidence and mortality rates of ADOD peak in the age group of 95 years and above. In terms of gender, in 2021, the ASIR and ASPR of Asian females were 135.71 and 795.07 respectively, while those of Asian males were 102.64 and 586.41 respectively.

At present, reversing Alzheimer's disease clinically still poses a challenge, with a scarcity of effective treatment methods. The limitations of drug therapy are particularly prominent [30]. Actively managing risk factors can slow disease progression. As living standards rise, the incidence of metabolic diseases like high systolic blood pressure, high BMI, and diabetes has grown significantly. In Asian countries, rapid economic development, along with intense competition and heavy life stress, has led to the spread of bad habits such as smoking and excessive drinking [31]. Analyzing from the perspective of risk factors, high fasting blood glucose has become the primary risk factor for the onset of ADOD. In 2021, in the Asian region, the proportion of DALYs caused by ADOD due to high fasting blood glucose was as high as 13.71 %. Further exploration of gender differences reveals that males are more significantly affected by behavioral risks such as smoking, while females are more vulnerable to metabolic risk factors such as high body weight. Research has confirmed that smoking can accelerate the development of dementia and exacerbate its severity [32]. Tobacco products contain chemicals like nicotine, tar, and carbon monoxide, which are toxic to the brain. Once in the body, they subtly damage normal brain functions, severely harming memory, thinking, and cognitive abilities. Smoking also greatly raises the risk of cardiovascular and respiratory diseases. For dementia patients, these added risks further undermine their frail health, seriously affecting their quality of life and disease prognosis

[33]. A number of previous studies have shown that in the countries along the Belt and Road, the consumption of tobacco products is a key risk factor for cancer [34]. Research has confirmed that adhering to the Mediterranean diet pattern can significantly reduce an individual's risk of developing Alzheimer's disease. This dietary structure is rich in antioxidants, anti - inflammatory nutrients, and healthy fats, playing a crucial role in maintaining normal cognitive function of the brain and preventing the occurrence and development of neurodegenerative diseases [35]. The modified Mediterranean ketogenic diet has caught scholars' attention. It could be a therapeutic intervention, reversing Alzheimer's-related pathological lipid changes. With its low-cost and low-risk edges, it's appealing in preventing Alzheimer's and treating early-stage patients [36]. Given that natural products have unparalleled significant advantages in terms of effectiveness and safety compared to traditional therapies, the great potential they hold in the field of Alzheimer's disease treatment deserves our high attention. Both in vitro and in vivo research results consistently indicate that phenolic-derived phytochemicals play a highly positive role in promoting the prevention of the development of Alzheimer's disease [36].

Among many pathogenic factors, microbiome dysbiosis is key in triggering Alzheimer's disease. Research shows that targeted interventions can reverse its pathological development. By precisely regulating the microbiome, we can optimize intestinal tight - junction proteins, reduce the permeability of intestinal and blood - brain barriers, and relieve inflammation in the intestines, blood, and brain. Through these synergistic measures, we can mitigate Alzheimer's pathology, slow cognitive decline, inhibit cognitive function deterioration, and delay disease progression [37].

5. Conclusion

The findings of this study offer valuable references to Asian countries and regions yet to fully research ADOD burden, helping them craft effective strategies. For relevant departments in Asia, the top priority is optimizing dementia-patient medical services. Meanwhile, they should boost public awareness, promote early-risk-factor screening, and aim for early diagnosis and treatment. Health management departments should coordinate, integrate local resources and facilities, and speed up improving the older adult care and geriatric medical systems, laying a solid foundation for the aging society in Asia.

Based on this chapter's analysis, we especially appeal to focus on countries and regions like China in Asia, where ADOD prevalence is rising fast. We must face population growth and aging challenges, note the disease's gender-specific traits, and combine multidisciplinary efforts for gender-targeted measures in Asia. On one hand, stay alert to key risk factors like high fasting blood glucose to cut the disease incidence at the source. On the other, keep enhancing new drug Research and Development (R&D) to improve patients' survival and quality of life in Asia.

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Ethics considerations

This study is a secondary data analysis research, and the authors did not directly collect consent to participate. However, all research activities were carried out in accordance with relevant national and international guidelines and regulations. No patients or the general public were included in the recruitment or implementation process of this study. All data from the Global Burden of Disease (GBD) in 2021 are publicly available and can be accessed at https://vizhub.healthdata.org/gbd-compare/.All data used and/or analyzed in this study can be obtained from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Jinxuan Guo: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Pin Wang:** Formal analysis. **Jin Gong:** Formal analysis. **Wenxian Sun:** Formal analysis. **Xiaodong Han:** Formal analysis. **Chang Xu:** Formal analysis. **Aidi Shan:** Formal analysis. **Xin Wang:** Formal analysis. **Heya Luan:** Methodology. **Shaoqi Li:** Methodology. **Ruina Li:** Methodology. **Boye Wen:** Methodology. **Runqi Chen:** Methodology. **Sirong Lv:** Methodology. **Cuibai Wei:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Data availability

http://ghdx.healthdata.org/gbd-results-tool (GBD study 2021 data resources were available online from the Global Health Data Exchange (GHDx) query tool).

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