



Research Article

Global epidemiological and indirect economic burden of neurological, mental, and substance use disorders: An analysis based on the global burden of disease data

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ABSTRACT

Objective: To evaluate the global disease burden and indirect economic costs of neurological, mental, and substance use disorders (NMSDs) from 1990 to 2023.

Methods: This study analyzed data on incidence, prevalence, and disability-adjusted life years (DALYs) for NMSDs using data from the Global Burden of Disease 2023 database. Joinpoint regression analysis was used to calculate average annual percentage change. Spearman correlation was applied to examine the association between age-standardized rates and socio-demographic index (SDI). The indirect economic burden was estimated using the human capital approach, incorporating age-adjusted productivity weights and gross domestic product (GDP) per capita.

Results: From 1990 to 2023, the absolute numbers of incident cases, prevalent cases, and DALYs for NMSDs increased substantially, with DALYs for neurological and mental disorders approximately doubling. Age-standardized rates demonstrated divergent trends across disease categories. For mental disorders, the age-standardized incidence, prevalence, and DALY rates increased by 15.00%, 24.00%, and 29.00%, respectively, with the overall burden rising markedly in 2019. In contrast, while the overall burden of substance use disorders declined, a notable exception emerged in high-income North America, where rising rates were observed specifically for opioid and cocaine use disorders. The burden of neurological and mental disorders was higher in females than in males, whereas substance use disorders showed the opposite pattern. The age-standardized DALY rate for motor neuron disease exhibited a significant positive correlation with SDI ($\rho_s = 0.82$, $P < 0.001$). The indirect economic burden and its share of GDP increased in most countries, while the share for substance use disorders in China declined by 46.19%.

Conclusion: The disease burden and economic costs of NMSDs increased globally from 1990 to 2023, with significant geographic, national, and demographic disparities. These findings highlight an urgent need for targeted resource allocation and integrated interventions.

1. Introduction

Neurological, mental, and substance use disorders (NMSDs) represent a heterogeneous group of brain disorders that stem from the intricate interplay of genetic, physiological, psychological, and social determinants.¹ NMSDs have become major public health challenges affecting human health and social development.² According to the 2022 estimates from the World Health Organization (WHO), over one billion people worldwide suffer from NMSDs, and health systems face significant gaps in meeting the needs of both new and existing patients.³ Over recent

years, the global disease spectrum has shifted from infectious diseases to chronic noncommunicable diseases. The total number of disability-adjusted life years (DALYs) for infectious diseases decreased from 874 million to 681 million, while those for chronic noncommunicable diseases increased from 1.45 billion to 1.80 billion. The burden attributable to NMSDs has significantly increased. Age-standardized DALY rates for anxiety, depression, and Alzheimer's disease have risen, placing these conditions among the top 25 causes of DALYs.⁴ This overall NMSD burden now exceeds that of any other disease category, including cancer and cardiovascular disease.⁵ Consequently, whether health resource al-

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location models have adapted to this epidemiological shift has become a central concern in the global public health arena.

The third edition of Disease Control Priorities (DCP-3) indicates that expenditures on care for NMSDs account for <1% of total government health spending,¹ revealing a severe imbalance between disease burden and resource allocation. A global shortage of specialists in NMSDs has created significant gaps in patient diagnosis, treatment, and care.⁶ In China alone, only 9.5% of individuals with depression receive treatment.⁷ These realities suggest that current healthcare resource allocation may be inadequate to address the evolving disease patterns and population health needs. This imbalance not only causes patient suffering but also leads to reduced work efficiency due to cognitive impairment or emotional and behavioral disturbances,⁸ resulting in decreased productivity and increased unemployment rates—creating substantial indirect economic burdens. Previous evidence has demonstrated that the indirect economic burden of brain disorders surpasses their direct medical and care costs.⁹ Although treating NMSDs has proven highly cost-effective (expanding treatment coverage for anxiety and depression yields a cost-benefit ratio of 1:3.3–1:5.7 when weighing economic and health benefits.¹⁰), the heavy indirect economic burden has prevented policymakers and health systems from prioritizing resource allocation. Therefore, to inform prevention and control priorities, resource allocation, and utilization optimization, it is essential to accurately assess the current burden of NMSDs based on available data and quantify its indirect economic burden.

The decision to adopt a unified analytical framework encompassing NMSDs is justified on several grounds. These three categories have been consistently grouped together in major global health policy frameworks—including the WHO Mental Health Action Plan and DCP-3—owing to their shared neurobiological substrates and their collective contribution to the global noncommunicable disease burden. Empirical evidence further points to substantive interconnections: substance use disorders demonstrate high comorbidity with mental disorders (e.g., alcohol use disorder and depression), and mental disorders such as depression are well-documented risk factors for neurological conditions including dementia and stroke. Beyond clinical overlap, they share key social determinants—including socioeconomic status, early-life adversity, and chronic stress—and collectively constitute the leading contributors to years lived with disability (YLDs) worldwide. Examining these conditions within a single framework thus facilitates the identification of cross-cutting patterns in disease burden distribution, shared determinants of health inequity, and potential avenues for integrated prevention and treatment that would otherwise remain obscured in condition-specific analyses.

According to the International Classification of Diseases, 11th Revision (ICD-11), NMSDs are classified into 39 categories. Common categories include: Alzheimer's disease, characterized pathologically by amyloid-beta deposits and hyperphosphorylated tau protein in the brain, and clinically by cognitive decline;¹¹ Parkinson's disease, a neurodegenerative disorder whose core mechanism involves progressive degeneration of dopaminergic neurons in the substantia nigra, clinically manifesting as bradykinesia, tremor, and postural instability;¹² motor neuron diseases, characterized by selective, progressive loss and degeneration of motor neurons primarily affecting upper and lower motor neurons, leading to progressive muscle weakness, atrophy, and pyramidal tract signs;¹³ headache disorders, including tension-type headache and migraine, characterized by recurrent or persistent headaches;¹⁴ anxiety and depression, arising from hypothalamic-pituitary-adrenal axis dysfunction causing emotional dysregulation;¹⁵ and substance use disorders, conduct disorders, and eating disorders, resulting from orbitofrontal-amygdala-hypothalamic circuit dysfunction leading to uncontrolled behavioral patterns.^{16–18} The burden imposed by different diseases on patients, health systems, and socioeconomic systems varies considerably. For example, the annual per capita expenditure for dementia patients is \$23,796,¹⁹ and the annual per capita direct costs for depression patients range from \$1,000 to \$2,500.²⁰ There-

fore, further category-specific analyses of the current disease burden are required.

Previous analyses of the NMSD burden have been limited to isolated studies, lacking a unified framework for comparative assessment.^{21–25} While some studies have estimated the direct economic burden—with direct healthcare expenditures reaching approximately \$1.7 trillion,²⁶ analyses of indirect economic burdens remain absent, preventing a comprehensive assessment of the overall economic impact. This study utilizes publicly available databases to analyze the disease burden and indirect economic burden of NMSDs across different countries (or regions) and populations globally from 1990 to 2023.

2. Methods

2.1. Data source

Data for this study were sourced from the Global Burden of Disease (GBD) database 2023 accessible via the GBD results tool at <http://ghdx.healthdata.org/gbdresults-tool>. This database provides estimates of disease burden data by age and sex since 1990 for 204 countries and regions, covering 375 diseases or injuries and 88 risk factors. All estimates are presented with 95% uncertainty intervals (UI). Estimates are reported in absolute numbers and as rates per 100,000 person-years. To account for differences in population age structures, age-standardization was applied using the GBD 2023 global standard population to derive age-standardized rates (ASRs). The mean value for each reported indicator represents the average of 250 samples drawn from the estimated distribution. The 95% UI corresponds to the 2.5th percentile and 97.5th percentiles within the sample results.⁴

2.2. Case definition

In the GBD 2023 database, causes of disease are categorized into four levels. Chronic noncommunicable diseases include neurological disorders, mental disorders, and substance use disorders. Because ICD-10 classifies substance use disorders as mental disorders, we included them in the analysis. To ensure data comparability, GBD 2023 employs case definitions based on ICD-10. Detailed definitions of NMSDs and their subcategories included in GBD 2023 are provided in Supplementary Table S1.

2.3. Definition of relevant indicators

2.3.1. Epidemiological indicators of disease burden

Epidemiological indicators include incidence, prevalence, and DALYs. These indicators are age-standardized using the GBD 2023 global standard population to derive age-standardized incidence rate (ASIR), age-standardized prevalence rate (ASPR), and age-standardized DALY rate (ASDR). Specific definitions of evaluation indicators are provided in the supplementary document.

2.3.2. Economic indicators of disease burden

Economic indicators for diseases encompass direct economic burden, indirect economic burden, and non-monetary burden. This study focuses solely on indirect economic burden, defined as the loss of current and future social and familial value resulting from reduced effective working capacity, shortened working hours, and decreased productivity due to disease, disability, and premature death. Estimation methods include the human capital approach and the friction cost approach. We selected the human capital approach, the widely accepted and most objective method for estimating indirect economic burden, because disease-specific DALYs are readily available from the GBD database. In contrast, the friction cost approach requires detailed macroeconomic data (e.g., friction period length) that are often unavailable in developing countries.^{27,28}

2.3.3. Socio-demographic index

Socio-demographic index (SDI) is a comprehensive indicator of development level used to holistically assess the socioeconomic development status of a country or region. It is a composite metric derived from the geometric mean of three factors: total fertility rate among individuals under 25 years old, mean years of education among the population aged 15 and above, and per capita income.²⁹ SDI value ranges from 0 to 1, where 0 represents the theoretical minimum level of development related to health and 1 represents the theoretical maximum level of development. Based on SDI values, countries and regions worldwide are categorized into five groups: low, lower-middle, middle, upper-middle, and high SDI regions. The calculation formula for SDI is provided in the supplementary document.

2.4. Data analysis

All statistical analyses were performed using R software (version 4.5.2, R Foundation for Statistical Computing, Vienna, Austria). Data organization and indirect economic burden estimation were conducted using Excel 2021 (Microsoft Corporation, Redmond, WA, USA). This study describes the disease burden and indirect economic burden across different years, ages, genders, SDI regions, and 204 countries, analyzing temporal trends in these metrics.

The Joinpoint regression analysis was used to partition long-term disease trends into distinct segments, assessing whether changes across different periods were statistically significant based on *P*-values or average annual percentage change (AAPC) values with their corresponding 95% confidence intervals (CI). It should be noted that the 95% UIs reported in GBD 2023 reflect uncertainty inherent in the disease burden estimation process, accounting for model-based variance across multiple data sources and analytical stages. In contrast, the 95% CIs reported in Joinpoint regression represent the statistical precision of the trend parameter estimates derived from the regression model. These two measures address different sources of uncertainty and are not directly comparable: UIs capture estimation uncertainty in the underlying disease metrics, while CIs reflect sampling uncertainty in the trend analysis. The weighted average of annual percentage change (APC) across segments yields the AAPC, which evaluates the overall average trend for a disease. When $P \leq 0.05$ and $AAPC > 0$, it indicates an upward trend in the burden over time; conversely, a downward trend is observed.^{30,31} We analyzed temporal trends in ASRs for neuropsychiatric diseases globally and across 21 GBD regions from 1990 to 2023, calculating AAPC. The specific calculation formula is as follows:

$$APC = [exp(\beta) - 1] \times 100\%$$

$$AAPC = \left[exp \left(\frac{\sum_{i=1}^k w_i \beta_i}{\sum_{i=1}^k w_i} \right) - 1 \right] \times 100\%$$

where β is the regression coefficient obtained through linear regression model fitting, β_i is the regression coefficient for each linear segment, representing APC within each time period, and w_i is the number of years in each time period.

Spearman correlation analysis was employed to evaluate the association between ASR and SDI using cross-sectional data for the year 2023. ASIR, ASPR, and ASDR were used as disease burden metrics in separate correlation analyses. Spearman correlation coefficients (ρ_s) and their corresponding *P*-values were calculated, with a significance level of $\alpha = 0.05$. The sign of ρ_s indicates the direction of association between ASR and SDI, while the magnitude of the absolute value of ρ_s reflects the strength of this association—values closer to 1 indicate a stronger correlation.

We calculated the indirect economic burden and its share of gross domestic product (GDP) from 1990 to 2023 using the human capital approach.^{29–31} The specific formula is:

$$\text{Annual indirect economic burden}$$

$$= \text{GDP per capita} \times \text{DALYs} \times \text{productivity weight}$$

To facilitate comparisons across years and countries, the GDP per capita was adjusted for purchasing power parity and expressed in constant 2017 international dollars, directly downloaded from the World Bank, accounting for inflation and cross-country price differences. Productivity weights were age-adjusted with values of 0.15 for ages 0–14, 0.75 for ages 15–44, 0.80 for ages 45–59, and 0.10 for ages 60 and above.³²

3. Results

3.1. Global trends in the burden of NMSDs

From 1990 to 2023, the absolute numbers of incident cases, prevalent cases, and DALYs for NMSDs and their subcategories showed an upward trend worldwide. DALYs for neurological disorders and mental disorders approximately doubled (increasing from 58 million to 117 million and from 83 million to 171 million, respectively). The global ASIR for neurological disorders remained relatively stable, with a net percentage change of <0.05%. However, the ASIR and ASPR for Parkinson's disease, along with ASDR for other neurological disorders, increased substantially, by 26.77%, 37.01%, and 152.43%, respectively. For mental disorders, the overall ASIR rose markedly in 2019, plateaued in 2020 and 2021 before declining rapidly; the ASPR and ASDR remained relatively stable before rising. Over the entire study period, the ASIR, ASPR, and ASDR for mental disorders increased by 15.00%, 24.00%, and 29.00%, respectively. ASDR for anxiety disorders and major depressive disorder rose by 65.09% and 41.05%, respectively, whereas idiopathic intellectual disability exhibited the largest decline, with a decrease of 12.58%. Although ASRs for substance use disorders and most of their subcategories have declined since 1990, cocaine and opioid use disorders showed increasing trends, with ASDR rising by 55.28% and 47.96%, respectively. Neurological disorders exhibited higher incidence, prevalence, and ASRs than mental disorders, but their DALY rates and ASDR were lower than those of mental disorders (Fig. 1, Supplementary Fig. S1).

3.2. Age and gender distribution of NMSDs worldwide

3.2.1. Neurological disorders

The incidence, prevalence, and DALY rates increased gradually with age, with the highest DALY burden observed among the elderly, primarily due to Alzheimer's disease and Parkinson's disease. The overall burden was greater in females than in males (ASDR for females: 1,584.31 per 100,000 person-years vs. ASDR for males: 1,147.88 per 100,000 person-years). The leading causes in females were headache disorders (migraine and tension-type headache), Alzheimer's disease and other dementias, and multiple sclerosis. Headache disorders were the most common condition across all age groups (Fig. 2, Supplementary Fig. S2–S4), though their ASR showed no significant upward or downward trend (Supplementary Fig. S1).

3.2.2. Mental disorders

The incidence, prevalence, and DALY rates peaked in the 10–19 age group and gradually declined thereafter. Generally, rates were higher in females than in males (ASDR: 2,239.62 per 100,000 person-years vs. 1,900.20 per 100,000 person-years). However, males had significantly higher incidence, prevalence, and DALY counts for autism spectrum disorder, attention-deficit/hyperactivity disorder, and conduct disorder. Except for conduct disorder, other types of mental disorders tended to persist throughout life after onset (Fig. 2, Supplementary Fig. S5–S7).

3.2.3. Substance use disorders

The incidence, prevalence, and DALY rates peaked at 30–34 years of age and declined gradually thereafter. These disorders exhibited the most pronounced gender disparities, with an ASDR of 607.85 per 100,000 person-years in males versus 235.28 per 100,000 person-years

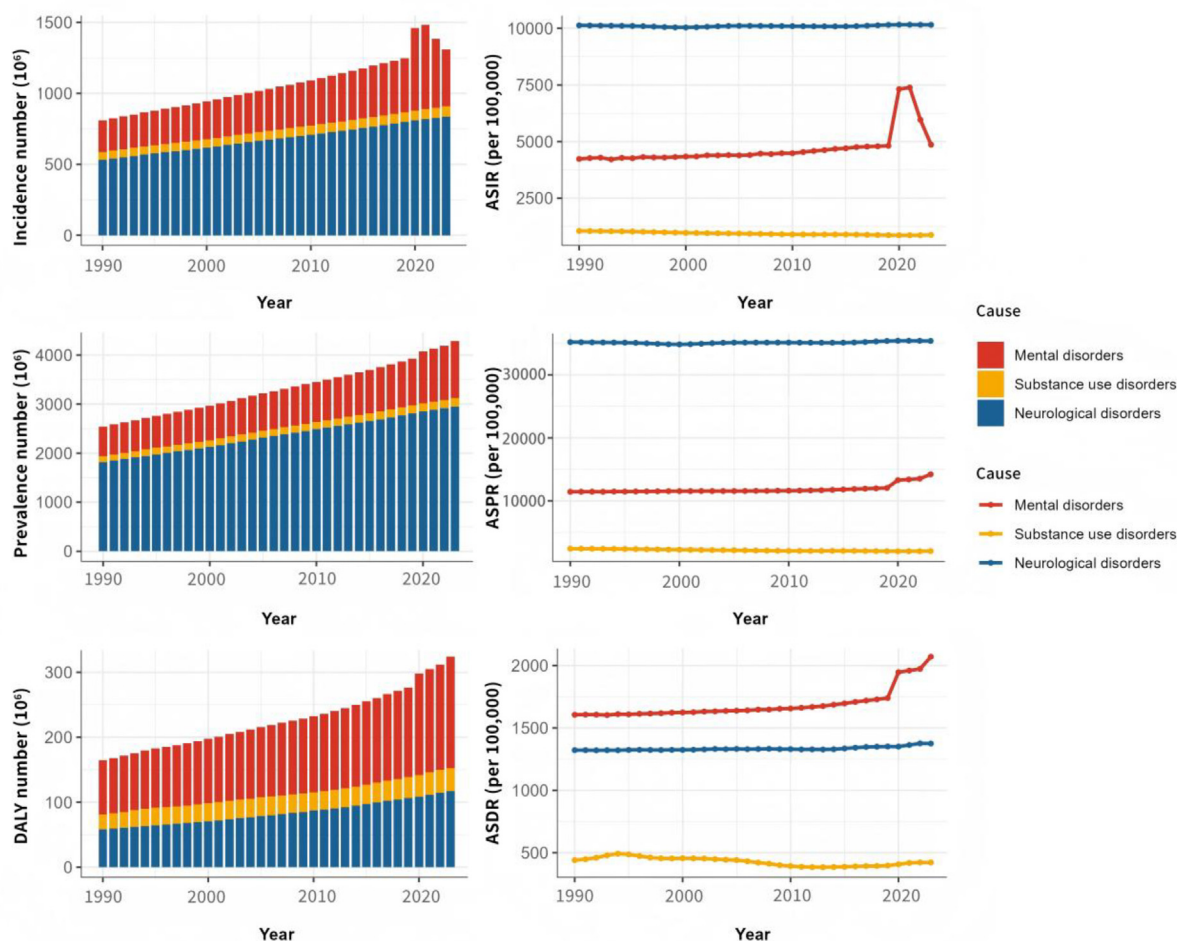


Fig. 1. Temporal trends in absolute numbers and age-standardized rates of incidence, prevalence, and DALYs for NMSDs globally, 1990–2023. NMSDs: neurological, mental, and substance use disorders; ASIR: age-standardized incidence rate; ASPR: age-standardized prevalence rate; ASDR: age-standardized DALY rate; DALYs: disability-adjusted life years.

in females (Fig. 2). Alcohol use disorders accounted for the highest incidence, prevalence, and DALYs among all substance use subtypes (Supplementary Fig. S8–S10). Across all subtypes, the increase in ASRs was larger in males than in females, while the decrease was smaller in males than in females. For cocaine use disorders, the ASDR increased by 71.98% among males but only 24.34% among females. For other substance use disorders, the ASDR decreased by 57.88% among females but only 2.58% among males (Supplementary Fig. S1).

3.3. Regional distribution of NMSDs

3.3.1. Neurological disorders

In high SDI areas, ASRs consistently remained at the highest levels (Fig. 3). Across 21 GBD regions, ASRs also showed no significant change with the corresponding AAPC ranging between 0 and 0.31. High-income North America had persistently high ASIR and ASPR, whereas East Asia had low ASRs. ASDR was high in tropical Latin America and low in South Asia. The absolute DALY number in South Asia was significantly higher than in other regions, with Oceania having the lowest (Supplementary Table S2–S4). In 2023, the top three contributors to ASDR were migraine, Alzheimer's disease, and idiopathic epilepsy, with migraine being the leading contributor globally and across 21 GBD regions (Supplementary Fig. S11). Except for motor neuron disease—which showed significant upward trends in Andean Latin American and the Caribbean, with increases of 1,489.55% and 1,180.85% respectively—no other neu-

rological subcategory exhibited pronounced changes (Supplementary Fig. S12–S14).

In 2023, ASIR and ASPR for neurological disorders were high in most European countries (e.g., Norway, Italy, the United Kingdom, Germany, and the Netherlands), the United States, Canada, Russia, and Brazil. Norway had the highest ASIR (13,277.60 per 100,000 person-years), and the Netherlands had the highest ASPR (45,361.06 per 100,000 person-years). China exhibited low ASIR and ASPR, but showed the highest increasing trends, with ASIR and ASPR increasing by 6.23% and 7.23%, respectively. The highest ASDRs were observed in most African countries (e.g., Zambia, Uganda, Eritrea, and Tunisia) along with Belgium, Germany, Saudi Arabia, Greenland, the United States, and Brazil, with Zambia recording the highest (1,788.46 per 100,000 person-years). Asia, Oceania, and some American countries (e.g., Peru, Argentina, and Cuba) had the lowest ASDR, with Iraq recording the fastest growth (16.43%) and Rwanda the largest decline (−18.40%).

3.3.2. Mental disorders

ASIR, ASPR and ASDR showed a clear increase in 2019 across all five SDI regions, followed by slower growth in 2020. Notably, the ASIR rose markedly in 2019, plateaued in 2020–2021, and then declined rapidly thereafter. ASIR remained highest in low SDI regions, while ASPR and ASDR consistently peaked in high-SDI regions (Fig. 3). At the GBD regional level, the ASIR for mental disorders was highest in Central Sub-Saharan Africa, whereas the ASPR and ASDR were relatively high in Australasia. The Southeast Asia had the lowest ASR. The most pronounced

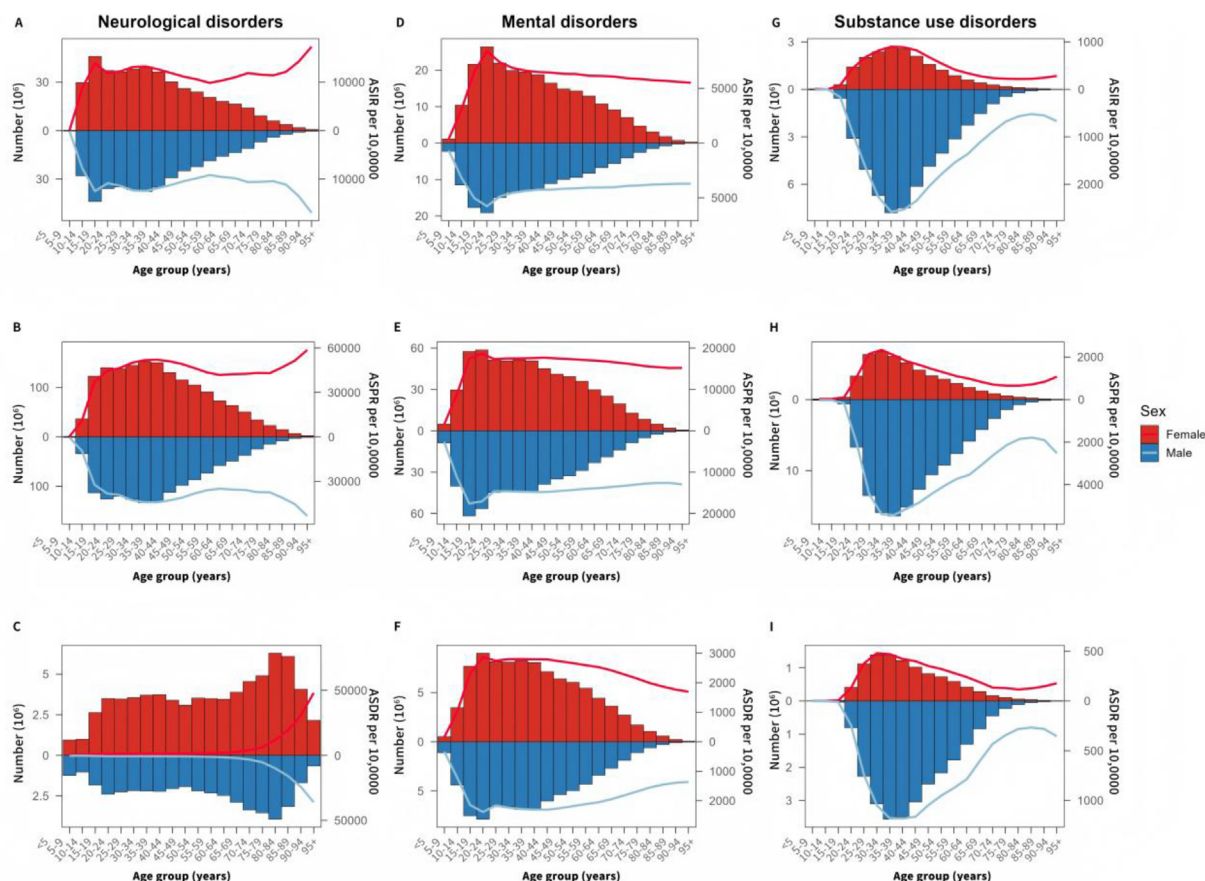


Fig. 2. Age- and sex-specific distribution of absolute numbers and age-standardized rates of incident cases, prevalent cases, and DALYs for NMSDs in 2023. (A–C) neurological disorders; (D–F) mental disorders; (G–I) substance use disorders.

increases in ASIR occurred in Western Europe (AAPC = 0.7201), Southeast Asia (AAPC = 0.6973), and East Asia (AAPC = 0.6320). ASPR and ASDR increased significantly in Australasia and Western Sub-Saharan Africa, with AAPCs exceeding 1 in both regions (Supplementary Table S2–S4). In 2023, anxiety disorders and major depressive disorder ranked as the top two conditions across all 21 GBD regions. Most subcategories showed increasing trends; in Australasia and Western Sub-Saharan Africa, the increases primarily driven by anxiety disorders, exhibiting ASDR increases of 149.48% and 117.43%, respectively. In high-income North America, autism spectrum disorders showed the largest increase, with an ASDR increase of 93.29% (Fig. 4, Supplementary Fig. S15–S17).

In 2023, ASIR for mental disorders was high in the Netherlands, the United Kingdom, and Syria; ASPR and ASDR showed similar distributions, with higher rates in the Netherlands, Portugal, the United Kingdom, Australia, Brazil, and Iran. The Netherlands exhibited the highest ASRs across all three metrics (ASIR: 10,357.47 per 100,000 person-years; ASPR: 22,892.78 per 100,000 person-years; ASDR: 3,555.85 per 100,000 person-years). Asian countries, particularly Southeast Asian nations (e.g., Myanmar, Laos, Thailand, and Timor-Leste), had low ASRs. ASRs showed an upward trend across all countries, with the United Kingdom experiencing the largest increases: ASIR 63.00%, ASPR 55.20%, and ASDR 64.30%.

3.3.3. Substance use disorders

ASRs declined overall, except in high SDI regions, where the ASDR increased by 85.29% (Fig. 3). The rates were highest in high-income North American and lowest in Western Sub-Saharan Africa. Across 21 GBD regions, the rates showed declining or stable trends, while high-income North America exhibited a marked upward trend, with an AAPC

of 4.1075 for ASDR (Supplementary Table S2–S4). Among all subcategories in 2023, alcohol use disorder had the highest ASR. In high-income North America, opioid use disorder showed the largest increase, with an ASDR rise of 754.38%. In tropical Latin America, cocaine use disorder showed marked increases in ASIR and ASPR, rising by 138.88% and 116.80%, respectively (Supplementary Fig. S18–S21). In 2023, Mongolia and the United States had the highest ASR. Mongolia showed the largest increase in ASIR, increasing by 27.69%, whereas the United States had the largest increases in ASPR (37.85%) and ASDR (284.02%). Canada showed a substantial ASDR increase (150.10%).

3.4. Association between ASRs and SDI

For anorexia nervosa, bulimia nervosa, and drug use disorders, the ASIR, ASPR, and ASDR each showed significant positive correlations with SDI, with all correlation coefficients $\rho_s \geq 0.69$. (Supplementary Table S5–S7). Similarly, the ASPR and ASDR of motor neuron disease showed significant positive correlations with SDI ($\rho_s = 0.89$ and 0.82 , respectively) (Supplementary Fig. S22, S23). In contrast, the ASDR of idiopathic epilepsy exhibited a significant negative correlation with SDI ($\rho_s = -0.69$; Supplementary Fig. S24).

3.5. DALYs attributed to NMSDs

YLDs accounted for the majority of the DALY burden across NMSDs, with proportions exceeding 59.00% for each category (Supplementary Fig. S25). Among neurological disorders subcategories, headache disorders (tension-type headache and migraine) accounted entirely for YLD, while other conditions contributed primarily to years of life lost (YLL), with YLL proportions ranging from 51.59% to 95.02%. Among

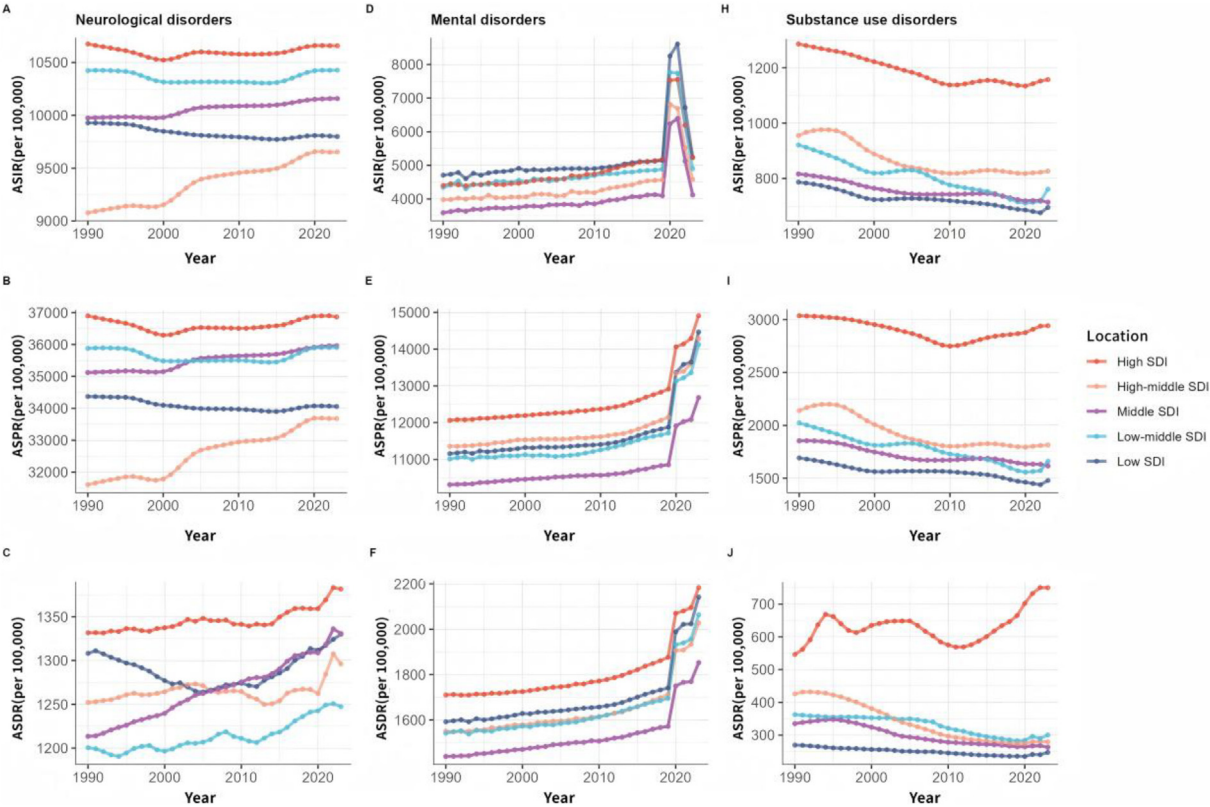


Fig. 3. Temporal trends in age-standardized rates of NMSDs across five SDI regions from 1990 to 2023. (A–C) neurological disorders; (D–F) mental disorders; (H–J) substance use disorders. SDI: socio-demographic index.

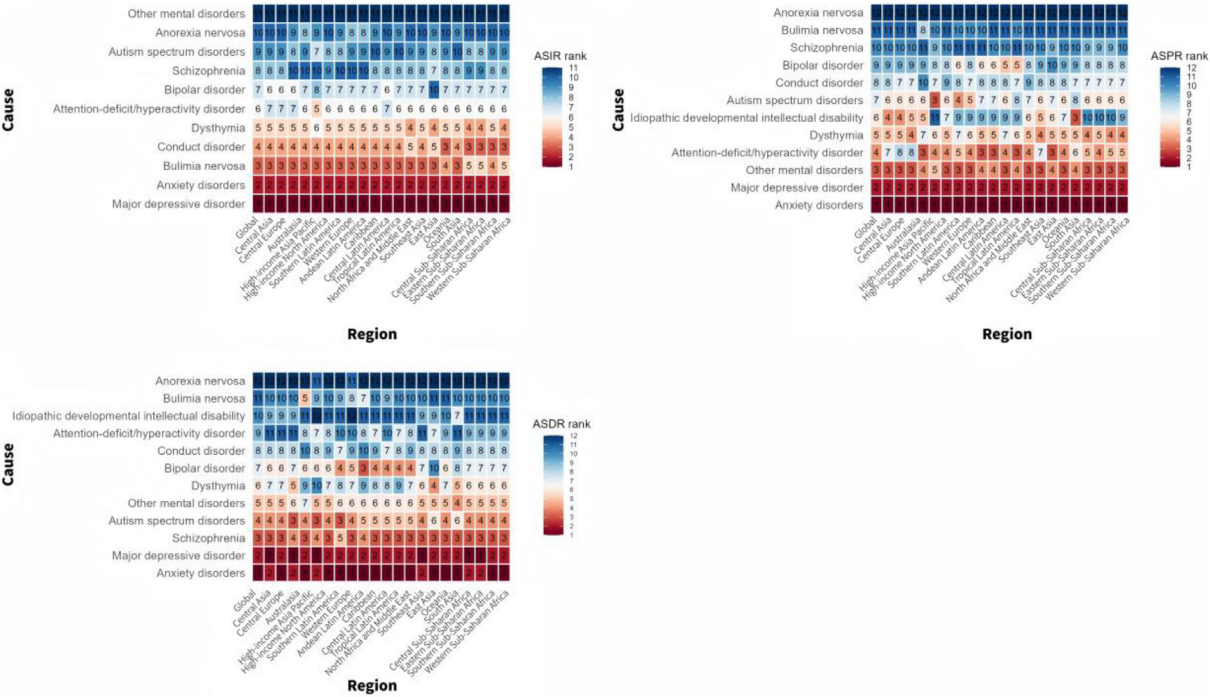


Fig. 4. Ranking of age-standardized rates for subcategories of mental disorders across 21 GBD regions in 2023.

mental disorders, only anorexia nervosa resulted in YLL (1.56%); all other subtypes contributed solely to YLD. Among substance use disorders, cannabis-related disorders contributed solely to YLDs; alcohol, opioid, and amphetamine use disorders predominantly resulted in YLDs, accounting for over 54.00% of the burden; and cocaine and other substance use disorders primarily contributed to YLLs, representing >54.00% of the burden (Supplementary Fig. S26).

3.6. Indirect economic burden of NMSDs

From 1990 to 2023, the global indirect economic burden increased by 216.73%, 270.64%, and 185.42% for neurological, mental, and substance use disorders, respectively, showing an overall upward trajectory. The proportion of indirect economic burden relative to GDP rose annually for neurological disorders, with a total rise of 12.33%. For mental disorders, the proportion rose sharply in 2019, stabilized in 2020 and 2021, and then resumed rapid growth, yielding an overall increase of 31.45%. Mental disorders imposed the heaviest indirect economic burden. Substance use disorders exhibited fluctuating patterns (Supplementary Fig. S27 and Table S8).

In both 1990 and 2023, the indirect economic burdens of NMSDs were relatively high in the United States, China, and India. Most countries exhibited upward trends, with Equatorial Guinea experiencing the fastest growth (neurological disorders: 6,053.89%; mental disorders: 8,087.07%; substance use disorders: 7,420.68%) (Supplementary Table S9–S11).

The share of indirect economic burden of neurological disorders in GDP was relatively high in most European countries (such as Moldova, Cyprus, Germany, and Italy) in both 1990 and 2023. Moldova had the highest share in 1990 (0.89%), while Cyprus had the highest in 2023 (1.06%). Beyond most European nations, Saudi Arabia, Zambia, Rwanda, and Greenland also exhibited substantial shares in 1990. Most countries showed increasing trends, with Japan, Cameroon, Libya, South Africa, Jordan, and Iran experiencing notable increases (> 30.00%), whereas Rwanda recorded the largest decrease, dropping by 26.86%. In 1990, the proportion for mental disorders was high in the Netherlands, Saudi Arabia, New Zealand, Cyprus, the United States, Greenland, Switzerland, Portugal, Chile, and Australia, with the Netherlands having the highest (1.56%). By 2023, Cyprus, the Netherlands, the United Kingdom, Australia, Brazil, and Iran showed high proportions, with Cyprus ranking first (2.44%). Except for Georgia, the proportion increased across all countries, with substantial growth in African nations (Cameroon: 96.77%; Central African Republic: 84.09%; Nigeria: 75.36%). In 1990, the share for substance use disorders was relatively high in Greenland (1.15%) and Russia (1.02%). By 2023, the highest proportions were in the United States (2.02%), Mongolia (1.26%), and Canada (1.05%). The United States, Mongolia, and Canada showed the most pronounced increases (> 100%), while China exhibited the largest decrease (−46.19%) (Supplementary Table S9–S11).

4. Discussion

Our findings indicate that the absolute numbers of incident cases, prevalent cases, and DALYs for NMSDs increased globally from 1990 to 2023, with mental disorders showing the largest absolute DALY increase (from 83 million to 171 million, a 1.05-fold rise), while age-standardized DALY rates for substance use disorders declined in most regions but rose by 85.29% in high SDI regions. Among disease subtypes, headache disorders, Alzheimer's disease and other dementias, anxiety disorders, major depressive disorder, and alcohol use disorders accounted for the greatest burden. These results suggest that although the overall burden of NMSDs continues to grow, the patterns of increase vary substantially across disease categories and regions.

These findings are broadly consistent with previous reports identifying population growth and demographic aging as the primary drivers of the rising absolute burden.^{33,34} This age-related pattern is particularly

evident for neurological disorders, where a significant disease burden in older age—predominantly attributed to Parkinson's and Alzheimer's disease—reinforces age as a risk factor for their onset.³⁵ In China, the annual aging rate has accelerated from <2.00% annually to 2.47%,³⁶ coinciding with the largest increases in incidence and prevalence of neurological disorders burdens observed in our study. This underscores the imperative for rapidly aging populations to provide essential care and treatment services for NMSDs, with a focus on early detection, disease mitigation, reduction of premature mortality, and effective treatment.³⁷

Regionally, the lower ASRs observed in low and lower-middle SDI regions compared to high-SDI regions likely reflect substantial under-ascertainment due to inadequate medical facilities, shortages of health-care personnel, and gaps in epidemiological surveillance.^{22,24} This data limitation inherently constitutes a form of health inequity.³⁸ Therefore, investing in data collection training and health information systems in low- and middle-income countries is an effective measure to achieve health equity and address the NMSD crisis.³⁹ The significant positive correlation between the ASDR of motor neuron disease and SDI, for instance, cannot be fully explained by data gaps alone; rather, it more likely reflects disparities in diagnostic capacity, access to neuroimaging, and availability of specialized treatment services.⁴⁰ This provides data support for incorporating rare but highly disabling and fatal neurological diseases into national essential health services and strengthening universal health coverage measures.⁴¹

The marked rise in mental disorder burden observed in 2019, driven primarily by anxiety and depression, is likely attributable to the impact of COVID-19 pandemic.⁴² In June 2020, the United States adults had rates of anxiety and depression symptoms that were three to four times higher than in the previous year.⁴³ The COVID-19 pandemic exposed the fragility of global mental health services, particularly in low- and middle-income countries, and while digital mental health interventions advanced rapidly, they also faced challenges, highlighting the urgent need to establish scalable digital service models that meet population demands.⁴⁴ The United Kingdom, which recorded the most significant increase in mental disorder burden, may attribute this to nearly a decade of fiscal austerity policies implemented since 2010. These policies reduced social security and mental health services while increasing tax burdens, exacerbating individual economic burdens, and intensifying the disease burden of mental disorders.^{45,46}

Of note, although mental disorders exhibit higher DALYs and ASDR than neurological diseases, their incidence and prevalence patterns diverge. This discrepancy likely stems from the nascent stage of effective diagnostic and therapeutic interventions for mental disorders, coupled with greater public willingness to allocate resources toward physical illnesses relative to mental health conditions.⁴⁷

The overall ASR for substance use disorders has declined, but opioid use disorders have continued to rise, particularly in high-income North America (especially the United States). In the late 1990s, aggressive pharmaceutical industry promoted prescription opioid use. Following regulatory controls, affected individuals shifted to illicit synthetic opioids such as fentanyl,⁴⁸ marking a more severe phase of the epidemic. Overdose deaths linked to synthetic opioids increased by 2.21 times relative to total opioid-related deaths.⁴⁹ Increasing funding for evidence-based treatment, assessment, and medication-assisted therapies could effectively mitigate this crisis.⁵⁰ Alcohol use disorder remains a leading cause disability, accounting for 36.4% of NMSD-related DALYs.⁵¹ A bidirectional relationship between substance use and mental disorders⁵² offers a new perspective for integrated treatment approaches for NMSDs. Currently, most neuropsychiatric and substance addiction treatment systems operate independently. Transitioning from single-disease to integrated care models represents the most cost-effective strategy.⁵³ Evidence suggests that integrated care reduces costs by approximately 4% while enhancing intervention effectiveness by about 6% compared to conventional care.⁵⁴

Notably, the declining share of indirect economic burden attributable to substance use disorders in China (−46.19% from 1990

to 2023) may reflect several concurrent developments: rapid economic growth has expanded the GDP denominator, outpacing growth in DALY estimates, while strict regulatory policies on opioid prescription and alcohol control, implemented since the early 2000s, have likely contributed to stabilized or reduced ASRs. Conversely, the dramatic increases observed in Equatorial Guinea—where the indirect economic burden of NMSDs grew by over 6,000% to 8,000%—may be partially attributable to oil-sector-fueled GDP expansion rather than genuine epidemiological worsening. The country's small baseline population combined with rapidly expanding economy produces amplifies percentage changes, necessitating cautious interpretation of these extreme fluctuations.

NMSDs and their subcategories exhibit distinct age- and gender-specific patterns. The overall burden of neurological and mental disorders was higher in females than in males, particularly for Alzheimer's disease and other dementias, headache disorders, and anxiety and depressive disorders, consistent with previous findings.^{55–58} This disparity may be attributed to fluctuations in estrogen levels during adolescence, postpartum, and perimenopause, which affect endocrine function,⁵⁹ or to gender-specific socioeconomic status and caregiving responsibilities.⁶⁰ The burden of mental disorders is particularly severe during adolescence. A study indicated that the burden among children aged 5–14 is projected to increase further,⁶¹ possibly due to developmental vulnerability of the prefrontal cortex-amygdala circuit during this period, which is highly sensitive to adverse environmental exposures such as parental divorce⁶² and early childhood adversity,⁶³ potentially leading to dysregulation in emotional control and executive functions.⁶⁴ Implementing effective prevention and early intervention during this neurodevelopmental high-risk period can promote brain maturation by influencing neuroplasticity, yielding long-term protective effects.⁶⁵ Economic evaluations indicated that interventions targeting adolescent mental disorders are cost-effectiveness. For instance, the economic benefits of preventing and treating common adolescent mental disorders over a decade are estimated to equate to 25% of the United Kingdom National Health Service's annual expenditure in 2021. Preventive interventions for anxiety and depression could reduce 7.3 million DALYs.⁶⁶ With respect to temporal trends in sex disparities, the sex gaps in substance use disorders have widened over the study period, with male ASDR increases exceeding female increases across most subcategories (e.g., cocaine use disorders: 71.98% in males versus 24.34% in females), while sex disparities in neurological and mental disorders have remained relatively stable. Regarding age of onset, mental disorders continue to peak during adolescence (ages 10–19), but emerging data suggest that an increasing burden among children aged 5–14, indicating a possible earlier onset that warrants monitoring in future surveillance.

Globally, health expenditures for NMSDs account for <1% of total government health spending.¹ Societal misconceptions and policy neglect often lead to reduced investment in these conditions.^{67,68} Our estimates of indirect economic burden provide actionable evidence for resource allocation decisions. The burden is substantial in populous nations (China and India) and high-income countries (the United States). In China and India—each with over 1.4 billion inhabitants—resources for NMSD interventions remain scarce, and treatment-seeking rates are low: only 8% of patients in China seek treatment, while India faces a treatment gap of 70%–92% for mental disorders.^{69,70} Addressing these barriers is crucial for reducing indirect economic burdens in populous nations. At the national level, the marked escalation in Equatorial Guinea's indirect economic burden is largely ascribed to the concomitant rapid per capita GDP. At the same time, healthcare system enhancements and expanded diagnostic coverage—propelled by economic progress—have led to the progressive identification of previously undetected cases. However, current healthcare infrastructure continues to fall short of addressing patient needs.^{71,72} Policy responses should encompass the reinforcement of physical infrastructure, augmentation of governmental fiscal allocations, assurance of essential drug availability, and systematic training specialized personnel in NMSD care.⁷² The proportion of indi-

rect economic burden relative to GDP varies considerably. Some countries face dual pressures of high economic burden and high ASDR: for neurological disorders, predominantly European nations (Germany, the United Kingdom, Italy, and Finland); for mental disorders, the Netherlands, Portugal, United Kingdom, Australia, Brazil, and Iran; and for substance use disorders, the United States and Mongolia. These nations should prioritize comprehensive prevention and control strategies tailored to their leading conditions. The most pronounced decline in the global share of substance use disorder burden was observed in China, which correlated with substantial decrease in drug-use-related DALYs achieved through long-term prevention and control policies, including strict supply control, extensive anti-drug education, rehabilitation services, and relevant legislative measures.^{73,74}

5. Limitations

This study has several limitations. First, as with all GBD 2023 analyses, these results are subject to the inherent constraints and limitations of the database: case definitions and diagnostic criteria vary across countries, and data gaps in low-income countries affect estimation accuracy. Comorbidity models may underestimate disease associations, particularly for mental disorders.²⁹ Additionally, YLLs estimates undercount mental disorder-related deaths coded as “suicide.” Second, the scope excludes infectious neurological diseases (e.g., meningitis) and cerebrovascular diseases (e.g., stroke), potentially underestimating the burden of neurological diseases. Third, the human capital approach relies heavily on DALYs and cannot disaggregate indirect burden components (e.g., absenteeism, reduced labor force, caregiver loss). Moreover, we did not calculate direct economic burden, potentially underestimating the economic burdens. Future research should incorporate direct economic burden assessments. Combining these with our indirect burden estimates will enable a total economic burden calculation to inform rational health resource allocation.

6. Conclusions

Between 1990 and 2023, despite varying trends in ASRs, their absolute numbers of incident cases, prevalent cases, and DALYs for NMSDs increased across all categories. The overall disease burden exhibited significant disparities across regions and populations. Among subtypes, Alzheimer's disease and other dementias, Parkinson's disease, headache disorders, anxiety disorders, depression, and alcohol use disorders accounted for the largest shares of the burden. Concurrently, the indirect economic burden of these diseases has shown an upward trend globally, while national health systems continue to face resource allocation shortfalls. These findings underscore the imperative for enhanced collaboration among global and national health systems to develop and implement targeted, comprehensive interventions aimed at reducing disease burden and narrowing cross-country disparities.

Author's contributions

Tao RS: data curation, formal analysis, funding acquisition, investigation, writing original draft, and writing – review & editing. Sun ZH: methodology, conceptualization, software, formal analysis, writing original draft, and writing – review & editing. Long RY: conceptualization, data curation, investigation, methodology, supervision, writing – review & editing. All authors have reviewed the final version of the manuscript.

Declaration of generative AI and AI-assisted technologies use

During the preparation of this study, the authors utilized DeepSeek and ChatGPT for language editing and polishing, and partial literature search tasks. All AI-assisted content was thoroughly reviewed and revised by the authors, who take full responsibility for the final

manuscript. No AI tools were used for data analysis, result interpretation, or the generation of core scientific conclusions. To protect privacy, all data input into these AI tools were non-identifiable aggregated statistical information and did not involve any individual-level data.

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Conflict of interest disclosure

The authors declare that they have no conflicts of interest.

Data availability

Data for this study are derived from the Global Burden of Disease Database 2023, available at <https://vizhub.healthdata.org/gbd-results/>.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.cmsj.2026.08.002](https://doi.org/10.1016/j.cmsj.2026.08.002).

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