BMJ Open

Burden and trends of multiple sclerosis in China from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019

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To cite: Li M, Zhou N, Duan S, *et al*. Burden and trends of multiple sclerosis in China from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. *BMJ Open* 2022;**12**:e066335. doi:10.1136/bmjopen-2022-066335

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-066335).

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Received 06 July 2022
Accepted 28 November 2022

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ABSTRACT

Objective To compare the burden of multiple sclerosis disease indicators in the Asia-Pacific countries, China and globally through the Global Burden of Disease 2019 (GBD2019) Database, and to analyse the changes of multiple sclerosis disease burden in China from 1990 to 2019.

Study design Observational study based on the Global Burden of Disease.

Setting The relevant incidence, prevalence, death and disability-adjusted life year (DALY) rates and corresponding age-standardised rates (ASRs) and sociodemographic index (SDI) in China, globally and in Asia-Pacific countries were extracted from the GBD2019 Database to further study the age-standardised incidence, prevalence and mortality, and the relationship between DALY rate and SDI.

Results Various disease burden indicators of multiple sclerosis in China are at low level in the world, and the prevalence, incidence and DALY rates have slowly increased from 1990 to 2019. During this period, the age-standardised prevalence rate (ASPR) of multiple sclerosis in China showed an upward trend, while the age-standardised death rate (ASDR), age-standardised DALY rate (ASR-DALY) and age-standardised incidence rate all decreased to varying degrees, which were roughly consistent with the global amplitude changes, and all indicators are similar to most countries in the Asia-Pacific region. As the value of the SDI increases, the ASPR of multiple sclerosis was trending upward, and the ASDR was trending downward.

Conclusion Compared with other countries in the Asia-Pacific region, China is in a low state of disease burden indicators. However, as a developing country and the most populous country in the world, the total number of patients is not small, and as a rare disease, the treatment cost is relatively expensive, and the treatment cost of the complications caused by the disease is not low. The construction of the medical security system should be strengthened to reduce its burden on individuals, families and society.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study provides a comprehensive description of the incidence, prevalence and deaths from multiple sclerosis in China.
⇒ This study assesses long-term (30-year) trends in the burden of multiple sclerosis in China, globally and in the Asia-Pacific region.
⇒ The Global Burden of Disease approach provides a standardised statistical approach that allows incidence, prevalence, mortality, and comparability between countries and time to reduce potential bias.
⇒ For each estimate reported in this study, we also provide a measure of uncertainty (uncertainty intervals) to reflect how much is known.
⇒ The main limitation is that the data were secondarily estimated data rather than the original surveillance data.

INTRODUCTION

Multiple sclerosis (MS) is a central nervous system disease in which the body's immune system attacks myelin and causes neurological disorders to gradually lose function. According to the current Chinese identification, MS is a rare disease and can be studied as a rare disease, and was included in the 'First Batch of Rare Diseases List' in May 2018.[1] The catalogue is selected by authoritative experts in different fields in accordance with certain working procedures based on the incidence of diseases in China's population, the level of medical technology, the burden of disease, the level of protection, etc, with reference to international experience. The catalogue was widely consulted and agreed upon by relevant ministries and industries. More women than men have MS. MS is one of the main causes of neurological deficits in young and middle-aged people. The age of onset is usually between 15 and 40 years old, mostly in early adulthood. The spectrum of clinical symptoms is relatively wide, depending on the affected part, and it can be manifested as limb weakness, sensory symptoms, vision loss, sphincter dysfunction, etc.[2] MS affects more than 2 million people worldwide; 25%

of whom live in low-income and middle-income countries.[3] From the global view, the number of MS deaths is on the rise.

The possible aetiologies and risk factors are susceptibility gene carrier, Epstein-Barr virus infection, smoking, vitamin D deficiency, adolescent obesity and 'latitude effect'. In addition, the global prevalence distribution of MS can be divided into high prevalence area (greater than 30/100 000), medium prevalence area (5–30/100 000) and low prevalence area (less than 5/100 000).[4] The incidence is high in Europe and North America, and most countries in the Asia-Pacific region are low-prevalence regions; however, there are some exceptions such as South Korea, Japan, New Zealand and Australia studied in this paper. With the improvement of the level of MS diagnosis and treatment, the number of detected cases has also increased year by year.[5]

Many countries and regions in the world do not have MS cases and related epidemiological data. More research is needed to make more accurate estimates in countries over the world including China. Using detailed national-level morbidity and mortality data, this article introduces the results of the Global Burden of Disease 2019 (GBD2019) MS disease burden study and discusses the differences in the global, Asia-Pacific and China MS disease burden. The current situation provides an empirical basis and a reference for formulating reasonable and effective MS prevention and control policies. By further exploring the relationship between disease burden and sociodemographic index (SDI) in different regions, suggestions are put forward to reduce the disease burden of MS and better protect the rights and interests of patients with MS.

MATERIALS AND METHODS

Data sources

The data sources of this study are all published on the Institute for Health Metrics and Evaluation (IHME) official website (http://ghdx.healthdata.org/), which is currently the most extensive and most credible database on disease burden in the world. The study, led by the IHME at the University of Washington in the USA, aims to assess the disease burden of 315 diseases, injuries and risk factors in 195 countries and regions around the world, and regularly publish the incidence, prevalence, death, and disability-adjusted life year (DALY) data, with data breakdowns by country, year, gender, attribution and age. Relevant data were downloaded from the Global Health Data Exchange website (http://ghdx.healthdata.org/gbd-results-tool).

Statistical analysis

The database uses the IHME Bayesian regression tool DisMod-MR V.2.1 for the incidence, prevalence, death, DALYs and other indicators of MS. Analyses, modelling and estimates are performed, normalised to the world population, and reported as age-standardised incidence, prevalence, mortality and DALY rates per 100 000 population.[6] After cleaning and arranging the stored data in this study, we use Excel and Origin V.2021a for tabulation and graphing. All estimates are generated with a 95% uncertainty interval (95% UI), including all uncertainties due to measurement error, bias and modelling, with the 95% UI taken from the 25th and 975th samples of 1000 percentile. Since the GBD Database has been age standardised

Table 1 Comparison of disease burden in the world, Asia-Pacific region and China, in 1990 and 2019

Categories	Global	Low-middle	Middle	High-middle	High	China
Incident cases						
1990	41 854	82.12	2569.47	18.82	990.79	2005.14
2019	59 345.44	128.29	3952.61	39.92	1319.2	2967.1
Percentage change between 1990 and 2019	41.79	56.22	53.83	112.11	33.15	48
Prevalent cases						
1990	1 022 936.64	1087.47	28 933.38	253.69	24 383.24	21 608
2019	1 756 792.02	1901.36	57 403.39	609.23	45 091.67	42 570
Percentage change between 1990 and 2019	71.70	74.84	98.4	140.15	84.93	97
Death cases						
1990	13 356	1947.18	1510.98	10.69	345.91	1223.95
2019	22 438.96	3079.43	2114.66	28.35	535.36	1803.54
Percentage change between 1990 and 2019	68	58.15	39.95	165.2	54.77	47.35
DALYs						
1990	726 065.6	1947.18	66 203.05	479.82	17 958.42	52 673.56
2019	1 159 831.84	3079.43	97 191.91	1175.79	26 608.54	71 439.34
Percentage change between 1990 and 2019	59.74	58.15	46.81	145.05	48.17	35.62

DALYs, disability-adjusted life years.

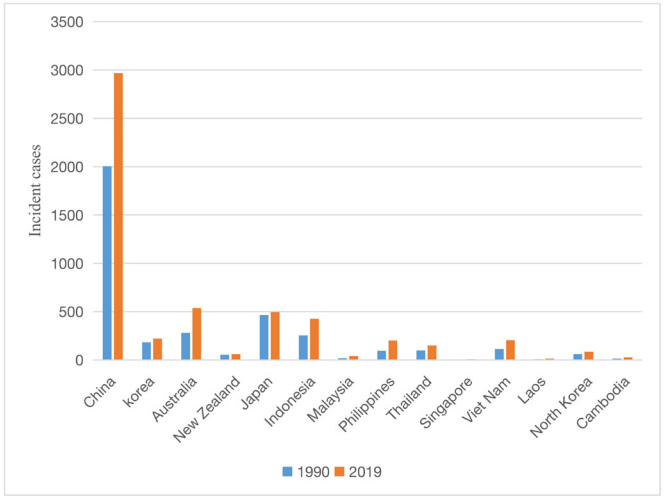

Figure 1 Comparison of the number new cases by country in the Asia-Pacific region in 1990 and 2019.

and given 95% UI, statistical analysis and graphing can be performed directly.

Indicator selection and interpretation

The countries selected in this paper are the countries in the Asia-Pacific region where the annual death toll from MS is greater than 1. A major feature of the Asia-Pacific region is the large number of countries and the large economic differences. There are both developed and developing countries here. There are highly developed urban countries and regions, as well as economically backward island countries; in this way, we can better study the relationship between MS and the level of social development. The SDI is a comprehensive measure of education level, per capita income and fertility rate. The score ranges from 0 to 1. The lower the value, the less developed the region is. The higher the value, the more developed the region is. There is an announcement to divide countries into five SDI quintiles: low (0–0.454743), low-middle (0.454743–0.607679), middle (0.607679–0.689504), high-middle (0.689504–0.8051290) and high (0.805129–1).[7] Because the SDI values of the Asia-Pacific countries involved in this article are not between 0 and 0.454743, the SDI values of the countries selected in this article are divided into four levels (low-middle, middle, high-middle, high). Incidence, prevalence, death, DALY rates and their age-standardised rates (ASRs) were also used to assess MS disease burden. According to the definition in the GBD2019 Study, the incidence rate refers to the proportion of new cases of MS per 100 000 population; the prevalence rate refers to the proportion of new and old patients with MS per 100 000 population; the mortality rate is the proportion of deaths per 100 000 people; DALY refers to the proportion of disabled life years and disabled life years per 100 000 people, which approximately reflects the gap between the current health status and the ideal status of the population.

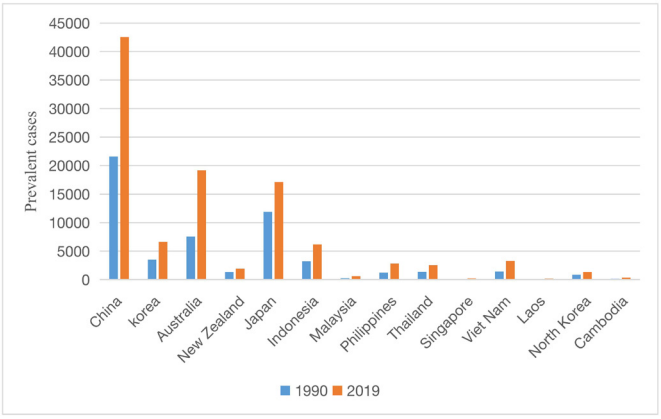

Figure 3 Comparison of the number of patients with the disease by country in the Asia-Pacific region in 1990 and 2019.

Patient and public involvement

No patients were involved in developing the aims, design or implementation of this study. No patients were involved

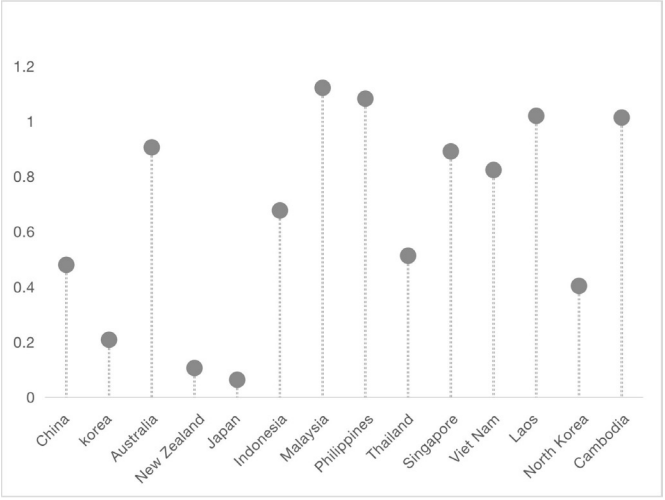

Figure 2 The growth rate of multiple sclerosis incidence in countries in the Asia-Pacific region from 1990 to 2019.

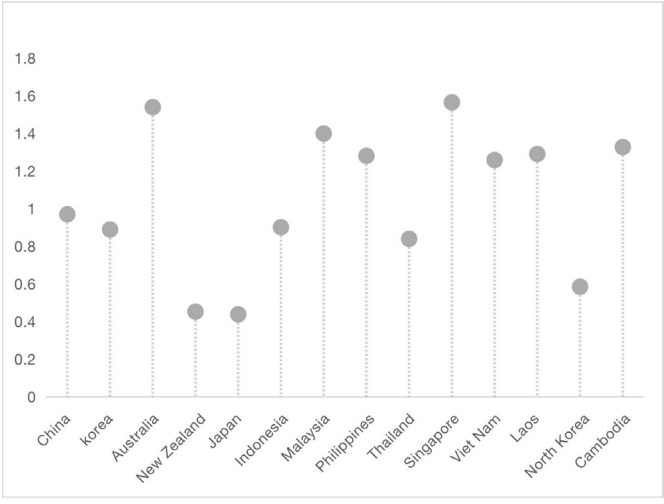

Figure 4 The growth rate of the number of people with multiple sclerosis in countries in the Asia-Pacific region from 1990 to 2019.

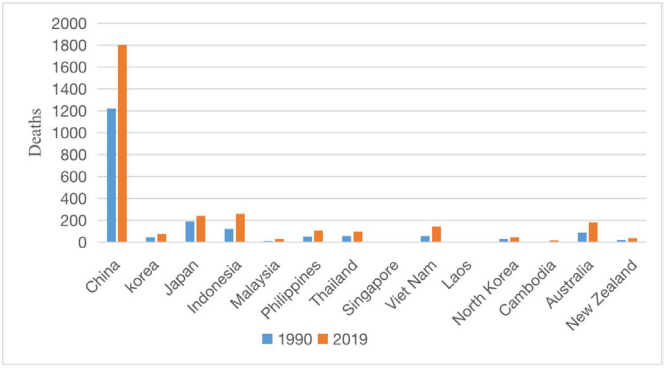

Figure 5 Comparison of deaths by country in the Asia-Pacific region in 1990 and 2019.

in the interpretation of study results or write up of the manuscript.

RESULTS

Incidence

In 2019, among the high-SDI regions in Asia-Pacific, Australia has the highest age-standardised incidence rate (ASRI) of 2.2 (95% UI: 1.91 to 2.48)/100 000, and Malaysia had an ASRI of 0.12 (95% UI: 0.10 to 0.15)/100 000) (online supplemental table 1). According to the GBD Database, the number of people with MS in the world increased from 41 854 cases in 1990 to 59 345.44 cases in 2019. This is an increase of 41.79% (table 1). In the Asia-Pacific region, Malaysia has the largest increase in the number of cases (112.11%), which is in a high-middle SDI region. Second only to Malaysia is the Philippines, which is in a middle-SDI region (108.20%). The least increase in the number of cases is Japan, which is in a high-SDI region (6.32%) (table 1 and figures 1 and 2). According to the SDI standard published by IHME in 2019, China is a middle-SDI country. In 1990, the number of MS cases in China was 2005.14. By 2019, the number of MS cases in China was 2967.1, an increase of 48%, and the

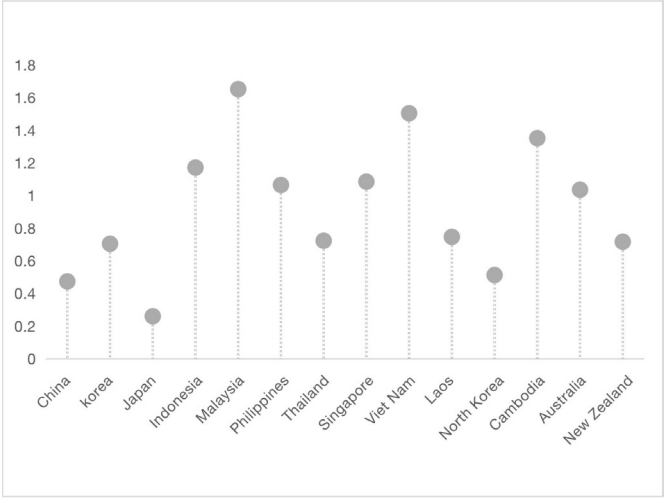

Figure 6 The growth rate of multiple sclerosis deaths by country in the Asia-Pacific region from 1990 to 2019.

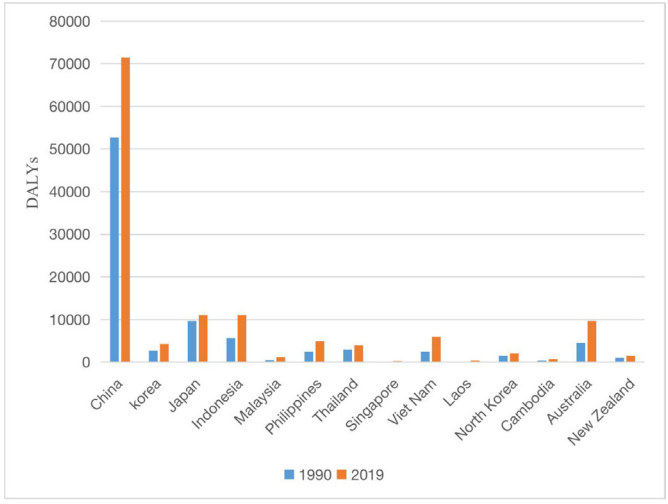

Figure 7 Comparison of disability-adjusted life years (DALYs) by country in the Asia-Pacific region, 1990 and 2019.

increase in the incidence rate was higher than that in the global level. Compared with other Asia-Pacific regions, the growth rate of the number of cases in China is lower than that in most countries (table 1). In 2019, the ASRI of MS in China was lower than that in most countries of the Asia-Pacific region, with little difference from the lowest ASRI in Malaysia. There was also a downward trend compared with the ASRI of MS in China in 1990 (online supplemental table 1).

Prevalence

According to statistics, the number of people with MS worldwide increased from 1 022 936.64 cases in 1990 to 1 756 792.02 cases in 2019, an increase of 71.7% (table 1). The largest increase in the number of patients in the Asia-Pacific region was in Singapore (165.49%) and the smallest increase was in Japan (43.87%), both of which belonged to high-SDI regions (figures 3 and 4). In 2019, among the Asia-Pacific regions, Australia had the highest

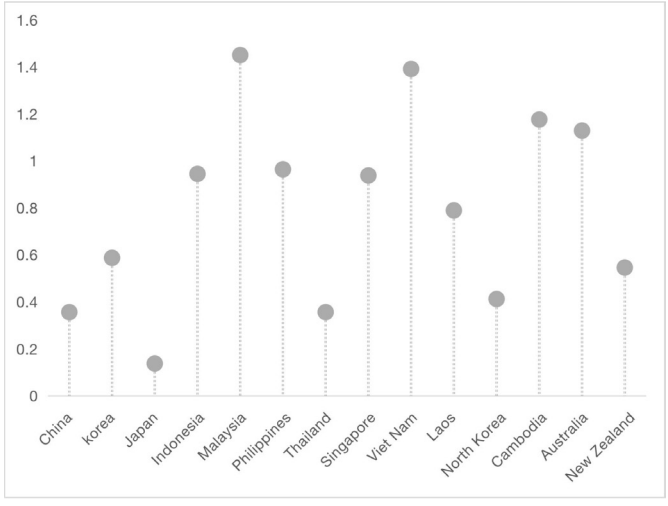

Figure 8 The growth rate of multiple sclerosis disability-adjusted life years by country in the Asia-Pacific region from 1990 to 2019.

Table 2 Indicators in different SDI regions over the past three decades

Year	1990	1995	2000	2005	2010	2015	2019	Mean
ASRI								
High SDI	0.782	0.806	0.912	0.916	0.924	0.938	0.896	0.751
High-middle SDI	0.24	0.233	0.23	0.23	0.23	0.23	0.23	0.232
Middle SDI	0.184	0.184	0.18	0.18	0.178	0.182	0.18	0.181
Low-middle SDI	0.13	0.13	0.13	0.13	0.13	0.13	0.12	0.129
ASPR								
High SDI	19.126	20.078	23.306	23.678	23.932	24.48	23.142	22.535
High-middle SDI	3.043	2.977	2.967	2.947	3.03	3.07	3.147	3.026
Middle SDI	2.298	2.295	2.327	2.343	2.381	2.445	2.478	2.368
Low-middle SDI	1.76	1.78	1.82	1.85	1.86	1.87	1.87	1.83
ASDR								
High SDI	0.27	0.278	0.288	0.28	0.264	0.254	0.25	0.269
High-middle SDI	0.153	0.15	0.147	0.14	0.137	0.133	0.13	0.141
Middle SDI	0.124	0.128	0.126	0.12	0.112	0.11	0.11	0.119
Low-middle SDI	0.09	0.1	0.1	0.09	0.1	0.09	0.1	0.096
ASR-DALYs								
High SDI	13.43	13.914	14.94	14.632	14.302	14.038	13.724	14.14
High-middle SDI	6.283	6.173	5.89	5.61	5.507	5.437	5.45	5.764
Middle SDI	5.056	5.234	5.242	4.594	4.42	4.364	4.408	4.824
Low-middle SDI	3.68	3.68	3.69	3.59	3.65	3.62	3.72	3.661

ASDR, age-standardised death rate; ASPR, age-standardised prevalence rate; ASR, age-standardised rate; ASRI, age-standardised incidence rate; DALYs, disability-adjusted life years; SDI, sociodemographic index.

age-standardised prevalence rate (ASPR) of 61.09 (95% UI: 51.70 to 70.06)/100 000, and Malaysia had the lowest ASPR of 1.87 (95% UI: 1.44 to 2.34)/100 000. Compared with 1990 and 2019, the ASPR of most countries is on an upward trend (online supplemental table 1). In 1990, the number of patients with MS in China was 21 608; but in 2019, it has reached 42 570, almost doubled (1.97 times), which is higher than the growth rate of the global number of patients (table 1). Compared with the growth rate of ASPR in 1990, China is also much higher than the global level. From the perspective of the Asia-Pacific region, the growth rate of China's ASPR (23.40%) is only lower than that of Australia (50.69%) (online supplemental table 1).

Deaths

The global death toll due to MS in 2019 was 22 438.96, an increase of 68.00% over the 13 356 deaths in 1990 (table 1). Compared with 1223 deaths in 1990, the number of MS deaths in China in 2019 increased by 47.35%, which is far lower than the growth rate of global deaths (table 1 and figure 5). The country with the largest increase in the number of deaths in the Asia-Pacific region was Malaysia with 165.20%, and the country with the smallest increase was Japan with 26.04%, similar to the incidence (figure 6). Compared with the global

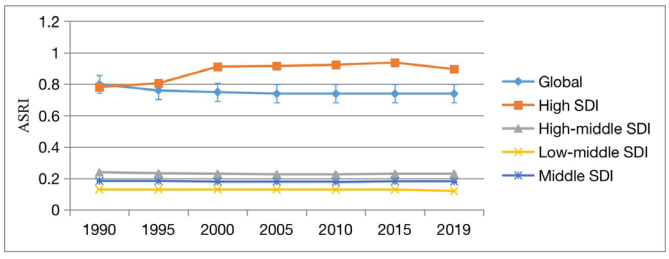

Figure 9 According to the 2019 SDI classification criteria, the distribution of ASRI in various SDI regions in the past 30 years. ASRI, age-standardised incidence rate; SDI, sociodemographic index.

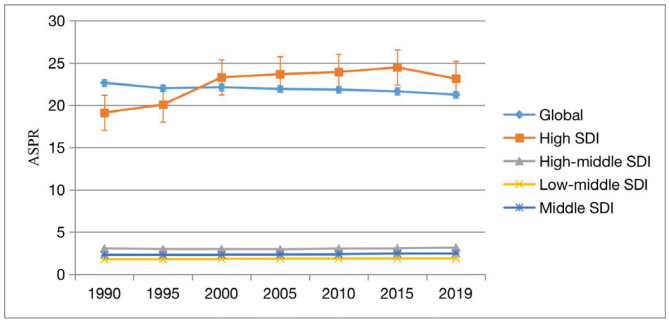

Figure 10 According to the 2019 SDI classification criteria, the distribution of ASPR in various SDI regions in the past 30 years. ASPR, age-standardised prevalence rate; SDI, sociodemographic index.

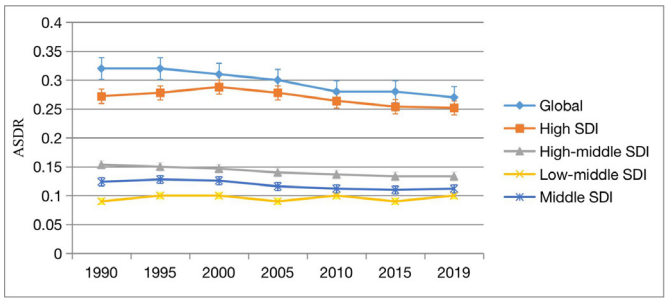

Figure 11 According to the 2019 SDI classification standard, ASDR is distributed in various SDI regions in the past 30 years. ASDR, age-standardised death rate; SDI, sociodemographic index.

age-standardised death rate (ASDR) in 1990, there is a downward trend in 2019, from 0.32 (95% UI: 0.28 to 0.42)/100 000 in 1990 to 0.27 (95% UI: 0.23 to 0.34)/100 000 in 2019. In 2019, in the Asia-Pacific region, New Zealand had the highest ASDR of 0.52 (95% UI: 0.35 to 0.62)/100 000, and the lowest was Singapore with 0.07 (95% UI: 0.04 to 0.09)/100 000 (online supplemental table 1). Compared with 1223 deaths in 1990, the number of MS deaths in China in 2019 increased by 47.35%, which is far lower than the growth rate of global deaths (table 1 and figure 5). Compared with ASDR in 1990, the trend of ASDR of MS in China is generally similar to the global situation, but the increase in global MS deaths (68.01%) is higher than that in China (47.35%), and the increase in global mortality (16%) is lower than that in China (30%), while the decline in global ASDR (15.63%) is lower than that of China (30.77%). In the Asia-Pacific region, China has the highest decline in ASDR, and both the death rate increase and the death toll increase are at a low level (online supplemental table 1, table 1 and figure 6).

Disability-adjusted life years

Globally, the DALYs of MS increased from 726 065.6 years in 1990 to 1 159 831.84 years in 2019, an increase of 59.74% (table 1). In the Asia-Pacific region, Malaysia has the largest growth rate (145.05%), followed by Vietnam (139.12%); and the smallest growth rate is Japan (13.74%) (figures 7 and 8). Globally,there was a small decrease in ASR-DALYs for MS, from 16.09 (95% UI: 13.80 to 19.34)/100 000 per year in 1990 to 13.96 (95% UI: 12.05 to 16.63)/100 000 per year in 2019. In 2019, from the Asia-Pacific region, Australia had the highest ASR-DALYs at 29.70 (95% UI: 28.85 to 36.39)/100 000 years, followed by New Zealand at 24.52 (95% UI: 18.80 to 29.15)/100 000 years; and Singapore's standardised DALY was a minimum 3.17 (95% UI: 2.14 to 3.85)/100 000 years (online supplemental table 1). The DALYs of MS in China increased from 52 673.56 years in 1990 to 71 439.34 years in 2019, an increase of 35.62%, much lower than the global DALYs (table 1). In 2019, China's ASR-DALY was 3.69 (3.02 to 4.75)/100 000, which was the last level in Asia-Pacific countries, and was similar to Singapore's ASR-DALYs (online supplemental table 1).

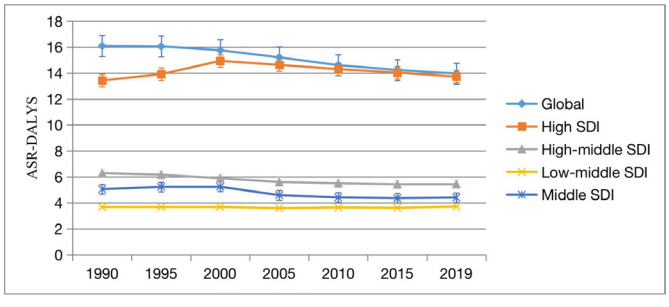

Figure 12 According to the 2019 SDI classification standard, the distribution of ASR-DALYs in various SDI regions in the past 30 years. ASR, age-standardised rate; DALYs, disability-adjusted life years; SDI, sociodemographic index.

Relationship between ASRs and SDI

The official website of GBD Research provides a detailed introduction of SDI values on a global, regional and national scale from 1990 to 2019. According to the 2019 SDI classification standards, the countries selected in this paper can be divided into low-middle, middle, high-middle and high. In general, there is a close relationship between various indicators and SDI. The higher the SDI value, the higher the value indicators. From 1990 to 2019, the change trend of ASRI in high-middle, middle and low-middle SDI regions was relatively stable, and the change range was small and similar. The ASRI of high SDI was much higher than that of other low-SDI regions. The lowest was 0.782/100 000 and reached the highest value of 0.938/100 000 in 2015 (table 2 and figure 9). In the past 30 years, the ASPR in the middle-SDI and high-SDI regions in the Asia-Pacific region has been on the rise. From 1990 to 1995, it was still lower than the global level, and in 2000 it exceeded the global level. In 2015, the ASPR value was 24.48/100 000, the highest level over the years (table 2 and figure 10). ASPR in other SDI regions is at a lower level. According to the collected data, from 1990 to 2019, the ASDR in different SDI regions showed a downward trend to varying degrees, and the MS cure rate in high-SDI regions was also higher than that in other SDI regions (table 2 and figure 11). The ASR-DALYs in the high-SDI regions were similar to those in the middle-SDI regions. In 2000, there was an increase of 14.94/100 000 and 5.242/100 000, respectively, and then maintained a downward trend until 2019. With the development of the SDI, the gap between the current health status and the ideal status of the population has gradually narrowed (table 2 and figure 12).

During the period from 1990 to 2019, China's SDI increased significantly. In 1990, the SDI value was significantly lower than the global average level. Since 2004, the SDI value has exceeded the global average level. In 2019, China's SDI value has been significantly higher than the global average level. In 2019, China's SDI value belongs to the middle-SDI region. With the growth of SDI, the ASPR of MS shows an upward trend, while ASDR and other indicators show a downward trend. In 2019, the ASDR of MS

in China was 0.9/100 000, the ASRI was 0.74/100 000 and the ASR-DALYs were 13.96/100 000 per year, which were lower than the global average.

DISCUSSION

By analysing data from the GBD Database, this study estimated the incidence, prevalence, death and DALYs of MS in the global and Asia-Pacific regions between 1990 and 2019, and the corresponding ASRs of the burden of disease in MS provide a new comprehensive assessment. In the Asia-Pacific region, the indicators in high-SDI regions are much higher than other low-SDI regions. This study found that in the case of the same ASPR, the ASDR and ASR-DALYs of patients with MS in high-SDI regions were generally lower than in areas with low SDI. The results are consistent with the results of other studies analysing MS.[8] In addition, the cure rate of MS in areas with high SDI is significantly higher than that in other countries, and ASDR of MS in the Asia-Pacific region has decreased to varying degrees. This study also found that regions with higher SDI values had higher prevalence rates, and the increased prevalence may be due to increased life expectancy of patients with MS and advances in the diagnosis of MS.[9] Over the past 20 years, MS has been misdiagnosed and missed. This phenomenon often occurs, and when patients cannot easily meet the diagnostic criteria or have atypical clinical and imaging features, it may interfere with the diagnosis of the diseased and affected population.[10] The current diagnosis of MS relies on the McDonald criteria, which use relevant laboratory tests, including MRI, to prove the MS in time and space, and can make an early diagnosis before the second clinical attack. Early treatment intervention provides the basis.[11] In order to detect and diagnose MS earlier, the McDonald MS diagnostic criteria were revised in 2017.[12] Changes in diagnostic methods and criteria mean that patients with MS can be diagnosed earlier in the disease trajectory, allowing patients to receive timely treatment and improve survival. In the Asia-Pacific region, the decline in ASDR in China is the largest, which may be related to the rapid increase in the level of SDI in China. China's economic level, medical technology and medical insurance policies have played a positive role in the treatment of MS. However, despite the diagnosis and treatment of MS in China, there is still a certain gap between the developed countries and the establishment of a large-scale, multicentre MS case database, the establishment of a long-term follow-up mechanism for patients with MS, and the improvement of early diagnosis and treatment of MS in grass roots hospitals.

The size of the MS drug market in 2019 was approximately US$21.8 billion. Since the Food and Drug Administration (FDA) approved the first MS treatment drug in 1993, 19 MS treatment drugs have been approved, of which 4 are in China.[13] The MS treatment drugs approved by the China FDA are beta-interferon, teriflunomide, fingolimod and siponimod. Among them, teriflunomide was launched in China in July 2018, and fingolimod in July 2019, and both have been included in Chinese medical insurance. In the new medical insurance list in 2021, the drug for the treatment of MS (fampridine) was approved in China and included in the national medical insurance within half a year, which fully reflects the importance China attaches to patients with MS to increase the availability of rare disease drugs and reduce the burden on patients. For the protection of drugs for rare diseases, different countries and regions have introduced different policies from the aspects of economic and administrative support to improve the accessibility of rare disease drugs. The main measures include tax credits, research and development support, registration fee reduction, trial design assistance, market exclusivity period and rapid approval.[14–16]

Finally, the economic burden of MS is not only related to its treatment, but also to its complications. Patients with MS with complications (such as high blood pressure, diabetes, ischaemic heart disease, chronic lung disease, depression and bipolar disorder) had high hospitalisation rates, which caused serious economic and social burden.[17] China also needs to strengthen the accessibility and affordability guarantee mechanism of rare disease drugs, solve the problem of less choice of treatment drugs due to the small patient population and the heavy burden caused by high drug prices, and establish a multilevel medical security system for rare diseases with multiparty participation to effectively reduce the disease burden of patients. Actively exploring its epidemiological law and its influence on the degree of social development is of great significance for guiding health policy formulation, improving the health level of the population and preventing the development of MS.

Limitation

There are still some limitations in this study. Although GBD Database has been widely used in the assessment of disease burden in various countries around the world, there are still some errors in the statistical data of each country, which need to be further investigated and improved. In the Asia-Pacific region, only one country in this paper belongs to the high-middle SDI region, which cannot fully reflect the disease burden of MS in high-middle SDI countries. The GBD Database also lacks relevant data for each province in China, which makes it impossible to further analyse the disease burden of MS between urban and rural areas in China.

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Funding This study was supported by the 2022 Basic Research Project of Liaoning Provincial Department of Education (LJKMR20221296).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethical approval was not obtained because the data included in this study were publicly available and de-identified data.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data sources of this study are all published on the IHME official website (http://ghdx.healthdata.org/), Data are available in a public, open access repository. All data are publicly available. Data are available on request.

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