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Global burden of Rabies in 204 countries and territories, from 1990 to 2019: results from the Global Burden of Disease Study 2019

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Abstract

Background: Rabies is an acute lethal infectious disease caused by lyssavirus infection. In 2018, the World Health Organization (WHO) proposed a global strategic plan to end human rabies deaths by 2030. However, systematic studies of the global rabies disease burden and epidemiological trends are scarce.

Methods: We extracted the disease burden and epidemiological data of global rabies in the preceding 30 years from the Global Burden of Disease (GBD) study 2019 and performed a comprehensive analysis.

Results: In 2019, the incident cases of rabies worldwide were 14075.51 (95% uncertainty interval, UI: 6124.33-21618.11), and the number of deaths was 13743.44 (95%UI: 6019.13-17938.53), both of which were lower than that in 1990. With the improvement of the Socio-demographic Index (SDI), the incident cases, the number of deaths, age-standardized incidence rate (ASIR) and death rate (ASDR), and disability-adjusted life years (DALYs) of rabies all showed downward trends. Adolescents and adults under the age of 50 represented the majority of rabies cases worldwide.

Conclusions: The global disease burden of rabies had declined over the past 30 years. Furthermore, the disease burden of rabies was closely related to the SDI level.

Keywords: rabies, global disease burden, prevalence, mortality, disability-adjusted life years

Background

Rabies is a viral disease that spreads amongst animals. Besides dogs, other domestic animals such as cats, ferrets, and cattle, are also susceptible of rabies. Human rabies is mainly caused by the infection of rabies virus after being bitten by a sick dog, and the virus then invades the central nervous system, resulting in acute and fatal encephalomyelitis (Laurent Dacheux 2011). Because some countries or regions lack a systematic and mandatory rabies reporting system, or because the reporting system lacks quality control, global rabies mortality are greatly underestimated, and rabies is also a neglected disease (Fooks et al. 2017). Rabies is a fully preventable disease, the incubation period following rabies virus infection is typically 2-8 weeks, although it can range from days to years. Once the infection develops symptoms, rabies is always fatal. Therefore, preventive measures should be taken as soon as possible for those at risk after being bitten by canines or other animals (Stringer 2003).

Preventive measures include wound treatment, vaccination, and injection of rabies immunoglobulin. However, in many developing countries, where canine rabies causes the majority of human cases, deaths occurred mostly due to a lack of access to affordable biological agents needed for effective postexposure prophylaxis (Rupprecht, Hanlon, and Hemachudha 2002). With extensive education and vaccine availability, rabies has been eliminated in some developed countries, such as western Europe, Canada, the United States of America (USA), Australia, Japan, and some Latin American countries (World Health Organization 2018).

Mastering the current global rabies disease burden and epidemic trend, and increasing

publicity, education, and investment in disease prevention and control are critical to the prevention and control of rabies. However, studies on the disease burden and prevalence of rabies worldwide are currently lacking. Therefore, based on the data from the GDB2019 in 204 countries and territories, this study comprehensively and systematically described and compared the prevalence of rabies in different socioeconomic index regions, and across countries globally. Additionally, the death toll, DALYs, and other information were also reported in this study. Knowledge of the current global disease burden and prevalence trends of rabies is critical to preventing and controlling the epidemic of rabies, as well as boosting disease prevention and control awareness, education, and investment.

Methods

Study data

Data for the disease burden of rabies were derived from the online data source tool, the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool), which is an ongoing global collaboration that uses all available epidemiological data to provide a comparative assessment of health loss from 369 diseases across 204 countries and territories (GBD 2019 Diseases and Injuries Collaborators 2020). GBD estimation process is based on identifying multiple relevant data sources for each disease or injury, including censuses, household surveys, civil registration and vital statistics, disease registries, health service use, air pollution monitors, satellite imaging, disease notifications, and

other sources. Each of these types of data is identified from a systematic review of published studies, searches of government and international organization websites, published reports, primary data sources such as the Demographic and Health Surveys, and contributions of datasets by GBD collaborators (GBD 2019 Diseases and Injuries Collaborators 2020). We acquired data on the incidence, death, ASIR, ASDR, DALYs, and estimated annual percentage change (EAPC) of rabies from 1990 to 2019 from GBD 2019 database.

The Socio-demographic Index (SDI), which is based on national-level income per capita, average years of education among people over the age of 15, and total fertility rate, was used to categorize the countries into five SDI quintiles (high, high-middle, middle, low-middle, and low levels).

Details about the study design and methods of GBD studies have been extensively described in existing GBD literature (GBD 2019 Risk Factors Collaborators 2020, GBD 2015 Diseases and Injuries Collaborator 2016, GBD 2019 Diseases and Injuries Collaborators 2020).

Data analysis

A secondary systematic descriptive analysis was conducted regarding the burdens of rabies in 204 countries and territories from1990 to 2019, and the findings were further investigated. The incidence, deaths, ASIR, ASDR, and DALYs of rabies in both genders and different age groups were also compared. Uncertainty intervals (UIs) were defined as the 2.5^{th} and 97.5^{th} values of the posterior distributions.

The association strengths between SDI level and ASIR, ASDR, DALYs, or EAPC were measured by Spearmanôs rank correlation coefficients. Moreover, Locally Weighted Scatterplot Smoothing curves were fitted to describe the change trends. All data management was performed using Microsoft Excel and SAS (version 9.4) and the figures were created using GraphPad Prism (version 9) or SAS (version 9.4). A *P* value of less than 0.05 was regarded as statistically significant.

Results

Rabies incidence burden worldwide

Globally, the number of patients with rabies decreased from 24,744.66 (95%UI: 9201.76-40728.99) in 1990 to 14,075.51 (95%UI: 6124.33-21618.11) in 2019, and the EAPC was -0.43% (95%UI: -0.64% to -0.2%) (Table S1). The ASIR of rabies decreased from 45.99 (95%UI: 17.74-75.23)/10,000,000 in 1990 to 18.45 (95%UI: 7.89-28.18)/10,000,000 in 2019. The higher the SDI level, the lower the rabies ASIR was (Figure 1-A). In 2019, the low SDI region had an ASIR of 48.70 (95%UI: 22.06 -85.80)/10,000,000, while the high SDI region was only 0.14 (95%UI: 0.07 to 0.19)/10,000,000 (Table S1). It showed that SDI level was significantly negatively correlated with ASIR of rabies. In terms of trend, in the past 30 years, the global rabies ASIR has shown a considerable downward trend, and it has decreased in different levels of SDI regions (Figure 1-A).

Between genders, the incidence cases and ASIR of rabies in males were higher than in

females in both 1990 and 2019 (Table S1); however, in the past 30 years, the ASIR of rabies has shown a downward trend for both men and women (Figure 1-A).

For different SDI regions, the prevalence of rabies in 2019 decreased compared to 1990. However, in high SDI areas, the number of rabies cases increased slightly from 15.26 (95% UI: 9.86-23.71) in 1990 to 18.08 (95% UI: 8.70-26.55) in 2019 (Table S1).

For different regions, in 1990, the number of rabies cases and ASIR in South Asia were both the highest, which were 15139.39 (95%UI: 5621.07-23976.88) and 149.76 (59.06-233.50)/10,000,000, respectively. In 2019, the region with the largest number of rabies cases was still South Asia, at 7287.84 (95%UI: 3560.98-12760.99), but it has dropped by more than 50% compared to 1990. In 2019, the region with the highest ASIR was Western Sub-Saharan Africa at 56.97 (95%UI: 16.28-92.62)/10,000,000 (Table S1). In 2019, the number of rabies cases and ASIR in Australasia were both the lowest, at 0.02 (95%UI: 0.02-0.03) and 0.02 (95%UI: 0.01-0.03)/10,000,000, respectively.

Compared with 1990, the EAPC of rabies ASIR in most regions showed a downward trend in 2019, that is, the incidence rate was declining over the past 30 years. However, the EAPC of rabies ASIR in Australasia and high-income North America showed slight growth, the number of rabies cases in these two regions in 2019 was 0.06 (95%UI: 0.04-0.08) and 3.48 (95%UI: 3.01-4.36), respectively (Table S1), which still belong to rabies-controlled regions.

For the 204 countries included in GBD 2019, the top three countries for ASIR rabies in 2019 were Nepal at 1.21 (95%UI: 0.40-2.10) per 100,000, Myanmar at 1.04 (95%UI: 0.30-1.91) per 100,000, and Niger at 0.92 (95%UI: 0.27-2.59) (Table S2). From the geographical point of view, the regions with high ASIR are mainly located in Southeast Asia, Africa, and Eastern Europe (Figure 2-A). In 2019, there were 92 countries or regions in the world where the ASIR was near 0, accounting for 45.1% of all countries (Table S2). From 1990 to 2019, The EAPC of rabies ASIR has been quite diversly geographically. The top three countries with the highest EAPC over the past 30 years were the Netherlands at 5.19% (95%UI: 2.02-13.20%), Puerto Rico at 2.75% (95%UI: 1.07-5.68%), and Greece at 2.23% (95%UI: 1.02-5.23%). A total of 31 countries or regions in the world had a positive EAPC of ASIR, accounting for 15.2% (Table S3), mainly in developed countries such as Northern Europe, North America, and Australia (Figure 2-B). In the remaining 174 countries with negative values in EAPC, Mexico, Costa Rica, and Brazil, which belong to South America, had experienced the fastest decline, with EAPC of rabies ASIR were -1.00% (95%UI: -1.00% to -1.00%), -0.99% (95%UI: -1.00% to -0.98%), and -0.99% (95%UI: -0.99% to -0.98%), respectively.

Rabies deaths and DALYs burden worldwide

Globally, the number of rabies deaths in 2019 was 13743.44 (95%UI: 6019.13-17938.53), almost half of that in 1990. The EAPC was -0.47% (95%UI: -0.63 to -0.20), indicating a global downward trend in rabies deaths over the past 30

years (Table S4). In 2019, rabies deaths in the high SDI region were 17.31 (95%UI: 8.84-23.94), a slight increase from 16.14 (95%UI: 9.62-29.35) in 1990. In other SDI regions, the number of rabies deaths in 2019 decreased compared with 1990. Since the mortality rate of rabies is nearly 100%, the number of rabies deaths and incidence is comparable.

For different countries, India had the most deaths from rabies in 2019 with 5206.34 (95%UI: 2096.03-6826.33) in number, followed by Nigeria with 1295.34 (95%UI: 299.35-2317.38) and Pakistan with 1198.21 (95%UI: 596.39-2719.79) ranking the third, Ethiopia the fourth with 921.91 (95%UI: 144.43-2666.32), and China the fifth with 719.07 (95%UI: 264.39-897.83). In 2019, a total of 34 countries in the world had zero rabies deaths (Table S5, Table S7).

In 2019, the global ASDR of rabies was 0.18 (0.08-0.24) per 100,000 people, 37.5% of that in 1990, and the EAPC was -0.62% (95%CI: -0.73 to -0.44%) (Table S4). Whether in 1990 or 2019, high SDI areas had lower ASDRs (Table S4). In high SDI regions, ASDR was approximately 0 in both 1990 and 2019. Therefore, on the whole, rabies in high SDI areas has been well controlled. Over the past 30 years, there has been a significant downward trend in global rabies ASDR, with a faster decline in low SDI regions (Figure 1-B). From 1990 to 2019, the ASDR due to rabies in male was higher than that in female across the different SDI regions (Figure 1-B).

DALYs represent the total health burden of a disease, which consist of years of life lost due to premature mortality (YLLs) and years of healthy life lost due to disability

(YLDs). In 2019, global rabies-related DALYs were 782052.30 (95%UI: 320289.68-1081217.50), which were 45.4% in 1990, and their EAPC were -0.55% (95%UI: -0.68 to -0.24%). From 1990 to 2019, the global rabies-related DALYs showed an overall downward trend. Rabies-related DALYs decreased in all SDI regions in 2019 compared with 1990 (Table S4). In 2019, among all SDI regions, the low SDI region had the highest rabies-related DALYs, which were 349618.54 (95%UI: 132906.01-601695.19) and were 581.4 times that of the high SDI region (Table S4).

In 2019, the global age-standardized DALYs rate was 10.59 (95%UI: 4.38-14.69)/100,000, almost 1/3 of that in 1990, with EAPC -0.64% (95%UI: -0.74 to-0.41%) (Table S4). From the perspective of trend, the age-standardized DALYs rate has shown a significant downward trend in the past 30 years globally and in all SDI regions, but the decline rate of low SDI regions, including low and low-middle SDI regions, is significantly higher than high SDI regions (Figure 1-C).

Age-related incidence of rabies

We further analyzed the incidence of rabies in different age groups. Globally, rabies incidence in the 0-14 age group was the highest among the four age groups (0-14 years, 15ï49 years, 50ï69 years, and 70+ years) in 1990. However, in 2019, the age 0-14 group and 15-49 group have similar incidence, and significantly higher than that in the middle age (50-69 years) and high age (70+ years) groups (Figure S1).

Globally, in the past 30 years, those aged 0-14 years had the highest rabies incidence, followed by 15-49 years and 50-69 years. The over 70 years group had the lowest

incidence of rabies. The gap in incidence between the 15-49 years and 0-14 years has gradually narrowed (Figure 3).

From 1990 to 2019, the incidence of rabies in all age groups in the world showed a downward trend. In low, low-middle, and middle SDI level areas, the rabies victims were mainly in the 0-14 years and 15-49 years young age group. However, in the middle-high and high SDI level areas, older aged 50-69 years and over 70 years occupied a larger proportion of rabies incidence (Figure 3). Globally, rabies incidence in 0-14 years showed a downward trend, while the 50-69 years and over 70 years showed obvious upward trends (Figure 3, figure S1).

Whether in 1990 or 2019, the incident cases of rabies in all age groups in high SDI areas were significantly smaller than in other regions. Globally, the rabies incidence cases in the 0-14 years group were 5089.27 (95% UI: 1930.99-7809.25) in 2019, only 38.9% of that in 1990, with a significantly higher decline than other age groups. The cases of rabies over 70 years in 2019 were almost the same as in 1990, both were approximately 1100 cases (Table S6).

Rabies disease burden and trend related to SDI level

The above results demonstrated that the disease burden of rabies is closely related to the SDI level. We further explored the rabies disease burden and trends related to SDI levels. A significant negative correlation was found between the age-standardized incidence and death rate of rabies and SDI ($R = -0.68$, $P < 0.001$) in 2019 (Figure 4 A-B). Also, the age-standardized DALYs rate showed a significant negative

correlation with SDI level (R = -0.7, $P < 0.001$, Figure 4-C).

However, the EAPC of ASIR (Figure 4-D), ASDR (Figure 4-E), Age-standardized DALYs (Figure 4-F) rates of rabies from 1990 to 2019 (%) showed a mild positive correlation with SDI levels in the past 30 years (R = 0.38, 0.38, and 0.37, respectively). Higher SDI level countries had a more positive value of EAPC (EAPC > 0); Most low SDI areas had negative EAPC values (EAPC < 0) (Figure 4-D, E, F).

Particularly noteworthy was the Netherlands, which appeared in the more scattered areas in the picture (combined with EAPC values and Figure 4-D, E, F). The EAPC of the disease burden of rabies in the Netherlands was the highest among all countries (Table S3). However, the Netherlands had relatively low rabies deaths with 0.03 in 1990 and 0.36 in 2019. Probably because there was only one rabies case in the Netherlands in 1997 (Schrijver, Veering, and Vis 1997), which was the first case in the Netherlands since 1963.

Discussion

GBD 2019 provides comprehensive data estimates of incidence, prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life-years (DALYs) due to 369 diseases and injuries, for the two sexes, and for 204 countries and territories (GBD 2019 Diseases and Injuries Collaborators 2020). Included in the GBD 2019 data, rabies is a neglected but still endangering zoonotic viral disease. Rabies can be prevented, but once the infected person has clinical symptoms, the fatality rate is almost 100% (World Health Organization 2018).

Therefore, providing global rabies disease burden and epidemiological data is of great significance for strengthening rabies disease control and vaccine research.

In the past 30 years, the global incidence cases, ASIR, death cases, ASDR, and DALYs of rabies have shown significant downward trends. In 2019, 13743.44 (95%UI: 6019.13-17938.53) people lost their lives due to rabies, still a big number. Hampson K, et al. reported the estimates of death from rabies were 59,000 (95% Confidence Intervals: 25-159,000) human deaths, more than that of GBD 2019 (Hampson et al. 2015). To the best of our knowledge, the possible reasons for the discrepancy can be summarized as follows. (1) Data resource variance. The data for our study were derived from GBD 2019, which is the most comprehensive worldwide observational epidemiological study (https://www.thelancet.com/gbd/about). The GBD estimation process is based on identifying multiple relevant data sources for each disease or injury, including censuses, household surveys, civil registration and vital statistics, disease registries, health service use, air pollution monitors, satellite imaging, disease notifications, and other sources. Each of these types of data is identified from a systematic review of published studies, searches of government and international organization websites, published reports, primary data sources such as the Demographic and Health Surveys, and contributions of datasets by GBD collaborators. Data in GBD were collected and analyzed by a consortium of more than 7,000 researchers in more than 156 countries and territories. However, data in Hampson K et al.ôs study were obtained from surveys involving the medical,

veterinary and laboratory sectors and were collected from 136 respondents (spanning all sectors and 45 countries). (2) Different statistical models. It is difficult to estimate the real number of deaths from rabies globally since a systematic, mandatory and quality rabies reporting system was lacking in some countries, and global rabies mortality is greatly underestimated (Fooks et al. 2017); therefore, the Bayesian compartmental model framework (DisMod-MR) was applied to evaluate all the available data on incidence, prevalence, remission, and mortality for disease in the GBD system. On the other hand, Hampson K et al. reported the estimated burden of rabies deaths using the probability decision-tree model framework (Hampson et al. 2015). (3) Different time periods. Our study period was from 1990 to 2019, allowing comparisons over time, across age groups, and among populations, whereas Hampson K et al. used the available data regarding human and animal rabies, dog bite incidence, control efforts, and associated economic costs from 2000 to 2013. This requires governments of all countries, especially low-income countries, to strengthen the investment and implementation of the rabies reporting system in the future.

However, it is noteworthy that rabies has approximately been eliminated in high-income countries or regions. In 2019, there were zero deaths from rabies reported in 34 of the 204 countries in the world (Table S7). Low-income countries or regions were the main victims of rabies. India had the highest number of deaths from rabies in 2019, it reached 5206.34 (95%UI: 2096.03-6826.33). Another large developing country, China, had 719.07 rabies deaths (95%UI: 264.39-897.83),

ranking fifth in the world. However, the death toll in Brazil was only 1.46 (95%UI: 1.28-1.68). This was inextricably linked to the introduction of canine vaccination campaigns and the expansion of post-exposure prophylaxis in Brazil (Duarte et al. 2021). Although the SDI level of Brazil was not higher than China. Therefore, the most important factors in the prevention and control of rabies may not be the socio-economic level, but the government investment, the construction of laws and regulations, public participation, and the utilization of funds. The success of rabies prevention and control in South America provided a good example for the global fight against rabies (Meske et al. 2021).

In addition, it is of note that in the past 30 years, although some high-income countries have eliminated rabies, the EAPC of rabies ASIR in 31 countries or regions has shown positive, that is, the incidence rate is increasing, and these lists are mainly distributed in developed countries such as Northern Europe, North America, and Australia. This suggests that the prevention and control of rabies should be strengthened not only in developing countries but also in developed regions, to prevent the resurgence of this acute fatal disease. Several measures could be considered: more active vaccination of high-risk groups, legislation to vaccinate all petsô dogs, and establishment of a rabies epidemic alert system, etc. Furthermore, cases imported from other high-risk areas and infection after being bitten by outdoor wild animals still occurred occasionally in high-income countries, which is the target of rabies prevention and control in the future (Parize et al. 2018; Gautret and Parola

2012; Sparkes et al. 2015).

Based on the data of GBD 2019, we found that the ASDR of rabies in males was higher than that in females globally and in different SDI regions over the past 30 years. The possible reason is men participate in more outdoor activities or physical labor than women, so they are more likely to be bitten by dogs and infected with the rabies virus. A study in China showed that male farmers were the main victims of rabies because they were more engaged in outdoor physical labor (Lu et al. 2021). Similar results have been found in studies in other countries (Abdulmoghni et al. 2021; Yibrah and Damtie 2015; Sudarshan et al. 2007; Kassiri et al. 2014; Ma et al. 2021). Therefore, it is important to provide outdoor workers with necessary protective measures, popularize the knowledge of prevention and control, and affordable vaccination services in areas with high rabies prevalence.

In addition, people aged 0-14 years and 15-49 years were more likely to become victims of rabies. Children aged 0-14 may be more likely to be bitten by dogs due to a lack of sufficient self-defense ability. From 1990 to 2019, the global incidence of rabies in children aged 0-14 has decreased year by year, while the number of middle-aged people aged 15-49 has hardly declined in the past 30 years (Figure 3). As a result, the gap between the incidence of rabies in the 0-14-year-old group and the 15-49-year-old group has gradually narrowed over the past 30 years. The possible reasons are as follows. Initially, more attention was given to children, and currently, a higher proportion of children bitten by dogs were taken post-exposure vaccinated

against rabies (Wang et al. 2022). Then, people aged 15-49 have more activities outdoor; therefore, are associated with increased risks of being bitten by dogs and developing rabies. Besides, the vaccination rate among middle-aged people after being bitten is comparatively low than children (Yurachai, Hinjoy, and Wallace 2020; Wang et al. 2022). Finally, pre-exposure vaccination has been administered to children in some countries with a high rabies burden and their effectiveness is observed, which also reduced the rabies incidence among children (Kamoltham et al. 2007; Kessels et al. 2017; Soentjens et al. 2021). In recent years, the proportion of rabies patients aged 50-69 years and over 70 years were increasing, which may be due to the aging of the population, more middle-aged and elderly people participated in outdoor activities, their defense ability was reduced, and they were more likely to be attacked by dogs. Adequate attention should be paid to these vulnerable groups, including enhanced knowledge and awareness, providing widespread and affordable vaccination services, et al. Indeed, some experts have called for extensive rabies vaccination of children to prevent the disease (Soentjens et al. 2021). Moreover, studies had shown that pre-exposure rabies prophylaxis in children was safe and effective, and it was also advocated by WHO in recent years (Kessels et al. 2017; Kamoltham et al. 2007; Malerczyk, Vakil, and Bender 2013). However, vaccinations for HIV-infected and other immunocompromised children may not produce adequate immunity. Therefore, this special population needs to be tested for post-vaccination antibody concentrations (Thisyakorn et al. 2000), and may even require booster or

rabies immunoglobulin (Chadwick and Geretti 2007; Geretti and Doyle 2010).

Unlike many other diseases, the GBD 2019 data did not include risk factors for rabies resulting from the lack of a sound mechanism for collecting and reporting rabies disease information in some countries (Taylor et al. 2017). The study by Taylor et al. (Taylor, Knopf, and Partners for Rabies 2015) showed that only 8 of the 91 countries surveyed did not have a mandatory reporting system for rabies. However, many countries had an ineffective surveillance system, and almost all of them were high and moderate rabies risk countries in Africa and Asia. In addition, many factors had an impact on the disease burden of rabies, such as the number of dogs, the level of immunity of dogs, human vaccination level, the effectiveness and accessibility of vaccines, and the awareness of rabies in the population, etc. However, these data are extremely lacking at present (Sessou et al. 2021; Mbilo et al. 2021; Dizon et al. 2022; Haupt 1999). In addition, there seemed to be an increasing trend of rabies cases caused by non-canine animals. This made it more difficult to study the risk factors related to rabies. However, lack of risk factors analysis is an important shortcoming of this study. We believe that research on risk factors will facilitate targeted measures to curb the incidence of rabies, especially in countries with a high rabies burden. This requires further research in the future, especially to strengthen the implementation of the statutory reporting system for rabies in various countries.

In 2018, the United Against Rabies (UAR) collaboration was jointly established by the World Health Organization, Food, and Agriculture Organization of the United

Nations, the World Organization for Animal Health, and the Global Alliance for Rabies Control. The Global Strategic Plan to end human deaths from dog-mediated rabies by 2030 (Zero by 30) was announced (World Health Organization, 2018). To achieve this ñzero by 30ò goal, the UAR proposed three major objectives: 1)effectively use vaccines, medicines, tools, and technologies; 2)generate, innovate and measure impact; 3)sustain commitment and resources (World Health Organization, 2018). The achievement of this great goal requires the active promotion and scientific management of the governments of various countries, and the participation of the whole society. Extensive vaccination may be the most prominent and effective measure, but there is still much room for improvement. It is also necessary to take economic, cultural, social, educational, and technological factors into account, especially in Asia and Africa where the rabies burden is high (Rupprecht and Salahuddin 2019; Haselbeck et al. 2021). Funding arrangements are also important because areas with low SDI levels are still the places with rabies endemic.

In the past 30 years, Mexico, Costa Rica, Brazil, and other South American countries had greatly curbed the epidemic of rabies because of the efforts of the government and the people. Therefore, although the goal of eliminating rabies by 2030 faces many difficulties, it is still possible to achieve it. In the future, we need more government funding, public participation, enterprise research and development, and, ultimately, the elimination of rabies.

Conclusion

The global rabies disease burden has shown a remarkable downward trend over the past 30 years. However, in economically underdeveloped countries, rabies still caused deaths and DALYs that cannot be ignored. The elimination of rabies requires the joint participation and efforts of the whole society.

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Author contributions

Hui Gan, Zhangkai J. Cheng, Baoqing Sun, and Zheng Zhu designed the study. Hui Gan and Xiangqing Hou collected and analyzed the data. Zheng Zhu and Hui Gan wrote the manuscript. Yiming Wang, Xiangqing Hou, Gaofeng Xu, Zhifeng Huang, Teng Zhang, Runpei Lin, Mingshan Xue, and Mingtao Liu edited the manuscript and provided valuable suggestions for study design and data analysis. All authors have approved the final version of this paper.

Conflict of interests

The authors declare no competing interests.

Availability of data and materials

The datasets analyzed during the current study are available in the IHME Data

(http://ghdx.healthdata.org/gbd-results-tool).

Ethical Approval statement

The data in this study were anonymized before its use. All methods were carried out in accordance with relevant guidelines and regulations.

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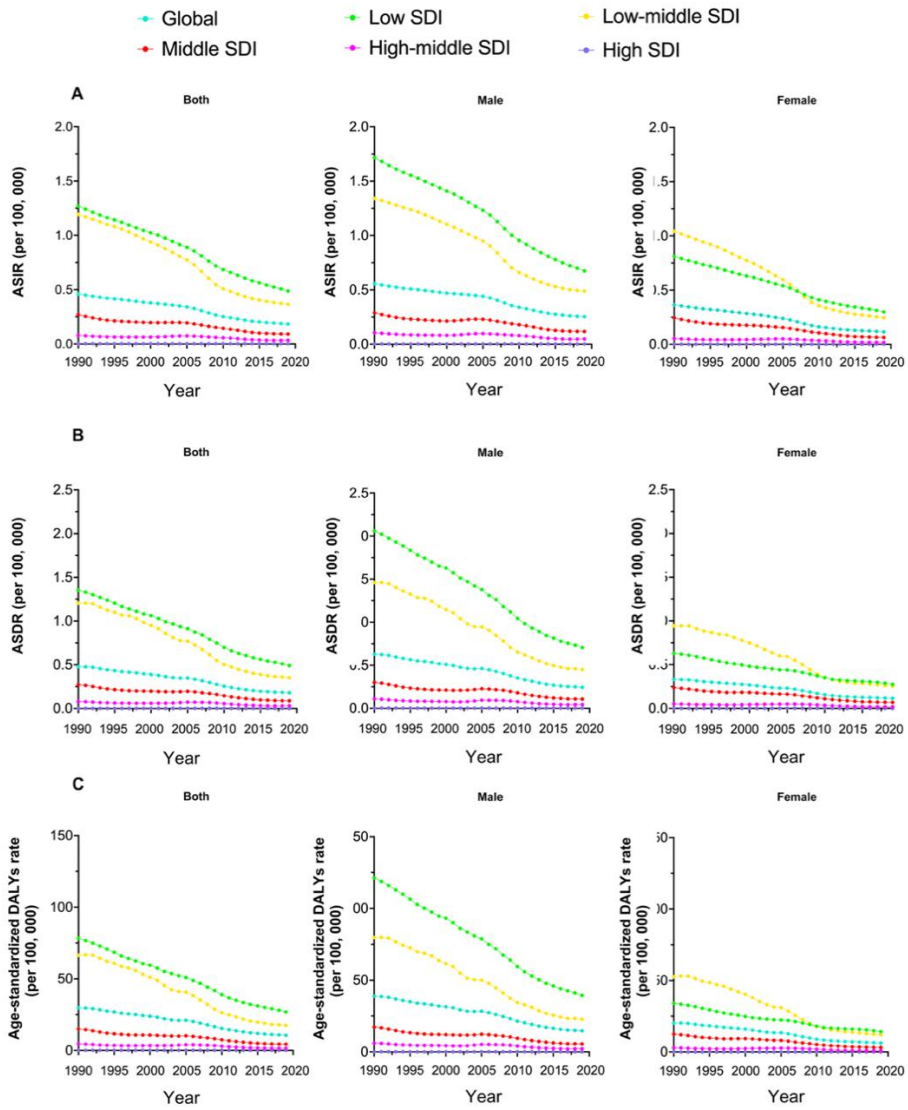
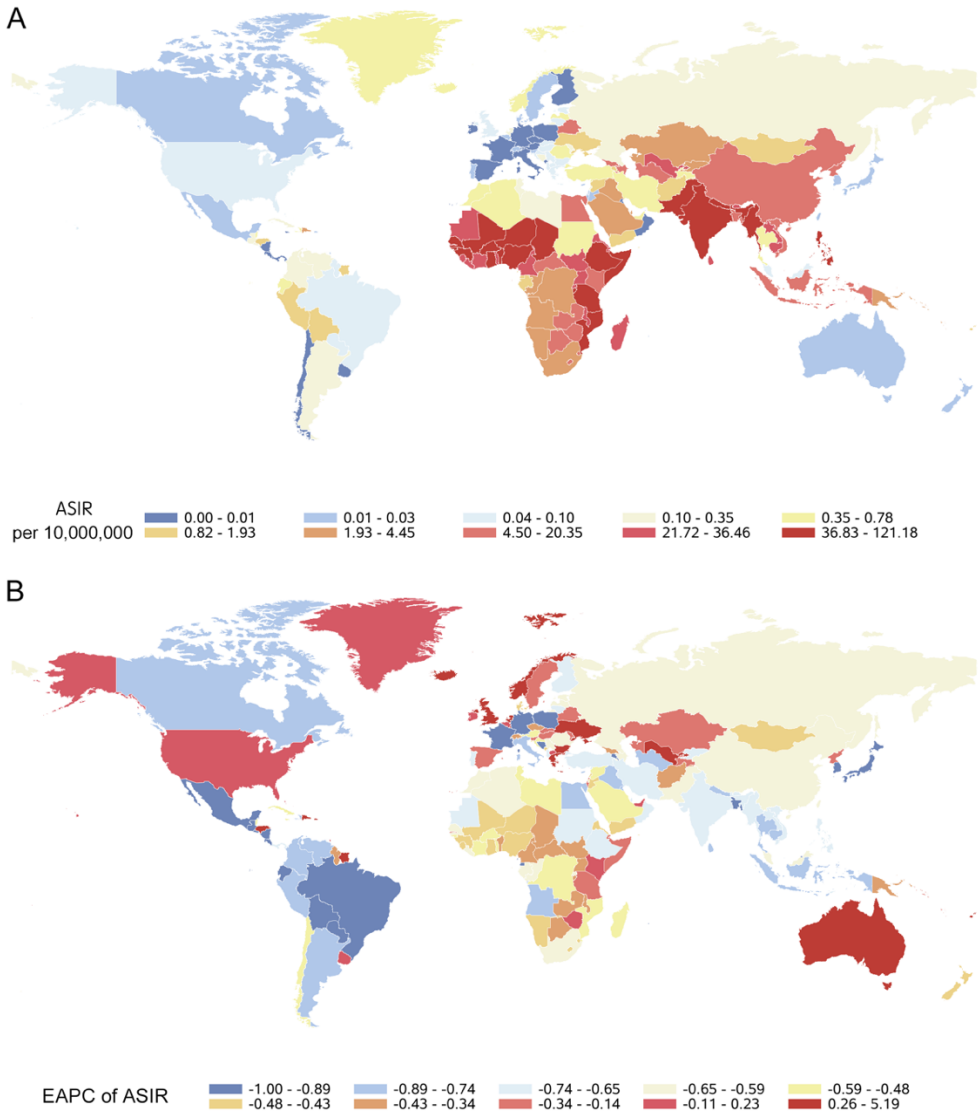
Figure 1. Age-standardized Incidence (A), Death (B), and DALYs (C) rate (per 100, 000) of Rabies globally with different gender and in different SDI areas.



ASIR: age-standardized incidence rate, DALYs: disability-adjusted life years,
ASDR: age-standardized death rate.

Figure 2. Age-standardized incidence rate (per 10,000,000) in 2019 (A) and EAPC of ASIR from 1990 to 2019 (B) of Rabies in 204 countries and territories.



A: The Age-standardized incidence rate of Rabies in 2019.

B: The EAPC of Rabies ASR from 1990 to 2019. ASR, age-standardized rate; EAPC, estimated annual percentage change.

Figure 3. The proportion of the four age groups for Rabies incident cases between 1990 and 2019 globally, and in low, low-middle, middle, high-middle, and high SDI quintiles. The populations were divided into four age groups: 0-14 years, 15ï49 years, 50ï69 years, and 70+ years

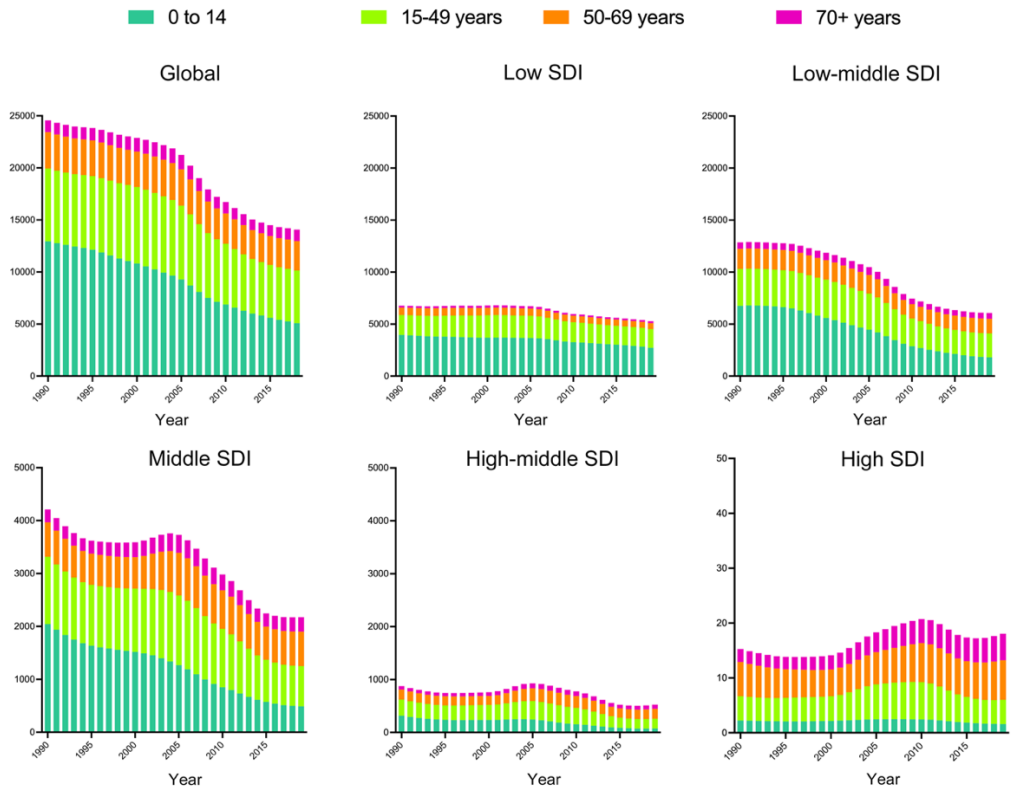


Figure 4. Rabies-related burden in 2019 and EAPC of the burden from 1990 to 2019 in countries and regions with different SDI levels.

Age-standardized incidence (A), Death (B), and DALYs (C) rate of Rabies in 1990. EAPC of ASIR (D), ASDR (E), Age-standardized DALYs (F) rate of Rabies from 1990 to 2019 (%). Every dot represented a country or territory and its color implied the region where the country or territory was located. ASIR: Age-standardized incidence rate, ASDR: Age-standardized death rate, DALYs: Disability-adjusted life years, EAPC: Estimated annual percentage change.