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Global time-trend analysis and projections of disease burden for neuroblastic tumors: a worldwide study from 1990 to 2021

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Abstract

Background Neuroblastoma and other peripheral nerve cell tumors (NB-PNT) are the most common extracranial solid tumors in children. This study aimed to describe the global burden of NB-PNT across different age groups and genders, including incidence, prevalence, mortality, and disability-adjusted life years (DALYs) in various countries and regions. Additionally, we analyzed changes in the disease burden over the past three decades and predicted future trends up to 2036.

Methods Using open data from the Global Burden of Disease (GBD) database (1990–2021), we provided a dynamic description of the disease burden of NB-PNT patients across different age and gender groups on a global scale. Joinpoint analysis was used to calculate the average annual percentage change (AAPC) to quantify trends in the burden of NB-PNT. Meanwhile, the Bayesian Age-Period-Cohort (BAPC) model was applied to predict the changes in disease burden up to 2036.

Results From 1990 to 2021, the global burden of NB-PNT increased significantly, with global prevalence rising from 41,456 to 56,326 cases. Gender and age disparities were evident, with male patients and patients aged 6–11 months exhibiting higher disease burden. Regional variations were observed, with higher disease burdens in regions with a higher sociodemographic index (SDI), although low-SDI regions showed a consistent upward trend. Overall, the prevalence of NB-PNT increased year by year (overall AAPC = 0.64% [0.56 − 0.72%]), with a slight decline in age-standardized mortality rates observed in 2019 ($APC_{2019-2021}$ = -2.02%). Projections indicate a slight decline in both incidence and mortality rates by 2036, with a more pronounced reduction in females.

Conclusions A higher burden of NB-PNT was evident among male patients and infants. The disease burden in low-SDI regions has increased in recent years, while a decline was observed in high-SDI regions. Over the past 30 years, the burden rose overall, although a decline in incidence was observed in 2019. Projections indicate a slight decrease in global incidence and mortality rates through 2036.

Keywords Cancer epidemiology, Neuroblastoma, Peripheral nerve cell tumors, Disability-adjusted life years, Incidence

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Introduction

Neuroblastoma (NB), a malignancy originating from neural crest cells, is the most common extracranial solid tumor in children. These tumors typically arise in the adrenal medulla or paraspinal sympathetic ganglia [1]. Other tumors that also originate from the sympathetic nervous system, such as ganglioneuroma (GN) and ganglioneuroblastoma (GNB), are part of the NB spectrum. Collectively, these tumors are referred to as peripheral neuroblastic tumors (PNTs) [2]. As one of the most common tumors in children and a leading cause of death, understanding its incidence and keeping abreast of the latest trends in incidence and mortality is crucial. However, limited information on these trends is currently available.

NB, which has the highest incidence rate within this spectrum, accounts for approximately 10% of all pediatric cancers and is responsible for 15% of cancer-related deaths in children [3]. Survival rates have improved over the past few decades [4, 5]. For instance, the five-year survival rate for high-risk NB patients younger than 30 years has increased from 29% in the 1990s to nearly 50% in the 2010s [6], largely due to advancements in myeloablative therapy and immunotherapy [7]. However, these mainstream survival data primarily originate from cohorts in developed regions, such as North America or Europe. In developing or underdeveloped regions, where these advanced treatment methods are not accessible, the epidemiology of NB may differ significantly, though this remains unclear. Additionally, factors such as changes in fertility rates, which have led to shifts in population structure, and the depletion of healthcare resources caused by the Coronavirus Disease-19 (COVID-19) pandemic in 2019 have introduced considerable uncertainty in the trends of incidence and mortality.

In this study, using data from the Global Burden of Disease (GBD) 2021 study [8], we reviewed the global rates and trends of incidence, mortality, and disease burden of PNT. We conducted a detailed comparison of gender- and age-specific differences, highlighting turning points in incidence trends over the past 30 years and projecting changes for the next 15 years. Additionally, we presented the epidemiological disparities in PNT across different economic regions. This study aims to serve as a valuable reference for policy planning and to support the improvement of cancer control measures.

Materials and methods

Data acquisition

The data used in this study were sourced from the GBD 2021 dataset, which provides comprehensive records on the incidence, prevalence, and mortality rates of over 300 diseases and injuries across 204 countries and regions, spanning the years 1990 to 2021 and stratified by age and sex [8]. Data on cancer prevalence, incidence, annual cancer-related deaths, disability-adjusted life years (DALYs), age-standardized incidence rate (ASIR) and age-standardized mortality rates (ASMR) attributable to neuroblastoma and other peripheral nervous cell tumors (NB-PNT) were obtained using the results tool from the Global Health Data Exchange (GHDx) (http://ghdx.healthdata.org/gbd-results-tool). These data were analyzed by year, age, region, and country. Countries and territories were categorized into five socio-demographic index (SDI) levels: low, low-middle, middle, high-middle, and high. Given the unique characteristics of NB incidence, patients under 5 years of age were further divided into five specific age groups: <28 days, 1–5 months, 6–11 months, 12–23 months, and 2–4 years. Patients aged 5 years and older were grouped in 5-year intervals, while individuals aged 50 years and above were classified into three additional groups: 50–74 years, 75–84 years, and 85 years and older. The 50–74 age group, for example, was formed by combining the 50–54, 55–59, 60–64, 65–69, and 70–74 age groups. The corresponding age-specific rates were calculated as the sum of the number of incidence or deaths in the included age groups divided by the total population of these groups, multiplied by 100,000.

Definition

In GBD 2021, NB-PNT was defined by the International Classification of Diseases (ICD) code 10th Revision (C47-C47.9). The subcategories C47.1-C47.9 correspond to tumors located in the upper limbs, lower limbs, chest, abdomen, pelvis, and other unspecified or uncategorized areas. It is important to note that within this broad category, NB is the primary type, but it also encompasses other relatively rare pathological types, such as GN, GNB, etc. Although NB is the dominant type, the patient population in this study exhibits a degree of heterogeneity.

The SDI, as estimated by GBD researchers, is expressed on a scale from 0 to 1. It is derived from three components: lag-distributed income (LDI) per capita, the average years of education for individuals aged 15 and older (EDU15+), and the total fertility rate for women under the age of 25 (TFU25) [9, 10, 11]. A higher SDI corresponds to a higher level of development at the country level. Based on this classification, 204 countries and territories were classified into five SDI categories: low, low-middle, middle, high-middle, and high.

DALYs represent the total number of healthy life years lost from the onset of an illness to death. DALYs are calculated as the sum of the years of life lost (YLLs) and the years lived with a disability (YLDs). DALYs provide a comprehensive assessment of the impact of NB-PNT, combining both non-fatal health outcomes and premature death. One DALY represents the loss of one full year of healthy life [12].

Age-period-cohort analysis

This study applied the age-period-cohort model to evaluate the disease burden of NB-PNT. Age effects reflect the influence of age-related changes on disease incidence rates, while period effects capture temporal factors that uniformly influence all age groups over time. Cohort effects represent the influence of early-life experiences and social determinants specific to particular birth cohorts. These effects also illustrate variations in mortality rates caused by generational differences in lifestyles or exposure to risk factors [13]. The log-linear regression model used in this analysis is expressed as follows [14, 15, 16]:

$$log\,(Y_i) = \mu + \alpha * age_i + \beta * period_i + \gamma * cohort_i + \epsilon$$

The incidence rate (Y_i) was modeled as a function of age, period, and cohort effects, with coefficients α, β and γ representing the respective contributions of age, period, and cohort. The intercept (μ) and the residual term (ϵ) accounted for the baseline level and unexplained variance, respectively. To implement the age-period-cohort model, data were organized into consecutive 5-year intervals covering the period from 1992 to 2021. Data from 1990 to 1991 were excluded due to their inability to align with the 5-year interval framework. Considering the disease characteristics, age was categorized into 14 groups. Children under 5 years of age were subdivided into five groups: <28 days, 1–5 months, 6–11 months, 12–23 months, and 2–4 years. For individuals aged 5–49 years, age was grouped into 5-year intervals, and those aged 50 years and older were excluded from the age-period-cohort analysis. A total of 19 birth cohorts, representing individuals born between 1943 and 2021, were identified for analysis. The average levels of age, period, and cohort effects were used as the reference categories. Statistical analysis was performed using the age-period-cohort online tool provided by the National Cancer Institute (http://analysistools.nci.nih.gov/apc/).

Statistical analyses

Descriptive analysis of the incidence rates, mortality, and DALYs for NB-PNT was conducted across defined age groups, gender, and years, with temporal trends plotted from 1990 to 2021. Age-standardized rates were calculated by adjusting the age structure based on the GBD world population standard. To visually represent the disease burden of NB-PNT across different countries and regions, we plotted global maps of incidence rates for each country. Temporal trends in disease incidence and variations in incidence and mortality rates by gender and age were depicted using line charts and bipartite plots. Consistent with prior studies [17], we use joinpoint regression analysis to assess trends in the disease burden of NB-PNT using joinpoint software (version 4.9.1.0). Annual Percentage Change (APC), Average Annual Percentage Change (AAPC), and 95% confidence intervals (CIs) were calculated. APC values greater than 0, less than 0, or $P > 0.05$ indicate statistically significant increases, decreases, or no significant changes in the trend of NB-PNT, respectively. The AAPC synthesizes the trends across the entire study period, with values greater than 0, less than 0, and equal to 0 indicating increasing, decreasing, or stable trends, respectively. To predict the incidence and prevalence rates, the Bayesian Age-Period-Cohort (BAPC) model was applied and analyzed using the Integrated Nested Laplace Approximation (INLA) package in R. A P-value of < 0.05 was considered statistically significant. All statistical analyses and visualizations were performed using R software (version 4.3.1). This study did not require ethical approval, as it did not involve direct interaction with or participation from human subjects. Data were accessed on 18 November 2024.

Results

The global burden of NB-PNT

The global and regional burden of NB-PNT and its trends are summarized in Table 1. In 1990, the global prevalence of NB-PNT was estimated at 41,456 (30,653 – 55,586) cases, with an age-standardized prevalence rate of 0.68 (0.50–0.91) per 100,000. In 2021, these values had increased to 56,326 (38,459 – 75,480) cases and 0.83 (0.57–1.12) per 100,000, respectively. The prevalence of the disease varied across regions, with areas of higher SDI showing a greater age-standardized prevalence. However, a declining trend in prevalence was identified in high-HDI regions, while an overall increase was noted in low-SDI regions. Regarding incidence, the global incidence rate increased from 5,854 (4,517–5,854) cases in 1990 to 10,867 (8,279–13,557) cases in 2021. This upward trend was evident across all regions, with the most pronounced increase occurring in low-SDI regions.

Globally, the death count and DALYs for NB-PNT in 1990 were 2,675 (2,298-3,318) and 185,391 (158,570 – 219,544), respectively. By 2021, these values increased to 5,194 (4,295-5,932) and 285,479 (227,709 – 341,110). We observed a reduction in the age-standardized mortality rate in high-SDI regions, decreasing from 0.097 (0.091-0.10) to 0.088 (0.080–0.095). Meanwhile, age-standardized mortality rates increased to different extents across other regions, with the most pronounced rise observed in middle and low-middle SDI regions.

The national burden of NB-PNT

Figure 1 illustrates the disease burden of NB-PNT across various countries. Fig. 1A shows the range of

Table 1 Global NB-PNT cases across all age groups and age-standardized prevalence, incidence, mortality, YLL, YLD, and DALY rates in 1990 and 2021

Measure	All-ages cases			Age-standardized rates per 100,000 people (95% UI)		
	1990	2021	Change (%)	1990	2021	Change (%)
Prevalence						
Global	41,456 (30653,55586)	56,326 (38459,75480)	35.9	0.68 (0.50,0.91)	0.83 (0.57,1.12)	22.1
High SDI	11,536 (9754,13524)	8807 (7434,10206)	-23.7	1.80 (1.52,2.11)	1.45 (1.20,1.70)	-19.4
High-middle SDI	8079 (6153,10439)	8032 (6057,10006)	-0.6	0.86 (0.66,1.12)	1.02 (0.76,1.28)	18.6
Middle SDI	10,480 (7275,14524)	14,707 (10257,19434)	40.3	0.53 (0.37,0.73)	0.79 (0.55,1.05)	49.1
Low-middle SDI	7725 (4799,12142)	15,184 (9220,15184)	96.6	0.45 (0.28,0.71)	0.79 (0.48,1.17)	75.6
Low SDI	3598 (1943,6601)	9554 (4263,16804)	165.5	0.40 (0.22,0.73)	0.58 (0.26,1.03)	45.0
Incidence						
Global	5854 (4517,5854)	10,867 (8279,13557)	85.6	0.11 (0.08,0.14)	0.15 (0.11,0.18)	36.4
High SDI	1869 (1615,2148)	2310 (2034,2571)	23.6	0.25 (0.21,0.29)	0.24 (0.21,0.27)	-4.0
High-middle SDI	1302 (1011,1667)	2350 (1913,2781)	80.5	0.13 (0.10,0.17)	0.19 (0.15,0.23)	46.2
Middle SDI	1353 (960,1848)	3022 (2296,3798)	123.4	0.074 (0.053,0.10)	0.14 (0.10,0.17)	89.2
Low-middle SDI	914 (579,1424)	2057 (1332,2964)	125.1	0.058 (0.038,0.089)	0.11 (0.071,0.16)	89.7
Low SDI	409 (233,750)	1120 (533,1938)	173.8	0.050 (0.029,0.091)	0.075 (0.037,0.13)	50.0
Death						
Global	2675 (2298,3138)	5194 (4295,5932)	94.2	0.051 (0.043,0.059)	0.068 (0.056,0.078)	33.3
High SDI	774 (732,808)	1048 (956,1124)	35.4	0.097 (0.091,0.10)	0.088 (0.080,0.095)	-9.3
High-middle SDI	614 (510,732)	1168 (964,1318)	90.2	0.062 (0.052,0.074)	0.082 (0.068,0.093)	32.3
Middle SDI	642 (530,737)	1503 (1238,1710)	134.1	0.038 (0.031,0.044)	0.065 (0.053,0.074)	71.1
Low-middle SDI	443 (342,581)	953 (726,1204)	115.1	0.030 (0.023,0.040)	0.052 (0.040,0.065)	73.3
Low SDI	199 (134,317)	517 (295,813)	159.8	0.026 (0.017,0.042)	0.037 (0.022,0.058)	42.3
DALYs	185,391 (158570,219544)	285,479 (227709,341110)	54.0	3.20 (2.75,3.78)	3.95 (3.11,4.77)	23.4
YLDs	3661 (2314,5480)	5582 (3664,8271)	52.5	0.062 (0.039,0.092)	0.079 (0.051,0.12)	27.4
YLLs	181,730 (154880,214933)	279,897 (223219,334085)	54.0	3.14 (2.68,3.70)	3.87 (3.05,4.76)	23.2

DALY: disability-adjusted life year; NB-PNT: neuroblastoma and other peripheral nerves cell tumors; SDI: socio-demographic index; UI: uncertainly interval; YLD: years lived with a disability; YLL: years of life lost

age-standardized incidence rates across countries. Some regions, such as North America, Australia, and Europe, have higher incidence rates, which are consistent with their relatively higher SDI, aligning with the previously mentioned conclusion regarding incidence differences across regions with varying SDI levels. Malta (0.56, 95% CI: 0.40–0.78) recorded the highest rate, followed by Tobago, Barbados, and Italy, while the countries with the lowest incidence rates include Tajikistan and Niger.

In terms of relative changes in incidence rates from 1990 to 2021, Liberia experienced the greatest decline, showing a 59.0% reduction. Niger and Greenland followed closely behind. On the other hand, Saint Vincent and the Grenadines recorded the most significant increase in incidence, rising by 2214.1%. The countries ranked second and third in terms of the largest increase were Guyana and Georgia, followed by Qatar and Equatorial Guinea. Overall, over the 31-year period, 25 countries and regions experienced a decrease in incidence rates, while 179 countries recorded an increase.

Gender disparities in the global burden of NB-PNT in different age groups

Figure 2 illustrates the prevalence, mortality rate, and DALYs across different age groups, stratified by gender. In terms of prevalence rates, the peak occurs at ages 0–2 years, with infants aged 6–11 months representing the primary high-risk group. After 11 months, the prevalence gradually declines with increasing age, and this decrease is more pronounced among female patients compared to males. Regarding the number of cases, the primary age range for male patients is 2–4 years, while for females, it is 5–9 years. Notably, the number of male patients exceeds that of female patients across all age groups (Fig. 2B), highlighting a gender disparity. The age distribution of mortality rates and DALYs shows some similarity to the prevalence distribution, with the primary peak occurring in infants aged 6–11 months. After this peak, the mortality rate in female patients decreases more rapidly with age compared to males. For patients aged over 50 years, mortality rates increase with age. Unlike the prevalence peak, the mortality peak for both male and female patients occurs at 6–11 months, and gender differences in mortality rates within this age group

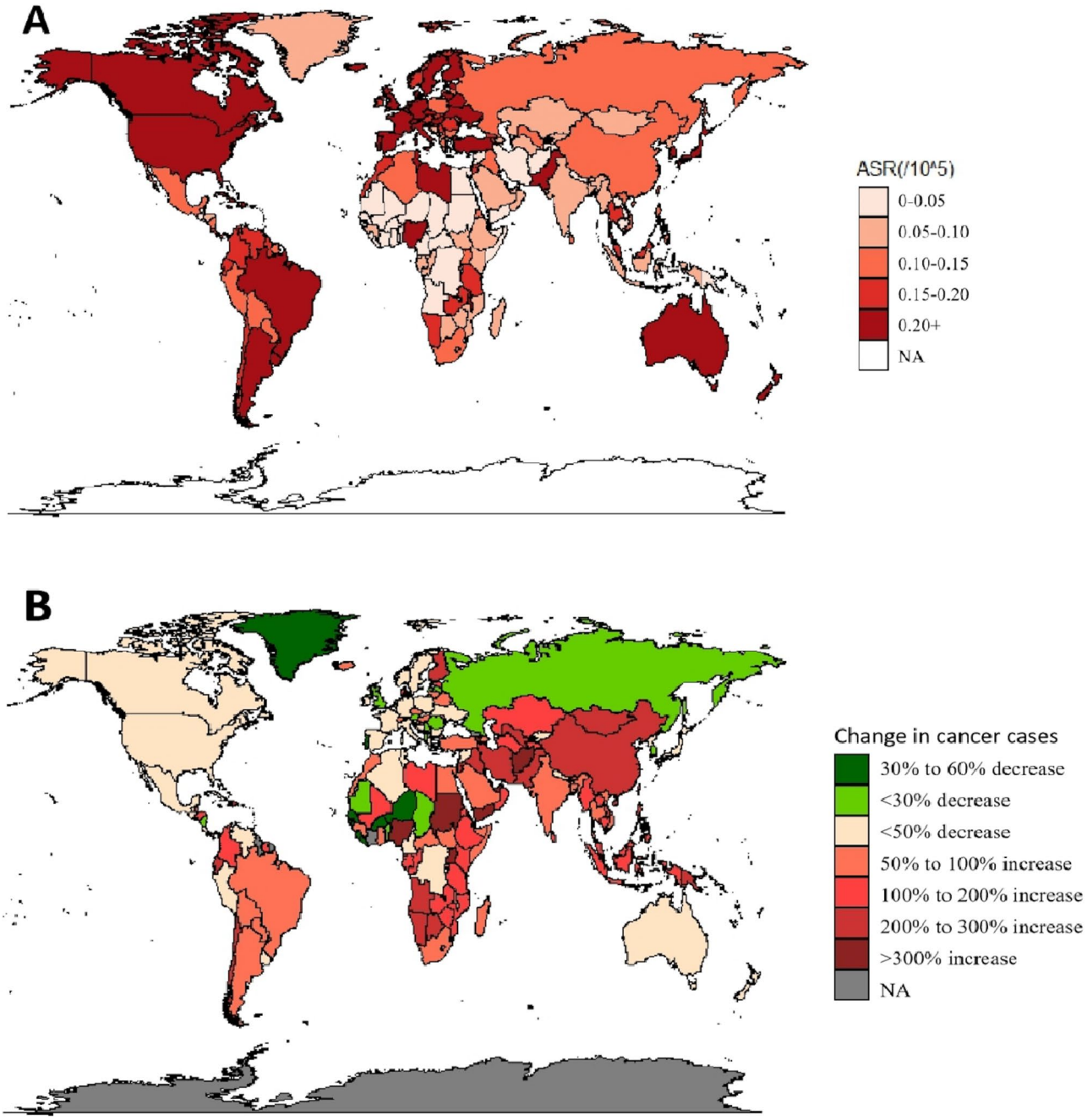

Fig. 1 The map showing the age-standardized incidence per 100,000 people (**A**) and changes in incidence from 1990 to 2021 (**B**) among various countries and regions

are minimal. Similarly, the peak age for DALYs also falls within the 6–11 month range.

Figure 3 presents the global prevalence and death counts, as well as the age-standardized prevalence and mortality rates, for patients of different genders from 1990 to 2021. The number of cases has increased year by year from 1990 to 2019, particularly after 2006. A turning point was observed in 2019, as prevalence rates declined in 2020 and 2021 compared to earlier years. During the same period, the age-standardized prevalence rate for males remained higher than that for females. In terms of mortality, both the number of deaths and the mortality rate exhibited a consistent year-on-year increase. The number of deaths in 2020 and 2021 remained stable compared to 2019. Similarly, the age-standardized mortality rate for males was higher than that for females during the same years.

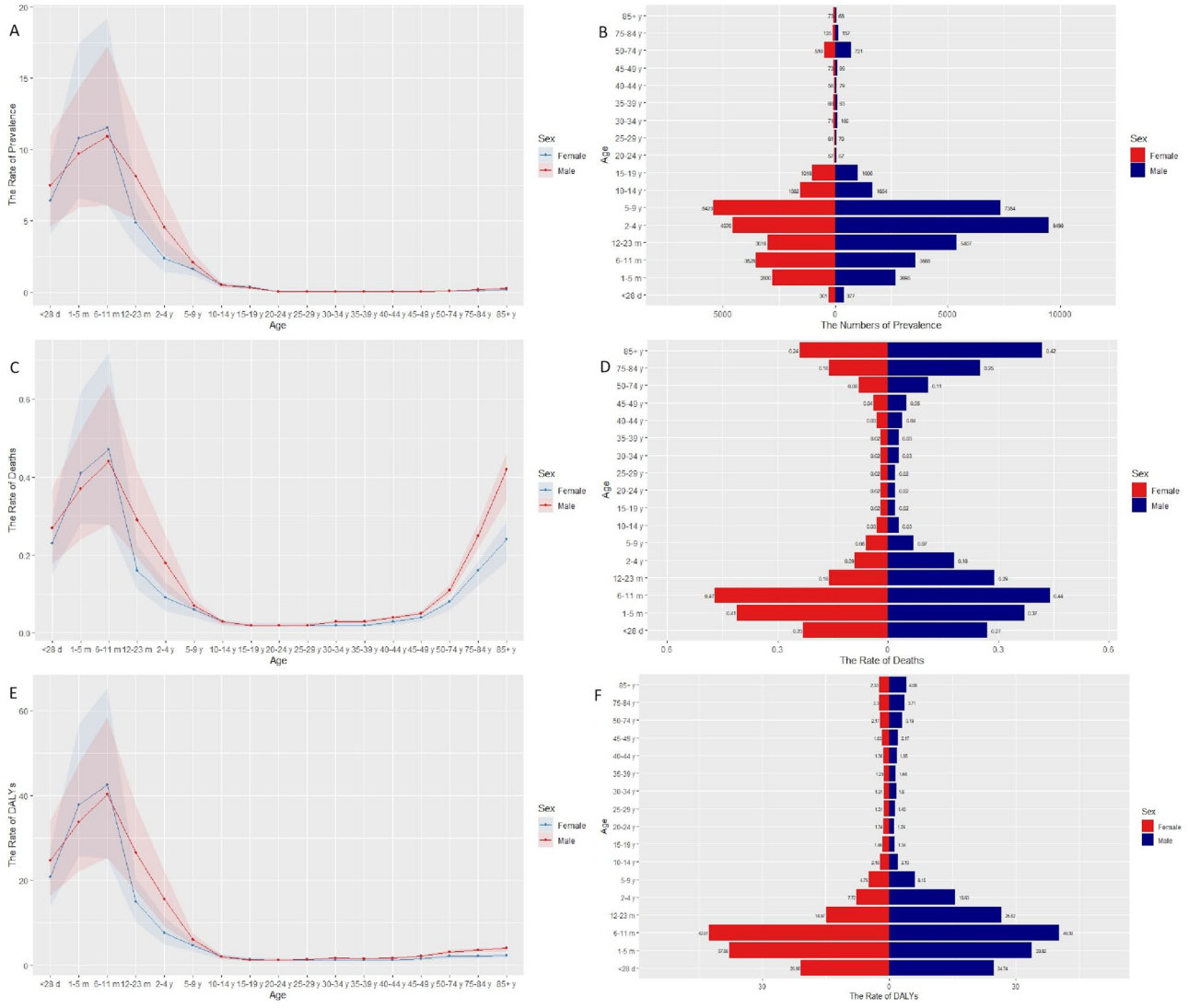

Fig. 2 Line graphs and bilateral charts of prevalence rate (**A**-**B**), mortality rate (**C**-**D**), and DALY rate (**E**-**F**) for patients in different age groups, with separate bilateral charts for males and females

Joinpoint analysis of global NB-PNT prevalence and mortality

The segmental trends of prevalence and mortality rate of NB-PNT were analyzed using joinpoint analysis, as illustrated in Fig. 4. Regarding prevalence, since 1990, the prevalence of NB-PNT has shown an annual increase (overall AAPC = 0.64% [0.56 – 0.72%]). However, a turning point occurred in 1999, with a slight decline in prevalence ($APC_{2000-2006}$ = -0.44%). In 2019, a more significant turning point was observed, characterized by a substantial decrease in prevalence ($APC_{2019-2021}$ = -5.09%). In terms of mortality, from 1990 to 2021, there was also an upward trend (overall AAPC = 0.94% [0.86 – 1.02%]), with a plateau phase similar to that observed in prevalence, occurring between 2000 and 2007 ($APC_{2000-2007}$ = -0.22%). In 2019, a turning point was observed, marked by a slight decline in age-standardized mortality rates ($APC_{2019-2021}$ = -2.02%). There were no significant differences in the trend of change between males and females, but male patients consistently exhibited higher prevalence and mortality rates than female patients during the same period.

Age, period and cohort effects on NB-PNT incidence

Figure 5 illustrates the age-period-cohort effect on the NB-PNT incidence rate. Fig. 5A shows the changes in incidence rates across different age groups. Fig. 5B presents the proportional changes in disease incidence across different years. A gradual upward trend in incidence rates is observed, with the incidence rate ratio for the population in 2019 compared to 2004 estimated at 1.17 (95% CI: 1.127–1.215), using 2004 as the baseline. Fig. 5C demonstrates the incidence rate ratios for different cohorts

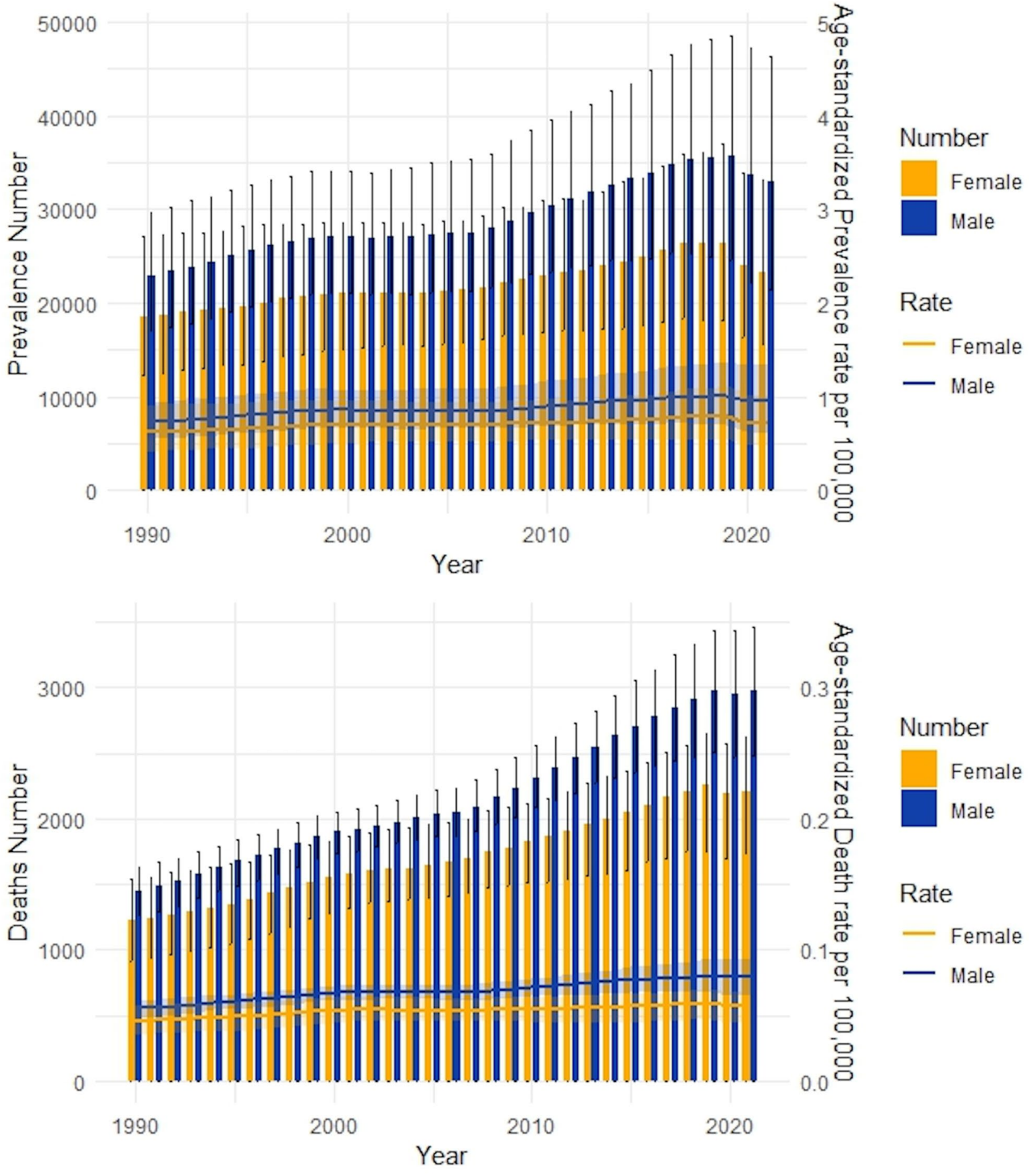

Fig. 3 Axis charts of prevalence number (upper chart) and death number (lower chart) for male and female patients, along with age-standardized prevalence and mortality rates

based on birth year, indicating that more recent birth cohorts exhibit higher incidence rates. The incidence rate ratio for the population born in 2017 compared to those born in 1972 is 1.401 (95% CI: 1.085–1.809). Fig. 5D illustrates the relationship between incidence rates and time periods for different age groups. The average annual change in incidence rates for each age group exceeds 0, indicating a consistent yearly increase in incidence across all age groups. Notably, the incidence rate for the 25–30 age group has a significantly higher annual increase

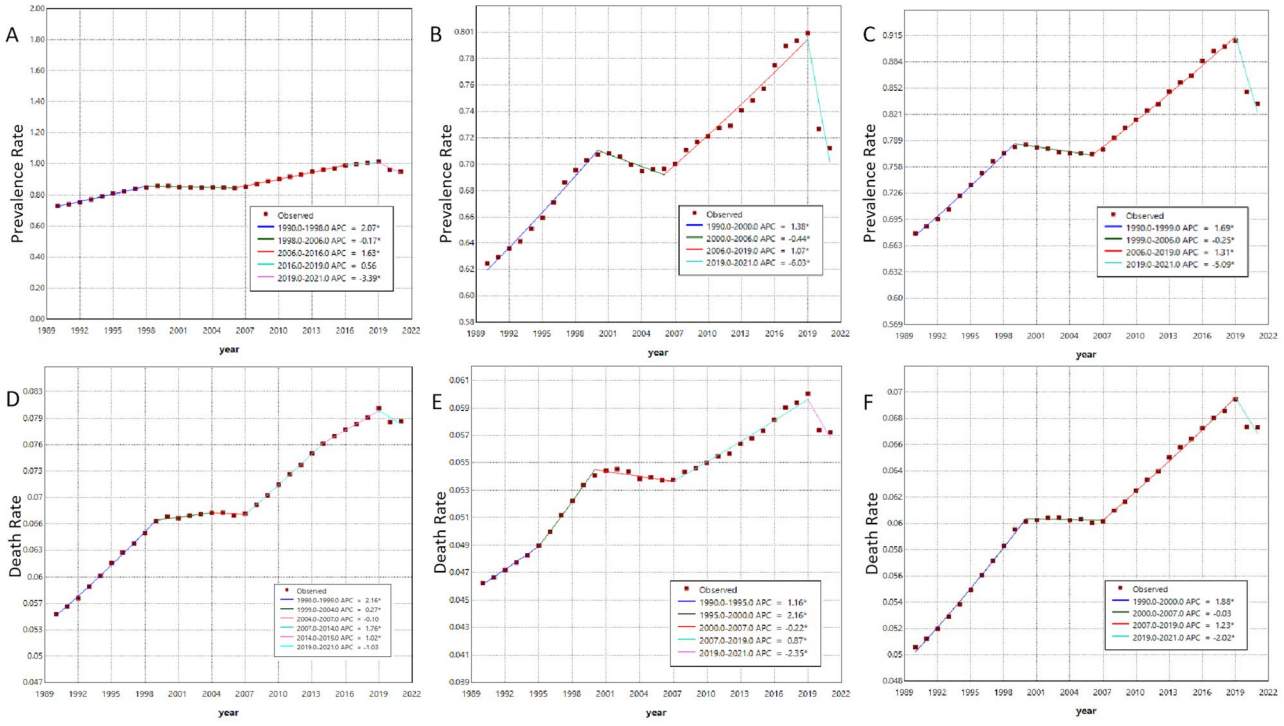

Fig. 4 The joinpoint analysis of prevalence (**A**-**C**) and mortality rates (**D**-**F**) for male patients, female patients, and the total population

(Ratio = 1.665, 95% CI = 1.298–2.032), while the annual increase in incidence for the 2–4 age group is relatively lower (Ratio = 0.494, 95% CI = 0.325–0.663).

Predictions of global incidence and death rates for NB-PNT

Based on the NB-PNT data from the GBD database spanning 1990 to 2021, we further projected the disease burden for the next 15 years, as depicted in Fig. 6. Our projections suggest that the incidence and mortality rates, as well as the number of new cases and deaths, are expected to decline in both sexes over the next decade. By 2036, the predicted ASIR is projected to decline to 0.14 per 100,000 in men and 0.10 per 100,000 in women. The predicted ASMR is projected to be 0.08 per 100,000 in men and 0.05 per 100,000 in women. A decline in both global incidence and mortality rates is anticipated for both sexes, with a greater reduction projected for females.

Discussion

As a rare disease, GBD 2021 provides the most comprehensive epidemiological data on NB-PNT spanning the past three decades. In this study, we found that, based on the GBD 2021 database, the incidence, prevalence, mortality, and disease burden of NB-PNT have exhibited an upward trend globally over the past three decades. The global number of new cases increased from 41,456 in 1990 to 56,326 in 2021, while the incidence rate rose from 5,854 cases per 100,000 population in 1990 to 10,867 per 100,000 in 2021, representing an 85.6% increase. Similarly, the global mortality rate from this disease nearly doubled compared to 1990. However, these trends varied across countries and regions. The findings of this study offer valuable epidemiological insights for researchers and policymakers worldwide and serve as a meaningful reference for developing disease management strategies.

NB primarily occurs in children, with most cases being diagnosed before the age of 5 [5]. The peak incidence occurs in infants under 1 year of age [18], which is consistent with our findings, where the highest incidence was observed between 6 and 11 months. It is important to note that due to misdiagnosis, the actual age of onset may be earlier than the statistical figures suggest. After the age of 2, the incidence of the disease significantly decreases, and no second peak in incidence is observed. The occurrence of NB in adults and older age groups is exceptionally rare, with the incidence being less than one in a hundred thousand. The overall annual incidence rate across all age groups has shown an increasing trend, particularly in adults, with a marked increase observed in the 25–30 age group in recent years. A study from the Texas MD Anderson Cancer Center reported 118 adult neuroblastoma cases with a median diagnostic age of 47 years [19]. Similarly, a single-center study from Italy that included all NB patients aged over 12 years treated within the past 20 years reported a median diagnosis age of 17 years [20]. As diagnostic capabilities continue to improve, the number of adult NB cases is expected to rise further.

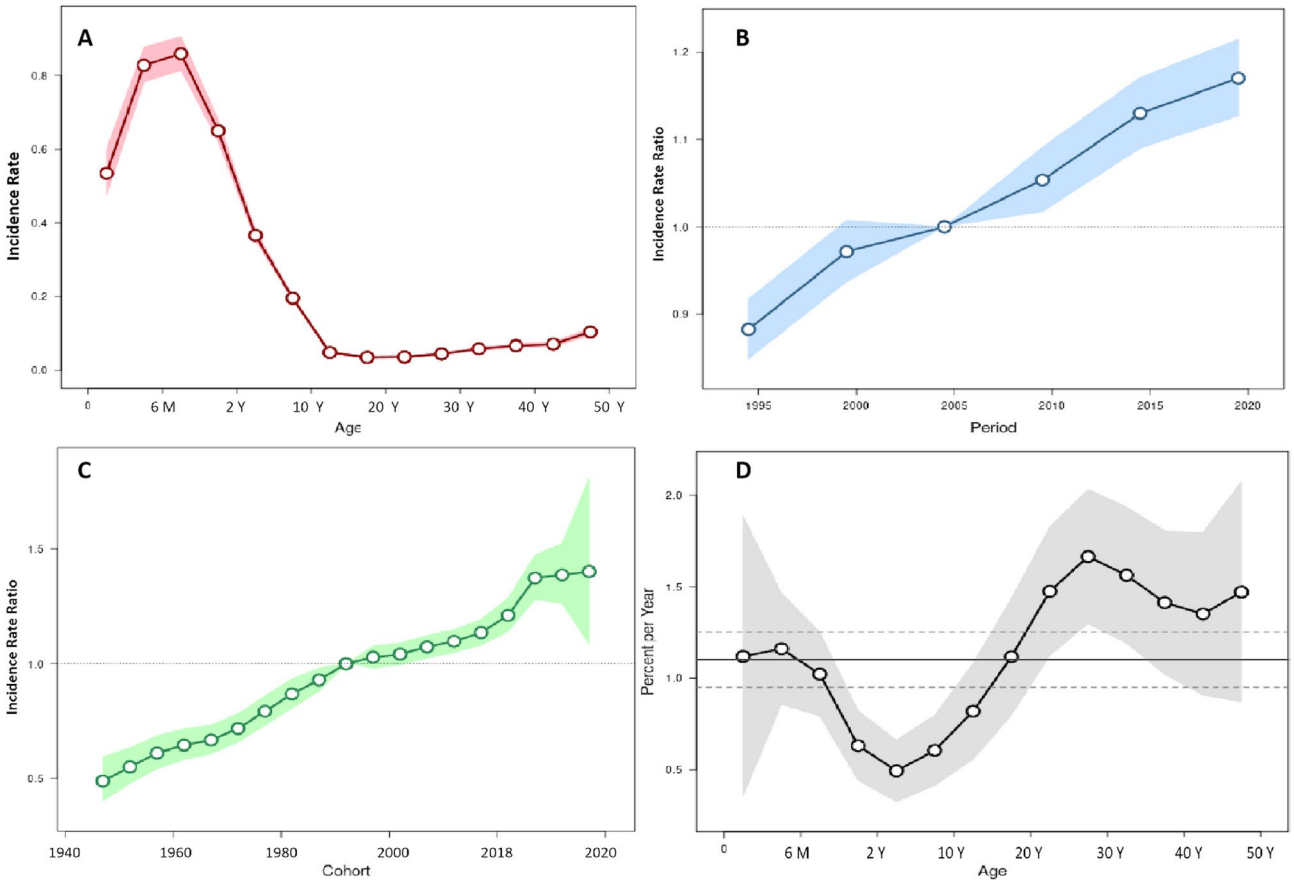

Fig. 5 Schematic of age-period-cohort model results. (**A**) changes in disease incidence for patients across different age groups. (**B**) proportional changes in disease incidence across different years. (**C**) changes in incidence rate ratios for different birth cohorts. (**D**) comparison of annual incidence rate trends across different age groups of patients

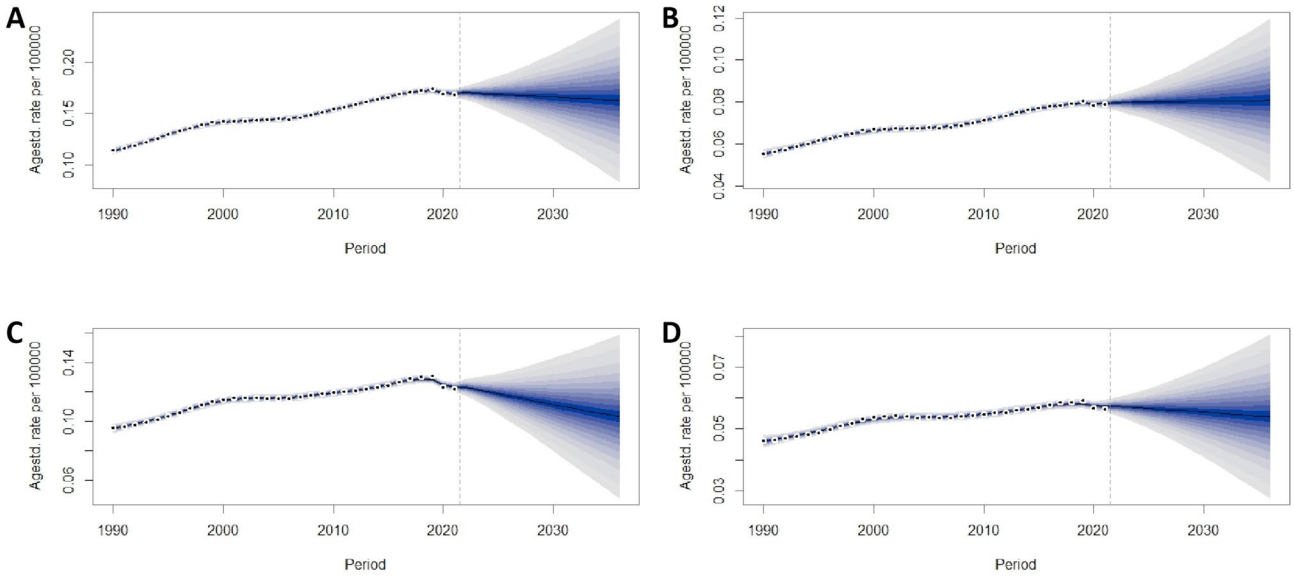

Fig. 6 Predicted trends in age-standardized incidence and mortality rates up to 2036

Although it is rare in both adolescents and adults, greater attention should be directed toward adult neuroblastoma cases, with an emphasis on standardizing treatment strategies. Furthermore, within the same age group, gender differences in incidence have been confirmed in multiple studies [5, 7]. Our research also reached similar conclusions, indicating that the incidence of NB is generally higher in males than females, and the decline in incidence with age is slower in males after the age of 1. This suggests that the age of onset for female patients tends to be more concentrated.

Due to the varying locations of tumor development, NB can exhibit diverse clinical manifestations [4]. Additionally, infants and young children have very limited ability to express clinical symptoms, which poses a significant challenge for the diagnosis of NB. Previous studies have suggested that in economically developed regions, such as Western Europe, the United States, Canada, Japan, Hong Kong, and Australia, the incidence of neuroblastoma is notably higher, primarily attributed to superior healthcare resources [21, 22]. In contrast, middle- and low-income countries, including regions in Africa, parts of East Asia, and South America, typically report lower incidence rates [23]. Furthermore, within North America, the incidence of NB is significantly higher among Caucasians compared to Black or Hispanic populations. However, this is likely attributable to differences in access to healthcare resources across different demographic groups. Currently, there is no strong evidence to support significant differences in the incidence of neuroblastoma across ethnic and racial groups [24]. In addition, some studies have observed a potential link between insufficient intake of vitamins and folic acid during pregnancy and an increased risk of NB in offspring [25, 26]. In low-income countries, inadequate prenatal care and nutrient intake may also contribute to elevated NB incidence.

Population transition is a key driver of changes in cancer burden. According to World Health Organization (WHO) population data, birth rates have steadily declined since the 21st century. Since the peak incidence of NB occurs in children under 1 year of age, it is highly sensitive to changes in population structure. However, despite the demographic shift, the incidence of NB continues to rise. A study based on the SEER database concluded that from 1975 to 2015, the number of new cases per decade gradually increased [27]. Our findings also indicate that this trend persisted up until 2019, indicating that additional factors could contribute to the rise in incidence. It is important to consider whether this is due to improvements in surveillance and diagnosis or changes in the distribution of potential risk factors. Conducting research on risk factors for rare diseases such as NB is particularly challenging. A review article provided detailed insights into potential risk factors for such diseases, indicating that factors such as maternal alcohol consumption during pregnancy and the use of diuretics may increase the risk of the fetus developing the disease [18]. However, since these findings are not conclusive, predicting the impact on the disease incidence trend remains difficult. Notably, since 2019, the incidence of NB-PNT has exhibited a downward trend. On one hand, this may be due to the strain on healthcare resources caused by COVID-19, especially in low-income countries. In high-income countries, the pandemic has also led to a decline in female fertility rates [28], further contributing to a decrease in the number of newborns. From 1990 to 2021, the changes in the annual incidence and mortality rates closely mirrored each other, suggesting that although chemotherapy methods for NB-PNT have improved over the past 30 years, there has been no significant reduction in the overall mortality rate. This is particularly true in middle- and low-income countries, where access to comprehensive treatment remains limited for patients [29]. This also highlights that the diagnosis and treatment journey for NB-PNT remains long and challenging. The urgent need for more effective treatment strategies is critical to reducing mortality and improving survival and prognosis for affected children.

Our study suggests that the incidence of NB-PNT is expected to maintain the downward trend observed since 2019, stabilizing or slightly declining. Based on global fertility trends, the majority of live births in the future are projected to shift from high-income countries to low-income countries. Consequently, the focus of disease prevention and treatment efforts must gradually shift toward middle- and low-income countries, with a particular emphasis on enhancing their diagnostic and treatment capacities over time.

This study has several limitations. First, GBD analyses are highly dependent on the quality and quantity of available data. In middle- and low-income countries or regions with poor healthcare infrastructure, data gaps due to regulatory issues may introduce biases in disease burden estimates. Second, because GBD categorizes PNT and NB under the same disease group for statistical purposes, the conclusions of this study may only partially reflect findings specific to NB and should not be interpreted as entirely equivalent. Third, misclassification or miscoding within disease registries could compromise the robustness and accuracy of the findings. Finally, the disease burden in any given region is shaped by diverse factors, including socioeconomic environment, ethnicity, genetics, and healthcare conditions. As a result, the findings of this study should not be directly extrapolated to specific regions, and further in-depth analysis is needed based on data specific to each country or region.

Conclusions

This study provided a comprehensive analysis of the global burden of NB-PNT over the past three decades. A higher burden of NB-PNT was evident among male patients and infants. The disease burden in low-SDI regions has increased in recent years, while a decline was observed in high-SDI regions. Over the past 30 years, the burden rose overall, although a decline in incidence was observed in 2019. Projections indicate a slight decrease in global incidence and mortality rates through 2036.

Abbreviations

AAPC	Average annual percentage change
APC	Annual percentage change
ASIR	Age-standardized incidence rate
ASMR	Age-standardized mortality rate
BAPC	Bayesian age-period-cohort
CI	Confidence interval
COVID-19	Coronavirus disease-19
DALY	Disability-adjusted life year
GBD	Global burden of disease
GHDx	Global health data exchange
GN	Ganglioneuroma
GNB	Ganglioneuroblastoma
ICD	International classification of diseases
NB	Neuroblastoma
NB-PNT	Neuroblastoma and other peripheral nerves cell tumors
PNT	Peripheral neuroblastic tumor
SDI	Socio-demographic index
UI	Uncertainly interval
WHO	World health organization
YLD	Years lived with a disability
YLL	Years of life lost

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Author contributions

All authors contributed to the conceptualization of the study. Y.T. and W.C. were responsible for methodology, data curation, investigation, formal analysis, writing– original draft and writing– review and editing. H.Z., J.S. and H.G. were responsible for data curation and investigation. Z.L. was responsible for project administration, supervision, funding acquisition and writing– review and editing. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

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