

# The evolving burden of pediatric solid tumors: A global analysis from 1990 to 2021

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## Abstract

**Background:** To evaluate the global incidence and mortality trends of seven major solid tumors (brain cancer, hepatoblastoma, kidney cancer, malignant bone tumors [MNBAC], neuroblastoma, retinoblastoma, and soft tissue sarcomas) in individuals aged 0–19 years from 1990 to 2021.

**Methods:** Using data from the Global Burden of Disease Study 2021, analyses were stratified by age, region, and sociodemographic index (SDI). Temporal trends were quantified via estimated annual percentage change (EAPC). A linear regression model evaluated the correlation between childhood meningitis mortality and SDI.

**Results:** In 2021, these tumors accounted for 96,913 new cases and 42,869 deaths worldwide. Brain cancer and MNBAC were the most common and fatal. Retinoblastoma showed the largest incidence increase, while neuroblastoma was the only tumor with rising mortality. Major regional disparities were observed, with East Asia having the highest brain cancer burden and sub-Saharan Africa experiencing the greatest retinoblastoma mortality. Incidence peaked in infants for hepatoblastoma, neuroblastoma, and soft tissue sarcomas, and in adolescents for bone tumors. Higher SDI correlated with higher neuroblastoma incidence, while lower-SDI regions had elevated mortality for multiple tumors.

**Conclusion:** Substantial global and regional disparities persist in the burden of pediatric solid tumors. Enhancing early detection in low-SDI regions and implementing targeted strategies for high-burden tumors such as brain cancer and MNBAC are essential to reducing mortality.

## Keywords:

Global burden of disease, incidence, mortality, pediatric cancer, solid tumors

## Introduction

Cancer is a major global health crisis, particularly for children and adolescents, who are highly vulnerable. Annually, around 400,000 children and adolescents are diagnosed with cancer worldwide, with solid tumors being particularly prevalent.<sup>[1,2]</sup> Despite remarkable advancements in cancer treatment, particularly in the realms of molecular genetics, immunotherapy, and precision medicine,

the therapeutic landscape for malignant solid tumors in children and adolescents remains fraught with challenges.<sup>[3-5]</sup> The long-term survival prospects for certain high-risk tumor types remain bleak, with effective radical treatment options still elusive. Furthermore, the potential long-term adverse effects and complications associated with treatment can severely compromise patients' quality of life.<sup>[6]</sup> This

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treatment quandary manifests in notable disparities across diverse global regions. In resource-constrained countries, the scarcity of medical resources, delayed diagnosis, and irregular treatment practices contribute to a cure rate for malignant solid tumors that is less than 30%.<sup>[7]</sup> This global imbalance in medical resource allocation further intensifies the disease burden of malignant solid tumors in children and adolescents.<sup>[8]</sup> To devise more targeted and efficacious prevention and control strategies, a profound comprehension of the epidemiological characteristics and trends of prevalent malignant solid tumors on a global scale is imperative.

The Global Burden of Disease Study (GBD) 2021 report highlights the need to prioritize health threats across 204 countries.<sup>[9]</sup> Leveraging the latest data from GBD 2021, this study will undertake a comprehensive analysis of incidence and mortality rates for seven relatively prevalent malignant solid tumors in children and adolescents worldwide. Our findings will furnish policymakers with reliable data, thereby fostering the development of tailored prevention and control strategies to address this pressing global health concern.

## Methods

### Data source and definition

In this study, malignant solid tumors occurring in individuals aged 0–19 were defined as such in children and adolescents. This analysis specifically focuses on seven prevalent solid tumors in children and adolescents: Brain and central nervous system cancer (brain cancer), hepatoblastoma, kidney cancer, malignant neoplasm of bone and articular cartilage (MNBAC), neuroblastoma and other peripheral nervous cell tumors (neuroblastoma), retinoblastoma, and soft tissue and other extraosseous sarcomas (STES). Quantitative indicators such as incidence, deaths, and associated rates for these tumors across diverse regions and ages globally were sourced from the GBD database (available at <https://vizhub.healthdata.org/gbd-results/>). Relevant data from systematic reviews of the literature, household surveys, health service access, civil registration and vital statistics data, surveillance data, and other sources were collected and identified for use in the GBD estimation process. The definition, processing, correction, and modeling of the data have been described elsewhere.<sup>[10,11]</sup>

Based on the SDI classification, spanning low, low-middle, middle, middle-high, and high categories, these countries and regions were further categorized into five groups.<sup>[10]</sup> The world was segmented into 21 regions, taking into account epidemiological similarity

and geographical proximity.<sup>[12]</sup> To delineate the age distribution of the disease burden, patients were stratified into seven distinct age groups: <1 year, 1–2 years, 2–4 years, 5–9 years, 10–14 years, and 15–19 years.

### Statistical analyses

Death counts and rates per 100,000 population were used as indicators, with 95% uncertainty intervals (UI) for accuracy. UI were computed based on the 2.5<sup>th</sup> and 97.5<sup>th</sup> percentiles obtained from 1000 samples for each variable.<sup>[13]</sup> To unravel key characteristics of the cancer burden, further analysis was conducted to examine differences across diverse geographical locations, countries, age groups, and SDIs. Simultaneously, the estimated annual percentage change (EAPC) in rates was estimated to illustrate trends in the burden of solid tumors in children and adolescents over time. Specifically, the following linear regression model was utilized for calculation:  $y = \alpha + \beta x + \varepsilon$ , where  $y$  represents the natural logarithm of the age-standardized rate,  $x$  represents the year, and  $\varepsilon$  is the error term. The EAPC value was derived using the formula  $100 \times (e^{\beta} - 1)$ , with its 95% confidence interval (CI) determined within the regression analysis framework. An EAPC with both its value and the upper limit of its 95% CI being negative signifies a decreasing trend over time; an EAPC with both its value and the lower limit of its 95% CI being positive indicates an increasing trend; an EAPC close to zero or statistically insignificant denotes stability or minimal change in the indicator over time.<sup>[10,11]</sup> Linear regression models were employed to explore the association between the burden of solid tumors and the SDI across regions and countries.<sup>[14,15]</sup> Statistical analyses and data visualization were executed using R (v4.4.2), with significance set at  $P < 0.05$ .

## Results

### Global incidence and mortality

Our analysis revealed seven major types of solid tumors accounted for 96,913.4 cases and 42,868.6 deaths annually, with incidence and mortality rates of 3.8 per 100,000 and 1.6 per 100,000, respectively. Additionally, brain cancer, MNBAC, and kidney cancer had the highest incidence rates, while brain cancer, MNBAC, and STES were the primary causes of death [Table 1].

From 1990 to 2021, the incidence rates of brain cancer, hepatoblastoma, kidney cancer, and STES declined, while those of MNBAC, neuroblastoma, and retinoblastoma increased. Notably, hepatoblastoma exhibited the most significant decline in incidence, with an EAPC of  $-2.1$  (95% CI  $-2.3$  to  $-2.0$ ). In contrast, retinoblastoma showed the most

## Key Message

*From 1990 to 2021, pediatric solid tumors caused significant global burden, with brain cancer and malignant bone tumors being the most incident and fatal types. Retinoblastoma incidence increased most, while neuroblastoma was the only tumor with rising mortality. Infants were most affected by hepatoblastoma and neuroblastoma, whereas adolescents faced higher risks from bone tumors and soft tissue sarcomas. These findings highlight the urgent need for early detection in resource-limited regions and targeted strategies for high-burden tumors.*

pronounced increase in incidence, with an EAPC of 1.3 (95% CI 1.0 to 1.6). In terms of mortality, hepatoblastoma had the most significant decline, with an EAPC of  $-2.6$  (95% CI  $-2.8$  to  $-2.5$ ). Conversely, neuroblastoma was the only solid tumor among the seven to show an increasing mortality trend [Figure 1 and Table 1].

### Regional incidence and mortality

The global burden of solid tumors in children and adolescents varies significantly by region. Brain cancer is the primary cause of incidence and mortality in most regions, with East Asia reporting the highest number of cases at 10,667.4 (95% UI 8,179.5–14,267.2), accounting for 61.2% of global incidence. South and Central Asia have high death tolls and mortality rates, respectively [Table 1, Figure 2, and S1]. MNBAC ranks second in many regions, especially in sub-Saharan Africa [Figure S1]. Kidney cancer is most incident in Southern Latin America, while neuroblastoma is prevalent in High-income Asia Pacific. The Caribbean has the highest STES incidence, and Eastern sub-Saharan Africa has the highest retinoblastoma incidence and mortality [Table 1 and Figure 2].

From 1990 to 2021, incidence and mortality trends differed by region and tumor type. High-income Asia Pacific saw a rise in brain cancer, while East Asia noted increases in MNBAC and retinoblastoma. Central Asia had growth in neuroblastoma and STES. Southern Sub-Saharan Africa saw a significant increase in kidney cancer. Hepatoblastoma declined in most regions except Australasia. Most regions saw declines in MNBAC, kidney cancer, STES, hepatoblastoma, and retinoblastoma mortality, but Southern Sub-Saharan Africa had increases in brain cancer, STES, kidney cancer, and retinoblastoma mortality. Brain cancer and neuroblastoma mortality trends were relatively balanced across regions [Table 1].

### National incidence and mortality

In 2021, India topped the list for neuroblastoma, hepatoblastoma, and MNBAC in terms of both incidence and mortality. China led in the incidence of brain cancer, kidney cancer, and retinoblastoma. Nigeria ranked first in the incidence and mortality of

STES, as well as in the mortality of kidney cancer. Monaco and Tajikistan had the highest incidence and mortality rates of brain cancer, respectively. For kidney cancer, Argentina and Malawi recorded the highest incidence and mortality rates. Malta and Malawi had the highest incidence and mortality rates for neuroblastoma. Tokelau ranked first in both the incidence and mortality rates of MNBAC, as well as in the incidence rate of retinoblastoma. Mali and Haiti had the highest incidence and mortality rates for hepatoblastoma and STES, respectively [Table 1, Figure S2, and Figure 3].

From 1990 to 2021, Ecuador experienced the fastest increase in incidence rate brain cancer, and both Ecuador and Turkmenistan had the fastest increases in mortality. For MNBAC, Saint Vincent and the Grenadines saw the most significant increases in both incidence and mortality, with EAPCs of 3.8 (95% CI 2.4–5.2) and 3.5 (95% CI 2.2–4.8), respectively. Mongolia had the fastest growth in both incidence and mortality for kidney cancer, with EAPCs of 7.4 (95% CI 6.0–8.8) and 6.1 (95% CI 4.8–7.5), respectively. Guyana had the fastest increases in both incidence and mortality for neuroblastoma, with EAPCs of 8.3 (95% CI 5.7–11.0) and 7.8 (95% CI 5.3–10.3), respectively. Armenia experienced the most significant increases in both incidence and mortality for retinoblastoma, with EAPCs of 18.3 (95% CI 14.4–22.4) and 14.4 (95% CI 10.7–18.2), respectively. Belarus had the fastest growth in both incidence and mortality for hepatoblastoma, with EAPCs of 6.5 (95% CI 5.4–7.6) and 5.3 (95% CI 3.7–7.0), respectively. Finally, Georgia had the most rapid increases in both incidence and mortality for STES, with EAPCs of 12.6 (95% CI 11.1–14.2) and 12.4 (95% CI 10.9–14.0), respectively (Table 1). These findings highlight the diverse trends in solid tumor disease burden across different countries over the past few decades.

### Burden of solid tumor by age

In 2021, an analysis of the age distribution characteristics revealed distinct patterns among seven types of solid tumors. Specifically, brain cancer incidence and mortality cases were predominantly observed in the 5–9 age group, with peak incidence

**Table 1: Global and regional burden of malignant solid tumors in children and adolescents in 1990 and 2021, and the changing trend from 1990 to 2021**

| Location        | Diseases       | 1990                        |                            |                            | 2021                  |  |  |
|-----------------|----------------|-----------------------------|----------------------------|----------------------------|-----------------------|--|--|
|                 |                | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95%UI)     | Death rate, n (95%UI) |  |  |
| Global          | Brain cancer   | 38816.6 (30302.6, 48085.6)  | 1.7 (1.3, 2.1)             | 25697.8 (19402.2, 32227.8) | 1.1 (0.9, 1.4)        |  |  |
|                 | Hepatoblastoma | 7063.7 (5798.8, 8280.7)     | 0.3 (0.3, 0.4)             | 4828.3 (3938.6, 5670.5)    | 0.2 (0.2, 0.3)        |  |  |
|                 | Kidney cancer  | 11077.5 (9103.0, 13051.4)   | 0.5 (0.4, 0.6)             | 4328.8 (3481.0, 5198.3)    | 0.2 (0.2, 0.2)        |  |  |
|                 | MNBAC          | 14750.0 (12236.1, 17658.0)  | 0.7 (0.5, 0.8)             | 7319.9 (6060.5, 8894.9)    | 0.3 (0.3, 0.4)        |  |  |
|                 | Neuroblastoma  | 4394.7 (3242.7, 5903.9)     | 0.5 (0.4, 0.6)             | 1711.8 (1431.9, 2037.1)    | 0.1 (0.1, 0.1)        |  |  |
|                 | Retinoblastoma | 4673.5 (3033.3, 5953.1)     | 0.2 (0.1, 0.3)             | 3179.8 (1819.0, 4172.8)    | 0.1 (0.1, 0.2)        |  |  |
|                 | STES           | 13194.2 (10307.6, 17690.5)  | 0.6 (0.5, 0.8)             | 5959.5 (4754.7, 8150.2)    | 0.3 (0.2, 0.4)        |  |  |
|                 | Brain cancer   | 2007.2 (1232.2, 3591.9)     | 0.7 (0.4, 1.3)             | 1699.4 (1037.3, 3102.7)    | 0.6 (0.4, 1.1)        |  |  |
|                 | Hepatoblastoma | 1431.5 (988.3, 1850.8)      | 0.5 (0.4, 0.7)             | 1012.4 (700.0, 1308.5)     | 0.4 (0.3, 0.5)        |  |  |
|                 | Kidney cancer  | 1258.4 (749.8, 1731.6)      | 0.5 (0.3, 0.6)             | 772.7 (465.8, 1046.8)      | 0.3 (0.2, 0.4)        |  |  |
| Low-SDI         | MNBAC          | 1896.0 (1346.9, 2610.2)     | 0.7 (0.5, 0.9)             | 1190.6 (903.6, 1623.1)     | 0.4 (0.3, 0.6)        |  |  |
|                 | Neuroblastoma  | 389.5 (216.1, 711.3)        | 0.1 (0.1, 0.2)             | 182.8 (122.3, 286.7)       | 0.1 (0.0, 0.1)        |  |  |
|                 | Retinoblastoma | 1411.8 (628.0, 1572.9)      | 0.4 (0.2, 0.6)             | 1139.7 (633.5, 1570.9)     | 0.4 (0.2, 0.6)        |  |  |
|                 | STES           | 3428.4 (2359.9, 5411.0)     | 1.2 (0.8, 1.9)             | 1863.4 (1347.3, 2838.3)    | 0.7 (0.5, 1.0)        |  |  |
|                 | Brain cancer   | 5667.1 (3947.4, 8376.8)     | 1.0 (0.7, 1.4)             | 4536.0 (3152.6, 6759.1)    | 0.8 (0.5, 1.1)        |  |  |
|                 | Hepatoblastoma | 1653.2 (1114.4, 2085.7)     | 0.3 (0.2, 0.4)             | 1167.0 (786.7, 1469.5)     | 0.2 (0.1, 0.2)        |  |  |
|                 | Kidney cancer  | 1554.7 (1105.2, 1980.9)     | 0.3 (0.2, 0.3)             | 790.5 (559.1, 1021.6)      | 0.1 (0.1, 0.2)        |  |  |
|                 | MNBAC          | 3532.4 (2480.7, 4479.6)     | 0.6 (0.4, 0.8)             | 2072.5 (1479.3, 2573.5)    | 0.4 (0.3, 0.4)        |  |  |
|                 | Neuroblastoma  | 832.4 (521.2, 1298.7)       | 0.1 (0.1, 0.2)             | 379.6 (287.8, 506.6)       | 0.1 (0.0, 0.1)        |  |  |
|                 | Retinoblastoma | 1198.3 (658.7, 1689.9)      | 0.2 (0.1, 0.3)             | 1133.6 (613.2, 1582.6)     | 0.2 (0.1, 0.3)        |  |  |
| Middle SDI      | STES           | 3455.8 (2484.4, 4760.9)     | 0.6 (0.4, 0.8)             | 1732.3 (1305.4, 2328.1)    | 0.3 (0.2, 0.4)        |  |  |
|                 | Brain cancer   | 14842.3 (10633.6, 18330.8)  | 1.9 (1.4, 2.4)             | 10577.9 (7579.9, 13031.9)  | 1.4 (1.0, 1.7)        |  |  |
|                 | Hepatoblastoma | 2649.0 (2302.6, 3055.9)     | 0.3 (0.3, 0.4)             | 1842.2 (1604.9, 2128.8)    | 0.2 (0.2, 0.3)        |  |  |
|                 | Kidney cancer  | 3818.7 (3173.4, 4504.5)     | 0.5 (0.4, 0.6)             | 1546.2 (1317.9, 1804.8)    | 0.2 (0.2, 0.2)        |  |  |
|                 | MNBAC          | 4199.8 (3424.2, 5278.8)     | 0.5 (0.4, 0.7)             | 2127.4 (1794.5, 2683.9)    | 0.3 (0.2, 0.4)        |  |  |
|                 | Neuroblastoma  | 1118.7 (777.4, 1554.6)      | 0.1 (0.1, 0.2)             | 467.8 (381.6, 545.2)       | 0.1 (0.0, 0.1)        |  |  |
|                 | Retinoblastoma | 907.5 (520.1, 1337.6)       | 0.1 (0.1, 0.2)             | 651.6 (385.7, 861.4)       | 0.1 (0.1, 0.1)        |  |  |
|                 | STES           | 3041.6 (2346.4, 3949.7)     | 0.4 (0.3, 0.5)             | 1314.6 (1000.3, 1690.5)    | 0.2 (0.1, 0.2)        |  |  |
|                 | Brain cancer   | 9797.7 (7820.2, 11552.7)    | 2.6 (2.1, 3.1)             | 6350.0 (5009.3, 7541.9)    | 1.7 (1.4, 2.0)        |  |  |
|                 | Hepatoblastoma | 996.9 (859.2, 1166.9)       | 0.3 (0.2, 0.3)             | 660.3 (567.9, 774.4)       | 0.2 (0.2, 0.2)        |  |  |
| High-middle SDI | Kidney cancer  | 3074.2 (2598.1, 3618.3)     | 0.8 (0.7, 1.0)             | 938.3 (798.6, 1112.1)      | 0.3 (0.2, 0.3)        |  |  |
|                 | MNBAC          | 3027.5 (2748.9, 3498.6)     | 0.8 (0.7, 0.9)             | 1225.2 (1116.3, 1423.2)    | 0.3 (0.3, 0.4)        |  |  |
|                 | Neuroblastoma  | 844.9 (639.9, 1090.9)       | 0.1 (0.1, 0.3)             | 306.7 (261.6, 357.5)       | 0.1 (0.1, 0.1)        |  |  |
|                 | Retinoblastoma | 605.5 (405.7, 899.1)        | 0.2 (0.1, 0.2)             | 213.6 (119.6, 326.9)       | 0.1 (0.0, 0.1)        |  |  |
|                 | STES           | 1571.2 (1311.6, 1941.3)     | 0.4 (0.4, 0.5)             | 574.9 (493.3, 720.3)       | 0.2 (0.1, 0.2)        |  |  |
|                 | Brain cancer   | 6470.5 (6254.7, 6692.9)     | 2.6 (2.5, 2.7)             | 2513.2 (2401.7, 2610.6)    | 1.0 (1.0, 1.0)        |  |  |

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Table 1: Contd...

| Location             | Diseases       | 1990                        |                            |                        |
|----------------------|----------------|-----------------------------|----------------------------|------------------------|
|                      |                | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95%UI) |
| Andean Latin America | Hepatoblastoma | 330.1 (312.2, 349.4)        | 0.1 (0.1, 0.1)             | 144.4 (133.1, 156.2)   |
|                      | Kidney cancer  | 1362.8 (1310.1, 1413.0)     | 0.5 (0.5, 0.6)             | 277.7 (267.9, 287.8)   |
|                      | MNBAC          | 2079.4 (1971.0, 2194.6)     | 0.8 (0.8, 0.9)             | 697.3 (663.1, 730.3)   |
|                      | Neuroblastoma  | 1205.3 (1015.7, 1416.4)     | 0.5 (0.4, 0.6)             | 373.4 (353.8, 391.7)   |
|                      | Retinoblastoma | 818.0 (684.0, 961.6)        | 0.3 (0.3, 0.4)             | 40.0 (32.8, 47.4)      |
|                      | STES           | 1684.6 (1566.4, 1821.6)     | 0.7 (0.6, 0.7)             | 468.8 (450.4, 489.8)   |
|                      | Brain cancer   | 310.3 (231.5, 470.5)        | 1.6 (1.2, 2.5)             | 240.0 (179.5, 352.9)   |
|                      | Hepatoblastoma | 39.5 (28.4, 51.9)           | 0.2 (0.1, 0.3)             | 27.7 (20.0, 36.5)      |
|                      | Kidney cancer  | 103.1 (85.1, 122.8)         | 0.5 (0.4, 0.6)             | 54.2 (44.5, 63.4)      |
|                      | MNBAC          | 198.8 (148.8, 254.1)        | 1.0 (0.8, 1.3)             | 104.1 (81.4, 131.0)    |
|                      | Neuroblastoma  | 42.6 (26.2, 64.1)           | 0.5 (0.4, 0.6)             | 18.3 (13.0, 24.0)      |
|                      | Retinoblastoma | 55.4 (30.8, 98.0)           | 0.3 (0.2, 0.5)             | 48.1 (28.4, 82.3)      |
|                      | STES           | 134.3 (87.6, 183.3)         | 0.7 (0.5, 1.0)             | 61.9 (42.2, 83.3)      |
|                      | Brain cancer   | 151.6 (138.2, 167.6)        | 2.4 (2.2, 2.7)             | 68.4 (64.3, 72.2)      |
|                      | Hepatoblastoma | 6.2 (5.5, 6.9)              | 0.1 (0.1, 0.1)             | 2.1 (1.8, 2.3)         |
|                      | Kidney cancer  | 27.9 (24.7, 32.0)           | 0.4 (0.4, 0.5)             | 6.5 (6.0, 7.1)         |
|                      | Australasia    | MNBAC                       | 65.6 (59.4, 72.0)          | 1.0 (0.9, 1.1)         |
| Neuroblastoma        |                | 29.9 (24.7, 36.7)           | 0.3 (0.2, 0.4)             | 8.4 (7.3, 9.6)         |
| Retinoblastoma       |                | 8.2 (6.0, 10.4)             | 0.1 (0.1, 0.2)             | 0.2 (0.2, 0.3)         |
| STES                 |                | 42.8 (37.1, 49.7)           | 0.7 (0.6, 0.8)             | 11.2 (9.9, 12.7)       |
| Brain cancer         |                | 220.0 (172.9, 369.6)        | 1.5 (1.1, 2.4)             | 153.6 (115.5, 279.1)   |
| Hepatoblastoma       |                | 11.5 (7.4, 16.7)            | 0.1 (0.0, 0.1)             | 8.0 (5.1, 11.7)        |
| Kidney cancer        |                | 84.5 (60.7, 109.5)          | 0.6 (0.4, 0.7)             | 41.8 (28.5, 56.3)      |
| MNBAC                |                | 116.9 (97.0, 150.9)         | 0.8 (0.6, 1.0)             | 56.3 (46.3, 73.2)      |
| Neuroblastoma        |                | 37.9 (25.2, 58.4)           | 0.0 (0.0, 0.1)             | 15.1 (11.3, 21.2)      |
| Retinoblastoma       |                | 13.8 (8.7, 20.8)            | 0.1 (0.1, 0.1)             | 5.5 (3.5, 7.9)         |
| Caribbean            | STES           | 157.1 (110.0, 219.5)        | 1.0 (0.7, 1.5)             | 77.4 (52.6, 110.1)     |
|                      | Brain cancer   | 555.4 (465.5, 696.8)        | 1.8 (1.5, 2.2)             | 427.0 (360.9, 538.7)   |
|                      | Hepatoblastoma | 114.7 (93.9, 143.7)         | 0.4 (0.3, 0.5)             | 79.1 (64.8, 99.4)      |
|                      | Kidney cancer  | 168.3 (137.5, 207.2)        | 0.5 (0.4, 0.7)             | 71.4 (58.5, 88.2)      |
|                      | MNBAC          | 182.4 (145.7, 225.5)        | 0.6 (0.5, 0.7)             | 80.4 (65.0, 96.4)      |
|                      | Neuroblastoma  | 13.5 (9.1, 20.3)            | 0.3 (0.2, 0.3)             | 5.7 (4.3, 7.5)         |
|                      | Retinoblastoma | 31.4 (12.9, 66.3)           | 0.1 (0.0, 0.2)             | 16.0 (7.4, 30.0)       |
|                      | STES           | 69.4 (52.1, 96.6)           | 0.2 (0.2, 0.3)             | 27.9 (21.2, 38.1)      |
|                      | Brain cancer   | 992.6 (924.7, 1085.8)       | 2.5 (2.4, 2.8)             | 672.8 (627.7, 730.0)   |
|                      | Hepatoblastoma | 43.1 (37.2, 50.1)           | 0.1 (0.1, 0.1)             | 28.1 (24.2, 32.7)      |
| Central Asia         | Kidney cancer  | 172.3 (152.8, 189.5)        | 0.4 (0.4, 0.5)             | 60.5 (54.2, 65.6)      |

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Table 1: Contd...

| Location                 | Diseases                  | 1990                        |                            |                         |
|--------------------------|---------------------------|-----------------------------|----------------------------|-------------------------|
|                          |                           | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death rate, n (95%UI)   |
| High-income Asia Pacific | Retinoblastoma            | 971.6 (563.9, 1356.9)       | 0.9 (0.5, 1.2)             | 942.5 (554.0, 1327.7)   |
|                          | STES                      | 1888.6 (1265.8, 3012.6)     | 1.7 (1.1, 2.7)             | 1033.2 (718.9, 1612.4)  |
|                          | Brain cancer              | 1041.1 (898.0, 1174.5)      | 2.1 (1.8, 2.3)             | 369.7 (303.7, 412.9)    |
|                          | Hepatoblastoma            | 100.1 (83.6, 118.9)         | 0.2 (0.2, 0.2)             | 47.1 (36.3, 59.1)       |
|                          | Kidney cancer             | 124.0 (111.4, 136.4)        | 0.2 (0.2, 0.3)             | 34.7 (31.9, 37.9)       |
|                          | MNBAC                     | 485.3 (428.4, 549.1)        | 1.0 (0.9, 1.1)             | 168.0 (141.6, 195.5)    |
|                          | Neuroblastoma             | 255.4 (209.8, 304.6)        | 0.6 (0.5, 0.7)             | 81.2 (73.2, 92.3)       |
|                          | Retinoblastoma            | 138.4 (107.3, 176.1)        | 0.3 (0.2, 0.4)             | 8.4 (6.0, 11.6)         |
|                          | STES                      | 321.4 (280.6, 377.8)        | 0.6 (0.6, 0.8)             | 91.9 (79.5, 109.7)      |
|                          | Brain cancer              | 2601.5 (2509.1, 2692.6)     | 3.2 (3.1, 3.3)             | 799.0 (788.4, 809.6)    |
|                          | Hepatoblastoma            | 110.0 (107.1, 113.0)        | 0.1 (0.1, 0.1)             | 37.6 (36.7, 38.5)       |
|                          | High-income North America | Kidney cancer               | 607.7 (587.9, 628.1)       | 0.7 (0.7, 0.8)          |
| MNBAC                    |                           | 634.9 (605.1, 662.3)        | 0.8 (0.7, 0.8)             | 191.4 (187.0, 196.2)    |
| Neuroblastoma            |                           | 488.4 (411.1, 577.2)        | 0.2 (0.2, 0.3)             | 147.4 (136.3, 157.4)    |
| Retinoblastoma           |                           | 445.2 (370.1, 529.0)        | 0.5 (0.5, 0.6)             | 14.0 (12.5, 15.5)       |
| STES                     |                           | 703.0 (654.0, 757.3)        | 0.9 (0.8, 0.9)             | 184.3 (180.6, 188.3)    |
| Brain cancer             |                           | 3557.4 (2455.6, 5235.1)     | 2.0 (1.4, 3.0)             | 2285.1 (1589.2, 3426.1) |
| Hepatoblastoma           |                           | 494.5 (363.2, 626.8)        | 0.3 (0.2, 0.4)             | 345.1 (254.0, 439.8)    |
| Kidney cancer            |                           | 1215.4 (759.1, 1699.9)      | 0.7 (0.4, 1.0)             | 309.5 (208.5, 416.8)    |
| MNBAC                    |                           | 1235.6 (786.7, 1551.9)      | 0.7 (0.4, 0.9)             | 616.6 (405.6, 761.7)    |
| Neuroblastoma            |                           | 250.9 (154.0, 402.8)        | 0.0 (0.0, 0.0)             | 101.4 (71.7, 145.0)     |
| Retinoblastoma           |                           | 114.4 (67.2, 180.1)         | 0.1 (0.0, 0.1)             | 77.8 (47.3, 122.7)      |
| Oceania                  |                           | STES                        | 1141.7 (834.7, 1682.4)     | 0.6 (0.5, 1.0)          |
|                          | Brain cancer              | 11.2 (5.6, 17.1)            | 0.3 (0.2, 0.5)             | 8.6 (4.3, 13.4)         |
|                          | Hepatoblastoma            | 2.9 (1.8, 4.9)              | 0.1 (0.1, 0.1)             | 2.1 (1.3, 3.6)          |
|                          | Kidney cancer             | 3.5 (2.4, 5.5)              | 0.1 (0.1, 0.2)             | 1.4 (1.0, 2.2)          |
|                          | MNBAC                     | 9.0 (4.3, 16.6)             | 0.3 (0.1, 0.5)             | 5.8 (2.7, 10.9)         |
|                          | Neuroblastoma             | 0.4 (0.2, 0.8)              | 0.1 (0.1, 0.2)             | 0.2 (0.1, 0.4)          |
|                          | Retinoblastoma            | 1.4 (0.5, 3.9)              | 0.0 (0.0, 0.1)             | 1.3 (0.4, 3.7)          |
|                          | STES                      | 3.0 (1.8, 4.9)              | 0.1 (0.1, 0.1)             | 1.4 (0.8, 2.3)          |
|                          | Brain cancer              | 4726.4 (2887.9, 7266.5)     | 0.9 (0.5, 1.3)             | 3910.3 (2418.3, 5982.5) |
|                          | Hepatoblastoma            | 1177.7 (706.7, 1587.7)      | 0.2 (0.1, 0.3)             | 833.9 (496.5, 1122.2)   |
|                          | Kidney cancer             | 816.7 (504.1, 1116.0)       | 0.2 (0.1, 0.2)             | 484.1 (296.5, 664.8)    |
|                          | South Asia                | MNBAC                       | 3212.0 (2108.3, 4123.6)    | 0.6 (0.4, 0.8)          |
| Neuroblastoma            |                           | 767.5 (442.2, 1216.3)       | 0.1 (0.1, 0.2)             | 358.1 (242.6, 494.0)    |
| Retinoblastoma           |                           | 954.0 (453.0, 1416.6)       | 0.2 (0.1, 0.3)             | 935.5 (441.3, 1395.8)   |
| STES                     |                           | 3114.9 (2024.1, 4114.6)     | 0.6 (0.4, 0.8)             | 1580.7 (1058.2, 2030.3) |
| Brain cancer             |                           |                             |                            | 0.3 (0.2, 0.4)          |

Contd...



**Table 1: Contd...**

| Location       | Diseases       | 1990                        |                            |                         |                        | 1990-2021                   |                            |                         |                        |                               |
|----------------|----------------|-----------------------------|----------------------------|-------------------------|------------------------|-----------------------------|----------------------------|-------------------------|------------------------|-------------------------------|
|                |                | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95% UI) | Death rate, n (95% UI) | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95% UI) | Death rate, n (95% UI) | EAPC of incidence, % (95% CI) |
| Global         | Kidney cancer  | 577.5 (427.0, 733.9)        | 0.5 (0.4, 0.7)             | 360.7 (261.5, 469.3)    | 0.3 (0.2, 0.4)         | 19922.5 (16061.8, 24531.8)  | 0.8 (0.6, 0.9)             | 1922.5 (1606.1, 2453.1) | -0.3 (-0.4, -0.2)      | -1.3 (-1.4, -1.2)             |
|                | MNBAC          | 747.3 (534.5, 975.5)        | 0.7 (0.5, 0.9)             | 392.3 (290.8, 500.5)    | 0.4 (0.3, 0.5)         | 2416.2 (1922.5, 3019.0)     | 0.1 (0.1, 0.1)             | 241.6 (192.3, 301.9)    | -2.1 (-2.3, -2.0)      | -2.6 (-2.8, -2.5)             |
|                | Neuroblastoma  | 174.4 (49.2, 326.7)         | 0.5 (0.4, 0.6)             | 77.6 (21.9, 121.9)      | 0.1 (0.0, 0.1)         | 3243.2 (2427.1, 4090.5)     | 0.1 (0.1, 0.2)             | 324.3 (242.7, 409.0)    | -0.3 (-0.4, -0.1)      | -1.0 (-1.2, -0.9)             |
|                | Retinoblastoma | 386.5 (184.0, 556.9)        | 0.4 (0.2, 0.5)             | 376.5 (179.4, 544.0)    | 0.4 (0.2, 0.5)         | 8573.6 (7257.2, 10618.1)    | 0.3 (0.3, 0.4)             | 857.4 (725.7, 1061.8)   | 0.5 (0.5, 0.6)         | 0.0 (-0.1, 0.1)               |
|                | STES           | 1042.2 (687.7, 1756.6)      | 1.0 (0.6, 1.6)             | 545.9 (365.1, 910.8)    | 0.5 (0.3, 0.8)         | 2094.7 (1546.6, 2658.7)     | 0.1 (0.1, 0.1)             | 209.5 (154.7, 265.9)    | 0.7 (0.5, 0.8)         | 0.4 (0.3, 0.6)                |
| Low-SDI        |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
| Low-middle SDI |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
| Middle SDI     |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |
|                |                |                             |                            |                         |                        |                             |                            |                         |                        |                               |

Contd...

**Table 1: Contd...**

| Location             | 2021                               |                                   |                               | 1990–2021                    |                               |                           |
|----------------------|------------------------------------|-----------------------------------|-------------------------------|------------------------------|-------------------------------|---------------------------|
|                      | Incidence cases, <i>n</i> (95% UI) | Incidence rate, <i>n</i> (95% UI) | Death cases, <i>n</i> (95%UI) | Death rate, <i>n</i> (95%UI) | EAPC of incidence, % (95% CI) | EAPC of death, % (95% CI) |
| High-middle SDI      | 7848.4 (6323.1, 9922.9)            | 2.6 (2.1, 3.3)                    | 2820.8 (2336.6, 3512.8)       | 0.9 (0.8, 1.2)               | 0.0 (-0.1, 0.2)               | -2.1 (-2.2, -1.9)         |
|                      | 359.6 (290.0, 448.1)               | 0.1 (0.1, 0.1)                    | 131.3 (108.8, 158.6)          | 0.0 (0.0, 0.1)               | -2.5 (-2.9, -2.1)             | -4.8 (-5.2, -4.5)         |
|                      | 1793.2 (1547.9, 2070.3)            | 0.6 (0.5, 0.7)                    | 278.2 (242.4, 314.3)          | 0.1 (0.1, 0.1)               | -0.5 (-0.7, -0.2)             | -2.9 (-3.0, -2.7)         |
|                      | 2183.8 (1684.3, 2547.4)            | 0.7 (0.6, 0.8)                    | 662.3 (510.6, 766.4)          | 0.2 (0.2, 0.3)               | -0.4 (-0.6, -0.2)             | -1.5 (-1.8, -1.2)         |
|                      | 780.8 (580.6, 984.8)               | 0.3 (0.2, 0.3)                    | 237.8 (185.8, 284.8)          | 0.1 (0.1, 0.1)               | 1.0 (0.7, 1.3)                | 0.3 (0.1, 0.6)            |
|                      | 934.7 (487.8, 1387.5)              | 0.3 (0.2, 0.5)                    | 59.3 (29.8, 85.6)             | 0.0 (0.0, 0.0)               | 4.0 (3.3, 4.6)                | -2.4 (-2.7, -2.1)         |
|                      | 836.8 (719.0, 987.3)               | 0.3 (0.2, 0.3)                    | 224.7 (193.5, 262.7)          | 0.1 (0.1, 0.1)               | -1.4 (-1.6, -1.3)             | -2.5 (-2.6, -2.4)         |
|                      | 6139.9 (5783.5, 6526.6)            | 2.6 (2.5, 2.8)                    | 1622.6 (1531.1, 1724.4)       | 0.7 (0.7, 0.7)               | 0.3 (0.2, 0.4)                | -1.1 (-1.1, -1.0)         |
|                      | 345.0 (314.7, 374.0)               | 0.1 (0.1, 0.2)                    | 85.2 (78.1, 91.6)             | 0.0 (0.0, 0.0)               | 0.7 (0.4, 0.9)                | -1.2 (-1.3, -1.2)         |
|                      | 1228.6 (1145.1, 1318.7)            | 0.5 (0.5, 0.6)                    | 146.9 (136.9, 155.8)          | 0.1 (0.1, 0.1)               | 0.2 (-0.0, 0.3)               | -1.6 (-1.7, -1.5)         |
|                      | 1686.6 (1567.1, 1808.7)            | 0.7 (0.7, 0.8)                    | 457.4 (430.6, 484.1)          | 0.2 (0.2, 0.2)               | -0.6 (-0.7, -0.4)             | -1.3 (-1.4, -1.1)         |
|                      | 871.6 (726.8, 1020.6)              | 0.4 (0.3, 0.4)                    | 243.1 (215.2, 270.2)          | 0.1 (0.1, 0.1)               | -0.8 (-1.0, -0.6)             | -1.1 (-1.3, -0.9)         |
|                      | 648.7 (488.8, 828.9)               | 0.3 (0.2, 0.4)                    | 12.4 (9.9, 15.0)              | 0.0 (0.0, 0.0)               | 0.4 (0.0, 0.8)                | -2.7 (-3.2, -2.1)         |
|                      | 1427.0 (1274.1, 1565.6)            | 0.6 (0.5, 0.7)                    | 328.5 (302.4, 349.3)          | 0.1 (0.1, 0.2)               | -0.4 (-0.6, -0.1)             | -1.0 (-1.2, -0.7)         |
| 499.0 (383.4, 667.4) | 2.1 (1.6, 2.8)                     | 288.1 (215.6, 371.7)              | 1.2 (0.9, 1.6)                | 1.1 (0.8, 1.3)               | 0.1 (-0.2, 0.4)               |                           |
| Andean Latin America | 15.5 (10.4, 22.4)                  | 0.1 (0.0, 0.1)                    | 9.9 (6.9, 14.4)               | 0.0 (0.0, 0.1)               | -3.7 (-4.1, -3.4)             | -4.1 (-4.4, -3.8)         |
|                      | 99.1 (76.0, 127.9)                 | 0.4 (0.3, 0.5)                    | 30.9 (23.9, 39.6)             | 0.1 (0.1, 0.2)               | -0.5 (-0.8, -0.3)             | -2.3 (-2.5, -2.1)         |
|                      | 202.2 (150.8, 266.3)               | 0.9 (0.6, 1.1)                    | 79.3 (59.5, 103.9)            | 0.3 (0.3, 0.4)               | -0.5 (-0.6, -0.4)             | -1.4 (-1.5, -1.3)         |
|                      | 41.8 (27.5, 58.4)                  | 0.2 (0.1, 0.2)                    | 15.4 (11.0, 20.4)             | 0.1 (0.0, 0.1)               | -0.3 (-0.6, -0.1)             | -0.9 (-1.0, -0.7)         |
|                      | 111.8 (62.1, 187.6)                | 0.5 (0.3, 0.8)                    | 26.1 (16.1, 42.6)             | 0.1 (0.1, 0.2)               | 2.4 (2.1, 2.7)                | -2.3 (-2.5, -2.0)         |
|                      | 70.0 (50.4, 96.0)                  | 0.3 (0.2, 0.4)                    | 23.8 (17.5, 32.9)             | 0.1 (0.1, 0.1)               | -2.3 (-2.6, -1.9)             | -3.3 (-3.6, -3.0)         |
|                      | 158.1 (134.4, 185.7)               | 2.1 (1.8, 2.5)                    | 52.1 (47.0, 58.1)             | 0.7 (0.6, 0.8)               | -0.3 (-0.4, -0.2)             | -1.4 (-1.5, -1.3)         |
|                      | 13.3 (10.4, 16.6)                  | 0.2 (0.1, 0.2)                    | 3.1 (2.5, 3.8)                | 0.0 (0.0, 0.1)               | 2.1 (1.8, 2.4)                | 1.0 (0.8, 1.3)            |
|                      | 28.9 (23.3, 35.4)                  | 0.4 (0.3, 0.5)                    | 3.6 (3.1, 4.3)                | 0.0 (0.0, 0.1)               | 0.1 (-0.5, 0.7)               | -2.0 (-2.4, -1.6)         |
|                      | 51.9 (44.0, 61.0)                  | 0.7 (0.6, 0.8)                    | 13.5 (11.4, 15.9)             | 0.2 (0.2, 0.2)               | -1.4 (-1.9, -0.9)             | -2.1 (-2.6, -1.6)         |
|                      | 30.3 (21.8, 41.1)                  | 0.4 (0.3, 0.5)                    | 8.3 (6.2, 10.9)               | 0.1 (0.1, 0.1)               | -0.5 (-0.8, -0.2)             | -0.6 (-0.8, -0.3)         |
|                      | 2.9 (1.5, 5.1)                     | 0.0 (0.0, 0.1)                    | 0.0 (0.0, 0.1)                | 0.0 (0.0, 0.0)               | -1.4 (-3.2, 0.4)              | -4.5 (-6.2, -2.8)         |
|                      | 52.6 (40.6, 66.8)                  | 0.7 (0.5, 0.9)                    | 11.4 (8.8, 14.5)              | 0.2 (0.1, 0.2)               | -0.5 (-1.3, 0.4)              | -1.1 (-1.9, -0.2)         |
|                      | 240.0 (186.1, 340.9)               | 1.6 (1.2, 2.2)                    | 161.4 (119.0, 245.1)          | 1.1 (0.8, 1.6)               | 0.5 (0.4, 0.6)                | 0.4 (0.3, 0.4)            |
| 7.1 (4.7, 11.0)      | 0.0 (0.0, 0.1)                     | 4.8 (3.1, 7.5)                    | 0.0 (0.0, 0.0)                | -1.5 (-1.8, -1.2)            | -1.6 (-1.9, -1.3)             |                           |
| 74.9 (55.5, 105.6)   | 0.5 (0.4, 0.7)                     | 31.1 (21.3, 47.4)                 | 0.2 (0.1, 0.3)                | -0.2 (-0.3, -0.0)            | -0.7 (-0.9, -0.5)             |                           |
| 107.5 (81.2, 145.5)  | 0.7 (0.5, 1.0)                     | 47.6 (35.6, 65.3)                 | 0.3 (0.2, 0.4)                | -0.0 (-0.2, 0.1)             | -0.1 (-0.2, 0.0)              |                           |
| 56.3 (36.3, 83.8)    | 0.4 (0.2, 0.5)                     | 21.8 (15.3, 31.1)                 | 0.1 (0.1, 0.2)                | 1.3 (0.8, 1.8)               | 1.2 (0.8, 1.6)                |                           |
| 4.4 (2.4, 7.4)       | 0.0 (0.0, 0.0)                     | 1.8 (0.9, 3.3)                    | 0.0 (0.0, 0.0)                | -2.4 (-3.4, -1.3)            | -2.5 (-3.2, -1.8)             |                           |
| 141.5 (90.7, 210.7)  | 0.9 (0.6, 1.4)                     | 63.6 (38.8, 94.7)                 | 0.4 (0.3, 0.6)                | -0.1 (-0.3, 0.0)             | -0.4 (-0.6, -0.2)             |                           |
| 822.0 (688.2, 978.4) | 2.4 (2.0, 2.8)                     | 559.4 (469.1, 668.3)              | 1.6 (1.4, 1.9)                | 1.3 (1.2, 1.5)               | 0.9 (0.7, 1.0)                |                           |
| Central Asia         |                                    |                                   |                               |                              |                               |                           |

Contd...

Table 1: Contd...

| Location              | 2021                        |                            |                         | 1990–2021             |                               |                           |
|-----------------------|-----------------------------|----------------------------|-------------------------|-----------------------|-------------------------------|---------------------------|
|                       | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95%UI)  | Death rate, n (95%UI) | EAPC of incidence, % (95% CI) | EAPC of death, % (95% CI) |
| Central Europe        | 42.4 (31.0, 56.8)           | 0.1 (0.1, 0.2)             | 28.0 (20.5, 37.3)       | 0.1 (0.1, 0.1)        | -3.0 (-3.5,-2.6)              | -3.2 (-3.7,-2.8)          |
|                       | 154.4 (125.8, 186.7)        | 0.4 (0.4, 0.5)             | 53.8 (43.6, 65.3)       | 0.2 (0.1, 0.2)        | 0.1 (-0.3, 0.5)               | -0.6 (-0.9,-0.4)          |
|                       | 218.0 (178.8, 264.5)        | 0.6 (0.5, 0.8)             | 83.6 (69.4, 99.3)       | 0.2 (0.2, 0.3)        | 0.5 (0.3, 0.8)                | 0.0 (-0.2, 0.3)           |
|                       | 22.5 (14.4, 32.7)           | 0.1 (0.0, 0.1)             | 8.4 (6.1, 11.7)         | 0.0 (0.0, 0.0)        | 2.8 (2.2, 3.4)                | 2.3 (1.8, 2.8)            |
|                       | 54.7 (28.0, 97.1)           | 0.2 (0.1, 0.3)             | 14.4 (7.8, 25.5)        | 0.0 (0.0, 0.1)        | 2.9 (2.1, 3.6)                | -0.1 (-0.5, 0.3)          |
|                       | 84.4 (64.6, 107.3)          | 0.2 (0.2, 0.3)             | 28.9 (22.3, 36.5)       | 0.1 (0.1, 0.1)        | 1.0 (0.5, 1.5)                | 0.4 (-0.1, 0.8)           |
|                       | 459.4 (404.5, 510.8)        | 2.0 (1.7, 2.2)             | 212.2 (188.9, 237.5)    | 0.9 (0.8, 1.0)        | -0.5 (-0.8,-0.3)              | -1.8 (-2.0,-1.6)          |
|                       | 8.9 (7.2, 11.0)             | 0.0 (0.0, 0.0)             | 3.5 (2.8, 4.3)          | 0.0 (0.0, 0.0)        | -3.0 (-3.6,-2.5)              | -4.9 (-5.3,-4.4)          |
|                       | 85.8 (75.5, 96.6)           | 0.4 (0.3, 0.4)             | 17.8 (15.8, 19.9)       | 0.1 (0.1, 0.1)        | 0.0 (-0.3, 0.3)               | -1.8 (-2.0,-1.6)          |
|                       | 105.2 (93.5, 119.0)         | 0.4 (0.4, 0.5)             | 34.2 (30.5, 38.5)       | 0.1 (0.1, 0.2)        | -2.7 (-3.1,-2.4)              | -3.6 (-3.9,-3.2)          |
|                       | 50.0 (38.3, 63.3)           | 0.2 (0.2, 0.3)             | 15.5 (12.7, 19.0)       | 0.1 (0.1, 0.1)        | -0.4 (-1.0, 0.1)              | -0.9 (-1.4,-0.4)          |
|                       | 17.6 (11.3, 27.2)           | 0.1 (0.0, 0.1)             | 1.2 (0.8, 1.9)          | 0.0 (0.0, 0.0)        | 0.2 (-0.5, 1.0)               | -4.7 (-5.3,-4.1)          |
|                       | 117.6 (101.3, 138.0)        | 0.5 (0.4, 0.6)             | 30.8 (26.7, 35.4)       | 0.1 (0.1, 0.2)        | 0.2 (0.0, 0.5)                | -0.7 (-0.9,-0.4)          |
|                       | 1056.7 (900.1, 1252.0)      | 1.2 (1.1, 1.5)             | 617.8 (528.8, 726.2)    | 0.7 (0.6, 0.9)        | 0.3 (0.0, 0.6)                | -0.4 (-0.6,-0.2)          |
| Central Latin America | 86.2 (66.4, 112.9)          | 0.1 (0.1, 0.1)             | 55.0 (42.5, 71.1)       | 0.1 (0.0, 0.1)        | -2.0 (-2.2,-1.8)              | -2.3 (-2.4,-2.1)          |
|                       | 318.5 (260.1, 387.5)        | 0.4 (0.3, 0.5)             | 98.9 (81.4, 120.7)      | 0.1 (0.1, 0.1)        | -0.3 (-0.5,-0.1)              | -1.7 (-1.9,-1.5)          |
|                       | 699.9 (616.0, 787.8)        | 0.8 (0.7, 0.9)             | 289.6 (256.8, 323.8)    | 0.3 (0.3, 0.4)        | 1.7 (1.4, 2.0)                | 1.2 (0.8, 1.5)            |
|                       | 175.1 (124.2, 241.5)        | 0.2 (0.1, 0.3)             | 63.1 (49.5, 80.6)       | 0.1 (0.1, 0.1)        | -0.2 (-0.9, 0.4)              | -0.6 (-1.2, 0.0)          |
|                       | 161.0 (104.7, 242.1)        | 0.2 (0.1, 0.3)             | 37.8 (25.9, 53.8)       | 0.0 (0.0, 0.1)        | 1.1 (0.4, 1.7)                | -2.5 (-2.9,-2.1)          |
|                       | 377.8 (323.0, 440.4)        | 0.4 (0.4, 0.5)             | 126.1 (109.3, 146.5)    | 0.1 (0.1, 0.2)        | -0.3 (-0.5,-0.1)              | -1.0 (-1.2,-0.9)          |
|                       | 228.8 (155.4, 315.1)        | 0.3 (0.2, 0.4)             | 185.9 (126.7, 256.3)    | 0.3 (0.2, 0.3)        | 0.2 (0.0, 0.4)                | 0.1 (-0.1, 0.2)           |
|                       | 96.5 (43.1, 177.1)          | 0.1 (0.1, 0.2)             | 67.9 (30.5, 128.1)      | 0.1 (0.0, 0.2)        | -4.1 (-4.3,-3.8)              | -4.1 (-4.3,-3.8)          |
|                       | 85.1 (56.3, 124.1)          | 0.1 (0.1, 0.2)             | 43.1 (28.5, 62.1)       | 0.1 (0.0, 0.1)        | -0.7 (-0.9,-0.5)              | -1.4 (-1.6,-1.2)          |
|                       | 238.8 (134.6, 389.7)        | 0.3 (0.2, 0.5)             | 140.3 (78.6, 231.4)     | 0.2 (0.1, 0.3)        | -0.2 (-0.4,-0.0)              | -0.6 (-0.7,-0.5)          |
|                       | 27.5 (16.1, 43.4)           | 0.0 (0.0, 0.1)             | 12.3 (8.5, 17.6)        | 0.0 (0.0, 0.0)        | -0.6 (-1.0,-0.2)              | -0.7 (-1.0,-0.3)          |
|                       | 71.6 (26.3, 146.7)          | 0.1 (0.0, 0.2)             | 65.9 (25.9, 126.1)      | 0.1 (0.0, 0.2)        | -1.2 (-1.4,-0.9)              | -1.4 (-1.7,-1.1)          |
|                       | 291.7 (185.4, 461.3)        | 0.4 (0.3, 0.6)             | 136.3 (86.9, 210.3)     | 0.2 (0.1, 0.3)        | -2.3 (-2.5,-2.1)              | -2.8 (-3.0,-2.5)          |
|                       | 10667.4 (8179.5, 14267.2)   | 3.1 (2.4, 4.1)             | 3711.7 (2803.3, 4960.4) | 1.1 (0.8, 1.4)        | -0.0 (-0.3, 0.2)              | -2.5 (-2.8,-2.3)          |
| East Asia             | 565.8 (401.6, 801.9)        | 0.2 (0.1, 0.2)             | 221.6 (160.3, 309.4)    | 0.1 (0.0, 0.1)        | -3.6 (-4.2,-3.1)              | -5.6 (-6.1,-5.2)          |
|                       | 1829.8 (1409.5, 2275.5)     | 0.5 (0.4, 0.7)             | 332.2 (250.5, 410.4)    | 0.1 (0.1, 0.1)        | -0.6 (-0.9,-0.3)              | -3.3 (-3.5,-3.1)          |
|                       | 2341.2 (1607.8, 2989.6)     | 0.7 (0.5, 0.9)             | 662.9 (455.9, 829.1)    | 0.2 (0.1, 0.2)        | 2.0 (1.4, 2.6)                | 0.3 (-0.4, 1.0)           |
|                       | 597.0 (408.2, 793.1)        | 0.2 (0.1, 0.2)             | 180.8 (130.5, 231.6)    | 0.1 (0.0, 0.1)        | 2.2 (1.7, 2.7)                | 1.2 (0.7, 1.7)            |
|                       | 1124.9 (444.1, 1762.9)      | 0.3 (0.1, 0.5)             | 74.0 (31.6, 110.6)      | 0.0 (0.0, 0.0)        | 5.9 (5.0, 6.8)                | -2.1 (-2.7,-1.6)          |
|                       | 311.0 (227.0, 474.4)        | 0.1 (0.1, 0.1)             | 84.4 (61.9, 126.2)      | 0.0 (0.0, 0.0)        | -4.2 (-4.4,-4.0)              | -5.7 (-5.9,-5.4)          |
|                       | 802.5 (752.9, 849.2)        | 1.7 (1.6, 1.8)             | 439.8 (417.1, 462.3)    | 1.0 (0.9, 1.0)        | -0.3 (-0.6,-0.1)              | -1.4 (-1.5,-1.2)          |
|                       | 57.7 (52.1, 63.1)           | 0.1 (0.1, 0.1)             | 25.9 (23.6, 28.3)       | 0.1 (0.1, 0.1)        | -1.1 (-1.9,-0.4)              | -2.6 (-3.1,-2.0)          |

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**Table 1: Contd...**

| Location                     | 2021                        |                            |                         | 1990–2021             |                               |                           |
|------------------------------|-----------------------------|----------------------------|-------------------------|-----------------------|-------------------------------|---------------------------|
|                              | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95%UI)  | Death rate, n (95%UI) | EAPC of incidence, % (95% CI) | EAPC of death, % (95% CI) |
|                              | 200.7 (184.3, 220.2)        | 0.4 (0.4, 0.5)             | 37.4 (34.6, 40.5)       | 0.1 (0.1, 0.1)        | -1.2 (-1.7, -0.6)             | -2.5 (-2.9, -2.1)         |
|                              | 278.7 (254.0, 302.2)        | 0.6 (0.6, 0.7)             | 92.5 (83.3, 100.6)      | 0.2 (0.2, 0.2)        | -3.6 (-4.0, -3.3)             | -4.1 (-4.6, -3.6)         |
|                              | 73.4 (53.4, 96.1)           | 0.2 (0.1, 0.2)             | 23.9 (18.7, 28.8)       | 0.1 (0.0, 0.1)        | -0.9 (-1.1, -0.6)             | -1.4 (-1.6, -1.2)         |
|                              | 51.9 (38.3, 71.8)           | 0.1 (0.1, 0.2)             | 4.8 (3.5, 6.4)          | 0.0 (0.0, 0.0)        | -0.3 (-0.8, 0.2)              | -3.8 (-4.1, -3.5)         |
|                              | 178.8 (153.0, 204.6)        | 0.4 (0.3, 0.4)             | 50.0 (43.2, 55.7)       | 0.1 (0.1, 0.1)        | -1.0 (-1.6, -0.5)             | -1.7 (-2.3, -1.1)         |
| Eastern sub-Saharan Africa   | 2123.4 (1482.7, 2930.0)     | 0.9 (0.7, 1.3)             | 1678.3 (1180.6, 2343.2) | 0.7 (0.5, 1.0)        | 0.5 (0.3, 0.7)                | 0.3 (0.2, 0.4)            |
|                              | 509.8 (296.9, 887.7)        | 0.2 (0.1, 0.4)             | 356.1 (208.9, 622.7)    | 0.2 (0.1, 0.3)        | -2.5 (-2.7, -2.4)             | -2.6 (-2.7, -2.5)         |
|                              | 1136.0 (604.3, 1694.1)      | 0.5 (0.3, 0.7)             | 552.8 (294.8, 830.2)    | 0.2 (0.1, 0.4)        | -0.3 (-0.5, -0.1)             | -1.1 (-1.3, -0.9)         |
|                              | 2282.7 (1546.7, 3664.2)     | 1.0 (0.7, 1.6)             | 1282.4 (878.0, 2055.5)  | 0.6 (0.4, 0.9)        | 0.2 (0.1, 0.3)                | -0.4 (-0.5, -0.3)         |
|                              | 565.8 (247.3, 1006.5)       | 0.2 (0.1, 0.4)             | 244.0 (121.5, 403.3)    | 0.1 (0.1, 0.2)        | 0.8 (0.4, 1.1)                | 0.6 (0.3, 0.9)            |
| High-income Asia Pacific     | 1265.0 (786.9, 1975.0)      | 0.6 (0.3, 0.9)             | 1058.1 (700.0, 1629.2)  | 0.5 (0.3, 0.7)        | -1.0 (-1.2, -0.8)             | -1.4 (-1.6, -1.1)         |
|                              | 1889.5 (1212.4, 2999.3)     | 0.8 (0.5, 1.3)             | 861.8 (571.5, 1428.2)   | 0.4 (0.3, 0.6)        | -2.3 (-2.4, -2.2)             | -2.9 (-3.0, -2.8)         |
|                              | 941.5 (793.6, 1070.1)       | 3.1 (2.6, 3.5)             | 190.1 (164.5, 207.6)    | 0.6 (0.5, 0.7)        | 1.6 (1.2, 2.0)                | -0.6 (-0.9, -0.2)         |
|                              | 37.6 (33.1, 44.5)           | 0.1 (0.1, 0.1)             | 8.5 (7.6, 9.9)          | 0.0 (0.0, 0.0)        | -1.8 (-2.6, -1.0)             | -4.3 (-4.8, -3.8)         |
|                              | 88.9 (77.7, 101.9)          | 0.3 (0.3, 0.3)             | 12.1 (11.1, 13.1)       | 0.0 (0.0, 0.0)        | 0.6 (0.3, 0.9)                | -1.9 (-2.0, -1.7)         |
|                              | 199.4 (178.7, 221.3)        | 0.6 (0.6, 0.7)             | 51.2 (46.4, 56.6)       | 0.2 (0.2, 0.2)        | -1.5 (-1.7, -1.3)             | -2.5 (-2.7, -2.2)         |
|                              | 150.1 (125.8, 173.5)        | 0.5 (0.4, 0.6)             | 41.7 (37.1, 46.7)       | 0.1 (0.1, 0.2)        | -0.6 (-1.0, -0.2)             | -1.0 (-1.3, -0.7)         |
|                              | 106.8 (74.0, 146.8)         | 0.3 (0.2, 0.5)             | 1.6 (1.2, 2.2)          | 0.0 (0.0, 0.0)        | 1.6 (0.7, 2.5)                | -3.0 (-3.7, -2.3)         |
|                              | 157.9 (137.1, 177.9)        | 0.5 (0.4, 0.6)             | 34.7 (30.9, 38.2)       | 0.1 (0.1, 0.1)        | -1.1 (-1.4, -0.8)             | -1.9 (-2.3, -1.6)         |
| High-income North America    | 2619.1 (2435.5, 2813.2)     | 2.9 (2.7, 3.1)             | 649.3 (612.8, 690.8)    | 0.7 (0.7, 0.8)        | -0.1 (-0.2, 0.0)              | -0.7 (-0.8, -0.6)         |
|                              | 179.2 (159.5, 200.1)        | 0.2 (0.2, 0.2)             | 44.7 (40.2, 49.7)       | 0.0 (0.0, 0.1)        | 1.7 (1.4, 1.9)                | 0.7 (0.5, 0.8)            |
|                              | 523.6 (486.7, 560.5)        | 0.6 (0.5, 0.6)             | 53.7 (50.7, 57.3)       | 0.1 (0.1, 0.1)        | -0.6 (-0.8, -0.5)             | -1.6 (-1.7, -1.5)         |
|                              | 765.1 (704.5, 818.5)        | 0.9 (0.8, 0.9)             | 211.6 (197.2, 225.5)    | 0.2 (0.2, 0.3)        | 0.2 (0.0, 0.3)                | -0.1 (-0.3, -0.0)         |
|                              | 354.0 (292.3, 417.2)        | 0.4 (0.3, 0.5)             | 99.3 (86.4, 112.8)      | 0.1 (0.1, 0.1)        | -1.1 (-1.3, -0.9)             | -1.3 (-1.5, -1.2)         |
|                              | 233.5 (159.4, 336.0)        | 0.3 (0.2, 0.4)             | 4.3 (3.3, 5.7)          | 0.0 (0.0, 0.0)        | -1.6 (-2.1, -1.1)             | -3.3 (-4.0, -2.7)         |
|                              | 657.5 (590.8, 719.1)        | 0.7 (0.7, 0.8)             | 155.2 (143.5, 165.5)    | 0.2 (0.2, 0.2)        | -0.4 (-0.5, -0.2)             | -0.7 (-0.9, -0.5)         |
| North Africa and Middle East | 5965.5 (4265.8, 7546.2)     | 2.5 (1.8, 3.2)             | 2623.7 (1878.7, 3267.0) | 1.1 (0.8, 1.4)        | 1.0 (0.8, 1.1)                | -0.3 (-0.4, -0.2)         |
|                              | 329.2 (258.3, 418.2)        | 0.1 (0.1, 0.2)             | 207.8 (163.1, 264.6)    | 0.1 (0.1, 0.1)        | -1.5 (-1.7, -1.2)             | -1.8 (-2.0, -1.6)         |
|                              | 1230.6 (972.2, 1531.2)      | 0.5 (0.4, 0.6)             | 213.6 (173.3, 262.0)    | 0.1 (0.1, 0.1)        | -0.2 (-0.4, 0.1)              | -1.5 (-1.7, -1.3)         |
|                              | 1802.0 (1461.1, 2258.5)     | 0.8 (0.6, 1.0)             | 708.2 (569.3, 890.6)    | 0.3 (0.2, 0.4)        | 0.3 (0.2, 0.4)                | -0.5 (-0.6, -0.4)         |
|                              | 365.5 (252.6, 511.6)        | 0.2 (0.1, 0.2)             | 119.3 (87.5, 158.5)     | 0.1 (0.0, 0.1)        | 0.9 (0.6, 1.2)                | 0.2 (-0.1, 0.4)           |
|                              | 230.5 (145.6, 358.8)        | 0.1 (0.1, 0.2)             | 43.6 (26.7, 70.0)       | 0.0 (0.0, 0.0)        | 2.0 (1.7, 2.3)                | -2.3 (-2.6, -1.9)         |
|                              | 596.9 (436.3, 911.6)        | 0.3 (0.2, 0.4)             | 207.6 (152.4, 308.8)    | 0.1 (0.1, 0.1)        | -2.7 (-2.9, -2.5)             | -3.4 (-3.6, -3.2)         |
| Oceania                      | 24.6 (13.3, 37.0)           | 0.4 (0.2, 0.6)             | 18.8 (10.3, 28.1)       | 0.3 (0.2, 0.4)        | 0.4 (0.4, 0.5)                | 0.5 (0.4, 0.5)            |
|                              | 4.0 (2.3, 7.1)              | 0.1 (0.0, 0.1)             | 2.8 (1.6, 4.9)          | 0.0 (0.0, 0.1)        | -1.2 (-1.5, -0.9)             | -1.2 (-1.5, -1.0)         |
|                              | 8.1 (5.3, 12.8)             | 0.1 (0.1, 0.2)             | 3.2 (2.1, 5.0)          | 0.0 (0.0, 0.1)        | 0.5 (0.3, 0.7)                | 0.5 (0.3, 0.8)            |

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Table 1: Contd...

| Location                    | 2021                        |                            |                         | 1990–2021             |                               |                           |
|-----------------------------|-----------------------------|----------------------------|-------------------------|-----------------------|-------------------------------|---------------------------|
|                             | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95%UI)  | Death rate, n (95%UI) | EAPC of incidence, % (95% CI) | EAPC of death, % (95% CI) |
|                             | 20.7 (7.5, 40.5)            | 0.3 (0.1, 0.6)             | 12.6 (4.3, 25.7)        | 0.2 (0.1, 0.4)        | 0.5 (0.3, 0.8)                | 0.4 (0.2, 0.6)            |
|                             | 0.7 (0.4, 1.3)              | 0.0 (0.0, 0.0)             | 0.4 (0.2, 0.6)          | 0.0 (0.0, 0.0)        | -1.2 (-1.7, -0.7)             | -1.2 (-1.7, -0.8)         |
|                             | 3.5 (1.0, 10.2)             | 0.1 (0.0, 0.2)             | 2.9 (0.8, 9.5)          | 0.0 (0.0, 0.1)        | 0.8 (0.5, 1.0)                | 0.5 (0.1, 0.8)            |
|                             | 4.8 (2.8, 8.4)              | 0.1 (0.0, 0.1)             | 2.1 (1.2, 3.7)          | 0.0 (0.0, 0.1)        | -0.6 (-0.8, -0.5)             | -0.7 (-0.9, -0.6)         |
| South Asia                  | 6144.9 (4858.3, 7983.4)     | 0.9 (0.7, 1.2)             | 4377.3 (3437.4, 5653.5) | 0.6 (0.5, 0.8)        | 0.1 (-0.0, 0.3)               | -0.4 (-0.5, -0.3)         |
|                             | 815.5 (632.7, 1044.5)       | 0.1 (0.1, 0.2)             | 559.5 (436.1, 716.6)    | 0.1 (0.1, 0.1)        | -1.7 (-1.8, -1.6)             | -1.8 (-1.9, -1.7)         |
|                             | 1043.8 (733.8, 1396.0)      | 0.2 (0.1, 0.2)             | 452.3 (311.9, 608.8)    | 0.1 (0.0, 0.1)        | 0.3 (0.2, 0.4)                | -0.7 (-0.8, -0.6)         |
|                             | 5197.2 (4149.7, 6529.2)     | 0.8 (0.6, 1.0)             | 2669.2 (2139.3, 3339.9) | 0.4 (0.3, 0.5)        | 0.9 (0.8, 0.9)                | 0.2 (0.1, 0.3)            |
|                             | 1496.1 (907.4, 2299.9)      | 0.2 (0.1, 0.3)             | 598.9 (412.9, 833.5)    | 0.1 (0.1, 0.1)        | 1.8 (1.4, 2.2)                | 1.2 (0.9, 1.6)            |
|                             | 1247.8 (670.9, 1931.4)      | 0.2 (0.1, 0.3)             | 674.3 (378.2, 1002.6)   | 0.1 (0.1, 0.1)        | 0.3 (-0.1, 0.8)               | -1.7 (-1.9, -1.5)         |
|                             | 1968.1 (1374.8, 3040.8)     | 0.3 (0.2, 0.4)             | 815.6 (586.2, 1234.2)   | 0.1 (0.1, 0.2)        | -2.2 (-2.3, -2.1)             | -2.9 (-3.0, -2.8)         |
| Southeast Asia              | 2303.5 (1673.1, 2819.1)     | 1.0 (0.7, 1.2)             | 1451.1 (1042.4, 1795.8) | 0.6 (0.5, 0.8)        | 0.4 (0.4, 0.4)                | -0.1 (-0.1, -0.0)         |
|                             | 252.4 (185.7, 346.6)        | 0.1 (0.1, 0.2)             | 163.8 (121.8, 226.1)    | 0.1 (0.1, 0.1)        | -3.0 (-3.2, -2.8)             | -3.2 (-3.4, -3.1)         |
|                             | 738.8 (593.9, 902.1)        | 0.3 (0.3, 0.4)             | 231.9 (186.2, 284.9)    | 0.1 (0.1, 0.1)        | 0.1 (-0.0, 0.1)               | -0.5 (-0.6, -0.4)         |
|                             | 1497.0 (1004.2, 1896.7)     | 0.7 (0.4, 0.8)             | 707.5 (477.1, 890.7)    | 0.3 (0.2, 0.4)        | 1.0 (0.9, 1.1)                | 0.5 (0.4, 0.6)            |
|                             | 345.6 (244.3, 469.3)        | 0.2 (0.1, 0.2)             | 126.3 (98.4, 159.2)     | 0.1 (0.0, 0.1)        | 0.9 (0.8, 1.1)                | 0.5 (0.4, 0.6)            |
|                             | 311.3 (171.8, 494.2)        | 0.1 (0.1, 0.2)             | 95.6 (42.5, 145.4)      | 0.0 (0.0, 0.1)        | 1.2 (1.0, 1.3)                | -1.5 (-1.6, -1.4)         |
|                             | 514.2 (385.5, 784.6)        | 0.2 (0.2, 0.3)             | 194.8 (146.5, 290.8)    | 0.1 (0.1, 0.1)        | -1.8 (-1.9, -1.8)             | -2.5 (-2.6, -2.4)         |
| Southern Latin America      | 293.7 (252.0, 345.8)        | 1.5 (1.3, 1.8)             | 143.9 (128.4, 159.8)    | 0.7 (0.7, 0.8)        | 1.4 (1.0, 1.8)                | 0.5 (0.2, 0.9)            |
|                             | 3.9 (3.2, 4.6)              | 0.0 (0.0, 0.0)             | 2.1 (1.8, 2.6)          | 0.0 (0.0, 0.0)        | 1.2 (0.9, 1.5)                | 0.4 (0.1, 0.7)            |
|                             | 222.4 (181.1, 269.9)        | 1.1 (0.9, 1.4)             | 22.6 (19.3, 26.1)       | 0.1 (0.1, 0.1)        | 0.9 (0.6, 1.1)                | -0.8 (-1.0, -0.6)         |
|                             | 159.5 (139.2, 183.0)        | 0.8 (0.7, 0.9)             | 57.1 (49.3, 66.7)       | 0.3 (0.3, 0.3)        | -0.8 (-1.0, -0.6)             | -1.3 (-1.5, -1.1)         |
|                             | 62.6 (44.3, 87.3)           | 0.3 (0.2, 0.4)             | 20.3 (15.0, 27.3)       | 0.1 (0.1, 0.1)        | 1.3 (0.9, 1.8)                | 0.8 (0.4, 1.3)            |
|                             | 26.0 (15.3, 39.3)           | 0.1 (0.1, 0.2)             | 1.6 (1.0, 2.3)          | 0.0 (0.0, 0.0)        | -1.0 (-1.7, -0.2)             | -4.5 (-5.1, -3.8)         |
|                             | 94.9 (73.0, 121.5)          | 0.5 (0.4, 0.6)             | 28.6 (22.7, 36.3)       | 0.1 (0.1, 0.2)        | 0.4 (0.1, 0.6)                | -0.3 (-0.5, -0.1)         |
|                             | 227.4 (166.5, 289.5)        | 0.7 (0.5, 0.9)             | 169.1 (123.8, 216.7)    | 0.5 (0.4, 0.7)        | 1.3 (1.1, 1.5)                | 1.2 (1.1, 1.4)            |
| Southern Sub-Saharan Africa | 39.7 (27.8, 53.4)           | 0.1 (0.1, 0.2)             | 27.8 (19.7, 37.3)       | 0.1 (0.1, 0.1)        | 0.1 (-0.2, 0.3)               | 0.1 (-0.2, 0.3)           |
|                             | 105.5 (84.4, 127.2)         | 0.3 (0.3, 0.4)             | 43.6 (35.0, 53.8)       | 0.1 (0.1, 0.2)        | 1.3 (0.8, 1.8)                | 0.7 (0.3, 1.1)            |
|                             | 132.5 (99.4, 187.6)         | 0.4 (0.3, 0.6)             | 68.0 (51.0, 98.2)       | 0.2 (0.2, 0.3)        | -0.0 (-0.3, 0.3)              | -0.1 (-0.5, 0.3)          |
|                             | 44.6 (28.4, 66.2)           | 0.1 (0.1, 0.2)             | 18.0 (13.5, 24.0)       | 0.1 (0.0, 0.1)        | 1.3 (0.8, 1.8)                | 1.1 (0.8, 1.5)            |
|                             | 51.6 (20.2, 91.6)           | 0.2 (0.1, 0.3)             | 30.5 (12.5, 55.6)       | 0.1 (0.0, 0.2)        | 3.0 (2.2, 3.7)                | 1.9 (1.4, 2.5)            |
|                             | 140.9 (96.8, 191.4)         | 0.5 (0.3, 0.6)             | 58.9 (41.3, 79.8)       | 0.2 (0.1, 0.3)        | 1.0 (0.6, 1.3)                | 0.8 (0.5, 1.1)            |
| Tropical Latin America      | 1195.3 (1011.1, 1373.8)     | 1.8 (1.5, 2.1)             | 717.8 (610.7, 823.5)    | 1.1 (0.9, 1.2)        | 0.7 (0.3, 1.1)                | 0.1 (-0.3, 0.5)           |
|                             | 39.9 (30.9, 48.9)           | 0.1 (0.0, 0.1)             | 25.7 (19.8, 31.4)       | 0.0 (0.0, 0.0)        | -1.5 (-1.8, -1.2)             | -1.7 (-2.0, -1.4)         |
|                             | 263.7 (220.4, 307.2)        | 0.4 (0.3, 0.5)             | 83.5 (69.6, 98.6)       | 0.1 (0.1, 0.1)        | 0.2 (-0.2, 0.5)               | -1.2 (-1.5, -0.8)         |

Contd...

**Table 1: Contd...**

| Location                   | 2021                        |                            |                        | 1990-2021             |                               |                           |
|----------------------------|-----------------------------|----------------------------|------------------------|-----------------------|-------------------------------|---------------------------|
|                            | Incidence cases, n (95% UI) | Incidence rate, n (95% UI) | Death cases, n (95%UI) | Death rate, n (95%UI) | EAPC of incidence, % (95% CI) | EAPC of death, % (95% CI) |
| Western Europe             | 512.7 (452.2, 576.5)        | 0.8 (0.7, 0.9)             | 215.9 (194.5, 239.5)   | 0.3 (0.3, 0.4)        | 0.6 (0.4, 0.9)                | 0.1 (-0.1, 0.4)           |
|                            | 255.5 (181.1, 338.6)        | 0.4 (0.3, 0.5)             | 92.7 (71.9, 113.3)     | 0.1 (0.1, 0.2)        | 0.7 (0.2, 1.2)                | 0.3 (-0.2, 0.7)           |
|                            | 74.3 (48.7, 105.3)          | 0.1 (0.1, 0.2)             | 19.6 (13.1, 26.9)      | 0.0 (0.0, 0.0)        | 0.2 (-0.2, 0.6)               | -2.9 (-3.3,-2.5)          |
|                            | 290.4 (242.1, 340.9)        | 0.4 (0.4, 0.5)             | 99.0 (83.5, 114.9)     | 0.1 (0.1, 0.2)        | 0.7 (0.4, 1.0)                | 0.0 (-0.3, 0.3)           |
|                            | 2498.8 (2331.0, 2672.8)     | 2.7 (2.5, 2.9)             | 694.4 (656.6, 736.0)   | 0.8 (0.7, 0.8)        | -0.0 (-0.1, 0.1)              | -1.3 (-1.3,-1.2)          |
|                            | 120.1 (104.7, 136.5)        | 0.1 (0.1, 0.1)             | 26.9 (23.8, 30.3)      | 0.0 (0.0, 0.0)        | 0.9 (0.7, 1.2)                | -0.7 (-0.9,-0.5)          |
|                            | 518.0 (465.2, 575.0)        | 0.6 (0.5, 0.6)             | 60.8 (55.4, 66.3)      | 0.1 (0.1, 0.1)        | 0.2 (-0.0, 0.4)               | -1.7 (-1.9,-1.6)          |
|                            | 760.6 (691.6, 828.2)        | 0.8 (0.8, 0.9)             | 192.5 (178.1, 206.8)   | 0.2 (0.2, 0.2)        | -1.1 (-1.3,-0.9)              | -1.9 (-2.2,-1.7)          |
|                            | 410.7 (324.9, 509.6)        | 0.4 (0.4, 0.6)             | 112.6 (95.4, 132.7)    | 0.1 (0.1, 0.1)        | -0.7 (-0.9,-0.4)              | -1.0 (-1.2,-0.8)          |
|                            | 363.7 (263.7, 461.8)        | 0.4 (0.3, 0.5)             | 5.0 (3.9, 6.4)         | 0.0 (0.0, 0.0)        | 1.3 (0.7, 1.9)                | -2.3 (-3.3,-1.4)          |
| Western sub-Saharan Africa | 662.0 (574.0, 751.8)        | 0.7 (0.6, 0.8)             | 145.0 (128.9, 160.2)   | 0.2 (0.1, 0.2)        | -0.2 (-0.5, 0.1)              | -0.9 (-1.3,-0.6)          |
|                            | 1262.8 (613.2, 1680.1)      | 2.1 (1.6, 2.8)             | 980.3 (482.9, 1303.7)  | 0.4 (0.2, 0.5)        | 0.8 (0.6, 1.0)                | 0.6 (0.5, 0.8)            |
|                            | 823.6 (590.2, 1092.9)       | 0.3 (0.2, 0.4)             | 570.6 (412.6, 754.3)   | 0.2 (0.2, 0.3)        | -2.5 (-2.6,-2.3)              | -2.5 (-2.7,-2.3)          |
|                            | 1691.9 (1056.7, 2362.5)     | 0.6 (0.4, 0.9)             | 864.2 (544.5, 1186.7)  | 0.3 (0.2, 0.4)        | 1.1 (0.9, 1.3)                | 0.4 (0.2, 0.5)            |
|                            | 2106.5 (1505.9, 2742.0)     | 0.8 (0.6, 1.0)             | 953.9 (687.0, 1253.1)  | 0.4 (0.3, 0.5)        | 0.5 (0.4, 0.7)                | -0.0 (-0.1, 0.1)          |
|                            | 668.0 (173.6, 1235.1)       | 0.2 (0.1, 0.5)             | 271.7 (69.2, 474.1)    | 0.1 (0.0, 0.2)        | 1.8 (1.4, 2.2)                | 1.5 (1.1, 1.9)            |
|                            | 760.2 (290.7, 1259.8)       | 0.3 (0.1, 0.5)             | 599.0 (251.7, 949.3)   | 0.2 (0.1, 0.4)        | -0.5 (-0.7,-0.3)              | -1.2 (-1.3,-1.0)          |
|                            | 1532.6 (981.5, 2491.4)      | 0.6 (0.4, 0.9)             | 697.6 (446.1, 1118.2)  | 0.3 (0.2, 0.4)        | -1.3 (-1.5,-1.2)              | -1.8 (-2.0,-1.6)          |

EAPC, estimated annual percentage change; SDI, sociodemographic index; UI, uncertain interval; CI, confidence interval; Brain cancer, Brain and central nervous system cancer; MNBAC, Malignant neoplasm of bone and articular cartilage; Neuroblastoma, Neuroblastoma and other peripheral nervous cell tumor; STES, Soft tissue and other extraosseous sarcomas. Rate, per 100 000 people

in the 1–2 age group and peak mortality in infants under 1 year old. Hepatoblastoma cases and related mortality were primarily concentrated in infants under 1 year old, whereas retinoblastoma primarily impacted children in the 2–4 age bracket. Kidney cancer and

neuroblastoma primarily struck individuals aged 2–4, with the highest incidence noted in the 1–2 age group and peak mortality in infants under 1 year old. MNBAC exclusively manifested in children older than 1 year, with incidence and mortality cases, as well

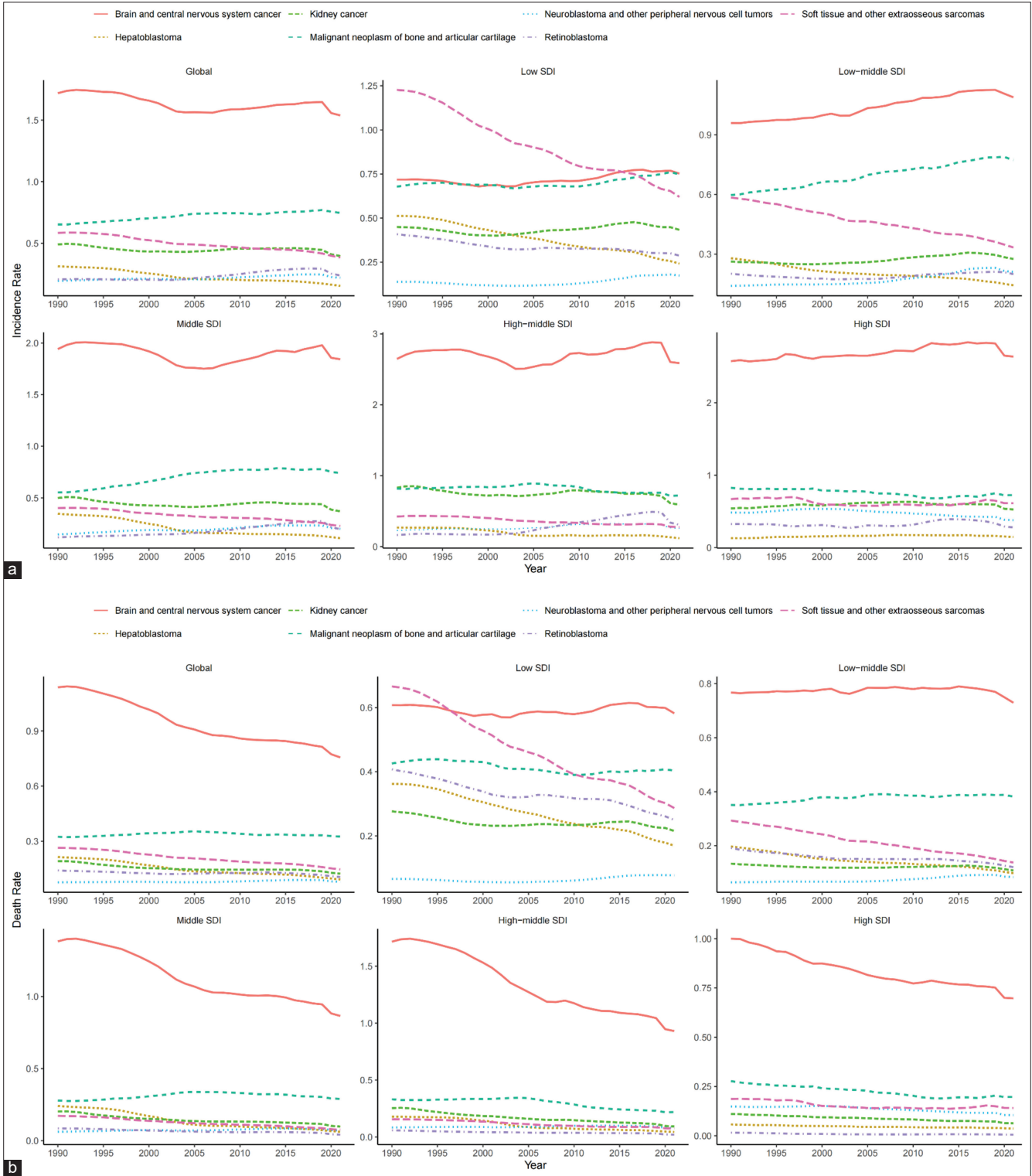


Figure 1: Epidemiologic trends of burden in global and five sociodemographic index regions of solid tumors from 1990 to 2021. (a) Incidence rate and (b) death rate

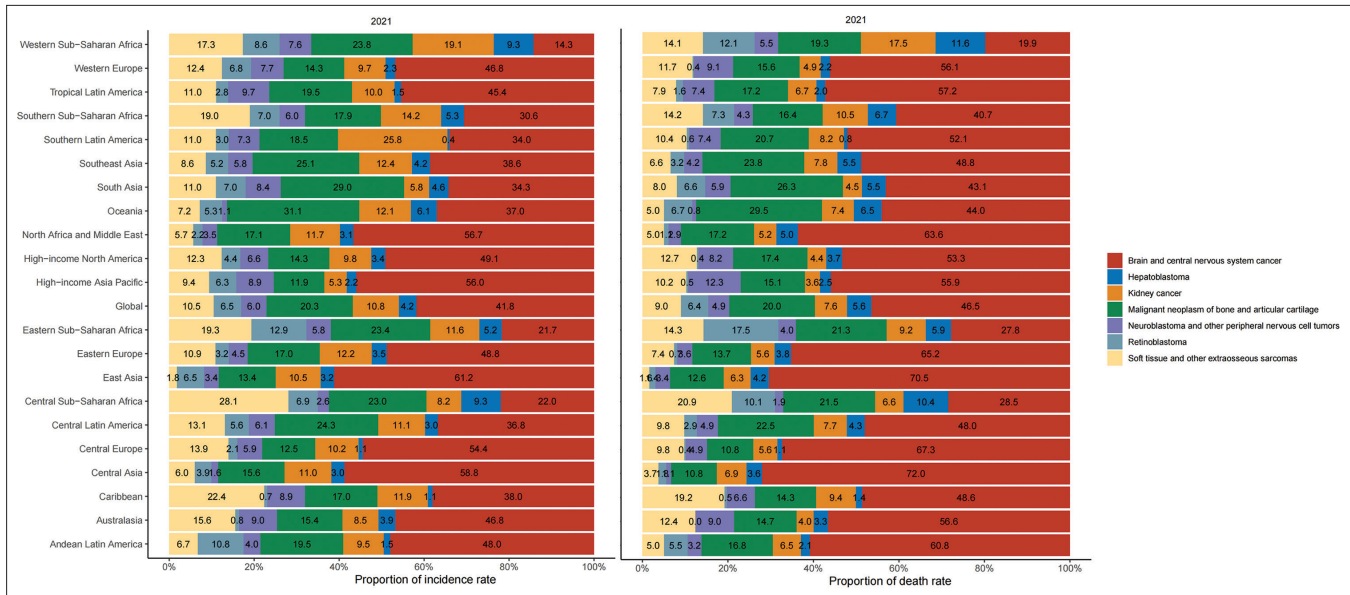


Figure 2: Regional incidence and death proportion of solid tumors burden in 2021

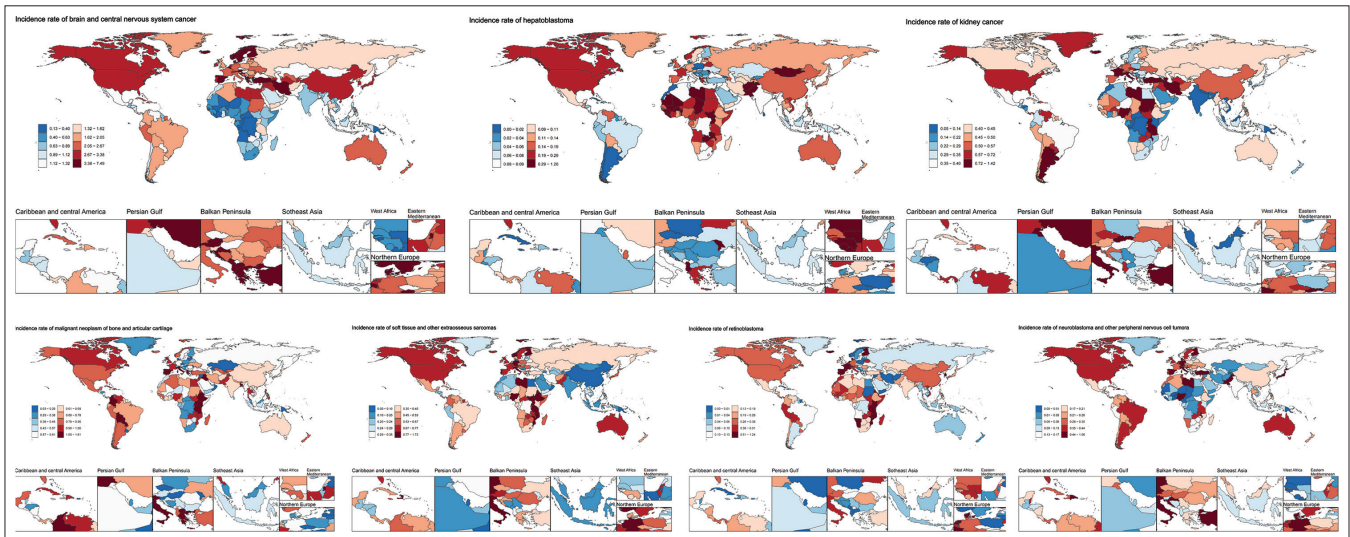


Figure 3: Incidence burden of solid tumors in 204 countries and territories in 2021

as corresponding rates, peaking in the 15–19 age group and increasing progressively with age. Notably, although the majority of STES cases and related deaths were concentrated in the 15–19 age group, infants under 1 year old had the highest incidence and mortality rates for this tumor type [Figure 4].

**Burden of solid tumor by SDI**

Among the five SDI regions, brain cancer had the highest incidence and mortality rates for solid tumors, followed by MNBC. Specifically, in 2021, the high-SDI region had the highest incidence rate of brain cancer, and it also had a relatively high incidence rate of neuroblastoma. In contrast, the low-SDI region had the highest incidence rates of hepatoblastoma and STES. The High-middle SDI

region had the highest incidence rates of kidney cancer and retinoblastoma. The low-middle SDI region had the highest incidence rate of MNBC. In terms of mortality, several types of tumors in the low-SDI region had high mortality rates, including MNBC, kidney cancer, hepatoblastoma, retinoblastoma, and STES. Notably, the High-middle SDI region had the highest mortality rate for brain cancer, and the high-SDI region had a high mortality rate for neuroblastoma [Table 1].

From 1990 to 2021, the incidence rates of brain cancer and kidney cancer remained relatively stable across all SDI regions. However, the incidence of MNBC gradually increased in regions with low-SDI, and neuroblastoma incidence increased in

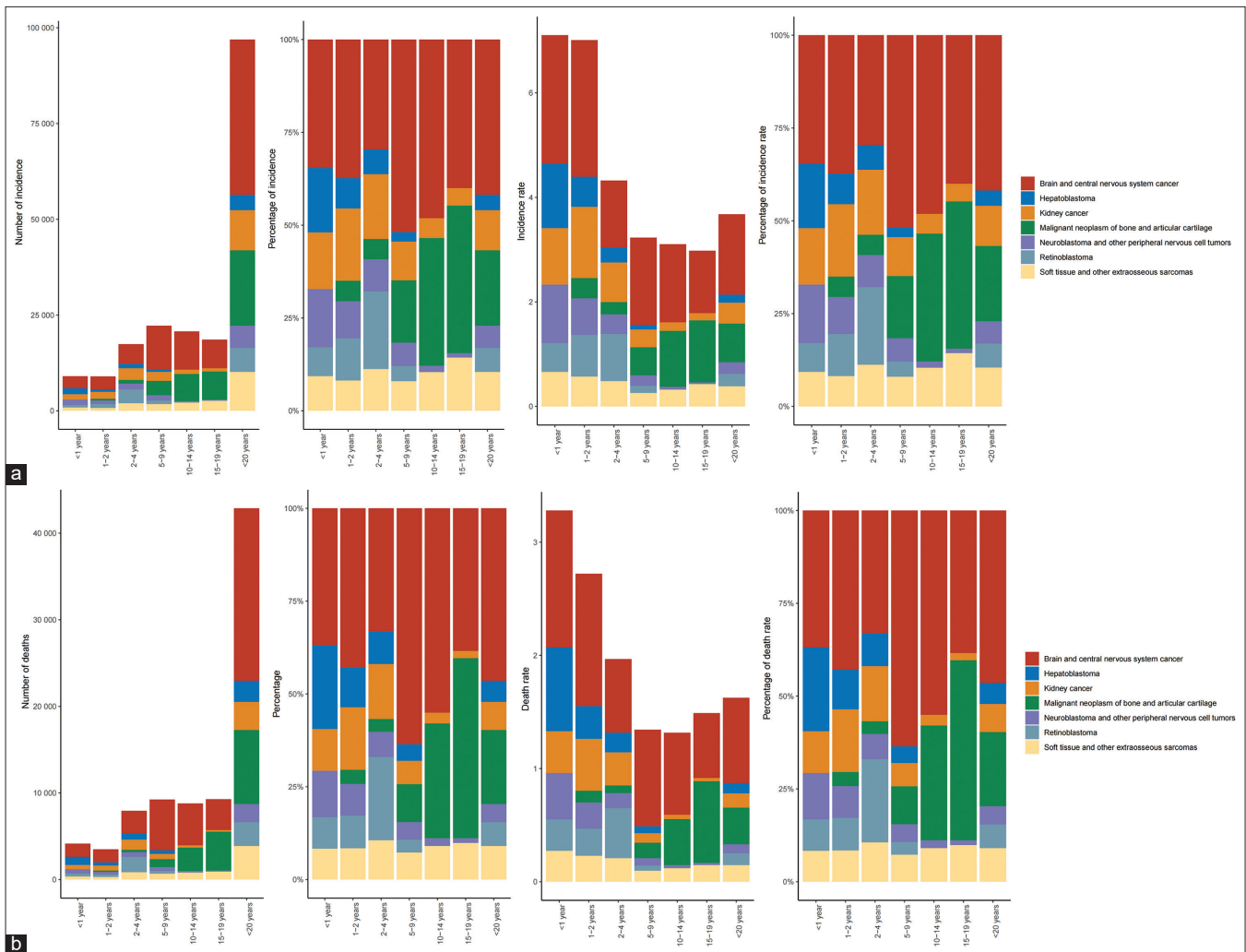


Figure 4: Age proportion of solid tumors burden in 2021. (a) Incidence rate and (b) death rate

all regions except high-SDI. Retinoblastoma showed an increasing trend in all regions except low-SDI, while hepatoblastoma and STES declined in most SDI regions. In terms of mortality, neuroblastoma mortality increased in all regions except high-SDI, and MNBAC mortality slightly increased in Low-middle and Middle SDI regions. The mortality burden of the other tumors declined in different SDI regions [Table 1 and Figure 1].

The relationships between the incidence and mortality rates of different types of cancer and SDI vary. As SDI increases, the incidence rates of brain cancer and neuroblastoma gradually increase, while the mortality rates of hepatoblastoma and retinoblastoma gradually decrease. The mortality rate of neuroblastoma increases with SDI. However, the correlations between the incidence and mortality rates of the other tumors and SDI are relatively weak or insignificant [Figures S3 and S4]. At the national level, there was no significant correlation

between the incidence and mortality rates of kidney cancer and SDI. The associations between the burden of the other tumors and SDI were similar to those at the regional level, indicating that the trends observed at the regional level are largely consistent with those at the national level [Figures S5 and S6].

### Discussion

Solid tumors seriously threaten children and adolescents' health, challenging global health policies and systems. Their impact requires urgent action. This study outlines incidence and mortality of seven major solid tumors affecting this age group worldwide, showing trends and disparities. In 2021, these tumors caused nearly 40% of new cancer cases and deaths in 0–19 year-olds globally. Brain cancer and MNBAC are prominent. Since 1990, MNBAC, neuroblastoma, and retinoblastoma incidence has risen, with neuroblastoma mortality also increasing,

needing constant monitoring, research, and targeted prevention.

Over the past few decades, remarkable advancements in multi-modal therapy and supportive care have substantially enhanced the prognosis of numerous types of malignant solid tumors among children and adolescents, as demonstrated by our study results.<sup>[16]</sup> However, substantial regional disparities persist. Brain cancer, which stands as the most prevalent solid tumor and the primary cause of cancer-related deaths in this age group, is particularly prominent in Asian regions, notably East and Central Asia. This disparity is largely attributed to variations in demographic factors, including race, parental age, and environmental exposures such as ionizing radiation and air pollution.<sup>[17,18]</sup> Research indicates that an older maternal age correlates with an accumulation of chromosomal and gene-level mutations in germ cells, thereby elevating the risk of brain cancer in offspring. Folate plays a pivotal role in nucleotide synthesis and repair; maternal folate supplementation during pregnancy aids in reducing the likelihood of chromosomal breaks and improper proto-oncogene activation, thereby offering protection against pediatric brain tumors.<sup>[19,20]</sup> Hence, enhancing basic maternal healthcare is imperative for mitigating the risk of brain tumors in these regions. The disease burden, particularly the mortality burden, associated with various tumors such as MNBC, STS, and retinoblastoma in sub-Saharan Africa, is markedly higher compared to other regions. This disparity is primarily driven by economic limitations, restricted access to healthcare facilities and professional medical care, the intricacy of treatment protocols, and the absence of effective early screening and diagnostic mechanisms. Consequently, pediatric tumors in this region frequently manifest as advanced and locally metastatic diseases, often without receiving any effective treatment. Furthermore, the presence of multiple comorbidities, including malaria, tuberculosis, malnutrition, and treatment-related toxicities, further exacerbates the decline in pediatric tumor survival rates in the region.<sup>[21,22]</sup> In response, there is a pressing need to augment medical assistance to sub-Saharan Africa, bolster its pediatric tumor diagnosis and treatment capabilities, and intensify the training of medical personnel. Neuroblastoma, a malignant tumor arising from primitive neural crest cells within the sympathetic nervous system, exhibits an escalating global incidence and mortality trend. The incidence is notably high in relatively developed regions, such as High-income Asia Pacific, potentially due to advancements in early detection technology,

enhanced screening initiatives, and heightened clinical awareness.<sup>[23]</sup> Conversely, the incidence of renal cancer is significantly elevated in Southern Latin America, which starkly contrasts with the pervasive high levels of arsenic in drinking water sources in this area. Studies have shown that prolonged arsenic exposure is linked to alterations in gene expression related to arsenic methylation, potentially increasing the risk of developing various tumors, including renal cancer.<sup>[24]</sup> While further in-depth research is required to elucidate the precise connection between arsenic contamination and renal cancer, the existing evidence will aid relevant countries in promoting public health awareness and intervention programs, as well as formulating urgently needed environmental policies for the region. Despite notable improvements in the survival rate of hepatoblastoma across most global regions, it has exhibited a notable surge in Australia. The reasons underlying this increase remain unclear, but potential contributing factors may include a significant rise in metastatic hepatoblastoma cases, advancements in diagnostic techniques, and changes in reporting practices.<sup>[25,26]</sup>

It is noteworthy that despite the fact that 80% of cancer patients reside in low- and middle-income countries, the incidence and mortality trends of various cancer types exhibit distinct patterns across different SDI regions, intricately intertwined with the SDI. Specifically, brain cancer holds the top position in both incidence and mortality across the five SDI regions, underscoring its significant contribution to the global cancer burden, particularly in regions with a higher SDI. This revelation underscores the formidable challenges still faced in the prevention and control of brain cancer, even in areas with relatively abundant medical resources.<sup>[27]</sup> Furthermore, MNBC demonstrates a high incidence across multiple SDI regions, particularly in those with a low-middle SDI, with mortality rates escalating in some areas. This may be attributed to the low rates of early diagnosis and limited treatment resources stemming from adverse socio-economic conditions.<sup>[28]</sup> Conversely, in regions with a higher SDI, despite the heightened incidence of kidney cancer, retinoblastoma, and hepatoblastoma, the mortality rates of these tumors have not risen concurrently, thanks to superior medical services, screening mechanisms, and heightened diagnostic awareness. This underscores the pivotal role of effective medical interventions in mitigating mortality. From a temporal trend perspective, while the mortality burden of most tumor types has decreased in various SDI regions, this positive shift has not been evenly distributed across all regions and tumor types. This suggests

that global cancer prevention and control strategies must become more nuanced and comprehensive. In devising future prevention and control strategies, it is imperative to bolster support for cancer prevention, early diagnosis, and treatment in low-SDI regions, while simultaneously addressing the emerging challenges in the prevention and control of specific tumor types in high-SDI regions, thereby fostering balanced progress in the global cancer prevention and control endeavor.

Moreover, there are disparities in the incidence of malignant solid tumors among different age groups of children and adolescents. Infants are more susceptible to brain cancer, neuroblastoma, kidney cancer, hepatoblastoma, and retinoblastoma, potentially due to their underdeveloped immune systems and high cell division rates.<sup>[29,30]</sup> Conversely, adolescents aged 15–19 are more affected by MNBAC and STES, possibly linked to their growth stage, active tissues, and increased life pressures.<sup>[31]</sup> Adolescents may overlook bodily abnormalities and hesitate to discuss health concerns, leading to delayed diagnosis and reduced survival rates.<sup>[32]</sup> To address these disparities, precise and personalized prevention and screening strategies tailored to different age groups and tumor types are crucial for early detection.

Pediatric solid tumors are challenging due to their rapid growth, aggressiveness, and tendency to spread, making prevention difficult. However, they often respond well to treatment and are cost-effective. To address this, early diagnostic capabilities and access to high-quality healthcare must be improved. This ensures timely referrals to pediatric oncology centers for accurate evaluations, diagnoses, and staging, enabling effective treatment and supportive care.<sup>[22]</sup> As global research progresses, new targets and drugs offer better prospects for pediatric patients.<sup>[33]</sup> For example, neuroblastoma treatment is shifting to more precise immunotherapy and targeted therapy, significantly improving survival rates and quality of life.<sup>[23]</sup>

This study, based on GBD 2021 estimates, offers insights into malignant solid tumors in children and adolescents globally but has limitations. Data are mainly from existing studies and stats, which may be incomplete or vary in quality. Regional comparisons may be biased due to different data collection methods. The study focuses on seven major tumors and excludes others, like extracranial germ cell tumors, and lacks detailed tumor classification, hindering understanding of specific tumor pathogenesis. For rare or specific tumors, it provides limited information. Proposed interventions rely on existing research and may be affected by

factors like medical resources, patient economics, and social support. Implementation must consider local feasibility and require continuous monitoring.

## Conclusion

This study offers an exhaustive examination of the incidence and mortality rates associated with seven primary malignant solid tumors affecting children and adolescents worldwide. It profoundly underscores the dire challenges posed by these tumors to adolescents' health and brings to light the stark disparities in their geographical distribution and across different socio-economic development levels. Notably, brain cancer and MNBAC predominate the global incidence and mortality scenario, posing a formidable risk to the survival prospects of the affected youth. We urge policymakers to prioritize this, develop tailored prevention and screening initiatives, and improve pediatric cancer survival rates and prognosis.

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## Ethical statement

For GBD studies, the Institutional Review Board of the University of Washington reviewed and approved a waiver of informed consent (<https://www.healthdata.org/research-analysis/gbd>).

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The study was not supported by any funding projects.

## Conflicts of interest

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

## Data availability statement

The data on the burden of disease are available from the Institute for Health Metrics and Evaluation at <https://www.healthdata.org/>.

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