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RESEARCH

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Global cancer statistics for adolescents and young adults: population based study

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Abstract

Background Accurate and up-to-date estimates of the global cancer burden in adolescents and young adults (AYA) are scarce. This study aims to assess the global burden and trends of AYA cancer, with a focus on socioeconomic disparities, to inform global cancer control strategies.

Methods AYA cancer, defined as cancer occurring in individuals aged 15–39, was analyzed using data from the Global Burden of Disease (GBD) 2021 study and the Global Cancer Observatory (GLOBOCAN) 2022 project. We examined the global burden by age, sex, geographic location, and Human Development Index (HDI), as well as its temporal trends. Primary outcomes included age-standardized incidence and mortality rates (ASIR, ASMR) and the average annual percent change (AAPC).

Results In 2022, an estimated 1,300,196 incidental cases and 377,621 cancer-related deaths occurred among AYAs worldwide, with an ASIR of 40.3 per 100,000 and an ASMR of 11.8 per 100,000. The most common cancers were breast, thyroid, and cervical, while the leading causes of death were breast, cervical, and leukemia. The incidence and mortality were disproportionately higher among females (ASIR: 52.9 for females vs. 28.3 for males; ASMR: 13.1 for females vs. 10.6 for males). Countries with higher HDI experienced a higher incidence of AYA cancers (ASIR: 32.0 [low HDI] vs. 54.8 [very high HDI]), while countries with lower HDI faced a disproportionately higher mortality burden (ASMR: 17.2 [low HDI] vs. 8.4 [very high HDI]) despite their relatively low incidence. Disproportionality and regression measures highlighted significant HDI-related inequalities. AYA cancer incidence was stable from 2000 to 2011 (AAPC: −0.04) but increased from 2012 to 2021 (AAPC: 0.53), driven by growing gonadal and colorectal cancers. Mortality decreased substantially from 2000 to 2011 (AAPC: −1.64), but the decline slowed from 2012 (AAPC: −0.32) probably due to increased deaths from gonadal cancers. These trends varied by sex, cancer type, geography, and HDI.

Conclusion AYA cancers present a significant and growing global burden, with marked disparities across sex, geographic locations, and HDI levels. Policymakers should prioritize equitable resource allocation and implement targeted interventions to reduce these inequalities, particularly in low-HDI regions and with regard to gonadal cancers.

Keywords Adolescents and young adults, Cancer, Incidence, Mortality, Global analysis, Trend, Disparities

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Background

Cancer constitutes a major global public health issue and ranks as the third leading cause of death globally, responsible for one in seven deaths in 2021 [1, 2]. While it predominantly affects older adults, cancer incidence in adolescents and young adults (AYAs) is relatively low, comprising about 5% of total cases [3, 4]. AYAs with cancer exhibit distinct biological, epidemiological, and clinical characteristics, markedly differing from those in children and older adults [5, 6]. In addition, they face a range of complex, age-specific challenges, including fertility preservation, long-term side effects, socioeconomic burden, and psychosocial issues [7–9]. For decades, AYAs with cancer have been under-recognized, underdiagnosed, and under-served, with fewer improvements in survival as compared to other age groups [10–13]. Thus, the specific needs, expectations, and treatment recommendations for AYAs with cancer merit special considerations to improve outcomes [6, 14].

Globally, the burden of AYA cancer is rising, with marked regional disparities in incidence and mortality [15–18]. In the last updated GBD 2019 study, there were 1.19 million new cancer cases and 396,000 cancer deaths globally among AYAs. Cancer was the fourth leading cause of death and the tenth leading cause of disease burden in this age group, contributing 23.5 million disability-adjusted life years. The recent updates from Global Cancer Observatory (GLOBOCAN) 2022 and the Global Burden of Disease (GBD) study provide an expanded dataset, improving the accuracy and coverage of cancer burden estimates [1, 2]. Combining insights from these databases offers a comprehensive view of the global AYA cancer burden, which is critical for developing targeted interventions and improving survival outcomes.

However, no studies have applied these latest estimates to assess the burden and unique challenges of AYA cancers, leaving gaps in our understanding of this population. This study aimed to assess the global burden and evolving trends of AYA cancers, focusing on patterns in incidence and mortality, as well as socioeconomic disparities related to sex, geography, and human development level. By highlighting these disparities, the findings can guide targeted cancer control strategies that address health inequities and improve resource allocation for this vulnerable population.

Methods

Study design

In this analysis, AYA cancer was defined as cancer occurring in individuals between the ages of 15 and 39 years, consistent with the broadly accepted age range recommended by the Adolescent and Young Adult Oncology Progress Review Group (AYAOPRG) [6, 10]. All available malignant cancer types in the GLOBOCAN 2022 database and GBD 2021 estimates categorized by the 10th Edition of the International Classification of Diseases (ICD-10) were examined. The list of ICD-10 codes mapped to the GLOBOCAN or the GBD cause list for cancer sites or types is available in previous reports [1, 2]. We excluded non-melanoma skin cancer (NMSC) (C44) and combined colon, rectum, and anus cancers into a single category of colorectal cancer (C18-C21). Ethical approval and informed consent were not required for this study, as it utilized publicly available, anonymized data aggregated at the population level.

Data source

We retrieved data from the GBD 2021 results available online at the Institute for Health Metrics and Evaluation (https://vizhub.healthdata.org/gbd-results/) and the International Agency for Research on Cancer's GLOBOCAN 2022 estimates available online at the Cancer Today (https://gco.iarc.who.int/today/en/dataviz/tables), respectively. We used data on Human Development Index (HDI) for each country from the United Nations, which is a comprehensive socioeconomic development indicator encompassing life expectancy, education level, and gross national income [19]. The study included 185 countries or territories, organized into 19 regions based on epidemiological similarities and geographical proximity (Table S1). In our analysis, Melanesia, Micronesia, and Polynesia were merged into a single category referred to as the Pacific Islands. Additionally, these countries were classified into four HDI categories based on their 2022 HDIs: low, medium, high, and very high (Table S2).

Overview of cancer burden estimates

Detailed information on the data sources and methodologies used to compile these results is provided in related publications and online platform [1, 2, 20, 21]. Here, we provide an overview of the cancer burden estimation process for GBD 2021 and GLOBOCAN 2022, with key differences between the two databases provided in Supplement (Table S3). The GBD 2021 study offers comprehensive estimates for 50 cancer types across 204 countries and territories. It draws on multiple sources, including cancer registries, vital registration systems, hospital records, clinical data, scientific literature, and input from the GBD collaborator network. Incidence data is primarily sourced from cancer registries, while mortality data comes from both registries and vital registration systems. When direct incidence data is unavailable, mortality-to-incidence ratios (MIR) are employed. Newly included cancers, such as Burkitt lymphoma and retinoblastoma, use registry data supplemented by mortality records. The study integrates the Healthcare Access and Quality Index to refine MIR estimates by identifying outliers. SEER*Stat data supports survival analysis, while clinical and hospital records estimate procedure-related disabilities, such as those following mastectomy or cystectomy. Advanced statistical tools, including DisMod-MR 2.1 and spatiotemporal Gaussian process regression, ensure data consistency across regions, age groups, and timeframes. Meanwhile, the GLOBOCAN 2022 project provides estimates for 36 cancer types across 185 countries and territories. Data sources include national and subnational cancer registries, mortality databases, and predictive models. It employs short-term prediction models for countries with reliable data, while MIR estimates—adjusted by the HDI—are used where data is limited. In cases where national registries are unavailable, neighboring countries' data serves as a proxy. Additionally, non-specific or ill-defined cases are redistributed into specific cancer categories to improve accuracy.

Statistical analysis

We acquired estimates of incidence and mortality for all cancers combined except NMSC and for each available cancer type at the global, regional, and national level. We reported estimates of absolute, proportional, and age-standardized rates (ASRs) of incidence (ASIR) and mortality (ASMR) for AYA cancer at global, regional, and national levels. Truncated age-standardized rate per 100,000 person-years was calculated using the formula $\frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100,000$ (where a_i is age-specific death rate for the i-th age group, w_i is the weight of the i-th age group in the standard population; and A is the total number of age groups). Age standardization was performed using the World Standard Population proposed by Segi and later modified by Doll et al. (Table S3) to ensure consistency and comparability across various data sources. To illustrate key patterns in the AYA cancer burden, we also compared differences across age groups, sexes, geographical locations, and human developmental levels. Temporal trend in ASRs was measured with the average annual percent change (AAPC), which was calculated with the Joinpoint Trend Analysis Software (Command-Line Version 5.2.0). The AAPC provides a summary of these trends over a specific period as a weighted average of the annual percent changes (APCs). Terms such as "increase" or "decrease" are used to describe statistically significant slopes (APC or AAPC) determined by two-sided tests. Trends that do not meet the threshold of significance are described as "stable". The relationships between country-level age-standardized rates and mortality-incidence ratios with the HDI were visualized using scatter plots, enhanced with locally weighted scatterplot smoothing regression lines, and analyzed using the Spearman's correlation analysis. Measures of absolute and relative health inequalities attributable to HDI were assessed using the Absolute Concentration Index and Slope Index of Inequality (for absolute inequalities), as well as the Relative Concentration Index and Relative Index of Inequality (for relative inequalities), all executed using the "healthequal" package [22]. All statistical analyses and graphics were conducted using R software (version 4.3.3).

Results

Global landscape of AYA cancer in 2022

In 2022, there were 1,300,196 new cancer cases and 377,621 cancer deaths in AYAs aged 15–39 years worldwide (Table 1). ASRs were 40.3 per 100,000 person-years and 11.8 per 100,000 person-years in terms of incidence and mortality, respectively.

The most commonly diagnosed AYA cancers included breast cancer, thyroid cancer, and cervical cancer. The leading contributors to AYA cancer deaths were breast cancer, cervical cancer, and leukemia. The burden of AYA cancers was notably higher among women than men (incidence: 52.9 [female] vs. 28.3 [male] per 100,000 person-years; mortality: 13.1 [female] vs. 10.6 [male] per 100,000 person-years), reflected in male-to-female ratios of 0.53 for incidence and 0.81 for mortality. This was primarily contributed by the markedly high burden of breast, thyroid, and cervical cancers among AYA women (Figure S1). As age advanced, both sexes experienced a notable rise in absolute numbers and ASRs of incidence and mortality, with women exhibiting a particularly rapid escalation (Fig. 1A). Consequently, the cancer burden was notably higher among young adults compared to adolescents. Moreover, the cancer profiles according to 5-year age intervals among AYAs varied substantially (Fig. 1B and Tables S4–8). The most common cancers among adolescent group were leukemia and thyroid cancer, and among those aged 20–39 years, breast and thyroid cancer (Fig. 1C). Leukemia accounted for the highest proportion of cancer deaths in the 15 to 29 age group, whereas breast cancer was the leading cause of death among those aged 30–39 years. Although thyroid cancer consistently ranked within the top two across all age subgroups, it accounts for less than 1% of AYA cancer deaths.

Geographic differences in burden of AYA cancer

Regionally, Australasia had the highest ASIR of 72.4 per 100,000 person-years in 2022, followed by Northern America (65.9 per 100,000 person-years) and Southern Europe (61.9 per 100,000 person-years) (Fig. 2A and Table S9). South Central Asia reported the lowest ASIR of 25.5 per 100,000 person-years, followed by Western Africa (26.8 per 100,000 person-years) and

Table 1 Burden of cancer incidence and mortality among AYAs worldwide in 2022

Cancer types	Estimated new cancer cases and ASR per 100,000 people per year									Estimated cancer-related deaths and ASR per 100,000 people per year								
	Both sexes			Men			Women			Both sexes			Men			Women		
	Cases	(%)	ASR	Cases	(%)	ASR	Cases	(%)	ASR	Deaths	(%)	ASR	Deaths	(%)	ASR	Deaths	(%)	ASR
All cancers excluded NMSC	1,300,196	100.0	40.3	458,124	100.0	28.3	842,072	100.0	52.9	377,621	100.0	11.8	170,340	100.0	10.6	207,281	100.0	13.1
Age groups																		
Breast	245,827	18.9	14.9	–	–	–	245,827	29.2	14.9	48,658	12.9	2.9	–	–	–	48,658	23.5	2.9
Thyroid	236,761	18.2	7.3	63,509	13.9	3.8	173,252	20.6	11.0	2107	0.6	0.1	630	0.4	0.0	1477	0.7	0.1
Cervix uteri	105,728	8.1	6.5	–	–	–	105,728	12.6	6.5	32,575	8.6	2.0	–	–	–	32,575	15.7	2.0
Leukaemia	64,704	5.0	2.2	37,560	8.2	2.5	27,144	3.2	1.9	40,364	10.7	1.4	23,610	13.9	1.5	16,754	8.1	1.1
Colorectum	59,520	4.6	1.8	30,796	6.7	1.9	28,724	3.4	1.8	22,776	6.0	0.7	12,496	7.3	0.8	10,280	5.0	0.6
Non–Hodgkin lymphoma	51,095	3.9	1.6	30,178	6.6	1.9	20,917	2.5	1.4	18,403	4.9	0.6	11,089	6.5	0.7	7314	3.5	0.5
Brain & CNS	46,828	3.6	1.5	27,126	5.9	1.7	19,702	2.3	1.3	26,943	7.1	0.9	16,258	9.5	1.0	10,685	5.2	0.7
Testis	42,732	3.3	2.7	42,732	9.3	2.7	–	–	–	3893	1.0	0.3	3893	2.3	0.3	–	–	–
Ovary	37,703	2.9	2.4	–	–	–	37,703	4.5	2.4	9846	2.6	0.6	–	–	–	9846	4.8	0.6
Liver & IBD	32,513	2.5	1.0	23,808	5.2	1.4	8705	1.0	0.6	26,188	6.9	0.8	19,363	11.4	1.1	6825	3.3	0.4
Trachea, bronchus and lung	31,681	2.4	1.0	15,696	3.4	1.0	15,985	1.9	1.0	15,189	4.0	0.5	9291	5.5	0.6	5898	2.8	0.4
Hodgkin lymphoma	31,117	2.4	1.1	17,493	3.8	1.2	13,624	1.6	1.0	4791	1.3	0.2	2815	1.7	0.2	1976	1.0	0.1
Lip, oral cavity	28,930	2.2	0.9	21,871	4.8	1.3	7059	0.8	0.4	12,211	3.2	0.4	9525	5.6	0.6	2686	1.3	0.2
Melanoma of skin	25,886	2.0	0.8	10,137	2.2	0.6	15,749	1.9	1.0	2321	0.6	0.1	1248	0.7	0.1	1073	0.5	0.1
Stomach	24,869	1.9	0.8	11,629	2.5	0.7	13,240	1.6	0.8	15,811	4.2	0.5	7551	4.4	0.5	8260	4.0	0.5
Kidney	17,712	1.4	0.5	10,710	2.3	0.6	7002	0.8	0.4	3133	0.8	0.1	1799	1.1	0.1	1334	0.6	0.1
Nasopharynx	17,238	1.3	0.5	11,390	2.5	0.7	5848	0.7	0.4	5925	1.6	0.2	3923	2.3	0.2	2002	1.0	0.1
Kaposi sarcoma	16,519	1.3	0.5	10,642	2.3	0.7	5877	0.7	0.4	8244	2.2	0.3	5216	3.1	0.3	3028	1.5	0.2
Corpus uteri	13,142	1.0	0.8	–	–	–	13,142	1.6	0.8	1571	0.4	0.1	–	–	–	1571	0.8	0.1
Oesophagus	9891	0.8	0.3	5746	1.3	0.3	4145	0.5	0.3	8005	2.1	0.2	4828	2.8	0.3	3177	1.5	0.2
Bladder	8962	0.7	0.3	6113	1.3	0.4	2849	0.3	0.2	1606	0.4	0.1	1058	0.6	0.1	548	0.3	0.0
Salivary glands	7515	0.6	0.2	3534	0.8	0.2	3981	0.5	0.3	1632	0.4	0.1	810	0.5	0.1	822	0.4	0.1
Pancreas	7343	0.6	0.2	3920	0.9	0.2	3423	0.4	0.2	4627	1.2	0.1	2770	1.6	0.2	1857	0.9	0.1
Prostate	5732	0.4	0.3	5732	1.3	0.3	–	–	–	1578	0.4	0.1	1578	0.9	0.1	–	–	–
Gallbladder	3913	0.3	0.1	1071	0.2	0.1	2842	0.3	0.2	2785	0.7	0.1	731	0.4	0.0	2054	1.0	0.1
Larynx	3562	0.3	0.1	2522	0.6	0.2	1040	0.1	0.1	1655	0.4	0.1	1185	0.7	0.1	470	0.2	0.0
Hypopharynx	3137	0.2	0.1	2134	0.5	0.1	1003	0.1	0.1	1731	0.5	0.1	1215	0.7	0.1	516	0.2	0.0
Multiple myeloma	3127	0.2	0.1	1852	0.4	0.1	1275	0.2	0.1	1564	0.4	0.1	943	0.6	0.1	621	0.3	0.0
Oropharynx	2937	0.2	0.1	2034	0.4	0.1	903	0.1	0.1	1047	0.3	0.0	730	0.4	0.0	317	0.2	0.0
Vulva	2814	0.2	0.2	–	–	–	2814	0.3	0.2	832	0.2	0.1	–	–	–	832	0.4	0.1

Table 1 (continued)

Cancer types	Estimated new cancer cases and ASR per 100,000 people per year									Estimated cancer-related deaths and ASR per 100,000 people per year								
	Both sexes			Men			Women			Both sexes			Men			Women		
	Cases	(%)	ASR	Cases	(%)	ASR	Cases	(%)	ASR	Deaths	(%)	ASR	Deaths	(%)	ASR	Deaths	(%)	ASR
Penis	2589	0.2	0.2	2589	0.6	0.2	–	–	–	499	0.1	0.0	499	0.3	0.0	–	–	–
Vagina	1171	0.1	0.1	–	–	–	1171	0.1	0.1	366	0.1	0.0	–	–	–	366	0.2	0.0
Mesothelioma	670	0.1	0.0	339	0.1	0.02	331	0.0	0.0	418	0.1	0.0	249	0.1	0.0	169	0.1	0.0

AYAs adolescents and young adults, *NMSC* non-melanoma skin cancer, *CNS* central nervous system, *IBD* intrahepatic bile ducts, *ASR* age-standardized rate

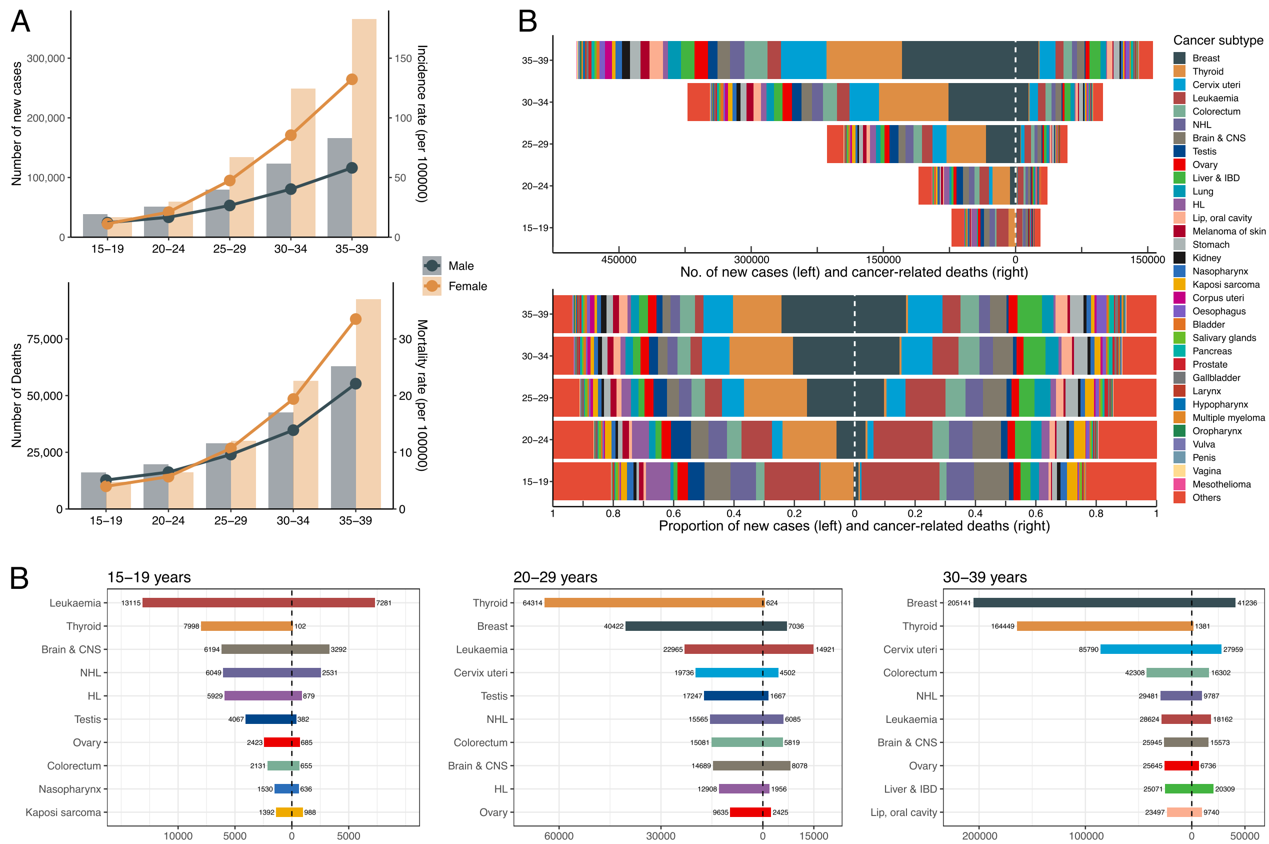

Fig. 1 Global burden of adolescent and young adult cancers, 2022. **A** Global age-specific counts and rates of incident cases and deaths by sex. **B** Global age-specific counts and proportion of incident cases and deaths by cancer type. **C** Global age-specific counts of incident cases and deaths for the 10 most common cancers

Middle Africa (29.6 per 100,000 person-years). ASMR was highest in Eastern Africa (22.3 per 100,000 person-years) and was lowest in Northern Europe (6.0 per 100,000 person-years). Women exhibited significantly higher AYA cancer burden than men across all regions, with the most pronounced gender disparity observed in Pacific Islands (Figure S1). The only exception is that ASMR was higher among AYA males in East Asia compared to females. There were also substantial geographic variations in AYA cancer profiles in terms of of incidence and mortality (Fig. 2B). Rankings of the relative burden of AYA cancer are summarized in Fig. 2C, depicted by ASIRs of AYA cancer across regions. The inter-category rankings revealed that Europe and Northern America had relatively higher incidences for most cancer types, with Southern Europe having the highest number of first-ranked cancer types across all categories. Intra-category rankings underscored that breast cancer ranked as the foremost cancer type among AYAs across the majority of regions. However, notable exceptions were observed in Eastern Asia and Eastern/Southern Africa, where thyroid and cervical cancers respectively exhibited the highest incidence rates.

At the national level, the burden of AYA cancer in 2022 showed significant variability across 185 countries or territories (Fig. 3A and Table S10). Malawi recorded both the highest ASIR (78.3 per 100,000 person-years) and the highest ASMR (50.3 per 100,000 person-years), followed by Hungary and Portugal. Conversely, the lowest incidence burden was observed in the United Arab Emirates (9.1 per 100,000 person-years), while Luxembourg had the lowest mortality burden (1.3 per 100,000 person-years). Breast cancer emerged as the most common cancer among AYAs across most countries, dominating both in incidence and mortality (Fig. 3B). In the remaining countries, cervical cancer, thyroid cancer, and Kaposi sarcoma ranked foremost in incidence, while leukemia, brain & CNS cancer, and cervical cancer held top positions in terms of mortality.

HDI-related disparities in burden of AYA cancer

The global burden of AYA cancer varied substantially across the four levels of the HDI, as detailed in

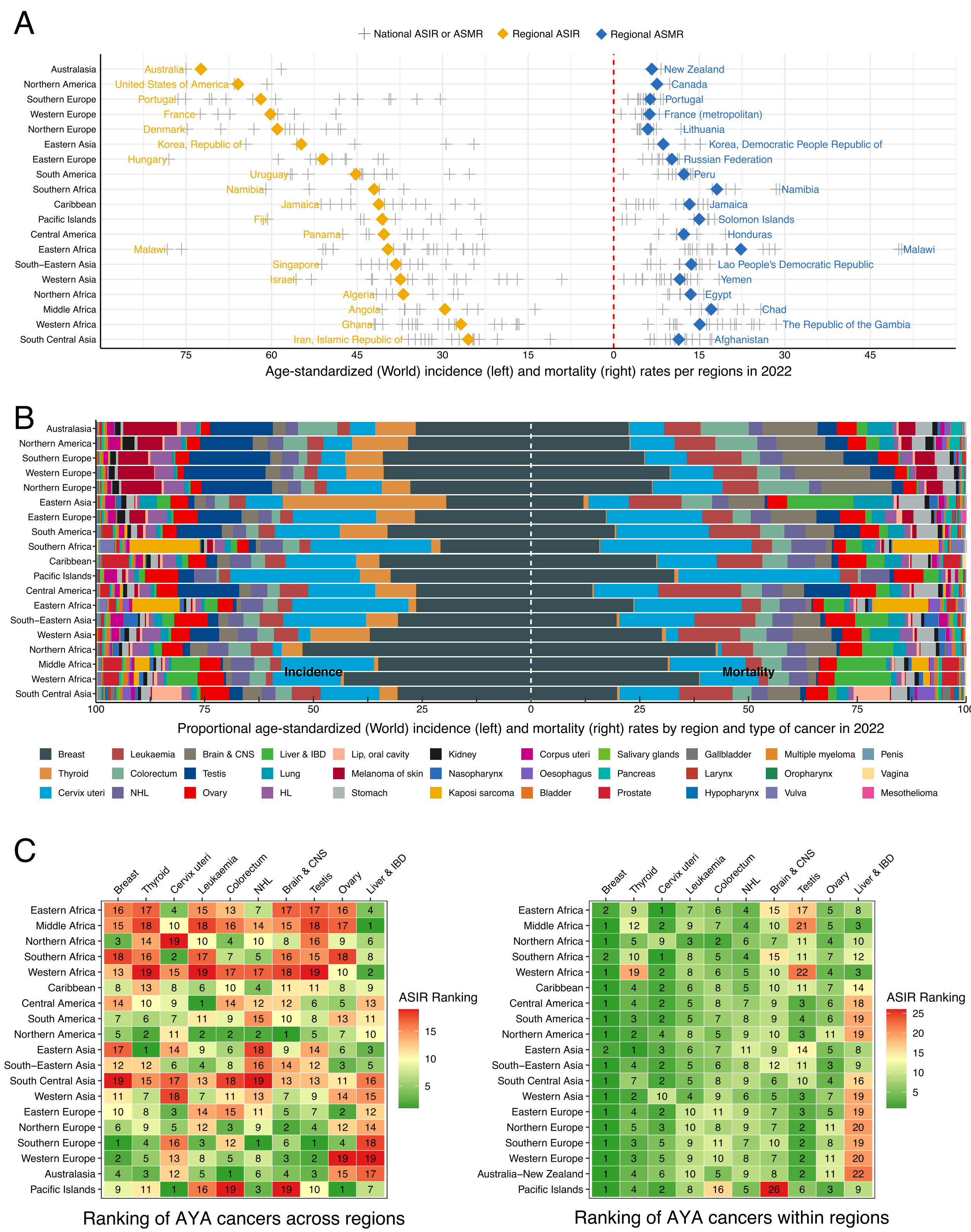

Fig. 2 Regional burden of adolescent and young adult cancers, 2022. **A** Age-standardized incidence and mortality rates by region, with national data included; countries with the highest rates within each region are highlighted. **B** Region-specific proportion of incident cases and deaths. **C** Rankings of the top 10 AYA cancer incidences across and within regions. Abbreviation: *ASIR* age-standardized incidence rate, *ASMR* age-standardized mortality rate, *AYA* adolescents and young adults

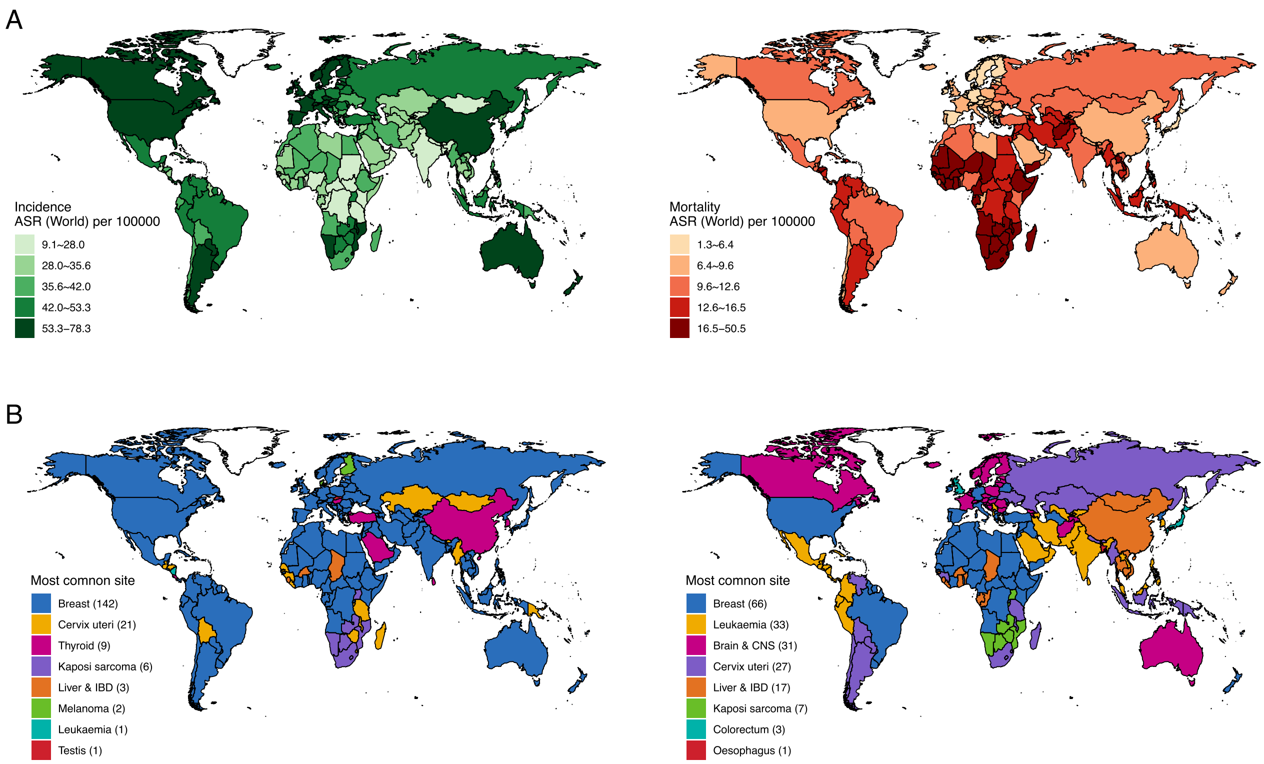

Fig. 3 National burden of adolescent and young adult cancers, 2022. **A** Global maps present the age-standardized rates of incidence and mortality in each country. **B** Global maps present the most common type of cancer incidence and mortality in each country

Table S11 and illustrated in Fig. 4A. The very high HDI countries showed the highest ASIR (54.8 per 100,000 person-years), while the medium HDI countries yielded the lowest (27.2 per 100,000 person-years). Notably, a decreasing step-wise gradient in ASMR was observed with increasing HDI levels; the highest ASMR was observed in the low HDI countries (17.2 per 100,000 person-years), with the lowest occurring in the very high HDI countries (8.4 per 100,000 person-years). Similar patterns were observed when further stratified by sex. Regarding the cancer profiles across HDI levels, the 5 most frequent cancer types accounted for approximately half of the total estimated number of incident cases and cancer deaths (Fig. 4B). Breast cancer accounted for the greatest proportion of new cases in the low, medium, and very high-HDI countries, while thyroid cancer ranked first in the high-HDI countries. Cervical cancer was another significant contributor to AYA cancer cases, representing the top five incident cancers across all HDI levels. These findings corresponded with the rankings of the incidence burden depicted by ASIRs (Fig. 4C). In terms of cancer-related deaths, breast cancer, leukemia, and cervical cancer were among the top five causes across all HDI levels. Breast cancer was the largest contributor to the mortality burden in low and very high-HDI countries, while leukemia was the leading cause of cancer-related death in medium and high-HDI countries.

The relationship between country-level ASIR, ASMR, or MIR, and HDI, are illustrated in Fig. 5A. Unexpected, a non-linear yet exponential relationship was observed between HDI and ASIR ($R=0.55$, $P<0.001$). As the HDI increased, the expected ASIR of AYA cancer initially maintained a relatively stable trajectory. However, a notable shift occurred in countries characterized by high to very high HDI, marking a transition towards an exponential growth pattern. Inconsistent with the disproportionately high ASIR associated with higher HDI, ASMR and MIR both decreased as HDI increased in a linear manner (ASMR: $R=-0.76$, $P<0.001$; MIR: $R=0.89$, $P<0.001$). Furthermore, with the continued elevation of HDI levels, the regional disparities surrounding expected ASMR and MIR gradually diminished. The associations between MIR and HDI stratified by top 10 AYA cancers are summarized in Figure S3. Comprehensive measures monitoring HDI-related inequalities in the burden of AYA cancer are detailed in Fig. 5B and Table S12. These results collectively highlight notable HDI-related health inequalities, both absolute and relative. Countries with higher HDI experience a disproportionately higher incidence of AYA

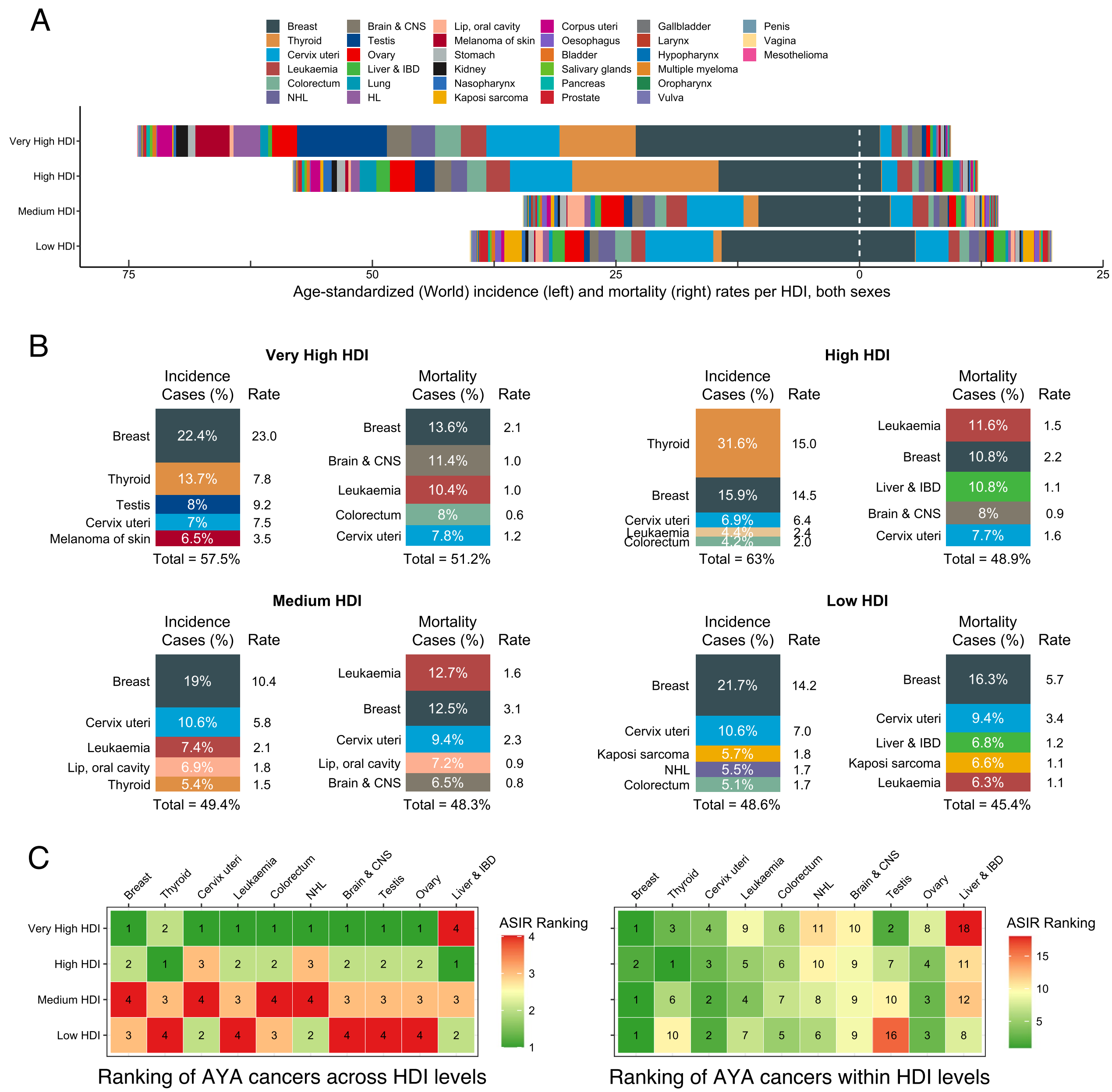

Fig. 4 Burden of adolescent and young adult cancers by HDI level. **A** HDI-specific age-standardized rates of incidence and mortality. **B** HDI-specific proportion and age-standardized rates of incidence and mortality for the 5 most frequent cancers. **C** Rankings of the top 10 AYA cancer incidences across and within different HDI levels. Abbreviation: *HDI* human development index

cancer, whereas countries with lower HDI suffer a disproportionately higher mortality burden.

Evolving trend of AYA cancer

The trends of AYA cancer incidence from 2000 to 2021 showed significant variations across different sexes, leading cancer types, geographical locations, and human development levels, as detailed in Table S13 and illustrated in Fig. 6. Overall, the incidence of AYA cancer slightly rose during the study period (AAPC: 0.17 [95% CI 0.09–0.24]), with the increase predominantly among females (AAPC: 0.22 [95% CI 0.15–0.29]) and rates remaining stable in males (AAPC: 0.09 [95% CI −0.02 to 0.19]) (Fig. 6A). It's noteworthy that the incidence of AYA cancer remained stable at the first decade and then followed an evident uptrend in the last decade, regardless of gender. Increases in the incidence of leading AYA cancer such as thyroid cancer, testicular cancer, breast cancer,

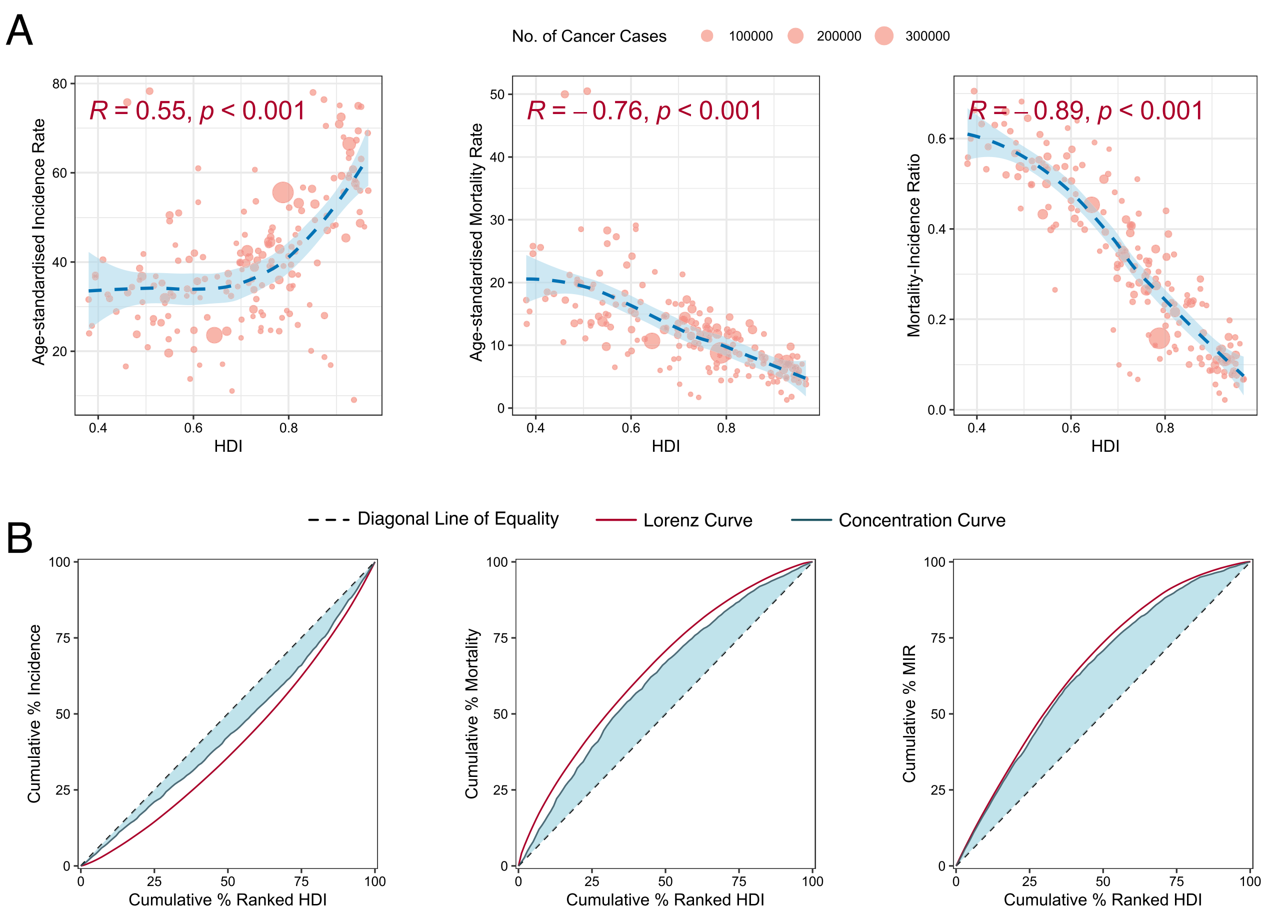

Fig. 5 HDI-related inequalities in burden of adolescent and young adult cancers, 2022. **A** Associations between the age-standardized incidence rate, age-standardized mortality rate, and incidence-mortality ratio with HDI. Each dot represents a country, with the size of the dot indicating the number of incidental cases in that country. **B** Concentration curve illustrating HDI-related inequalities in age-standardized rates and incidence-mortality ratio. Abbreviation: *HDI* human development index

ovarian cancer, brain & CNS cancer, colorectal cancer, and non-Hodgkin lymphoma were recorded (Fig. 6B). In contrast, significant decreases were noted in liver cancer and leukemia. Nationally, Saudi Arabia (AAPC: 3.00 [95% CI 2.68–3.31]) experienced the most significant increase, while Luxembourg (AAPC: −2.15 [95% CI −2.60 to −1.70]) saw the largest decline (Table S13 and Figure S2). Regionally, the most pronounced increase was observed in Western Asia (AAPC: 1.38 [95% CI 1.22–1.54]), and the most notable decline in Southern Africa (AAPC: −1.85 [95% CI −2.89 to −0.79]) (Fig. 6C). When assessed by human development levels, incidence in very high HDI countries remained stable (AAPC: −0.02 [95% CI −0.13 to 0.09]), whereas significant increases were observed in countries with low to high HDI, with the most substantial rise noted in the high HDI countries (AAPC: 0.93 [95% CI 0.76–1.10]) (Fig. 6D).

Substantial decreases in the ASMR of AYA cancer were observed for both sexes throughout the study period (Fig. 6A and Table S13). Mortality declines in leading AYA cancer included liver cancer, leukemia, cervical cancer, non-Hodgkin lymphoma, colorectal cancer, and brain & central nervous system cancer (Fig. 6B). Conversely, significant increases were recorded in testicular cancer, breast cancer, and ovarian cancer. The vast majority of regions experienced significant declines in AYA cancer mortality, with the exceptions of Northern Africa and Central America (Fig. 6C). Moreover, a significant decline in ASMR was observed across all human development levels, with more pronounced decreases in regions with higher HDI (Fig. 6D). Notably, the downtrend in the ASMR of AYA cancers slowed in the past decade, manifesting as a slowdown decline in ASMR in more regions or an accelerated increase in ASMR in some hormone-related cancers, such as testicular cancer, breast cancer, and ovary cancer (Figure S4 and Table S14).

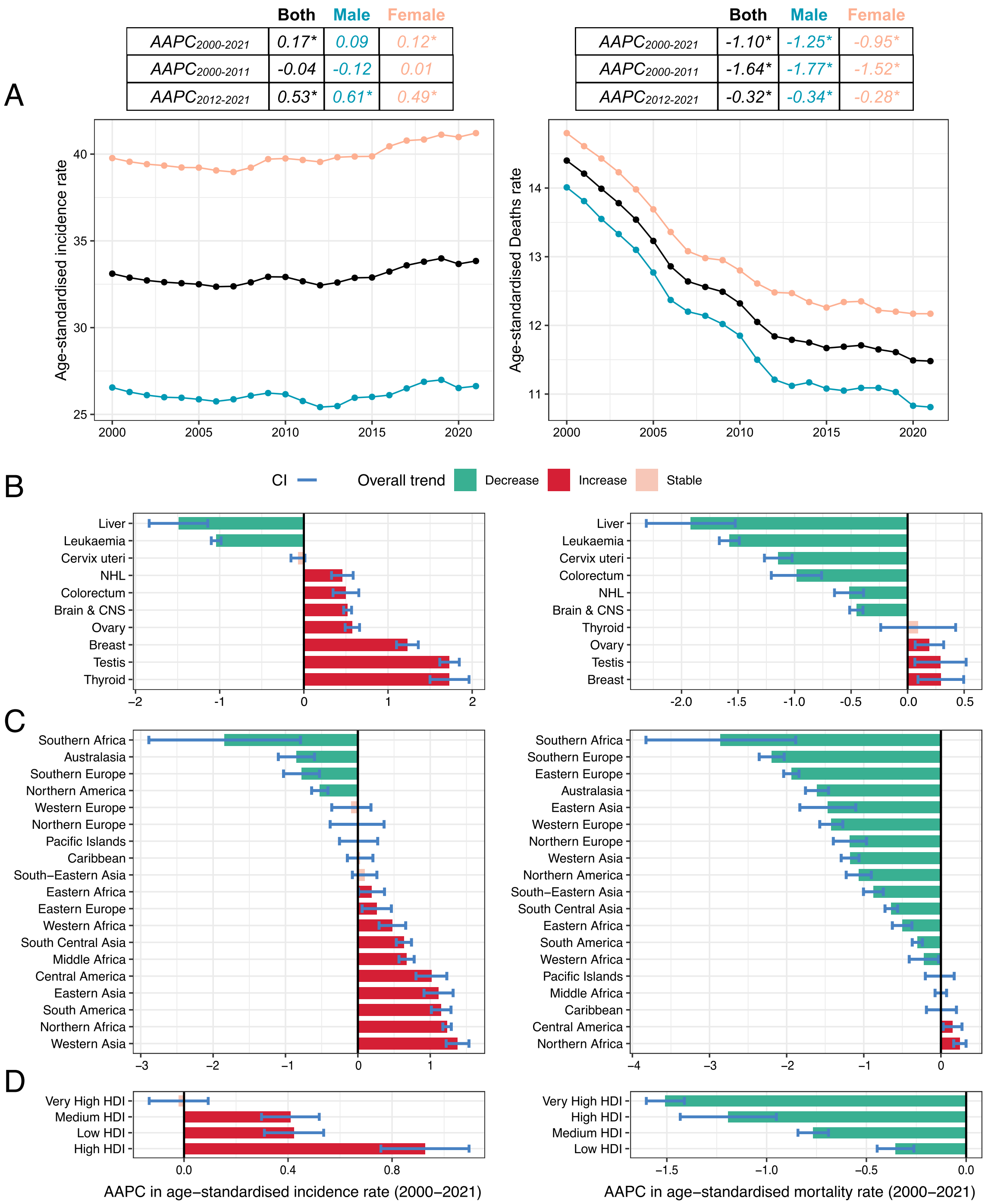

Fig. 6 Temporal trend in burden of adolescent and young adult cancers from 2000 to 2021. **A** By sex. **B** By the 10 most frequent cancer type. **C** By region. **D** By HDI. Abbreviation: *AAPC* average annual percent change, *HDI* human development index. Source: The Global Burden of Disease Study 2021

Discussion

To the best of our knowledge, this study is the first to provide a comprehensive and up-to-date evaluation of the global burden and emerging trend of AYA cancer by integrating the two most well-established cancer databases. Our research updates and expands the epidemiological evidence concerning the cancer burden in this demographic, offering detailed profiles and new insights. We confirm the substantial burden of cancer among AYAs and identify an upward trend of incidence alongside a slowdown decline in mortality rates in recent years. Most importantly, our analysis also uncovers significant variations in the cancer burden and trend within the AYA population, with disparities based on age, sex, geographic location, and human developmental level.

The extended AYA age range of 15–39 years, as proposed by the Adolescent and Young Adult Oncology Progress Review Group, includes more common epithelial carcinomas typically seen in older adults, such as breast, cervical, and colorectal cancers, leading to a significantly altered cancer profile distribution [6, 10, 14]. In line with previous studies, our results have confirmed the notably heterogeneity in spectrum of cancer by age group within this patient population [3, 15, 18]. A defining feature of cancer epidemiology in AYAs is the predominance of females [23]. Our results showed that the incidence rate of AYA cancers in females was 1.9 times higher than that in males. Our study results emphasize the effectiveness of these cancer control measures, as evidenced by the curbed increase in the incidence rate of cervical cancer and the continuous decline in the incidence rate of liver cancer during the study period. While many AYA cancers are not strongly influenced by behavioral risk factors such as tobacco, alcohol, or nutrition, they may interact synergistically with other risk factors. Given the noticeable increase in obesity-related cancers, maintaining a healthy weight, engaging in regular exercise, limiting alcohol intake, and avoiding smoking remain effective and cost-efficient preventive strategies for reducing incidence and improving prognosis in AYAs.

Our study revealed that the incidence rate of AYA cancers has shown a noticeable increase in the past decade, largely driven by the fast increase of colorectal cancer and gonadal cancers. This has led to a slowdown in the decline of adolescent and young adult cancer mortality rates since 2012, in stark contrast to the significant decreases seen in earlier years. Our findings are to some extent consistent with established epidemiological data indicating that the demographics of cancer patients are increasingly shifting from older individuals to younger people [2, 24]. Previous studies have identified such common cancers as breast, thyroid, colorectal and cervical cancers are increasing in people younger than 50. In our analysis, cancers closely related to hormones or obesity, such as testicular cancer, breast cancer, thyroid cancer, ovarian cancer, and colorectal cancer, have shown the most significant increase. Such increases may reflect shifts in lifestyle, rising obesity rates, evolving environmental risk factors, and improvements in screening and early detection technologies [25]. Prospective life-course cohort studies that incorporate biomarker and omics analyses of specimens collected during early life are essential for understanding the etiology behind the rising incidence of AYA cancers and for developing targeted prevention strategies. Additionally, the role of overdiagnosis cannot be overlooked, particularly for cancers like thyroid, breast, and testicular cancers, where enhanced screening and early detection methods may identify slow-growing or indolent tumors. Studies have indicated that these cancers are among those most commonly subject to overdiagnosis [26–28]. This raises important questions about the balance between early detection and the potential harms of unnecessary treatment.

Our study confirmed significant HDI-related health inequalities in the burden of AYA cancers, with high and very high-HDI countries experiencing markedly higher incidence rates. The disproportionately higher incidence of AYA cancers in these regions can be attributed to several factors, including variations in genetic predispositions and risk factor exposures, differences in detection and diagnostic capabilities, the implementation of preventive and public health measures, and incomplete data collection and reporting mechanisms in low-HDI settings [29, 30]. In our study, breast, thyroid, and testicular cancers, often linked to germline mutations when they occur in young individuals, are identified as major contributors to the higher incidence of AYA cancers in high and very high HDI countries. Consistent with the GLOBOCAN 2012 study, our findings reveal that the burden of thyroid cancer is significantly greater in high and very high-HDI countries, with incidence rates being ten times higher than in low and middle-HDI countries [15]. This correlation with human development levels likely reflects changes in diagnostic practices of thyroid cancer in high-income Western countries and East Asia over the past decades [26, 31]. On the other hand, the cancer burden reported for low HDI countries, such as sub-Saharan Africa, might be underestimated due to limited access to appropriate diagnosis and care, constraints in technical workforce and infrastructure, and low-quality cancer data systems compared with those in developed countries [29].

Our analysis showed considerably higher mortality rates for most AYA cancers in lower HDI countries compared to higher HDI countries. This is unexpected, as low HDI countries had disproportionate low incidence rates for AYA cancers. However, variations in mortality reflect not only differences in incidence but also disparities in cancer spectrum, early diagnosis, healthcare availability, and other factors [32, 33]. Consistent with previous epidemiological data, AYA cancers in low HDI countries are more likely to be fatal, while cancers with better prognoses are more common in high HDI countries [15]. In addition to differences in the distribution of cancer types, variation in mortality within the same cancer type also contributes to the higher cancer mortality observed in low HDI countries. For many AYA cancers, such as breast, cervical, and non-Hodgkin lymphoma, where mortality can be effectively reduced through active prevention, early diagnosis, and effective treatment, we observed that the MIR is more strongly correlated with HDI. These findings collectively support the opportunity and importance of improving healthcare systems to reduce AYA cancer mortality in low HDI countries.

In this study, we have for the first time combined the latest cancer data from GBD 2021 and GLOBOCAN 2022 to assess the global burden of cancer among adolescents and young adults, offering several significant advantages. Due to methodological improvements and the inclusion of more population-based cancer registry data, the current iterations of both GBD 2021 and GLOBOCAN 2022 provide more accurate and reliable estimates than previous data. More specifically, GBD offers extensive time trend and multidimensional health data, while GLOBOCAN focuses on detailed cancer burden data. This complementarity allows for a more comprehensive analysis, providing valuable information to policymakers and researchers, thereby enhancing global cancer prevention and control efforts. However, there are important limitations to acknowledge. Firstly, integrating and comparing data from GBD 2021 and GLOBOCAN 2022 can be complex due to the different modeling methods and data sources used by each, inevitably leading to some data inconsistencies [34]. In this study, we did not integrate the data but conducted sectional and longitudinal analyses separately, using uniformed standardized age groups and country classifications. Therefore, it is essential to consider the specific limitations of each database when processing and interpreting the relative results. Secondly, the accuracy of cancer burden estimates in both the GBD and GLOBOCAN databases largely depends on the original data reported by cancer registries and vital registration systems worldwide. This implies that in some developing countries lacking healthcare resources and reliable registration systems, insufficient cancer diagnosis and reporting may result in underestimated cancer burden estimates [29]. Currently, both the International Agency for Research on Cancer and the Institute for Health Metrics and Evaluation are committed to collaborating with partners worldwide to produce timely, pertinent, and scientifically sound evidence that sheds light on global health conditions. Lastly, the COVID-19 pandemic caused significant disruptions to cancer services, resulting in major delays in diagnosis and treatment. The GLOBOCAN 2022 estimates do not account for the pandemic's impact, as they are primarily based on pre-2020 data, leaving the long-term effects on cancer survival and mortality uncertain.

Conclusions

This study updates and expands the epidemiological evidence on the global burden and trends of AYA cancers, emphasizing the substantial and growing cancer burden. Significant HDI-related health disparities were confirmed in the burden of AYA cancers, with gonadal cancers showing the most pronounced increase in incidence and mortality over the past decade. Policymakers should prioritize equitable resource allocation and implement targeted interventions to address these disparities, particularly in low-HDI regions and with regard to gonadal cancers.

Abbreviations

AYA	Adolescents and young adult
GLOBOCAN	Global Cancer Observatory
GBD	Global Burden of Disease
AYAOPRG	Adolescent and Young Adult Oncology Progress Review Group
ICD	International Classification of Diseases
NMSC	Non-melanoma skin cancer
HDI	Human development index
MIR	Mortality-to-incidence ratio
ASR	Age-standardized rate
ASIR	Age-standardized incidence rate
ASMR	Age-standardized mortality rate
AAPC	Average annual percent change
APC	Annual percent change

Supplementary Information

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Supplementary Material 1.

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Author contributions

WZL and JXH conceived and designed the study. JXH, WHL, WW, and JL supervised the study. WZL, HRL and XWL designed the statistical analysis plan and WZL performed the statistical analysis. All authors contributed to the acquisition, analysis, verification, or interpretation of data. WZL drafted the manuscript. All authors revised the manuscript and gave final approval of the version to submission. JXH and WHL contributed equally to this work and are joint corresponding authors.

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Availability of data and materials

All analyzed data are retrieved from the GBD 2021 results available online at the Institute for Health Metrics and Evaluation (IHME) (https://vizhub.healthdata.org/gbd-results/) and the International Agency for Research on Cancer's

(IARC) GLOBOCAN 2022 estimates available online at the GCO (https://gco.iarc.who.int). The processed data generated in this study are included in this article and its supplementary files. Any other information are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was not required for this study, as it utilized publicly available, anonymized data aggregated at the population level.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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