Cancer Incidence and Mortality among Children and Adolescents: a Narrative Review

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Incidência e Mortalidade por Câncer entre Crianças e Adolescentes: uma Revisão Narrativa

Incidencia y Mortalidad por Cáncer entre Niños e Adolescentes: una Revisión Narrativa

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Abstract

Introduction: Cancer in children and adolescents aged 0-19 years is a public health problem in both developed and developing countries. It is considered rare and distinct when compared to cancer in adults. They present patterns of incidence and mortality vary throughout the world, with approximately 80% of childhood cancers occurring in low human development countries, with access to poor quality health care services. **Objective:** To present an overview of cancer in children and adolescents aged 0-19 years, with an emphasis on describing the results of population-based studies for incidence and mortality in different geographic regions in the World and Brazil. **Results:** Overall cancer incidence rates in children and adolescents aged 0-19 years old ranged from 50 to 200 cases per million per year in different countries and continents. In Brazil, the median incidence rates were 154.3 per million. Mortality declined in several parts of the world, being considered the second cause of death in developed countries. **Conclusion:** The information from the cancer registries are indispensable in coping with cancer in the pediatric population, especially in developing countries, where the impact of cancer is poorly understood, while its effect on the population is increasing. Improvements in the adoption of integrated treatment strategies should be considered to improve cancer mortality rates in children and adolescents in Brazil and in the World.

Key words: Adolescent; Child; Incidence; Mortality; Neoplasms; Electronic Health Records.

Resumo

Introdução: O câncer em crianças e adolescentes com idade entre 0-19 anos configura-se como um problema de saúde pública tanto nos países desenvolvidos como nos países em desenvolvimento. É considerado raro e distinto quando comparado com o câncer em adultos. Apresenta padrões de incidência e mortalidade que variam em todo mundo, sendo que aproximadamente 80% dos cânceres infantis ocorrem nos países com baixo índice de desenvolvimento humano, com acesso aos serviços de cuidado à saúde de baixa qualidade. **Objetivo:** Apresentar um panorama geral do câncer em crianças e adolescentes com idade entre 0-19 anos com ênfase na descrição dos resultados de estudos de base populacional para incidência e mortalidade nas diferentes regiões geográficas no Mundo e no Brasil. **Resultados:** As taxas de incidência gerais para o câncer em crianças e adolescentes com idade entre 0-19 variaram entre 50 e 200 casos por milhão por ano em diferentes países e continentes. No Brasil, a mediana das taxas a incidência foi de 154,3 por milhão. A mortalidade apresentou declínio em várias partes do mundo, sendo considerada a segunda causa de morte em países desenvolvidos. **Conclusão:** As informações dos registros de câncer são indispensáveis no enfrentamento do câncer na população pediátrica, principalmente nos países em desenvolvimento, onde o impacto do câncer é pouco conhecido, ao passo que seu efeito sobre a população está aumentando. Melhorias na adoção de estratégias de tratamento integrado devem ser consideradas para melhorar as taxas de mortalidade por câncer em crianças e adolescentes no Brasil e no Mundo.

Palavras-chave: Adolescente; Criança; Incidência; Mortalidade; Neoplasias; Registros Eletrônicos de Saúde.

Resumen

Introducción: El cáncer en niños y adolescentes de entre 0-19 años se configura como un problema de salud pública tanto en los países desarrollados y en los países en desarrollo. Se considera raro y distinto cuando se compara con el cáncer en adultos. Se presentan patrones de incidencia y mortalidad que varían en todo el mundo, siendo que aproximadamente el 80% de los cánceres infantiles ocurren en los países con bajo índice de desarrollo humano, con acceso a los servicios de cuidado de la salud de baja calidad. **Objetivo:** Presentar un panorama general del cáncer en niños y adolescentes con edad entre 0-19 años con énfasis en la descripción de los resultados de estudios de base poblacional para incidência y mortalidad en las diferentes regiones geográficas en el Mundo y en Brasil. **Resultados:** Las tasas de incidencia general para el cáncer en niños y adolescentes de entre 0-19 varían entre 50 y 200 casos por millón por año en diferentes países y continentes. En Brasil, la mediana de las tasas la incidencia fue de 154,3 por millón. La mortalidad ha disminuido en varias partes del mundo, siendo considerada la segunda causa de muerte en los países desarrollados. **Conclusión:** La información de los registros de cáncer es indispensable en el enfrentamiento del cáncer en la población pediátrica, principalmente en los países en desarrollo, donde el impacto del cáncer es poco conocido, mientras que su efecto sobre la población está aumentando. Las mejoras en la adopción de estrategias de tratamiento integrado deben ser consideradas para mejorar las tasas de mortalidad por cáncer en niños y adolescentes en Brasil y en el Mundo.

Palabras clave: Adolescente; Niño; Incidencia; Mortalidad; Neoplasias; Registros Electrónicos de Salud.

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INTRODUCTION

Pediatric cancer, defined as cancer in children and adolescents from 0 to 19 years of age[1-3], is a public health problem in both developed and developing countries. It is considered rare when compared to cancer in adults, accounting for only a small proportion of the global burden of cancer, ranging from 0.5% to 4.6% of all malignant tumors[4-6], and with approximately 80% of pediatric cancers occurring in countries with low human development indices (HDI) and low-quality access to healthcare services[6,7].

Pediatric cancers are distinct entities from the cancers occurring in adults and should be studied separately due to the differences in primary sites, histological origins, and clinical presentation[8]. While cancer in adults is associated with various risk factors such as smoking, diet, occupation, and exposure to other carcinogenic agents, the causal associations in pediatric cancer have been explored less and the possible mechanisms involved in this process remain largely unknown[4-5]. Studies suggest an association with genetic, hereditary, and immunological predisposition, environmental exposure to genotoxic agents, ionizing radiation, electromagnetic fields, and others[9-11].

Studies that allow assessing epidemiological characteristics and differences in developed and developing countries are essential, since these populations are exposed to different environments, socioeconomic conditions, and risk factors[12]. The identification of these geographic differences, especially in genetically related populations, can provide backing for possible etiological associations and has been used to support hypotheses on the association between lifestyle exposures and the risk of pediatric cancer, especially leukemia[13].

Data from population-based cancer registries (PBCR) on incidence and mortality contribute not only to understanding the etiology of the disease, but also to monitoring changes in the impact, quality of care, and treatment of pediatric cancers[12].

Given the above, this review aims to present an overview of cancer in children and adolescents 0-19 years of age, emphasizing the results of population-based studies on incidence and mortality in different geographic regions of the world and Brazil.

Classification of cancer in children and adolescents

Cancer in children (0-14 years) has its own classification, the International Classification of Childhood Cancer, third edition (ICCC-3). Based on morphology rather than primary tumor site (as in adults), this classification was designed for international epidemiological purposes and standardization of information in population-based registries, allowing comparison of information on incidence and survival in different regions and time periods. The use of an international classification system is especially important in the field of pediatric oncology, in which the low incidence requires rigorous procedures to ensure comparability of the case series [14].

ICCC-3 classifies cancer in 12 main groups, subdivided into 47 subgroups: I. leukemias and myeloproliferative and myelodysplastic diseases; II. lymphomas and reticuloendothelial neoplasms; III. central nervous system and miscellaneous intracranial and intraspinal neoplasms; IV. tumors of the sympathetic nervous system; V. retinoblastoma; VI. renal tumors; VII. hepatic tumors; VIII. malignant osseous tumors; IX. soft tissue sarcomas; X. germ cell, trophoblastic, and other gonadal neoplasms; XI. carcinomas and other malignant epithelial neoplasms; XII. other malignant tumors not otherwise specified [14].

Cancer in adolescents and young adults (15-24 years) presents a different pattern from that in children and adults. In 2002, Birch *et al.*[15] proposed a specific classification for this age bracket, the Brazilian version of which is called the Classification Scheme for Tumors in Adolescents and Young Adults (CAAJ in Portuguese), which has been incorporated by Brazil's population-based cancer registries since 2015.

Cancer epidemiology children and adolescents

Studies have shown that cancer incidence in children and adolescents differs between geographic regions and has increased over time in all age brackets. An annual increase of approximately 1% has been seen in the last three decades in Europe, North America, Australia, and elsewhere, although the upward rate appears to have stabilized in the last decade[16-19].

PBCR around the world have reported overall annual childhood cancer incidence rates ranging from 50 to 200 cases per million children in different countries. The range of tumor types differs between populations[17,20-29], with particularly rare childhood tumors having incidence rates varying from 1 per million, such as hepatoblastoma, to 50 per million for the most common subgroup, acute lymphoblastic leukemia (ALL)[2].

The explanation for differences in total incidence worldwide is largely unknown, although it probably relates to differences in exposure to risk factors, together with genetic factors that affect the individual's likelihood of developing cancer[30]. In equatorial Africa, for example, Burkitt's lymphoma accounts for some 50% of all childhood cancers, and the AIDS epidemic in many African countries led to a substantial increase in Kaposi's sarcoma, which shows a higher incidence than Burkitt's lymphoma in these regions[30-32]. In addition, some types of

cancer can vary according to the degree of socioeconomic development, such as ALL, very common especially in countries with populations with high socioeconomic status. Evidence of this is provided by the drop in the incidence of Burkitt's lymphoma and the increase in ALL incidence in the Gaza Strip, coinciding with a period of rapid economic growth[33]. Another cancer related to economic status is non-hereditary retinoblastoma, with a higher incidence in less developed populations, suggesting an association with low socioeconomic status and perhaps an infectious etiology. Contrasting with this, the incidence of Wilms' tumor and Ewing's sarcoma varies widely along ethnic lines, suggesting an important role for genetic predisposition. These tumors may originate from embryonic cells that persist after birth, or from intrauterine oncogenic events[1,4,30-36].

Global cancer incidence in children and adolescents

Based on estimates from GLOBOCAN 2012, global cancer incidence in children 0-14 years of age for all types of cancer except non-melanoma skin cancers was 88 per million, or 98 per million in boys and 76 per million in girls. In more developed regions it was 145 per million, compared to 81 per million in less developed regions. In North America (Canada and USA) it was 165 per million, in Europe 139 per million, Oceania 120 per million, Latin America and the Caribbean 109 per million, Africa 85 per million, and Asia 75 per million[6].

A European study based on data from the *Automated Childhood Cancer Information System* (ACCIS) analyzed cancer trends in children and adolescents. The study analyzed 62 PBCR located in 19 European countries, totaling 113 thousand new cancer cases in children (0-14 years) and 18 thousand in adolescents (15-19 years) from 1970 to 1999. In the 1990s, age-adjusted incidence rates were 140 per million in children and 157 per million in children and adolescents (0-19 years). In three decades, global incidence increased 1.0% per year in children, with an increase in most types of tumors, and 1.5% in adolescents[1].

As for distribution of tumors by age bracket, neuroblastoma (28%) was the most frequent type of tumor of infants under 1 year of age. In children 1-4 years of age, the most frequent cancers were leukemias (41%), and in the 5-9-year group they were CNS tumors (28%). From 10 years upward, embryonic tumors like retinoblastoma, nephroblastoma, and hepatoblastoma nearly disappeared, while other cancers became more frequent, mainly lymphomas, carcinomas, germ cell tumors, and osseous tumors. In adolescents, lymphomas accounted for 25% and carcinomas 20% of the total. As for incidence, the most frequent types of tumors in children were leukemias, with 44.8 per million, CNS tumors (29.8 per million), and lymphomas (15.5 per million). In adolescents, the highest incidence rates were in lymphomas (47.4 per million), carcinomas (38.1 per million), CNS tumors (24.6 per million), germ cell tumors (24.5 per million), and leukemias (23.4 per million)[1].

Steliarova-Foucher *et al.*[37] recently analyzed a decade of information (2001-2010) from 153 registries in 62 countries, departments, and territories. Overall age-adjusted incidence was 140.6 per million in children (0-14 years) and 155.8 per million in 0-19 years of age. The most common cancers were leukemia (46.4 per million), followed by CNS tumors (28.2 per million), and lymphomas (15.2 per million). In adolescents 15-19 years of age, age-specific incidence was 185.3 per million, and the most common cancers were lymphomas (41.8 per million) and the group of epithelial tumors and melanoma (39.5 per million). Incidence also varied considerably by region, type of cancer, sex, age, and ethnic group. Since the 1980s, the overall rate of cancers in children 0-14 years of age also increased from 124.0 to 140.6 per million.

In the United States, two studies based on data from the *Surveillance, Epidemiology, and End Results (SEER) Program* analyzed cancer incidence in children and adolescents. Siegel *et al.*[38] found age-adjusted incidence of 171.01 per million from 2001 to 2009. The overall rate for all cancers combined remained stable over time, with an increase in the overall trend for African-Americans 0-19 years of age (annual percent change, APC:1.3% [95%CI: 0.2;2.5]), and for thyroid cancer in both sexes (APC: 4.9% [95%CI: 3.2;6.6]) and specifically among adolescents and in the Northeast, South, and West of the USA, and renal carcinoma (APC: 5.4% [95%CI: 2.8;8.1]). Extracranial and extragonadal germ cell tumors and melanoma showed decreasing rates. Burkhamer, Kriebel, and Clapp[39] found that incidence from 1975 to 2012 increased by 0.67% a year in males and 0.62% in females, resulting in a total increase of more than 25% in 38 years. The largest annual increases in incidence were in non-Hodgkin lymphoma (NHL) (2.16% in females; 1.38% in males), thyroid cancer (2.12% in females; 1.59% in males), acute myeloid leukemia (AML) (1.73% in females), and testicular cancer (1.55% in males).

Cancer incidence in children and adolescents in Brazil

In Brazil, based on data from PBCR, the median percentage of tumors in the pediatric population (0-14 years) was 2%, while in children and adolescents (0-19 years) it was 3% and in adolescents and young adults (15-29 years) it was 4.3%. Among the neoplasms, leukemia was the most frequent type of cancer with 33% for cases in the age group 0-14 years and 26% in the 0-19-year bracket. In the age group 0-14 years, CNS tumors were

the second most frequent tumor, with 16%, followed by lymphomas with 14%, while in the age group 0-19 years, lymphomas were the second most frequent tumor, followed by CNS tumors, with 14% and 13%, respectively. Adolescents and young adults showed a different pattern from other age brackets. The carcinomas group was the most frequent with 34%, followed by lymphomas (12%) and skin tumors, including melanomas and carcinomas (9%). Leukemias in this age bracket accounted for 8% of all neoplasms, with median incidence rates of 21.21 per million in both sexes. Overall age-adjusted incidence was 126.65 per million in children 0-14 years, 139.99 per million in the 0-19-year bracket, and 236.16 per million in the 15-29-year bracket[40].

In the last decade, three Brazilian studies analyzed data on childhood cancer incidence[41-43]. De Camargo *et al.*[41] analyzed data on childhood cancer incidence in 14 PBCR (corresponding to 15% of the population of Brazilian children and adolescents) and showed median rates of 154.3 per million children and adolescents 0-19 years of age. Children 1-4 years of age showed the highest incidence rates. In all 14 PBCR, leukemia was the most frequent cancer, with rates ranging from 67.5 per million in Goiânia to 21.0 per million in Salvador, followed by lymphoma and CNS tumors in most of the PBCR. De Camargo *et al.*[42] analyzed childhood cancer incidence rates according to socioeconomic status (SES) in the regions for embryonic tumors such as retinoblastoma, neuroblastoma, Wilms' tumor, and medulloblastoma. Regional variations were observed, directly associated with SES, mainly for neuroblastoma and retinoblastoma rates. Ferreira *et al.*[43] analyzed the incidence of lymphomas in children and adolescents according to social exclusion index (SEI) as a proxy for socioeconomic status, and found that higher SEI correlated with higher incidence of Hodgkin's lymphoma (HL) (p=0.06), but without reaching statistical significance.

Cancer mortality in children and adolescents

Mortality rates in children and adolescents with cancer have also shown different geographic patterns, as well as a decline in various parts of the world[44-45]. In developed countries, cancer is the second leading cause of death in children 0-14 years of age, accounting for approximately 5% of deaths in this age bracket. The proportion is lower in developing countries (approximately 1%), due to the deaths caused by infectious diseases[2].

Global cancer mortality in children and adolescents

Based on GLOBOCAN 2012 estimates, global cancer mortality in children from all types of types of cancer (except for non-melanoma skin cancer) was 43 per million, or 48 per million in males and 38 per million in females. In less developed regions it was 45 per million, and in the more developed regions it was 26 per million. It was 50 per million in Africa, 45 per million in Latin America and the Caribbean, 43 per million in Asia, 31 per million in Oceania, 29 per million in Europe, and 23 per million in North America (Canada and USA)[6].

In Europe, based on data from the World Health Organization (WHO), Bosetti *et al.*[44] found that childhood cancer mortality decreased continuously from 1990 to 2007 (from 52 to 35 per million in boys and from 43 to 28 per million in girls). However, there were differences in mortality patterns by geographic region. In 2005-2007, childhood cancer mortality rates were higher in countries of Eastern Europe (49 and 39 per million in boys and girls, respectively) and Southern Europe (40 and 31 per million in boys and girls, respectively) when compared to Western Europe (31 and 25 per million in boys and girls, respectively) and Northern Europe (32 and 25 per million in boys and girls, respectively).

Chatenoud *et al.*[45], assessing childhood cancer mortality patterns in various areas of the world, analyzed WHO mortality data from 24 countries of the Americas, Asia, and Oceania from 1970 to 2007. Starting in 1970, mortality from all childhood cancers decreased from approximately 80 to 30 per million boys and from 60 to 20 per million girls in North America and Japan. Latin American countries reported rates of approximately 50 and 40 per million boys and girls, respectively, in 2005-2007, and similar to the rates reported in more developed regions in the early 1980s. In addition, analyses of geographic patterns and time trends in various countries showed that in the last 35 years, childhood cancer mortality decreased by approximately 60% in countries like the USA, Canada, and Puerto Rico, meaning the prevention of approximately 2,800 deaths per year.

In the United States, Smith *et al.*[46], aimed at assessing progress in cancer treatment, analyzed cancer mortality trends in children and adolescents under 20 years of age from 1975 to 2010. Their analysis showed that cancer mortality in this age bracket underwent a significant decline from 2002 to 2010 (APC: -2.4% [95%CI: -3.2;-1.7]), similar to that seen in 1975-1998 (APC -2.7% [95%CI: -2.8;-2.5]). Significant declines in mortality were seen in all age groups (<20 years, 15-19 years, and <15 years). The age group <20 years showed a significant decline in ALL (APC: -3.1), AML (APC: -2.3), NHL (APC: -4.40), HL (APC: -7.6), and ganglioneuroblastoma (APC: -1.9), CNS tumors (APC: -1.1), and gonadal tumors (APC: -6.1). In addition, from 2000 to 2010 the age group 15-19 years showed mortality rates greater than or equal to the age group <15 years.

Ferlay *et al.*[6], Bosetti *et al.*[44], and Chatenoud *et al.*[45] reported the rates in per 100 thousand, but for purposes of comparison we converted them to per million.

Cancer mortality in children and adolescents in Brazil

In Brazil, Ferman *et al.*[47] analyzed childhood cancer mortality (0-14 years) in the country's five major geographic regions over the course of three decades. In general, age-adjusted mortality rates showed a trend towards stability throughout the country (36.91 deaths per million in 1979 and 39.83 deaths per million in 2008), with a decrease in childhood cancer mortality rates in the South and Southeast (1.2 to 1.6% per year, respectively), stability in the Central-West, and an increase in the North and Northeast. Mortality from all childhood cancers from 1979 to 2008 showed a slight but significant decline (approximately 0.5% per year) in boys (average annual percent change, AAPC: -0.34), and stability in girls (AAPC: -0.03). When tumors were analyzed separately, mortality from leukemia decreased significantly throughout the period (14.33 deaths per million in 1979 and 13.83 deaths per million in 2008).

Another Brazilian study analyzed trends in cancer mortality among adolescents and young adults 15-29 years of age in 1979-2013. This study found mortality rates of 54 per million in the 15-19-year group, 61 per million in the 20-24-year group, and 88 per million in the 25-29-year group. Leukemias, lymphomas, and CNS tumors showed the highest rates in all the age groups. Uterine cervical cancer rates were highest in the 25-29-year age group. There was a significant increase in mortality trends in the North and Northeast for all groups of tumors, especially CNS tumors. A small decrease in the mortality rate from lymphomas was observed in the South and Southeast[48].

The Brazilian National Cancer Institute José Alencar Gomes da Silva (INCA)[40], in its most recent publication on cancer mortality in children, adolescents, and young adults in Brazil, found cancer to be the second leading cause of death in children, adolescents, and young adults (0-29 years). In 2009-2013, the mean age-adjusted mortality rate was 32.07 per million in the age bracket 0-14 years, 44.22 per million in the age bracket 0-19 years, 54.01 per million in the age bracket 15-19 years, and 66.97 per million in the age bracket 15-29 years. Among the leading causes of death from cancer in children 0-14 years of age, leukemias showed the highest mortality rate (14.94 deaths per million), followed by CNS tumors (10.26 deaths per million), and NHL (2.70 deaths per million) in both sexes. The same pattern was maintained in adolescents and young adults (15-29 years), with leukemias as the type of cancer with the highest mortality (13.96 deaths per million), followed by CNS tumors (9.56 per million) and NHL (5.14 per million), while uterine cervical cancer was the leading cause of cancer mortality in females 25-29 years of age.

CONCLUSION

This review reports the results of analyses performed in the last decade on cancer incidence, mortality and trends in children and adolescents, furnishing up-to-date information on the overall scenario and behavior of the disease in various geographic regions. Data from cancer registries are thus essential for dealing with cancer in the pediatric population, especially in developing countries, where little is known about the impact of cancer, while its effect on the population is increasing. The elucidation of the extent of cancer in this population allows cancer control programs to be planned efficiently, implementing not only prevention strategies, but also standards of care through improvement in the adoption of comprehensive treatment strategies in order to improve cancer mortality rates in children and adolescents in Brazil and the world.

CONTRIBUTIONS

All the authors contributed to all stages of the article.

CONFLICT OF INTEREST

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REFERENCES

1. Steliarova-Foucher E, Stiller C, Kaatsch P, Berrino F, Coebergh JW, Lacour B. et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCIS project): an epidemiological study. Lancet. 2004;364(9451):2097-2105. Cited in: PubMed; PMID: 15589307.
2. Boyle P, Levin B, editors. World Cancer Report 2008. Lyon, France: International Agency for Research on Cancer; 2008.
3. American Cancer Society. Cancer Facts & Figures 2014. Atlanta: American Cancer Society; 2014.
4. Parkin DM, Stiller CA, Draper GJ, Bieber CA. The international incidence of childhood cancer. Int J Cancer. 1988,42(4):511-520. Cited in: PubMed; PMID: 3170025.

5. Buka I, Koranteng S, Vargas AR. Trends in childhood cancer incidence: review of environmental linkages. Pediatr Clin North Am. 2007,54(1):177-203.
6. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al., editors. GLOBOCAN 2012: estimated cancer incidence and prevalence worldwide in 2012 v1.0. Lyon, France: International Agency for Research on Cancer; 2013. (IARC CancerBase; no. 11).
7. Stewart BW; Wild PW, editors. World Cancer Report 2014. Lyon, France: International Agency for Research on Cancer; 2014.
8. Little J. Introduction**.** In: Little J. Epidemiology of Childhood Cancer. Lyon, France: IARC; c1999. P.1-9. (IARC Scientific Publications; 149).
9. Stiller CA. International patterns of cancer incidence in adolescents. Cancer Treat Rev. 2007;33(7):631-645. Cited in: PubMed; PMID: 17329031.
10. Linabery AM, Ross JA. Trends in childhood cancer incidence in the U.S. (1992–2004). Cancer. 2008, 112(2):416–432. Cited in: PubMed; PMID: 18074355.
11. Matthes R, Ziegelberger G, editors. Risk factors for childhood leukaemia. Radiation Protection Dosimetry. 2008;132(2 Spec No):107–274.
12. Valsecchi MG, Steliarova-Foucher E. Cancer registration in developing countries: luxury or necessity? Lancet Oncol. 2008;9(2):159-167. Cited in: PubMed; PMID: 18237850.
13. Greaves M. Infection, immune responses and the aetiology of childhood leukaemia. Nat Rev Cancer. 2006;6(3):193-203. Cited in: PubMed; PMID: 16467884.
14. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, Third Edition. Cancer. 2005;103(7):1457–1467. Cited in: PubMed; PMID: 15712273.
15. Birch JM, Alston RD, Kelsey AM, Quinn MJ, Babb P, McNally RJ. Classification and incidence of cancers in adolescents and young adults in England 1979-1997. Br J Cancer. 2002;87(11):1267-1274. Cited in: PubMed; PMID: 12439716.
16. Stiller CA, Desandes E, Danon SE, Izarzugaza I, Ratiu A, Vassileva-Valerianova Z, et al. Cancer incidence and survival in European adolescents (1978–1997). Report from the automated childhood cancer information system project. Eur J Cancer. 2006;42(13):2006–2018. Cited in: PubMed; PMID: 16919767.
17. Baade PD, Youlden DR, Valery PC, Hassall T, Ward L, Green AC, et al. Trends in incidence of childhood cancer in Australia, 1983–2006. Br J Cancer. 2010; 102(3):620–626. Cited in: PubMed; PMID: 20051948.
18. Baba S, Ioka A, Tsukuma H, Noda H, Ajiki W, Iso H. Incidence and survival trends for childhood cancer in Osaka, Japan, 1973–2001. Cancer Sci. 2010;101(3):787–792. Cited in: PubMed; PMID: 20132215.
19. Kohler BA, Ward E, McCarthy BJ, Schymura MJ, Ries LA, Eheman C, et al. Annual report to the nation on the status of cancer, 1975–2007, featuring tumors of the brain and other nervous system. J Natl Cancer Inst. 2011;103(9):714–736. Cited in: PubMed; PMID: 21454908.
20. Parkin DM, Ferlay J, Hamdi-Chérif M, Sitas F, Thomas JO, Wabinga H, et al., editors. Cancer in Africa: epidemiology and prevention. Lyon, France: IARC Press; 2003. Chapter 5, Childhood cancer; p. 381-396. (IARC Scientific Publications; 153).
21. Fajardo-Gutiérrez A, Juárez-Ocaña S, González-Miranda G, Palma-Padilla V, Carreón-Cruz R, Ortega-Alvárez MC, et al. Incidence of cancer in children residing in ten jurisdictions of the Mexican Republic: importance of the Cancer registry (a population-based study). BMC Cancer. 2007;7:68. Cited in: PubMed; PMID: 17445267.
22. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990–2001: incidence and survival. Int J Cancer. 2008;122(11):2607–2611. Cited in: PubMed; PMID: 18324630.
23. Bao PP, Zheng Y, Wang CF, Gu K, Jin F, Lu W. Time trends and characteristics of childhood cancer among children age 0-14 in Shanghai. Pediatr Blood Cancer. 2009;53(1):13-61. Cited in: PubMed; PMID: 19260104.
24. Lacour B, Guyot-Goubin A, Guissou S, Bellec S, Désandes E, Clavel J. Incidence of childhood cancer in France: National Children Cancer Registries, 2000–2004. Eur J Cancer Prev. 2010;19(3):173–181. Cited in: PubMed; PMID: 20361423.
25. Moradi A, Semnani S, Roshandel G, Mirbehbehani N, Keshtkar A, Aarabi M, et al. Incidence of childhood cancers in Golestan province of Iran. Iran J Pediatr.2010;20(3):335–342. Cited in: PubMed; PMID:23056726.
26. Wiangnon S, Veerakul G, Nuchprayoon I, Seksarn P, Hongeng S, Krutvecho T, et al. Childhood cancer incidence and survival 2003–2005, Thailand: study from the Thai Pediatric Oncology Group. Asian Pac J Cancer Prev. 2011;12(9):2215–2220. Cited in: PubMed; PMID: 22296359.
27. Kaatsch P, Spix C, editors. German Childhood Cancer Registry. Annual Report 2011. Mainz (Germany): Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) at the University Medical Center of the Johannes-Gutenberg University Mainz; 2012.
28. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, et al., editors. SEER Cancer Statistics Review, 1975-2010. [Internet]. Bethesda, MD: National Cancer Institute; 2013. [accessed 20

April 2018]. Available from: https://seer.cancer.gov/csr/1975_2010/.

29. Moreno F, Loria D, Abriata G, Terracini B; ROHA network. Childhood cancer: incidence and early deaths in Argentina, 2000–2008. Eur J Cancer. 2013;49(2):465–473. Cited in: PubMed; PMID: 22980725.
30. Magrath I, Steliarova-Foucher E, Epelman S, Ribeiro RC, Harif M, Li CK, et al. Paediatric cancer in low-income and middle-income countries. Lancet Oncol. 2013;14(3):104-116. Cited in: PubMed; PMID: 23434340.
31. Amir H, Kaaya EE, Manji KP, Kwesigabo G, Biberfeld P. Kaposi's sarcoma before and during a human immunodeficiency virus epidemic in Tanzanian children. Pediatr Infect Dis J. 2001;20(5):518–521. Cited in: PubMed; PMID: 11368110.
32. Aka P, Kawira E, Masalu N, Emmanuel B, Brubaker G, Magatti J, et al. Incidence and trends in Burkitt lymphoma in northern Tanzania from 2000 to 2009. Pediatr Blood Cancer. 2012;59(7):1234–1238. Cited in: PubMed; PMID: 22618958.
33. Ramot B, Magrath I. Hypothesis: the environment is a major determinant of the immunological sub-type of lymphoma and acute lymphoblastic leukaemia in children. Br J Haematol. 1982;50(2):183–89. Cited in: PubMed; PMID: 6977370.
34. Stiller CA, Parkin DM. Geographic and ethnic variations in the incidence of childhood cancer. Br Med Bull.1996;52(4): 682-703. Cited in: PubMed; PMID: 9039726.
35. Ferlay, F Bray, P Pisani, Parkin DM. editors. GLOBOCAN 2002: cancer incidence, mortality and prevalence worldwide v2.0. Lyon, France: International Agency for Research on Cancer; 2004. (IARC CancerBase; no. 5).
36. Kaatsch P, Steliarova-Foucher E, Crocetti E, Magnani C, Spix C, Zambon P. Time trends of cancer incidence in European children (1978-1997): report from the Automated Childhood Cancer Information System project. Eur J Cancer. 2006;42(13):1961-1971. Cited in: PubMed; PMID: 16919764.
37. Steliarova-Foucher E, Colombet M, Ries LAG, Moreno F, Dolya A, Bray F, et al. International incidence of childhood cancer, 2001-10: a population-based registry study. Lancet Oncol. 2017;18(6):719-731. Cited in: PubMed; PMID: 28410997.
38. Siegel DA, King J, Tai E, Buchanan N, Ajani UA, Li J. Cancer incidence rates and trends among children and adolescents in the United States, 2001-2009. Pediatrics. 2014;134(4):e945-955. Cited in: PubMed;PMID: 25201796.
39. Burkhamer J, Kriebel D, Clapp R. The increasing toll of adolescent cancer incidence in the US. PLoS One. 2017;24;12(2):e0172986. Cited in: PubMed; PMID: 28235028.
40. Instituto Nacional de Câncer José Alencar Gomes da Silva. Incidência, mortalidade e morbidade hospitalar por câncer em crianças, adolescentes e adultos jovens no Brasil: informações dos registros de câncer e do sistema de mortalidade. [Internet]. Rio de Janeiro: INCA; 2016. [Accessed 20 April 2018]. In: http://www1.inca.gov.br/wcm/incidencia/2017/pdf/versao-completa.pdf
41. de Camargo B, Santos MO, Rebelo MS, Reis RS, Ferman S, Noronha CP, et al. Cancer incidence among children and adolescents in Brazil: first report of 14 population-based cancer registries. Int J Cancer. 2010; 126(3): 715-720. Cited in: PubMed; PMID: 19642142.
42. de Camargo B, Ferreira JM, Reis RS, Ferman S, Santos MO, Pombo-de-Oliveira MS. Socioeconomic status and the incidence of non-central nervous system childhood embryonic tumors in Brazil. BMC Cancer. 2011;11:160. Cited in: PubMed; PMID: 21545722.
43. Ferreira JM, Klumb CE, Reis RS, Santos MO, Oliveira JF, de Camargo B, et al. Lymphoma subtype incidence rates in children and adolescents: first report from Brazil. Cancer Epidemiol. 2012; 36(4):e221-e226. Cited in: PubMed; PMID: 2552334.
44. Bosetti C, Bertuccio P, Chatenoud L, Negri E, Levi F, La Vecchia C. Childhood cancer mortality in Europe, 1970-2007. Eur J Cancer. 2010; 46(2):384-394. Cited in: PubMed; PMID: 19818600.
45. Chatenoud L, Bertuccio P, Bosetti C, Levi F, Negri E, La Vecchia C. Childhood cancer mortality in America, Asia, and Oceania, 1970 through 2007. Cancer. 2010. 116(21):5063-5074. Cited in: PubMed; PMID: 20629033.
46. Smith MA, Altekruse SF, Adamson PC, Reaman GH, Seibel NL. Declining childhood and adolescent cancer mortality. Cancer. 2014;120(16):2497-2506. Cited in: PubMed; PMID: 24853691.
47. Ferman S, Santos MO, Ferreira JM, Reis RS, Oliveira JF, Pombo-de-Oliveira MS, et al. Childhood cancer mortality trends in Brazil, 1979 –2008. Clinics (São Paulo). 2013;68(2):219-224. Cited in: PubMed; PMID: 23525319.
48. Balmant NV, de Souza Reis R2, de Oliveira Santos M2, Pinto Oliveira J2, de Camargo B. Trends in cancer mortality among adolescents and young adults in Brazil. J Adolesc Young Adult Oncol. 2017;6(2):341-347. Cited in: PubMed; PMID: 28051344.

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