



Socioeconomic inequalities in cancer incidence and access to health services among children and adolescents in China: a cross-sectional study

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Summary

Background Despite the substantial burden caused by childhood cancer globally, childhood cancer incidence obtained in a nationwide childhood cancer registry and the accessibility of relevant health services are still unknown in China. We comprehensively assessed the most up-to-date cancer incidence in Chinese children and adolescents, nationally, regionally, and in specific population subgroups, and also examined the association between cancer incidence and socioeconomic inequality in access to health services.

Methods In this national cross-sectional study, we used data from the National Center for Pediatric Cancer Surveillance, the nationwide Hospital Quality Monitoring System, and public databases to cover 31 provinces, autonomous regions, and municipalities in mainland China. We estimated the incidence of cancer among children (aged 0–14 years) and adolescents (aged 15–19 years) in China through stratified proportional estimation. We classified regions by socioeconomic status using the human development index (HDI). Incidence rates of 12 main groups, 47 subgroups, and 81 subtypes of cancer were reported and compared by sex, age, and socioeconomic status, according to the third edition of the International Classification of Childhood Cancer. We also quantified the geographical and population density of paediatric oncologists, pathology workforce, diagnoses and treatment institutions of paediatric cancer, and paediatric beds. We used the Gini coefficient to assess equality in access to these four health service indicators. We also calculated the proportions of cross-regional patients among new cases in our surveillance system.

Findings We estimated the incidence of cancer among children (aged 0–14 years) and adolescents (aged 15–19 years) in China from Jan 1, 2018, to Dec 31, 2020. An estimated 121 145 cancer cases were diagnosed among children and adolescents in China between 2018 and 2020, with world standard age-standardised incidence rates of 122·86 (95% CI 121·70–124·02) per million for children and 137·64 (136·08–139·20) per million for adolescents. Boys had a higher incidence rate of childhood cancer (133·18 for boys vs 111·21 for girls per million) but a lower incidence of adolescent cancer (133·92 for boys vs 141·79 for girls per million) than girls. Leukaemias (42·33 per million) were the most common cancer group in children, whereas malignant epithelial tumours and melanomas (30·39 per million) surpassed leukaemias (30·08 per million) in adolescents as the cancer with the highest incidence. The overall incidence rates ranged from 101·60 (100·67–102·51) per million in very low HDI regions to 138·21 (137·14–139·29) per million in high HDI regions, indicating a significant positive association between the incidence of childhood and adolescent cancer and regional socioeconomic status ($p < 0·0001$). The incidence in girls showed larger variation (48·45% from the lowest to the highest) than boys (36·71% from lowest to highest) in different socioeconomic regions. The population and geographical densities of most health services also showed a significant positive correlation with HDI levels. In particular, the geographical density distribution (Gini coefficients of 0·32–0·47) had higher inequalities than population density distribution (Gini coefficients of 0·05–0·19). The overall proportion of cross-regional patients of childhood and adolescent cancer was 22·16%, and the highest proportion occurred in retinoblastoma (56·54%) and in low HDI regions (35·14%).

Interpretation Our study showed that the burden of cancer in children and adolescents in China is much higher than previously nationally reported from 2000 to 2015. The distribution of the accessibility of health services, as a social determinant of health, might have a notable role in the socioeconomic inequalities in cancer incidence among Chinese children and adolescents. With regards to achieving the Sustainable Development Goals, policy approaches should prioritise increasing the accessibility of health services for early diagnosis to improve outcomes and subsequently reduce disease burdens, as well as narrowing the socioeconomic inequalities of childhood and adolescent cancer.

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Introduction

Cancer is one of the leading causes of death among children and adolescents worldwide.^{1,2} The reported incidence rate of childhood and adolescent cancer is greater in high-income countries than in low-income and middle-income countries (LMICs);³ however, more than 80% of the total number of childhood cancer cases occur in LMICs.⁴ Although two studies in China reported the

national incidence of childhood and adolescent cancer using population-based cancer registry data from 2000 to 2015, the results probably underestimated the incidence because of the absence of high-quality reporting of childhood cancers and missing data from the floating populations in China (ie, those who moved out of their household regions for more than 6 months), who are approximately 16% of the population.^{5,6} The Global

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Research in context

Evidence before this study

We searched PubMed, Google Scholar, and China National Knowledge Infrastructure without language restrictions for articles published from Jan 1, 1990, to July 31, 2022, using the search terms “childhood or adolescent”, “cancer incidence”, “social determinant of health”, “health service”, and “inequality”. Two studies reported the incidence of childhood cancer using data from 2000 to 2015 in China; however, the results appeared to be an underestimation of incidence (eg, one showed that the incidence was 96.03 per million for children and adolescents aged 0–19 years and the other showed 87.1 per million for children aged 0–14 years). Another study by the International Incidence of Childhood Cancer reported an incidence of 135.0 cases per million for children and adolescents aged 0–19 years, but it included only six high-quality registries from 1990 to 2013, all of which were concentrated in more high-income cities, and did not reflect regional variation in China. Some studies have suggested that the distributions in human resources for health were uneven and inequalities in health services could lead to large disparities in incidence rates of childhood cancer. To the best of our knowledge, no studies have reported the association between accessibility to health services and the incidence rates of childhood and adolescent cancers in China, and few studies have provided quantifiable evidence in low-income and middle-income countries.

Added value of this study

Based on the nationwide, largest, specialised, hospital-based childhood cancer surveillance system, we conducted a national cross-sectional study of incidence rates and access to health services among children and adolescents with cancer from different socioeconomic statuses in China using large-scale data from Jan 1, 2018, to Dec 31, 2020. Our findings indicate that the world standard age-standardised incidence rates of cancer were 126.48 (95% CI 125.45–127.50) per million for children and adolescents. We observed a large regional disparity in the cancer incidence among children and adolescents, which was significantly positively associated with regional socioeconomic status ($p < 0.0001$). The higher sex ratio (of boys to girls) of overall incidence in poor socioeconomic areas compared with rich socioeconomic areas indicated that cancer incidence among girls might be more sensitive to socioeconomic status.

For the first time, the accessibility of health services (diagnoses and treatment institutions of paediatric cancer, paediatric beds, paediatric oncologists, and pathology workforce) have been reported in China. We found that the population densities of paediatric oncologists and pathology workforce, and the geographical densities of all health services were significantly associated with socioeconomic status. In particular, geographical densities had higher inequalities than population densities. Accessibility to health services increased in line with increased socioeconomic status, which resulted in higher reported incidence rates of childhood cancer. Furthermore, a clear increasing trend of proportions of cross-regional patients (patients diagnosed outside their region of residence) with decreasing human development index levels was observed overall and in 11 main cancer groups of patients.

Implications of all the available evidence

The national substantial burden of childhood and adolescent cancer in China has been vastly underestimated in previous reports from 2000 to 2015. The available evidence reveals the socioeconomic inequalities in childhood and adolescent cancer incidence and accessibility of health services, and confirms the positive associations among them. Children and adolescents with cancer in regions of a lower socioeconomic status face greater challenges than regions of a higher socioeconomic status, with regards to the poorer accessibility of health services, which has been ignored and is an ongoing public health issue. Our research showed the proportion of newly diagnosed patients with childhood and adolescent cancer across all regions were more than 30% of the participants in most cancer groups in lower socioeconomic areas, with long-term additional associated non-medical expenses. These findings suggest that building the capacity of paediatric cancer health services should be one of the criteria for promoting regional centres for children's health and regional centres for cancer, which could contribute to reducing accessibility inequalities, ensure access to early diagnosis, and reduce the financial burden. It is also necessary to promote collaboration between health systems and equally effective social systems, such as families, schools, communities, and social charities, to improve personal and social awareness and investment for childhood and adolescent cancer.

Burden of Disease Study 2019⁷ results only used International Classification of Disease (ICD) categories to classify cancer types. The incidence of childhood and adolescent cancer in terms of socioeconomic inequality in China has never been reported.

The lower reported incidence rates than in high-income countries might be related to incomplete reporting systems or poor diagnosis capacities because of inadequate health systems in LMICs.⁸ The capacity of health services is one of the evaluation indicators of a health system, and itself acts as a social determinant of health.⁹ In China, several studies have shown the inequality in the distribution of health resources;^{10,11} however, the health service capacity for childhood and adolescent cancer has never been reported at the national and regional levels. Some researchers have suggested that inequalities in health service capacity could lead to large disparities in the incidence and survival rates of childhood cancer.^{12–15} Understanding the association between incidence rate, health service accessibility, and socioeconomic status, on the basis of quantifiable evidence, is essential for prioritising health policy decisions and developing cancer control strategies in response to the WHO Global Initiative for Childhood Cancer.¹⁶

In China, with the universal coverage (with 96·3% of the population having essential health insurance) of health insurance and the implementation of a cross-provincial medical insurance payment and settlement system, children and adolescents with cancer can choose their health-care providers across hospitals or provinces without the limitations of a referral model.¹⁷ Various referrals can be provided by the National Center for Children's Health, the Regional Center for Children's Health, and designated medical institutions and treatment collaborative groups. In this context, establishing a hospital-based cancer surveillance system is essential to provide data for formulating the framework of childhood cancer control, as a way to achieve the Sustainable Development Goal of reducing premature mortality from non-communicable diseases by a third and to promote wellbeing.¹⁸ On June 12, 2019, the National Center for Pediatric Cancer Surveillance (NCPCS) received approval by the National Health Commission to build a nationwide, specialised, and hospital-based cancer surveillance system for children and adolescents, designed to continuously collect information on cancer cases in China.¹⁹ The NCPCS provides a unique background to conduct this research on incidence of childhood and adolescent cancers and health services accessibility.

We aimed to estimate the incidence rates of childhood and adolescent cancers by socioeconomic status, sex, and age group from 2018 to 2020 in China, on the basis of the third edition of the International Classification of Childhood Cancer (ICCC-3).²⁰ We aimed to provide quantifiable evidence of inequality in access to health services with regards to diagnosis across socioeconomic regions. We further explored the

association between the inaccessibility of health services in terms of diagnosis and incidence rates of childhood and adolescent cancers.

Methods

Study design and data sources

We did a national cross-sectional study in China to assess the most up-to-date cancer incidence in Chinese children and adolescents. Records of hospital admission events were extracted from the NCPCS and national Hospital Quality Monitoring System (HQMS) databases.²¹ From 31 provinces, autonomous regions, and municipalities (hereafter referred to as 31 provinces; appendix p 8) in mainland China, we obtained the numbers of diagnoses and treatment institutions of paediatric cancer and paediatric oncologists from the HQMS database, data on the Human Development Index (HDI),²² population size,²³ the geographical area,²⁴ the number of paediatric beds,²⁵ and pathology workforce²⁶ from public databases (appendix p 3). The term diagnoses and treatment institutions of paediatric cancer refers to tertiary public hospitals that have obtained the practice licence of a hospital and carry out the diagnosis and treatment of paediatric cancers. The term paediatric oncologist refers to doctors who have obtained the licensure of a practising physician and carry out the diagnosis and treatment of paediatric cancers (including some doctors who have received standard training for specialists in oncology). The term pathology workforce includes all pathologists and pathology technicians.

Identification of new incidence cases

The NCPCS conducts nationwide, hospital-based cancer surveillance among patients aged 0–19 years who were admitted to hospital in China, covering 425 surveillance sites in 31 provinces. Multiple paediatric cancer report cards being issued for only one individual with cancer, resulting from multiple hospital admission records, were reported to the NCPCS by surveillance sites from Jan 1, 2017, to Dec 31, 2020. The NCPCS then established unique identifiers to link multiple report cards to the one individual (appendix p 4). To exclude patients who had been diagnosed before this surveillance, we used a 12-month washout period (Jan 1, 2017, to Dec 31, 2017) to identify new incidence cases in 2018, a 24-month washout period (Jan 1, 2017, to Dec 31, 2018) to identify new cases in 2019, and a 36-month washout period (Jan 1, 2017, to Dec 31, 2019) to identify new incidence cases in 2020 (appendix p 5), meaning that only cancers in individuals who were not being diagnosed or treated during the washout period were considered new incidence cases (appendix p 5),²⁷ and we defined the earliest date of hospital admission after Dec 31, 2017, as the date of diagnosis (appendix p 6). The incidence rate was calculated on the basis of the province of residence, regardless of the province where the new incidence case was diagnosed. On the basis of this process, we

See Online for appendix

For more on the cross provincial medical insurance payment and settlement system see <http://www.nhsa.gov.cn/>

For more on various referrals see <http://www.nhc.gov.cn/>

established the NCPCS new incidence case database for 2018–20.

Procedures

We extracted information from the NCPCS case database on individuals aged 0–19 years with all cancers, non-malignant tumours, or dynamic undetermined or unknown tumours of the CNS and reproductive system. The standard set of variables included in this study were age, sex, province of diagnosis (the province where the patient was admitted to hospital), province of residence (the province where citizens lived continuously for more than 1 year as their main area of residence, except for official business, labour dispatch, medical treatment, etc), admission event data, and information on the cancer (ie, date of diagnosis, code of International Classification of Diseases, tenth revision [ICD-10], site, morphology, and behaviour). All surveillance sites registered disease codes according to the ICD-10 and the International Classification of Diseases for Oncology, third edition. We categorised all cases on the basis of ICC-3 (appendix p 7) using the conversion rules from International Classification of Diseases for Oncology, third edition, to convert disease codes to ICC-3.²⁸

We excluded new incident cases if they met the following exclusion criteria: if the patient had secondary, recurrent, or non-first-diagnosed metastatic tumours; or if the patients resided in areas outside the 31 provinces of mainland China or their country of citizenship was not China. Registration standards and quality control procedures during and after case reporting were established according to the quality control standard of the International Agency for Research on Cancer (IARC).^{29–31} Detailed quality control procedures including uniqueness, integrity, validity, and logic verification have been described elsewhere.¹⁹

This NCPCS project was approved by the ethics committee of the Beijing Children's Hospital, Capital Medical University (Beijing, China; IEC-C-006-A04-V.06). With the ethics committees' approval, informed consent of the patient was waived in this study.

Classification of socioeconomic status and indicators

We assigned socioeconomic status using the HDI.³² On the basis of the percentile of the HDI, we divided the 31 provinces of residence and diagnosis into six regions: very low HDI regions (≤ 10 th percentile), low HDI regions (>10 th to 25th percentile), lower-middle HDI regions (>25 th to 50th percentile), upper-middle HDI regions (>50 th to 75th percentile), high HDI regions (>75 th to 90th percentile), and very high HDI regions (>90 th percentile; appendix p 8). We classified the age of patients into five groups: younger than 1 year, 1–4 years, 5–9 years, 10–14 years, and 15 years and older.

reported if they were lower than 0.05 per million. We calculated the proportions of cross-regional patients per the total new cases of their region of residence in the NCPCS database. All analyses were done using SAS version 9.4 and R version 4.0.3. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting recommendations (appendix p 18).³⁶

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We estimated the incidence of cancer among children (aged 0–14 years) and adolescents (aged 15–19 years) in China from Jan 1, 2018, to Dec 31, 2020. After quality control, 181471 (98.52%) of 184193 records of hospital admission were included in the NCPCS hospital admission record database, 274484 (94.93%) of 289158 records of hospital admission were included in the HQMS hospital admission record database, and 76468 (97.01%) of 78827 new cases were included in the NCPCS case database (appendix pp 19–20). The number of hospital admission records in the NCPCS database was 66.11% of that in the HQMS database.

Overall, 121145 children and adolescents were estimated to be diagnosed with cancer in China from Jan 1, 2018, to Dec 31, 2020, with an average world standard age-standardised incidence rate of 126.48 (95% CI 125.45–127.50) per million (table 1). The incidence of cancer was higher in adolescents (137.64 [95% CI 136.08–139.20] per million) than in children (122.86 [121.70–124.02] per million). Children younger than 5 years had the highest incidence rate, whereas children aged 5–9 years had the lowest incidence rate, and subsequently the rate increased with increasing age. The patterns in the data by age were similar between boys and girls. Although incidence was similar between children and adolescents among boys (133.18 per million vs 133.92 per million), a higher incidence rate was observed in adolescents compared with children

among girls (111.21 per million vs 141.97 per million; table 1).

Leukaemias, CNS tumours, and lymphomas were ranked as the top three main cancer groups with the highest incidence rates among children, whereas malignant epithelial tumours and melanomas, leukaemias, and CNS tumours were the three cancer types with the highest incidence rates among adolescents. Among children and adolescents, lymphoid leukaemias were the most common subgroup (21.96 [55.82%] of 39.34 per million) of leukaemias. The incidence rates of all subgroups of leukaemias were higher in boys than in girls. Thyroid carcinomas accounted for 54.47% (5.60 of 10.28 per million) of all malignant epithelial tumours and melanomas. The incidence of thyroid carcinomas was 3.45 times (9.04 vs 2.62 per million) more common in girls than in boys (appendix pp 21–28).

Figure 1 shows the composition of the top ten specific cancers with the highest incidence by sex and age. The ranking of the top ten cancers varied among different age and sex groups. Neuroblastoma and ganglioneuroblastoma were the most common cancer types in both girls and boys younger than 1 year, accounting for 15.84% of all incidence cases in boys and 14.35% of all incident cases in girls (appendix pp 29–30). The second most common cancer in this age group was different in girls (retinoblastoma) and boys (hepatoblastoma). Among those aged 1 year or older, the incidence rate of precursor cell leukaemias was the highest in all groups except for adolescent girls, in whom thyroid carcinomas had the highest incidence. Neuroblastoma and ganglioneuroblastoma were the second most common cancer in both girls and boys aged 1–4 years. In children aged 5 years and older and in adolescents, the second most common cancer group was acute myeloid leukaemias.

The overall incidence of cancer in children increased with increasing HDI ($p < 0.0001$), despite some fluctuations among different age groups (table 2). Although incidence in girls and boys aged 0–14 years had similar changing patterns, girls showed larger variation (48.45% from the lowest to the highest) than boys

	Number of estimated cases (number of registered cases)			ASR/WSR per million (95% CI)		
	Boys	Girls	All	Boys	Girls	All
0–14 years*	52 478 (35 909)	38 654 (26 311)	91 132 (62 220)	133.18 (131.97–134.39)	111.21 (110.11–112.32)	122.86 (121.70–124.02)
0–4 years	22 084 (16 559)	16 688 (12 495)	38 772 (29 054)	179.68 (177.31–182.05)	150.69 (148.40–152.98)	165.94 (164.29–167.59)
<1 year	3874 (3090)	3181 (2504)	7054 (5594)	204.55 (198.13–211.01)	186.82 (180.33–193.31)	196.15 (191.56–200.72)
1–4 years	18 210 (13 469)	13 508 (9991)	31 718 (23 460)	175.15 (172.60–177.69)	144.13 (141.71–146.57)	160.44 (158.68–162.21)
5–9 years	12 778 (10 271)	9035 (7220)	21 813 (17 491)	88.71 (87.17–90.24)	71.32 (69.85–72.79)	80.57 (79.50–81.64)
10–14 years	17 616 (9079)	12 931 (6596)	30 547 (15 675)	128.75 (126.85–130.65)	108.71 (106.84–110.59)	119.43 (118.09–120.77)
15–19 years	15 690 (7613)	14 324 (6635)	30 013 (14 248)	133.92 (131.82–136.01)	141.97 (139.65–144.30)	137.64 (136.08–139.20)
0–19 years*	68 168 (43 522)	52 977 (32 946)	121 145 (76 468)	133.36 (132.31–134.41)	118.74 (117.75–119.73)	126.48 (125.45–127.50)

WSR=world standard age-standardised rate. ASR=age-specific rate. *WSR data.

Table 1: Number of new cases and incidence rates of childhood and adolescent cancer by sex and age group in China, 2018–20

(36·71% from lowest to highest) in different HDI regions. Data for the overall incidence of cancer in adolescents also increased with increasing HDI levels ($p < 0\cdot0001$), but with greater fluctuations. The magnitude of the change was smaller in adolescent girls (31·05%) than in adolescent boys (37·09%; table 2).

Regional variations for specific cancer groups were heterotonic (figure 2). Among children, a clear trend of increasing incidence rate with increasing HDI levels was observed for lymphomas, CNS tumours, neuroblastoma, retinoblastoma, malignant bone tumours, and soft tissue sarcomas.

Geographical density of all health services (Gini coefficients of 0·32–0·47) had higher inequalities in population density (Gini coefficients of 0·05–0·19; table 3). The geographical density of all health services increased significantly with increasing HDI ($p = 0\cdot012$ for hospital beds and treatment institutions, $p = 0\cdot0050$ for hospital beds, $p = 0\cdot012$ for paediatric oncologists, and $p = 0\cdot0001$ for pathology workforce), whereas only the geographical density of paediatric oncologists ($p = 0\cdot049$) and pathology workforce ($p = 0\cdot0090$) had a significant correlation with the level of HDI (table 3).

Overall incidence rates of childhood cancer and adolescent cancer showed an increasing trend with increasing geographical density of all health services and population density of the majority health services, except hospital beds (figure 4). However, the incidence of adolescent cancer sharply decreased in regions with the highest geographical and population densities of all health services (appendix pp 31–38).

The overall proportion of cross-regional patients among all cases of childhood and adolescent cancers was 16·6%, and the highest proportions were seen in neuroblastoma (56·54%) and in low HDI regions (35·14%). An increasing trend of proportions of cross-regional patients was observed with decreasing HDI levels for most cancer groups, despite some fluctuations among groups, except for CNS tumours, renal tumours, lymphomas, and soft tissue sarcomas, which followed the trend without fluctuations (figure 5).

Conclusion

To our knowledge, this study is the first to use national, population-based data from NCPDS and HQMS databases in 2018 and 2020, to provide comprehensive data on up-to-date cancer incidence among children and adolescents in China classified using the ICCC-3. We also revealed inequalities in cancer incidence and accessibility to relevant health services across socio-economic regions of China. Our findings provide novel insights into the implications of socioeconomic inequality on the burden of childhood and adolescent cancers in the population.

In 2018 and 2020, newly diagnosed cancer cases among children and adolescents in China were approximately 40 000 cases per year, which is similar to the

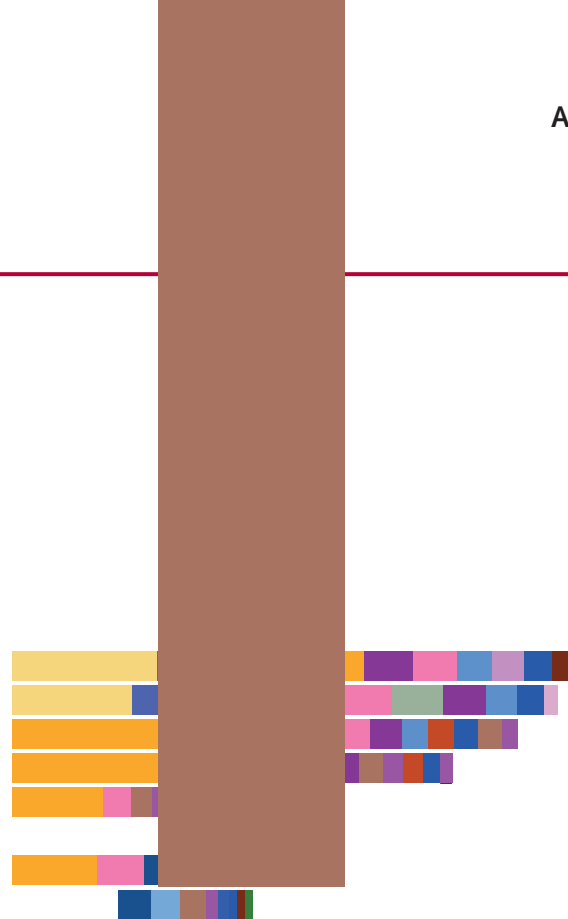


Figure 1: Incidence rates of the top 10 most common childhood-specific and adolescent-specific cancers for each sex and age group in China, 2018–20. NK cell=natural killer cell.⁰¹

Global Burden of Disease Study 2019 and GLOBOCAN 2020 estimates.^{7,37} Our estimated world standard age-standardised incidence rate of childhood and adolescent cancer was similar to the rate reported by the IARC,³³ but much higher than the rate of Chinese National Central Cancer Registry.³⁶ The incidence rates of the main cancer groups were generally lower than those reported in North America, Europe, and Australia, especially among adolescents, but similar to those in Japan.^{2,33,38} However, it is worth noting that as a common childhood solid tumour, hepatoblastoma showed a higher incidence rate in China than that reported in most other countries.^{38–40} Based on our findings, it is necessary to conduct more research programmes focusing on factors associated with specific cancer types that are common among Chinese children and adolescents.

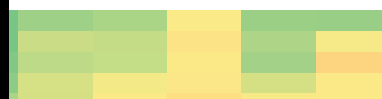
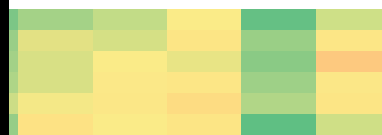
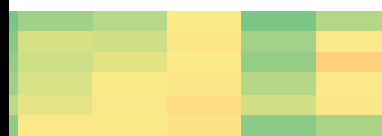
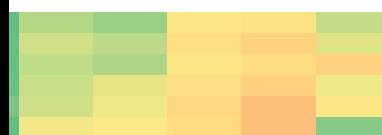
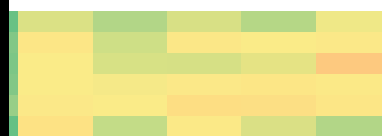
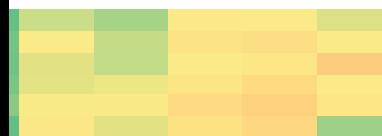
The IARC incidence reports used data from six high-quality registries of Chinese National Central Cancer Registry from 1990 to 2013,³³ and the overall cancer incidence in China was weighted towards those children and adolescents observed in these registries, which could not reflect regional variation. As the gold standard for providing information on cancer incidence, improving data quality and coverage is a necessary element in the role of population-based cancer registries in cancer control. However, it was inevitable that some childhood cancer cases in population-based registries in China would be missed because of the large floating population, and the fact that the number of cases

	Very low HDI	Low HDI	Lower-middle HDI	Upper-middle HDI	High HDI	Very high HDI	p value for trend
Boys							
0-14 years*	105.03 (103.96-106.11)	125.99 (124.80-127.16)	133.38 (132.16-134.58)	137.45 (136.22-138.68)	143.59 (142.33-144.85)	139.12 (137.98-140.45)	<0.0001†
0-4 years	135.05 (128.10-142.07)	171.11 (165.41-176.78)	176.86 (171.99-181.74)	187.11 (182.50-191.71)	196.36 (190.94-201.78)	192.53 (178.66-206.33)	<0.0001
<1 year	159.39 (141.10-177.80)	190.36 (175.23-205.36)	188.26 (175.22-201.20)	219.04 (206.14-232.00)	230.7 (215.88-245.59)	239.31 (199.64-280.66)	0.0001
1-4 years	130.03 (122.54-137.59)	167.48 (161.34-173.61)	174.84 (169.60-180.12)	181.54 (176.61-186.44)	189.98 (184.18-195.79)	184.57 (170.03-199.34)	<0.0001
5-9 years	81.54 (76.21-86.81)	82.81 (79.14-86.50)	90.05 (87.04-93.04)	91.04 (88.00-94.05)	91.99 (88.48-95.49)	84.44 (75.31-93.43)	0.034
10-14 years	96.88 (91.01-102.78)	122.11 (117.55-126.64)	131.64 (128.01-135.26)	131.12 (127.39-134.84)	139.44 (134.88-144.02)	136.13 (123.03-149.43)	<0.0001
15-19 years	113.43 (106.75-120.21)	138.57 (133.32-143.85)	133.83 (129.74-137.94)	132.55 (128.47-136.61)	144.25 (139.43-149.10)	105.22 (94.09-116.47)	0.091
0-19 years*	107.08 (106.16-108.05)	129.07 (128.03-130.10)	133.49 (132.43-134.54)	136.25 (135.18-137.31)	143.75 (142.66-144.85)	130.82 (129.87-131.96)	<0.0001†
Girls							
0-14 years*	86.40 (85.42-87.37)	107.95 (106.88-109.06)	105.37 (104.29-106.44)	116.43 (115.29-117.56)	122.41 (121.25-123.58)	128.26 (127.05-129.42)	<0.0001†
0-4 years	109.73 (103.16-116.38)	147.90 (142.31-153.44)	140.31 (135.77-144.88)	159.35 (154.84-163.85)	167.21 (161.91-172.49)	171.99 (158.33-185.49)	<0.0001
<1 year	133.12 (115.30-150.42)	174.13 (159.05-189.44)	155.32 (142.96-167.73)	203.26 (189.98-216.37)	226.73 (211.11-242.29)	247.36 (203.83-289.25)	<0.0001
1-4 years	104.89 (97.77-111.97)	142.98 (137.03-148.96)	137.68 (132.79-142.57)	151.70 (146.95-156.47)	156.20 (150.62-161.76)	159.22 (145.13-173.40)	<0.0001
5-9 years	62.34 (57.50-67.28)	69.72 (66.14-73.31)	69.07 (66.27-71.85)	73.68 (70.74-76.59)	75.38 (72.01-78.80)	76.89 (67.83-85.98)	0.0075
10-14 years	85.78 (79.92-91.63)	104.02 (99.54-108.48)	105.08 (101.59-108.55)	112.55 (108.84-116.28)	120.41 (115.85-125.01)	129.90 (116.35-143.54)	<0.0001
15-19 years	123.55 (116.48-130.62)	138.57 (133.32-143.85)	133.83 (129.74-137.94)	132.55 (128.47-136.61)	144.25 (139.43-149.10)	105.22 (94.09-116.47)	0.091

among children and adolescents accounts for less than 1% of the total number of cases of cancer.³⁵ The establishment of the NCPCS marks the beginning of an independent childhood cancer registry in China, a milestone in the national plan for oncology and child health. As the largest, specialist, and only nationwide hospital-based childhood cancer surveillance system, the NCPCS covered nearly 70% of hospital admission records from Jan 1, 2017, to Dec 31, 2020, for childhood and adolescent cancer in December 2021. The NCPCS has not only taken into account all variables of the cancer case files of the IARC and the resident cancer case report cards of the Chinese National Central Cancer Registry, but also collected detailed diagnostic and treatment information. Based on the aforementioned details, it is clear that the NCPCS has an indispensable and complementary role in the application of population-based cancer registry data sources to assess the cancer burden in China. The NCPCS can also provide a basis for long-term follow-ups of treatment records and prognosis, to support the standardisation of age-applicable guidelines for cancer detection and treatment, and for the evaluation of future progress.

Consistent with global studies showing disparities in incidence rates across countries with different socioeconomic statuses,³³ we observed a significant positive association between incidence rates of childhood and adolescent cancers and regional socioeconomic status in China; and our results also provide strong evidence that health systems might have an important role in socioeconomic inequalities in cancer incidence. Previous studies have shown that the geographical distribution of general paediatric care services was highly skewed in China.^{10,41} Paediatricians with higher education levels and those with well resourced tertiary hospitals are both clustered in well developed regions, which reflects a higher capacity for diagnosis and treatment. The international and intranational unequal distribution of health services for children is a global problem, especially in LMICs, where resources are even more scarce.^{42,43}

In 2020, approximately 70% of inpatient medical care expense within the insurance scope was covered by health insurance in China, with the nationwide implementation of the cross-provincial medical insurance payment and settlement system further helping to break the limitations



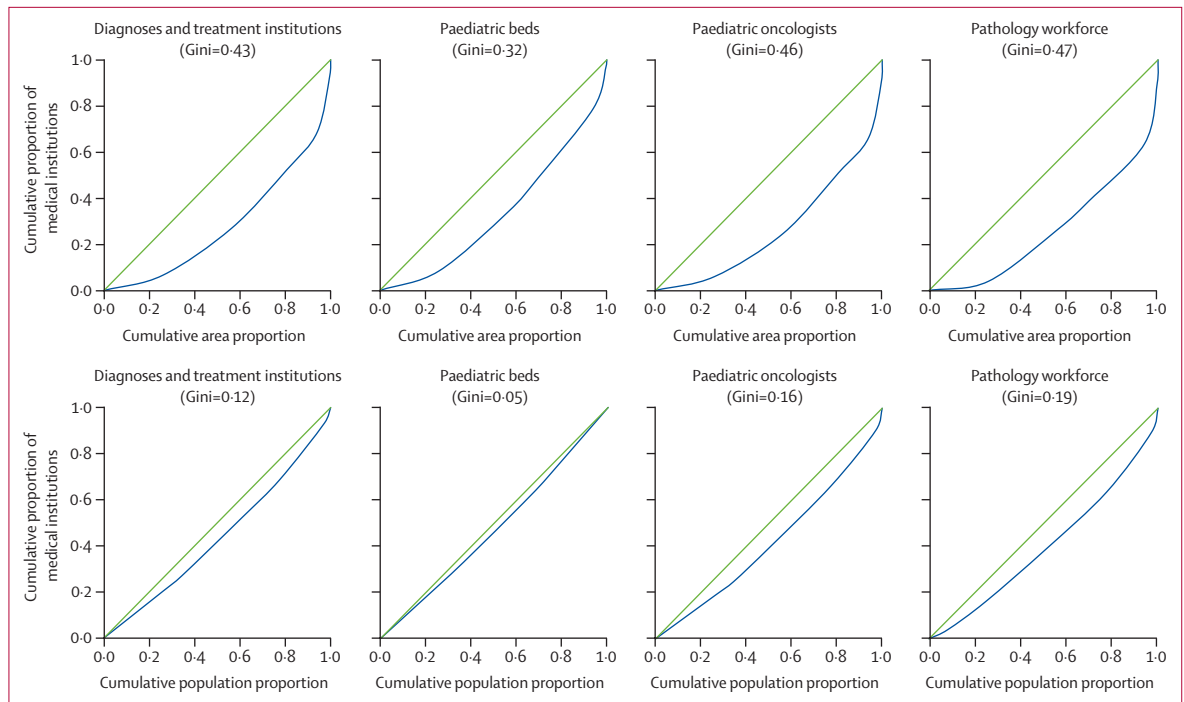


Figure 3: Distributions of health service indicators adjusted for geographical area or for childhood and adolescent populations in six human development index regions in China, 2020

The health service indicators included: the numbers of diagnoses and treatment institutions of paediatric cancer, the number of paediatric beds, the number of paediatric oncologists, and the number of pathology workforce.

	Diagnoses and treatment institutions of paediatric cancer		Paediatric beds		Paediatric oncologists		Pathology workforce	
	Geographical density	Population density	Geographical density	Population density	Geographical density	Population density	Geographical density	Population density
Very low HDI	0.04	4.11×10^{-3}	11.84	1.10	0.76	0.07	0.48	0.04
Low HDI	0.21	5.06×10^{-3}	40.76	0.97	3.82	0.09	2.85	0.07
Lower-middle HDI	0.12	3.99×10^{-3}	30.83	1.06	2.04	0.07	2.33	0.08
Upper-middle HDI	0.18	4.86×10^{-3}	45.50	1.23	3.56	0.10	3.21	0.09
High HDI	0.77	6.36×10^{-3}	119.02	0.98	14.42	0.12	14.84	0.12
Very high HDI	3.23	0.01	306.66	1.20	86.40	0.34	88.82	0.35
p value	0.012*	0.051*	0.0050*	0.53	0.012*	0.049*	0.0060*	0.0090*

Geographical density is the number of diagnosis and treatment institutions of paediatric cancer, paediatric beds, paediatric oncologists, and pathology workforce per 1000 km² geographical area. Population density is the number of diagnoses and treatment institutions of paediatric cancer, paediatric beds, paediatric oncologists, and pathology workforce per 1000 childhood and adolescent population. HDI=human development index. *We replaced each geographical density and population density with a log transmission in linear regression models.

Table 3: Geographical and population densities of diagnoses and treatment institutions of paediatric cancer, paediatric beds, paediatric oncologists, and pathology workforce in China, 2020

of an unequal distribution of health services. According to our surveillance data, poorer socioeconomic regions had a higher proportion of cross-regional patients, especially for neuroblastomas and retinoblastoma, with proportions of nearly or more than 50%. However, because of increased non-medical expenses, a long time to receiving health services, and the inconvenience of children travelling long distances, health service accessibility inequality is still an obstacle of early

diagnosis, which results in a lower reported cancer incidence rate in poor socioeconomic regions than in rich socioeconomic regions.

Of note, the highest sex ratio (boys to girls) was reported in regions with lower HDI levels, which suggested that cancer incidence among girls might be more sensitive to socioeconomic status. Globally, LMICs generally have higher sex ratios (in boys than girls) of cancer incidence among children and adolescents than in high-income

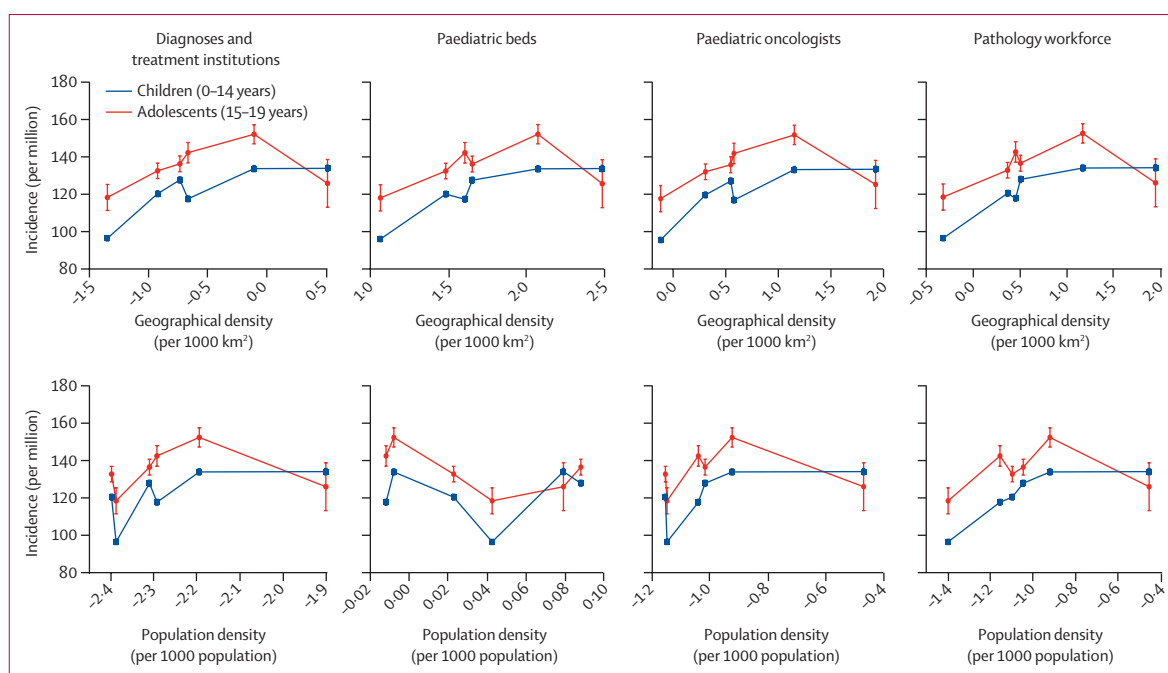


Figure 4:

	Leukaemias	Lymphomas	CNS tumours	Neuroblastomas	Retinoblastoma	Renal tumours	Hepatic tumours	Malignant bone tumours	Soft tissue sarcomas	Germ cell tumours	Malignant epithelial tumours and melanomas	Overall cancers
Very low HDI	20.65	26.92	43.87	41.79	57.80	36.32	42.54	24.92	37.21	31.93	28.15	30.08
Low HDI	32.32	34.99	41.27	48.36	69.14	35.36	38.64	27.12	37.14	33.41	22.47	35.14
Lower-middle HDI	19.97	34.48	41.15	46.12	74.09	25.62	29.19	23.35	31.66	31.48	19.53	27.61
Upper-middle HDI	8.63	18.51	26.20	25.76	54.02	15.98	13.57	20.15	19.63	16.71	9.64	16.60
High HDI	5.07	15.74	22.44	18.28	42.14	13.39	13.10	12.46	15.44	14.95	10.39	12.90
Very high HDI	3.21	2.27	0.76	2.42	6.25	9.72	6.00	3.95	0.93	2.73	3.26	2.97
All regions	15.06	24.91	32.12	31.58	56.54	22.42	22.66	20.70	25.00	23.38	15.44	22.16

Figure 5: The proportions of cross-regional patients in overall and 11 main cancer groups among children and adolescents in China by HDI, 2018–20. Cross-regional patients are patients diagnosed outside their region of residence. HDI=human development index.

countries.³³ On the basis of the political commitment in the 2030 UN Agenda for Sustainable Development,¹⁸ more attention should be paid to girls who have cancer in the process of diagnoses, treatment, and prognosis.

Compared with children, we found that adolescents have a higher overall incidence of cancer and a different spectrum of cancer types having the highest incidence, with greater sex differences in the most common cancer types and corresponding incidence rates. We also found a sharp decline in the incidence of adolescent cancer in regions with the highest accessibilities of health services.

One possible reason for the decline is that some cancers could be diagnosed earlier in childhood in these regions, and this possibility is worth being further evaluated by combining tumour staging and survival data. Under the influence of many unique physiological characteristic, adolescents face different cancer risks and disease burdens to children and adults.⁴⁴ Building on China's substantial achievements in reducing child mortality, adolescent health and child health have been equivalently placed on the priority list in the Health China 2030 document.⁴⁵ Multisectoral control plans for adolescent

cancer are a start to addressing the social and environmental determinants of health that put adolescents at risk, and ultimately affect the overall health of this population.⁴⁶

Given the little understanding of causes of most childhood cancers and their high mortality without appropriate and timely diagnosis and treatment, strategies should focus on increasing the accessibility of health services for early diagnosis to reduce disease burden. A better understanding of the childhood and adolescent cancer burden at the national and regional level is the first step towards developing childhood cancer control plans. The COVID-19 pandemic is likely to further exacerbate previously existing socioeconomic inequalities faced by children and adolescents with cancer. In the post-pandemic period, there is an urgent need for policy makers to increase the allocation of resources, such as improving medical facilities and the paediatric oncology workforce in lower socioeconomic areas. In the process of promoting the hierarchical diagnosis and treatment system in China, the capacity-building of paediatric cancer health services should be one of the criteria for establishing regional centers for children's health and regional centers for cancer. The integration between primary health-care institutions maternal and child health-care hospitals and regional centres for children's health and national centres for children's health should also be strengthened, especially in regions with a lower geographical accessibility of health services. Internet Plus^{47,48} medical services and artificial intelligence health care should be boosted as an effective measure to narrow regional gaps, giving patients at the grassroots level, especially those in remote areas, more access to quality health services. Health knowledge disseminations need to be carried out through school and community platforms to promote the recognition and awareness of common symptoms of childhood and adolescent cancer among parents and school doctors. Targeted early diagnosis programmes, such as popularising the early diagnosis of retinoblastoma through eye disease screening and visual acuity assessment among children aged 0–6 years nationwide, are also necessary.

Our study has several limitations. First, our estimates of incidence rates could be underestimated because of the following reasons. The estimation of cases relied on records from the HQMS database, which includes nearly all tertiary hospitals, but only some secondary hospitals.²¹ However, based on our surveillance, less than 0.05% of new cases were diagnosed in non-tertiary hospitals. Additionally, there was a paucity of outpatient data in the NCPDS and HQMS databases. In the context of universal health insurance coverage in China, the number of patients who were diagnosed in outpatient clinics without subsequent admission to hospital was low. Meanwhile, death certificates and underdiagnosed cases were not adjusted for. Second, we used at least

12 months as a washout period to identify new cases, which might lead to the slight overestimation of some cancers because cases who were diagnosed or treated before the washout period may be incorrectly considered as new cases. We further assessed the effect of different washout periods on the number of new cases, and found that a 1.01% overestimation might exist compared with using a 36-month washout period. Third, 18.33% of new cases were classified into the unspecified diagnostic subgroups because of the undetailed morphology codes, highlighting the importance of targeted training registrars to improve the data quality. Fourth, we did not further analyse the intraregional and intraprovincial disparities, because the estimated incidence rate in each province could be unstable because it was based on only 3 years' worth of data. Fifth, we evaluated the accessibility of paediatric oncologist and pathology workforce only by their numbers; their professional abilities should be surveyed and analysed in the future. Finally, more social determinants of health indicators (such as diagnostic equipment and individual-level socioeconomic data) should be evaluated in future surveys in addition to the four indicators used in this study.

In conclusion, through a combination of cancer incidence and health service access data, this study reveals the substantial burden of childhood and adolescent cancer in China, which might have been substantially underestimated and long neglected, as well as the quantifiable evidence of socioeconomic inequalities faced by children and adolescents with cancer in LMICs. Our analysis provides baseline data and a roadmap for targeted policies and precision public health programmes for alleviating the disease burden and socioeconomic inequalities in the Sustainable Development Goals era in China, and further expansion and improvement of the nationwide childhood cancer registry will be the only way to assess its effectiveness at the national and subnational levels.

Contributors

XN, ZL, XL, XZ, GB, YiL, and JZhan developed the study concept and drafted the analyses plan. ZL, XL, XZ, XX, YuL, CJ, YX, ZD, and YZe collected the data. ZL, RZ, and XL carried out data quality control. GB, XZ, YiL, and ZY sorted out the rules of disease coding conversion. XL, YiL, XZ, and ZL did the analysis and prepared the results. GB and XZ made the figures and tables. XN, ZL, YiL, XZ, XL, and GB wrote the first draft of the paper. YZh and XN revised the manuscript of the paper. GF directed the statistical methods. HW, XM, HZ, YS, MG, QZ, SW, JZhao, YZe, and YG provided professional guidance on childhood cancer. All authors provided input into interpretation of the results and content of the paper. XN, ZL, XL, XZ, GB, and YiL had full access to all data in the study and verified the data, and are responsible for the integrity and accuracy of the data and the decision to submit the manuscript. All authors revised the report and approved the final version before submission.

Declaration of interests

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Administration of Hospitals Incubating Program (PG2022024). GB reports a grant from the National Natural Science Foundation of China (82104470). All other authors declare no competing interests.

Data sharing

Data sources of HDI, the population aged 0–19, and geographical area are listed by regions in the appendix (p 8). Data sources of health services are listed by regions in the appendix (p 9). References cited by data sources can be viewed. The National Center for Pediatric Cancer Surveillance (NCPCS) hospital admission record database and Hospital Quality Monitoring System hospital admission record database are listed in the appendix (pp 12–14). The NCPCS new incidence case database from this study, including deidentified individual participant data and all codes used for generating the results, will be made available upon publication to members of the scientific and medical community for non-commercial use only, upon email request to ncpcs@bch.com.cn. According to the Personal Information Protection Law of China, individual participant data in our study will not be made available publicly.

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