

## Estimated National and State Level Incidence of Childhood and Adolescent Cancer in India

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**Background:** Hitherto, incidence burden of childhood cancer in India has been derived from GLOBOCAN data. Recent analyses have challenged whether this accurately measures the true incidence of childhood cancer.

**Objective:** To use observed data rather than simulation to estimate the number of children (0-14 years), as well as number of children and adolescents (0-19 years), in India who develop cancer every year at the national and state/union territory (UT) level.

**Methods:** Age-specific (five year groups), sex-specific, and state/UT specific population data from India Census 2011 was used. Global average incidence rates from the International Incidence of Childhood Cancer 3 (IICC3) report were used. Incidence rates per million person-years for the 0-14 years and 0-19 years age groups were age-adjusted using the world standard population to provide age-standardized incidence rates, using the age-specific incidence rates for individual age groups (0-4 years, 5-9 years, 10-

14 years, and 15-19 years).

**Results:** The national number of children (0-14 years) and children and adolescents (0-19 years) that may develop cancer every year based on 2011 census are 52,366 and 76,805 persons respectively. Cancer type specific incidence is provided for each state/UT for these age ranges. This national incidence is approximately double of the GLOBOCAN 2018 estimates of incidence of children diagnosed and registered with cancer and the differential is greater in girls.

**Conclusion:** Our analysis proposes new estimates of incident childhood cancer cases in India for children and adolescents. Future regional, national and international research on childhood cancer epidemiology and healthcare accessibility would help further refine these estimates.

**Keywords:** Cancer registry, Epidemiology, Incidence, Population data.

Defining the local incidence of cancer is a key first step towards developing a comprehensive cancer control strategy [1]. In the context of childhood cancer, such information helps to understand disease etiology, improve access to care, plan investments in service delivery, advocate resource allocation, and measure the quality of different components of the health system [1].

Estimates of global and country-specific cancer and childhood cancer burden are provided by multiple groups. The recently published GLOBOCAN 2018 study [2], coordinated by the International Agency for Research on Cancer, provides comprehensive global childhood cancer incidence estimates and is commonly used by the World Health Organization and governments for planning cancer control. In 2018, the study estimated that 200,166 new children, age 0-14 years, were diagnosed and registered with cancer globally, of whom 28,712 (14.3%) were from India [2].

Recent analyses have questioned the accuracy of GLOBOCAN data for estimating the incidence of

childhood cancer [3]. The local incidence of childhood cancer varies substantially in the published data including that from India [4,5]. It has been hypothesized that under-diagnosis and consequently under-registration, which is disproportionately high in low and middle income countries (LMIC), leads to an "incidence gap" and under-estimates the cancer burden, and are hence not reflected in the GLOBOCAN 2018 data [6]. This theory has been further substantiated by independent simulation-based studies that have estimated the annual global childhood cancer burden is nearly 45% greater than that historically reported, between 360,000 to 400,000, when children who develop cancer but are never registered are counted [7,8].

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Due to perceived incomplete case-finding, misdiagnosis within the fragmented Indian health system and significantly lower incidence-rates of childhood cancer in India, the currently reported childhood cancer from GLOBOCAN 2018 likely represent an underestimate [5,9]. In this study, we aim to use observed data

rather than simulation to estimate the number of children (0-14 years), as well as number of children and adolescents (0-19 years), in India who develop cancer every year. Additionally, we report these data at the national and state/union territory (UT) level for the purposes of supporting cancer control planning.

## METHODS

Age-specific (five year groups), sex-specific, and state/UT-specific population data from India Census 2011 was used [10]. These data pre-date the division of Andhra Pradesh in 2014 and Jammu and Kashmir in 2019 and hence considers these states as a whole. Conducted every 10 years since 1872, phase one of the 2011 census began on 1<sup>st</sup> April 2010 and included house-listing and collecting information for the National Population Register. The second phase was the population enumeration phase done from 9 to 28 February, 2011.

Global average incidence rates from the International Incidence of Childhood Cancer 3 (IICC3) report were used [4]. Conducted by the International Agency for Research on Cancer with the specific purpose of collecting and disseminating childhood cancer data, IICC-3 is the third monograph following from IICC-1 published in 1988 and IICC-2 published in 1998. Only population based cancer registries were invited. The target period covered the years starting with 1990, and targeted the age range of 0-19 years. IICC-3 uses observed data on cancer incidence from countries or regions covered by population-based cancer registries and unlike GLOBOCAN does not extrapolate to produce selected national, regional or global cancer burden estimates.

Incidence rates per million person-years for the 0-14 years (children) and 0-19 years (children and adolescents) age groups were age-adjusted using the world standard population to provide age-standardised incidence rates, using the age-specific incidence rates for individual age groups (0-4 years, 5-9 years, 10-14 years, and 15-19 years).

*Statistical analyses:* Number of incident cases for 0-14 years, 0-19 years and individual age groups (0-4 years, 5-9 years, 10-14 years, and 15-19 years) was calculated by multiplying incidence rates with the denominator population for the country and each state/UT. To get cancer-specific incident cases according to the International Childhood Cancer Classification third edition in 0-14 years age group, cancer-specific incidence rates were multiplied with the denominator population for the country and each state/UT [11]. As cancer-specific incidence rates were not available for 0-19 year

age group, cancer-specific incident cases for this age group were obtained by adding incident cases in the 0-14 year age group derived above and cancer-specific incident cases in the 15-19 year age group. To derive the cancer-specific incident cases in 15-19 year age group, cancer-specific incidence rates for this age group were multiplied with the denominator population for the country and each state/UT.

## RESULTS

Using globally observed data and local population estimates, the national number of children (0-14 years) and, children and adolescents (0-19 years) that may develop cancer every year are based on 2011 census as 52,366 and 76,805 persons, respectively (**Table I**). The national incidence for boys and girls of 0-14 years of age are 29,425 and 23,045 persons, respectively, and 42,160 boys and 33,694 girls for those 0-19 years of age. Uttar Pradesh, Bihar, Maharashtra, West Bengal and Madhya Pradesh are the five states with the largest absolute burden of disease (**Table I**). Leukemias, central nervous system (CNS) tumors and lymphomas are the three most common cancers in the 0-14 years age group contributing to 33.0%, 20.1% and 10.8% of the total burden (**Table II**), and account for 27.0%, 16.8% and 13.9%, respectively of the total burden in the 0-19 years age group (**Table III**).

## DISCUSSION

The National Cancer Registry Program (NCRP) in India provides data for the observed individual population based cancer registries which include all patients with cancer diagnosed and registered, and cover less than 10% of the Indian population [12]. The NCRP report, however, does not extrapolate to provide an estimate of the national incidence of childhood cancer. National estimates used for cancer control planning in India are provided by the GLOBOCAN 2018 models that are built using individual cancer registry data from the NCRP report, national vital statistic data sets and economic development covariates [2,12]. In this analysis, using internationally standardized incidence rates and population-estimates from India, we found that the incidence of childhood cancer is 54.8% larger in 0 to 14 years age range (52366 vs 28712) and 50.3% larger in 0 to 19 years age range (76805 vs 38640) compared to GLOBOCAN 2018. We hypothesize the large observed difference between the two estimates is due to the substantial number of cases that are not diagnosed and/or registered in India [6-8].

For health systems planning, calculating both the number of patients who will develop cancer and the

Table I Age- and Gender-Specific Incident Cases of Cancer in Children and Adolescent in States and Union Territories of India

	0-4 y	5-9 y	10-14 y	15-19 y	0-14 y, boys	0-14 y, girls	0-14 y, both	0-19 y, boys	0-19 y, girls	0-19 y, both
Incidence rate (per million)	187.9	107.6	114.4	185.3	151.4	129.4	140.6	163.2	143.6	155.8
India	21196	13657	15182	22334	29425	23045	52366	42160	33694	76805
Andaman & Nicobar	5	3	4	6	7	6	13	11	9	20
Andhra Pradesh	1181	786	938	1500	1696	1370	3064	2514	2080	4656
Arunachal Pradesh	27	18	21	29	38	32	69	54	46	101
Assam	604	381	399	569	792	649	1441	1114	932	2075
Bihar	2399	1618	1592	1755	3285	2591	5866	4404	3476	7976
Chandigarh	15	10	11	19	22	16	37	33	24	58
Chhattisgarh	477	297	330	482	629	522	1151	893	763	1680
Dadra & Nagar Haveli	7	4	4	6	9	7	15	12	9	22
Daman & Diu	4	2	2	5	4	3	8	8	5	13
Delhi	260	165	189	309	372	273	642	552	409	971
Goa	19	11	13	21	25	20	45	37	30	67
Gujarat	1026	628	703	1087	1405	1056	2453	2028	1563	3632
Haryana	444	269	305	496	625	440	1059	917	659	1590
Himachal Pradesh	102	64	73	119	142	109	250	207	164	376
Jammu & Kashmir	266	152	162	229	341	257	596	473	371	853
Jharkhand	686	445	470	594	924	749	1672	1276	1045	2352
Karnataka	948	564	656	1080	1247	1008	2253	1840	1519	3405
Kerala	461	275	323	484	604	497	1101	868	736	1627
Lakshadweep	1	1	1	1	1	1	2	2	2	3
Madhya Pradesh	1404	889	980	1380	1911	1511	3417	2710	2175	4946
Maharashtra	1759	1057	1228	1969	2389	1829	4206	3507	2736	6317
Manipur	48	31	36	53	67	54	121	96	80	179
Meghalaya	76	42	44	60	90	75	166	124	107	234
Mizoram	23	13	13	20	27	23	50	39	33	73
Nagaland	37	25	28	43	53	42	95	77	63	142
Odisha	686	438	497	727	934	765	1698	1328	1129	2493
Puducherry	18	11	12	19	23	19	42	33	28	62
Punjab	401	255	296	522	590	412	996	892	637	1543
Rajasthan	1372	865	959	1355	1900	1446	3336	2683	2097	4836
Sikkim	8	6	8	12	13	11	23	19	16	36
Tamil Nadu	992	597	707	1159	1325	1068	2391	1956	1619	3624
Tripura	61	36	41	66	79	64	143	114	97	214
Uttar Pradesh	3829	2697	2960	4269	5691	4363	10026	8143	6383	14700
Uttarakhand	174	114	131	208	250	191	440	366	289	663
West Bengal	1378	887	1048	1678	1913	1566	3478	2830	2363	5265

Table II International Childhood Cancer Classification Type-Specific Incident Cases of Cancer in Children 0-14 Years of Age in States and Union Territories of India

	Leukemias	Lymphomas	CNS tumors	SNS tumors	Retino-blastoma	Renal tumors	Hepatic tumors	Bone tumors	Soft tissue sarcomas	Germ cell tumors	Epithelial tumors <sup>a</sup>	Other <sup>b</sup>
Incidence rate (per million)	46.4	15.2	28.2	10.4	4.5	8.2	2.3	5.7	8.9	4.9	4.6	1.2
India	17281	5661	10503	3873	1676	3054	857	2123	3315	1825	1713	447
Andaman & Nicobar	4	1	3	1	0	1	0	1	1	0	0	0
Andhra Pradesh	1011	331	615	227	98	179	50	124	194	107	100	26
Arunachal Pradesh	23	7	14	5	2	4	1	3	4	2	2	1
Assam	476	156	289	107	46	84	24	58	91	50	47	12
Bihar	1936	634	1177	434	188	342	96	238	371	204	192	50
Chandigarh	12	4	8	3	1	2	1	2	2	1	1	0
Chhattisgarh	380	124	231	85	37	67	19	47	73	40	38	10
Dadra & Nagar Haveli	5	2	3	1	0	1	0	1	1	1	0	0
Daman & Diu	3	1	2	1	0	0	0	0	0	0	0	0
Delhi	212	69	129	47	21	37	11	26	41	22	21	5
Goa	15	5	9	3	1	3	1	2	3	2	1	0
Gujarat	809	265	492	181	79	143	40	99	155	85	80	21
Haryana	349	114	212	78	34	62	17	43	67	37	35	9
Himachal Pradesh	82	27	50	18	8	15	4	10	16	9	8	2
Jammu & Kashmir	197	64	120	44	19	35	10	24	38	21	20	5
Jharkhand	552	181	335	124	54	98	27	68	106	58	55	14
Karnataka	744	244	452	167	72	131	37	91	143	79	74	19
Kerala	363	119	221	81	35	64	18	45	70	38	36	9
Lakshadweep	1	0	0	0	0	0	0	0	0	0	0	0
Madhya Pradesh	1128	369	685	253	109	199	56	139	216	119	112	29
Maharashtra	1388	455	844	311	135	245	69	171	266	147	138	36
Manipur	40	13	24	9	4	7	2	5	8	4	4	1
Meghalaya	55	18	33	12	5	10	3	7	10	6	5	1
Mizoram	17	5	10	4	2	3	1	2	3	2	2	0
Nagaland	32	10	19	7	3	6	2	4	6	3	3	1
Odisha	560	184	341	126	54	99	28	69	107	59	56	14
Puducherry	14	5	8	3	1	2	1	2	3	1	1	0
Punjab	329	108	200	74	32	58	16	40	63	35	33	9
Rajasthan	1101	361	669	247	107	195	55	135	211	116	109	28
Sikkim	8	3	5	2	1	1	0	1	1	1	1	0
Tamil Nadu	789	259	480	177	77	139	39	97	151	83	78	20
Tripura	47	15	29	11	5	8	2	6	9	5	5	1
Uttar Pradesh	3309	1084	2011	742	321	585	164	406	635	349	328	86
Uttarakhand	145	48	88	33	14	26	7	18	28	15	14	4
West Bengal	1148	376	698	257	111	203	57	141	220	121	114	30

CNS – central nervous system, SNS – sympathetic nervous system. <sup>a</sup> also includes melanomas, <sup>b</sup> also includes unspecified.

Table III International Childhood Cancer Classification Type-Specific Incident Cases\* of Cancer in Children 0-19 Years of Age in States and Union Territories of India

	Leukemias	Lymphomas	CNS tumors	SNS tumors	Retino-blastoma	Renal tumours	Hepatic tumors	Bone tumors	Soft tissue sarcomas	Germ cell tumors	Epithelial tumors <sup>a</sup>	Other <sup>b</sup>
India	20716	10699	12901	3958	1676	3223	1001	3859	4870	4501	6474	784
Andaman & Nicobar	5	3	3	1	0	1	0	1	1	1	2	0
Andhra Pradesh	1242	670	776	232	98	190	60	241	298	286	420	49
Arunachal Pradesh	27	14	17	5	2	4	1	5	6	6	8	1
Assam	563	284	350	109	46	88	27	103	131	118	168	21
Bihar	2206	1030	1365	441	188	355	107	374	494	415	566	77
Chandigarh	15	8	10	3	1	2	1	3	4	4	5	1
Chhattisgarh	454	233	283	87	37	71	22	84	106	98	140	17
Dadra & Nagar Haveli	6	3	4	1	0	1	0	1	1	1	2	0
Daman & Diu	3	2	2	1	0	0	0	1	1	1	1	0
Delhi	259	139	162	49	21	40	13	50	62	59	87	10
Goa	18	10	11	3	1	3	1	3	4	4	6	1
Gujarat	977	510	609	186	79	151	47	184	231	216	312	37
Haryana	426	226	266	80	34	65	21	81	102	96	140	17
Himachal Pradesh	101	54	63	19	8	15	5	19	24	23	33	4
Jammu & Kashmir	232	116	144	45	19	37	11	42	54	48	68	9
Jharkhand	643	315	399	126	54	102	31	114	147	129	181	23
Karnataka	910	487	568	171	72	140	44	175	218	208	304	36
Kerala	438	228	273	83	35	68	21	82	103	96	139	17
Lakshadweep	1	0	1	0	0	0	0	0	0	0	0	0
Madhya Pradesh	1340	681	834	258	109	210	65	246	312	284	406	50
Maharashtra	1691	899	1055	319	135	260	82	324	403	383	557	66
Manipur	48	25	30	9	4	7	2	9	11	11	15	2
Meghalaya	64	32	40	12	5	10	3	11	15	13	18	2
Mizoram	20	10	12	4	2	3	1	4	5	4	6	1
Nagaland	38	20	24	7	3	6	2	7	9	8	12	1
Odisha	672	348	419	128	54	105	32	125	158	146	211	25
Puducherry	17	9	10	3	1	3	1	3	4	4	5	1
Punjab	409	225	256	76	32	62	20	81	99	97	144	16
Rajasthan	1309	666	815	252	107	205	63	241	306	279	398	49
Sikkim	10	5	6	2	1	1	0	2	2	2	3	0
Tamil Nadu	967	520	604	181	77	148	47	187	232	222	325	38
Tripura	57	30	36	11	5	9	3	11	14	13	19	2
Uttar Pradesh	3965	2047	2469	758	321	617	192	738	932	861	1238	150
Uttarakhand	177	95	111	33	14	27	9	34	42	40	59	7
West Bengal	1406	755	878	264	111	216	68	271	337	322	472	55

\*Incidence rate for each of the major cancer types for the 0-19 years age group were not available and the burden was estimated by adding incident cases in the 0-14 year age group and 15-19 year age group (incidence rates for the cancer subtypes for the ages 15-19 were available); CNS: central nervous system; SNS: sympathetic nervous system; <sup>a</sup>also includes melanomas; <sup>b</sup>also includes unspecified

**WHAT IS ALREADY KNOWN?**

- Incidence burden of childhood cancer in India has been derived from GLOBOCAN data.

**WHAT THIS STUDY ADDS?**

- The national number of children (0-14 years), and children and adolescents (0-19 years) that may develop cancer every year in India (based on census 2011) are 52366 and 76805 persons, respectively.
- This is approximately double the previous estimates of incidence of children diagnosed and registered with cancer.

number of patients who are diagnosed and registered is critical information. Knowing the current healthcare utilization needs presently is critical for states to make allocation decisions today. However, as cancer control plans typically are written as multi-year plans, identifying the gap between the observed and expected cases is important. In particular, as strategies to improve access and referral are often built into national cancer control plans, these calculations can inform prioritization, decision-making, monitoring procedures and budgeting.

Not only is the incidence of diagnosed and registered (GLOBOCAN 2018) approximately half of those who develop cancer (our estimates), **Suppl. Table I** shows this differential varies by age, gender and cancer. The estimated proportion of girls diagnosed and registered with cancer is 10% less than boys. This aligns with the narrative of female children with cancer experiencing relatively greater barriers to accessing healthcare [5,13-15]. Similarly the differential of the GLOBOCAN 2018 estimates and those from our analysis is greatest in CNS tumors and lowest in leukemias. This may reflect the relatively sick nature of leukemia patients, and easy availability of automated blood counts and bone marrow examination as compared to more sophisticated and technology dependent interventions like neuroimaging and neurosurgery. There is also a component of under-ascertainment in diagnosed CNS tumors as currently NCRP datasets exclude tumors with 'benign' or 'uncertain' behavior and such tumors constitute 40-50% of CNS tumors in children and adolescents [16].

Limitations of our analysis are that we are using the 2011 census data and hence have likely slightly over-estimated the incidence of new cases. Although the population of India is projected to peak around 2050, that for children ages 0-19 years is expected to peak between 2010 to 2020. And hence one can argue that the burden in 2011 will be higher by a few percentage points than the burden in 2020 and beyond. The census 2011 however remains the most reliable estimates of population at the state and union territory level and hence was used. It is also difficult to be more precise to the relative

contributions of under-diagnosis versus under-registration although there is some evidence to support that under-diagnosis is the main component of 'incidence gap' in the burden [17]. The contribution of under-diagnosis and under-registration may vary across states depending on the healthcare accessibility but in our analysis we have assumed that it is same across states.

Perhaps the most important question in regard to our estimates is its reliability and accuracy. While there is a degree of uncertainty around the burden, its reliability can be inferred from two arguments. Firstly, is the central tenet that environment plays a minor role in the etiology of childhood cancer hence the variation in the incidence of childhood cancer across the world is limited [4,18]. Secondly, under-diagnosis and other aspects of impaired healthcare access like delayed diagnosis, abandonment of treatment, etc. are well-recognized issues in LMICs [5,14,17,19,20]. Our estimates of 45-50% under-diagnosed children mirrors other recently published data which reached similar conclusions using differing methodologies [7,8].

In conclusion, our analysis proposes new estimates of incident childhood cancer cases in India. We also provide estimates at state and union territory level. This has enormous implications for all childhood cancer stakeholders who aim to provide access, treatment and chance of long-term cure to every child with cancer. It also suggests that access to diagnosis is as big, if not a bigger problem, than access to complete treatment and needs to be tackled early and urgently. Future regional, national and international research on childhood cancer epidemiology and healthcare accessibility would help further refine these estimates.

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**Supplementary Table I Comparison of Childhood Cancer Burden Estimates by GLOBOCAN and Our Analysis**

	0 to 14 years age			0 to 19 years age		
	Globocan	Our Estimate	% Diagnosed & Registered	Globocan	Our Estimate	% Diagnosed & Registered
<b>Total</b>	<b>28712</b>	<b>52366</b>	<b>54.8</b>	<b>38640</b>	<b>76805</b>	<b>50.3</b>
Boys	17468	29425	59.4	22960	42160	54.5
Girls	11244	23045	48.8	15680	33964	46.2
Leukemia*	11056	17281	64.0	13637	20716	65.8
Lymphoma*	3591	5661	63.4	5019	10699	46.9
CNS tumours*	3626	10503	34.5	4638	12901	36.0
Kidney tumours*	1466	3054	48.0	1578	3223	49.0
Liver tumours*	421	857	49.1	481	1001	48.1

\*Only those cancers were selected where the ICD site classification aligns closely with the ICC morphology classification

CNS – central nervous system