

Expected number of childhood cancers in Italy from 2001 to 2015

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ABSTRACT

The total number of children with incident cancer in Italy has never been specifically estimated. Specialized population-based Childhood Cancer Registries have only been operating in Piedmont (CCRP) and in the Marche region, while general population cancer registries cover about 20% of the Italian population. The number of expected cases of childhood cancer (0-14 years) in Italy in the period 2001-2015 has been estimated using CCRP incidence rates and annual percentage changes. The expected number of cases of all cancer types were 8,132, 8,672 and 8,944 in the periods 2001-2005, 2006-2010 and 2011-2015 respectively. These figures help evaluate the allocation of resources for the care of child cancer patients in Italy, and to estimate the number of cases expected to enter clinical trials.

Key words: childhood, cancer, expected number.

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In Italy, population-based cancer registries cover almost 20% of the population.¹ In addition to the general Cancer Registries, two specialized Childhood Cancer Registries have been operating in Piedmont (CCRP)² and in the Marche region³ from 1967 and 1990, respectively. These cover 6% and 2% of the child population of Italy, respectively. Furthermore, a hospital-based registry covering almost all of the country was set up by the Italian Association of Pediatric Hematology and Oncology (AIEOP) in 1989.⁴ Incidence rates of childhood cancer measured by the population-based Italian Cancer Registries are remarkably similar, with higher rates in measured by the specialized registries than the general registries. However, variations in incidence rates do not appear to be systematically related to geographic trends. On the contrary, variations appear to occur randomly across the country.⁵

The aim of this study is to estimate the number of expected cases of cancer (all types together and main tumour types) in children under the age of 15 for the period 2001-2015 in Italy. Estimates are based on

population projections from the Italian National Institute of Statistics (ISTAT)⁵ and on the incidence rates and annual percentage changes calculated using CCRP records.² The present study could help estimate the resources needed for childhood cancer care in different geographic areas of Italy and the proportion of children entering multicenter clinical studies.⁴

Design and Methods

Piedmont is a highly industrialized region in the north-west of Italy. In 2001, the total population was 4,213,294. While the general population was stable, the childhood population decreased sharply from approximately 800,000 in 1975-79 to 500,000 in 1999-2001 due to decreasing birth rates.⁶

The CCRP has recorded cancer incidence in children (age 0-14 years) resident in the region since 1967. Data collection and coding procedures have been previously reported,^{2,6} and were homogeneous throughout the entire period of activity of

Table 1. Estimated number of childhood cancers (0-14 years) in Italy for the periods 2001-05, 2006-2010, and 2011-2015, by cancer groups with statistically significant APC of incidence rates.

Time period	Geographic Area	Leukemia [¶]		Acute Lymphoblastic Leukemia		Central Nervous System Tumors		Sympathetic Nervous System Tumors		Soft Tissues Sarcomas		Germ Cell Tumors		All Tumors	
		CIR ¹	CIT ² APC%* 1.0	CIR ¹	CIT ² * APC%* 1.2	CIR ¹	CIT ² * APC%* 2.3	CIR ¹	CIT ² * APC%* 2.3	CIR ¹	CIT ² * APC%* 1.4	CIR ¹	CIT ² * APC%* 3.0	CIR ¹	CIT ² * APC%* 1.3
2001-2005	North-Western	562	574	449	460	481	504	177	186	99	102	46	49	1,850	1,899
	North Eastern	405	413	324	332	345	362	128	134	71	73	33	35	1,330	1,365
	Central	424	432	338	346	366	383	133	139	75	77	35	37	1,404	1,441
	Southern	683	696	541	554	601	629	210	220	124	127	57	60	2,287	2,347
	Islands	314	320	248	254	277	290	95	100	57	59	26	28	1,052	1,079
	Italy	2,387	2,436	1,900	1,946	2,070	2,168	744	779	425	437	197	209	7,923	8,132
2006-2010	North-Western	574	615	458	497	490	575	173	202	100	110	45	55	1,872	2,049
	North Eastern	415	445	331	360	355	417	123	144	72	79	32	39	1,352	1,480
	Central	436	468	348	378	372	437	132	155	76	84	34	42	1,425	1,560
	Southern	683	732	545	592	584	685	215	252	121	133	56	69	2,251	2,464
	Islands	309	331	246	268	266	311	96	113	55	61	25	31	1,021	1,118
	Italy	2,417	2,591	1,927	2,095	2,067	2,425	739	867	423	467	192	237	7,922	8,672
2011-2015	North-Western	547	616	434	500	477	627	157	206	96	114	42	60	1,801	2,103
	North 394	444	312	360	346	455	112	147	70	83	30	43	1,303	1,521	
	North Eastern	424	477	337	388	368	484	123	162	74	88	33	47	1,393	1,626
	Southern	667	752	532	614	573	752	201	264	116	137	52	74	2,181	2,547
	Islands	300	338	239	276	258	339	90	119	52	62	24	34	983	1,147
	Italy	2,332	2,627	1,854	2,139	2,022	2,657	683	897	409	483	181	258	7,661	8,944
2001-2015	Italy	7,136	7,654	5,681	6,180	6,160	7,250	2,166	2,543	1,257	1,387	570	704	23,505	25,748

*Estimate accounting for the Age-adjusted Annual Percent Change (APCs) estimated by Dalmaso et al.⁶ ¶APCs in the period 1977-2001 for acute lymphoblastic leukemia and acute non-lymphatic leukemia, and 1967-2001 for all other cancer types. ¹CIR: constant incidence rate; CIT: constant incidence trends

the CCRP. All the diagnoses are coded using the ICD-O-2⁷ classification and then grouped according to the International Classification for Childhood Cancer (ICCC).⁸ Personal, medical and follow-up data were routinely collected for each patient with a confirmed residence in Piedmont.

The expected number of cases of selected childhood cancer types in Italy up to the year 2015 was calculated on the basis of the age specific incidence rates (per million children) recorded in Piedmont for the period 1997-2001. In the calculation, rates were corrected according to the time trends observed in Piedmont. Correction factors were based on the annual percent changes (APCs) in the period 1977-2001 for acute lymphoblastic leukemia and acute non-lymphatic leukemia, and in the period 1967-2001 for all other cancer types.⁶ The different time interval for leukemias was chosen to exclude the apparent impact of improved diagnostic methods in the early 1970s.⁶

APCs were estimated using Poisson regression analysis and adjusted for age and sex. The APC is computed as $100 \times (RR-1)$, where RR is the relative risk of a given

year with respect to the previous one adjusted for age and sex. Incidence time trends were taken into account to estimate the expected number of cases only if the calculated APCs were statistically significant ($p \leq 0.05$), otherwise it was assumed that the 1997-2001 incidence rates were stable and could be used for prediction.⁶

The national population figures stratified by calendar year, age and geographic area of residence for the period 2001-2015 were obtained from ISTAT and were based on census data, inter-census estimates and demographic projections. Notably, the ISTAT population projections are explicitly based on the assumption that, in the period 2005-2015, 150,000 persons will immigrate to Italy each year.⁵

Results and Discussion

Table 1 and 2 show the expected number of cases for each five year period, major cancer categories and Italian geographic areas, as defined by ISTAT.⁵ In particular, Table 1 shows the expected number of cases

Table 2. Estimated number of childhood cancers (0-14 years) in Italy for the periods 2001-05, 2006-2010, and 2011-2015, by cancer categories with stable incidence rates.

Time period	Geographic area	Acute non-lymphoblastic leukemia	Lymphomas	Hodgkin lymphoma	Non-Hodgkin lymphoma	Retino-blastoma	Renal tumors	Hepatic tumors	Bone sarcomas	Carcinomas
2001-2005	North-Western	94	221	105	49	47	116	12	38	52
	North Eastern	68	158	74	35	34	84	8	27	37
	Central	72	171	81	38	35	87	9	29	41
	Southern	118	290	140	63	54	136	14	50	69
	Islands	55	135	65	29	25	62	6	23	32
	Italy	406	974	465	214	195	484	49	166	231
2006-2010	North-Western	96	227	108	50	45	116	11	39	53
	North Eastern	70	165	78	37	32	84	8	28	39
	Central	73	172	82	38	35	89	9	29	41
	Southern	115	271	129	59	57	141	14	46	64
	Islands	52	125	60	27	25	63	6	21	30
	Italy	407	960	456	211	193	492	48	163	226
2011-2015	North-Western	94	231	111	51	40	107	11	40	54
	North Eastern	69	169	82	37	28	77	8	29	40
	Central	73	176	84	39	32	84	8	30	41
	Southern	112	265	125	59	52	135	13	45	62
	Islands	51	120	57	27	24	61	6	21	28
	Italy	399	961	459	213	175	463	46	165	225
2001-2015	Italy	1,212	2,895*	1,380*	637*	563	1,440	143	1,257	682

* Expected number of Burkitt and unspecified lymphomas were not estimated as specific categories. However, in the period 1997-2001, they represented 19% and 81% of the remaining lymphomas respectively.

by cancer categories whose APCs were statistically significant. The estimates are calculated both accounting and not accounting for the APC, ie. assuming constant time trends or constant incidence rates respectively. Table 2 shows the expected number of cases for those cancer categories characterized by non-statistically significant APCs.

On average, 1,600–1,700 cancer cases are expected to occur yearly. However, according to the estimated APC, the annual number of cases is expected to rise from the 1,626 new cases per year for the period 2001-2005, to 1,789 cases for the period 2011-2015. About 40% of all estimated cases will occur in northern Italy, 18% in central Italy, and 42% in southern Italy and the Islands.

The expected number of children developing leukemia, assuming rates remain stable, is 2,387 cases during the first five years, 2,417 during the second and 2,332 during the last five year period. Furthermore, if APCs are accounted for, a further 518 cases are expected to occur. In both instances, approximately 80% will be cases of acute lymphoblastic leukemia (ALL). Among the estimated cases of lymphomas, about 50% will be Hodgkin lymphomas, ranging from 456–465 cases in the 3 five year periods, and 20% will be non-Hodgkin lymphomas. The expected number of Burkitt and unspecified lymphomas were not estimated as specific categories. However, in the period 1997-2001, they represented 19% and 81% of the remaining lym-

phomas respectively. The number of expected central nervous system (CNS) tumor cases will decrease from 2,070 in the period 2001-05 to 2,022 in the period 2011-15 assuming rates remain stable. On the contrary, if APCs are accounted for, a further 1,090 cases is expected to occur in the period 2001-2015. The number of sympathetic nervous system (SNS) tumors will range from 744 in the first five years to 683 in the third five year period assuming stable rates, while the overall estimated number of extra cases according to the APCs is 377. Nearly 93% of all SNS tumors are expected to be neuroblastomas.

Descriptive epidemiologic studies can provide measures of burden of disease, impact on assistance and on health care provision and help plan pediatric oncology units. The present estimates of cases of childhood cancer expected in Italy, updating those published in 1992,⁹ are important for the allocation of resources for pediatric cancer care. The national population projection are based on assumptions of constant immigration rates, improving average life expectancy, and increasing fertility over the time period 2005-2015. Furthermore, our estimates have been calculated taking into account two possible scenarios: constant incidence rates over time or constantly increasing incidence time trends. In particular, we based our estimates on the following assumptions: a) for the cancer types with statistically significant

APCs, the incidence time trends are assumed to remain constant throughout the investigated time period; b) rates for cancer types will remain constant at the level estimated for the period 1997-2001; c) incidence rates and APCs estimated in Piedmont are representative of Italy as a whole, and can, therefore, be used to make nationwide projections. The trend for leukemias shows both an increase over the long term and short term variations.¹⁰ Since we calculated estimates for a long period and for wide time intervals, we expect the long term trend to prevail. As for CNS, the trend has been steady for 30 years and, therefore, it is reasonable to believe that there will be a further increase at the same pace. A strong increasing time trend for the incidence of neuroblastoma incidence in infants has appeared in recent years. If the APC used for prediction were estimated in the last time period rather than in the whole registration period, this would have led to a much larger number of estimated cases. The present paper provides a range of estimates for each cancer category with a statistically significant increasing incidence time trend.

The overall difference between the two estimates over the entire period is 2,748 cases, of which 19% (518) leukemias, 18% (499) ALL, 40% (1090) CNS tumors, 14% (377) SNS tumors, 5% (130) bone sarcomas and 5% (134) germ cell tumors. The assumption of homogeneous incidence rates and APC across Italy is the most reasonable operational hypothesis that can be obtained from the available data. It is supported by the small variation of incidence measured by the different cancer registries.¹ Given the small number of cases

recorded in the period 1997-2001, more detailed estimates were not drawn. In particular, 18 PNET and 6 glioma were identified among the CNS tumors, while 11 rhabdomyosarcoma and 14 non-rhabdomyosarcoma were identified among the soft tissue sarcomas. The estimation of an expected number of cases using unstable incidence rates estimates might have been misleading.

In absolute terms, the largest number of expected cancer cases will be leukemias, in particular ALL, and CNS tumors. In relative terms, the largest increase is estimated to occur among germ cells tumors and central and sympathetic nervous system tumors.

The authors believe that the most likely scenario is to be found between the two groups of estimates. For example, the incidence of neurological tumors is steadily increasing while increases in the incidence of leukemia is not constant. Nevertheless, in terms of planning healthcare resources, the estimates accounting for increasing trends should be considered as the upper limit for evaluating resources for childhood cancer care in Italy over the next ten years and for assessing the proportion of cases which can receive adequate care within multicenter clinical trials.

Author's Contributions

IB: conception and data analysis; MMM: conception and data analysis; ED: data analysis; PD, MLM: conception; MG: data analysis; FM: conception and data analysis; CM: conception and data analysis; GP: conception and data analysis.

Conflict of Interest

The authors reported no potential conflicts of interest.

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