Chapter 1. Introduction

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RATIONALE FOR THIS PUBLICATION

Cancer is predominantly a disease of older people. The risk of developing cancer is about 1 in 500 by age 15 years and about 1 in 5 by age 75 years. Although cancer is rarer in children than in adults, it is the leading cause of disease-specific deaths for children in many countries. The types of cancer that occur in childhood are quite different from those that are typical in adulthood. The major cancer types, when reported for all ages combined, are carcinomas of the breast, prostate, lung, colorectum, cervix uteri, and stomach [1], whereas in children the most commonly affected sites are the haematopoietic system, the central nervous system (CNS), and embryonal tissues [2].

The young age and the differences in the frequency of occurrence and in the spectrum of tumours suggest distinctive etiological paths for these tumours. About one third of the total cancer burden is thought to arise as a result of exposure to external factors, such as smoking, viruses, or diet, most of them modifiable. The proportion of cancers that are due to known causes in children probably does not exceed 5–10%, and the causes include heredity, ionizing radiation, and viral infections [3, 4, 5]. Other exposures have also been studied, such as parental factors, non-ionizing radiation, environmental pollution, and diet, but the evidence is not conclusive.

Large population-based studies have shown a steady annual increase of 0.6% in the incidence of childhood cancer over the past 20–30 years [2, 6, 7]. Although some of this increase may be ascribed to improved detection and registration of tumours [8], the persistence of these trends over the decades compels scientists to search for other contributing causes.

International Incidence of Childhood Cancer, Volume III (IICC-3) provides the most complete, standardized data on childhood cancer incidence around the world. This publication was specifically designed to appropriately address the particular features of childhood cancers, such as low frequency of occurrence, distinctive cancer types, variation between populations, patterns by age and sex, and diversity of data sources.

HIGHLIGHTS OF THIS VOLUME

Numbers of cases and incidence rates are presented by diagnostic categories of the updated International Classification of Childhood Cancer (ICCC), as described in Chapter 3. This classification defines the types of tumours included in the statistics and comprises all malignancies, as well as non-malignant tumours of the CNS.

The childhood age range considered includes adolescents (the age group 15–19 years), in accordance with previous large-scale studies [6, 9, 10], to enable the presentation in detail of incidence rates that are inadequately represented in statistics produced for all ages. The choice of the age range 0–19 years for IICC-3 enabled description of the tumour types that are common before age 15 years but whose incidence further increases or peaks in the age group 15–19 years, such as bone tumours, germ cell tumours, and thyroid carcinomas. ICCC is arguably well adapted to classify tumours occurring in adolescence [11], especially compared with the International Classification of Diseases (ICD) coding system [12], which is used for the presentation of cancer data in publications that are not focused on the childhood age range, such as the *Cancer Incidence in Five Continents* series (https://ci5.iarc.who.int/). The trend of including the age group 15–19 years with childhood cancer data has been to a large extent motivated by the discovery of less-favourable treatment outcomes in adolescents compared with children and the ensuing need for a specific focus on this neglected population. In response to these findings, several paediatric cancer registries have extended the covered population up to age 19 years, as evidenced in the current volume. However, the IICC-3 age range remains 0–14 years for those paediatric cancer registries that did not collect data on patients aged 15 years or older. For the sake of comparisons, data are provided as much as possible for the age groups 0–14, 15–19, and 0–19 years. To address variability of tumour types and incidence rates over the childhood age range, the incidence statistics for the registries are also presented for infants (age < 1 year) and the age groups 1–4, 5–9, and 10–14 years.

A set of customized criteria was developed to evaluate the quality and comparability of each submitted dataset. The datasets selected for publication in IICC-3 complied with the requirements of the peer-review process established by the editors of this volume, as described in Chapter 2. More than 300 registries operating in 82 countries and territories on five continents provided data deemed to be of high enough quality, and 65 registries were also able to supply cancer and population data for two or more ethnic groups. In total, information on 774 549 unique cancer cases from non-overlapping areas and time periods is available in IICC-3 (Table A.5), including 556 628 cases in the age range 0–14 years and 217 921 cases in the age range 15–19 years. Of these cases, about 40% were registered in Europe, 32% in North America, 17% in Asia, 7% in Latin America and the Caribbean, and less than 5% each in Africa and Oceania (Table 1.1).

Table 1.1. Scope of IICC-3: total absolute numbers (N) and percentage contribution (%) of cancer cases from non-overlapping areas and periods, non-overlapping population covered by contributing cancer registries in 2010, estimates of 2010 world population by age and continent [17], and estimated IICC-3 coverage in 2010

	Cases total period						Population in 2010					
Age (years)	0–19		0–14		15–19		0–14			15–19		
Continent	(N)	(%)	(N)	(%)	(N)	(%)	IICC-3 (N)	Continent (N)	Coverage (%)	IICC-3 (N)	Continent (N)	Coverage (%)
Africa	28 820	3.7	23 178	4.2	5 642	2.6	23 164 247	434 762 176	5.3	2 881 990	110 058 813	2.6
America, Latin and the Caribbean	54 380	7.0	43 917	7.9	10 463	4.8	25 961 422	165 059 645	15.7	5 100 519	55 333 040	9.2
America, North	250 549	32.3	168 954	30.4	81 595	37.4	65 996 816	67 910 619	97.2	23 933 182	24 388 039	98.1
Asia	129 129	16.7	91 560	16.4	37 569	17.2	67 771 204	1 073 983 845	6.3	19 642 721	369 273 598	5.3
Europe	286 686	37.0	212 764	38.2	73 922	33.9	75 627 558	113 899 254	66.4	19 897 016	43 155 104	46.1
Oceania	24 985	3.2	16 255	2.9	8 730	4.0	5 237 261	8 808 596	59.5	1 823 095	2 817 777	64.7
Total	**774 549**	**100.0**	**556 628**	**100.0**	**217 921**	**100.0**	**263 758 508**	**1 864 424 135**	**14.1**	**73 278 523**	**605 026 371**	**12.1**

The estimated coverage of the world population by the registries selected for inclusion in IICC-3 was 14% for children aged 0–14 years and 12% for adolescents aged 15–19 years in 2010, the year with the largest number of person-years, but the proportion covered varied extensively between the continents (Table 1.1; Fig. 1.1) and over time (Fig. 1.2). Registries in Africa contributed the largest annual number of person-years in 2006, those in Europe in 2004, those in the Americas and Asia in 2010, and those in Oceania in 2011.

IICC-3 includes the most up-to-date data that each registry could provide in the framework of data collection for this study, starting by default with 1990. Although the period of contribution varied by registry, the largest number of registries contributed data for 2010 (Fig. 1.2). The starting year of contribution was most often 1998 (56 registries), and the final year of contribution was most often 2012 (184 registries). The average length of the registration period included in IICC-3 was 15.8 years, and 108 registries provided data for 20 or more years. The long study period enabled the accumulation of a sufficient number of cases to provide relatively stable incidence rates even for small registration areas.

The variety and quantity of data available enabled the production of 518 tables showing incidence statistics for 515 different datasets and 116 comparative tables in which incidence statistics from the contributors are compared for each selected diagnostic category. Given the space limitations of a book to be printed, a great deal of material is available online only at https://iicc.iarc.who.int/. The contents of both the book and the online resources are described in Chapter 5.

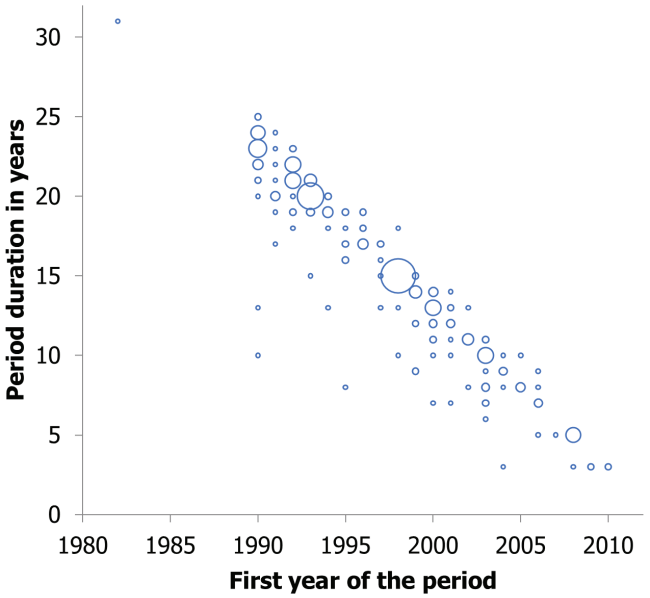

Fig. 1.2. Variation in the length and timing of the periods contributed by the registries to IICC-3. The areas of the bubbles represent the number of registries (ranging between 1 and 52) for each combination of the first year and the duration of the contributory period.

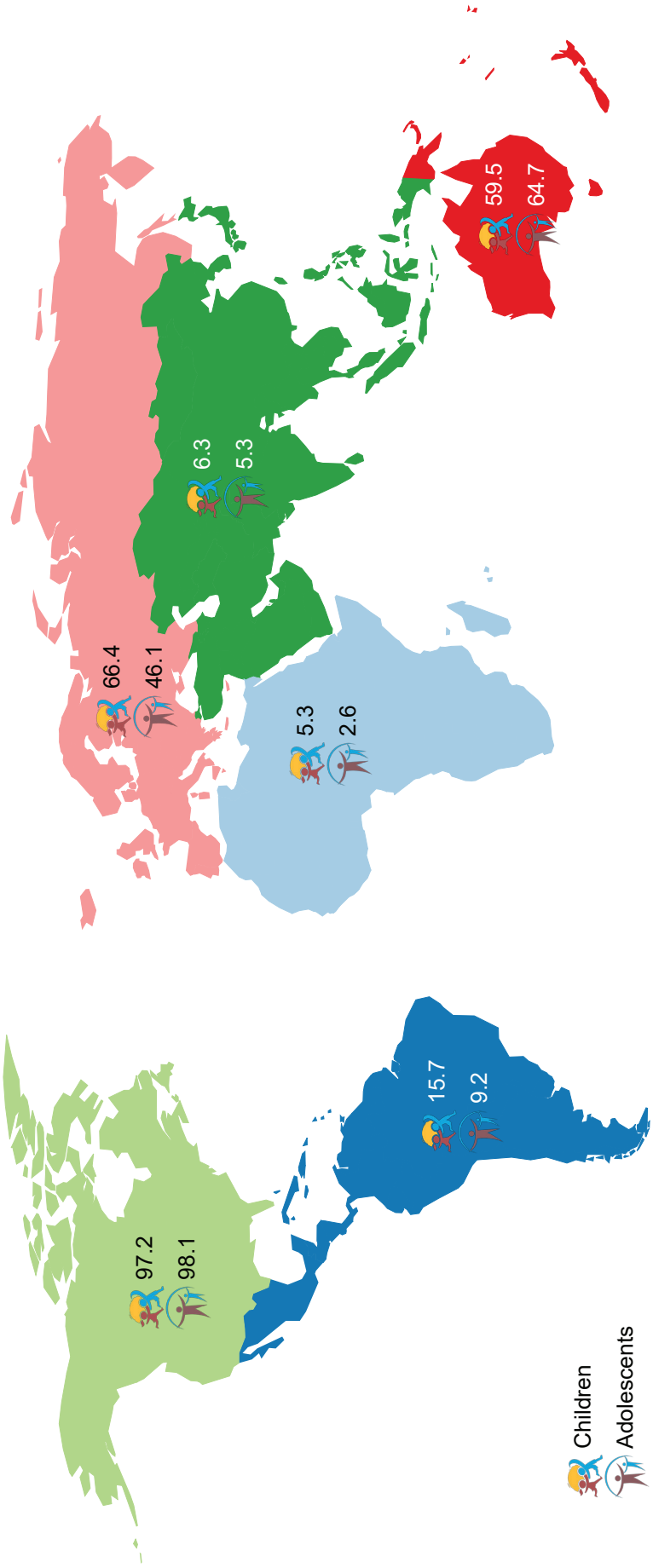

Fig. 1.1. Percentage of the population of children (age 0–14 years) and adolescents (age 15–19 years) covered by the registries contributing to IICC-3 in 2010, by continent.

THE IICC SERIES

IICC-3 is the third volume in a series, in which the first volume (IICC-1) targeted the decade of the 1970s [13] and the second volume (IICC-2) covered roughly the 1980s [14]. In all three volumes, the methodology of data collection, validation, analysis, and evaluation was supported by international standards recommended by the International Association of Cancer Registries (IACR). Although IICC-3 was conceived with the same principles as the two previous volumes, this publication is enriched by several novel attributes, one of which is the inclusion of adolescents, as mentioned above.

Only population-based cancer registries were invited and accepted to contribute to IICC3. This decision reflects the growing registration coverage, including in low-income countries, and the aim to describe the occurrence of childhood cancers for use in prevention and public health research. Because of much sparser registration coverage, the earlier volumes included case series from hospital or histopathology databases without a link to any underlying population; 18 such datasets were published in IICC-1 and 8 in IICC-2 (Table A.1).

The third edition of ICCC (ICCC-3) [11], which is based on the coding system of the third edition of the International Classification of Diseases for Oncology (ICD-O-3) [15], was modified for the purposes of this publication, taking into account ICD-O-3.1 [16] and several successive new editions of the WHO Classification of Tumours series (https://whobluebooks.iarc.who.int/), as described in Chapter 3. Despite an effort to maintain comparability with the classification of childhood cancer used in the previous volumes of IICC, some differences in the reported rates between the volumes and registries could reflect, to some extent, changes in classification.

The IICC series is produced by the International Agency for Research on Cancer (IARC) in collaboration with IACR. All contributors to IICC-3 were encouraged to join IACR to ensure the continued international coherence of the data collected in their cancer registry.

Table 1.2. Number of countries and territories, registries, and datasets included in each of the three volumes of IICC, by continent and overall

Continent	Countries and territories			Registries			Datasets		
	IICC-1	IICC-2	IICC-3	IICC-1	IICC-2	IICC-3	IICC-1	IICC-2	IICC-3
Africa	9	9	14	10	9	21	13	11	29
America, Latin and the Caribbean	6	8	16	8	9	38	8	9	42
America, North	2	2	2	21	26	70	11	31	241
Asia	13	13	17	20	27	58	22	33	69
Europe	15	21	29	25	55	109	24	55	113
Oceania	4	3	4	5	11	12	7	10	21
Total	**49**	**56**	**82**	**89**	**137**	**308**	**85**	**149**	**515**

As shown in Table 1.2, the number of countries and territories represented in IICC-3 has increased by almost 50% since IICC-2. The number of registries has grown 3.5-fold compared with IICC-1 and has doubled since IICC-2. The number of tables presenting different datasets has increased across the volumes, from 85 in IICC-1 to 515 in IICC-3 (Table 1.2). A dataset refers to a single cancer registry, to one of the ethnic groups defined within the registry, or to a pool of several registries operating in one country. Although the number of datasets expanded most in North America – specifically, the ethnically diverse datasets that constituted the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results (SEER) Program in the USA – the number of datasets presented also increased considerably in the other continents, compared with the previous volumes (Fig. 1.3).

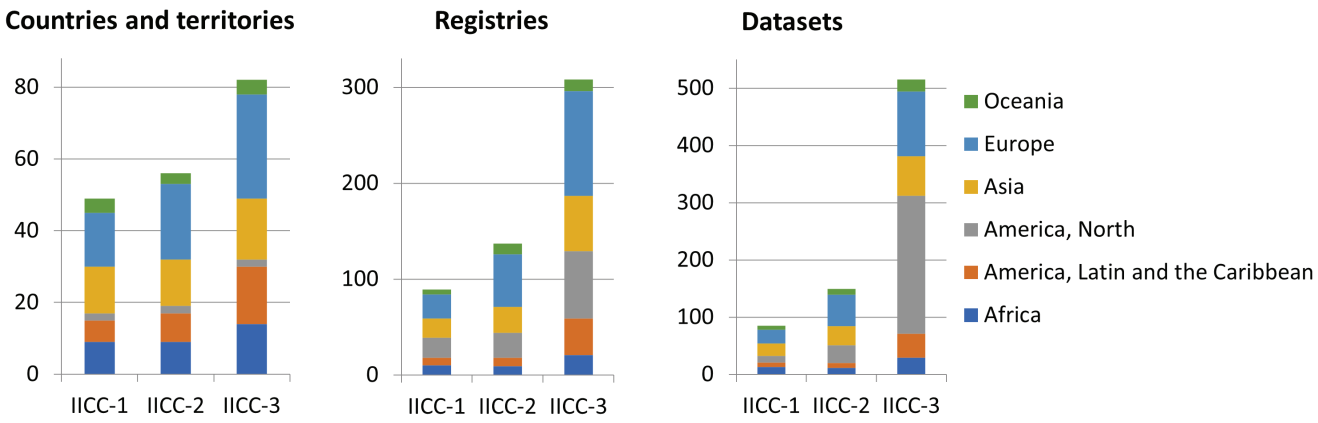

Fig. 1.3. Number of countries and territories, registries, and datasets included in each of the three volumes of IICC, by continent.

Among this large number of contributing entities, relatively few were present in all three volumes (Fig. 1.4; Table A.1). The contributors that are no longer present include the hospital or pathology case series reported in the first two volumes, primarily from Africa, Asia, and Oceania; also, some population-based cancer registries have ceased to exist. In several registries, the data were available but could not be shared because of the introduction of national laws on data protection that could not be complied with in the framework of an international study of this global scope. It is hoped that continued international collaboration will stimulate the development of mechanisms that would enable the sharing of these data in the future.

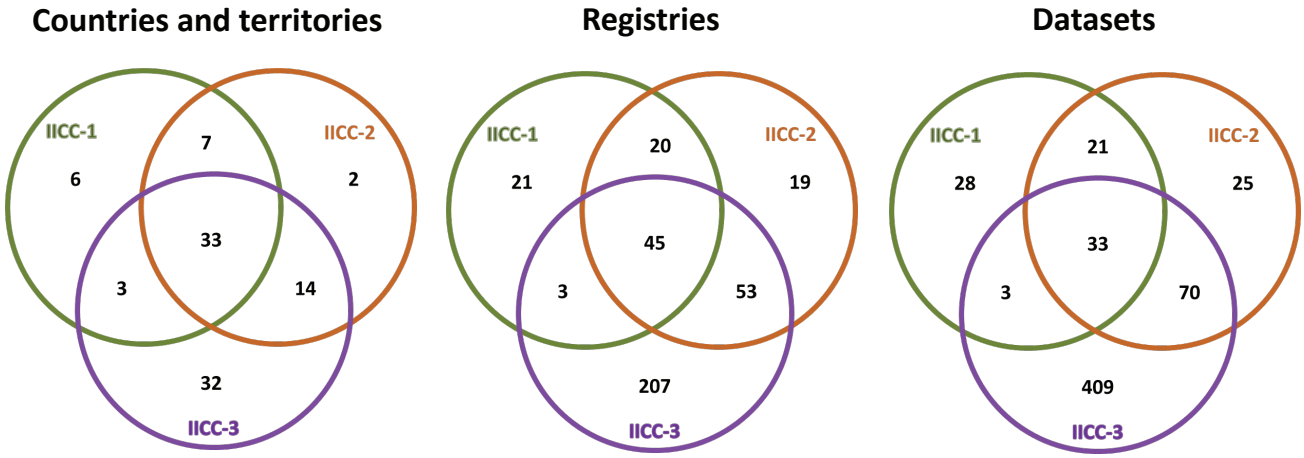

Fig. 1.4. Numbers of contributions to the three volumes of IICC.

With the publication of this third volume of IICC, an expectation may emerge to evaluate time trends using the IICC data from the three volumes. However, such assessment would be possible only after careful reprocessing of the databases from the three volumes, for several reasons. First, the tumours were classified according to a slightly different classification in each of the three volumes, which affects the comparability of the resulting rates. Second, some registries will have continued to modify the data they hold after records for the relevant years were submitted for the respective volumes of IICC, and the extent of the introduced changes is likely to differ between the calendar years and registries. Furthermore, improved registration processes and greater centralization of care for children with cancer have probably resulted in more complete case ascertainment and thereby an apparent increase in incidence rates. Readers should also be aware of possible changes in the proportions of unspecified diagnoses across volumes. Finally, the length of the periods covered by individual registries in the three volumes may be very different or, exceptionally, overlapping. For all these reasons, great caution should be exercised in making all but the most informal comparisons of the published incidence rates across the three volumes.

In the following chapters, the methods of data collection, processing, analysis, and presentation are described and the strengths and limitation of the released data are highlighted, to enable informed readers to make the best use of the results of this wide international collaboration, to the advantage of current and future generations of children.

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