

# Epidemiology of childhood cancer and the SACCSG tumour registry

**Childhood cancer is relatively rare, but it is still the second most common cause of death in children in Western countries.**

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Childhood cancer is relatively rare, comprising less than 1% of cases of malignant disease.<sup>1</sup> Cancer is the second most common cause of death in children in Western countries, while in Africa it is not even ranked among the 10 most common causes of death. Infections, nutritional disease, HIV and tuberculosis remain the most important paediatric health problems in developing countries. In developed countries, more than 80% of children with malignancies can be cured, but unfortunately most children with cancer live in developing countries, where the cure rate is much lower.<sup>2</sup> In 2009 South Africa's population was approximately 49 million, of whom 15 500 000 were in the age group 0 - 14 years.<sup>3</sup> This translates to over 31% of the population, while in the USA and Western Europe the corresponding figures are 20%<sup>4</sup> and 17%,<sup>5</sup> respectively.

There is a need to understand malignant disease in children to find more efficient ways of treating it. Such a task is usually approached at four different levels: (i) the molecular and sub-molecular level (biochemistry, cell biology, immunology and genetics); (ii) the tissular or organ level (pathology); (iii) the patient level (clinical medicine); and (iv) the population level (epidemiology – factors that govern the occurrence and distribution of a disease in a given population).<sup>6</sup> The combined data thus obtained create a comprehensive picture of the disease, leading to more effective prevention and cure.

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## *Contribution of epidemiology to prevention and cure*

This contribution is considerable and manifests at many levels. Firstly, **descriptive epidemiology** focuses on the characteristics of the population affected by a given malignancy, such as age group, geographical distribution, sex and ethnicity. It provides information on the incidence and mortality of a given cancer over years, enabling

the assessment of efficacy of various therapeutic interventions. It also identifies new syndromes and risk factors for known diseases. For example, by establishing that acute lymphoblastic leukaemia (ALL) is the most frequent cancer in childhood (up to 25% of all cancers),<sup>7</sup> the study indicated that research of the causes, diagnosis and cure would lead to major gains by reducing the burden of malignant disease in children. However, epidemiological studies have found that in parts of Central Africa the most commonly encountered childhood cancer is not ALL, but Burkitt's lymphoma, constituting almost 50% of all malignancies in children.<sup>8</sup> Therefore, in that geographical area, targeting Burkitt's lymphoma instead of ALL would be more effective in terms of population health.

**Analytical epidemiology** tests hypotheses formulated on the basis of descriptive studies. It mainly compares a population group with exposure to a hypothetical risk factor with an unexposed group, and measures the incidence and prevalence of disease in both. Consequently it determines the strength of the influence of the risk factor studied. Another analytical method consists of following up cohorts of people in time, noting the incidence of the disease studied and the exposure to various potential risk factors.

Epidemiological studies have contributed to understanding that most childhood cancers originate in the genetic make-up of the embryo or *in utero*. The occurrence of retinoblastoma, for example, was described in families and led to the discovery of its origin in a mutation of the RB1 tumour suppressor gene.<sup>9</sup> Retinoblastoma constitutes about 3% of all cancers in children. Another typical example of an intrauterine event leading to childhood cancer is fetal exposure to diethylstilboestrol, which was prescribed for 3 decades during the last century to prevent fetal loss. Girls born to the mothers who had been on this drug developed clear cell carcinomas of the vagina and uterine cervix. An epidemiological study<sup>10</sup> highlighted the high risk of cancer in women exposed to diethylstilboestrol *in utero*, leading to contraindication of the drug during pregnancy. Other risk factors for early childhood cancer have also been identified by epidemiological methods, e.g. infection with the Epstein-Barr virus that causes Burkitt's lymphoma.

The analysis of cancer survival data provides important insight into the effectiveness of various therapeutic protocols. An equally important field where epidemiological methods are applied is the study of survivors of childhood cancer, e.g. with high rates of secondary malignancies, organ failure and infertility.<sup>11</sup>

## Data sources

Epidemiological studies use complex statistical calculations to test the correlation of phenomena observed in populations. Primary sources can be divided into population data and disease data. Population data for epidemiological research in South Africa are provided by Statistics South Africa, a governmental organisation. The South African Children's Tumour Registry incorporates information on malignant disease. It was started in 1987 as an initiative of the South African Children's Cancer Study Group (SACCSG) and is the result of collaboration of all paediatric oncology units in the country. While the data are presented regularly at conferences and congresses, only a small section has been published.<sup>12</sup> To my knowledge there is no other dedicated children's cancer registry in Africa, although the International Association of Cancer Registries has 60 African members.<sup>13</sup> However, only 17 of these are national registries and the remainder are regional or hospital records. These records include both children and adults with cancer; therefore some meaningful data pertaining only to children may be missed.

The South African Children's Tumour Registry is a central repository of data provided by individual, hospital-based registries in the country. While such registries record data on all patients presenting to paediatric oncology services, children who died without being seen at a hospital, as well as those treated by private oncologists or other paediatric sub-specialists, e.g. neurosurgeons, may not be recorded. Therefore, by its very nature, a central registry of hospital-based registries cannot be complete. It is nevertheless the most efficient and sustainable way of obtaining data that can be used in statistical research, because it does not require substantial expenditure. The minimum data that can be collected in a hospital-based registry are: demographic information (name, age, sex, address),

tumour type, localisation and stage, histological type, treatment and outcome, and yearly follow-up results. Should the patient die, the date and cause of death must be recorded.<sup>14</sup>

## Analytical epidemiology tests hypotheses formulated on the basis of descriptive studies.

There are plans for starting a national registry, maintained by the Department of Health, in which childhood cancer data can be reported by following a more comprehensive procedure, e.g. by designating cancer as a notifiable disease. Such a measure would result in more accurate reporting; however, data collected would remain hospital based.

An alternative source of cancer information is the National Cancer Registry, a pathology-based registry of the National Health Laboratory Service. However, this source has several shortcomings with regard to children's cancer: an unknown number of cases were not registered as they were diagnosed only clinically, sometimes assisted by identifying tumour markers in serum (e.g. hepatocellular carcinoma); children are on the same register as adults (as mentioned above, child-specific data may be missed); some clinical data were not communicated to the laboratories; and many laboratories decided to discontinue contributing to the register for fear of consequences arising from disclosing information that may be private.<sup>15</sup>

A population-based registry would be closer to accurately reflecting the occurrence of malignant disease. To compile accurate data, patients for such a registry should be actively sought. Registrars should contact departments of pathology, departments of radiology that

incorporate radiotherapy, other hospital departments (e.g. surgery), chemical pathology and haematology laboratories, outpatient and private clinics, and laboratories. They should also study death certificates and by the means described above identify cases of cancer, extracting and entering the data in the registry.<sup>16</sup>

Currently, however, the South African Children's Tumour Registry remains the main source of statistical data for epidemiological studies in this particular field.

The objectives of the Children's Tumour Registry are the following: to accurately present age-specific incidences, the relative frequencies of various neoplasms, the prevalence of children's cancer and individual malignancies, and their distribution according to age, sex, ethnicity and geographical area. It also assesses subtype, stage and outcome of malignancies. The information collected has the potential to assist scientific analysis, planning and research.

Table I is a synopsis of the number of childhood cancers recorded in the South African Children's Tumour Registry from 1997 to 2007 by year and type of tumour.

The annual incidence of tumours in South African children aged 0 - 14 years varied between 33.4 and 47.2 per million from 2003 to 2007, much lower than in the USA or Europe. In Europe, for example, the annual incidence of cancer in this age group was 140 per million in 1990, increasing by 1% per year for the last 3 decades.<sup>1</sup> The explanation for this discrepancy is either non-diagnosis or lack of reporting.

In South Africa leukaemia is the most common malignancy in childhood, representing 25.35% of all cancers, which is similar to rates in other countries. While brain tumours and leukaemia comprise almost half of childhood malignancies in developed countries, in South Africa brain tumours represent only 13.44% of the total cancers diagnosed in children. Even with

**Table I. Registered cases in the Children's Tumour Registry, 1997 - 2007**

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	Total
Leukaemia	146	157	142	177	162	140	162	208	154	139	150	1 737
Lymphoma	69	83	66	98	85	83	88	86	98	78	89	923
Brain	62	61	100	78	80	85	106	104	94	82	69	921
Nephroblastoma	64	85	75	84	104	62	72	94	71	73	61	845
Neuroblastoma	38	25	37	44	29	30	27	41	29	31	41	372
Retinoblastoma	40	44	35	55	46	41	42	42	57	52	33	487
Liver	12	7	13	17	17	14	12	8	13	14	16	143
Soft-tissue sarcomas	58	59	44	73	54	65	64	73	65	43	53	651
Bone	22	25	20	22	26	31	25	28	34	48	28	309
Germ cell	20	27	27	24	20	21	20	17	19	15	13	223
Other	15	19	16	44	25	26	22	22	16	19	15	239
Total	546	592	575	716	648	598	640	723	650	594	568	6 850

substantial underreporting, the difference in incidence of this form of cancer between South Africa and much of the developed world is remarkable.

These simple calculations illustrate the utility of the cancer registry in the national effort to improve the health of the population. For example, the registry data confirmed that in South Africa, as in many other countries, the efforts to prevent, diagnose and treat leukaemia more effectively would lead to a substantial reduction in the cancer risk in children.

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### In a nutshell

- Childhood cancer is a relatively rare disease, comprising less than 1% of total cancers.
- Childhood cancer is the second most common cause of death in children in First World countries.
- Eighty per cent of all childhood cancers occur in developing countries where the survival rate is low.
- Childhood cancers can be cured in more than 80% of cases in developed countries.
- A tumour registry is an essential tool for obtaining information about age-specific incidences, relative frequencies of various neoplasms, prevalence of children's cancer and individual malignancies and their distribution according to age, sex, ethnicity and geographical area.
- Epidemiological studies of cancer include factors affecting the incidence and prevalence of the disease as a way to infer possible trends and causes. Most childhood cancers are due to genetic defects or intrauterine exposure to oncogenic factors.
- The South African Children's Tumour Registry was established in 1987 at the initiative of SACCSG and is the only one in Africa dedicated exclusively to childhood cancer.
- Leukaemia is the most common malignancy diagnosed in children.
- Childhood cancer is significantly underreported in South Africa.

#### Mission Statement

To contribute to the wellbeing of children with cancer and related life-threatening blood disorders, and their families.

#### Donor Information

Public donations enable the vital work of CHOC to continue. To donate R20 to the CHOC Childhood Foundation SA simply text the word **CHOC** to **40808** (VAS rates apply) or phone 086 111 3500.

Keeping  
more than  
**hope** alive.

What to watch out for



#### Seek

Medical help early for persistent symptoms



#### Eye

White spot in the eye, new squint, blindness, bulging eyeball



#### Lump

Abdomen and pelvis, head and neck



#### Unexplained

Fever for over two weeks, loss of weight and appetite, pallor, fatigue, easy bruising or bleeding



#### Aching

Bones, joints, back, and easy fractures



#### Neurological

Change or deterioration in walking, balance, speech or behaviour, regression of milestones, early morning vomiting and/or headache for more than a week, enlarging head.

### Saint Siluan Warning Signs

If you detect any of these warning signs in a child, please SMS the **name of your province** to **34486**. A CHOC representative will contact you shortly thereafter. (SMS cost R2)



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