NATIONAL CANCER REGISTRY

Division of the National Health Laboratory Service

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Table of Contents

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Thelle Mogoerane Regional Hospital

Tygerberg Hospital

Union for International Cancer Control (UICC)

Universitas Hospital

Vermaak Laboratories

World Health Organization (WHO)

Wits Donald Gordon Medical Centre

List of Figures

List of Tables

Acronyms and Abbreviations

ASR	: Age-Standardised Incidence Rate
CHOC	: Childhood Cancer Foundation South African
CNS	: Central Nervous System
NDoH	: National Department of Health, South Africa
EPBCR	: Ekurhuleni Population-Based Cancer Registry
GICC	: Global Initiative for Childhood Cancer
GICR	: Global Initiative for Cancer Registry
IACR	: International Association of Cancer Registries
IARC	: International Agency for Research on Cancer
ICCC-3	: International Classification of Childhood Cancer, Third Edition
ICDO-3	: International Classification of Diseases for Oncology, Third Edition
NICD	: National Institute for Communicable Diseases
NCR	: National Cancer Registry, South Africa
PBCR	: Population-Based Cancer Registries
POPI Act	: Protection of Personal Information Act, South Africa
SA	: South Africa
SSA	: sub-Saharan Africa
STATSSA	: Statistics, South Africa
WHO	: World Health Organization
WSP	: World Standard Population

EXECUTIVE SUMMARY

Cancer surveillance is the responsibility of the National Cancer Registry (NCR) in South Africa (SA). In 2011, the South African National Department of Health enacted Regulation No. 380 of the National Health Act (Act 61 of 2003), which formally established the NCR as its delegated agency for the collection of cancer surveillance information and made cancer a reportable disease. This is the fourth annual childhood cancers report using the International Classification of Childhood Cancers Third Edition (ICCC-3) by the NCR. This 2021 report includes the age-group 15-19 years old for the first time. The inclusion of adolescents aged 15 - 19 aligns with international childhood classification standards; and also due to the need to know more about cancers in this age group within the South African context. A total of 1378 cancers were diagnosed in children aged 0 - 19 years old in South Africa in 2021. This equated to an overall age-standardized rate of 63.5 cases per million (95%CI: 53.1-75.7). We found the most common cancer group diagnosed to be leukaemias and the second most common cancers were lymphomas. Approximately 32% of the cases (n=437) were diagnosed in children aged 0 - 4 years old, followed by the 15 – 19 year age group (n=339; 24%). Our results are comparable to results from within the African region and global trends. Annual reports of childhood cancers are the first step towards improving reporting of childhood cancers and raising awareness of the incidence of childhood cancers.

INTRODUCTION

The National Cancer Registry (NCR) is responsible for cancer surveillance in South Africa (SA). This includes the systemic collection, storage, analysis, interpretation and reporting of cancer cases [1]. The NCR achieves cancer surveillance through its pathology-based cancer registry, its sentinel population-based cancer registries located in the Gauteng and Kwa-Zulu Natal provinces and the childhood cancer registry.

For the NCR to accurately report cancer incidence, the South African Department of Health enacted Regulation No 380 of the National Health Act (Act 61 of 2003), which formally appointed the National Cancer Registry (NCR) as its delegated agency for the collection of cancer surveillance information [2]. This regulation made cancer a reportable disease with every healthcare worker obliged to report confirmed cancers to the NCR [2,3].

There is a need for accurate childhood cancer estimates globally, but this is particularly difficult and scarce in sub-Saharan Africa (SSA) [4,5]. One of the reasons is that childhood cancers are rare compared to adult cancers [6]. Diagnosis of childhood cancers is also challenging as it may mimic communicable diseases common in SSA, with the additional challenges of inadequate diagnostic abilities in resource-poor settings. Survival rates of childhood cancers in low- and middle-income countries are far lower, approximately 30%, compared to high-income countries where the survival rate is approximately 80%. This was recently highlighted in the Global Initiative for Childhood Cancer (GICC) of the World Health Organization (WHO); which was launched to improve cancer outcomes for children with cancer and to attain a survival rate of 60% by 2030 [7].

Cancers affecting children have been identified as a national priority in South Africa and work is underway on drafting a "Childhood Cancer Strategic Framework" [8]. This is the fourth standalone report on childhood cancers using the International Classification of Childhood Cancers Third Edition (ICCC-3) [9]. The report is much needed to guide both clinicians and policymakers to improve childhood cancer awareness, screening, diagnosis, treatment and outcomes. For this report, childhood cancers are defined as malignant tumours diagnosed in children aged 0 - 19 years old. Previously, the

reports only included up to 0 - 14years old. With this report we now include the age-group 15-19years to align the childhood cancers report with international standards. This is because cancers in adolescents are more similar to those in younger children than adults as these cancers have different causes, treatments and outcomes compared to adult cancers, making it important to track them within the paediatric context and also the South African context.

Background

In 2021, South Africa reported a population of approximately 60.14 million, with children aged 0 - 19 years old comprising ≈36,5% of the population [10]. The distribution of males and females aged 0 - 19 years old is comparable (Figure 1).

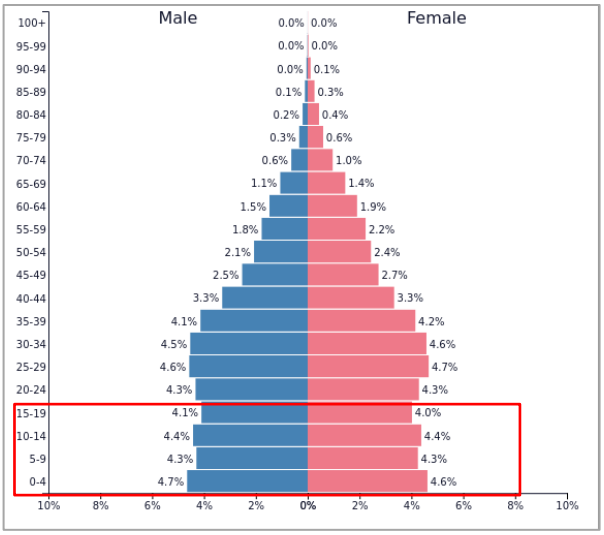

Figure 1: Population pyramid of South Africa (2021). Age groups 0 - 19 years highlighted in red.

In South Africa, there are currently 13 paediatric oncology units housed within the public sector health facilities in the country. Figure 2 shows the distribution of paediatric oncology units within the public health sector of South Africa.

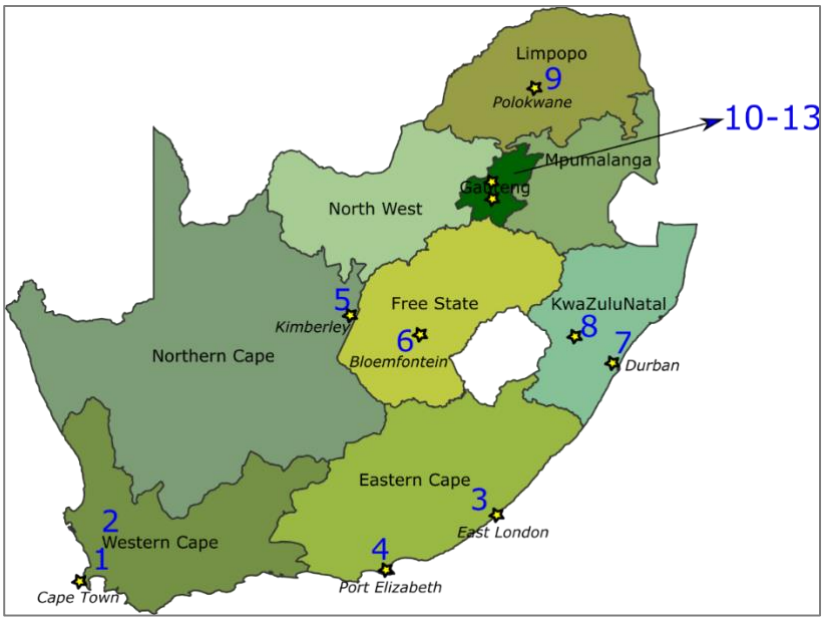

Figure 2: Distribution of major public health facilities with paediatric oncology units in South Africa, 2022.

The sites are (1) Red Cross War Memorial Children's Hospital (2) Tygerberg Hospital (3) Frere Hospital (4) Port Elizabeth Provincial Hospital (5) Robert Mangaliso Sobukwe Hospital (6) Universitas Academic Hospital (7) Inkosi Albert Luthuli Central Hospital (8) Greys Hospital (9) Pietersburg Hospital (10) Charlotte Maxeke Johannesburg Academic Hospital (11) Chris Hani Baragwanath Academic Hospital (12) Steve Biko Academic Hospital (13) Dr George Mukhari Academic Hospital

METHODS

Data sources

The NCR currently includes all reported pathologically-diagnosed cases of childhood cancers (0 - 19 years) within the annual pathology-based cancer incidence report using the International Classification of Diseases for Oncology Third Edition (ICD-0-3) classification system. However, this is an under-estimation of incidence as it only captures cancers diagnosed pathologically (histology, cytology, bone marrow aspirate or trephine). The pathology-based cancer registry includes data from both private and public laboratories. The Ekurhuleni Population-Based Cancer Registry (EPBCR) also reports on all childhood cancer cases identified through both active and passive case finding as detailed in the EPBCR reports (11).

Regulation 380 of the National Health Act of 2003 made cancer a reportable disease with every healthcare worker obliged to report confirmed cancers to the NCR. The NCR has set up a dedicated email for direct reporting of paediatric cancers from healthcare workers (12). These cancer notifications sent by clinicians, from both private and public sectors, are a valuable data source as it allows cases to be identified that may have been diagnosed without a pathology report, or cases diagnosed outside of the population-based registry demarcation to be identified.

For this report, data from the pathology-based cancer registry, the EPBCR, cancer notifications sent by clinicians and other sources such as private treatment centres from various sites throughout the country (Appendix 2) were used. The data from the these sources were combined to create one comprehensive national dataset (Figure 3). Duplicate cases were removed. All new cancer cases diagnosed from 01 January 2021 to 31 December 2021 were included. Furthermore, these cases were checked against the previous year's dataset to ensure reporting of only new cases within the year. Cases that were not South African residents were excluded i.e. specimens sent to laboratories from other countries or patients with home address based in other countries. Using the ICD-0-3, the cancers have been classified into 12 main groups and 48 sub-groups according to the third edition of the International Classification of Childhood Cancer (ICCC-3) [9]. The 12 main groups are I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases (*Leukaemias*) II. Lymphomas and reticuloendothelial neoplasms (*Lymphomas*), III. Central Nervous System (CNS) and miscellaneous intracranial and intraspinal neoplasms (*malignant CNS tumours),* IV. Neuroblastoma and other peripheral nervous cell tumours (*Sympathetic nervous system tumours),* V. Retinoblastomas (*Retinoblastomas*), VI. Renal tumours (*Renal tumours*), VII. Hepatic tumours (*Hepatic tumours*), VIII. Malignant bone tumours (*Malignant bone tumours),* IX. Soft tissue and other extraosseous sarcomas (*Soft tissue sarcomas*), X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads (*Germ cell tumours*), XI. Other malignant epithelial neoplasms and malignant melanomas (*Malignant epithelial neoplasms),* and XII. Other and unspecified malignant neoplasms (*Other and unspecified malignant tumours*).

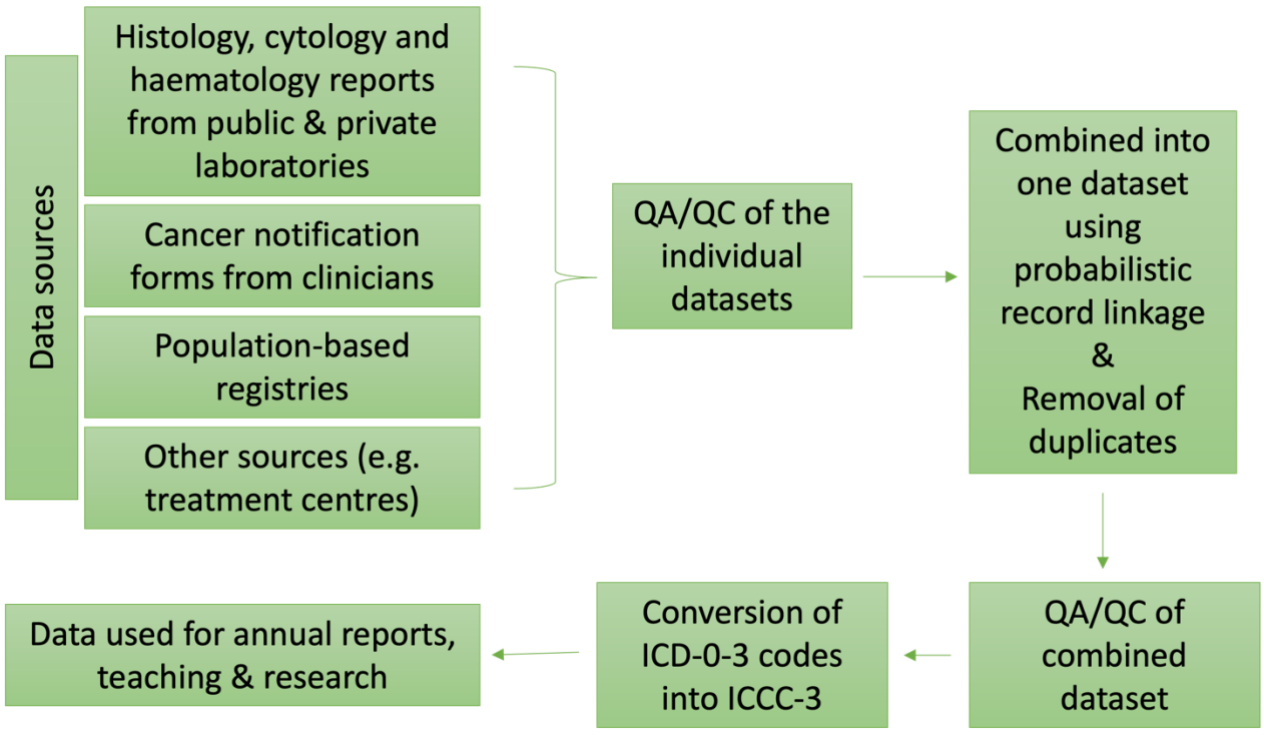

Figure 3: Data sources and data flow to create a comprehensive national dataset of childhood cancers in South Africa, 2021.

Confidentiality

The NCR adheres to the National Health Laboratory Services (NHLS), the International Agency for Research on Cancer/International Association of Cancer Registries (IARC/IACR) guidelines and the Protection of Personal Information Act (POPI Act) to ensure the preservation of confidentiality [11]. Cancer statistics are released in an anonymised and aggregated format in annual reports published on the NCR website.

Statistical Methods

The results are presented as:

- the number of new cancer cases,
- the percentage of all new cancer cases,
- Age-Specific Incidence rates (ASIR) per million
- Age-Standardised Incidence Rate (ASR) per million

The results are further stratified by:

- sex (Male and Female),
- by ICCC-3 groups and sub-groups (Appendix 3)
- age groups (4-year interval e.g. 0 - 4 years, 5 - 9, 10 – 14, 15 - 19)

For Age standardization, the Segi-World Standard Population (WSP) is used as per international cancer registration norms. STATSSA mid-year population data for South Africa is used as a denominator.

The Calculation methods are as follows:

$$\textbf{Crude} = \frac{\textbf{Number of new cases}}{\textbf{Mid-year population}} \times \textbf{1, 000,000}$$

$$\textbf{WSP weighting} = \frac{\textbf{WSP (for each age group)}}{\textbf{Total WSP for all age groups}}$$

$$\textbf{ASR} = \textbf{Crude X WSP weighting}$$

RESULTS

A total of 1378 cancers were diagnosed in children aged 0 – 19 years old in South Africa in 2021. This equated to an overall age-standardized rate of 63.5 cases per million (95% CI: 53.1 – 75.7) (Table 2). Incidence rates were comparable in boys compared to girls (incidence sex ratio was 1.11 boys:1 girl (Table 2). Approximately 32% of the cases (n=437) were diagnosed in children aged 0 - 4 years old, followed by the 15 – 19 year age group (n=339; 24%) (Table 2). The 2021 dataset indicates that the NCR pathology registry is missed at least 33% of all childhood cancers (n= 458).

Cancer Incidence by type

The most common cancer diagnosed in children was leukaemia, which accounted for 20% of all cancers diagnosed in children aged 0 – 19 years with an ASR of 12.75 per million children (95% CI: 11.28 - 14.36) (Table 2). Of the leukaemias, lymphoid leukaemias were the most commonly diagnosed (Table 3) with an ASR of 7.81 per million (95% CI: 6.67 - 9.09) with the highest incidence being found in the

0 - 4 years and 5 - 9 years age groups with an age-specific incidence rate of 11.83 and 8.74 cases per million respectively.

Lymphomas were the second most common cancer group diagnosed in children, with the highest number of cases (n=103) occurring in the 15 - 19 years age group with an age-specific incidence rate 21.1 per million (Table 2). Non-Hodgkin lymphomas (except Burkitt lymphoma) and Hodgkin lymphomas were the most common type of lymphomas diagnosed (Table 2). There were 30 cases of "Other and unspecified malignant neoplasms" making it the least commonly diagnosed cancer in children in 2021.

Cancer Incidence by sex

Of the 1378 cancers diagnosed, 52.5% (n=724) were diagnosed in boys and 47.0% (n=648) were diagnosed in girls (Figure 5). There were six cases (0.4%) reported with unknown sex.

Lymphoid leukaemia and nephroblastomas were the two most common cancers among both boys and girls. Non-Hodgkin lymphomas (except Burkitt lymphomas) is one of the top five commonly diagnosed cancers in boys, but not in girls (Table 1). Similarly, acute myeloid leukaemias is one of the top five commonly diagnosed cancers in girls but not in boys (Table 1).

Table 1: Most commonly diagnosed childhood cancers by sex, South Africa, 2021

Boys	**n**	**(%)**
(Ia) Lymphoid leukaemias	81	11.2
(VIa) Nephroblastoma and other nonepithelial renal tumours	67	9.3
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	60	8.3
(IIa) Hodgkin lymphomas	54	7.5
(IXd) Other specified soft tissue sarcomas	54	7.5
Girls	**n**	**(%)**
(Ia) Lymphoid leukaemias	86	13.3
(VIa) Nephroblastoma and other nonepithelial renal tumour**s**	52	8.0
(IIa) Hodgkin lymphomas	43	6.6
(IXd) Other specified soft tissue sarcomas	42	6.5
(Ib) Acute myeloid leukaemias	40	6.2

Table 2: Cancer Incidence for children 0-19 years old by main cancer groups as defined by the 21 main groups per the ICCC-3, South Africa (2021).

	Number of cases							Rates per Million							
								Age-Specific Rates							
Cancer Group	**Age 0-4**	**Age 5-9**	**Age 10-14**	**Age 15-19**	**All ages**	**Ratio (M/F)**	**%**	**ASIR 0-4**	**ASIR 5-9**	**ASIR 10-14**	**ASIR 15-19**	**Crude**	**ASR**	**LCL**	**UCL**
I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases	101	75	63	37	276	0.9	20.0	17.6	13.1	11.1	7.6	12.53	12.75	11.28	14.36
II. Lymphomas and reticuloendothelial neoplasms	30	47	52	103	232	1.7	16.8	5.2	8.2	9.2	21.1	10.53	10.43	9.13	11.87
III. CNS and miscellaneous intracranial and intraspinal neoplasms	49	52	48	13	162	0.9	11.8	8.5	9.1	8.5	2.7	7.36	7.33	6.24	8.56
IV. Neuroblastoma and other peripheral nervous cell tumours	36	9	8	5	58	0.8	4.2	6.3	1.6	1.4	1.0	2.63	2.82	2.14	3.65
V. Retinoblastoma	66	9	1	0	76	1.1	5.5	11.5	1.6	0.2	0.0	3.45	3.88	3.05	4.85
VI. Renal tumours	74	41	7	3	125	1.3	9.1	12.9	7.2	1.2	0.6	5.68	6.07	5.05	7.23
VII. Hepatic tumours	19	7	2	3	31	0.8	2.2	3.3	1.2	0.3	0.6	1.41	1.52	1.03	2.15
VIII. Malignant bone tumours	5	5	32	45	87	1.4	6.3	0.9	0.9	5.6	9.2	3.95	3.82	3.06	4.72
IX. Soft tissue and other extraosseous sarcomas	26	38	50	82	196	1.4	10.8	4.0	6.1	6.2	11.5	6.77	6.70	5.66	7.87
X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads	12	7	10	17	46	0.5	3.3	2.1	1.2	1.8	3.5	2.09	2.11	1.54	2.82
XI. Other malignant epithelial neoplasms and malignant melanomas	11	12	32	51	106	1.3	7.7	1.9	2.1	5.6	10.4	4.81	4.72	3.86	5.71

XII. Other and unspecified malignant neoplasms	11	7	6	6	30	0.7	2.2	1.9	1.2	1.1	1.2	1.36	1.39	0.94	1.99
Total	**437**	**306**	**296**	**339**	**1378**	**1.1**	**100**	**76.0**	**53.5**	**52.2**	**69.5**	**62.6**	**63.5**	**53.1**	**75.7**

Ratio (M/F): male-to-female ratio
ASIR: Age-specific incidence rates per million
Crude: crude rates expressed per million aged 0-19 years
ASR: age-standardized incidence rate per million (World Standard population)
LCL: Lower 95% confidence intervals for the ASR
UCL: Upper 95% confidence intervals for the ASR

Table 3: Cancer incidence for children 0 - 14years old by sub-groups as defined by the ICCC-3, South Africa (2021)

	Number of cases							Rates per Million Age-Specific Rates							
Cancer type	**Age 0-4**	**Age 5-9**	**Age 10-14**	**Age 15-19**	**All**	**Ratio (M/F)**	**%**	**Age 0-4**	**Age 5-9**	**Age 10-14**	**Age 15-19**	**Crude**	**ASR**	**LCL**	**UCL**
I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases															
(Ia) Lymphoid leukaemias	68	50	35	15	168	0.9	12.2	11.83	8.74	6.17	3.07	7.63	7.81	6.67	9.09
(Ib) Acute myeloid leukaemias	20	18	19	18	75	0.9	5.4	3.48	3.15	3.35	3.69	3.41	3.41	2.68	4.28
(Ic) Chronic myeloproliferative diseases	2	2	2	1	7	1.3	0.5	0.35	0.35	0.35	0.20	0.32	0.32	0.13	0.66
(Id) Myelodysplastic syndrome and other myeloproliferative diseases	4	0	1	0	5	1.5	0.4	0.70	0.00	0.18	0.00	0.23	0.25	0.08	0.57
(Ie) Unspecified and other specified leukaemias	7	5	6	3	21	0.8	1.5	1.22	0.87	1.06	0.61	0.95	0.96	0.59	1.47
II. Lymphomas and reticuloendothelial neoplasms															
(IIa) Hodgkin lymphomas	5	14	23	55	97	1.3	7.0	0.87	2.45	4.05	11.27	4.40	4.32	3.50	5.27
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	9	17	26	41	93	1.9	6.7	1.57	2.97	4.58	8.40	4.22	4.13	3.33	5.07
(IIc) Burkitt lymphoma	7	13	1	2	23	6.7	1.7	1.22	2.27	0.18	0.41	1.04	1.07	0.67	1.60
(IId) Miscellaneous lymphoreticular neoplasms	9	0	0	0	9	0.8	0.7	1.57	0.00	0.00	0.00	0.41	0.47	0.21	0.88
(IIe) Unspecified lymphomas	0	3	2	5	10	2.3	0.7	0.00	0.52	0.35	1.02	0.45	0.44	0.21	0.81
III. CNS and miscellaneous intracranial and intraspinal neoplasms															
(IIIa) Ependymomas and choroid plexus tumour	10	7	5	4	26	0.9	1.9	1.74	1.22	0.88	0.82	1.18	1.21	0.79	1.77
(IIIb) Astrocytomas	9	6	11	4	30	0.8	2.2	1.57	1.05	1.94	0.82	1.36	1.35	0.91	1.93
(IIIc) Intracranial and intraspinal embryonal tumours	13	13	8	4	38	1.7	2.8	2.26	2.27	1.41	0.82	1.73	1.75	1.23	2.40
(IIId) Other gliomas	13	16	12	0	41	0.7	3.0	2.26	2.80	2.11	0.00	1.86	1.85	1.33	2.52

(IIIe) Other specified intracranial and intraspinal neoplasms	4	10	12	1	27	0.6	2.0	0.70	1.75	2.11	0.20	1.23	1.17	0.77	1.70
(IIIf) Unspecified intracranial and intraspinal neoplasms	0	0	0	0	0	0	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.17
IV. Neuroblastoma and other peripheral nervous cell tumours															
(IVa) Neuroblastoma and ganglioneuroblastoma	35	8	5	2	50	0.9	3.6	6.09	1.40	0.88	0.41	2.27	2.47	1.83	3.25
(IVb) Other peripheral nervous cell tumours	1	1	3	3	8	0.6	0.6	0.17	0.17	0.53	0.61	0.36	0.35	0.15	0.70
V. Retinoblastoma															
(V) Retinoblastoma	66	9	1	0	76	1.1	5.5	11.48	1.57	0.18	0.00	3.45	3.88	3.05	4.85
VI. Renal tumours															
(VIa) Nephroblastoma and other nonepithelial renal tumours	73	39	6	2	120	1.3	8.7	12.7	6.82	1.06	0.41	5.45	5.84	4.84	6.99
(VIb) Renal carcinomas	1	2	1	1	5	1.5	0.4	0.17	0.35	0.18	0.20	0.23	0.23	0.07	0.53
(VIc) Unspecified malignant renal tumours	0	0	0	0	0	0	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.17
VII. Hepatic tumours															
(VIIa) Hepatoblastoma	19	4	1	1	25	0.8	1.8	3.30	0.70	0.18	0.20	1.14	1.25	0.81	1.84
(VIIb) Hepatic carcinomas	0	3	1	2	6	1.0	0.4	0.00	0.52	0.18	0.41	0.27	0.26	0.10	0.58
(VIIc) Unspecified malignant hepatic tumours	0	0	0	0	0	0	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.17
VIII. Malignant bone tumours															
(VIIIa) Osteosarcomas	0	4	29	34	67	1	4.9	0.00	0.70	5.11	6.97	3.04	2.89	2.24	3.68
(VIIIb) Chondrosarcomas	0	0	0	4	4	3	0.3	0.00	0.00	0.00	0.82	0.18	0.18	0.05	0.47
(VIIIc) Ewing tumour and related sarcomas of bone	3	1	1	6	11	3	0.8	0.52	0.17	0.18	1.23	0.50	0.52	0.26	0.92
(VIIId) Other specified malignant bone tumours	0	0	2	1	3	2	0.2	0.00	0.00	0.35	0.20	0.14	0.13	0.03	0.38
(VIIIe) Unspecified malignant bone tumours	2	0	0	0	2	0	0.1	0.35	0.00	0.00	0.00	0.09	0.10	0.01	0.36
IX. Soft tissue and other extraosseous sarcomas															
(IXa) Rhabdomyosarcomas	9	22	16	18	65	2	4.7	1.57	3.85	2.82	3.69	2.95	2.90	2.23	3.69
(IXb) Fibrosarcomas, peripheral nerve sheath tumours, and other fibrous neoplasms	1	0	1	2	4	0	0.3	0.17	0.00	0.18	0.41	0.18	0.18	0.05	0.47
(IXc) Kaposi sarcoma	2	2	2	11	17	1	1.2	0.35	0.35	0.35	2.25	0.77	0.78	0.45	1.25
(IXd) Other specified soft tissue sarcomas	11	8	13	18	50	1	3.6	1.91	1.40	2.29	3.69	2.27	2.27	1.68	2.99

(IXe) Unspecified soft tissue sarcomas	0	3	3	7	13	1	0.9	0.00	0.52	0.53	1.43	0.59	0.57	0.30	0.98
X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads															
(Xa) Intracranial and intraspinal germ cell tumours	2	2	2	0	6	0.5	0.4	0.35	0.35	0.35	0.00	0.27	0.27	0.10	0.59
(Xb) Malignant extracranial and extragonadal germ cell tumours	2	1	1	3	7	0.8	0.5	0.35	0.17	0.18	0.61	0.32	0.33	0.13	0.67
(Xc) Malignant gonadal germ cell tumours	6	3	6	12	27	0.4	2.0	1.04	0.52	1.06	2.46	1.23	1.24	0.81	1.80
(Xd) Gonadal carcinomas	0	0	1	2	3	2.0	0.2	0.00	0.00	0.18	0.41	0.14	0.13	0.03	0.39
(Xe) Other and unspecified malignant gonadal tumours	2	1	0	0	3	0.5	0.2	0.35	0.17	0.00	0.00	0.14	0.15	0.03	0.43
XI. Other malignant epithelial neoplasms and malignant melanomas															
(XIa) Adrenocortical carcinomas	1	0	0	0	1	0	0.1	0.17	0.00	0.00	0.00	0.05	0.05	0.00	0.27
(XIb) Thyroid carcinomas	0	1	5	9	15	1.1	1.1	0.00	0.17	0.88	1.84	0.68	0.66	0.37	1.09
(XIc) Nasopharyngeal carcinomas	0	0	6	2	8	3.0	0.6	0.00	0.00	1.06	0.41	0.36	0.33	0.14	0.66
(XId) Malignant melanomas	3	0	0	4	7	0.8	0.5	0.52	0.00	0.00	0.82	0.32	0.34	0.14	0.70
(XIe) Skin carcinomas	2	2	3	4	11	2.7	0.8	0.35	0.35	0.53	0.82	0.50	0.50	0.25	0.89
(XIf) Other and unspecified carcinomas	5	9	18	32	64	1.1	4.6	0.87	1.57	3.17	6.56	2.91	2.84	2.19	3.63
XII. Other and unspecified malignant neoplasms															
(XIIa) Other specified malignant tumours	8	5	2	2	17	0.9	1.2	1.39	0.87	0.35	0.41	0.77	0.81	0.47	1.29
(XIIb) Other unspecified malignant tumours	3	2	4	4	13	0.4	0.9	0.52	0.35	0.70	0.82	0.59	0.59	0.31	1.01
Total	**437**	**306**	**296**	**339**	**1378**	**1.1**	**100**	**76.0**	**53.4**	**52.2**	**69.4**	**62.6**	**63.5**	**46.4**	**87.7**

Ratio (M/F): male-to-female ratio
ASIR: Age-specific incidence rates per million
Crude: crude rates expressed per million aged 0-19 years
ASR: age-standardized incidence rate per million (World Standard population)
LCL: Lower 95% confidence intervals for the ASR
UCL: Upper 95% confidence intervals for the ASR

Cancer Incidence by age-groups

The majority of childhood cancers were diagnosed in children aged 0 - 4 years (n=437, 31.7%) (Table 2). The annual incidence of the most common cancers by age group is shown in Table 4. Lymphoid leukaemias were found across all age groups in varying percentages (11.9%-16.7%) except in 15 - 19year olds.

Table 4: Most commonly diagnosed childhood cancers by age group, South Africa, 2021.

Cancer Type	No. of cases	(%)
0 - 4 years		
(VIa) Nephroblastoma and other nonepithelial renal tumours	73	16.7
(Ia) Lymphoid leukaemias	68	15.6
(V) Retinoblastoma	66	15.1
(IVa) Neuroblastoma and ganglioneuroblastoma	35	8.0
(Ib) Acute myeloid leukaemias	20	4.6
5 - 9 years		
(Ia) Lymphoid leukaemias	50	16.3
(VIa) Nephroblastoma and other nonepithelial renal tumours	39	12.8
(IXa) Rhabdomyosarcomas	22	7.2
(Ib) Acute myeloid leukaemias	18	5.9
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	17	5.6
10 - 14 years		
(Ia) Lymphoid leukaemias	35	11.9
(VIIIa) Osteosarcomas	29	9.8
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	26	8.8
(IIa) Hodgkin lymphomas	23	7.8
(Ib) Acute myeloid leukaemias	19	6.4
15-19 years		
(IIa) Hodgkin lymphomas	55	16.2
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	41	12.0
(VIIIa) Osteosarcomas	34	10.0
(XIf) Other and unspecified carcinomas	32	9.4
(Ib) Acute myeloid leukaemias	18	5.31

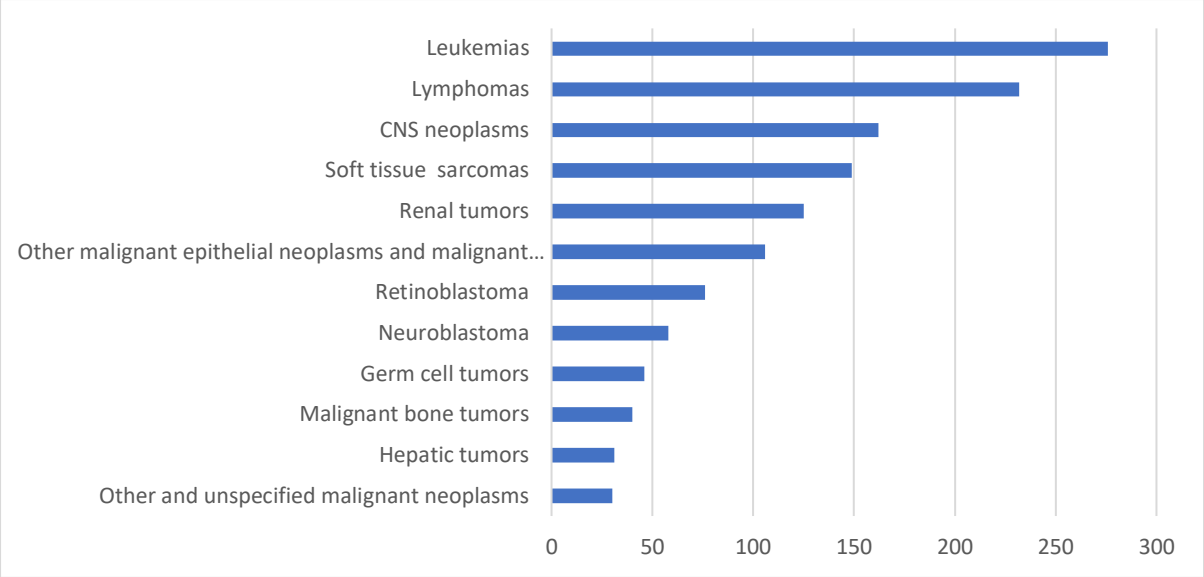

Figure 4: Number of childhood cancer cases per main group as classified by the ICCC-3, South Africa, 2021.

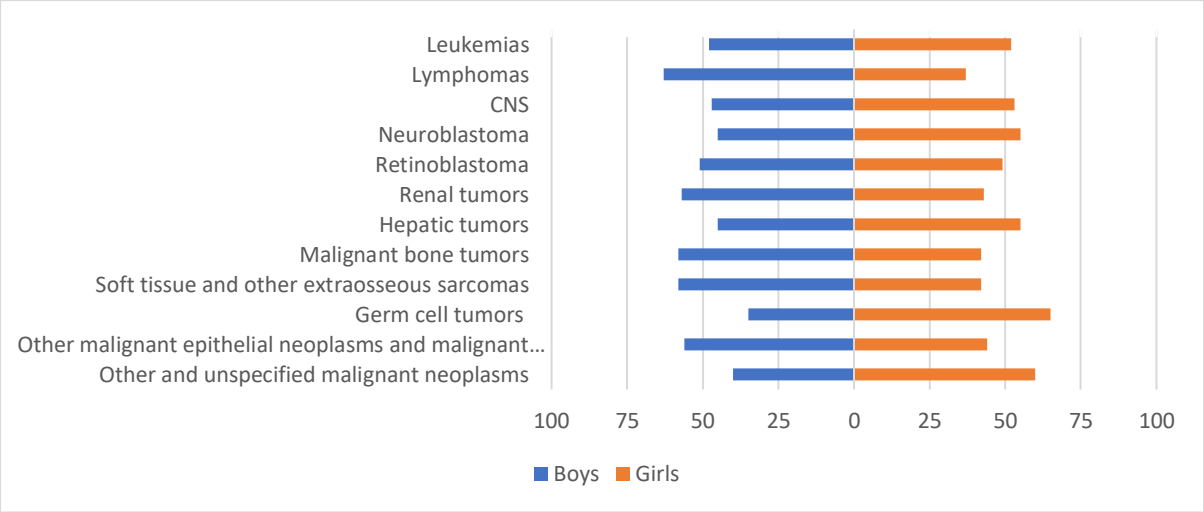

Figure 5: Distribution of childhood cancers by cancer type and sex, South Africa, 2021

Cancer Incidence by population group

This report looks at the distribution of cancers per population groups. It was found the lymphoid leukaemias were the most common type of cancer across all population groups (Figure 6). There were 45 patients (≈3%) where population group could not be assigned.

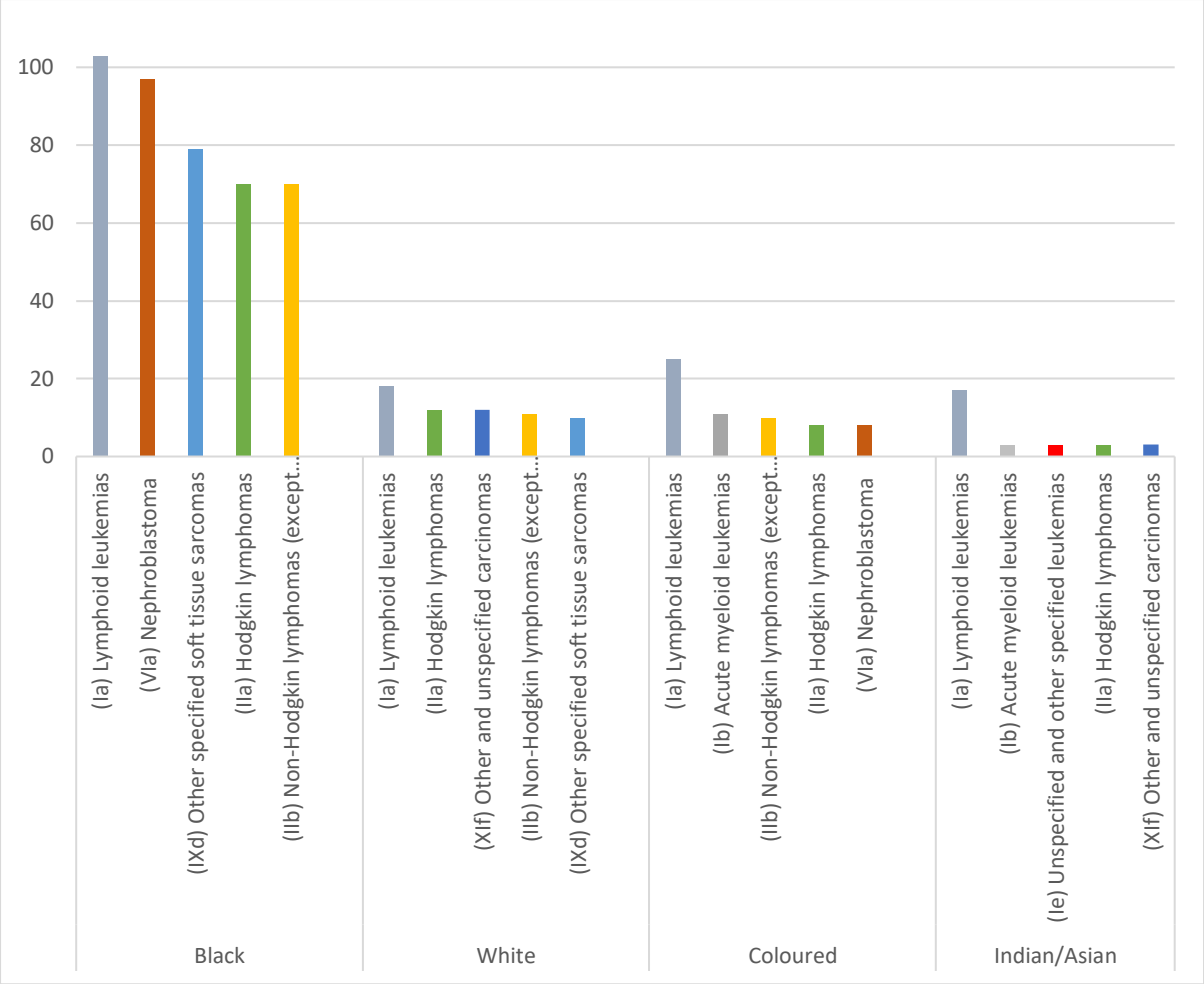

Figure 6: Top five cancers, as per ICCC-3 subgrouping, per population group in children aged 0-19 years in South Africa, 2021

DISCUSSION

This is the fourth annual report on childhood cancer incidence by the National Cancer Registry of South Africa. A total of 1378 cancers cases were recorded in children aged 0 - 19 years old, with an overall ASR of 63.5 per million. The total number of cases are higher compared to 2020 (n=1048) due to the inclusion of the age group 15 - 19 years old. The overall ASR of 63.5 per million is higher than the previous reported ASRs of 59.8 per million – 62.4 per million using NCR childhood reports from the period 2018 - 2020.

Similar to the previous published reports, we found the most common cancer group diagnosed to be leukaemias (20.1%), followed by lymphomas (16.8%). This is in line with previous reports on childhood cancers in South Africa [12,13].

The absolute number of CNS tumours reported in 2021 (n = 162, 11.8%) is higher than 2020 (n=149), it was the third most common cancer in 2021 similar to 2020. This highlights that the number of CNS tumours is be under-diagnosed and/or under-reported as it is not in line with global trends of being the second most commonly diagnosed childhood cancer [5,13]. Soft tissue sarcomas (10.8%) were the fourth most common cancer in 2021, with rhabdomyosarcomas being the most common sub-type. Kaposi sarcoma, an AIDS-defining cancer, was most common in the 15-19year old age group (n= 11). Renal tumours (9.0%) were the fifth most common cancer, predominantly nephroblastomas sub-type, which was most prevalent in the 0 - 4 years old age group comparable to global trends [14]

Most childhood cancer cases were diagnosed in children aged 0 – 4 years old (n = 437; 31.7%). The age-specific incidence rates were highest in children aged 0 - 4 years (76.0 per million) group similar to global patterns[14]. The lowest rates were in the 10 - 14 years old (52.2 per million). Globally the most common cancer in children aged 0 – 4 years is leukaemia, however rates in sub-Saharan Africa (SSA) have always been lower than the global rates [14]. The trend in South Africa is similar to SSA, where leukaemias were the most frequently diagnosed cancer in the 0 - 4 years age group but at lower rates compared to global rates [14]..Osteosarcoma was the most commonly diagnosed malignant bone tumour, with the highest incidence recorded in the 15-19 year old group (n = 34) followed by the 10-14 age group (n= 29) following line with global trends that it tends to occur in older children [15] .

The ratio of boys diagnosed with cancers compared to girls is 1.1:1. Similar to reported global trends, we saw a higher incidence of germ cell and gonadal tumours in girls compared to boys [14].

The 2021 dataset indicates that the NCR pathology registry is missed at least 33% of all childhood cancers. Of the missed cancers, 41.5% were haematological malignancies (leukaemias and lymphomas)

and 17% were brain tumours. Although two new data sources have been added in 2021, there is still room for improvement to build a more comprehensive national dataset to provide accurate incidence rates childhood cancers in South Africa. Although population groups were included in this report, there were 45 patients (3%) where population group could not be assigned. This highlights the need to improve collection of demographic details from the source for more in-depth analysis.

Annual reports of childhood cancers by the NCR are a key step towards improving reporting of childhood cancers and raising awareness of the incidence of childhood cancers. Inclusion of 15-19 year adolescents should provide additional information regarding the incidence of cancers in this age group. Nationally, paediatric oncologists have identified the need for targeted interventions for adolescents to receive appropriate referral, treatment and follow-up within the local South African healthcare setting. Efforts are ongoing to improve reporting by including information on staging and survival. These are currently limited by poor access to clinical information for staging and poor reporting of vital status.

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Appendix 1: Cancer Notification Form

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

National Health Act, 2003 (Act No. 61 of 2003)
Regulation Number 380

Republic of South Africa
Department of Health

CANCER REGISTRATION FORM

To be completed in duplicate in **BLOCK LETTERS**.
Please mark with ☑ the CORRECT box, where required.
Original to be submitted to the National Cancer Register and copy to be retained:
To be submitted to the National Cancer Register via:
e-mail: cancer.registry@nhls.ac.za
fax: 011 489 9132 / 011 489 9152
Post: PO Box 1038, Johannesburg, 2000

A. PARTICULARS OF INDIVIDUAL

1. Name of facility

USE PATIENT STICKER *if available*

2. Surname

3. Full names

4. Date of birth

5. Folder number

6. Sex ☐ Male ☐ Female

7. ID number/Passport number

8. Race group ☐ African ☐ Coloured ☐ White ☐ Indian ☐ Other _____

9. Area of residence

9.1 City/town/village

9.2 Postal code **9.3 How long at this address?** ☐☐ years

Please record place of birth if not the same as current address

9.4 City/town/village

9.5 Postal code

B. RISK FACTOR PROFILE

10. Usual occupation of patient
(If retired, give type of work done for most of working life)

11. Type of industry/business
(eg Mining, farming etc)

12. Did the patient ever smoke tobacco? ☐ Yes ☐ No ☐ Unknown

13. Did the patient ever consume alcohol regularly? ☐ Yes ☐ No ☐ Unknown
(that is, more than once a week)

14. HIV status ☐ Negative ☐ Positive ☐ Unknown

C. CLINICAL AND LABORATORY DETAILS

15. Date of diagnosis

16. Cancer diagnosis and Histology **17. ICD-10** ☐☐☐.☐

Please give all information available on the site, laterality, histology and behaviour of the tumour

_____

_____

18. Grade ☐ Well differentiated ☐ Moderately differentiated ☐ Poorly differentiated ☐ Unknown/Not applicable

19. Stage ☐ Primary/localised ☐ Metastatic ☐ Unknown/Not applicable

20. Invasiveness ☐ In-situ ☐ Invasive

21. Basis of diagnosis ☐ Clinical ☐ Clinical with investigation ☐ Cytology/histopathology ☐ Molecular ☐ Death Certificate

22. Prescribed treatment ☐ Surgery ☐ Radiation ☐ Chemotherapy ☐ Other ☐ Palliation ☐ Alternative ☐ None

INFORMANT PARTICULARS

Name (Print) _____

MP/NC Number

Signature _____ Date _____

OFFICE CODING

☐☐☐.☐

M - ☐☐☐☐ / ☐ / ☐

Appendix 2: Sites cancer notification forms received from (paediatric cases), 2021

- Chris Hani Baragwanath Academic Hospital
- Charlotte Maxeke Johannesburg Academic Hospital
- Ethekwini Hospital and Heart Complex
- Frere Hospital
- Greys Hospital
- Inkosi Albert Luthuli Central Hospital
- Netcare Clinton Hospital
- P.E. Provincial Hospital (Paediatric Oncology)
- Robert Mangaliso Sobukwe Hospital
- Steve Biko Academic Hospital
- Tygerberg Hospital
- Universitas Hospital
- Wits Donald Gordan Medical Centre
- Red Cross War Memorial Children's Hospital
- Stanger Hospital
- Polokwane Hospital
- South African Oncology Consortium
- ICON Oncology

Appendix 3: International Classification of Childhood Cancer, 3rd edition

Site Group	ICD-O-3 Histology (Type)	ICD-O-2/3 Site
I Leukaemias, myeloproliferative diseases, and myelodysplastic diseases		
(a) Lymphoid leukaemias	9820, 9823, 9826, 9827, 9831-9837, 9940, 9948	C000-C809
(b) Acute myeloid leukaemias	9840, 9861, 9866, 9867, 9870-9874, 9891, 9895-9897, 9910, 9920, 9931	C000-C809
(c) Chronic myeloproliferative diseases	9863, 9875, 9876, 9950, 9960-9964	C000-C809
(d) Myelodysplastic syndrome and other myeloproliferative diseases	9945, 9946, 9975, 9980, 9982-9987, 9989	C000-C809
(e) Unspecified and other specified leukaemias	9800, 9801, 9805, 9860, 9930	C000-C809
II Lymphomas and reticuloendothelial neoplasms		
(a) Hodgkin lymphomas	9650-9655, 9659, 9661-9665, 9667	C000-C809
(b) Non-Hodgkin lymphomas (except Burkitt lymphoma)	9591, 9670, 9671, 9673, 9675, 9678-9680, 9684, 9689-9691, 9695, 9698-9702, 9705, 9708, 9709, 9714, 9716-9719, 9727-9729, 9731-9734, 9760-9762, 9764-9769, 9970	C000-C809
(c) Burkitt lymphoma	9687	C000-C809

(d) Miscellaneous lymphoreticular neoplasms	9740-9742, 9750, 9754-9758	C000-C809
(e) Unspecified lymphomas	9590, 9596	C000-C809
III CNS and miscellaneous intracranial and intraspinal neoplasms		
(a) Ependymomas and choroid plexus tumour	9383, 9390-9394	C000-C809
(b) Astrocytomas	9380	C723
	9384, 9400-9411, 9420, 9421-9424, 9440-9442	C000-C809
(c) Intracranial and intraspinal embryonal tumours	9470-9474, 9480, 9508	C000-C809
	9501-9504	C700-C729
(d) Other gliomas	9380	C700-C722, C724-C729, C751, C753
	9381, 9382, 9430, 9444, 9450, 9451, 9460	C000-C809
(e) Other specified intracranial and intraspinal neoplasms	8270-8281, 8300, 9350-9352, 9360-9362, 9412, 9413, 9492, 9493, 9505-9507, 9530-9539, 9582	C000-C809
(f) Unspecified intracranial and intraspinal neoplasms	8000-8005	C700-C729, C751-C753
IV Neuroblastoma and other peripheral nervous cell tumours		
(a) Neuroblastoma and ganglioneuroblastoma	9490, 9500	C000-C809
(b) Other peripheral nervous cell tumours	8680-8683, 8690-8693, 8700, 9520-9523	C000-C809
	9501-9504	C000-C699, C739-C768, C809
V Retinoblastoma	**9510-9514**	**C000-C809**
VI Renal tumours		
(a) Nephroblastoma and other nonepithelial renal tumours	8959, 8960, 8964-8967	C000-C809
	8963, 9364	C649
(b) Renal carcinomas	8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8143, 8155, 8190-8201, 8210, 8211, 8221-8231, 8240, 8241, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8401, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8576	C649
	8311, 8312, 8316-8319, 8361	C000-C809
(c) Unspecified malignant renal tumours	8000-8005	C649
VII Hepatic tumours		

(a) Hepatoblastoma	8970	C000-C809
(b) Hepatic carcinomas	8010-8041, 8050-8075, 8082, 8120-8122, 8140, 8141, 8143, 8155, 8190-8201, 8210, 8211, 8230, 8231, 8240, 8241, 8244-8246, 8260-8264, 8310, 8320, 8323, 8401, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8576	C220, C221
	8160-8180	C000-C809
(c) Unspecified malignant hepatic tumours	8000-8005	C220, C221
VIII Malignant bone tumours		
(a) Osteosarcomas	9180-9187, 9191-9195, 9200	C400-C419, C760-C768, C809
(b) Chondrosarcomas	9210, 9220, 9240	C400-C419, C760-C768, C809
	9221, 9230, 9241-9243	C000-C809
(c) Ewing tumour and related sarcomas of bone	9260	C400-C419, C760-C768, C809
	9363-9365	C400-C419
(d) Other specified malignant bone tumours	8810, 8811, 8823, 8830	C400-C419
	8812, 9250, 9261, 9262, 9270-9275, 9280-9282, 9290, 9300-9302, 9310-9312, 9320-9322, 9330, 9340-9342, 9370-9372	C000-C809
(e) Unspecified malignant bone tumours	8000-8005, 8800, 8801, 8803-8805	C400-C419
IX Soft tissue and other extraosseous sarcomas		
(a)Rhabdomyosarcomas	8900-8905, 8910, 8912, 8920, 8991	C000-C809
(b) Fibrosarcomas, peripheral nerve sheath tumours, and other fibrous neoplasms	8810, 8811, 8813-8815, 8821, 8823, 8834-8835	C000-C399, C440-C768, C809
	8820, 8822, 8824-8827, 9150, 9160, 9491, 9540-9571, 9580	C000-C809
(c) Kaposi sarcoma	9140	C000-C809
(d) Other specified soft tissue sarcomas	8587, 8710-8713, 8806, 8831-8833, 8836, 8840-8842, 8850-8858, 8860-8862, 8870, 8880, 8881, 8890-8898, 8921, 8982, 8990, 9040-9044, 9120-9125, 9130-9133, 9135, 9136, 9141, 9142, 9161, 9170-9175, 9231, 9251, 9252, 9373, 9581	C000-C809
	8830	C000-C399, C440-C768, C809
	8963	C000-C639, C659-C699, C739-C768, C809

	9180, 9210, 9220, 9240	C490-C499
	9260	C000-C399, C470-C759
	9364	C000-C399, C470-C639, C659-C699, C739-C768, C809
	9365	C000-C399, C470-C639, C659-C768, C809
(e) Unspecified soft tissue sarcomas	8800-8805	C000-C399, C440-C768, C809
X Germ cell tumours, trophoblastic tumours, and neoplasms of gonads		
(a) Intracranial and intraspinal germ cell tumours	9060-9065, 9070-9072, 9080-9085, 9100, 9101	C700-C729, C751-C753
(b) Malignant extracranial and extragonadal germ cell tumours	9060-9065, 9070-9072, 9080-9085, 9100-9105	C000-C559, C570-C619, C630-C699, C739-C750, C754-C768, C809
(c) Malignant gonadal germ cell tumours	9060-9065, 9070-9073, 9080-9085, 9090, 9091, 9100, 9101	C569, C620-C629
(d) Gonadal carcinomas	8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8143, 8190-8201, 8210, 8211, 8221-8241, 8244-8246, 8260-8263, 8290, 8310, 8313, 8320, 8323, 8380-8384, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8573, 9000, 9014, 9015	C569, C620-C629
	8441-8444, 8450, 8451, 8460-8473	C000-C809
(e) Other and unspecified malignant gonadal tumours	8590-8671	C000-C809
	8000-8005	C569, C620-C629
XI Other malignant epithelial neoplasms and malignant melanomas		
(a) Adrenocortical carcinomas	8370-8375	C000-C809
(b) Thyroid carcinomas	8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8190, 8200, 8201, 8211, 8230, 8231, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8430, 8440, 8480, 8481, 8510, 8560-8573	C739
	8330-8337, 8340-8347, 8350	C000-C809
(c) Nasopharyngeal carcinomas	8010-8041, 8050-8075, 8082, 8083, 8120-8122, 8130-8141, 8190, 8200, 8201, 8211, 8230, 8231, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8430, 8440, 8480, 8481, 8500-8576	C110-C119
(d) Malignant melanomas	8720-8780, 8790	C000-C809

(e) Skin carcinomas	8010-8041, 8050-8075, 8078, 8082, 8090-8110, 8140, 8143, 8147, 8190, 8200, 8240, 8246, 8247, 8260, 8310, 8320, 8323, 8390-8420, 8430, 8480, 8542, 8560, 8570-8573, 8940, 8941	C440-C449
(f) Other and unspecified carcinomas	8010-8084, 8120-8157, 8190-8264, 8290, 8310, 8313-8315, 8320-8325, 8360, 8380-8384, 8430-8440, 8452-8454, 8480-8586, 8588-8589, 8940, 8941, 8983, 9000, 9010-9016, 9020, 9030	C000-C109, C129-C218, C239-C399, C480-C488, C500-C559, C570-C619, C630-C639, C659-C729, C750-C768, C809
XII Other and unspecified malignant neoplasms		
(a) Other specified malignant tumours	8930-8936, 8950, 8951, 8971-8981, 9050-9055, 9110	C000-C809
	9363	C000-C399, C470-C759
(b) Other unspecified malignant tumours	8000-8005	C000-C218, C239-C399, C420-C559, C570-C619, C630-C639, C659-C699, C739-C750, C754-C809
Not Classified by ICCC or in situ		