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Dedication

This inaugural childhood cancer report is dedicated to

the late Dr Elvira Singh (1976 – 2022)

Acknowledgements

The National Cancer Registry (NCR) would also like to thank all individuals, organisations and relevant stakeholders that played a critical role in the operations of the Childhood Cancer Registry.

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Steve Biko Academic Hospital

Tambo Memorial Regional Hospital

Tembisa Regional Hospital

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

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Acronyms and Abbreviations

AFCRN	: African Cancer Registry Network
ASR	: Age-Standardised Incidence Rate
CNS	: Central Nervous System
NDoH	: National Department of Health, South Africa
EPBCR	: Ekurhuleni Population-Based Cancer Registry
GICC	: Global Initiative for Childhood Cancer
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
NCR	: National Cancer Registry, South Africa
POPI Act	: Protection of Personal Information Act, South Africa
SA	: South Africa
SAMRC	: South African Medical Research Council
SAOC	: South African Oncology Consortium
SACTR	: South African Children's Tumour Registry
STATSSA	: Statistics, South Africa
WHO	: World Health Organization
WSP	: World Standard Population

EXECUTIVE SUMMARY

There is a need for accurate childhood cancer estimates globally, but this is particularly difficult and scarce in sub-Saharan Africa. 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. The NCR currently includes all reported pathology-diagnosed cases of childhood cancers (0-14 years) within the annual pathology-based cancer incidence report. This is the first time the National Cancer Registry is publishing a standalone report on childhood cancers using the International Classification of Childhood Cancers Third Edition (ICCC-3). A total of 975 cancers were diagnosed in children aged 0-14years old in South Africa in 2018. This equated to overall age standardized rate of 59.8 cases per million (95%CI: 48.6-73.2). We found the most common cancer group diagnosed to be leukaemias and following global trends, and the second most common cancers were lymphomas aligning with previous reports on childhood cancer incidence from SA. Almost half of all the cases (n=441) were diagnosed in children aged 0-4years old. Most of the results within the report are comparable to results from within the region and global trends. Annual reports of childhood cancers are the first step towards improving reporting of childhood cancers and raising awareness on the incidence of childhood cancers. Efforts are ongoing to receive data from all possible data sources.

INTRODUCTION

In South Africa (SA), the National Cancer Registry (NCR) is responsible for cancer surveillance which includes the systemic collection, storage, analysis, interpretation and reporting of cancer cases (1). The NCR achieves this through its pathology-based registry and its first sentinel population-based cancer registry located in the Ekurhuleni district, Gauteng province. Annual reports with incidence rates are published for each of these registries.

In order 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 established 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 health-care worker obliged to report confirmed cancers to the NCR (2,3).

For the purpose of this report, childhood cancers are defined as malignant tumours diagnosed in children aged 0-14 years old. 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 20%, 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).

Although there is no standalone childhood cancer policy currently in South Africa, “cancers of childhood, adolescence and young adulthood” have been identified as a national priority and work is underway to draft a “Childhood Cancer Strategic Framework” (8). This highlights the need for the NCR to produce annual childhood cancer reports and provide accurate cancer incidence rates to guide policymakers nationally and globally. This is the first time the National Cancer Registry is publishing

a standalone report on childhood cancers using the International Classification of Childhood Cancers Third Edition (ICCC-3) (9).

Background

In 2018, South Africa reported a population of approximately 58 million, with children aged 0-14 years old comprising ≈30% of the population (10). The distribution of males and females aged 0-14 years old is comparable (Figure 1).

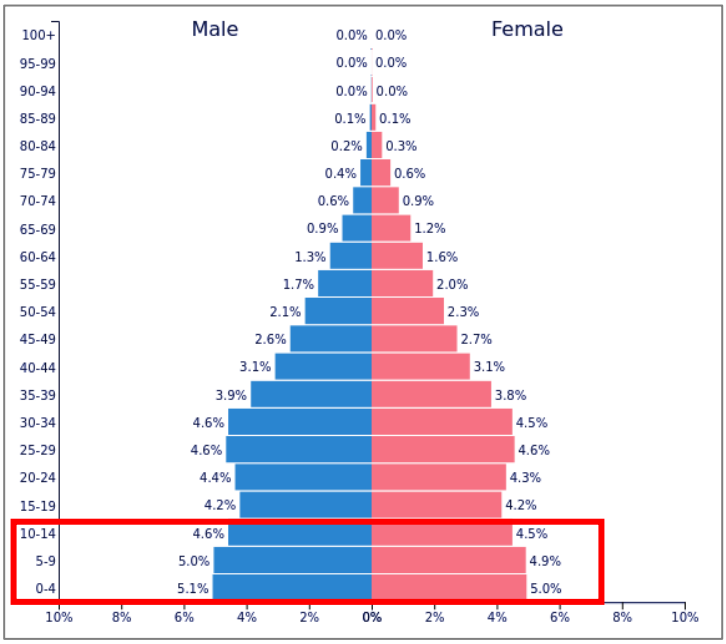

Figure 1: *Population pyramid of South Africa (2019). Age groups 0-19 years highlighted in red.*

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.

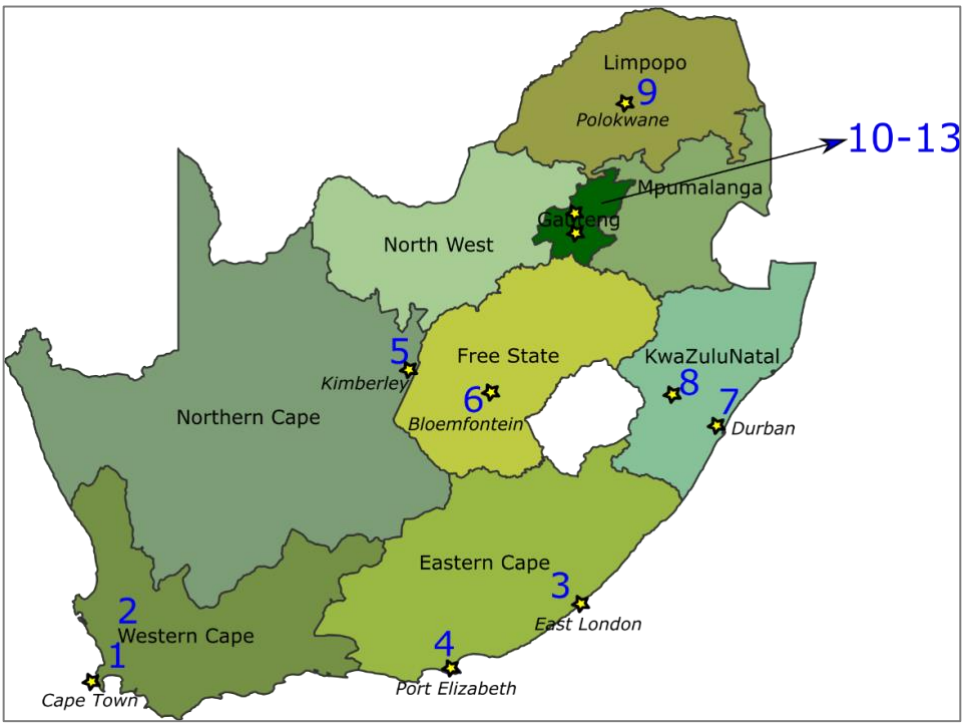

Figure 2: Distribution of major public health facilities with paediatric oncology units in South Africa, 2022.

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 pathology-diagnosed cases of childhood cancers (0-14 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 2018 EPBCR report (11).

As previously mentioned, Regulation 380 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). 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 EPBCR jurisdiction.

For this report, data from the pathology-based cancer registry, the EPBCR and cancer notifications sent by clinicians from various sites throughout the country (Appendix 2) were used. The data from the three sources were linked to create one comprehensive national dataset (Figure 3). Duplicate cases were deleted. All new cancer cases diagnosed from 01 January 2018 to 31 December 2018 were included. Cases that were not of 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. 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*).

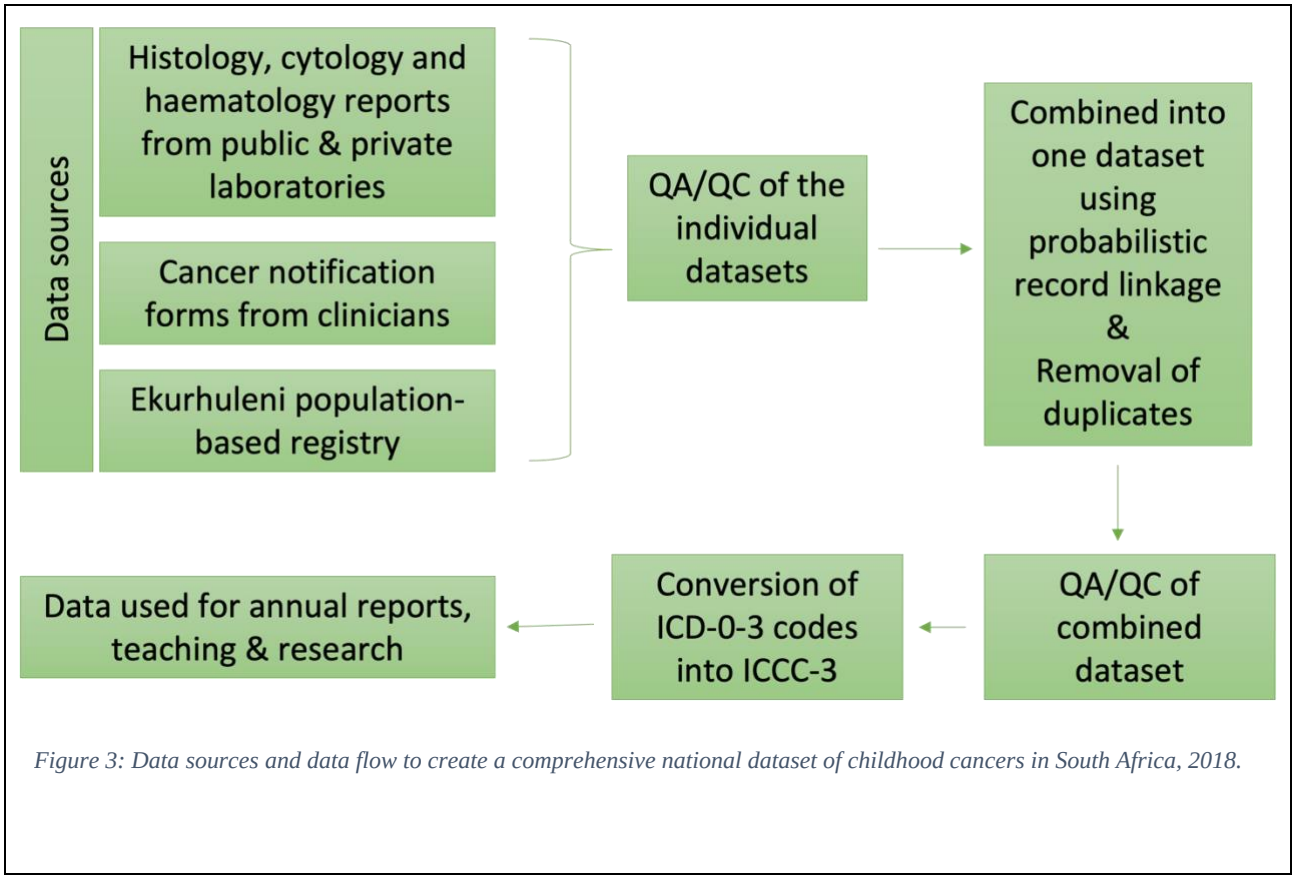

Figure 3: Data sources and data flow to create a comprehensive national dataset of childhood cancers in South Africa, 2018.

Confidentiality

The NCR adheres to the NHLS, the IARC/IACR guidelines and the POPI Act to ensure the preservation of confidentiality (13). Cancer statistics are released in an 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 (ASpIR) 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)

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 975 cancers were diagnosed in children aged 0-14years old in South Africa in 2018. This equated to overall age standardized rate of 59.8 cases per million (95%CI: 48.6-73.2) (Table 1).

Of the 975 cases, 240 cases (24.6%) were found both in the NCR registries and cancer notifications sent by clinicians. Approximately 50% of the cases came from the NCR pathology-based registry and/or the EPBCR. The remaining cases 245 (25%) were reported by clinicians.

Incidence rates were slightly higher in boys compared to girls (incidence sex ratio was 1.17: 1 boy: girls (Table1).

Cancer Incidence by type

The most common cancer diagnosed in children was leukaemia, which accounted for 19% of all cancers diagnosed in children aged 0-14yrs with an ASR of 11.47 per million children (95%CI 9.89-13.24) (Table 1). Of the leukaemias, lymphoid leukaemias were the commonly diagnosed (Table 2) with an ASR of 7.69 per million (95%CI: 6.41-9.16) with the highest incidence being found in the 0-4 years

and 5-9 years age groups with an age-specific incidence rate of 8.6 and 8.7 cases per million respectively.

Lymphomas were the second most common cancer group diagnosed in South Africa, with the highest number of cases (n=77) occurring in the 10-14 age group with an age-specific incidence rate 14 per million (Table 1). Non-Hodgkin lymphomas (except Burkitt lymphoma) and Hodgkin lymphomas were the most common type of lymphomas diagnosed (Table 2). Only 18 cases of hepatic tumours were diagnosed making them the least commonly diagnosed cancers in children in 2018. However of the 18, 77.7% (n=14) were diagnosed in children aged 0-4 years old.

Cancer Incidence by sex

Of the 975 cancers diagnosed, 53.9% (n=526) were diagnosed in boys and 46% (n=448) were diagnosed in girls (Figure 4). There was one case (0.1%) diagnosed with unknown sex.

Table 1: Cancer incidence for children 0-14years old by main cancer groups as defined by the 12 main groups per theICCC-3, South Africa (2018)

	Number of cases						Rates per Million Age-specific Rates						
Cancer Group	**Age 0-4**	**Age 5-9**	**Age 10-14**	**All ages**	**Ratio (M/F)**	**Relative Freq (%)**	**ASpIR 0-4**	**ASpIR 5-9**	**ASpIR 10-14**	**Crude**	**ASR**	**LCL**	**UCL**
I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases	75	72	42	189	1.2	19.4	13.23	12.57	7.9	11.31	11.47	9.89	13.24
II. Lymphomas and reticuloendothelial neoplasms	50	47	77	174	2.2	17.8	8.82	8.21	14.49	10.41	10.27	8.79	11.92
III. CNS and miscellaneous intracranial and intraspinal neoplasms	66	50	20	136	1.2	13.9	11.64	8.73	3.76	8.14	8.42	7.05	9.96
IV. Neuroblastoma and other peripheral nervous cell tumours	38	11	1	50	1.3	5.1	6.7	1.92	.19	2.99	3.27	2.42	4.31
V. Retinoblastoma	57	3	0	60	1.1	6.2	10.05	.52	0	3.59	4.06	3.10	5.22
VI. Renal tumours	70	25	5	100	.8	10.3	12.35	4.37	.94	5.98	6.46	5.25	7.86
VII. Hepatic tumours	14	2	2	18	.6	1.8	2.47	.35	.38	1.08	1.18	0.70	1.86
VIII. Malignant bone tumours	4	10	39	53	.8	5.4	.71	1.75	7.34	3.17	2.97	2.22	3.89
IX. Soft tissue and other extraosseous sarcomas	43	47	35	125	1	12.8	7.58	8.21	6.59	7.48	7.50	6.23	8.94
X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads	12	7	11	30	.4	3.1	2.12	1.22	2.07	1.80	1.81	1.22	2.59
XI. Other malignant epithelial neoplasms and malignant melanomas	10	8	19	37	1.5	3.8	1.76	1.4	3.58	2.21	2.17	1.53	3.00
XII. Other and unspecified malignant neoplasms	2	1	0	3		0.3	.35	.17	0	0.18	0.19	0.04	0.56
Total	**441**	**283**	**251**	**975**	**1.17**	**100.0**	**77.8**	**49.4**	**47.2**	**58.3**	**59.8**	**48.6**	**73.2**

Ratio (M/F): male-to-female ratio
ASpIR: Age-specific incidence rates per million
Crude: crude rates expressed per million aged 0-14 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 2: Cancer incidence for children 0-14years old by sub-groups as defined by the ICCC-3, South Africa (2018)

Cancer type	*Number of cases*						*Rates per Million Age-specific Rates*						
	Age 0-4	Age 5-9	Age 10-14	All	Ratio (M/F)	Relative freq (%)	ASpIR 0-4	ASpIR 5-9	ASpIR 10-14	Crude	ASR	LCL	UCL
I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases													
(Ia) Lymphoid leukaemias	49	50	28	127	1	13.0	8.6	8.7	5.3	7.6	7.7	6.4	9.2
(Ib) Acute myeloid leukaemias	19	13	9	41	1	4.2	3.3	2.3	1.7	2.5	2.5	1.8	3.4
(Ic) Chronic myeloproliferative diseases	0	1	2	3	1	0.3	0.0	0.2	0.4	0.2	0.2	0.0	0.5
(Id) Myelodysplastic syndrome and other myeloproliferative diseases	3	0	0	3		0,3	0.5	0.0	0.0	0.2	0.2	0.0	0.6
(Ie) Unspecified and other specified leukaemias	4	8	3	15	1	1.5	0.7	1.4	0.6	0.9	0.9	0.5	1.5
II. Lymphomas and reticuloendothelial neoplasms													
(IIa) Hodgkin lymphomas	19	20	34	73	3	7.5	3.3	3.5	6.4	4.4	4.3	3.4	5.4
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	20	20	35	75	2	7.7	3.5	3.5	6.6	4.5	4.4	3.5	5.5
(IIc) Burkitt lymphoma	7	5	7	19	4	1.9	1.2	0.9	1.3	1.1	1.1	0.7	1.8
(IId) Miscellaneous lymphoreticular neoplasms	3	1	0	4	3	0.4	0.5	0.2	0.0	0.2	0.3	0.1	0.7
(IIe) Unspecified lymphomas	1	1	1	3	1	0.3	0.2	0.2	0.2	0.2	0.2	0.0	0.5
III. CNS and miscellaneous intracranial and intraspinal neoplasms													
(IIIa) Ependymomas and choroid plexus tumour	20	3	3	26	2	2.7	3.5	0.5	0.6	1.6	1.7	1.1	2.5
(IIIb) Astrocytomas	12	16	6	34	1	3.5	2.1	2.8	1.1	2.0	2.0	1.4	2.9
(IIIc) Intracranial and intraspinal embryonal tumours	23	12	4	39	1	4.0	4.1	2.1	0.8	2.3	2.5	1.7	3.4
(IIId) Other gliomas	4	14	2	20	1	2.1	0.7	2.4	0.4	1.2	1.2	0.7	1.8
(IIIe) Other specified intracranial and intraspinal neoplasms	4	3	3	10	2	1.0	0.7	0.5	0.6	0.6	0.6	0.3	1.1
(IIIf) Unspecified intracranial and intraspinal neoplasms	3	2	2	7		0.7	0.5	0.3	0.4	0.4	0.4	0.2	0.9

Cancer type	Number of cases						Rates per Million Age-specific Rates						
	Age 0-4	Age 5-9	Age 10-14	All	Ratio (M/F)	Relative freq (%)	ASpIR 0-4	ASpIR 5-9	ASpIR 10-14	Crude	ASR	LCL	UCL
IV. Neuroblastoma and other peripheral nervous cell tumours													
(IVa) Neuroblastoma and ganglioneuroblastoma	37	11	0	48	1	4.9	6.5	1.9	0.0	2.9	3.1	2.3	4.2
(IVb) Other peripheral nervous cell tumours	1	0	1	2	1	0.2	0.2	0.0	0.2	0.1	0.1	0.0	0.4
V. Retinoblastoma	57	3	0	60	1	6.2	10.1	0.5	0.0	3.6	4.1	3.1	5.2
VI. Renal tumours													
(VIa) Nephroblastoma and other nonepithelial renal tumours	70	25	4	99	1	10.2	12.4	4.4	0.8	5.9	6.4	5.2	7.8
(VIb) Renal carcinomas	0	0	1	1		0.1	0.0	0.0	0.2	0.1	0.1	0.0	0.3
(VIc) Unspecified malignant renal tumours	0	0	0	0		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2
VII. Hepatic tumours													
(VIIa) Hepatoblastoma	10	2	1	13	1	1.3	1.8	0.3	0.2	0.8	0.9	0.5	1.4
(VIIb) Hepatic carcinomas	2	0	1	3		0.3	0.3	0.0	0.2	0.2	0.2	0.0	0.6
(VIIc) Unspecified malignant hepatic tumours	2	0	0	2	1	0.2	0.3	0.0	0.0	0.1	0.1	0.0	0.5
VIII. Malignant bone tumours													
(VIIIa) Osteosarcomas	2	7	32	41	1	4.2	1	6	2.5	2.3	1.6	3.1	2
(VIIIb) Chondrosarcomas	1	0	2	3	2	0.3	0	0	0.2	0.2	0.0	0.5	1
(VIIIc) Ewing tumour and related sarcomas of bone	1	3	4	8	1	0.8	1	1	0.5	0.5	0.2	0.9	1
(VIIId) Other specified malignant bone tumours	0	0	0	0		0.0	0	0	0.0	0.0	0.0	0.2	0
(VIIIe) Unspecified malignant bone tumours	0	0	1	1		0.1	0	0	0.1	0.1	0.0	0.3	0
IX. Soft tissue and other extraosseous sarcomas													
(IXa) Rhabdomyosarcomas	25	29	10	64	1	6.6	5	2	3.8	3.9	3.0	5.0	25
(IXb) Fibrosarcomas. peripheral nerve sheath tumours, and other fibrous neoplasms	6	0	1	7	3	0.7	0	0	0.4	0.5	0.2	0.9	6
(IXc) Kaposi sarcoma	2	3	4	9	1	0.9	1	1	0.5	0.5	0.2	1.0	2
(Ixd) Other specified soft tissue sarcomas	7	12	14	33	1	3.4	2	3	2.0	1.9	1.3	2.7	7
(Ixe) Unspecified soft tissue sarcomas	3	3	6	12		1.2	1	1	0.7	0.7	0.4	1.2	3

	Number of cases						Rates per Million Age-specific Rates						
Cancer type	**Age 0-4**	**Age 5-9**	**Age 10-14**	**All**	**Ratio (M/F)**	**Relative freq (%)**	**ASpIR 0-4**	**ASpIR 5-9**	**ASpIR 10-14**	**Crude**	**ASR**	**LCL**	**UCL**
X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads													
(Xa) Intracranial and intraspinal germ cell tumours	1	3	1	5		0.4	0.2	0.5	0.2	0.3	0.3	0.1	0.7
(Xb) Malignant extracranial and extragonadal germ cell tumours	2	0	2	4		0.4	0.3	0.0	0.4	0.2	0.2	0.1	0.6
(Xc) Malignant gonadal germ cell tumours	9	4	6	19	1	2.1	1.6	0.7	1.1	1.1	1.2	0.7	1.8
(Xd) Gonadal carcinomas	0	0	1	1		0.1	0.0	0.0	0.2	0.1	0.1	0.0	0.3
(Xe) Other and unspecified malignant gonadal tumours	0	0	1	1		0.1	0.0	0.0	0.2	0.1	0.1	0.0	0.3
XI. Other malignant epithelial neoplasms and malignant melanomas													
(Xia) Adrenocortical carcinomas	1	0	0	1		0.1	0.2	0.0	0.0	0.1	0.1	0.0	0.4
(XIb) Thyroid carcinomas	0	1	3	4	1	0.4	0.0	0.2	0.6	0.2	0.2	0.1	0.6
(XIc) Nasopharyngeal carcinomas	0	0	2	2	1	0.2	0.0	0.0	0.4	0.1	0.1	0.0	0.4
(XId) Malignant melanomas	0	1	3	4	1	0.4	0.0	0.2	0.6	0.2	0.2	0.1	0.6
(XIe) Skin carcinomas	1	2	0	3		0.3	0.2	0.3	0.0	0.2	0.2	0.0	0.5
(XIf) Other and unspecified carcinomas	8	4	11	23	1	2.4	1.4	0.7	2.1	1.4	1.4	0.9	2.1
XII. Other and unspecified malignant neoplasms													
(XIIa) Other specified malignant tumours	1	0	0	1		0.1	0.2	0.0	0.0	0.1	0.1	0.0	0.4
(XIIb) Other unspecified malignant tumours	1	1	0	2		0.2	0.2	0.2	0.0	0.1	0.1	0.0	0.4
Total	**441**	**283**	**251**	**975**		**100**	**77.8**	**49.4**	**47.3**	**58.3**	**59.8**	**41.9**	**87.2**

Ratio (M/F): male-to-female ratio
ASpIR: Age-specific incidence rates per million
Crude: crude rates expressed per million aged 0-14 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

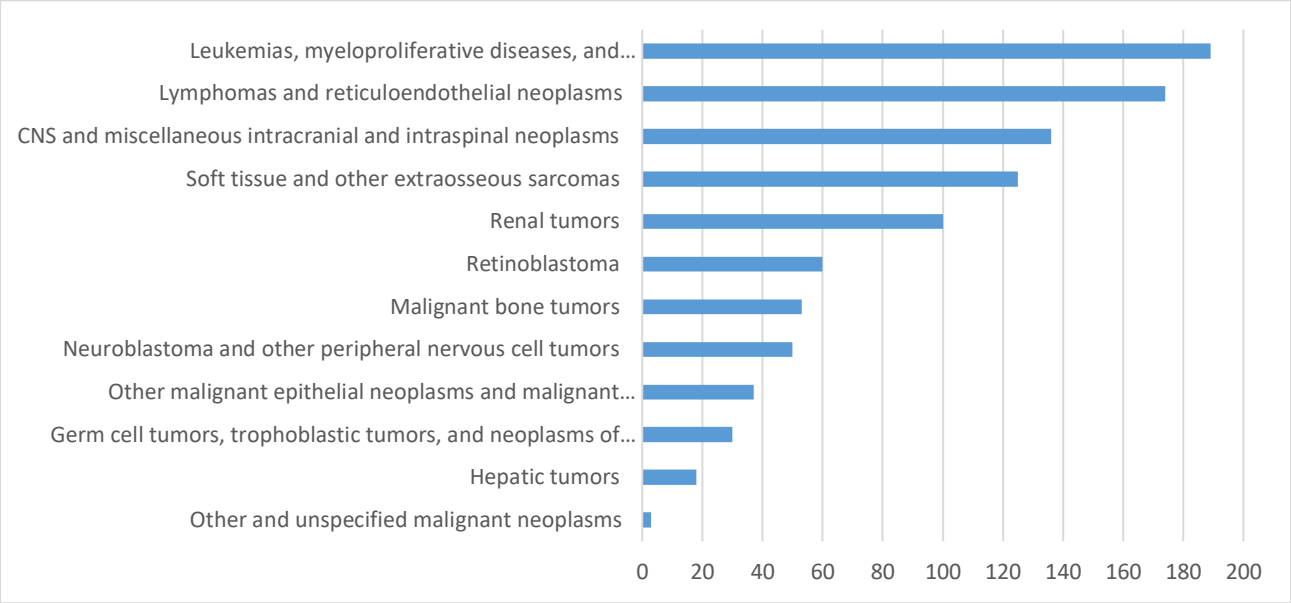

Figure 4: Number of childhood cancer cases per main group as classified by the ICCC-3, South Africa, 2018.

Lymphomas were more commonly diagnosed in boys (69%) compared to girls (31%), whereas Germ cell tumours were more commonly diagnosed in girls (73.3%) compared to boys (26.7%).

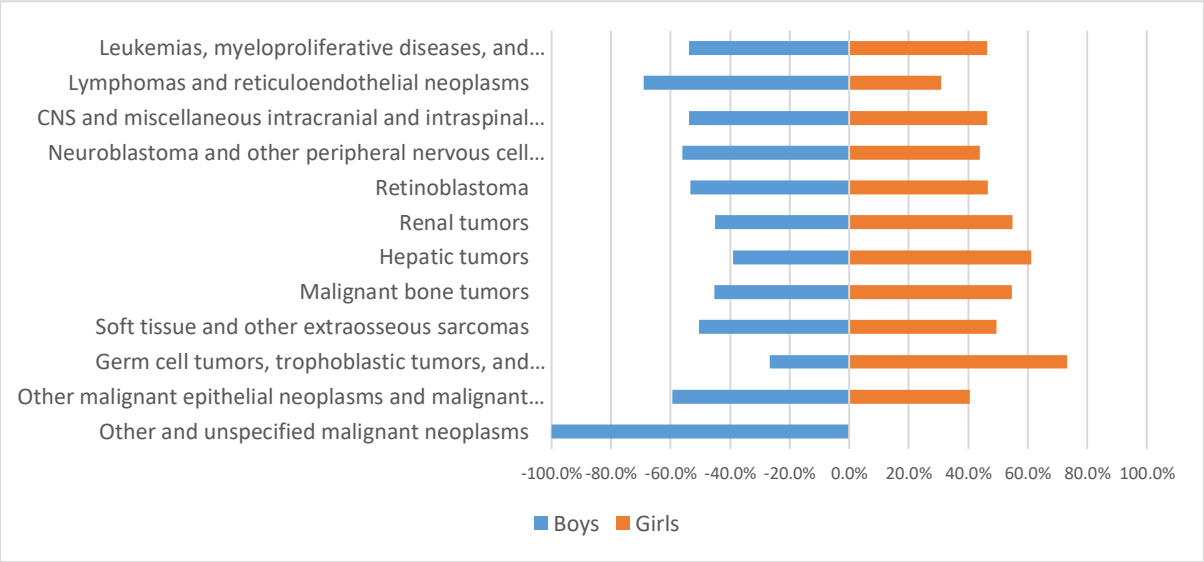

Figure 5: Distribution of childhood cancers by cancer type and sex, South Africa, 2018

Lymphoid leukaemias, non-Hodgkin lymphomas, nephroblastoma and rhabdomyosarcomas were among the top five cancers diagnosed in boys and girls with lymphoid leukaemias being the most commonly diagnosed cancer in both groups (Table 3). Hodgkin lymphomas were the second most commonly diagnosed cancer in boys but they were not in the top five cancers for girls.

Table 3: Most commonly diagnosed childhood cancers by sex, South Africa, 2018

Boys	**n**	**(%)**
(Ia) Lymphoid leukaemias	70	13.3%
(IIa) Hodgkin lymphomas	56	10.6%
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	45	8.6%
(VIa) Nephroblastoma and other nonepithelial renal tumours	44	8.4%
(IXa) Rhabdomyosarcomas	36	6.8%
Girls	**n**	**(%)**
(Ia) Lymphoid leukaemias	56	12.5%
(VIa) Nephroblastoma and other nonepithelial renal tumours	55	12.3%
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	30	6.7%
(IXa) Rhabdomyosarcomas	28	6.3%
(V) Retinoblastoma	28	6.3%

Cancer Incidence by age-groups

Almost half of all childhood cancers were diagnosed in children aged 0-4 years (n=441, 45.2%) (Table 1). Annual incidence of the most common cancers by age group is shown in Table 4. Although found in varying percentages (11.1%-17.7%), lymphoid leukaemias were found across all the three age-groups.

Table 4: Most commonly diagnosed childhood cancers by age group, South Africa, 2018.

Cancer Type	**No. of cases**	**(%)**
0-4 years		
(VIa) Nephroblastoma and other nonepithelial renal tumours	70	15.90%
(V) Retinoblastoma	57	12.90%
(Ia) Lymphoid leukaemias	49	11.10%
(IVa) Neuroblastoma and ganglioneuroblastoma	37	8.40%
(IXa) Rhabdomyosarcomas	25	5.70%
5-9 years		
(Ia) Lymphoid leukaemias	50	17.70%
(IXa) Rhabdomyosarcomas	29	10.20%
(VIa) Nephroblastoma and other nonepithelial renal tumours	25	8.80%
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	20	7.10%
(IIa) Hodgkin lymphomas	20	7.10%
10-14 years		
(IIb) Non-Hodgkin lymphomas (except Burkitt lymphoma)	35	13.90%

(IIa) Hodgkin lymphomas	34	13.50%
(VIIIa) Osteosarcomas	32	12.74%
(Ia) Lymphoid leukaemias	28	11.20%
(IXd) Other specified soft tissue sarcomas	14	5.57%

DISCUSSION

This is the first report on childhood cancer incidence by the National Cancer Registry of South Africa. A total of 975 cancers cases were recorded in children aged 0-14 years old. The overall ASR of 59.8 per million is higher than previously reported ASR of 45.7 per million children using NCR data from the period 2000-2006 (14) and 45.2 per million from period 1987-2007 by the South African Children's Tumour Registry (SACTR) (15). The higher incidence rate is likely a result of a comprehensive national dataset created by linking the various data sources. As there is a lack of unique identifiers in the SA healthcare system, this is the first time data sources have been linked using probabilistic record linkage to achieve a more complete estimate of childhood cancers.

We found the most common cancer group diagnosed to be leukaemias (19.4%), followed by lymphomas (17.8%). This is in line with previous reports on childhood cancers in South Africa (16,17). However globally, leukaemias and tumours of the central nervous systems (CNS) are the two most common cancers. In South Africa, tumours of the central nervous system were ranked third (13.9%). The difference between global and South African rates of CNS tumours may be result of under-diagnosis and/or under-reporting (5,17).

Soft tissue sarcomas (12.8%) were the fourth most common cancer, with rhabdomyosarcomas (n=64,) being the most prominent sub-group. Previous studies have shown that soft tissue sarcomas have a higher incidence in Black South African children compared to White South African children (14); and that the NCR has recorded higher numbers of soft tissue sarcomas compared to other data sources (15). With the public health sector servicing 80% of the South African population, the high number of soft tissue sarcomas could be due to most of the NCR pathology reports coming from the National Health Laboratory Services (NHLS) public sector laboratories. Renal tumours, predominantly

nephroblastomas, were the fifth most common childhood cancer. Renal rumours were most prevalent in the 0-4 years old age group comparable to global trends (18).

Almost half of all the childhood cancer cases were diagnosed in children aged 0-4years old. The age-specific incidence rates were the highest in children aged 0-4 years (77.8 per million) group similar to global patterns (18). The lowest rates were in the 10-14 years old (47.2 per million).Globally the most common cancer in children aged 0-4years is leukaemia, however rates in sub-Saharan Africa have always been lower than the global rates (18). Similarly, in South Africa, leukaemias were the most frequently diagnosed cancer in the 0-4 years age-group but at lower rates compared to global rates.

More boys were diagnosed with cancers compared to girls, at a ratio of 1.2. This is also in line with global ratio of 1.37, although the reasons for this still remain unclear, it is hypothesized that the discrepancy in developing countries could be a result of more cases occurring in boys than girls due to unknown reasons, but also due to sociocultural norms where boys are more likely to be taken to health care facilities for further investigation and treatment (18). Similar to reported global trends, we saw that a higher incidence of germ and gonadal tumours in girls compared to boys (18).

In 2018, less than 10 cases of Kaposi sarcoma were diagnosed (Table 2), with 44% of the cases being diagnosed in the 10-14yers age group. Incidence rates of Kaposi sarcoma in children have been decreasing due to the wide-spread roll-out of antiretroviral therapy, particularly among HIV-positive pregnant women (19,20) with a consequent reduction in mother-to-child transmission of HIV.

The low incidence of Burkitts lymphoma (ASR 1.1 per million, 95%CI:0.7-1.8) diagnosed in South African children compared to other sub-Saharan countries may be due to differences in exposure to infectious diseases such as Epstein Barr virus and malaria (14,21).

Childhood cancer is underreported in South Africa. The NCR previously reported 742 cases in ages 0-14 years old in its 2018 annual statistics report (22). Annual reports of childhood cancers are the first step towards improving reporting of childhood cancers and raising awareness on the incidence of childhood cancers. Misdiagnosis and delay in diagnosis of childhood cancers are major barriers in improving outcomes. There is a need for increased index of suspicion for childhood cancers by

clinicians as childhood cancers may mimic other infection-related diseases within the South African context (23). Although data from various sources were used, there is still room for improvement to build a more comprehensive national dataset to provide accurate incidence rates. The current dataset indicates that the NCR pathology registry is missing approximately 25% of all childhood cancers. Of the missed cancers, 70% were haematological malignancies (leukaemias and lymphomas) and brain tumours. Efforts are ongoing to strengthen and motivate reporting of cancers diagnosed in children from all possible data sources to provide an accurate snapshot of childhood cancers in South Africa. This is much-needed to guide both clinicians and policymakers to improve childhood cancer awareness, screening, diagnosis, treatment and outcomes.

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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) 2018

- 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

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

Site Group	ICD-O-3 Histology (Type)	ICD-O-2/3 Site	Recode
I Leukaemias, myeloproliferative diseases, and myelodysplastic diseases			
(a) Lymphoid leukaemias	9820, 9823, 9826, 9827, 9831-9837, 9940, 9948	C000-C809	011
(b) Acute myeloid leukaemias	9840, 9861, 9866, 9867, 9870-9874, 9891, 9895-9897, 9910, 9920, 9931	C000-C809	012
(c) Chronic myeloproliferative diseases	9863, 9875, 9876, 9950, 9960-9964	C000-C809	013
(d) Myelodysplastic syndrome and other myeloproliferative diseases	9945, 9946, 9975, 9980, 9982-9987, 9989	C000-C809	014
(e) Unspecified and other specified leukaemias	9800, 9801, 9805, 9860, 9930	C000-C809	015
II Lymphomas and reticuloendothelial neoplasms			
(a) Hodgkin lymphomas	9650-9655, 9659, 9661-9665, 9667	C000-C809	021
(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	022
(c) Burkitt lymphoma	9687	C000-C809	023
(d) Miscellaneous lymphoreticular neoplasms	9740-9742, 9750, 9754-9758	C000-C809	024

(e) Unspecified lymphomas	9590, 9596	C000-C809	025
III CNS and miscellaneous intracranial and intraspinal neoplasms			
(a) Ependymomas and choroid plexus tumour	9383, 9390-9394	C000-C809	031
(b) Astrocytomas	9380	C723	032
	9384, 9400-9411, 9420, 9421-9424, 9440-9442	C000-C809	032
(c) Intracranial and intraspinal embryonal tumours	9470-9474, 9480, 9508	C000-C809	033
	9501-9504	C700-C729	033
(d) Other gliomas	9380	C700-C722, C724-C729, C751, C753	034
	9381, 9382, 9430, 9444, 9450, 9451, 9460	C000-C809	034
(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	035
(f) Unspecified intracranial and intraspinal neoplasms	8000-8005	C700-C729, C751-C753	036
IV Neuroblastoma and other peripheral nervous cell tumours			
(a) Neuroblastoma and ganglioneuroblastoma	9490, 9500	C000-C809	041
(b) Other peripheral nervous cell tumours	8680-8683, 8690-8693, 8700, 9520-9523	C000-C809	042
	9501-9504	C000-C699, C739-C768, C809	042
V Retinoblastoma	**9510-9514**	**C000-C809**	**050**
VI Renal tumours			
(a) Nephroblastoma and other nonepithelial renal tumours	8959, 8960, 8964-8967	C000-C809	061
	8963, 9364	C649	061
(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	062
	8311, 8312, 8316-8319, 8361	C000-C809	062
(c) Unspecified malignant renal tumours	8000-8005	C649	063
VII Hepatic tumours			
(a) Hepatoblastoma	8970	C000-C809	071

(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	072
	8160-8180	C000-C809	072
(c) Unspecified malignant hepatic tumours	8000-8005	C220, C221	073
VIII Malignant bone tumours			
(a) Osteosarcomas	9180-9187, 9191-9195, 9200	C400-C419, C760-C768, C809	081
(b) Chondrosarcomas	9210, 9220, 9240	C400-C419, C760-C768, C809	082
	9221, 9230, 9241-9243	C000-C809	082
(c) Ewing tumour and related sarcomas of bone	9260	C400-C419, C760-C768, C809	083
	9363-9365	C400-C419	083
(d) Other specified malignant bone tumours	8810, 8811, 8823, 8830	C400-C419	084
	8812, 9250, 9261, 9262, 9270-9275, 9280-9282, 9290, 9300-9302, 9310-9312, 9320-9322, 9330, 9340-9342, 9370-9372	C000-C809	084
(e) Unspecified malignant bone tumours	8000-8005, 8800, 8801, 8803-8805	C400-C419	085
IX Soft tissue and other extraosseous sarcomas			
(a)Rhabdomyosarcomas	8900-8905, 8910, 8912, 8920, 8991	C000-C809	091
(b) Fibrosarcomas, peripheral nerve sheath tumours, and other fibrous neoplasms	8810, 8811, 8813-8815, 8821, 8823, 8834-8835	C000-C399, C440-C768, C809	092
	8820, 8822, 8824-8827, 9150, 9160, 9491, 9540-9571, 9580	C000-C809	092
(c) Kaposi sarcoma	9140	C000-C809	093
(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	094
	8830	C000-C399, C440-C768, C809	094
	8963	C000-C639, C659-C699, C739-C768, C809	094
	9180, 9210, 9220, 9240	C490-C499	094

	9260	C000-C399, C470-C759	094
	9364	C000-C399, C470-C639, C659-C699, C739-C768, C809	094
	9365	C000-C399, C470-C639, C659-C768, C809	094
(e) Unspecified soft tissue sarcomas	8800-8805	C000-C399, C440-C768, C809	095
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	101
(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	102
(c) Malignant gonadal germ cell tumours	9060-9065, 9070-9073, 9080-9085, 9090, 9091, 9100, 9101	C569, C620-C629	103
(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	104
	8441-8444, 8450, 8451, 8460-8473	C000-C809	104
(e) Other and unspecified malignant gonadal tumours	8590-8671	C000-C809	105
	8000-8005	C569, C620-C629	105
XI Other malignant epithelial neoplasms and malignant melanomas			
(a) Adrenocortical carcinomas	8370-8375	C000-C809	111
(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	112
	8330-8337, 8340-8347, 8350	C000-C809	112
(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	113
(d) Malignant melanomas	8720-8780, 8790	C000-C809	114

(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	115
(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	116
XII Other and unspecified malignant neoplasms			
(a) Other specified malignant tumours	8930-8936, 8950, 8951, 8971-8981, 9050-9055, 9110	C000-C809	121
	9363	C000-C399, C470-C759	121
(b) Other unspecified malignant tumours	8000-8005	C000-C218, C239-C399, C420-C559, C570-C619, C630-C639, C659-C699, C739-C750, C754-C809	122
Not Classified by ICCC or in situ			**999**