ASSESSING THE STATUS AND CHALLENGES OF PEDIATRIC ONCOLOGY IN LOW AND MIDDLE-INCOME COUNTRIES

by

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ABSTRACT

In the past decade, an increased global effort has been directed towards improving pediatric oncology status in low and middle-income countries (LMICs). Several international organizations and large consortiums have collaborated to undertake this effort, such as the United States (U.S.) National Cancer Institute (NCI), The Middle East Cancer Consortium, African Cancer Registry Network, The Middle East Childhood Cancer Alliance, Pediatric Oncology East and Mediterranean (POEM) Group and others. However, underreporting of incidence, mortality, and survival rate of childhood cancer in LMICs have so far limited the global community from understanding the true scale of the problem. Underestimating the extent of pediatric cancer in LMICs creates a massive challenge and plays a significant role in delaying improvement of pediatric cancer medical care.

In this study, a rapid review and data assessment from publicly available databases and literature was performed to define the status of pediatric cancer data in low-income countries (LICs) and compare it to that of high-income countries (HICs). This assessment revealed that the amount of pediatric cancer data published in HICs was significantly larger compared to LICs, especially for African countries. The analysis also highlighted the existence of a significant discrepancy of pediatric cancer data reported by different sources in LICs, whereas there was a minimal discrepancy in data reported in HICs.

To better understand the extent of data underreporting in LICs, a questionnaire was sent to cancer registries in selected African countries to assess the factors that might impact the process and quality of data collection and reporting. The results of the questionnaire highlighted that limited resources of registries, staff workload, lack of training, access to diagnostic tools and underrepresentation of their data in global databases were some of the factors that mostly

contributed to pediatric cancer data underreporting. Results also indicated that incidence rates reported by cancer registries were not comparable with those reported by global databases, thus confirming the discrepancy outlined in the data assessment.

To further investigate underreporting in LICs and collect pediatric data directly from cancer centers, a fieldwork trip in Egypt took place in 2018. The outcome of interviews and meetings during the visit illustrated that lack of resources, access to therapies, and access to diagnostic tools and protocols were key gaps and challenges that those cancer centers faced. Moreover, future collaborations and action plans were established, and data digitalization and training programs were the main two action plans prioritized.

In summary, the combined outcome of the rapid review and data assessment, cancer registries questionnaire, and field trip suggested that there is a significant underreporting of pediatric cancer data and discrepancy in data reported in LICs. Additionally, cancer hospitals, centers, and registries face tremendous challenges and gaps that negatively impact data collection and reporting. Therefore, there is an urgent need for the global community to establish strategies to quantify the true scale of pediatric cancer, which should lead to allocate sufficient funds to improve pediatric cancer medical care in LICs.

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List of abbreviations

ACS	American Cancer Society
AFCRN	African Cancer Registry Network
ALL	Acute Lymphocytic Leukemia
AML	Acute Myeloid Leukemia
ASR	Age-standardised Average Annual Incidence Rate
BL	Burkitt Lymphoma
CAR-T	Chimeric Antigen Receptor Cell Therapy
CCDI	Childhood Care Data Initiative
CCSS	Childhood Cancer Survivor Study
CDC	Center for Disease and Control Prevention
CI5	Cancer Incidence in Five Continents
CNS	Central Nervus System
CPI	Checkpoint Inhibitors
CSC	Cancer Stem Cells
CT	Computed Tomography
DCCR	The Danish Childhood Cancer Registry
ECO	European Cancer Observatory
GCO	Global Cancer Observatory
GP	General Pediatricians/Practitioners
GPCR	Gharbiah Population-based Cancer Registry
HBCRs	Hospital-Based Cancer Registries
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HICs	High-Income Countries
HPV	Human Papilloma Virus
IARC	International Agency for Research on Cancer
ICU	Intensive Care Unit
IICC	The International Incidence of Childhood Cancer
INFORM	Individualized Therapy for Relapsed Malignancies in Childhood
LICs	Low-Income Countries
LMICs	Low- and Medium-Income Countries
MRD	Minimal Residual Disease
MRI	Magnetic Resonance Imaging
NCCP	National Cancer Control Plan
NCI	National Cancer Institute
NGOs	Non-Governmental Organizations

NGS	Next Generation Sequencing
NSCR	Nigerian National System of Cancer Registries
OCMU	Oncology Center in Al Mansoura University
PBCRs	Population-Based Cancer Registries
POINTE	Paediatric Oncology International Network for Training and Education
POEM	Pediatric Oncology East and Mediterranean
PSA	Prostate Specific Antigen
QC	Quality Control
SEER	Surveillance, Epidemiology, and End Results Program
SIOP	International Society of Pediatric Oncology
SMN	Secondary Malignant Neoplasms
SNPs	Single Nucleotide Polymorphisms
SSC	Squamous Cell Carcinoma
TARGET	Therapeutically Applicable Research to Generate Effective Treatments
UK	United Kingdom
UNDP	United Nations Development Program
USA	United States of America
WCC	World Child Cancer
WCRF	World Cancer Research Fund
WHO	World Health Organization

1 CHAPTER 1: INTRODUCTION

1.1 Overview of Cancer

Cancer is considered one of the deadliest diseases, with increasing cases every year (Roy & Saikia, 2016). The NCI defined cancer as "a term for diseases in which abnormal cells divide without control and can invade nearby tissues" (National Cancer Institute, 2021). This uncontrolled proliferation of abnormal cells is a result of multiple mutations in genes regulating proliferation and cell death (American Cancer Society, What Is Cancer?, 2020). In general, most cancer types could be described as an aggressive, resistant, and relapsed disease. The ability of cancer cells to rapidly metastasize and invade multiple organs makes it an aggressive disease. The low response rate of cancer to treatment and the ability of cancer to escape the immune system characterizes it as a resistant disease. Finally, the recurrence of cancer after multiple treatments and the rate of relapsed cancer patients defines it as a relapsed condition (Bajaj, Diaz, & Reya, 2020).

Cancer is not a single disease, even though the term cancer is always used for diagnosis, but it consists of hundreds of diseases, which creates complexity in developing therapies (Surveillance, Epidemiology, and End Results). The heterogeneity of cancer is not only observed between different types of cancers, but also within the same type and sub-types. Multiple tumors of the same types in the same patient represent significant heterogeneity and result in different treatment response. This clonal heterogeneity occurs when a patient might have multiple sub-clones originating from the same tumor (cancer stem cell), which have differential responses to treatment because of different mutations (Dagogo-Jack & Shaw, 2018).

1.1.1 Biology of cancer

The transformation of normal cells into cancer cells, also called carcinogenesis, starts with uncontrolled cell division of normal cells (Johns Hopkins, 2021). The process of this transformation involves various steps and stages. First, a normal cell transforms to an initiated cell, then to preneoplastic cell, which transforms to neoplastic cell and finally to cancer cell that metastasizes and forms malignant tumor (Figure 1.1) (Medicine LibreTexts, 2020).

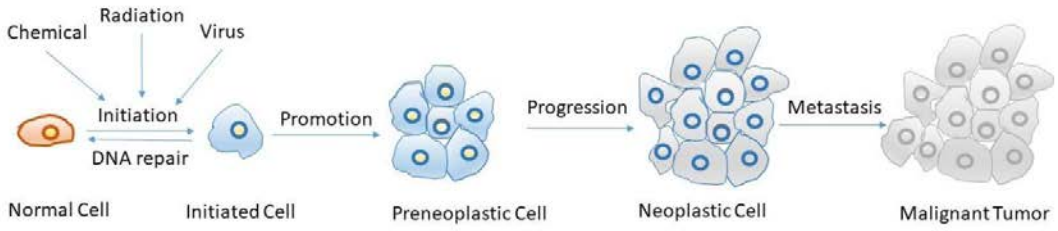


Figure 1.1 The transformation process of normal cell to malignant tumor
(Taken from (Medicine LibreTexts, 2020))

The development of cancer cells is a result of multiple genetic mutations and abnormalities. Genetic mutations in two major classes of genes, tumor suppressor genes and oncogenes, are the main drivers of cancer development and metastases. Tumor suppressor genes, such as P53, in a normal setting should stop the transformation of normal cells to cancer (Chial, 2008). Oncogenes are mutated genes that work as pro-growth and promote cell proliferation and differentiation, such as HER2 (Kontomanolis, et al., 2020). However, there are various changes in other genes and proteins that also contribute to this transformation (National Cancer Institute, The Genetics of Cancer, 2017). In addition, many mechanisms were identified to be involved in the development of the disease such as genomic instability and loss of proteostasis (Aunan, Cho, & Søreide, 2017).

Cancer cells that initiate tumors are called cancer stem cells (CSC), which have the ability to continuously divide, proliferate, and generate clones (Rycaj & Tang, 2015). Once the tumor is developed, malignant cells will escape and metastasize to other tissues and organs through the blood and lymphatic system (Cooper, 2000). One of the main features of cancer cells, solid tumors and lymphomas is the ability to form new blood vessels, a process called angiogenesis, to enable access to oxygen and nutrition (Cree, 2011).

1.1.2 Types of cancer

There are more than hundred types of cancers that are dependent on the cell of origin, and they vary in their frequency and distribution. The primary site of cancer initiation is what would determine the naming and diagnosis of cancer types, and it is called the primary cancer (Johns Hopkins Medicine, 2021). Also, cancers are defined by the cell type of origin, mutations, and characteristics (Cooper, 2000). For example, there are many different types of B cell lymphomas. Every type of cancer differs in its morphology, genotype, phenotype, and response to treatments (Alizadeh, et al., 2000). The main two categories of cancer types are blood cancers and solid tumors cancers. Blood cancers, also called hematological malignancies, include leukemia, lymphoma, and multiple myeloma, whereas solid tumors are originated in other organs (American Cancer Society, What Is Cancer?, 2020). Another way to categorize types of cancers is based on the type of cell where the cancer is originated. For example, carcinomas start in epithelial cells, sarcomas originate in bone tissues, muscles or fibrous tissues, and lymphomas originates in the lymphatic system (Johns Hopkins, 2021). Additionally, other types of cancers begin in other parts of the body. Tumors categorized as central nervus system (CNS) start in the brain or spinal cord, melanoma originates in the skin, and ovarian cancer develops in the ovary (American Cancer Society, What

Is Cancer?, 2020). Finally, cancers that originate from glandular tissues like lung, breast, prostate, or colon are known as adenocarcinomas, which are defined as subtypes of carcinomas. In general, lung, breast, and colorectal cancers are the most common cancer types globally (WCRF, 2021).

1.1.3 Age distribution

Cancer could be classified as an age-related disease, given that the risk of developing cancer increases by age. Aging and cancer are connected at a molecular level due to the decline of organ functions and weakening of the immune system, which is vital to fight cancer (Fan, et al., 2019). Moreover, by living longer, more mutations could be accumulated, and the risk that some of these mutations will give rise to a tumor would be higher (Davidović, 1999) (Figure 1.2). Studies demonstrated that the median age of cancer diagnosis is 66 years, and the highest cancer incidence occur between the age of 75-84 (Aramillo Irizar, et al., 2018). Data from the same study also revealed that at 50 years of age, the transformation rate from premalignant cells to cancer cells is the fastest. However, there are types of cancers that are more common in children and young adults (adolescents), such as bone and brain cancers. Recently, a population-based analysis demonstrated a significant increase in cancer incidence under the age of 50, suggesting that this increase could be related to environmental exposure and obesity (Sung, Siegel, Rosenberg, & Jemal, 2019).

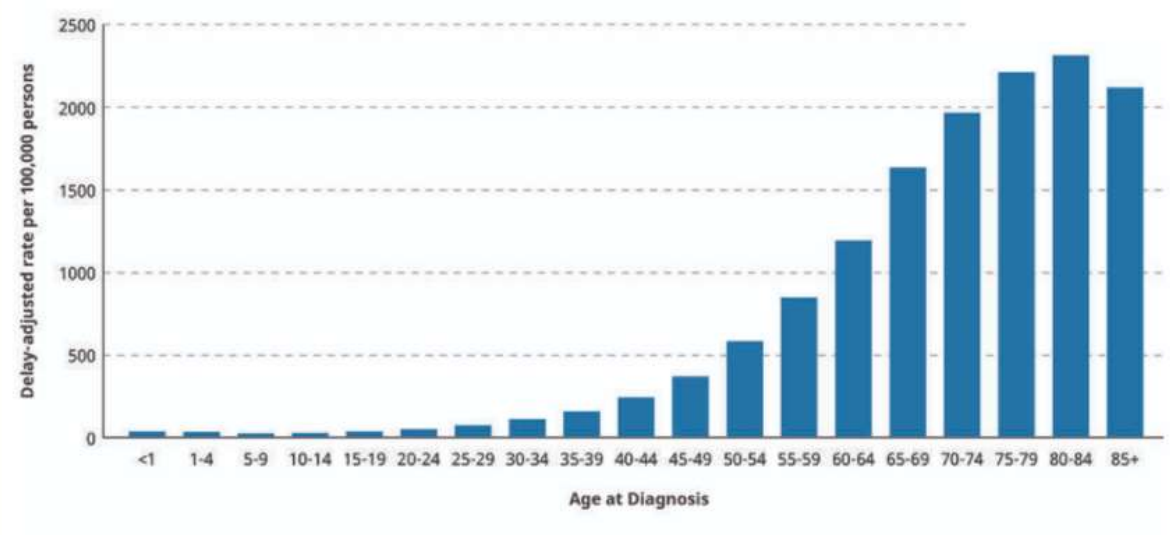


Figure 1.2 Age distribution of incidence rate for all cancer types and both sexes
Date source: SEER 2013-2917. National Cancer Institute
(Taken from (National Cancer Institute, 2021))

1.1.4 Cancer incidence and mortality

The World Health Organization (WHO) reported that, in 2018, 18 million new cases of cancers were diagnosed. Cancer was the second leading cause of death in 2018 after heart disease, with an estimated mortality incidence of approximately 9.6 million people. In 2018, the most prevalent cancer types were lung, breast, and prostate cancers, respectively, and kidney cancer had the lowest prevalence. Additionally, the primary cancer related mortality was associated with lung and breast cancers (Mattiuzzi & Lippi, 2019).

There is an overall increase of cancer incidence worldwide, with predictions suggesting that incidence will increase by 62% in 2040 (World Health Organization, 2021). GLOBOCAN is a database commonly used as a source to obtain global cancer data on survival, incidence, and mortality (GLOBOCAN 2020, Database Provides Latest Global Data on Cancer Burden, Cancer

Deaths, 2020). A global increase in cancer cases between the year of 2018 and 2020 has been already reported by GLOBOCAN 2020 statistics report. In 2020, 19.3 million new cancer cases and 10 million deaths were reported (Sung, et al., 2021). In addition, the GLOBOCAN 2020 report indicated that breast cancer was the most common cancer (2.3 million cases) and its incidence exceeded lung cancer, followed by colorectal, prostate and stomach cancer. However, lung cancer remains the primary cancer related death (1.8 million death) followed by colorectal, liver, stomach, and breast cancers (Sung, et al., 2021).

Data indicate that cancer incidence and the types of common cancers reported in HICs differ from those reported in LICs. In HICs, lung and colon cancer are the most common cancers reported. However, in LMICs stomach cancer is the most common cancer, followed by liver, esophageal, and cervical cancer ((Torre, Siegel, Ward, & Jemal, 2016)). Furthermore, the increase of cancer incidence in LMICs was higher compared to HICs, and this difference was approximately 2-3-fold (Sung, et al., 2021). Factors that might have contributed to this increase are discussed in the cancer risk factor section 1.1.5. A study also indicated that by 2030 cancer burdens in LMICs will rise by 60% (Duncan, Cira, Barango, & Trimble, 2019).

Prognosis and the stage of cancer at diagnosis determine the 5-years survival rate of the cancer patient. Stages of cancers are defined by multiple staging criteria, such as those defined by the American Cancer Society (ACS) (Mattiuzzi & Lippi, 2019). The type of cancer is also another element that determine the 5-years survival rate. For example, Hodgkin's lymphoma has good survival rate, even if diagnosed in a late stage. On the other hand, pancreatic cancer has a low survival rate, even if early diagnosed (Ilic & Ilic, 2016). The worst overall prognosis was observed in esophagus, liver, and pancreas cancers. In contrast, thyroid and prostate cancer have the best

prognosis with a nearly 100% 5-year survival rate (American Cancer Society, Survival Rates for Prostate Cancer, 2021) (Torre, Siegel, Ward, & Jemal, 2016). This is cancer survival not an overall survival, as older patients may die from other causes. Notably, the prognosis of prostate cancer differs in the UK compared to the U.S, as prostate cancer is the second most common cause of cancer death in the UK. Generally, prevention approaches, early detection and screening, and access to effective therapies could improve the overall survival rate of many cancers (Torre, Siegel, Ward, & Jemal, 2016). For example, early detection by routine mammogram screening for breast cancer and PSA screening for prostate cancer has a great impact on improving clinical outcome for both cancer indications. To achieve further improvement, global collaborations, and effective strategies to advance cancer medical care are still needed (Mattiuzzi & Lippi, 2019).

1.1.5 Cancer risk factors

For decades, epidemiology studies have been investigating factors that might be associated with cancer. Some of these studies highlighted that developing cancer is associated with various risk factors, such as environmental exposure to carcinogens or toxins, smoking, obesity, family medical history, diet, and lifestyle (Willett, 2002). It has been also reported that risk factors differ from region to region based on socioeconomic status and the presence of specific viruses and diseases. Some risk factors are linked to a broad number of cancer types, while other risk factors are linked to a specific type of cancers. For example, smoking and poor diet are linked to several cancers. Similarly, higher cancer incidence is reported in areas with high consumption of animal fats and lack of physical exercise compared to areas with high consumption of fresh fruit and vegetables (van't Veer, Jansen, Klerk, & Kok, 2000). Examples of how specific risk factors could be linked to a specific type of cancer are presented in this paragraph. Breast cancer is associated

with changes of reproductive patterns, hormonal therapies, long use of oral contraceptives and excessive alcohol consumption (de Menezes, Bergmann, & Thuler, 2013). Liver cancer is significantly linked to infection of hepatitis B virus (HBV) or hepatitis C virus (HCV) especially hepatocellular carcinoma (HCC), which represents approximately 90% of liver cancer (Llovet, et al., 2016). The high prevalence of HBV and HCV in LICs contributes to the high incidence of liver cancer in these regions. Esophageal cancer cases are significantly high in an area defined as "esophageal cancer belt," which extends from northern Iran through the Central Asian republics to north-central China. Studies suggest that the increase of incidence in this region could be due to high consumption of hot food and drinks as well as poor diet (Mosavi-Jarrahi & Mohagheghi, 2006). Squamous cell carcinoma (SCC), which is the most common type of esophageal cancer, is linked to lack of nutrition, and intake of high temperatures food and drinks (Abnet, Arnold, & Wei, 2018). Published data revealed that gastric cancer cases are high in U.S. and Europe due to obesity (Sung, Siegel, Rosenberg, & Jemal, 2019). Melanoma and other skin cancers are highly correlated with sun exposure that causes DNA damage to the skin (Raimondi, Suppa, & Gandini, 2020). Risk factors that are associated with adult cancer are different from those associated with pediatric cancer (Stanford Children's Health, 2021). Pediatric cancer risk factors will be discussed in section (1.3.1.21.3.1.2)

1.2 Overview of pediatric Cancer

In the past decades, childhood cancer rate has significantly increased and has become the leading cause of mortality amongst children (National Cancer Institute, 2021). A drastic increase was observed between 2001 and 2014 and was primarily associated with environmental exposures, such as hazardous substances in the water (radioactive materials uranium and radium), soil, and

food (Cancer Treatment Center of Ameria, 2020) (Osterweil, 2018). With more than 200,000 children diagnosed with cancer every year, pediatric cancer is a global challenge and should be addressed as a global health priority (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017). Despite the reported increase of its incidence, pediatric cancer is a relatively rare disease compared to other childhood diseases and to adult cancer.

1.2.1 Difference between Adult and pediatric cancer

Pediatric cancer age is defined in the U.S by The American Academy of Pediatrics as (0-21), in the UK as (0-18), and most cancer registries report pediatric data for age (0-14). The average age at pediatric cancer diagnosis is 5 years for the group of children age (0 to 14), while the average age for cancer diagnosis in adults is 65.

Studies have shown that pediatric cancer differs biologically from adult cancer, and it is therefore considered as a different disease (Kattner, et al., 2019). One of the main characteristics that distinguishes pediatric cancer tumors is that they contain much fewer genetic alterations compared to adult tumors (Gröbner, et al., 2018). Furthermore, the genes and mutations that drive pediatric cancer are different from those that drive the development and progression of adult cancer (Children's Hospital of Philadelphia, 2018). The distribution of mutations and the role of microenvironment are dissimilar as well. Additional differences between adult versus pediatric types of tumors were observed in disease development, progression, and response to treatment. Pediatric oncologists demonstrate that it is a misperception to assume that pediatric cancer patients are “small” adult cancer patients (Fred Hutchinson Cancer Research Center, 2021). Therefore, adjusting the adult treatment dose to pediatric by accounting for different weight, metabolism and other covariates does not necessarily translate to similar efficacy and response to treatment

observed in adults. Hence, challenges in drug development for adult cancer are unlike those in pediatric cancer. Since cancer therapies are primarily developed for adults, developing therapies for childhood cancer is an urgent unmet medical need.

1.2.2 Advancement in pediatric cancer therapies

In the past two decades, the evolution of precision medicine has had a significant impact on improving the cancer treatment success rate and decreasing toxicity of therapeutic agents (Forrest, Geoerger, & Janeway, 2018). Matching the right patient to the right treatment, based on tumor genetic profiling, has increased patient benefits in clinical trials (Hadjadj, Deshmukh, & Jabado, 2020). Implementing precision medicine in pediatric oncology clinical trials has been recently initiated, and data from these trials have shown the positive impact of utilizing genetic alteration data in patient selection decision (Forrest, Geoerger, & Janeway, 2018). Examples of these initiatives are the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) initiative in the U.S., and Individualized Therapy for Relapsed Malignancies in Childhood (INFORM) in Europe (Hadjadj, Deshmukh, & Jabado, 2020). Furthermore, the development of novel technologies and platforms that support the concept of identifying specific tumor's genetic signatures, such as Next Generation Sequencing (NGS), led to creating valuable data libraries, which contain large amounts of sequencing data that allowed identifying mutations. These data have enabled identification of predictive biomarkers that, when implemented in clinical trials, substantially improved cancer cure and survival rate (Goswami, 2016). As a result of these improvements, it was recently reported that the 10-year survival rate of pediatric leukemia patients increased from 27 to 81% in a period of thirty years (Westhoff, et al., 2018).

The advancement of immunotherapy has changed the treatment landscape of oncology and improved the general clinical response. Immunotherapy approaches aim to enable the immune system to recognize cancer cells and kill them. Data indicated that some types of cancer that are resistant to other therapies have a higher response rate to immunotherapy drugs (Sanmamed & Chen, 2018). Generally, immunotherapy drugs are more tolerated with fewer side effects compared to other drug classes, such as chemotherapy (Riley, June, Langer, & Mitchell, 2019). Recently, several immunotherapies drug classes were approved for pediatric cancer, including antibodies, checkpoint inhibitors (CPI), and Chimeric Antigen Receptor (CAR)-T cell therapy (Hutzen, et al., 2019). Applying immunotherapy methods in pediatric cancer has shown a great potential in increasing efficiency without the side effects of chemotherapy (Hutzen, et al., 2019).

1.2.3 Gaps in pediatric cancer research

Despite the recent advancement in pediatric oncology landscape, there are still numerous gaps and areas of improvement that need to be addressed. For example, the number of approved drugs for pediatric cancer is significantly lower compared to adult cancer. Between 1980-2017, only 11 drugs were approved by the FDA for pediatric cancer (Barone, Casey, McKee, & Reaman, 2019). On the other hand, the FDA approved 20 cancer drugs for adult patients just in 2020 (Bean, 2020). Several potential factors might have contributed to the limited number of approved drugs for pediatric cancers. For example, pediatric cancers harbor smaller number of mutations compared to adult cancer, which could lead to the limited targeted therapies identified (Kattner, et al., 2019). Also, pediatric cancer is rare compared to adult cancer. Therefore, a limited number of patients are receiving therapy, a small market and insignificant financial incentives are accessible for pharmaceutical companies (Angelini, Pritchard-Jones, & Hargrave, 2013).

Developing more effective and less toxic therapies for childhood cancer has been a challenge. Long term side effects of most cancer therapies are hurdles given that pediatric patients live longer. One of the main reported side effects appearing in later stage of pediatric patients is secondary malignancies, also called secondary malignant neoplasms (SMN), which is due to chemotherapy and DNA damage from radiation treatment (Choi, Helenowski, & Hijiya, 2014). Another gap in the pediatric oncology field is the low number of clinical trials compared to trials for adult cancer (Chiaruttini, Felisi, & Bonifazi, 2018). This gap might be due to the limited number of pediatric patients available to be enrolled in clinical trials needed to generate meaningful data that would lead to drug approval (Downs-Canner & Shaw, 2009). Increasing the number of pediatric cancer clinical trials would require international and global cooperation to recruit sufficient numbers of patients with these relatively rare cancers.

1.3 Status of pediatric cancer in HICs vs LICs

Although the recent advances in pediatric oncology treatment have led to higher survival and cure rates globally, only HICs have experienced this improved benefit. Data revealed that 80% of children with cancer treated in HICs are cured, whereas children in LMICs display lower cure rates due to factors including limited access to sufficient medical care, late-stage disease at time of diagnosis and misdiagnosis (Ribeiro, Antillon, Pedrosa, & Pui, 2016). In the past decade, an increased global effort has been directed towards improving pediatric oncology condition in LICs. Although LICs have made tremendous progresses in treating common pediatric diseases, such as malaria, pneumonia and gastroenteritis, mortality rates for most pediatric cancers are still close to 100% (Haileamlak, 2016). Roughly, 94% of pediatric cancer related deaths worldwide occur in LMICs (Pritchard-Jones, et al., 2013). Recently, the WHO and St. Jude Children's Hospital

initiated a partnership to fill the gap between differences in cure and survival rates between HICs and LICs. However, to achieve this goal, significant efforts to improve data reporting and effective strategies to access affordable therapeutics need to be defined (St. Jude Children's Research Hospital).

1.3.1 Epidemiology of pediatric cancer

1.3.1.1 Types of pediatric cancer

Pediatric cancers include leukemia, brain and spinal cord tumors, neuroblastoma, Wilms tumor (WT), lymphoma (Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma, and bone cancer (osteosarcoma and Ewing sarcoma) (American Cancer Society , Types of Cancer that Develop in Children, 2019). Moreover, the most common type of childhood cancer globally is leukemia, followed by central nervous system (CNS) cancer and lymphomas (Steliarova-Foucher, et al., 2017).

1.3.1.2 Risk factors and geographical distribution of pediatric cancer in HICs vs LICs

The prevalence of pediatric cancer across regions differs due to various environmental and social factors, including pollutions, chemicals and toxins exposure, low socioeconomic status, lifestyle, the presence of specific disease or viruses, and nutritional deficiencies (Sherief, et al., 2015). For example, in sub-Saharan regions of Africa, there is an increased risk to develop certain types of pediatric cancers, such as Burkitt lymphoma, where Epstein-Barr virus and malaria are common (American Childhood Cancer Organization, 2021). Similarly, in countries with high incidence of HIV virus, such as Zimbabwe and Uganda, Kaposi sarcoma cases are higher (American Childhood Cancer Organization, 2021) (Table 1.1).

Table 1.1 Examples of association between pediatric cancer types and known factors in African countries

African countries	Most common types of childhood cancer	Known association factors
Zimbabwe	Kaposi sarcoma, Wilms tumor, non-Hodgkin lymphoma, retinoblastoma, and acute lymphocytic leukemia	Kaposi sarcoma and HIV (El-Mallawany, McAtee, Campbell, & Kazembe, 2018)
Uganda	Burkitt lymphoma, Kaposi sarcoma, WT, and retinoblastoma	Burkitt lymphoma and Epstein-Barr virus and malaria Kaposi sarcoma and HIV virous (Joko-Fru, et al., 2018)
Kenya	ALL, retinoblastoma, WT, Burkitt lymphoma, and Hodgkin lymphoma	Burkitt lymphoma and Epstein-Barr virus and malaria (El-Mallawany, McAtee, Campbell, & Kazembe, 2018)

Common types of pediatric cancer in HICs vary from those in LICs. A published report by WHO displays this difference of cancer distributions. Even though leukemia is the most common type of pediatric cancer in the world, it is a very rare form of cancer in sub-Saharan Africa (World Health Organization, 2021). However, there is a possibility that the prevalence of Leukemia in Africa is low due to misdiagnosis, as symptoms of leukemia are vague (Chen & Mullen, 2017). Other common types of cancer in HICs are brain and CNS, lymphomas, and neuroblastoma (Magrath, et al., 2013). The most common types of pediatric cancer in Africa are lymphomas, nephroblastoma, Kaposi sarcoma and retinoblastoma (Stefan D. C., 2015) (Table 1.2).

Table 1.2 Distribution of the most common types of pediatric cancer

The most common types of pediatric cancer		
HICs	LMICs	Africa
Leukemia	Retinoblastoma	Lymphoma
Brain and CNS	Neuroblastoma	Nephroblastoma
Lymphomas	Wilms' tumor	Kaposi sarcoma
Neuroblastoma	Burkitt's lymphoma	Retinoblastoma

Race and ethnicity could also increase the risk of developing specific forms of cancer and impact response to cancer therapies and overall survival rates (Kahn, et al., 2019) (Figure 1.3). For example, a study reported that white, non-Hispanic children have a higher chance to develop pediatric cancer compared to black, non-Hispanic or Hispanic children (NY Department of Health). Data from the same study also illustrated that the incidence rate of pediatric lymphoma and CNS in white, non-Hispanic children is higher compared to black, non-Hispanic and Hispanic children. Data suggested that variations of occurrence of single nucleotide polymorphisms (SNPs) amongst different racial groups could contribute to this disparity (Moore, Hubbard, Williams, & Spector, 2020). Furthermore, a study on 67,000 pediatric patients investigating the impact of race and ethnicity on mortality showed that Hispanic and black children have a higher risk to die of cancer compared to white, non-Hispanic children (Delavar , Barnes, Wang, & Johnson, 2020). This difference could be due to the limited access to diagnostic tests, treatments, and medical care as well as poverty, socioeconomic status, and genetic components (Blakemore, 2018).

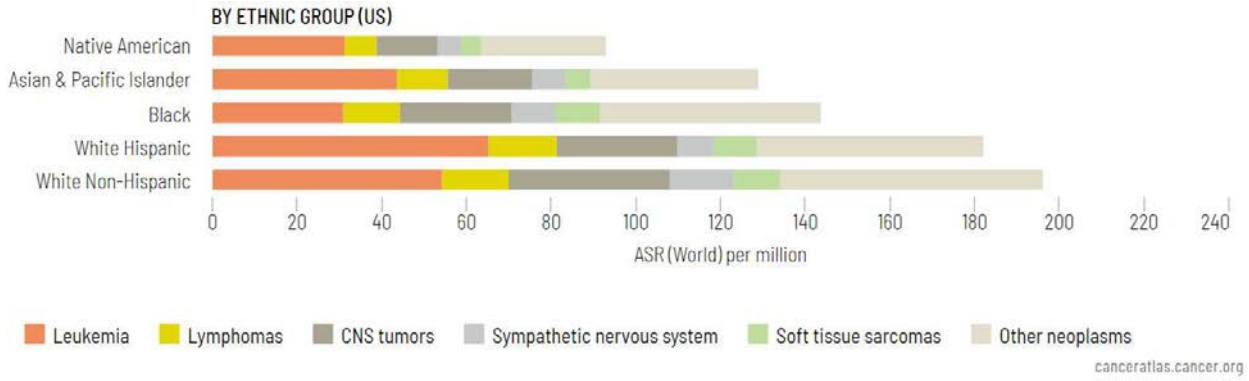


Figure 1.3 Age-standardized cancer incidence rate by ethnic group per cancer type 2001-2010 (Taken from The Cancer Atlas, (The Cancer Atlas, 2021))

The role of nutrition deficiency has been implicated to impact cancer prevention and linked to poorer treatment response (Ladas, 2019). Lack of a proper diet affects metabolism, weakens the immune system of the cancer patient, and increases the risk of developing infection (Kim, 2019). Lange et al. reported a statistically significant association of poor survival in pediatric acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) with underweight and overweight (Lange, et al., 2005). Recently, the World Cancer Research has re-iterated the significance of lifestyle during and after cancer care, summarizing decades of supportive scientific evidence (Ladas, 2019).

1.3.1.3 Global incidence and mortality of pediatric cancer in HICs vs LICs

Incidence of pediatric cancer varies across regions and is determined by various factors (Figure 1.4). Data demonstrated that pediatric cancer incidence and mortality rates in some LICs are much higher compared to HICs (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017). In 2017, a study reported that incidence rate was 4.6% in Sub Saharan Africa and 0.5% in HICs (Parkin & Stefan, 2017). Additionally, four out of five new pediatric cancer cases were reported to occur in

LICs (Joko-Fru, et al., 2018). Published data showed that 8% of total pediatric cancer patients live in HICs, and 21% are located in LICs (US Chilhood Cancer Statistics, 2021). It is important to note that the average age in HICs versus LMICS is significantly higher, which implies that a significant proportion of the population in LMICs are under the age of 15. For example, the median age in the U.S is 38 and in Malawi is 18 years. The average age combined with incidence rate reported could suggest that there are more children with cancer in LMICs than HICs (Sudharsanan & Bloom, 2018). In Africa, cancer incidence is much higher compared to the U.S. and European countries (Pritchard-Jones, et al., 2013). However, it is very challenging to estimate the accurate incidence and survival rates in most low-income regions, like sub-Saharan Africa, due to limited population-based data (Joko-Fru, et al., 2018).

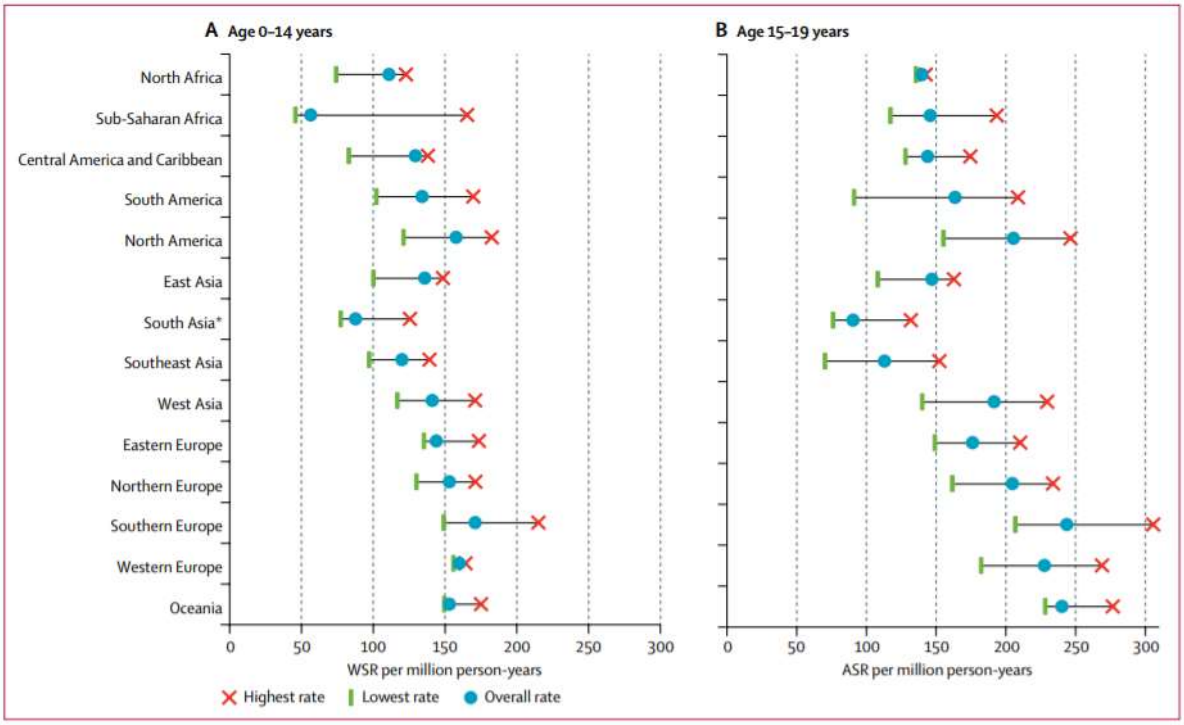


Figure 1.4 Incidence rate of pediatric cancer by region
(Taken from (Steliarova-Foucher, et al., 2017))

The difference in survival and cure rate between HICs and LICs is also significant. For example, data from the American Childhood Cancer Organization indicated that the 5-year survival rate in HICs is 79.8%, whilst in LICs is 7.4% (US Chilhood Cancer Statistics, 2021). The survival rate in Cote d'Ivoire was reported to be as low as 5% (Hadley, Rouma, & Saad-Eldin, 2012). In Europe, the 5-year survival rate for Acute Lymphocytic Leukemia (ALL) is approximately 86%, (Bonaventure, et al., 2017), and the 5-year survival in LICs such as Pakistan is 52.9% (Jabeen, Ashraf, Iftikhar, & Belgaumi, 2016). In Denmark, the 5-year survival rate of all pediatric cancer combined is 86% (Schrøder, et al., 2016). It is important to note that in LICs regions, 55% of pediatric cancer patients die before they receive a diagnosis. This percentage is much lower in HICs and reported to be 6% (US Chilhood Cancer Statistics, 2021). Finally, the cure rate in HICs is 80% versus 20% in LICs (World Health Organization, 2021). To contextualize the difference of pediatric cancer status in HICs versus LICs, Figure 1.5 illustrates the percentage of pediatric cancer patients that live in both regions, incidence rates, percentage of children die before diagnosis, 5-year survival rate, and cure rate.

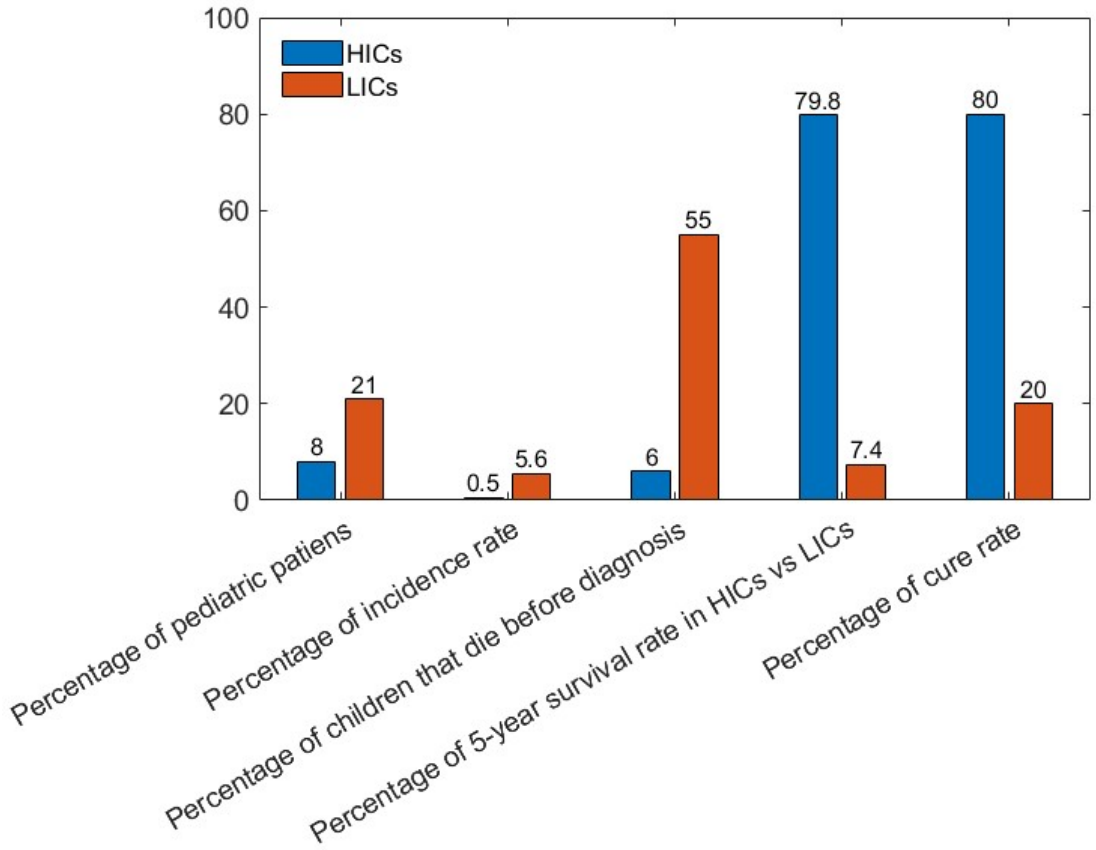


Figure 1.5 The difference of pediatric cancer status in HICs versus LICs

1.4 Challenges throughout the pediatric cancer patients' journey in LICs

The challenges during the pediatric cancer patients' journey, starting with having initial symptoms through receiving treatment, represents a significant burden on the children and their families. In LICs, these challenges include, lengthy processes to get the right diagnosis, delay in receiving treatment, logistics to reach hospitals emotional distress and financial burden (Basbous, et al., 2021). When parents are notified of the tragic diagnosis of their child, the emotional conflict and struggle are overwhelming and cause major changes in the family's dynamics (Attia, 2016). These challenges will be discussed in detail in the following sections.

1.4.1.1 Diagnosis

Receiving the right diagnosis in a timely manner is critical for pediatric cancer patients. When children start developing symptoms, parents face confusion and frustration for not knowing the cause behind these symptoms. Numerous tests need to be performed, and several doctor's visits have to be scheduled. One of the main difficulties is the waiting time to see a doctor and receive a diagnosis. Studies have demonstrated that in Sub-Saharan Africa, a patient could wait up to 6 months until seeing an oncologist and up to additional 3 months to receive a diagnosis (Price, Ndom, Atenguena, Mambou Nouemssi, & Ryder, 2012). This delay is usually due to the limited capacity and resources of healthcare systems across LICs, which are not sufficient to accommodate the number of cancer cases of adult and pediatric patients. For example, Cameroon has only one cancer hospital (Yaounde General Hospital) serving a population of 18.8 million. Therefore, there is a substantial delay before physicians can provide medical support to the patients (Price, Ndom, Atenguena, Mambou Nouemssi, & Ryder, 2012). Another factor that could delay cancer diagnosis is the social prejudices associated with a cancer diagnosis in specific cultures or tribes and the mistrust of "western" medicine. In these circumstances, families will rather choose to go to spiritual healers instead of receiving medical treatment in hospitals (Maillie, Masalu, Mafwimbo, Maxmilian, & Schroeder, 2020). Since WHO reports that cancer prevention, early detection and early diagnosis are the main pillars to improve caner medical care (Attia, 2016), the impact of the delayed diagnosis could significantly worsen the clinical outcome and decrease the survival rate.

1.4.1.2 Treatment

Discussing treatment options that are available and affordable for families in LICs countries poses another challenging task that negatively adds confusion and uncertainties. Studies have

shown that, in addition to delayed diagnosis, patients also experience additional delay in receiving treatment due to limited medical resources. This delay impacts clinical outcome and lead to progression of disease and increased mortality rate (Hanna, et al., 2020). Many children that die of cancer could be easily treated if they were diagnosed early and provided with the proper cancer therapy. Price et al. reported that approximately 500,000 cancer patients died in sub-Saharan Africa, and the mortality could have been much lower if patients were diagnosed and treated earlier (Price, Ndom, Atenguena, Mambou Nouemssi, & Ryder, 2012). On the other hand, in HICs, such as Denmark, the estimated median time between pediatric cancer patient diagnosis and starting treatment is 7 days (Schrøder, et al., 2016). Another challenge is the limited access to effective and tolerable therapies that are readily available in HICs. Generally, therapeutic options are associated with significant physical pain and side effects, which contribute to increase an already substantial burden for pediatric cancer patients and their families. In HICs, patients have access to better pain management and supportive care, which is limited in LMICs (Morriss & Roques, 2018). In an effort to minimize the delay in providing treatment to pediatric patients, cancer centers in LICs often try to get access and optimize medical protocols that are used and developed in HICs (Haileamlak, 2016). However, implementation of these protocols is challenging without access to drugs and supportive care (Hewamana, et al., 2021). Moreover, applying protocols will be ineffective without adequate training of nurses, clinicians, pathologists, radiologists, and surgeons. To mitigate this gap, cancer centers in LICs are initiating "twinning programs" with advanced HICs centers not only to access treatment protocols but to also obtain the necessary training for their medical staff (Hopkins, Burns, & Eden, 2013).

1.4.1.3 Geographical distance and transportation

Logistics to access hospitals and cancer centers also represent a substantial burden for families and children in LICs. The limited number of hospitals and cancer centers covering large populations in under-developed countries creates a significant geographic challenge that requires patients to travel for hours to reach the hospital. Traveling time could be more than 7 hours (Price, Ndom, Atenguena, Mambou Nouemssi, & Ryder, 2012). The limited resources of cancer centers in rural areas could force patients to travel to bigger cities to seek for better cancer care. Limited medical training of health care professionals within remote areas might also require families to reach out to more advanced medical facilities (Cancedda, et al., 2015). Spending hours in transportation while receiving chemotherapy or radiation therapy could be extremely difficult for children and their families. It is quite common that in LICs patient's family would have to arrange accommodation near the hospital and travel long distances back home the next day, which is socially inconvenient and financially challenging.

1.4.1.4 Social and emotional factors

Emotional distress is another massive challenge in the journey of pediatric cancer patients. A study conducted by (Edwards & Greeff, 2017) on South African children highlighted that 92% of the pediatric patients suffered from emotional challenges with shock, fear, anxiety, depression, and post-traumatic distress frequently reaching clinical levels. Many children were also reported to miss school and experience intense stress due to separation from their families if admitted into hospitals (Edwards & Greeff, 2017). Furthermore, having larger families and caring for multiple children while one of them is battling cancer creates additional burden and instability.

1.4.1.5 Financial burden

While the financial consequences of pediatric cancer are devastating across all countries, the challenges faced by families in LICs are even more problematic. Financial burden is not only limited to the cost of treatment but expands to all aspects of the patient journey. Examples include unplanned hospitalization, transportations to hospitals and cancer centers, accommodations if hospitals are located in other cities. Hospitalization has been very common for pediatric cancer patients (Attia, 2016), with costs that could reach thousands of dollars, especially if the child needs a procedure or treatment for infection (Warner, Kirchhoff, Nam, & Fluchel, 2015). Studies have demonstrated that the cost of hospitalization for pediatric cancer is significantly higher compared to any other pediatric illnesses. The type of cancer could also impact the cost of treatment and hospitalization. Published data highlighted that the highest hospitalization cost is for leukemia ($55,700) followed by non-Hodgkin lymphoma ($46,900). Additionally, the consequence of frequent, unexpected hospitalization might force parents to change or quit their jobs, which leads to unemployment (Warner, Kirchhoff, Nam, & Fluchel, 2015). Although cancer patients in most LMICs could get access to funded treatment and hospitalization, they are forced to seek treatment in private facilities because public hospitals are often at full (Turner, et al., 2019).

1.5 Pediatric cancer data reporting

Pediatric cancer data reported in the public domain is limited compared to adult cancer data, which might contribute to the fact that the general knowledge about pediatric cancer is significantly less compared to adult cancer (Ishihara, Ohno, Fujii, Hara, & Soda, 2017). Recently, several efforts have been initiated to improve pediatric cancer data generation, collection, reporting, and access. However, these initiatives focus only on data in HICs. Therefore, including data from LICs would

improve pediatric cancer data access and reporting globally. Examples of these initiatives are discussed in section (1.5.2).

1.5.1 Significance of accessing accurate pediatric cancer data

The ability to develop accurate, high-quality databases that can be readily accessed and analyzed will accelerate the improvement of pediatric cancer medical care. Accessing data for clinical decision-making led to the development of the concept of "Big data". The need for creating large databases was not limited to determining cancer incidence and mortality. Rather, the entire scientific community needed access to clinical and molecular datasets to have a better understanding of the biology of the disease, answer questions and develop scientific hypotheses. High-quality, publicly available cancer databases containing information about drug efficacy, toxicity and adverse events associated with treatment would have a great impact on improving regimens, drug safety (Mandawat, Eberly, & Border, 2019) and design of clinical trials to assess the effect of novel therapeutic modalities (McFatrich, et al., 2020).

1.5.2 Large scale pediatric cancer datasets examples and initiatives

There are several examples of global initiatives and collaborations that improved pediatric cancer data availability and access.

1.5.2.1 St. Jude cloud-based platform

St. Jude Children's Research Hospital was opened in 1962 with the aim to improve cure of pediatric cancer patients (St. Jude Children's Research Hospital). The hospital has recently launched a cloud-based platform, in collaboration with DNAnexus and Microsoft, to collect large genomic data that were made available to researchers. The platform currently contains information

from 5000 pediatric cancer patients and will be expanded to include information from an additional 10000 patients. The cloud provides access to tools for data analysis and visualization to enable researchers to utilize data from the pediatric cancer genomic project and clinical genomics (St. Jude Cloud, 2021).

1.5.2.2 Childhood Cancer Survivor Study (CCSS)

A registry-based study called Childhood Cancer Survivor Study (CCSS) was successfully conducted to collect survival status of over 30,000 pediatric cancer patients in the U.S. and Canada (Leisenring, et al., 2009). The study was initiated in 1994 and funded by the NCI. The data from this study focused on long term follow-up of pediatric patients who survived 5 years or more. St. Jude Children's Research Hospital is facilitating this collaboration, which includes approximately 31 hospitals and cancer centers from the U.S. and Canada (St. Jude Children's Research Hospital, 2021). The impact of the data from this study has been critical to understanding the risk factors and long-term side effect of cancer treatment on pediatric patients.

1.5.2.3 Childhood Cancer Data Initiative (CCDI)

The NCI has recently initiated the Childhood Cancer Data Initiative (CCDI) project to collect and analyze large-scale pediatric cancer data in the U.S. (Mandawat, Eberly, & Border, 2019). The goal of this initiative is to provide researchers and oncologists with access to these datasets and develop tools for data analysis. Data will be obtained from patients located anywhere in the U.S. Preclinical, clinical, and public health research data will be included in those datasets. Data will enable oncologist to better diagnose, characterize the disease and determine the optimal therapies, which will ultimately improve pediatric cancer care (National Cancer Institute, Childhood Cancer Data Initiative, 2021).

1.5.3 Gaps in pediatric cancer data

Despite these recent initiatives, availability of high-quality, accessible pediatric cancer datasets remains limited, especially in LICs. Several efforts utilizing modeling and simulations methods have been recently undertaken to predict global childhood cancer incidence more accurately (Ward, Yeh, Bhakta, Frazier, & Atun, 2019). While these model-based meta-analyses are useful to fill gaps of data underreporting, they are not accurate in predicting cancer incidence and mortality in countries without cancer registries.

1.6 Data underreporting in LICs

1.6.1 Impact of data underreporting

Data underreporting of incidence, mortality, and survival rate of childhood cancer in LICs have so far limited the global community from understanding the magnitude of childhood cancer in LICs and the true burden of the disease. Data underreporting has created a massive challenge and has played a significant role in delaying the improvement of pediatric cancer medical care (Paapsi, et al., 2017). Providing accurate data of pediatric cancer incidence, survival and mortality rates is essential to facilitate the development and implementation of effective strategies for detection, screening, and treatment to improve survival rate. Additionally, accurate reporting would enable allocating sufficient funds to improve medical care and support the development of registries with improved data quality control (Gupta, Rivera-Luna, Ribeiro, & Howard, 2014).

1.6.2 Factors that might contribute to data underreporting in LICs

Social and economic factors could contribute to data underreporting in LICs. One of these factors is the lack of awareness about cancer symptoms, which results in death of children before

their cases are even reported to hospitals (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017). In countries with limited access to affordable diagnostics and appropriate screening tests, children are often misdiagnosed (for example, lymphoma misdiagnosed as tuberculosis) (Hannan, 2016). Moreover, many patients from rural and remote locations struggle to cover the traveling costs to hospitals and cancer centers in larger cities. As a result, they miss the necessary follow-up after treatment, and their records are not updated. Additionally, in some LICs, medical files and reports are not available in hospitals and providers because patients are allowed to take them home. Finally, clinicians are not required by law to report new cancer cases to registries (Tangka, et al., 2016).

1.7 Cancer Registries

1.7.1 The role of cancer registries

Cancer registries have a critical role in reporting cancer data, such as incidence and mortality rates, to enable defining the true scale of the disease and implement strategic control plans (Parkin, The role of cancer registries in cancer control, 2008). The role of registries has been evolving throughout the years from a basic role of only collecting number of cancer cases to providing data about tumor histology, stage of disease and treatment. This data has had a great impact on health policies and strategies to improve cancer medical care. Cancer registries have also become a vital source in epidemiological research by providing patients' demographic data and cancer patterns (Parkin, The evolution of the population-based cancer registry, 2006)

1.7.2 The different types of cancer registries

There are two main types of cancer registries: population-based (PBCR) and hospital-based cancer registries (HBCR) (IARC Publications). Hospital-based cancer registries collect data on patients from a given hospital or institute, whilst population-based cancer registries collect data on

a population scale, such as a city or a state. Population-based registries provide information about cancer patterns and changes over a period of time. Moreover, they contribute to the overall cancer control plan in a country (National Cancer Institute, Hospital-Based Registries).

1.7.3 Lack of resources across cancer registries in LICs

Limited resources in cancer registries in LICs create a great challenge and plays a major role in data underreporting. The limited number of employees involved in data management, collection, and quality control negatively impact data reporting (Tangka, et al., 2016). There are very limited data to quantify the resources needed to operate a cancer registry. It is critical to understand the real cost of running cancer registries to allow the appropriate allocation of funds, administrative personnel, researchers, data managers, computers, and quality control tools required for cancer registry operation (Tangka, et al., 2016). Despite the limited resources in African countries, there is improvement in data reporting and the quality of cancer registries (Omonisi, Liu, & Parkin, 2020). There is an increased number of cancer registries in Africa, as well as increase cancer control plans that encourage data reporting. However, additional population-based registries are needed. Countries with no cancer registries face the problem that most cancer centers and hospitals do not have electronic patient records and have only paper records, which makes data reporting to registries very difficult and inaccurate. Collaborations and partnerships are key components to establish, sustain, and improve cancer registries.

1.8 Objectives of the research

The introduction of the thesis highlighted several issues and gaps in the status of pediatric cancer in LICs that need to be resolved. A few of these issues were selected and prioritized to be addressed in this research. First, underreporting of pediatric cancer data in LICs is a critical issue

that has a significant impact on understanding the true status of the disease and the consequent allocation of sufficient resources. Second, sources of data used by global databases are likely inaccurate. Therefore, several metrics, including incidence and mortality rates, reported by global databases, are probably imprecise. Third, there are numerous potential factors that might contribute to data underreporting and inaccuracy, which need to be highlighted and prioritized. Finally, there are insufficient cancer registries in LICs.

To investigate the above issues and gaps, several objectives were outlined in this research. The main objectives are:

1. There were attempts to estimate the real number of childhood cancer cases and mortality observed in hospitals and cancer centers in selected LICs. However, accessing the data was not possible.
2. To determine whether pediatric cancer data collected from hospital and cancer center records were comparable with data reported in databases and registries.
3. To investigate whether there is a discrepancy between data reported by different publicly available databases and pinpoint the reasons leading to this discrepancy.
4. To identify potential factors that might contribute to underreporting of pediatric cancer data and explore approaches that could improve reporting of childhood cancer incidence and mortality in LICs.
5. To investigate how cancer registries in LICs collect, store, and report pediatric cancer data and identify challenges and gaps that they face.

1.9 Structure of the thesis

In chapter two, an assessment of global publicly available databases was performed to explore which databases reported pediatric cancer data and what type of data was included. Additionally, analysis of overlapping pediatric cancer data from different databases on selected LICs was presented and results were compared. This comparison was to investigate whether there was a discrepancy in data reported between databases. Furthermore, evaluation of pediatric cancer incidence reported from cancer registries and literature was assessed to explore the representation of data from LICs in global public domain.

In chapter three, data obtained from a questionnaire developed to collect pediatric cancer data from selected African local and national cancer registries was presented and analyzed to assess the extent of data underreporting. The questionnaire was designed to investigate whether African cancer registries collected pediatric cancer data and gathered information about the methods used to obtain the data. Data were analyzed to determine whether there is a discrepancy between cancer incidence reported by the registry versus what was reported by publicly available databases. Data analysis was performed to enable the identification of the main challenges that cancer registries face and identify factors that could contribute to data underreporting and data discrepancy in LICs.

In chapter four, a field trip that took place in Egypt in 2018 was presented. The aim of the trip was to collect data from pediatric cancer patient's records in hospitals and cancer centers directly to compare it to published data. This comparison was to investigate pediatric cancer data underreporting in LICs and determine whether a discrepancy might exist. In addition, six cancer centers were visited and interviewed to identify the main challenges they face and assess how data

is collected, stored, and reported. Finally, a future work plan was developed to improve data collection and reporting in four cancer centers.

In chapter five, a summary of key findings from the research was outlined. In addition, limitations of the data analysis and data availability were discussed. Finally, recommendations for future research and additional analysis were proposed.

2 CHAPTER 2: RAPID REVIEW AND ASSESSMENT OF PUBLICLY AVIALABLE PEDIATRIC CANCER DATA

2.1 Introduction

A rapid review and data assessment on publicly available pediatric cancer data in LICs are presented in this chapter. The aim of the analysis was to investigate whether there is a discrepancy of pediatric cancer incidence reported from global databases, literature, and cancer registries. In addition, a data assessment was conducted to explore potential trends of pediatric cancer incidence across data reported in the literature. Finally, an assessment of the distribution of cancer registries in LICs was performed to determine the impact of the presence or absence of cancer registries on pediatric cancer data reporting.

The flow diagram presented in Table 2.1 outlines the questions addressed in the assessment as well as the steps that were followed to collect the necessary data and conduct the analysis. The flow diagram also shows the data sources used and the type of analysis performed.

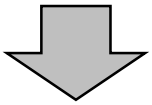
Table 2.1 A flow diagram outlines the steps and sources of data assessment and analysis conducted

Is there a discrepancy of pediatric cancer cases and incidence reported between databases?
A: Collected publicly available pediatric cancer data from different databases 1. Identified global databases that will be included in the analysis by Google search and searching websites of known academic cancer centers and cancer organizations. For example: Dana Farber Cancer Institute, St Jude Children's Research Hospital, Jimmy Fund, SIOP, National Cancer Institutes. 2. Databases that include only adult cancer data or have very limited pediatric cancer data were excluded since they would not allow for comparative analysis. Thus, a total of twelve databases were included in the analysis.

3. Identified the regions and countries that the databases cover to determine whether the databases are global, regional, or local.
4. Evaluated data reported in each database to define types of data reported, challenges, limitations, how to access the data, source of the data, references used, and if data is up to date.

B: Comparative Analysis

1. A comparative analysis of reported cancer incidence was performed to investigate whether there is a discrepancy among datasets reported
2. Assessment focused on African countries as a case study



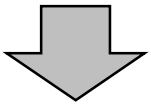
Evaluation of pediatric cancer incidence reported from literature

A: Data collection

1. Search for literature was performed in PubMed using the following keywords: pediatric cancer incidence, childhood cancer cases, pediatric cancer in LICs, pediatric cancer statistics, childhood cancer, and cancer registries.
2. Data was collected from several publications that reported population-based or simulation-based pediatric cancer incidence.
3. Evaluation of the types of data reported, years covered, and the methods used in the reported analyses was performed.
4. The content and data of the articles were assessed to determine the relevance to the aim of the analysis.
5. Investigated the data sources used in the articles and the references to assess data accuracy and explore possible duplication.

B: Comparative analysis and identification of potential incidence rate trends

1. A comparative analysis of the data was planned to determine if there was a discrepancy of pediatric cancer incidence reported among these articles.
2. Investigation of potential trends of pediatric cancer incidence for a given country/region was done.
3. Assessment focused on African countries as a case study.



Representation of cancer registries in reporting pediatric cancer data in LICs vs HICs

1. Assessment of the distribution of cancer registries in HICs compared to LICs was performed.

2. Identified which countries have population-based or national-based registries and which countries do not have any registry at all.
3. Assessment focused on African countries as a case study.

2.2 Is there a discrepancy of pediatric cancer cases and incidence reported on LICs between databases?

To investigate whether there is a discrepancy between pediatric cancer data reported by global databases, data were collected from different databases, and a comparative analysis was performed.

2.2.1 Evaluation of publicly available databases and resources

Publicly available pediatric cancer incidence and number of cases from global databases were collected to evaluate the accuracy and quality of these data. Some of the databases included in the analysis are: GLOBOCAN, WHO, International Incidence of Childhood Cancer (IICC), the International Agency for Research on Cancer (IARC), Surveillance, Epidemiology, and End Results (SEER), Global Cancer Observatory (GCO) and African Cancer Registry Network (AFCRN). A summary of databases and sources was created to illustrate the type of data, data format, how the data was collected, its limitations, and how to get access to the data (Table 2.2). Data collected from these databases largely varied and lacked overlap of key metrics to conduct a comprehensive comparison. Therefore, datasets collected were considered fragmented and incomplete. Furthermore, approximately 50% of the major global databases investigated reported the status of pediatric cancer in the U.S. and European regions but lacked meaningful representation of Africa.

Table 2.2 Pediatric cancer databases and data sources included in the analysis

Organization		Regions covered	Type of Data	General notes/source of data
WHO	World Health Organization	Global	• Statistics in pediatric cancer • Data visualization tools • Incidence, mortality, and survival • Cancer types in 185 countries • Prediction of future cancer rated worldwide • Cancer risk factors	• Date integrated with other databases in a data platform called The Global Cancer Observatory (GCO) which is an interactive web-based platform presenting global cancer statistics from several sources like: International Agency for Research on Cancer (IARC) Section of Cancer Surveillance (CSU), including GLOBOCAN; Cancer Incidence in Five Continents (CI5); International Incidence of Childhood Cancer (IICC); and Cancer Survival in Africa, Asia, the Caribbean and Central America (SurvCan).
GCO	Global Cancer Observatory	Global	• Platform that is linked to other databases • Incidence, mortality, and survival	• Using data of IARC's Section of Cancer Surveillance (CSU), including GLOBOCAN; cancer Incidence in five continents (CI5); International Incidence of Childhood Cancer (IICC); and Cancer Survival in Africa, Asia, the Caribbean and Central America (SurvCan)- Data of 15 countries are included www.survcan.iarc.fr/
CDC	Centers for Disease Control and Prevention	U.S.	• CDC cancer statistics in U.S. only • The global data only from other resources • Incidence, mortality, and survival	• Global data is from SEER, WHO, ACS, cancer Atlas and other organizations
NCI	National Cancer Institute	U.S.	• Cancer statistics in U.S only • Incidence, mortality, survival, prevalence, and statistics by race and ethnicity • Data by state	• Only global data is from SEER (Surveillance, Epidemiology, and End Results)

ACS	American Cancer Society	U.S	• Cancer statistics in the U.S • Incidence, mortality, survival	• No global data
ACCO	American Childhood Cancer Organization	U.S Global	• Statistics of pediatric cancer in U.S • Limited statistics of global pediatric cancer • Incidence and mortality • Disease type, age, ethnicity, and sex.	• Data sources are: National Cancer Institute's (NCI), SEER Program • U.S data collected from 10 sites (5 states and 5 cities) • Very limited international data • International data are from (IARC) 2016 press release
ACCIS	Automated Childhood Cancer Information System	E.U	• Data on cancer incidence and survival.	• Only data on European region • Data from 50 population-based cancer registries in 19 European countries
ECO	European Cancer Observatory- The EUREG database	E.U	• The ECO platform provides a comprehensive system of information on cancer burden in Europe • Cancer incidence, prevalence, mortality and survival	• ECO is a project developed at the IARC in partnership with the (ENCR) in the framework of the EUROCOURSE project supported by the European Commission. • Data from 40 European countries • Data is connected to EUCAN, EUREG and EUROCIM platforms
Cancer Research UK		E.U U.K Global	• Cancer incidence, mortality, survival, risk, and diagnosis • UK and worldwide	• The source of global data is the Global Cancer Observatory platform, IARC, and GLOBOCAN
GLOBOCAN		Global	• Estimates of the incidence, mortality and prevalence from major types of cancer, at national level, for 184 countries. • Online analysis tools	• Some data from IARC • Data from 185 countries
CAN/SA	Cancer South Africa Statistics	Africa Global	• Data on incidence and mortality • Global cancer statistics • South Africa Cancer Statistics	• Data sources are GLOBOCAN, WHO, IARC, CDC..etc • Most updated report of South Africa data in 2016
AFCRN	African Cancer Registry Network	Africa	• New cases of cancer diagnosed and mortality	• Must submit a request to access the database

			• Every cancer case file contains 14 variables on each case	• Data of the AFCRN database are from 22 African cancer registries

It is important to note that the amount of published pediatric cancer data related to African countries is very limited, likely due to the absence of data documentation into local registries. Moreover, published data are often not collected during the same period of time, which prevents an appropriate comparison. For example, datasets from several sources for Egypt, Malawi and Ghana lack time overlap (Table 2.3).

Table 2.3 Lack of time overlap in published data for Egypt, Malawi, and Ghana

Dataset	Egypt	Ghana	Malawi	Year
GLOBOCAN 2012 data set	✓	✓	✓	2012
Dataset from Cancer of childhood in sub-Saharan Africa paper	X	X	✓	2003-2010
IARC /WHO dataset International Incidence of Childhood Cancer (IICC3)	✓	X	X	1999-2010 Only Gharbia registry
CI5 IARC report	X	X	X	Up to 2007
African Cancer Registry Network (AFCRN)	X	✓	✓	Varies

2.2.2 Comparative analyses to determine whether there is a discrepancy

` and registries frequently publish incomplete data because small hospitals and minor cancer centers often do not report the data. Furthermore, comparison of the incidence and mortality rates reported across global databases revealed discrepancies, suggesting that the data sources were inaccurate (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017). For example, there was a ~20%

difference in total childhood cancer incidence in Africa reported by WHO versus incidence from GLOBOCAN database in 2012 (Table 2.4) (Ferlay, et al., 2015) (WHO, 2012).

Table 2.4 GLOBOCAN versus WHO Pediatric cancer data for Africa in 2012 Ages 0-14

Cancer	WHO Africa	GLOBOCAN Africa
All cancers excl. non-melanoma skin cancer	29341	36428
Bladder	182	210
Brain, nervous system	1220	2065
Colorectum	71	99
Gallbladder	2	2
Hodgkin lymphoma	1260	1652
Kaposi sarcoma	2081	2131
Kidney	2899	3577
Larynx	21	21
Leukemia	3123	4858
Lip, oral cavity	372	423
Liver	548	707
Lung	22	72
Melanoma of skin	66	73
Multiple myeloma	68	74
Nasopharynx	230	324
Non-Hodgkin lymphoma	6296	6994
Oesophagus	11	15
Other pharynx	50	55
Pancreas	1	1
Stomach	97	115
Thyroid	120	129

These data highlighted a discrepancy in the number of pediatric cancer cases reported in 18 out of 21 (82%) of cancer types reported. In addition, the greatest disparity was observed in leukemia followed by brain, nervous system, non-Hodgkin lymphoma, and Hodgkin lymphoma (Figure 2.1).

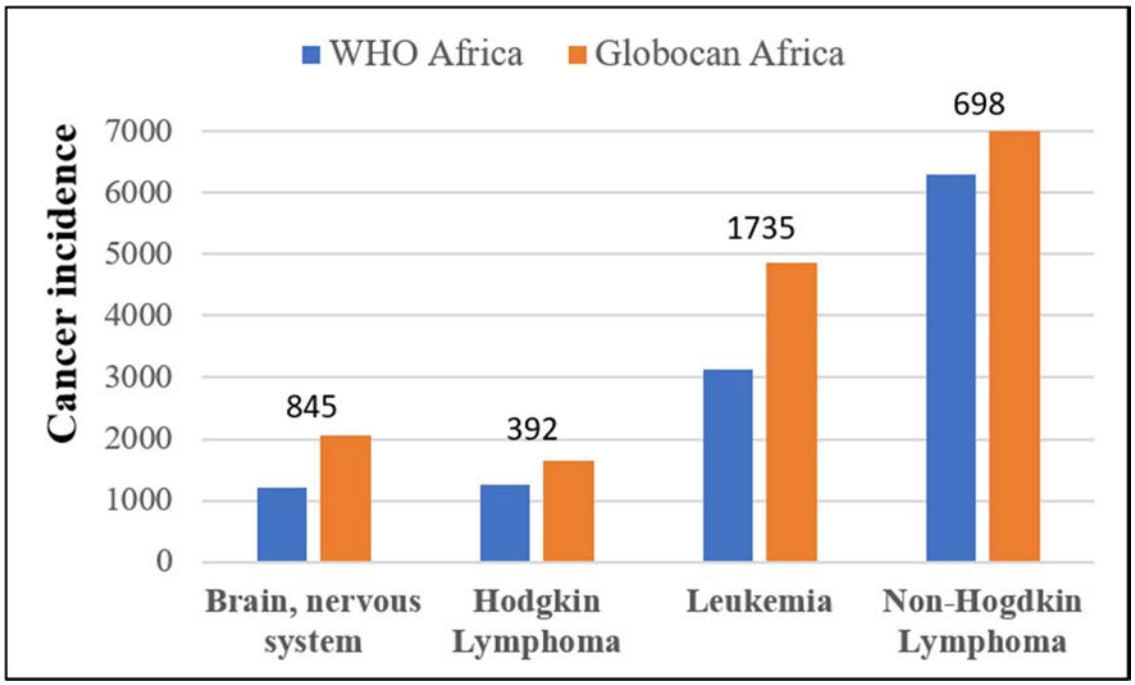


Figure 2.1 GLOBOCAN versus WHO data for pediatric cancer incidence ages 0-14 in Africa. Data for the year of 2012

Pediatric cancer incidence rate in Africa reported by GCO versus The Cancer Atlas also differ (Table 2.5). GCO reported an incidence rate of 9.0 per 100,000 populations in 2020 (Global Cancer Observatory, 2020), and The Cancer Atlas reported an incidence rate of approximately 17.0 per 100,000 in 2010 (The Cancer Atlas, 2021). Since the incidence rates were reported over different periods of time, and because incidence rate generally increases over time, the value of 17.0 reported by Cancer Atlas should be likely higher in 2020. Therefore, this observation suggests that there is a significant discrepancy in data reported among databases for Africa.

Table 2.5 Pediatric cancer incidence rate for Africa reported by GCO versus The Cancer Atlas

Source	Incidence rate in Africa
Global Cancer Observatory	9.0
The Cancer Atlas	17.0

Data from large global databases are frequently used by other small databases and referenced for publications, which contributes to further propagation of inaccurate data. For example, the Cancer South Africa Statistics reports data from GLOBOCAN and IARC databases. Furthermore, small hospitals and cancer centers in rural areas have limited resources to obtain accurate records or implement acceptable data quality measures. As a result, data from these sources is not reliable to be included in national databases or registries (Tangka, et al., 2016). Moreover, the absence of electronic records in numerous cancer centers in LICs, which only have paper patient's records, is a great obstacle to document or report data (Rossman, et al., 2021). On the other hand, pediatric cancer data reported by different databases for HICs is comparable with minimal variation. For example, the incidence rate reported for the U.S. by GCO is 17.2 per 100,000 populations (Global Cancer Observatory, 2020) versus 17.4 reported by The American Cancer Society (The American Cancer society, 2018) (Table 2.6). Similarly, the pediatric cancer incidence rates reported for the U.K by three different databases (GCO, European Cancer Observatory (ECO), and Cancer Research U.K) are 16.4, 16.6 and 16.7, respectively (Table 2.7) (Global Cancer Observatory, 2020) (European Cancer Observatory) (Cancer Research UK). This observation was also consistent with published studies that compared pediatric cancer incidence data from different databases and showed that the difference observed in U.S or EU regions was minimal (Johnston, et al., 2021).

Table 2.6 Pediatric cancer incidence rates for the U.S. reported by GCO and The American Cancer Society

Source	Incidence rate in U.S
Global Cancer Observatory	17.2
American Cancer Society	17.4

Table 2.7 Pediatric cancer incidence rates for the U.K reported by GCO, ECO and Cancer Research UK

Source	Incidence rate in U.K
Global Cancer Observatory	16.7
European Cancer Observatory	16.6
Cancer Research UK	16.4

Additional reliable tools that could improve data access and reporting are still needed. One of the major achievements was the development of the global interactive web-based platform, "The Global Cancer Observatory (GCO)". This platform reports global cancer statistics from various sources: The WHO, International Agency for Research on Cancer (IARC's), Section of Cancer Surveillance (CSU) - including GLOBOCAN, Cancer Incidence in Five Continents (CI5), International Incidence of Childhood Cancer (IICC) - and Cancer Survival in Africa, Asia, the Caribbean and Central America (SurvCan). This platform has the potential to improve cancer data collection and reporting globally, and it could decrease the discrepancy observed among various databases in LICs.

2.3 Evaluation of pediatric cancer incidence reported from literature

To investigate whether there is a discrepancy between pediatric cancer incidence reported in the literature on LICs, data were collected from articles, and a comparative analysis was performed. This analysis focused on the African region as a case study. The process and steps of this evaluation were listed in the flow diagram (Table 2.1).

2.3.1 Assessment of published pediatric cancer incidence data on LICs

Data of pediatric cancer incidence in African countries were collected from the literature to determine whether there is a discrepancy amongst data reported. Additionally, assessment of data

sources used and referenced in these articles was conducted. To identify potential publications that could be included in the comparative analysis, a search for articles was performed in PubMed and Google search. Titles, abstracts, and conclusions of articles were reviewed to determine the relevance of the content of the analyses. The key measures that were defined to determine whether an article was included in the analysis were: if the article reported pediatric cancer incidence or number of cases for patients ages 0-14, if data reported was for African countries or regions, and if years covered were overlapping with other studies to allow proper comparison. The number of articles assessed, elimination steps, and rationale for elimination and/or inclusion are illustrated in the flowchart (Figure 2.2).

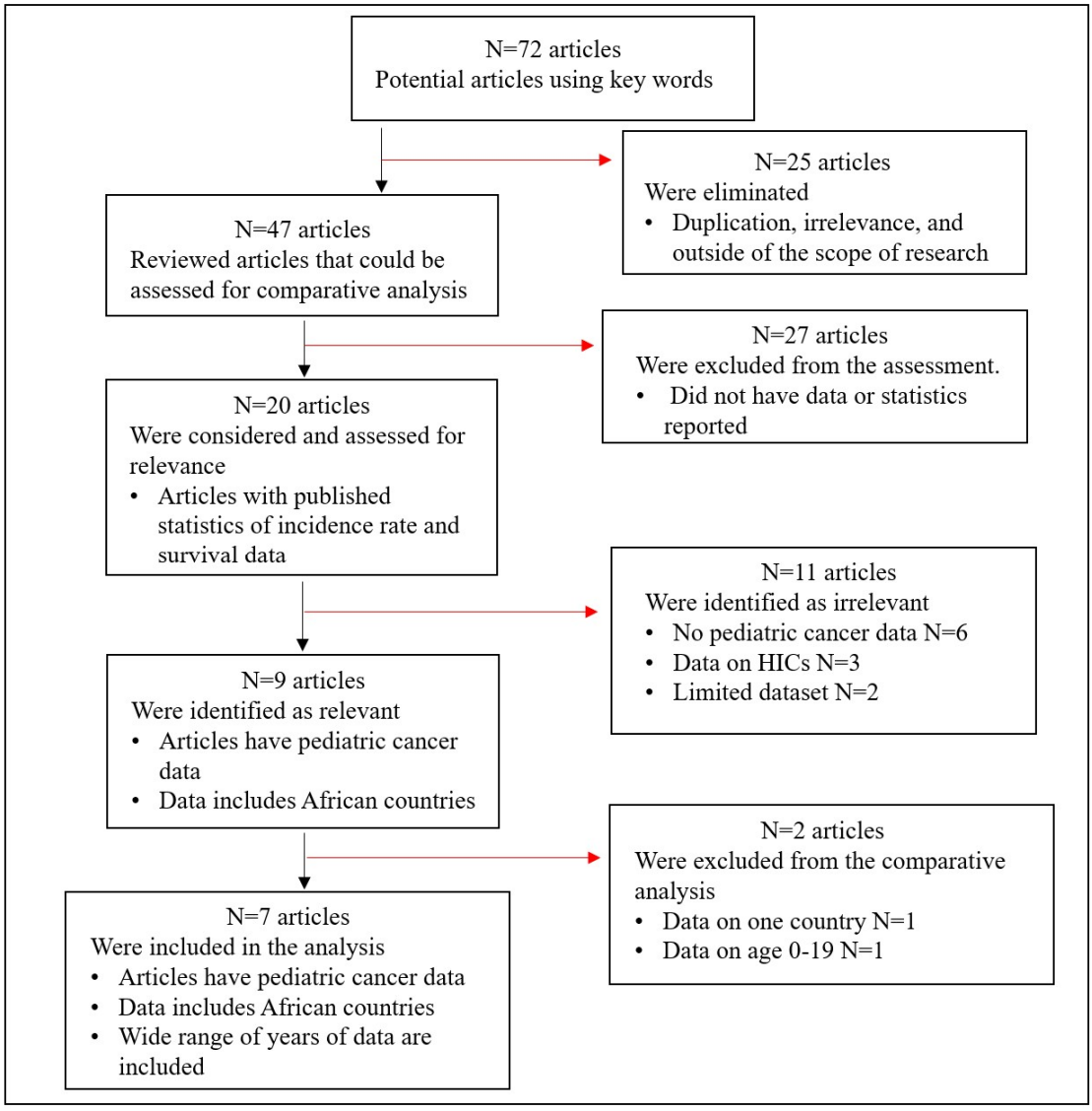


Figure 2.2 Flowchart illustrating the process of inclusion/exclusion of articles for the comparison analysis

In the preliminary search, approximately 72 articles were screened, and 25 articles were eliminated due to duplication, irrelevance, or because the topic was outside the scope of research. The remaining 47 articles were classified to be potential for further evaluation. However, only 20 were relevant for further assessment. Information about these 20 articles - including title, first author, year published, countries/regions covered, years covered in the data reported, and whether the

article is relevant - was gathered and presented in (Table 2.8). The main elimination criteria used at this phase was whether an article did not report data or statistics. For example, even though the eliminated 27 articles addressed various topics that are related to pediatric cancer, such as medical care advancement, biology of the disease, challenges, gaps, and data underreporting, no data were reported. Additional evaluation on the data reported by the 20 articles was done to determine whether the data was suitable for the analysis. 11 out of 20 articles were eliminated because of the following: only adult cancer data was reported (N=6), data were focused on pediatric cancer in HICs (N=3), or datasets reported were limited to be included in the analysis (N=2). Data from the remaining 9 articles was further evaluated, and 2 articles were subsequently excluded because data was reported for only one country (N=1), or for patients aged 0-19 without the possibility to subgroup the ages 0-14 (N=1). The final 7 articles were deemed to be suitable for the comparative analysis of pediatric cancer incidence in Africa.

Table 2.8 List of potential articles that were evaluated to be included in the comparative analysis

Title of the article	Year published	Reference	Countries/ region covered	Years covered	Is the article relevant ?	Reason/ comment
Cancer of childhood in sub-Saharan Africa	2017	(Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017)	Sub-Saharan Africa	2001-2013	Yes	Covering wide range of African countries and years of data
Cancer Incidence in Egypt: Results of the National Population-Based Cancer Registry Program	2014	(Ibrahim, Khaled, Mikhail, Baraka, & Kamel, 2014)	Egypt	2008-2011	Yes	Limited pediatric cancer data
Cancer Statistics, 2019	2019	(Siegel, Miller, & Jemal, 2019.)	USA	2011-2015	No	Data covers HICs

Cancer Statistics for Adolescents and Young Adults, 2020	2020	(Miller, et al., 2020)	USA	2020	No	No pediatric cancer data. Data included on ages 15-19, 20-29, and 30-39 years
Cancer Statistics, 2016	2016	(Siegel, Miller, & Jemal, Cancer statistics, 2016, 2016)	USA	2016	No	Data covers HICs
Childhood and Adolescent Cancer Statistics, 2014	2014	(Ward, DeSantis, Robbins, Kohler, & Jemal, 2014)	USA	2014	No	Data covers HICs
Childhood cancer: Estimating regional and global incidence	2021	(Johnston, et al., 2021)	Global	2015	Yes	Large dataset covering several countries
Childhood cancer health outcomes in egypt: ten-year real-world evidence from children's cancer hospital 57357 – egypt (CCHE) and comparison with results from England	2019	(Soliman, et al., 2019)	Egypt	2007-2017	No	Limited dataset and no incidence data
Childhood cancer incidence in South Africa, 1987 - 2007	2015	(Stefan, et al., 2015)	South Africa	1987 - 2007	Yes	Covering only one region in Africa
Cancer incidence in Cotonou (Benin), 2014–2016 First results from the cancer Registry of Cotonou	2019	(Egue, Gnangnon, Akele-Akpo, & Maxwell Parkin, 2019)	Benin	2014–2016	No	No pediatric cancer data
Estimating the total incidence of global childhood cancer: a simulation-based analysis	2019	(Ward, Yeh, Bhakta, Frazier, & Atun, 2019)	Global	2015 projected to 2030	Yes	Large dataset covering several countries
Global Cancer Incidence and Mortality Rates and Trends—An Update	2016	(Torre, Siegel, Ward, & Jemal, 2016)	Global	2003–2007	No	No pediatric cancer data

Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries	2021	(Sung, et al., 2021)	Global	2019-2020	No	No pediatric cancer data
Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017 A Systematic Analysis for the Global Burden of Disease Study	2019	(Fitzmaurice , et al., 2019)	Global	1990 - 2017	No	No pediatric cancer data
International incidence of childhood cancer, 2001–10: a population-based registry study	2017	(Steliarova-Foucher, et al., 2017)	Global	2001-2010	Yes	Large dataset covering several regions. Years covered are not for every country
Patterns of Distribution of Childhood Cancer in Africa	2015	(Stefan D. C., 2015)	Africa	2000 - 2010	Yes	Pediatric cancer data covering several countries
Population-Based Cancer Registration in Sub-Saharan Africa: Its Role in Research and Cancer Control	2020	(Omonisi, Liu, & Parkin, 2020)	Sub-Saharan Africa	2020	No	No pediatric cancer data
Sustainable care for children with cancer: a Lancet Oncology Commission	2020	(Atun, et al., 2020)	Global	2012-2018	Yes	Large dataset covering several countries. Years covered vary for every country
Temporal trends in childhood cancer survival in Egypt, 2007 to 2017: A large retrospective study of 14 808 children with cancer from the Children's Cancer Hospital Egypt	2021	(Soliman R. M., et al., 2021)	Egypt	2007-2017	No	Limited dataset and no incidence data

Trends in childhood cancer incidence in sub-Saharan Africa: Results from 25 years of cancer registration in Harare (Zimbabwe) and Kyadondo (Uganda)	2021	(Stoeter, et al., 2021)	Sub-Saharan Africa	1991-2015	Yes	Pediatric cancer data on African countries

2.3.2 Comparative analysis of data reported from literature and exploration of potential trends

The limited number of publications that reported pediatric cancer incidence, specifically, for African countries prevented a comprehensive comparative analysis. This limitation is not uncommon in the field of pediatric cancer, and it was also reported in other studies (Ward, Yeh, Bhakta, Frazier, & Atun, 2019). In an attempt to mitigate this gap, modeling and simulation approaches have been recently undertaken by several groups to predict the global incidence of childhood cancer (Johnston, et al., 2021).

A comprehensive review was completed for the 7 articles selected for the comparative analysis. Information about the type of study (population-based or model-based), type of data used, source of data, and age of population covered was collected from these 7 articles and listed in Table 2.9. The main characteristics that differentiated the articles were also explored. For example, 5/7 articles used African cancer registries as a source of data, 3/7 articles compared their cancer incidence data with other databases and identified discrepancies, 2/7 articles used modeling approaches to predict incidence rate, whilst 5/7 performed analysis on population-based data from various sources. Data sources used by articles included cancer registries, SEER, GLOBOCAN, IARC, ICCC-3, IICC-3, GCC, and WHO.

Table 2.9 List of the final 7 articles that were selected for the comparative analysis

Paper number	Title of the article	years covered	Type of data	Population covered	Sources of data	Comparison with other articles
1	Cancer of childhood in sub-Saharan Africa	2001-2013	population -based data	Pediatric cancer 0-14 (Africa)	16 cancer registries - members of AFCRN	Comprehensive article with data per country/African regions and cancer type
2	Childhood cancer: Estimating regional and global incidence	2015	A Baseline Model (BM) was constructe d- applied to population data	Pediatric cancer 0-14 (Global)	SEER, ICCC-3, IICC-3 and GCC, GLOBOCA N and WHO	Data by region and not by country - Results were compared to GLOBOCAN 2018
3	Childhood cancer incidence in South Africa, 1987 - 2007	1987 - 2007	population -based data	Pediatric cancer 0-14 (Africa)	Data from Tumor registry, United Nations, and Statistics South Africa	Data reported by country with overall incidence rate
4	International incidence of childhood cancer, 2001–10: a population-based registry study	2001–2010	population -based registry study	Pediatric cancer 0-19 (Global)	International Association of Cancer Registries and 153 registries from 62 countries	Data reported by region by cancer type
5	Patterns of Distribution of Childhood Cancer in Africa	2000 - 2010	population -based registry study	Pediatric cancer 0-14 (Africa)	Registry centers in Africa registered with the IARC, African centers registered with AORTIC and SIOP Africa	Data reported by country by cancer type. Data for every country covering different years range. The study compared data with GLOBOCAN 2012
6	Sustainable care for children with cancer: a Lancet Oncology Commission	2012-2017, 2018	modeling based study	Pediatric cancer 0-14 (Global)	Population based cancer registries	Data was compared to other studies including data from GLOBOCAN

7	Trends in childhood cancer incidence in sub-Saharan Africa: Results from 25 years of cancer registration in Harare (Zimbabwe) and Kyadondo (Uganda)	1991-2015	population -based registry study	Pediatric cancer 0-19 (Africa)	Population-based cancer registries	Data reported by country with overall incidence and by cancer type

In this section, articles will be referred to as paper 1-7 (Table 2.9). After the datasets from the 7 articles were extracted, significant limitations to conduct the analysis were identified. The variation of how data was reported by these articles prevented a proper comparison of the pediatric cancer incidence. For example, most articles reported data either by country or by region, but not the combination of both. Therefore, it was not possible to isolate data from individual countries out of grouped regions or assume that data from a single country was representative of an entire region. Similarly, the lack of overlap for a given year or a specific range of years among datasets prevented an adequate data comparison. Furthermore, datasets from some articles reported data that covered different periods of time within each country, such as paper 1 (Table 2.10) (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017). All of these limitations prevented conducting a proper comparative analysis.

Table 2.10 ASR/per million for 13 African countries reported by paper1
Data taken from (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017)

Paper1 Cancer of childhood in sub-Saharan Africa, 2017			
Country	**Region**	**Year**	**ASR/per million**
The Gambia	West Africa	2002-2011	27.6
Guinea	West Africa	2001-2010	30.6
Niger	West Africa	2001-2009	51.7
Botswana	South Africa	2003-2008	70.3
Nigeria	West Africa,	2003-2012	80.6

Ethiopia	East Africa	2011–2013	95.7
Mauritius	East Africa	2003-2012	97.2
Zimbabwe	East Africa	2003-2013	108
Reunion	East Africa	2002-2008, 2022	109.6
Mali	West Africa	2006-2014	119.4
Uganda	East Africa	2003-2012	151
Kenya	East Africa	2007-2011	152.3
Malawi	East Africa	2003–2010	308.2

However, several trends were observed across pediatric cancer incidence data in African countries (Figure 2.3). Incidence data for Uganda displayed a fluctuation of the age-standardized average annual incidence rate (ASR) across different years. ASRs reported in Uganda were 151 by paper 1, 182.7 by paper 3, 69.9 by paper 5, and 146.6 by paper 7. The most significant difference was observed in data reported by paper 5, which highlighted a noticeable decrease in the incidence rate between the years of (2000-2008) (Figure 2.3A). For Zimbabwe, ASRs reported were 108 by paper 1, 111.6 by paper 3, 120 by paper 5, and 130 by paper 7 (Figure 2.3B). These data showed that the ASRs reported for Zimbabwe were similar, with only a slight increase in the data reported by paper 7. Moreover, ASRs reported for Mali were 119.4 by paper 1, 77.7 by paper 3, and 67.8 by paper 5, which showed a clear discrepancy among articles (Figure 2.3C). Finally, ASRs reported for Nigeria were 80.6 by paper 1, 70.5 by paper 3, and 67 by paper 5, which indicated a slight overall discrepancy (Figure 2.3D). Data reported by paper 1 for Nigeria suggested a higher ASR compared to the other articles, which might be due to data variability associated with coverage of a wider range of time. Overall, data suggest that ASRs reported by paper 5 were generally lower compared to other articles. Data sources used by this article and types of analysis were investigated as a potential factor that might have led to this observation. However, no clear association was identified.

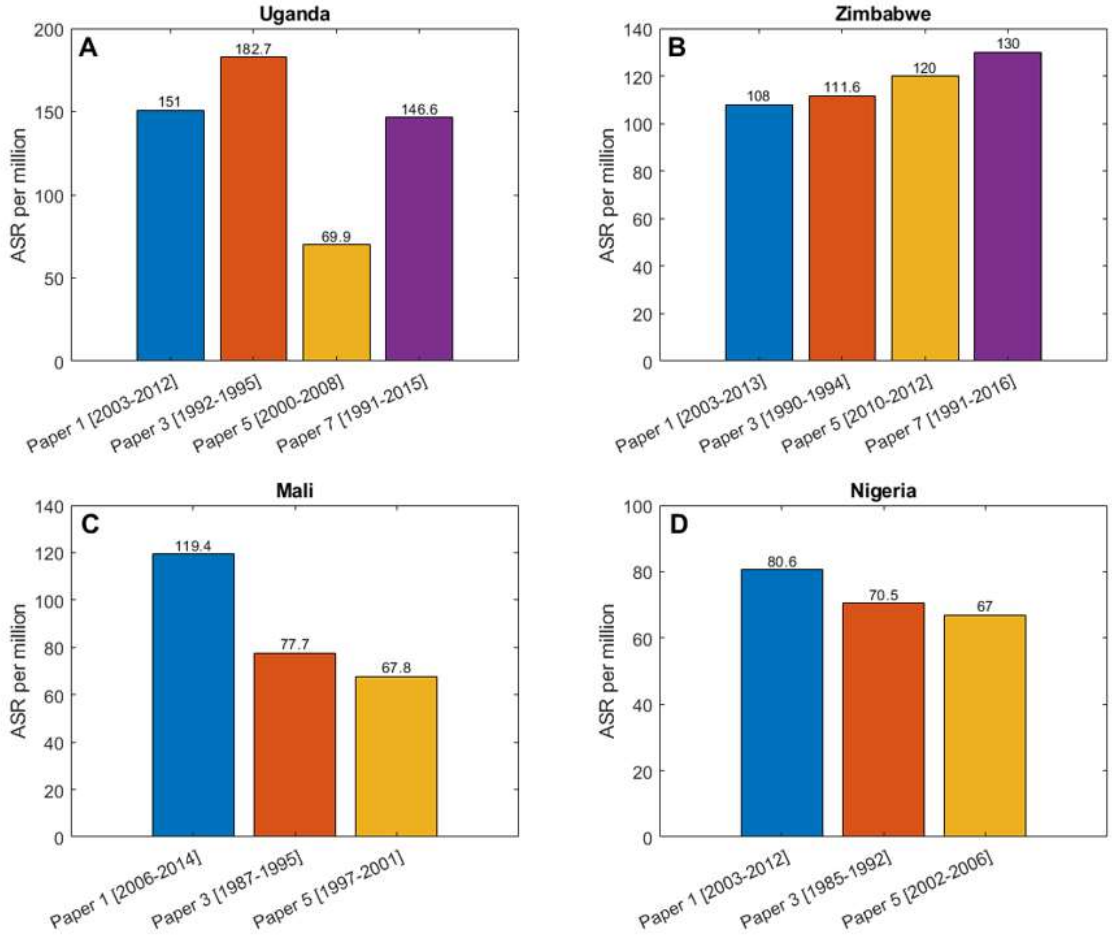


Figure 2.3 ASRs per million reported by articles for Uganda (A), Zimbabwe (B), Mali (C), and Nigeria (D).
Blue bars represent paper1, orange bars paper3, yellow bars paper5, and purple bars paper7

A comparison of incidence rates by regions was also attempted. However, ASRs were reported across articles without time overlapping or consistency in regions. Therefore, a proper comparative analysis was not possible. ASRs were reported in more than one article over a similar period of time only for North Africa. ASRs reported for North Africa were 182.4 by paper 2, 109 by paper 4, and 105.4 by paper 6 (Table 2.11).

Table 2.11 ASR/per million reported for North Africa region

Article/paper	Country	Year covered	ASR/per million
Paper 2	North Africa	2015	182.4
Paper 4	North Africa	2001-2010	109
Paper 6	North Africa	2018	105.4

Data from paper 1 showed that the lowest incidence rate was in Gambia and Guinea with ASR of 27.6 and 30.6, respectively. On the other hand, the highest ASR reported was 308.2 in Malawi. The intermediate ASR reported for the remaining countries ranged between 70-152.3 (Table 2.10). Notably, the countries with lowest ASRs were in West Africa (Gambia, Guinea, and Niger), whereas the countries with the highest ASRs were East Africa (Malawi, Kenya, and Uganda), indicating that incidence rate in East Africa region is higher compared to countries in West Africa (Stefan, Bray, Ferlay, Liu, & Maxwell Parkin, 2017).

This data assessment across literature highlighted the gap of limited available pediatric cancer data in African regions and the urgent need to improve data reporting. To overcome this limitation, studies utilized simulation-based data to generate pediatric cancer incidence rates. Ward and colleagues published a simulation-based global childhood cancer incidence for 200 countries in 2015 and predicted a number of new cases between 2015 to 2030 (Ward, Yeh, Bhakta, Frazier, & Atun, 2019). The authors considered in their simulation model various variables and regional based factors, such as genetic alterations, environmental risk factors, and pattern of population growth. To estimate the number of cases in countries without registries, a geographical proximity of neighboring country-based approaches was used with the assumption of same cancer incidence. The authors predicted that 6.7 million new cases of pediatric cancer will occur between 2015 and 2030. Moreover, they estimated that 92% of the new cancer incidence will be in LMICs.

Various studies indicated that the incidence of pediatric cancer in HICs is very close to the accurate estimate (Shah, Kayamba, Peek, & Heimburger, 2019). Since this analysis revealed gaps in the amount of pediatric cancer incidence data available in LICs, it is reasonable to assume that the number of cancer incidence reported in LICs is very low compared to real numbers. Hence, if we assume that the proportion of pediatric population in a specific LICs and HICs is the same, then one would expect similar number of cancer incidence. However, social and economic factors that might impact cancer development should also be considered.

2.4 Representation of cancer registries in reporting pediatric cancer data in LICs versus HICs

The role of cancer registries in data collection and reporting is essential (Curado, 2019). One of the key potential factors that might contribute to data underreporting in LICs is the minimal geographical distribution of cancer registries and the capacity at which they can operate (Znaor, et al., 2018). In LICs, there are limited number of population-based registries, and most of the countries have national or hospital-based registries. A study published by Siddiqui et al. in 2018 showed that 40% of the LICs do not have registries at all (Siddiqui & Zafar, 2018). Globally, only 60% of the countries have quality population-based cancer registries, and these registries usually cover only a small percentage of the population (Ward, Yeh, Bhakta, Frazier, & Atun, 2019). The work of Siddiqui et al. clearly highlighted the underrepresentation of data from LICs in the global cancer statistics. On the other hand, the presence and distribution of population-based registries cancer registries in HICs have been well established. The first population-based cancer registry in HICs was established in Germany in 1929 and in the U.S. in 1940 (IARC Publications). Most of cancer centers and hospitals in HICs are connected to these registries (American Cancer Society,

2021). Pediatric cancer data in HICs, such as European region, are covered by more than 200 cancer registries (Steliarova-Foucher, et al., 2015). In contrast, numerous studies highlighted the underrepresentation of data from LICs in global databases (Piñeros, Mery, Soerjomataram, Bray, & Steliarova-Foucher, 2021). There is a significant difference between the percentage of pediatric cancer patients ages 0-14 covered by registries in HICs versus LICs. For example, only 5.3% of pediatric cancer patients are covered by cancer registries from Africa compared to 97.2 from the U.S. and 66.4 from Europe (Piñeros, Mery, Soerjomataram, Bray, & Steliarova-Foucher, 2021). The representation of data reported in global statistics from HICs and LICs also significantly differs (Henson, et al., 2020). A study collected data from 190 countries to identify countries that have population-based registries, hospital-based registries or do not have registries at all (Siddiqui & Zafar, 2018). In this study, the presence and absence of registries in the country was correlated with income status and available health policies. Results of the correlation analysis showed that 75% of HICs have national registries compared to only 22% of LICs. Additionally, 50 (26%) of the 190 countries investigated did not have any kind of cancer registry (Figure 2.4).

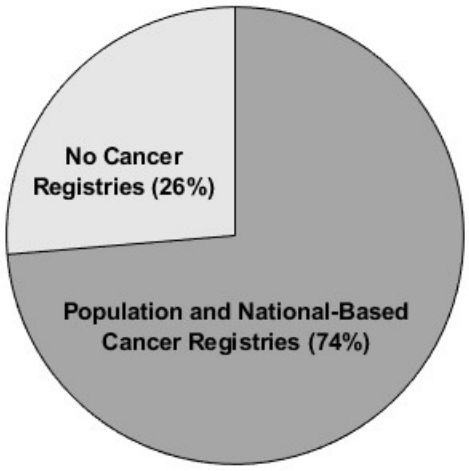


Figure 2.4 Availability of cancer registries in 190 countries
(Data taken from (Siddiqui & Zafar, 2018))

Out of the 140 countries with a registry, 99 (71%) had a population-based registry and 81 (58%) had national registries. Only 4 out of 29 LICs have registers, and 35 out of 50 LMICs have registries. An assessment of the distribution of cancer registries in African countries was also performed in this study. 24 out 40 (60%) African countries have registries, and 16 out of 40 (40%) have no registries or there is no data available. This analysis suggested that it is critical to encourage LICs to establish cancer registries and improve the reporting of high-quality pediatric cancer data. Establishing cancer registries will improve the assessment of cancer burden and enhance cancer medical care (Siddiqui & Zafar, 2018). It is crucial to improve data collection and reporting in LICs. Therefore, governments should implement policies that mandate hospitals, cancer centers, registries, and health providers to collect and report data. Also, encouraging local and national cancer registries to report quality data to global databases could improve data reporting and might expand the access to pediatric cancer data.

3 CHAPTER 3: INVESTIGATION OF CANCER REGISTRIES IN AFRICA AND REPORTING OF PEDIATRIC CANCER DATA

3.1 Introduction

Pediatric cancer data underreporting in LICs has been highlighted by many publications and presented in SIOP conferences. Data suggest that the actual number or pediatric cancer cases in LICs is much higher than what is reported. To assess the extent of data under-reporting of pediatric cancer in LICs, a questionnaire was designed to collect data from local and national cancer registries in selected African countries. The questions focused on pediatric cancer data collection and reporting. The questionnaire contained six sections that covered several topics, including general information about the registry, collection of pediatric cancer data, sources of pediatric cancer data, type of pediatric cancer data, use of cancer registry results in pediatric cancer control, and resources and challenges in collecting pediatric cancer data. Data from this survey might enable a better understanding of the flow of data collection and identifying factors that could contribute to data underreporting and data discrepancy. The questionnaire was conducted in collaboration between the University of Birmingham, Birmingham UK, and The African Cancer Registry Network, Oxford UK. The data collected will help with the aims of the AFCRN, which are to improve the effectiveness of cancer surveillance in sub–Saharan Africa by providing expert evaluation of current problems and technical support to remedy identified barriers, with long-term goals of strengthening health systems and creating research platforms for the identification of problems, priorities, and targets for intervention. The questionnaire was sent to 30 cancer registries,

and 15 registries (50%) responded. 6 out of 15 registries were population-based, and the remaining 9 were hospital-based registries. Data analysis was performed and discussed in sections 3.4 and 3.5 of this chapter, respectively.

3.2 Objectives of the questionnaire

The objectives of the cancer registries questionnaire are the following:

1. Design a comprehensive questionnaire to capture all relevant information needed for the assessment.
2. Send the questionnaire to many African cancer registries, affiliated with AFCRN, to gather a wide-ranging dataset.
3. Receive data on time.
4. Understand the setup of cancer registries.
5. Assess cancer registries resources and funding.
6. Understand the data flow between cancer centers, cancer hospitals and cancer registries.
7. Investigate how pediatric cancer data was collected and the process of data collection.
8. Identify the sources of data collected, formatting of the data, and the quality of data collected in cancer registries.
9. Identify the main challenges that cancer registries faced in collecting pediatric cancer data or that prevented registries from collecting the data.
10. Develop hypotheses regarding factors that might contribute to pediatric cancer data underreporting in Africa and other LICs.

3.3 Methods and procedure to develop the questionnaire

A meeting with AFCRN was held to discuss the objectives and the design of the questionnaire. In addition, a study proposal was sent to AFCRN to outline the rationale, methods, and timelines of the study. AFCRN shared a template of a questionnaire that was conducted in 2014 to address similar questions, but in the context of adult cancer data (template is included in the appendix). AFCRN template was modified and adjusted to suit pediatric cancer data questionnaire. A draft of the developed questionnaire was sent to AFCRN to obtain input and feedback. Finally, the questionnaire was sent to cancer registries by AFCRN on our behalf.

The questionnaire was predominantly based upon tick-boxes with some sections for free text. It should only take 20-40 mins to complete it. Once the questionnaire was sent out, registries were given 2 weeks to complete it. Reminders were sent out on day 7 and day 11. The aim was to collect data from all AFCRN-affiliated cancer registries by the end of September 2019. The complete set of data was received by December 2019. The questionnaire data was collated and analyzed. Further analysis will be conducted in conjunction with the AFCRN to identify areas of strengths and areas that require improvement.

3.4 The questionnaire for African cancer registries

The questionnaire for African National Cancer Registries, (QANCR 2019), was focused on pediatric cancer data collection in Africa. The six sections of questions listed in the questionnaire are:

1. General information about the registry.
2. Collection of pediatric cancer data.

3. Sources of pediatric cancer data.
4. Type of pediatric cancer data.
5. Use of cancer registry results in pediatric cancer control.
6. Resources and Challenges in collecting pediatric cancer data.

The complete questionnaire is included in the appendices of the thesis

3.5 Data analysis and results

The questionnaire was sent to 30 cancer registries across Africa to fully characterize the pediatric cancer data collection and reporting across the whole continent. The list of the 30 registries is presented in Table 3.1. These cancer registries were chosen because of their affiliation with AFCRN. However, only 15 registries (50%) participated in this study and responded. Some registries did not participate due to language barrier, as they requested the questionnaire to be translated to French or local languages. Information about registries can be found at the AFCRN website (African Cancer Registry Network, 2021)

Table 3.1 List of Cancer registries that received the African cancer registries questionnaire
Information about registries can be found at AFCRN Website (African Cancer Registry Network, 2021)

National and Local African Cancer Registers (30)			
Cancer Registry	Country	Responded	Not responded
Cotonou Cancer Registry	Benin		
National Cancer Registry	Botswana		
Registre des Cancers d'Abidjan	Cote d'Ivoire		
Swaziland National Cancer Registry	Eswatini		
Addis Ababa City Cancer Registry	Ethiopia		
Gambia Cancer Registry	Gambia		
Kumasi Cancer Registry	Ghana		

Registre de Cancer de Guinée	Guinea		
Eldoret Cancer Registry	Kenya		
Nairobi Cancer Registry	Kenya		
Malawi Cancer Registry	Malawi		
Registre des cancers du Mali	Mali		
Mauritius National Cancer Registry	Mauritius		
Registro de Cancro de Beira	Mozambique		
Maputo Cancer Registry	Mozambique		
Namibian Cancer Registry	Namibia		
Registre des Cancers du Niger	Niger		
Abuja Cancer Registry	Nigeria		
Calabar Cancer Registry	Nigeria		
Nigerian National System of Cancer Registries	Nigeria		
Ibadan Cancer Registry	Nigeria		
Registre des cancers de Brazzaville	République du Congo		
Registre des cancers de la Réunion	Reunion Island		
Seychelles National Cancer Registry	Seychelles		
South Africa Eastern Cape Province Cancer Registry	South Africa		
National Cancer Registry (NCR-SA)	South Africa		
Gulu Cancer Registry	Uganda		
Kampala Cancer Registry	Uganda		
Zambia National Cancer Registry	Zambia		
National Cancer Registry (Harare & Bulawayo)	Zimbabwe		

Figure 3.1 illustrates the 11 countries that participated in the questionnaire, which include Benin, Eswatini, Mali, Mozambique, Niger, Nigeria, République du Congo, Reunion Island, Seychelles, South Africa, and Uganda (Map Chart, 2021). To better contextualize the distribution of the countries, three geographical clusters were defined. The north cluster included Mali, Niger, Nigeria, and Benin; the central cluster included Congo, Uganda, and Seychelles; the south cluster included Mozambique, South Africa, Eswatini and Reunion Island.

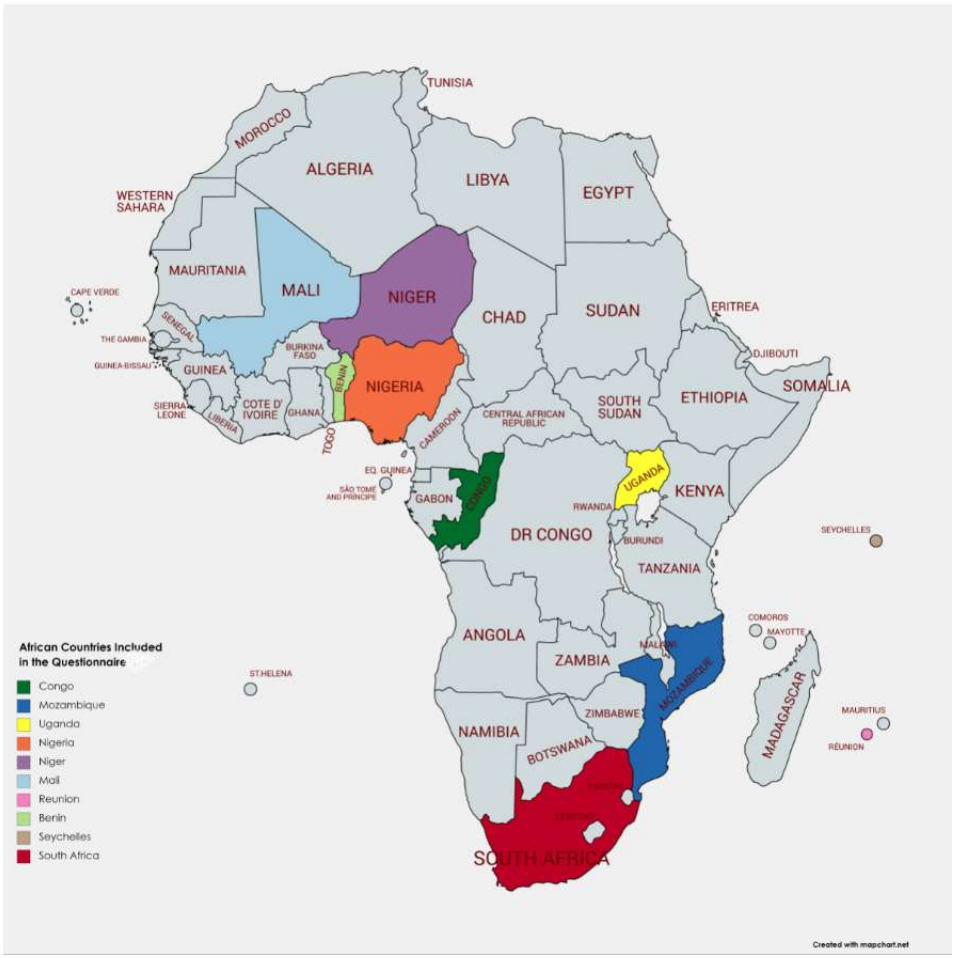


Figure 3.1 Map of countries that participated in the African cancer registries questionnaire (Map Chart, 2021)

3.5.1 General information about the registries

General information about cancer registries that participated in the questionnaire are presented in Table 3.2. The country population data were obtained from the world meters website and represent the statistics from 2019 (Worldometers, 2021) also contextualizes the proportion of children ages 0-14 in every country. Data was obtained from The World Bank website and represent the statistics from 2019 (The World Bank Group, 2019). Statistics of 2019 was chosen given that the questionnaire was conducted in the same year.

Table 3.2 General information about cancer registries participated in the questionnaire

Cancer Registry	Country	Region	Type of registry	Country population	Proportion of pediatric country population ages 0-14
Cotonou Cancer Registry	Benin	Littoral	Population based	12,123,200	42%
Eswatini National Cancer Registry	Eswatini	Hhohho	Population based	1,160,164	38%
Registre des cancers de Bamako	Mali	Bamako	Hospital based	20,250,833	47%
Beira Cancer Registry	Mozambique	Beira	Hospital based	31,255,435	44%
The Maputo Cancer Registry	Mozambique	Eastern Africa	Hospital based	31,255,435	44%
Registre des cancers du	Niger	Afrique de l'ouest	Hospital based	24,206,644	50%
Calabar Cancer Registry	Nigeria	Cross River State	Population based	206,139,589	44%
Ekiti Cancer Registry	Nigeria	Southwest	Population based	206,139,589	44%
The Ibadan Cancer Registry	Nigeria	Ibadan	Hospital based	206,139,589	44%
Registre des cancers de Brazzavill	République du Congo	Brazzaville	Hospital based	5,518,087	42%
Registre des Cancers de la Réunion	Réunion Island	Reunion Island	Hospital based	895,312	32%
Seychelles National Cancer Registry	Seychelles	East Africa	Hospital based	98,347	24%
National Cancer Registry	South Africa	South Africa	Hospital based	59,308,690	29%
Gulu Cancer Registry	Uganda	Northern Uganda	Population based	45,741,007	47%
Kampala Cancer Registry	Uganda	Central	Population based	45,741,007	47%

3.5.1.1 Staff working in the registry

The first set of questions covered general information about the registries. A key factor to understand is staffing levels in each registry. Hence, Question 1.1 focused on reporting the estimated average of full-time equivalent (FTE) of staff working in the cancer registry, such as statisticians, registrar and medical staff (including nurses/consultants/pathologists). Results from this question showed that the National Cancer Registry in South Africa had the highest number of

FTEs (12.1), while Kampala Cancer Registry in Uganda had the lowest number of FTEs (1) (Figure 3.2).

Results also indicated that the staff type working in the registries included medical staff, registrar, programmer, administration, statistician, epidemiologist, management and other. Staff listed as other included control verification, data capture and retrieve case files. The allocation of types of staff across registries showed that 13 out 15 registries had registrars, 13 out of 15 registries had other medical staff, 12 out of 15 registries had statisticians, 11 out of 15 registries had administration staff, and 11 out of 15 registries had management staff. Registries that did not have registrars reported that they have other type of staff responsible for data collection, for example the National Cancer Registry in South Africa allocated epidemiologist to collect data. In some registries a fraction of an FTE was reported as a staff type. For example, The Kampala Cancer Registry in Uganda has only one FTE that was allocated as 0.1, 0.2, 0.2 and 0.5 FTE across different staff types. Therefore, we would predict that the same person is performing all tasks or there are multiple people who are dedicated to a specific responsibility as part time employees.

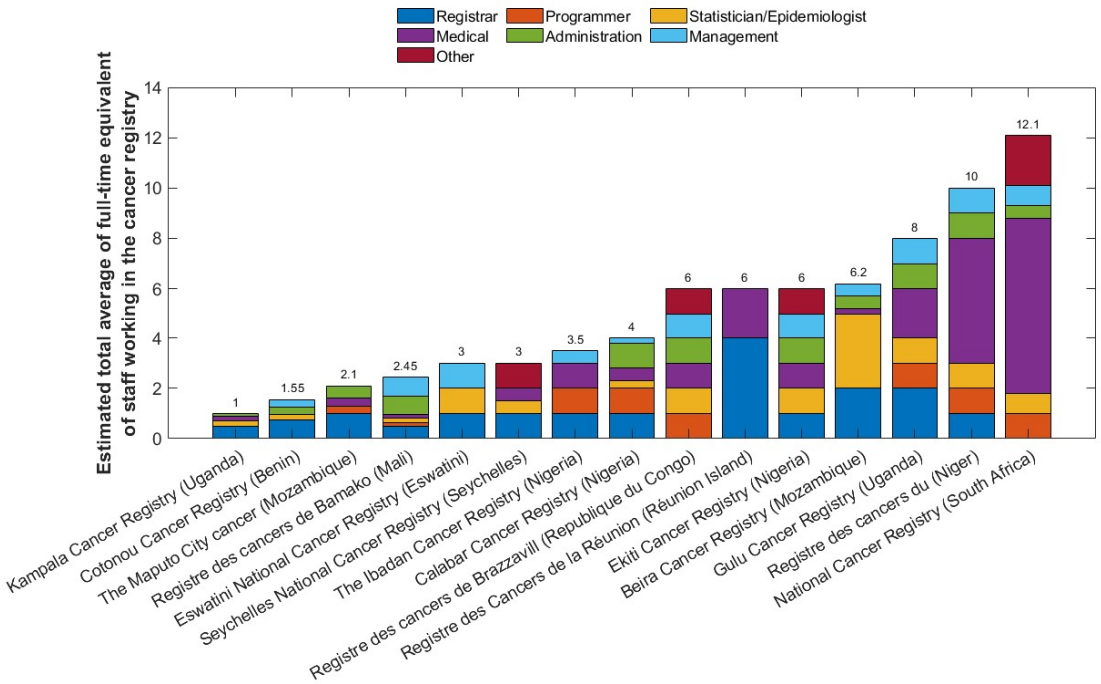


Figure 3.2 Estimated total average of FTEs of staff working in cancer registries (by registry) Colors represent the different types of FTEs, stacked bars denote the fraction of total FTEs, and numbers are the cumulative number of total FTEs.

3.5.1.2 Distribution of staff in cancer registries

To characterize the distribution of staff categories and determine the proportion of each staff type across registries, question 1.1, stating "please indicate the average full-time equivalent (FTE) of staff working in the cancer registry", was included. Results indicated that medical staff represented the highest percentage of staff type across registries (27.8%) followed by registrar (22.4%), statistician/epidemiologist (13.6%), management (10.7%), administration (10.2%), programmers (8.6%) and others (6.7%), as illustrated in Figure 3.3.

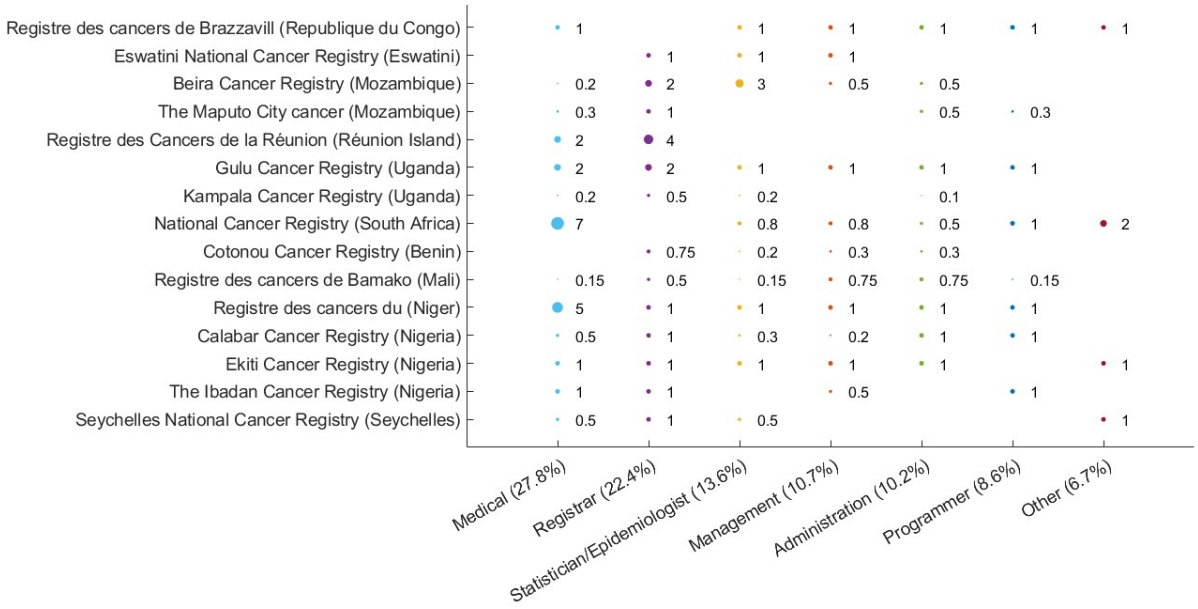


Figure 3.3 Distribution of staff type working in cancer registries (by category).
Dot plot illustrating the distribution of staff category by registry. Size of the dot represent the number of staff workers.

The National Cancer Registry in South Africa and the Registre des cancers du in Niger had the highest number of medical staff, with 7 and 5 FTEs, respectively. On the other hand, the Beira Cancer Registry and Maputo City Cancer Registry in Mozambique and the Kampala Cancer Registry in Uganda had the lowest number of medical staff, with 0.2, 0.3 and 0.2 FTEs, respectively. The medical staff of all other registries ranged between 0.5 and 2 FTEs. The highest prevalence of registrars was reported by the Registre des Cancers de la Réunion in Reunion Island (4), and the lowest prevalence of registrar was indicated by the Registre des cancers de Bamako in Mali (0.5) and the Kampala Cancer Registry in Uganda (0.5). All the remaining registries reported a prevalence ranging between 0.75 and 2. Whilst the Beira Cancer Registry in Mozambique had the highest number of statistician/epidemiologist (3), the Registre des cancers de Bamako in Mali had the lowest number of statistician/epidemiologist (0.15), and the reported range for other

registries was between 0.2 and 1. The representation of all the other staff types, including management, administrative, and programmer, across registries was between 0.1 and 2.

Registries with high medical staff appeared to have low registrars (Figure 3.3). For example, the National Cancer registry in South Africa had seven medical staff and no registrar, and the Registre des cancers du in Niger had five medical staff and only one registrar. Since it was not reported whether medical staff was also collecting data in these registries, it is unclear whether the low representation of registrars could negatively impact the data collection efficiency or the high representation of medical staff in the registry could improve the data interpretation and increase quality of data entry. In the Registre des Cancers de la Reunion in Reunion Island, the only two types of staff reported were medical and registrar, which raise the question whether the responsibilities of both staff types would also cover administration, management and statisticians' roles.

To identify and compare FTE workload across registries, an in-depth analysis was performed by contextualizing the number of FTEs with the population covered, the proportion of pediatric population, and the number of pediatric cancer cases reported. This analysis was conducted to highlight challenges and lack of resources faced by registries, and it is described in section 3.5.6 after the above metrics were defined.

3.5.1.3 Funding supporting the registry

Limited funding is a challenge for many cancer registries in Africa, as reported in multiple publications (Lingwood, et al., 2008). To better understand the extent of this challenge, question 1.2 was included to assess the sources of funding that support each registry. A list of funding

resources was provided in the questionnaire. The results of this question indicated that the most common source of funding was local governments followed by hospitals (Figure 3.4).

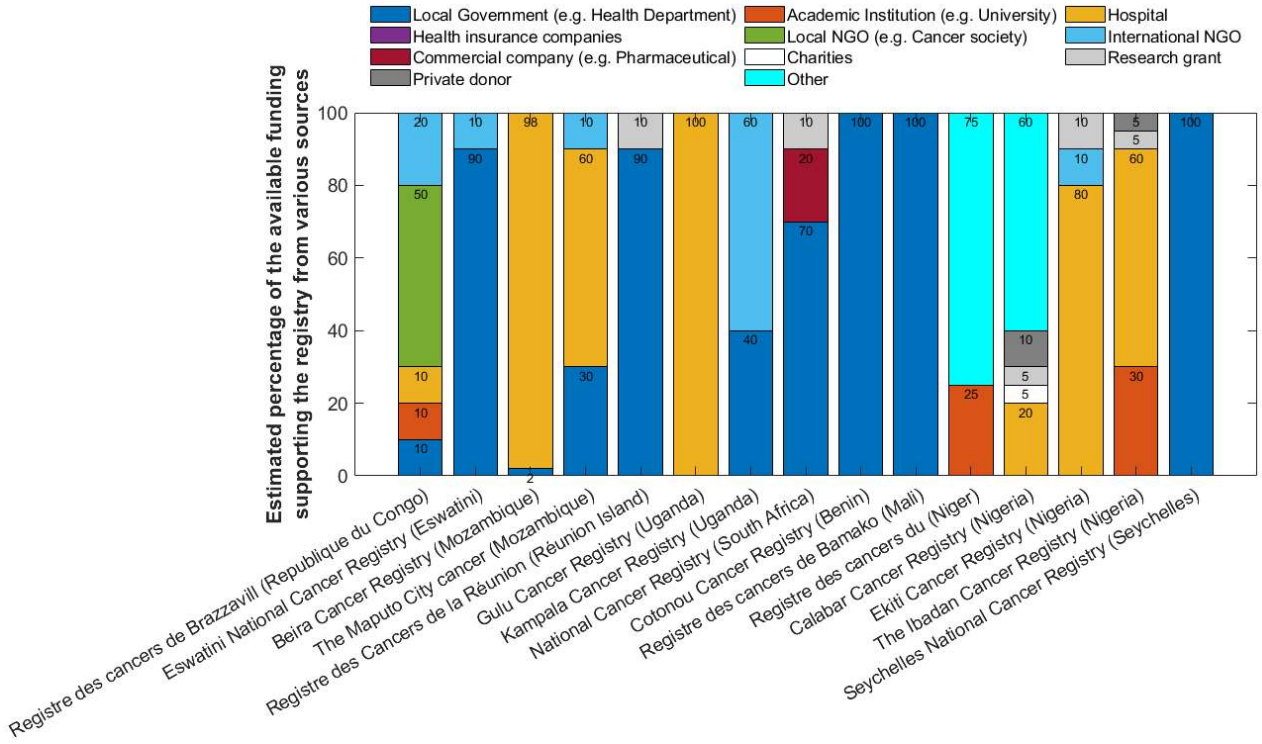


Figure 3.4 Estimated percentage of the available funding supporting the registries
Colors represent the different types of funding sources, and stacked bars represent the fraction of source funding by category per registry.

Ten registries (67%) were reported to receive funding from local governments. Across those, three were entirely funded by local governments (Cotonou Cancer Registry in Benin, Registre des cancers de Bamako in Mali, and Seychelles National Cancer Registry in Seychelles), three were mostly funded by local government (Eswatini National Cancer Registry in Eswatini, Registre des Cancers de la Reunion in Reunion Island, and National Cancer Registry in South Africa), and the remaining four were partially funded by local government. Moreover, 5 out of 15 registries did not receive any funding from local governments (Gulu Cancer Registry in Uganda, Registre des Cancers du in Niger, and the Calabar Cancer registry, Ekiti Cancer Registry, and the Ibadan Cancer

Registry in Nigeria). If registries are entirely or mostly funded by local governments and the country is a LIC, it is reasonable to assume that the amount of funds receiving to support data collection and reporting would be minimal. In addition, it is not clear whether governments could influence the process of decision-making and impact the way data are collected and reported, which was not addressed by the questionnaire.

The second most reported source of funding was hospitals. 7 out of 15 registries received funding from this source, with 5 registries mostly funded by the hospitals and 2 receiving minimal financial support from hospitals. The 5 registries mostly funded by hospitals were Gulu Cancer Registry in Uganda, Beira Cancer Registry in Mozambique, Ekiti Cancer Registry in Nigeria, Ibadan Cancer Registry in Nigeria, and Maputo City Cancer Registry in Mozambique. The 2 registries receiving minimal funding from hospitals were Registre des cancers de Brazzaville in Congo, and Calabar Cancer Registry in Nigeria.

The least common source of funding were charities, private donors, and commercial companies, respectively. The minimal representations of charities, private donors, local NGOs and commercial companies might pinpoint the need for increasing awareness about the importance of supporting cancer registries and their central role in reporting data. Moreover, the general low-income status of these countries does not facilitate contribution from local sources. Expanding interactions and communication with these sources might result in better collaborations and provide additional support.

Intermediate source of funding included international NGOs followed by academic institution and research grants. Data from Figure 3.4 revealed a marginal contribution of funding from international NGOs, with low number of registries receiving funding and low percentage of

contribution for a given registry. This result might indicate that NGOs contributions are limited due to some local regulations on receiving international funding. NGOs might also not be aware of the extent of limited resources that cancer registries encounter. Increasing visibility of cancer registries in LICs, by collecting and reporting more data to international databases, could attract the attention of the global community and eventually direct additional support. In addition, participating in international conferences could increase scientific collaborations and increase visibility.

Data also showed that registries within the same country receive funding from completely different sources. For example, in Uganda one registry was entirely funded by hospitals (Gulu Cancer Registry), and the other registry (Kampala Cancer Registry) was funded by local government and an international NGO. It was unclear why local government would allocate funding to only one registry or why only one registry received funding from an international NGO. A possible hypothesis is that the location of the registry and the area covered could have an impact on the funding stream. For example, The Kampala Cancer Registry is covering a large population area, including the capital city, which may influence the local government to provide funding. On the other hand, the Gulu Cancer Registry is located in the St. Mary's Hospital Lacor in the north of Uganda, and it could be therefore entirely funded by the hospital (African Cancer Registry Network, Uganda - Gulu Cancer Registry, 2017). A similar pattern was observed in Mozambique, where The Maputo Cancer Registry received funding from an international NGO, local government, and hospitals while the Beira Cancer Registry received funding mostly from hospitals. In this example as well, the location of Maputo Cancer Registry, covering a large area including the capital city, could be a potential explanation for receiving funding from an international NGO.

Factors that could determine the resource of funding allocated to cancer registries in this region need to be explored further.

Another observation is that none of the three registries from Nigeria received any funding from local government. These registries are funded by hospitals, academic institution, private donors research grant, international NGO, and other sources that were not reported. Based on published data, all three registries are part of the Nigerian National System of Cancer Registries (NSCR) which oversees all cancer registries in Nigeria and might facilitate allocation of funding (Nigerian National System of Cancer Registries).

3.5.2 Collection of pediatric cancer data

The second section of the questionnaire addressed the collection of pediatric cancer data. Whilst it is clear that all the cancer registries collect data on adult cancer cases, it is less clear how many reported collecting data on pediatric patients. Thus, we asked each registry to report on: 1) the overall population covered by the registry to calculate the incidence rate; and 2) the population of children age between 0-14 covered by the registry. The response to this question is illustrated in Figure 3.5.

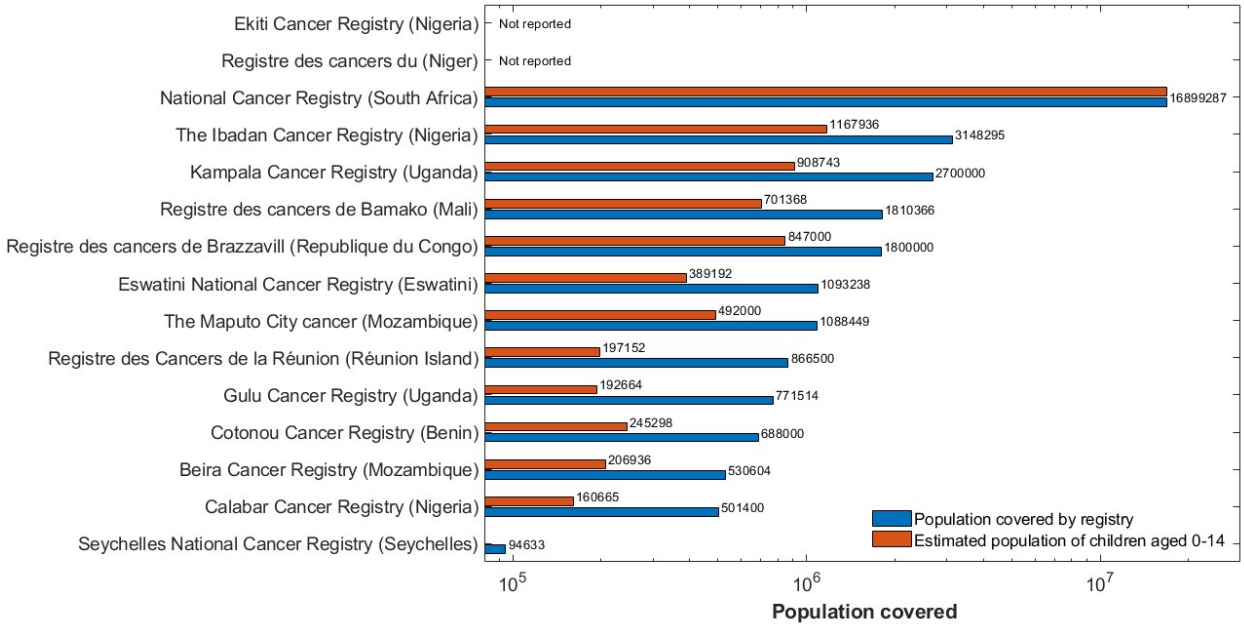


Figure 3.5 Population covered by the registry
Blue bars represent the total populations, and the red bars represent the pediatric population (children ages 0-14).

The National Cancer Registry in South Africa covered the largest populations. This registry collected data only from pediatric cancer patients and covered 16,899,287 children with age between 0-14 years. In contrast, all other registries covered a population that integrated both adult and pediatric patients, with a median proportion of children to adult equal to 36.3% and a standard deviation equal to 19.9%. The Ibadan cancer registry in Nigeria covered the second largest population, comprised of 3,148,295 people, followed by Kampala Cancer registry in Uganda, which covered 2,700,000 people. The smallest populations covered by registries were reported by Beira Cancer registry in Mozambique, Calabar Cancer registry in Nigeria, and Seychelles National Cancer registry in Seychelle with 530,604, 501,400, and 94,633 people, respectively. The population covered by registries within the same country were reported with a wide range. For

example, in Nigeria the Ibadan Cancer Registry covered a population that was 6 times larger than the population covered by the Calabar Cancer Registry.

Looking at the distribution of FTEs and population covered, data showed that the National Cancer registry in South Africa had 12 FTEs and covered a population of approximately 17 million, while Kampala Cancer Registry in Uganda had only one FTE and covered a population of approximately 3 million people. The lack of resources to collect or report data by the Kampala registry is noticeably clear. Overall, patterns in the ratio of FTEs to population covered across registries may be reflective of insufficient resources and inequality of distributing the resources that the majority of cancer registries encounter. Additional analysis about the workload of FTEs across registries is presented in Section 3.5.7.

In Table 3.3 is reported the proportion of pediatric cancer patients covered by registry, which was calculated by dividing the covered population of children ages 0-14 by the total population covered by registry. Results indicated that 100% of population covered by The National Cancer Registry in South Africa are pediatric cancer patients, whereas the percentage decreased to 47% in Registre des cancers de Brazzavill in Republique du Congo, 45% in The Maputo City Cancer Registry in Mozambique, 39% in Both Beira Cancer Registry in Mozambique and in Registre des cancers de Bamako in Mali, 37% in The Ibadan Cancer Registry in Nigeria, 36% in Cotonou Cancer Registry in Benin and Eswatini National Cancer Registry in Eswatini, 34% in Kampala Cancer Registry in Uganda, 32% in Calabar Cancer Registry in Nigeria, 25% in Gulu Cancer Registry Uganda, and 23% in Registre des Cancers de la Réunion in Reunion Island. Two registries out of fifteen (13.3%) did not provide data about the fraction of pediatric population they covered.

Table 3.3 The proportion of pediatric cancer patients covered by registry, which was calculated by dividing the covered population of children ages 0-14 by the total population covered by registry.

Cancer Registry	Country	# of FTEs	Population covered by registry	Population covered ages 0-14	Proportion of children 0-14
Cotonou Cancer Registry	Benin	1.5	688,000	245,298	36%
Eswatini National Cancer Registry	Eswatini	3	1,093,238	389,192	36%
Registre des cancers de Bamako	Mali	2.5	1,810,366	701,368	39%
Beira Cancer Registry	Mozambique	6.2	530,604	206,936	39%
The Maputo City Cancer Registry	Mozambique	2	1,088,449	492,000	45%
Registre des cancers du	Niger	10	NA	NA	NA
Calabar Cancer Registry	Nigeria	6	501,400	160,665	32%
Ekiti Cancer Registry	Nigeria	4	NA	NA	NA
The Ibadan Cancer Registry	Nigeria	3.5	3,148,295	1,167,936	37%
Registre des cancers de Brazzavill	République du Congo	6	1,800,000	847,000	47%
Registre des Cancers de la Réunion	Réunion Island	6	866,500	197,152	23%
Seychelles National Cancer Registry	Seychelles	3	94,633	NA	NA
National Cancer Registry	South Africa	12	16,899,287	16,899,287	100%
Gulu Cancer Registry	Uganda	8	771,514	192,664	25%
Kampala Cancer Registry	Uganda	1	2,700,000	908,743	34%

To determine how pediatric cancer data was collected, question 2.2 was designed. Specifically, the main objective was to understand whether the registry reached out to hospitals to collect data, or hospitals reached out to registries to report data, or both. Reported results showed that 73% of registries reached out to hospitals to collect data, 7% of registries indicated that hospitals voluntarily reported data to registry, and the remaining 20% reported that they applied both approaches (Figure 3.6). Registries that reach out to hospitals were located in Republique du Congo, Eswatini, Mozambique, Reunion Island, Uganda, Benin, Mali, and in Nigeria. The registry in South Africa was the only one that collected pediatric cancer data from hospitals that voluntarily

reported data to the registry. Registries that used both approaches were in Niger, Seychelles and one registry in Nigeria.

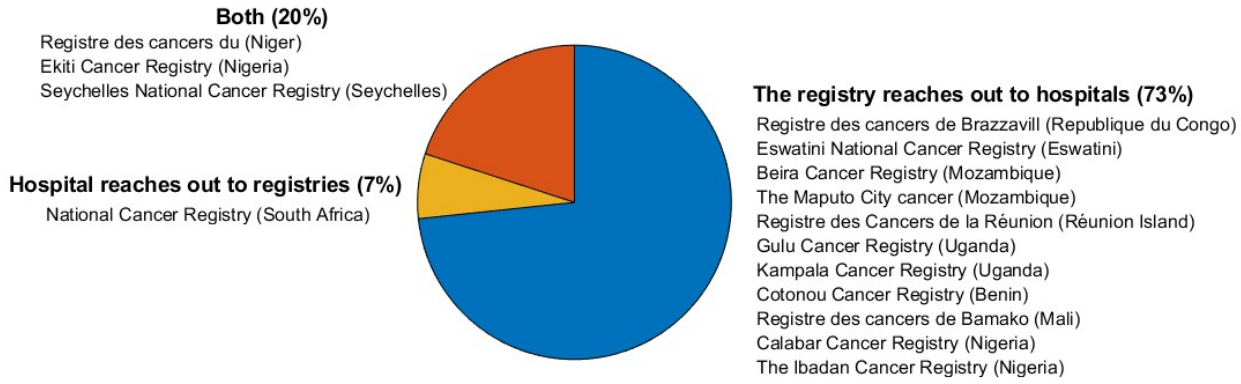


Figure 3.6 Approaches used in collecting the pediatric cancer data

To investigate whether there was an association between the number of FTEs working in the registries and the approach they used to collect data (whether registries reached out to hospitals or hospitals reached out to registries), additional analysis was performed. Results suggested that there was no correlation between number of FTEs working in the registry and the approach used. Registries reached out to hospitals for data collection independently of the staff capacity. Additionally, there was no association between whether registries were located inside a hospital or not with the approach used to collect data.

Question 2.3 and 2.4 were follow-up questions to question 2.2. In question 2.3, information about the name of the hospitals that registries reached out to was listed. In question 2.4, the names of hospitals that voluntarily reached out to registries were collected. This information was not included in this result chapter. However, the number of hospitals involved in data collection was captured to illustrate the magnitude of sources used in data reporting (Table 3.4).

Table 3.4 Number of hospitals involved in data collection

Registry	Country	# of hospitals that registry reach out to collect data	# of hospitals that reach out to registry to report data
Cotonou Cancer Registry	Benin	10	0
Eswatini National Cancer Registry	Eswatini	3	1
Registre des Cancers de la Réunion	France (Reunion Island)	9	0
Registre des cancers de Bamako	Mali	2	0
Beira Cancer Registry	Mozambique	3	0
The Maputo City Cancer Registry	Mozambique	3	1
Registre des cancers du	Niger	6	0
Ekiti Cancer Registry	Nigeria	NA	NA
Calabar Cancer Registry	Nigeria	1	0
The Ibadan Cancer Registry	Nigeria	11	0
Registre des cancers de Brazzavill	République du Congo	7	1
Seychelles National Cancer Registry	Seychelles	1	0
National Cancer Registry	South Africa	0	19
Gulu Cancer Registry	Uganda	9	0
Kampala Cancer Registry	Uganda	10	0

The Cotonou Cancer Registry in Benin reached out to 10 hospitals. Eswatini National Cancer Registry in Eswatini reached out to 3 hospitals, while 1 hospital voluntarily report data to the registry. Registre des Cancers de la Réunion in Reunion Island reached out to 9 hospitals. Registre des cancers de Bamako in Mali reached out to 2 hospitals, Beira Cancer Registry in Mozambique reaches out to 3 hospitals, The Maputo City Cancer Registry in Mozambique reached out to 3 hospitals, and only one hospital report data to the registry. Registre des cancers du in Niger reached out to 6 hospitals, and Calabar Cancer Registry and The Ibadan Cancer Registry in Nigeria reached out to 1 hospital and 11 hospitals, respectively. Registre des cancers de Brazzavill in Congo reached out to 7 hospitals, and 1 hospital reports data to the registry. Seychelles National Cancer Registry in Seychelles reached out to 1 hospital, the National Cancer Registry in South Africa collected data

from 19 hospitals that voluntarily report data to the registry, and Gulu Cancer Registry and Kampala Cancer Registry in Uganda reached out to 9 and 10 hospitals, respectively.

Results from question 2.2 and the follow-up questions 2.3 and 2.4 did not correspond accurately. Question 2.2 addressed how the pediatric cancer data was collected, whether cancer registries reach out to hospitals for data collection or hospitals voluntarily report data to the registry. The follow-up questions asked which hospitals do cancer registry reach out to, and which hospitals reach out to registry to report data. The three registries that reported using both approaches (Registre des cancers du in Niger, Ekiti Cancer Registry and Seychelles National Cancer Registry) only provided the names of the hospitals they reached out to. Therefore, it is not clear whether they were contacted by hospitals or did not provide this information. On the other hand, the Eswatini National Cancer Registry, the Maputo City Cancer Registry and the Seychelles National Cancer Registry reported to have only reached out to hospitals but followed-up by providing names of hospitals that contacted these registries. Therefore, the identified discrepancy was reported.

Further analysis was performed to explore potential association between the location of registries (whether they are in capital cities or rural areas) and the number of hospitals involved in data collection. Results illustrated in Figure 3.7 highlighted a significant overlap of the number of hospitals involved in data collection, thus suggesting that there was no correlation.

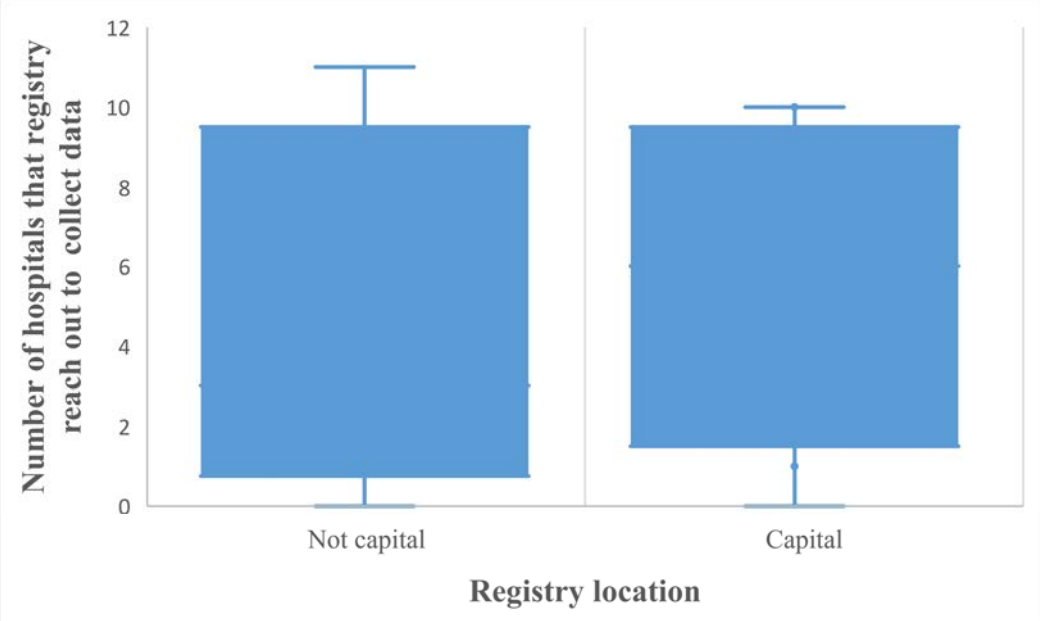


Figure 3.7 Comparison of number of hospitals that reached by the registry versus location of registries.

3.5.2.1 Collection of pediatric cancer data by staff types

To identify who collected the pediatric cancer data in the registries, question 2.5 was included. Results revealed that: 1) in 66.67% of registries, data was collected by registrar only; 2) in 6.67% of registries, data was collected by epidemiologists only; 3) in 6.67% of registries, data was collected by registrar and epidemiologist; 4) in 6.67% of registries, data was collected by registrar and medical students; 5) in 6.67% of registries, data was collected by registrar, epidemiologist, administration and social worker; and 6) 6.67% of registries did not respond to the question (Figure 3.8). Registrars were dominantly responsible for data collection across cancer registries. In cancer registries that did not have a registrar, epidemiologists were responsible for data collection. Moreover, administration staff, social workers and medical students were involved in data collection despite that their main responsibilities did not include this task, likely due to lack of personnel resources and limited number of staff. For example, Calabar Cancer Registry in

Nigeria reported that administrative staff and social workers collected data. Also, Registre des cancers de Bamako in Mali reported that medical students were involved in data collection. If tasks of data collection and reporting were beyond the area of expertise for staff working in registries, that could create additional burden on FTEs and might lead to jeopardizing the quality of data entry and control.

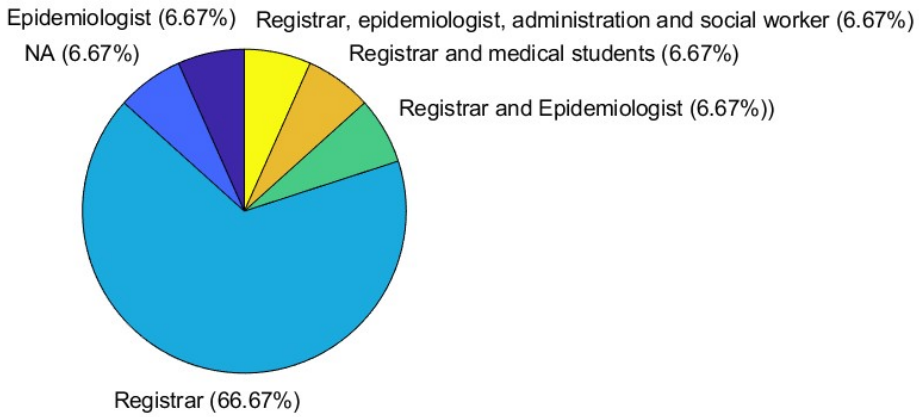


Figure 3.8 Collection of pediatric cancer data in cancer registries by staff types

3.5.2.2 Connection of data to other local or international registries

The aim of question 2.6 was to determine whether registries connected their data to other local registries. Figure 3.9A illustrates the answers provided in the questionnaire. Data showed that 4 out of 15 (27%) registries have their data connected to other local registries. These registries were Ekiti Cancer Registry in Nigeria, Registry des cancers de Bamako in Mali, National Cancer Registry in South Africa and Registre des cancers da la Reunion in Reunion Island. The low prevalence of connection between local registries could be due to the lack of collaboration and the disconnect of data exchanges. It is unclear, however, whether this disconnect is associated to limited communication, registry location, or absence of other local registries in the country. For

example, the Ekiti Cancer Registry in Nigeria reported to be connected to other local registries, but the Calabar Cancer Registry and the Ibadan Cancer registry in Nigeria did not. This result was surprising given that these registries are part of both NSCR and AFCRN, which hypothetically could aid in linking registries and increase interactions.

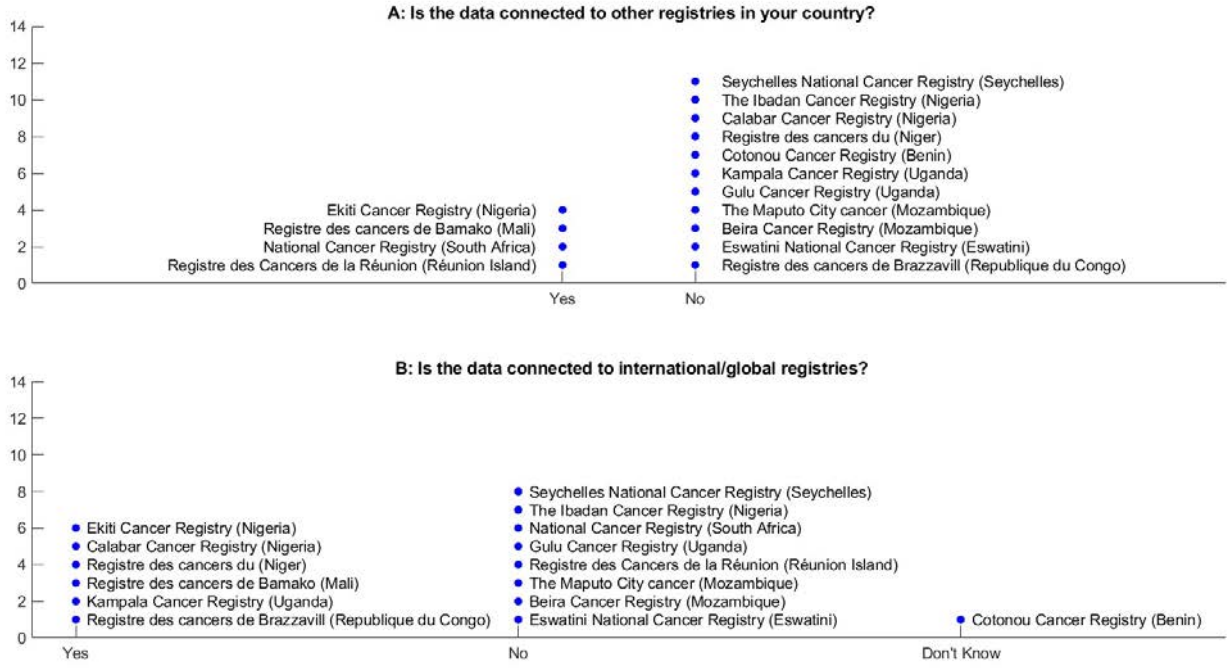


Figure 3.9 Connection between registries with other local or international registries

The assessment of whether registries connected their data to other international or global registries was an important aspect to investigate data sharing and reporting in the region. Hence question 2.7 was designed. Figure 3.9 highlights that 6 out of 15 (40%) registries had data connected to international registries, while 8 out of 15 (53%) did not, and 1 out of 15 (7%) did not provide an answer. Surprisingly, the response regarding data connection to international or global registry compared to data connection to local registry showed favorable number for international and global registries. Registries did not report which local or international registries their data were

connected to, and available sources that would confirm this information could not be identified. It would have been beneficial to add a question in the questionnaire to outline the reason for not connecting the data.

The type of database that is used is also an important aspect of how easily data can be collected and compared between registries. There are several different options including publicly available software, such as CANReg, or registries that may have their own in-house system. Evaluating how many registries are using CANReg5 database was addressed in question 2.8. CANReg5 database is an open platform that was developed by the International Agency for Research on Cancer in collaboration with the International Association of Cancer Registries (IACR). Members of the Association obtain an access to this software free of charge. CANReg5 tool could be used in cancer registry data storing, data entry and analysis. CANReg5 is an improved version of CANReg4, after enhancement of functions and features (International Association of Cancer Registries). For example, an improved database engine was implemented in the CANReg5, which enabled multiuser capabilities (International Association of Cancer Registries, 2021). CANReg5 became available in 2010, and it has a feature to support the process of data migration from CANReg4 (International Association of Cancer Registries, A brief introduction to CanReg5, 2012).

When registries were asked which data bases were being used, the response indicated that 12 out of 15 (80%) registries used CANReg5 database, while 3 out of 15 (20%) registries did not use it (Figure 3.10). The three registries that did not use CANReg5 used instead CANReg4 or a local database on Microsoft Access. Notably, one of the registries that did not use CANReg5 is the Ibadan Cancer Registry in Nigeria, even though the other 2 registries from Nigeria who participated

in the questionnaire used CANReg5. Using standardized databases, tools, and platforms to collect and analyze data is an important factor for improving the quality of data collection. In addition, integration of data from multiple registries could facilitate easier data access and normalization. It is not clear why some registries are not using this platform despite the free access, and there was no publicly available information to explain the reason.

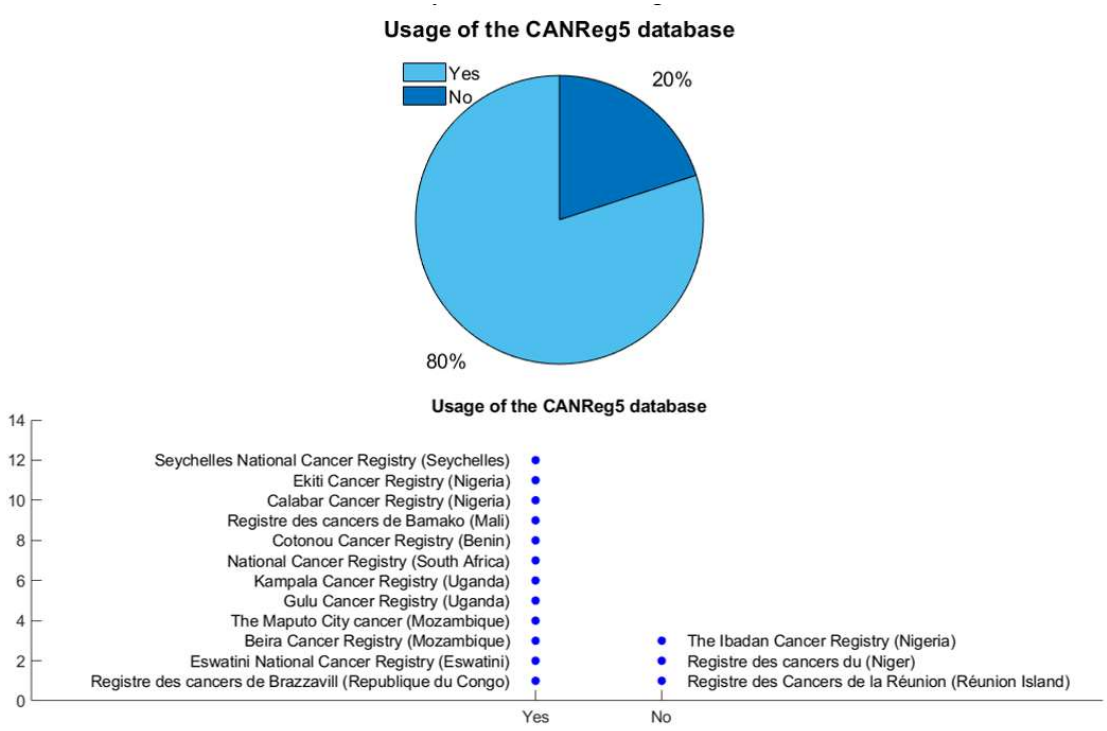


Figure 3.10 ***Usage of CANReg5 database***

3.5.3 Sources of pediatric cancer data

The third section of the questions aimed to gather information about the sources of pediatric cancer data used in data collection. Question 3.1 was incorporated to explore whether registries were collecting data from hospitals treating childhood cancer. Results revealed that 12 out of 15 registries collected childhood cancer data, and 3 out of 15 did not collect childhood cancer data (Figure 3.11). The three registries that indicated they did not collect pediatric cancer data are:

Calabar Cancer Registry in Nigeria, Beira Cancer Registry in Mozambique, and Eswatini National Cancer Registry in Eswatini. The proportion of children from the population covered in the area by these registries are 32%, 39% and 36%, respectively. Hence, it is unclear why these registries do not collect pediatric cancer data. However, there are multiple cancer registries in Nigeria and Mozambique, which may suggest that specific registries are designated to collect pediatric cancer data. There is no information available in the public domain to explain or confirm the response reported to this question.

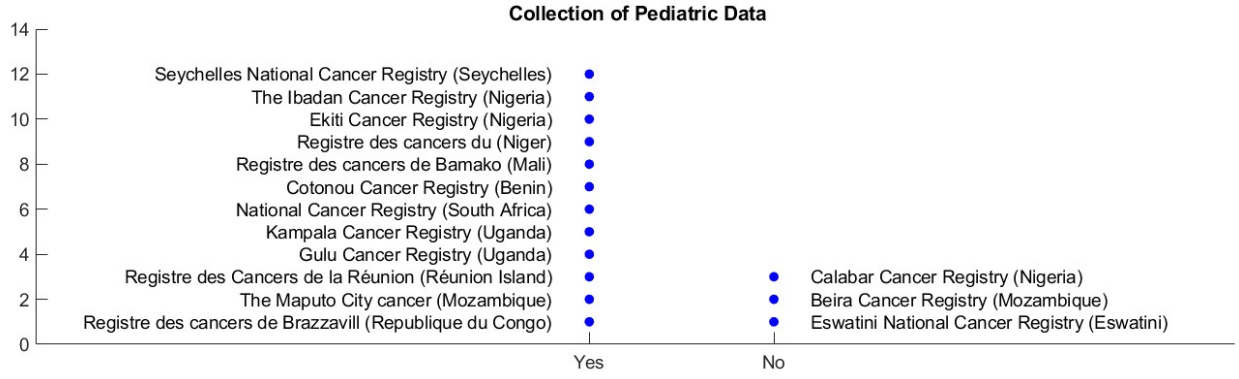


Figure 3.11 Collection of data from hospitals treating childhood cancer

The aim of question 3.2 was to identify sources used by registries to collect pediatric cancer data. Hence, a list of potential data sources was provided to registries in the questionnaire for selection. Registries were also asked to indicate the prevalence of various sources utilized. The sources provided included imaging departments (CT and/or MRI, ultrasound, X rays), radiotherapy departments, pathology lab, hematology lab, public hospital, specialist oncology units, private hospital/clinic, health insurance providers, neurosurgery and other. As illustrated in Figure 3.12, pathology labs were the most common source used to collect data followed by hematology labs, public hospitals, private hospitals/clinics, imaging departments, specialist oncology units,

radiotherapy department, neurosurgery, and health insurance providers, respectively. Registre des Cancers de la Réunion in Reunion Island collected data from an additional source, which is the regional cancer network.

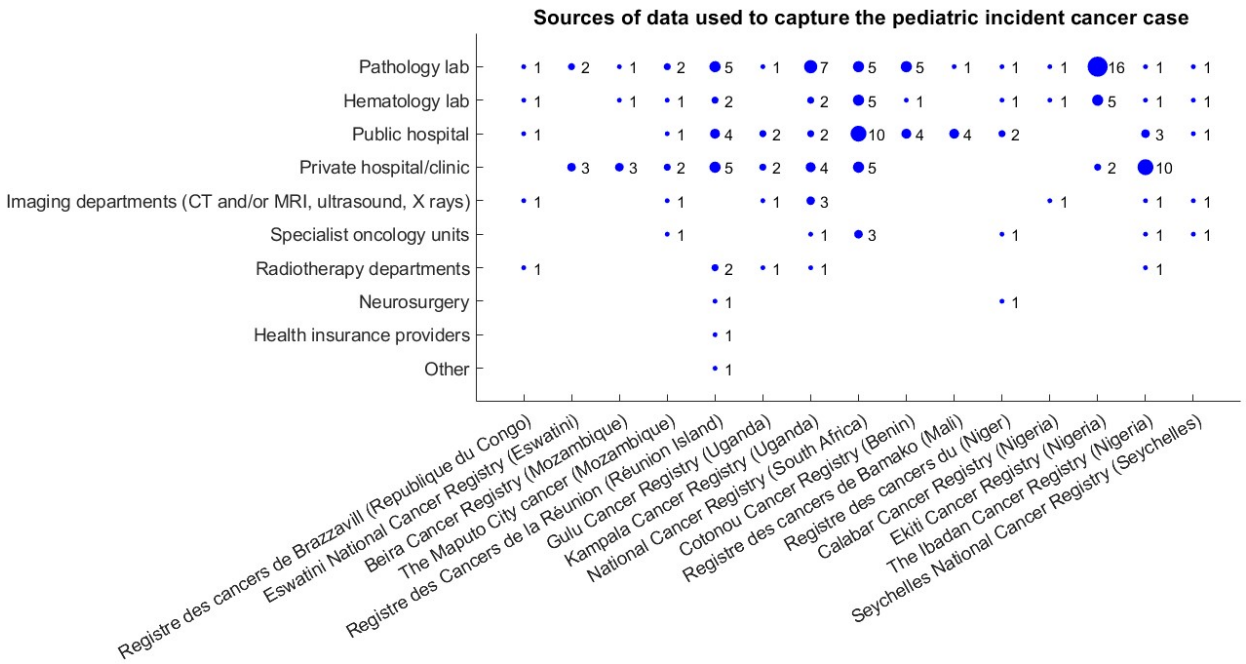


Figure 3.12 Sources of data used to capture the pediatric cancer incidence in each registry
Dot plot illustrating the distribution of sources of data used to capture pediatric cancer incidence by each registry. Size of the dot represents the number of sources used.

Results showed that 15 out of 15 registries collected data from pathology labs. The highest number of pathology labs used by a registry was 16 by the Ekiti Cancer Registry in Nigeria. Moreover, 12 out of 15 registries used hematology labs to collect data. The 3 registries that did not use hematology labs were: Eswatini National Cancer Registry in Eswatini, Gulu Cancer Registry in Uganda, and Register des Cancers de Bambako in Mali. The highest number of hematology labs used by a registry was 5 (The National Cancer Registry in South Africa and Ekiti Cancer Registry in Nigeria). Public hospitals were used for data collection by 11 out of 15 registries. The 4 registries

that did not use public hospitals were Eswatini National Cancer Registry in Eswatini, Beira Cancer Registry in Mozambique, Calabar Cancer Registry and Ekiti Cancer Registry in Nigeria. The highest number of public hospitals used was 10 by The National Cancer Registry in South Africa. Furthermore, 9 out of 15 registries used private hospitals and clinics in data collection. The highest number of private hospitals used was 10 by the Ibadan Cancer Registry in Nigeria. The imaging department was used by 7 out of 15 registries, and 6 out of 15 registries used specialist oncology units. Finally, 5 out of 15 registries used radiotherapy departments to collect data, and the Registre des Cancers de la Réunion in Reunion Island was the only registry to use either neurosurgery department, health insurance company or other sources. Even though three cancer registries reported that they did not collect pediatric cancer data in question 3.1, they reported in this follow-up question that they used some of the sources to collect data. It is not clear whether they misunderstood the current question or provided a wrong answer to the previous one.

A few trends were observed in the data collected from question 3.2. The first trend highlighted that the registries underutilized imaging departments to collect CT, MRI and ultrasound scans, despite that these tools provide extremely valuable data for the diagnosis and prognosis of childhood cancer. This could be due to the high cost of CT scans, MRI, and the imaging equipment as well as the limited availability of scans in cancer hospitals. Based on publicly available sources, the estimated cost of an MRI in Uganda is approximately 650,000 Ugandan Shilling, which is equivalent to 185 U.S dollars (Nabawanuka, 2014). Moreover, the cost of the CT scan in Nigeria ranges between 34,000 and 40,000 Nigerian Naira, which is roughly 97 U.S dollars (Osakwe, 2017). Another trend showed that registries from the same country relied on different sources for data collections. For example, only one of the 2 registries in Mozambique (The Maputo Cancer

Registry) used public hospitals as a source for data collection, but the Beira Cancer Registry used private hospitals. Moreover, one of the registries used 6 sources while the other used only 3 sources to collect data. In Uganda, one of the two registries (Gulu Cancer Registry) did not use hematology labs for data collection despite being a common source of data across registries. This registry utilized pathology labs, public hospitals, and private hospitals as a source of data collection. In addition, the total number of data sources utilized by the Gulu Cancer Registry was 7 compared to a total of 20 sources used by the Kampala Cancer Registry. In Nigeria, one of the three registries relied heavily on pathology labs for data collection (16 labs) compared to the other 2 registries that used only one pathology lab. In addition, one of the three registries in Nigeria used 7 sources for data collection compared to 3 sources used by the other 2 registries. This variation of data source utilized across registries in the same country could be due to geographical location of the registry, the distance to the data source, agreements with the source of data, or the number of populations covered by the registry.

Reporting death data is critical in assessing cancer mortality rates and it is an important component in evaluating the burden of cancer. Thus, question 3.3 was incorporated in the questionnaire to verify if registries used death certificates as a source of information on cancer cases. Results showed that 67% of registries used death certificates, and 33% did not use death certificates as a source of information. Based on what was reported by cancer registries, hospitals were the most common source to access death certificates compared to birth and death registration departments (Figure 3.13). Cancer registries, which did not collect death certificates, did not explain whether this was due to lack of resources or regulations that limits their access to the data. Some LICs might apply restrictions to accessing death certificate data or lack in efficiency to

process the data request (Sankoh, et al., 2020). Thus, improving the process of collecting death certificates is needed to provide a more realistic estimation of mortality rates in LICs.

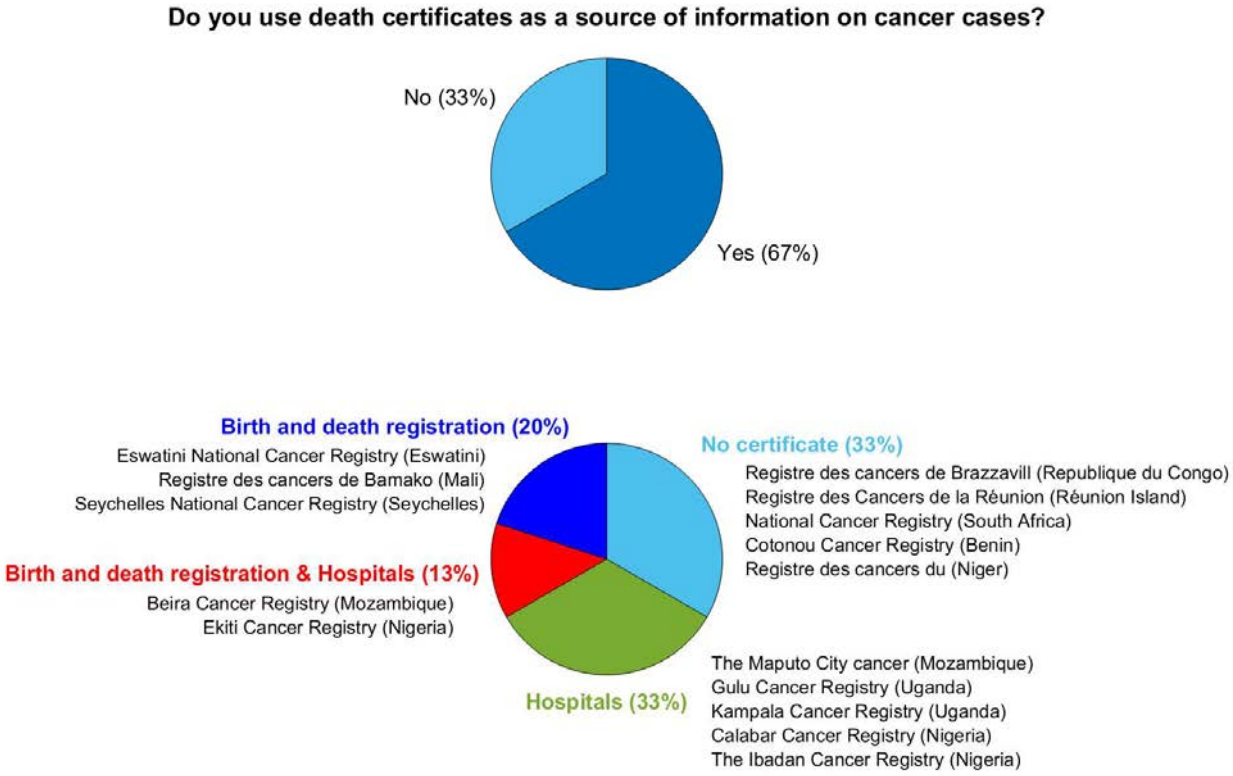


Figure 3.13 Usage of death certificates as a source of information on cancer cases

To investigate whether data collection by registries was obtained by voluntary collaboration or was a part of legal or formal agreement question 3.4 was included. Based on the response to this question (Figure 3.14), 9 out of 15 registries collected data through voluntary collaboration, 4 out of 15 registries collected data as part of legal agreement, 3 out of 15 registries collected data through formal framework, and 1 out of 15 registries did not provide an answer. In addition, 2 registries that collect data through voluntary collaboration also collected data through legal agreements. The combination of both approaches could be beneficial and might lead to an efficient

data collection process. Based on the data reported from cancer registries, it was not clear what type of legal agreements or formal framework were in place to collect data.

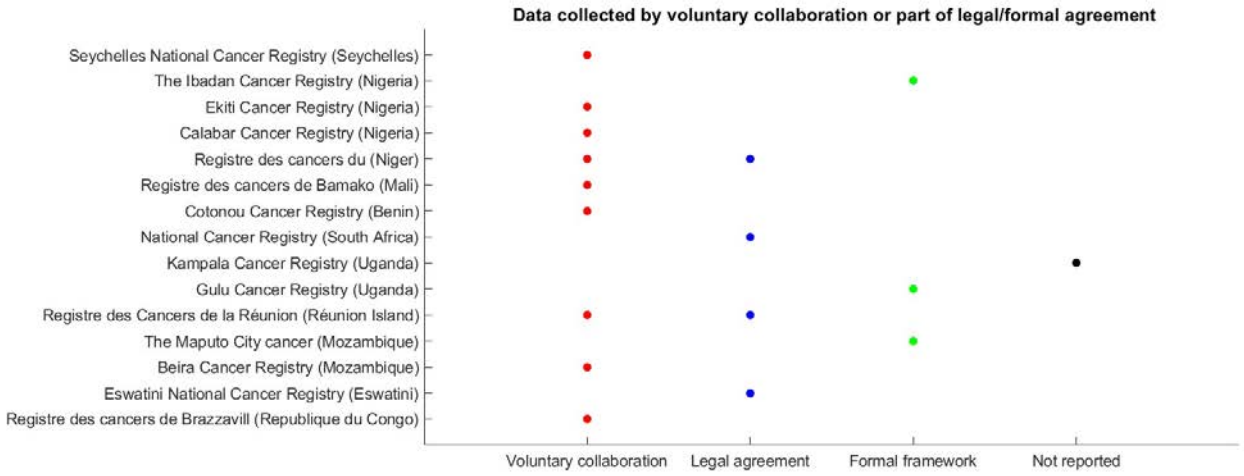


Figure 3.14 Data collection by voluntary collaboration and/or as part of a legal/formal agreement between registries and data sources

To investigate whether cancer registries recorded data on all pediatric cancer cases or only on residents of the population-base question 3.5 was incorporated. Another aim of this question was to understand the magnitude of pediatric cancer cases reported by cancer registries in the past 12 months, and whether these cases were reported for the entire population covered or only for residents. This information could allow contextualizing the current available resources at each registry in terms of population covered and data entries. Results showed that 7 out of 15 registries recorded data on all pediatric cancer cases from the sources used by the registry (Figure 3.15). Moreover, 6 out of 15 registries collected data only on residents of the population-base, and 2 out of 15 registries did not provide an answer. In addition, the response to this question from registries within the same country was consistent in Mozambique and Uganda. The 2 registries in Mozambique recorded data on all pediatric cancer cases, and the 2 registries in Uganda recorded

data only on residents. On the other hand, the responses from the three registries in Nigeria were not consistent. For example, The Ibadan Cancer Registry recorded data on all pediatric cancer cases, the Calabar Cancer Registry recorded data only on residents, and Ekiti Cancer Registry did not provide an answer.

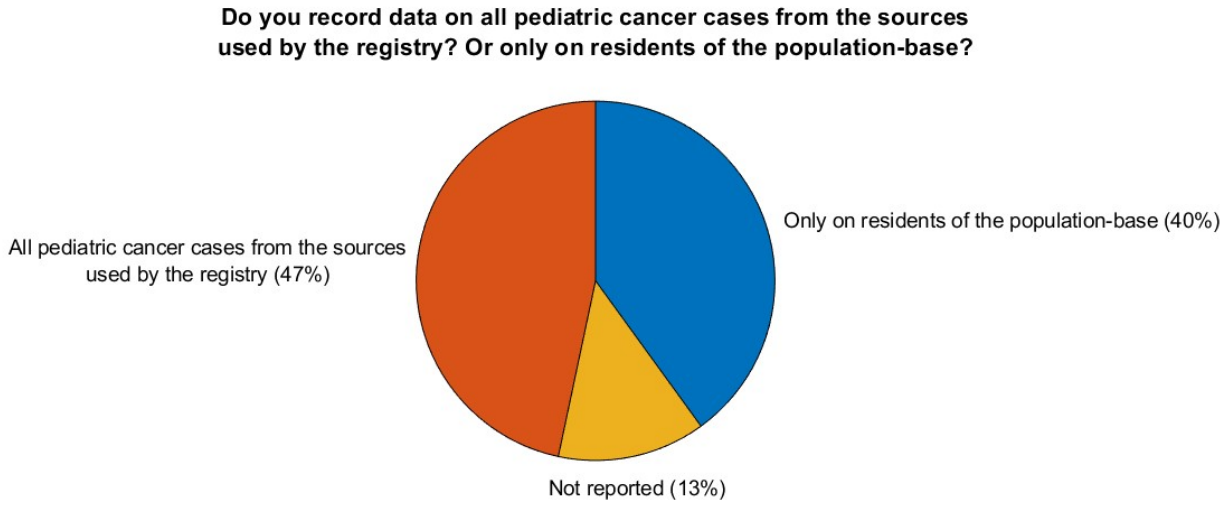


Figure 3.15 Collection of data on all pediatric cancer cases from the sources used by the registry versus data collected only from residents of the population-base

The approximate number of pediatric cancer cases registered in the last 12 months (2019/2020) was evaluated in question 3.6. The National Cancer Registry in South Africa had the highest number of pediatric cancer cases, with 2000 cases reported in the last 12 months. The Kampala Cancer Registry in Uganda was the second highest with 1500 cases. Overall, the total number of cases reported by the remaining 13 registries combined was significantly smaller compared to the number of cases reported by the first 2 registries (Figure 3.16). Registre des cancers de Bamako in Mali reported 131 cases, The Maputo City Cancer Registry in Mozambique 120, Registre des cancers de Brazzavill in Congo 104, The Ibadan Cancer Registry in Nigeria 61, Gulu Cancer Registry in Uganda 54, Registre des Cancers de la Réunion in Reunion Island 35,

Registre des cancers du in Niger 30, Cotonou Cancer Registry in Benin 23, Ekiti Cancer Registry in Nigeria 7, Beira Cancer Registry in Mozambique 16, Eswatini National Cancer Registry Eswatini 15, Calabar Cancer Registry in Nigeria 10, and Seychelles National Cancer Registry in Seychelles 5. Data illustrated that, in Nigeria, the number of cases reported across the 3 registries were similar, with 10, 17 and 61 cases, respectively. Notably, in Uganda, the number of cases reported by the 2 registries were significantly different (1500 and 54).

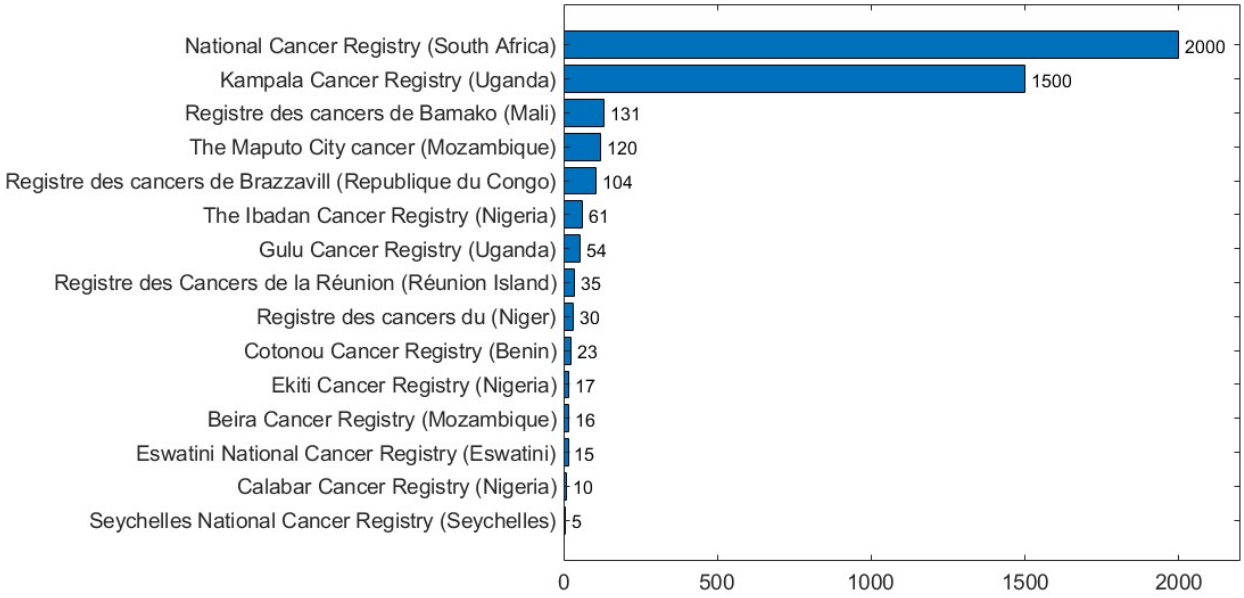


Figure 3.16 The approximate number of pediatric cancer cases registered in the last 12 month (2019/2020)

To understand differences in cases reported from registries across and within countries, a table listing the incidence of pediatric cancer cases per 100,000 population was generated (Table 3.5). The incidence was computed by dividing the number of pediatric cancer cases by the pediatric population covered by the registry and multiplying this ratio by 100,000. Data revealed that the incidence of pediatric cancer cases across countries varied widely, with the highest incidence reported in the Kampala Cancer Registry in Uganda (165.1) and the lowest incidence reported in

the Eswatini National Cancer Registry (3.9). This variation could be due to the difference in population number covered by the registry or environmental and socioeconomic factors resulted in increasing cancer incidence in particular areas.

Table 3.5 Pediatric cancer cases and the incidence rate per 100K populations

Cancer Registry	Country	Pediatric country population ages 0-14	Pediatric population covered by registry ages 0-14	Number of pediatric cancer cases reported by registry in the last 12-month (2019-2020) ages 0-14	Pediatric cancer incidence per 100K population covered by registry ages 0-14	Predicted new pediatric cases per year per country population ages 0-14
Cotonou Cancer Registry	Benin	5,091,744	245,298	23	9.4	477
Eswatini National Cancer Registry	Eswatini	440,862	389,192	15	3.9	17
Registre des cancers de Bamako	Mali	9,517,892	701,368	131	18.7	1,778
Beira Cancer Registry	Mozambique	13,752,391	206,936	16	7.7	1,063
The Maputo City Cancer Registry	Mozambique	13,752,391	492,000	120	24.4	3,354
Registre des cancers du	Niger	12,103,322	NA	30	NA	NA
Calabar Cancer Registry	Nigeria	90,701,419	160,665	10	6.2	5,645
Ekiti Cancer Registry	Nigeria	90,701,419	NA	17	NA	NA
The Ibadan Cancer Registry	Nigeria	90,701,419	1,167,936	61	5.2	4,737
Registre des cancers de Brazzavill	République du Congo	2,317,597	847,000	104	12.3	285
Registre des Cancers de la Réunion	Réunion Island	286,500	197,152	35	17.8	51
Seychelles National Cancer Registry	Seychelles	23,603	NA	5	NA	NA
National Cancer Registry	South Africa	17,199,520	16,899,287	2000	11.8	2,036
Gulu Cancer Registry	Uganda	21,498,273	192,664	54	28.0	6,026
Kampala Cancer Registry	Uganda	21,498,273	908,743	1500	165.1	35,486

Data from Table 3.5 also illustrated that the incidence of pediatric cancer cases per 100K population ages 0-14 within countries was either similar or significantly different depending on the country investigated. For example, in Nigeria the incidence of pediatric cancer cases was comparable across registries, with the Calabar Cancer Registry reporting a value of 6.2 per 100K and the Ibadan Cancer Registry reporting a value of 5.2 per 100K. In contrast, the incidence of pediatric cancer cases in Mozambique and Uganda varied significantly, with values ranging from 7.7 to 24.4 per 100K in Mozambique and from 28 to 165.1 per 100K in Uganda. Overall, these results suggested that there is a significant difference of incidence rate within the same country. This difference could be due to various risk factors that contribute to increasing the number of pediatric cancer cases, such as environmental, socioeconomic and others.

To investigate whether the pediatric cancer incidence rate reported by registries was comparable to that reported by publicly available sources, additional analysis was performed. Publicly available data was obtained from the WHO and GLOBOCAN 2020 datasets and used for this analysis (Table 3.6). Pediatric cancer cases were reported for 10 out of 11 countries, as data on Reunion Island were not available. Notably, publicly available datasets do not overlap in the same year period. The total number of pediatric cancer cases, in the selected countries, was reported by WHO and GLOBOCAN for the year of 2020. In contrast, the number of pediatric populations per country was only available for the year of 2019 and not for 2020. The incidence rate was computed using the data reported in 2019 and 2020 based on the assumption that the number of pediatric populations in 2019 was equal to that in 2020, which should not significantly bias the estimation of the true incidence rate in 2020. Incidence rate was calculated by dividing pediatric cancer cases by the total number of pediatric populations in the country and multiplying it by 100,000.

Comparison between incidence rates obtained from cancer registries and publicly available databases is illustrated in Table 3.6. Incidence rates for Benin, Eswatini, Mali, Mozambique, Niger, Nigeria, République du Congo, South Africa and Uganda were retrieved from the GLOBOCAN database using a dynamical browser (International Agency for Research on Cancer, 2021). Incidence rates for Eswatini, Mozambique, Nigeria, Seychelles, South Africa and Uganda were retrieved from the Cancer Country Profile WHO database, which provided cancer pediatric information and statistics for several African countries (WHO, Cancer Country Profile, 2020).

Table 3.6 Pediatric cancer incidence rate reported by registries and obtained from publicly available sources

Cancer Registry	Country	Pediatric cancer incidence per 100K population covered by registry ages 0-14	Pediatric cancer incidence per 100K population by WHO	Pediatric cancer incidence per 100K population by GLOBOCAN	Number of pediatric cancer cases reported in 2020 by WHO	Number of pediatric cancer cases reported in 2020 by GLOBOCAN
Cotonou Cancer Registry	Benin	9.4	NA	5.0	NA	257
Eswatini National Cancer Registry	Eswatini	3.9	9.8	4.5	43.0	20.0
Registre des cancers de Bamako	Mali	18.7	NA	10.6	NA	1,013
Beira Cancer Registry	Mozambique	7.7	13.5	11	1,853	1,580
The Maputo City Cancer Registry	Mozambique	24.4				
Registre des cancers du	Niger	NA	NA	5.7	NA	688
Calabar Cancer Registry	Nigeria	6.2	13.1	7.3	11837	6647
Ekiti Cancer Registry	Nigeria	NA				
The Ibadan Cancer Registry	Nigeria	5.2				
Registre des cancers de Brazzavill	République du Congo	12.3	NA	5.6	NA	129
Registre des Cancers de la Réunion	Réunion Island	17.8	NA	NA	NA	NA
Seychelles National Cancer Registry	Seychelles	NA	8.5	NA	2	NA

National Cancer Registry	South Africa	11.8	9.8	8.3	1688	1430
Gulu Cancer Registry	Uganda	28.0	13.2	9.8	2833	2110
Kampala Cancer Registry	Uganda	165.1				

Results highlighted that incidence rates from WHO and GLOBOCAN were comparable with those reported from the registry in South Africa. In contrast, significant discrepancy was detected between incidence reported from registries in all the other countries compared to public databases. For example, in Benin the incidence rate reported by the registry was 9.4 compared to 5.5 reported by GLOBOCAN, in Mali the incidence rate reported by registry was 18.7 versus 10.6 reported by GLOBOCAN, and in Uganda a significant discrepancy was observed between incidence rates reported by the two registries (28.0 and 165.1) compared to those reported by WHO and GLOBOCAN (13.2 and 9.8), respectively. These three examples might suggest that public databases could be underreporting the true pediatric cancer incidence in these countries. On the other hand, the incidence rates reported in Nigeria by two registries were 6.2 and 5.2, whilst the incidence rates reported by WHO and GLOBOCAN were 13.1 and 7.3, respectively. This result could imply that publicly available databases might be overreporting the true incidence rate in Nigeria. In Eswatini, the incidence rate reported by the registry (3.9) was comparable to the rate reported by GLOBOCAN (4.5) but varied from the one reported by WHO (9.8). In Mozambique, the outcome of the comparison led to a mixed interpretation of the results. The incidence rates reported by the two registries in Mozambique were 7.7 and 24.4, while the WHO and GLOBOCAN reported incidence rate of 13.5 and 11, respectively. Therefore, selecting 7.7 as incidence rate for comparison could suggest that databases are overreporting data, whereas choosing 24.4 as incidence rate would suggest that the databases are underreporting data. In Niger, Seychelles, and

Reunion Island, comparison between incidence rates was not possible due to the absence of data by either the registries or the publicly available databases. Interestingly, pronounced discrepancies among data from WHO and GLOBOCAN databases was also detected for incidence rates reported for Eswatini, Nigeria, and Uganda.

Assuming that the pediatric cancer incidence reported by the registries was representative of the whole country would hypothetically enable predicting the total number of pediatric cancer cases per country using the total pediatric population. Based on this assumption, the total number of cases per country was predicted by multiplying the incidence rate by the country pediatric population and divided it by 100,000 (Table 3.5).

Access to databases is a critical aspect of data collection and reporting. Therefore, the aim of question 3.7 was to understand whether cancer registries were able to access computer databases to gather all information necessary to register a child with cancer. Reported response revealed that 40% of registries could access computer databases to gather all information needed to register a child, 40% of registries could not, and 20% of registries could sometimes collect the information needed to register a child (Figure 3.17).

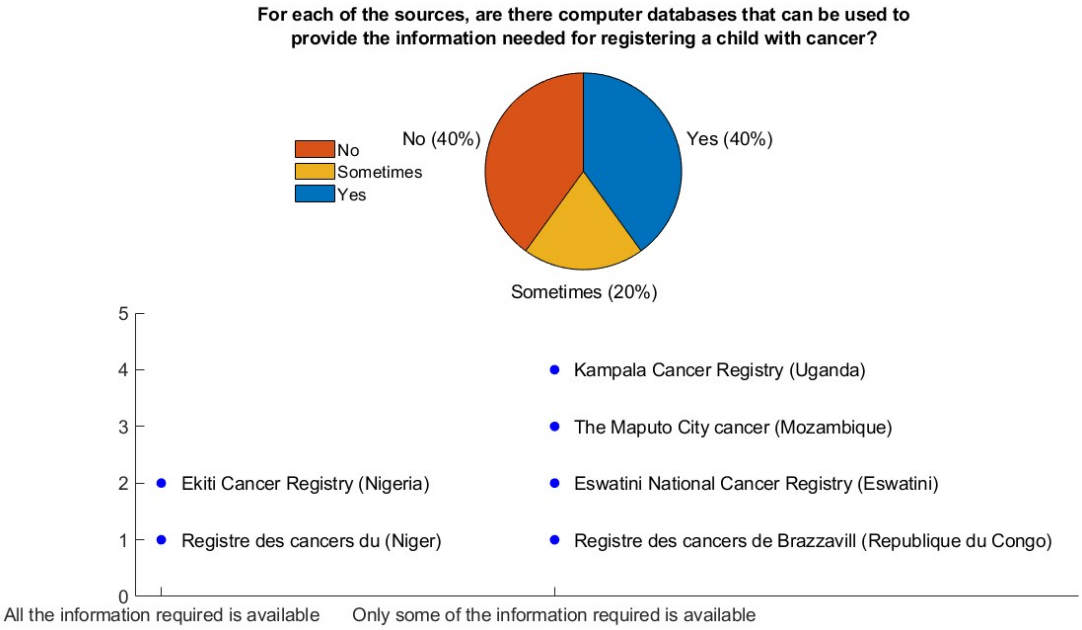


Figure 3.17 Access to computer databases that can be used to provide the information needed for registering a child with cancer

3.5.4 Types of pediatric cancer data

The fourth section of the questionnaire was designed to evaluate the type of pediatric cancer data collected by the registry. To this end, three questions were included in the questionnaire. In question 4.1.1, registries were asked what test results and diagnosis data were collected. Results demonstrated that 14 out of 15 registries collected tumor biopsy data, 10 out of 15 registries collected bone marrow aspirate data, 9 out of 15 registries collected blood test results, 6 out of 15 registries collected current treatment information, 3 out of 15 registries collected previous treatment data, and 2 out 15 registries collected initial treatment data. Question 4.1.2 was focused on listing patients' contact information and follow-up data. Analysis of provided responses showed that 13 out of 15 registries collected contact data, 12 out of 15 registries collected date of last contact, 11 out of 15 registries collected phone number of parents or guardian of the child and status at the last contact, 5 out of 15 registries collected date of next follow-up appointment, and 4

out of 15 registries collected long term survival data. Question 4.1.3 was added to explore whether registries collected stage of the disease data. Results indicated that 13 out of 15 registries collected stage of the disease data, 9 out of 15 registries collected laterality (for retinoblastoma patients), and 8 out of 15 registries collected information about the system used in staging the disease. A summary of the responses to the three questions is reported in (Table 3.7). Data indicated that previous and initial treatments were collected by small number of registries, which could suggest that there are gaps in the accuracy of assessment of the current treatment. The absence of information about previous treatment and its clinical outcome could significantly impact the response to the current treatment. Data also revealed that a small number of registries collected long term survival data, which could lead to misreporting survival and mortality rates in a given county. Collecting incomplete data sets could lead to pediatric cancer data underreporting.

Table 3.7 Types of pediatric cancer data collected

4.1.1 Test results and diagnosis data	**Total # of registries**	**Percentage**
Tumor biopsy results	14/15	93.3%
Bone marrow aspirate data	10/15	66.7%
Blood test results	9/15	60%
Current treatment	6/15	40%
Previous treatment	3/15	20%
Initial treatment	2/15	13.3%
4.1.2 Contact information and follow-up		
Name of contact person	13/15	86.7%
Date of last contact	12/15	80%
Phone number of parents or guardian of the child	11/15	73.3%
Status at the last contact	11/15	73.3%
Date of next follow up appointment	5/15	33.3%
Long term survival	4/15	26.7%
Other	1/15	6.7%
4.1.3 Stage of disease data		
Stage of the disease	13/15	86.7%
Laterality (for retinoblastoma patients)	9/15	60%
The system used in staging the disease	8/15	53.3%

To assess whether registries in LICs collect the same type of data collected by registries in HICs, a comparison was performed. This comparison revealed that registries in HICs generally collect more data and detailed information about pediatric patients. For example, The Danish Childhood Cancer Registry (DCCR) reported that data collected include "tumor type, extent of disease (localization of metastases), date of diagnosis, date of start of therapy, type of therapy, treatment protocol, response to initial therapy, date of cessation of therapy, relapse, yearly follow-up, and disease status "(alive in complete remission, alive with active disease, development of secondary malignancy, death: date and cause of death)" (Schrøder, et al., 2016). Similarly, data collected by cancer registries in the U.S. includes medical history, diagnosis, tumor types, previous treatment, and follow-up (National Cancer Registrars Association, 2021). Differences observed in types of data collected may highlight the need for registries in LICs to improve their process of data collection.

3.5.5 Use of cancer registry results in pediatric cancer control

The fifth section of the questionnaire aimed to assess how cancer registries utilized data in pediatric cancer control. Question 5 investigated whether the registry had any formal contact with local or national department/s of health. Response showed that 60% of registries had formal contact with both local and national health departments, 20 % of registries had contact with national ministry of health, 13% had contact with local health department, and 7% had no contact with any health department (Figure 3.18). As a follow up question on the contact of registries with health departments, question 5.2 assessed the registry interactions with local and/or national health departments. Three types of potential interactions to select from were provided in the questionnaire:

1) during joint meeting; 2) response to requests for information on cancer; or 3) planning of cancer services (including cancer surveillance and screening planning). Results indicated that 13 out of 15 registries had contact with health departments either by one or more ways of interaction, and 2 out of 15 registries did not provide an answer (Figure 3.19).

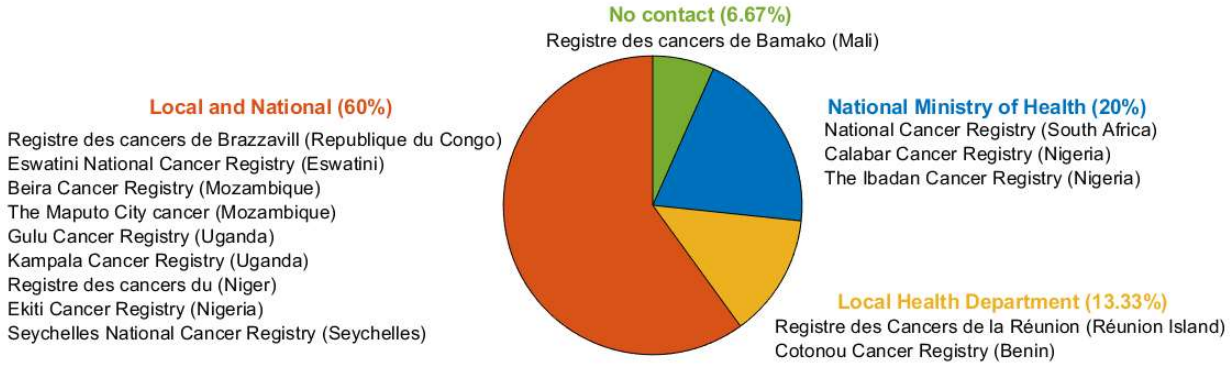


Figure 3.18 Formal contact between registries and departments of health

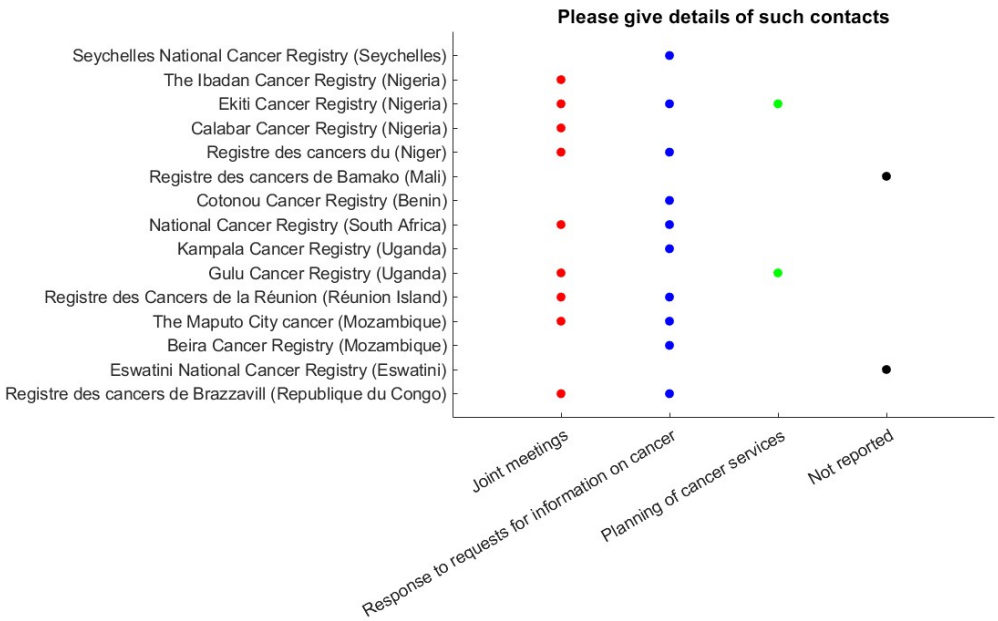


Figure 3.19 Types of interactions between registries and departments of health

Given the importance of having cancer control plan in every country, question 5.3 was included to address the existence of a national plan in the country/region where registries are located. Cancer control plans provide a defined strategy to control cancer by health authorities in the country for five or more years. The cancer control plan usually covers a wide spectrum of stages including, prevention, screening, diagnosis, treatment, cancer data reporting, and overseeing cancer registries. Response to this question indicated that 87% of registries had a national cancer control plan in place. These registries are in Congo, Eswatini, Mozambique, Reunion Island, Uganda, South Africa, Niger, Nigeria, Benin, and Seychelles. The cancer control plans in these countries include a pediatric cancer plan. 13% of registries did not have a plan. Among the registries that had a plan in place, 9 registries indicated that ministry of health was responsible for the plan, and 4 registries reported that the national cancer control was responsible for the plan. Moreover, 76% of registries that had a plan indicated that a member of the cancer registry was involved in preparing the plan, whereas 15% reported that no one was involved, and 7% did not provide an answer (Figure 3.20)

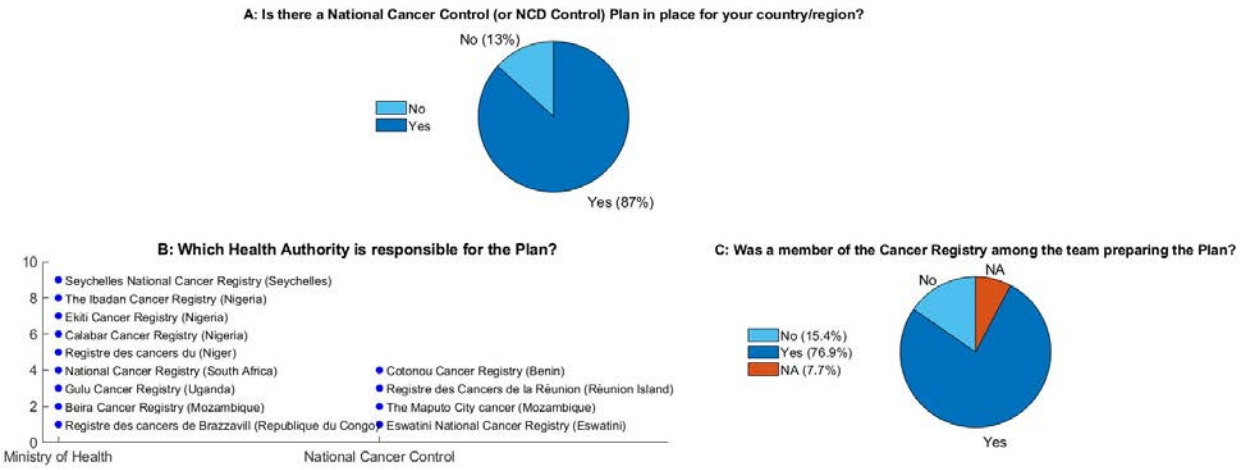


Figure 3.20 National cancer control (or NCD Control) plan in place in each country/region

A: Pie plot illustrating whether registries had a national cancer control plan in place. B: Dot plot depicting the health authority responsible for the plan. C: Pie plot showing the contribution of registries in preparing the plan

GLOBOCAN database is a source of cancer incidence and mortality in approximately 186 countries worldwide. The aim of question 5.5 was to assess the inclusion of pediatric cancer data from registries in GLOBOCAN published data in 2018. 7 out of 15 registries had their data included in the GLOBOCAN 2018 national estimate, 4 out of 15 registries did not have their data included, and 4 out of 15 registries did not know if their cancer data was included in GLOBOCAN national estimate (Figure 3.21).

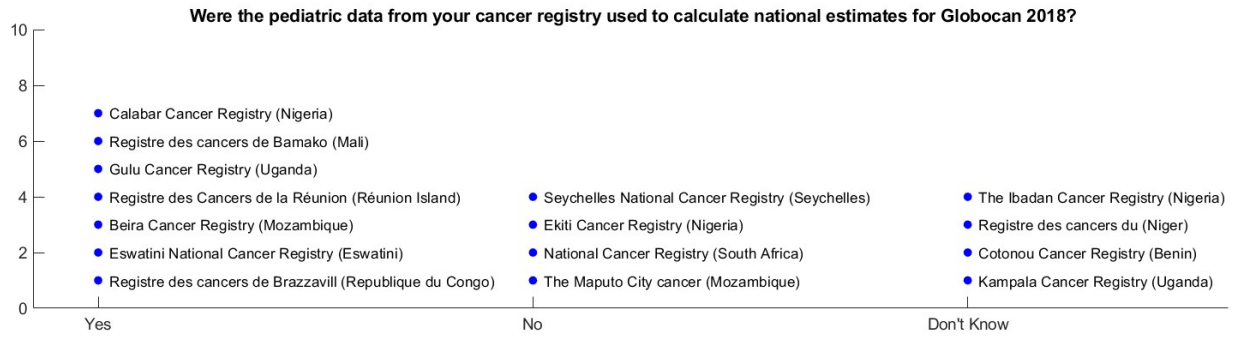


Figure 3.21 Inclusion of the pediatric cancer data from cancer registries in GLOBOCAN 2018

Factors that could have contributed to the lack of awareness of the 4 registries about including their data in GLOBOCAN national estimate were explored. For example, the ratio of number of FTEs working in the registry to the number of populations covered, as an indication of the workload per FTE, provided a possible pattern of association with this outcome. 3 out of the 4 registries had a small number of FTEs (1, 1.5 and 3.5), which could generally impact the capacity of staff performance. However, the 4th registry had 10 FTEs with low workload assessment. Hence, this assumption might not apply for this registry.

The presence of cancer registry in public domain could be an indication of the extent of involvement and contribution of the registry in reporting data. Additionally, it could create opportunities for visibility, potential collaborations, and increase funding to improve data reporting. To assess if registries had been mentioned in the public media, question 5.6 was included in the questionnaire. Results showed that 67% of registries was mentioned in the public media, 13% was not mentioned, and 20% did not know (Figure 3.22).

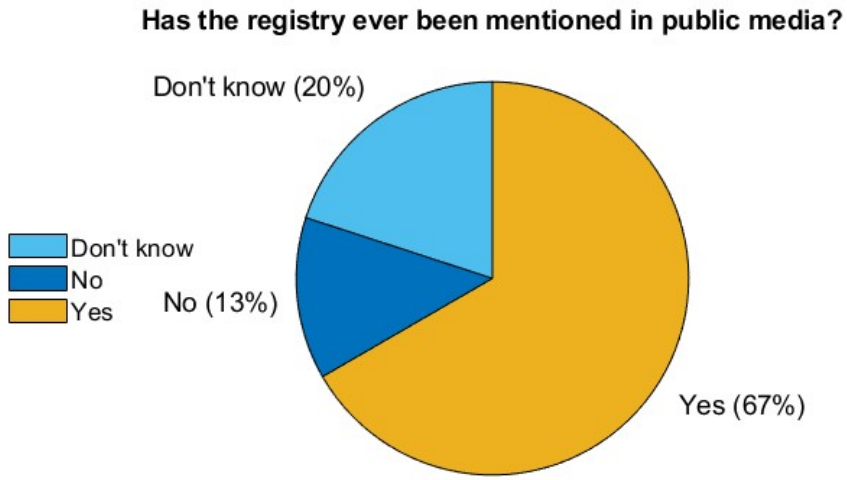


Figure 3.22 Assessment of whether the registries were mentioned in the public media

3.5.6 Resources and challenges in collecting pediatric cancer data

The sixth section of the questionnaire focused on the resources and challenges in collecting pediatric cancer data. Question 6.1 was integrated to verify whether the current resources were sufficient to allow cancer registries to collect pediatric cancer data. 13 out of 15 (87%) registries indicated that the resources were not sufficient, and 2 out of 15 (13%) registries indicated that their current resources were sufficient to collect pediatric cancer data (Figure 3.23A). The 2 registries reporting that their current resources were sufficient communicated that these resources were funded 100% and 90% by the local government. On the other hand, three registries indicating that

their current resources were not sufficient also communicated that these resources were funded 100% and 90% by the local government. Therefore, the source of funding appeared not have a strong impact on the resource sufficiency. A possible explanation is that the amount of funding received from local government varied significantly. Additionally, by exploring data from the registries reporting that their resources were not sufficient, it appeared that the pattern of funding sources and the combination of sources allocated to a given registry also did not impact whether resources were sufficient or not. As a follow up question, registries were asked to indicate what additional resources might be needed to collect pediatric cancer data. Based on the response provided, the most needed resource was funding followed by personnel, training, computers, transportations, logistics, and office space, respectively (Figure 3.23B).

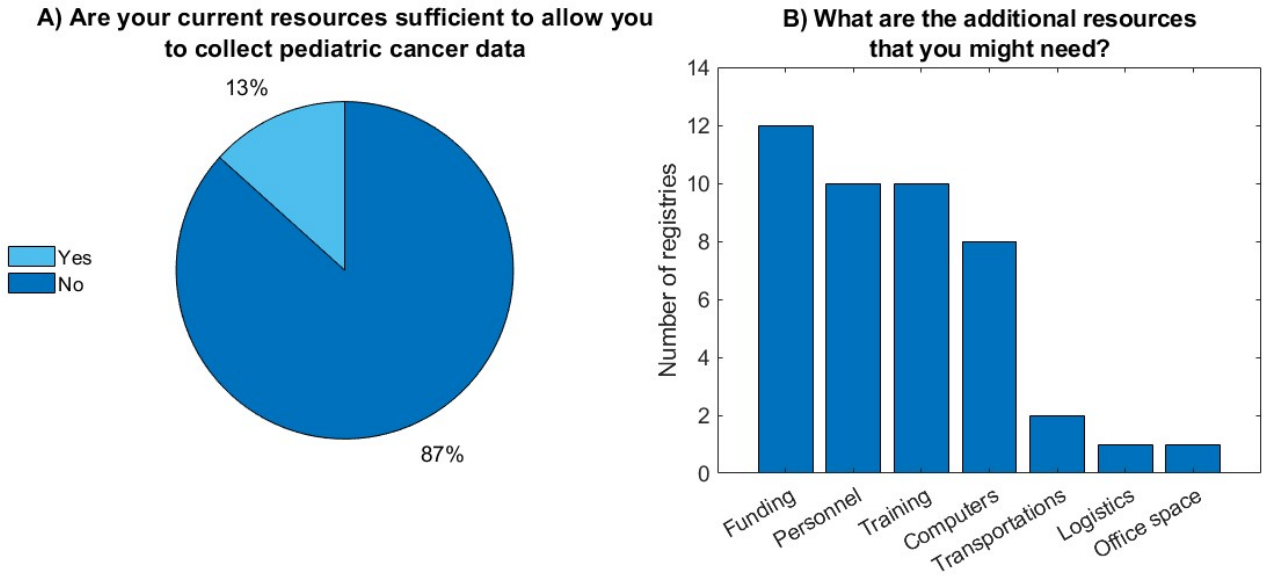


Figure 3.23 Resources to collect pediatric cancer data
A: Pie plot illustrating the percentage of registries that had sufficient and insufficient resources to collect pediatric cancer data. B: Bar plot visualizing the ranked-ordered additional resources needed to collect pediatric cancer data

To identify if it was possible for cancer registries to collect more completed datasets on childhood cancer and in a larger area, question 6.2 was added to the questionnaire. 93% of registries

responded that more complete datasets could be collected, and 7% of registries did not provide an answer (Figure 3.24A). As a follow-up question, registries were requested to list additional resources that would be needed to expand data collection in larger areas. Based on the response provided, personnel was the most needed resource followed by funding, transportations, computers, and training, respectively. In addition, some registries indicated that there was a need for additional resources in logistics, presence of pediatric oncologists/surgeons, power supplies and internet (Figure 3.24B).

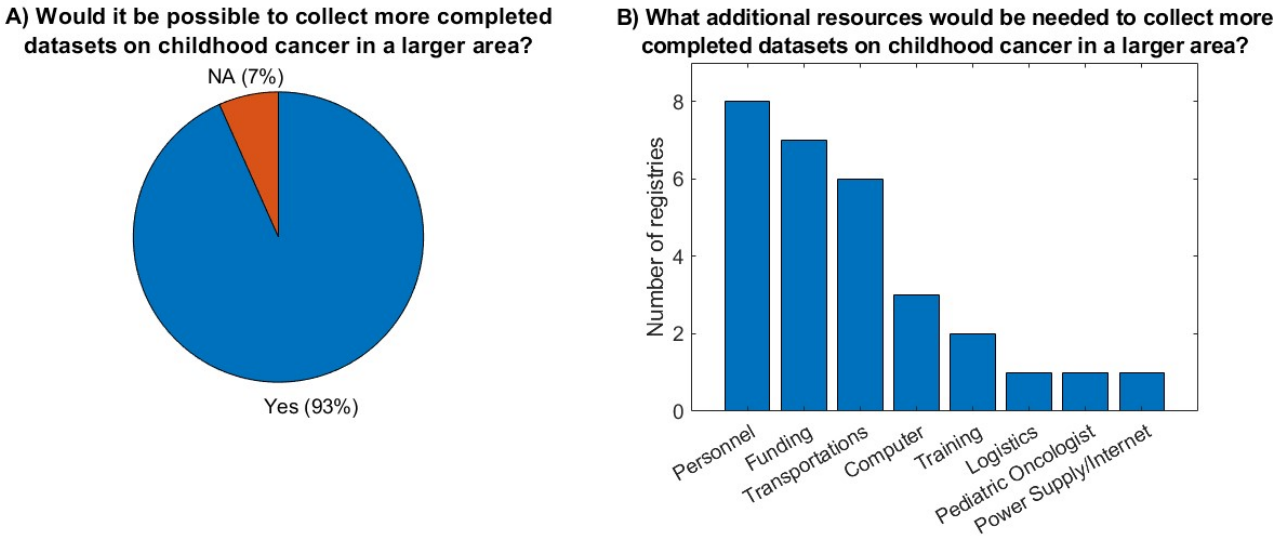


Figure 3.24 Collection of datasets on childhood cancer in larger areas
A: Pie plot visualizing the percentage of registries indicating that more completed dataset could be collected. B: Bar plot listing the ranked-ordered additional resource needed to collect more completed datasets on childhood cancer in larger areas

To identify the main challenges that cancer registries face in collecting pediatric cancer data question 6.3 was included. This question was in a free text format to allow registries to list all that is applicable for their own registry/country. 13 out of 15 registries provided an insight on the challenges they encountered, 1 out of 15 stated that there were no challenges in collecting pediatric cancer data, and 1 out of 15 did not provide an answer. The lack of funding was a common

challenge across several registries, and it appeared to be one of the most impactful factors in limiting the cancer registries capacity to collect data. Limited amount of personnel was another frequent challenge, given the population covered by each registry. Lack of training represented another great challenge in data collection for cancer registries, who clearly highlighted how cancer registry staffs, registrars and medical personnel at hospitals needed specialized training. Moreover, training on the updated staging guidelines at hospitals and cancer centers is needed to assure accurate data recording. However, it is unclear how/which cancer staging methods are currently used by clinicians in notification forms.

In some countries, cancer registries indicated that there is a deficiency of medical expertise, specialized pediatric oncologist, oncology facilities, and epidemiologist. Moreover, the insufficient number of pathologists, pathology services and absence of equipment created a great obstacle in childhood cancer diagnosis and impacted capturing the real incidence of pediatric cancer. Accessing critical and accurate data/information was another challenge that cancer registries faced. For example, the absence of data sources to capture patient survival, follow-up and archival data made data collection extremely difficult. Unavailability of updated national population data was an additional issue that limited data integration and accurate analysis. Furthermore, lack of computers and digital tools, transportation and office space were additional challenges that prevented cancer registries from performing data collection properly. Finally, some registries highlighted that lack of awareness about childhood cancer symptoms and treatment was a problem that significantly impacted early diagnosis and survival of childhood cancer.

As an example, one of the registries provided the following challenges as the main obstacles in collecting pediatric cancer data: “1- Lack of awareness: of the need to notify of childhood

cancers & and why it is important to do so. 2- Staging of childhood cancers. It is unclear how/which staging clinicians use currently in notification forms. We also have a lack of resources to be able to host a training for the new Toronto staging guidelines to be implemented. 3- Comprehensive list of data sources. No updated list of national pediatric oncologists/ hematologists readily available. Identifying new data sources solely depends on word of-mouth, particularly within the private sector. 4- Outcome (survival) status is almost never reported, and we don't have the resources to follow-up each recorded incident case. 5- Lack of expertise in childhood cancers' pathology and registration within NCR itself. Epidemiologists do not necessarily have a medical background which may affect quality of registry". Another example provided by another cancer registry was the following: "1-Lack of trained registrars, 2-There is no specialized pediatric oncology facilities in the country, so data are difficult to collect, 3-Lack of pathologists (the percentage of microscopic verification is low), 4-People are poor with low access to diagnosis and treatment (the burden is underestimated), 5-We need more support and recognition from the Ministry of Health. pediatric cancer data should be mandatory".

3.5.7 Additional analysis integrating several metrics

3.5.7.1 Workload per FTE across registries

To better contextualize the extent of lack of resources faced by registries in LICs, the data presented in sections 1-6 was integrated and analyzed. For example, associating number of FTEs, with reported cancer cases, population covered, and proportion of pediatric cancer data would provide an insight into the workload burden faced by registry stuff and how this workload could impact the amount and quality of data reporting. Therefore, Table 3.8 was assembled to highlight this information and report metrics that could be used to address this analysis.

Table 3.8 Number of populations covered by an FTE

Registry	Country	# of FTEs	Population covered by registry (million)	Population covered by 1 FTE (million)	Cluster
Kampala Cancer Registry	Uganda	1	2,700,000	2,700,000	central
National Cancer Registry	South Africa	12.1	16,899,287	1,396,635	south
The Ibadan Cancer Registry	Nigeria	3.5	3,148,295	899,513	north
Registre des cancers de Bamako	Mali	2.45	1,810,366	738,925	north
The Maputo City Cancer Registry	Mozambique	2.1	1,088,449	518,309	south
Cotonou Cancer Registry	Benin	1.55	688,000	443,871	north
Eswatini National Cancer Registry	Eswatini	3	1,093,238	364,413	south
Registre des cancers de Brazzavill	Republique du Congo	6	1,800,000	300,000	central
Registre des Cancers de la Réunion	Réunion Island	6	866,500	144,417	south
Calabar Cancer Registry	Nigeria	4	501,400	125,350	north
Gulu Cancer Registry	Uganda	8	771,514	96,439	central
Beira Cancer Registry	Mozambique	6.2	530,604	85,581	south
Seychelles National Cancer Registry	Seychelles	3	94,633	31,544	central
Registre des cancers du	Niger	10	NA	NA	north
Ekiti Cancer Registry	Nigeria	6	NA	NA	north

The workload burden faced by registry staff was quantified using the number of FTEs per population covered. This metric was computed by dividing the number FTEs working in a registry by the total population covered and multiplying this ratio by 1,000,000. Data demonstrated that there was a significant inequality of workload burden between registries across countries that participated to the questionnaire. The Kampala Cancer Registry, the National Cancer Registry, the Ibadan Cancer Registry and the Registre des cancers de Bamako had the highest workload burden, with 1 FTE covering approximately 2.7, 1.4, 0.9 and 0.74 million people across the population covered, respectively. In contrast, the Gulu Cancer Registry, the Beira Cancer Registry and the Seychelles National Cancer Registry had the lowest workload burden, with 1 FTE covering approximately 96, 86 and 32 thousand people across the population covered, respectively. All other registries had an intermediate workload burden, with 1 FTE covering approximately 125-518 thousand people across the population covered.

3.5.7.2 Workload per FTE in registries within the same country

Further analysis revealed a significant inequality of workload burden between registries within the same country. For example, the workload burden of the Kampala Cancer Registry was 28-fold higher compared to that of the Gulu Cancer Registry in Uganda. Similar patterns were observed in Nigeria (The Ibadan Cancer Registry versus Calabar Cancer Registry) and Mozambique (Maputo City Cancer Registry versus Beira Cancer Registry), with fold-change in workload burden between registry equal to 7.2 and 6.0, respectively. In all these cases, the reported inequality was due to larger populations that needed coverage and smaller number of FTEs covering those populations. Therefore, geographical location in high density population areas within the same country can lead to different workloads, create discrepancy in allocating resources and potentially contribute to data underreporting.

3.5.7.3 The impact of geographical location of registry on data collection

To better understand the impact of geographical location on the extent of data underreporting, a similar analysis was conducted across clustered regions. Three clusters were defined by grouping countries in north, central and south Africa. Results of this analysis indicated that there was no clear pattern between geographical location and inequality of workload burden, as significant differences were observed across all countries grouped in the same cluster. Therefore, although these registries already face a severe lack of personnel and resources, the geographical location in high density population areas could add an additional layer that can negatively impact the quality of the data collected and reported.

3.6 Discussion

The cancer registries questionnaire was conducted in selected countries in Africa to address potential factors that could contribute to pediatric cancer data underreporting in LICs. The questionnaire enabled a better understanding of the setup of cancer registries, registries resources and funding, and data flow between cancer centers, hospitals and registries. The process of collecting and reporting data and the main challenges that registries faces were also investigated. In this section, the results of the questionnaire were grouped into four main categories for discussion. These categories are resources in cancer registries, pediatric cancer data sources, cancer control plans, and challenges that the registries encounter.

3.6.1 Resources in cancer registries

The massive gap identified when comparing resources available for cancer registries in LICs versus HICs revealed an imbalance and inequality in accessing sufficient resources (Horton & Gauvreau, 2015). Published data revealed that budget allocated for health and medical system, per person per year, across sub-Saharan Africa are extremely inadequate compared to the budget in HICs. For example, in the U.S. the approximate budget per person per year reaches $7285. On the other hand, in LICs this budget could range between $17 to $819 per person per year. Additionally, Horton *et al* demonstrated that the difference in resources available for cancer registries in LICs compared to HICs was clearly linked to the quality of data reported (Horton & Gauvreau, 2015). Furthermore, this comparison revealed that resources significantly impacted the percentage of population covered by registries. The percentage of population covered by cancer registries in HICs is approximately 80% compared to only single digit percentage in LICs.

Lack of resources that cancer registries encounter in LICs, especially in Africa, have been demonstrated by several publications (Curado, 2019). Despite the crucial role of cancer registries in providing data that enable governments to assess cancer burden, the funding and support provided to registries is very minimal. The cancer registries questionnaire highlighted the extent of limited resources and raised possible negative impact on collecting pediatric cancer data. The limited resources were illustrated via several aspects. The first aspect was the gap between the number of FTEs working in the registry and the distribution of staff types with respect to the number of populations covered by each registry. This comparison demonstrated the significant workload and burden on FTEs working at the registries. As an example, the Kampala Cancer Registry in Uganda had only one FTE covering a population of 2.7 million. The consequence of such deficiency in resources could be one of the major factors contributing to data underreporting in this region. The impact is not only restricted on the amount of data that should have been collected, but also on the quality of data reported. It was noted by 93% of registries that if they have had access to sufficient resources, they would have been able to collect more complete sets of data and cover larger areas, which clearly emphasizes the need to increase support. Moreover, the quality of data could be compromised by FTE work overload, which might lead to missing data or inaccuracy of data recording.

The second aspect of lack of resources reported in the questionnaire was the distribution of staff types across registries. It was clear that the allocation of staff types was insufficient to meet the need for assigning accurate roles and responsibilities across registries, which also has implications on data reporting. Delegating an FTE to collect, report, or analyze data without the proper knowledge or training would negatively affect the quality of data handled.

The third aspect was the lack of funding illustrated by 13/15 registries that reported that their funding was insufficient. The limited funding and the low representation of international communities and NGOs, as a source of funding, was one of the main conclusions of the funding section in the questionnaire. A study investigated the approximate cost needed to operate cancer registries in LICs, which highlighted the need to share such data with stakeholders to enhance awareness and increase support (Tangka, et al., 2016). Tangka *et al*. demonstrated that the cost of operating a registry in LICs is high and includes significant fixed cost. The cost to register a cancer patient in LICs would range between $3.77 to $15.62 U.S dollars. In addition, more than half of registries expenses goes to wages of employees. Allocating proper funding is critical for the sustainability of the cancer registries in LICs and could have a significant impact on reducing data underreporting.

In summary, analysis of the resources available in cancer registries showed an evident pattern of imbalance in resources distribution across countries and registries within the same country.

3.6.2 Pediatric cancer data sources

3.6.2.1 Approaches used in data collection

Not all cancer registries that participated in the questionnaire collected data from hospitals treating pediatric cancer. However, most cancer registries (12/15) reported that they collected pediatric cancer data. The three registries that did not collect pediatric cancer data did not explain the reason why they did not. It was unclear if there are other cancer registries in the country collected this data. In South Africa, the National Cancer Registry is completely dedicated to collecting pediatric cancer data. Based on information from the South Africa cancer registries website, there are another 2 cancer registries – the National Pathology-Based Cancer Registry and

the Ekurhuleni population-based cancer registry – that collected adult cancer data (National Institute for Communicable Diseases , 2021).

Cancer registries reported different approaches and various data sources utilized to collect data. It appeared that the percentage of cancer registries reaching out to hospitals to collect data was significantly higher than the percentage of registries that were approached by hospitals or cancer centers to report data (only one registry). This outcome may suggest that the frequency of registries reaching out to hospitals could lead to an increased burden and responsibilities on cancer registries given that they are the main drivers for cancer data collection. Encouraging hospitals and cancer centers to voluntarily report data and be more involved in the process of data collection might be useful to ensure more accurate data reporting. In fact, mutual collaboration between both cancer registries and hospitals could be the most efficient model for data collection and reporting (Gakunga & Parkin, 2015).

3.6.2.2 The use of data sources

Cancer registries reported the use of multiple data sources. Pathology labs were the most common source used, and the health insurance providers were the least source used for data collection (1/15 registries). The reason why health insurance provides were not a common source for data collection in most of the countries that participated in the questionnaire is because people do not have health insurance. Moreover, one of the main observations regarding data sources, as shown in figure 3.12, was the pronounced underutilization of imaging departments. Missing imaging data, which are a source for diagnosis and clinical response, could lead to data underreporting. Overall, the average number of sources used by a registry was 11.2 and the median

was 7. This result was comparable with what was published by a similar study (Gakunga & Parkin, 2015).

3.6.2.3 Death certificates as a sources of data

Death certificates are valuable source for cancer survival, mortality, and cure rates reported by registries. Mortality data are crucial components in computing statistics that could lead to estimating the cancer burden in each country. The availability of such estimates is needed by governments to develop effective cancer prevention and control plans. When registries were asked whether they used death certificated to collect data, the response showed that a third of registries did not. Missing mortality data across many registries could lead to data underreporting of death incidence, long term follow-up data and cause of death. A study reported that, in LICs, accessing death certificates is challenging, and the reliability of information obtained from death certificates might be questionable, which could be the reason why only 1% of death is reported in LICs (Sankoh, et al., 2020). In general, the number of African countries using death registration is very minimal compared to other countries in different regions. Results from a survey that was conducted by the Economic Commission for Africa (ECA) revealed that only 18 out of 54 African countries record and report data of annual deaths. Moreover, the same study showed that death registration systems in African regions only capture one in three deaths (Sankoh, et al., 2020). For example, in Nigeria, published data demonstrated that in 2017 only 10% of death cases were registered, and between 2008 and 2017 the WHO did not have any death data reported for Nigeria in their database (Makinde, et al., 202). Data underreporting could be critical in Nigeria, the largest populated country in Africa and 7th largest country in the world, with prediction that by 2050 their population will reach 400 million and be the 3rd largest country in the world (Makinde, et al., 202). Currently,

based on the NSCR, there are 11 population-based cancer registries and 20 hospital-based cancer registries in Nigeria (Nigerian National System of Cancer Registries, 2018). In general, there are cancer control initiatives and tremendous efforts to improve data collection and reporting in Nigeria (al-Haddad, et al., 2015).

It is evident that underreporting of death data is still common in LICs, and there are meaningful efforts by cancer registries to improve it. On the other hand, in HICs, such as the U.S., death data reporting is enforced by health authorities, which could be the most efficient way to ensure data reporting. The CDC implemented a program to improve accuracy of cancer mortality data and to ensure that death certificates would be easily accessed, reviewed and quality-controlled (United States Cancer Statistics, 2021).

3.6.2.4 Data collection from all cancer cases or only residents

The response reported by cancer registries regarding whether they collected data on all pediatric cancer cases or only on residents revealed that 47% of registries collected data on all pediatric cancer cases. Registries that collected data only on residents, might have missed large sets of data, which could contribute to data underreporting. It was not clear why some registries collected data only on residents, and whether other registries in the same country covered larger population areas and included all cases. Although population-based cancer registries (PBCRs) are usually responsible for collecting data on all cancer cases, some registries did not follow this concept (Omonisi, Liu, & Parkin, 2020). Additionally, public data revealed that PBCR is covering only 2% of populations in Africa, which needs immediate improvement (List & O'Connor , 2020).

3.6.3 Cancer control plans

WHO defined cancer control plans as "public health programs designed to reduce cancer incidence and mortality and improve quality of life of cancer patients, through the systematic and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment, and palliation, making the best use of available resources" (World Health Organization, 2021) Cancer control plans are instrumental to improving cancer medical care, especially in LICs. Published data showed that survival rate, mortality rate, and quality of reported data differ between countries that have established cancer control plans versus countries that did not have cancer control plans in place (Shah, Kayamba, Peek, & Heimburger, 2019). It was clear that more favorable outcome was observed in countries with cancer control plans. 87% of cancer registries that participated in the questionnaire reported that they have a national cancer control plan. This was a reasonable outcome given the economic status of most countries in that region and the limited resources. In addition, all cancer control plans across those countries included pediatric cancer plans, which could eventually improve pediatric cancer care and data reporting. It was unclear why the response regarding the existence of cancer control plans from the two registries in Uganda was not consistent. One registry confirmed that there was a cancer control plan while the other registry reported that there was not a cancer control plan. However, based on published data, Uganda has a cancer control plan, so technically, the percentage reported in the questionnaire should have been 93% (Orem & Wabinga, 2009). There are initiatives to improve pediatric cancer care in Uganda through collaborative efforts between health authorities and patients' families. One of these initiatives is focused on establishing the Uganda Child Cancer Foundation, which provides various services such as distribute awareness, help in accessing treatment, social support for patients and

their families, and advocate for cancer prevention (Orem & Wabinga, 2009). Furthermore, based on a study investigating pediatric cancer control in Africa, Mali has a cancer control plan (Weaver, Yao, Renner, Harif, & Lam, 2015), despite the response provided in the questionnaire stated that they did not. This discrepancy could be an indication that the registry is not aware of cancer regulations at a national level. Combining the data reported in the questionnaire with what is publicly available would suggest that all the countries that participated in the questionnaire had a cancer control plan in place.

Although the existence of cancer control plans is critical, implementing and enforcing the guidelines of the plan is what makes the plans impactful. The role of governments and health authorities to monitor cancer centers and cancer registries to ensure following the plan guidelines, data collection and data quality control is significantly needed (International Cancer Control Partnership). Since cancer incidence is notably increasing in Africa, cancer control plans are becoming essential to establish and prioritize short term and long term strategies for cancer control (Stefan, et al., 2013). For pediatric cancer, the status of enforcing and applying cancer control plans in Africa has improved. For example, in Nigeria, the plan includes a strategy for immunization of children against HPV and hepatitis B to prevent cancer associated with these viruses. Additionally, the plan aims to establish pediatric cancer screening facilities and prevention programs (Nigeria National Cancer Control Plan 2018). Another example is the cancer control plan in Eswatini, which includes educational and awareness programs for parents about pediatric cancer that could facilitate cancer prevention and early detection. Also, Eswatini cancer control plan includes providing social support for pediatric cancer patients and their families (National Cancer Prevention and Control Strategy, 2019)

3.6.4 Challenges that cancer registries encounter

Responses provided in the questionnaire highlighted various types of challenges that cancer registries in Africa are facing to collect pediatric cancer data. The results of the questionnaire were comparable to what have been published about challenges in collecting pediatric cancer data in LICs (Curado, Voti, & Sortino-Rachou, 2009). The medical system in most African countries lacks basic infrastructure, such as access of pediatric cancer patients to cancer screening, diagnosis, treatment, and palliative care (Anwar & Boulos, 2012). A study indicated that, out of 53 African countries, only 21 have radiotherapy, which highlights the deficiency of proper medical care they encounter (Anwar & Boulos, 2012). The challenges faced by cancer registries were not only limited staff, resources and funding (as discussed in section 3.5.1), but also included access of basic elements like computers, databases, office space and transportation. For example, results of the questionnaire illustrated that 40% of registries did not have access to database to register a child, which could lead to either missing data or recorded data as hard copies. Medical records that are reported as hard copies could be lost or damaged, and they might be difficult to retrieve for follow-up appointments. This issue could be considered as a major contributor in pediatric cancer data underreporting.

Another challenge that was reported in the questionnaire was the minimal number of pediatric oncologists compared to the population covered. Published data revealed that 31 African countries have less than 10 oncologists covering a population of 100,000 people, and in some countries the number decreased to 1 or 2 oncologists (Ribeiro, et al., 2008). Conversely, in the U.S. and U.K., the allocation of physicians to populations covered was reported to be approximately 230 physicians per 100,000 population (Hadley, Rouma, & Saad-Eldin, 2012). Some cancer registries

also highlighted that there was no updated list of national pediatric oncologists/hematologists in their countries, which might impact data exchange and quality of data reported.

The lack of training across personnel in cancer registries, cancer centers and hospitals has been one of the major challenges that was reported by registries. Also, the frequent transfer of trained personnel has been a hurdle. The significant negative impact of this challenge was recognized by health authorities in Africa aiming to improve the situation. For example, the African Organization for Research and Training in Cancer initiated the African Cancer Network Project in 2012 (Stefan D. C., Cancer Care in Africa: An Overview of Resources, 2015). This project had many goals, including the improvement of training of healthcare workers and providing opportunities for collaborations between cancer centers in Africa and advanced cancer centers in HICs. Another example is the Paediatric Oncology International Network for Training and Education (POINTE) that was initiated by SIOP (van Heerden, et al., 2020). POINTE provided partnering opportunities between LICs and HICs pediatric cancer centers to improve pediatric cancer care and offered access to training and educational materials for health care workers (POINTE, 2018).

Finally, cancer registries emphasized that the poverty of population and their lack of awareness about pediatric cancer had been an underestimated burden, and additional support and recognition from the national health authorities is significantly needed.

3.7 Conclusions

Cancer registries that participated in the questionnaire experience limited resources and encounter numerous challenges to collect or report pediatric cancer data. It was evident that registries are covering large populations compared to their capacity and resources. Even though

most registries reported that they collect pediatric cancer data, it was clear that limited access to data sources and basic tools create a hurdle to report more data and cover larger areas of populations. Additionally, results illustrated discrepancy in distribution of resources across cancer registries even within the same country. One of the major outcomes of the questionnaire was to identify various potential factors that might have contributed to pediatric cancer data underreporting in this region. For example, the burden of workload per FTE, minimal funding, low number of oncologists, access to computers and databases, and lack of training of staff could be powerful indicators that impact data reporting and the quality of data reported. Furthermore, the limited connection of data reported from cancer registries to international databases was also described. Cancer registries that collect pediatric cancer data seemed to have access to hospitals that report data. However, six of these registries are not connected to global or international registries, which raised the question on how their data was globally reported. Overall, the results reported in the questionnaire were comparable to those published by various studies. Finally, it is important to note that cancer registries are making tremendous efforts to improve data collection and reporting despite the difficult circumstances and challenges they face. Efforts by local governments, healthcare providers, and international organizations have been made to enhance pediatric cancer medical care in Africa and LICs, in general. However, additional support and increase awareness about the real burden of pediatric cancer in LICs is nonetheless significantly needed.

3.8 Future work

Sending a follow-up questionnaire to the same cancer registries that participated in this questionnaire could be useful to collect more results and improve the overall analysis. Moreover,

including additional registries across other African countries might allow a better assessment in addressing factors that might contribute to data underreporting within these countries. Translating the questionnaire to French or local language would allow a larger participation. Furthermore, to have a comprehensive view about the process, challenges, and workflow in collecting pediatric cancer data in Africa, it would be extremely valuable to conduct a questionnaire from hospitals and cancer centers. Such a questionnaire could enable identifying additional gaps or approaches to improve interactions between cancer centers and registries to enhance pediatric cancer data reporting. Finally, sending a similar questionnaire to cancer registries in HICs might be beneficial to underline the inequality between the pediatric cancer status in LICs and HICs. Results could also facilitate exploring methods that could be applied to improve data reporting in LICs.

4 CHAPTER 4: FIELDWORK FOR PEDIATRIC CANCER DATA COLLECTION

4.1 Introduction

One of the approaches that could be used to investigate pediatric cancer data underreporting in LMICs is to compare published data with data collected directly from cancer hospitals and cancer centers. To identify sources of patient's records data that could be collected directly from hospitals and cancer centers, a field trip to three countries in Africa was designed in 2018. The fieldwork was originally planned in Egypt, Ghana, and Malawi. However, the trip took place only in Egypt because the completion of hospital visits required more time than expected and did not allow continuing the trip in the other two countries. A list of the main hospitals and cancer centers in Egypt, Ghana, and Malawi was compiled in preparation for the fieldwork, but only the list of the main hospitals in Egypt is presented in this section (Table 4.1).

Table 4.1 A list of the main cancer hospitals and cancer centers in Egypt

Cancer Hospitals/cancer centers in Egypt			
Hospital/Center	**Address**	**Website**	**City**
57357 Children Cancer Hospital	Magra El-Eyoun, El-Sayeda Zainab	https://www.57357.org/	Cairo
National Cancer Institute	Al Kasr Al Aini, Misr Al Qadimah	http://www.nci.cu.edu.eg/	
Abu El Reesh Hospital	Al Kasr Al Aini Al Munira	https://www.telemedfoundationevents.com/abu-elreesh/	
Al Salam Hospital	Sadaat St. Gawarhi, Salaam City	NA	
Ain Shams Uni Hospital	El-Khalifa El-Maamoun, Abbasia	http://hospitals.asu.edu.eg//english/	
Harmal Hospital	Dar AlSalam,	NA	

Nasser Institute	1351 Nile Corniche, Shoubra	http://www.nasserinstitute.com/	
Cairo University Hospital	Al Kasr EL Ainy	http://medicine.cu.edu.eg/beta1/index.php/en/	
Specialized oncology center	12 Doky st. Doky	NA	
El Sheikh Zayed Specialized Hospital	6th of October - Sheikh Zayed	http://www.zayedhospital.com	
Hayat Hospital	33, Moustfa Kamel St, Smouha	http://hayatcancerhospital.co	Alexandria
Cancer Research Institute- Alexandria University	165 Borg El Arab	http://mri.alexu.edu.eg/index.php/en/	
Oncology Center- Mansoura University	60 Elgomhoria st, children hospital	http://ocmu.mans.edu.eg/en/	Mansoura
Zagazig University Oncology Institute	Hehia, Harayah Raznah	http://english.zu.edu.eg/ZuDetails.aspx?ID=209	Al Zagageig
Tanta cancer center- A Branch of 57357	Tanta Qism 2, Gharbia	NA	Tanta
Benha Children Hospital	Qism Banha, Qalyubia Governorate	NA	

Egypt was selected as a case study because it is my home country, which enabled me to utilize connections in the medical field to establish collaborations. My involvement in the pediatric cancer sector started when I founded a non-profit organization to provide medical and financial support to unprivileged pediatric cancer patients in Egypt. Leading this organization since 2003 has enabled establishing networks in the pediatric oncology medical care. Working with families of pediatric patients has provided a clear insight into the challenges that they face and the magnitude of the burden they experience. Additionally, interacting with cancer hospitals and centers has provided an opportunity to recognize the limited resources and difficult conditions of their working environment.

The total population of the Arab Republic of Egypt in 2020 was reported to exceed a 100 million. The two major cities in Egypt are Cairo (capital city), with a population of 20.901 million,

and Alexandria, with 5.281 million. The proportion of pediatric population is approximately 33.6% (Worldometers, 2021) and the median age is 24 years (Index Mundi, 2020). Published data indicated that the number of pediatric cancer cases reported in Egypt in 2020 was 6803 (WHO, Cancer Country Profile: Egypt, 2020), the ASR for the whole population was 166.6 per 100K (Ibrahim, Khaled, Mikhail, Baraka, & Kamel, 2014), and the survival rate was 30% (El Malla, et al., 2017). In addition, the GLOBOCAN 2020 report indicate that the total number of new cancer cases in Egypt was approximately 135K in 2020, which is an ASR of 1.35 (GLOBOCAN, 2020). There is only one cancer registry in Egypt, which is the Gharbiah Population-based Cancer Registry (GPCR) in the Gharbiah governorate (Ibrahim, Khaled, Mikhail, Baraka, & Kamel, 2014). This cancer registry is located 60 miles north of the capital city, was established in 1936, and became a national population-based in 2007 (Ibrahim & Mikhail, 2015). GPCR covers a population of 4 million people, which represent a small fraction of the total population of the country (Corley, et al., 2015). Public hospitals in Egypt are funded by the government and rely primarily on public donations. As a consequence, resources allocated are insufficient with respect to the number of people utilizing these facilities. Additionally, Egypt has no established medical insurance system, which forces patients who would not use public hospitals to pay for medical care out of pocket. Private cancer hospitals and clinics provide improved medical care, but at an extremely high cost given the average income for the majority of the population. With the increase of adult and pediatric cancer incidence in Egypt, there is an urgent need to improve cancer medical care and establish additional cancer registries to improve data collection and reporting (Corley, et al., 2015).

4.2 Aims of the field trip

The aims of the fieldwork in Egypt were the following:

1. Initiate and establish collaboration with key pediatric oncologists at hospitals and cancer centers.
2. Assess how pediatric cancer data is collected and reported.
3. Investigate how pediatric cancer data is utilized in decision making for patient's treatments, understanding the status of pediatric cancer in Egypt, and improving medical care.
4. Collect data from pediatric cancer patient's records, which include cancer incidence, cancer type, survival, cure, and mortality rates.
5. Analyze collected data and compare them to the published data to investigate whether a discrepancy might exist.
6. Identify the main challenges that hospitals and cancer centers face, which would be beneficial to address several questions that were posed in this research.
7. Understand the organization structure of the facilities and evaluate the staff available for pediatric care from the interviews and tours conducted during the trip.

4.3 Methods

In this section are discussed the details of the planning for the field work that was conducted in Egypt. Moreover, the structure of the face-to-face meetings and questions that were asked during these interviews are introduced.

4.3.1 Field work planning

The focus of the planning phase was to create an effective workflow for the fieldwork to facilitate data collection. The steps that were implemented to organize the fieldwork in Egypt are presented in the flow chart (Figure 4.1), and the list of main cancer hospitals and cancer centers in Egypt is reported in Table 4.1.

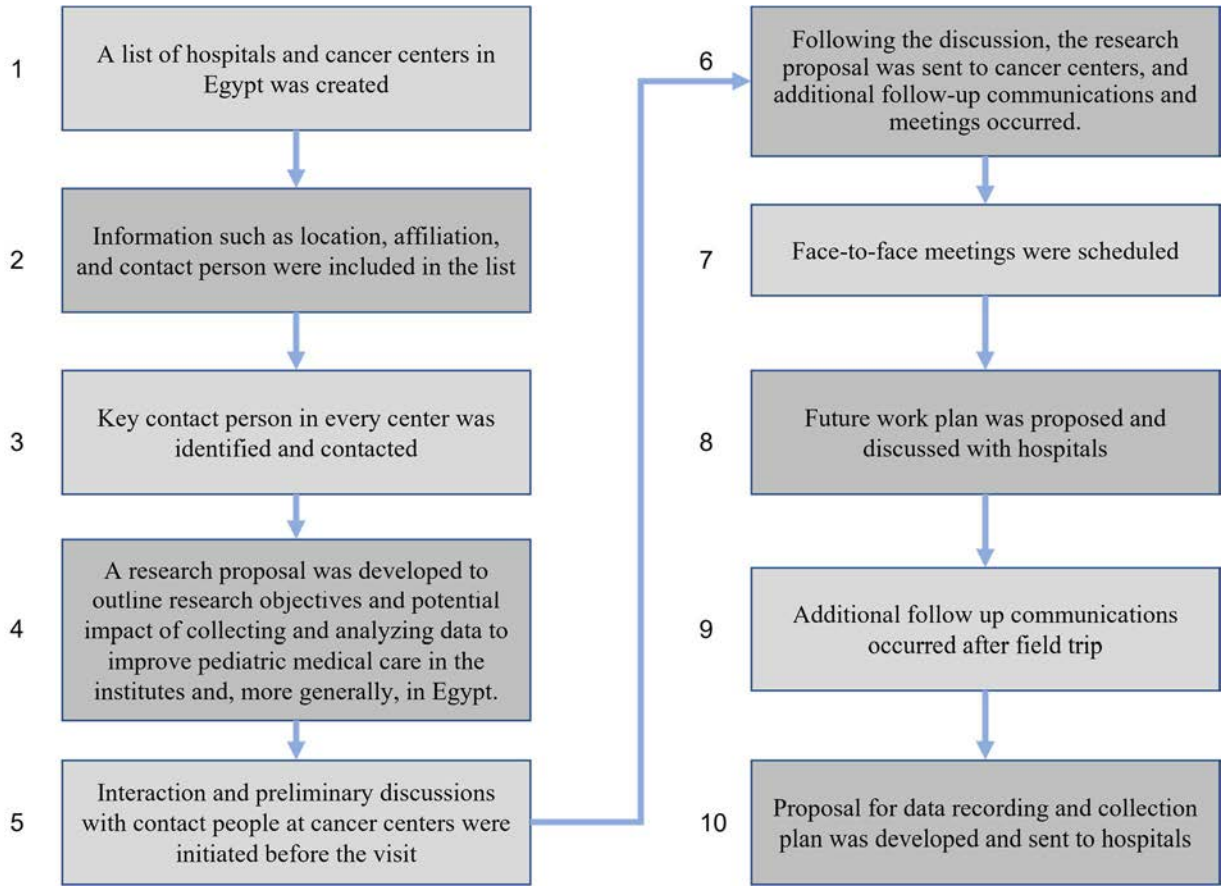


Figure 4.1 Workflow and steps implemented to plan the field trip to Egypt

4.3.2 Structure of face-to-face meetings and interviews

During the face-to-face meetings, several questions were posed. These questions were designed to enable a better understanding of the operational and medical capacity that each of the cancer centers has. In addition, these questions were posed to assess the availability and feasibility of accessing their pediatric cancer data. The first category of questions was related to resources and addressed the sources of funds, number of staff working in the hospital, population covered by the hospital, and the size of the hospital. The second category was focused on the medical care that they provide, and the questions covered the structure of the facility, access to diagnostic tools,

access to cancer therapies, treatment protocol, and if they are following international or risk adapted protocol approach. The third category was related to data collection and data storing, and these questions covered the type of data they collect, if they have a database, how they store patients' records and information (hardcopies or digitalized), and their affiliation with a cancer registry. Finally, the last category of questions was associated with the main challenges they face and if they have any specific infrastructure issues.

4.4 Results of the fieldwork

Although one of the main goals of the fieldwork was to collect pediatric cancer data, the trip turned into a survey and research interviews. Therefore, the aims of the research related to data collection and analysis were postponed. However, what was accomplished in the trip was valuable for addressing several questions posed in the thesis. Information gathered during the interviews and meetings with medical staff provided a deep insight into the general status of pediatric cancer in Egypt, funding sources, staffing, structure of the hospital, access to treatment, how pediatric data are collected and stored, key challenges they face, and areas for improvement. During this trip, six hospitals and cancer centers were visited in Cairo, Alexandria and Mansoura. The three cities are located in the north of Egypt, as illustrated in the map depicted in Figure 4.2 (nationsonline.org, 2021).

Figure 4.2 Map of Egypt showing the location of the three cities that were visited during the field trip.
(Map was taken and adapted from (nationsonline.org, 2021))

A list of hospitals and cancer centers visited in Egypt in 2018 is presented in Table 4.2. In addition, a map illustrating the location of the four hospitals and cancer centers visited in Cairo is shown in Figure 4.3

Table 4.2 List of hospitals and cancer centers visited in Egypt

Cancer hospitals/cancer centers visited in Egypt		
Hospital/Center	**Address**	**City**
57357 Children Cancer Hospital	Magra El-Eyoun, El-Sayeda Zainab	Cairo
National Cancer Institute	Al Kasr Al Aini, Misr Al Qadimah	

Cairo University Hospital	Al Kasr EL Ainy	
Ain Shams Uni Hospital	El-Khalifa El-Maamoun, Abbasia	
Cancer Research Institute- Alexandria University	165 Borg El Arab	Alexandria
Oncology Center- Mansoura University	60 Elgomhoria st, children hospital	Mansoura

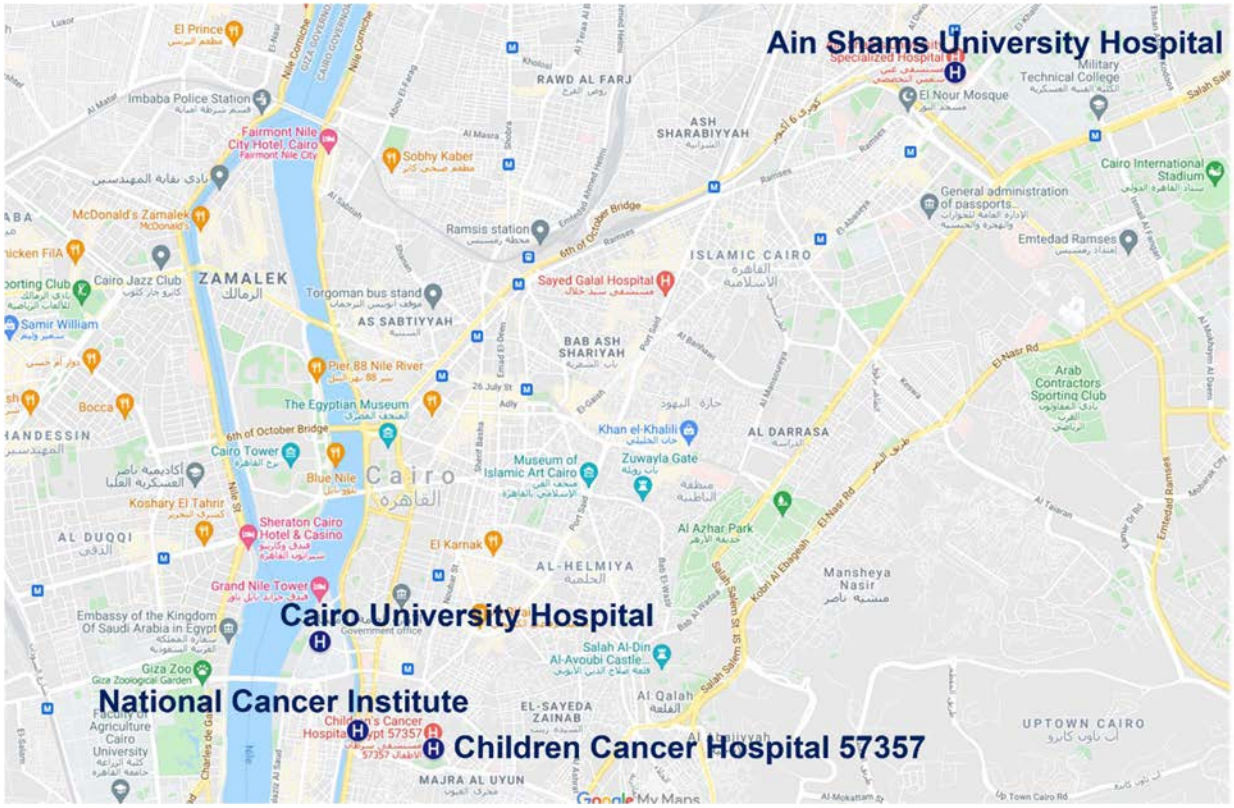


Figure 4.3 A map of Cairo illustrating the location of the four cancer hospitals and cancer centers that were visited during the field trip

4.4.1 Data collection from hospitals and cancer centers visited in Egypt

4.4.1.1 Ain Shams University hospital

The first hospital we visited was Ain Shams University Hospital in Cairo, which was established in 1984 (http://asush.asu.edu.eg/en). On February 11th, 2018, we met with the Dr. Samia Girgis, the duty manager of Ain Shams Uni hospitals and head of infection control unit

(professor of clinical pathology, faculty of medicine), and three pediatric medical oncologists; Dr. Fatma Ebeid, Dr. Iman Ragab, and Dr. Nayera Hazaa. A tour of the hospital and of the pediatric cancer unit was given. The hospital heavily relies on public donations, limited government funds and non-profit support. Lack of funds, resource and social support not only impairs the ability of the hospital to effectively treat the patients, but also results in adding additional roles and responsibilities on medical doctors. For example, medical staff often arrange fundraising activities to provide financial support for the treatment expenses of their patients. The limited financial resources available at this hospital also forces medical doctors to administer patients with dosing regimens that are below those recommended in the treatment protocol. Thus, although doctors currently attempt to closely follow clinical protocols developed by The Children's Oncology Group (COG) or The International Society of Pediatric Oncology (SIOP), they often risk adapt treatment protocols based on available levels of drug supply and supportive care resources. Several gaps and challenges that impact the doctor's ability to provide high quality medical care to pediatric patients were also identified. Supportive care, especially for leukemia patients, is one of the most common problems.

Significant rates of infection-related deaths in AML patients present another common issue that the Ain Shams cancer center facing. Hence, they apply complete isolation strategy of patients to reduce the risk of infection, which creates additional unnecessary burden to already distressed families. Majority of the infection-related deaths are due to parents' lack of knowledge about the risk of infection after their children's immune system is compromised.

Access to therapeutic agents and anti-fungal drugs is another major problem due to the high cost. Despite that the Ain Shams center have negotiated lower costs with various pharma companies, they were still not able to access the necessary drug supply. Thus, joining the clinical

trial network, a network of clinicians and researchers, was identified as a potential solution to access therapeutic agents with reduced costs and improved supply schedules. This center has also been developing an outreach program to educate parents and healthcare workers to recognize the signs and symptoms of pediatric cancers. However, the program was only supported for a limited time due to lack of resources. Despite the Ain Shams cancer center capacity and extremely limited resources, they treat approximately 60 pediatric oncology patients a year including several patients from surrounding governorates and neighboring countries. Ain Shams cancer center sends some of the new diagnosed patients to 57357 Children Cancer hospital in Cairo due to the limited numbers of beds (20 beds in the pediatric oncology unit). Also, with only 15 staff in the pediatric oncology unit, the medical personnel are limited.

All the above listed issues contribute to create an environment where collection of high-quality data of pediatric patients is not the main focus. The Ain Shams center also does not have a computerized database. A large amount of patient's records is stored as hard copies, with a few records uploaded into excel spreadsheets. Therefore, accessing data from this hospital was not possible.

4.4.1.2 57357 Children Cancer Hospital

The second cancer center visited in Cairo was the 57357 Children Cancer Hospital (https://www.57357.org/), which was built in 2003 with a current capacity that reached 320 beds. The visit took place on February 12th, 2018. During the visit, we met with Dr. Sherif Abouel Naga, the CEO, Dr. Mohamed Aggag, the CMO, and Dr. Aya Nassar, the Head of Professional Development. The tour of the hospital was an opportunity to explore the inpatient and outpatient clinics, as well as research laboratories. The hospital had a vision of establishing a pediatric cancer

facility to serve all Egyptian governorate and neighboring countries. The hospital was built using a significant amount of public fundraising, and it is at full capacity. Currently, they are building another large pediatric oncology hospital for outpatients and inpatients alongside the 57357 hospital. The standard of the facilities is high, and access to drugs, radiotherapy, CT scanners, MRI and additional resources is provided. The center actively collaborates with St. Jude Hospital in the United States and applies pediatric oncology treatment protocols of St. Jude Hospital to treat their patients. Also, they have a small early discovery research department with dedicated laboratories. The facility has large areas for children's art and physical activities to engage children while they receive treatment as well as a small internal school for inpatient children. We met with several researchers and the bioinformatics team, and they provided us with information about how they established and adapted their protocols and performed data analysis. The 57357 hospital has built an established database and computerized system for data analysis. This system is connected to the second site of the hospital located in a city called Tanta. Tanta is the fifth largest populated city in Egypt, and it is located approximately 100 km north of Cairo. Accessing the data from both sites of the 57357 hospital was critical for this project due to the amount of data they have from all governorates across the country. However, although pediatric cancer data are stored in a database, accessing data was not possible because the hospital declined the collaboration and did not share the data.

4.4.1.3 National Cancer Institute

The third center visited was the National Cancer Institute in Cairo on February 12th, 2018. (NCI - http://www.nci.cu.edu.eg/). The NCI was established in 1950, and it is affiliated with Cairo University. The capacity of the NCI is 550 beds and serves patients from all governorates. During

the visit, meetings took place with Dr. Emad Ebeid, the head of the institute, Dr. Hisham Fahmi, Lecturer at Pediatric Hematology and Oncology, Dr. Wael Zekri, and other pediatric oncologists and research members. The building is in extremely poor conditions, crowded, poorly resourced, and maintained. The center relies on donations and very limited government funding. However, recently, they started to receive funds from United States Agency for International Development (USAID) and the United Nations Development Program (UNDP). There were a lot of patients in waiting areas, reflecting the difficult conditions in which this center operates. During the meetings several issues and gaps were discussed. The doctors were keen to develop research facility, establish research laboratories and explore the possibility to initiate research collaborative efforts. They also shared how difficult the working conditions were and highlighted the limited resources and lack of basics infrastructure. As per our conversation, the doctor reported that they see roughly 250 patients and 20 new cancer patients were diagnosed daily. These numbers include adult and pediatric patients from Cairo and several surrounding governances. The NCI does not have a database or a reliable computerized system for patient's records, which limits their ability to access patient's data. Moreover, the center lost years of patient's data due to poor storing conditions of the hard-copy records. The medical doctors informed us that the data lost contained lots of information that could have been extremely beneficial to adjust the treatment protocols and optimize subsequent treatment of relapsed pediatric patients. The head of the NCI highlighted a few gaps and issues that needed to be addressed to improve the oncology medical care at the institute. The main priority was to implement a database and a user-friendly computerized system to store over 20 years of hard-copy data and patient's records. Additional support was needed to provide training for medical staff and develop online teaching material to educate patient's families

on how to manage aspects of patient care after diagnosis of disease due to preventable conditions such as nutrition or infections.

Given the magnitude of data that the NCI retains, it would have been a great source of pediatric cancer data collection. However, accessing the data was not possible because the institute still needs to implement a digitalized system to record patients' data.

4.4.1.4 Cairo University Hospital

Cairo University Hospital (https://cu.edu.eg/Home) is affiliated with the Medical School of Cairo University, and during our visit we met with the head of the institute. The meeting was brief since they did not treat any pediatric cancer patients. Once a diagnosis is confirmed, the patient is sent to other pediatric cancer centers or hospitals. The only issue reported by the hospital was the limited funds and resources, which contributes to diverting patients to alternative facilities. This hospital could not be used as a source of pediatric cancer data because they only treat adult patients.

4.4.1.5 Cancer Research Institute in Alexandria

The cancer research institute in Alexandria (http://mri.p.alexu.edu.eg/) is affiliated with Alexandria University. The visit took place on February 13th, 2018, and we met with the head of the cancer center Dr. Shady Fadel, the Associate Professor of Clinical Oncology. This new pediatric oncology center, established in 2018, is located approximately 60 km outside the city of Alexandria. The location might create a commute burden for patients and might require appropriate transportation between the hospital and the city, which is currently missing. When we visited the hospital, they communicated that they were planning to serve other nearby regions, including Matrouh, Alexandria, El Beheira, and Kafr El Sheikh. The center is a new facility completely

dedicated to pediatric oncology. The main building is mostly empty and surrounded by a large area of unconstructed land. Thus, the center has the potential to expand in the near future. At the time of our visit, there was only one pediatric oncologist, three residents and two specialized clinicians. The vision was to create a high standards facility with inpatients capacity of 80 beds. One of the issues that the director of the hospital highlighted was the lack of regulations in Egypt regarding oncologist who treat pediatric patients, which results into several cases of misdiagnosis and application of wrong treatment protocols. Another issue brought to our attention was that the number of pediatric oncologists in Egypt is significantly low because adult oncology practice is much more profitable than pediatric oncology is. Thus, the estimated ratio of pediatric oncologists to the pediatric population is approximately 1 to 15 million. During our conversation, a few areas that needed immediate support for improvement were highlighted. These areas included: 1) education of GPs and families about pediatric cancer signs and symptoms to increase earlier presentation and diagnosis; 2) training and education of nurses and management staff at all levels; and 3) general cleaning and hygiene standards in the hospital to decrease the spread of disease. Another problem identified was the lack of necessary personnel to support the daily activities of the center. At the time of the visit, the hospital relied on only two trained pathologists with limited resources. The center also needed a radiotherapy facility, nutritionists, social workers, and supportive care. Furthermore, access to more affordable and consistent drug supply, development of consistent treatment protocols, publicity and media support for fundraising and data management systems were the main priorities to improve the standard of care provided to the pediatric patients. Another highlighted gap was the development of a specialized program for kids to provide artwork and physical activities while the children undergo their treatment.

As many other hospitals in Egypt, this cancer center did not have a database, and their patient's records of eight years were stored on hard copies, which created a challenge in terms of accessing, using and sharing the data. The hospital has tried to use the Pediatric Oncology East and Mediterranean (POEM) group for data reporting to address this problem, but the approval process has so far represented a great challenge. Overall, the Alexandria hospital is developing a research program to establish a competitive cancer center with high standards for pediatric care. However, establishing basic medical care might be an optimal way to utilize their limited resources rather than developing a research program. The lack of data digitalization was a great limitation to collect data from this hospital as well.

4.4.1.6 Oncology Center in Al Mansoura University

The Oncology Center in Al Mansoura University was visited on February 14th, 2018 (OCMU- http://ocmu.mans.edu.eg/en/). Al Mansoura is the capital of the Dakahlia Governorate, which is located about 130 Km north-east from Cairo. During the visit, meetings took place with several key medical staff including, Dr. Mohamed Hegazy, the Head of the Oncology Institute, Dr. Ahmed Mansour, Head of the Pediatric oncology unit and Consultant to the minister of higher education and Scientific research, Prof. Mohammed Sallah, the Director of MU International Relations Office. Also, we met with pediatric oncologists; Dr. Dina Reda, Dr. Hagar Gamal, Dr. Suzy Abdel Mabood, and Dr. Ahmad Darwish. We were given a tour around the current center and the expansion areas. The hospital relies on public donations and limited government funding. The population of the Dakahlia Governorate in 2018 was 6.57 million, and the center receives approximately 3.5 million patients annually (adult/pediatric) from Al Mansoura and several surrounding governorates, which counts for 53% of population. Amongst these patients, roughly

200 new cases of pediatric oncology are diagnosed per year. The hospital is ambitious in improving their facilities and standards for patient's care. Using funding from public donation, the center is increasing the inpatients capacity from 40 beds to 80 beds and opening a new ICU unit. However, given the huge number of patients treated in this hospital, the center is planning to open another site in a smaller city, called Gamasa. OCMU has a computerized system and a database for patient's records, and all data is documented including retrospective data. The hospital database will be connected to the new pediatric oncology site in the city of Gamasa. However, their database is not connected to any other registry, even the Gharbia registry, which is the only local cancer registry in Egypt. The major gaps they have highlighted and areas that need improvement are supportive care, access to consistent laboratory diagnostic tests, cancer cytogenetics kits, minimal residual disease (MRD) analysis, training program (research and clinical) and access to medications. Therefore, the OCMU would like to join the clinical trials network through the UOB, which will allow them to access therapeutic agents and established protocols. Additionally, a future plan to access OCMU data was discussed. Although this hospital had developed a database to retain their patient's records, we could not collect any pediatric cancer data before a collaboration agreement was defined.

4.4.2 Hospitals and cancer centers that were not visited

In addition to the cancer centers/hospitals that were visited during the fieldwork, there were many other pediatric cancer centers in Egypt that were not visited due to limited time and conflict of schedules. Examples of hospitals that were not visited in Cairo include Al Demerdash hospital, Harmal Hospital, Abu El Reesh and Nasser Institute. Centers not visited in other cities were the Benha Children Hospital and the Zagazig University Oncology Institute. Accessing data from these

hospitals and cancer centers would be instrumental to assembling a comprehensive dataset that could improve the significance of the data analysis. Hence, preliminary discussions with medical oncologists at these centers were initiated and follow-up in-person meetings were planned for future fieldworks.

4.5 Discussion and conclusions

4.5.1 Establishing collaborations with cancer centers

The field trip was a great opportunity to establish collaborations with pediatric oncologists in Egypt. During the trip, we had meetings where we exchanged knowledge and had productive discussions about ways to improve the pediatric cancer medical care in their institute and, generally, in Egypt. Several areas of potential collaborative efforts were defined, such as digitalizing pediatric cancer data, joining the clinical trial networks, exchanging treatment protocols, and participating in training programs. Moreover, work plans and follow-up activities were discussed and outlined, and more detailed information is provided in section (4.6). Overall, the outcome of field trip with respect to establishing collaborations with pediatric cancer institutes in Egypt was highly successful.

4.5.2 Data collection and general approximate statistics

One of the main objectives of the fieldwork was to collect pediatric cancer data directly from cancer centers and compare it to published data. Unfortunately, data was stored as paper records across most hospitals visited, which prevented us from accessing the data and achieve this goal. This outcome could potentially change after completing the project of data records digitalization. However, during our meetings, medical doctors verbally provided data and approximate statistics

reflecting the current pediatric cancer status in Egypt. For example, the NCI reported that acute lymphocytic leukemia (ALL) is the most common type of pediatric cancer in Egypt, and acute myeloid leukemia (AML) represent around 30% of pediatric cancer cases. In addition, approximately 300 cases of renal cancer were diagnosed in the last 10 years with a survival rate of 70%. Al Mansoura cancer center reported that 20 new cases of Burkitt lymphoma are diagnosed in Egypt every year. Finally, Alexandria hospital reported that roughly 7000 pediatric patients are newly diagnosed every year in Egypt.

Given that the data collected was extremely limited and potentially inaccurate, we were not able to directly compare it to publicly available data to fulfill the primary objective of the field trip. Therefore, data comparison across cancer hospitals and identification of possible data discrepancy will be conducted when digitized data become available.

4.5.3 Main challenges and issues

The main outcome of the meetings during the field work was the identification of five major common issues among cancer centers in Egypt. The issues are the following:

1. A common factor emerged across all the hospitals visited: these centers operate under extremely limited financial resources and rely on public donations. Thus, the standard and quality of the services provided to the pediatric patients is poor.
2. One of the most common issues across cancer centers is the lack of databases and computerized data documentation. Patient's records are stored as hard copies and rarely organized into computerized databases. Thus, large amounts of clinical pediatric data accumulated over many years often get lost or is not available to be shared with other centers. Hence, medical doctors cannot access critical clinical information that could be used to improve their ability to diagnose

and treat pediatric patients. Moreover, the lack of data documentation represents a great challenge to define the real incidence, survival, cure and mortality rate of childhood cancer in the country, which significantly impacts the accuracy of allocating sufficient funds to improve the pediatric cancer medical care. When databases are organized and computerized, they are often not connected to local or global registry so that key data is not shared. The absence of databases at cancer centers and the lack of interconnection with established databases is mainly due to limited funds and shortage of medical staff.

3. Another major issue across cancer centers is the limited training available for medical staff and nurses. The need to establish training programs to enhance knowledge of the medical staff, pathologists and young residents is greatly needed. Educational and awareness programs for parents after the cancer diagnosis of their children is also critical. Many children die from infection and complications that could be prevented if parents have received necessary information and guidance.
4. Access to affordable medications and new therapies is another common challenge and has a significant impact on the survival and cure rate in the country. The high cost of chemotherapy is an enormous obstacle that limits children from receiving treatments. The limited opportunities of LMICs to enroll in international clinical trials also contribute to this problem because it prevents access to free drugs and essential medical support.
5. Major infrastructure gaps and limited social and supportive care greatly impact the medical care provided.

It was important to highlight the difference of resources that the 57357 hospital has and its access to cancer treatment and advanced protocol compared to other cancer hospitals and cancer

centers. Overall, the distribution of pediatric cancer care observed across centers in these large cities it is highly likely to be the same in smaller cities.

4.6 Post-fieldwork action plans and future direction

In this section, more detailed information about post-fieldwork action plans that were agreed upon during our visit is outlined. Out of numerous potential areas for collaboration, two main action plans were prioritized. These plans are data digitalization and training programs for GPs.

4.6.1 Data digitalization

Since one of the main objectives of this research was to determine whether there was a discrepancy between published data and data collected from cancer centers, accessing data from both sources is a fundamental step. However, after the fieldwork, it became clear that accessing data from hospitals in Egypt was challenging due to the absence of databases and poor data documentation in most of the centers that were visited. This represents a great obstacle to access the data and has a significant impact on the timeline for collecting and analyzing the data. Therefore, a strategy to upload patient's paper records into a database was proposed. The action plan to implement this strategy was comprised of three components, which are listed below.

4.6.1.1 Provide tools for data collection

Currently, efforts are on-going to explore and evaluate approaches to provide these cancer centers with data collection tools and establish data collection systems. These efforts include implementing databases, providing computers and funding salaries of personnel to upload the data. The process involves continuous discussions and liaise with various partners at cancer centers,

WCC organization and Merck KGaA to assess data collection strategies and prioritize the next steps.

4.6.1.2 Hiring data managers

To facilitate uploading the hardcopy patient's records into a database, hiring qualified full-time personnel is necessary. The anticipated timeline to complete the data upload is twelve months. Therefore, the number of employees necessary to upload the data within this timeline will vary depending on the number of patient's records accumulated by the different centers over time. Once the retrospective data is stored in a database, it is critical to assure that cancer centers will continue uploading the data in a timely manner. A funding scheme for maintaining the data entry might be needed and is under evaluation.

4.6.1.3 Facilitating the development of the database

In order to build an optimized database, various available databases will be interrogated and compared to evaluate differences and select the most appropriate one. There are currently two options to be evaluated. The first option is to use the CanReg5 databases used by the WCC, which could be provided to the various hospitals at no cost. The second option is to develop a customized database built by a software developer who offered this service at no cost. Irrespectively of the choice, the proposed database should be implemented as a simple excel based system to enable easy access of hospital staff to improve data documentation. The computerized database should also be interconnected with databases of local and global registries to facilitate the exchange and accessibility of the stored data.

Currently, there are very limited pediatric cancer data collected and reported from Egypt. Accessing this data is instrumental to defining the real medical need and allocating the necessary

funds to provide effective treatment solutions. Therefore, the development of the proposed database is critical and highlights the relevance of the proposed research plan.

4.6.2 Educational and training programs

The second action plan prioritized was the access of cancer centers to educational and training programs. This prioritization was due to the significant need of pediatric oncologists, medical staff, and nurses to receive the proper training in their area of expertise. The negative impact of undertrained staff on cancer medical care in Egypt was clearly communicated from all cancer centers and hospitals visited. Thus, accessing educational and training programs would enable medical staff to get exposure to advanced and up-to-date clinical practices in oncology. Since the university of Birmingham has an established relationship with the WCC organization, their training program was recommended. This funded program will focus on training GPs and healthcare workers. In addition, the program will provide training and educational materials to support parents after their children receive a cancer diagnosis. Such a program could have a significant impact on improving the pediatric cancer medical care across hospitals and cancer centers.

5 CHAPTER 5: SUMMARY AND FUTURE WORK

5.1 Summary of key findings

The assessment and analysis performed on data published by global databases highlighted that there is limited pediatric cancer data reported compared to adult cancer data, with clear underrepresentation of data from LICs. For example, approximately 50% of the major global investigated databases reported pediatric cancer data for the U.S. and European regions but lacked meaningful representation for Africa. Data analysis from these databases also showed discrepancy between data reported. Additionally, reviewing data from literature and publications on pediatric cancer data clearly indicated data underreporting, which was associated with the underrepresentation of cancer registries of LICs.

The cancer registries questionnaire that was conducted in selected African countries illustrated the extent of limited resources and workload that FTEs experience given the size of populations covered. Results from the questionnaire confirmed that incidence rates reported by cancer registries were not comparable with incidence rates reported by global databases. This discrepancy was also observed among databases used for this comparison. Additionally, various gaps and challenges that cancer registries face in LICs were identified. The most common gaps include lack of funding and training, limited number of pediatric oncologists, and small number of FTEs. Some of these gaps could be mitigated or resolved to improve data collection and reporting.

The field trip to Egypt was an opportunity to assess the real status of pediatric cancer medical care in LICs and the challenges that these cancer centers and hospitals face. Cancer centers that were visited experience limited resources, minimal funding, and stressful working conditions. In

addition, inadequate training of health care professionals was identified as one of the major challenges that significantly impact cancer medical care. Due to lack of digitalization of patients' records in cancer centers in Egypt, accurate pediatric cancer data collection and reporting is nearly impossible. Moreover, the number of pediatric cancer patients seen by hospitals and cancer centers are different from what is reported by databases.

In conclusion, the common outcome from the database analysis, literature review, cancer registries questionnaire and the field trip is the pronounced discrepancy between pediatric cancer data reported by all sources, which is highly indicative of pediatric cancer data underreporting in LICs. The second common outcome is the significantly limited resources and challenging conditions that cancer hospitals and cancer centers face, which has a great impact on cancer medical care in general.

5.2 Limitations of analysis

In this section some of the factors that have prevented a more complete analysis of the data collected are discussed. The limited pediatric cancer data for LICs available in the public domain creates a major challenge, which prevents performing comprehensive analyses and reaching accurate conclusions. Lack of publicly available datasets that overlap on the same period of time is another limiting factor that restricts opportunities to conduct appropriate comparison and assess accuracy. Moreover, the limited information published about cancer hospitals, cancer centers, and cancer registries in LICs impacts the ability to perform further assessments on their work model, structure, resources, and capacity.

The cancer registries questionnaire that was designed to investigate pediatric cancer data collection and reporting in African countries provided valuable results and information that were utilized in this thesis. However, the number of registries that participated was small (15) and represented only 11 countries out of 54 countries in Africa. The minimal participation was likely due to a language barrier, given that the questionnaire was provided in English. Translation of the questionnaire to local language should increase the number of cancer registries that could have participated. Expanding the participation could have added broader insights into the results of the questionnaire. Also, the questionnaire did not specify selection criteria to include cancer registries; rather, it was sent to all registries that were members of the AFCRN network. This factor might have decreased the geographical and population diversity of cancer registries that participated in the questionnaire. Furthermore, additional questions should have been added to the questionnaire to gather further details. For example, having obtained information about the role of each FTE and the structure of the registry would have provided a better understanding of the data collection process and workflow.

One of the main objectives of the field trip to Egypt was to collect pediatric cancer data from hospitals and cancer centers and compare it with data published in global databases. However, the absence of digitalized patients' records in most cancer centers and the loss of years' worth of hard-copy data due to poor storage conditions impeded data collection. Therefore, the inability to collect data from hospitals and cancer centers during the field trip to Egypt negatively impacted the outlined research plan and led to an incomplete assessment. Moreover, the field trip was originally planned to take place in more than one country. However, the length of time that was required for

logistics, scheduling meetings, and executing visits in Egypt limited the trip to only one country, which is not a sufficient representation for LICs in Africa.

5.3 Recommendations for future research

Recommendations for future work and analysis are proposed in this section. Additional data analysis could be performed to expand the scope of this research and aid to a more comprehensive assessment. For example, investigation of published pediatric cancer data from LICs, beyond African regions, would provide a broader insight about the status of pediatric cancer in other regions. Pediatric cancer data underreporting is a critical gap that needs to be resolved. Hence, exploring and tackling potential elements that could decrease underreporting might improve data collection, reporting, and accuracy in LICs. A few of these elements include allocating sufficient resources, provide training, and improving access to diagnostic tests.

Follow-up interactions with cancer registries that participated in the questionnaire could resolve issues that were not addressed in the original questionnaire. Some of these issues are the differences of funding sources between registries within the same country, rationale to why some registries did not collect pediatric cancer data, and why some cancer registries were not aware that a cancer control plan was established nationally. Obtaining and incorporating data from a questionnaire on cancer hospitals and cancer centers would be of a great benefit to investigate the hospital's side of data collection. This could provide a comprehensive view on the process of data reporting and collection in LICs.

Follow-up visits to Egypt might be useful to expedite the initiation of the data uploading work plan that was agreed upon during the field trip. Additionally, analysis of the data that will be

uploaded into database might enable achieving one of the primary goals of the field trip, which was to estimate the pediatric cancer incidence in Egypt. Finally, field trips to other African LICs might enhance the understanding of the real status of pediatric cancer medical care in Africa more generally.

6 CHAPTER 6: REFERENCES

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APPENDICES

Questionnaire for African National Cancer Registries (QANCR 2019) Pediatric Cancer data collection

Objectives of the study:

This survey is conducted in collaboration between the University of Birmingham, Birmingham UK, and The African Cancer Registry Network, Oxford UK. The main goal of this survey is to determine what pediatric data are collected by cancer registries, and how, in sub-Saharan Africa. The questions should only take 20-30mins and will address the methods used to obtain patient data, sources of data, type of data collected, and the main challenges that cancer registries face. To fill in the boxes, right click using your mouse and fill in.

Thank you for your time and contribution. We will let you know the outcome of the survey as soon as we have collated and analyzed the data.

Riham Iadevaia, Dr. Farhat Khanim, and Dr. Max Parkin

Contact Information:

Name	Institution	Email
Riham Iadevaia	University of Birmingham	[redacted]
Dr. Farhat Khanim	University of Birmingham	[redacted]
Dr. Max Parkin	The African Cancer Registry Network (AFCRN)	[redacted]

Registry name: ……...

Country: …….. Region: ……

Address: ……

……

Year established……..

Full Name: …….

Position: …….

Date: ……...

Signature: …….

1. General information about the registry

1.1. Please indicate the average full-time equivalent (FTE) of staff working in the cancer registry. Examples: Two half-time registrars would count for 1 FTE. The registry chief might work as an epidemiologist for 0.3 FTE, 0.5 as a clinician and 0.2 as a manager.

- ☐ - Registrar (e.g. collection, registration, checking)
- ☐ - Programmer (e.g. database management, automation and output)
- ☐ - Statistician/epidemiologist (e.g. methods, analysis, interpretation, communication)
- ☐ - Medical (e.g. pathology, coding, communication)
- ☐ - Administration (e.g. secretarial support)
- ☐ - Management (e.g. direction)
- ☐ - Other (please specify) ……...

1.2. Please estimate the percentage of the available funding supporting the registry from each of the different sources listed:

Percentage	Source	Comments
	Local Government (e.g. Health Department)	

	Academic Institution (e.g. University)	
	Hospital	
	Health insurance companies	
	Local NGO (e.g. Cancer society)	
	International NGO	
	Commercial company (e.g. Pharmaceutical)	
	Charities	
	Research grant	
	Private donor	
	Other	
100%		

2. Collection of pediatric cancer data

2.1. The population base (Target population):

What is the population-base of the registry (the population for which you aim to calculate incidence rates)? ……...

Name of cities/towns/ geographical areas covered ……..

……...

Estimated population of children aged 0-14…….

2.2. How is the pediatric cancer data collected? Please check all that apply:

☐ The registry reaches out to hospitals and cancer center for data collection

☐ Hospitals and cancer centers voluntarily report pediatric cancer data

☐ Both

☐ Other, please specify ……. ……

2.3. Which hospitals and cancer centers do you reach out to for pediatric cancer data? Please use Section (A) in the following table

2.4. Which hospitals and cancer centers voluntarily report pediatric cancer data? Please use Section (B) in the following table

Name of institution (A)	Distance to hospital	Frequency of data collection/update
…… …… …… …… …… …… …… …… …… …… …… …… …… …… …… …… …… …… ……	…….... …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. …….. ……..	☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly
Name of institution (B)	Distance to hospital	Frequency of data collection/update
…… …… ……	…….... …….. ……..	☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly ☐Monthly ☐Quarterly ☐Yearly

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2.5. Who collects the pediatric cancer data?

☐ Registrar ☐ Statistician ☐ Epidemiologist ☐ Administration ☐ Other

If other, please specify ……

2.6. Is the data connected to other registries in your country? ☐ Yes ☐ No ☐ Don't know

If yes, which ones? ……...

2.7. Is the data connected to international/global registries? ☐ Yes ☐ No ☐ Don't know

If yes, which ones? ……

2.8. Do you use the CANReg5 database?

☐ ☐

Yes No

If No, which database are you using?.....

3. Sources of pediatric cancer data

3.1 Do you collect data from hospitals treating childhood cancer? ☐ Yes ☐ No

If yes, how many? ……

3.2 Which of the listed sources of data are used to capture the pediatric incident cancer cases in your registry? Please select all that apply and indicate how many?

☐ Imaging departments If yes, how many? ……..
(CT and/or MRI, ultrasound, X rays) …….

☐ Radiotherapy departments If yes, how many? ……..

☐ Pathology lab If yes, how many? ……..

☐ Hematology lab If yes, how many? ……..

☐ Public hospital If yes, how many? ……..

☐ Specialist oncology units If yes, how many? ……..

☐ Private hospital/clinic If yes, how many? ……..

☐ Health insurance providers If yes, how many? ……..

☐ Neurosurgery If yes, how many? ……..

☐ Other ……

3.3 Do you use death certificates as a source of information on cancer cases?

☐ Yes ☐ No

If yes, what is the source used?

☐ Birth and death registration?

☐ Hospitals (mortuary)

☐ Other ……

3.4 Please specify whether the data collected is by voluntary collaboration or is it part of a legal/formal agreement between the registry and the data sources

☐ Voluntary collaboration ☐ Legal agreement

☐ Formal framework ☐ Other ……

3.5 Do you record data on all pediatric cancer cases from the sources used by the registry? Or only on residents of the population-base?

3.6 If ALL cases, what is the approximate number of pediatric cancers registered in a recent year:

a) Total cases…….

b) Cases from the registry population-bases……..……

3.7 For each of the sources-are there computer databases that can be used to provide the information needed for registering a child with cancer

☐ Yes ☐ No ☐ Sometimes …….

If yes,

☐ All the information required

☐ Only some of the information required

4. Type of pediatric cancer data

4.1 What type of pediatric cancer data have you collected? Please select all that apply

4.1.1 Test results and diagnosis data:

☐ Tumor biopsy results ☐ Bone marrow aspirate data ☐ Blood test results

☐ Current treatment ☐ Previous treatment

☐ Initial treatment – if yes, how do you define the initial treatment? ……

…….

4.1.2 Contact information and follow up:

☐ Name of contact person ☐ Phone number of parents or guardian of the child

☐ Date of last contact ☐ Status at the last contact

☐ Date of next follow up appointment

☐ Long term survival

4.1.3 Stage of disease data:

☐ Stage of the disease ☐ The system used in staging the disease

☐ Laterality (for retinoblastoma patients)

Other …….....

……..

5. Use of cancer registry results in pediatric cancer control

5.1. Does the registry have any formal contact with the department/s of health?

☐ Yes ☐ No ☐ Don't know

Contact with local Health Department ☐ Yes ☐ No

Contact with Ministry of Health (national) ☐ Yes ☐ No

5.2.Please give details of such contacts

☐ Joint meetings

☐ Response to requests for information on cancer

☐ Planning of cancer services (including cancer surveillance, screening planning)

Please specify:

5.3. Is there a National Cancer Control (or NCD Control) Plan in place for your:

☐ Country or ☐ Province/Region?

☐ Yes ☐ No ☐ Don't know

If YES,

a. Which Health Authority is responsible for the Plan?

……..

b. Was a member of the Cancer Registry among the team preparing the Plan?

☐ Yes ☐ No ☐ Don't know

5.5. Were the pediatric data from your cancer registry used to calculate national estimates for Globocan 2018?

☐ Yes ☐ No ☐ Don't know

If NO, what was the reason: ……..

……

5.6 Has the registry ever been mentioned in public media?

☐ Yes ☐ No ☐ Don't know

6. Resources and Challenges in collecting pediatric cancer data

6.1 Are your current resources sufficient to allow you to collect pediatric cancer data?

☐ Yes ☐ No

If No, what are the additional resource that you might need? Please select all that apply

☐ Personnel ☐ Funding ☐ Training ☐ Computers ☐ Other……

6.2 Would it be possible to collect more completed datasets on childhood cancer and in a larger area?

☐ Yes ☐ No

If yes, what additional resources would be needed to accomplish this? Please specify

……

……

……

……

could this be done for:

☐

The whole country

☐ Part of the country (Please specify) ……..

……...

6.3 In your opinion what are the main challenges you face in collecting pediatric cancer data/information

1- ……..……..

2- ……..……..

3- ……..……..

4- ……..……..

5- ……

Additional comments:

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