UNIVERSITY of RWANDA

ACCESS TO CHILDHOOD CANCER ESSENTIALS DRUGS IN RWANDA

By

Dr Jean Nepomuscene NKURUNZIZA

Registration number: 11111593

A dissertation submitted in partial fulfilment of the requirements for the Degree of MASTER OF MEDICINE IN GENERAL PAEDIATRICS.

School of medicine and pharmacy

College of Medicine and Health Sciences/ University of Rwanda

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August 2021

CERTIFICATION FOR EXAMINATION

The undersigned certify that they have read and hereby recommend for acceptance by the University of Rwanda a dissertation entitled "**Access to childhood cancer essential drugs in Rwanda**" in partial fulfillment of the requirements for the degree of Master of Medicine (Pediatrics) of the University of Rwanda.

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DECLARATION

I declare that this dissertation contains my own work except where specifically acknowledged.

Dr Jean Nepomuscene NKURUNZIZA

11111593

Signature:

Date: 21 December 2021

DEDICATION

To my Creator, I thank you for the courage and determination to realize the completion of this work.

To my special wife, Joyeuse NDUWAYO

To our children, IGANZE NKURUNZIZA Grady Loan and GWIZA NKURUNZIZA Ciella

To my mother and my late father

To my brothers, sisters, and in-law family

I dedicate this work.

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May God bless you.

GLOSSARY ITEMS

EMLs: Essential Medicine Lists

HIC: High Income Countries

LMICs: Lower and Middle Income Countries

UR: University of Rwanda

CHUK: (University Teaching Hospital of Kigali)

CMHS: College of Medicine and Health Sciences

KFH: King Faisal Hospital

MOH: Minister of Health

RBC MPPD: Rwanda Biomedical Center Medical Procurement and Production Division

WHO: World Health Organisation

NCDs: Non-Communicable Diseases

EMs: Essential Medicines

NEMLs: National Essential Medicines Lists

EMLc: Essential Medicine List for children

RNEC: Rwanda National Ethic Committee

EAC: East African Community

PI: Principal Investigator

UN: United Nation

SDGs: Sustained Development Goals

POSIT: Paediatric Oncology System Integration Tool

RMS: Rwanda Medical Supply

elMIS: electronic Logistics Management Information System

MINECOFIN: Minister of finance and economic planning

RPPA: Rwanda public procurement agency

SPN: Special procurement notice

GPN: General procurement notice

BCCE: Butaro Cancer Center of Excellence

VEN: Vital Essential Non-essential

GMP certificate: Good Manufacturing practice certificate

DTC: Drugs and Therapeutic Committee

MDG: Millennium Development Goals

ABSTRACT

Background: Childhood cancers are curable. Access to essential childhood cancer drugs has proven a direct effect on reducing mortality of paediatric cancer in developed countries with an 80% cure rate contrary to 90% of paediatric cancer deaths in LMICs where ineffective care is distributed. To decrease childhood cancer mortality in LMIC, availability of good quality and affordable essential childhood cancer drugs is required.

Objectives: This study aimed to identify determinants of paediatric cancer drug access in Rwanda.

Methods: Qualitative method using policy and thematic analysis was used. Data collection was done using health policies analysis and semi-structured interviews with fifteen stakeholders involved in paediatric cancer care and cancer drugs procurement in Rwanda.

Results: Eight policies and guidelines related to drug procurement and cancer treatment were analysed. Fifteen stakeholders including policymakers with policy preparation, procurement and regulatory roles (n=8), non-governmental organisation (n=1) with cancer treatment center funds, and service providers, with clinical and pharmacy-related roles (n=6), were interviewed. Four major themes emerged from participant interviews that highlighted a number of barriers, solutions, and facilitators as determinants of childhood cancer drug access have been formed that included: (i) Limited prioritization for pediatric cancer; (ii) weak procurement and supply chains; (iii) high childhood cancer drug costs, and (iv) lack of systems to optimize pharmacovigilance. After policies analysis, there are gaps in policies specific to childhood cancer. Policy related to childhood cancer need to be developed as a rapidly growing domain that needs good attention. In Rwanda there is poor access to essential childhood cancer drugs, the barriers expressed by the study mostly is related to a limited budget, disseminated procurement, expensive drugs, and lack of generic anti-cancer drugs. Most of these barriers push procurement for doubtable quality drugs. Solutions given by the study participants to improve access to affordable good quality childhood anti-cancer drugs are pool procurement in the country or combined with other countries based on accurate data and good budget specific to cancer as a rapidly growing domain. Good budget and bulk procurement stimulate cancer drugs suppliers with well-known quality to enter in a tender, good solution to cancer care.

Conclusion: This study reveals the need for systemic consideration of childhood cancer at the national level related to greater policy attention and coordination and a more systematized approach to procurement and supply chain management for essential childhood cancer drugs in Rwanda.

Keywords: childhood cancer, essential drugs, Rwanda

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CHAPTER 1. INTRODUCTION

1.1. BACKGROUND

Rwanda is an enclosed crowded low-income country in sub-Saharans Africa. Wellness program in Rwanda is mostly served in public hospitals and is coming to the fore in free enterprise. Majority of patients are insured by mutual health insurance (CBHI) (1,2). Rwanda health system consists of referral, provincials and District Hospitals with health centers and posts, community based health workers and private hospitals (3) Rwanda has a well-established referral system, from community based health workers until referral teaching hospitals where most patients with cancer are diagnosed and treated. This well-established referral system has significantly improved mortality and morbidity as patients meet concerned physicians for diagnosis or treatment in a short time.

Reducing paediatric deaths is one of Millennium Development Goals target; as low-income and lower- middle-income countries (LMICs) advance toward the achievement of this target, creativity to reduce the burden of non-communicable diseases, including paediatric cancer need to be highlighted. United Nations (UN) Sustainable Development Goals for 2030, declared in September 2015 include the reduction of early mortality from NCDs, where cancer is important part (4).

Globally there were 18.1 million new cancer cases and 9.6 million cancer deaths worldwide in 2018 (5). The number of new cases is expected to increase by more than 70% over the next 20 years to reach 22 million (6). Global, a child is confirmed with cancer every three minutes (7). Roughly 200 000 children and adolescents are confirmed with cancer every year worldwide (8). In Denmark, one of the developed countries, the annual incidence of paediatric cancer rate is around 14 cases per 100 000 children below 15 years of age (9). In the United States, the mean annual incidence rate for all cancers in people below 20 years is 14.9 cases per 100,000 person-years (10).

The proportion of paediatric cancer in sub-Saharan countries amid all cancers was 1.4% to 10.0% in Ghana and Rwanda (11). 80% of paediatric cancer cases live in the lower-middle-income country where Rwanda as EAC member is located (12). In many cases, these children have small or no access to essential childhood cancers drugs, only 20% of diagnosed children receive effective care and 90% of paediatric cancer deaths now occur in poor countries where ineffective care is distributed (7,13). A major impediment to paediatric cancer effective care in LMICs is lack of essential medicines (8)(14). In developed countries with multi modalities therapy and team workers action in the management of paediatric cancers, there is a significant

reduction of mortality related to cancer in children with an 80% of cure rate (15). In LMICs where East African countries including Rwanda located and where preponderance of paediatric cancer, cure rates are far lower(12).

Strong care of paediatric cancer require unbiased access to good anti- cancer and supportive dugs (16). limited access to cancer curative therapies and limited numbers of health professionals with specialized cancer training was a major factor of mortality in LMIC including Rwanda (17). Restricted access to paediatric cancer drugs is the main factor contributing to the low survival rate of paediatric population in Rwanda as LMIC. This study analysed determinants of childhood Cancer Essential Drug Access in Rwanda.

1.2. PROBLEM STATEMENT

Access to childhood cancer essentials can significantly improve health outcomes. One of the key components of drug access at both the institutional and national levels in LMICs is the genuine, sustained, and competitively-priced purchase of essential drugs (18). Poor access to treatment is partly due to market inefficacy that restrict the availability of affordable products that have been approved by a stringent regulatory authority, such as the regulatory authorities of the US or European Union. In many LMICs, including Rwanda, the small and unpredictable procurement volumes currently observed are not attractive to manufacturers, who find most of their market in wealthy countries. This lead to high prices, limited bid response , and shipping delays, forcing countries to procure from lower-quality manufacturers. In addition, high distributor mark-ups along the supply chain add cost and reduce competition. Poor access to chemotherapies forces providers to delay care, change patient regimens mid-course, or use sub-optimal regimens, all leading to fewer patients receiving treatment and worse health outcomes.

The African oncology market is currently small; many countries, individually, do not procure some products in sufficient quantities to meet manufacturers' minimum order quantities. This challenge increases the cost of production for manufactures, limits countries' negotiating power, and ultimately results in higher prices paid for medicines and diagnostics.

Currently, in Rwanda, guideline on management of non-communicable disease suggests chemotherapy production from provincial hospitals, referral hospitals and teaching hospitals(3). This is not practical as only BCCE and KFH currently provide chemotherapy. Despite MOH's voluntary to provide cancer care, little data available on determinants of childhood cancer drug access continue to limit easy accessibility to pediatric essential cancer drugs. This study, therefore, sought to investigate barriers to pediatric cancer essential drugs access in the Rwandan context.

1.3. RESEARCH QUESTIONS ADDRESSED BY THIS STUDY

There are two key questions guiding this investigation:

- ✓ What health and procurement policies and practices are in place and how do they structure paediatric cancer drug access in the Rwandan health system?
- ✓ What are the key determinants of childhood cancer drug access in Rwanda?

1.4. RESEARCH AIMS AND OBJECTIVE

1.4.1. STUDY AIM:

- ✓ To identify determinants of paediatric cancer drug access in Rwanda, with attention to the macroeconomic and health system context.

1.4.2. STUDY OBJECTIVES:

To achieve the aforementioned aim, this study had two primary objectives:

- ✓ To describe current policies and practices related to childhood cancer drug procurement and provision within Rwanda.
- ✓ Identify the system-related key determinants of access to paediatric cancer drugs within Rwandan health system.

CHAPTER 2. LITERATURE REVIEW

At the 2012 World Health Assembly, member states agreed to reduce premature mortality from non-communicable diseases (NCDs) by 25% by 2025, among them childhood cancer included (11,12). For the achievement of the goals, WHO set some measures among them is expending Essential Medicines Lists for diseases which government should meet. The list is available to governments in all countries as a developmental guide to the national essential medicines lists (NEMLs), which supports the purchase of essential medicines for the public sector (20). Paediatric malignancy medicines are on the WHO model list of Essential Medicines for Children (EMLc) (20). To achieve these goals for reduction of NCDs mortality, universal health coverage through access to affordable good quality essential drugs had been set as part of no 3 sustainable development goals by 2030(21,22). Access to essential treatments for cancer is the key determinants of childhood cancer outcome. Treatment of paediatric cancer is a huge success of modern medicine but in the lower-middle-income country is still a problem due to limited access. Currently, more than 80% of children with cancer receiving modern multidisciplinary treatments in developed countries are cured (12).

According to Global Access to Essential Medicines for pediatric Cancer study, 42.1% of patients in low- and middle-income countries do not have full access to chemotherapy kits (23). With this poor accessibility to childhood cancer drugs, a big percentage 80% of paediatric cancer are in lower and middle-income countries (12). Access to medicines is regulated by numerous factors in health care system, including drugs availability, accessibility, acceptability, affordability, and quality (24).

Poor access to essential medicines for managing chronic diseases and cancers is a big issue in low-income and middle-income countries including Rwanda as an East African member (14). Morbidity from pediatric cancer is second only to unintentional injuries in high-income countries, in low-income countries, it hardly hits the radar screen compared with death from infectious disease (17).

In first world countries, multimodal therapy treat more than 80% of paediatric cancers, Survival rates for Wilms tumor, Burkitt's lymphoma, and ALL in HICs are higher than 85%, 90%, and 85%, respectively (17,19,25). In contrast to the heartening progress in HICs, childhood cancer survival remains low in LMICs including Rwanda (13). Over 90% of children with cancer are diagnosed in low- and middle-income countries (LMICs), where mortality is high (19).

In LMICs, where the majority of paediatric cancer reside, cure rates are far lower as essential childhood cancer accessibility is poor (13). Access to cancer drugs is a difficult issue, involving

phenomena from drug development to delivery. Challenges related to cancer drugs are evident across common domains of access: **availability, accessibility, acceptability, affordability, and quality** (24)**.**

Availability: Essential cancer drug availability measures the number of unexpired drugs in a health facility in relation to all expected number of childhood essential drugs on the list elaborated by WHO to constructively give essential health services. The elements that guide the availability of drugs in the health system are the inaccessibility of drug prices, under budgeting especial in the public sector, inability to accurately predict the needs and unsuitable acquisition in the supply chain, and weak Cooperation between government and non-government in providing access to essential medicines (26).

Accessibility touch on to the capacity for individuals to get the treatments needed for their health regardless of age, income, or other factors (27). Paediatric cancer drugs are often lacking in LMICs due to weak supply management system such as inadequate inventory management, broken supply channels, affordable prices of essential medicines, and inadequate infrastructure for transportation and storage. These complications are exacerbated by socioeconomic and geographic complexity in many LMICs, primarily poverty and rural influences patients' ability to obtain the medicines they need (24) (28).

Acceptability is the overall capability and desire of the patient to use the medicines and the caregiver to give the medicine as planned (29). Despite the availability of potent molecules, there is deficiency of paediatric formulations as syrups compare to adults formulations. Childhood cancer treatments are unique in that requisite sterile injectable formulation; therefore, they are relatively complex to manufacture, require refrigeration and have limited shelf lives. In addition, they are administered according to body weight or body surface area, making it difficult to prescribe doses suitable for different stages of child development in the case of vials or pills that minimize waste. .. These characteristics often put pressure on drug acceptance for both healthcare providers and patients, especially in LMICs (24).

Affordability refers to connections between cost, price, and solvency. It addresses issues related to drug pricing, drug purchasing methods, and the impacts of these factors on access to drugs.

Globally, high price of cancer therapy poses a challenge to cancer suffers and governments alike mostly in LMIC. The generic anti-cancer formulation has been formed, cost related boundaries continue (30). These boundaries are based on a variety of phenomena, including limited national budget and competing health system priorities; small fragmented markets for paediatric cancer

treatments; slim industry profit margins due to patent expiry; and lack of public or employer-based insurance scheme coverage (24).

Quality integrates pharmacovigilance, efficacy and address issues related to drug origin such as counterfeiting, poor manufacturing, and poor quality control. The most important generic production capacity for pediatric cancer treatments is the double-edged sword. It lowers prices but spreads production, which complicates drug origin assessments and therefore quality assurance. These guarantees are still compromised in many low- and middle-income countries by weak or non-existent pharmacovigilance systems compared to decentralize and often maze-like drug supply and supply systems (24). Governments must control the manufacture, procurement, storage, distribution, supply, and sale of medicines to guarantee the drug's safety and efficacy.

In Rwanda 700 paediatric cancer patients are anticipated to be diagnosed each year (31). An analysis of cancer registries from 2007 to 2011 displayed 320 paediatric cases enrolled throughout Rwanda, The PIH with Butaro Cancer Center of Excellence which provides the only free source of cancer care in the country recorded only 102 children with cancer diagnosed from July 2012 to June 2013, very low number compared to the expected number, this comes as consequences for difficult accessibility of childhood cancer care (31).

This discrepancy might indicate significant level of cancer that has not been diagnosed and treated in the paediatric individuals (7). Butaro Cancer Center of Excellence receives selected types of cancer due to the lack of all modalities of cancer treatment and inaccessibility of all essential childhood cancer drugs. As a single semi-public center of cancer treatment in Rwanda which is located in a rural area of the northern province of the country, and most paediatric cancer are diagnosed at referral hospitals mostly KFH and CHUK, all patients are not accessing the center.

Some of the patients who don't reach to Butaro site, others don't complete treatment courses due to stock out or absconding to treatment due to inaccessibility and unaffordability of cancer treatment. All these factors lead to poor adherence, if paediatric cancer treatments are available in multiple centers may improve patient's care that can improve the survival rate for children with cancers.

Access to essential anti-cancer drugs is one of major determinants of childhood cancer outcome worldwide. WHO Essential Medicines List sets the fundamental standards that governments in all countries must meet in their supply of drugs (20).

World Health Organisation plan on access to medicines is focused on evidence-based selection of essential drugs, coherent purchase of quality-guaranteed products, affordability and efficiency

of patients and medical systems, fair dispensation networks to ensure general access to needed medicines. These joined task within the pharmaceutical department need to be addressed concomitantly to guarantee that patients can have timely access to needed treatments (20). Guarantee access to such medicines is a clear component of the broader right to health enshrined in international human rights conventions (19,32). Based on the WHO list of cancer essential medicine, this study explored policies and practices related to childhood cancer drug procurement at the CHUK, KFH, Butaro cancer center of excellence, and RBC MPPD as institutional in charge of medications procurement in Rwanda and barriers impending ACCESS.

Essential medicines are those solving health care priorities in the population and be always available in operating health systems at all times at affordable price to patients (20). Universal availability of essential medicines in the public sector is essential to promote fairness of access which decreases mortality.

They are many contributing factors of mortality including shortage of facilities to treat cancer, delayed consultation, shortage of multidisciplinary team care, some children consulted with malnutrition leading to power chemotherapy tolerance, concomitant infection, ignorance, poverty causing poor adherence, lack of chemotherapy, or other modalities like radiotherapy which mostly increase mortality related to cancer, equitable access to affordable healthcare including essential medicines is one of the challenges.

This study identified available medicines in Rwanda national EMLs based on WHO list of EMLs and identify determinant factors of poor access to childhood cancer essentials drugs at CHUK, KFH, Butaro Cancer Center of Excellence, and RBC MPPD as a center of national public drug procurement

Despite this good achievement of childhood cancer care in developed countries and WHO strategies on childhood cancer drug access in LMICs, mortality is still high in these developing countries including Rwanda, this study identified some barriers and enablers of paediatric cancer drug access in Rwanda and possible modalities of cancer treatment.

One of the key components of drug access at both the institutional and national levels in LMICs is the genuine, sustained, and competitively-priced acquisition of essential drugs(18).

CHAPTER 3. RESEARCH METHODOLOGY

3.1. STUDY DESIGN

This study was a qualitative case study design. It was explored through the identification of different factors interacting in access to essential childhood cancer drugs in Rwanda. Its focus is upon drawing the meaning from the ideas and experiences of participants (33).

3.2. STUDY SITE

This study explored determinants of paediatric cancer drug access within Rwandan health system.

3.3. STUDY POPULATION

Sampling was purposive to include stakeholders involved in childhood cancer care, systems of drug procurement and supply, and/or cancer policy and program development. Stakeholders were picked out via policy documents and academic literature study and snowballing techniques involving participant referral. Stakeholders were contacted by email or by telephone and invited to participate in the study, and required to sign an informed consent form before interview initiation.

3.4. INCLUSION CRITERIA

Stakeholders involved in childhood cancer care, systems of drug procurement and supply, and/or cancer policy and program development. These roles included individuals engaged in cancer policy and programming at the national level, procurement officers at CHUK, KFH, Butaro Cancer Center of Excellence, RBC MPPD members as institutions in charge of drug procurement and MOH.

3.5. EXCLUSION CRITERIA

Persons who are not taking care of children with cancer and are not engaged with cancer policy or programming. Also, persons who refused to sign consent.

3.6. RISKS

There were no physical risks or discomforts to participants in this study, as it consisted only of a confidential one-on-one interview.

The most considerable risk anticipated in this study was emotional distress that could rise from parents with children with cancer and the patient's side was excluded in the study. We gave light to stop the interview if a participant was not comfortable. However, no subject stopped the interview.

There was also a minor social risk of disclosing participants' socially private information. To avoid this, we gave enough explanation to the participant about the concept of research and policy of privacy before starting the interview. We kept all information confidential.

No legal risks, no financial risks to both the researcher and the participants

3.7. BENEFITS TO SUBJECTS

There were also no direct benefits from participating in the study. However, in the future, policymakers may use the information shared by subjects when deciding whether and how to improve access to therapies for children with cancer.

3.8. SAMPLING AND ENROLMENT

3.8.1. QUALITATIVE DATA COLLECTION

Qualitative data collection was derived from: (1) structured searches of the published and grey literature on the health system context, childhood cancer care, and health technology policy in participating jurisdictions; and (2) in-depth, semi-structured interviews with stakeholders involved in childhood cancer care, systems of drug procurement and supply, and/or cancer policy and program development in Rwanda. Data sources included governmental and non-governmental documents, academic articles, media sources, organizational and transcripts from qualitative interviews. Stakeholders were contacted by email or by telephone and invited to participate in the study.

The PI and supervisors developed semi-structured qualitative interview guides focused on cancer medicine availability in a public health. Interviews were audiotaped, transcribed verbatim, and translated into English. Relevant literature and interview transcripts were imported into and inductively coded using excel. The PI and a second reviewer coded to confirm data coding and increase reliability

3.9. SAMPLE SIZE

Sample size in a qualitative study was determined by saturation of data which is the gold standard by which the purposive sample sizes are determined (Polkinghorne, 2005) (34). Guest et al 2006 postulate that six to twelve subjects are adequate to achieve saturation(35). For this study, the PI interviewed fifteen stakeholders who could speak to childhood cancer drug access, and saturation was reached.

3.10. MEASUREMENTS AND STUDY INSTRUMENTS

Interviews were semi-structured, lasted about 30 -40 minutes each, and were based on an interview guide developed for this study.

3.11. DATA ANALYSIS and MANAGEMENT

Before each interview, the participant was briefed about the confidentiality and non-use of names. During the transcription, a unique patient code was used PRA or SP or NGO followed by a number of codes. The first code PRA stands for Policy and Regulatory Authority, second code

SP stands for Service Provider, third stands for Non-Governmental Organization the number means numbering order of interview. Transcriptions and translations were stored in a password-secured computer. Transcription was done by the PI and double-checked by a research assistant trained on qualitative data transcription and supervisors. No translation was performed as the interviews were taken in English. Analysis was done using the qualitative manner in the following 6 steps:

1. Familiarization with data where we carefully listened to the audio recordings several times to gain a sense of content, then transcript the data.
   Transcription was done by the PI or by a data-transcriber
2. After identification of important features of the data that might be relevant to answering the research question, coding and thematic analysis was done using Microsoft Excel.
3. Identification of thematic framework. After reviewing the codes and collated data themes have been condensate.
4. Indexing: we grouped and analyzed different codes within themes based on similarities and differences. Then we sorted themes into categories and subcategories.
5. Charting: we read all collated extracts for each category and see if they appear to form coherent patterns.
6. Mapping: We defined and refined the categories and analyze them within themes

3.11.1. DOCUMENTS REVIEW ANALYSIS

Data analysis of documents was undertaken in the following steps: Transcripts and data from desk reviews were read, organized, and familiarized. Sections related to childhood cancer drugs procurement, provision, policy and strategy statements, and regulations were noted. All relevant data with respect to research questions were analyzed.

3.12. STUDY LIMITATION

One potential limitation includes limited access to different stakeholders as a result of time constraints or constraints in recruitment. This limitation was minimized by focusing the recruitment of participants critical to paediatric cancer drug policy, procurement, and supply chain management, and then snowball sampling.

3.13. COMPENSATION/REIMBURSEMENT

Subjects did not receive any compensation for their involvement in the study, nor did they incur any out-of-pocket costs for participating in the research.

3.14. ETHICAL CONSIDERATION

3.14.1. INFORMED CONSENT

Informed consent was obtained with a written consent form after a full explanation of the objectives of the study.

3.14.2. CONFIDENTIALITY ASSURANCES

All data collected remains anonymously coded and presented. By signing the consent form, the subject agreed to allow the research team (PI and supervisors) to view their research data. The subject received a copy of the research consent form. The data created from this study was stored in a secure and locked location. Only research team can access the data. The audio recordings of the interviews were transcribed by a professional transcription company and PI. They were no audio recordings, without any identifying information attached. Any identifying information on the audio recording was removed or uses pseudonyms when the interview was transcribed. At the end of the study, the data are retained as long as needed.

3.14.3. ETHICAL APPROVAL

The research proposal was reviewed and approved at the pediatric departmental level, the CMHS Institutional Review Board *(No 027/CMHS IRB/2020),* and the National Ethics committee (FWA Assurance No.00001973 IRB 00001497 of IORG0001100) before approaching the participants and starting data collection.

3.15. CONFLICT OF INTEREST (REAL OR APPARENT)

There were no conflicts of interest

CHAPTER 4. RESULTS

4.1. DETERMINANTS OF CANCER DRUG ACCESS

To study determinants of childhood cancer essential drugs access, analysis of documents related to current health policies and analysis of key-informant interviews with health system stakeholders has been taken in place.

4.1.1. DOCUMENT ANALYSIS OF CURRENT HEALTH POLICIES AND STRATEGIES

To understand the determinants of cancer drug access in Rwanda, we conducted analysis of the documents to review what policies and strategies have been established within the Rwandan context to guide practice and procedures around drug access, procurement, and supply.

Eight national health-related documents were evaluated, which included policies and guidelines describing drugs procurement and supply chain management nationally and institutionally. Table 1 provides an overview of the relevant documents reviewed. Although no specific policy focussing on paediatric cancer exists in Rwanda, there are many policies and strategies in place to guide cancer drug procurement, supply, and delivery mechanisms. Foundational to this process is the establishment of adequate methods for forecasting the need for paediatric cancer medicines. The MoH, through the RBC division of non-communicable disease, supports a national cancer registry to have adequate data on cancer to facilitate drug planning. This data is to be completed by district hospitals, provincial hospitals, referral hospitals, teaching hospitals, which are then provided to the MoH. With this data, institutions in charge of public drug procurements, such as RMS, refine their budgets for drug procurement, a process predominantly procured from international manufacturers. As it relates to childhood cancer, data that tracks disease incidence is not well documented, and as such, results in weak data systems for guided policymaking on childhood cancer.

Table 1: Overview of relevant Rwandan health policies

Document tittle	Document type	Timeline	Vision/mission/objective	Main actors	AUTHOR
National Health sector Policy	Policy	2015-2020	To ensure universal accessibility of equitable and affordable quality health services for all Rwandan	MOH	MOH
National guideline for management of Non-Communicable Diseases (NCDs)	guideline	2016	Non communicable disease management	MOH NCD program from RBC	MOH
Rwanda National Health Insurance Policy	Policy	2010	To provide a national framework for strategies and actions aimed at assuring that all residents of Rwanda can be enrolled in a health insurance plan that provides access to quality health care	Policymakers, MOH	MOH
Public procurement user guide	guideline	2010	To enhance the ability of Government officials and suppliers to work in mutual understanding for the interest of both parties and in transparency	- MINECOFIN - RPPA	Minister of Finance
Liste de medicaments essentiels national	Guideline	2010	To ensure harmony in treatment, procurement, and reimbursement	Policymakers, MOH	MOH
national list of essential medicines for adults	guide	2015	To help direct prescribers and dispersers on the product to be prescribed and dispensed at each level of the health system	Policymakers, MOH	MOH
Pharmacy policy 2016	policy	2016-2020	Rwanda's population health is improved through the sustainable provision and rational use of intrinsically high quality medical services that are accessible and affordable in fair manner	Minister of health -Rwanda medical supply -health insurances -private pharmacy wholesale	MOH
Guideline on submission of documentation for registration of human medical products through FDA 2020	Guideline	2020	To provide guidance to applicants and authority in managing applications for human medicinal products	Rwanda FDA	-MOH -RFDA

4.1.1.1. DRUG FINANCING AND PROCUREMENT

According to the 2016 National Pharmacy Policy, health commodities are financed through fiscal budgetary allocation, insurances scheme, development partners, the private sector, and out-of-pocket expenditure. The budget of the RMS, as a public institution under the MoH finance, is allocated across a broad spectrum of competing disease priorities. Due to limited public sector capital, the budget attributed to cancer drugs is small compare to demand.

Cancer drugs finance is low compare to estimated procurement need. The country does not have a dedicated budget from paediatric cancer drugs. Strategies to address this limited capital in terms of cancer drugs included the potential creation of a dedicated national paediatric drugs budget within the national drugs budget if possible paediatric oncology drugs budget and private investment or NGO funds. This will solve the problem of poor cancer drugs availability.

As specified in the 2016 National Pharmacy Policy, the procurement process is mainly fulfilled by the Rwanda-MPPD currently changed to Rwanda Medical Supply, referral hospitals, BUFMAR, and private pharmacy wholesalers. For public procurement of health commodities, including childhood cancer essential drugs an international bidding competitive bidding is used for the procurement process(36). The procurement process is following the general rule of procurement proposed by the Rwanda public procurement authority (RPPA) as outlined in Figure 1(37).

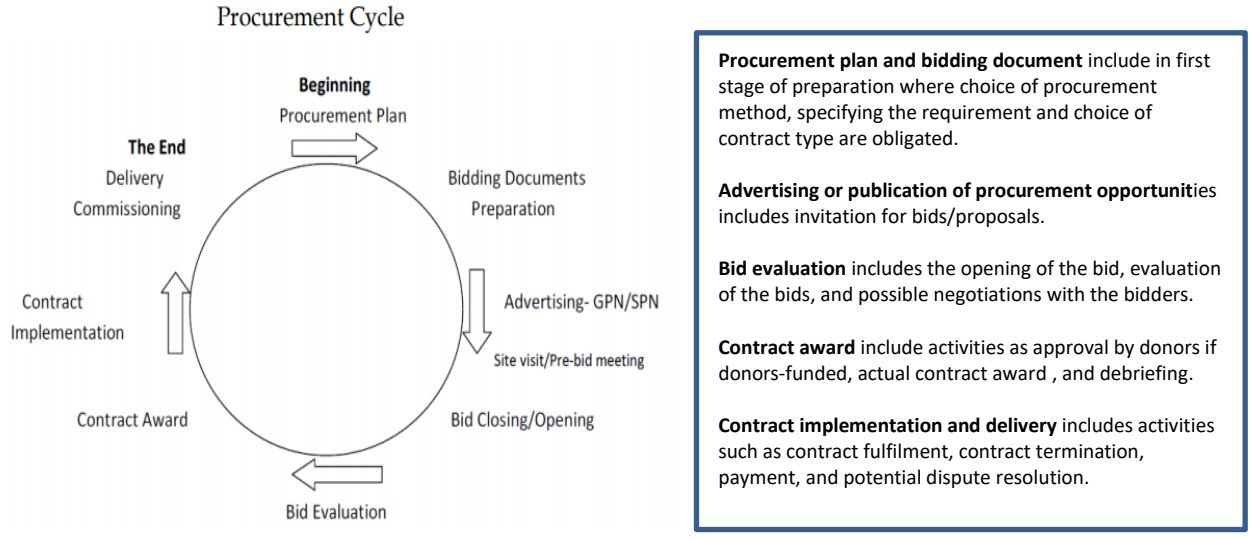

Figure 1. Rwanda public procurement user guide (30)

During the procurement planning process and the preparation of the bidding documents, the procuring agency shall ensure that there is enough allocated budget and shall be compliant with regulations governing budget execution. Every procurement is associated with tender as

specified in article 18 of the RPPA guideline. State that the threshold for procuring without tendering is for purchases whose value does not exceed one hundred thousand Rwanda francs (37).

Cancer drugs experience greater procurement limitations as there is no local industry and no local pharmaceutical company supplying cancer drugs. The global pharmaceutical industries are not interested to supply cancer drugs in a small country like Rwanda as they are not targeting the big market in Rwanda. This lack of interested suppliers had the effect of lack of competitive bidding in terms of the tender which leads to the high cost of cancer drugs. For small domains like childhood cancer drugs to allow direct negotiations with cancer drugs producers like industry rather than passing through tender by delivery for a certain signed contract like in two years might be helpful. there are currently multiple drug procurement agencies and they are not interested in burden of procuring small amounts of drugs, creation of cancer drugs procurement agency, this would increase volumes of drugs, providing a platform for negotiating better prices.

4.1.1.2. DRUG REGISTRATION

During the process of drug registration, an applicant sent a letter online or hard copier with attached drug registration fees payment to Rwanda FDA, Rwanda FDA screen for completeness which takes 30 working days and if complete the document is scheduled for assessment for safety, quality by verifying Good Manufacturing Practice certificate from manufacturer and efficacy assessment. Assessment is based on the first in and first out rule but priorities are intended in case of emergency. The drug registration processes take nine months. In pediatric populations, medications are in different formulations, forms, different strengths, and different sizes. As pediatric drugs have different categories of forms, size, formulations, and each category proceed with registration process its self and with registration fees(1250$) payment which is high compare to procured volume, this is regarded as a barrier to access childhood cancer drugs which are mostly exported from outside of the country.

This process might discourage supplying pharmaceutical companies that are not targeting a big market in the country. This has a big impact on access to childhood cancer essential drugs as inside the country no pharmaceutical supplier or industry producing anti-cancer drugs.

4.1.1.3. DRUG PRICING

The cancer drugs prices are high in Rwanda as no industry producing the cancer drugs in the country and due to poor availability cause few retail pharmacies fixing their prices. The pharmacy policy of 2016 states lack of national pharmaceutical products pricing in both private and public institutions, this has an impact on health commodities prices to be high. In public institutions there is a tariff with a top-up of 20% at each entity but not in private institutions. The

creation of national drugs prices index might be one of the solutions to cancer drugs affordability.

Insurance Coverage Role of health insurances in easy accessibility and affordability of health care is undisputable like Community-Based Health Insurance CBHI used by the majority of Rwandan change Rwandan life, as a member of the insurances does not become stranded at home because of quick access to health care. Rwanda national health insurance policy (April 2010) outlines population coverage by any health insurance is 96% with CBHI coverage of 90%, in terms of cancer care they were poor health insurance coverage in cancer care like CBHI is not covering chemotherapy which leads to poor drug availability and affordability. The policy marker should discuss with insurance to cover cancer essential drugs which may improve cancer care by improving affordability

4.1.1.4. CHILDHOOD CANCER TREATMENT GUIDELINES

In the health sector policy of January 2015, the policy-makers expressed cancer as NCD prevention and control services to be not yet available across the health care system (HR capacities, diagnostic and treatment technologies) and existing services are not affordable and accessible to all. Like national cancer control plan is not yet well installed and this causes limited cancer care advocacy. This has a very bad impact where for example currently few cancer drugs entities procured through public drug procurement and this causes limited accessibility of anti-cancer drugs in the country.

Clinical practice guidelines are developed to help health care workers and patients to get allocate care for their circumstances. Working cancer centers play a key role in developing and promoting treatment guidelines in hospitals and play a big role in national treatment guideline development. Different stakeholders are basing on these guidelines to prepare tenders, procurement, and supply. The table below provides national guideline for the management of non-communicable diseases.

Table 2. National guideline for management of Non-Communicable Diseases (NCDs)

HEALTH CARE LEVEL	PERSONNEL REQUIRED	SERVICE OFFERED RELATED TO CANCER CARE
Referral hospitals and teaching hospitals	-Nurse -Medical Officer -Physician(Internist) Pathologists -Gynaecologist -Surgeons -Paediatrician -Radio-oncologist -Medical oncologist –Clinical Pharmacist	Same as DH Services plus -Surgery -Chemotherapy -Research -Pathologic interpretation
Provincial hospital	Nurse -Medical Officer -Family Physician -Physician (Internist) - Pathologists- -Gynaecologist -Surgeon -Paediatrician	**District hospital service delivery+** -Surgery -Chemotherapy -research
District hospital	-Nurse - Medical Officer - Social Worker -Community Health Office	**Health center service delivery +** -Coordination/M&E -Research – Cancer Registry
Health post and health centers	-Nurse -Social Worker -Community Health Officer	**Community service delivery+** -Screening of cervical lesions using VIA - Cryotherapy -Referral for screened positive clients for further management -Centre for outreach - Palliative care
Community service	Community health worker	Community awareness on cancer prevention and early detection. Home-based palliative care - Referral and linkage

According to NCD guidelines of 2016 all provincial, referral, and teaching hospitals should treat cancer at least by providing chemotherapy. In practice except for screening and diagnosis of cancer no cancer drugs are available in referral even provincial hospitals which impedes access. Policymakers should be responsible for the follow-up of these guidelines and transition in practice for the policies as written.

4.1.1.5. SELECTION OF NATIONAL DRUG FORMULARY AND ESSENTIAL MEDICINES LIST

The national drug formulary was selected based on treatment guidelines, WHO essential medicines lists, VEN developed list, and some disease priorities. According to the NEML of

2015, the list was elaborated under the guidance of the minister of health in collaboration with its institutions like RBC, physicians from different country hospitals, and consultants from different NGOs like WHO(38). According to national pharmacy policy 2015, the selection of medicines to NEML depend on the prevailing disease, treatment guidelines, level of health care delivery, and financial resources.

The first selected list in Rwanda has been elaborated in 1991; the last published national essential medicines list which is the 6th edition was published in 2015 and has a party of cancer drugs. This NEML was revised every 5 years based on current guidelines and new disease prevalence. Rwandan NEML sets regulatory standard for medicines considered meeting the priority health needs and guiding public and non-government agencies including retail pharmacies in domestic medicines procurement. Many health insurances policies including CBHI used by many populations are strict on coverage of medications on the NEML. Childhood cancer care is improving quickly based to new research as one disease-causing high mortality and morbidity, The challenge comes to drugs that are not on NEML for cancer as its availability become a problem and when available its insurance coverage becomes a problem, the researcher suggest a clear process for adding a new entity to NEML without waiting 5 years for reviewing NEML, this will help insurance coverage not only that will help in availability by procurement by public and private sector institutions.

Table 3. 2015 Rwanda NEML for paediatric cancer compared to 2019 WHO EML for childhood cancer.

Name of drug	Available on WHO EMLc	Available Rwanda NEMLc
Arsenic trioxide concentrate for solution for infusion: 1 mg/mL	+	X
Bleomycin for injection powder form: 15 mg (as sulfate) in vial.	+	+
Calcium folinate Injection: 10 ml ampoule with 3 mg/ mL. **Tablet: 25 mg, 15 mg; 5 mg.**	+ +	X X
Carboplatin Injection: 50 mg/5 mL; 150 mg/15 mL; 450 mg/45 mL; 600 mg/60 m	+	+
Asparaginase for injection Powder form: vial of 10 000 IU	+	+
Cisplatin Injection: 50 mg/50 mL; 100 mg/100 mL.	+	+
Cyclophosphamide Powder for injection: 500 mg in vial. **Tablet: 25 mg; 50 mg**	+ +	+ +
Cytarabine Powder for injection: 100 mg in vial.	+	X
Dacarbazine Powder for injection: 100 mg in vial.	+	X
Dactinomycin Powder for injection: 500 micrograms in vial.	+	+
Daunorubicin for injection powder form: vial of 50 mg (hydrochloride)	+	+
Doxorubicin Powder form for injection: 10 mg; 50 mg	+	+

(hydrochloride) in vial		
Etoposide Capsule: 50 mg; 100 mg. **Injection: 20 mg/ mL in 5- mL ampoule.**	+ +	X X
Fluorouracil Injection: 50 mg/ mL in 5- mL ampoule	+	+
Hydroxycarbamide Solid oral dosage form: 1g, 500 mg, 400mg, 300mg, 250 mg; 200 mg	+	+
Ifosfamide Powder form for injection: 2-g vial, 1-g vial, 500 mg vial.	+	+
Irinotecan Injection: 2 mL vial with 40 mg; 5 mL vial with 100 mg; 25mL vial 500mg.	+	+
Mercaptopurine Tablet: 50 mg.	+	+
Methotrexate Powder form for injection: 50 mg (as sodium salt) in vial. Tablet: 2.5 mg (as sodium salt)	+ +	+ +
Oxaliplatin Injection: 10 mL vial with 50 mg; 20 mL vial with 100 mg, 40 mL vial with 200 mg. Powder form for injection: 50 mg, 100 mg in vial.	+	+
Paclitaxel Powder form for injection: 6 mg/ mL.	+	+
Pegaspargase* Injection: 3,750 units/5 mL in vial	+	X
Procarbazine Capsule: 50 mg (as hydrochloride)	+	X
Realgar-Indigo naturalis formulation Tablet: 270 mg (containing tetra-arsenic tetra-sulfide 30 mg)	+	X
Thioguanine Solid oral dosage form: 40 mg	+	X
Vinblastine Powder form for injection: 10 mg (sulfate) in vial	+	X
Vincristine Powder for injection: vial with 1 mg; 5 mg (sulfate).	+	+
All-trans retinoic acid (ATRA) Capsule: 10 mg.	+	X
Dasatinib Tablet: 20 mg; 50 mg; 70 mg; 80 mg; 100 mg; 140 mg	+	X
Imatinib Tablet: 100 mg; 400 mg.	+	+
Nilotinib Capsule: 150 mg; 200 mg.	+	X
Rituximab* Injection (intravenous): 100 mg/10 mL in 10- mL vial; 500 mg/50 mL in 50- mL vial.	+	X
Filgrastim Injection: 120 micrograms/0.2 mL; 300 micrograms/0.5 mL; 480 micrograms/0.8 mL in pre-filled syringe 300 micrograms/mL in 1- mL vial, 480 micrograms/1.6 mL in 1.6- mL vial	+	X
Dexamethasone Injection: ampoule of 1 mL with 4 mg (as disodium phosphate salt). **Oral liquid: 2 mg/5 mL** **Tablet: 4mg, 2 mg.**	+ + +	X X X
Injectable Hydrocortisone Powder form : 100 mg (as sodium succinate) in vial.	+	+
Parenteral Methylprednisolone : 40 mg/ mL (as sodium succinate) in 1- mL single dose vial and 5- mL multi-dose vials; 80 mg/ mL (as sodium succinate) in 1- mL single-dose vial	+	+

Prednisolone syrup: 5 mg/ mL **Tablet: 25, 5 mg**	+ +	+ X
Allopurinol pill: 100 ; 300 mg.	+	+
Mesna Injection: 100 mg/ mL in 4- mL and 10- mL ampoules. Tablet: 400 mg; 600 mg.	+ +	X X

+: available **X: not available.**

The above table compares the Rwanda national essential medicines to WHO pediatric EML for cancer. Even though the World health organization sets the list to guide country-level drug prioritization in NEML selection, there is a big discrepancy in between. This table has 47 WHO essential childhood cancer drug forms with only 24 drug forms available in Rwanda NEML which shows a discrepancy of 48.9%.

4.1.1.6. DRUGS SUPPLY, DISTRIBUTION, AND STOCK MANAGEMENT

National store RMS was in charge of drugs procurement and distribution in general. When drugs arrived in the country they were stored in a good warehouse where quantification, own quality checking, and registration in the online system eLMIS were done in order to inform the periphery pharmacies the drugs are available. According to the periphery request they distribute to these pharmacies which were most of the time the district pharmacies or referral hospitals pharmacies then the district pharmacies distribute in the district hospital pharmacies and health centers. For the essential childhood cancer drugs which are mostly used at Butaro cancer of excellence, there are two parallel lines where PIH as an NGO funding the center do their own procurement international and they receive medications without passing through RMS, but there were few drugs passing through RMS then distributed to Butaro cancer center of excellence. The cancer drugs store was monitored daily but also online electronic system eLMIS where most of the pharmacies report the stock status of the drugs to help to monitor drugs stock status at a peripheral level even at a national level so that there was a rare problem of stock out or expired drugs.

This monitoring system was for all medications. There is no particular system for tracking childhood cancer drugs.

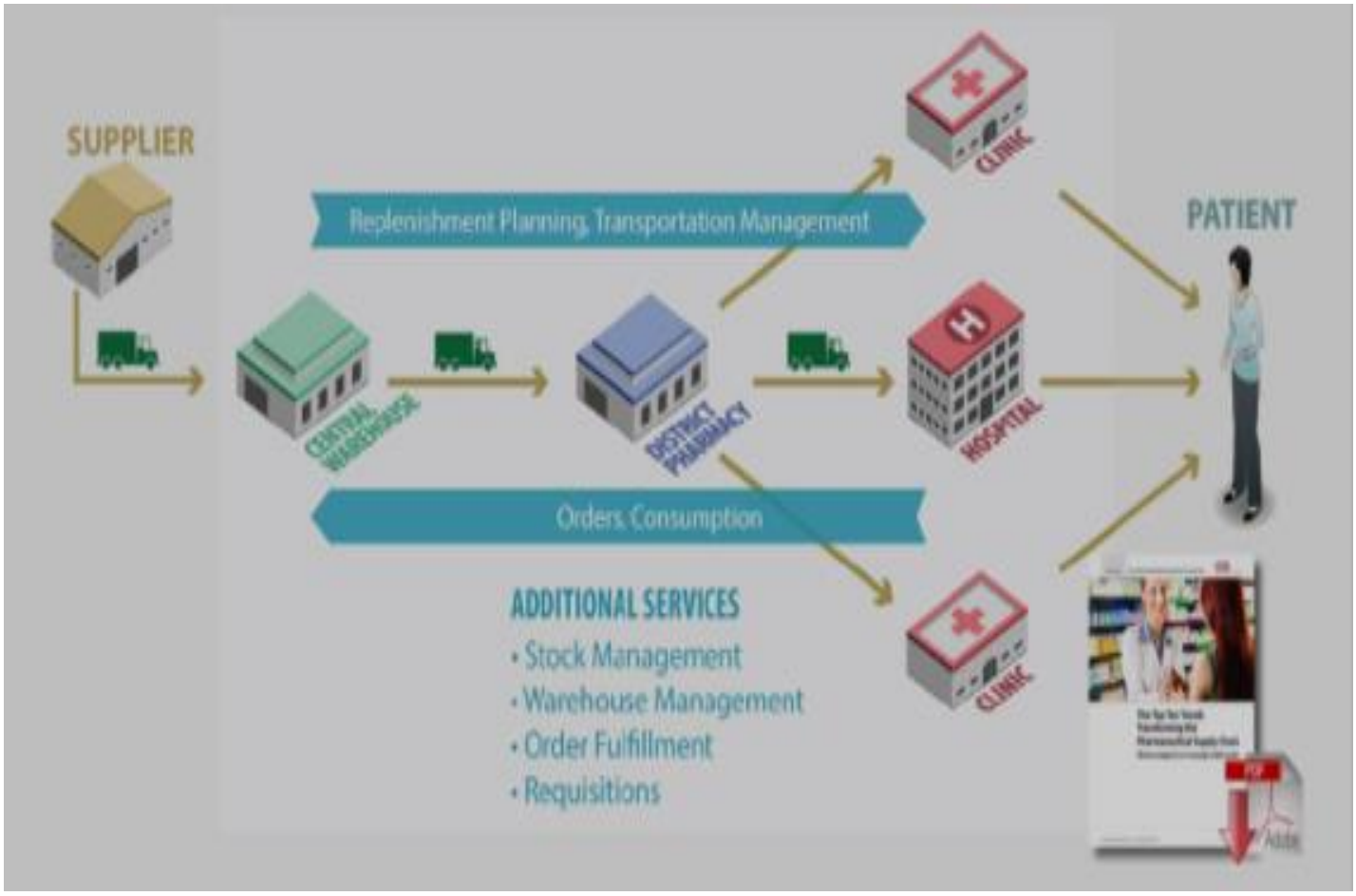

Figure 2. Drug distribution channel in Rwanda

Rwanda health care network produced by A Cloud-Based Pharmaceutical Supply Chain Network in Rwanda in 2015.

In terms of cancer drugs procurement, PIH as the main actor in public cancer care with the collaboration of the Minister of Health support Butaro Cancer Center of Excellence by providing medications. Partners in Health primarily procure from the manufacturers rather than RMS. KFH as a single private institution with cancer care used to procure international and when has stock out of medications it collaborates with Butaro Cancer Center of Excellence so that there is no discontinuity of care to the patients. Figure 3 demonstrates current procurement and supply processes.

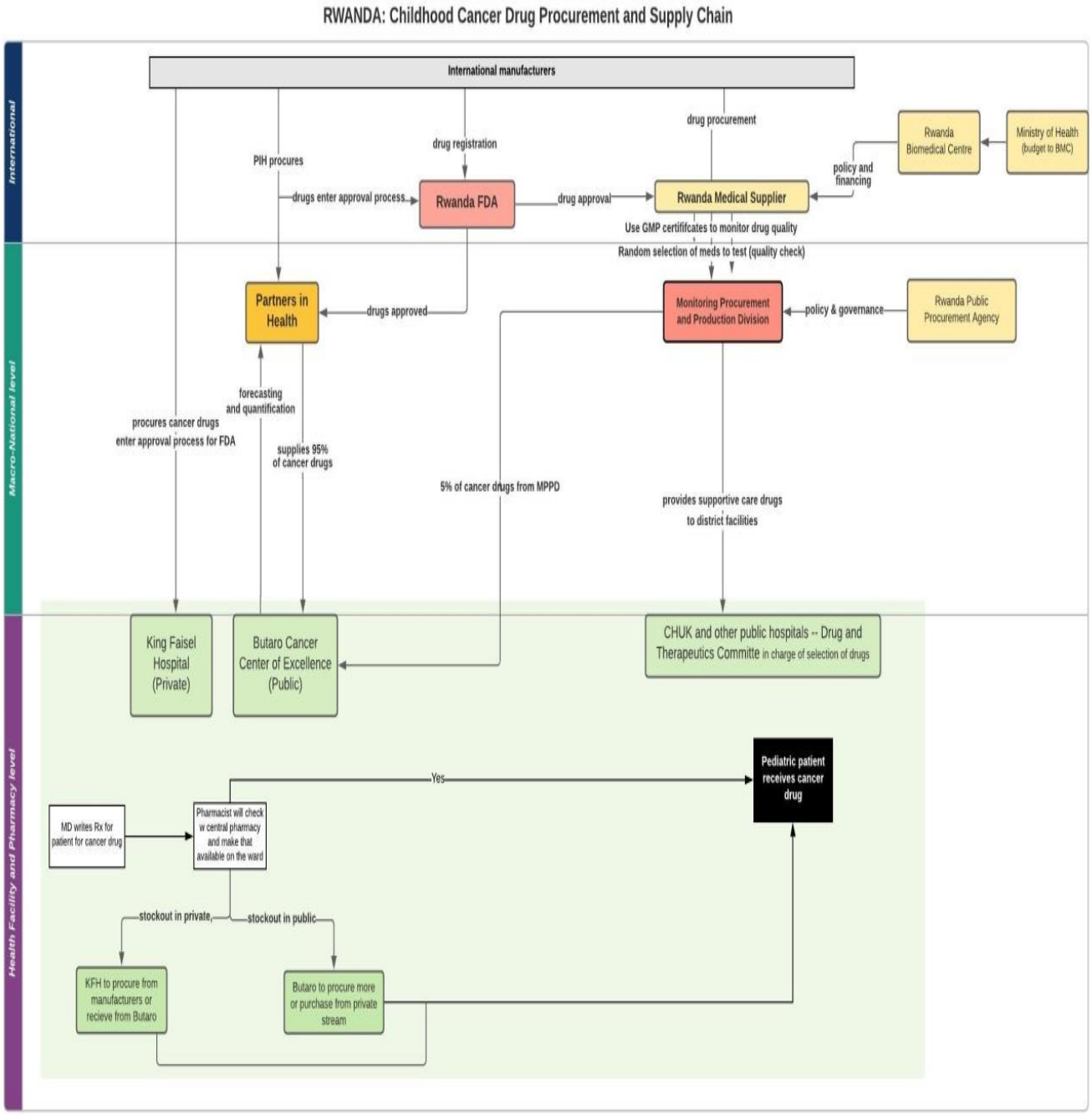

Figure 3. Rwanda childhood cancer procurement and supply chain

Cancer drugs procurement is done internationally as no industry for anti-cancer medicine is available in the country. Rwanda medical supply ex-MPPD as public procurement center with capacity of international procurement after revising budget and health policy related to VEN drugs from MOH and RBC, procure international respecting guideline of public procurement as proposed by Rwanda Public Procurement Agency. KFH as private institutions and PIH as non-Government organizations also procure international. Rwanda FDA as a center in charge of pharmacovigilance and quality monitoring every drug should pass through it for approval and registration before being used in the country. After approval from FDA, RMS stores medications

in their warehouse then supply in the district pharmacy and referral hospital according to their request. PIH supplies Butaro cancer center of excellence under their partnership and KFH supplies its pharmacy. Patients receive cancer medications in public from Butaro cancer center of Excellence and in private from KFH which are the two most common centers supplying chemotherapy in the county. They are working into connections so that if medications are not available at KFH, the pharmacist request at Butaro cancer center of excellence in order not to delay or interrupt patients' care.

Table below summarize key **Challenges facing Paediatric Cancer treatment from the policy document review**

Table 4: Summary of key challenges facing paediatric cancer treatment from the policy documents review

Policy	There is no specific policy focussed on paediatric cancers. There are many policies and strategies in place to guide cancer drug procurement, supply, and delivery mechanisms
Forecasting need	Weak structures for determining the burden of paediatric cancers and therefore inadequate information on the required drugs
Budgeting	There is a limited public budget for financing cancer drugs There is no dedicated budget line for paediatric cancer medications
Procurement	Paediatric cancer drugs are subject to the international bidding process. Low volumes of drugs are a disincentive to the pharmaceutical industries Lack of local manufacturing further limits access to the drugs. Lack of a central procurement agency in -charge of procuring cancer drugs
Drug registration	Lengthy process of registration – 30 months registration, 9 months ascertainment of good manufacturing practice Relatively expensive process - $1250 US per drug Registration of paediatric medication more expensive because different forms (liquid/tablet/injectable, sizes are treated as different drugs subject to the same registration process.
Cost to consumer	Lack of a policy on pricing of pharmaceutical products in private and public institution. Public institutions having a 20% tariff markup Paediatric cancer treatment is not included in the Rwanda national health policy
Cancer care	National cancer control policy is not well installed Limited access to cancer related HR, diagnostic and treatment services
Essential medicine	24 /47 drugs included in the WHO paediatric essential drug list are on the Rwanda NEML
Supply and distribution	Public -private partnership Parallel supply and distribution

4.1.2 KEY-INFORMANT INTERVIEWS WITH HEALTH SYSTEM STAKEHOLDERS

The challenges of accessing paediatric cancer drugs identified through the review of policies were confirmed by the key person interviews who further elaborated on the issues. In addition, pharmacovigilance emerged as a key issue. To analyse the determinants of paediatric cancer drug access through the perspectives of system stakeholders, 15 stakeholders were interviewed from **June 21st, 2020** to **December 13th, 2020**. The interviewed stakeholders include policymakers with policy, procurement, and regulatory roles (n=8), non-governmental organisation (n=1) with cancer treatment center funds and service providers, with clinical and pharmacy-related roles (n=6). Table 4 provides a summary of the categorizations used to describe stakeholders at each level of the health system.

Table 5. Summary of stakeholders interviewed and their role in childhood cancer care

Stakeholders	Role in childhood cancer care	institutions
Service Provider (SP)	-provision of childhood cancer treatment -order and purchase of childhood cancer drugs	**-CHUK** **-KFH** **-Butaro Cancer Center of Excellence**
Non-Governmental Organisation(NGO)	-fund childhood cancer care financial and social -procure childhood cancer drugs - hospital partnership support in cancer treatment	**-PIH**
Policy Regulatory Authority(PRA)	-provide a budget of drugs -national procurement, distribution, and storing -quality and pharmacovigilance monitoring -provision of drug license and registration of drugs -insurance coverage for childhood cancer	**-MOH** **-RBC** **-RMS former MPPD** **-Rwanda FDA** **-RSSB**

Despite the governmental acknowledgment of childhood cancer on national policy agendas, as shown in Rwanda national guideline for the management of non-communicable disease 2016, multiple challenges impede access to essential childhood cancer drugs. In this study, four major themes emerged from participants interviews that highlighted a number of barriers, solutions, and facilitators of childhood cancer drug access have been formed that included: (i) Limited prioritization for pediatric cancer; (ii) weak procurement and supply chains; (iii) high childhood cancer drug costs, and (iv) lack of systems to optimize pharmacovigilance.

Table 5 below summarizes the themes and categories involved in this study of access to essential childhood cancer drugs

Table 6. Summary of themes, subthemes, and categories analysed from participants' interviews.

Themes	Subthemes	Categories
Limited prioritization for paediatric cancer care	-low budget for cancer drugs	- limited national prioritization for paediatric cancer treatment - small number of cancer treatment center - poor health insurance coverage of essential childhood cancer drugs
Weak procurement and supply chains	-segregated procurement	- Low cancer drugs volume order as a barrier to Procurement - Drug registration and supply
High costs of childhood cancer drugs		-Small volume of cancer drug order - National index drugs prices and insurance coverage -limited Generic drugs use
Lack of systems to optimize pharmacovigilance		- Quality challenge -pharmacovigilance inspection

4.1.2.1 LIMITED PRIORITIZATION FOR PAEDIATRIC CANCER CARE

Limited prioritization for pediatric cancer care is shown in limited national prioritization for pediatric cancer treatment, small number of cancer treatment center, and poor health insurance coverage for essential childhood cancer drugs.

LIMITED NATIONAL PRIORITIZATION FOR PEDIATRIC CANCER TREATMENT

Limited national prioritization for pediatric cancer care and treatment emerged as a prominent theme across participants interviewed. The national public procurement institutions RMS ex-MPPD, with capabilities for international procurement and few other distributing pharmacies in the country like BUFMAR are not interested in cancer drugs procurement. Most public hospitals have a mandate to procure exclusively through RMS except referral and teaching hospitals. Even though referral hospital and teaching hospital policy allowed them to procure national even international, they are not capable to procure international due to a restricted budget, or volume needed low compare to needed by manufacturer to produce. Referral hospitals procure from national procurement institutions which are RMS or other few procurement agencies with an agreement to MOH but most of them don't procure cancer drugs. The limited ability of RMS

considered as national procurement agency in term of procurement of cancer drugs explain poor cancer care in the public hospitals. Lack of most of the essentials childhood cancer drugs in public procurement comes as a big barrier to the availability of these entities in most public hospitals and also explains limited national prioritization of pediatric cancer drugs.

> "*There is only palliative drugs and some emergent cancer drugs in referral and teaching hospitals, no chemotherapy available and even hospitals senior management staffs don't put anti-cancer drugs in priority like infectious medications and others during budget plan*" (Service provider).
> "*We as referral hospital work with RMS ex-MPPD in drugs procurements, and other few procurement agencies with capabilities to deal with the international procedures. This very helpful during procurement for hospitals in many drugs but when it comes to cancer drugs most these procurement agencies are not procuring anti-cancer drugs, it causes lack of cancers medications*" (Service Provider)

Study participants further described that lack of budget specific to childhood cancer essentials poses an additional barrier to drug availability, as the budget for cancer drugs, therefore, competes with the budget for other communicable and non-communicable diseases, and most of the budget is spent on infectious disease. This limited budget is largely the result of population demand for other competing disease priorities. Participants stated that little public budget has conducted to annual limited funds to paediatric cancer treatment procurement. Insufficient funds lead to inefficient procured drugs resulting experienced more prolonged unavailability and periodic stock out. Childhood cancer drugs are expensive and, so, this becomes hard to prioritize cancer which can siphon off a huge chunk of an institutional budget. Based on how cancer drugs procurement is special as it requires good funds compare to other drugs needed by the majority of people this causes undermining of cancer sector budget and cause the problem of availability. This undermining cancer budget provided by the government, demonstrate limited cancer prioritization compare to infectious disease with many funds.

> *"Not only childhood cancer drug, there is no specific stakeholders for cancer drugs in general. The Government only itself providing a combining budget for drugs procurement in public procurement supply. It's not like HIV or malaria which have other stakeholders, even government don't provide a specific budget to cancer but provide a budget to medications in general which most of the time used in other needed drugs with many populations need like malaria and other infectious disease and anti-cancer drugs are procured in small volume compared to needs*". (Policy regulatory authority)

The solution of availability of childhood cancer drugs may be possible with the prioritization of cancer as a rapidly growing domain. It requires teamwork between policymaker, service provider and private sector investment as the childhood cancer domain is growing and demands a lot of power in their management, combined power like from procurement base to good inventory might be a good availability solution.

A policy and regulatory authority further emphasized childhood cancer as a rapidly growing domain that needs good attention and a good budget as most childhood cancers are curable with the availability of affordable good quality drugs. They suggest better distribution of drugs budget especially this for cancer as this is special sector rapidly growing who need a good budget, and this may improve childhood cancer essential drugs availability.

> "*No budget identified to cancer drugs only, Rwandan governments vote the budget of the healthy commodity in general and establish how it can be used. MOH provides a budget to RBC and RMS ex MPPD. MPPD which is the center of drugs store and procurement distribute the budget including those of childhood cancer drugs. As cancer drugs are expensive in general they are having few cancer entities compare to needed, if the specific budget for cancer drugs is available as some of the infectious disease budgets is programmed with a specific team or program for follow up it might improve the availability of essential childhood cancer drugs '* (policy and regulatory authority)

SMALL *NUMBER OF CANCER TREATMENT CENTER*

Currently, there is only one semi-public cancer treatment center in Butaro—the Butaro Cancer Center of Excellence (BCCE)—sponsored by Partner in Health (PIH) that provides childhood cancer care and treatment and only one private hospital KFH providing cancer care. Although they offer cancer care, not all childhood cancer diseases are covered. For cancers not treated by BCCE and KFH, they are transferred outside of the country to look for care if they can afford to. Barriers to accessibility can then result, as patients may be challenged to access care and treatment that is too far to reach. Limited prioritization is shown with a lack of cancer treatment services in public hospitals with a mandate to provide chemotherapy like teaching hospitals, referral hospitals, and provincial hospitals.

> "*In the country, there is only one public center providing anti-cancer drugs and there is a minimum number of patients traveling outside to get the cancer drugs, this show difficult accessibility to cancer care, we still have room for improvement on patient accessibility so that patient will not have to walk the long distance to get access to care, other cancer treatment centers are needed to increase geographic accessibility of cancer drugs*."(Policy regulatory authority)

Solutions proposed by most study participants were to extend cancer delivery service in every corner of the country by putting cancer treatment center in every provincial, referral, and teaching hospital so that accessibility will be good but again to increase resources in cancer service so that many types of cancer will be covered inside of the country.

> " *We need amelioration on patient accessibility so that patient will not have to walk long distance to get access to care, other treatment centers are needed like in referral and teaching hospitals to increase geographic accessibility of cancer drugs'* (Policy regulatory authority).

POOR HEALTH INSURANCE COVERAGE OF ESSENTIAL CHILDHOOD CANCER DRUGS

Study participants further described Limited prioritization for paediatric cancer *drugs* in the health system as there are poor cancer drugs coverage by health insurances especially CBHI.

Lack of chemotherapy coverage by CBHI used by more than 80% of the Rwandan population considered as national health insurance, complicate cancer drugs accessibility and affordability. This implicates limited cancer unit consideration compared to infectious disease block with drugs that has subsidies and full insurances coverage. This discourages most public hospitals with the ability to procure anti-cancer drugs as most of their clients are covered by CBHI. Private insurance cover medications from private pharmacies, but access to childhood cancer essential drugs become an issue as anti-cancer drugs investment from the private sector also is limited due to the way the anti-cancer drugs are expensive.

> "*Anti-cancer drugs are expensive, not every manufacturer capable for manufacturing them and not again every pharmaceutical company able to retail them, not every patient afford these drugs, little insurance cover these medications. These factors complicate availability in the private sector and make accessibility a big issue and this cause problem of accessibility.*" (Service provider)

> "*Based to way anti-cancer drugs are too expensive, if insurances coverage like CBHI with limited budget without any subsidies from donors or government, they may siphon insurance budget even related to other diseases, insurance needs discussion with the government before starting coverage and current there are discussion in place with good progress*"(Policy regulatory authority)

Health insurance coverage for essential childhood cancer drugs can be a long-standing solution for improved accessibility of affordable cancer care services. Government and insurance voluntaries on prioritizations of cancer care as a rapidly growing domain in this century might be a solution to access to essential childhood cancer drugs.

4.1.2.2. WEAK PROCUREMENT AND SUPPLY CHAINS

The **segregated procurement** of cancer drugs was noted as a prominent issue driving to complex tendering processes through a long time for new drug registration process and low order cancer drugs volume.

LOW CANCER DRUGS VOLUME ORDER AS BARRIER TO PROCUREMENT

Segregated procurement from procuring agencies has proven as a barrier to procurement. Low minimum order cancer drugs quantities from different institutions like PIH and RMS, as well as a lack of centralized data for forecasting, remain critical barriers to drug availability. Lack of coherent drugs procurement between procurement agencies has proven a barrier, as described by RMS participants when they procured cancers drugs and Butaro Cancer Center of Excellence procured their drugs, as the requested volume is small, there is a tendency of rejection of the request by the suppliers. Segregated procurement from different agencies in the same country causes price elevation, which is a barrier to affordability and availability.

> "RMS Ex-*MPPD RBC interacts with the minister of health as the boss and public health institution as clients, in terms of procurement childhood cancer drugs we are interacting with supplier companies PIH also supply childhood cancer drugs to BCCE but we are not interlinked due to their drugs are delivered cost-free to patients while RMS are selling medications that are why most of the time RMS may bring some entities and are not bought as there are free drugs at BCCE*."(Policy Regulatory Authority).

> "*Rwanda as a small country has the issues of forecasting volume, the request we have are small compare to the minimum needs of most factory. When we go with the purchase order of small quantities, sometimes they neglect or reject the request which became a problem for cancer drugs procurement. And always it requires a supplier to deliver those medicines at high prices from retail pharmacies. It means that when we have a big volume of the item needed, it facilitates the manufacturer to produce many products and react quickly at request at low prices*." (Service provider)

Rwanda as a small country with a small purchase volume of drugs, accessing drugs in adequate quantities proves challenging as most suppliers target large markets. These low quantities, therefore, limit the available supplier pool for childhood cancer medicines. The procurement volume of drugs problems was aggravated in a small sector like paediatric oncology that the forecasted paediatric cancer drugs were smaller than those needed by many pharmaceutical companies to produce and supply.

As a solution to these barriers, participants spoke of combining the pharmaceutical purchasing power of Rwanda like combining procurement of PIH supporting Butaro Cancer Center of Excellence and RMS supplying most of the public hospitals. Participants noted that a pooled procurement approach across the EAC may be a suitable solution to increase the purchasing power as compared to a single country. Participants expressed pooled regional procurement as a strategy to improve the availability of standard quality and affordable pharmaceuticals, including childhood cancer drugs. This pooled procurement should be a sustainable solution if based on good inventory at the national level from accurate data from different treatment centers.

> "*We need to see how we can approach those pharmaceutical companies to be able to negotiate the discount especially in Africa where people do not have enough financial means for buying those drugs, we should have accessible prices, this cannot be done in isolation, we can do it as regional may be at EAC level, why not at sub-Saharan countries or African union, once there are big volumes you can be able to negotiate a better price to those cancer drugs. This may solve the problem of availability as no company will reject the request as it happens with isolated small volume request and of course it will resolve accessibility and affordability problem*." (Policy and regulatory authority)

> "*Access barriers to be overcome we need to get into pool procurement or bark purchase, we need to combine more molecules more quantities for different partners may be in the country even in the region so that we can procure a big quantity. If bark procurement happens, it will increase availability and accessibility of affordable cancer*." (Policy and regulatory authority)

DRUG REGISTRATION AND SUPPLY

Drug processing and the cost of registering new drugs prove challenges for potential suppliers of cancer drugs mostly coming from outside of the country as inside the country most companies are not interested in the cancer drugs market.

> "In *Rwanda FDA, the new drug registration cost around 1250$ is somehow high compare to the requested volume and some companies refuse to pay the fees as first of all procured volume is small and supplying companies are not sure for continuity of market. And it became hard to convince the company to register every new drug*." (Service provider)

As described by participants, the cost of drug registration with the Rwanda FDA is discouraging to most international supplying companies when they receive low-volume requests. Additionally, a limited number of interested suppliers may be subject to international delays in drug delivery which can pose a challenge for drugs arriving in a timely fashion.

> "*The availability of cancer drugs suppliers is an issue, there are no local suppliers we can trust who can supply anti-cancer medications and some time we got the problem with the external suppliers like delaying our product and sometimes refusing our request as it is small compare to requested amounts to register new drugs*." (Service provider)

Study participants noted that many of these upstream challenges related to drugs entering the system have downstream consequences as limited stock may enter the supply chain. A proposed solution to the suppliers by the study participants is the creation of incentives; some participants suggested giving subsides to cancer drugs, such as cost-free registration at the Rwanda FDA level since other drugs require money for registration or orphan drugs. Subsidization may be a solution to attract the suppliers of childhood cancer drugs to increase availability and affordability. Some participants suggested discounts with big pharmaceutical companies for cancer to supply immediately to national stock without intermediaries by giving a certain contract for supply as some companies fear the low market and market sustainability**.**

> "*two ways can be used during procurement of cancer drugs possible, going through open tender like we are doing for those other medications when the public tender is out, interested people can submit their bid, and this is even what is recommended by RPPA to be in transparency. In the cancer drugs framework contract with manufacturers, let's say Rwanda can go and negotiate with the industry on quantity and prices and may sign a contract for 5 years without every year passing through these open tenders, this can improve the availability of cancer drugs*." (Policy and regulatory authority)

The improvement of the procurement process including the improvement of process of new drugs registration will play a great impact on the availability of affordable good quality childhood cancer essentials drugs. The sustainable measure of procurement will play a great impact on accessibility as many hospitals will accomplish their mission of cancer care in every province of the country.

4.1.2.3 HIGH COSTS OF CHILDHOOD CANCER DRUGS

Interviewed stakeholders described a variety of affordability barriers to access that included expensive drugs, lack of generic drugs, and poor insurance coverage. Facilitators to the affordability of childhood cancer essential drugs were also noted that included advocacy on insurance coverage, PIH support for chemotherapy delivery. Stakeholders emphasized the high cost of childhood cancer drugs as a major challenge in accessing childhood cancer drugs. Poor

affordability of anti-cancer drugs for children appeared driven by both international and national factors that included: low order volumes contributing to higher and more volatile pricing by manufacturers, lack of price control within pharmacies, lack of generic drugs available to reduce drug costs as well as poor health insurance coverage for patients accessing medicines.

SMALL VOLUME OF CANCER DRUG ORDER

Low order volume of cancer drugs was emphasized by participants as a large contributor to the high costs of the drugs. This fragmented procurement with low volume results in a limited potential for negotiating and bargaining with manufacturers. Low volume procurement causes limited capacity to buy from the big company as requiring minimum volume for the industry to produce are not targeted, they procure from other unknown or retails pharmaceutical companies at a high price. These circumstances pose a challenge at the national level as drug costs become quite high.

> "*When we prepare our request, they are few quantities. When we go to procurement to international supply, no one is interested in our request with these few quantities unless we direct purchase to retails pharmacies. Due to low quantities of these drugs, many supplies are not interested and this has impacted a lot on the availability of drug and affordability as even given medications are expensive*." (Policy regulatory authority)

NATIONAL INDEX DRUGS PRICES AND INSURANCE COVERAGE

In addition to low order volumes, a lack of price control within pharmacies emerged as another barrier to affordability. Lack of a national index price for pharmaceutical products on private and public pharmacies hinders regulations on drug pricing in the country. Public institutions have a percentage mark up to 20%, and private pharmacies have no regulations in place. As stated by one service provider:

> "*There are no cancer drugs in public procurement chain and if anti-cancer drugs are not available at Butaro cancer center of excellence, the patients get out in private pharmacy in order to buy medications, these pharmacies are selling their medication at elevated prices compare to the normal price*." (Service provider).

Further, limited health insurance coverage for patients under medicines was an additional barrier to affordability. Health insurance is one-way countries encourage in order to have universal equitable health service, but when it comes to cancer some insurance hesitates to cover chemotherapy drugs cost which becomes a burden to patients and the entire family as increased costs for the patients and their families. Children with cancer are not eligible for treatment under CBHI. As described by one service provider:

> "*Health insurance had partial coverage like CBHI doesn't cover chemotherapy but they do pay for surgery and diagnostic modalities, insurance still need discussion to show them how childhood cancers are curable if well cared*.' (Service provider)

Private insurance covers anti-cancer drugs, but the high cost of anti-cancer drugs and delays in drug acquisition that render some schemes no longer eligible result in significant access barriers. Some proposed solution to affordability by case study participants was:

To enhance the affordability of anti-cancer drugs, participants suggested: strengthening insurance coverage and generating known drugs prices**.** Participants emphasized the need for policymakers to create a national price drug index and to routinely follow up with all pharmacies to ensure proper pricing of medications.

> "*Rwanda MOH is working on national pharmaceutical products prices index; I think this will have a good impact on affordability as every medication will be sold on known prices."* (Policy and regulatory authority)

LIMITED GENERIC DRUGS USE

Further, the lack of cheaper generic anti-cancer drugs available in the country is an additional barrier that arose. Generic drugs are mostly the ones recommended in the essential medicines list as they are cheap in comparison to brand drugs; but, most of the anti-cancer drugs are brand. As outlined by one policy and regulatory authority:

> "*There is a problem of availability for the generic anti-cancer drugs which are cheap and this limits affordability. Most of these drugs are still branded by the manufacture and they are very expensive. As in general, the essential medicines are generic drugs which are affordable to everyone, this comes as a barrier to many companies involved in drugs procurement as it is difficult to find generic anti-cancer drugs*." (Policy and regulatory authority)

Furthermore, participants suggested that generic drugs would decrease the prices of medications and increase affordability as currently, most anti-cancer medications are brand medications. The lack of generic drugs available limits affordability because most insurance relies on generic drugs and if branded drugs are available, the insurances refuse cost coverage.

> "*Insurances prefer generic medicines because they are cost-effective, they are affordable and the expenditure will be reduced if found generic drugs, insurance have a policy for generic use over specialty drugs*." (Policy and regulatory authority)

Grouped bark pool procurement based on good inventory is a good solution to affordability as it gives chance to prices negotiation from industry or pharmaceutical supply

4.1.2.4 LACK OF SYSTEMS TO OPTIMIZE PHARMACOVIGILANCE

The Rwanda Food and Drugs Authority (RFDA) monitor and ensure the quality of drugs imported in the country and follow drugs pharmacovigilance. Every new drug procured into the system, therefore, has to be registered by RFDA in order to prevent forgery of medications and to test the quality of medications entering in the country. In this study, quality, as it was associated with access referred to drug efficacy and safety. Barriers to quality and national and institutional challenges with pharmacovigilance were noted by participants

QUALITY CHALLENGE

A lack of systems to support pharmacovigilance emerged as a determinant of access, particularly as such processes hindered access to quality drugs for patients. Regulatory authorities highlighted that barriers to quality emerged from the lack of an in-house laboratory for monitoring the quality of cancer drugs and lack of site visits to the industry producing anti-cancer drugs in order to confirm what is written on the paper reflects what medication contains. As described by one service provider:

> "*No laboratory inside the country to test the quality of cancer drugs, only GMP paper is relied on before purchase of drug.no counterchecking if these papers reflect reality*." (Service provider)

Concerns about the quality of available anti-cancer drugs were frequently related to affordability subject. Known drugs supplying companies with good quality cancer drugs are expensive, which pushes purchase cancer drugs from companies with debatable quality. Many stakeholders expressed that high drug costs contributed to the procurement of unknown quality drugs.

Study participants explain how low purchased volume may contribute to poor quality of drugs, because like most of the time the known companies with good quality drugs are requiring a minimum volume of drugs in order to produce. Most of the time country demand of cancer drugs is small compare to minimum order required by most of factories, procurement is done with companies or retail pharmacies which agreed to delivery medications which most of the time their quality of drugs is doubtable.

> "*When it comes to cancer drugs, they are known companies with good quality of drugs which are largely from the USA or Europe but their requirement including minimum quantity to manufacture, expensive drugs, all of the requirement are not meant by most of the developing countries which push them to work with the Indian company which their quality is still debatable but with affordable drugs, need to check their quality certificate.*" (Policy and regulatory authority)

Solutions proposed by study participants for the quality of essential childhood cancer drugs included pooling procurement with other countries which might give power for procurement from the known company with good quality drugs while still processing Rwanda in-house quality control drugs checking. Cancer treatment center's ability to prepare syrup friendly to children might be a good solution to good quality for acceptable drugs for children.

PHARMACOVIGILANCE INSPECTION

For pharmacovigilance-related surveillance, the Post-marketing Surveillance Commission relies primarily on clinical or medical reports related to side effects or drug ineffectiveness. Clinicians demonstrate unhappiness with Rwanda's FDA feedback after a drug side effect communicated. Poor drug side effect reporting and late action on reported side effect have an impact on patients

even clinician using the medications as one policy and regulatory authority described:

> "*Rwanda FDA with role of identifications and monitoring and reporting on any drug related problem causing to the clients. This drugs report should work if many structures play their role to improve this important section, because mostly there are poor connections from the patient to health care provider and final to the regulatory authority*." (Policy and regulatory authority)

Study participants were suggesting the creation of an online system for drugs side effect reporting from the health center to the national level which may solve the problem of delayed or poor reporting and missed side effect caused by the drug. Pharmacovigilance committee from Rwanda FDA should work in a team with clinician by reporting feedback on reported drug effects.

CHAPTER 5. DISCUSSION

5.1. DETERMINANTS OF CHILDHOOD CANCER DRUG ACCESS

This work contributed little, but growing set of literature that increases comprehension of health policies and guidelines for children with cancer in Rwanda and through analyzed stakeholders' interviews on access to essential childhood cancer drugs in Rwanda as LMIC, provides barriers and facilitators of essential cancer drugs access in Rwanda. The results focus on health policies analysis and themes from fifteen interviewed participants on five domains of childhood essentials cancer drugs access. **.** In this study current health policies documents enhancing cancer drugs access were analyzed as stated **drug financing and procurement, childhood cancer treatment guidelines, national drug formulary and essential medicines list selection, drugs supply, distribution, and stock management.** The formed themes were: **Limited prioritization for pediatric cancer; weak procurement and supply chains; high childhood cancer drug costs, and lack of systems to optimize pharmacovigilance**

5.1.1. DRUG FINANCING AND PROCUREMENT

According to the national 2016 Pharmacy Policy Rwanda, health commodities are financed through a number of sources, including, fiscal budgetary allocation, insurance schemes, development partners, private sector, and out-of-pocket expenditure(36). This pharmacy financing procedure is well documented, but not implemented as envisioned as out-of-pocket spending by families, either at the point of service or via private insurance and external finance are mostly used. This domestic financing of cancer drugs with external financial support has been reported in many LMIC contrary to high-income countries where public and insurance finance play a great role in cancer drugs finance(39). Infectious diseases are prioritized to a greater extent compared to NCDs and most of the budget was spent on infectious medications. Similar experiences were noted in Trinidad and Tobago and another in Botswana(31;32). Possible Strategies to address this limited fund and good use of available budget included potential creation of national oncology budget and if possible paediatric cancer drugs budget even with advancement for use of generic drugs as money-saving manner as suggested in other study done for childhood cancer in Africa and the study done by WHO on the pricing of cancer and its effects suggesting the use of generic labels compared to their originator equivalents, yielding expenditure savings and 2020 GLOBOCAN on enhancing global access to cancer medicine (42,43,44).

5.1.2. CHILDHOOD CANCER TREATMENT GUIDELINES

Childhood cancer treatment guideline is necessary in order to have best practice in term of treatment, prevention, and budget. There is a national treatment guideline for non-communicable diseases including cancer but its usage is low, the most reason as explained in 2015 national

health policy is limited human resources capacities, diagnostic and treatment technologies. The lack of implementation of the national guideline has been reported in many lower-middle-income countries because of inadequate facilities and mainly budget (45). Proving adequate facilities may be a solution for follow-up of cancer treatment guidelines.

5.1.3. NATIONAL DRUG FORMULARY AND ESSENTIAL MEDICINES LIST SELECTION

WHO created a list of essential medicines for cancer and avail it to countries in order to help them in preparation of NEML and procurement. It is mandatory for every country to have a good NEML in order to help the population. There is a difference in childhood cancer essential medicines list in NEMLc compare to WHO EMLc, this explained the lack of childhood cancer essential drugs in many hospitals that have a mandate to treat these children with cancer. The gap to Rwanda NEMLc from WHO paediatric EML apropos of essential childhood cancer drugs was indication of a drug policy domain that abandoned paediatric cancer. This showed a clear lack of priority in agenda-setting at hospital levels, NCD program level, and at national level. The discrepancy of drugs of NEMLc and WHO EMLc has been reported even in another middle-income country study like Ghana(46). The presence of medicines on the national essential medicines list does not explain availability. The Presence of a strong national essential medicines list for childhood cancer based on recent strong evidence on childhood cancer has been suggested as a solution to cancer care affordability and accessibility. Most health insurances are based to the list of essential medicines in order to prepare list for coverage. The same experience has been reported in Croatia (47)

5.1.4. DRUGS SUPPLY, DISTRIBUTION, AND STOCK MANAGEMENT

Cancer drugs are procured and supplied by RMS, PIH, and KFH. PIH as an NGO in partnership with BCCE they request cancer medications international and supply immediately BCCE where are used by patients. RMS as a national center of procurement after receiving medications from the international supply, they distribute medications according to the request mostly to district pharmacy and referral hospitals, then district pharmacies distribute to the district hospital and health center where patient receive the medications. KFH as private institutions procure international or national medications and receive the medications in the pharmacy stock and patients receive medications according to physician's prescriptions. About stock management, there is an online system e-LMIS helping in controlling daily quantity pharmacy store status. It helps to prevent stock out of medications. In general, the process of drug distribution and stock management is effective and reliable. The hospitals providing cancer treatment are working in connections so that there is no drugs interruption to the patients while another hospital has regimens. The use of an online system of stock management is a reliable solution to prevent

stock out and expired medications. The use of an online system of stock monitoring also has been recommended in a study done in South Africa on ARV supply chain to improve distribution (48).

5.1.5. LIMITED PRIORITIZATION FOR PEDIATRIC CANCER DRUG

Limited prioritization has been shown in limited prioritization for pediatric cancer at national level, small number of cancer treatment center in the country, and poor health insurance coverage of essential childhood cancer drugs.

LIMITED NATIONAL PRIORITIZATION FOR PEDIATRIC CANCER

Of the essential childhood cancer medicines recommended in the Rwanda national essential medicines list for children, few are available in public hospitals, only Butaro Cancer Center of Excellence under PIH funds providing anti-cancer drugs to children other supposed to provide cancer drugs are not providing. This explained to lack of childhood cancer drugs in normal public procurement done by RMS. Lack of essential childhood cancer drugs in public hospitals has been reported in many other studies including a study done in Rwanda and another in Mexico on prices, availability, and affordability of medicine(49,50)**.** Limited coordinated childhood cancer data at national level, this problem of childhood cancer data limits the optimization of political will to mobilize for cancer support as well as for greater private sector investment in cancer drugs procurement and NGO support. Data challenges are acknowledged in other LMIC settings, such as Ghana and the Caribbean countries as a barrier to access essential paediatric drug (41,46).

Most of the drug's budget is spent on infectious disease over the cancer drugs during procurement as expressed by study participants. This shows minimal prioritization of cancer over other diseases. The minimal prioritization of cancer care also has been noted in a study done in Ghana on health system determinants of access to essential paediatric cancer treatments (46).

SMALL NUMBER OF CANCER TREATMENT CENTER

In Rwanda, only two centers can provide chemotherapies which complicate the accessibility of cancer drugs. What we reported in this paper were poor accessibility based to limited cancer treatment center as only PIH funded center which Butaro Cancer Center of Excellence was working and KFH working privately. Based on NCDs guideline chemotherapy should be provided from provincial hospitals, referral hospitals and teaching hospitals(3). Few cancer treatment centers complicate travel to center which lead to treatment abandonment or delay in treatment as is shown in another study done in rural area of West Virginia(51). Extension of treatment centers in every teaching, referral, provincial hospitals might be a good solution to easy accessibility.

POOR HEALTH INSURANCE COVERAGE OF ESSENTIAL CHILDHOOD CANCER DRUGS

Health insurances is one of the measures taken by most of countries in order to try to practice universal health coverage, in Rwanda many populations are covered by different health

insurances mostly CBHI considered as national health insurance covering more than 80% of populations. Lack of childhood cancer drugs coverage by CBHI considered as national public health insurance was considered as limited prioritization of cancer care at national level. The same experience was recorded in Ghana where the national health insurance covers limited medications from the essential medicine list for children(46). CBHI and other health insurances coverage of essential childhood cancer drugs might play a great role in childhood cancer care, government especially the minister of health discussion with health insurance guaranty future childhood cancer care.

5.1.6. WEAK PROCUREMENT AND SUPPLY CHAINS

Weak procurement and supply chain was shown with segregated low volume order and difficult drug registration and supply. Poor availability of essential childhood cancer drugs has been associated with a limited budget during drug procurement but also a poor system of anti-cancer drugs procurement. This is isolated institution procurement where currently each institution did separate procurement with small quantity order which decreases prices negotiations and some industries and supplier neglect the request. National combined procurement and if possible regional combined procurement or group purchase under framework contract that guarantee supply through established public channels has been proposed as a solution of procurement and at the same time solutions of availability in this study. This also has been suggested in the study of improving strategy of procurement of health commodities and many middle-income countries studies(40,41,46,52).

LOW VOLUME ORDER AS BARRIER TO PROCUREMENT

Most drugs are procured by RMS then distribute to other health facilities. For cancer drugs, there is small request as RMS intervenes in public procurement chains coordination and few other facilities providing cancer drugs procure separately. The PIH supporting BCCE and KFH providing cancer drugs procure international beside RMS. The segregated procurement in a small field like pediatric cancer complicates procurement as most supplying companies and industries demand minimum volume to produce. Some requests are rejected by the suppliers. The big requests are prioritized over small requests and this has impact of delay supply. The problem of low volume request complicating procurement has been noted in many middle-income countries of the Caribbean region (53).

DRUG REGISTRATION AND SUPPLY

Every new entity before procurement should be registered at RFDA, the new drug registration process takes nine months of processing drugs, and 1250$ for registering a drug. long time for new drug registration and the high amount required to register a new entity in Rwanda FDA before used in the country has been reported as a factor discouraging many drugs suppliers.

Stuck of new drugs registration had been reported in other studies in the Caribbean and Ghana(46,53). Cancer drug procurement from outside of the country free of taxes and free RFDA registration could be good facilitation for suppliers as suggested in another study from a middle-income country where anti-cancer drugs are procured as branded drugs free of charges and fast which improve drugs supply delay as new drug process improve (46). To improve the availability and affordability of childhood cancer drugs that are not produced inside the country, the attraction of outside suppliers is a cornerstone. Many suppliers are targeting the big market, the small country like Rwanda need to stimulate the supplier, some mechanisms the study proposed was facilitation in drug registrations through Rwanda FDA by reduction of fees of new entities registration and decrease of new drug processing time and easy provision of importing visa and license, taxes reduction or free taxes on anti-cancer. Taxes reduction on cancer drugs as an act to improve supply and affordability has been suggested in another study on availability, Price, and Affordability of Anticancer Medicines in china (30) .

5.1.7. HIGH COSTS OF CHILDHOOD CANCER DRUGS

High cost of childhood cancer drugs was associated with small volume of cancer order, lack of national drugs prices index, limited insurance coverage, and limited use of generic anti-cancer drugs

SMALL VOLUME OF CANCER DRUG ORDER

In terms of procurement, the RMS which is a national procurement center, KFH private institution providing anti-cancer drugs, Butaro Cancer Center of Excellence under PIH funds providing cancer drugs procure cancer drugs internationals, this separated institutions procurement decrease volume of requested drugs which complicate procurement as most of the cancer factors require minimum volume to produce that is not reached. Grouped power at national level even region might be a good solution to access as suggested by study participants even in other studies done in the middle-income countries where Rwanda is located(15,39). Group-based procurement through existing collaborative initiatives, such as EAC, African Union countries combined cancer drugs pooling may come as a solution to procurement(30,31).

The good solution of affordability suggested by most of the case participants is coordinated pool procurement in Rwanda or in the region where Rwanda is located. The pooled procurement has been reported as a solution in many middle-income countries like Ghana, Botswana, etc (55).

NATIONAL DRUGS PRICES INDEX AND INSURANCE COVERAGE.

Currently, Rwanda has good health insurance coverage CBHI, RSSB, MMI, etc, this facilitates health care delivery. But most cytotoxic drugs for childhood cancer are not covered by health insurance especially public health insurance (CBHI) covering more than 80% of the population. The affordability challenge to cancer drugs due to poor insurance coverage has been reported even in Ghana (46). When cancer drugs are covered by insurance due to the way they are

expensive, even some percentage not covered by insurance becomes a challenge to patients. The financial stress on patients or parents with children with cancer disease has been reported in many other countries as reported in a WHO study done in 2018 on the pricing of cancer medicines and its impact (44)(30). The poor affordability was reported in another study done by BIZIMANA et al on price, availability, and affordability of medicine in Rwanda which shows poor affordability of chronic disease drugs (49). Therefore, more financial support is needed on patients or parents with children diseased with cancer. Rwanda Government should negotiate with health insurance for coverage of essentials cancer drugs and the government should provide some subsidies or provide 100% coverage in cancer drugs to improve affordability which will have a great impact on childhood cancer outcomes. The 100% government coverage of medications has been suggested in a study done in Rwanda on the availability of essential NCDs drugs as a factor that might improve accessibility(56).

In Rwanda, the costs of drugs to the patients in public health facilities are set with a top-up of 20% margin over the initial cost from supplier, as instructed by the minister of health, but the prices in private pharmacies are set based on their need. This is related to the lack of national drugs index price which should control prices in both private and public pharmacies. This is a big barrier to cancer drugs affordability as currently few anti-cancer drugs pass through public procurement, patients in need were using private pharmacies who sell at the highest prices, this explains poor cancer drugs affordability and regimen interruption to patients. The problem of drug pricing has been reported in the pricing of cancer medicine and its impact study done by WHO done in 2018(44). The problem of high prices in private pharmacies in Rwanda had also been reported in other studies like the study done by KAYUMBA et al on prices, availability, and affordability of medicines in Rwanda and many other studies done in the middle country(49). Therefore aggressive pricing policies are needed to disrupt this ongoing problem of affordability.

LIMITED GENERIC DRUGS USE.

Most of the anti-cancer drugs are patent, still protected by the producer. There is a lack of generic entities which pushes to use the branded drugs, this is not allowed by most insurances that cover essential medicine list and most are generic drugs. The use of generic drugs is a good way to increase the availability and affordability of childhood cancer drugs. Initiative approach for RMS considered as a national public procurement agency for procurement for generic anti-cancer drugs might highly increase availability and affordability to the population as suggested in many other studies on access to childhood cancer essential(46,57).

5.1.8. LACK OF SYSTEMS TO OPTIMIZE PHARMACOVIGILANCE

Lack of system to optimize phamacovigilance of childhood cancer essential drugs has been explained by quality challenge and limited phamacovigilance inspection.

QUALITY CHALLENGE

Drugs quality was checked by Rwanda FDA. Rwanda FDA is a new institution still in process for development, currently no in-house laboratory for checking the quality of cancer drugs except basing on paper for good manufacturing practice. Despite well-known good quality companies from Europe or America, insufficient budget, low volume of demanded cancer drugs not reaching minimum quantity for the industry to produce, all of these factors push to procure from an unknown company. Insufficient budget pushing procurement from low-quality cancer supplier companies has been mentioned in many middle-income countries like the study on Health system determinants of access to essential medicines for children with cancer in Ghana(46) The bark pool procurement at national level might come as a solution to quality as it gave power to procurement from good quality companies..

PHARMACOVIGILENCE INSPECTION

Adverse drugs reaction and ineffectiveness of drugs is followed by RFDA. They are reported by end-users which are patients. The patients are under the care of clinicians including physicians, nurses, and allied health sciences practitioners. The barriers come from the gap in communication between the team. While drugs circulating in the country, good reporting for drugs side effects like an online system of reporting was suggested as a manner of adequate pharmacovigelance data reception at national level.

5.2. STRENGHTHS AND LIMITATIONS

As far as we know, this work constitutes the first case study of a detailed qualitative method of determinants of access to essential medicines for childhood cancer in the context of Rwanda's healthcare system.This study collected data from stakeholders in single not all public hospital (CHUK), single not all private hospital (KFH), PIH funded hospital which is Butaro Cancer Center of Excellence, RMS, Rwanda FDA, RBC, and MOH. Due to COVID 19 pandemic, quantitative analysis of the study has not been done, as instruction preventing travel from one district hospital to another limits data collection to BCCE. Furthermore, our results on barrier and facilitator on access to childhood cancer essential drugs in Rwanda were findings from stakeholders from Public and private stakeholders who concluded good political will in policy monitoring and bulk large volume with well-prepared regulations of procurement might be the solution of access to childhood cancer essential in Rwanda, for further research many private sectors and NGOs should be interviewed. The small number of policies and guidelines accessed (8) in this study limited our ability to get generalized conclusions. Only accessed policies and guidelines were few due to time constraints, this comes as a limitation as few policies were reviewed, for the reviewed policies and guidelines were showing some factor humping drugs access to a country like a long period of new drug process around 9 months and cost of new drugs registration which is elevated but also lack of policy specific to childhood cancer drugs. Pool procurement of childhood cancer essential drugs is a strong solution to good quality drug availability and affordability.

Further research is needed to assess health determinant factors of access to childhood cancer essential drugs on health system context in Rwanda on availability, affordability, and quality by assessing drugs pharmacovigilance.

CHAPTER 6. CONCLUSION AND RECOMMENDATIONS

6.1. CONCLUSION:

Although there is good progress in childhood cancer care in developed countries, there is still a gap in access to childhood cancer essential drugs in Rwanda as a middle-income country. This study identified barriers and facilitators of access to childhood cancer essentials drugs in Rwanda. Policy and guidelines in place not taking into consideration childhood cancer as a rapidly growing domain that needs political voluntary in terms of budget allocation and special procurement process. RMS in charge of public procurement drugs lacks accurate cancer data and insufficient budget which pushed them to concentrate on infectious disease drugs which are affordable with adequate data and where pool procurement is possible.

This poor procurement of cancer drugs in the public procurement chain cause poor availability of medicines in the public hospitals which explained poor access. Poor access to public hospitals pushed parents with cancer diseased children to consult private institutions and pharmacies, where prices of medications are high as no rule regulating their prices and with poor insurance coverage as like CBHI used by most of the population, were not covering medications outside of public institutions which make affordability a challenge. Insufficient budget with solitary different institutions procurement with small volume instead of grouped large volume bulk Procurement at national level or a regional level were not favoring procurement from known good quality supplier companies which explain the mostly doubtable quality of cancer drugs.

As solutions suggested by the study were joining power from different countries like EAC country in terms of procurement which would increase demanded volume, this would increase negotiation power from known good quality drugs supplier companies for prices reduction. The grouped procurement might have a direct impact on the availability of cancer drugs which will facilitate easy accessibility of affordable childhood cancer drugs. This might be sustainable if political will of putting in place the clear policy of cancer or childhood cancer drugs procurement as rapidly growing domains requiring special interventions by giving subsidies and a special program of new drug processing through Rwanda FDA which will attract many cancer drugs supplier to bring their entities in the country as a no local supplier of cancer drugs available in Rwanda. National drugs prices index was suggested as solutions of affordability to cancer drugs from private institutions as the price of drugs should be set at national level. A well-equipped cancer treatment center with the ability to prepare syrup friendly to children may increase drug acceptability and accessibility to children and decrease drug wastage.

6.2. RECOMMENDATIONS

To government of Rwanda

- ✓ To provide enough budget for cancer as a rapidly increasing domain.

To the Ministry of Health:

- ✓ To elaborate childhood cancer policy.
- ✓ To improve national cancer registry
- ✓ To advocate for chemotherapy health insurance especial CBHI

To RMS

- ✓ To Strengthen systems for procurement of pediatric cancer drug needs

TO RFDA

- ✓ To improve FDA approval processes
- ✓ To build an in-house laboratory for quality checking

TO REFERRAL AND PROVINCIAL HOSPITAL like CHUK:

- ✓ To create a pediatric cancer treatment unit.

To PIH:

- ✓ Extend cancer treatment program in other provinces of the country not only northern in Butaro cancer center of excellence

To the next researchers:

- ✓ To research on Incidence and prevalence of pediatric cancer in Rwanda
- ✓ To conduct a study on adverse and Toxic Effects of Childhood Cancer Treatments in Rwanda
- ✓ To conduct research on factors affecting access to follow up care on survival of childhood cancer in Rwanda

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APPENDICES

APPENDIX1

ACCESS TO CHILDHOOD CANCER ESSENTIALS STUDY GUIDE

INTERVIEW DATE/TIME: _____

Pre-interview

- Review purpose of study and why participant selected
- Review and collect informed consent
    - Review anonymity conditions
    - Review withdrawal rights (any point during/after conduct of interview)
- Describe nature/structure of interview
- Review the interview guide in entirety. Identify key sections to focus on given the interviewee's background and role.

Introduction

- State date
- State professional role
    - ☐ Politician/civil servant/policymaker
    - ☐ Health professional (physician, pharmacist, allied health)
    - ☐ Civil society representative
    - ☐ Other (specify) _____

Preamble

- This study is one part of a project examining drug access for children with cancer in low and middle income countries (LMICs) Rwanda. It is focused on describing and analyzing the health system determinants of childhood cancer drug access, and identifying opportunities to improve access.
- The project seeks to improve context-sensitive understanding of the challenges related to childhood cancer drug access, to enable stable and appropriate procurement and supply management by local institutions and governments..

Study Objectives

1. Describe policies and practices related to childhood cancer drug procurement and provision in participating jurisdictions; and

2. Analyze the key determinants of childhood cancer drug access in health system context.

Desk Review

Review of existing academic and grey literature to summarize available knowledge on:

1. National policy and legal framework for pharmaceuticals, with focus on cancer drugs and supportive care agents (including evaluation of NCCP, assessment of national formulary against EMLc, etc)
2. Clinical guidelines or standards of care for treatment of childhood cancers
3. Procurement systems and practices, including pharmaceutical budgets and allocation to childhood cancer
4. Quality assurance practices
5. Distribution systems, including inventory management (e.g. storage, forecasting, etc)
6. Monitoring and evaluation systems

Interview

Guiding questions:

1. **What is your role/your organization's role in the procurement of (childhood) cancer drugs?**
2. **What do you see as the major barriers to (childhood) cancer drug access in Rwanda or institution? How could access be improved?**

Part I. Policy and Economic Issues
A. Policy and Legal Framework
i. National medicine policy

- Is there a national medicine policy , or written document specifying national goals for the pharmaceutical sector and/or a framework for coordinating this sector?
    - PROBE: For example, components of a national medicine policy might include legislative and regulatory frameworks, choice of essential medicines, and/or financial strategies
- What is the role of national regulatory authorities in ensuring patient access to pediatric cancer medicines? PROBES:
    - What is the purview of these authorities? How do they relate to international regulatory bodies and/or recommendations from regulatory authorities internationally?

- How are regulatory authorities involved in decision-making regarding local pharmaceutical production?
- What are the regulations and incentives for quality insurance of local pharmaceutical production?

ii. Intellectual Property and Access to Medicines

- How do national and international intellectual property regulations influence access to childhood cancer medicines in your country?
- Are there regulatory barriers to introducing generic competition for childhood cancer medicines?

B. Financing and Sustainability

i. Affordability (from system, institutional, and patient perspectives)

- What are the implications of the current financing mix/model for:
  - Drug purchasing and prices?
  - Drug affordability at the institutional and patient levels?
  - Resource sustainability for the procurement of childhood cancer care drugs?
  - Priority setting and resource allocation for childhood cancer programs and services?
  - Equity of access to childhood cancer medicines?
- How does the financing for childhood cancer care (including drugs) differ from that for cancer care and control in adults?
- What factors contribute to intra- and inter-national differences in the pricing of childhood cancer medicines?
  - PROBE: How do manufacturer pricing schemes and taxes along the pharmaceutical supply chain contribute to this?
- Health Insurance
  - Please describe the scope of health insurance coverage for cancer care and childhood cancer care. PROBES:
    - Are all childhood cancers covered by public funding or is coverage limited to only specific childhood cancers, certain populations or certain age groups of children/adolescents with cancer?
    - If funding is limited to specific cancers or populations, which ones and why were those ones selected (cost effectiveness, level of supportive care necessary, achievable cure rates, etc.)?

        - Is public coverage limited to specific sites of care (i.e. only government hospitals) or is there also partial payment of private care facilities)?
        - In general, do patients have access to public or employer-based health insurance?
- Patient Perspective
    - What are the cost-related barriers for patients to access childhood cancer medications in your institution and country?
        - PROBE: Are these medications available in generic formulations? How are off-patent cytotoxic drugs financed?
        - PROBE: Is there any form of regionally pooled purchasing for childhood cancer medications?

The following questions should be answered through **desk review** if possible:

i. Resource Distribution

- Please describe the existing systems of governance/organization for pooling and distributing funds for:
    - The health system
    - Cancer care
    - National Cancer Control Plan (NCCP) directed programs, if a NCCP exists
    - Childhood cancer care
    - PROBE: What, if anything, could be improved in terms of pooling and distributing of funds?
- How are resources allocated within the national health system? PROBES:
    - General health priorities? Disease priorities? Target groups? Target regions? Level of care (primary/secondary/tertiary)? Types of care (preventive/early diagnosis/curative treatment/palliative care)?
    - Is there a formula used for resource allocation?
    - How are cancer program budgets used, if at all, at the national, regional, district and/or community levels?
    - *If there is a National Cancer Control Programme (NCCP):* How has the NCCP influenced: the structures/systems for pooling and distributing of funds?
    - What, if anything, would you change about how resources are allocated for the national health system?
- What is the budget allocation for childhood cancer in Rwanda or your institution? How much is actually spent on childhood cancer care? PROBES:

- Absolute amount per year and the proportion from total health expenditure indicating the currency and year of estimation
- If a national cancer center exists, its annual operating budget and proportion spent on childhood cancer

- Please describe the main modalities and streams of funding for the childhood cancer care continuum in relation to health system components (primary care, diagnosis and referral, tertiary care, palliative care, survivorship care). PROBES:
  - Are designated bundles of resources allotted to specific childhood cancer diagnoses? Or are system components (e.g. hospital services, physician services, medicines, etc) funded through distinct mechanisms? Or is it a mix of the above? Please describe.
  - Is there funding in your country to cover non-treatment related costs for cancer such as travel, food, and/or accommodation for families?
  - What components of medical care are patients/families required to self-fund? What out of pocket costs are typically incurred by patients/families?
  - If so, specify who provides these funds and the proportion of cost/amounts.
  - How do government subsidies, national health insurance, private foundations, public-private relationships, and user charges influence funding?
  - What roles do international organizations, such as the United Nations, pharmaceutical donations, and donor funding play in financing medications?

Service		**Source(s)**	**Mechanism**	**Proportion**
Hospital services (in-patient bed, DI, surgery, pathology, radiation, supportive care)		Government		
		NGO		
		Employer		
		PHI		
		OOP		
Physician services				
Allied health services				
Medicines	Chemotherapy			
	Supportive			
	Opioids			
Out-pt/community diagnostic services (lab, DI, biopsy,				

pathology)			
Ancillary/indirect costs (travel, accommodation, food)			

Source	**Mechanism**	**Proportion**
Government	General taxation Payroll Earmarked	
Civil society	Charitable donation	
International donor	Government ODA Twinning institution International institution Innovative financing	
Private	Out of pocket costs User fees Medical savings accounts Private insurance Employer-based insurance	

- Please describe how the following receive payment:
    - Health care institutions in general?
    - NCCP supported programs?
    - Cancer treatment centers?
    - PROBE:
        - Does the payment mechanism for programs and institutions encourage or discourage productivity in any way? Honesty and quality assurance? Improved patient outcomes?

Part II. Pharmaceutical Management

A. Selection

- Is there a national drug formulary? Please provide.
    - PROBE: Who manages the national formulary? What governance and oversight mechanisms exist for the national formulary? Who sets priorities for pharmaceutical policy? What is the process for adding/removing products from the formulary?
    - PROBE: What factors influence the selection of this list? – e.g., prevalence of diseases, cost-benefit ratio, scientific data

- PROBE: What, if any, barriers exist to national formulary compliance with World Health Organization (WHO) essential medicines list (EML) recommendations?

- Do you have a National Drug Price Reference Index? Please provide.

B. Procurement

i. Managing procurement

- Who is responsible for obtaining childhood cancer medicines – e.g., the patient, physicians/providers, the treating institution
    - PROBE: Through what channels are these medicines obtained – public/central medical stores, private outlets, private foundations?
- How are cancer medicines procured at the national level? – e.g., open or closed tender, direct procurement, competitive negotiation, purchasing from international procurement agencies?
    - PROBE: What principles or strategies dictate this procurement? – e.g., Procurement of generic medicines, pharmaceutical quality standards, limitation of procurement to essential medicines, competitive procurement?
    - PROBE: What purchasing models are followed? – e.g., annual purchasing, scheduled purchasing, perpetual purchasing?
- What is the role of global health initiatives (e.g., Pan American Health Organization (PAHO) Strategic Fund) in procurement?
- What is the role of civil society actors such as non-governmental organizations (NGOs) in procurement?
- Is procurement of childhood cancer medicines distinct than for other classes of medicines?
    - PROBE: How, if at all, do the procurement structures in the health system, disease programs, adult cancer programs, and pediatric cancer care programs interact? Do they use the same supply chain management systems?
- Are there national procurement laws which govern this process?

ii. Quality assurance

- What quality assurance programs exist for essential cancer medicines (national, institutional)? Are they put to routine use? – e.g., selection of suppliers with acceptable quality standards; quality assurance for packing, storage, delivery, and recording; appropriate management of quality concerns
- Are there issues of drug safety and efficacy for EML medications, such as counterfeiting, improper production, and inadequate quality surveillance?

iii. Quantification

- What processes exist to determine the amount of medication required for procurement? – e.g.
    - Consumption method (based on past use) - what data and supply systems does this come from?
    - Morbidity method (predicts theoretical quantities needed for specific diseases) – requires data on morbidity and patient visits to quantify
    - Proxy consumption method – based on data from other facilities, regions, and countries
    - PROBE (if applicable): Given that procurement is at a national level, please describe how medications are coordinated and shared across institutions?
    - PROBE: How is the quantification process performed? Manually or computer-based? Centralized (government) or decentralized (peripheral warehouses, health facilities)?
- How does procurement relate to national drug formulary provisions?

C. Distribution

i. Managing Distribution

- How are medicines supplied to government and non-governmental health services?

Strategy	Description	Proportion
Central medicine stores	Procurement and distribution by central government unit	
Autonomous supply agency	Procurement and distribution by autonomous or semi- autonomous agency	
Direct delivery system	Medicines delivered directly by suppliers to facilities; government selects suppliers, but does not store and distribute medicines	
Primary distributor	Government establishes contract with one or more	

	primary distributors and/or suppliers	
Primarily private supply	Private pharmacies provide medicines to public-sector patients	

- Please describe the process by which essential cancer medicines are distributed? – e.g.,
    - System type: Geographic or population coverage? Push or pull system?
    - Information system: What systems exist for inventory control, records and forms, consumption reports?
    - Storage: How are sites selected, what materials-handling systems exist?
    - Delivery: Are medicines collected or delivered? Is this done in-house or via a third party?

ii. Inventory Management

- How accurate and current are stock records for medicines? Are there regular reports on inventory, operating costs, and consumption patterns?
    - PROBE: What criteria are used to determine which medicines are held in stock all the time? (e.g. – VEN classification of vital, essential, nonessential)
- Are there significant or frequent problems with the supply (e.g. shortages) and/or availability of essential childhood cancer drugs in public sector health facilities? Are there identifiable (perceived) reasons for these shortages or excesses? What is the evidence for this? PROBES:
    - Is there a process in place to identify, prevent, and/or address medication stock outs in the country or public sector facilities?
    - How is the amount of safety stock held in storage facilities determined?
    - Is there a process to ensure stock for rapid availability of antibiotics for childhood cancer patients presenting with fever and neutropenia?
    - When was the most recent stockout? For what medicine? How was the issue solved?
    - How do people obtain chemotherapeutics, antimicrobials, and pain medications when they are not available? E.g. purchasing from the private sector, outside pharmacies, importing/black market?
    - How would you describe the turnaround time, or the time taken to deliver and fill an order after it is received?

- Please describe any systems in place for monitoring the supply and usage of medications and other therapeutics for the treatment of childhood cancer? PROBES:
    - Please describe which individuals and/or departments are responsible for this task. Is this a separate job within each department? Is the same system used within departments?
    - Are there routine access problems with supplies important to childhood cancer care, such as blood culture bottles, contrast agent, pathology stains?
    - Is expiry of drugs / consumables perceived to be an important challenge with drugs and logistics supply management?
    - How are pediatric pharmacists involved in supply chain management for antineoplastic drugs?
    - Are there intra-institutional and inter-institutional policies to minimize waste of essential cancer medicines?

iii. Local manufacturing & Importation

- Please describe the importation and/or port-clearing process for childhood cancer medicines? Are these processes managed in-house or privately?
- What are the types of pharmaceutical manufacturers that operate in your country (multinational companies, hospital-based firms, etc.)?

iv. Transportation

- Which authority manages the transportation of childhood cancer medicines? Is the contracted out? What quality assurance programs exist?

D. Use

i. Provider Perspective

- What strategies exist to encourage rational use of childhood cancer medicines? – e.g.,
    - Educational – Training of prescribers, distributing printed materials, using standardized international protocols
    - Managerial – Supervision, feedback, structured approaches like forms or guidelines
    - Economic – Financial incentives, reimbursement
    - Regulatory – Pharmaceutical registration, restrictions, limited medicine lists
    - PROBE: What factors contribute to irrational use? – e.g., polypharmacy, use of ineffective medicines, incorrect use of effective medicines

- PROBE: What types of medicine-use data is collected, including both quantitative or qualitative? (e.g., pharmaceutical supply orders, patient registry data, patient interviews)

- What supports exist for ideal medicine dispensing practices? – e.g., prepackaging, labelling, record keeping, etc.
- What systems exist to ensure pharmacovigilance – product quality, monitoring of adverse drug reactions, and monitoring of medication errors?
    - PROBE: Do these differ for childhood cancer medicines in particular?

ii. Patient Experience

- How do socioeconomic and geographical factors, such as poverty and rurality, affect patient patients' abilities to access essential cancer medicines?
- What challenges arise for patients and providers due to unique characteristics of childhood cancer medicines – e.g., sterile injectable formulations, dosing by weight or body surface area
    - PROBE: Does the availability of formulations and/or their preparation influence childrens' abilities to take these medicines? – e.g., Are liquid formations available? Who is responsible for compounding medications (pharmacists, physicians, patients)?
- How would you describe the overall patient and provider experience with pediatric cancer treatment in your institution and country overall?

Part III. Management Support Systems

A. Planning and Administration

- What management support exists for the pharmaceutical supply system (processes of selection, procurement, distribution, and use)?
- What measures exist to control excess costs in the pharmaceutical supply system? – e.g., price comparison analyses, expiry data analyses, hidden cost analyses
- Who is responsible for financial planning and managing accounting systems related to childhood cancer medicines, locally and nationally?

B. Organization and Management

- What measures exist to protect against security breaches such as theft, bribery, and fraud for childhood cancer medicines?
- How is the supply of pharmaceuticals managed at the facility or hospital level?
- Please describe any processes to procure and manage medical and laboratory supplies required in the treatment of childhood cancer.

- PROBE: Is there national coordination of purchasing for these supplies? Is there data on the consumption and use of these supplies? Is there appropriate collaboration with front line staff in making these decisions? Do donations play a role in supplying these materials?

C. Information Management

- Please describe any systems that exist for monitoring and evaluating access to childhood cancer medicines in your institution and/or country – e.g., supervisory visits, routine data reporting, special studies to answer targeted questions when needed, needs assessments
- Is there a centralized or distributed pharmaceutical management information system? – e.g., record-keeping documents, feedback reports, performance indicators
    - PROBE: To what degree is this process computerized vs. manually recorded?

D. Human Resources Management

- Are there human resources issues that adversely impact patients' abilities to access childhood cancer medicines? – e.g., adequacy of training, salaries, and staff
    - PROBE: Is there specialized training for pharmacists or others who prepare and administer pediatric cancer medications?

Post-interviews

- Thank participant

APPENDIX2

Consent form for participation in a study on "Access to childhood cancer essential "

Identification: _____ Date: _____

By signing the form below, I confirm that the consent form has been explained to me in terms that I understand.

I consent for participating in this study. I understand that the information may be used in the medical record, for purposes of medical teaching, or publication in medical textbooks or journal and electronic publications. By consenting to this study participation I understand that I will not receive payment from any party. Refusal to consent to this study participation is accepted,

I understand that the results of this study may be read by members of general public, in addition to scientists and medical researchers that regularly use these publications in their professional education. If I have any questions or wish to withdraw this consent in the future, I will contact:

Dr NKURUNZIZA Jean Nepomuscene, neponziza@gmail.com,0788258451

Dr Aimable KANYAMUHUNGA, kanyamuhungaa@gmail.com, +250788670200

Names of person giving connsent: _____ Signature

Signature of investigator

UBURENGANZIZA BWO KWITABIRA UBUSHAKASHATSI KU KUBONEKA KW"IMITI YINGENZI YA KANSERI MU RWANDA

UMWIRONDORO ITARIKI

Mukuzuza iyi nyandiko nemeye ko basobanuriye ibijyanye nubushakatsi ndabyumva kandi ndabyemera.

Nemeye kwitabira ubushakashatsi,numvise ko amakuru azavamo ashobora kwifashishashwa kwa muganga,mu kwigisha,no mubitabo,no kuri murandasi.

Mu kwemera kujya mu bushakashatsi nta mafaranga nzahabwa. Kwanga kujya muri ubu bushakashatsi biremewe.

Numvise ko ibizava mu bushakashatsi bizabonwa numuntu wese,abashakashatsi nabandi bahanga.

Numvise ngize ikibazo cg shaka kuva muri ubu bushakashatsi nyuma .nzashaka

1. Dr NKURUNZIZA Jean Nepomuscene, neponziza@gmail.com, 0788258451

2. Dr KANYAMUHUNGA Aimable, kanyamuhungaa@gmail.com, 0788670200

Izina ryuwemeye kujya mu bushakashatsi isinya

……. ……..

Umushakashatsi isinya

…… ……

APPENDIX3

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 18th/February/2020

Dr Jean Nepomuscene NKURUNZIZA
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 027/CMHS IRB/2020

Your Project Title ***"Access to Childhood Cancer Essential Drugs"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
		Yes	No (Reason)	
Name of Members	**Institute**		**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 17th February 2020, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 18th February 2020

Expiration date: The 18th February 2021

Professor GAHUTU Jean Bosco
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:

- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

APPENDIX4

REPUBLIC OF RWANDA/REPUBLIQUE DU RWANDA

NATIONAL ETHICS COMMITTEE / COMITE NATIONAL D'ETHIQUE

Telephone: (250) 2 55 10 78 84
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Ministry of Health
P.O. Box. 84
Kigali, Rwanda.

FWA Assurance No. 00001973
IRB 00001497 of IORG0001100

February 24th,2020

Dr. Jean Nepomuscene NKURUNZIZA
Principal Investigator
School of Medicine and Pharmacy, CMHS, UR

Review Approval Notice: No. 128/ RNEC/ 2020

Your research Project:**" Access to Childhood Cancer Essential Drugs"** has been **approved** by the Rwanda National Ethics.

This decision is based on the approval from the **School of Medicine and Pharmacy, CMHS, UR** dated on 18th February 2020

Date of Approval: February 18, 2020
Expiration date: February 18, 2021

Sincerely,

RWANDA NATIONAL ETHICS COMMITTEE R.N.E.C P.O BOX:84 KIGALI

Dr. Jean-Baptiste MAZARATI
Chairperson, Rwanda National Ethics Committee.