THE ECONOMIC OUTCOME OF ANTIMICROBIAL STEWARDSHIP IN A HOSPITAL SETTING: THE CASE OF GERTRUDE'S CHILDRENS' HOSPITAL

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A thesis submitted in partial fulfilment of the requirement for the award of Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance of the University of Nairobi

November, 2023

DECLARATION

I, Lihanda Bevin Likuyani, declare that this thesis is my original work and has not been presented for the award of any other degree or to any other university.

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Approval by supervisors

This is to certify that this thesis has been submitted for examination with our approval as supervisors.

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DEDICATION

I would like to dedicate this thesis to my wife, Anita Wairimu, and son, Gabriel Likuyani.

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LIST OF ABBREVIATIONS AND ACRONYMS

AM	Antimicrobial
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship Program
ABSD	Antibiotic Shillings Per Patient Day
AMSD	Antimicrobial Shillings Per Patient Day
ASP	Antimicrobial Stewardship
AWaRE	Access, Watch and Reserve classification
CDC	Centers for Disease Control and Prevention
CLABSI	Central line associated blood stream infection
DDD	Defined Daily Doses
EMR	Electronic Medical Records
GCH	Gertrude's Children's Hospital
GDP	Gross Domestic Product
ICT	Information and Communication Technologies.
IPC	Infection Prevention and Control
MRSA	Methicillin-resistant Staphylococcus aureus
PHIS	Pediatric Health Information System
UCLA	University of California, Los Angeles
UoN	University of Nairobi
USB	Universal Serial Bus
US CDC	United States Center for Disease Control and Prevention
VAP	Ventilator associated pneumonia.
WHO	World Health Organization

DEFINITION OF OPERATIONAL TERMS

Antibiotic cycling: the use of an antibiotic as first line therapy for a specific period of time then alternating that antibiotic with one of a different class but same spectrum of activity for the same duration, then repeating the cycle.

Antimicrobial agent: a drug or medicine that kills or inhibits growth of bacteria, fungi, parasites or viruses.

Antimicrobial resistance: a situation where a micro-organism becomes progressively unresponsive to antimicrobial agents.

Antimicrobial stewardship program: refers to a coordinated program that encourages the effective and efficient use of antimicrobial agents to improve therapeutic outcomes, reduce antimicrobial resistance and reduce morbidity and mortality due to drug resistant microbes.

AWaRe classification: classification of antibiotics into Access, Watch and Reserve, taking into account their impact on antimicrobial resistance, to emphasize the importance of their appropriate use.

Defined daily doses: refers to the average assumed maintenance dose per day for a drug used for its main indication in adults

DDD per 1000 patient days the number of DDDs of a drug utilized on average on any given day in a representative group of 1000 patients.

DDDs per 100 bed days: estimates the proportion of inpatients receiving one DDD of a given drug.

Leapfrog antibiotics: antibiotics that are not necessarily the first line treatment but are used for empirical treatment.

Persuasion strategies: focuses on education of the clinicians and thereafter auditing their prescribing behavior and providing relevant feedback.

Restrictive strategies: antimicrobial stewardship strategy involving limitation of general antimicrobial agent use and involves formulary restriction, antibiotic cycling and requirements for authorizations of antibiotic prescribing.

Structural strategies: antimicrobial stewardship strategy involving the introduction of infrastructure that aids in effective and efficient use of antibiotics.

ABSTRACT

Background

The Centre for Disease Control and Prevention has strongly advocated for the planning and implementation of antimicrobial stewardship (AMS) programs in a bid to fight antimicrobial resistance (AMR). The World Health Organization has included antimicrobial resistance (AMR) in the list of top ten public health concerns. It leads to increased cost of treatment, prolonged hospital stays, treatment failure and at times death. Implementing AMS programs requires allocation of significant financial resources and therefore it is important for stakeholders to understand the economic and financial impact of these initiatives. Although various authors have conducted studies on the economic impact of AMS in hospitals, not much has been done in the Kenyan context.

Objectives

The main objective of the study was to investigate the economic outcome of implementing antimicrobial stewardship interventions at Gertrude's Children Hospital (GCH).

Methodology

A mixed method study involving collection of both qualitative and quantitative data was carried out for the period between 2015-2022. Five AMS committee members were interviewed and responses were validated by review of AMS meeting minutes, periodic AMS reports and hospital guidelines on use of antibiotics. Purposive sampling was done, where the Chief Pharmacist identified the participants who met the inclusion criteria. The economic outcome of the AMS program was assessed through review of retrospective pre-post data on antibiotics consumption and the cost attached. Data was extracted from the electronic medical record software used at the hospital. A comparison of antibiotic use before and after implementation of AMS program was done to assess changes in consumption and cost. The pre-phase was 2015-2018 while

post-phase was 2019-2022. Qualitative data was analyzed by content analysis while quantitative data was analyzed using STATA version 13.0 software. Alpha was set at 0.05.

Results

AMS interventions implemented at GCH include structural, restrictive and persuasive strategies. Structural strategies implemented at GCH include digitization through an electronic medical records (EMR) software, antibiograms, pro-calcitonin testing, rapid diagnostic testing of respiratory viruses as well as penicillin allergy testing. No decision support software was in place to help in rational antibiotic prescribing. Restrictive strategies included restriction of antibiotic prescribed particularly for surgical prophylaxis and a pre-authorization policy for all reserve antibiotics. Education of hospital staff on AMR and AMS principles was also a key strategy for Gertrude's children's hospital. Implementation of these strategies was done at estimated total annual cost of $84,229. This figure includes $5,200 in capital costs and $79,029 in recurrent costs. This annual recurrent cost included a figure of $58,896 incurred in form of full-time equivalent salaries (FTE). There was an overall 25.4% decrease in consumption of selected antibiotics between the pre-AMS phase (2015-2018) to post-phase (2019-2022), from 137.8 Defined Daily Doses (DDDs) to 112.4 DDDs. Consumption of imipenem/cilastatin (-81%), meropenem (-54.7%), from 9.05 DDDs to 4.09 DDDs and vancomycin (-54.4%), from 1.85 DDDs to 0.84 DDDs. However, increased consumption was seen with cefotaxime (44%) and clindamycin (22%) injections. The number of patients exposed to the study antibiotics reduced from 39143 (pre-AMS) to 37425 (post-AMS).In terms of cost, Antimicrobial Shillings per patient Day (AMSD) decreased by 9.3% in the first year (2018) and by 33.3% in 2019, there was a very slight increase in 2020 (0.5%). Antibiotic Shillings Per patient Day (ABSD) then increased in 2021 by 4.2%. 2022 saw a drop by 29.2% in 2022.

Conclusion

AMS program implementation at Gertrude's Children's Hospital was associated with a decreased consumption and expenditure on target antibiotics. This finding should serve to encourage the implementation of such a program across all level 4, 5 and 6 hospitals in Kenya as it promotes rational use of antimicrobial agents while saving costs for the hospital.

1.0 CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND

World Health Organization (WHO) defines antimicrobial resistance (AMR) as a state whereby bacteria, viruses and parasites are unresponsive to antimicrobial agents leading to significant increases in morbidity and mortality[1]. Due to AMR, patients experience prolonged length of hospital stays, readmissions, increased costs of management of disease and sometimes death[2]. It is estimated that AMR causes 23,000 deaths in the USA and 25,000 in the European Union annually. In Africa we lose an estimated 700,000 people annually. Antimicrobial resistance is expected to cause approximately 10 million deaths by 2050 worldwide, 4.1 million of these deaths expected to come from Africa[3].

There are several factors that may lead to AMR which include: use of antimicrobial agents in agriculture, increased levels of global interconnectedness leading to spread of the resistant microbes and general overuse of antibiotics[3]. Studies have shown in Africa, health seeking behavior is different as compared to the west. The population does not go to a hospital or clinic as the first line of contact when unwell. Indeed it has been noted that, 31.7% of the population do not consult a doctor while 26.4% obtain antibiotics over the counter[4]. There has not been recent innovations in regard to development of new antibiotics and therefore it is imperative that something is done to protect the effectiveness of the range of antimicrobial agents that are in current use[4].

Antimicrobial stewardship (AMS) can be referred to as the efficient and effective management of antibiotics with a bid to optimize their use[5]. The United States Centers for Disease Control and Prevention (US CDC) has proposed seven core elements that are key to the success of any antimicrobial stewardship program (AMS). These include hospital leadership, accountability, pharmacy expertise, action, tracking, reporting and education[6]. Antimicrobial stewardship programs aid in limiting AMR through prevention of antimicrobial overuse, optimization of therapeutic outcomes and reducing rates of hospital acquired infections and healthcare costs[5].

1.2 PROBLEM STATEMENT

Antibiotic resistance is one of the leading challenges facing healthcare delivery in the world. In fact, the World Health Organization (WHO) has included AMR in its top ten list of the biggest public health dangers facing the human species. Indeed, AMR contributes to increased cost of treatments, prolonged

hospital stays, treatment failure and even death. It is projected that by 2050, increase in antimicrobial resistance may lead to close to 10 million deaths yearly, an overall Gross Domestic Product (GDP) decrease and close to losses of 100 million dollars[2].

In this regard, many institutions including the US Centre for Disease Control and Prevention have strongly advocated for the implementation of antibiotic stewardship programs. The main goals for this program is to not only reduce the cases of antibiotic resistance, but also to optimize clinical outcomes[7]. However, for these programs to run effectively, adequate resources have to be allocated. Consequently the administration and other stakeholders need to understand the economic and financial impact of these initiatives[8].

Although many investigators have done several studies geared towards assessing the economic impact of AMS programs, not much has been done in the Kenyan context. In addition, most of these studies have not factored in the costs related to implementing these programs[9]. It is therefore not possible to understand whether AMS program strategies implemented in the Kenyan setting have had any positive influence on rational antibiotic utilization and cost savings to both the hospital and the patients.

This study therefore investigated the economic implications of AMS programs at Gertrude's hospital, a private hospital in Kenya that has implemented AMS. It sought to find out the costs involved in implementing the program, its impact on antibiotic utilization and other costs accrued by the hospital, and cost implications for the patients. The study also aimed to increase the body of knowledge with regard to feasibility and economic impact of AMS programs.

1.3 RESEARCH QUESTIONS

1. What were the types and costs of antimicrobial stewardship interventions implemented at Gertrude's Children Hospital?
2. What is the outcome of antimicrobial stewardship interventions on antibiotic consumption and costs at Gertrude's Children Hospital, four years before and after implementation of the AMS program?

1.4 RESEARCH OBJECTIVES

1.4.1 Main Objective

The main objective of this study was to investigate the economic outcome of implementing antimicrobial stewardship interventions on antibiotic consumption and costs at the Gertrude's Children Hospital from 2015 to 2022.

1.4.2 Specific Objectives

The specific objectives were to:

1. Identify the types of antimicrobial stewardship interventions implemented at Gertrude's Children Hospital between 2015-2022.
2. Identify the costs of antimicrobial stewardship interventions implemented at Gertrude's Children Hospital between 2015-2022.
3. Determine the change in antibiotic consumption before and after implementation of the AMS program between 2015-2022.
4. Determine the change in antibiotic cost before and after implementation of the AMS program between 2015-2022.

1.5 STUDY JUSTIFICATION

Antimicrobial resistance is a global problem fueled by misuse, over-use and inappropriate use of antibiotics. This leads to increased duration of hospital stay, costs of treatment and mortality. Many global health organizations such as the WHO and the CDC have advocated for the implementation of antimicrobial stewardship programs aimed at reducing cases of antimicrobial resistance and optimizing clinical outcomes. The economic impact of these programs particularly in the Kenyan context has not been studied and therefore this study sought to assess this impact at Gertrude's hospital. This study was expected to provide data on the impact of AMS on antibiotic utilization, expenditure on antibiotics and overall drug costs per patient. It was also aimed at establishing the interventions and costs involved in setting up and implementing AMS programs in the hospital set up.

Before this, study there was no data on the economic impact of AMS programs in Kenya. In addition, most of the global data available did not factor in the costs involved in implementing these programs. This study therefore sought to fill this knowledge gap and as well add to the existing global body of knowledge on this subject. Kenya has adopted an inter-ministerial approach towards its fight against AMR and came up with the "National policy on prevention and containment of antibiotic resistance." This policy aims at increasing awareness and understanding of AMR. This study shall therefore add to the existing body of knowledge available to the Ministry of Health in its initiative around antimicrobial stewardship programs.

Apart from the Ministry of Health, Kenya, other stakeholders that shall gain from this study include the administration of Gertrude's hospital who shall be able to assess the economic viability of the program. At the global level this study shall add to the body of knowledge available to international bodies such as the

WHO and CDC in their efforts related to AMS. The study findings shall help in assessment of the economic feasibility of these programs. As a result, hospital administrators will have tangible data to inform their decisions on this subject. The findings of this study shall be disseminated through publications, national policy briefs, continuous medical education and conference presentations.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1 ANTIMICROBIAL STEWARDSHIP PROGRAMMES

The United States Centers for Disease Control and Prevention define AMS as the concerted efforts made by institutions geared towards measurement and improvement on how antibiotics are prescribed by clinicians and how they are utilized by the patient[6]. Other authors have defined AMS as organized efforts that aim to enhance the effective and efficient use of antimicrobial agents so as to enhance therapeutic outcomes in patients, limit AMR, reduce the spread of multidrug resistant microbes and as well reduce wastage of resources, thereby reducing costs[10].

A Cochrane review identified key strategies in the implementation of AMS. These strategies may be divided into three main classes; structural, persuasive or the restrictive models[11]. The structural model involves the introduction of infrastructure that aids in effective and efficient use of antibiotics. An example given by Huebner in 2019 is digitization of records or decision support systems[10]. This infrastructure gives the healthcare providers tools that encourage rational use of antimicrobial agents.

The persuasive model focuses on education of the clinicians and thereafter auditing their prescribing behavior and providing relevant feedback. The prescribers are provided with relevant information either through training, workshops or continuous medication on the appropriate use of antimicrobial agents. Their prescriptions are then audited to find out if they are in compliance with the principles of rational prescribing of these medicines.

The restrictive model involves general restriction of antimicrobial agent use thereby limiting misuse and encouraging rational use. Activities may include formulary restriction, antibiotic cycling and requirements for authorizations of antibiotic prescribing[10]. Formulary restriction involves discouraging misuse by limiting the scope of antimicrobials available for the prescribers. Antibiotic cycling involves the use of an antibiotic as first line therapy for a specific period of time then alternating that antibiotic with one of a different class but same spectrum of activity for the same duration, then repeating the cycle. Pre-authorization requires prescribers to seek approval prior to prescribing certain antibiotics. Other strategies may include establishment of hospital prescribing guidelines, early conversion from intravenous to oral medications and de-escalation (Akpan et al., 2016). The strategies are presented in Table 2.1 [11] and Figure 2.1 [12].

Table 2.1: **Strategies of implementation of antibiotic stewardship programs as per Cochrane groupings [11].**

Strategy	Objective	Examples
Structural	Provide support and institute control	Digitization of records and decision support systems
Restrictive	Define rules and implement standards	Formulary restriction, antibiotic cycling and preauthorization
Persuasive	Provide information and feedback	Educational information, reminders and feedback

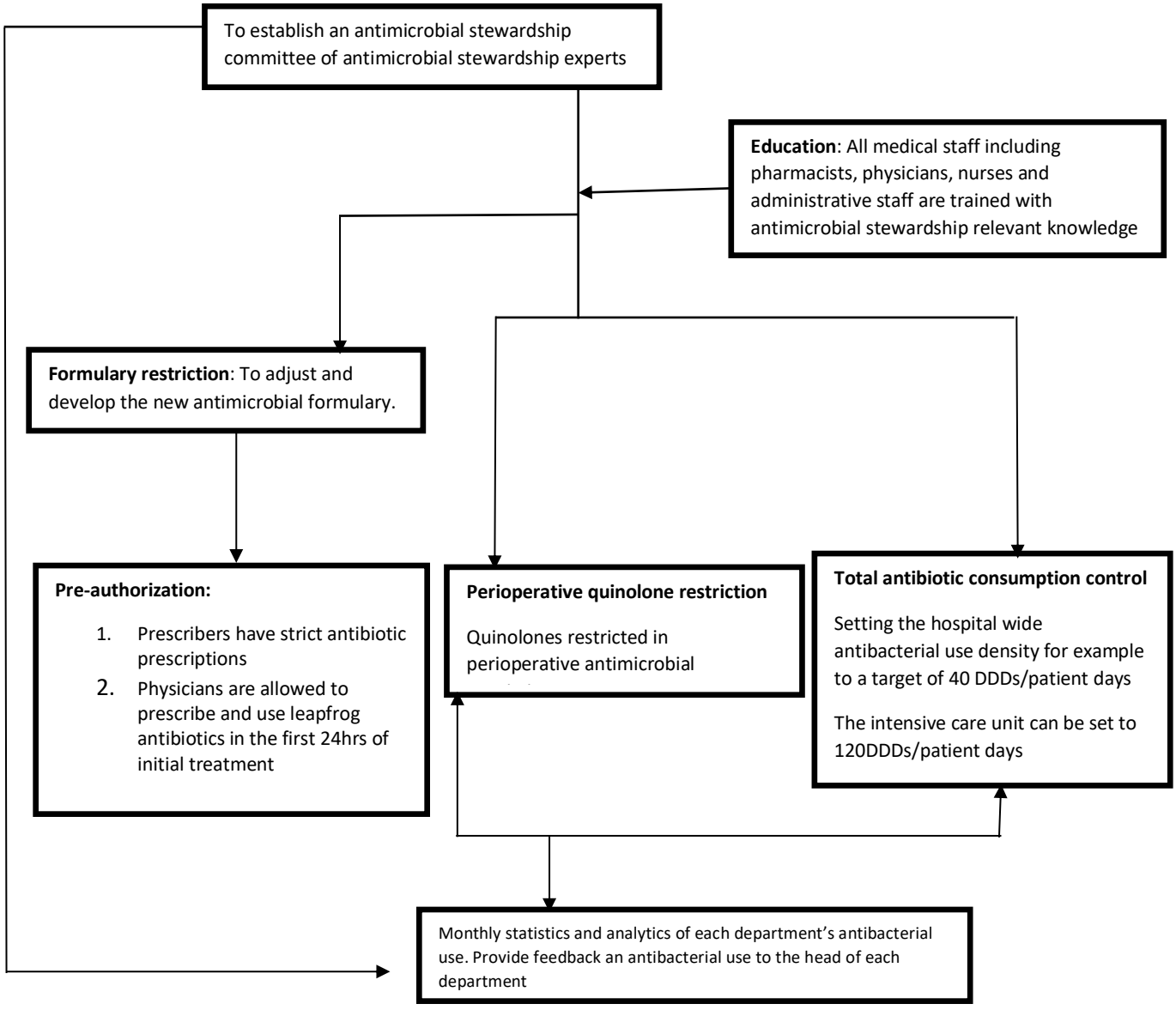


Figure 2.1 Flow chart explaining the strategies employed in antimicrobial stewardship programs (Hou et al., 2014)

Figure 2.1 shows that AMS programs begin with establishment of an antimicrobial stewardship committee and continues with a consistent monitoring and feedback system.

2.1.1 Core elements of hospital antimicrobial stewardship programs

Optimizing antibiotic use is a complex process that requires careful planning and effective execution. Different hospitals offer different contexts in terms of the challenges they face in management of antibiotic use; this therefore means that there is no "one size fits all" when it comes to how to implement AMS programs[13]**.** However, there are key elements that can guide any hospital or health institution establish a functional AMS program allowing flexibility to a certain degree[6]**.**

For an AMS program to be successful, leadership buy-in is paramount[6]**.** This is vital because the Chief Executive Officer, for the case of private hospitals and Chief Officer of Health, in the context of public hospitals, make the final decision on how resources are allocated in their respective institutions. In this regard if these leaders are on board, this can ensure that adequate levels of financial, human and information technology resources are allocated towards the program.

An accountable person should be appointed to ensure management of the program and monitoring outcomes. This could be a physician or a pharmacist. In a scenario where the chairperson is a physician it is recommended that a pharmacist should be brought on board to co-lead the program. Their expertise is viewed as crucial in driving the implementation process[13]**.**

Putting into action pre-determined strategies is vital for success of AMS. This may involve conducting audits on clinician prescribing, giving feedback and instituting pre-authorization strategies among other interventions. Other core elements include tracking of prescription patterns and impact of instituted interventions, reporting to stakeholders on the overall progress and educating the relevant healthcare workers on and optimizing the use of antibiotics and resistance[6]**.**

2.1.2 Guidelines on antimicrobial stewardship programs and implementation in Kenya

In 2019, Kenya established a National Antimicrobial Stewardship Inter Agency Advisory Committee (NASIC) and Technical Working Groups (TWGs) at the National Level. Thereafter the Ministry of Health came up with guidelines aimed at guiding the health workforce to implement antibiotic stewardship programs[14]**.** This was done because several studies had shown that antimicrobial resistance was becoming a growing menace in the country.

A review done in 2020 showed that indeed Kenya has a National Action Plan (NAP) on AMR that is aligned to the WHO global action plan (GAP) [15]**.** Kenya was only one of the few countries in Africa with antimicrobial stewardship programs. The guidelines therefore provide direction on the framework, approach and available resources that aid implementation of AMS programs down to the county level. Kenya launched a National AMR surveillance strategy mainly hinged on the laboratories, established a central data repository on the same and as well joined the Global Antimicrobial Resistance Surveillance System[16]**.**

The counties were encouraged to form county advisory committees on AMS but as at the year 2020, out of the forty seven counties only two had established the same [16]**.** It was noted that implementation of AMS programs in the country was constrained by lack of prioritization by the key stakeholders and inadequate resource allocation on the same. However, the National Medicines and Therapy Committees had success in reviewing the Essential Drug List, incorporating the AWaRE classification[16]**.** For these programs to be successful it was noted that it was important to have consistent stakeholder engagement and lobbying for increased resource allocations while establishing frameworks that shall ensure adequate monitoring and evaluation of the same.

2.2 OUTCOME OF ANTIMICROBIAL STEWARDSHIP PROGRAMS

2.2.1 Economic outcome of antimicrobial resistance: A global and local perspective

Antimicrobial resistance has a far reaching global and local economic impact[17]. At the local level, studies have shown an increase in hospital stays of between 3-46 days which in some cases may cause a deprivation of a nation's workforce thereby lowering a country's Gross Domestic Product (GDP). The same studies show an increase of hospital costs by between US$238 to US$16,496[2]**.**

At the global level the World Bank summarizes the economic impact of AMR in five major predicted future scenarios; It is expected that by 2050, AMR will lead to a fall of between 1.1-5% in annual Gross Domestic Product (GDP) causing a significant increase in poverty levels. The global real exports may decrease by between 1.1-3.8% while global healthcare costs are expected to increase by 700 billion dollars. It is as well expected that the global livestock output is expected to decrease by close to 5%.

2.2.2 Quality measures for assessment of economic outcome

The measures for assessment of economic impact of AMS programs can be divided into four main groups; structural, initial outcomes, other outcome and process measures[5]**.** The assessment of structural measures may be done through the use of the CDC checklist of the core elements of an AMS program[6]**.**

In initial outcome measures, focus is on antimicrobial consumption. The most efficient and preferred manner to implement this is through collection of routine antimicrobial consumption data[5]**.** From this, priority is given to the indicators DDD/100(0) patient days and/or DDD/admission. Proportion of DDDs in AWaRE group is also a beneficial outcome measure. Other outcome measures include measures focused on assessment of clinical outcomes such as average length of stay, mortality and readmission rates. Process measures are auxiliary measures used to assess whether the new AMS practices are being implemented from day to day[5]**.** Examples include the amount of time taken to carry out an AMS training.

2.2.3 Challenges in evaluating economic outcome of antimicrobial stewardship programs

Economic evidence is key in determining the value of a health intervention such as an AMS program[18]. In assessing this economic impact of AMS, cost effectiveness and cost utility analyses are central in determining the opportunity cost of implementing an AMS program. Examples of challenges in evaluating economic impact of AMS programs include difficulty in capturing long term resource allocations and the costs of negative external costs[19]**.**

Determining the time horizon in assessing the impact of the AMS is another challenge. Many economic evaluations have been born from inadequate choice of time horizon. The costs and benefits accrued from AMS programs transcend generations, therefore confining this just to a selected time may give a false quantification of these two parameters[19]**.** Antimicrobial stewardship interventions may have a societal impact such as availability of a healthy workforce. These benefits extend beyond the boundaries of the hospital implementing the program[19]**.** Since the chosen population do not work, it is a challenge to measure the societal impact.

2.2.4 Economic outcome of antimicrobial stewardship

The main objectives of antimicrobial stewardship programs are to enhance clinical outcomes and reduce cases of antibiotic resistance. However, for the resource providers it is important to understand the financial and economic impact that these programs have in their institutions[20]**.**

In this regard researchers in different settings have endeavored to investigate the impact of AMS programs from an economic perspective. These researchers have employed various study designs including systematic reviews [9] and prospective interventional studies[21]**.** However quasi experimental design is the most popular. This entails collecting data before and after implementation of the set-out AMS strategies and assessing impact therein.

The main outcomes assessed in these studies featured mainly change in defined daily doses (DDD) from the point of drug utilization, antibiotic acquisition costs and changes in costs to the patient. Table 2.2 is a summary of studies that assessed the economic impact of AMS programs.

Table *2.2*: Studies on economic outcome of antimicrobial stewardship

Research	**Study site**	**AMS strategy**	**Study design**	**Results**
Abubakar et al, 2019, Nigeria	Two public tertiary hospitals involving 464 surgical procedures	protocol development, educational meetings, audit & feedback	Pre and post intervention study	The DDD (antibiotic prophylaxis) from 16.6 to 12.8/procedure Cost of surgical antimicrobial prophylaxis decreased by $4.2
Fukuda et al,2014, Japan	429 bed-capacity community hospital	Audit and interventional feedback Dose optimization De-escalation Training	Before-after	Antimicrobial costs decreased by 25.8% Aminoglycoside use reduced by 80%
Cook & Gooch,2014, USA	904 bed -capacity tertiary care teaching hospital	Restriction Training Guidelines	Prospective interventional (2001-2013)	62.8% reduction in antibiotic use
Bartlett & Siola,2014, USA	155 bed-capacity community hospital	Restriction Parenteral to oral conversion Review & feedback	Quasi-experimental, before-after	Decreased acquisition cost of antibiotics by 25.5% Increased number of discharges in a month by 8.5% Antimicrobial DDD decreased from 1627 to 1338/1000 patient days
Borde et al, 2014, Germany	1600 bed tertiary hospital	Guideline revision Information & education	Before-after	Overall reduction in antibiotic use Cephalosporins (-37%) Fluoroquinolones (-43%)

		Regular ward rounds Intensified infectious disease consultation. Audit and feedback		
Cisneros et al,2013, Spain	1251bed capacity Teaching hospital	Training Guidelines	Before-after	42% reduction in antibiotic consumption
Vettese et al,2013, USA	253 bed capacity Non-teaching hospital	Review & feedback Parenteral to oral conversion Dose optimization	Before-after	Reduction of average cost of antibiotics from $ 219867 to $137805 (-37%)
Teo et al, 2011, Singapore	1700 bed capacity General hospital	Prescriber education Prospective review & feedback De-escalation of therapy Dose optimization Parenteral to oral conversion	Before-after	Acquisition costs of antibiotics reduced by S$198575 (9.9%) Cost saved by patient in the same period was S$91194
Bassetti et al, 2000, Italy	2500 bed capacity hospital	Restriction Formulary guidelines	Before-after	Average cost of antibiotics reduced from 4.53 euros to 4.18 euros. Consumption of ceftazidime & tazobactam/piperacillin reduced by 52% and 26% respectively
Mercer et al, 1999, USA	360 bed capacity Community hospital	Restriction Guidelines Pre-authorization	Cost comparative before-after	26% reduction in IV antibiotics, 10% in oral antibiotics 24% cost reduction in cost per patient

These studies show that implementation of AMS programs leads to an overall decrease in antibiotic utilization and consumption, reduced antibiotic acquisitions costs, reduced antibiotic use related costs and a decrease in costs per patient.

2.3 CONCEPTUAL FRAMEWORK

Antimicrobial stewardship is a program that requires careful planning coupled with significant investments. Once this is done, there are a myriad of benefits that can be accrued from implementing this program. AMS activities involve incurring implementation costs by the facility and this further translates to key benefits through the program. These benefits together with the costs attached are discussed in Figure 2.3.

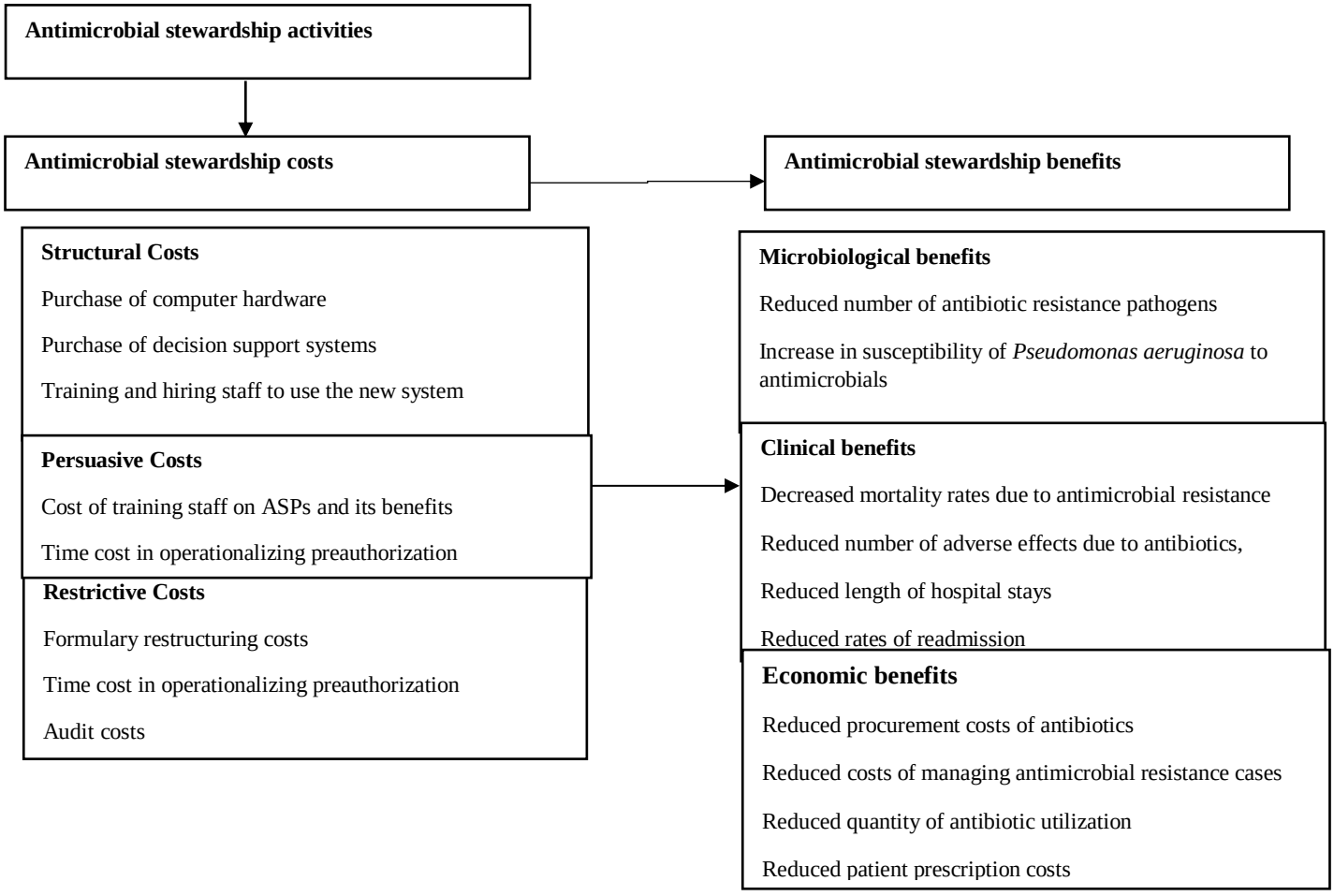


Figure 2.*2*: Conceptual map showing key variables in assessing impact of antimicrobial stewardship programs

2.3.1 Categories of variables in the conceptual framework

In this framework there are two main categories of variables: independent and dependent variables. Independent variables are the interventions and costs involved in setting up and implementing an AMS program. These include structural, persuasive and restriction-related costs such as purchase of computers,

training and costs related to prescription auditing. Dependent variables include the benefits accrued from implementing the AMS program. These include economic, clinical and microbiological benefits. In this study looking at the economic outcomes, the dependent variables also include quantity of antibiotics consumed and the procurement costs spent on these antibiotics.

2.3.2 Costs incurred in implementation of antimicrobial stewardship

Antimicrobial stewardship programs result in considerable benefits to the institution. However, with these benefits come considerable costs attached. It should be noted that not many studies have been conducted with the objective of analyzing the costs involved in implementing a AMS program. That being noted, some institutions in the United States have reported massive investments in AMS, incurring costs of between $17,000 to $388500[8].

The costs involved in implementing an AMS is contingent on the strategies the institution uses in implementing the program. This, according to Cochrane review groupings, could either be structural, restrictive or persuasive[10]. If the strategy chosen is structural, this involves for example computerization of clinical information which enhances decision making with regards to antibiotic use. This therefore will involve purchase of computers and establishing and electronic health information system which has AMS support. Studies in the United States have reported a cost of $58,300 and $145,000 for purchase of an AMS enabled health information software and computers of between $800 and $1500 [8]. Structural interventions could also include purchase of laboratory equipment.

Restrictive interventions, in some studies have been referred to as the principle strategy that gives the AMS a strong foundation to succeed[7]. In this intervention, institutions focus on setting rules and restrictions that limit scope of antibiotic use to those in their formulary, institute pre-authorization policies allowing only clinicians with training on AMS use to approve use of antibiotics.

Persuasive interventions are also a mainstay in implementation of a AMS program. This strategy involves training the healthcare workers on antimicrobial stewardship, carrying out audits and having in place a feedback program. Costs in this intervention include training costs, travel costs (for AMS related activities) and sitting allowances for the AMS committee. In general overall budgeted costs of implementing AMS program in the United States, excluding one-time costs range between $17000 to approximately $388,500 per year[8].

Time costs are also invested in AMS programs from the planning, implementation and the evaluation phase. The committee and the other stakeholders in the hospital invest a lot of time in ensuring the program

is successful. This is in the form of the aforementioned trainings, strategy meetings and other AMS activities that they would normally be engaged in. Most AMS programs allocate between 50-100% of at least one of their staff's time to AMS activities[22]**.** Time costs can be quantified using the opportunity costs that the hospital incurs through their staff engaging in AMS activities instead of other traditional hospital activities. A study by Zacharia in 2016 showed that some United States hospitals incur AMS personnel costs of between $17000 to $134,100[8]**.**

2.3.3 Factors that determine the cost of an antimicrobial stewardship program

The cost of a program is strongly dependent on the human and infrastructural resources dedicated to the program[23]**.** It is recommended that the bed capacity of the hospital should drive the full time equivalent (FTE) allocated to implementing an AMS program by pharmacists and physicians. The higher the bed capacity, the higher the allocated FTE[24]**.** This higher FTE translates to higher costs incurred in ensuring that the program remains effective. The other components of the AMS program as well determines the cost of the program. If the program includes all AMS strategies including structural, restrictive and persuasive this leads to a more costly program as compared to programs that miss any of these strategies.

2.3.4 Benefits of antimicrobial stewardship and indicators of these benefits

A number of benefits can be accrued to both the patient and the healthcare institution in implementation of antimicrobial stewardship. These can broadly be classified into three main categories; economic benefits, clinical benefits and microbiological benefits[25]**.**

2.3.4.1 Economic benefits of antibiotic stewardship programs

Many researchers have endeavored to assess the economic benefits of implementing an antimicrobial stewardship program. This is because administrators are always keen on looking at running an institution in a more cost-effective and efficient manner. Some of these benefits include reduction in procurement costs, decreased costs of case management of antimicrobial resistance as well as consumption of antimicrobial agents. Many studies have shown huge economic benefits of AMS in hospitals through analysis of consumption and cost saving of antibiotics[26]**.**

Antibiotic consumption was either presented as percentage change or as WHO defined anatomical therapeutic chemical (ATC)/defined daily doses (DDD). These were either normalized to 1000 bed days [27] or 100 bed-days.[28] The cost related benefits were either presented as absolute figures, percentage changes in cost or both.

Studies done in the United States and Europe have shown cost savings ranging from $2.50-$2650 per patient [26] while others reported a reduction in antibiotic expenditure of 43% [27] and 28.5%[7]. In antibiotic utilization, studies have reported significant decrease in consumption post implementation of AMS ranging from 10.5DDD/1000 bed days to 375 DDD patient days[15].

2.3.4.2 Clinical Benefits of antimicrobial stewardship programs

Implementation of AMS in the hospital could have a number of clinical benefits. These include improved cure rates, decreased cases of treatment failure, reduced number of adverse effects due to antibiotics, reduced rates of *Clostridium difficile* infections, reduced length of hospital stays and rates of readmission[6]. Authors like Al-Omari et al in 2020 showed the incidence of ventilator associated pneumonia (VAP) and central line associated blood stream infection (CLABSI) reduced after implementation of AMS[7].

2.3.4.3 Microbiological benefits of antimicrobial stewardship programs

Combating antimicrobial resistance is at the heart of antimicrobial stewardship programs[6]. This benefit can mainly be assessed through finding out the percentage of patients with antimicrobial resistant organisms compared to those with antimicrobial susceptible infections. Cultures and the laboratory unit play a crucial role in obtaining valid results[25]. A study conducted in 2020 showed a significant increase in susceptibility of *Pseudomonas aeruginosa* to antimicrobials including amikacin, ciprofloxacin and cefepime after implementation of an AMS program[27].

2.4 METHODOLOGICAL APPROACHES OF ASSESSING THE IMPACT OF ANTIMICROBIAL STEWARDSHIP PROGRAMS

A number of methodological approaches and study designs have been employed in evaluating the impact of antimicrobial stewardship programs. Although randomized control trials (RCT) are considered to rank high up in hierarchy of evidence, this method has not been popular mainly due to ethical concerns, cost implications and logistical challenges[25]. Despite this, a number of RCTs measuring impact of AMS have been done including one where a pilot cluster randomized control trial[29]. In this study, at pre-AMS phase, point prevalence data was obtained on antibiotic use as well as data on antibiotic utilization. This was then compared to the same data collected post-AMS.

In majority of published literature, the most dominant methodological approaches are observational studies and in particular, interrupted time series studies. In one such study, the investigators compared antibiotic

utilization and cost in pre- and post- implementation of AMS in four hospitals in Qassim, Saudi Arabia[7]**.** They used data mining software to extract relevant data focusing on only ten restricted antimicrobials that have a broad- spectrum of activity. These included antimicrobials such as imipenem/cilastatin, piperacillin/tazobactam, ciprofloxacin and moxifloxacin.

A similar study was done in 2019 by Wang et al which involved analyzing trends pre- and post-AMS implementation[28]. They studied trends in antimicrobial utilization and intensity of use, antimicrobial prophylaxis in Type I incision operations, rates of antimicrobial resistance in common gram-negative bacilli and methicillin resistant *Staphylococcus aureus* (MRSA).

In assessing utilization of antibiotics at the hospital set-up, DDD were the main estimate used. These were either normalized to 1000 bed days [27] or 100 bed-days[28]**.** Other measured outcomes included comparing total cost of antimicrobials, assessing antimicrobial resistance patterns, comparing length of hospital stays, assessing readmissions, mortality and incidence of hospital acquired infections.

As seen in this literature review, a lot of studies have covered the impact of antimicrobial stewardship programs on antibiotic utilization and costs. However, there is paucity of data in the context of Kenya of this impact. In addition, costs related to implementation of these programs has not been well covered in the Kenyan context and this study aimed to fill this literature gap.

3.0 CHAPTER THREE: METHODOLOGY

3.1 STUDY DESIGN

This was a mixed methods study as it entailed the collection of both qualitative and quantitative data. It was a pharmacoeconomic study that entails cost consequence analysis. This design was chosen as it entailed collection of data on the cost of implementation of AMS interventions. The consequences thereafter were evaluated mainly through retrospective review of data on antibiotic consumption and cost. This study was conducted in three phases; The first phase entailed a key informant interview, the second, a pre-post data analysis and the third involved costing. The methodologies of each of these phases based on the research objectives are described separately in this chapter.

3.2 STUDY SITE

The study was conducted in Gertrude's Children's hospital, one of the region's largest private pediatric hospitals. The hospital serves approximately 300,000 outpatients annually through its clinics around Nairobi and 9000 in patients annually with a bed capacity of 100 patients. It is a tertiary teaching and referral hospital established in 1947 and focused on serving patients between 0-21 years of age.

Gertrude's hospital is a non-profit organization and the largest pediatric hospital in the East African region. It has 27 pediatric specialties and 14 outpatient centers in and around Nairobi County. The hospital is known as the gold standard for the best practice in quality, safety and management depicted by its accreditation by the Joint Commission International (JCI) USA. This study site was selected because it is one of the few hospital facilities in Kenya that has a well-established AMS program and the hospital was interested in evaluating the impact of the implemented AMS program. The site also has a well-established health management system and data relevant to the study can be accessed through their electronic systems.

3.3 KEY INFORMANT INTERVIEWS TO IDENTIFY THE TYPES AND COSTS OF ANTIMICROBIAL STEWARDSHIP INTERVENTIONS

3.3.1 Study design

This was a mixed methods study involving key informant interviews. It involved collection of both qualitative and quantitative data.

3.3.2 Study population

The key informants in this study were individuals who had an in-depth knowledge on the implementation and operational costs of the antimicrobial stewardship program at Gertrude's Children's Hospital. The main purpose of key informant interviews was to collect information from a wide range of people including physicians, pharmacists, accountants, nurses and administrators who are members of the antimicrobial stewardship committee or were directly involved in the implementation of the AMS program at Gertrude's Children's hospital.

These committee members with their insider knowledge and understanding provided insight on the specific AMS interventions and costs incurred in implementation of the program. These individuals were tasked on providing information on the AMS interventions implemented and the attendant costs. The study period covered was between 2015 to 2022. This period was chosen because the Chief Pharmacist indicated that the antimicrobial stewardship interventions at the hospital began in 2018.

3.3.3 Eligibility Criteria

3.3.3.1 Inclusion criteria

Participants were included in the study if they met any of the following criteria;

i. The Chief Pharmacist or any other pharmacist directly involved in implementation of the AMS program at GCH
ii. The person in charge of special programs (including AMS) at the GCH
iii. The accountant or financial officer directly involved in the implementation of the AMS program.
iv. The current and past chair of the AMS program committee

The list was not limited to the above criteria and additional members were included as suggested by the interviewees. The individuals were required to give informed consent.

3.3.3.2 Exclusion criteria

Participants not included in the study were;

i. Employed for less than a full calendar year as it was deemed that they were new and may not have in-depth knowledge of implementation of the program.
ii. Unavailability for interview between the time periods April- July 2022
iii. Failed to give informed consent

A total of five key informants, all current members of the AMS committee, were eligible, provided consent and subsequently interviewed. These included, the Chief Pharmacist, the AMS pharmacist (AMS secretary), AMS chairperson (pediatrician), microbiologist and administration representative. The thematic areas covered during the interview include; AMS interventions and how they were implemented, capital and recurrent costs incurred, guideline development, compliance assessment and challenges faced.

3.3.4 Sample size and sampling procedure

Purposive sampling was conducted aiming at obtaining maximum information. This sampling approach was selected because it is appropriate for qualitative studies aimed at getting maximum information. According to the principles of sampling for key informant interviews by UCLA Center for Health Policy Research, a sample size of between 4-10 informants is adequate or until saturation point is achieved is adequate [30].

The hospital's chief pharmacist was requested to assist with the recruitment process by providing a list with contacts and offices of personnel who were potentially eligible. The researcher either called or physically visited the individuals to make an appointment for a formal visit. The participant was allowed to select a time and place for a more formal appointment. During the first visit, eligibility was confirmed using the eligibility checklist in appendix F. If eligible, participant was asked to provide an informed consent. During the consenting process, the objective and purpose of the study was explained to the participants. They were also made aware of their rights and the interview was only administered if the participant was willing and available at a time that was convenient for him or her. Consenting was done in a private room to maintain privacy and confidentiality.

3.3.5 Sources of data, data collection instrument and procedures

The data that was collected included both qualitative and quantitative data. These included data on the types of AMS interventions implemented at the hospital and the related costs. Key informant interviews were the main source of this data and it was validated through review of records.

The interview was done with the aid of a key informant interview guide presented in appendix G. This was administered by the researcher who was accompanied by a research assistant. The research assistant made

written notes as well as made observations for non-verbal ques. The interviews were conducted both online and face to face depending on the preferences of the interviewees. For interviewees who gave permission, an audio record of interview was done. Non-verbal cues including eye contact, hand gestures and facial expressions were recorded to validate authenticity of responses.

The interview was designed to collect information on the human resources and all activities that were involved in implementation of the AMS program at the hospital. These resources included but not limited to time, personnel, meetings, trainings and equipment, and database reconfiguration. Where possible the attendant costs were obtained. Where possible documentary evidence was requested for, this included evidence of meetings and receipts and these were used to validate the interviews.

3.3.8 Variables

The key variables in this objective were AMS interventions implemented at GCH as well as direct and hidden costs incurred in implementing the program. AMS interventions in this study included all the measures put in place to aid in the rational use of antimicrobials. These measures included restrictive, structural and persuasive strategies that GCH implemented to prevent antibiotic misuse. Direct costs included all foreseen costs that could be directly traced and tracked to a particular AMS activity for example costs for of purchasing laboratory equipment. Hidden costs included all unforeseen costs related to instituting the AMS program.

3.3.9 Data analysis

Qualitative data was analyzed through narrative thematic analysis. This involved 5 main stages including; (a) data organization, (b) deriving a general sense of the information, (c) coding, (d) establishing categories and themes and finally, (e) data interpretation. Data organization began with transcribing audio recordings after the interview. During transcription, any patterns and themes were noted in the transcript margin. Coding was then done manually through re-reading the transcripts and identifying recurrent words, ideas and patterns from the data. Interpretation involved studying the categories and corresponding codes to determine if there were any themes or patterns that provided insight on the AMS stewardship activities at Gertrude's Children's hospital.

Continuous variables were presented as sums and means. Categorical variables were presented as frequencies and percentages. Descriptive statistics, analyzing the costs of AMS implementation were done estimating frequency and percentages and creating combo charts were made by Excel (version 2019;

Microsoft Corp, Redmond, WA). The quantitative costs were analyzed using inferential t test and Mann-Whitney test using STATA software version 13.0. Alpha was set at 0.05.

3.4 PRE-POST STUDY TO INVESTIGATE THE CHANGE IN ANTIBIOTIC PROCUREMENT EXPENDITURE AND UTILIZATION

3.4.1 Study design

A pre-post quasi-experimental study design was used to analyze the outcomes of the AMS by comparing antibiotic utilization and cost data. The designated periods were pre (2015-2018) and post (2019-2022) AMS program initiation for inpatients at GCH.

3.4.2 Study population

Five antibiotics were chosen from the Access AWaRe group while seven and three antibiotics were chosen from the watch and reserve groups respectively. Making a total of 15 antibiotics included in the study. These antibiotics were selected to have a complete representation of all the AWaRe classes while focusing on those whose supplies were consistently available during the study period. These medicines were used to determine the antibiotic consumption within the study period (2015-2022). The selected antibiotics included;

i. **Access:** amikacin, amoxicillin/clavulanic acid, clindamycin, gentamicin, benzylpenicillin.
ii. **Watch:** azithromycin, cefepime, cefotaxime, ceftazidime, ceftriaxone, clarithromycin, vancomycin.
iii. **Reserve:** imipenem, meropenem, piperacillin/tazobactam.

3.4.3 Eligibility criteria for selection of antibiotics

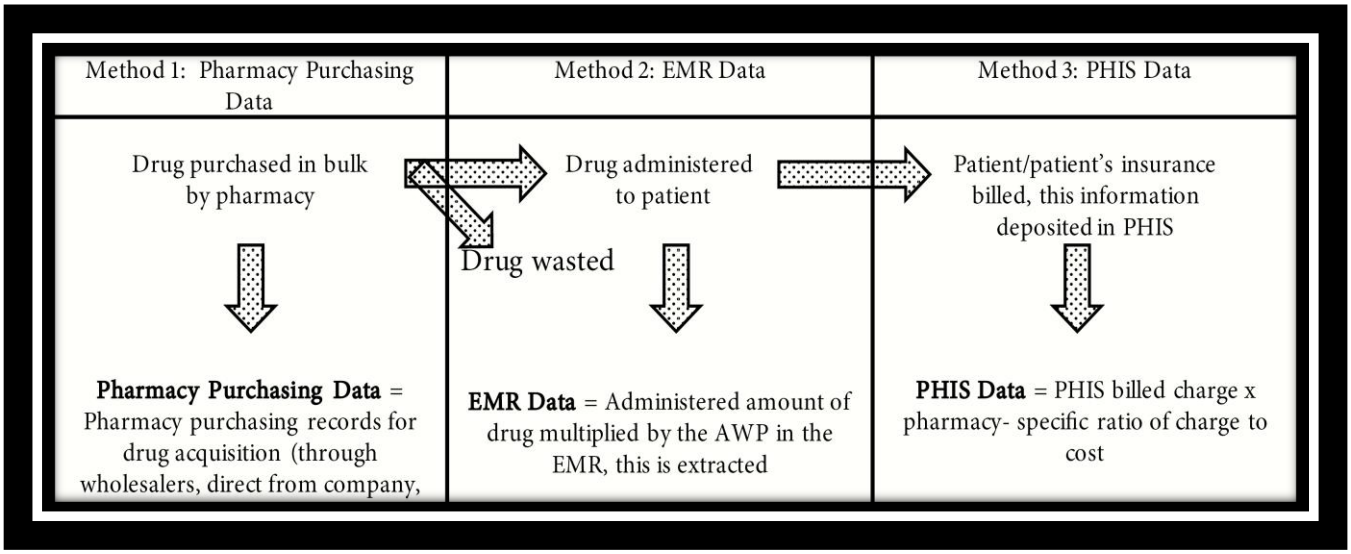
3.4.3.1 Inclusion criteria

Antibiotics were included if they were prescribed for;

i. Patients admitted at the hospital within the study period (2015-2022)
ii. Patients who received any of the chosen antibiotics in the Access, Watch Reserve (AWaRe) classes
iii. Antibiotics administered by oral or parenteral routes.

3.4.4 Types and sources of data on antibiotic consumption

In this research objective, data that was collected was mainly quantitative and included antibiotic consumption data and the costs attached on the same. As shown in Figure 3.1 , consumption data was collected from three sources (Parker et al., 2017): pharmacy purchasing data for drug acquisition costs, patient level data which was obtained from the electronic medical records as well as patient invoices and billing obtained from the pediatric health information system (KRANIUM®) used at the hospital.



EMR*: *Electronic Medical records, AWP-Average Wholesale Price, PHIS- Pediatric Health Information system

Figure 3.1: Sources of antibiotic consumption data at Gertrude's Children Hospital

3.4.5 Data collection instrument

A data recording sheet was used to document data on chosen antibiotics and their consumption levels. Baseline characteristics was compared in the pre-phase and post-phase including comparing demographic parameters such as sex, age groups, as well as the admitting wards.

3.4.6 Data collection procedure

The Information and Communication Technology (ICT) department was asked to provide weekly or monthly data on utilization and acquisition costs of antibiotics for the study period (2015-2022). However, this data was only available in form of annual reports. Access to data was requested from the hospital management through the head of ICT department. All data was password protected. In the electronic medical records, each medicine administered to a patient and attached costs was documented.

3.4.8 Variables for the pre-post study

Antibiotic consumption referred to the quantity of antibiotics used by patients expressed in DDDs per 1000 patient days [32]. Antibiotic costs included the amount in shillings attributed to the antibiotics consumed.

3.4.9 Data Analysis for the pre-post study

Data on antibiotic consumption was gathered and reported in terms of defined daily doses (DDDs) as recommended by the WHO Collaborating Centre for Drug Statistics Methodology [32]. The DDD per 1000 patient days was calculated by dividing the cumulative use of a specific antibiotic (in grams) by a defined daily standard dose for that drug and then expressing it per every 1000 patient days [32]. The patient days were calculated by counting the number of days a patient was admitted in the ward receiving the respective antibiotic. Days which did not include administration of the antibiotics in question were not included as true patient days. Thereafter current acquisition prices were used for all cost comparisons to account for any changes in those costs over the studied period.
Total expenditures for all antibiotics s were calculated and divided by the applicable total number of patient-days to derive a figure for "antibiotic shillings per patient day" (ABSD). Actual cost savings related to the AMS was calculated by subtracting the ABSD for each of the four study years from the ABSD for the baseline year (the year before the launch of the AMS); each difference was then multiplied by the number of patient-days for the specific year.

All categorical data were presented as frequencies and percentages while continuous data were presented as means and standard deviations of the mean. Changes in antibiotic consumption and cost were calculated as the frequency and percentage differences between two or more time periods through Excel software (version 2019; Microsoft Corp, Redmond, WA). The pre- and post-AMS periods were compared for time related changes in antibiotic consumption and cost. Shapiro Wilk test was used to test whether the data was normally distributed and according to the distribution the paired t-test or Wilcoxon signed rank test were utilized for inferential statistical analysis. STATA version 13 was utilized to conduct this analysis. Alpha was set at 0.05

3.5 COSTING METHODOLOGY

3.5.1 Costing perspective and horizon

The costing perspective was the provider (Gertrude's Children's Hospital) whereby the costs incurred by the hospital before and after implementation of the antimicrobial stewardship program were considered. The time horizon for costing was 2015-2022, pre-AMS (2015-2018) and post-AMS (2018-2022). The implementation costs included all costs incurred since the inception of the program to date.

3.5.2 Types of costs included.

The focus of this study was on both capital and operational costs. Another concept that was considered is time costs. When implementing an AMS program, considerable time is taken by pharmacists, doctors and other cadres in ensuring every intervention is in place and is sustainable. Personnel salaries were used to value time expended with the current year (2022) set as the base year used to value these salaries.

The time required for performing AMS activities for all hospitalized patients under antibiotic therapy were estimated and converted into hours per week. The actual time spent on patient reviews of each AMS activity was taken as an estimate during the key informant interviews. Full-time equivalents (FTEs) were measured according to labor laws in Kenya as 40 hours per week [33].

3.9 DATA MANAGEMENT

Interviews were transcribed within twenty-four hours of data collection. All audio recordings were destroyed immediately after transcription in order to hide the identity of the interviewees. The interviews were recorded in MS Word document that were password protected. All data was backed up in a USB disk which was always kept under lock and key.

Access to data was requested from the hospital management on 5th March 2022 prior to any data collection. To ensure confidentiality, unique patient identifiers were used instead of patient names or inpatient numbers. All data was password protected to limit access and unwarranted manipulation of the data. Any documents linking the collected data to patient information was kept under lock and key and access only limited to the principal investigator.

Data obtained was entered into STATA version 13 and a database created. Data back up and cleaning were done every three days. Data was stored on an external USB drive.

3.6 QUALITY ASSURANCE

All data obtained from key informants, electronic medical records and other sources were double checked by the researcher r during data entry. The final report underwent inspection and quality audit as per the Good Clinical Practice (GCP) standards and protocols outlined by the ICH (2010). A pre-test was carried out for feasibility and quality of the data collection tools. The data collection instruments were altered based on the results of the pre-test.

The research assistant was a nurse and underwent training before starting data collection. Training included how to record good notes during key informant interviews and how to properly fill questionnaires.

3.8 ETHICAL CONSIDERATIONS

Ethical approval for this study was obtained from both the Kenyatta National Hospital- University of Nairobi Ethics and Research Committee (Appendix A: **Ref. No. P987/12/2021)** and Gertrude's Children's Hospital Research and Ethics Committee (Appendix B). Gertrude's Children Hospital was informed about the study through an oral presentation regarding the purpose and procedures to be carried out. There were no incentives provided to the hospital. However, the findings on conclusion of the study, were shared with the Chief Pharmacist of Gertrude's Children's Hospital through a copy of this thesis. Confidentiality was observed and the extracted data stored securely through passwords and all recordings were destroyed.

4.0 CHAPTER FOUR: RESULTS

This chapter includes results on the AMS interventions put in place and nature and types of costs involved in implementing the same. It also includes data in relation to changes in antibiotic consumption and procurement costs pre- and post- implementation of the AMS program at Gertrude's Children's Hospital in 2018.

4.1 Finding on the key informant interviews on how antimicrobial stewardship program was implemented

A total of five key informants, all current members of the AMS committee, were eligible, provided consent and subsequently interviewed. These included, the Chief Pharmacist, the AMS pharmacist (AMS secretary), AMS chairperson (pediatrician), microbiologist and administration representative. The thematic areas covered during the interview include; AMS interventions and how they were implemented, capital and recurrent costs incurred, guideline development, compliance assessment and challenges faced.

4.2 Antimicrobial stewardship interventions implemented at Gertrude's Children's Hospital

All members indicated that AMS interventions and associated capital costs were incurred in 2018. The interventions covered all three Cochrane groupings of structural, persuasive and restrictive strategies and were implemented in the inpatient, outpatient and emergency departments.

Structural strategies implemented at GCH include purchase of computers, installation of internet connectivity and an electronic medical records (EMR) software referred to as KRANIUM®. Other structural interventions were implemented in the laboratory including antibiograms, pro-calcitonin testing, rapid diagnostic testing to detect respiratory viruses as well as penicillin allergy testing. No decision support software was in place to help in rational antibiotic prescribing.

The informants noted that there were restrictive strategies implemented at the hospital geared at defining rules and implementing standards around use of antibiotics. This included formulary restriction of antibiotics such as cephazolin use for surgical prophylaxis.

4.2.1 Compliance to guidelines for surgical prophylaxis at Gertrude's children's hospital

An example of a graphical representation depicting compliance to the guidelines to the use of antibiotics in surgical prophylaxis is shown in figure 4.1. Withdrawal of antibiotics previously readily available in theatres and pre-authorization policy for all reserve antibiotics were some of the other strategies implemented by the AMS committee.

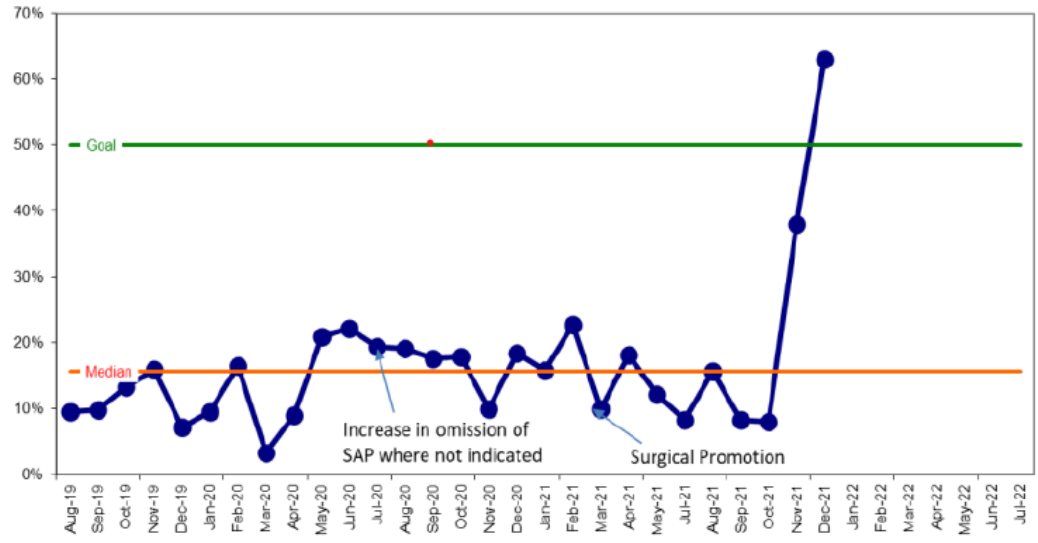


Figure 4.1: Compliance to the guidelines for surgical prophylaxis at Gertrude's children hospital (Source: *GCH AMS committee)*

4.2.3 Compliance to restrictive antibiotic prescribing

Figure 4.2 shows a graph depicting the level of compliance to restrictive antibiotic prescribing. Restriction of cephazolin use in the hospital theatre was subject to when it was prescribed only by the surgeon with a clear indication.

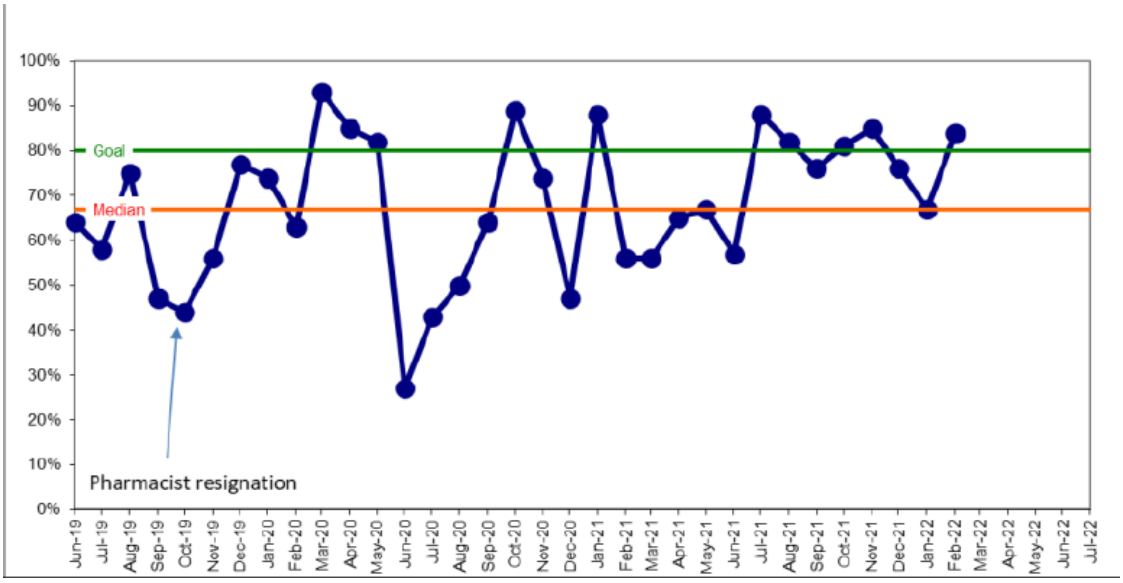


Figure 4.2: Compliance to restrictive antibiotic prescribing at Gertrudes children hospital (Source: GCH AMS committee)

In regard to pre-authorization, an AMS pharmacist assessed the appropriateness of the initial antibiotics which were empirically prescribed and authorized once it was deemed appropriate. If it was not appropriate, the AMS Pharmacist liaised with the prescriber and together they determined best regimen. Standard treatment guidelines borrowed from the Ministry of Health, were also put in place to guide antibiotic prescribing in key conditions including management of pneumonia, urinary tract infections, skin and soft tissue infection, bacteremia, *Clostridium difficile* infection among others.

Persuasive AMS strategies were implemented that included providing training to staff around antimicrobial resistance and importance of AMS. The trainings were conducted physically, virtually and the committee was exploring the establishment of an e-learning portal for the same exercise. Prospective audit and feedback to monitor compliance was also conducted to ensure all key guidelines including use of restricted antibiotics were adhered to. All responses received were validated through use of various reports including reserve antibiotic report, AMS meeting minutes as well as standard treatment guidelines.

4.3 Costs involved in implementing the antimicrobial stewardship program at Gertrude's

There were various costs involved in starting and implementing the antimicrobial stewardship program at GCH. These are discussed in the following sections.

4.3.1 Cost of time spent on antimicrobial stewardship activities

Key informants provided salary and fringe support data for AMS committee members. It was noted that none of the AMS committee members carried out AMS activities as a full-time job. All members stated that they engaged in other activities of healthcare delivery and performed antimicrobial stewardship over and above these activities with an FTE hours range of 0.3-0.5; median 0.375. As shown in Table 4.1, the yearly approximated FTE costs ranged from $1,920 to $1,120 (median $20,000) and a total FTE cost of $58,880. It was noted that the AMS chairperson and the chief pharmacist spent the most time in the AMS implementation because they are head of their respective departments and had key influence on the administration to create impact through their AMS initiatives.

Table 4.1: Costs of time related to implementation of antimicrobial stewardship program at Gertrude's Children's Hospital

AMS Committee Member	Hours spent weekly on AMS activities	Hours per year(52x)	FTE	Monthly income ($)	Annual income ($)	FTE Costs ($)
AMS secretary (Pharmacist)	15	780	0.375	800	9,600	3,600
AMS Chairperson (Pediatrician)	20	1040	0.5	1,867	22,404	11,202
Chief Pediatrician	16	832	0.4	1,867	22,404	8,962
Clinical Pathologist	15	780	0.375	1,867	22,404	8,402
Medical Officer	12	624	0.3	1,000	12,000	3,600
IPC coordinator	16	832	0.4	534	6,408	2,563
Nurse	12	624	0.3	534	6,408	1,922
Nurse	12	624	0.3	534	6,408	1,922
Consultant intensivist	12	624	0.3	1,867	22,404	6,721
Chief Pharmacist	20	1040	0.5	1.667	20,004	10,002
Total	**150**	**7800**	**3.75**	**12,003**	**150,444**	**58,896**

4.3.2 Capital Costs incurred in implementing antimicrobial stewardship activities at Gertrude's Children's Hospital.

It was noted that GCH laboratory had purchased certain equipment to implement AMS. These included a penicillin allergy testing machine with a current (2022) market price of $200. The hospital also purchased computers at an estimated total cost of $5000. Total capital costs were estimated at $5,200.

4.3.3 Recurrent costs incurred in implementing antimicrobial stewardship activities at Gertrude's Children's Hospital.

As shown in Table 4.2, direct recurrent costs included antibiograms at an annual cost of $2,800, leasing EMR software ($4,800), internet & communication services ($80), pro-calcitonin test kits ($4,800), AMS meetings refreshments ($133), training and education ($1,667) as well as $333 spent on AMS related travels. Indirect costs included electricity and cleaning at combined current estimated cost of $800 For the shared costs such as EMR software lease, internet and utility costs, assumption was that AMS activities consumed 5% of the total of these costs.

Table 4.2: Annual costs incurred in implementing the AMS program at GCH

Item	Quantity	Cost ($)	Total Cost ($)
Capital Costs			
Penicillin allergy testing machine	1	200	200
Computers	15	333	5,000
Sub-total			**5,200**
Recurrent costs			
Direct Costs			
Antibiogram: Blood culture testing kits	120	23	2,800
Electric medical records (Kranium) software	12	400	4,800
Internet & Communication	12	133	1,600
Pro-Calcitonin test kit	120	40	4800
Rapid diagnostic kits for viral infections	120	27	3200
AMS meeting(refreshments)	4	33	133
Training & workshop materials	100	17	1,667
Travel cost	10	33	333
Time costs (FTE)			58,896
			78,229
Overhead costs			
Electricity	12	33	400
Cleaning	12	33	400
			800
Total Costs			**84,229**

4.4 Participants recruited to assess antibiotic consumption and cost

During the study a total of 320,259 patients were screened for eligibility, of these, 76,568 (23.9%) met the inclusion criteria. A total of 243,691 (76.1%) patients were excluded for the following reasons; 107,984(33.7%) did not receive any antibiotics, 89352 (27.9%) received antibiotics that were not included in the study, 46355 (14.5%) received the target antibiotics through routes other than parenteral or oral (Figure 4.3).

A total of 76,568 patients who received at least one of our selected antibiotics during their inpatient stay from 2015 to 2022 were included in the study. Of this number 39,143 (51.1%) represented the pre-phase subjects while 37425 (48.9%) represented the post-phase.

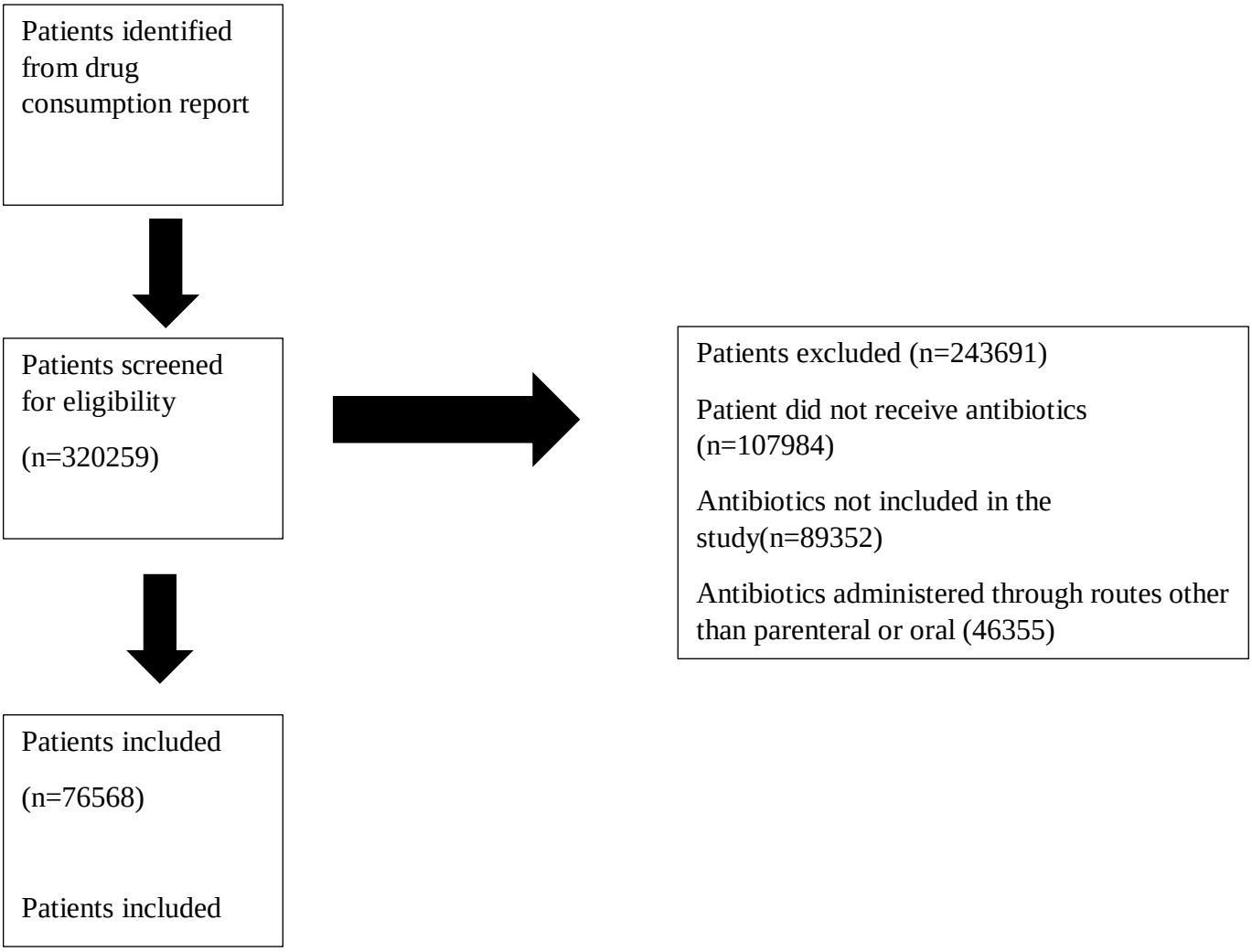


Figure 4.3: Consort diagram of participants included in the antibiotic consumption study at Gertrude's children hospital.

4.5 Socio-demographic characteristics of the study participants.

The characteristics of the study participants are summarized in Table 4.3. As shown in the table there was a statistically significant difference in gender between the pre-AMS and post-AMS however there was no statistical significance difference in age.

Table 4.3: Socio-demographic characteristics of patients in the antibiotic consumption study at GCH

Variable	Study Phase		P-value
	Pre-AMS	Post-AMS	
Sex n (%)			
Male	20476 (52.31)	19442 (51.95)	**0.33**
Female	18667 (47.69)	17983 (48.05)	
Age (Years: Median [IQR])	9 [7-13]	6 [4-9]	**<0.001**
Ward number n (%)			
0	1303 (3.33)	4327 (11.56)	**0.83**
1	37148 (94.89)	31016 (82.87)	
2	253 (0.65)	30 (0.08)	
3	154 (0.39)	1430 (4)	
10	222 (0.57)	148 (0).4	
13	2 (0.01)	0 (0)	
38	1 (0)	0 (0)	
39	2 (0.01)	3 (0.01)	
43	40 (0.1)	206 (0.55)	
44	12 (0.03)	13 (0.03)	
69	10 (0.03)	0 (0)	
83	0 (0)	252 (0.67)	
91	0 (0)	1 (0)	
TOTAL	n (%)	n (%)	

The median age pre-AMS was 9 [7-13] while in the post-AMS phase was 6 [4-9], three years younger than the former. In both phases male participants were more with a 52.3% and 52.0% in pre and post phases respectively. Most participants were recruited from ward 1 having 94.9% of the participants pre-AMS and 82.87% in the post-AMS phase.

4.6 Antibiotics included in the study

As shown from Table 4.4, a total of 15 antibiotics met the inclusion criteria and were included in the study. 5 of these were from Access class, 7 from Watch class and 3 from Reserve class of the AWARE classification.

Table 4.4: List of antibiotics included in the study

ANTIBIOTIC	ATC CODE	AWARE CATEGORY
AMIKACIN	J01GB06	Access
AMOXICILLIN/CLAVULANIC ACID INJ	J01CR02	Access
CLINDAMYCIN INJ	J01FF01	Access
GENTAMICIN	J01GB03	Access
BENZYLPENICILLIN	J01CE01	Access
AZITHROMYCIN TABS	J01FA10	Watch
CEFEPIME	J01DE01	Watch
CEFOTAXIME	J01DD01	Watch
CEFTAZIDIME	J01DD02	Watch
CEFTRIAXONE	J01DD04	Watch
CLARITHROMYCIN INJ	J01FA09	Watch
VANCOMYCIN	J01XA01	Watch
IMIPENEM/CILASTATIN	J01DH51	Reserve
MEROPENEM	J01DH02	Reserve
PIPERACILLIN/TAZOBACTAM	J01CA12	Reserve

4.7 Economic Impact of AMS on consumption and acquisition cost of antibiotics

As shown from both Figure 4.4 and Table 4.6, in the years leading to the implementation of the AMS, there was an observed rise in antibiotic consumption (expressed in both mg and DDD's per 1000 patient days). Antibiotics having the highest consumption included ceftriaxone (79 DDDs), amoxicillin/clavulanic acid injection (76 DDDs), azithromycin (41 DDDs), meropenem (13 DDDs) and amikacin (12 DDDs). Antibiotics least consumed at the hospital were imipenem/cilastatin (0.06 DDDs) cefotaxime (0.6 DDDs), clindamycin (1.4 DDDs) and piperacillin/tazobactam (1.6 DDDs). Most of the antibiotics included in the study were administered parenterally.

An overall 18.5% decrease in consumption of selected antibiotics was observed between the pre-AMS phase (2015-2018) to post-phase (2019-2022). The most significant reduction in consumption was observed with imipenem/cilastatin (-81%), meropenem (-54.7%) and vancomycin (-54.4%). However increased consumption was seen with cefotaxime (44%) and clindamycin (22%) injections

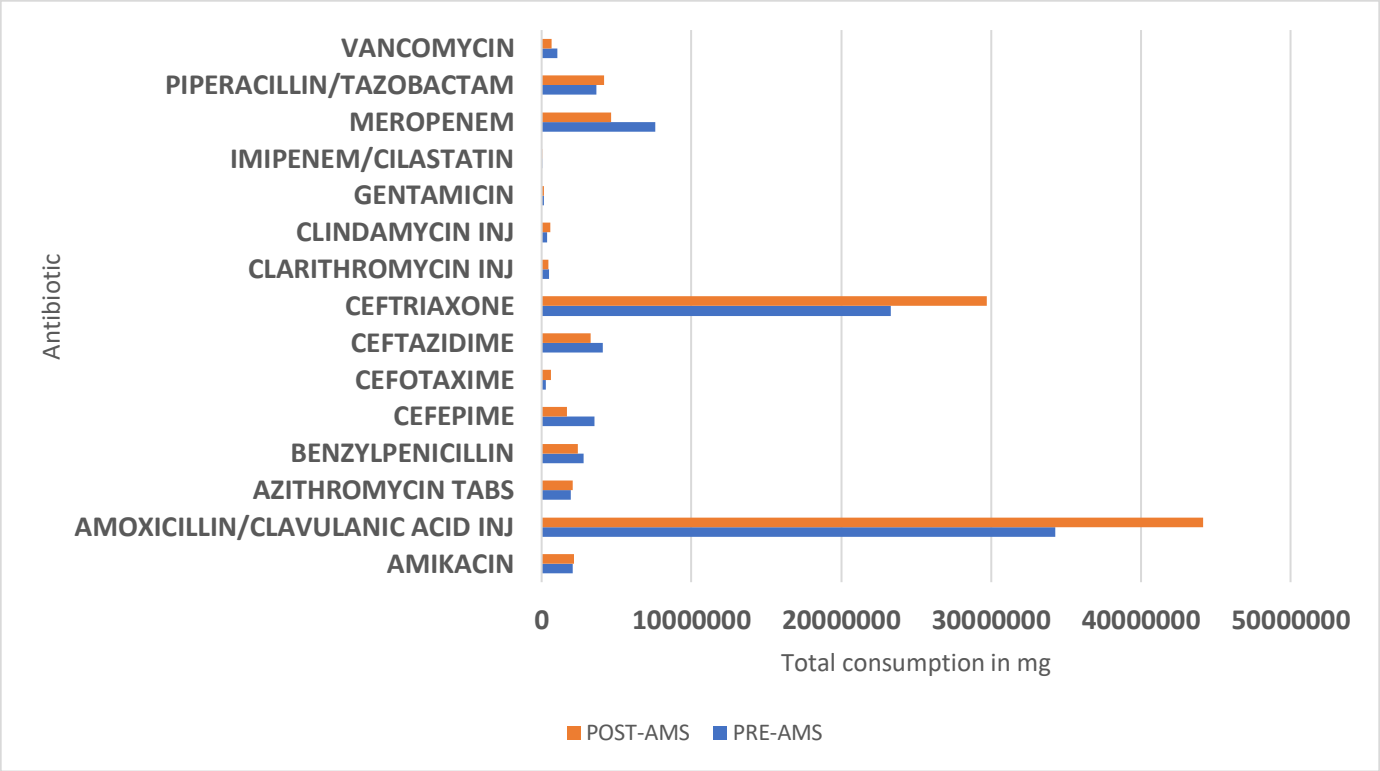


Figure 4.4: Consumption of antibiotics in milligrams during pre- and post-antimicrobial stewardship interventions at Gertrude's Children's Hospital

Table 4.6: Defined Daily Dose (DDD) per 1000 Patient-Days for Selected Antibiotic at Gertrude's children hospital

ANTIBIOTIC	Pre-AMS	Post AMS	Change	P-value
AMIKACIN	7.15	5.425615	-24.1173	0.001
AMOXICILLIN/CLAVULANIC ACID INJ	40.43116591	35.83255	-11.374	
AZITHROMYCIN TABS	22.96878981	17.8992	-22.0716	
BENZYLPENICILLIN	2.761785462	1.739006	-37.0333	
CEFEPIME	3.076704391	1.135716	-63.0866	
CEFOTAXIME	0.245643931	0.354517	44.32145	
CEFTAZIDIME	3.667822963	2.14303	-41.5722	
CEFTRIAXONE	40.85974581	38.66682	-5.36696	
CLARITHROMYCIN INJ	1.80743319	1.176393	-34.9136	
CLINDAMYCIN INJ	0.667399506	0.817478	22.48708	
GENTAMICIN	2.371198747	1.489458	-37.1854	
IMIPENEM/CILASTATIN	0.053786427	0.010082	-81.2563	
MEROPENEM	9.050128104	4.097703	-54.7222	
PIPERACILLIN/TAZOBACTAM	0.89525381	0.753026	-15.8869	
VANCOMYCIN	1.853497686	0.844591	-54.4326	
Total	137.8603557	112.3852	-18.479	

As shown in figure 4.6, Antibiotic shillings per patient day (ABSD), which had consistently increased yearly, prior to implementation of AMS, decreased by 9.3% in the first year (2018) and a further drop by 33.3% in 2019, there was a very slight increase in 2020 (0.5%). Antibiotic shillings per patient day then increased in 2021 by 4.2%: this trend was due almost exclusively due to a large increase in consumption of amoxicillin/clavulanic acid injection (19 DDDs) s. 2022 saw a drop of ABSD by 29.2% in 2022.

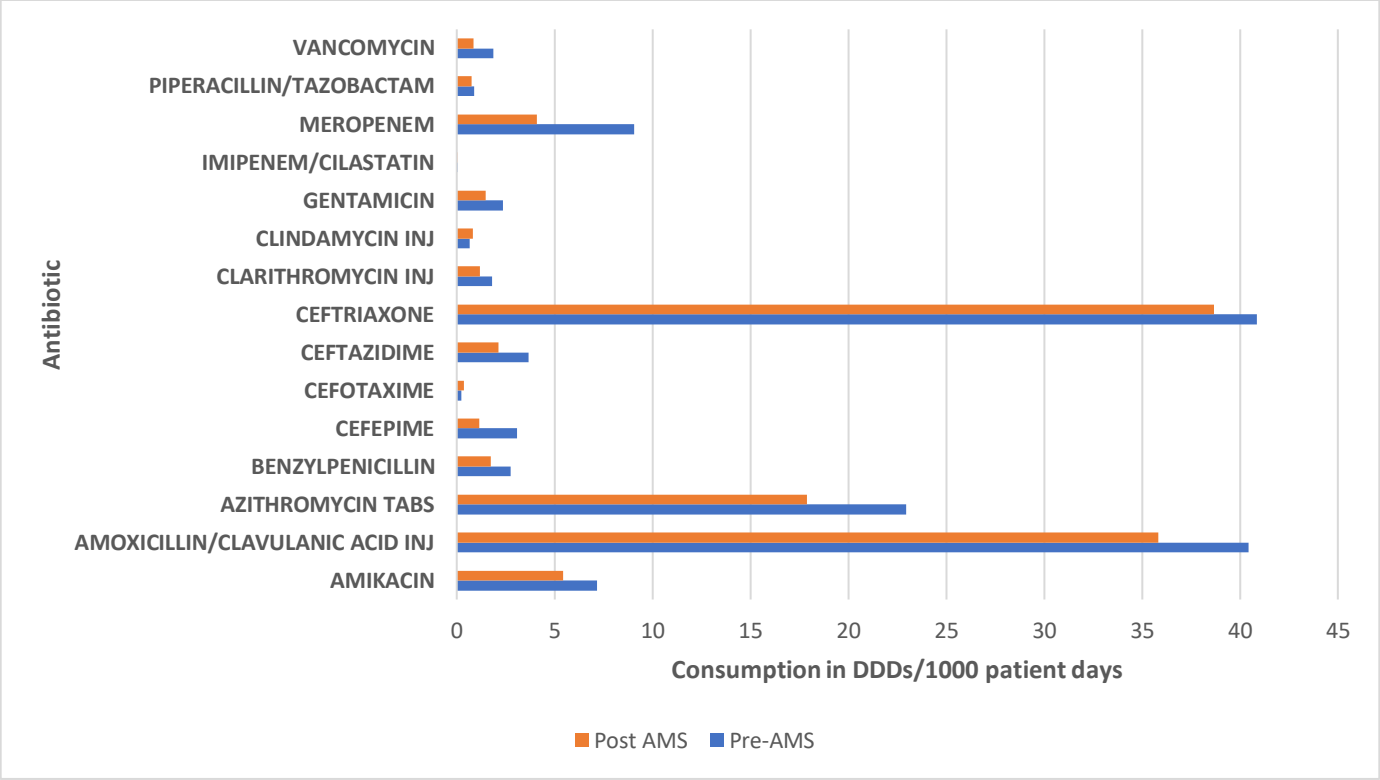


Figure 4.5 Consumption of antibiotics in DDDs/1000 patient days during pre- and post-antimicrobial stewardship interventions at Gertrude's Children's Hospital

The high consumption of amoxicillin/clavulanic acid injection was mainly due to its many advantageous pharmacokinetic properties including high bioavailability, high volume of distribution and a broad spectrum of antimicrobial activity against both gram-positive, gram-negative bacteria as well as beta lactamase producing strains. Among the antibiotics that were included in the study ceftriaxone, had the highest consumption with a total of 79 DDDs. For 2018-2022 the actual cost savings attributable to AMS activities ranged from KES 6,492,430.78 to 53,662,905.91.

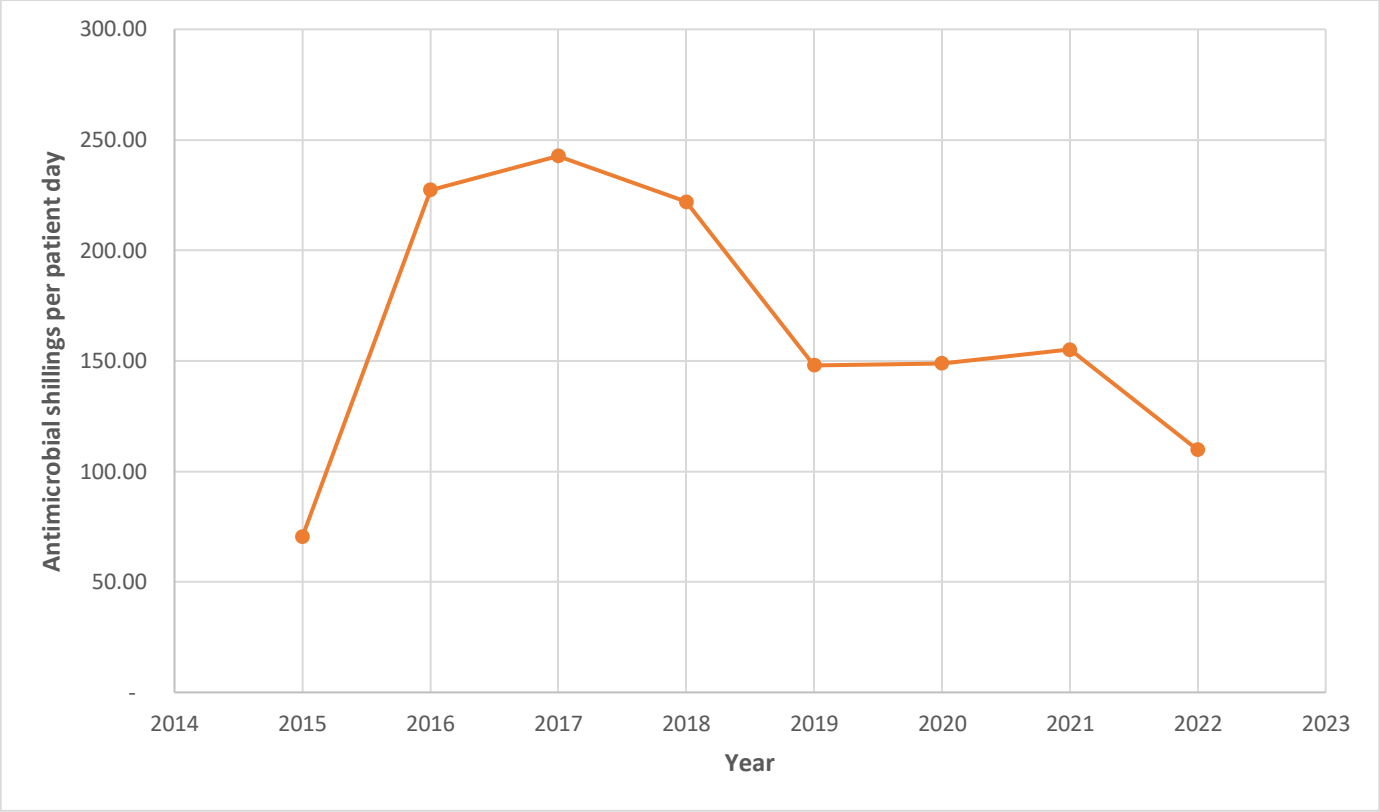


Figure 4.6: Effect of antimicrobial stewardship on antibiotic expenditure at Gertrude's children's hospital pre- and post-antimicrobial stewardship program

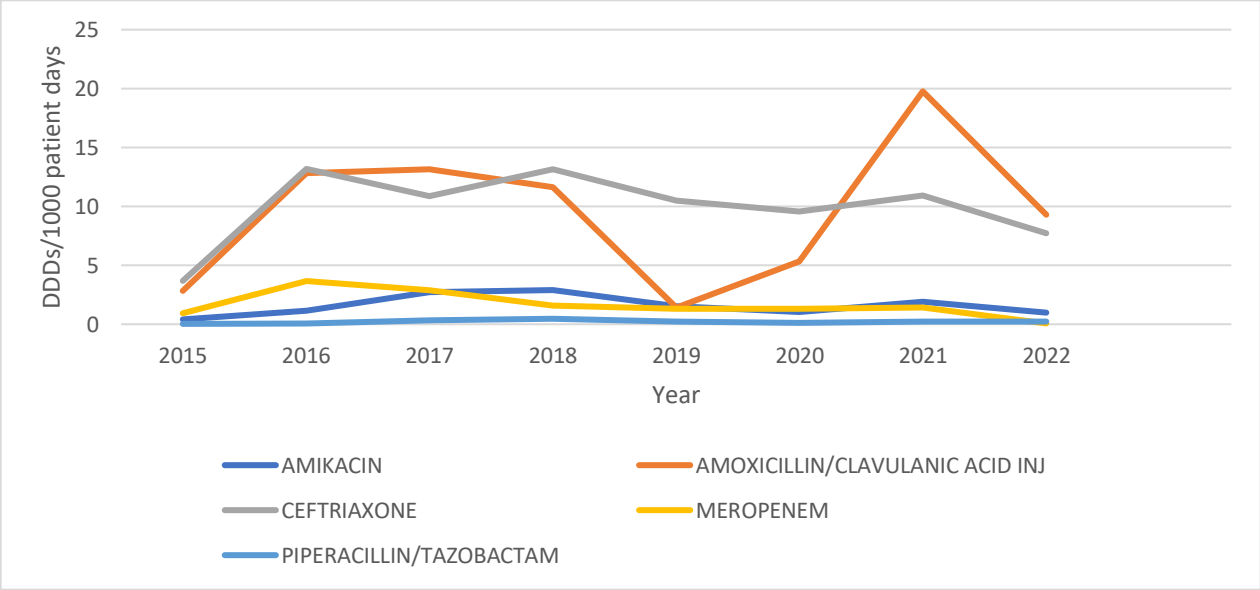


Figure 4.7 Antibiotic consumption at GCH before and after implementation of AMS program expressed as defined daily doses (DDDs) per 1000 patient days

4.7 Cost savings attributed to decreased antibiotic consumption

As shown in table 4.7 there was a progressive increase in actual cost savings in relation to antibiotic consumption from the year 2018 (KES 6,492,430.78) to 2022 (KES 53,662,905.91).

Table 4.7: Estimated cost savings associated with the AMS program implemented at GCH between 2018 and 2022.

0Year	Total Antibiotic expenditures (KES)	Patient Days	Antibiotic shillings/patient day (ABSD)	Actual Savings compared to 2017 (KES)
2015	20,027,679.43	284238	70.46	
02016	62,439,270.08	274675	227.32	
2017	63,708,510.31	262557	242.65	
002018	69,763,324.77	314267	221.99	6,492,430.78
02019	59,181,619.93	399758	148.04	37,818,218.83
2020	40,668,320.16	273292	148.81	25,644,999.23
2021	70,165,866.45	452346	155.12	39,594,261.08
2022	44,318,680.17	403804	109.75	53,662,905.91

5.0 CHAPTER FIVE: DISCUSSION

Assessment of the impact of an AMS program on antibiotic consumption within a hospital is a crucial part of any AMS strategy to identify any shortcomings or evaluate benefits of the AMS interventions[7]. Because assessing all metrics may not be practical and feasible, it was therefore necessary to use those that were most relevant to this setting. This study therefore evaluated the economic impact through use of WHO recommended DDDs to assess consumption and antibiotics shillings per patient days to assess impact on cost.

The findings reveal that the AMS program implemented at Gertrude's Children's hospital led to an overall decrease in consumption of antibiotics as well as a decrease in antibiotics expenditures. This is in line with other similar studies conducted in various settings[34–37]. With this decrease in use and expenditure on antibiotics, it is as well expected that other indirect expenses may decrease. The study by Fukuda et al published in 2014 for example showed that antimicrobial stewardship programs contributed to the reduction of the antimicrobial therapy costs in a community hospital with 429 beds[34]. Another study by Borde et al showed a significant intervention-related decrease in the use of cephalosporins and fluoroquinolones[36]. J. M. Cisneros et al. were able to show a significant decrease in antibiotic consumption through an educational antimicrobial stewardship program[37].

The data also indicate that there was financial savings after implementing the AMS interventions at the hospital. Although, as shown in this study, implementing these interventions are costly, previous studies have confirmed an overall economic benefit in rational use of high-cost antibiotics. The overall reduction in the hospital's cost regarding antibiotics by 84% (53,662,905.91) in this report is higher than a similar study reporting a 41.3% decline in procurement expenditures on antibiotics [27]. The reason for this difference is because in the Kenyan setting antimicrobial stewardship in general is relatively new and therefore the impact is bigger than in countries like the United States where the programs have been run for

a longer period of time. This finding of cost reduction can be used to re enforce policy on implementation of AMS programs in health facilities.

The AMS program at GCH has been consistently implemented since 2018 with the aim of ensuring the rational use of antibiotics. This is achieved through the selection of the right antibiotic, for the right indication, at the right cost, to the right patient, at the right time and with the right dose and route, thereby ensuring least amount of harm comes to the patient. GCH to some extent utilized all three groupings of the Cochrane Review of AMS interventions; structural, persuasive and restrictive [11].

A key strategy that the AMS committee leverages on is education (persuasive) of prescribers and other healthcare providers [38] including distribution of guidelines (such as surgical prophylaxis), physical lectures, referring trainees to online material (WHO) as well as exploring ways to carry out self-paced learning modules developed by the committee members. The hospital also conducts audit and feedback activities (both in form of oral and written reports) particularly on surgical prophylaxis guidelines compliance as use of reserve antibiotics.

Structural strategy is a key pillar of implementation of a successful AMS program [11]. GCH acknowledged this and implemented key structural inputs to achieve this through equipping the laboratory as well as other departments in the hospital [15]. These include digitization of patient records through an online based EMR software (KRANIUM), purchase of computers, internet and other channels of communication. In the laboratory, the hospital has a penicillin allergy testing kit that ensures that patients are not at risk of violent adverse penicillin related reactions. The laboratory also purchases blood culture kits that allow development of antibiograms to assess antimicrobial susceptibility at the hospital [39].

The hospital also conducts pro-calcitonin testing to find out whether the infections seen in the patients are caused by bacterial or viral microorganisms [40]. In this way they are able to determine, for example a pneumonia diagnosis is caused by bacteria or virus.

Restriction is a key strategy in implementation of AMS at GCH. The committee ensures that antibiotics are not easily and readily available in the theatres thus preventing misuse. Among the antibiotics restricted is cephazolin that the committee ensures is only availed in the theatre when the surgeon orders it and there is a rational indication for the same. Compliance to the guidelines of surgical prophylaxis was poor at only between 5-25% and this was due to teething challenges and resistance from the user departments. However, from September 2021, there was a significant increase in compliance from September 2021 attributed to withdrawal of excess quantities of antibiotics from the surgical department and intense education initiatives on rational use of antibiotics.

In 2005, Drummond et al recommended considering both capital and operational costs. These can further be specified, in the context of AMS programs into implementation costs, operational costs (human resource and/or equipment costs for implementing the AMS program), antimicrobial costs, length of stay costs, morbidity and/or mortality costs, societal costs (such as loss of productivity), acquisition costs and other miscellaneous costs. In this study it is estimated that the annual cost of AMS at GCH is KES 12,152,000. Majority of this cost goes to payment of staff having an FTE cost of KES 8,832,000 annually. This finding is consistent with previous data on funding of AMS activities in pediatric hospitals [41] where high amounts of AMS budgets were dedicated to payment of salaries or FTE. It is not clear whether these huge budgetary allocations translate to improvement of the benefits derived from these AMS activities. However, the consensus from the key informants was that institutional financial support needed to be increased as it was not in congruence with the scope of work they intended to achieve. Institutional commitment is a key quality measure used to rank children's hospital[42].

Assessment of the economic impact of AMS interventions implemented at the hospital level is a key strategy in evaluating whether there are tangible benefits in implementing the program [7,9,10]. Given that it was not feasible and realistic to assess all the quality indicators, it was important to choose the most

relevant metric for this setting. DDDs were used to assess antibiotic consumption as this has been termed as the most efficient and sustainable measure [5].

A key finding in this study was that ceftriaxone and amoxicillin/clavulanic acid injections had the highest consumption. This is in agreement with other studies and surveys done both in Kenya and other countries in the African context[43]. Ceftriaxone, a third generation cephalosporin has been noted to be the most prescribed and administered antibiotic for both inpatient and ambulatory care in hospitals [44]. This is due to its broad-spectrum antimicrobial activity against lung, urinary tract, bone, skin and central nervous system infections. Its activity against other multi-drug resistant bacteria such as Enterobacteriaceae makes it a highly powerful arsenal in the fight against infectious diseases. Ceftriaxone's positive safety profile, affordability and a long half-life that allows once or twice daily dosage are other key benefits that may encourage overuse[45].

Ceftriaxone resistance within the sub-Saharan region has been shown to be high and increasing [46] where sixty percent of patients on ceftriaxone got inappropriate dose, frequency or duration. [44]. The best strategy to alleviate this growing resistance is through controlling the prescription of this antibiotic through strong antibiotic stewardship programs. Establishing appropriate standard treatment guidelines and continuous survey of resistant strains is also key in ensuring this resistance does not become unmanageable.

The use of amoxicillin/clavulanic acid injection was the highest consumed access antibiotic and its use was quite variable. Amoxicillin/clavulanic acid is a preferred antibiotic largely due to the nature of its broad spectrum activity It was noted that in 2021 in particular there was a huge surge in use due to the COVID-19 pandemic where the use of the drug was its highest. Although the two highly consumed antibiotics were from the access and watch classes, in a different study done in a private hospital in Kenya, reserve antibiotics were consumed more than the access antibiotics.

Conducting a similar study in a public hospital may pose several challenges and limitations. For example, the lack of consistent supplies of medicines in these health facilities may directly affect consumption related data. Therefore, it would be difficult to determine whether any impact on consumption was due to the AMS program or resource related factors. Another challenge is that public hospitals may lack the necessary financial resources to adequately implement an AMS program. Therefore, consumption may be observed not to change but it could be because of limitations in implementation and therefore no impact felt.

5.1 Strengths and Limitations

There are no studies cited in Kenya estimating the costs of implementing an AMS program and the economic impacts such a program would have at the hospital level. The strength of this study is that it shows the positive economic savings AMS programs can have when implemented at the hospital setting.

The economic impact of the AMS program at Gertrude's Children's hospital has to be analyzed in the context of several limitations. First, the study was limited by the chosen study design; the pre-post quasi experimental study. Despite the analysis showing apparent association between the AMS interventions and reduced consumption of antibiotics, definite causality cannot be determined due to lack of control for confounding due to other potential causes such as improved procurement practices and shifts in prescribing practice. Secondly the study did not include assessment of change in length of hospital stay, cost of managing resistance, change in rates of hospital acquired infections among other potential indirect economic benefits of the program. Thirdly not all antimicrobials and dosage forms were included in the study as this scope was constrained by time and finances.

6.0 CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

AMS program implementation at Gertrude's Children's Hospital was associated with a decreased consumption and cost of target antibiotics. This finding should serve to encourage the implementation of such a program across all level 4, 5 and 6 hospitals in Kenya. This will improve overall patient safety and therapeutic outcomes while at the same time saving both the patient and the hospital unnecessary expenses.

6.2 Recommendations

Based on these results, having a vibrant AMS program implemented at the hospital setting is vital in promoting the rational use of antibiotics. As a national policy, it may be time to aggressively implement AMS programs in all health facilities in the country to not only improve the quality of care but as well save hospitals millions of shillings. The antimicrobial stewardship program, by enabling patients to use the right medication at the right time, reduce the unnecessary costs and unnecessary burden to patients.

This study incorporated a small cohort of antibiotics and it is therefore recommended that future studies should focus on antimicrobials not included in this study. Individual Cochrane groupings (structural, restrictive and persuasive) should be analyzed separately on their effectiveness in promoting rational antimicrobial use. It is also recommended that studies on long term economic effects such as mortality and infection rates should be carried out. A further analysis should be done to determine whether an outright purchase of the health management information system is more cost effective compared to the current leasing plan they have in place.

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APPENDICES

APPENDIX A: KNH/UON ERC APPROVAL

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10th May, 2022

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University of Nairobi

Dear Bevin,

RESEARCH PROPOSAL: THE ECONOMIC IMPACT OF ANTIMICROBIAL STEWARDSHIP IN A HOSPITAL SETTING; THE CASE FOR GERTRUDE'S CHILDREN'S HOSPITAL (P987/12/2021)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P987/12/2021.** The approval period is 10th May 2022– 9th May 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Chair, Dept. of Pharmacy, UoN
Supervisors: Prof. Faith Okalebo, Pharmacology and Pharmacognosy Unit, UoN
Dr. Margaret Oluka, Pharmacology and Pharmacognosy Unit, UoN

APPENDIX B: GERTRUDE'S CHILDREN HOSPITAL ETHICS AND RESEARCH COMMITTEE APPROVAL LETTER

Gertrude's
CHILDREN'S HOSPITAL
Quality healthcare for children

August 24, 2022

To : Chief Pharmacist

PERMISION TO COLLECT DATA IN GERTRUDE'S CHILDRENS' HOSPITAL

This is to confirm that **Dr. Lihanda Bevin Likuyani** has received approval from the Hospital's Ethical Review Board to conduct a study "**The Economic Impact of Antimicrobial Stewardship in A Hospital Setting: The Case for Gertrude's Childrens' Hospital"**

By way of this letter, authority is granted to access and collect data in Gertrude's Children'sHospital: Pharmacy related to the study.

Kindly accord him the necessary assistance.Regards,

Dr. Thomas Ngwiri

HEAD OF CLINICAL SERVICES

APPENDIX C: CONSENT FORM

PARTICIPANT INFORMATION AND CONSENT FORM

ADULT CONSENT

FOR ENROLLMENT IN THE STUDY

(To be administered in English or any other appropriate language e.g., Kiswahili translation)

Title of Study: THE ECONOMIC IMPACT OF ANTIMICROBIAL STEWARDSHIP AT A HOSPITAL SETTING: THE CASE FOR GERTRUDE'S CHILDREN'S HOSPITAL.

Principal Investigator\and institutional affiliation: DR. LIHANDA BEVIN LIKUYANI, MPHARM STUDENT, UNIVERSITY OF NAIROBI

Co-Investigators and institutional affiliation:

PROF FAITH OKALEBO, UON

PROF. MARGARET OLUKA, UON

DR. SUSAN MUTUA, GERTRUDE'S CHILDREN'S HOSPITAL

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will requestyou to sign your name on this form. You should understand the general principles which apply to all participants in medical research: i) Your decision to participate is entirely voluntary ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal

iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and

Research Committee protocol No. **P987/12/2021**

WHAT IS THIS STUDY ABOUT?

The researchers listed above are interviewing individuals who **are members of the Antimicrobial Stewardship Committee at Gertrude's Children's Hospital and have an in-depth knowledge of the AMS program implemented at the hospital.** The purpose of the interview is to find out **the AMS interventions and costs incurred in implementation of the program**. Participants in this research study will be asked questionsabout the nature of the AMS interventions and the costs attached to the same.

There will be approximately **4-10** participants in this study randomly chosen. We areasking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:
You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 30minutes and will cover topics such as antibiotic resistance and stewardship.

After the interview has finished**,** we will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you include: further clarifications on responses as well as request for documents to validate results.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questionsyou do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

Participating in this study will cost you 30 minutes of your time. There will be no monetary costs involved.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

CONSENT FORM (STATEMENT OF CONSENT)

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participantin a research study.

I agree to participate in this research study:	**Yes**	**No**
I agree to have (define specimen) preserved for later study:	Yes	No
I agree to provide contact information for follow-up:	Yes	No

Participant printed name: _____

Participant signature / Thumb stamp_____ **Date** _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: DR. BEVIN LIKUYANI **Date**: **3RD JANUARY 2022**

Signature 

Role in the study: ***principal investigator***

For more information contact **DR. BEVIN LIKUYANI** at **+254725154328** from

8.00am to **5pm**

Witness Printed Name (*If witness is necessary, A witness is a person mutually acceptable to boththe researcher and participant*)

Name_____ Signature /Thumb stamp: _____

Contact information _____ Date; __

APPENDIX D: DECLARATION OF CONFIDENTIALITY FORM

STUDENT CONFIDENTIALITY AGREEMENT

Title of Research Project: **THE ECONOMIC IMPACT OF ANTIMICROBIAL STEWARDSHIP AT A HOSPITAL SETTING: THE CASE FOR GERTRUDE'S CHILDREN'S HOSPITAL**

Principal Investigator: DR. LIHANDA BEVIN LIKUYANI

I understand that I may have access to confidential information about study sites and participants. By signing this statement, I am indicating my understanding of my responsibilities to maintain confidentiality and agree to the following:

- I understand that names and any other identifying information about study sites and participants are completely confidential.

- I agree not to divulge, publish, or otherwise make known to unauthorized persons or to the public any information obtained in the course of this research project that could identify the persons who participated in the study.

- I understand that all information about study sites or participants obtained or accessed by me in the course of my work is confidential. I agree not to divulge or otherwise make known to unauthorized persons any of this information, unless specifically authorized to do so by approved protocol or by the local principal investigator acting in response to applicable law or court order, or public health or clinical need.

- I understand that I am not to read information about study sites or participants, or any other confidential documents, nor ask questions of study participants for my own personal information but only to the extent and for the purpose of performing my assigned duties on this research project.

- I agree to notify the local principal investigator immediately should I become aware of an actual breach of confidentiality or a situation which could potentially result in a breach, whether this be on my part or on the part of another person.

Signature  Date: **03-01-2022** Name **LIHANDA BEVIN LIKUYANI**

APPENDIX E: ASSURANCE ON CONFIDENTIALITY

All information obtained from your records and interviews conducted will be kept confidential and used for the purpose of this study only. Your records will be kept under lock and key and information will be accessible to authorized persons only.

Contacts

For any further information about this study, you may contact me, my academic department or the Kenyatta National Hospital/University of Nairobi Ethics and research Committee using the contacts provided below:

Lihanda Bevin Likuyani,
Department of pharmacology and pharmacognosy
School of Pharmacy,
University of Nairobi
P.O Box 157-00202 KNH. Tel: 0725154328

Prof. Faith Okalebo,
Department of Pharmacology and Pharmacognosy
School of Pharmacy, University of Nairobi
P.O Box 19676- Nairobi. Tel: 07374343204

The Chairperson,
The Kenyatta National Hospital/University of Nairobi Research and Ethics Committee,
P.O Box 19676- Nairobi. Tel: 020-2726300 Ext 44102

APPENDIX F: ELIGIBILITY CHECKLIST

STUDY TITLE: THE ECONOMIC IMPACT OF ANTIMICROBIAL STEWARDSHIP IN A HOSPITAL SETTING: THE CASE FOR GERTRUDE'S CHILDRENS' HOSPITAL

Eligibility Checklist	
Principal Investigator:	Participant ID:

ELIGIBILITY CRITERIA All supporting documentation for each answer shall be maintained and this document should be retained in the subject's research file.

Inclusion Criteria	**Comments (if applicable)**	**Yes**	**No**
An employee of Gertrude's children's hospital			
Directly involved in implementation of the AMS program at Gertrude's Children's hospital			
Gives an informed consent	Date Consent Signed: _____		

Eligibility Checklist Completed by:

Signature of Research Assistant **Date (MM/DD/YYYY)**

Printed Name of Research Assistant

If any answers to inclusion criteria are 'no', then participant is not eligible to be enrolled.

The subject is: ☐ **eligible** / ☐ **ineligible** for participation in the above-named study based on the inclusion/exclusion criteria as verified by a qualified investigator.

Verified by:

Signature of Investigator **Date (MM/DD/YYYY)**

LIHANDA BEVIN LIKUYANI

Printed Name of Investigator

APPENDIX G: KEY INFORMANT INTERVIEW GUIDE

The goal of this interview is to identify resources and structures necessary to run a successful antimicrobial stewardship program at Gertrude's Children's Hospital.

1. Does your hospital have an antimicrobial stewardship program?

- ○ Yes
- ○ No

2. Are you involved in your hospital's antimicrobial stewardship program?

- ○ Yes
- ○ No

3. Who is the lead of your hospital's antimicrobial stewardship program?

- ○ Physician
- ○ Pharmacist
- ○ Physician and pharmacist co-lead
- ○ Other (specify) _____

4. What is your title?

- ○ Physician
- ○ Pharmacist
- ○ Other _____

5. What is your role within your hospital's antimicrobial stewardship program?

- ○ Physician lead
- ○ Physician participant
- ○ Stewardship pharmacist
- ○ Data analyst
- ○ Other _____

6. Do you have additional training in infectious diseases (ID) or stewardship?

- ○ Yes, residency trained in ID
- ○ Yes, certificate in stewardship (e.g. MAD-ID, SIDP)
- ○ No

7. Are you board-certified or board-eligible in Infectious Diseases?

- ○ Yes
- ○ No

8. Is antimicrobial stewardship part of your written job description?

- ○ Yes (1)
- ○ No (2)
- ○ Not sure (3)

9. Number of years your stewardship program has existed (exact dates).

_____

10. Is there a written policy for antimicrobial stewardship at your institution?

- ○ Yes
- ○ No
- ○ Not sure

11. In which settings does your antimicrobial stewardship program work? (all that apply)

- ☐ Inpatient (which wards)
- ☐ Outpatient
- ☐ Emergency department
- ☐ Long-term care facility
- ☐ Other _____

12. How are you compensated for your antimicrobial stewardship duties?

- ○ Hourly, at the rate you bill for your clinical work
- ○ Hourly, at below the rate you bill for your clinical work
- ○ Hourly, at above the rate you bill for your clinical work
- ○ Hourly, not sure what rate in comparison to clinical work
- ○ Flat yearly rate (bonus or stipend)
- ○ Incorporated into your salary as a full-time equivalent (FTE)
- ○ Not compensated for this work
- ○ Other (specify) _____

13. Does your hospital have an electronic medical record (EMR)?

- ○ Yes
- ○ No

14. Which EMR does your primary hospital use?

- ○ EPIC
- ○ MEDITECH
- ○ CPSI Computer Programs and Systems
- ○ Cerner Corporation
- ○ Allscripts
- ○ NextGen Healthcare
- ○ Homegrown system
- ○ Other _____
- ○ I do not know

15. What technology add-ons does your AMS have? (all that apply)

- ☐ None
- ☐ ABX Alert (ICNet)
- ☐ Dynamic Monitoring Suite (VigiLanz)
- ☐ EPIC AMS Module
- ☐ EpiQuest Live
- ☐ Theradoc (Premier)

☐ Other (specify) _____

16. How much did this technology cost? _____

17. Does your main hospital offer computerized decision support at the time of antibiotic prescribing?

○ Yes

○ No

○ Not sure

18. If yes, how much did this cost? _____

19. Is your main hospital's laboratory on-site?

○ Yes

○ No

20. Which of the following Microbiology interventions does your AMS program/hospital offer? (all that apply)

☐ Antibiogram

☐ Cascade reporting of antibiotics

☐ Rapid diagnostic testing of respiratory viruses

☐ Rapid diagnostic testing of blood specimens (specify platform used)
_____

☐ Rapid identification of Staphylococcus aureus

☐ Procalcitonin testing

☐ None of the above

☐ Other _____

21. How much did it cost to set up this laboratory AMS features?

22. Does your hospital have a mechanism for ordering providers to review antibiotics (all or selected) at 48-72 hours after initiation for continued appropriateness (antibiotic time-out)?

- ○ Yes
- ○ No
- ○ Not sure

23. If no, what are the barriers to implementation of an antibiotic time-out at your main hospital? (all that apply)

- ☐ IT/technical issues
- ☐ Not an institutional priority at this time
- ☐ Provider resistance
- ☐ Other (specify) _____

24. Does your AMS require prior authorization of selected restricted antibiotics (e.g. restricted formulary)?

- ○ Yes
- ○ No

25. If No, what are the barriers to implementation of a prior authorization system at your hospital? (all that apply)

- ☐ Lack of time/dedicated personnel for approvals
- ☐ Provider resistance
- ☐ Not an institutional priority at this time
- ☐ Other (specify) _____

26. What percentage of the time are restricted antimicrobials approved by the following? (sum to 100%)

_____ AMS Pharmacist
_____ Attending Medical Officer
_____ Consultant
_____ Unrestricted release is allowed during certain times
_____ Other

27. Does your AMS perform prospective audit and feedback of selected antibiotics?

- ○ Yes
- ○ No

28. If No, what are the barriers to performing prospective audit and feedback of antibiotics at your hospital? (all that apply)

- ☐ Not enough dedicated time
- ☐ Lack of personnel with ID or stewardship training
- ☐ Not an institutional priority
- ☐ Other/additional comments (specify) _____

29. How does your facility practice prospective audit and feedback activities?

- ○ Centralized model: Dedicated AMS team (e.g. AMS pharmacist and/or physician) does review and feedback for the targeted patients
- ○ De-centralized model: Clinical pharmacists (e.g. pharmacists rounding on the wards) do review and perform antimicrobial stewardship interventions as part of their usual work flow
- ○ Mixed model: Some areas of the facility are covered by a centralized AMS team, and others (e.g. ICU) are covered by the de-centralized clinical pharmacists
- ○ Other (please describe) _____

30. How many days per week is prospective audit and feedback of antibiotics done at your hospital?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7

31. Please specify the percent contribution each group makes to all prospective audit and feedback activities (must add up to 100%)

_____ Pharmacist with training in infectious disease
_____ Pharmacist with AMS training
_____ Pharmacist without specific ID or stewardship training
_____ Attending physician
_____ Other

32. If yes, how many hours per week do you personally spend doing prospective audit and feedback?

_____

33. How does your program focus your efforts for prospective audit and feedback? (all that apply)

- ☐ All patients receiving antibiotics
- ☐ Patients on selected antibiotics or combinations of antibiotics
- ☐ Patients on certain number of antibiotics (specify number) _____
- ☐ Patients on antibiotics for a certain amount of time (specify duration, in days) _____
- ☐ Patients on specific services or units (specify) _____
- ☐ Patients with specific syndromes
- ☐ Laboratory-based trigger (e.g. drug level, microbiology result)
- ☐ Other (specify) _____

34. Does your AMS routinely perform audit and feedback of treatment for the following specific infectious diseases syndromes? (all that apply)

- ☐ Bacteremia
- ☐ Skin and soft tissue infections
- ☐ Bacteriuria
- ☐ Use of antibiotics in the setting of Clostridium difficile infection
- ☐ Pneumonia
- ☐ Surgical prophylaxis
- ☐ Febrile neutropenia
- ☐ Sepsis

☐ Other (please specify) _____

☐ My program does not provide stewardship based on syndrome

35. Average number of patients your AMS reviews on days that prospective audit and feedback is done

○ < 10

○ 10-20

○ 21-40

○ 41-60

○ > 60

36. Average number of patients your AMS provides feedback on during days that prospective audit and feedback is done

○ < 5

○ 6-10

○ 11-5

○ 16-20

○ 21-25

○ 26-30

○ > 30

37. How do you contact primary providers? (all that apply)

- [ ] Text/text page
- [ ] Telephone
- [ ] Email
- [ ] Communication in the chart
- [ ] Other _____

38. How are conflicts resolved between the AMS and the primary service/provider? (select best answer)

- ○ Primary service/provider makes ultimate decision
- ○ ID consultation mandated
- ○ AMS has authority to override primary service/provider
- ○ There is no official policy at my main hospital
- ○ Other _____

39. Does your main hospital have facility-specific practice guidelines?

- ○ Yes
- ○ No

40. Which facility-specific practice guidelines does your facility have? (all that apply)

- [ ] Pneumonia
- [ ] Urinary tract infection
- [ ] Skin and soft tissue infection
- [ ] Bacteremia
- [ ] Clostridium difficile infection
- [ ] Surgical prophylaxis
- [ ] Empirical treatment of MRSA
- [ ] Empirical treatment of Pseudomonas
- [ ] Febrile neutropenia
- [ ] Other _____

41. Does your facility monitor adherence to treatment guidelines?

- ○ Yes
- ○ No

42. Does your hospital's pharmacy support the following initiatives?

	Yes (2)	No (3)	Not sure (4)
Automatic dose adjustment for organ dysfunction	○	○	○
Vancomycin PK monitoring	○	○	○
Aminoglycoside PK monitoring	○	○	○
Extended infusion of beta-lactam antibiotics	○	○	○
Automatic stop orders	○	○	○
IV to PO conversion	○	○	○

43. Does your AMS program have a way to arrange for allergy testing for penicillin-allergic patients?

○ Yes

○ No

44. Does your facility offer any AMS support for outpatient interventions? (all that apply)

☐ Upper respiratory tract infections

☐ Urinary tract infections

☐ Outpatient Parenteral Antibiotic Therapy (OPAT)

45. Which measures does your AMS routinely monitor and trend at least once per year? (all that apply)

- ☐ Number of prospective audit and feedback recommendations made to teams
- ☐ Type of prospective audit and feedback recommendation made
- ☐ Whether prospective audit and feedback recommendation was accepted
- ☐ Antibiotic use in days of therapy (DOT)
- ☐ Antibiotic use in length of therapy (LOT)
- ☐ Antibiotic use in defined daily doses (DDD)
- ☐ Antibiotic purchasing costs
- ☐ *Clostridium difficle* infections
- ☐ Drug-resistant organisms
- ☐ Special project/iniative-based outcomes
- ☐ Other (please specify) _____
- ☐ My AMS does not monitor any measures at this time

46. In the past two years, has your program demonstrated effectiveness in any of the following areas? (all that apply)

- ☐ Cost savings/cost avoidance
- ☐ Decreased antibiotic utilization
- ☐ Decreased *Clostridium difficile* infection
- ☐ Decreased rate of drug-resistant organisms
- ☐ Other _____

- [ ] Our AMS has not demonstrated any of the above

47. Who primarily prepares your AMS reports?

- ○ Medical Officer/Physician
- ○ Pharmacist
- ○ Data analyst
- ○ Other _____

48. Who receives the AMS reports? (all that apply)

- [ ] Quality improvement committee
- [ ] Medical executive committee/hospital leadership
- [ ] Pharmacy and therapeutics
- [ ] Infection control committee
- [ ] Clinicians
- [ ] Other _____

49. Does your AMS provide education to the following groups? (all that apply)

- ☐ Providers
- ☐ Pharmacists
- ☐ Nurses
- ☐ Trainees
- ☐ Patients
- ☐ Other _____
- ☐ None of the above

50. How much does it cost the hospital to provide this education?

51. Please specify the full-time equivalent (FTE) components (% effort) dedicated solely to your AMS (all that apply, enter numbers > 100% if there are two or more individuals contributing significant time)

% effort

0 20 40 60 80 100 120 140 160 180 200

52. The financial resources for my AMS are adequate

- ○ Strongly agree
- ○ Somewhat agree
- ○ Somewhat disagree
- ○ Strongly disagree

53. My program needs the following resources: (all that apply)

- ☐ Physician FTE (specify % effort needed) _____
- ☐ Pharmacist FTE (specify % effort needed) _____
- ☐ Data analysis FTE (specify % effort needed) _____
- ☐ Administrative FTE (specify % effort needed) _____
- ☐ Technology/software (5)
- ☐ Other (6) _____

54. Which of these factors (if any) do you see as barriers to successful implementation of your stewardship program? (all that apply)

- ☐ Financial resources (1)
- ☐ Lack of dedicated time (PharmD and/or MD) (2)
- ☐ Not a hospital administration institutional priority (3)
- ☐ Resistance from providers (4)
- ☐ Insufficient IT infrastructure (5)
- ☐ None of the above (7)
- ☐ Other (specify) (8) _____

Comments

_____

_____

_____

_____

_____

APPENDIX H: GERTRUDE'S CHILDREN'S HOSPITAL ANTIMICROBIAL STEWARDSHIP PROPOSAL 2022

PRESERVE THE MIRACLE FOR OUR CHILDREN

- ANTIMICROBIAL STEWARDSHIP AT GERTRUDE'S CHILDREN HOSPITAL KENYA

ABSTRACT

Gertrude's Children's Hospital (GCH) established the Antimicrobial Stewardship Program in 2018 to optimize the use of antimicrobials in the hospital by ensuring the selection of the right antibiotic, for the right indication (right diagnosis), to the right patient, at the right time, with the right dose and route, causing the least harm to the patient and future patients.

We have had successful initiatives targeting the in-patient use of antimicrobials. These included promoting compliance with the Surgical Antibiotic Prophylaxis Guidelines as well as Use of Restricted (Reserve) Antimicrobials through prospective audit and feedback. We plan to conduct our first Point Prevalence Survey in May-2022 and thereafter make interventions based on the findings.

However, use of antimicrobials in the out-patient department where about 1,000 patients are seen each day across the network of sixteen facilities has remained suboptimal. Compliance with the hospital Standard Treatment Guidelines (STG) remains low especially with regard to the choice of antimicrobial mostly due to insistence by parents/guardians for a particular brand and inadequate documentation by prescribers to justify reason for not using the first line.

The overall goal of the project is to develop Gertrude's Children's Hospital (GCH) to be a Centre of Excellence in Antimicrobial Stewardship, exercising appropriate antimicrobial use in both the in-patient and out-patient settings.

The planned outputs are:

1. To achieve training of targeted healthcare professionals involved in prescribing, dispensing, administration, and monitoring of antimicrobials ≥ 80%

2. To achieve complete STG adherence for > 50% of prescriptions for the common infections managed at the out-patient department

3. To establish weekly Antimicrobial ward rounds

4. To increase awareness among patients and families on Antimicrobial Resistance

The project will target members of hospital committees responsible for appropriate use of antimicrobials, clinical staff in out-patient department as well as patients and families. There will be 25 members of the Medicines and Therapeutics Committee (MTC) and Antimicrobial Stewardship Committee (ASC) Members; 93 Prescribers; 68 Pharmacy Staff and 300,000 patients seen per year.

The Project is to be run by a core team of four (4) members of the ASC comprising of Consultant Paediatrician/Infectious diseases physician (*ASC Chair*); Chief Paediatrician; Chief Pharmacist and Pharmacist (*ASC Secretary*)

The Main Project Activities are:

1. Review of the Standard Treatment Guidelines

2. Establishment of Antimicrobials Prescribing decision support system in the Hospital Management Information System (HMIS)

3. Capacity Building of Healthcare Professionals

4. Patient and Families Engagement: a. Development/update of IEC Materials for Parents and Children

b. Undertake responsible antibiotic use campaigns targeting patient and families

c. Conduct surveys on the public awareness of Antimicrobial Resistance using the WHO AMR Awareness Survey Tool

APPENDIX I: SAMPLE RESERVE ANTIBIOTIC COMPLIANCE REPORT PREPARED BY GERTRUDE'S CHILDREN'S HOSPITAL