This is a peer-reviewed, accepted author manuscript of the following research article: Gwebu, P., Meyer, J., Schellack, N., Matsebula-Myeni, Z., & Godman, B. (Accepted/In press). A web-based point prevalence survey of antimicrobial use and quality indicators at Raleigh Fitkin Memorial Hospital, Eswatini and the implications: PPS study in Eswatini. *Hospital Practice*, 1-12.

A web-based point prevalence survey of antimicrobial use and quality indicators at Raleigh Fitkin Memorial Hospital in the Kingdom of Eswatini and the implications

Prudence C. Gwebu[ab], Johanna C. Meyer[bc], Natalie Schellack[d], Zinhle C. Matsebula-Myeni[ae], and Brian Godman[b,f,g]

[a] Department of Pharmacy, Raleigh Fitkin Memorial Hospital, Manzini, Eswatini
[b]Division of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Molotlegi Street, Ga-Rankuwa, Gauteng, South Africa.
[c]South African Vaccination and Immunisation Centre, Sefako Makgatho Health Sciences University, Molotlegi Street, Ga-Rankuwa, Gauteng, South Africa.
[d]Department of Pharmacology, Faculty of Health Sciences, University of Pretoria, Gauteng, South Africa
[e]Cerium Scientific, Office Warehouse 8, King Mswati 111 Avenue, Matsapha, Eswatini
[f] Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK. Email: Brian.Godman@strath.ac.uk
[g]Centre of Medical and Bio-allied Health Sciences Research, Ajman University, Ajman, United Arab Emirates

Corresponding author: Prudence Ceb'sile Gwebu, Department of Pharmacy, Raleigh Fitkin Memorial Hospital, Ligusha Street, Manzini, Eswatini, M200; Tel: +268 76081604; Email: ntombiep@gmail.com

Key Words: Antimicrobial utilisation; Antimicrobial resistance; Point Prevalence Survey; Eswatini; web-based mobile App

Abstract

Objectives: Currently there is limited knowledge regarding antimicrobial utilisation patterns among public hospitals in Eswatini. This is a concern given rising resistance rates among African countries. This study aimed to address this by determining antimicrobial utilisation patterns using a point prevalence survey (PPS) methodology at Raleigh Fitkin Memorial (RFM) Hospital. The findings would be used to identify potential interventions to improve future antimicrobial utilisation. **Method**: A PPS was conducted using a web-based application (App). Antimicrobials were categorised according to the World Health Organization (WHO) Access, Watch, and Reserve (AWaRe) classification. Each ward in the hospital was surveyed in one day using patient files. All patients in the ward, admitted by 08h30 on the day of the survey, were included. Ethical clearance was granted by the university and Eswatini Ethics. **Results**: Overall, 68 patient files in 12 wards were surveyed, with 88.2% (60/68) receiving at least one antimicrobial. The most widely prescribed antimicrobials were amoxicillin (24.5%), and ceftriaxone IV (21.6%), mostly from the Access group (69.9%), and zero from the Reserve group. In the past 90 days prior to admission, most patients (60.3%; 41/68) were not receiving any antimicrobials. Of concern was that antimicrobial use was empirical for all patients (100%) with mostly parenteral administration (88.3%; 91/103). In addition, the majority of surgical prophylaxis patients (80%; 12/15) were given an extended course post surgery. There was also no documented switch or stop dates, or patient culture and drug sensitivity results. **Conclusion**: Antimicrobial utilisation is high at RFM hospital. Identified targets for quality improvement programmes include encouraging earlier switching to oral antimicrobials, reducing extended use for surgical prophylaxis and encouraging greater sensitivity testing and documentation stop dates. The development of the App appreciably reduced data collection times and analysis, and would be recommended for use in other public hospitals.

1. Introduction

The management of infectious diseases relies on the appropriate use of antimicrobials to reduce subsequent morbidity and mortality [1]. However, as the effectiveness of a number of antimicrobials is decreasing through increasing antimicrobial resistance (AMR) rates [2], the world is facing a major predicament of how infections will be treated in the future, with increasing AMR increasing morbidity, mortality and costs [3-7]. This has resulted in a number of global strategies to try and reverse rising AMR rates. This includes the development of the One Health Approach by the World Health Organization (WHO) in September 2017 and the launch of National Action Plans (NAPs) to reduce AMR, including the Kingdom of Eswatini [8-11]. The WHO defines 'One Health' as an approach whereby multiple sector stakeholders design and implement programmes, legislation, research and policies with the intention to achieve better public health outcomes by addressing health threats amongst humans, animals and the environment as a unit [11,12]. A key area is the need for up-to-date antimicrobial usage and surveillance data.

The 2011 Global Antibiotic Resistance Partnership – South Africa (GARP-SA) situation analysis identified the need for a response to address rising AMR levels and the increasing number of multidrug resistant bacterial infections among healthcare settings in South Africa [13,14]. According to Mendelson and Matsoso and others [15,16], baseline antimicrobial use data can help identify pertinent programmes to improve future antimicrobial use and reduce AMR [5,16].

The WHO Global Strategy for Containment of Antimicrobial Resistance states that AMR is fuelled by inappropriate use of antimicrobials, especially overuse and misuse for minor infections as well as incomplete treatment courses [17]. A surveillance study conducted by Systems for Improved Access to Pharmaceuticals and Services, Management Sciences for Health (SIAPS-MSH) in Eswatini indicated that at least 52% of patients were prescribed at least one antibiotic in 2015, which is much higher than the recommended 20-26% by the WHO in ambulatory care [18]. Since then, the final draft of the Kingdom of Eswatini NAP to curb AMR was made available at the end of 2017, with the Government fully committed to curbing the spread of AMR in the country [8]. This is needed given the findings in ambulatory care in 2015 [18], from a study undertaken in Piggs Peak Government Hospital between 2014 and 2015 showing that the physicians in the hospital prescribed a range of antibiotics to treat patients with community acquired pneumonia with limited following of current national guidelines [19].Ncube et al (2020) identified a general need to improve the prescribing of medicines in the Kingdom given the extent of inappropriate prescribing [20].

Consequently, this study aimed to build on these studies and the recent draft of the NAP by determining the prevalence of antimicrobial consumption using the PPS method at Raleigh Fitkin Memorial (RFM) Hospital in Eswatini. The objective was to identify potential areas for quality improvement programmes in this leading hospital in the Kingdom. RFM currently has an Infection Prevention and Control (IPC) officer who is part of an ongoing Antimicrobial Stewardship (AMS) Committee. In addition, the pharmacy reviews all inpatient prescriptions on a daily basis and is the secretariat of the AMS committee. However, the IPC committee has recently been inactive. Consequently, implementation of recommendations from the AMS committee are currently a challenge in Eswatini. It is anticipated that this research will help to address this as well as recommend areas for AMS activities in line with the goals of the national NAP.

2. Materials and Methods

2.1 Study design

This was an observational, descriptive quantitative study with a PPS design using a purposely developed App. This builds on similar methodology to measure prevalence among public sector hospitals in Botswana and subsequently across South Africa using the purposely developed App [21-24].

2.2 Study population and sample

RFM has 350 beds, which is less than the WHO upper limit of 500 hospital beds for sampling. Consequently, no sampling was applied as all in-patients were eligible to participate in the study. Each in-patient ward within the hospital was surveyed only once. Although the wards in the hospital were not all surveyed on the same day, all beds in one single ward were completely surveyed on one single day. In cases where data collection was interrupted by ward rounds, files not completely surveyed were collected later to complete the survey, as all file numbers were captured, as well as the time of admission to allow for patient reviews to proceed during ward rounds. This was to ensure that the denominator (number of admitted patients) is calculated correctly and reflects only those patients admitted by 08H30 on the day of the survey.

In-patient hospital wards were categorised into the following 12 disciplines: Paediatric ward, neonatal ward, adult male medical ward, adult female medical ward, COVID-19 ward, adult male surgical wards, adult female surgical wards, paediatric and adult intensive care unit, private ward, labour ward, post-partum ward, and gynaecological ward. These were further categorised into 6 wards (Table 1). However, some wards had no patients at the time of the study for various reasons. The private ward was closed so that critically ill female medical ward patients could be transferred to it as the roof in the female medical ward had collapsed and was being renovated at the time of the study. The gynaecology ward was also closed at the time, with all patients referred to another hospital. Furthermore, patient admissions were being reduced where possible in line with COVID-19 protocols.

The study population included all neonates, paediatric and adult in-patients who were in the ward at 08h30 on the day of the survey. For the purpose of calculating the point prevalence of antimicrobial use, basic data was collected on all patients, and this served as the denominator. The denominator data was the total number of inpatients at 08h30 in the ward surveyed and the total number of beds in the ward surveyed. Detailed data was subsequently collected for only those patients who were on antimicrobial therapy, which served as the numerator. This included patients taking one or more of any of the antimicrobials, except topical antimicrobials, antituberculosis treatments and antivirals chronically.

For surgical patients, the administration of any prophylactic antibacterial was recorded if administered during the previous 24 hours. The reason for this was to code the duration for example, prophylaxis, as either 1 dose, 1 day, or >1 day. This was because previous studies among low- and middle-income countries (LMICs), including African countries, had shown prolonged administration of antimicrobials for surgical prophylaxis, which is a concern [25-29]. Definitions for medical prophylaxis were similar to other studies [21,22,24,30].

2.3 Data collection

Data was collected over a period of two weeks (25 January 2021 to 8 February 2021) and completed all wards within this time frame. Patients' medical files served as the main data collection source. Data was collected by reviewing patient medical records and information was captured on the data collection instrument (web-based App, on a Knack platform) [22,24]. This included data on previous antibiotic use when available in the patients' notes. No patient was interviewed and any lack of information in the file, was recorded as such.

The researcher collected the data with a team of third year pharmacy technician students who were completing their pharmacy diploma in August 2021. The students were trained on the data collection procedures, 8 hours in total, spread over 2 days. Training was given in the form of an oral presentation with practical illustrations, using examples, where all data collectors were given the exact procedure for collecting the relevant data from the patients' medical files. The training also included a mini pilot study involving all data collectors to determine if they fully understood the data collection instrument. The data collectors were also given an opportunity to explore and use the App on their phones for a week before actual data collection commenced, to enhance their familiarity with the App and the electronic data collection instrument.

2.4 Data analysis

The data was captured on the web-based App and exported to Microsoft Excel® spread sheets. Data was checked for accuracy and correctness prior to analysis using SPSS Version 20 for Windows, in consultation with a statistician. This was a descriptive, explanatory analysis since the study was quantitative. Categorical variables were calculated as frequencies and percentages.

Antimicrobials prescribed were analysed according to the WHO Anatomical Therapeutic Chemical (ATC) classification (ATC level 5) [31], the dose, frequency and route of administration. Appropriateness of the prescribed antimicrobials with guidelines were evaluated based on the national Essential Medicines List (EML) and Standard Treatment Guidelines (STGs) [32], with adherence to guidelines increasingly seen as good quality prescribing in hospitals [33-35]. We also assessed antimicrobial utilisation based on the WHO AWaRe list (Access, Watch and Reserve) [36]. The Access list of antibiotics are recommended first-line or second-line treatments for key infections and should be routinely available, with those in the Watch list recommended first- or second-choice treatments for specific infections with a greater potential for antibiotic resistance. Those in the Reserve list should be last resort antibiotics used under specialist guidance due to concerns with resistance development [36]. The AWaRe list is increasingly being used across countries and settings to improve future antimicrobial prescribing [23,37-40].

In addition, whether antibiotic sensitivity analysis was requested and subsequently acted upon, and whether treatment was empiric or not. Alongside this, the route of administration with concerns that prolonged intravenous administration can increase the length of stay in hospitals adding to the costs [41,42].

2.5 Ethical approval

Ethical approval from the Sefako Makgatho University Research Ethics Committee (SMUREC/P/121/2020: PG) and the local national Eswatini National Health Research Review Board (ENHRRB-FWA00026661/IRB00011253). Permission was thereafter obtained from the Hospital Administrator of RFM Hospital, with patient confidentiality strictly maintained. Authorised personnel in the wards were given an explaination about the purpose of the study and given assurance regarding the confidentiality of patients personal health information.

3. Results

3.1 Overview of patient demographics

A total of 68 in patient files were surveyed from the 12 wards, which were categorised as shown in Table 1. There were 71 potential patient records at the time of the survey; however, for 3 patient records, data capturing was incomplete, hence excluded from the final sample and analysis. The adult surgical ward had the most patients admitted (32.4%; 22/68), including 59.1% (13/22) male and 40.9% (9/22) female patients. Overall, 88.2% (60/68) of the patients whose medical records were reviewed, were prescribed at least one antimicrobial. Of the 60 patients prescribed an antimicrobial, 65% were females and 35% were males.

Table 1: Wards categorisation for surveyed patient files at Raleigh Fitkin Memorial hospital (n=68)

Category of wards	In-patient hospital wards	Number of patients
Adult ICU	Intensive care unit	**2**
Adult medical ward	Private ward	**0**
	Female medical ward	**6**
	Male medical ward	**2**
	Isolation COVID-19 ward	**3**
Adult surgical ward	Female surgical ward	**9**
	Male surgical ward	**13**
Neonatal medical ward	Special care and neonates	**17**
Obstetrics and gynaecology ward	Labour ward	**0**
	Postpartum ward	**9**
	Obstetrics and gynaecology ward	**0**
Paediatric medical ward	Children's ward	**7**
Total		**68**

3.2 Antimicrobial Utilisation

The summary of antimicrobials utilised per ward category is shown in Table 2. A total of 103 antimicrobials were prescribed to the 60 patients. Patients in the adult surgical wards were prescribed the most antimicrobials (28.2% of the total prescribed; 29/103) followed closely by patients in the neonatal medical ward at 27.2% (28/103). Table 2 illustrates that out of the 103 antimicrobial prescriptions, the top five antibiotics prescribed were amoxicillin (24.5%), followed by ceftriaxone (21.6%), gentamicin (14.7%), metronidazole (12.7%) and cloxacillin (9.8%). All these antimicrobials were from the Access group, with the exception of ceftriaxone which belongs to the Watch group.

Table 2: Antimicrobial utilisation per ward (n=103)

Antimicrobials prescribed with ATC codes	In-patient hospital wards						Antibiotics prescribed	
	Adult ICU	Adult medical	Adult surgical	Neonatal medical	Obstetrics & gynae-cology	Paediatric medical	Number	Percentage (%)
Amoxicillin J01CA04		1	5	13	4	2	**25**	**24.5%**
Azithromycin J01FA10		1					**1**	**1.0%**
Benzathinebenzylpenicillin J01CE08					1		**1**	**1.0%**
Benzylpenicillin J01CE01				1			**1**	**1.0%**
Ceftriaxone J01DD04	1	7	5	1	4	5	**23**	**21.6%**
Ceftriaxone combinations J01DD54					1		**1**	**1.0%**
Ciprofloxacin J01MA02			1				**1**	**1.0%**
Clindamycin J01FF01			1				**1**	**1.0%**
Cloxacillin J01CF02	1	1	7			1	**10**	**9.8%**
Combinations of long-acting sulphonamides J01ED20		2					**2**	**2.0%**
Combinations of short acting sulphonamides J01EB20		1					**1**	**1.0%**
Doxycycline J01AA02		1					**1**	**1.0%**
Erythromycin J01FA01			1				**1**	**1.0%**
Fluconazole J02AC01		1					**1**	**1.0%**
Gentamicin J01GB03			1	12	1	1	**15**	**14.7%**
Meropenem J01DH02		2		1			**3**	**2.9%**
Metronidazole (oral/rectal) P01AB01		1	1				**2**	**2.0%**
Metronidazole (parenteral) J01XD01		1	7		3	2	**13**	**12.7%**
Number per ward	**2**	**19**	**29**	**28**	**14**	**11**	**103**	
Percentage (%) per ward	**1.9%**	**18.4%**	**28.2%**	**27.2%**	**13.6%**	**10.7%**		

Patients in the adult ICU consumed the least (1.9%; 2/103) antimicrobials. Of the 103 antimicrobials prescribed, 40.8% (42/103) were for prophylaxis (medical and surgical) and 59.2% (61/103) for treatment. This is further illustrated in Table 3 and Table 4, which provide additional details on the ward types, the antimicrobials prescribed and the percentage per ward category whether prescribed for prophylaxis (n=42 of total antimicrobials prescribed) or treatment (n=61). Where an antimicrobial was prescribed for prophylaxis, 64.3% (27/42) of antimicrobials were prescribed for medical prophylaxis and 35.7% (15/42) for surgical prophylaxis.

Table 3: Antimicrobial used for prophylaxis (n=42)

	In-patient hospital wards						Antimicrobials prescribed	
Antimicrobials with ATC codes	Adult ICU	Adult medical	Adult surgical	Neonatal medical	Obstetrics & gynae-cology	Paediatric medical	Number	Percentage (%)
Amoxicillin J01CA04		1	1	9	4		**15**	36.6%
Azithromycin J01FA10							**0**	0.0%
Benzathinebenzylpenicillin J01CE08					1		**1**	2.4%
Benzylpenicillin J01CE01							**0**	0.0%
Ceftriaxone J01DD04			3		2		**5**	9.8%
Ceftriaxone combinations J01DD54					1		**1**	2.4%
Ciprofloxacin J01MA02							**0**	0.0%
Clindamycin J01FF01							**0**	0.0%

Cloxacillin J01CF02			3				**3**	7.3%
Combinations of long-acting sulphonamides J01ED20		2					**2**	4.9%
Combinations of short acting sulphonamides J01EB20		1					**1**	2.4%
Doxycycline J01AA02							**0**	0.0%
Erythromycin J01FA01			1				**1**	2.4%
Fluconazole J02AC01							**0**	0.0%
Gentamicin J01GB03				8	1		**9**	22.0%
Meropenem J01DH02							**0**	0.0%
Metronidazole (oral/rectal) P01AB01		1					**1**	2.4%
Metronidazole (parenteral) J01XD01			2		1		**3**	7.3%
Number per ward	**0**	**5**	**10**	**17**	**10**	**0**	**42**	
Percentage (%) per ward	**0%**	**11.9%**	**23.8%**	**40.5%**	**23.8%**	**0%**		

Table 4: Antimicrobial use for treatment and their indications (n=61)

Indications	**In-patient hospital wards**						**Antimicrobials prescribed**	
	Adult ICU	**Adult medical**	**Adult surgical**	**Neonatal medical**	**Obstetrics & gynae-cology**	**Paediatric medical**	**Number**	**Percentage (%)**
ASB; Asymptomatic bacteriuria			3				**3**	**4.8%**
BAC; Laboratory-confirmed bacteraemia			1				**1**	**1.6%**
BJ; Bone and Joint Infections			3			1	**4**	**6.5%**
BRON; Acute bronchitis		1				4	**5**	**8.1%**
CNS; central nervous system		2	2	6		1	**11**	**19.4%**
CSEP; Clinical sepsis		1	1				**2**	**3.2%**
CVS; Cardiovascular infections		2					**2**	**3.2%**
CYS; Symptomatic lower urinary tract infection		1					**1**	**1.6%**
EYE; eye infections				1		2	**3**	**4.8%**
GUM; Prostatitis			1				**1**	**1.6%**
ML; Malnutrition						3	**3**	**4.8%**
NA; Not applicable for antimicrobial use other than treatment		2		2			**4**	**6.5%**
OBGY; Obstetric or gynaecological infections				2	4		**6**	**9.7%**
PNEU; Pneumonia		2					**2**	**3.2%**
PYE; Symptomatic upper urinary tract infection			1				**1**	**1.6%**
SST; Soft tissue infections	2		2				**4**	**6.5%**
UND; Completely undefined		3	1				**4**	**6.5%**
No Indication			4				**4**	**6.5%**
Number per ward	**2**	**14**	**19**	**11**	**4**	**11**	**61**	
Percentage (%) per ward	**3.3%**	**23.0%**	**31.1%**	**18.0%**	**6.6%**	**18.0%**		

Table 4 shows that central nervous system infections (19.4%; 12/62) was the most common type of infection for which an antimicrobial was prescribed, followed by obstetrics and gynaecology infections (9.7%; 6/62). Most infections for which an antimicrobial was prescribed were for patients in the adult surgical ward (31.1%; 19/61) and the neonatal and paediatric wards (18%; 11/61). There was no indication in the patients' files for four (6.5%) of the antimicrobials, prescribed in the adult surgical wards.

6

3.3 Quality Indicators

Intravenous administration of antimicrobials was high (88.3%), followed by the oral route (10.7%) and intramuscular route (1%). The majority of prescribed antimicrobials were from the Access group (69.9%) followed by the Watch group (29.1%) with none from the Reserve group. Only one antimicrobial (1%), i.e., fluconazole could not be classified using the AWaRe tool (Table 5).

Table 5: Quality indicators summary

Indicator		Number	Percentage (%)
Route of administration (n=103)	Intravenous	**91**	**88.3%**
	Oral	**11**	**10.7%**
	Intramuscular	**1**	**1%**
AWaRe Classification (n=103)	Access	**72**	**69.9%**
	Watch	**30**	**29.1%**
	Reserve	**0**	**0%**
	Unclassified	**1**	**1%**
Purpose for use (n=103)	Prophylaxis	**42**	**40.8%**
	Treatment	**61**	**59.2%**
Item prescribed from STG/EML (n=103)	Yes	**103**	**100%**
	No	**0**	**0%**
Antibiotics in the past 90 days (n=68)	Yes	**3**	**4.4%**
	No	**41**	**60.3%**
	Unknown	**24**	**35.3%**

Out of all patients who received an antimicrobial for surgical prophylaxis, 80.0% (12/15) were given an antimicrobial for more than one day. None of the patients surveyed had cultures performed at RFM or had culture results recorded in their files. In addition, there were no documented stop dates in the patients' files.

Very few (4.4%; 3/68) patients had antimicrobials documented in their files as being prescribed in the past 90 days and 60.3% (41/68) had no recording of antimicrobials used prior to admission. However, 35.3% (24/68) of the patients' files surveyed had 'unknown' documented for treatment prescribed 90 days prior to admission.

4. Discussion

We believe this is the first PPS study undertaken in Eswatini. Of all patients that were admitted, 88.2% were given at least one antimicrobial, which is higher than seen overall in the global PPS, with hospitals in Africa reporting the highest use (50%) and Eastern Europe the lowest (27.4%) [33]. However, these high rates are similar to Iraq (93.7%) and Pakistan (77.6%) [43,44]. This rate in this study is also appreciably higher than seen in a recent study conducted among 18 public sector hospitals in South Africa at 33.6% [23]. This suggests the overuse of antimicrobials in this hospital in Eswatini, which is of concern. Consequently, more lessons need to be adopted from South Africa for full implementation of ASPs in RFM with re-activation of the IPC committee for better patient outcomes at RFM hospital, although there are still areas of concern in South Africa [45-47]. We cannot be certain whether the lack of routine culture and sensitivity testing (CST) could have contributed to high antimicrobial use at RFM hospital, and will be investigating this further.

The most common infection in this study was central nervous system related infections mostly amongst neonates as opposed to respiratory infections in this age group (19.4% of prescribed antimicrobials). This is different to other PPS studies and requires further research to determine possible causes for this anomaly [23,28-30,44]. However, this may reflect differences in the profile of admitted patients in this study versus other PPS studies conducted across Africa. For instance, high rates of HIV were seen among in-patients in Botswana in their PPS with obstetrics and gynaecology infections the most common infection, and sexually transmitted diseases were the most common infection seen among ambulatory care patients in Botswana [21,48]. This is very different compared to higher-income countries [33].

The most prescribed antibiotic in our study was amoxicillin (Access group) followed by ceftriaxone (Watch group), which is similar to other studies including the Global PPS where penicillins with β-

7

lactamase inhibitors were the most prescribed antimicrobials [27,30,33]. Overall, 69.9% of antimicrobials prescribed were from the Access group (Table 5), marginally higher than the rate of 55.9% seen by Skosana *et al.* in South Africa [23], and higher than the countries who participated in the Global PPS [33]. This is not necessarily an indication of appropriate prescribing but emphasis should be on the use of narrow spectrum antimicrobials first line. The antimicrobial guidelines developed in 2019 for Eswatini should suggest this practice when reviewed in 2022, with routine monitoring of subsequent prescribing against national guidance, which as mentioned is increasingly seen as a key quality improvement goal [21-33-35]. Encouragingly, no antibiotics from the Reserve group were prescribed.

Encouragingly as well, all prescribed antimicrobials (100%) were from the STG/EML of Eswatini [32]. This was similar to the findings in Ethiopia and Eritrea, where all antibiotics (100%) were prescribed from their national EML [49,50]. This could be due to the fact that public sector hospitals in LMICs including Eswatini receive most of their medicines from government suppliers, which typically supply medicines based on the national EML [51,52]. This encourages prescribers to adhere to the EML, resulting in high compliance rates with the national EML.

The adult surgical ward had the highest number of antimicrobials prescribed (28.2%) followed by the neonatal ward (27.2%). The latter could be due to prescriber inexperience and fear with the lack of functional immune systems in neonates leading to high prophylaxis use, and we will also be exploring this further. The WHO also recommends beta lactam penicillins and aminoglycosides for neonatal sepsis [53]. The least number of antimicrobials prescribed were in the adult ICU. We are not sure of the reasons for this.

Identified areas of concern included extended antimicrobial prescribing for the prevention of surgical site infections (SSIs) where 80.0% of surgical patients (12/15) were given an antimicrobial for more than one day. This is an issue since extending prophylaxis beyond the first 24 hours after surgery can lead to adverse events as well as increased risk of resistance adding to the costs [25,26,54]. We have seen that appropriate ASPs instigated among LMICs have reduced extended prophylaxis to prevent SSIs thereby providing guidance to the RFM hospital [26].

Another area of concern was that 88.3% of patients had their antimicrobials administered intravenously (IV). This is similar though to the situation in Eritrea and Ethiopia as well as a number of other African countries [21,28,49,50,55]. However, future research should look into evaluating the appropriateness of the IV route at all times as part of any ASP especially if there is limited switching before discharge. Alongside this, evaluate further the rationale behind the current lack of CST as part of any ASP in view of the need to continually update antibiograms to improve future empiric prescribing. In Ethiopia, the prescribing of broad spectrum antibiotics was normal practice and the healthcare professionals did not see the need for CST [49]. However, this needs further investigation in RFM hospital to guide future activities. Potentially, the hospital could instigate training of key stakeholders on CST as well as routinely making available specimen bottles on all wards for sample collection prior to antibiotic administration. This could potentially be achieved through the Pharmacy and Therapeutics Committee (PTC), which is already functional in the hospital, with a subgroup responsible for enhancing appropriate antimicrobial prescribing through the IPC and subsequent ASPs building on activities in other countries [46,56,47]. This is because RFM hospital currently lacks specialties in microbiology and infectious diseases with the internist more focused on non-communicable diseases. The findings from this study could also put pressure on hospital management to improve laboratory facilities as part of re-introducing the IPC to help attain NHP goals. In addition, address capacity issues in the hospital as well as ensure routine availability of necessary consumables and reagents to encourage greater CST. The implementation of pertinent antimicrobial guidelines should be strengthened by ASPs as well as by the re-introduction of the IPC, which combined with increasing PTC activities [45,58,59]. We have seen improved antimicrobial prescribing in other sectors in Eswatini following the implementation and monitoring of guidelines [60].

Once quality improvement programmes have been instigated including encouraging earlier switching, reducing extended prophylaxis for SSIs and encouraging greater documentation of stop and start dates, repeated PPS studies should be undertaken to monitor the impact of these programmes in line with the goals of the NAP. The findings can be used to instigate additional programmes where needed.

Prior exposure to antimicrobials could also result in the development of resistant antimicrobials and is also of concern for future ASPs. It was encouraging that 60% of the studied patients, with data taken from their files, were not on any antibiotic prior to admission, but we cannot be certain this is a true reflection or that patients were knowledgeable on what antimicrobials are. We would also like to examine this issue further in future studies and also determine the knowledge gap among patients.

We are aware of a number of limitations of this study. These include the fact that this study was only undertaken in one hospital in Eswatini and the sample size was too small to generalize the findings to Eswatini as a whole. The presence of COVID-19 called for changes in admission criteria during the study and the capacity of the hospital was also compromised due to infrastructure and other concerns. In addition, some wards had to be rapidly converted to COVID-19 isolation wards and some procedures such as elective surgeries had to be suspended. Another limitation was that the data source was only patient files. However, this is not unique to this PPS study. Despite these limitations, we believe the results are robust and provide a good starting point for the development of pertinent ASP activities as well as future PPS studies in Eswatini.

5. Conclusion

In conclusion, this study revealed that the use of antimicrobials was extremely high in RFM hospital and the most widely prescribed antimicrobials among in-patients were amoxicillin (beta lactam penicillin) and ceftriaxone (3rd generation cephalosporin) followed by gentamicin (aminoglycoside). Target areas for future quality improvement programmes included strengthening CST to guide future empiric use, review of patients on day three for potential switching from IV to oral antimicrobials where possible, reducing the use of extended prophylaxis for SSIs and greater documentation of start and stop dates in patients' files. The App developed and tested in South Africa made the PPS easy to conduct and not time consuming in a resource limited setting such as Eswatini, and should be used in future PPS studies.

Acknowledgements
The authors are grateful to Mr. Sikhumbuzo Dlamini, the RFM statistician for the statistical analysis of the data. The authors are also grateful to the Ministry of Health and the RFM hospital management for allowing us to collect data. Finally, the authors thank the third year pharmacy diploma students and the pharmacy technician, Mr. Matenga, for assistance with data collection.

Data availability
Further details are available from the authors on request

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The analysis and write-up was self funded by the authors.

Conflict of Interest Statement
The authors have no relevant conflicts of interest to declare.

References

1. Medina E, Pieper DH. Tackling Threats and Future Problems of Multidrug-Resistant Bacteria. Curr Top Microbiol Immunol. 2016;398:3-33.
2. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022.
3. Founou RC, Founou LL, Essack SY. Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. PLoS One. 2017;12(12):e0189621-e.
4. Hofer U. The cost of antimicrobial resistance. Nat Rev Microbiol. 2019;17(1):3.
5. Godman B, Egwuenu A, Haque M, Malande OO, Schellack N, Kumar S, et al. Strategies to Improve Antimicrobial Utilization with a Special Focus on Developing Countries. Life. 2021;11(6).
6. Pérez-Lazo G, Abarca-Salazar S, Lovón R, Rojas R, Ballena-López J, Morales-Moreno A, et al. Antibiotic Consumption and Its Relationship with Bacterial Resistance Profiles in ESKAPE Pathogens in a Peruvian Hospital. Antibiotics. 2021;10(10):1221.
7. Čižman M, Mioč V, Bajec T, Paragi M, Kastrin T, Gonçalves J. Correlation between Antibiotic Consumption and Resistance of Invasive Streptococcus pneumoniae. Antibiotics. 2021;10(7):758.

8. USAID, SIAPS. Development of Swaziland's National Antimicrobial Resistance Containment Strategic Plan. 2018. Available at URL: https://siapsprogram.org/wp-content/uploads/2018/03/18-032-AMR-Technical-Report_Jan2018.-V.4.final_.pdf
9. WHO. GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE. 2015. Available at URL: https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1.
10. Iwu CD, Patrick SM. An insight into the implementation of the global action plan on antimicrobial resistance in the WHO African region: A roadmap for action. Int J Antimicrob Agents. 2021;58(4):106411.
11. WHO. One Health. 2017. Available at URL: https://www.who.int/news-room/questions-and-answers/item/one-health
12. Mendelson M, Brink A, Gouws J, Mbelle N, Naidoo V, Pople T, et al. The One Health stewardship of colistin as an antibiotic of last resort for human health in South Africa. Lancet Infect Dis. 2018;18(9):e288-e94.
13. Duse AG. The Global Antibiotic Resistance Partnership (GARP). S Afr Med J. 2011;101(8 Pt 2):551.
14. Schellack N, Benjamin D, Brink A, Duse A, Faure K, Goff D, et al. A situational analysis of current antimicrobial governance, regulation, and utilization in South Africa. Int J Infect Dis. 2017;64:100-6.
15. Mendelson M, Matsoso MP. THE SOUTH AFRICAN ANTIMICROBIAL RESISTANCE STRATEGY FRAMEWORK. AMR CONTROL 2015:54-61. Available at URL: http://globalhealthdynamics.co.uk/wp-content/uploads/2015/06/08_Mendelson-Matsotso.pdf
16. Kim B, Kim Y, Hwang H, Kim J, Kim SW, Bae IG, et al. Trends and correlation between antibiotic usage and resistance pattern among hospitalized patients at university hospitals in Korea, 2004 to 2012: A nationwide multicenter study. Medicine. 2018;97(51):e13719.
17. WHO. WHO Global Strategy for Containment of Antimicrobial Resistance. 2001. Available at URL: https://www.who.int/drugresistance/WHO_Global_Strategy_English.pdf
18. Chevaux T. Fighting AMR in Resource-Limited Settings: Experiences in Swaziland. 2015. Available at URL: https://siapsprogram.org/2015/07/31/fighting-amr-in-resource-limited-settings/
19. Zwane SP, McGee S-AM, Suleman F. A Comparative Cost Analysis of Antibiotic Treatment for Community Acquired Pneumonia (CAP) in Adult Inpatients at Piggs Peak Government Hospital in Swaziland. Frontiers in public health [Internet]. 2018; 6:[303 p.].
20. Ncube NBQ, Knight L, Bradley HA, Schneider H, Laing R. Health system actors' perspectives of prescribing practices in public health facilities in Eswatini: A Qualitative Study. PLoS One. 2020;15(7):e0235513-e.
21. Anand Paramadhas BD, Tiroyakgosi C, Mpinda-Joseph P, Morokotso M, Matome M, Sinkala F, et al. Point prevalence study of antimicrobial use among hospitals across Botswana; findings and implications. Expert Rev Anti Infect Ther. 2019;17(7):535-46.
22. Kruger D, Dlamini NN, Meyer JC, Godman B, Kurdi A, Lennon M, et al. Development of a web-based application to improve data collection of antimicrobial utilization in the public health care system in South Africa. Hosp Pract. 2021;49(3):184-93.
23. Skosana PP, Schellack N, Godman B, Kurdi A, Bennie M, Kruger D, et al. A point prevalence survey of antimicrobial utilisation patterns and quality indices amongst hospitals in South Africa; findings and implications. Expert Rev Anti Infect Ther. 2021;19(10):1353-66.
24. Skosana PP, Schellack N, Godman B, Kurdi A, Bennie M, Kruger D, et al. A national, multicentre, web-based point prevalence survey of antimicrobial use and quality indices among hospitalised paediatric patients across South Africa. Journal of Global Antimicrobial Resistance. 2021.
25. Mwita JC, Souda S, Magafu M, Massele A, Godman B, Mwandri M. Prophylactic antibiotics to prevent surgical site infections in Botswana: findings and implications. Hosp Pract. 2018;46(3):97-102.
26. Mwita JC, Ogunleye OO, Olalekan A, Kalungia AC, Kurdi A, Saleem Z, et al. Key Issues Surrounding Appropriate Antibiotic Use for Prevention of Surgical Site Infections in Low- and Middle-Income Countries: A Narrative Review and the Implications. Int J Gen Med. 2021;14:515-30.
27. Momanyi L, Opanga S, Nyamu D, Oluka M, Kurdi A, Godman B. Antibiotic Prescribing Patterns at a Leading Referral Hospital in Kenya: A Point Prevalence Survey. J Res Pharm Pract. 2019;8(3):149-54.
28. Ogunleye OO, Oyawole MR, Odunuga PT, Kalejaye F, Yinka-Ogunleye AF, Olalekan A, et al. A multicentre point prevalence study of antibiotics utilization in hospitalized patients in an urban secondary and a tertiary healthcare facilities in Nigeria: findings and implications. Expert Review of Anti-infective Therapy. 2022;20(2):297-306.

29. Afriyie DK, Sefah IA, Sneddon J, Malcolm W, McKinney R, Cooper L, et al. Antimicrobial point prevalence surveys in two Ghanaian hospitals: opportunities for antimicrobial stewardship. JAC Antimicrob Resist. 2020;2(1):dlaa001.
30. Okoth C, Opanga S, Okalebo F, Oluka M, Baker Kurdi A, Godman B. Point prevalence survey of antibiotic use and resistance at a referral hospital in Kenya: findings and implications. Hosp Pract. 2018;46(3):128-36.
31. WHO. Anatomical Therapeutic Chemical (ATC) Classification. 2021. Available at URL: https://www.who.int/tools/atc-ddd-toolkit/atc-classification
32. Ministry of Health, Kingdom of Eswatini. Standard Treatment Guidelines and Essential Medicines List. 2021
33. Versporten A, Zarb P, Caniaux I, Gros MF, Drapier N, Miller M, et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Lancet Glob Health. 2018;6(6):e619-e29.
34. Campbell SM, Meyer J, Godman B. Why Compliance to National Prescribing Guidelines is Important Especially across Sub-Saharan Africa and Suggestions for the Future. Biomed Pharm Sci 2021;4 (316):1-7.
35. Niaz Q, Godman B, Campbell S, Kibuule D. Compliance to prescribing guidelines among public health care facilities in Namibia; findings and implications. Int J Clin Pharm. 2020;42(4):1227-36.
36. Sharland M, Pulcini C, Harbarth S, Zeng M, Gandra S, Mathur S, et al. Classifying antibiotics in the WHO Essential Medicines List for optimal use-be AWaRe. Lancet Infect Dis. 2018;18(1):18-20.
37. Hsia Y, Lee BR, Versporten A, Yang Y, Bielicki J, Jackson C, et al. Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): an analysis of paediatric survey data from 56 countries. Lancet Glob Health. 2019;7(7):e861-e71.
38. Klein EY, Milkowska-Shibata M, Tseng KK, Sharland M, Gandra S, Pulcini C, et al. Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000-15: an analysis of pharmaceutical sales data. Lancet Infect Dis. 2021;21(1):107-15.
39. Mustafa ZU, Salman M, Yasir M, Godman B, Majeed HA, Kanwal M, et al. Antibiotic consumption among hospitalized neonates and children in Punjab province, Pakistan. Expert Rev Anti Infect Ther. 2021:1-9.
40. Saleem Z, Hassali MA, Godman B, Fatima M, Ahmad Z, Sajid A, et al. Sale of WHO AWaRe groups antibiotics without a prescription in Pakistan: a simulated client study. J Pharm Policy Pract. 2020;13:26.
41. van den Bosch CM, Hulscher ME, Akkermans RP, Wille J, Geerlings SE, Prins JM. Appropriate antibiotic use reduces length of hospital stay. J Antimicrob Chemother. 2017;72(3):923-32.
42. Cyriac JM, James E. Switch over from intravenous to oral therapy: A concise overview. J Pharmacol Pharmacother. 2014;5(2):83-7.
43. Kurdi A, Hasan AJ, Baker KI, Seaton RA, Ramzi ZS, Sneddon J, et al. A multicentre point prevalence survey of hospital antibiotic prescribing and quality indices in the Kurdistan regional government of Northern Iraq: the need for urgent action. Expert Rev Anti Infect Ther. 2021;19(6):805-14.
44. Saleem Z, Hassali MA, Versporten A, Godman B, Hashmi FK, Goossens H, et al. A multicenter point prevalence survey of antibiotic use in Punjab, Pakistan: findings and implications. Expert Rev Anti Infect Ther. 2019;17(4):285-93.
45. Brink AJ, Messina AP, Feldman C, Richards GA, Becker PJ, Goff DA, et al. Antimicrobial stewardship across 47 South African hospitals: an implementation study. Lancet Infect Dis. 2016;16(9):1017-25.
46. Schellack N, Bronkhorst E, Coetzee R, Godman B, Gous A, Kolman S, et al. SASOCP position statement on the pharmacist’s role in antibiotic stewardship 2018. Southern African Journal of Infectious Diseases. 2018;33:28-35.
47. Engler D, Meyer JC, Schellack N, Kurdi A, Godman B. Compliance with South Africa's Antimicrobial Resistance National Strategy Framework: are we there yet? J Chemother. 2021;33(1):21-31.
48. Mashalla Y, Setlhare V, Massele A, Sepako E, Tiroyakgosi C, Kgatlwane J, et al. Assessment of prescribing practices at the primary healthcare facilities in Botswana with an emphasis on antibiotics: Findings and implications. Int J Clin Pract. 2017;71(12).
49. Demoz GT, Kasahun GG, Hagazy K, Woldu G, Wahdey S, Tadesse DB, et al. Prescribing Pattern of Antibiotics Using WHO Prescribing Indicators Among Inpatients in Ethiopia: A Need for Antibiotic Stewardship Program. Infect Drug Resist. 2020;13:2783-94.

50. Amaha ND, Berhe YH, Kaushik A. Assessment of inpatient antibiotic use in Halibet National Referral Hospital using WHO indicators: a retrospective study. BMC Res Notes. 2018;11(1):904.
51. Godman B, Haque M, Leong T, Allocati E, Kumar S, Islam S, et al. The Current Situation Regarding Long-Acting Insulin Analogues Including Biosimilars Among African, Asian, European, and South American Countries; Findings and Implications for the Future. Front Public Health. 2021;9:671961.
52. Meyer JC, Schellack N, Stokes J, Lancaster R, Zeeman H, Defty D, et al. Ongoing Initiatives to Improve the Quality and Efficiency of Medicine Use within the Public Healthcare System in South Africa; A Preliminary Study. Front Pharmacol. 2017;8:751.
53. Fuchs A, Bielicki J, Mathur S, Sharland M, Van Den Anker JN. Reviewing the WHO guidelines for antibiotic use for sepsis in neonates and children. Paediatr Int Child Health. 2018;38(sup1):S3-s15.
54. Cooper L, Sneddon J, Afriyie DK, Sefah IA, Kurdi A, Godman B, et al. Supporting global antimicrobial stewardship: antibiotic prophylaxis for the prevention of surgical site infection in low- and middle-income countries (LMICs): a scoping review and meta-analysis. JAC Antimicrob Resist. 2020;2(3):dlaa070.
55. Labi AK, Obeng-Nkrumah N, Dayie N, Egyir B, Sampane-Donkor E, Newman MJ, et al. Antimicrobial use in hospitalized patients: a multicentre point prevalence survey across seven hospitals in Ghana. JAC Antimicrob Resist. 2021;3(3):dlab087.
56. Mashaba TP, Matlala M, Godman B, Meyer JC. Implementation and monitoring of decisions by pharmacy and therapeutics committees in South African public sector hospitals. Expert Rev Clin Pharmacol. 2019;12(2):159-68.
57. Chigome AK, Matlala M, Godman B, Meyer JC. Availability and Use of Therapeutic Interchange Policies in Managing Antimicrobial Shortages among South African Public Sector Hospitals; Findings and Implications. Antibiotics. 2019;9(1).
58. Mpinda-Joseph P, Anand Paramadhas BD, Reyes G, Maruatona MB, Chise M, Monokwane-Thupiso BB, et al. Healthcare-associated infections including neonatal bloodstream infections in a leading tertiary hospital in Botswana. Hosp Pract. 2019;47(4):203-10.
59. Akpan MR, Isemin NU, Udoh AE, Ashiru-Oredope D. Implementation of antimicrobial stewardship programmes in African countries: a systematic literature review. J Glob Antimicrob Resist. 2020;22:317-24.
60. Ness TE, Streatfield AE, Simelane T, Korsa A, Dlamini S, Guffey D, et al. Evaluating antibiotic use and developing a tool to optimize prescribing in a family-centered HIV clinic in Eswatini. PLoS One. 2021;16(1):e0244247.

12