A systematic approach to improve rational medicine use in Eswatini

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Abstract

Studies on rational medicine use (RMU) have mainly focused on identifying, quantifying, and addressing irrational use without exploring reasons behind this irrational use. In addition, minimal work has been conducted on irrational use of medicines in the context of the growing burden of non-communicable diseases (NCDs). This PhD research examined medicine use in Eswatini, (previously Swaziland) between April 2017 and March 2019, with a focus on prescribing practices linked to specific diagnoses. It further explored factors influencing RMU, which included testing the effects of a short intervention - prescription audit and feedback coupled with small group education - on prescribing practices in health facilities.

This intervention study employed a mixed methods approach with both quantitative and qualitative components. RMU was assessed based on the World Health Organization/ International Network for the Rational Use of Drugs (WHO/INRUD) prescribing indicators at three time points: baseline, post intervention and post follow-up. Baseline results were used to design an unblinded intervention in 32 health facilities, randomly allocated to intervention (16) and control (16) arms. The intervention, prescription audit coupled with small group education, was designed based on baseline findings. Percentage of prescriptions with at least one antibiotic was used to allocate facilities to intervention and control arms. The intervention was rolled out in two visits, two months apart to intervention facilities. Descriptive statistics, mean difference-of-differences (MD), and multilevel mixed logistics models were performed to analyse data, comparing intervention and control facilities. Analyses of RMU are provided nationally and disaggregated to regional levels, as well as by diagnoses and level of care. In the qualitative component, semi-structured interviews were conducted to ascertain perspectives of policy makers, supervisors, and frontline managers across the four regions of the country at baseline (39 participants) and at the end of the study (28 participants). Drawing on Social Practice Theory, these interviews explored the material (health system context), competence (provider) and cultural (patient and provider) factors influencing prescribing practices.

The research documented widespread irrational use of medicines in Eswatini. Most WHO/INRUD prescribing indicators, except prescribing of injections, were outside the WHO recommended standards. Although not reaching statistical significance, small changes were documented

immediately post intervention: the average number of medicines per prescriptions increased more in control than intervention facilities (mean difference of differences (MD) = -0.23; p = 0.48); generic prescribing increased in both groups, more in control facilities (MD = -4.38; p = 0.35); antibiotics prescribing decreased slightly in both intervention and control facilities, with a higher decrease in control facilities (MD = 7.06; p = 0.26). A statistically significant increase in the use of antibiotics in control facilities was observed at the end of the follow-up period (MD = -8.31, p = 0.03, 95% CI = -15.74 - -0.89). Improvement in prescribing indicators was observed more in secondary than primary level facilities. Most of these changes, however, were not sustained at the end of the follow-up period. Polypharmacy and high levels of antibiotic prescribing persisted in all regions, with some regional variations (notably in the Shiselweni and Lubombo regions). Importantly, our study found a previously unreported finding that antibiotics were frequently prescribed for chronic non-communicable conditions (26% at baseline, 23% post intervention, and 24% post follow up period).

A variety of factors contributing to irrational use of medicines were reported by participants. Material factors included: poor use of standard treatment guidelines, lack of RMU policies, poorly functioning pharmaceutical and therapeutics committees, stock-outs of medicines, lack of pharmacy personnel in primary healthcare facilities, and restrictions of medicines by level of care (secondary vs primary healthcare). Provider-related factors included: inadequate knowledge, experience and practice ethic, symptomatic prescribing and high patient numbers. Patient-related factors included late presentation, language and the perceived patient pressure on providers to prescribe many medicines.

This research concludes that there is irrational use of medicines in Eswatini, when assessed against WHO recommended standards. The lack of impact of this intervention, when combined with the qualitative findings, indicates that irrational use of medicine is a complex problem that is beyond prescribers and supervisors in facilities alone to resolve. Improving rational medicines use in Eswatini requires mixed interventions and concerted effort from a range of stakeholders and policy makers in both the ministries of health and finance.

The thesis offers a number of recommendations for strengthening policy and practice to promote RMU in Eswatini. These include drawing on the tools used in this research to develop an ongoing system using data from the client management information system (CMIS) of monitoring and evaluation (M&E) of medicine use at facility, regional and national levels; and linking M&E to the strengthening of facility Pharmaceutics and Therapeutics Committees (PTC) as well as to national planning for the country. In this regard, the research provides a baseline against which to evaluate future strategies. Recommendations are also made on RMU training of frontline managers, supervisors, and policy makers, and on the role and availability of pharmacy personnel in support of RMU at all levels of care.

Findings of this research and the recommended strategies are likely to have relevance for other similar, low-middle-income settings. The research fills a number of gaps in the literature on RMU in Eswatini, namely, prescribing and use of medicines in health facilities, regions and levels of care, including reasons behind certain prescribing practices. It further provides information on use of medicines in the management of chronic non-communicable disease. Finally, it is recommended that future studies focus on system-level factors, in particular, the effect of availability of pharmacy personnel, availability of stock and stock management practices on rational use of medicines.

Keywords

Appropriate medicines use

Medicines use

WHO prescribing indicators

Rational medicine use

Prescribing practices

Prescriber attitudes

Swaziland

Eswatini

Social practice theory

Theoretical domains framework

Abbreviations

ACE	Angiotensin Converting Enzyme
ADR	Adverse Drug Reaction
AIDS	Acquired Immune Deficiency Syndrome
AMR	Antimicrobial Resistance
ARB	Angiotensin Receptor Blocker
ART	Antiretroviral Therapy
ARV	Antiretroviral
CCB	Calcium Channel Blocker
CI	Confidence Interval
CKD	Chronic Kidney Disease
CMIS	Client Management Information System
CMS	Central Medical Stores
CVD	Cardiovascular Disease
DDPS	Deputy Director Pharmaceutical Services
DM	Diabetes mellitus
EML	Essential Medicines List
FIP	International Pharmaceutical Federation
GINA	Global Initiative for Asthma
HCW	Healthcare Worker
HIV	Human Immunodeficiency Virus
HTN	Hypertension
IDF	International Diabetes Federation
INRUD	The International Network for the Rational Use of Drugs
JNC	Joint National Committee
KI	Key Informant
LMIC	Low- and middle-income Country
MoH	Ministry of Health
MSH/SIAPS	Management Sciences for Health/Systems for Improved Access to Pharmaceuticals and Services
NCD	Non-communicable Diseases
NDoH	National Department of Health
NEMLC	National Essential Medicines List Committee
NEMP	National Essential Medicines Policy
NHP	National Health Policy
NPP	National Pharmaceutical Policy
PI	Principal Investigator
PTC	Pharmaceutics and Therapeutics Committee
RCT	Randomised Controlled Trial
RHMT	Regional Health Management Team
RHO	Regional Health Office
RMU	Rational Medicine Use
SPT	Social Practice Theory
STG	Standard Treatment Guidelines
TB	Tuberculosis
TDF	Theoretical Domains Framework

TTM	Trans Theoretical Model
URTI	Upper Respiratory Tract Infection
WHO	World Health Organization

Preface

I declare that "A systematic approach to improve rational medicine use in Eswatini" is my own work. It is being submitted to the University of the Western Cape for the first time and has not been submitted for any examination or qualification in any other University. I also declare that I have acknowledged all sources used in this work.

Name: Nondumiso Beauty Queeneth Ncube

Signature: NNcube

Date: 27 July 2020

Dedication

I dedicate this work to my two girls - Imanathi and Yenzokuhle Ncube, to encourage you to be hard-working girls that break every societal barrier to reach your potential! I also dedicate it to my late parents: Mr Meshack Jabulani and Mary Ginindza for sacrificing all they had for me to get an education. Though you physically are not with me, you are in my heart always. Mom, you so much believed in education, I know you are super proud of me for pushing to the highest qualification!

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CHAPTER 1: INTRODUCTION

Medicines have the potential to save lives and are essential components of health systems. The World Health Organization (WHO) states that medicines are used rationally when patients are prescribed and dispensed correct affordable medicines in appropriate doses, and for an optimum duration to meet individual patient and community needs (Holloway & Van Dijk, 2011; WHO, 1985). Irrational use of medicines is a global problem that results in mismanagement of patients, wastage of critical resources and unnecessary public health problems (Holloway & Van Dijk, 2011). Examples of factors leading to irrational use include lack of use of clinical guidelines, improper self-medicating, and overuse of injections and antibiotics (Holloway & Van Dijk, 2011). Many studies attribute irrational medicine use to healthcare providers, patient factors, including pressurizing the healthcare provider to prescribe medicines when they are not indicated, have been mentioned as contributors to irrational use (De Geest & Sabaté, 2003). Worldwide, over 50% of medicines are sold, prescribed, and dispensed inappropriately (World Health Organization, 2002).

In response to this problem, in 1984, the World Health Assembly requested the Director-General of the WHO to call an experts' meeting of governments, patients' and consumers' organizations, and pharmaceutical entities to deliberate on methods that could be employed to ensure that medicines are used rationally (WHO, 1985). The meeting, named "Conference of Experts on the Rational Use of Drugs", was held in Nairobi (Kenya) in 1985; and the report of the meeting was published in 1986 to ensure its wide dissemination (WHO, 1985). It was at this meeting that experts came up with the concept of Rational Medicine Use (RMU).

The conference delegates defined RMU as the process of ensuring that medicines are given to the right patient to address their clinical needs, in appropriate doses meeting their individual needs, for an appropriate period, and at the lowest cost to the individual and their community (WHO, 1987). Medicine use is rational (appropriate, proper, correct) when patients receive the appropriate medicines, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost both to them and the community. Irrational (inappropriate, improper, incorrect) use of medicines is when one or more of these conditions is not met (Holloway & Van Dijk, 2011). Examples of irrational use of medicines are when: there is an overuse of injections in cases where oral dosage formulations are as effective; patients self-medicate prescription medicines; prescribers fail to prescribe according to clinical guidelines; antimicrobials are used inappropriately; and when too many medicines are used for a single patient (World Health Organization, 2002). The WHO then devised strategies to address irrational use of medicines including implementation of country policies on Essential Medicines Lists (EMLs) and Standard Treatment Guidelines (STGs), intervention research, as well as monitoring, measuring, and evaluating interventions.

The first Model List of Essential Medicines to help countries develop context-specific national lists was developed in 1977 by the WHO to address irrational use of medicines (WHO, 1977; World Health Organization, 2002). The EML was to be adapted into country policies that address the use of medicines. Since 1977, the WHO Expert Committee has met every two years to update the Model List. The latest EML for adults (the 21st edition) and EML for children (7th edition) were updated in June 2019 (World Health Organization, 2019a, 2019b).

In 1989, the WHO supported and collaborated with a group of professionals (The International Network for the Rational Use of Drugs - INRUD) to conduct intervention research as a strategy to address irrational use of medicines (Laing, 1990). The first phase of this work was to develop a set of indicators called the WHO/INRUD Indicators. The WHO/INRUD indicators look at key factors such as prescribing, health facility and patient care. The research was aimed at testing interventions for improving the rational use of medicines mainly in low resource settings (Laing, 1990). The INRUD built on earlier work which assessed the impact of essential drugs programmes that was conducted in Yemen (Hogerzeil, Sallami, Walker, & Fernando, 1989); and work which tested a regulatory strategy (using the EML) to improve prescribing in Uganda (Christensen & Anokbonggo, 1990). Research conducted by the INRUD resulted in the development of the WHO/INRUD indicators that are still used today to investigate the use of medicines in primary health care facilities (Hogerzeil et al., 1993; World Health Organization, 1993). Hogerzeil et al. reported on how the WHO/INRUD indicators were used in 12 developing countries to improve prescribing practices and behaviors in developing countries.

The WHO/INRUD medicine use indicators are divided into three core groups: Health facility indicators, prescribing indicators, and patient care indicators (World Health Organization, 1993). These indicators are objective measures that can be used to describe medicine use patterns in a health facility, a country, or a region (World Health Organization, 1993). Medicine use indicators can also be used to investigate performance problems in health facilities or individual health care providers (World Health Organization, 1993). Among other indicators, the WHO/INRUD indicators, can be used in intervention studies as measurable outcomes for evaluation, and the methods can be replicated in other settings and results compared.

To date, most studies have focused on first consultation for acute disease or have not specified the type of disease or condition being studied. These studies have mainly focused on describing medicine use practices for outpatient encounters and reporting on irrational use of medicines in more general terms. Research has also focused on strategies to improve RMU, including education, supervision, restrictions on prescribing, and provision of financial incentives for rational prescribing that have been used to address irrational use of medicines (Ross-Degnan et al., 1997; Rowe et al., 2018). Slight improvements in rational use of medicine were shown in studies evaluating the impact of written and face-to-face educational strategies on prescribing practices; with face-to-face interventions having higher impact (Santoso, 1996). Educational interventions alone did not result in sustainable improvements in RMU amongst health workers in Zimbabwe (Trap, et al, 2001). Adding regular supervision (two visits in six months for that study) to the educational strategy resulted in great improvements in measurable medicine use indicators (Trap et al., 2001). Furthermore, the study showed that coupling education with supervision ensured sustained improvements in clinical practice (Trap et al., 2001). A review of audit and feedback strategies to improve prescribing practices concluded that the intervention was effective and improved adherence to evidence-based practices (Ivers et al., 2012). The authors, however, highlighted that patient outcomes are hardly ever measured, thus questioning if improvement in clinical practice automatically improves patient outcomes (Ivers et al., 2012).

Consumer oriented strategies that have been effective in improving RMU are self-management and monitoring programmes involving medicine management pharmacists (Ryan et al., 2014). Educational interventions coupled with counselling or self-management skills training, financial incentives, and delays in prescribing antibiotics have all been shown to have potential in improving medicine use, though the effects of different interventions were inconsistent (Ryan et al., 2014). Similar to health care providers, education alone showed inconsistent effects in changing measurable outcomes though it did improve consumers' knowledge on medicines allowing them to make informed choices (Ryan et al., 2014).

Though strategies to identify medicine use problems in developed and developing countries are available, research around RMU for specific contexts, diseases, and populations has been poorly reported (Ryan et al., 2014). A search of literature on studies evaluating medicine use using the WHO/INRUD indicators for non-communicable diseases (NCDs) revealed very few studies.

Non-communicable diseases are on the rise in low- and middle-income countries mainly due to unhealthy diets, physical inactivity, harmful use of alcohol and use of tobacco, and urbanization. An analysis of prescribing policies and availability of NCD medicines in the Western Balkan Countries showed that prescribing policies and tools being used in these countries were not substantiated by scientific evidence nor did they follow national nor international guidelines (Pekez-Pavlisko et al., 2017). The global status report on non-communicable diseases (2014) states that NCDs were the leading cause of death in 2012 (68% equating to 38 million of the world's 56 million deaths); with most of the deaths being premature at less than 70 years of age (Riley & Cowan, 2014). The reported figures showed that of the global deaths due to NCDs, 28 million of them (82%) were from low- and middle-income countries (Riley & Cowan, 2014). By 2017, the global percentage of people dying from NCDs had gone up to 70% (World Health Organization, 2017). More studies are needed to assess appropriate use of NCD medicines.

Globally, there is a shortage of studies that address rational use of medicines, particularly in the context of a growing burden of NCDs (WHO, 2006). This PhD research aimed to fill this gap by studying rational use of medicines in Eswatini (previously Swaziland) with a focus on WHO/INRUD prescribing indicators including the use of medicines in relation to the diagnoses recorded. The research also supports policy and practice in Eswatini, where literature on medicine use practices is particularly scant, by providing a baseline on prescribing practices in the country.

1.1 Study Setting

The Kingdom of Eswatini (previously Swaziland) is a landlocked country in Southern Africa sharing its borders with South Africa and Mozambique. The country has an estimated surface area of 17,364 square kilometres and, according to the 2017 Census Preliminary Results, a population of 1,093,238 people (Eswatini, 2017). Most of the population (about 77%) resides in rural areas (World Health Organization (WHO), 2015). Eswatini has an estimated life expectancy of 54 years, and has over 50% of its population below 18 years of age (World Health Organization (WHO), 2015). The country is classified as a lower middle income country (World Health Organization

(WHO), 2015). The country is divided into four regions: Hhohho, Manzini, Shiselweni and Lubombo.

1.1.1 Administration of the Health Sector

The country's health system consists of an informal sector which is not regulated by any authority, and where health care is provided by traditional healers. Healthcare is also provided through Western-based services, which forms the formal sector and includes both private and public services. Most of the population that use Western medicine access healthcare services through government-owned or faith-based public facilities (Swaziland Ministry of Health and Social Welfare, 2006). Faith-based public sector facilities are not for profit, are mainly supported by the government, and are not essentially different from government facilities in Eswatini.

The Ministry of Health (MoH) is responsible for ensuring that national health-related administrative and executive functions are performed adequately in the country. It also provides guidance on essential health care package delivery to all levels of healthcare countrywide. The MoH decentralises its activities to regional health offices (RHO) in the four regions, and the RHOs are responsible for the implementation of national health plans and policies. At the regional level, the regional health management team (RHMT) provides technical leadership in the implementation processes. The RHMT comprises of the regional health administrator (overall in-charge), a senior matron from the regional office, senior medical officers and matrons from hospitals and health centers, clinic supervisors (senior nurses based at the regional health office who oversee several clinics in the region), a pharmacist, and other health professionals depending on their availability.

When this study commenced in 2016, the public sector health care delivery system was made up of three referral government and faith-based hospitals: Good Shepherd Hospital, a faith-based hospital in the Lubombo region; Raleigh Fitkin Memorial Hospital, a faith-based hospital in the Manzini region; and Mbabane Government Hospital, the National referral hospital situated in the Hhohho region. In addition, each of the four regions has other hospitals, and these are:

- Pigg's Peak Government Hospital in the Hhohho region;
- Hlathikhulu Government Hospital in the Shiselweni region;
- Mankayane Government Hospital in the Manzini region;

- Lubombo Referral Hospital in the Lubombo region;
- The National Psychiatric Hospital (specialized referral hospital) in the Manzini region;
- The National TB Hospital (specialized referral hospital) in the Manzini region.

The country also has five secondary level (level 2) health centres (which provide primary health care and act as referrals for primary health care facilities, and hence offer outpatient and inpatient services), eight public health units, and 211 clinics (providing outpatient primary health care), and 29 specialized facilities (e.g. army and police hospitals and clinics) At primary level (level 1) there also are community-based health care workers such as rural health motivators and human immunodeficiency virus/human immune deficiency disease (HIV/AIDS) and tuberculosis (TB) programme volunteers. Community health care workers are trained to provide basic health service delivery in the communities. In public and faith-based facilities, health services are accessed in clinics (primary healthcare) in which prescribing and dispensing is handled by nurses (a few clinics have pharmacy assistants); health centres (primary and secondary healthcare) where prescribing is done by nurses and doctors with pharmacy technicians managing and dispensing medicines; and hospitals (primary, secondary and tertiary healthcare) in which doctors and nurses prescribe while pharmacists and pharmacy technicians manage and dispense medicines (Swaziland Ministry of Health and Social Welfare, 2006).

When data collection for this study commenced in 2016, most of the sampled facilities were using paper-based registers, prescription booklets and notepads to prescribe medicines; with only three facilities using an electronic system – Client Management Information System (CMIS).

Table 1 below illustrates the distribution of health facilities by type and region across the country when this study commenced in 2016.

Table 1: Distribution of health facilities by type and region

Facility type	Region: *Hhohho*	*Lubombo*	*Manzini*	*Shiselweni*	**Total**
National Referral Hospital	1	1	1	0	**3**
Regional Hospital	1	1	1	1	**4**
Specialised Hospital	0	0	2	0	**2**
Health centre	2	1	0	2	**5**
Public Health Unit	2	1	2	3	**8**
Clinic with Maternity	4	12	7	2	**25**
Clinic without Maternity	49	33	76	28	**186**
Specialized Facility	10	4	14	1	**29**
Total	**69**	**53**	**103**	**37**	**262**

Source: MOH (2011) Service Availability Mapping

In Eswatini, there is no medical school; hence doctors qualify outside the country. When the data collection commenced in 2017, there had recently been a school of pharmacy established in the country and the first cohort of pharmacists graduated in 2016. Furthermore, there was a nursing college that provided training for pharmacy technicians; the first cohort graduated in 2015. With pharmacy cadres qualifying in-country, the country's health system took a move to mainly employ locally qualified staff. This resulted in contracts for most pharmacy technicians who were initially enrolled into the study in 2016/2017 not being renewed, meaning that this group of participants were not available at the end of the intervention in 2018. Also, the pharmaceutical structure changed in 2017; with posts for regional pharmacists being available and individuals recruited into these positions in 2017/18.

In public sector and faith-based facilities, medicines are dispensed as a comprehensive healthcare package with a charge of about $1 (SZL 15) in secondary level facilities and about $0.33 (SZL 5) in primary level facilities. This fee covers consultation and medicines and excludes tests such as laboratory tests and x-rays. If medicines are not available in public sector and faith-based health facilities, patients are provided with a prescription and advised to buy medicines from private facilities.

1.1.2 Procurement and Supply of Medicines for the Public Sector

Within the formal health system, the procurement unit at the Central Medical Stores (CMS) procures medicines and medical supplies through the government tender board for the public sector, including faith-based health facilities. The CMS receives all supplies and serves as the country's central depot where medicines are stored before distribution to facilities. All public sector and faith-based facilities, regardless of level of care, order medicines directly from the CMS.

1.1.3 Use of medicines

The WHO has several generic guidelines and frameworks for improving the use of medicines and suggests that these be used by countries to improve their medicine use and management (World Health Organization, 1993, 2002). Some countries have adopted the frameworks as they are while others adapted them to meet the needs of their specific contexts. Eswatini is mainly guided by WHO guidelines in many areas of patient management. A search of literature on medicine use in Eswatini was conducted. The principal investigator (NBQN) searched the Ministry of Health website and physically went to their offices to request for unpublished material. The implementing partner (MSH/SIAPS) also provided some documents. Literature and document review helped us to understand policies in place around medicine use in Eswatini and helped us align our interviews with the gaps identified in the policy documents and literature (see Appendix 3 for documents reviewed).

The country has some guiding documents on how medicines should be used. The 2011 National Health Policy (NHP) has no information on the quality of patient care or rational use of medicines. However, it reported a shortage of pharmaceutical personnel in the country as only 48 pharmacists were registered, and few of these were working in the public sector (Swaziland Ministry of Health and Social Welfare, 2006). The Central Medical Stores (CMS) which is responsible for procuring and storing medicines and medical supplies for the country, as well as distributing the supplies to health facilities, was run by five pharmacists and eight pharmacy technicians (Swaziland Ministry of Health and Social Welfare, 2006).

The latest Swaziland National Pharmaceutical Policy (NPP) states that the country does not have mechanisms for monitoring medicine use by health workers and the general public mainly due to lack of the necessary tools, staff and resources (Kingdom of Swaziland Ministry of Health, 2011). The document mentions that existing prescribing and dispensing practices need to be rationalised and streamlined through the development of various RMU tools and staff training (Kingdom of Swaziland Ministry of Health, 2011).

Non-governmental organisations such as Management Sciences for Health/Systems for Improved Access to Pharmaceuticals and Services (MSH/SIAPS) have done substantial work including the establishment of the Standard Treatment Guidelines/Essential Medicines List (STG/EML) and the National Essential Medicines List Committee (NEMLC). They have also undertaken activities to strengthen facility-level Pharmaceutics and Therapeutics Committees (PTCs), and have provided training on medicine management indicators such as ABC and vital, essential, non-essential (VEN) analyses. The training has mainly focused on methods that help inform the quantification process to minimise stock-outs of medicines, and little has been done on RMU. Also, trained personnel mainly worked with antiretroviral (ARV) and to a lesser extent TB medicines as infectious diseases programmes ran parallel to all other healthcare services in the country. In 2011, efforts were made through donor funds to have dispensing for all conditions happen under one roof to minimise stigma particularly for patients on antiretroviral therapy (ART). Though the dispensing has been consolidated, healthcare personnel managing other conditions (besides HIV and TB) have received minimal training around RMU.

1.1.4 Existing interventions to promote rational use of medicines

The first edition of the STG/EML of Common Medical Conditions in the Kingdom of Swaziland was published in 2012 (Government of the Kingdom of Swaziland Ministry of Health & AIDS Relief, USAID, 2012). In 2014 MSH/SIAPS facilitated the formation of the national essential medicines list committee (NEMLC) whose mandate is to maintain a straight-forward detailed process for implementing the use of STGs and updating it to meet local public health needs (Systems for Improved Access to Pharmaceuticals and Services, 2016). At the 75th International Pharmaceutical Federation (FIP) World Congress held in Germany in 2015, SIAPS presented information about how they strengthened a PTC to check for and contain antimicrobial resistance

(Getahun et al., 2015). Besides the availability of the STG/EML and the FIP presentation, there is a paucity of literature on other measures that Eswatini has taken to address RMU.

1.2 Problem Statement

Strategies to identify and quantify medicine use problems in developed and developing countries are available. However, reasons behind irrational use of medicines, research around RMU for specific contexts, diseases, and populations have been poorly reported. Like other settings, Eswatini had minimal information on overall rational use of medicines, rational use for specific diseases as well as use of medicines at different levels of care. To address medicines use practices in public sector and faith-based facilities in Eswatini, in 2013 MSH/SIAPS conducted a survey which revealed that no RMU post-graduate training was taking place in the country, though some on-the-job training was occurring (Kunene et al., 2013). The NPP further mentions that existing prescribing and dispensing practices need to be rationalised and streamlined through the development of various RMU tools and staff training. The current Swaziland Pharmaceutical Strategic Plan (2011-2016), still in existence in 2020, highlights the lack of structures in place to address RMU in the country. These include unavailability of advertising and promotion regulations, lack of initiatives to enforce generic prescribing and dispensing, absence of a mechanism to coordinate functioning and performance of PTCs except review of meeting minutes, and unavailability of mechanisms to enforce use of the STG/EML along with lack of mechanisms to review the current STG/EML (Kunene et al., 2013).

As the country does not have recently updated country-specific guidelines, the first and current treatment guidelines (STG/EML), though mainly tailored for primary healthcare, are those that all levels of care in the country are meant to utilise (Government of the Kingdom of Swaziland Ministry of Health & AIDS Relief, USAID, 2012). A review of literature on RMU practices after publication of the STG/EML did not reveal any studies evaluating impact or informing future development of guidelines. In 2014, MSH/SIAPS facilitated the formation of the NEMLC, and the committee's mandate is to implement a detailed process for promoting the use of STGs and updating these guidelines to meet local public health needs. Processes to review the STG/EML published in 2012, started in 2019 and had not been completed by the time this study was concluded. Another initiative to promote RMU involved facilitating the development of a PTC to identify and contain antimicrobial resistance (Getahun et al., 2015). A report produced in 2017 to address frequent stock out of medicines in the country called for "the monitoring of prescribing of pharmaceuticals in order to ensure adherence to STGs and avoid irrational use of medicines" (The Government of the Kingdom of Swaziland, 2017). Besides these interventions, there is a paucity of literature on other measures that Eswatini has taken to measure or address RMU.

In the context of minimal work on the rational use of medicines in Eswatini, this PhD research examined prescribing practices and factors influencing prescribing practices in the country. Furthermore, the study involved the implementation of an intervention for improving prescribing practices, and evaluated these practices at the end of the intervention. Findings from the study could inform policy development and interventions to monitor and improve the rational use of medicines in the country and similar contexts.

1.2.1 Aim

The aim of the research was to investigate medicine use in public sector and faith-based health facilities with a focus on prescribing practices aligned to recorded diagnoses and factors related to this in Eswatini, on the basis of which an intervention for improving prescribing practices in the country was designed, implemented and evaluated. In this study, diagnoses were categorized as acute or chronic (non-communicable diseases).

1.2.2 Objectives

a) To describe the medicine use situation, specifically prescribing aligned to recorded diagnoses (acute and chronic), investigate reasons for medicine use practices, assess policy around medicine use, and identify factors promoting/impeding rational use of medicines for the management of acute conditions and NCDs in Eswatini.
b) To design and implement an intervention to improve rational medicine use (RMU) appropriate to the Eswatini context.
c) To evaluate the impact of the RMU intervention on prescribing practices.

The study was carried out in three phases: a baseline survey to assess prevailing prescribing patterns (April 2016 – March 2017); intervention implementation (March 2018 – August 2018) and follow-up (September 2018 – February 2019); and evaluation of prescribing practices at the end of the intervention (October 2018) to determine if the intervention had an effect on prescribing practices and whether intervention effects were sustained (March 2019). More detail on the phases will be covered in subsequent chapters.

The next chapter (Chapter 2) is a literature review, which details evidence on the rational use of medicines – including NCDs - in developed and developing countries as well as strategies that have been used to promote rational use of medicines, highlighting the knowledge gaps in the field as a whole.

CHAPTER 2: LITERATURE REVIEW

This chapter presents a review of literature on rational use of medicines in developed and developing countries. It further details studies that have been conducted to investigate irrational medicine use, measure it, intervene, and evaluate effects of interventions that promote rational medicine use. The chapter also presents literature on rational use of medicines and non-communicable diseases (NCDs).

The burden of disease has changed over the years because of changes in lifestyle, urbanization, and migration of people. To understand and address the ever-growing problem of irrational medicine use, different interventional studies have been performed, with most literature focusing on providers' use of medicines (Holloway & Van Dijk, 2011). Literature on consumers' use of medicines is scarce. The choice of medicine for a particular patient is influenced by factors such as prescriber's knowledge and habits, availability of resources in the healthcare system, prescriber's academic background, government regulations, input from the patient, and influence from the prescriber's colleagues (Dias, 2012). In most cases, a visit to a healthcare professional results in at least one medicine being prescribed (Soumerai, McLaughlin, & Avorn, 2005). Soumerai and Avorn (1987) conducted an analysis in the US in which physicians were grouped according to background characteristics such as specialty, urban versus rural practice, age, certification by the board of physicians, size of practice, and intensity of previous target medicine use. Findings from the analysis showed that these characteristics had no effect on prescribing practices. However, a follow-up reinforcement visit to a targeted physician showed this action to be a predictor of prescribing change (Soumerai & Avorn, 1987). The authors state that this finding suggests that repetition and positive reinforcement are crucial in changing prescribing behaviour (Soumerai & Avorn, 1987).

The establishment of efficient systems and processes for measuring medicine use is, therefore, crucial. Measuring medicine use for inpatients is possible, but can be challenging for ambulatory patients (Soumerai et al., 2005). A strategy to measure medicine use that has been used in many studies involves assessing prescribing patterns. There are various reasons for irrational use of medicines. These include prescribing errors such as omissions and oversights (McDonald, 1976); over-promotion of medicines by pharmaceutical sales representatives (Avorn & Soumerai, 1983); prescribers' lack of considerations of the cost of medicines; prescribers not keeping abreast with developments in pharmacology; pressure from patients and their families; and medical aid coverage (Schwartz et al., 1989). Irrational medicines use has also been attributed to factors such as improper advertising, over-work of healthcare professionals, an oversupply of some medicines, and lack of skills and knowledge on RMU (Holloway & Van Dijk, 2011). Lack of practice of evidence-based medicine and decision making, pressure from co-health workers, and high patient volumes which do not allow enough consultation time have also been mentioned as factors promoting irrational medicine use (Dias, 2012; Soumerai et al., 2005).

Holloway and Van Dijk (2011) highlight the importance of measuring the use of medicines (i.e. prescribing, dispensing and patient use) and understanding the reasons before making efforts to address the identified problem. Measurable outcomes for monitoring medicines use include the amount, type of, and the reasons for irrational use (Holloway & Van Dijk, 2011).

The WHO/INRUD indicators have many uses including: increasing awareness on appropriate prescribing, and identifying priorities for action e.g. inclusion of widely prescribed medicines into country essential lists, and quantifying impact of an intervention (Hogerzeil et al., 1993).

2.1 Investigating Irrational Use of Medicines

Globally, the WHO/INRUD indicators have been used to investigate medicine use practices. Most studies have been descriptive cross-sectional surveys to highlight the extent of irrational use of medicines. To assess rational use of medicines in low- and middle-income countries (LMICs), Holloway et al conducted a 10-year review of empirical evidence on patterns of medicine use and intervention effects in primary care facilities. This review revealed that there was little improvement in prescribing practices over time; the average number of medicines prescribed per patient increased from 2.1 to 2.8, and prescribing of antibiotics from 45% to 54% (Holloway, Ivanovska, Wagner, Vialle-Valentin, & Ross-Degnan, 2013).

In Ethiopia, the WHO/INRUD indicators were used to assess medicines use patterns. This study reported that prescribing and dispensing practices were good, however, irrational use of antibiotics, and the average number of medicines per prescription were reported to need intervention (Bilal et al., 2016). Irrational prescribing and use of medicines has also been reported in places such as Yemen, Mali, Sudan, Thailand, and Uganda (Abdo-Rabbo, 2003; Mahmoud et al., 2014; Maiga et al., 2006; Ogwal-Okeng et al., 2004; Pongsupap & Lerberghe, 2006; Yousif & Supakankunti, 2016). In Pakistan, the WHO/INRUD core indicators were used to assess medicine use patterns in 10 primary health facilities in a province. For prescribing indicators, this study found that there was polypharmacy (the average number of medicines per prescription was 3.4 (SD = 0.8) - optimal range = 1.6-1.8); low generic prescribing (71.6% - optimal value = 100%); overuse of antibiotics (48.9% - optimal range = 20.0-26.8%); overuse of injections (27.1% - optimal range = 13.4-24.1%); and prescribing of medicines from the EML was not at 100% (93.4% - optimal value = 100%) (Atif, Sarwar, Azneem, et al., 2016).

A systematic review of prescribing practices conducted in 11 African countries showed that prescribing in the African region was not in line with WHO recommendations: more so in private than in public sector facilities. This study showed that the average number of medicines prescribed per patient encounter was 3.1, generic prescribing was at 68%, antibiotic prescribing was 46.8%, use of injections was 25%, and the percentage of medicines prescribed from the EML was 88% (Ofori-Asenso et al., 2016).

In Kermanshah Province, Iran, irrational use of medicines was also reported among rural family physicians. Prescribing indicators in this study were as follows: average number of medicines per prescription = 3.14; generic prescribing = 95.1%, use of antibiotics = 52.1%, use of injections = 24.4%, and prescribing medicines from the EML was at 95.9% (Ahmadi & Zarei, 2017).

Most studies report on the overuse of antibiotics. Though antibiotics are used to manage bacterial infections (Mohlala et al., 2010), scenarios where antibiotics have been used for non-bacterial infections are reported in literature (Desta et al., 1997; Llor & Bjerrum, 2016; Ncube, Solanki, Kredo, & Lalloo, 2017; Olayemi, Akinyede, & Oreagba, 2006; Risk et al., 2013a). Antibiotics can sometimes be used as empiric treatment of cellulitis (Raff & Kroshinsky, 2016) otitis media (Bareeqa & Ahmed, 2018), and apparent pneumonia (Mathur et al., 2018). The importance of using antibiotics rationally to avoid antimicrobial resistance (AMR), a rising global concern, cannot be over-emphasised. Irrational use of antibiotics along with poor adherence to treatment guidelines has been reported in South Africa (Gasson et al., 2018)

2.2 Measuring Medicine Use

Most medicine use problems are associated with prescribing practices. To extensively study prescribing practices, researchers in developed and developing countries have used the

WHO/INRUD prescribing indicators. Though WHO/INRUD indicators have widely been used, a recent study conducted in Namibia showed that these indicators had low sensitivity and/or specificity and the accuracy to assess prescribing practices in ambulatory care in Namibia was poor (Niaz et al., 2019). Prescribing indicators enable a researcher to observe outpatient prescribing practice and to compare medicine use patterns within facilities, regions and countries, ultimately enabling evaluation of a population's medication prescriptions as well as identifying those medicines that are frequently used (Farias et al., 2007). However, some settings have shown that countries' standard treatment guidelines are not often aligned with the WHO medicine use indicators (Kagoya et al., 2020). There are six WHO/INRUD prescribing indicators (Hogerzeil et al., 1993; World Health Organization, 1993) and they are discussed below. In this study the detailed definitions used in the WHO 1993 manual have been used exactly as described in this global standard.

1) Average number of medicines per encounter

This indicator is used to measure polypharmacy, a scenario where many medicines are used to manage one patient (Masnoon et al., 2017). When measuring this indicator, combination medicines are counted as one, and all medicines are included in the calculation regardless of whether they were dispensed or not (World Health Organization, 1993).

2) Percentage of medicines prescribed by generic name

This indicator makes it possible to measure the proportion of medicines that were prescribed by generic name (World Health Organization, 1993). Further investigations can then be performed to identify the medicines that are prescribed by brand name.

3) Percentage of prescriptions with one or more antibiotic prescribed

This indicator is useful in evaluating overuse of antibiotics, a practice which contributes to antimicrobial resistance - a phenomenon whereby the microbes become resistant to the medicine (Munita et al., 2016).

4) Percentage of prescriptions with one or more injection prescribed

This indicator evaluates overuse of injections. Injectable medicines are generally more expensive, labor intensive, require administration by trained personnel, require strict adherence to aseptic procedures, and are painful at the administration site as compared to oral dosage formulations (Gyawali et al., 2014).

5) **Percentage of medicines prescribed from the essential medicines list**

This indicator makes it possible to measure the degree to which prescribers adhere to national medicines lists or provincial/regional formularies (World Health Organization, 1993). In addition to controlling costs, prescribing within the essential medicines lists ensures that common conditions in a population are managed optimally (Vooss & Diefenthaeler Silveira, 2011). Table 2 shows the optimal values of the prescribing as recommended by the WHO.

Table 2: WHO/INRUD Prescribing Indicators

Drug use indicator	Optimal Value
Average number of medicines prescribed per patient encounter	<2
Percentage of medicines prescribed by generic name	100 %
Percentage of prescriptions that had one or more antibiotic prescribed	≤30 %
Percentage of prescriptions that had one or more injection prescribed	≤10 %
Percentage of medicine prescribed from essential medicines list or formulary	100 %

Source of information: (World Health Organization, 1993, 2002)

2.3 Interventions to Promote Rational Use of Medicines

Methods that have proven to be effective in promoting rational prescribing of medicines in developed countries include structured order forms, focused educational programmes, face-to-face education targeting specific individuals on a particular prescribing problem, and well developed and properly introduced guidelines with feedback (Hogerzeil, 1995; Rowe et al., 2018). Hogerzeil recommended that these interventions be tested in developing countries, and stressed the importance of using clearly defined methods with standardised tools and a reference standard when studying interventions to improve the use of medicines (Hogerzeil, 1995). The use of transparent methods and a reference standard allow researchers to measure and evaluate the impact of different interventions, and also allow for studies to be replicated in other settings and for comparisons between contexts, countries, regions, and facilities to be made (Hogerzeil, 1995). Hogerzeil recommended the use of treatment protocols as a reference standard to study rational prescribing particularly when conducting audits (Hogerzeil, 1995).

Amongst methods used to change healthcare professionals' behaviours, tailored interventions are often recommended (Baker et al., 2015). Tailoring is a process that involves a minimum of three steps: identifying determinants of healthcare practice, designing implementation interventions matching the determinants, and finally applying and assessing the implementation interventions (Wensing et al., 2011). Tailored interventions approaches are designed to bring about changes in healthcare practices after assessing determinants of those practices in a setting (Wensing et al., 2010).

A review of the literature on tailored interventions to overcome identified barriers to professional or healthcare outcomes showed that there was no single way of tailoring interventions to change professional practice (Baker et al., 2010). The authors state that interventions tailored to prospectively identify barriers to change health professionals' practices are more likely to improve practice compared to disseminating guidelines, educational material or not intervening at all (Baker et al., 2010). The authors recommended that further research be conducted to ascertain which are tailored interventions that work so as to report on ways used to identify barriers to change, and explain how this informed the process of tailoring the intervention (Baker et al., 2010).

In developing countries, many studies have been conducted to look at prescribing patterns; though the literature on the impact of interventions to change medicine use practices is limited (Le Grand et al., 1999). A systematic review of interventions to improve the use of medicines in primary care settings found strong evidence to support the use of strategies that targeted behavior (Ross-Degnan et al., 1997). Though prescribers' knowledge on RMU has been used as an outcome measure for interventions (Walker et al., 1990), Hogerzeil argued that adequate knowledge does not always translate to rational prescribing behaviour since there are other factors that influence prescribing such as patient demand, prescriber's preference based on their experience, marketing of medicines, etc. (Hogerzeil, 1995). Santoso (1996) highlighted that prescribing practices are influenced by economic, regulatory, educational, and managerial factors (Santoso, 1996).

In line with factors influencing prescribing behaviour, Hogerzeil divided strategies to promote rational prescribing into four categories:

1) Educational strategies

These strategies include face-to-face interactions, seminars, printed material and bulletins. Educational interventions are most widely used to disseminate information. In the 1980s, Leventhal and Cleary suggested that one-on-one educational methods can be effective in changing health behaviour (Leventhal & Cleary, 1980). This finding was supported by various studies that looked at prescribing behaviours (Avorn & Soumerai, 1983). The one-on-one approach particularly worked for pharmaceutical sales representatives who visit medical doctors and pharmacists to market their products (Soumerai et al., 2005). Avorn and Soumerai found that these visits, coupled with printed material, reduced the prescribing of medicines in problematic categories for about nine months after the start of the intervention (Avorn & Soumerai, 1983). In support of the face-to-face interaction with the prescriber, Schaffner et al. showed that inappropriate prescribing of targeted medicines reduced when practitioners were visited by "physician-counsellors" (Schaffner et al., 1983).

Avorn & Soumerai (1983) argue that though many educational interventions exclusively rely on dissemination of printed material such as medicine therapy protocols, newsletters and medicine bulletins to provide information; which are not enough for correcting problems with prescribing. The authors' findings were that the printed material alone did not change prescribing practices (Avorn & Soumerai, 1983).

In Indonesia, a three-arm study was conducted comparing: small group face-to-face education conducted in facilities, formal seminars conducted at the district level, and a control arm aimed to improve appropriate prescribing of medicines in the management of acute diarrhea (Santoso, 1996). Participants in the two experimental arms were also provided with written material on the management of the condition. The interventions were given once-off with no follow-up monitoring or supervision. Findings from this study showed equal effectiveness for the experimental interventions in the improvement of prescribers' knowledge levels (Santoso, 1996). Literature from other studies looking at educational interventions also shows that printed material has minimal influence on prescriber behaviour (Avorn & Soumerai, 1983) and that if a change is noticed it is for a short period (Berbatis et al., 1982; Schaffner et al., 1983).

Since most interventions on improving prescribing had been tested in developed countries, efforts were made in the early 1990's to study the use of medicines in developing countries. Laing et al.

suggested that printed material be developed through wide consultation and feedback, and be disseminated by intensive educational programmes as had been done in Uganda (Christensen & Anokbonggo, 1990), Zimbabwe (Laing & Ruredzo, 1989) and Yemen (Hogerzeil et al., 1989).

Printed educational materials have yielded greater effects in improving RMU if coupled with other methods such as group process and case management, audit, and supervision (Ross-Degnan et al., 1997). Findings also showed that training had varied effects with regard to duration; and variations were attributed to differences in the quality of training and the presence or absence of supervision (Ross-Degnan et al., 1997). A randomised controlled trial in Zambia to evaluate the effect of educational seminars on RMU and patient quality of care showed that the intervention positively influenced prescribers. Fewer patients were prescribed antibiotics (i.e. rational use of antibiotics) and the quality of care improved (recording of history taking, examination and diagnosis) (Bexell et al., 1996). The study concluded that a systematically organised continuing education programme with repeated seminars could significantly improve healthcare professionals' management of patients including prescribing of medicines (Bexell et al., 1996).

In 1996, in a primary healthcare setting in Mexico, a 4-stage study of physicians' prescribing patterns was conducted. The stages were: baseline to evaluate physicians' prescribing behaviour; intervention using a managerial peer review committee and an interactive educational workshop; post-intervention evaluation of short-term impact; and follow-up of long-term impact 18 months after the workshop (Pérez-Cuevas et al., 1996). Improvements in prescribing patterns from baseline to post workshop were noted. These improvements, however, dropped at the end of the follow-up period to almost baseline values. The authors concluded that interactive educational strategies and managerial interventions have the potential to improve physicians' prescribing practices but may not be sustained (Pérez-Cuevas et al., 1996). Multifaceted interventions are reported to often produce desired results (Bbosa et al., 2014). Other studies in literature also echo that interventions may have positive impacts on rational use of medicines but those impacts tend to drop post intervention (Ibrahim, Wertheimer, & Babar, 2017; Trap et al., 2001).

A review of global methodologies reported to have positive impacts in improving pharmaceutical use in primary care settings in developing countries was conducted in 1997. Findings from the review showed that printed material had no impact; while training of healthcare professionals using role playing, lectures, giving healthcare professionals opportunities to practice skills, and group problem-solving were found to improve medicines use (Ross-Degnan et al., 1997). The authors also found that multimodal strategies including focusing on a single outcome at a time, using opinion leaders as trainers, repeated sessions, and training at the work site all improved medicines use (Ross-Degnan et al., 1997).

Self-instruction material has also been used to address irrational prescribing. Soumerai et al. (2005) describe self-instruction programmes as those that try to increase individual physician involvement and clinical relevance thus making these interventions beneficial over didactic material alone. On the other hand, it is argued that participatory learning is important in improving physician practice patterns (Eisenberg & Eisenberg, 1998). A review of studies that used self-instruction material also showed that printed educational material may be useful in laying the foundation for more effective approaches (Soumerai et al., 2005). In support of this finding, it was shown that in situations where the use of certain medicines poses risks to the patients prescribers may reduce prescribing those medicines using information from various sources (Soumerai et al., 2005).

Prescribers' academic backgrounds and experience afford them knowledge on medicines. However, there are uncertainties as to how information is shared among prescribers and with patients. In healthcare knowledge, translation methods such as educational programmes, reminders, and feedback have been used though these have not been rigorously evaluated (Wensing et al., 2010). Wensing et al. (2010) reported that active self-study material/websites including active educational interventions such as outreach-based visits were likely to be effective. The authors also reported that though interventions vary in their methodological quality, the effect of individual approaches in changing health professionals' behaviours was minimal (around 10%) (Wensing et al., 2010).

2) Managerial strategies

These strategies include restrictions on prescribing e.g. maximum number of medicines per prescription, patient co-payment strategies, structured prescription forms, budget or cost restrictions, and endorsement of prescriptions by higher qualified consultants (Hogerzeil, 1995; Holloway, Rosella, & Henry, 2016). Managerial interventions target prescribers and guide the decisions they make through limiting medicines available for them to prescribe (Eriksen et al., 2017), monitoring use of guidelines and providing supervision, and auditing prescriptions and giving feedback to prescribers (Dias, 2012). Interventions that enforce policies such as national essential medicines policies and those forcing prescribers to adhere to national guidelines are reported to promote rational use of medicines (Chao et al., 2018). Though enforcing adherence to treatment guidelines may be effective in promoting RMU, literature shows that adherence to these guidelines is often poor (Dogan et al., 2016)Many authors advocate providing information to healthcare professionals on their practice and performance as a popular strategy to improve professional practice. However, reporting of patient-specific listings of prescribed medications showed that reporting detailed medicine use profiles for individual patients without clear suggestions for behavioural change or follow-up did not affect busy physicians' prescribing habits (Soumerai et al., 2005).

Managerial strategies involving effective monitoring and supervision, group process, regular audit and feedback were found to have moderate to large impacts on certain targeted practices (Ross-Degnan et al., 1997). It is crucial for the monitoring and supervision to be supportive to prescribers so that they do not view the process as punishment (Dias, 2012). The authors recommended that interventions be explored further while tracking the sustainability of the improvements they make in a broader range of problem practices.

A systematic review of the effects of audit and feedback on patient outcomes and healthcare professionals' practice showed that the strategy can be effective in improving practice though the effects are usually small to moderate (Jamtvedt, Young, Kristoffersen, Thomson O'Brien, & Oxman, 2003). Another review found that feedback to healthcare professionals influences clinical practice to a certain extent if it is part of a broader strategy that is aimed at decision makers who already concur with the process of reviewing their practice (Mugford et al., 1991). Adding interventions such as reminders, opinion leaders, outreach, incentives, patient educational material, a practice-based seminar, self-study, and assistance in developing a recall system/office system/quality improvement tool to audit and feedback had no overall increase in effect, though these processes showed mixed results (Jamtvedt et al., 2003).

3) Economic strategies

These are strategies in which incentives are offered to healthcare providers, health facilities and patients. Economic interventions are health system-oriented and involve the provision of financial incentives such as reimbursement to prescribers (Dias, 2012). Financial incentives impact how medicines are used, hence health systems need to have processes in place that ensure that financial incentives do not promote irrational use of medicines. Some interventions that have been implemented in certain settings to minimise irrational medicine use through financial incentives include: not allowing prescribing doctors to dispense/sell medicines, implementing flat dispensing fees regardless of the price of individual medicines, charging user fees per medicine and not per prescription, and only allowing medicine reimbursements if prescribing is in line with national clinical guidelines (World Health Organization, 2002).

4) **Regulatory strategies**

These are strategies such as critical review of medicines and product information, patient information leaflets and data sheets before market approval, scheduling of medicines, and specifying prescriber levels for each medicine. Regulatory interventions come into play in situations where the health system has policies that promote the use of generic medicines, have specifications as to who can prescribe and dispense different medicines (e.g. scheduling of medicines in South Africa and Eswatini), and removal from the market of questionable medicines (Dias, 2012). Regulatory interventions are also system-oriented and put restrictions on what prescribers can prescribe.

To improve physicians prescribing, Soumerai et al. (2005) conducted reviews of studies that looked at non-regulatory and non-commercial interventions such as prescription audits plus feedback, pharmaceutical detailing, government warnings, printed educational material, reminders at the time of prescribing, and physician-counsellor approaches. Studies looking at the prescription audits and feedback to prescribers suggested that ongoing feedback could be effective in increasing prescription of generics and prescribers' compliance with treatment guidelines (Soumerai et al., 2005). Educational computer-generated reminders on specific medicines improved knowledge on those medicines; though this knowledge change was not evident after the messages stopped (McDonald, 1976).

Though interventions combining managerial and economic strategies have been shown to be more effective and sustainable in promoting RMU, only 25% of reported interventions use either economic or managerial interventions (Holloway et al., 2016).

2.4 Methods to Evaluate Interventions that promote rational use of medicines

Interventions to measure medicine use have been conducted widely, but literature on evaluation of interventions to show evidence of their impact is scarce. Different kinds of studies such as time series (Zhen et al., 2018), mixed methods (Santoso, 1996), and systematic reviews (Johnson & May, 2015) have been used to study interventions for promoting rational use of medicines.

In 1996 Santoso reported on a randomised controlled trial (RCT) that he conducted to evaluate the efficacy of a small group face-to-face and a formal educational seminar intervention in promoting appropriate prescribing for acute diarrhea. The interventions were given once-off without follow-up. Findings from this study showed that both interventions were effective in reducing prescribing of antimicrobial agents for the management of acute diarrhea (Santoso, 1996). Another educational intervention, interactional group discussion – an innovative behavioural intervention, showed significant improvements in medicine use again using an RCT model with randomisation by facility (Prawitasari Hadiyono et al., 1996). An RCT of prescribing training in a South African province showed that training changed prescribing behavior; with the positive effects of the training lasting three months after the intervention (Meyer et al., 2001). A study conducted as a follow on to an RCT that involved training and education of healthcare providers and consumers on appropriate prescribed and encouraging healthcare providers to review their colleagues' prescribing practices, yielded positive long term and sustained results in reducing the antibiotic prescribing rate (Wei et al., 2019). Wei et al. (2019) recommended constant refresher trainings for healthcare providers and ongoing prescription audits to maintain effects of education as an intervention. Though educational interventions seemed to yield positive results in promoting rational use of medicines some studies showed that such interventions do not work all the time. Findings from a cluster RCT using educational meetings and group detailing as an intervention, showed that the intervention did not have significant improvements in increasing adherence of prescribers to ward lists or hospital drug formularies (Plet et al., 2014).

To study the effect of antibiotic stewardship interventions (audit with feedback and academic detailing) in selected wards in hospitals in Norway, a cluster RCT showed that the intervention increased adherence of prescribers to national guidelines (Wathne et al., 2018). Furthermore, the study showed that healthcare workers discussions on prescribing behaviours and setting targets to change prescribing practices promoted rational use of medicines (Wathne et al., 2018). A parallel-group cluster RCT conducted in primary care facilities in the United Kingdom used electronic health records to deliver an intervention which was multicomponent and included a webinar, monthly reports of general practice-specific data for antibiotic prescribing and decision support tools to inform appropriate antibiotic prescribing for respiratory infections. This study yielded positive results in reducing antibiotic prescribing for self-limiting respiratory tract infections over the 12 months during which the intervention was rolled out (Gulliford et al., 2019). In developing countries, an assessment of the effectiveness of antimicrobial stewardship programs in primary health care facilities in showed that the implementation of such problems was poor (Brinkmann & Kibuule, 2020).

In summary, to study and evaluate medicine use practices in developing countries, the following interventions have been used: availability and use of STGs, availability and use of up-to-date and context specific EMLs, availability of established and functional PTCs, problem-based pharmacotherapy undergraduate education based on national STGs, and problem-based in-service education of healthcare practitioners as part of their continuous professional development (Laing, Hogerzeil, & Ross-Degnan, 2001). Education alone was reported to have unsustainable improvements; but when coupled with direct supervision over a period - the combined interventions were shown to improve the efficacy and effectiveness of RMU practices (Trap, Todd, Moore, & Laing, 2001). A review of the effect of implementing RMU interventions in developing and transitional countries was conducted using information extracted from the WHO database between 2002 and 2008 (Holloway & Henry, 2014). Findings from this review showed that implementing medicine policies that promoted undergraduate teaching on STGs, free access and availability of essential medicines, and existence of a quality use of medicines promotion unit at the ministry of health improved rational use of medicines (Holloway & Henry, 2014).

Interventions such as interactive group processing on RMU among healthcare practitioners or consumers, educating pharmacists and medicine representatives on how to give productive advice on health and medicine use, and allocating government resources encouraging active participation of consumer organisations in public education on medicines showed to have potential to improve medicine use but needed further testing (Trap et al., 2001). Time series that study medicine management processes over time are also reported in literature (Trap et al., 2016, 2020).

2.5 Sustainability of interventions implemented in sub-Saharan Africa

Literature shows that interventions implemented in sub-Saharan Africa are difficult to sustain. A systematic review conducted in 2015 reported that 46% of outcomes from interventions implemented in the region were sustained for interventions focusing on communicable diseases, mainly HIV/AIDS and malaria (Iwelunmor et al., 2016). In the review, factors identified to facilitate sustainability of interventions both early on and after intervention implementation were community ownership and mobilization, while changes in the society and the state of the ecological and social systems were barriers that influenced the sustainment of interventions in sub-Saharan Africa (Iwelunmor et al., 2016). Medicine shortages in the African region also make it difficult to sustain interventions for promoting rational use of medicines (Modisakeng et al., 2020).

2.6 Rational Medicine Use and NCDs

Non-communicable diseases (NCDs) are an increasing public health concern world over. Globally, NCDs kill about 71% of people (41 million) every year; with 15 million (37%) deaths happening in the 30 to 69 year age group, and most deaths (85%) occurring in low- and middle-income countries (LMICs) (World Health Organization, 2018). The NCDs have been categorised into four broad groups: diabetes (which accounts for 1.6 million deaths annually), respiratory diseases (accounting for 3.9 deaths annually), cancers (accounting for 9 million deaths annually), and cardiovascular diseases (contributing the highest proportion of NCD deaths annually at 17.9 million) (The World Health Organization, 2018). Increased blood glucose (diabetes), and increased blood pressure (hypertension) are increased by factors such as lack of physical activity and unhealthy diets which are fueled by ageing populations, as well as unplanned urbanization and globalization of unhealthy lifestyles (The World Health Organization, 2018).

Cardiovascular diseases (CVDs), a group of disorders of the heart and blood vessels, are the highest cause of death the world over. Low- and middle-income countries are most affected by NCDs, with 37% of deaths occurring due to CVDs in this region (World Health Organization, 2017). Hypertension (HTN), also referred to as raised blood pressure, is defined as a systolic and/or diastolic blood pressure ≥ 140/90mmHg (WHO, 2013). In 2015, hypertension was more prevalent in women than in men (24.1% vs 20.1%) and more hypertensive people were residing in low- and middle-income countries (World Health Organization, 2013). Since 2010, Eswatini has experienced a surge in non-communicable diseases (NCDs). The Steps Survey conducted in 2010 showed that 43.8% of the population was overweight while 20.5% was obese. Twenty-five percent of the population (24.5%) had increased blood pressure, and of these 78.9% were not on blood pressure lowering medication. Routinely collected data showed that in 2017, NCDs accounted for 30% of outpatient cases and 14% of the inpatient cases (Akl et al., 2014). The follow-on Steps Survey conducted in 2014 showed that of the 3281 participants included in the survey, 17.3% women and 7.2% of men had uncontrolled increased blood pressure (WHO, 2014). Of note is that 87% of women and 72.8% with increased blood pressure were not on treatment (WHO, 2014). Literature attributes the increase in prevalence of HTN to ageing, population growth, and behavioural risk factors including obesity, sedentary lifestyles, unhealthy diets, over consumption of alcohol, and stressful lifestyles (Jarari et al., 2015).

It is crucial for people with hypertension to be identified early and linked to care. Care for hypertensive people includes counselling on lifestyle modification (healthy eating, increased physical activity, smoking cessation) as well as management with pharmacological agents (World Health Organization, 2017). Pharmacological agents used for the management of HTN belong to four classes: diuretics, β-blockers, calcium channel blockers, and renin–angiotensin inhibitors.

Evidence from studies conducted in clinical settings shows that reducing blood pressure with antihypertensive medicines improve clinical outcomes such as reducing the risk of heart failure, stroke, myocardial infarction, end-stage renal disease and revascularisation procedures (World Health Organization, 2013). The Joint National Committee (JNC 8) guidelines, published in 2014, highlight the importance of controlling both systolic and diastolic blood pressure and states specific cut-offs that should be used for age and comorbidity (Armstrong, 2014). Though in the past diuretics were recommended as first line medicine to control hypertension, the JNC 8 guidelines recommend the addition of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) to diuretics as first line medicines (Armstrong, 2014; Jarari et al., 2015). As second- and third-line therapy, the JNC 8 guidelines recommend increased doses of first line medicines or combinations of thiazide diuretics, ACE inhibitors, calcium channel blockers (CCBs) and ARBs (Armstrong, 2014). Furthermore, the guidelines recommend that hypertension management be limited to four classes of medicines: ACE inhibitors, ARBs, calcium-channel blockers and thiazide diuretics (Armstrong, 2014).

Regarding age, the JNC 8 guidelines state that blood pressure in patients ≥60 years without kidney disease, the goal BP level should be <150/90 mmHg. The goal BP should be <140/90 mmHg in patients over ≥60 years who also have chronic kidney disease (CKD) or diabetes or both conditions, and those patients between 18 and 59 years old without major comorbidities (Armstrong, 2014). Though several guidelines, particularly the latest JNC 8, are available to guide clinicians in the management of hypertension, evidence shows that the guidelines are rarely used (Jarari et al., 2015). In some settings, e.g. Kenya, training has been shown to improve adherence to guidelines (Mbui et al., 2017).

A hospital based study in Ethiopia looking at prescribing patterns for antihypertensive medicines found that HTN was mainly managed with one medicine; with hydrochlorthiazide (60.2%) being the most prescribed medicine, followed by enalapril (17.5%), while atenolol was the least prescribed medicine (1.6%) (Abegaz et al., 2017). The hydrochlorthiazide and enalapril combination was highly prescribed as dual therapy (53.7%), followed by hydrochlorthiazide plus nifedipine (29.4%), while hydrochlorthiazide combined with atenolol was least prescribed (3.5%) (Abegaz et al., 2017). Hydrochlorthiazide combined with atenolol and enalapril was the commonly prescribed triple therapy (40%), while enalapril plus spironolactone and nifedipine was hardly prescribed (11.1%) (Abegaz et al., 2017). This study concluded that twice daily dosing of antihypertensive medicine was more effective in controlling blood pressure compared to once-daily dosing (Abegaz et al., 2017). Prescribing patterns for HTN in Kenya showed that prescribers highly complied (75%) to treatment guidelines; and this adherence to guidelines was attributed to training of prescribers (Mbui et al., 2017).

In a Nigerian study, and contrary to the Ethiopian study, most of the hypertensive patients were on multi-medicines therapy, and less than 20% were on monotherapy (Adejumo et al., 2017). Diuretics were the most prescribed class of antihypertensives (64.7%), followed by calcium channel blockers (54.9%), and angiotensin converting enzyme inhibitors (44.6%) (Adejumo et al., 2017). In this study, though prescribing for HTN complied with recommended guidelines, the authors reported that blood pressure control on these patients was unsatisfactory (Adejumo et al., 2017). A study in India also showed that mono-therapy (48.94%) was often used in managing hypertension, followed by fixed dose combinations (35.04%) and use of multi-medicines (16.01%) (Rachana, 2014). However, contrary to the Nigerian and Ethiopian study where diuretics were most prescribed, the most commonly prescribed antihypertensive class of medicines were the calcium channel blockers (38.59%) followed by beta blockers (24.07%) (Rachana, 2014).

The NCD, type 2 diabetes mellitus (T2DM), a metabolic disorder, occurs when the pancreas fails to produce enough insulin or when the body is unable to utilise the insulin hence the insulin stays in the blood circulation for long times (World Health Organization, 2016). The condition is characterised by raised blood glucose levels and, if poorly managed, leads to complications that can result in death (World Health Organization, 2016). In 2014, the WHO estimated that globally 422 million adults were diabetic, and prevalence had doubled from 4.7% in 1980 to 8.5% in 2014 (World Health Organization, 2016). The International Diabetes Federation (IDF) projected that the global proportion of adults with diabetes will increase by 55% in 2040; with Africa projected to increase by 140.9% (IDF, 2017).

Type 2 diabetes mellitus is on the increase particularly in LMICs due to increasing urbanization, which has come along with lifestyle changes (Guariguata et al., 2014). Reduced physical exercise, obesity, and aging populations play a part in increasing the prevalence of type 2 diabetes globally (Ginter & Simko, 2013). A study conducted in the UK between 2004 and 2014 showed a 2.05% increase in diabetes prevalence particularly for patients aged 16-34 years of age, with higher prevalence rates observed in men (Zghebi et al., 2017). On the contrary, in India, T2DM was most prevalent in the age group 51- 60 years, and women (54% vs 46%) were mostly affected (Sharma et al., 2016). In 2015, the prevalence of diabetes in Africa was 3.2% (2.1 – 6.7%), and although the region is predominantly rural (61.3%), most of the people with diabetes (58.8%) resided in cities (IDF, 2017). Though the African region is predominantly rural (61.3%), most diabetic people (58.8%) live in cities and in the highly populated countries - Ethiopia (1.3 [0.8-3.5] million), Nigeria (1.6 [1.2-3.8] million), the Democratic republic of Congo (1.8 [1.5-2.2] million), and South Africa (2.3 [1.2-4.6] million) (The Society for Endocrinology, 2017). Notably, Africa has the highest proportion (66.7%) of people living with diabetes who have not been diagnosed (IDF, 2017).

The International Diabetes Federation reported that the prevalence of diabetes among the 20-79 years old age group in Eswatini was 2.5% (CI 1.5 - 4.3) and the projected prevalence for 2045 is 3% (CI 1.9-4.9) (IDF, 2017). The proportion of people who had not been diagnosed with diabetes was reported to be 49.7% (IDF, 2017). A survey conducted in 2014 in Eswatini revealed that

14.2% (N= 2892) of participants had increased blood glucose step (Ministry of Health Swaziland Government, 2014).

Though the global burden of T2DM is high, some measures can be put in place to prevent or delay the onset of the disease. Such measures include: avoidance of tobacco, eating a healthy diet (avoiding intake of saturated fats and sugar), achieving and maintaining a healthy body weight, and increasing physical activity (World Health Organization, 2016). To reduce NCD-related mortality countries need to actively monitor the burden of NCDs, identify quick wins in managing these and set country-specific priorities to manage NCDs.

A study looking at prescribing patterns of antidiabetic medicines in an Italian population of adults above 65 years of age between 2010 and 2014 showed that 33.9% of patients were treated with monotherapy in 2010 vs 38.6% in 2014 (Orlando et al., 2015). This study showed that the proportion of patients on metformin (biguanide) increased from 18.2% (2010) to 23.7% (2014), while that of patients on sulphonylureas decreased to 7.2% in 2014 vs 11% in 2010 (Orlando et al., 2015). Similarly, in Brazil, 60% of diabetic patients were treated with monotherapy; with 32% of the patients on metformin and 24.6% on glibenclamide (Guidoni et al., 2012). A study in India also showed that metformin was predominantly prescribed as monotherapy (42.3%) and as well as in combination therapy (6.9% in combination with glimepride, 4.6% in combination with glibenclamide, 2.9% in combination with pioglitazone, and 1.71% respectively in combination with gliclazide and voglibose) (Venkateswaramurthy et al., 2016). Another study conducted in an Indian hospital on patients with T2DM showed that the most commonly used medicine for the condition was insulin (86.7%), then biguanides (35.8%), and sulfonylureas (28.0%) (Sharma et al., 2016). A prospective study carried out on outpatients in a tertiary level hospital in Mumbai showed that the average number of antidiabetic medicines per prescription was 1.4, and although sulphonylureas were the most prescribed class of medicines, metformin was commonly prescribed as monotherapy. This study also found that there was a high use of insulin in type 2 diabetes (Agarwal et al., 2014).

Asthma is another NCD that the world is battling with. The WHO defines asthma as a chronic disease of the air passages of the lungs which inflames and narrows them (World Health Organization, 2020). In 2016, it was estimated that 339 million people globally had asthma, with children predominantly affected by the disease (Vos et al., 2017). The WHO estimated that globally, 417 918 people died from asthma-related illnesses in 2016 (Vos et al., 2017); with most deaths occurring in low-and lower-middle income countries (World Health Organization, 2020). Risk factors for developing asthma include inhaled particles that may irritate airways or trigger allergic reaction (World Health Organization, 2020). Asthma can be triggered by exercise, air pollution and allergic reactions. In some cases, asthma is spontaneous and characterised with shortness of breath and wheezing, chest tightness and coughing, especially at night or early morning (Ait-Khaled et al., 2008). In Eswatini, the prevalence of clinical asthma was estimated to be at 9.7 of the population (To et al., 2012). Asthma is under diagnosed and poorly managed; for instance, in South Africa less attention is paid to asthma partly because the health system is overwhelmed with communicable respiratory illnesses such as pneumonia and TB (Zar & Lalloo, 2013).

To help diagnose asthma, a patient who presents with chest symptoms (cough, breathlessness and/or wheezing often at night) that have daily variations and cause the patient to wake up at night should be suspected of having asthma (Ait-Khaled et al., 2008). Such patients should be carefully examined; any other alternative diagnosis excluded, and if the symptoms persist the diagnosis of asthma should be confirmed. A spirometer should be used to measure lung function and confirm airway obstruction (Schellack et al., 2019). If obstruction is present, the use of a bronchodilator (short-acting β2-agonist) can reverse the obstruction (Schellack et al., 2019). If it is not possible to diagnose asthma using a spirometer, a peak flow meter can be used (Schellack et al., 2019).

Asthma can be managed using non-pharmacological and pharmacological interventions. The long term goals of managing asthma are to minimize risks of persistent air flow obstruction, exacerbations of asthma, side effects of medicines, and asthma-related mortality (Global Initiative for Asthma, 2020). Non-pharmacological interventions include: maintaining a healthy diet, weight reduction, physical activity, dealing with emotional stress, smoking cessation, and avoidance of indoor allergens, occupational exposures, and medications that exacerbate asthma (such as non-steroidal anti-inflammatory medicines) (Global Initiative for Asthma, 2020). For pharmacological management, the Global Initiative for Asthma (GINA) no longer recommends treatment with short-acting β2-agonist (SABA) alone. The reason for this is that evidence shows that frequent use of SABA only increases the risk of asthma exacerbations and does not protect patients from severe exacerbations (Global Initiative for Asthma, 2020). The GINA recommends symptomatic use or daily low dose inhaled corticosteroid (ICS)-containing controller treatment to reduce the risk of serious asthma in adolescents and adults suffering from asthma (Global Initiative for Asthma, 2020).

Studies on rational use of medicines have mainly focused on quantifying the magnitude of irrational use of medicines using the WHO/INRUD indicators. Reasons behind irrational prescribing and use of medicines have not been explored particularly in the growing phase of NCDs. To extensively study prescribing practices in Eswatini we used the conceptual framework discussed in Chapter 3.

CHAPTER 3: STUDY FRAMEWORKS

3.1 Conceptual Framework

To study rational medicine use practices among policy makers at the National Department of Health (NDoH) and frontline medicine managers (prescribers (doctors and nurses), and pharmacy personnel (pharmacists, pharmacy technicians and pharmacy assistants)) in Eswatini, the study used a theory informed implementation intervention (the Theoretical Domains Framework (French et al., 2012)) in phases, as illustrated in Figure 1.

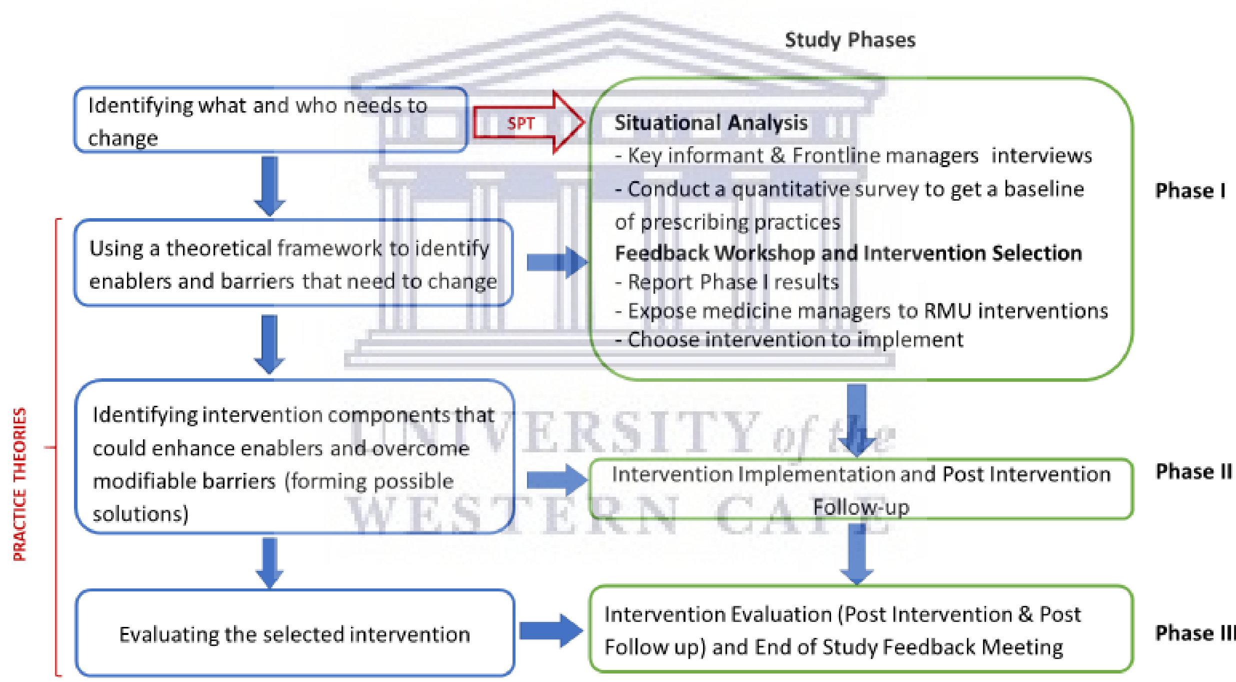

Figure 1: Study theories and procedures

The study was conducted in three phases:

Phase 1

A situational analysis to establish practices and processes in place regarding RMU practices in the country was conducted. This phase helped us identify possible pathways of change, as well as enablers and barriers to these pathways. Theories of behavior change were then used to design and implement a rational medicine use intervention to improve RMU in prescribing practice.

Phase 2

To enhance enablers and overcome modifiable barriers of change in RMU practices, an RMU intervention was implemented with frontline medicine managers in selected facilities across the four regions of the country.

Phase 3

During this phase, outcomes were measured to ascertain if there were changes in RMU practices pre- and post-the intervention in intervention and control facilities. The WHO/INRUD prescribing indicators were used as objective outcomes while participants' perspectives on change were used as subjective outcomes.

In conceptualising the study, we realised that prescribing is influenced by both internal (behaviour – what people do) and external factors (skills, resources, peer influence). The importance of understanding why people behave in a certain way was key for us to address prescribing practices in the country. Generally, practice comprises of several different elements linked together. Reckwitz (2002) states that practice is made up of three elements: competence, meaning and materials. Competence is the practical consciousness, shared understanding of appropriate performance, and deliberately cultivated skill; meaning is defined by mental activities, motivational knowledge and emotion; and materials are the tools, the human body itself, infrastructure, hardware and objects (Reckwitz, 2002).

We used the social practice theory (SPT) to determine the relationship between practice and the context of Eswatini within which prescribers function. The SPT was chosen as it is able explore the relationship between context and practice (Reckwitz, 2002). The SPT was used to study current prescribing practices to identify who, among frontline medicine managers, needs to change for medicines to be prescribed rationally.

Factors influencing prescribing behaviour and the SPT

As outlined in Chapter 2, the literature highlights a range of provider, patient and health system factors that influence prescribing behaviour. Table 3 maps these factors onto the SPT domains.

Table 3: Factors affecting prescribing behaviours and how they link to the SPT

Type of Factor and SPT Element	Factors
Provider (Competence)	Practitioner's experience and level of education, inadequate training of healthcare providers, visits by pharmaceutical sales representative (Fadare et al., 2018; Kamuhabwa & Kisoma, 2015; Prosser et al., 2003; Vancelik et al., 2007), physician's age and gender (Carrin, 1987; Watkins et al., 2003), prescribers' perception that the patient wants certain medicines and fear that not giving antibiotics will lead to patients having medical complications (Altiner et al., 2007; Birhanu Demeke et al., 2017; Cockburn & Pit, 1997; Kumar et al., 2003; Vazquez-Lago, Lopez-Vazquez, López-Durán, Taracido-Trunk, & Figueiras, 2012; Wood et al., 2013), fear that prescribers will lose patients if they do not give in to their demands (Ofori-Asenso et al., 2016).
Patient-provider interaction (shared meaning)	Patient expectations and demands (Ofori-Asenso et al., 2016).
Health system context (Material)	Health systems factors such as lack of continuous professional development, lack of structures that provide updated and evidence-based information on medicines in current use, patient load, and influences of pharmaceutical representatives (Chigome et al., 2020; Kamuhabwa & Kisoma, 2015; Prosser et al., 2003; Vancelik et al., 2007), socio-economic characteristics of the environment in which practice is conducted, health demand (Watkins et al., 2003), availability of materials to work with (Baker & Klein, 1991; Forster & Frost, 1991), and availability of funds to procure medicines (Morton-Jones & Pringle, 1993). Limited financing for healthcare and commodities such as medicines has also been cited to influence prescribing behaviours and result in poor adherence to national treatment guidelines (Yang et al., 2014a). Poor adherence to treatment guidelines due to health system factors has been reported in Sierra

	Leone (De Bruycker et al., 2013), Botswana (Fugelli et al., 2002), and China (Song et al., 2014). Poorly functioning Pharmacy and Therapeutics Committees (PTCs), and poor implementation of decisions taken by PTCs have also been cited to have a negative effect on prescribing practices (Mashaba et al., 2019; Umnuaypornlert & Kitikannakorn, 2014).

In addition to using the SPT to study prescribing practices in Eswatini, the trans theoretical model (TTM), a model that uses stages of change to bring together processes and principles of change from well-studied theories of behaviour change was used to conceptualise how frontline medicine managers can change intentional behaviour (Prochaska et al., 1992).

The TTM was chosen over other models of behaviour change as it is an inclusive and comprehensive theory that combines fundamental constructs from other theories, hence helpful in understanding change in a variety of behaviours (Glanz et al., 2014). According to the TTM, change happens as one goes through a series of stages (Figure 2) and this happens over time. Progression through the stages can be linear or non-linear and most of the time people will recycle through the stages or regress to earlier stages.

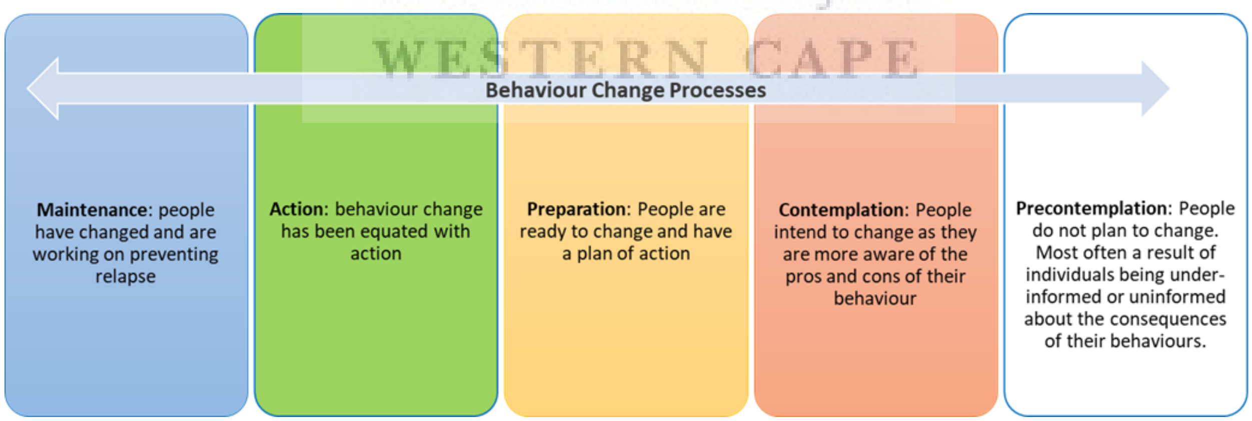

Figure 2: The stages of change model (adapted from sphweb.bumc.edu)

The TTM, along with the SPT, was operationalised in studying perspectives of health system actors on prescribing patterns in Eswatini. The theoretical framework employed in conducting the overall study is detailed in section 3.2.

3.2 Theoretical Framework

Studies highlight that implementation research is better accomplished if there is theory underlying the design and implementation of an intervention (Improved Clinical Effectiveness through Behavioural Research Group (ICEBeRG), 2006; Johnson &May, 2015). This study focused on changing medicine managers' existing RMU practices in Eswatini, hence the need to base the study on theory. French et al. (2012) highlight that using theory to develop implementation interventions allow the process to draw on practical issues, theory, and evidence. Literature shows that no one theory of analysing human behaviour has proven to be effective in changing behaviour (Noar & Zimmerman, 2005) nor proven to be the best in conducting implementation research (Grol et al., 2007; Lippke & Ziegelmann, 2008).

The Theoretical Domains Framework (TDF) was developed and validated using an expert consensus to identify a theory that addresses both organisational and psychological factors that shape health practitioners' clinical behaviour changes (Michie et al., 2005). During the consensus process, a set of 12 domains were identified as umbrellas to factors that influence clinical practitioners' behaviours and behaviour changes. These were: professional/social identity and role; skills; knowledge; beliefs about capabilities; goals and motivation; attention, memory, and decision processes; beliefs about consequences; resources and environmental context; emotion; social influences; nature of behaviours; and behavioural regulation (French et al., 2012). The authors further mention that the TDF provides an extensive framework that can be used for an array of interventions and has a potential to cover barriers to change (French et al., 2012).

The TDF (a four-step approach) was used to design and implement an RMU intervention for medicine managers in Eswatini. Medicine managers' perspectives of existing RMU practices and gaps in the country were explored using the social practice theory (SPT) of behaviour change. Practice theories and the model proposed by Grol et al. for developing an implementation plan for healthcare was used to plan and implement a RMU intervention with facility medicine managers in the Ministry of Health (Cosby, 2006).

Justification for the four-step approach in conceptualising the study

Studies show that there is no single strategy that has proven to work in changing professional practice (Wensing et al., 1998). Aligning the concept of change with medical practitioners, the authors conducted a systematic review including studies from 1980 to 1994 to collate evidence around innovations to change clinical practice. Findings from this review state that successful change is practical in situations where the people who need to change have the necessary skills, motivation, and knowledge to adopt the new practice (Wensing et al., 1998). The review also concluded that frameworks adopting multifaceted interventions are more effective in changing professional practice; a finding also echoed by Hogerzeil et al. in 2011. A systematic overview of systematic reviews on the effectiveness of behaviour change interventions conducted in 2015 showed that combining interventions was more effective in changing professional healthcare behaviour (Johnson & May, 2015). These findings led us to propose a four-step approach in conducting our research on RMU in Eswatini.

This systematic four-step approach, the theoretical domains framework (TDF), is recommended by French et al (2012) for designing and implementing behaviour change interventions. Below are the steps:

1) Identifying who needs to change (the problem behaviour);
2) Using a theoretical framework to identify enablers and barriers that need to be addressed (assessing the problem);
3) Identifying intervention components that could enhance enablers and overcome modifiable barriers (forming possible solutions); and
4) Identifying methods that can be used to measure and understand behaviour change (evaluating the selected intervention) (French et al., 2012).

The TDF approach was chosen for this study as it is beneficial in allowing researchers to base implementation interventions on theoretical approaches to changing behaviour (French et al., 2012). The TDF also allows researchers to investigate explicitly and implement behaviour change techniques (French et al., 2012). Our study focused on changing medicine managers' existing RMU practices in Eswatini. The social practice theory (SPT) of behaviour change was used to analyse medicine managers' behaviours towards RMU practices. The SPT was used as it not only focuses on the individual's behaviour but recognizes that behaviours are influenced by other external factors such as the material world (context) and systems of production and provision that they function under (Morris et al., 2012). Reckwitz states that under the SPT, individual practices or routines are often shaped by contextual factors (Reckwitz, 2002). The SPT model of analysing human behaviour is relatively new in designing and implementing interventions though it has been greatly used to study energy (Chatterton, 2011). The model has been chosen by various researchers over individualist approaches to analysing human behaviour as it encompasses other drivers of behaviour that are beyond individual decision-making processes (Chatterton, 2011). According to Chatterton, socially-oriented methods of analysing behaviour are useful in gaining insights into the processes and structures that generate behaviour (Chatterton, 2011). He further argues that individualist approaches have not been effective in creating expected changes as they tend to work around existing policies and function as "corrective" action. Socially- orientated approaches, on the other hand, help in developing new strategies for changing behaviour involving multiple stakeholders, and may only involve getting these stakeholders to continue what they do on a daily basis but in a different manner (Chatterton, 2011).

The stages of change model, also known as the trans-theoretical model (TTM) could have been used in studying medicine managers' behaviours in this study as it is a cognitive model that categorises individuals along a continuum of behaviour change (Morris et al., 2012). The logic behind the TTM is that individuals at the same stage are faced with similar problems and barriers, and the same type of intervention should suffice to assist these individuals (Nisbet & Gick, 2008). Since medicine managers targeted by this study were at different stages (i.e. different levels of knowledge from their professional backgrounds, experience and expertise in the prescribing and medicine use) and are faced with differing challenges, the TTM would have not been appropriate to analyse their behaviour.

Another individualistic approach of analysing behaviour - the theory of planned behaviour - could have been used to study patterns of medicine use in Eswatini. However, as this theory is centered on an individual's attitudes and beliefs (Morris et al., 2012), it could not be used for this study as it does not pay attention to contextual factors that may also contribute to behaviour. The same reason for not using the theory of planned behaviour applies to why we could not use the health belief model, which only focuses on individuals' behaviours being shaped by their perceived threats to their well-being (Morris et al., 2012). The next chapter (Chapter 4) details the methods that were followed in conducting this study.

CHAPTER 4: METHODOLOGY

This chapter gives detailed information on the procedures that were followed in conducting the study.

The study was conducted using a tailored intervention that was developed in a collaborative way. The intervention was implemented using a randomized pre-post with control group design. The study was conducted in three phases as illustrated in Figure 1 (p.31). The timeline for the study is presented in Table 4.

Table 4: Study Timeline

Phase of the Study	Activity	Timeline
Phase I	**Baseline Survey** - Quantitative aspect - Qualitative aspect (7 KI interviews and 32 interviews with Frontline managers)	April 2016 – March 2017
	First Feedback meeting and intervention selection.	February 2018
Phase II	Intervention piloting	March 2018
	Intervention roll out: - 2 visits, 2 months apart to 16 intervention facilities) - Six months follow up period	March 2018 – August 2018 September 2018 – February 2019
Phase III	**End of study Evaluation** Data collection - Post Intervention (quantitative) - Post Follow up (quantitative and qualitative)	*October 2018 March 2019
	End of study Feedback Meeting	February 2020

* Post intervention data for the month October 2018 was collected retrospectively in March 2019

4.1 Phases of the Study

4.1.1 Phase 1: Situational analysis (Objective 1)

The situational analysis was conducted using a concurrent mixed methods approach employing quantitative and qualitative methods. The Principal Investigator (NBQN) visited all 32 included facilities to collect quantitative and qualitative data and conducted key informant interviews and observations. Data from the situational analysis was presented in a feedback workshop to which all study participants were invited.

4.1.1.1 Quantitative Component

The quantitative component of the situational analysis involved a review of facility records to measure medicine use. Drawing on the WHO/INRUD prescribing indicators, medicine use patterns by region, level of care and diagnoses were evaluated.

Study Design

A retrospective record review of prescriptions from 1 April 2016 to 31 March 2017 was undertaken to document prescribing practices in randomly selected public sector and faith-based facilities in Eswatini. Three of the selected facilities did not have prescribing records; hence for these facilities prospective prescriptions from 1 May 2017 to 30 November 2017 were collected.

Sampling

A two-stage sampling strategy was employed to sample facilities (stage 1) and individual prescriptions (stage 2). Sampling for facilities and prescriptions has been thoroughly investigated by the INRUD group which recommends a minimum of 20 facilities and 30 prescriptions per facility (Hogerzeil et al., 1993). Hogerzeil et al. (1993) recommend 30 randomly selected outpatient encounters with prescriber per facility, as statistical simulation studies conducted on prospective prescriptions in multiple developing countries showed that this sample size yields meaningful findings (Hogerzeil et al., 1993). The authors further recommend a review of a minimum of 100 prescriptions per prescriber or per facility to compare medicine use by individual prescriber or facility (Hogerzeil et al., 1993).

Sampling of facilities: a sample size calculation using 95% confidence interval, 5% p-value and 80% power gave us a sample size of 158. Since this was a study towards a PhD qualification with limited funding, it was not possible to conduct the study in all 158 facilities. For the purpose of this study, a sampling frame of 325 public and faith-based facilities that receive essential medicines from the CMS was obtained from CMS. The CMS codes facilities by region and these codes were used to assign facilities to the four regions (Hhohho, Manzini, Lubombo, and Shiselweni) in the country. Specialised facilities (i.e. national referral hospital, psychiatric hospital, tuberculosis (TB) hospital and those facilities governed by other bodies such as the police services and the army) were excluded from the sampling frame, leaving 286 eligible facilities. Clinics only provide primary healthcare and are staffed with nurses, while health centers and hospitals provide primary and secondary healthcare. A patient can choose to attend at any level of care they want to go to regardless of presenting condition. Very ill patients are referred from clinics to health centres or hospital depending on the proximity.

From the 286 facilities, one hospital per region (4) and all health centres in the country (5) were purposively included leaving 277 facilities to sample clinics from. To sample clinics, we used a random sequence to select five clinics per region and inflated the sample of clinics per region by 20% (making six clinics per region) to allow for non-response. A total of 24 clinics (six per region) were included in the sample, making the overall sample size 33. One facility (a clinic) in the Shiselweni region was closed on the day the principal investigator (NBQN) went to collect data. Efforts were made to find out about the functioning of this facility and reasons that were beyond the research team were given. Since we had inflated the sample of clinics, the research team decided to drop this facility leaving the total number of facilities at 32. Appendix 1 is a map showing included facilities and their distribution across the country. Figure 3 shows the sampling of facilities, their allocation to intervention and control arms, and the total number of facilities analyzed at the end of the study.

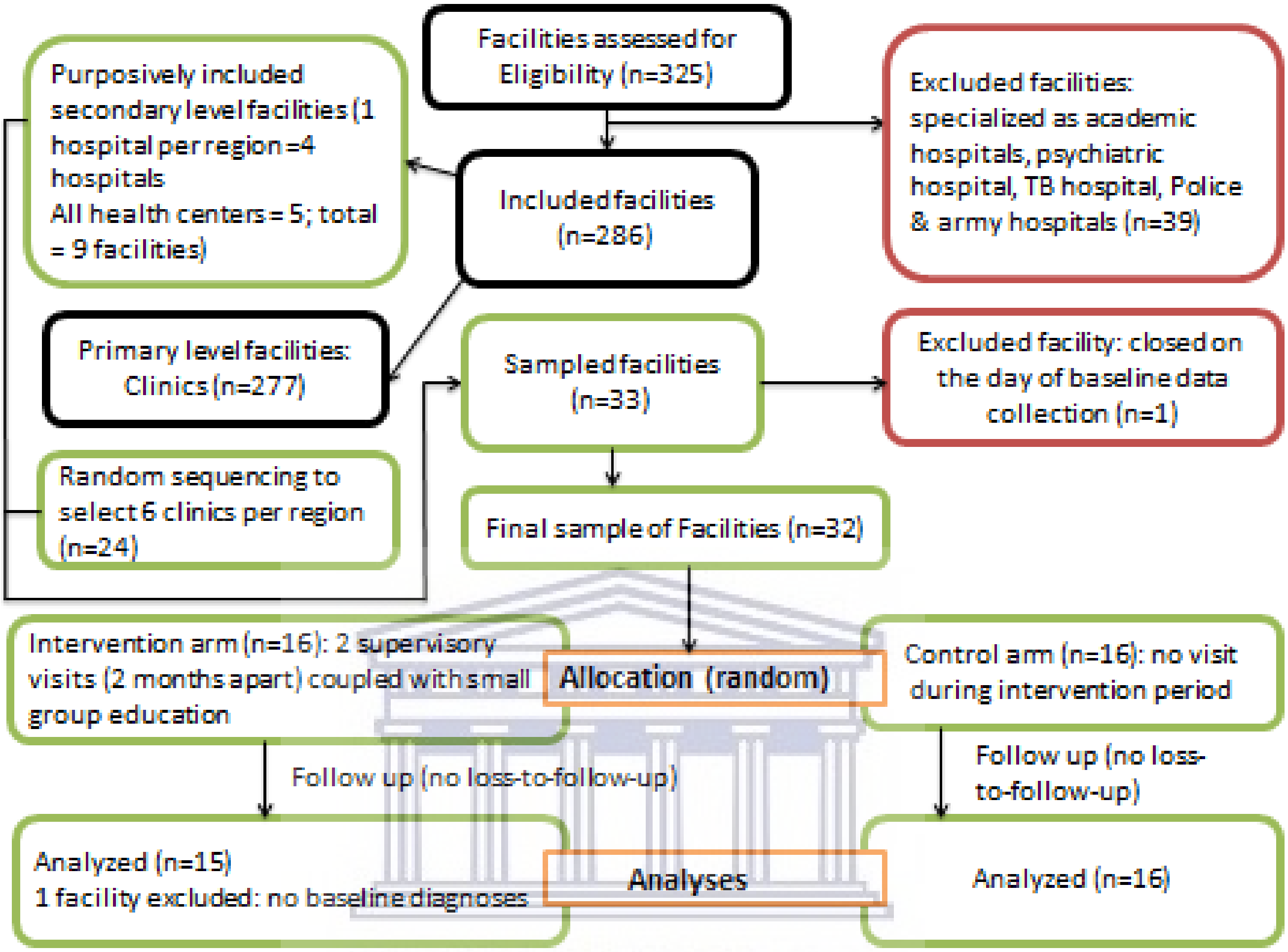

Figure 3: Flow chart showing sampling, allocation, and analyses of facilities

Inclusion criteria: hospitals, health centers, and clinics that receive medicines from the CMS (public sector and faith-based).

Exclusion criteria: national referral hospitals, specialized clinics, and public health units were excluded in the study as the kind of patients that are seen in these facilities and the type of care is different from the rest of the facilities.

Sampling of prescriptions: at the time the study started, in hospitals and health centres prescribers (doctors) had prescription books that they were using to prescribe except for one facility that had no prescribing record available in the facility; while nurses prescribed in a curative registers. Complete prescription books were kept in data or storerooms at these facilities for a minimum of five years. Each prescription in the book had an original copy and two carbon copies; the original prescription and a carbon copy were torn out and given to the patient while the second carbon copy remained in the prescription book – retrospective prescriptions for the study were collected from the carbon copies in the prescription books. Clinics were using patient curative registers to document prescribing information. Some higher-level facilities were also using these curative registers in addition to the prescription books. Two facilities were using the electronic patient management system – client management information system (CMIS), and one facility was prescribing on the Slack application. Slack is an American cloud-based application that allows teams to message each and brings all communication to one place and integrates tools already used by the teams. One can open different channels within the application, and access to the application and channels can be restricted by a person/few people who are able to give rights to users. The prescription (paper-based and electronic) has information such as patient age, gender, date of prescription, history (prescriber's notes), diagnoses and treatment prescribed.

To sample prescriptions in each facility, we followed Hogerzeil et al. (1993)'s recommendation of 100 outpatient encounters per facility to allow researchers to make comparisons between facilities (Hogerzeil et al., 1993). One hundred prescriptions (50 acute and 50 chronic) were randomly selected from the paper-based and electronic systems.

Prescriptions for outpatient encounters were collected from the curative register and prescription books in facilities that were using paper-based systems and the CMIS and Slack for those facilities that were using electronic systems. Prescriptions for antiretroviral therapy (ART), tuberculosis (TB), and family planning were not included in this study as prescriptions for these conditions are captured and recorded in different registers from the curative register. For facilities using prescription books, random sampling of prescriptions between 1 April 2016 and 31 March 2017 (one year's prescribing was utilized to characterize the facilities) was undertaken to select prescription books from which prescriptions would be collected using a two-stage random sampling method (to sample prescription books and actual from sampled prescription books prescriptions).

A two-stage random sampling strategy was used to select pages in the curative register from which prescriptions would be sampled, and the individual prescriptions. Each page in the curative register can record 37 prescriptions, so we multiplied 37 by the number of pages with prescriptions during the data collection period to get the sampling population. To calculate the sampling interval (SI) we divided the sampling population by the sample size of 50 prescriptions. The SI was multiplied by a random number (generated in Excel) to get the first prescription. Depending on whether the sampled prescription was acute or chronic (according to diagnosis recorded), we looked down the list of prescriptions to find the next recorded acute or chronic prescription i.e. a randomly selected acute prescription was coupled with the next available chronic prescription. To sample the second prescription, we added the SI to the number for the first prescription and looked down the list to couple it with acute/chronic prescription. This procedure was repeated until all 100 prescriptions were sampled. Similar principles of sampling were followed to sample prescriptions from CMIS and Slack.

A total of 3200 outpatient prescriptions were randomly selected from the 32 facilities. Prescriptions that were complete and had legible handwriting were included; if a prescription was illegible, the next legible prescription was included. Penicillins and other antibacterial agents, anti-infective ophthalmic and dermatologic agents, and antidiarrheal agents (excluding agents reserved for use as anti-tuberculosis agents like streptomycin) were included. For each prescription, data on the WHO 1993 standard prescribing indicators were collected exactly according to the definitions in this manual.

Data Collection

The principal investigator (NBQN) visited all 32 facilities to collect data. Data were collected using a paper-based WHO/INRUD prescribing indicators data collection tool (Appendix 2) and later transferred onto an Excel® spreadsheet on a password-protected laptop by NBQN and a research assistant (SN) using double data entry. Spreadsheet compare® was then used to check for data quality and paper-based data collection tools were consulted for any discrepancies.

Data Analyses

Quantitative data was coded and captured into an Excel spreadsheet and analysed using Excel and Stata (Version 15). Data was tested for normality using the Shapiro test. Descriptive statistics were done using the WHO/INRUD prescribing indicators (average number of medicines, average percentage of medicines prescribed by generic name, average percentage of prescriptions with one or more antibiotics, average percentage prescriptions with one or more injections, and percentage of medicines on EML). Baseline analyses were performed by facility (32), level of care, region, acute or chronic diagnoses, and the five most frequent acute and chronic diagnoses. Data collected at the level of patient (or prescription) was analysed at the level of patient while adjusting for clustering at two levels: region and facility. The analysis in this case was done using multilevel mixed logistic models since the outcome was binary. Data collected at the level of facility was analysed as independent facilities, clustered by region. Multiple linear regression was used to analyse these data as the outcomes were continuous variables and normally distributed. Robust standard errors were calculated from the clustering by region.

4.1.1.2 Qualitative Component

Study design

A qualitative exploratory study design was used to conduct the situational analysis. Data was collected using semi-structured interviews with key informants (KIs) from the ministry of health, central medical stores, an implementing partner (MSH/SIAPS) and frontline medicine managers in the 32 facilities sampled to get their perspectives on medicine use practices in the country. At facility level, semi-structured interviews were conducted along with non-participatory observations of day-to-day medicine-related activities performed by medicine managers. Lived realities of facility medicine managers in operationalising RMU through their interaction with the health system in Eswatini were explored using the epistemology of constructionism. The constructionist epistemology was used in the qualitative research as it identifies the participant as resourceful, active, and reflective in the construction of meaning as opposed to being a passive receiver of meaning (Creswell, 2013).

Semi-structured interviews with key informants and facility medicine managers

Sampling strategy and study design

Purposive sampling of KIs at the NDoH, the CMS, MSH/SIAPS and frontline medicine managers from all levels of healthcare (hospitals, health centers, and clinics) was performed. At facility level, an invitation to participate in the study was extended to decision makers such as matrons and senior medical officers; prescribers such as doctors and nurses; and people who order, dispense, and counsel patients on medicines such as pharmacists, pharmacy technicians, and nurses. One frontline manager (doctor, nurse, pharmacist, pharmacy technician, or pharmacy assistant) from each of the 32 randomly selected facilities was interviewed. Table 5 provides characteristics of respondents by cadre and level of care.

Table 5: Study participants' characteristics

Characteristics	Cadre (Number and Region)
Key Informants (N=7)	
Ministry of Health (National level of care)	Pharmacist (1)
Implementing Partner	Pharmacist (1)
Ministry of Health (Central level of care)	Pharmacist (1)
Ministry of Health (Regional level of care)	Nursing Matron (4: 1 from each region)
Frontline Managers (N=32)	
Ministry of Health (Secondary level of care)	Medical Officer (1: Lubombo region) Pharmacist (2: 1 from Hhohho and 1 from Shiselweni regions) Pharmacy Technicians (6: 4 from health centres [2 from Hhohho; 2 from Shiselweni] and 2 from hospitals [1 from Shiselweni and 1 from Manzini])
Ministry of Health (Primary level of care)	Nurse (23: 6 from Manzini; 5 from Shiselweni; 5 from Lubombo; 7 from Hhohho)*

*One clinic from the Hhohho region was wrongly coded as a facility in the Lubombo region by the central medical stores - it was analyzed under the Hhohho region. One clinic in the Shiselweni region was closed during data collection.

A qualitative exploratory study design was used to conduct this study. A qualitative exploratory study is defined as a study that allows researchers to investigate topics that have received minimal attention in the past and are not well defined (Hunter et al., 2018). Further, qualitative exploratory study designs allow study participants to contribute information towards building knowledge in the area under study (Reid-Searl & Happell, 2012).

Data Collection and Processing

A semi-structured interview guide (Appendix 5) informed by the SPT and covering themes such as knowledge of RMU, prescribing practices, enablers and barriers to the rational use of medicine, and interventions available to promote RMU was used to conduct one-on-one interviews with key informants. A similar interview guide (Appendix 6), but focusing on RMU activities and functioning in facilities, was used to conduct one-on-one interviews with frontline healthcare providers. Interviews were conducted between April and September 2017. Semi-structured in-depth interviews were used to collect data on medicine use practices in public sector and faith-based facilities in Eswatini. Semi-structured in-depth interviews were used as they employ the use of an interview guide with open ended questions to allow a range of responses from participants in a comprehensive and systematic manner to obtain the desired information (DiCicco-Bloom & Crabtree, 2006). Interview guides were piloted on healthcare professionals from facilities that were not in the sample (for frontline managers) and the CMS (for KIs). All interviews were conducted in English and the interviews lasted between 20 and 60 minutes. No repeat interviews were carried out.

The principal investigator (NBQN, a female PhD student) approached KIs and requested them to participate in the study after giving verbal and written information on the study. In facilities, the principal investigator (NBQN) introduced herself to management using the permission letter from the MoH and management guided on participants to be approached. NBQN conducted key informant interviews in offices in the MoH headquarters, implementing partner's office, and CMS; while a quiet office with minimal disturbance was used in health facilities. Interviews were audio recorded (all except one non-consenting participant), and were supplemented by field notes using a reflexive journal by NBQN. Some of the participants were people that NBQN previously worked with while practicing as a pharmacist in Eswatini, while others were not known to the principal investigator. Interviews were transcribed at the end of each day by a research assistant (SN) and the PI read the transcripts as soon as they were transcribed. For frontline managers, data saturation, a phenomenon achieved when the data gathered no longer brings out new information (Robson & McCartan, 2016), was achieved by the 15th interview. However, since the PI was collecting quantitative data from 32 facilities, she continued conducting interviews in all facilities. A research assistant transcribed the interviews and saved transcripts onto a password-protected laptop. Some participants (3 key informants) were interested to review transcripts and they were given the opportunity to do so (member-checking) before finalization of the transcripts. Frontline managers were not keen on reviewing their transcripts.

Data Management

For identification of the information source and anonymity, key informant quotes were coded as KI_Cadre_Level of care_Region; and frontline managers' quotes as FM_Cadre_Level of care_Region.

Data Analyses

Transcribed data and field notes were analysed deductively using Robson's (2011) five phases of thematic coding analysis (TCA); the first stage of which is familiarisation through reading and re-reading (literally, interpretively and reflexively). The PI (NBQN) re-checked all the transcripts for completeness and correctness. NBQN read the transcripts over and over to familiarise herself with the data and reflect on the actual interviews. As NBQN is a pharmacist who has worked in Eswatini, it was important for her to dissociate herself from the findings and her knowledge on medicine use practices in the country to objectively report on the information coming from the transcripts. The second phase involved coding. Two transcripts were randomly selected and independently coded by NBQN and LK (who co-authored the manuscript published for the qualitative baseline survey; (Ncube et al., 2020)), and captured on Atlas.ti software. Quotable quotes were extracted. Notes and memos were made from the selected transcripts to inductively generate the initial codes. NBQN and LK discussed their independent codes identifying similarities and differences through a discursive process. Using the initial codes, NBQN and LK developed a codebook. The codes were grouped into themes (third phase) and then used to construct different thematic maps. Thematic maps helped to structure and describe the themes, and ultimately unearth crucial information at different levels to understand medicine use patterns in the country. Suggestion of using different levels of themes (super-ordinate themes – "global level"; groups of basic themes – "organising level"; and "basic level") as stipulated by Attride-Stirling were operationalised to create thematic networks. Sub-themes with identical concepts were grouped deductively into final themes provided by the SPT framework (Attride-Stirling, 2001). An iterative process of cross-checking themes (fourth phase) against coded data was done to ensure that the networks are a true reflection of the data. Thematic networks (fifth phase) were then used to make comparisons between different aspects of data to interpret the patterns of medicine use in Eswatini. NBQN used the codebook to analyse the remaining transcripts. The reorganising of codes was achieved in a discursive process with all the authors of the manuscript.

The TDF domains were used deductively during coding along with sub-codes created from these domains as appropriate. Inductive coding was also performed for issues emerging from the data to give a rich description of the data (Braun & Clarke, 2006). The TDF was operationalised as literature shows that the TDF allows explicit investigation of clinical behaviour as well as implementation of behaviour change techniques (French et al., 2012).

The social practice theory (SPT) of behaviour change was used to analyse KIs' and frontline medicine managers' behaviours regarding medicine use practices. This theory was used as it not only focuses on the individual's behaviour but recognizes that human behaviours are influenced by other external factors such as the material world (context) and systems of production and provision that they function under (Morris et al., 2012).

Feedback Workshop and Intervention Selection

The goal of the meeting was to engage stakeholders involved in policy development of RMU, senior level medicine managers and frontline medicine managers on existing medicine use practices in Eswatini, and, using a collaborative participatory approach, to select an RMU intervention to be tested in Eswatini. The meeting lasted half a day and was held in Mbabane. Meeting attendants included policy makers from the National Department of Health, CMS and an implementing partner, regional medicine managers, and some frontline medicine managers from the included facilities. Baseline quantitative and qualitative findings were presented to participants. Various strategies (managerial, educational, economic, and regulatory) that can be employed to improve medicine use practices were also presented to participants. Participants were then divided into two groups in which they discussed baseline findings and decided on an intervention appropriate to be tested in Eswatini to improve rational use of medicines.

At this meeting, the participants agreed that small group on-site training coupled with supportive supervision would be appropriate for Eswatini's setting; and this was the adopted intervention to be tested. Detailed proceedings of this meeting are presented in Chapter 6. At this stage, no facility had been randomized to the intervention or control arms. Participants at the workshop were informed that they would be randomly selected to be either intervention or control facilities.

4.1.2 Phase II: Intervention Design and Implementation (Objective 2)

Intervention Design

Baseline results were used to inform the design of the intervention. There was high usage of antibiotics across the country and one region had a high use of injections. Also, there were some chronic conditions that were prescribed antibiotics. The intervention was designed around the problematic areas identified during the baseline survey i.e., inappropriate use of antibiotics and overuse of injections. Training material addressing general use of antibiotics and injections, including guidance from WHO on the acceptable values of WHO/INRUD prescribing indicators and on management of NCDs (hypertension, diabetes, asthma, and arthritis), was developed to be used during small group on-site trainings.

Allocation of facilities to Intervention and Control Arms

Results from Phase I were used to rank facilities from best to worst performing according to the WHO/INRUD prescribing indicators. Antibiotics use was the key indicator used for ranking. Best performing facilities were those that had the lowest percentage of use of antibiotics while worst performing facilities were those that used more antibiotics. After ranking facilities, random numbers generated in Excel were used to allocate facilities to the intervention and control arms. On the list of the random numbers, for each pair of intervention and control facilities, the higher number was allocated to an intervention and the lower number to the control facility. This was done to pair similar performing facilities (see Appendix 7 for allocation of facilities to intervention and control arms).

Intervention Development and Piloting

Results from Phase 1 were used to inform the development of educational material for the small-group on-site sessions. Educational material was around inappropriate use of antibiotics for NCDs (hypertension, diabetes, asthma, and arthritis) and the management of these NCDs according the Eswatini STG/EML, and WHO guidance (see Appendix 8).

The intervention was piloted on a small sample of central level and frontline medicine managers in early March 2018 in other facilities that were not part of the study to allow researchers to assess the feasibility of delivering the intervention and identify processes that needed to be clarified and simplified. Piloting also allowed the research team to adequately plan for effective implementation of the intervention on the included facilities.

Intervention Roll-out

The intervention was planned to be rolled out in three visits, two months apart, to the intervention facilities.

First Intervention visit

The first intervention visits (to 16 intervention facilities) were conducted from late March 2018. During the first intervention visit, the PI collected 30 random prescriptions from the previous month and analysed these using the WHO/INRUD prescribing indicators on-site. Results from the 30 prescriptions were presented along with Phase 1 facility results to a small group of frontline facility managers (prescribers – doctors and nurses, pharmacists, and pharmacy technicians) who were willing and available for the session. On average the meetings were attended by 4 people (range = 3-20); and meetings lasted 30 minutes (range = 20-60) on average. NBQN provided refreshments for the meetings. Findings of the on-site prescription audit were used to adapt messages shared during the feedback session. Performance comparisons were made between baseline and visit 1 findings and intensive discussions around optimal and problematic prescribing were held. Participants highlighted factors that affect prescribing practices, which were both internal and external factors. Supportive supervision on how they could improve prescribing was given. The prescription audit and feedback coupled with supportive supervision intervention was rolled out in all 16 intervention facilities. Information gathered during the discussions that emanated from the small groups was used to adapt messages for the following visit and if more information was requested during a visit, the PI ensured that information was available immediately after that visit or by the following visit. Visit 1 notes are available in Appendix 9.

Second Invention Visit

Visit 2 intervention roll out visits were conducted from May 2018 until August 2018. Similar procedures to those conducted during visit 1 were conducted, except that the 30 random prescriptions were collected from the date of visit 1 to the day before visit 2 for all intervention facilities (about two months' data). Visit 2 notes are available in Appendix 10.

Third Intervention Visit

Unfortunately, the PI injured her ankle after visiting only two facilities for visit 3 and was unable to complete the last round of intervention visits. Thus, the evaluation of the impact of the intervention was of only two visits to intervention facilities. A similar evaluation occurred in the

Zimbabwe supervision study described by Trap (Trap et al., 2001). In that study, four supervisory visits were planned but only two were undertaken due to external factors (fuel shortages). The evaluation however showed positive results.

After the last intervention visit (i.e., last visit 2 visit) facilities were followed up for six months (October 2018 to March 2019; facilities were not visited during this time but left to function as they normally do) at the end of which post-intervention data for the two time points was collected from all 32 facilities.

4.1.3 Phase III: End of Study Evaluation, Feedback Meeting, and Policy Recommendations (Objective 3)

To evaluate the quantitative components of the study a cross-sectional survey, as conducted at baseline, was repeated at the end of the intervention and at the end of the follow-up period. However, at the end of the intervention and follow-up periods 25 of the 32 facilities (78%) were using the electronic system (CMIS). We collected all prescriptions for the month of October 2018 to assess prescribing patterns post the intervention and all prescriptions for the month of April 2019 to assess prescribing patterns post the follow-up period. To randomly select 100 prescriptions per facility for each of the two periods we created a column of random numbers using the random function on Excel. These random numbers were then sorted using the random column from the smallest number to the largest. The first 100 prescriptions on this list were then selected as the sample for each of the two periods per facility.

Outcomes of the intervention were tested using paired data at each facility and within the pairs of matched facilities. Mean differences/changes using paired t-tests across three time points (baseline, post intervention, and post follow up) were conducted. We also looked at differences within facilities between baseline and post-intervention. An analysis of mean differences between the intervention and control groups calculated as a difference of differences subtracting the control from intervention indicators was also conducted. A negative difference meant that the control group increased more than intervention group; while a positive difference meant that the intervention group increased more than control group.

Analysis for the effect of the intervention on the outcomes over time, while controlling for confounders, was conducted at facility level using linear regression models. The longitudinal repeated measures nature of the data was adjusted for using clustered robust standard errors at the facility level. Within-subjects effect of time (3 time points: baseline, post intervention, post follow-up) was specified as well as between subjects effects of level of care (1 or 2), region (4 regions), type (chronic or acute) and group (intervention or control). An interaction between time and group was tested to assess the effect of the intervention over time. This was the effect of interest in the models. Interaction effects (effect of the intervention) were plotted on profile plots with adjusted marginal means. The analysis was used for the outcomes, which were relatively normally distributed i.e., average number of medicines, percentage of medicines prescribed by generic name, and percentage of prescriptions with antibiotics. Percentage injections and EML were transformed using logarithms and analysed in the same way.

Qualitative interviews using a semi-structured interview guide were conducted with six key informants who were interviewed pre-intervention. The 7th key informant could not be interviewed as the implementing partner (MSH/SIAPS) interviewed at baseline stopped supporting pharmaceutical services in the country around June 2018, and a new partner which mainly focused on supply chain took over. Frontline medicine managers from 10 purposively selected intervention facilities and 13 purposively selected control facilities were also interviewed. Included facilities were those that gave substantive information during the baseline survey. Data management procedures followed during Phase I (for qualitative and quantitative components) were repeated in Phase III.

Post intervention findings were presented in a half-day national meeting held in Mbabane. Participants at this meeting also made some policy recommendations.

End-of-Study Feedback Meeting and Policy Recommendation

The goal of the meeting was to present end-of-study results of the study to senior Ministry of Health officials, policy makers, medicines regulatory officials, central level pharmaceutical officials and frontline medicine managers. Furthermore, the meeting aimed to discuss these findings and get participants to discuss information they would like to see in the discussion section of the thesis along with recommendations for the study.

4.2 Ethics Statement

The study was approved the University of the Western Cape Senate Research Committee (Ethics Reference Number: BM/16/4/2) (Appendix 11) and the National Health Research Review Board (Appendix 12) in the Kingdom of Eswatini. The Ministry of Health in Eswatini further granted permission (Appendix 13) for the study to be conducted in healthcare facilities in the country.

The study was explained to participants before participation and they were told that they had the right to decline to answer any question they were uncomfortable with. An information leaflet (Appendix 14), which participants kept for reference whenever necessary, with contact details for the principal investigator and the Deputy Director Pharmaceutical Services, was provided to participants. Participants willing to be part of the study were given the information leaflet to read, and the PI further explained information on the leaflet and allowed participants to ask questions. Consenting participants gave written consent (Appendix 15). No incentives were provided for being part of this study. The use of the data collection tools for quantitative record reviews, semi-structured qualitative interviews, and audio-recorders for qualitative interviews were explained to participants. Furthermore, the benefits and risks of being part of the study, and lack of incentives for participating were explained to participants. Data was stored on a secured password protected computer; only the investigators had access to the data.

The next chapter (Chapter 5) details study findings.

CHAPTER 5: RESULTS

The results are presented in this chapter as Phase 1 – the quantitative and qualitative aspects, followed by Phase III – quantitative and qualitative aspects. Phase II was the intervention design and roll-out – as detailed in Appendices 9 and 10. Feedback meetings proceedings are detailed at the end of this chapter. Below are study results for Phase I (baseline survey) and Phase III (post intervention and post follow-up evaluation) as quantitative and qualitative components.

5.1 Phase 1

5.1.1 Quantitative Component

Results for this phase are presented as follows: overall presentation of WHO/INRUD indicators by region and level of care; and acute/chronic diagnoses, by region and level of care and the top five acute/chronic diagnoses.

Overall WHO/INRUD indicators by region and level of care

An average of 105 prescriptions were collected per facility making a total of 3345 (from 32 facilities, four regions and two levels of care) prescriptions that were included in the analysis by the WHO/INRUD prescribing indicators. More facilities were primary level of care (Level 1) compared to secondary level of care (Level 2) - 71.9% versus 28.1% - and Hhohho had the highest number of prescriptions -1012 (30.3%), followed by Shiselweni - 866 (25.9%), Manzini - 835 (25%), and the least prescriptions were from Lubombo region - 632 (18.9%). The results for the WHO/INRUD prescribing indicators were reported by region as shown in Table 6.

Table 6: Regional WHO/INRUD Prescribing Indicators

Regions	Sample size (N)	Average Number of Medicines per prescription	Medicines prescribed by generic name (%)	Prescriptions with at least one antibiotic (%)	Prescriptions with at least one injection (%)	Medicines prescribed from EML (%)
Hhohho	10	3.53	74	57	14	93
Lubombo	7	3.76	71	52	8	92
Shiselweni	9	3.45	78	54	8	93

Manzini	6	3.97	70	57	6	89
National	**32**	**3.70**	**74**	**54**	**10**	**92**

The pattern of medicine use by the average number of medicines prescribed per prescription by facility and region are shown in Figure 4. The national average number of medicines prescribed per prescription was 3.7 (range 2.54 – 7.19).

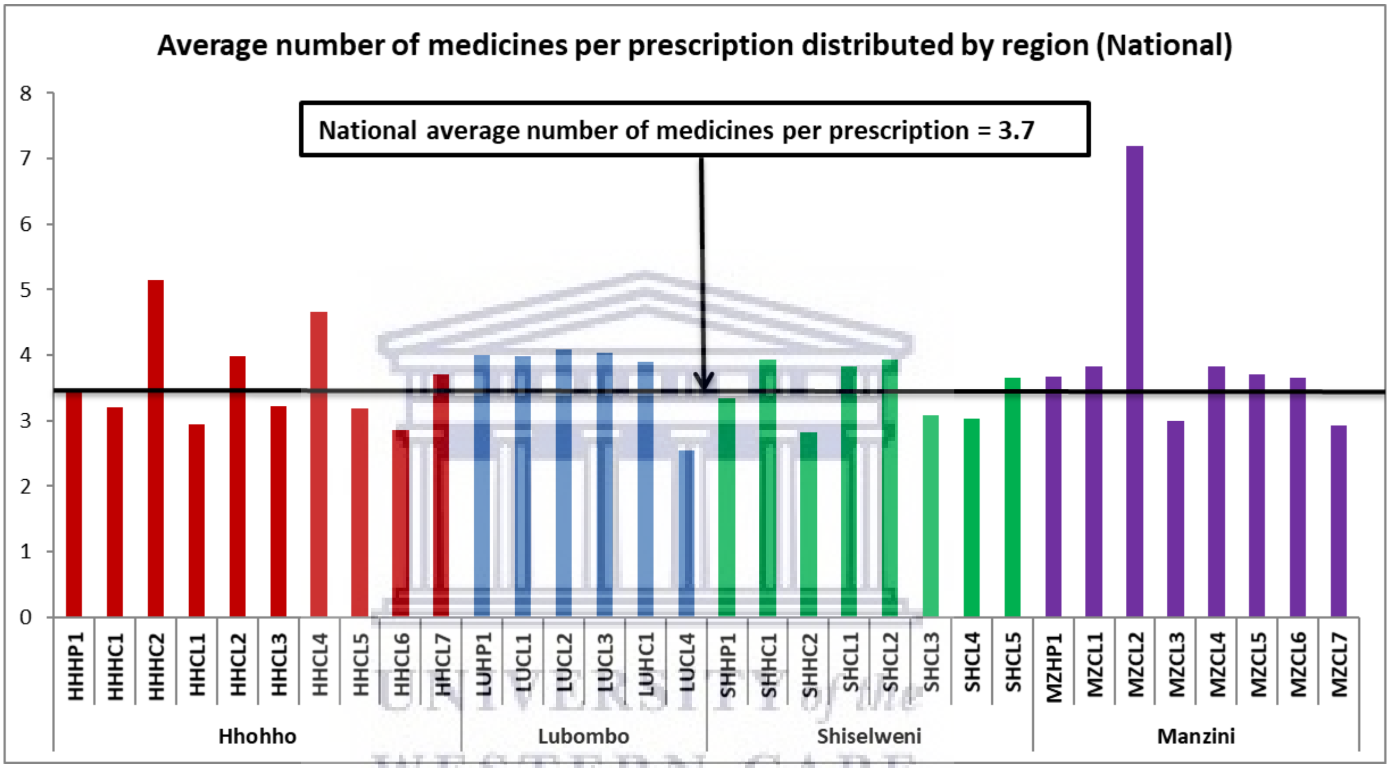

Figure 4: Average number of medicines prescribed per prescription

For the average number of medicines prescribed per prescription, there was no difference between the two levels of care (3.7). The coefficients for level 2 (health centres and hospitals) was negative relative to level 1(clinics), but very close to 0. Manzini and Lubombo regions had a significantly higher average number of medicines prescribed per prescription than Hhohho region ($p<0.001$). Shiselweni region was not different from the Hhohho region (Table 6).

The pattern of medicine use by generic prescribing is represented in Figure 5; the national average number of medicines prescribed by generic name was 74% (range 51% - 95%).

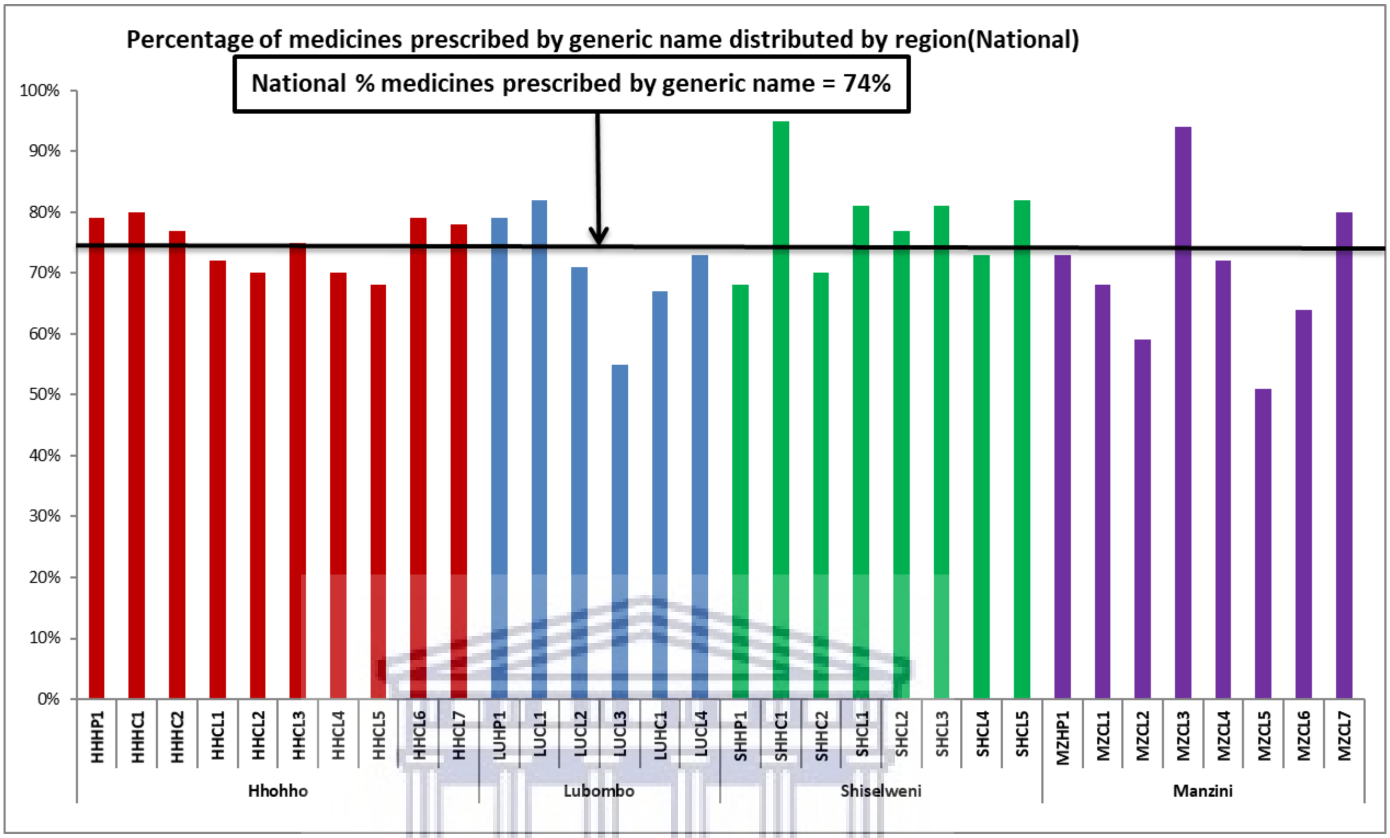

Figure 5: Percentage of medicines prescribed by generic name

For percentage of medicines prescribed by generic name, there was no difference between the two levels of care. Manzini (70%) and Lubombo (71%) regions had a significantly lower percentage of medicines prescribed by generic name than Hhohho (74%) region (p=0.002 and 0.003 respectively). Shiselweni (78%) region had a significantly higher percentage of medicines prescribed by generic name than Hhohho region (p<0.001).

Nationally, 54% (range 29% - 73%) of prescriptions had at least one antibiotic prescribed as shown in Figure 6.

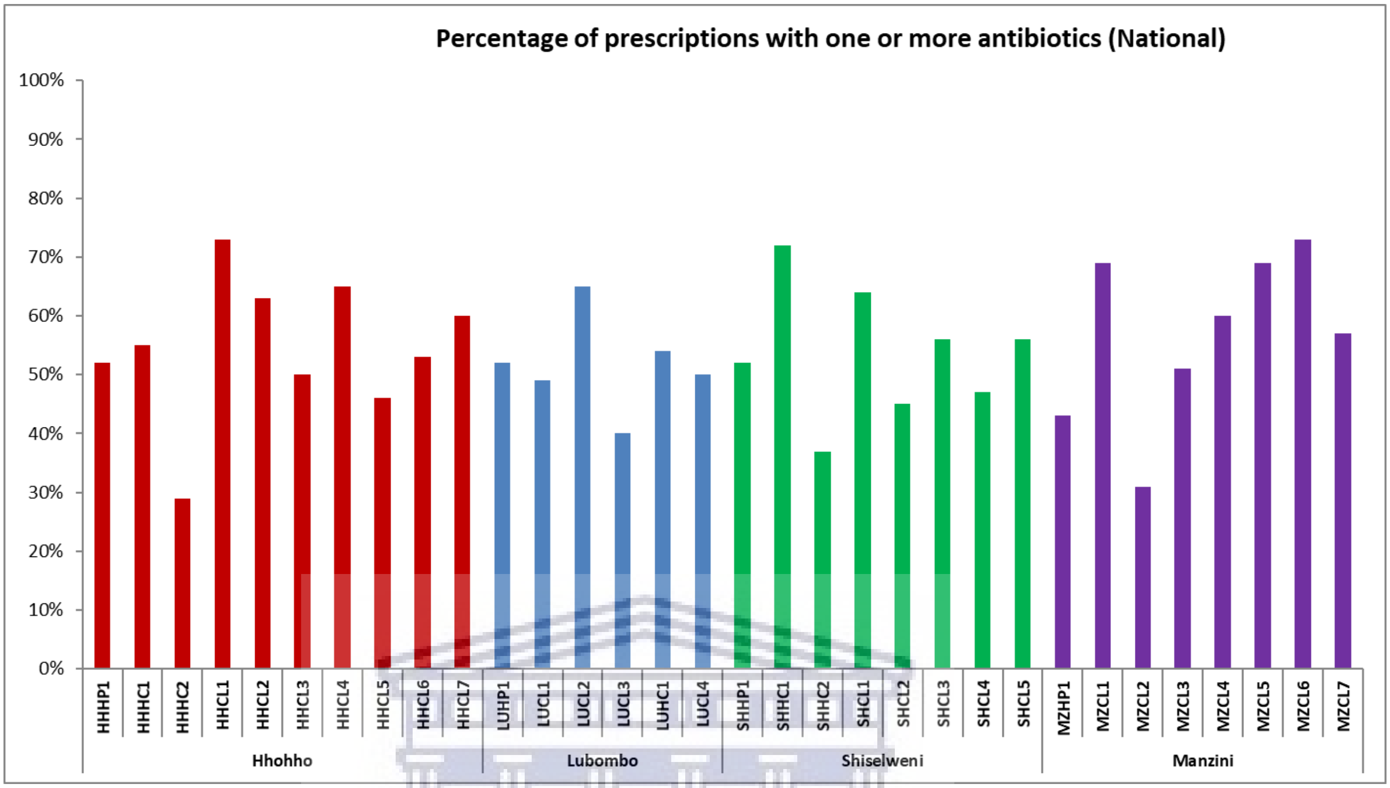

Figure 6: Percentage of prescriptions with at least one antibiotic prescribed

For percentage of prescriptions with at least one antibiotic, there was no difference between the two levels of care. Shiselweni and Lubombo regions had a significantly lower percentage of antibiotics than Hhohho region (p=0.001 and <0.001 respectively). Manzini region showed no difference from Hhohho in terms of percentage of prescriptions with at least one antibiotic.

The national average of prescriptions with injections prescribed was 10% (range 1% -35%) as shown in Figure 7.

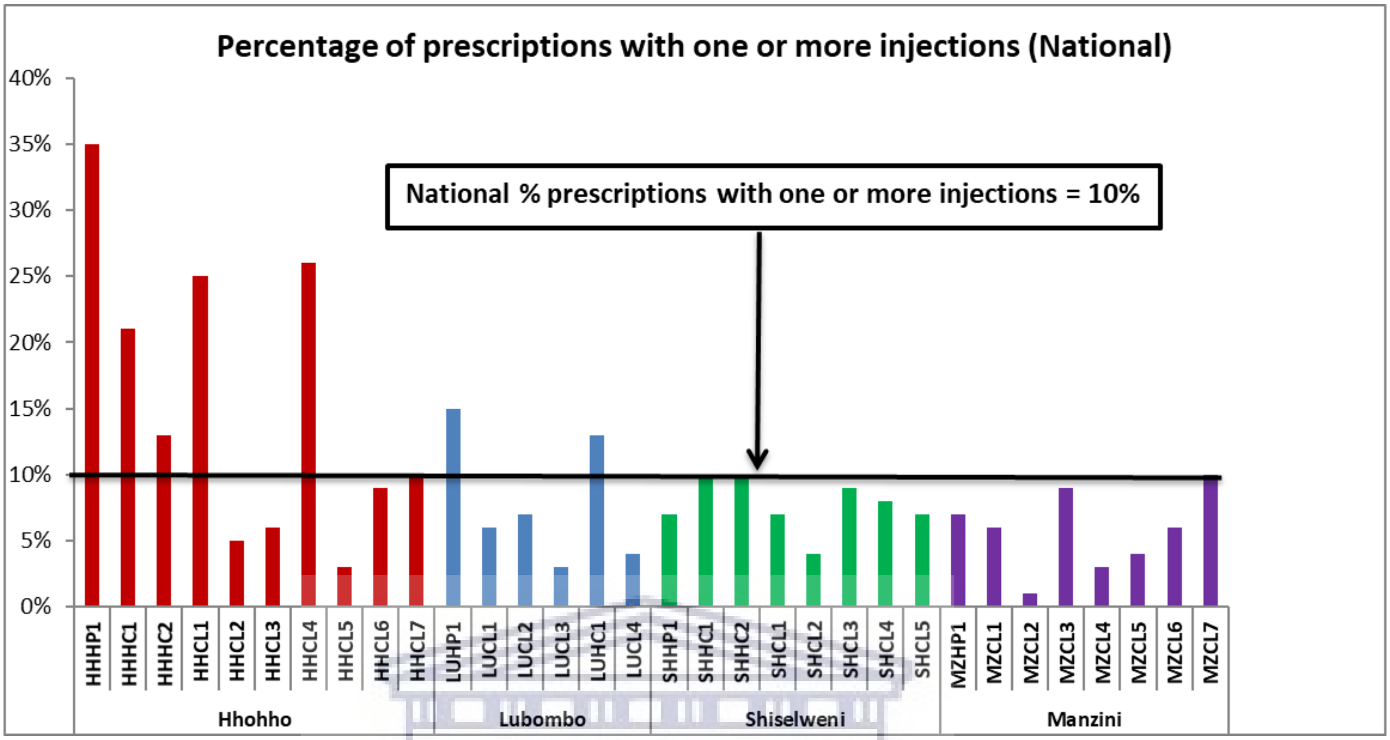

Figure 7: Percentage of prescription with one or more injections

The percentage of prescriptions with injections variable was skewed; therefore, it was transformed using a logarithm. The resulting variable was normally distributed. The result of the model with the transformed dependent variable shows that there was a significant difference between the levels of care, with level 2 having a higher percentage of prescriptions with injections than level 1 (p=0.047). Manzini, Shiselweni and Lubombo regions had a significantly lower percentage of prescriptions with injections than the Hhohho region (p<0.001).

For percentage of medicines prescribed from the EML (Figure 8), there was no difference between the two levels of care. Manzini (92%) and Lubombo (94%) regions had a significantly lower percentage of medicines on the EML than Hhohho (96%) region (p=0.001 and < 0.001 respectively). Shiselweni (96%) region had a similar percentage of medicines on the EML to the Hhohho region.

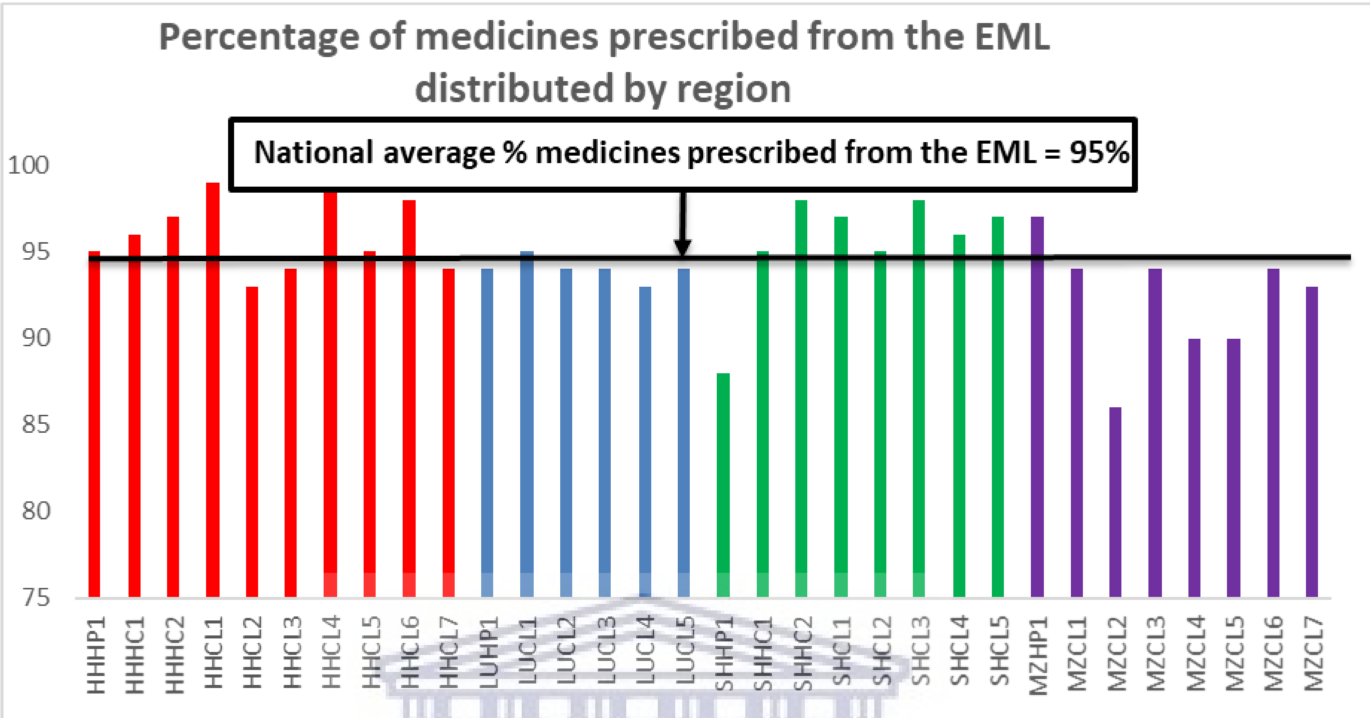

Figure 8: Percentage of medicines prescribed from the EML

Acute and Chronic Diagnoses

There was data on acute or chronic diagnoses for 3234 (97%) of the patients: 1938 (57.9%) acute and 1296 (38.7%) chronic. Most of the missing data on diagnosis was from one facility which was using the electronic system CMIS. Table 7 shows the WHO/INRUD prescribing indicators reported by acute and chronic diagnoses.

Table 7: Acute/Chronic WHO/INRUD Prescribing Indicators

Diagnosis	Average Number of medicines	Generics (%)	Antibiotics (%)	Injections (%)
Acute	3.48	69	75	13
Chronic	4.09	79	25	5

Acute and Chronic Diagnoses by Region and Level of care

Table 8 shows the percentages of level 1 and level 2 care for acute or chronic diagnoses by region without considering the clustering by facility. Data from Table 7 suggests that there were similar percentages of chronic and acute patients between the four regions at each level of care. Across the regions it appeared that chronic patients were more likely to be cared for at level 2 while acute patients at level 1. However, this was not true for the Shiselweni region.

Table 8: Chronic versus acute diagnosis by region and level of care

				Level of Care 1 (clinics)		**Level of Care 2 (hospitals and health centres)**	
				Count (N)	**Percentage (%)**	**Count (N)**	**Percentage (%)**
Region	**Hhohho**	Chronic or Acute	Acute	438	60.5%	144	50.2%
			Chronic	286	39.5%	143	49.8%
	Lubombo	Chronic or Acute	Acute	252	61.0%	125	57.1%
			Chronic	161	39.0%	94	42.9%
	Manzini	Chronic or Acute	Acute	384	60.9%	52	50.5%
			Chronic	247	39.1%	51	49.5%
	Shiselweni	Chronic or Acute	Acute	346	61.5%	197	67.0%
			Chronic	217	38.5%	97	33.0%

The multi-level mixed effects logistic model used to estimate the odds of chronic versus acute diagnoses by the two different levels of care whilst adjusting the standard errors of the estimate for 2 levels of clustering (by facility and by region) showed that level 2 was 1.19 times more likely (95% CI 0.82 – 1.73) to care for chronic patients vs. acute patients but the difference was not statistically significant (p=0.35).

Top five acute and chronic diagnoses

The most common chronic and acute conditions were identified and the WHO/INRUD prescribing indicators were calculated as shown in Table 9.

Table 9: WHO/INRUD Prescribing Indicators by top five chronic and acute conditions

Condition	N	Av. No of Drugs	% Generics	% Antibiotics	% Injections
Chronic Conditions (N = 1346)					
HTN Plus	547	4.37	78	37	9
HTN	434	4.01	86	17	1
DM Plus	187	4.21	73	52	12
Asthma	116	2.97	55	51	5
DM	62	4.18	80	24	6
Acute Conditions (N = 655)					
URTI	235	3.49	66	87	10
URTI Plus	162	3.66	68	61	9
Diarrhoea	90	3.82	68	88	4
Diarrhoea Plus	88	3.73	75	38	15
Abscess	80	1.94	77	93	25

Top diagnoses were recorded as follows: Diabetes (DM), hypertension (HTN), diabetes mellitus plus other conditions (DM plus), hypertension plus other conditions (HTN plus), upper respiratory tract infections – (URTI), and diarrhoea plus other conditions (diarrhoea plus), upper respiratory tract infection plus other conditions (URTI plus), and diarrhoea plus other conditions (Diarrhoea plus). Arthritis was not among the top diagnoses; however, of the 13 records for arthritis, 38% were prescribed antibiotics.

A multi-level mixed effects logistic model used to estimate the odds of chronic vs acute diagnoses by the region whilst adjusting for level of care and adjusting the standard errors of the estimate for the effect of clustering by facility showed that none of the regions were statistically different from the reference region (Hhohho) in terms of chronic or acute diagnoses.

5.1.2 Qualitative Component

Thirty-nine participants were included in this study, consisting of a mix of doctors, nurses, pharmacists, and pharmacy technicians (Table 5. Their ages ranged from 21 – 57 years, and they had been practicing for periods ranging from 1-30 years (median = 12.7 years). Table 10 summarizes the categories, themes and sub-themes that emerged from the data.

Table 10: Summary findings on qualitative interviews

Categories	Themes	Sub-themes
Current practices	Training of personnel in facilities	• Some facilities trained some not • In-service • Workshop setting
	Prescription practices	• Prescribing according to STG/EML • Prescribing outside STG/EML
	Prescription influences	• Pressure from patients • Symptomatic prescribing • Time and High patient volumes – prescriber writes out as many medicines for patient to make sure they do not come back with more complaints
	Patient monitoring	• No prescribing record kept at facility
Factors affecting RMU	Enablers	• Training from CMS, ICAP, MSH and MSF • STG/EML • Community improvement project in line with the 2020 vision • Facility-based formulary • Monthly staff meetings • Weekly clinical meetings • PTC in mother facility • SOPs from the ministry • Teamwork in patient management
	Barriers	• Providers uncomfortable consulting guidelines in front of patients • Stock-outs • Guideline recommends medicine not available at level of care (clinics) • No teamwork in patient management • No human resource for pharmacy • Unqualified staff dispensing medicines • Polypharmacy to satisfy patient • No pre-service orientation on guidelines for foreign doctors -Foreign doctors prescribing irrationally • Long lead times for stock delivery from CMS

		• Inadequate/inconsistent amounts of stock received from CMS • Lack of communication on stock availability between facilities and CMS • Lack of knowledge on inventory management • Polypharmacy for NCDs • No direct communication with regional pharmacist • No training on RMU • Prescribing outside guideline due to severity of conditions • No transfer of skill from older to younger generation • Facilities not ordering enough quantities from CMS • Medicines with short shelf-lives pushed to facilities • Overuse of antibiotics • Little attention paid to NCDs • Different practice ethics by different prescribers • No guideline on who in the nursing cadre can and cannot prescribe • Poor history taking • Absence of RMU policies in the country • Patients taking too long to present to facility • Patients dissatisfied with less medicines • Difficult to practice on patients if prescribing is irrational • Language barrier: foreigners and the elderly • Patients discontinue taking chronic medicines due to stock-outs and having to buy medicines out of pocket
Interventions to improve RMU	Existing	• STG/EML • Clinical meetings • Training • Medicine labels done in SiSwati
	Recommended	• Functional PTCs • Training of prescribers on prescribing • Training on inventory management • Consistent supply of medicines • Development of facility-based formularies • CPD for pharmacy personnel • Guideline review and update • Supervision and mentorship • Widening the list of medicines available at primary health care and health centre levels

		• Development, implementation, and monitoring of RMU policies • Having nurses specially trained on RMU and making them available in all facilities • In-service training • Deploying doctors on full-time basis in clinics • Prescribers willing to change prescribing practices/culture • Research feedback to be given to participants • Deployment of pharmacy assistants to clinics • Pre-service training for foreign doctors • Site visits to clinics by pharmacist

Key themes that emerged from the data included contextual, healthcare provider, and patient-oriented factors. Themes were organized around the SPT elements (material, meaning and competence), factors identified in literature to affect prescribing practices, and factors emerging from the data[1] (Appendix 4). For identification of the information source and anonymity, key informant quotes were coded as KI_Cadre_Level of care_Region; and frontline managers' quotes as FM_Cadre_Level of care_Region.

Health system context factors (Material)

This section highlights factors that participants reported to affect prescribing practices in line with how literature suggests that the context within which practice happens affects rational use of medicines. Availability of policy to guide RMU practices, availability and use of the STG/EML, availability of essential medicines, lack of pharmacy personnel in primary levels of care, restrictions of medicines by level of care, and active Pharmaceutics and Therapeutics Committees (PTCs) in hospitals and health centres were reported as health system factors (material) that affect prescribing and rational use of medicines.

[1] Baseline qualitative findings are published in this article: 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. Published 2020 Jul 9. doi:10.1371/journal.pone.0235513

Availability of policies to guide RMU practices

Frontline healthcare providers mentioned that the country had no policies to guide RMU, and this made it difficult for healthcare professionals to practice RMU without guiding policies. One frontline healthcare provider mentioned that due to lack of policies there was no guidance on who in the nursing cadre can and cannot prescribe, and this resulted in irrational prescribing.

Availability and use of the STG/EML

Information from key informants highlighted that public sector prescribing practices were influenced by the current STG/EML, which were mainly targeted at primary health care (though they can still be used at secondary and tertiary levels of healthcare). Until the latest guidelines published in 2012, Eswatini did not have country-specific guidelines. The current STG was a starting point to mainly guide clinics which provide primary healthcare and are only managed by nurses with no doctors and pharmacists; though the EML is comprehensive and includes all medicines available in the country at the different levels of care. The Ministry of Health had planned to then develop a more comprehensive guideline at a later stage. However, key informants highlighted that targeting the STG at primary level of care resulted in secondary and tertiary level facilities prescribing outside the guidelines.

> *"At tertiary level they say our STG is skewed a lot towards primary health care and doesn't provide for their guidance. And of course it is a little bit true… there is some truth to it because you know at tertiary level we can do with a little bit of a revision and we do both tertiary level and primary health care level [guideline needs to be revised for both primary and tertiary level], because at primary health care level we know that we do not have medical practitioners so we thought those are the ones that needed the guidance the most that's why we started with them (KI_P_N_H)."*

Key informants also reported that the STG/EML was outdated as it was published in 2012. However, KIs reported that availability of the STG/EML positively influenced rational use of medicine as some facilities used the STG/EML to develop their own (facility-specific) formularies. Though the STG/EML was seen to promote rational use of medicines, key informants reported that adherence to these guidelines seemed poor.

"We have put in place some contingency measures to try and guide or to try and coerce people to use medicines rationally by putting in place standard treatment guidelines. But when we follow with our facilities, we have realised that it is not used as such because some of them when you visit facilities, they have to look for the STG within their cabinets and stuff, yet you'd expect it on the desk where they are working with it (KI_P_N_H)."

A reason that was cited by key informants to possibly result in poor adherence to guidelines was that frontline healthcare providers were not comfortable to use the guidelines in front of patients.

"Because people think that [pause] I don't know it has not been proven so I want to believe it's a perception of the health care workers, because they tend to think that if they flip through their STG the patient will think they do not know, each time they are treating them they have to be checking but maybe with a mobile app on their smart phone the fears will be allayed (KI_P_IP_H)."

Key informants further reported that poor adherence to the STG/EML resulted in overuse of antibiotics which will soon contribute to the global problem of antimicrobial resistance. On the contrary, frontline healthcare providers validated overuse of antibiotics by reporting that most of the conditions that patients presented with required management with antibiotics.

Restrictions of medicines by level of care

Frontline healthcare providers highlighted the difficulty for them to adhere to treatment guidelines due to restrictions on availability of medicines at certain levels of care. An example cited was the unavailability of ceftriaxone and azithromycin at primary healthcare levels yet the latest guidelines for managing sexually transmitted infections recommend these medicines as first line therapy and for them to be available at primary healthcare level. Furthermore, frontline healthcare providers, particularly in clinics and health centres aired their frustration on certain medicines that were, according to the guidelines, not available at these levels of care yet they see many patients who need such medicines. Health centre level frontline providers questioned restriction of some medicines to hospital level, yet there were doctors in health centres who could manage patients the same way they would be managed in hospitals.

"I want to believe that the ministry of health has got the presentation on power point made by Facility Y in which we are asking the ministry to revise some parts that are in the

guideline to make more drugs available for health centres and clinics. We know that in Swaziland there are drugs that you can't find in clinics. There are drugs that you can't find in health centre though those drugs are available in the country (FM_MO_Sec_L)."

In such cases frontline healthcare providers from clinics and health centres mentioned that they referred patients to hospitals and it is often geographically difficult for patients to access these. Most medicines for managing NCDs were reported to not be allocated for use in primary healthcare facilities in the STG and hence not available at primary level facilities. The following are medicines for management of NCDs available at primary level of care: for hypertension - only hydrochlorthiazide; for diabetes – none of the medicines are available at primary level; for arthritis – indomethacin, colchicine, allopurinol, acetylsalicylic acid, and procaine penicillin/erythromycin [for osteomyelitis] are indicated for primary level use). Antibiotics were also reported as medicines that are not available at primary level of care; these were: penicillins (amoxicillin + clavulanic acid, flucloxacillin), all cephalosporins, sulphonamides (trimethoprim/sulphamethoxazole (400/80) injection), Macrolides/lincosamides/streptogramins (clarithromycin, clindamycin), aminoglycoside (streptomycin and vancomycin injections), quinolones (ciprofloxacin 250mg tablet, while the 500mg tablet is indicated for primary level use), and nitrofurantoin.

Availability of essential medicines

Frontline healthcare providers reported that essential medicines were constantly out of stock at the CMS and in health facilities. Stock-outs were reported as barriers that affect adherence to the STG/EML and rational use of medicines. Due to frequent unavailability of medicines, frontline healthcare providers reported that they often find themselves out of options on what to prescribe for the patients, and at the same time, found it difficult to send patients home with no medicines to alleviate their suffering. In such instances, frontline healthcare providers reported that they send patients to private sector facilities and sometimes prescribe out of the STG/EML and give medicines that might not be appropriate for the condition. Frontline healthcare providers stated that patients needed to have money to buy medicines and for transport to get to private sector facilities. Medicines that were reported to constantly be out-of-stock were those for managing NCDs. Often, patients would report to not have money to travel and buy medicines and such patients then discontinue taking their NCD medicines, compromising their management.

Some reasons that were cited for stock-outs of essential medicines were poor stock management practices which result in inadequate amounts ordered from the CMS.

> *"I think there are challenges with stock ordering from the facilities. You find that they run out because they haven't ordered the right quantities due to poor stock management practices (KI_P_C_M)."*

Delayed ordering by facilities, long lead times for CMS to deliver in facilities, inconsistent/inadequate supply of medicines by the CMS, and poor communication on stock availability between the CMS and facilities were also reported to affect stock availability and ultimately RMU.

> *"We only hear about stock shortages from facilities when they now are complaining that they are not getting their order, so there is no transparent communication between the central medical stores and the facility or at least the region (KI_P_C_M)."*

Lack of pharmacy personnel in primary levels of care

Frontline healthcare providers reported that clinics do not have pharmacy personnel, and this made it difficult for nurses to manage facility stocks of medicines (monitoring average monthly consumptions, quantities to order, and share slow-moving stock with other facilities to minimize expiries) as their professional qualification does not equip them to do this work. Though frontline healthcare providers reported that they receive off-and-on-site intermittent trainings on stock management from the CMS and implementing partners, they highlighted that not all nurses in a facility would receive the training. Furthermore, rotations of nurses between facilities resulted in some facilities having no nurses trained on stock management.

Inactive PTCs

Key informants and frontline healthcare providers reported that health centres and hospitals had PTCs, however, most were reported to not function adequately. Information gathered from some participants highlighted that monitoring of activities of PTCs was through meeting minutes that are submitted to the MoH headquarters. On probing about activities performed by PTCs, participants mentioned that meetings mainly discussed errors in prescribing; and due to prescribers feeling as if they were targeted during these, they often did not attend meetings. This resulted in committee members not forming a quorum and hence cancelling most meetings, ultimately rendering PTCs inactive in facilities. Clinics reported that they have monthly/weekly meetings which they used to discuss all issues pertaining their facilities – including prescribing patterns.

Patient Factors (Meaning)

This section reports on the effects of cultural conventions, expectations, and socially shared meaning on rational use of medicines. Themes reported to affect prescribing were mainly patient factors. Frontline healthcare providers reported that patients took too long to present to facilities. By the time they did, ailments would have progressed to complications, making it difficult for providers to treat these patients according to the STG/EML. Frontline providers also reported that patients demanded more medicines (an issue resulting in polypharmacy) and were not comfortable to leave the healthcare facility with no or few medicines.

> *"There also is also pressure from the patient that require a lot of variety of medicine. Patients are not satisfied if they are going away with maybe three types of medicines when they leave the facility, ah maybe they have a flu or headache or maybe a simple injury, you discover that they are not satisfied once they give, if you just give them one or two medicines, they want many (FM_PT_Sec_S)."*

To increase the number of medicines, frontline providers mentioned that prescribers end up prescribing medicines with no or little proven effectiveness. Frontline providers also mentioned that they sometimes prescribe and dispense a lot of medication to try and cover all ailments that the patients could be suffering from.

> *"uhm, yah we can benefit but once we had, we want to give the best care to our clients, we want to give extra actually if I can say so we don't want the client to come back with such a case that you gave me this drug what, what, what (FM_N_Prim_L)".*

On probing, the medicines that were reported to be most prescribed to increase medicine numbers were multivitamins, vitamin B complex, methyl salicylate and low doses of calcium gluconate. Key informants highlighted that polypharmacy was not just because of patients demanding many medicines from healthcare providers. They reported that polypharmacy for NCDs was very high, due to poor consulting practices by some healthcare providers.

"When it comes to chronic medications - that is where we have observed the worst case the most because you find that the prescriber, before even the chronic patient comes in for their diabetes or hypertension, the prescriber has started writing something on their prescription book the first two being a pain killer or even some multivite without assessing the patient and not knowing what is wrong with them. I mean does it mean everyone who leaves the hospital must have a pain killer, does it mean everyone is in pain - so that's why we say we have picked up elements of irrational use which we need to tell people to solve… Evidence of that is that at times when they [patients] are given some of these [medicines], because they know their core medicines that they need to take, and then the others [medicines] they will tell you "oh I still have that at home", so it shows that they are keeping it they're not taking it they are just taking their BP medication because that is their basic medication so they know that the others are just for pain if I may call them that […Laughs…](KI_P_N_H)."

Possible reasons for polypharmacy as stated by one frontline healthcare provider were poor adherence to the STG/EML, ignorance and poor knowledge.

"I think it's ignorance, lack of knowledge, not following the standard treatment guideline or even trying to please the patient (FM_P_Sec_H)".

Language was also cited as a patient factor that affected rational use of medicines. In facilities that were close to the border, frontline providers mentioned that they had patients that came to access healthcare from Mozambique and it was difficult to communicate with them. Also, providers reported that the elderly often struggled to understand instructions on how to use the medicine they were prescribed which left frontline providers uncertain if such patients used the medicines correctly.

Provider factors (Competence)

Provider-oriented factors that were reported to affect rational prescribing were: symptomatic prescribing, high patient volumes, competence, individual prescriber practice ethic, poor teamwork in patient management, and poor documentation practices. Frontline healthcare providers reported that irrational use of medicines is sometimes driven by symptomatic prescribing; where prescribers treat symptoms and not the diagnosis.

"The treatment is according to symptoms, so if you are sneezing you get items for sneezing, if you are coughing you get something for coughing and if you have an itchy eye you get something for the itchy eye. Itchy nose you get something for the itchy nose, if you have irritating throat, they give you something for irritating throat, list continuous like that, instead of making a proper diagnosis: what is the proper diagnosis, maybe the person has got one diagnosis which is flu, or which is respiratory tract infection. Just treat the disease, what do they do, treat each symptom with each medication (FM_PT_Sec_L)."

Regarding patient volumes, frontline healthcare providers reported that they sometimes prescribe as many medicines as possible to cover symptoms reported by patients and ensure that they do not come back to the facility the following day and increase patient numbers.

In this study, healthcare provider knowledge and embodied skills, as highlighted by the SPT, were reported to affect prescribing practices. Health system actors reported that actors at all levels of care in the country were poorly trained on rational use of medicines, and this resulted in inappropriate use of medicines in health facilities. Though some RMU training for frontline healthcare providers was happening, key informants reported that this training was not streamlined and policy makers were not privy to information on who has and has not been trained as they were not receiving training reports from facilitators.

Frontline healthcare providers reported that Eswatini did not have pre-service orientation of foreign-qualified healthcare professionals on RMU and use of the STG/EML.

"Their competence is not tested, in terms of prescribing or their knowledge on the disease patterns that are affecting the Southern region as well as the patterns again that affect the local region. They struggle in the early days to uh to understand the disease pattern that we do have so at the end of the day they just prescribe anything maybe according to whatever they have been trained, so there is also a general problem of not following the treatment guideline of which they are there (FM_PT_Sec_H)".

Different practice ethics by prescribers were reported to also affect rational use of medicines in Eswatini. One key informant mentioned that some prescribers were not comfortable to consult guidelines in front of patients.

"Because people think that […pause…] I don't know it has not been proven so I want to believe it's a perception of the health care workers because they tend to think that if they flip through their STG the patient will think they do not know, each time they are treating them they have to be checking but maybe with a mobile app on their smart phone the fears will be allayed (KI_P_IP_H)."

On probing to find how the issue of frontline healthcare providers not being comfortable to consult guidelines in front of patients could be solved, health system actors suggested the use of a mobile application.

Poor teamwork in the management of patients was also reported to result in irrational use of medicines. Pharmacy staff mentioned that prescribers were not comfortable with suggestions made by pharmacy personnel on adjusting prescriptions to meet the patients' needs and often felt undermined.

"The pharmacy personnel call that prescriber when they receive a prescription and feel there is some irrational use of medicines to discuss the issues. However, a lot of times the pharmacy staff come across challenges when they do this as some of the prescribers then feel undermined, offended, and most of the time they refuse to change the prescription (FM_PT_Sec_H)."

If pharmacy staff changed the prescription, the patient often went back to the prescriber to question the change. This caused disputes between pharmacy staff and prescribers which resulted in disciplinary meetings being called for pharmacy staff.

"It's like they really don't want to be corrected and so they called a meeting against pharmacy so our challenge is tight, but now we don't call them now you look at the prescription and you see what you can do (FM_PT_Sec_S)."

Furthermore, frontline providers reported that "being used to doing things in a certain way" resulted in inappropriate use of medicines.

"So, the weakness there is training, and not only training it's again changing the culture and the practice and culture … The tendency is, you see if we have a problem, we talk maybe in a therapeutic committee today and hope that people will bring sort of change,

then after that the graph just goes down. People change into their old practices that's why I said it's a culture, a culture is difficult to change for someone who is, maybe, they have been taught at school that this is what they are supposed to do and so you know trying to change that culture is a long process (FM_P_Sec_M)."

Poor or no documentation of prescribing information in some facilities was reported as another factor affecting rational use of medicines. Key informants highlighted that they were not sure if facilities with no records of prescribing information did this due to lack of knowledge on the importance of documentation and record keeping. On probing as to how it was possible for a facility to not have such records, key informants reported that at a single facility the doctor/nurse writes a prescription on a notepad that the patient takes it to the pharmacy and no record of the prescription remains in the prescriber's room. Only one facility had this situation and thus the overall results were not substantially affected. Once the prescription has been filled in the pharmacy, the patient takes the original prescription with them leaving the facility with no record of what was prescribed and dispensed for the patient.

Contrary to information from key informants on record keeping, frontline healthcare providers reported that they knew and understood the importance of keeping patient records in facilities. However, the government was constantly stocked out on prescription booklets in which each prescription is triplicate. Once the prescription has been written, the first and second copies are given to the patient to take to the pharmacy for dispensing of medicine – one copy stays in the pharmacy after dispensing while one copy leaves with the patient. The third copy remains with the prescriber; hence, there then is a record of each patient that stays with the prescriber and another with the pharmacy which are kept in the facility.

Beyond identifying factors that affect rational use of medicine, health system actors had recommendations on how RMU can be promoted in the country. Such recommendations included: functional PTCs; on- and off-site training of prescribers on appropriate use of medicines and inventory management; pre-service training for healthcare providers who qualify outside Eswatini; review and update of the STG/EML; supervision and mentorship of facility staff on medicines; widening the list of medicines available at primary health care level; development, implementation and monitoring of RMU policies; and availability of nurses trained on RMU in all facilities.

5.2 Phase III: Post Intervention and Post Follow-up Evaluation

This section will detail and compare quantitative results for the three time periods: baseline, post intervention, and post follow-up. It will also report on qualitative results for interviews conducted at the end of the follow-up period.

5.2.1 Quantitative Component

Overall WHO/INRUD Indicators (All facilities)

A total of 32 facilities were included in this study. On average, 100 prescriptions post intervention and 105 prescriptions post follow-up were collected/extracted in each of the 32 facilities making a total of 3201 post intervention and 3290 post follow-up prescriptions analysed during the post intervention phase. Sixteen facilities were randomly assigned to the intervention arm, and 16 were assigned to the control arm. All facilities in both arms were included in analyses by overall indicators, level of care, and region. One facility in the intervention arm was excluded from post intervention and post follow-up diagnoses analyses as it did not have diagnoses at baseline (see Figure 3).

Average number of medicines per prescription

There was a slight decrease in the average number of medicines per prescription from baseline to post-intervention to post follow-up periods for both intervention and control facilities as shown in Figure 9.

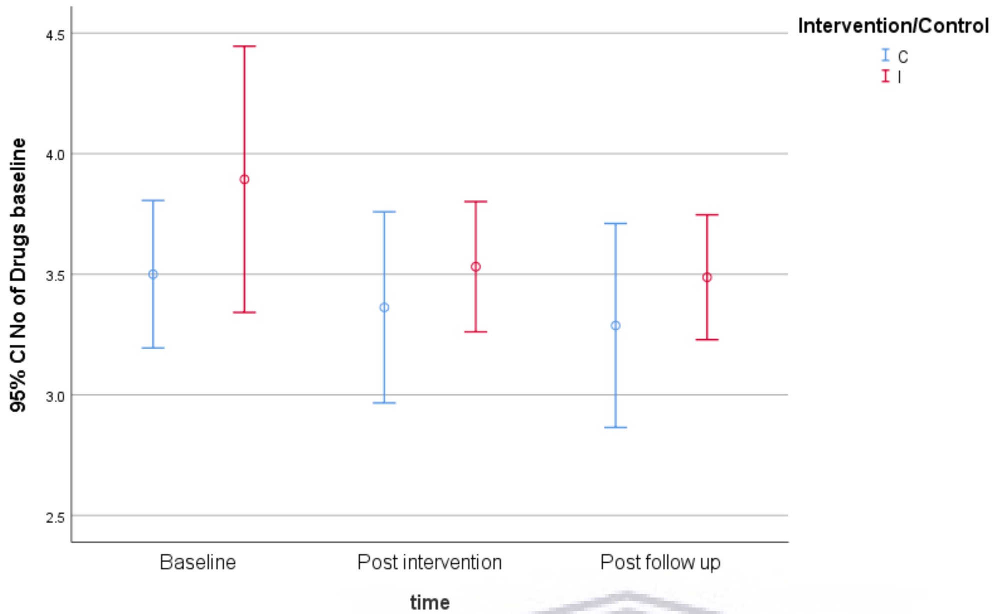

Figure 9: Average number of medicines per prescription from baseline to post-follow up

For this indicator, though there was a decrease in the average number of medicines per prescription in both intervention and control facilities between baseline and post intervention, and values remained the same at the end of the follow up period, none of the mean differences were statistically insignificant as shown in Table 11.

Table 11: Mean difference in differences of average number of medicines per prescription from baseline to post intervention and post follow up between intervention and control facilities

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in number of medicines between baseline and post intervention	-0.71	30	0.48	-0.23	0.32	-0.87	0.42

Difference in number of medicines between baseline and post follow-up	-0.60	30	0.55	-0.19	0.32	-0.86	0.47
Difference in number of medicines between post intervention and post follow-up	0.30	30	0.77	0.031	0.11	-0.18	0.25

Generic Prescribing

An increase in the percentage of medicines prescribed by generic name was observed from baseline through post-intervention to post-follow up in both intervention and control facilities. A higher increase however was observed in facilities in the control group compared to those in the intervention as shown in Figure 10.

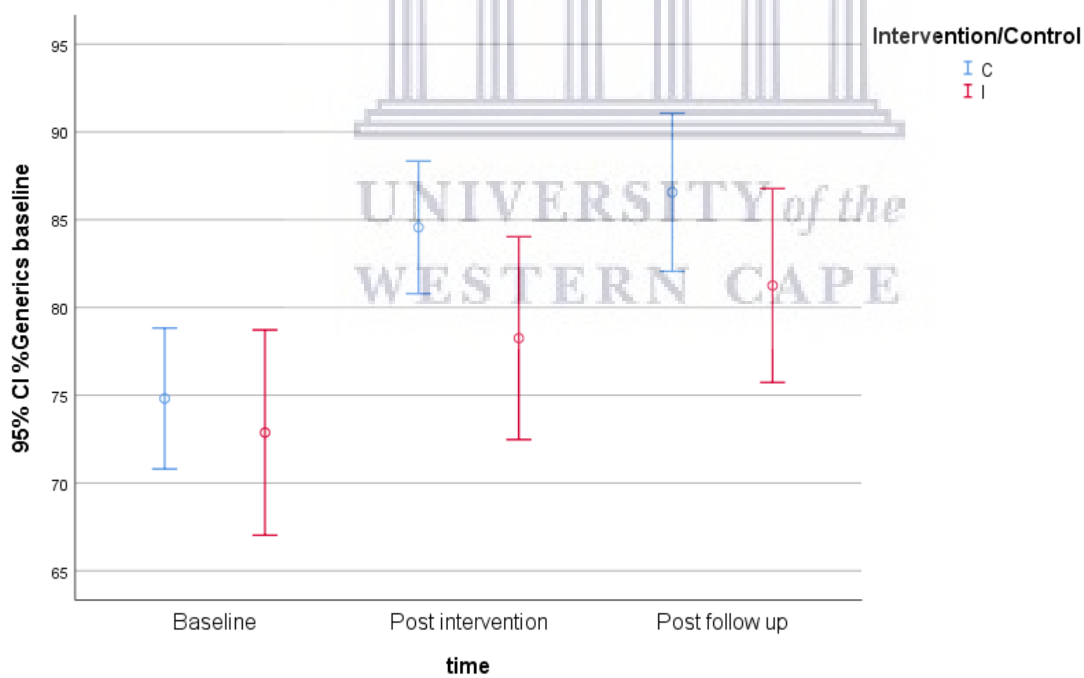

Figure 10: Percentage of medicine prescribed by generic name from baseline to post follow-up period

The mean differences at the three time points for percentage of medicines prescribed by generic name were statistically insignificant as shown in Table 12.

Table 12: Mean difference in differences of percentage of medicines prescribed by generic name from baseline to post intervention and post follow up between intervention and control facilities

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in percent of medicines prescribed by generic name between baseline and post intervention	-0.95	30	0.35	-4.38	4.60	-13.76	5.00
Difference in percent of medicines prescribed by generic name between baseline and post follow-up	-0.81	30	0.42	-3.38	4.16	-11.87	5.12
Difference in percent of medicines prescribed by generic name between post intervention and post follow-up	0.54	30	0.59	1.00	1.85	-2.77	4.77

Antibiotics Prescribing

The percentage of prescriptions with antibiotics prescribed dropped slightly from baseline to post-intervention for both intervention and control facilities with a higher drop in control facilities. The percentage bounced back to values even higher than baseline values post the follow-up period in both arms as shown in Figure 11.

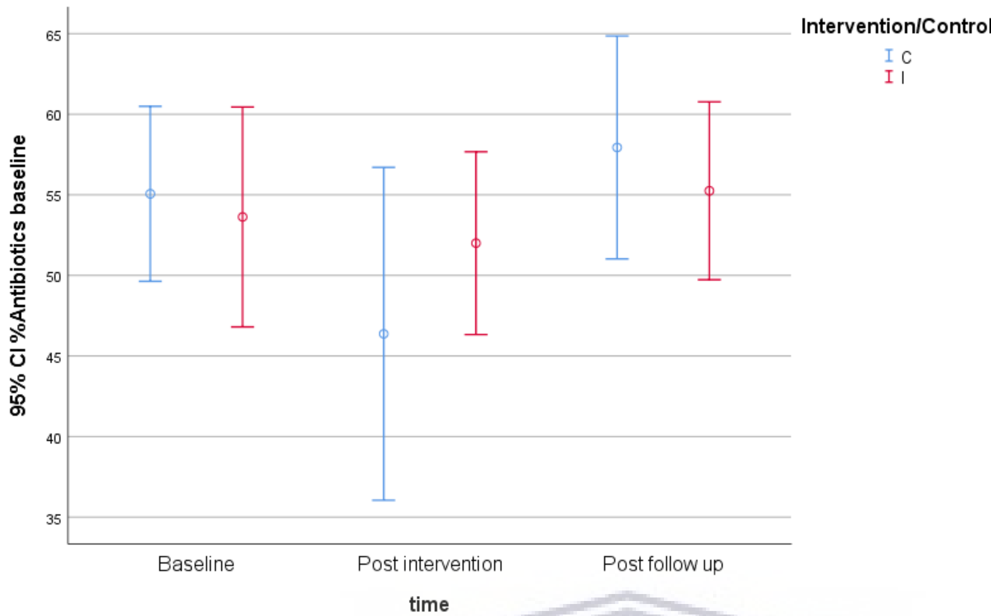

Figure 11: Percentage of prescriptions with at least one antibiotic at baseline, post intervention and post follow-up periods

The mean difference in percentage of prescriptions with antibiotics between post intervention and post follow-up was significantly larger than zero and statistically significant (mean difference = -8.31, p = 0.03, 95% CI = -15.74 - -0.89) as shown in Table 13. The negative difference meant that the control group experienced a greater increase between these time points than the intervention group.

Table 13: Mean difference in differences in percentage of prescriptions with antibiotics from baseline to post intervention and post follow-up between intervention and control facilities

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in percent of prescriptions with at least one antibiotic between baseline and post intervention	1.15	30	0.26	7.06	6.14	-5.48	19.61
Difference in percent of prescriptions with at least one antibiotic between baseline and post follow-up	-0.29	30	0.77	-1.25	4.25	-9.94	7.44
Difference in percent of prescriptions with at least one antibiotic between post intervention and post follow-up	-2.29	30	***0.03****	-8.31	3.64	-15.74	-0.89

*Statistically significant at p≤0.05

Injections Prescribing

Percentage of prescriptions with injections decreased from baseline to post intervention period in both intervention and control facilities; and slightly increased post the follow-up period with a higher increase observed in control facilities as shown in Figure 12.

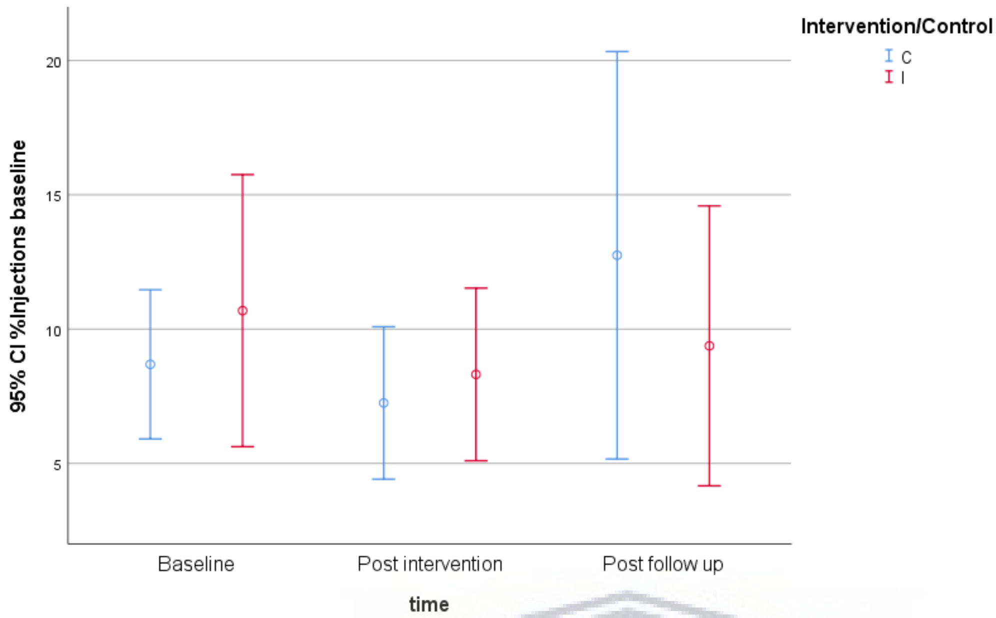

Figure 12: Percentage of prescriptions with an injection prescribed at baseline, post intervention and post follow up periods

The mean differences for percentage of prescriptions with injections were statistically insignificant as shown in Table 14.

Table 14: Mean difference in differences in percentage of prescriptions with injections from baseline to post intervention and post follow up between intervention and control facilities

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in percent of prescriptions with injections between baseline and post intervention	-0.37	30	0.71	-0.94	2.51	-6.06	4.18
Difference in percent of prescriptions with	-1.21	30	0.24	-5.38	4.45	-14.47	3.72

injections between baseline and post follow-up							
Difference in percent of prescriptions with injections between post intervention and post follow-up	-1.26	30	0.22	-4.44	3.54	-11.66	2.78

Prescribing from the EML

The percentage of medicines prescribed from the EML dropped from baseline to post intervention with a higher decrease in intervention than control facilities. At the end of the follow-up period, the percentage of medicines prescribed from the EML increased for both intervention and control facilities as shown in Figure 13.

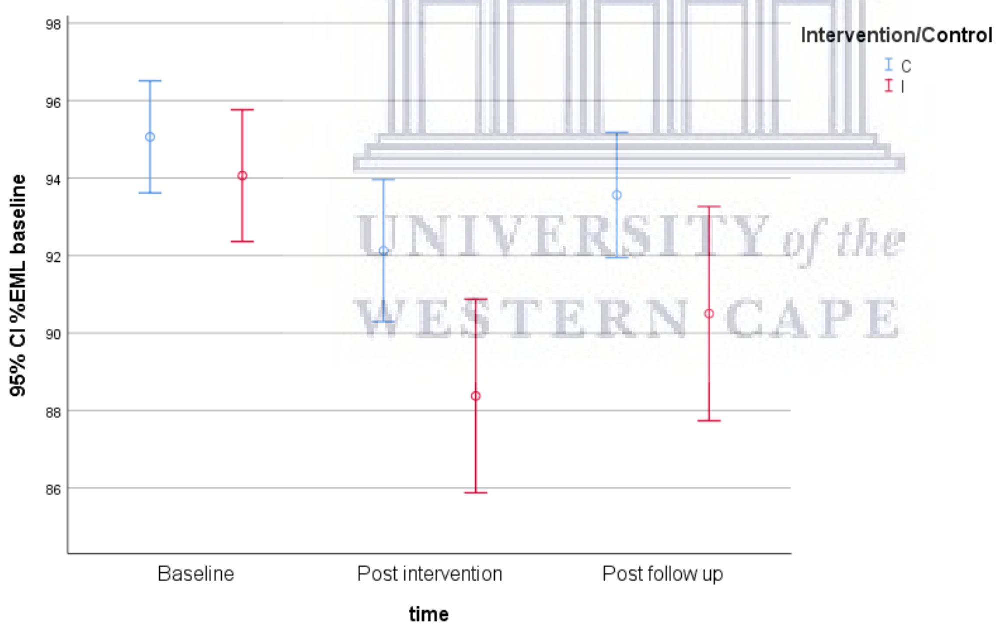

Figure 13: Percentage of medicines prescribed from the EML at baseline, post intervention and post follow up periods

Statistical significance was observed in the mean difference in the percentage of medicines prescribed from the EML between baseline and post intervention (mean difference = -2.75, p=

0.02, 95% CI = -4.99 - -0.51) as shown in Table 15. The negative difference meant that the intervention decreased more than the control.

Table 15: Mean difference in differences in the percentage of medicines prescribed from the EML between baseline and post intervention between intervention and control facilities

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in percentage of medicines prescribed from the EML between baseline and post intervention	-2.51	30	***0.02****	-2.75	1.10	-4.99	-0.51
Difference in percentage of medicines prescribed from the EML between baseline and post follow-up	-1.95	30	0.06	-2.06	1.06	-4.22	0.10
Difference in percentage of medicines prescribed from the EML between post intervention and post follow-up	0.68	30	0.50	0.69	1.01	-1.37	2.75

*Statistically significant at $p \leq 0.05$

Acute and Chronic Diagnoses

Acute Diagnosis

Average number of medicines per prescription

For acute conditions, the average number of medicines per prescription decreased for both intervention and control facilities from baseline to post intervention. The decrease in the average number of medicines was sustained at the end of the follow-up period as shown in Figure 14.

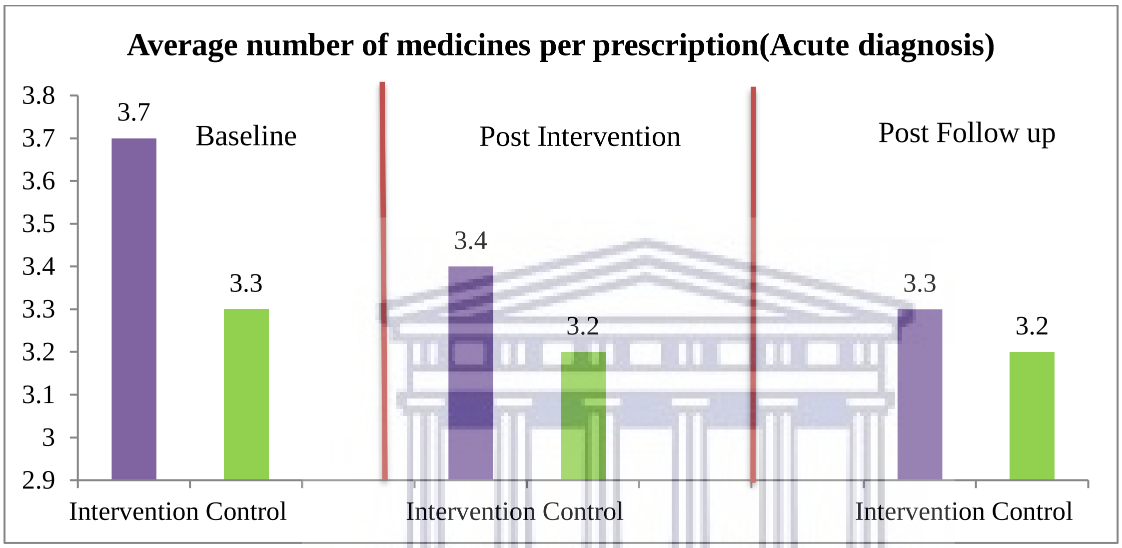

Figure 14: Average number of medicines per prescription - acute diagnosis

Generic prescribing

The percentage of medicines prescribed by generic name for acute conditions increased in both intervention and control facilities from baseline to post intervention. At the end of the follow-up period the percentage continued increasing for control facilities while there was a drop in intervention facilities as shown in Figure 15.

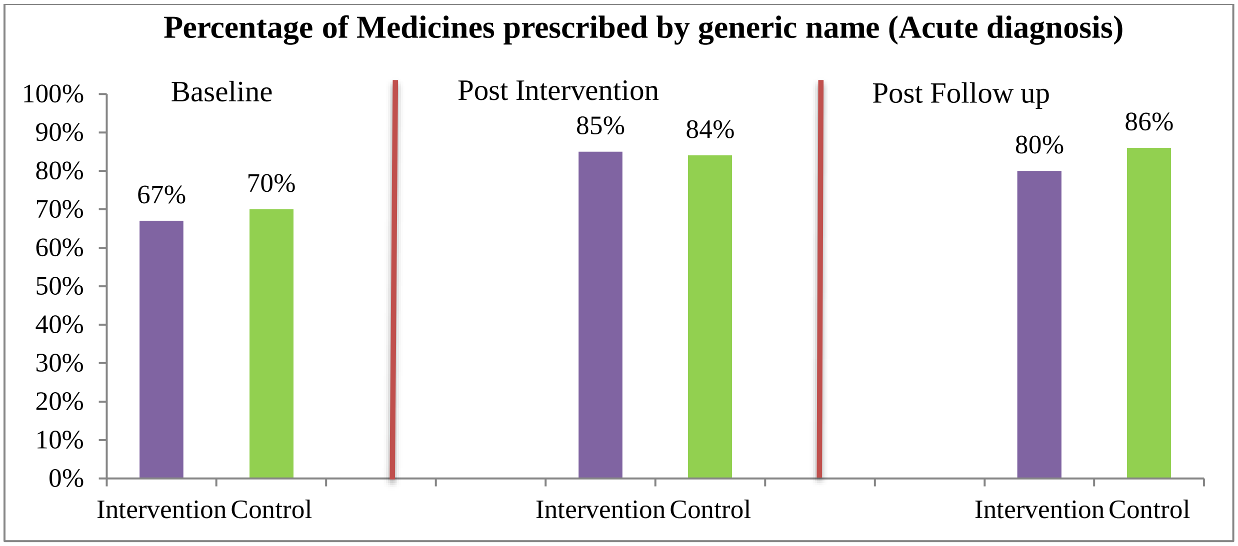

Figure 15: Percentage of medicines prescribed by generic name (acute diagnosis)

Antibiotics prescribing

For acute diagnosis, the percentage of prescriptions with antibiotics decreased in both intervention and control facilities from baseline to post intervention. This decrease was not sustained as the percentages had increased at the end of the follow-up with period; with a higher increase observed in control facilities as shown in Figure 16.

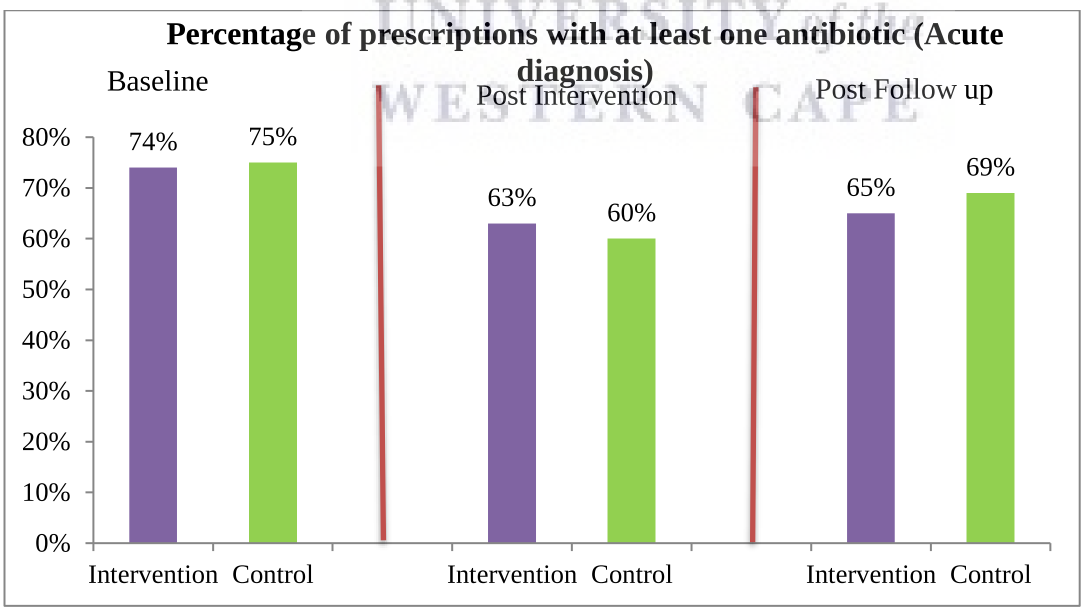

Figure 16: Percentage of prescriptions with at least one antibiotics (acute diagnosis)

Injections prescribing

In both intervention and control facilities the percentage of prescriptions with injections decreased from baseline to post intervention for acute conditions. At the end of the follow-up period the percentages increased with a higher increase observed in control facilities as shown in Figure 17.

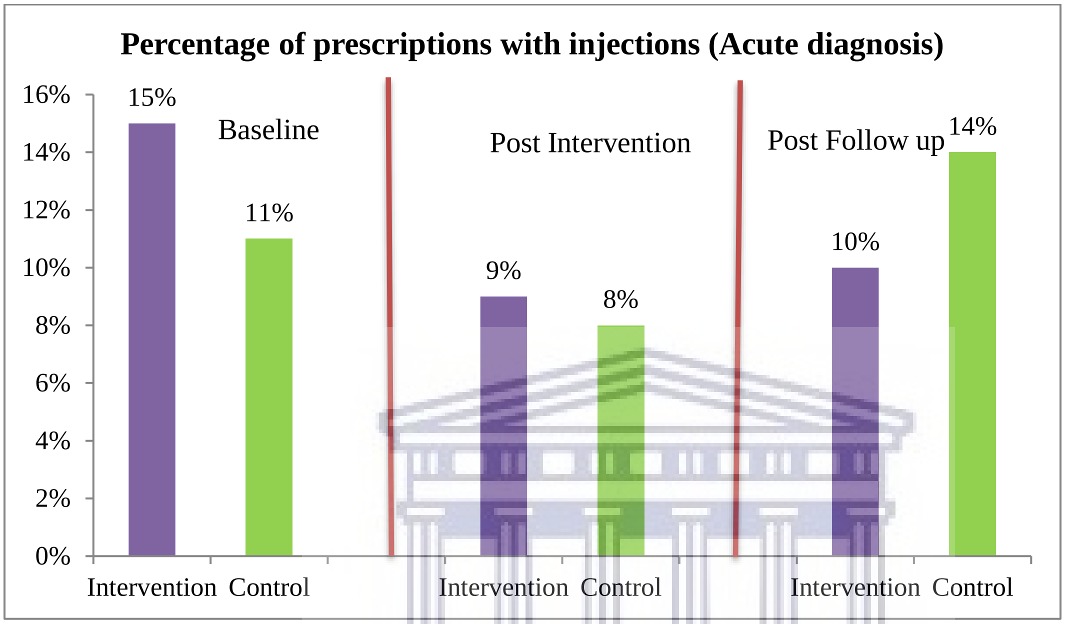

Figure 17: Percentage of prescriptions with injections (acute diagnosis)

Prescribing from the EML

For acute conditions, the percentage of medicines prescribed from the EML decreased from baseline to post intervention for both intervention and control facilities; and the highest decrease was observed in intervention facilities. A slight increase in percentages was observed at the end of the follow-up period in both intervention and control facilities as shown in Figure 18.

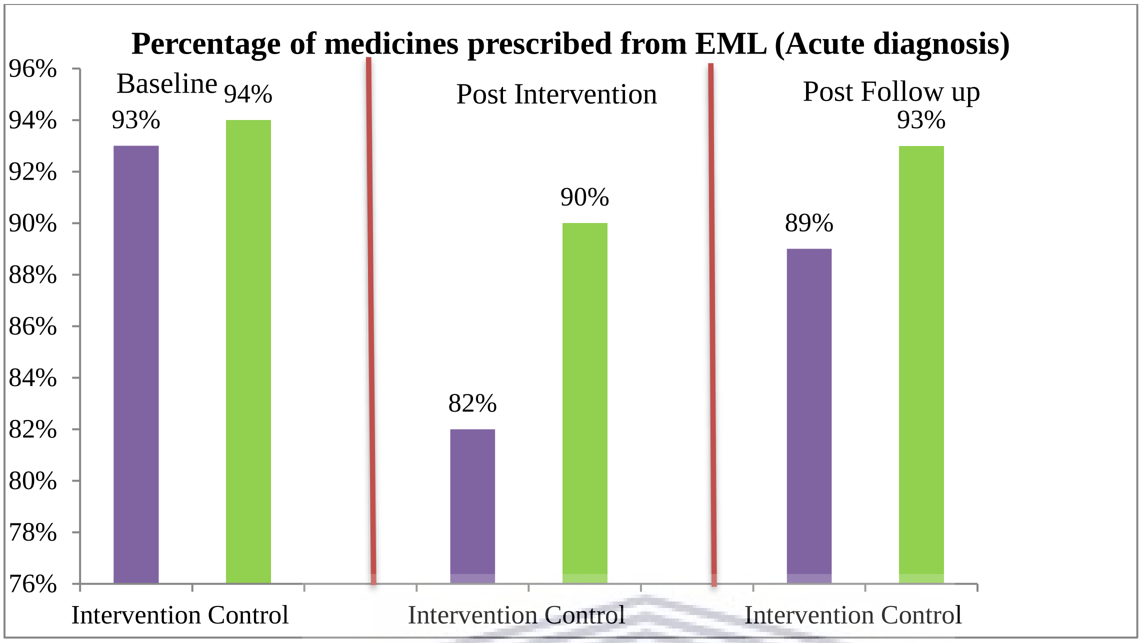

Figure 18: Percentage of medicine prescribed from the EML (acute diagnosis)

Comparison of prescribing indicators by intervention and control groups for acute conditions

When comparing the WHO/INRUD prescribing indicators for the intervention and control groups for acute conditions, the mean difference in differences of percentage of medicines prescribed from the EML between baseline and post intervention was the only statistically significant indicator (mean difference = -2.85, 95%CI = -5.64 - -0.07, p = 0.05) as shown in Table 16. The negative value of the mean difference shows that the number of medicines prescribed from the EML decreased at this time point. To show a positive effect of the intervention, the mean difference for this indicator should have been positive. All other mean differences of prescribing indicators were statistically insignificant as shown in Appendix 16.

Table 16: Mean difference in differences in percentage of medicines prescribed from the EML between baseline and post intervention (acute conditions) between intervention and control facilities

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in percentage of medicines prescribed from the EML between baseline and post intervention	-2.10	29	***0.05**	-2.85	1.36	-5.64	-0.07
Difference in percentage of medicines prescribed from the EML between baseline and post follow-up	-1.90	29	0.07	-2.72	1.43	-5.63	0.20
Difference in percentage of medicines prescribed from the EML between post intervention and post follow-up	0.29	30	0.78	0.45	1.55	-2.72	3.62

*Statistically significant at p≤0.05

Chronic diagnosis

Average number of medicines per prescription

For chronic conditions, the average number of medicines per prescription dropped in both intervention and control facilities from baseline to post intervention. The drop was sustained at the end of the follow-up period in intervention facilities while control facilities had a 0.2 drop from post intervention as shown in Figure 19.

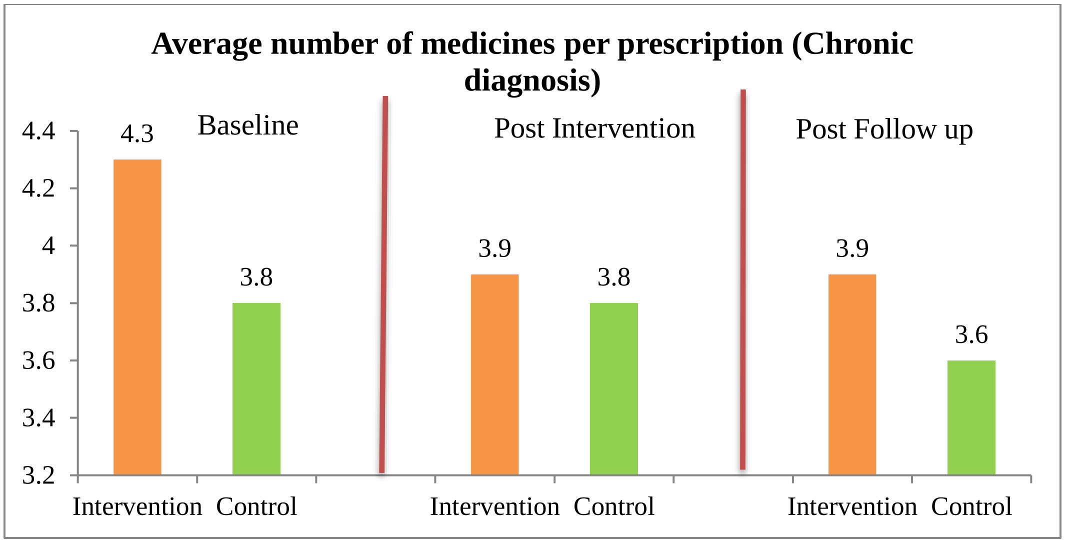

Figure 19: Average number of medicines per prescription (Chronic diagnosis)

Generic prescribing

Percentage of medicines prescribed by generic name for chronic conditions increased from baseline to post intervention; the increase was sustained post the follow-up period as shown in Figure 20.

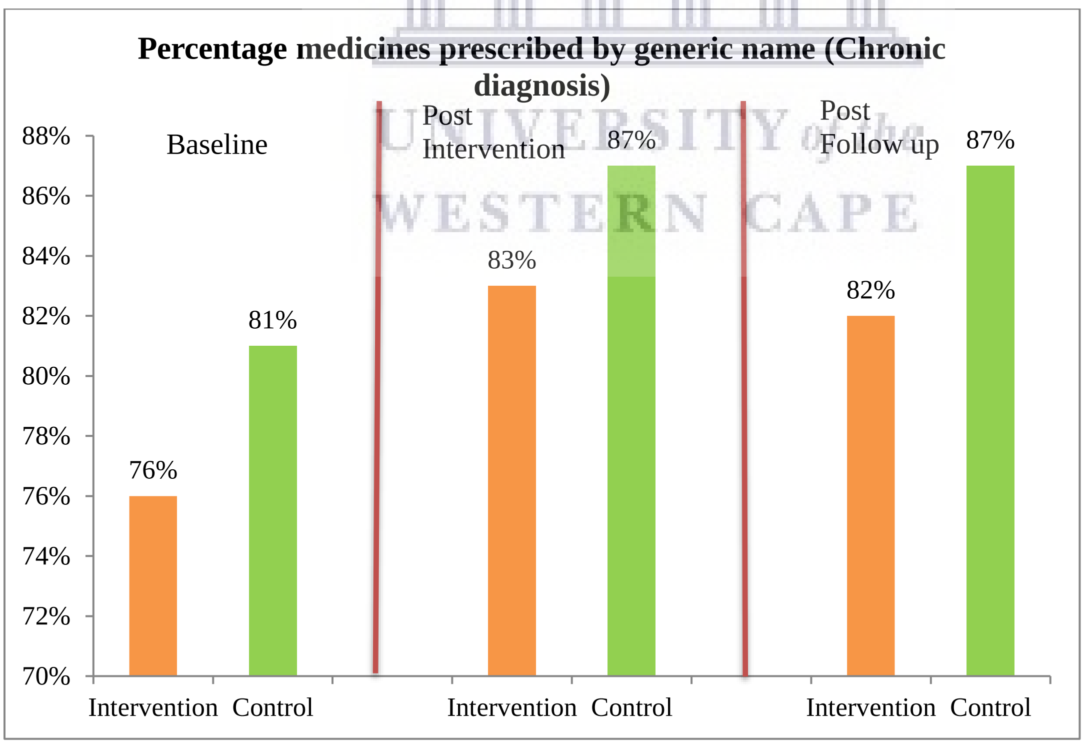

Figure 20: Percentage of medicines prescribed by generic name (chronic diagnosis)

Antibiotics prescribing

A small decrease in prescribing of antibiotics for chronic conditions was observed in both intervention and control facilities as the percentage of prescriptions with antibiotics decreased from baseline to the post intervention period as shown in Figure 21. Slight increases in antibiotic prescribing in both intervention and control facilities were observed at the end of follow-up period.

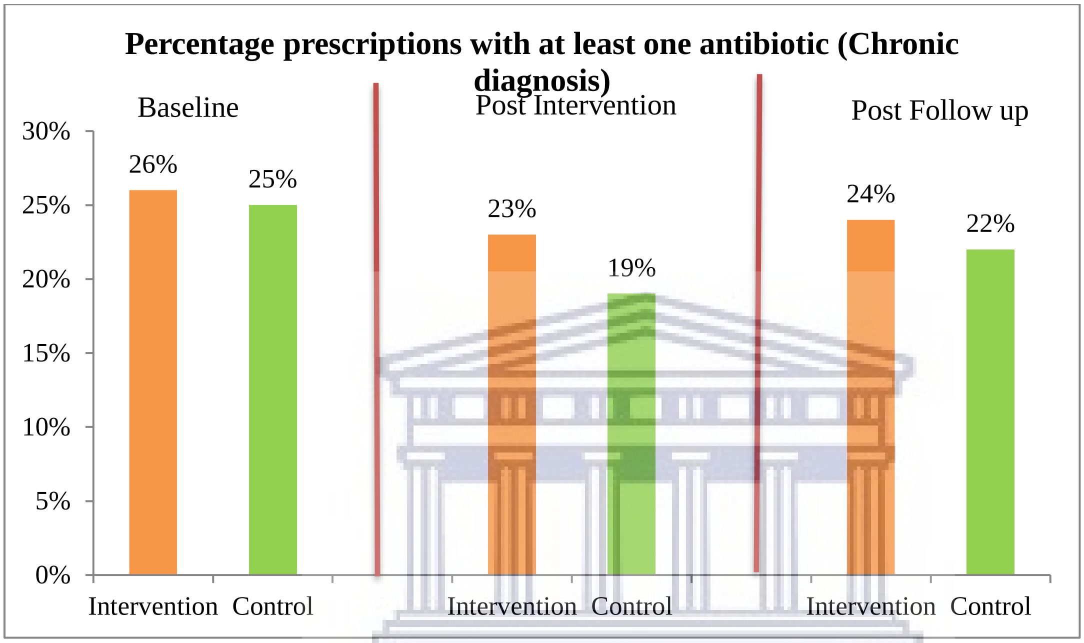

Figure 21: Percentage of prescriptions with at least one antibiotic prescribed (chronic conditions)

Injections prescribing

Prescribing of injections for chronic conditions decreased from baseline to post intervention in both intervention and control facilities as shown in Figure 22. However, this decrease was not sustained as at the end of the follow-up period the percentage of prescriptions with an injection had doubled compared to baseline in intervention facilities and rose to a percentage higher than that at baseline for control facilities.

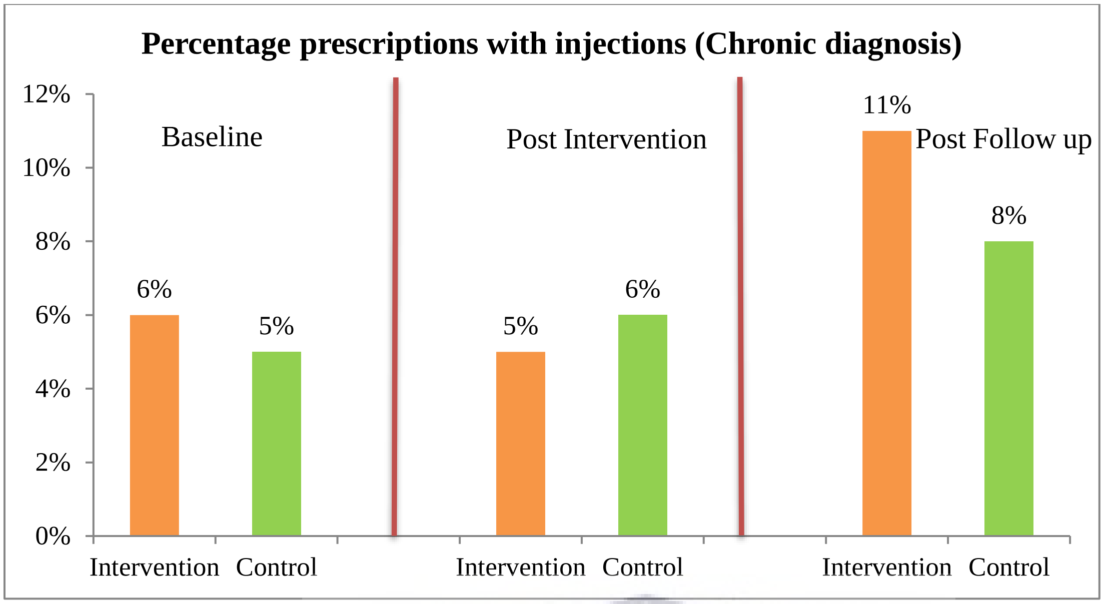

Figure 22: Percentage of prescriptions with injections (chronic diagnosis)

Prescribing from the EML

For chronic conditions, a slight decrease in percentage of medicines prescribed from the EML were observed from baseline to post intervention in intervention facilities; and the value slightly increased at the end of the follow-up period. In control facilities, a 0.1% decrease in medicines prescribed from the EML was observed from baseline to post intervention; this decrease was sustained at the end of the follow-up period as shown in Figure 23.

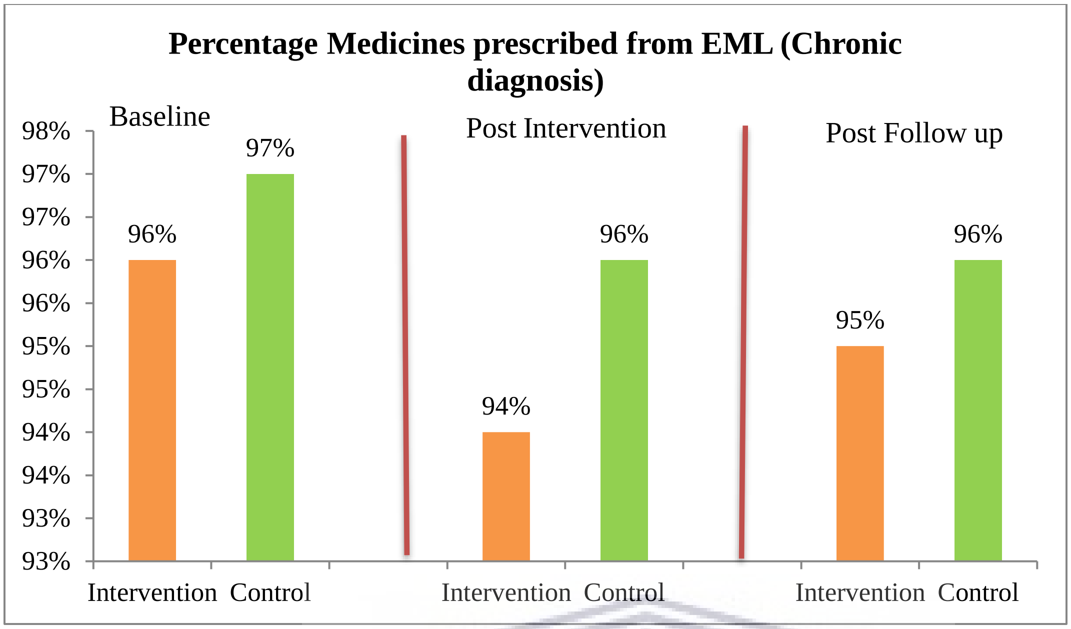

Figure 23: Percentage of medicines from EML (chronic conditions)

Comparison of prescribing indicators by intervention and control groups for chronic conditions

When comparing the mean differences in differences for the WHO/INRUD prescribing indicators between the intervention and control groups for chronic conditions, none of the mean differences were statistically significant (Appendix 16).

WHO/INRUD Indicators by region (All facilities)

Average number of medicines per prescription

The average number of medicines prescribed per prescription decreased in all four regions from baseline to post intervention with the highest decrease observed in the Manzini region as shown in Table 17. The average further dropped for Shiselweni and Lubombo regions post follow-up; remained as it was in Manzini region, while it increased in the Hhohho region. However, these changes were not statistically significant.

Table 17: Average number of medicines per prescription (regions)

WHO/INRUD Indicator	Average Number of Medicines per Prescription		
Region	**Baseline**	**Post Intervention**	**Post Follow up**
Manzini	4.0	3.4	3.4
Shiselweni	3.5	3.3	3.1
Lubombo	3.8	3.7	3.6
Hhohho	3.5	3.4	3.5

Generic prescribing

The percentage of medicines prescribed by generic name increased from baseline to end of follow-up period for all the regions; with the highest increase in the Lubombo region as shown in Table 18. However, these changes were not statistically significant.

Table 18: Percentage of medicines prescribed by generic name

WHO/INRUD Indicator	Percentage Medicines Prescribed by Generic Name		
Region	**Baseline (%)**	**Post Intervention %)**	**Post Follow up (%)**
Manzini	70	75	78
Shiselweni	80	86	88
Lubombo	71	85	88
Hhohho	75	81	83

Antibiotics prescribing

The percentage of prescriptions with antibiotics prescribed decreased from baseline to post intervention in all regions, with the highest decrease (9%) in the Shiselweni and Lubombo regions, 7% in Manzini, and only 2% in the Hhohho region as shown in Table 19. However, at the end of the follow-up period, the percentage of prescriptions with antibiotics increased to approximately baseline values for all regions; with the Shiselweni region having a 3% higher value than the baseline value. These changes, however, were not statistically significant.

Table 19: Percentage of prescriptions with antibiotics prescribed

WHO/INRUD Indicator	**Percentage Prescriptions with Antibiotics**		
Region	**Baseline (%)**	**Post Intervention %)**	**Post Follow up (%)**
Manzini	57	50	58
Shiselweni	54	45	57
Lubombo	52	43	54
Hhohho	57	55	56

Injections prescribing

The percentage of prescriptions with an injection prescribed decreased from baseline to post intervention in all regions. The Hhohho region experienced a higher decrease (4%) compared to the other regions as shown in Table 20. At the end of the follow-up period, the percentage of prescriptions with an injection in the Shiselweni region increased by 5% over the baseline value, while the other regions had values the same or just above baseline values. However, these changes were not statistically significant.

Table 20: Percentage of prescriptions with injections prescribed

WHO/INRUD Indicator	Percentage Prescriptions with Injections		
Region	**Baseline (%)**	**Post Intervention %)**	**Post Follow up (%)**
Manzini	6	5	7
Shiselweni	8	7	13
Lubombo	8	7	8
Hhohho	15	11	16

Availability of the EML

All facilities in the Shiselweni and Lubombo regions had the EML throughout the study period, while 90% of facilities in the Hhohho region and 88% of facilities in the Manzini region had the EML (Table 21).

Table 21: Availability of the Essential Medicines List in Facilities

WHO/INRUD Indicator	Availability of EML		
Region	**Baseline (%)**	**Post Intervention (%)**	**Post Follow up (%)**
Manzini	88	88	88
Shiselweni	100	100	100
Lubombo	100	100	100
Hhohho	90	90	90

Prescribing from the EML

Over 90% of medicines prescribed during the study were from the EML for all regions. Post the intervention, values in the Lubombo and Manzini regions dropped below 90% and by the end of the follow up period only Manzini had a value below 90% as shown in Table 22. However, these changes were not statistically significant.

Table 22: Percentage of medicines prescribed from the EML

WHO/INRUD Indicator	**Percentage of Medicines Prescribed from the EML**		
Region	**Baseline (%)**	**Post Intervention %)**	**Post Follow up (%)**
Manzini	92	87	89
Shiselweni	96	92	93
Lubombo	94	89	92
Hhohho	96	92	93

WHO/INRUD Indicators by Level of Care (All facilities)

The sample had nine secondary level facilities (4 hospitals and 5 health centers) and 23 primary level facilities (clinics). Due to the small sample of secondary compared to primary level facilities, analyses for this section were conducted to report on changes that occurred within each level of care during the study but not on changes by intervention or control groups. There were no statistically significant changes by level of care that occurred during this study.

Average number of medicines per prescription

In both primary and secondary levels of care the average number of medicines prescribed per prescription decreased from baseline to the end of the follow-up period as shown in Figures 24 and 25.

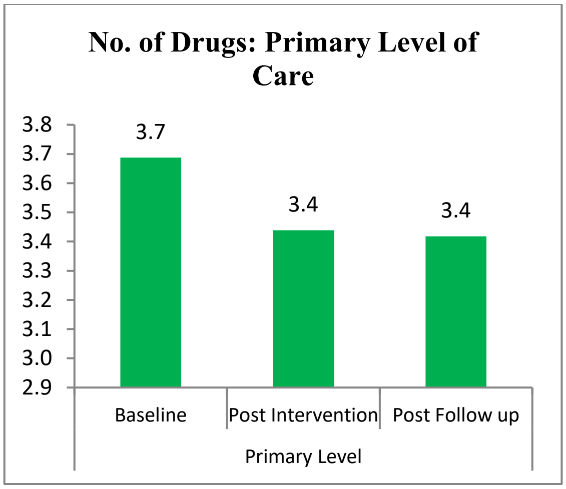

Figure 24: Average number of medicines per prescription (primary level of care)

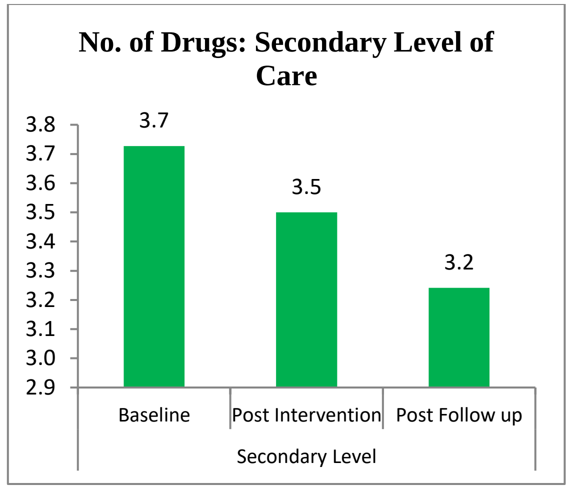

Figure 25: Average number of medicines per prescription (secondary level of care)

Generic Prescribing

A higher increase in the percentage of medicines prescribed by generic name (9% versus 4%) was observed in primary versus secondary level of care facilities from baseline to post intervention (Figure 26 and Figure 27). A continued increase was observed in both primary and secondary level of care facilities at the end of the follow-up period.

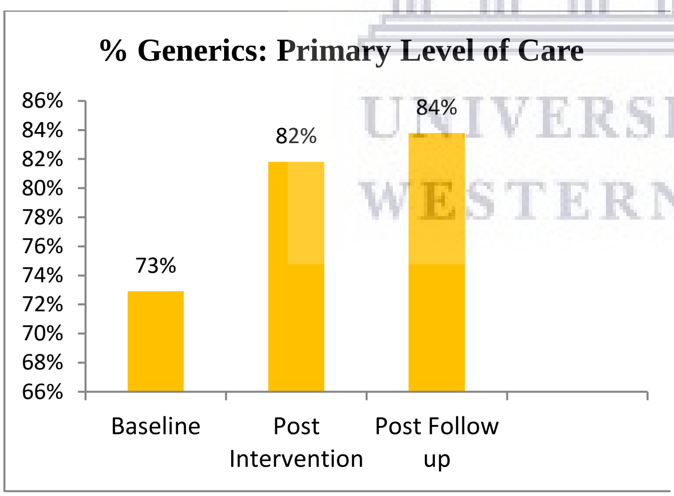

Figure 26: Percentage of medicines prescribed by generic name (primary level of care)

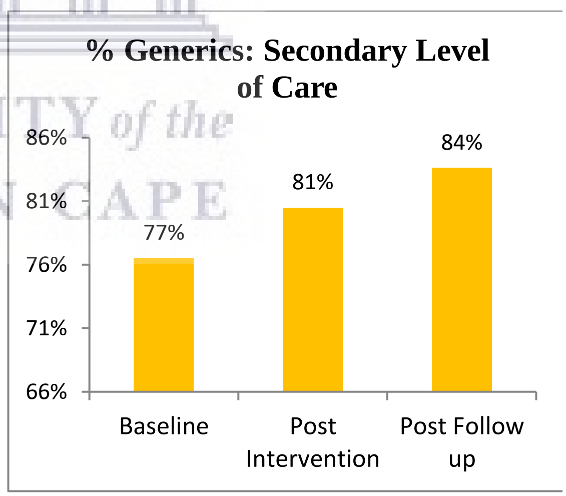

Figure 27: Percentage of medicines prescribed by generic name (secondary level of care)

Antibiotics prescribing

The percentage of prescriptions with antibiotics decreased from baseline to post intervention in both types of facilities (Figure 28 and Figure 29). At the end of the follow-up period, the percentage of prescriptions with an antibiotic had increased to a value higher than the baseline value for primary care facilities, while the secondary level facilities percentage had increased but was still lower than the baseline value.

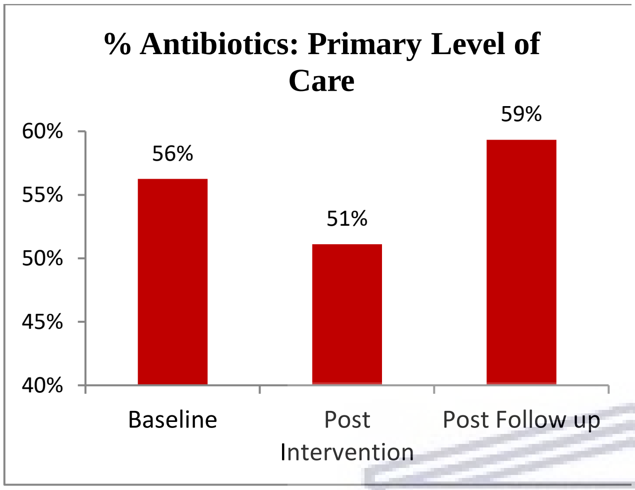

Figure 28: Percentage of prescriptions with antibiotics (primary level of care)

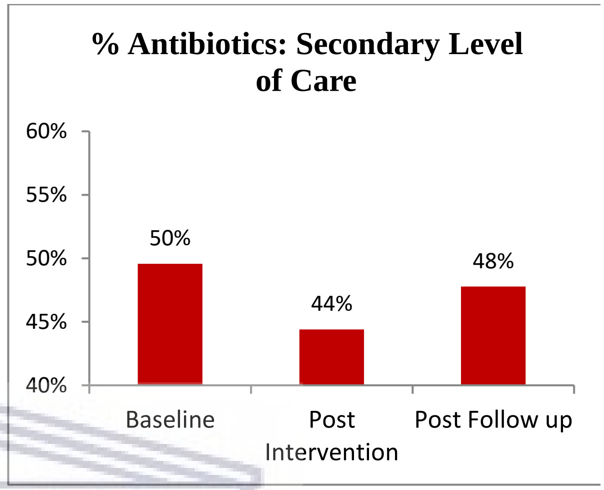

Figure 29: Percentage of prescriptions with antibiotics (secondary level of care)

Injections prescribing

A decrease in the percentage of prescriptions with injections was observed from baseline to post intervention for both levels of care; with the highest decrease observed in secondary level facilities as shown in Figures 30 and 31. At the end of the follow-up period, though both levels of care increased by 4%, the increase for primary level facilities was higher than the baseline value.

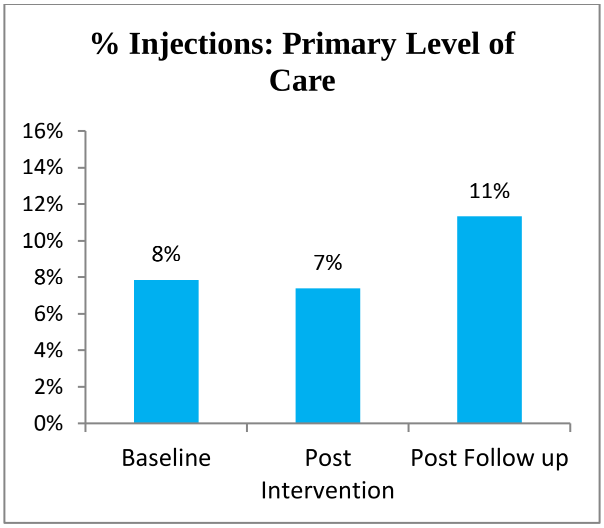

Figure 30: Percentage of prescriptions with injections (primary level of care)

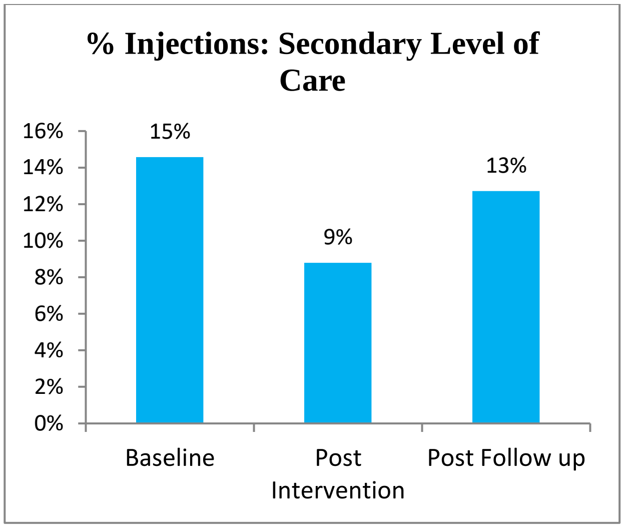

Figure 31: Percentage of prescriptions with injections (secondary level of care)

Prescribing from the EML

The percentage of medicines prescribed from the EML slightly decreased from baseline to post intervention and slightly increased at the end of the follow-up period for both primary and secondary level of care facilities (Figures 32 and 33).

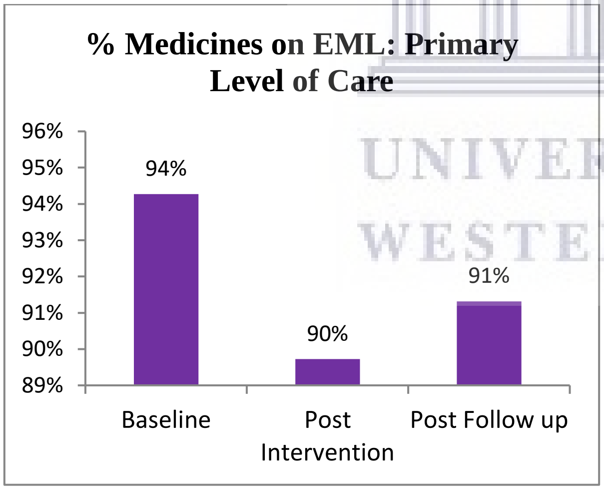

Figure 32: Percentage of medicines prescribed from the EML (primary level of care)

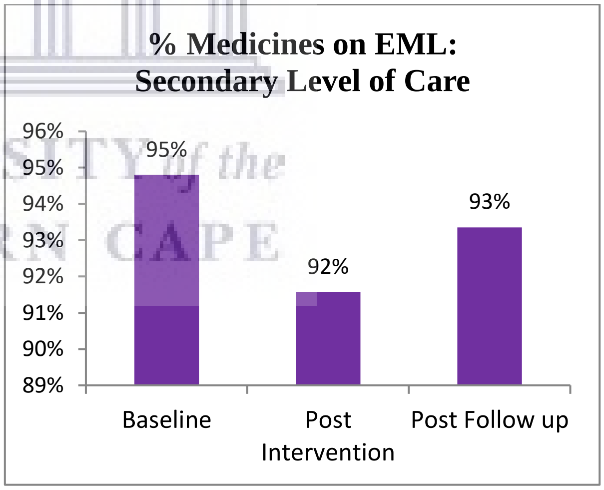

Figure 33: Percentage of medicines prescribed from the EML (secondary level of care)

Regression Analyses

The multiple linear regression model analysed at facility level to assess the effect of the intervention over time, while controlling for confounders, showed the following:

(i) Average number of medicines per prescription

The interaction between time and intervention was not statistically significant (p=0.55), meaning that the change over time in terms of average number of medicines per prescription was not dependent on the intervention. The intervention did not have an effect on the average number of medicines prescribed per prescription as the intervention group had on average 0.42 more medicines than the control group (p=0.34) after adjusting for time, level of care, region and diagnosis. Results also showed that the average number of medicines per prescription was similar in the four regions, level of care, and intervention vs control group at all the time points. The changes in the average number of medicines per prescription over time were not significant. However, there was a significantly higher mean number of medicines in chronic vs acute prescriptions. The results are shown in Table 23 and Figures 34-37.

Table 23: Regression analyses for average number of medicines per prescription

Number of medicines	Coefficient	Standard Error	t	p-value	95% CI
Chronic vs Acute	0.60	0.68	8.17	0.00	0.42 – 0.70
Region (baseline = Hhohho)					
Lubombo	0.21	0.31	0.69	0.50	-0.42 – 0.84
Manzini	0.24	0.31	0.78	0.44	-0.39 – 0.88
Shiselweni	-0.38	0.26	-0.14	0.89	-0.57 – 0.50
Level of Care (2 vs 1)	-0.28	0.21	-0.13	0.90	-0.46 -0.40
Intervention vs Control	0.42	0.44	0.96	0.34	-0.47 – 1.32
Time					
Post intervention	-0.15	0.18	-0.86	0.40	-0.52 – 0.21
Post Follow up	-0.17	0.24	-0.72	0.48	-0.66 – 0.32
Interaction between time and intervention	-0.10	0.17	-0.61	0.55	-0.45 – 0.24
Constant	2.73	0.47	5.84	0.00	1.78 – 3.68

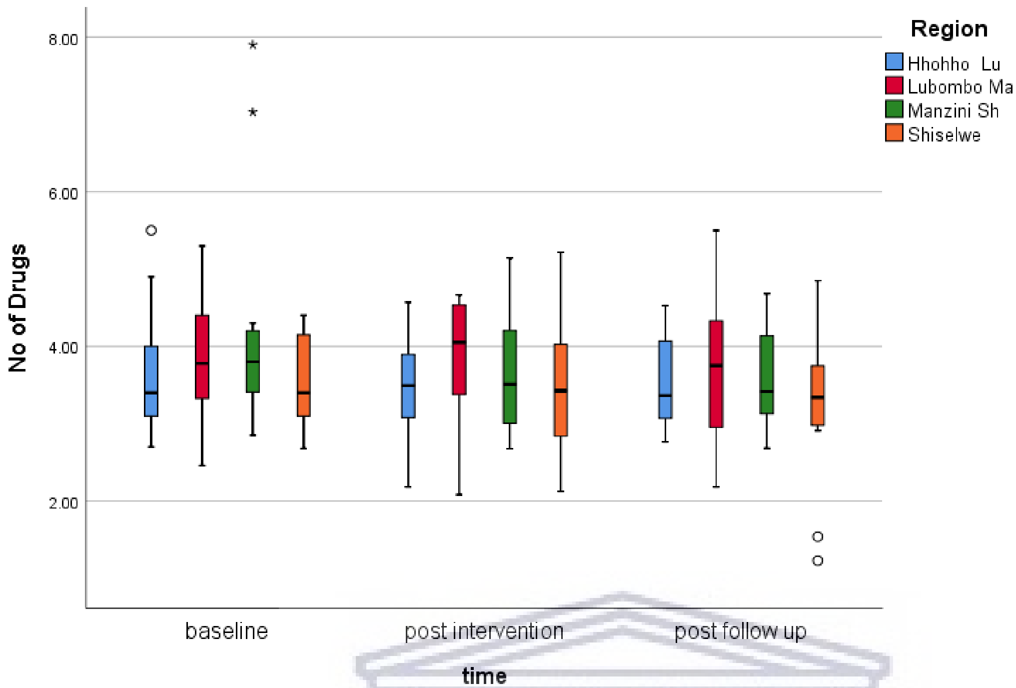

Figure 34: Changes in the average number of medicines per prescription over the three time periods

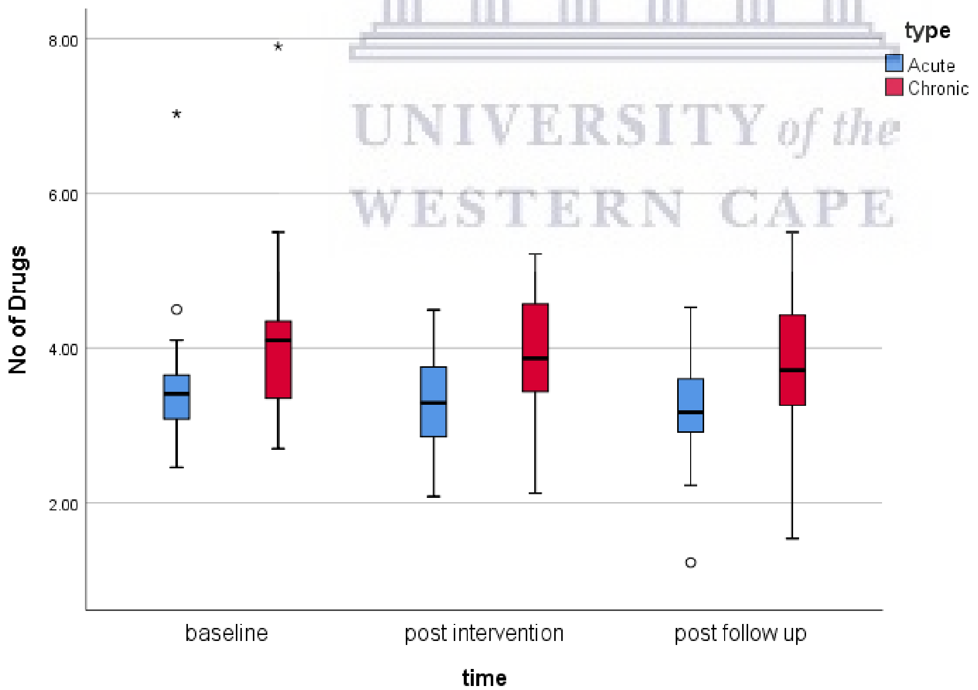

Figure 35: Changes in the average number of medicines per prescription over the 3 time periods (by diagnosis)

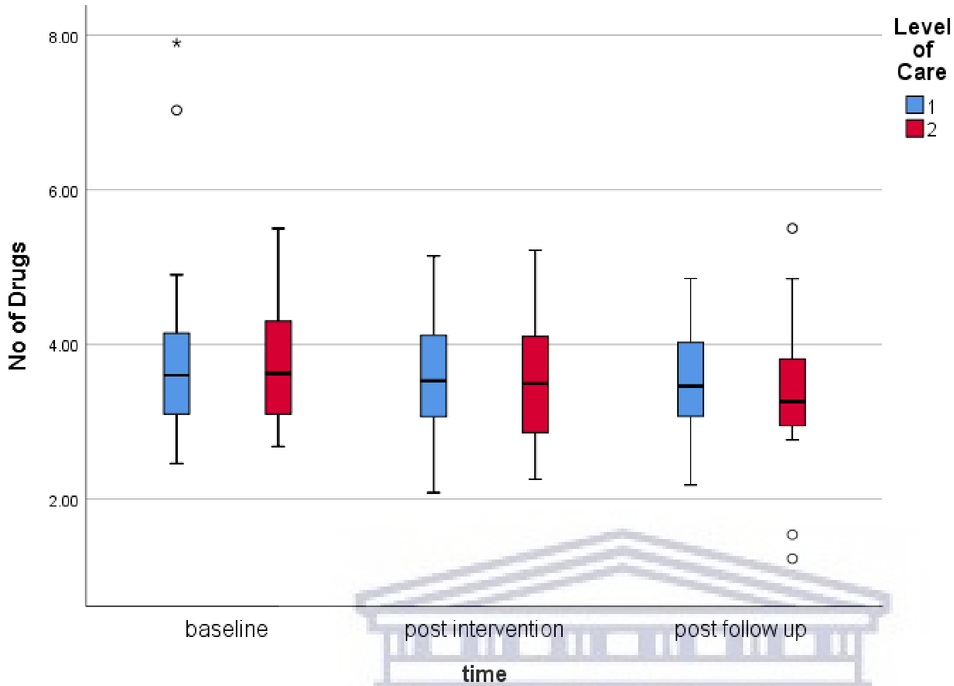

Figure 36: Changes in the average number of medicines per prescription over the 3 time periods (by level of care)

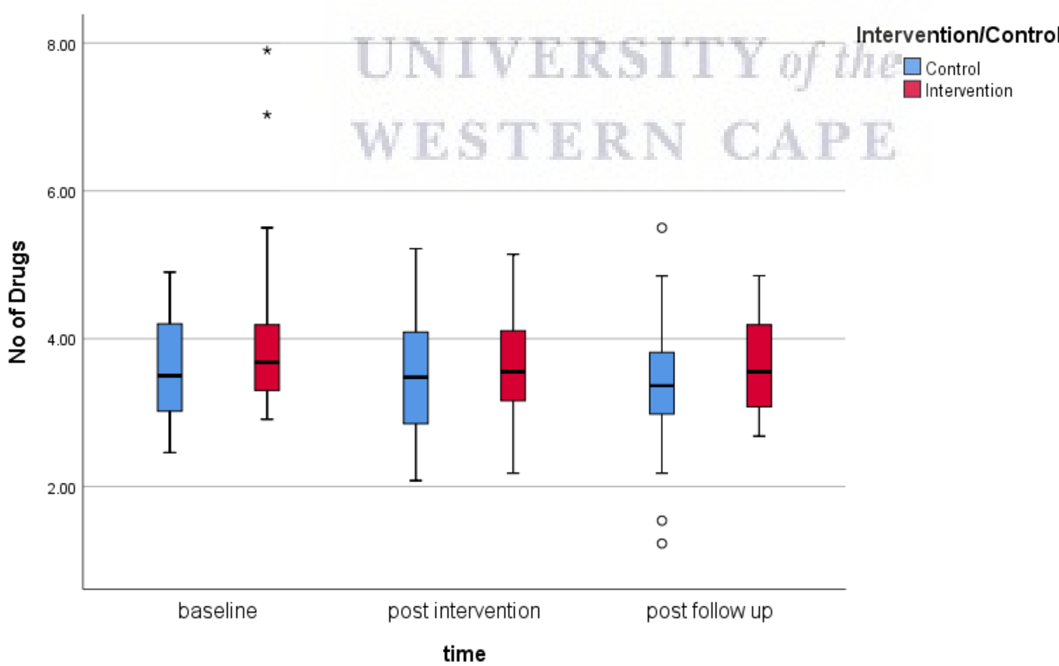

Figure 37: Changes in the average number of medicines per prescription over the 3 time periods (by intervention and control groups)

(ii) Generic prescribing

The interaction between time and intervention was not statistically significant (p=0.86), meaning that the change over time in terms of average percentage generics prescribed was not dependent on the intervention. The intervention did not have an effect on the average percentage of generics as the intervention group had on average 1.06% less medicines prescribed by generic name than the control group (p=0.77) after adjusting for time, level of care, region and diagnosis. Results also showed that the average percent of generics was similar in the four regions, and level of care at all the time points. The changes in the average percentage of medicines prescribed by generic name over time were significant between baseline and post intervention as well as between baseline and post follow-up. In each case, the percentage of generics increased (p=0.001 and p<0.001 respectively). There was also a borderline significantly higher mean percent of medicines prescribed by generic name in chronic vs acute prescriptions (p=0.05). The results are shown in Table 24 and Figures 38-41.

Table 24: Regression analyses for medicines prescribed by generic name

Percent Generics	Coefficient	Standard Error	t	p-value	95% CI
Chronic vs Acute	3.60	1.76	2.04	0.05	-0.0009–7.20
Regions (baseline = Hhohho)					
Lubombo	0.49	3.05	0.16	0.87	-5.74 – 6.71
Manzini	-7.37	3.86	-1.91	0.07	-15.24– 0.50
Shiselweni	2.50	3.21	0.78	0.44	-4.05 – 9.04
Level of Care (2 vs 1)	-1.90	2.38	-0.80	0.43	-6.74 – 2.96
Intervention vs Control	-1.06	3.87	-0.27	0.79	-8.95 – 6.83
Time					
Post intervention	11.47	3.28	3.50	0.001	4.78 – 18.16
Post Follow up	10.82	2.51	4.30	0.000	5.69 – 15.94
Interaction between time and intervention	-0.39	2.12	-0.18	0.86	-4.72 – 3.94
Constant	72.33	5.42	13.35	0.000	61.28– 83.38

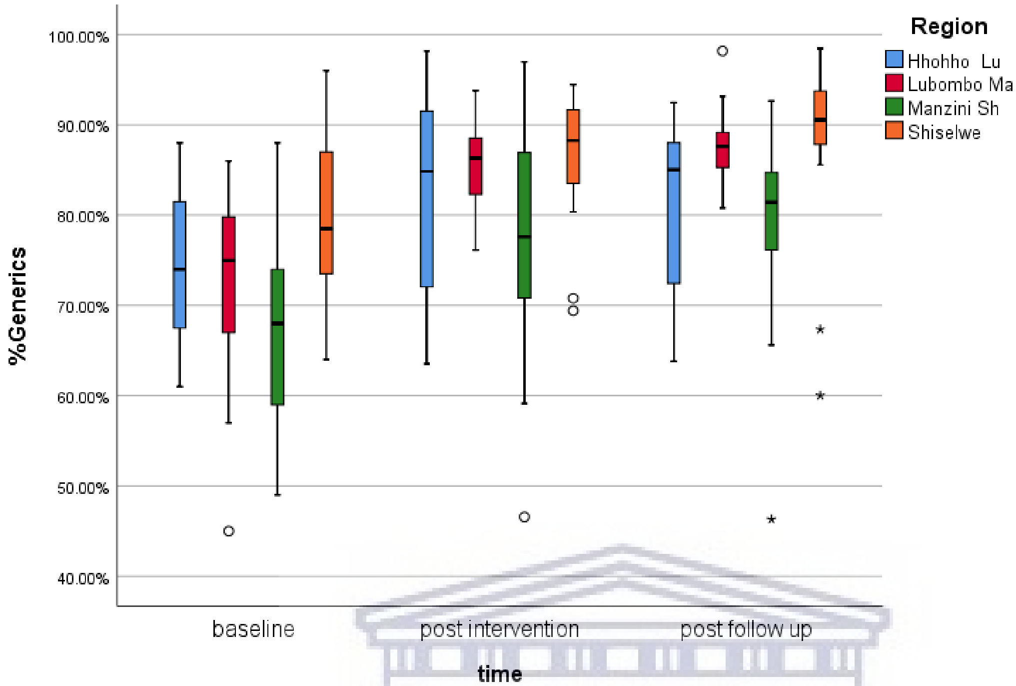

Figure 38: Changes in medicines prescribed by generic name over the 3 time periods

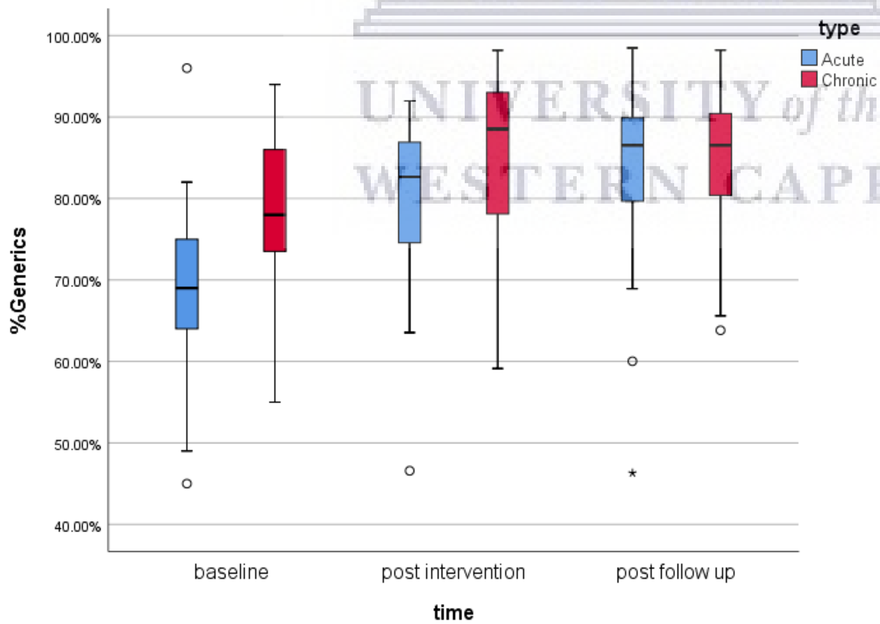

Figure 39: Changes in medicines prescribed by generic name over the 3 time periods (by diagnosis)

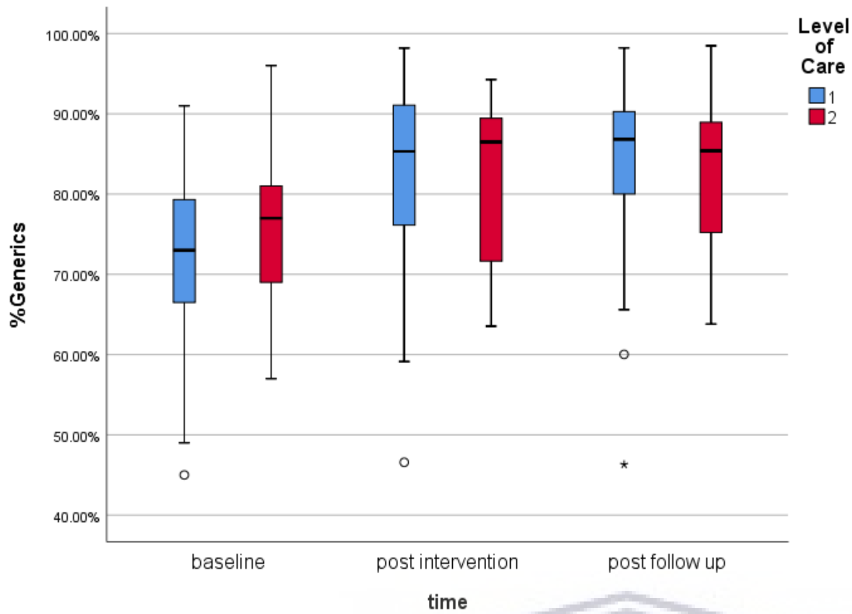

Figure 40: Changes in medicines prescribed by generic name over the 3 time periods (level of care)

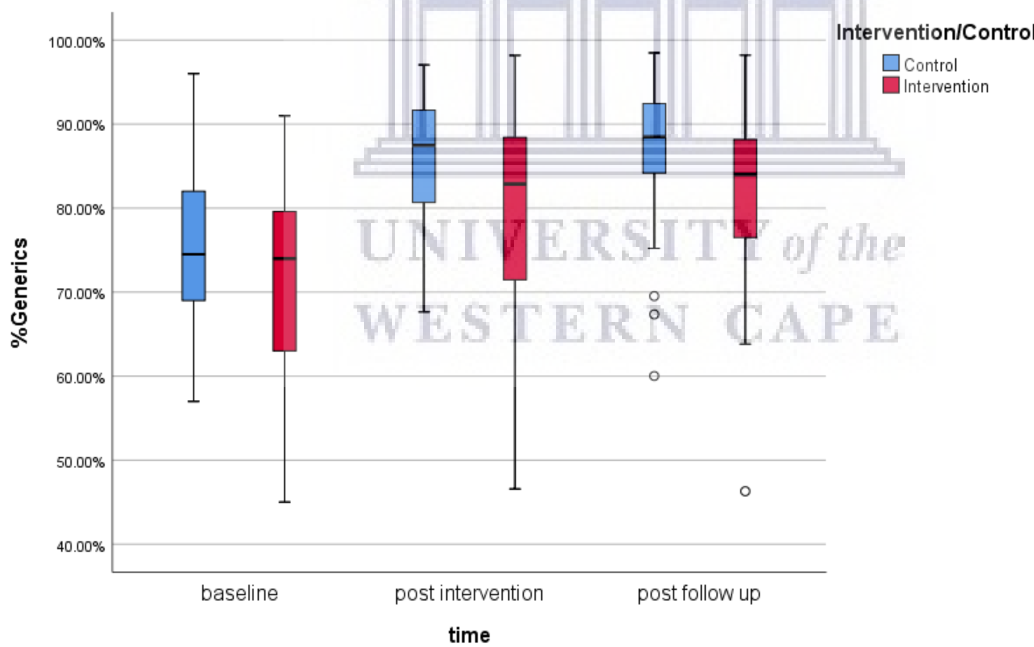

Figure 41: Changes in medicines prescribed by generic name over the 3 time periods (by intervention and control groups)

(iii) Antibiotic prescribing

The interaction between time and intervention was not statistically significant (p=0.72), meaning that the change over time in terms of average percentage of prescriptions with at least one antibiotic prescribed was not dependent on the intervention. The intervention did not have an effect on the average percentage of antibiotics as the intervention group had on average 0.62% more antibiotics than the control group (p=0.88) after adjusting for time, level of care, region and diagnosis. Results also showed that the average percent of antibiotics was similar in the four regions at all the time points. The second level of care had significantly lower percentage antibiotics than the first (p=0.02). The changes in the average percentage of antibiotics over time showed a significant reduction between baseline and post intervention but not between baseline and post follow-up. There was also a highly significantly lower mean percent of antibiotics in chronic vs acute prescriptions (p<0.001). The results are shown in Table 25 and Figures 42-45.

Table 25: Regression analyses for percentage of prescriptions with antibiotics

Percent antibiotics	**Coefficient**	**Standard Error**	**t**	**p-value**	**95% CI**
Chronic vs Acute	-44.52	2.03	-21.91	0.000	-48.66 - -40.37
Region baseline = Hhohho					
Lubombo	-2.94	4.14	-0.71	0.48	-11.38 – 5.51
Manzini	0.60	3.99	0.15	0.88	-7.54 – 8.75
Shiselweni	-3.36	3.61	-0.93	0.36	-10.73 – 4.00
Level of Care (2 vs 1)	-5.81	2.45	-2.37	0.02	-10.80 - -0.81
Intervention vs Control	0.62	3.92	0.16	0.88	-7.38 – 8.61
Time					
Post intervention	-8.56	2.77	-3.08	0.004	-14.22 - -2.90
Post Follow up	-4.55	2.50	-1.82	0.08	-9.65 – 0.55
Interaction between time and intervention	-0.67	1.83	-0.36	0.72	-4.14 – 3.07
Constant	125.65	5.46	23.01	0.000	114.52–136.79

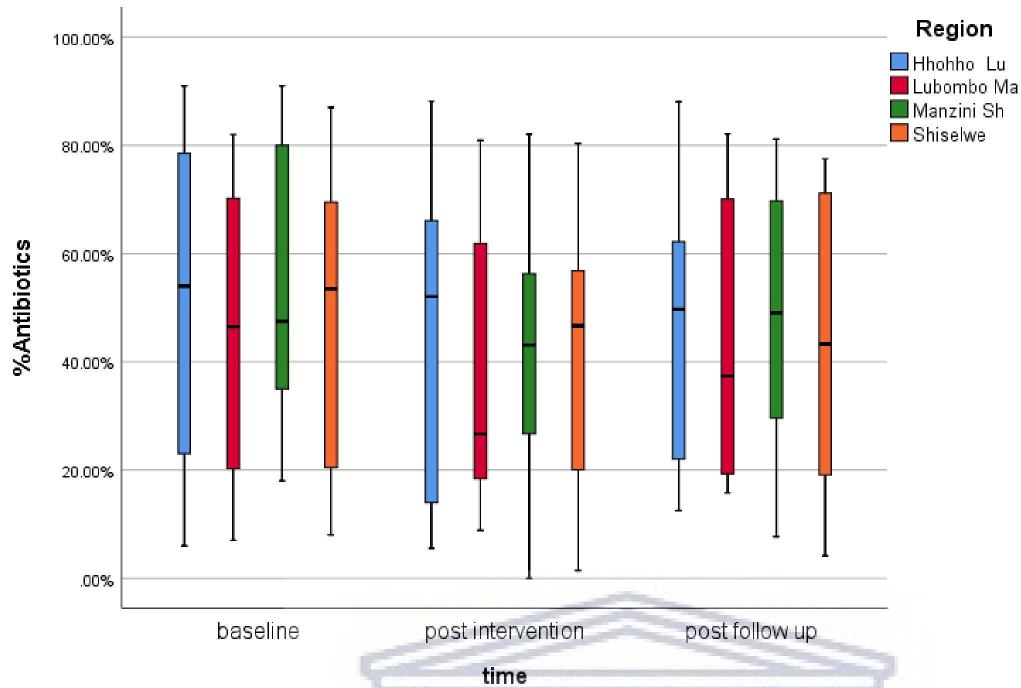

Figure 42: Changes in antibiotic prescribing over the 3 time periods

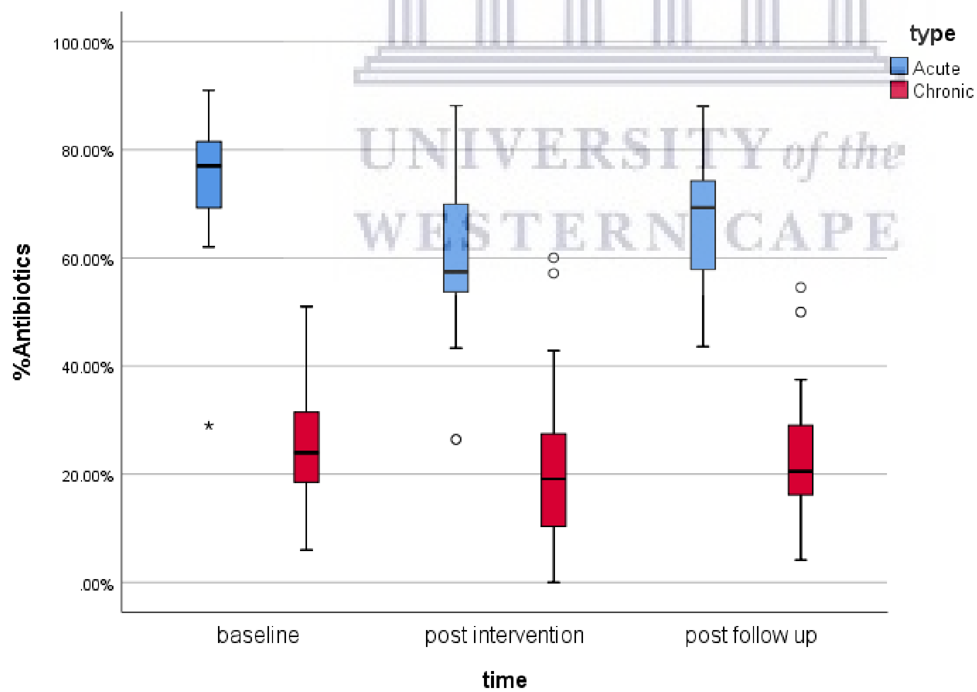

Figure 43: Changes in antibiotic prescribing over the 3 time periods (by diagnosis)

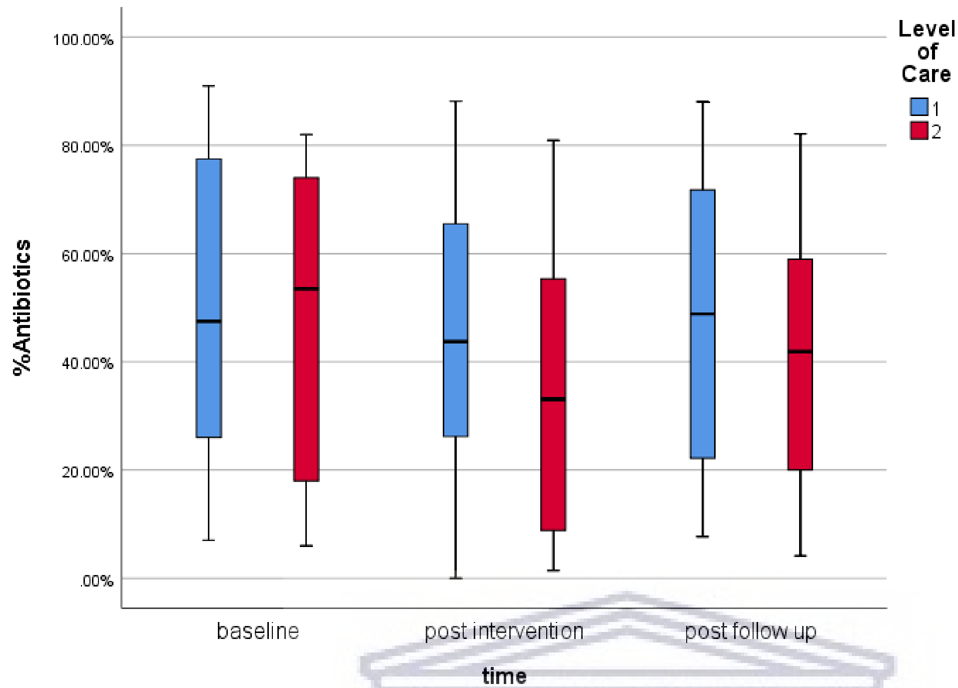

Figure 44: Changes in antibiotic prescribing over the 3 time periods (by level of care)

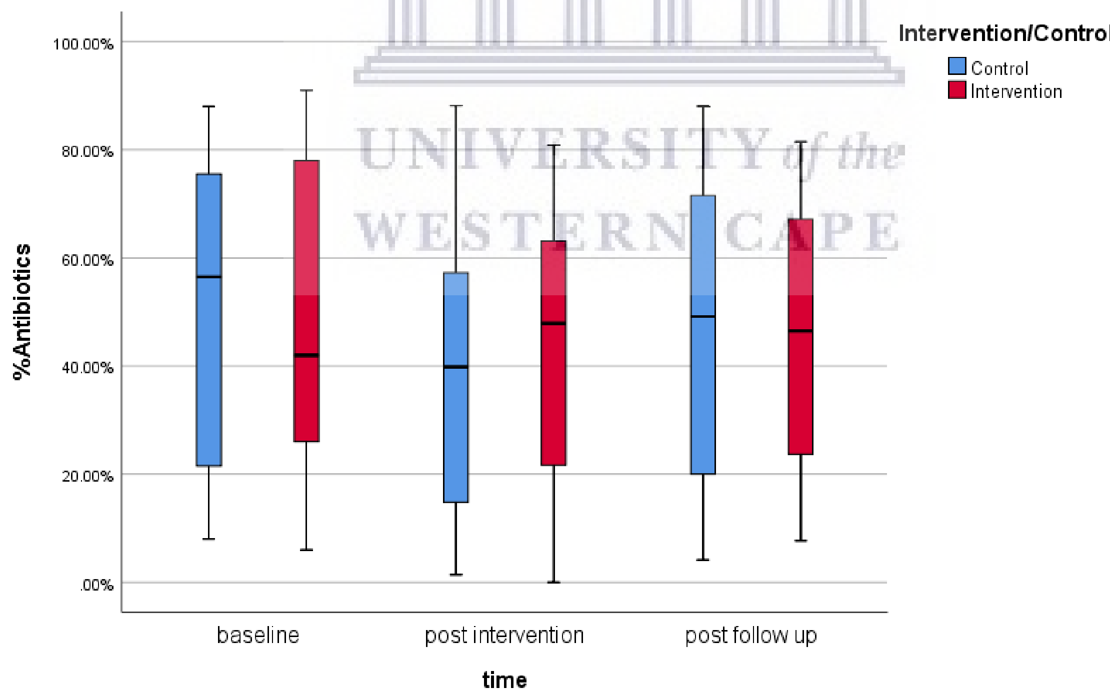

Figure 45: Changes in antibiotic prescribing over the 3 time periods (by intervention and control groups)

(iv) Injections prescribing

The logarithm of percent injections was used as the outcome. The interaction between time and intervention was not statistically significant (p=0.72), meaning that the change over time in terms of average percentage of prescriptions with at least one injection prescribed was not dependent on the intervention. The intervention did not influence the average percentage of injections (p=0.74) after adjusting for time, level of care, region, and diagnosis. Results also showed that the average percent of injections was similar in the four regions at all the time points except significantly lower in Manzini than Hhohho (p=0.03). The second level of care was not difference from the first (p=0.17). The changes in the average percentage of injections over time showed a significant reduction between baseline and post intervention but not between baseline and post follow-up. There was also a highly significantly lower mean percent of injections in chronic vs acute prescriptions (p<0.001). The results are shown in Table 26 and Figures 46-49.

Table 26: Regression analyses for percentage prescriptions with injections prescribed

Log injections	Coefficient	Standard Error	t	p-value	95% CI
Chronic vs Acute	-1.01	0.21	-4.73	0.000	-1.45 - -0.58
Region baseline = Hhohho					
Lubombo	0.33	0.29	0.11	0.91	-0.56 – 0.63
Manzini	-0.76	-.34	-2.22	0.03	-1.47 - -0.06
Shiselweni	-0.25	0.28	-0.87	0.39	-0.82 – 0.33
Level of Care (2 vs 1)	0.37	0.27	1.40	0.17	-0.17 – 0.91
Intervention vs Control	-0.11	0.34	-0.33	0.74	-0.81 – 0.58
Time					
Post intervention	-0.45	0.22	-2.07	0.05	-0.90 - -0.06
Post Follow up	-0.32	0.30	-1.06	0.30	-0.93 – 0.30
Interaction between time and intervention	0.07	0.21	0.36	0.72	-0.35 – 0.50
Constant	1.72	0.44	3.87	0.001	0.81 – 2.62

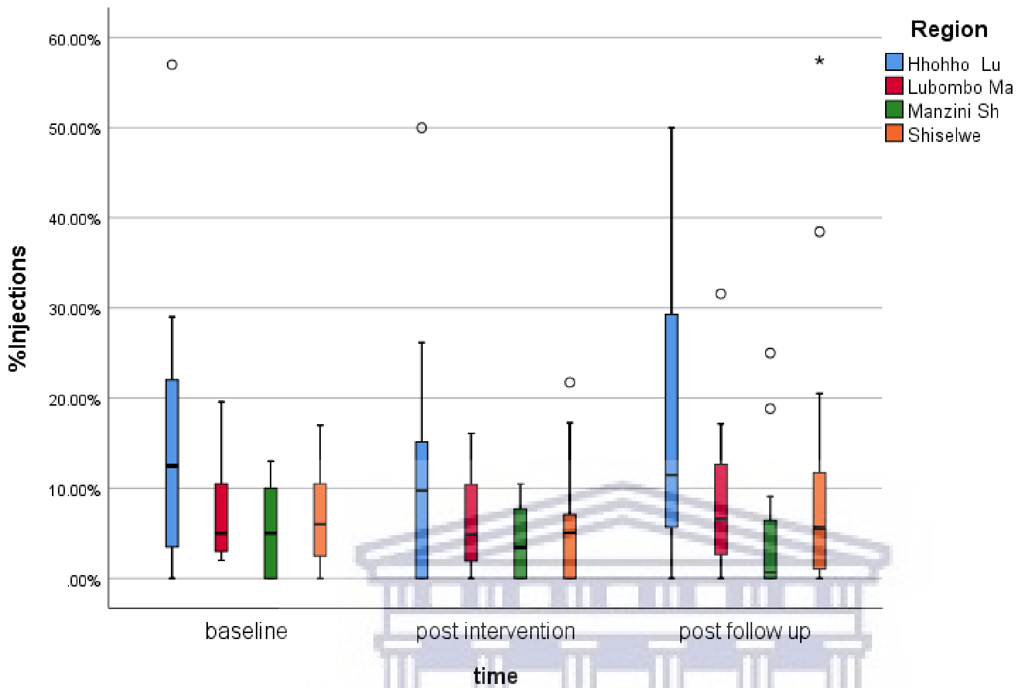

Figure 46: Changes in injection prescribing over the 3 time periods

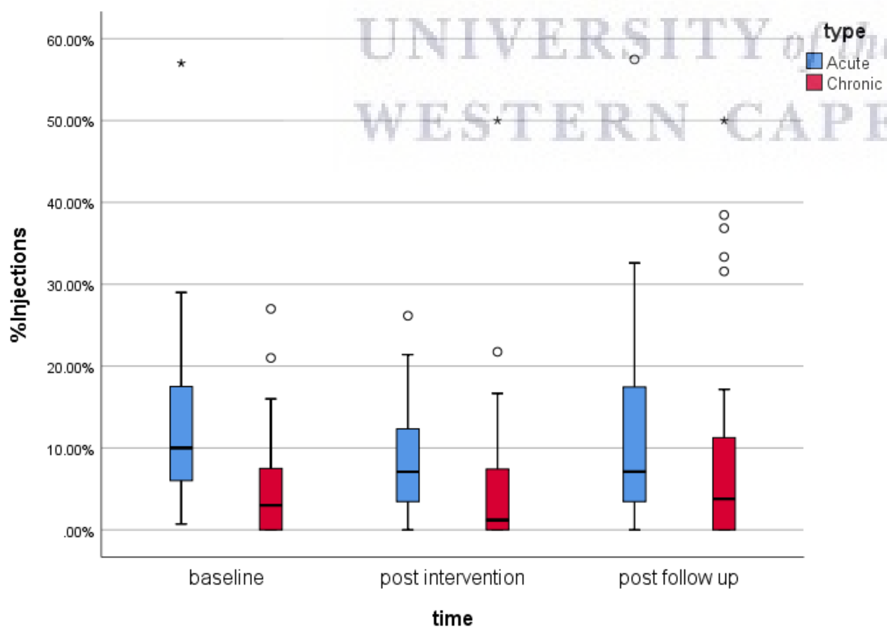

Figure 47: Changes in injections prescribing over the 3 time periods (by diagnosis)

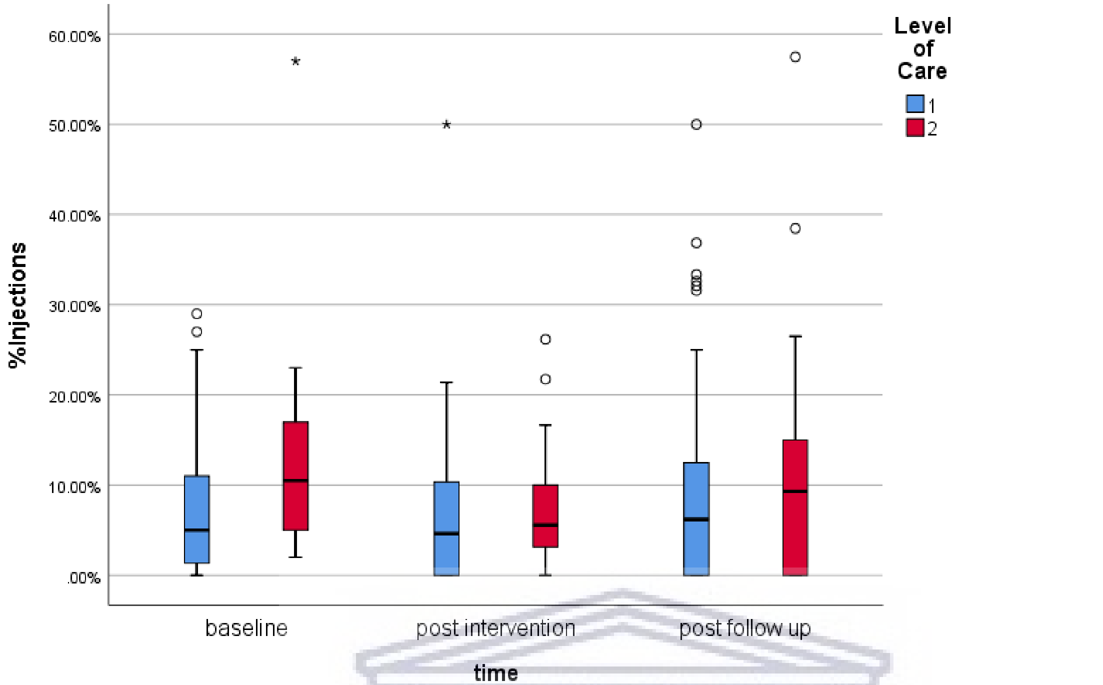

Figure 48: Changes in injections prescribing over the 3 time periods (by level of care)

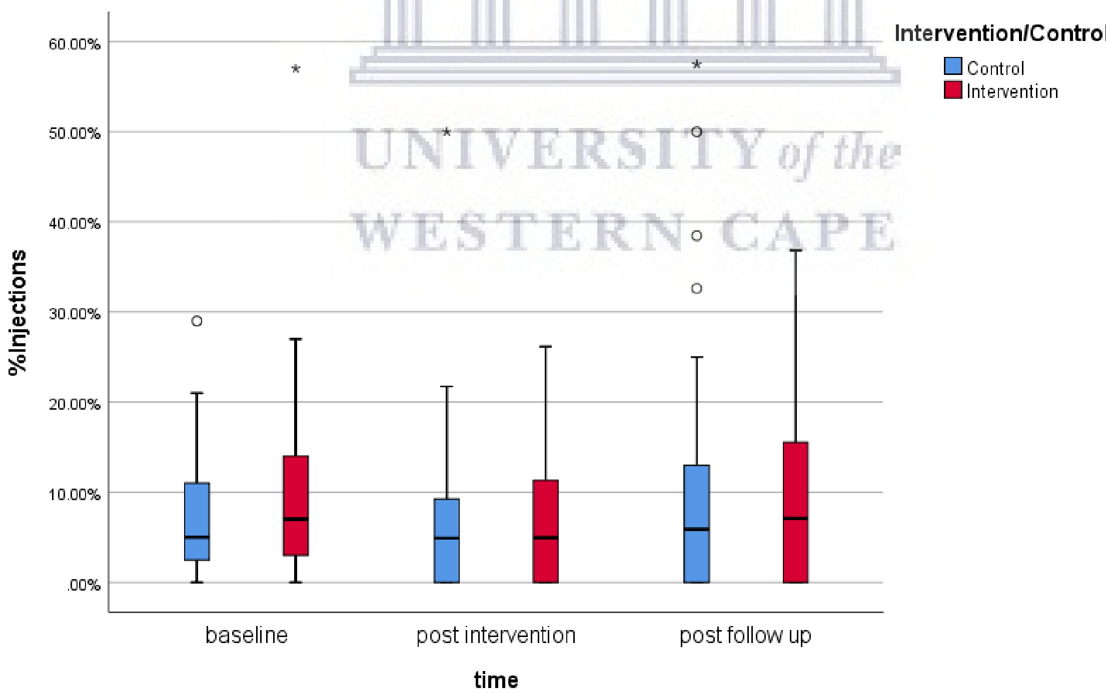

Figure 49: Changes in injections prescribing over the 3 time periods (by intervention and control groups)

(v) Prescribing EML medicines

The interaction between time and intervention was not statistically significant (p=0.14), meaning that the change over time in terms of average percentage of medicines prescribed from the EML was not dependent on the intervention. The intervention did not influence the average percentage of medicines prescribed from the EML (p=0.32) after adjusting for time, level of care, region, and diagnosis. Results also showed that the average percent of medicines prescribed from the EML was similar in the four regions at all the time points. The second level of care was not different from the first (p=0.32). The changes in the average percentage of medicines prescribed from the EML over time showed a significant reduction between baseline and post intervention but not between baseline and post follow-up. There was also a highly significantly higher mean percent of EML in chronic vs acute prescriptions (p<0.001). The results are shown in Table 27 and Figures 50-53.

Table 27: Regression analyses for percentage of medicines prescribed from the EML

Percent Medicines from EML	Coefficient	Standard Error	t	p-value	95% CI
Chronic vs Acute	5.68	0.81	7.05	0.000	4.03 – 7.32
Region baseline = Hhohho					
Lubombo	0.18	1.32	0.14	0.89	-2.50 – 2.87
Manzini	-1.84	1.66	-1.11	0.28	-5.22 – 1.54
Shiselweni	0.11	1.35	0.08	0.94	-2.65 – 2.87
Level of Care (2 vs 1)	0.97	0.96	1.01	0.32	-0.98 – 2.92
Intervention vs Control	-1.26	1.25	-1.01	0.32	-3.82 – 1.29
Time					
Post intervention	-3.74	1.29	-2.91	0.007	-6.36 - -1.12
Post Follow up	-1.04	0.59	-1.74	0.09	-2.24 – 0.17
Interaction between time and intervention	-0.63	0.41	-1.52	0.14	-1.48 – 0.21
Constant	86.37	2.29	37.68	0.000	81.69 – 91.04

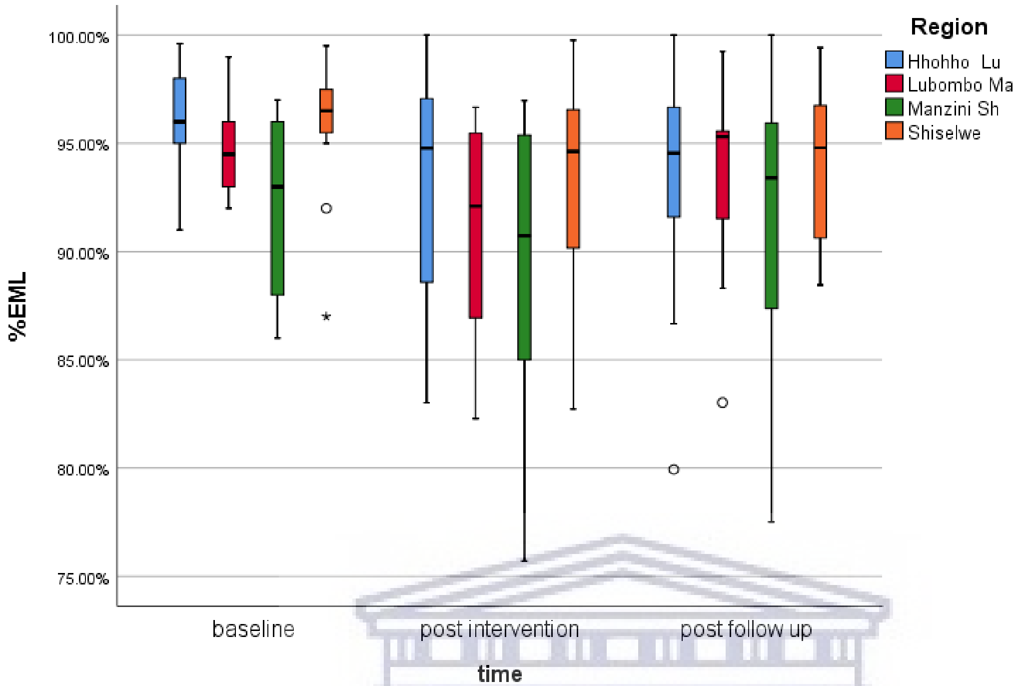

Figure 50: Changes in prescribing medicines from the EML

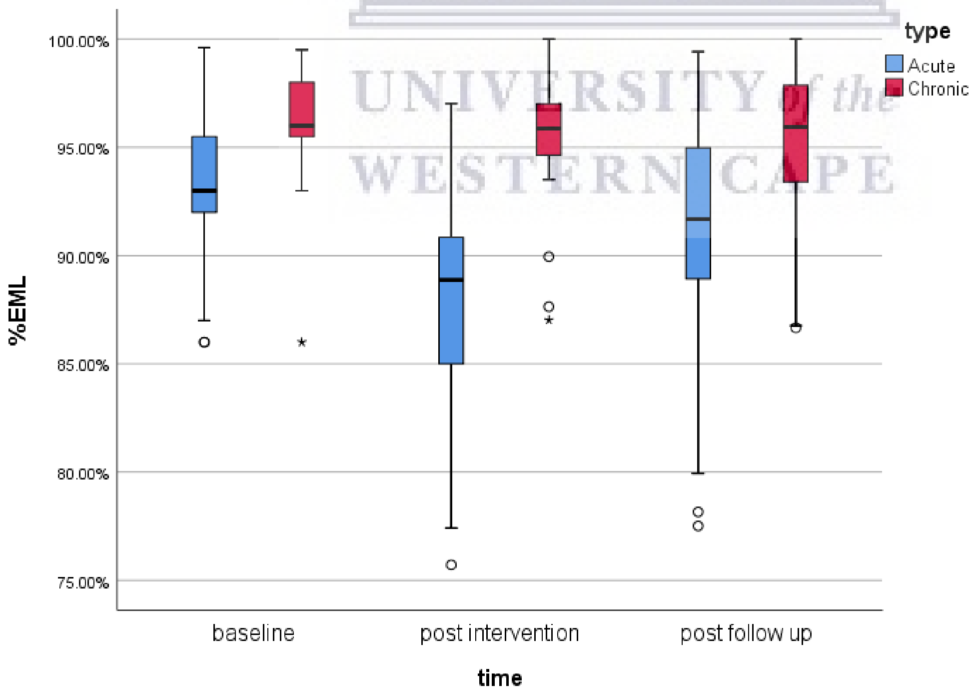

Figure 51: Changes in prescribing medicines from the EML (by diagnosis)

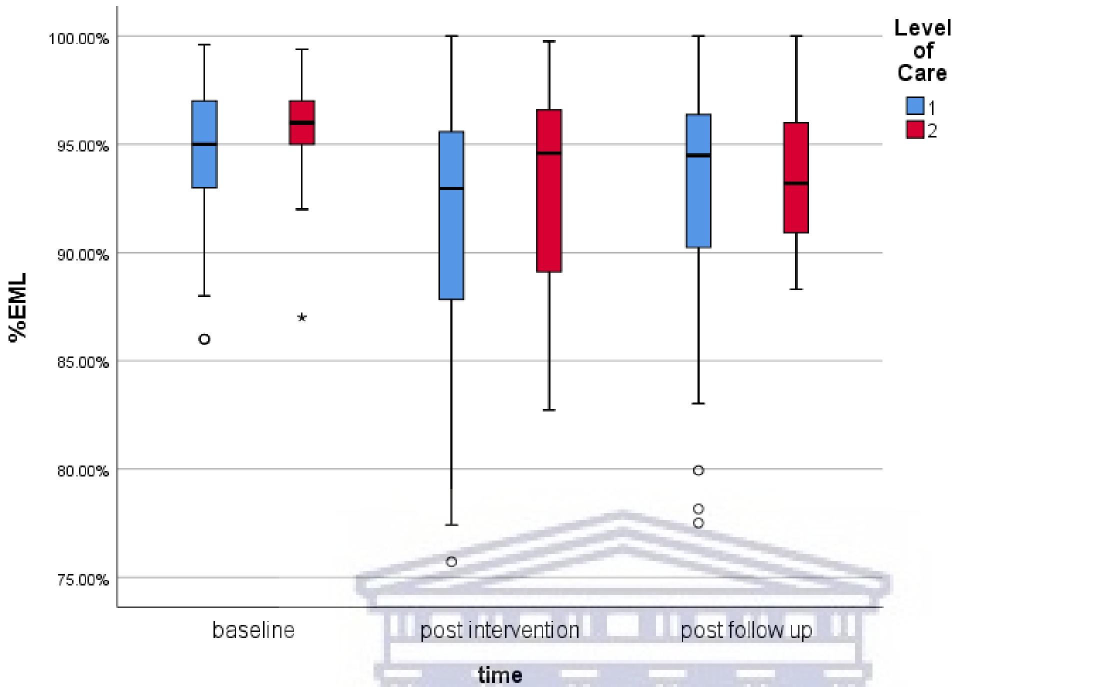

Figure 52: Changes in prescribing medicines from the EML (by level of care)

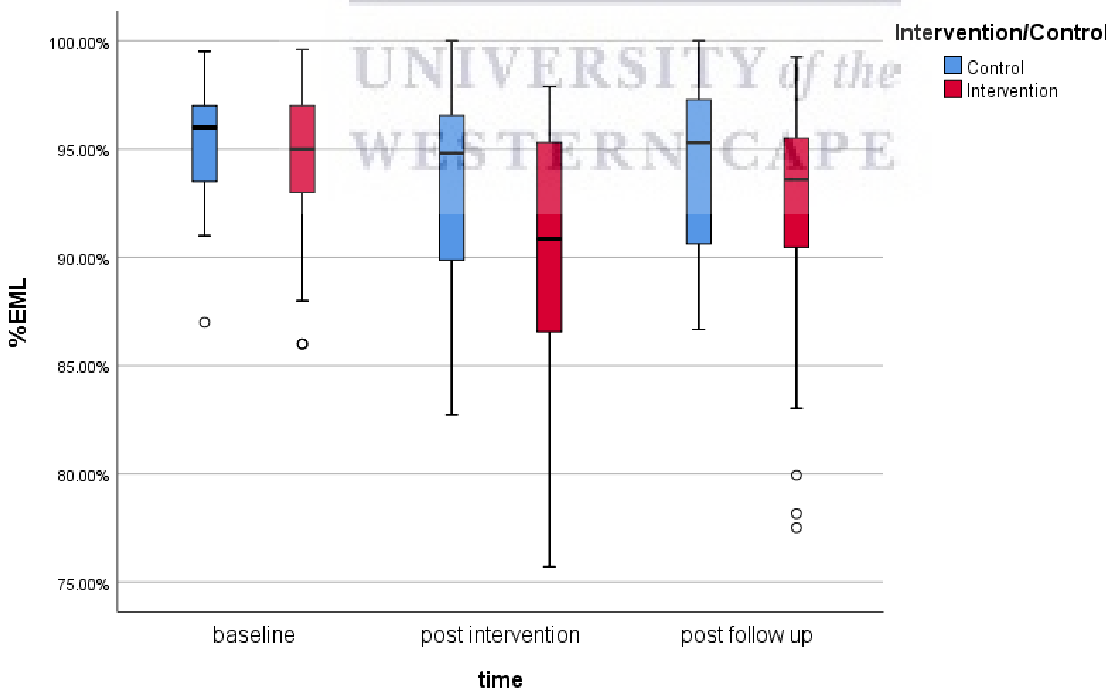

Figure 53: Changes in prescribing medicines from the EML (by intervention and control groups)

Although the sample sizes were small for the intervention and control groups (15 facilities and 16 facilities respectively), intragroup analyses (secondary analyses) were conducted to determine whether there were some potential changes in indicators during the three time periods.

5.2.2 Qualitative Component

At the end of the follow-up period 23 interviews were conducted with frontline managers using a semi-structured interview guide. The interviews were not conducted in all 32 facilities included in the study as by the 23rd interview we had reached saturation. Of the 23 frontline managers interviewed, 10 were from facilities that had been allocated to the intervention arm and 13 were from facilities allocated to the control arm. Six key informants were also interviewed using a semi-structured interview guide (one from national level, one from central medical stores and one from each of the four regions). The information coming from key informants was not as rich as that coming from frontline managers as they reported to not be directly involved in the day-to-day running of facilities and for them it was difficult to report on whether the study had an impact on how medicines were being used in facilities. Furthermore, some of the key informants were newly appointed and did not know much about the study. Frontline managers gave the richest information.

When visited at the end of the study, some facilities in the control arm seemed to have not made any changes to their prescribing practices though they were aware of problematic areas in prescribing and use of medicines identified in the baseline survey. Regarding the number of medicines per prescription, some facilities reported that they felt the standard recommended by WHO did not take into account symptoms that a patient presents with, hence they found it difficult to prescribe a maximum of three medicines per prescription.

"*So, the 2 to 3 really I kind of disagree but if it is one illness then we do not exceed the 3 medicines because with flu it's usually the 3 which is cold and flu, vitamin c and the cough syrup, so on the drugs it depends on what the patient is presenting.*" [FM_N_Prim_H]

Some facilities in the intervention arm reported to have made efforts to reduce the number of medicines per prescriptions. However, frontline managers reported that patients generally relate the number of medicines prescribed and dispensed to the amount they pay as consultation fees. Though this was the case, frontline managers reported that they educated patients on the importance of getting as few medicines as possible to improve compliance and adherence and reduce side effects.

"*You know, we were giving, the last time you were here, we were giving them the 2, strictly 2, and some patients were like…since they pay 5 Emalangeni they [patients] say "this hospital no longer gives us medication, E2.50 per medication" and we tell them that you are not paying for the medication and they think we are cheating them*." [FM_N_Prim_L]

Use of antibiotics

Facilities reported that the use of antibiotics decreased after baseline findings from the study made them aware of how they were using antibiotics. They mentioned that they used existing facility platforms such as PTCs and multidisciplinary teams (MDTs) to share information on overuse of antibiotics. Frontline managers reported that they felt that sharing information in PTCs only was not adequate as most facility staff are not part of the PTC as opposed to the MDTs which comprise of most staff and have frequent meetings. When asked whether the intervention rolled out had influenced the use of antibiotics in facilities, frontline managers generally responded in the affirmative.

"*Yes, it has decreased because we had talks even in the MDT besides the PTC because PTC is a smaller group yet in the MDT there are more people, so we did address it*." [FM_PT_Sec_H]

"*We spoke to the staff actually because it used to be PHU that would say if a child is sick they should get an antibiotic, it used to be public health units (PHU); and the issue of giving antibiotics when someone has flu, we then addressed it ourselves.*" [FM_PT_Sec_S]

"*In that part of antibiotics I think we as a pharmacy we had a PTC meeting after your presentation we then had a meeting as a committee and we discussed this thing of antibiotics where we reached an agreement as to how many antibiotics that should be in a prescription when referring to the data that you had collected. Yes, so that's really the only part we put more focus on, the antibiotic part, as a PTC meeting, we had a further discussion using your presentation then we discussed how we are supposed to improve our prescriptions but only the part of antibiotics which has improved.*" [FM_P_Sec_M]

Frontline managers also mentioned that during the intervention they started doing internal audits to find out where the overuse of antibiotics and injections was coming from. Their audits revealed that amoxicillin was being used as ward stock. In most cases, patients who present to the facility at night are admitted. Internal facility audits then showed that such patients would generally be prescribed antibiotics; and such practice increases the use of antibiotics.

"*…the overuse of the antibiotics because what we also found is that antibiotics were being dispensed as a ward stock especially Amoxil, so when patients would come at night they would be given antibiotic for two days of which that won't help the patient and you find that the next time they come back they are even worse than before and the bacteria is resistant to the Amoxil*." [FM_PT_Sec_H]

Facilities, particularly those in the intervention arm, mentioned that after being exposed to this study's procedures - the prescription audits and feedback coupled with small group education - they were noticing a decrease in the use of antibiotics for chronic conditions.

"*Well it has also improved on that part, it used to happen when doing refills that you would see that last month a person was prescribed amoxil and when they come again the following month they are prescribed amoxil, it's like they just copy the previous script without really assessing the client, but then it is decreasing gradually*." [FM_PT_Sec_H]

"*Yes, it has because you would find that each and every patient that has come to refill will leave with an antibiotic. When we look at the medical encounter, if it was before, there would have been an antibiotic but now we don't have so it has decreased*" [FM_PT_Sec_H]

"*Yes it has [use of antibiotics for NCDs has gone down], though the problem there [use of antibiotics for chronic conditions] is that if you try to talk to the practitioners they've got a reason. They tell me the patient they gave that antibiotic because there was a reason. They talk of core infection when they try to explain away the use of the antibiotic*." [FM_PT_Sec_S]

Though some facilities' frontline managers reported that the study had positively affected the use of antibiotics, some facilities reported that there still was irrational use of antibiotics.

"*But by merely looking at these results I would say we still have a challenge with polypharmacy and overuse of antibiotics*." [FM_PT_Sec_S]

Provider factors similar to those cited at baseline, such as prescribing antibiotics to make sure the antibiotic takes care of the ailment and patients do not return to the facility with no improvement of symptoms, persisted at the end of this study.

"*But you find that I end up prescribing the antibiotic because I don't want the patient to come back with the same issue tomorrow. Sometimes the patient will say they didn't have money to come to the clinic, so rather than having them go and come back another day I just end up giving the antibiotic, and when you notice and visit some other clinics you do find the stock out of antibiotics*." [FM_N_Prim_L]

Some frontline managers reported the use of antibiotics was warranted for patients who presented very ill with high temperatures.

"*We follow each patient's problem, sometimes you find that a patient will come in very sick and has a high fever and all those things, I know it could be viral or whatever but we don't take chances we do give (laughs)antibiotic especially Amoxil.*" [FM_N_Prim_H]

Contrary to WHO recommendations and standard on use of antibiotics, some frontline managers understood the baseline findings from this study to mean that each prescription should have two antibiotics. These facilities continued to use more antibiotics, being cautious to not prescribe more than two per prescription. Furthermore, frontline managers reported that though they were aware that they should not be using antibiotics unnecessarily, they still continued to.

"*We use them a lot, I understand the fact that they should not be many per prescription as we say they should not be more than 2, that I understand, but sometimes we do use antibiotics unnecessarily*." [FM_N_Prim_M]

"*Yes, but in the back of our minds we know we are not supposed to give them, so are trying to limit giving out antibiotics if it's not necessary*." [FM_N_Prim_L)

Though there were positive reports on use of antibiotics decreasing during the course of the study, some facilities reported that they were still be prescribing a lot of antibiotics. Frontline managers reported that although baseline study findings and intervention visits made them aware of the overuse of antibiotics, the use was not decreasing considerably.

"*It's not ok because every prescription even if you can go take a look you will find Amoxil*." [FM_PT_Sec_S]

Use of Injections

Frontline managers mentioned that they sometimes opt to prescribe injections because patients do not finish the course of medicines prescribed.

"*Some patients will tell you that they don't usually finish the course of medications so obviously you then opt for the injection, because we also try to run away from some issues. For instance, with antibiotics we try to avoid resistance so then when the patient tells you they don't finish the course so you end up giving injection*." [FM_N_Prim_M]

Patient Factors

Patient factors similar to those reported at baseline were also reported to affect rational prescribing and use of antibiotics in health facilities.

"*We are above 30%, even if you could have a look now you would see. We have even ran out of Amoxil 500, we are above and I think it's mainly because we are inside town and people start by first treating themselves before coming to the clinic. They start at XYZ [hospital] and they get panado there without an antibiotic then they go buy the antibiotic themselves and if they don't buy it themselves, they then come here and inform you that they are from XYZ [hospital] but they were not given the antibiotic and the symptoms are still there, mind you that is only in 2 days. So, they come here sometimes just because they want the antibiotic.*" [FM_N_Prim_S]

Informants mentioned that irrational use of antibiotics is sometimes fueled by patients who start treatment and do not finish the course of antibiotics, and sometimes share a course of treatment with relatives.

"*We do tell them but then they do take it and sometimes even incorrectly and they don't finish the course or you find that they give some of the pills to some of their relatives and they come to us having already started taking the antibiotic.*" [FM_N_Prim_S]

Frontline managers reported that though they knew the correct medicines to prescribe, they often felt pressured by patients to prescribe certain medicines. If they refuse to give in to patients' demands, patients will then embarrass them in public and say that they are incompetent.

"*... because they complain of their bodies are low on energy and when you don't give them the black pills [vitamin B Complex] they come back and knock again asking for the black pills. The fact we deal with a community every day, it's better for those in larger facilities because they don't see the same person every day and you meet them outside the clinic and they tell you that you never gave them the right care and medication and that's embarrassing*." [FM_N_Prim_L]

Effects of study

Frontline managers reported that the study positively impacted the way they prescribe and dispense medicines in their facilities.

"*Your coming has helped, because whenever I want to do something I remember your words "hey limit the medicines per prescription"*." [FM_N_Prim_L]

***"**(laughs) we are now educated on that part; we know you don't have to order a long list of drugs so we try to make it 3 at most 4 at worst case scenario they should not go past 5"* [FM_N_Prim_S]

Facilities also reported that through the information shared during the study they were making an effort to improve their prescribing practices to rationally use medicines. Changes in staff were cited as factors that potentially negatively impacted positive interventions as new staff might have not been involved in the study and might have their own entrenched prescribing practices that cannot be changed overnight.

"*You emphasized on using the guidelines, and I would say gradually we are trying though I am not on the outpatient side anymore where the prescriptions work more but then I would say somehow there is a change, we are trying to follow the guidelines as much as we can. Although sometimes there are changes in staff then it depends on individuality because as individuals our beliefs vary. Otherwise, truly speaking, I feel like there has been that change*." [FM_N_Sec_H]

"*ok, they [intervention visits] were helpful in a way that instead of us just prescribing, like we said we prescribe so that money comes into the company [laughter], somehow the nursing it would divert to the other side, so it [intervention visits] was helping in bringing us back into line so that when prescribing we just prescribe exactly the things that the patient needs instead of prescribing for other benefits, so it helped.*" [FM_N_Prim_H]

Some facilities were not sure if the study had affected prescribing of antibiotics as they felt that there were reasons beyond their control that resulted in them prescribing antibiotics.

"*I'm not sure, but we have a challenge with the community. Because the community once you don't give antibiotics, the same person comes back tomorrow for treatment again and then that makes you look like you don't know what you are doing if the same person keeps coming and coming and with them its psychological because they also tell you I want this pill that is maroon and so forth so if you don't give that pill the notion is that you haven't helped that person*." [FM_N_Prim_L]

Some facilities felt that the study had capacitated them to be aware of how they prescribe antibiotics. However, they felt over-prescribing multivitamins was not a big issue as they prescribed multivitamins and some elements to "boost" patients.

"… but it is usually on the antibiotics where we focus on mainly, but the multivitamins I don't see a problem with giving multivitamins because here in the rural area we don't get the three basic food groups so we try to boost by giving them some vitamins (laughs) but we are very careful on the antibiotics but for the multivitamins please allow us(laughs) but for the antibiotics we are prescribing fine except for the vitamins like calcium and BCo [vitamin B Complex] but they are usually not many from what I have observed." [FM_N_Prim_S]

"*Ok, for us I think we are giving 2 to 3 it's only that maybe we can add some especially with children but even with adults sometimes we do have multivitamins and all those. That's not medication but to boost immune system because the elderly like your BCo and some diclofenac and medicine for bones, muscles, and the rubbing stuff then they are happy. Sometimes we have diclofenac injection - we would give them some injection, we would give them some rubbing stuff including the tablets to take home and maybe some BCo if we do have and some calcium, so they will be happy they have received lots of medicines.*" [FM_N_Prim_H]

Frontline managers in the intervention arm reported that they found the small group education during intervention visits helpful. However, they mentioned that people tend to go back to what they were doing if there is not a constant reminder, particularly from someone who is not part of the team on irrational prescribing and use of medicines.

"*The talks help but that is not enough because they have a tendency that today they hear you but two or three months down the line they are back to doing what is not right. So, it would help if someone from outside can come to teach polypharmacy and if there is provision for food during the workshop then lots of people will attend too(laughs).*" [FM_PT_Sec_H]

Generally, informants (key informants and frontline managers) reported to have liked the participatory nature of the study. They liked being engaged and decisions taken with them.

"*Well I think when you first started this study, I believe all stakeholders were involved, because sometimes you guys just do the things in the offices and leave out the nurses who work directly with the patients, so [with this study] we also get the regular update. It [the manner in which the study was conducted] can help as well with the overuse of antibiotics."* [FM_N_Prim_M]

Frontline managers reported that they found the study, particularly the intervention visits (small group education), helpful as it addressed some outdated information in the STG/EML.

"*The study has helped us because I think with the aldomet case for the pregnant women it showed when you came you helped us on that, because the standard treatment guidelines still show that aldomet should be used to treat hypertension; even with the salbutamol which is still being recommended to treating asthma.*" [FM_N_Prim_M]

Some facilities in the control arm felt the study had a positive impact on their medicine use practices.

"*It gave us an idea as to how we are prescribing as a hospital because even when we thought we were doing right the study gave us an idea that even when we want to improve which parts can we improve on in terms of prescribing*." [FM_P_Sec_S]

Facilities also reported that the first consultative meeting had impacted on how they use injections.

"*There is an improvement, mostly because we used to supply some injectable antibiotics to the OPD (out patients' department) but now we stopped we are giving them to the normal wards, because if someone is at OPD it means they can take drugs orally so no need for injections, so we now supply the wards. At the OPD we now mostly supply STI injectables not just any, that's the decision we made after the study*." [FM_P_Sec_M]

Some frontline managers mentioned that they had not seen effects of the study as prescribers were still prescribing the same way they did at baseline. What fueled irrational prescribing was that most of the doctors were new and had not been engaged on the baseline study findings.

"*so nothing has changed people are still prescribing the same way they used to before and unfortunately, most of the doctors are new to the facility now since the first visit so, they prescribe the way they think it's supposed to be*." [FM_P_Sec_M]

Regarding realising effects of the study, frontline managers reported that although the study seemed to have positively impacted prescribing, the good prescribing practices did not last.

"*That one is a little bit tricky, because prescribers have got a tendency of saying when you speak to them today, maybe this week, they will do but the following week they are back to square one. That's what I've noted. That we can speak and have understanding but before you know it they are back to square one. It's a trend that you talk about it, they do it but the following week they are back to old methods. So I don't know how we can deal with it*." [FM_PT_Sec_S]

Facilities reported that during the intervention visits and just after the visits prescribing of antibiotics improved. However, they reported that once the visits stopped, prescribers reverted to overusing antibiotics as they were before they were made aware of overuse through the study.

"I won't bother hiding it from you, but benzathine is used very often at this facility. You came and spoke to us because they (prescribers) even saw the numbers and we sat down, it was me and the nurses and you spoke to us about it [overuse of antibiotics and injections] and it improved and we were no longer abusing the benzathine. But unfortunately by the look of things, now it is getting back to the old ways, it is now increasing so in the percentage I would say it is around 30% the usage of benzathine. So, yes they use if a lot, I am not sure if we would need training for that. Thing is you find that if the tablet for that condition is not available, they feel benzathine is for treating multiple diseases so that play a role in increasing the usage, because there is nothing else to give, yet you emphasized on that you have to beg the patient to come back later than to give what is not supposed to be given." [FM_PA_Prim_M]

Furthermore, informants highlighted that the study could potentially help the government to have an idea of how medicines are being used in the country.

"*In fact the study will help to show the government what is happening in the country, that under normal circumstances this is what should be done but it is not happening thus it will help to put all that should be in place to be in the right position so that our work will be made easier. So, if they [the government] have a buy-in it will be very good… but if the resources we need to function properly are not in place then we are not providing good service to the community.*" [FM_N_Prim_M]

When asked if the informants felt the study could have been done any differently, they generally liked the way the study was conducted.

"*I think so far it is good, I don't know where you can improve but so far, I felt it is okay, it helped us a lot more especially on the antibiotics it helped us coz we saw how other hospitals were doing and we felt like we were better (laughs) so we felt we were doing the right thing so we want to do much better going forward.*" [FM_P_Sec_M]

Interventions that facilities implemented following the study

After being made aware of baseline study findings, some facilities implemented interventions to improve rational use of medicines in their facilities. One facility in the control group developed a facility-based data collection tool using the INRUD indicators (Appendix 17) that they use to collect data, analyse and present to their PTC on how the facility was performing. Another facility in the intervention arm developed a monitoring and evaluation form, placed in the pharmacy, to monitor the use of antibiotics.

"*It is used by us here at pharmacy, to see that out of 200 prescriptions we have seen let me say 70 prescriptions that had antibiotics, so that we can be able to see whether the use of antibiotics is reducing or increasing because we have to try to be below 50 percent.*" [FM_P_Sec_S]

Challenges to rational use of medicines in facilities

Stock-outs and inconsistent supply of essential medicines, as cited at baseline, was cited even at the end of the study as a factor that compromises rational prescribing and use of medicines.

"*Most medicines are out of stock from the CMS and this result in prescribers prescribing outside the treatment guidelines. Also, the 2018 STI guidelines recommend use of new medicines like* *azithromycin which is not available from CMS. In PTC, the facility enforces use of treatment guidelines, but this is always a challenge because there always are stock outs*." [FM_P_Sec_S]

"The inconsistent supply of medication plays a big part as we end up not prescribing the way we are supposed to and we end up giving medication just because you don't want the patient to leave empty handed. For example, with the asthma drugs, since we are no longer supposed to use salbutamol tabs and syrup because it causes palpitations and it might cause cardiac problems in the long term but then when we do not have the spray what are we supposed to do? I cannot turn back the client seeing that they are having an asthma attack, so it becomes tricky yet if the drug supply was consistent the drugs we are not supposed to use we wouldn't be using. Methyldopa or aldomet is for pregnant women with hypertension but now what is happening we don't have HCTZ on stock, yet we have hypertensive clients in the community then what do we do" [FM_N_Prim_M]

An issue highlighted during baseline data collection in 2017 came up again during the post follow-up period data collection process. Informants mentioned that NCD medicines were not available at primary levels of care, and this compromised rational use of medicines.

"*[when NCD medicines are not available in stock] It's either we tell them to go to XYZ [hospital] or then we have to think hard and count and break up some of the pills and try to figure out how they can drink the 500mg medication in order to get to their dose of 850mg. That is usually the challenge when it comes to NCDs*." [FM_N_Prim_S]

High workload was cited as a factor that compromises rational use of medicines in primary healthcare facilities. Frontline managers mentioned that due to the amount of work they have to do on a daily basis; they never have enough time to dedicate to pharmaceutical management.

"*It's not a lie we are ignoring the pharmacy management on purpose; it's just that the workload is too much, because if we are going to do the counting, we find ourselves knocking off at 8pm then when are we going to get home?*" [FM_N_Prim_S]

Geographical access to some healthcare facilities was also cited as a factor that potentially promotes irrational use of medicines. Some frontline managers mentioned that it was difficult for CMS to deliver their stock, particularly during the rainy season. Unavailability of stock then made it difficult for these facilities to prescribe and use medicines rationally.

"*Another thing is where we are being a rural area, the infrastructure is a barrier on its own because they always complain that our road is not nice, so they are reluctant to come here most of the time especially in summer once the rains start, it's usually better in winter when it's not raining, so they have to think twice before they come here. Once it starts raining the roads become slippery and there no alternative route to take for them to get here so that also causes the late deliveries as they will focus on those they can reach easily.*" [FM_N_Prim_H]

Changes during the study

Changes, including the change in the structuring of the pharmaceutical cadre to have regional pharmacists who conduct supervisory visits and support to facilities, and introduction of CMIS, occurred during the course of the study. Participants were asked if they were aware of any changes that happened during the study and if these changes had an effect on rational medicine use. Frontline managers mentioned that introduction of CMIS positively affected RMU by reducing polypharmacy.

"*On that part I will speak from my experience. With the CMIS what normally is like they don't want to write a lot of things, lot of drugs, from the facility I come from because we used it for almost 6 months but with the introduction the polypharmacy decreased*." [FM_N_Prim_M]

"*It's really helping us even with limiting the amount of drugs, because when you are writing on paper you think you are giving out a small number of drugs and you keep adding but with the system you that you've filled up a whole page and then you count and see the unnecessary drugs and delete them so it's helping*." [FM_N_Prim_L]

Though frontline managers felt CMIS improves RMU, they still highlighted some negative effects that the system had on rational use of medicines. Healthcare providers, particularly nurses, mentioned that they had challenges with CMIS as they were not familiar with some of the preloaded diagnoses. Furthermore, some medicines were not preloaded on the system and this made prescribing challenging.

"*Some things are not available on CMIS, some of the diagnoses are not on the system and it's only the ones that doctors use most of the time that show that I as a nurse cannot use to diagnose someone.*" [FM_N_Prim_S]

"However, when it comes to diagnosing it's not as good too, I am not sure whether those diagnoses are from Europe or what (laughs), when you are diagnosing here you find common diagnosis, for version 1.6 when I wanted fungi I would just it immediately but here it is difficult to find, they have grouped the diagnosis in a different way now which is not easy to find so you end up maybe putting skin condition." [FM_N_Prim_S]

"*It's been causing headaches I won't lie to you, some of the drugs are not on the system, you can't update some things and sometimes you can give [prescribe] a patient some medication but when you check later you find it is not reflecting on the system so, it is still a headache.*" [FM_N_Prim_L]

Facilities also reported that CMIS does not allow them to do stock management and this affects their stock management practices.

"*Another thing with CMIS is that we are unable to count accurately because some of the medications are not on the system so they end up being skipped as opposed to when we were counting manually and then we end up ordering wrongly sometimes and not ordering the right amounts*" [FM_N_Prim_S]

Availability of regional pharmacists was cited as a factor that has positively contributed towards promoting rational use of medicines. Frontline managers reported that regional pharmacists have helped to improve communication on stock availability with CMS and further support with new information around medicines and borrowing medicines from other facilities as stop gap measures during stock outs.

"Before it was bad, it was bad until they provided us with regional pharmacist. Now that we have a regional pharmacist, we don't even bother calling CMS because now when I tell her that at Facility X we are facing such an issue she is quick to respond and give feedback to say that "yes I have talked to them and this is what they are saying" so the communication has improved." [FM_PA_Prim_M]

"*We do try to call and she tries to help where she can and if not ask us to borrow from our neighboring clinics, we do bother XXX a lot.*" [FM_N_Prim_H]

"It helps us a lot because when we have a problem we consult and they inform us if there is any new information regarding medicines, for instance they did come during the time where we had a

serious shortage of drugs when CMS was closed I think she was visiting all facilities, so she was checking, and if she sees that maybe we have a surplus of a certain drugs she would take the surplus and give it to another facility and take surplus from other facilities to give to us in the drug where we are having a shortage. They helped also with the issue of expired drugs which had stayed for a long time but they helped to facilitate and we were able to ship them out though we still have some of them." [FM_N_Prim_S]

Also, frontline managers reported that regional pharmacists conduct on-site trainings for facilities on stock management practices, which helps them keep adequate stock that enables them to practice RMU.

"…*he did give us an in-service training basically on stock management. If we have stock, we are able to prescribe rationally.*" [FM_PT_Sec_S]

Recommendations to improve RMU

Frontline managers reported that it would be helpful for them to have easily accessible reference material with key material that does not require a lot of effort to page through.

"*Another thing that helped is the use of charts like this one on the wall it gives clear direction as to how to manage diarrhea so for the common conditions it would be nice to have those charts in the examination rooms so it's easy to refer than having to sometimes page a book, and this chart tells you exactly when to give out antibiotics {laughs} so, it's important that we get these reminders.*" [FM_N_Prim_M]

Informants mentioned that refresher trainings and prescription audits could potentially improve rational use of medicines.

"Having the refresher trainings would help a lot even the audits like you are doing now can help in reminding ourselves on the right methods to follow and getting feedback from you guys to see where we are and where we need to improve." [FM_N_Prim_M]

Healthcare providers in facilities also felt that mentoring and supervisory visits from external people on rational use of medicines could promote rational use of medicines. They mentioned that prescribers tend to listen to external people as opposed to listening to their colleagues (pharmacy) in the facility.

"*So far it can be that if there can be a way whereby someone from outside can to speak to the nurses because I feel like they respond better when someone from outside speaks than with us and sometimes if possible, to get like handouts [used during intervention visits] that the nurses can see and place in their consulting rooms that can also support me when I need to make a correction on a prescription, so I can show that this is the way to do this. So, if that can happen I would be happy and also if someone can sit us down and talk to us especially on the antibiotics and the practice of polypharmacy coz on that one they have gone back to square one, back to square one I tell you, because you give allergex you give cold & flu give panado, cold and flu incorporates all this but then they prescribe all these. So, I think the trainings would help if someone can come teach us and those handouts whenever possible*." [FM_PA_Prim_M]

Informants also mentioned that making some medicines (particularly NCD medication) available at primary level of care could promote rational medicine use.

"Another thing can be that some of the drugs are not essential to clinics [according to the EML] yet we need them, drugs like aldomet we do not get, and being in a community that is situated in a rural area and then patients have to travel to get the drug in a hospital, and most of them do not have the funds to travel long distances so they end up defaulting on some treatments. On the essential drug list there are drugs that are missing which I think we [primary level of care] are supposed to be getting. For example, here comes a pregnant woman, delivers here and they are now bleeding, we don't have any means of controlling the bleeding because we don't have the drugs to help control the bleeding for women who are delivering they are only accessed at hospital level. You can also find that a patient is brought here having convulsions but we can't help because we don't have those drugs yet those are emergency cases, so the drugs that we can use during emergency cases are very limited in our facility. That is according to the essential drug list for small facilities like us which are not included, some of these drugs we do get from partners but from CMS you can't order syntocinon because they will say "syntocinon at XYZ clinic, what for?"
[FM_N_Prim_S]

Availability of pharmacy personnel in primary healthcare facilities was cited as a factor that could also promote rational use of medicines.

"*I think it they can deploy the rightful people in the right departments, have adequate staff for that particular position maybe it can be better, coz I think if we had pharmacist of pharm tech they would be able to alert us if we are now prescribing lots of antibiotics for example and also advice on the correct dosage coz I might know what I am supposed to give but for example, I see someone suffering from a skin condition like scabies, we learnt late that the patient has to apply the bb cream for 3 days and then take a break, so a pharm tech would have better knowledge on that aspect than us and they will tell the person the right things.*" [FM_N_Prim_H]

Around the issue of pharmacy personnel, informants recommended that regional pharmacists should have transport to allow them to support facilities on pharmaceutical issues.

"*... maybe it's due to transport because I think if they do have transport regularly, they would visit us, especially us who don't have pharm techs as I think there are some things that she can help us to fix as some things I might not be able to fix, so they should come and we talk."* [FM_N_Prim_S]

Frontline managers also mentioned that the country needs to have up-to-date guidelines, use of which should be enforced by the government to promote rational medicine use.

"*I think if the guidelines can be updated and if the government can have a way of enforcing or making sure that people are adhering to the guidelines. Number 2 would be that we should always have stock available because then people opt for something else if maybe the oral is not available or if there is no other alternative for the medication they wanted. We also need the continuous trainings every now and then to make sure we are on the right track. Then maybe for interactions and everything we need a system, the CMIS to be other systems that state that this drug interacts with this one on the system, just when you put it on CMIS it tells you that this drug interacts with this one; that can help too.*" [FM_PT_Sec_S]

The next chapter (Chapter 6) will detail consultative workshops that were conducted as part of the study.

CHAPTER 6: CONSULTATIVE WORKSHOPS

These were important participatory parts of the study that brought together investigators and study participants to deliberate on study conduct, processes, and findings. Consultative Workshop 1 was at the end of Phase 1; at this stage facilities had not been allocated to intervention and control arms. The purpose of this meeting was to report on Phase 1 findings, expose participants to a range of interventions for promoting rational use of medicines, and, as a collective, decide on an intervention to be tested in Eswatini. Consultative meeting 2 was at the end of Phase 3 and included participants from both intervention and control facilities. The purpose of this meeting was to report on overall study findings (i.e. from baseline through end of intervention to end of follow up period), and have participants deliberate on issues they would like to be highlighted in the discussion section of the thesis and further recommend how study findings can be translated into action. The reason for involving participants in the decision on the intervention to test in Eswatini was for the participants to feel that they have been involved and for them to own the processes followed during this study. Furthermore, we wanted to capacitate them to be able to continually monitor medicine use in their facilities. The two feedback meetings are detailed below.

6.1 First Consultative Workshop and Intervention Selection

On the 20th of February 2018 stakeholders from the MoH (national level, regional level, facility level and CMS) and an implementing partner (MSH/SIAPS) gathered to participate in a half-day consultative feedback meeting and workshop, which took place at the Mbabane Government Hospital Laboratory Conference room in Mbabane. The overall goal of the meeting was to engage stakeholders involved in policy development around RMU, senior level medicine managers and frontline medicine managers on existing medicine use practices in Eswatini, and, using a collaborative participatory approach, to select an RMU intervention to be tested in Eswatini. Workshop participants included KIs (4) and some frontline medicine managers (20) from the facilities that are part of the study. Facilitators were from the School of Public Health, University of the Western Cape: the PI (NBQN), and supervisors (Dr. Hazel Bradley and Prof Richard Laing).

The objectives of the workshop included:

- Presenting study procedures and findings;
- Engaging KIs and frontline medicine managers in discussions around the findings;

- Exposing KIs and frontline medicine managers to a range of interventions for promoting rational use of medicines;
- As a collective, choosing an intervention that can promote RMU in Eswatini to be implemented in Phase II of the study.

6.1.1 Workshop Materials

Several documents were developed to conduct the feedback meeting and workshop:

- Feedback and workshop agenda included in Appendix 18.
- Participant List included in Appendix 19.
- Information Leaflet included in Appendix 14.
- Situational analysis PowerPoint presentation.
- Strategies to improve medicine use PowerPoint presentation.

The meeting was chaired by the Ministry of Health and officially opened by the Deputy Director of Pharmaceutical Services in Eswatini. The research assistant (SN) took meeting notes. The chairperson explained that the meeting was part of a bigger study and mentioned that information gathered from the meeting would be used to report on the study. The chairperson further gave meeting attendants information sheets with more information on the study and attendants were asked to consent for proceedings of the feedback meeting and workshop to be reported.

The PI (NN) presented procedures that were followed in conducting the situational analysis and the quantitative and qualitative findings of this phase of the study. Meeting attendants were given an opportunity to ask questions.

Prof. Laing then presented strategies that can be used to promote medicine use. The strategies included: prescription audit and feedback to healthcare providers (prescribers, pharmacists, and dispensers) with supervision, large and small group training/education of healthcare providers on RMU, structured supervision with multiple supervisory visits, and regulatory approaches. Stakeholders were given an opportunity to ask questions.

Participants were then allocated to small groups and using the results from the situational analysis, participants were asked to deliberate in small groups on what intervention(s) could be implemented to promote appropriate use of medicines in Eswatini. In plenary, we went over the different recommendations to improve medicine use from the groups. These included: hosting a radio talk on the local radio health slot that aired on Thursday mornings, having large group off-site trainings for frontline medicine managers on RMU, and mentoring/supervising facilities on medicine use (i.e. identifying irrational use of medicines and supportively assisting medicine managers to improve prescribing practices).

6.1.2 Discussions

This section summarises the discussions at the feedback meeting and workshop. Participants appreciated the study and highlighted how the study acted as an "eye opener" for them. Discussions and reflections on the results from the situational analysis showed that participants were willing to prescribe rationally but they cited several factors that influenced prescribing. They mentioned that they were not aware of policies around RMU or the WHO guidance on how one should prescribe. Factors that participants highlighted as influencing prescribing practices included: lack of knowledge and skills to measure and evaluate medicine use, poor guidance/mentoring/supervision on rational use of medicines, the STG/EML limiting certain levels of care to prescribe certain medicines, poor documentation of prescribing information, poor inventory management, and frequent stock-outs of essential medicines.

Pros and cons of participants' recommendations of interventions to be tested in the meeting were discussed in detail with evidence given on which interventions have proven to be effective. At this meeting, the participants agreed that small group on-site training coupled with supportive supervision would be appropriate for Eswatini's setting; and this was the adopted intervention to be tested.

Investigators used a participatory approach to decide on an intervention to be implemented in Eswatini to improve rational use of medicines. Participatory approaches in research are advantageous in that participants develop and carry a sense of ownership of the research (Jagosh et al., 2012). Furthermore, participatory approaches build a base for the intervention; if participants are involved in the planning of the intervention, they tend to own it (Jagosh et al., 2012). Participatory research also allows participants (policy makers and frontline managers in this study) to be intensively involved in the study such that when study findings are available they are able to translate research to action (Cargo & Mercer, 2008; Israel et al., 1998; O'Fallon & Dearry, 2002).

6.2 Second consultative Workshop

On the 4th of February 2020 participants from the MoH (national level, regional level, facility level and CMS) gathered to participate in a half-day consultative feedback meeting and workshop, which took place at the Mbabane Government Hospital Laboratory Conference room in Mbabane. The overall goal of the meeting was to present end-of-study results to senior Ministry of Health officials, policy makers, medicines regulatory officials, central level pharmaceutical officials (4) and frontline medicine managers (18). Furthermore, the meeting aimed to discuss these findings and encourage the participants to discuss information they would like to see in the discussion section of the thesis along with recommendations for the study. Facilitators were from the School of Public Health, University of the Western Cape: the PI (NBQN), and supervisors (Dr. Hazel Bradley and Prof Richard Laing).

The objectives of the workshop included:

- Presenting study procedures and findings
- Engaging meeting participants in discussions around the findings
- Having meeting participants discuss information they would like to see in the final study report

6.2.1 Workshop Materials

Several documents were developed to conduct the feedback meeting:

- Meeting agenda included in Appendix 20.
- Participant List included in Appendix 21.
- PowerPoint presentation of results.

The meeting was chaired by the Ministry of Health and officially opened by the Deputy Director of Pharmaceutical Services in Eswatini. Mr. Willie Siduna (WS), a PhD student at the School of Public Health, UWC took meeting notes. The Chairperson explained that the meeting was a follow-on to a meeting held in 2018 that shared baseline findings on RMU in the country and during which the intervention (prescription audit and education) was decided on as appropriate for Eswatini. She then mentioned that the purpose of the meeting held on 4 February was for the investigators to present results post implementing the intervention. Dr. Hazel Bradley then presented the meeting overview where she explained how the presentation of the findings would be done. She emphasized that after the presentation participants would have a group work session to discuss their understanding of the results and give input. Dr. Bradley explained that information gathered from group work would go into the final study report. The Deputy Director of Pharmaceutical Services (DDPS) in Eswatini then gave welcome remarks. In her welcoming statements she highlighted the importance of RMU in Eswatini given the dwindling financial resources and rising antimicrobial resistance. She also mentioned that she would like these findings to be presented to all senior staff in the Ministry of Health. The DDPS further encouraged active participation of participants as she believed that the study had generated evidence needed for evidence-based decision making and provided recommendations for what needs to be done to improve RMU.

The PI (NBQN) then presented an overview of the baseline survey, intervention selection and implementation, quantitative results post the intervention, and quantitative/qualitative results post the follow up period. Meeting attendants were given an opportunity to ask questions and the questions asked included:

- Did the study look at availability of medicines?
- Are there differences in prescribing patterns between facilities with pharmacy technicians and those without? This information is important for the office of the DDPS as it is useful when motivating for more posts for pharmacy technicians.

Some comments from participants and investigators were:

- There is still a lot of work to be done to address over-prescribing of antibiotics. To address the use of antibiotics in NCDs, health care providers need to exhaust other means of therapy before resorting to medicinal therapy e.g. addressing dietary issues for diabetes. An example given was that diabetic patients should be encouraged to have okra (*ligusha*) after meals as it limits the glycemic load of food eaten.
- Eswatini needs to combine strategies to intervene in RMU.
- Study findings show that there is no pre-service training for prescribers to orient them on prescribing in Eswatini.
- Feedback from one facility on how information obtained from the baseline survey was used to implement an intervention (prescription audit and feedback during PTC meetings and

training of nurses rotating to out-patient department) which was improving the use of medicine in this facility was shared.

6.2.2 Group work

Participants were split into two groups - the focus of this session was to get participants to discuss issues they feel should be included in the discussion, recommendations, and conclusion sections of the final thesis report.

Group 1 discussions

Composition: 3 pharmacists (from hospitals and the region), 3 nurses (from hospitals and clinics)

Reaction to study results

- Group members were surprised at the use of antibiotics in chronic illnesses. They mentioned that antibiotics could have been used for an acute illness that was not included in the diagnoses.

Comments from Group 1

- One group member made this comment - "*I was part of the baseline survey and I am surprised that to this day NCDs are still being prescribed antibiotics*".
- Prescribers justify the overuse of amoxicillin. One doctor said she prescribed it because there were no cough medicines in the facility. Participants felt that most often amoxicillin is prescribed to replace any other medicine that is out of stock.
- A member of the group asked - "*What other methods can be used at facility level to improve use of antibiotics?"* In response to this question, group members highlighted the importance and need for prescribers to confirm the presence of bacterial infection before prescribing an antibiotic.
- Group members were disturbed by the fact that there were no doctors present in the feedback meeting.
- Group members emphasised the need for teamwork among health care workers (HCWs). An example cited was that when pharmacy technicians correct prescriptions from prescribers, the two cadres often fight.
- Team members highlighted the need for collaboration of health care workers at all levels of care. The group mentioned that a factor that resulted in inappropriate use of medicines

was doctors not attending clinical meetings including PTCs. Members mentioned that collaborations/teamwork would not be possible if health care workers do not meet and address critical issues particularly on RMU.

- Participants also highlighted human resource issues that potentially affect RMU. They mentioned that in some facilities, particularly clinics, the same nurse prescribes and dispenses to a patient. In such instances there are no checks on whether the prescribing is in line with the diagnosis or whether the correct medicine has been prescribed and dispensed to the patient.
- Results of the study showed minimal differences between the intervention and control facilities. When participants were asked whether they were surprised with the findings they mentioned that they were not, as it is difficult to change behaviour. Also, participants mentioned that some patients pressurise the prescriber to prescribe medicines for them.

  "When you are new in a facility, you are placed at the out-patient department which is very busy, at times even without undergoing orientation. This is where some habits come from."
- Overuse of injections: group members mentioned that the elderly often report to feel better if they get an injection. Group members also mentioned that there was high usage of injections in hospitals and health centres for patients who present after hours as it was easier to just give the patient an injection than to call the pharmacy person on duty to open the pharmacy and dispense medicines to patients.

Recommendations from Group 1

- Higher level MoH personnel should have access to this study so that they are aware of the issues around high use of antibiotics and polypharmacy. Polypharmacy at times is not on purpose – HCWs do not have sufficient knowledge and need to be educated on RMU. Polypharmacy results in drug-drug interactions and adverse drug reactions which are expensive to treat. Results from this study will go a long way in influencing RMU and ultimately budget control in the MoH.
- Regional pharmacists can impact RMU through supervision and support. However, though they have been appointed, they face challenges with transport to get to facilities. Regional

pharmacists should visit every pharmacy at least once a year – this could go a long way to improve RMU.

- There is need to have pharmacy personnel at all levels of care.
- The Eswatini health system has focused so much on HIV and neglected other conditions. Though clinical development/implementing partners are the main drivers of the focus on HIV, the MoH is also diverting most effort towards HIV. The HIV world is slowly becoming interested in NCDs because HIV positive clients are getting NCDs as they get older.
- The MoH should address root causes of irrational medicine use such as unavailability of medicines, prescribing, and patient education.
- Education of prescribers on generic names *"some HCWs are not familiar with generic names of medicines – this could contribute to polypharmacy as a prescriber who does not know the generic name can refill medicines without knowing what they are."*
- There is need to make pharmaceutical information on management of common conditions available to prescribers e.g. avoiding prescribing cold and flu tablets plus paracetamol plus chlorpheniramine OR vitamin B Complex plus multivitamins.
- STGs: Enforce use of STGs. *"STGs are readily available, but we as HCWs do not use them. People just cut and paste from the patient's treatment history."*, and *"It is good that STGs are currently undergoing revision, though some facility level personnel are not keen to participate in the STG/EML revision process – HCWs should be oriented on the STGs. The STG roll-out strategy should be extensive"*
- An electronic application of the STGs would be helpful to improve RMU.
- Educating patients on RMU as they sometimes come to a prescriber with certain expectations and discuss therapeutic and non-therapeutic options with the patient. *"Some patients feel that the more the medicines, the better the treatment they got."* Participants felt that community education, in a language they will understand, was crucial to improving RMU in consumers. Suggestions on how to do this included the use of images to illustrate how antibiotics work on bacteria and how the microbes become resistant to the antibiotics.

Group 2 discussions

Composition: 4 pharmacists (1 national level: policy, 1 from CMS, 2 from hospital), 2 pharmacy technicians from health centres, 3 nurses from clinics.

Reactions to results

- The research has opened eyes for the HCWs – they now realise that a lot of money can be saved if we address polypharmacy (it increases the drug budget, adverse drug reactions (ADRs), and impact on drug shortages) and overuse of antibiotics (prevent ADRs and AMR)
- Polypharmacy is entrenched in staff and patients. Patients demand a lot of medication. Even if they are given a few, they start reporting symptoms that they did not have before, to increase the number of medicines. Patients think that for every symptom, there must be a medicine. Education is needed for both HCWs and patients.
- Generic prescribing: this is a challenge as sometimes HCWs do not know the generic names. As a result, if medicines are prescribed using generic names, the nurse that refills the prescription will refill all medicines even if there was an antibiotic. This increases the number of medicines and could potentially perpetuate AMR.
- Injections: the elderly like to be injected, so they request for these. The reflection of use of injections in the results could potentially be a low reflection of the use of injections. Most people who present in the evening/night get injections. However, these injections are not recorded on prescribing records.
- Prescribing from the STG/EML: prescribers do not consult these. Currently the STG/EML is being revised. HCWs from facilities were requested to contribute to the process as the response is very low.
- High use of antibiotics (amoxicillin in particular): patients present the prescriber with a list of medicines they want, and most often including amoxicillin. HCWs give in to patients' demands. Some HCWs think that amoxicillin fixes everything. If there are medicine shortages and the HCW does not have the right medicine to prescribe, they just prescribe amoxicillin.
- It is difficult to practice RMU if stocks of medicines are inadequate.

Recommendations from Group 2

- There needs to be strong collaborations between the MoH and research. Findings from research should be used to implement interventions (research to action).
- HCWs at all levels of care (facility to regional to national) should also collaborate to promote rational use of medicines. Prescribers should be more involved in rational use.
- Facilities that have implemented the intervention tested in this study have shown positive results. These facilities should be used as references to scale up processes.
- Regional pharmacists need to be supported with transport so that they can conduct meaningful supervisory visits to facilities.
- STG/EML should be included in basic training of HCWs. All HCWs should be oriented to the STG/EML. The MoH needs to work with the Swaziland Medical and Dental Association and Nursing Council to ensure that HCWs are oriented and competent before being posted to facilities.
- Timely revisions of the STG/EML should happen as science is constantly changing.
- PTCs should have in-service training for HCWs in facilities. Nurse prescribing audit and feedback can be used to understand prescribing practices of nurses who normally do not sit in PTCs. Their training can then be tailored based on findings of the audit.
- Regional pharmacists could use CMIS to routinely perform prescribing audits and then target facilities with problematic prescribing.
- HCWs should re-emphasise non-pharmacological management to patients.
- Patient education in appropriate language is key to address irrational use of medicines. HCWs often report that patient volumes are high hence they do not have time to explain everything to each patient – this is an excuse, every HCW should make time to properly consult each patient.
- Patients who request to be prescribed amoxicillin should be educated using a language they understand (pictures, local language) that it is only used for bacterial infections.
- For HCWs, messages around use of antibiotics for bacterial infections need to be strengthened.

To wrap the meeting up, NBQN thanked the office of the Deputy Director Pharmaceutical Services (ODDPS), participants from facilities and supervisors for making this research a success. In her closing statements, NBQN encouraged the ODDPS to adopt some of the processes followed in this study to strengthen pharmaceutical services and rational use of medicines in the country. The next chapter (Chapter 7) discusses study findings.

CHAPTER 7: DISCUSSION

This chapter discusses findings and processes followed in conducting the study. In this study, prescribing indicators changed though most of these changes were not statistically significant as will be discussed. Participants enjoyed being part of the study and felt it had an impact in improving prescribing and medicine use practices. During the study, some specific system developments implemented by the MoH facilitated the changes while some were barriers to change as will be discussed in this chapter. Furthermore, participants felt that processes followed in conducting this study could be adopted by the department of pharmacy and used to closely monitor prescribing and medicine use practices at national, regional and facility levels.

To extensively discuss study findings, the discussion consists of the following subsections:

- Baseline survey (quantitative and qualitative components);
- End of study evaluation (quantitative and qualitative components);
- Processes followed in conducting the study (allocation of facilities to the intervention and control arms, first consultative meeting (sharing baseline findings and intervention selection), Intervention design and implementation and final consultative meeting),
- Strengths and limitations of the study.

7.1 Baseline Survey

7.1.1 Quantitative Component

Baseline findings of this study showed that there was polypharmacy in Eswatini as evidenced by the national average number (3.7) of medicines per prescription above the WHO (1993) recommended standard of two to three medicines per prescription. Polypharmacy, similar to Eswatini, has been reported in Southern India (Atif, Sarwar, Azeem, Umer, et al., 2016). To further highlight the widespread practice of polypharmacy, a systematic review of studies conducted in 10 African countries between 1995 and 2015 found the overall average number of medicines per prescription to be 3.1 (Ofori-Asenso et al., 2016). Other developing countries that have reported values higher than the WHO recommended standard are Yemen (3.8) and Mali (3.2) (Abdo-Rabbo, 2003; Maïga et al., 2003); while Sudan (2.55), Thailand (2.85), Namibia (2.6 – 2.8), and Uganda

(2.9) (Kagoya et al., 2020; Ogwal-Okeng et al., 2004; Pongsupap & Lerberghe, 2006; Yousif & Supakankunti, 2016) have reported values closer to the upper limit.

Polypharmacy could be due to co-morbidities suffered by people in the African region. Though this may be the case, Eswatini needs to ensure that medicines prescribed per patient are necessary, as it is costly to the health system to over prescribe. In addition, the use of unnecessary medicines can give rise to adverse events which are expensive to manage. It is notable that for both diabetes mellitus and hypertension, when reported as a single diagnosis, the average number of medicines was only slightly less than for combined diagnoses. In addition to the chronic medicines, chronic conditions were most frequently prescribed medicines such as paracetamol, multivitamins, vitamin B complex, and methyl salicylate, which could have increased the average number of medicines per prescription.

At baseline, the national average for percentage of medicines prescribed by generic name was just over 70%. The WHO recommends that all medicines (100%) be prescribed by generic name. Though generic prescribing in Eswatini is lower than recommended standards, the country is performing better than other areas that have recorded much lower rates of generic prescribing (Soumerai et al., 2005; World Health Organization, 2002). Low generic prescribing negatively affects health systems as branded medicines tend to be more expensive than their generic counterparts.

The national average percentage of prescriptions that had one or more antibiotics prescribed was a little over 50%. The rate of antibiotic prescribing was higher than the WHO recommendation of below 30% (World Health Organization, 1993). Overuse of antibiotics is not peculiar to Eswatini as other settings have also reported this problem. Sudan reported a slightly higher percentage (54.7%) (Yousif & Supakankunti, 2016), than Eswatini while 10 African countries collectively reported 46.8% (Ofori-Asenso et al., 2016). Prescribing rates lower than those observed in Eswatini, though still higher than recommended standards, have been reported in the Eastern Mediterranean region (53.6%), Western Pacific (50.8%), South East Asia (47.9%), Africa (45.9%), Europe (40.9%), and Latin America (37%) (Holloway et al., 2013).

Overuse of antibiotics results in antimicrobial resistance (AMR) – a global concern, as health systems run the risk of not being able to treat resistant strains of bacteria (Munita & Arias, 2016).

As with most Southern African countries, Eswatini is burdened with the HIV endemic and the HIV/TB co-infection, which may contribute to the high use of antibiotics. Though HIV infection does not necessarily require the use of antibiotics, it potentially increases the prevalence of opportunistic bacterial infections, which need to be treated with antibiotics (Mohlala, Peltzer, & Mafuya, 2010). In Eswatini prescriptions for antiretroviral therapy and tuberculosis are recorded in different registers and were not included in this study. Though efforts were made to exclude ART and TB prescriptions, this study probably included some prescriptions for patients on ART and TB who had opportunistic bacterial infections.

Regarding diagnoses, this study's findings, though not significant, showed that patients with chronic illnesses were more likely to be seen in secondary level facilities than primary level facilities. This could be because primary level facilities are managed by nurses only, whereas there are doctors at the health centres and hospitals, and most of the medicines for the management of chronic illnesses are not indicated for the primary level of care. With the increase of NCDs in Eswatini, policy needs to change to ensure that NCD medicines are available at primary levels of care.

The top five chronic conditions identified in this study were: diabetes mellitus (DM), DM + other conditions, hypertension (HTN), HTN + other conditions, and asthma. The top five acute conditions were: upper respiratory tract infections (URTIs), URTI + other conditions, diarrhea, diarrhea + other conditions, and abscess. This study revealed inappropriate use of antibiotics as these were prescribed for non-communicable conditions such as asthma (51%), diabetes mellitus (24%), and hypertension (17%); an observation that has not been documented in literature. Neither the Eswatini STG/EML nor published literature recommends the use of antibiotics for non-communicable diseases. The use of antibiotics for chronic conditions picked up in this study has not been previously documented in literature. Further investigations need to be done to ascertain reasons for prescribing antibiotics for NCDs. In addition, antibiotics were prescribed for upper respiratory tract infections (87%) despite evidence that upper respiratory tract infections are mostly of viral origin and self-limiting and need not be managed with antibiotics (Desta et al., 1997; Llor & Bjerrum, 2016; Ncube, Solanki, Kredo, & Lalloo, 2017; Olayemi et al., 2006; Risk et al., 2013b). Also, further studies need to be conducted to ascertain the high usage of antibiotics in the management of diarrhea; more in diarhhea as a single diagnosis than diarrhea with other conditions – a finding that has not been reported in literature.

The empiric use of antibiotics, according to clinical judgement without laboratory testing to confirm the infectious agent and whether it will be susceptible to the antibiotic prescribed, is common practice. Though evidence shows that antibiotics may be used empirically for cellulitis (Raff & Kroshinsky, 2016), otitis media (Bareeqa & Ahmed, 2018) and apparent pneumonia (Mathur et al., 2018) among other conditions; most of the conditions that were prescribed antibiotics in the baseline survey (e.g. NCDs, cough and upper respiratory tract infections) were not according to the Eswatini STG/EML. Interventions targeted at reducing overuse of antibiotics in public sector and faith-based facilities are imperative, particularly for non-communicable diseases and diarrhea for which there are no indications in the national treatment guidelines.

Baseline findings for this study showed that the national average of prescriptions with injections prescribed (10%) was within the recommended WHO standard of less than 20%. This finding showed that Eswatini was using less injectable medicines, and performing better than the European (17.2%), East Mediterranean (20.1%) and West Pacific (23.2%) regions (Ofori-Asenso et al., 2016). Though the use of injections was below the WHO recommendation, inappropriate use was observed, as injections were prescribed for hypertension. The national treatment guidelines and literature do not specify use of injections in the management of hypertension.

Study findings showed that primary and secondary level facilities performed similarly in prescribing medicines from the EML; and there was no significant difference between regions, showing that prescribers in Eswatini adhere to the EML. Eswatini performed well on this indicator, similar to other settings reported in literature (Eriksen et al., 2017).

7.1.2 Qualitative Component

Baseline findings of this study showed that there was inappropriate use of medicines in Eswatini. An interaction of health system context factors, provider factors and patient factors were found to affect rational use of medicines. Reported health system factors such as poor adherence to guidelines, stock outs of essential medicines, unavailability of RMU policies, lack of RMU training for healthcare professionals, and poor functioning of PTCs negatively affected prescribing practices. Poor adherence to standard treatment guidelines is not peculiar to Eswatini as similar findings have been reported in Sierra Leone (De Bruycker et al., 2013), Botswana (Fugelli et al., 2002), and China (Song et al., 2014). The importance of adhering to national treatment guidelines cannot be over emphasized as national guidelines are developed as a strategy to improve rational use of medicines.

Poor inventory management and poor communication on stock availability both resulting in stock outs of essential medicines were reported to affect rational use of medicines in the country. Unavailability of essential medicines compromises prescribing according to national guidelines. In Eswatini, the Ministry of Health receives its financial budget from the Ministry of Finance. Unavailability of essential medicines could be due to lack of funds by the Ministry of Finance, delays in the release of the budget by the Ministry of Finance for health commodities, and poor stock management by the CMS and facilities. These assumptions need to be explored further to ascertain reasons behind unavailability of essential medicines in Eswatini. Eswatini is not the only country suffering stock outs of essential medicines. In South Africa, procurement processes have been highlighted to result in medicine shortages (Modisakeng et al., 2020). Negative effects on stock levels due to limited financing of health commodities from the government are not unique to Eswatini. In China, limited financing from local governments was reported to influence reduction of medicine stocks and negatively affect service delivery to local consumers (Yang et al., 2014). To improve medicine availability and promote RMU in Eswatini, concerted efforts to ensure timely availability of funds for health commodities between the Ministries of Health and Finance, and inventory management, need to be strengthened.

Pharmaceutics and therapeutics committees (PTCs) were reported to be in place in health centres and hospitals. However, informants reported that these PTCs were not as active as they expected them to be. In settings where PTCs are in place and active such as South Africa, literature shows that there is lack of guidelines on implementation of decisions by PTCs; PTCs need to be strengthened in to be able to adequately manage medicines formularies, and the performance of PTCs needs to be monitored and evaluated (Chigome et al., 2020; Mashaba et al., 2019; Matlala et al., 2020). Poor performance of PTCs has also been reported in rural Thailand where they reported that, among other factors, the performance of hospital PTCs was compromised by professional and personal prejudices and conflicts, poor performance monitoring, poor communication, lack of a standardised way of selecting medicines and over-stretched committee members (Umnuaypornlert & Kitikannakorn, 2014). Efforts to ensure that PTCs, as custodians of medicines in health facilities, are actively performing their duties need to be strengthened to improve the rational use of medicines in Eswatini.

Prescriber-oriented factors that result in irrational use of medicines reported in this study included: the prescriber’s knowledge, personal preference and experience in clinical management of patients, and prescribers not being comfortable to consult guidelines in front of patients. Irrational use of medicines due to prescriber-oriented factors is not unique to Eswatini as literature shows that insufficient prescriber knowledge, their personal beliefs, and their fear that not giving certain medicines lead to patient complications contribute to irrational prescribing of medicines (Altiner et al., 2007; Birhanu Demeke et al., 2017; Cockburn & Pit, (1997); Kamuhabwa & Kisoma, 2015; Kumar et al., 2003; Vazquez-Lago et al., 2012; Wood et al., 2013). Availability of national policies on RMU and a standardised orientation programme for recently qualified healthcare professionals could help address these prescriber-oriented factors.

Baseline findings of this study also showed that patient factors, where patients influence prescribers to prescribe certain medicines for them, affect prescribing practices and rational use of medicines. Similar findings have been reported in Tanzania (Massele & Mwaluko, 1994a). Literature further shows that in the private sector patients are thought to negatively influence prescribers’ prescribing practices since prescribers are likely to lose patients if they do not give in to their demands (Ofori-Asenso et al., 2016).

Engagement of stakeholders in the different Ministries responsible for availability of medicines, capacitation of healthcare professionals (such as Ministry of Health and Ministry of Finance), up-to-date STG/EMLs, functioning PTCs, patient education, and supportive supervision on rational use of medicines could potentially improve RMU in Eswatini.

7.2 End of study evaluation

7.2.1 Quantitative Component

When indicators were aggregated across intervention and control arms, there were a few significant differences across the three time periods. Differences that occurred appeared to be related to the progressive introduction of CMIS' prescribing and reporting systems which affected the intervention and control facilities at different times as CMIS was not introduced at the same time in intervention and control facilities. Key indicators that changed were the use of generics and medicines prescribed from the essential medicines list. Although there was a reduction in the use of antibiotics from baseline to post intervention by region, level of care, and for acute and chronic diagnosis more in intervention than control facilities; these changes were not statistically significant. This study also showed that the reductions that happened at the end of the intervention were not sustained, as by the end of the follow up period most values of the WHO/INRUD indicators bounced back to baseline and even higher values for some indicators. The use of antibiotics had increased and was even higher than at baseline. A comparison of this study's findings and a similar study conducted in Zimbabwe shows that in the Zimbabwean study some indicators were not affected by the intervention i.e. did not change, while others that were under the direct control of healthcare workers in facilities changed significantly in the desired direction (Trap et al., 2001). Unlike the Trap study, we had no direct control over all indicators, and any changes observed in this study were either due to the intervention or health system changes that happened during the study.

Overall Indicators

The average number of medicines prescribed per prescription decreased in both intervention and control facilities (this difference was not statistically significant), and during assessment by acute and chronic diagnosis to levels close to the WHO recommended standards. Though the average number of medicines decreased, it did not decrease to levels as recommended by the WHO, and this meant that there is polypharmacy in Eswatini. Polypharmacy is common in African countries, as shown in a systematic review conducted between 1995 and 2015 (Ofori-Asenso et al., 2016). Though polypharmacy may be problematic in South Africa, literature shows that African countries' (Eswatini included) treatment guidelines are often not aligned with the WHO recommendation of two-to-three medicines per patient encounter (Niaz et al., 2019). The validity of the WHO/INRUD indicators in African settings needs to be investigated further. Qualitative findings of this study highlighted that prescribers give in to patient demands, and also prescribe as many medicines as possible to ensure patients do not come back to the facility. Such practices could result in the higher average number of medicines per prescription and ultimately, irrational use of medicines. Irrational use of medicines due to patient-related factors has been reported in literature across Africa (Massele & Mwaluko, 1994b; Ofori-Asenso et al., 2016).

Positive effects occurred during the study as the percentage of medicines prescribed by generic name increased in both intervention and control facilities as well as for acute and chronic diagnosis from baseline to end of study. A higher increase in generic prescribing was observed in control facilities compared to intervention facilities. Though the increase was statistically significant, it cannot be attributed to the intervention, more so because a greater change was observed in control facilities. Various changes occurred in the country during the study. These changes include a wide roll-out of the electronic system, CMIS, to 78% of facilities at the end of the follow-up period compared to 6% of facilities at baseline. The electronic system has most medicines preloaded in generic names. Furthermore, CMIS uses pull down menus for generic prescribing – forcing people to prescribe by generic name. In both intervention and control facilities the increase did not reach the WHO recommended standard of 100%. Though generic prescribing in Eswatini did not get to the recommended value, the country still performed better than values reported in Pakistan (71.6%) (Atif, Sarwar, Azeem, Naz, et al., 2016) and 11 countries in Africa (68%) (Ofori-Asenso et al., 2016).

A short-term reduction in prescribing of antibiotics both in the intervention and control arms was observed. The decrease was not sustained as the use of antibiotics increased beyond baseline values at the end of the follow up period in both arms, with a higher statistically significant increase in the control arm. Eswatini performed similarly to other countries in the sub-Saharan African region that also showed poor sustainability of healthcare intervention, including those for promoting rational use of medicines (Iwelunmor et al., 2016; Modisakeng et al., 2020).

A sustained decrease through post intervention to post follow up in antibiotics use was observed in prescriptions with acute diagnosis; while for chronic diagnosis, the use of antibiotics decreased from baseline to post intervention in both arms, and by the end of the follow-up period increased in both arms. A comparison of intervention and control arms on use of antibiotics showed statistically insignificant decreases, meaning that though there was a decrease in the use of antibiotics, using this study's findings we cannot conclude that the intervention had a positive effect. Eswatini is not the only country battling with overuse of antibiotics, where intervening has not yielded desired effects. A systematic review conducted in LMICs to assess the effects of interventions implemented to promote rational use of medicines found that antibiotic prescribing increased from 45% to 54% over a 10-year period (Holloway et al., 2013).

The intervention implemented in this study aimed to reduce use of antibiotics for non-communicable chronic conditions. Though a short-term decrease from baseline to post intervention was observed in this study, this reduction was not sustained. The use of antibiotics for NCDs shows that Eswatini, just like other settings reported in literature, is struggling with the use of antibiotics for non-bacterial infections (Desta et al., 1997; Llor & Bjerrum, 2016; Ncube, Meintjes, & Chola, 2014; Olayemi et al., 2006; Risk et al., 2013).

Though there was a general decrease in the use of antibiotics over time, other interventions that have been shown to reduce antibiotic use in literature still need to be explored in Eswatini. These include availability of policies that will advocate for implementation of a national antimicrobial resistance containment strategy; availability of a functional department dedicated to promoting rational use of medicines within the Ministry of Health which will ensure functional PTCs in health centres, hospitals, and regions; and availability of a medicines information centre (Holloway et al., 2016).

Though statistically insignificant at the end of the study, this study showed a decrease in the use of injections in both the intervention and control arms, acute diagnosis (the use remained low for chronic diagnosis i.e., did not change), and level of care, with a sustained decrease in facilities in the intervention arm. The reduction in the use of injections in the control arm from baseline to post intervention could have been due to sensitisation of healthcare workers on inappropriate use of injections during the first consultative meeting. However, the effect in the control arm was not sustained as at the end of the follow-up period the use of injections increased in facilities in the control arm. Furthermore, the use of injections increased and almost doubled in facilities in the intervention arm at the end of the follow-up period. Further research needs to be conducted to ascertain why facilities in the intervention arm experienced a greater increase in the use of injections at the end of the follow-up period.

A negative effect was observed on the percentage of medicines prescribed from the EML as a statistically significant decrease in prescribing from the EML was observed in this study. The introduction of CMIS, which comes with preloaded medicines, not only affected generic prescribing but also prescribing of medicines from the EML. It is possible that most of the preloaded medicines are not from the EML, and this could have resulted in the decrease in prescribing medicines from the EML observed in this study. However, further studies need to be conducted to validate this assumption. An intervention that could help to increase prescribing from the EML would be availability of and adherence to a National Essential Medicines Policy (NEMP) that will enforce prescribing from the EML, as well as availability of EML medicines. Operationalisation of the NEMP has been shown to promote rational medicine use, particularly in primary care settings (Chao et al., 2018).

WHO/INRUD Indicators by Region

In this study, the average number of medicines per prescription decreased while generic prescribing increased throughout the study period in all four regions. The use of antibiotics decreased from baseline to post intervention in all regions. However, the decrease in use of antibiotics was not sustained as values increased at the end of the follow-up period; more so in the Shiselweni region. Shiselweni region could have had a higher increase due to the fact that most facilities in this region were in the control arm (only one facility was in the intervention arm), hence the time effect of the information shared at the first consultative meeting in February 2018 had waned off by the time post-intervention and post follow-up data was collected in March 2019. The use of injections decreased from baseline to post intervention in all regions. The decreases were not sustained at the end of the follow-up period particularly in the Shiselweni region where the post follow-up value was almost double the baseline value. Again, the effect of most facilities being in the control arm could have had the negative effect on the use of injections in the Shiselweni region.

Prescribing from the EML decreased throughout the study in all four regions. Reasons behind this decrease could not be explained by this study's processes. Since availability of the EML did not change throughout the study, introduction and use of CMIS could have negatively impacted this indicator. As already stated, the assumption of a negative effect on prescribing medicines from the EML needs to be explored further. There were no significant differences on the intervention between regions.

WHO/INRUD Indicators by Level of Care

Desired results, i.e., reduction in the average number of medicines per prescription in both primary and secondary level facilities throughout the study were observed in this study. Also, positive effects were observed in generic prescribing, which increased, more in primary level facilities compared to secondary level facilities. The reason for the highest increase observed in primary level facilities could be that the study sample had more primary level (23) than secondary level (9) facilities. A short term, desired, effect of reducing the use of antibiotics in both levels of care was observed although the use increased at the end of the follow-up period, more in primary than secondary level facilities. Similarly to antibiotics use, desired short-term effects of reduction in the use of injections post intervention at both levels of care; with the use increasing beyond WHO recommended values in secondary level facilities at the end of the follow-up period, were observed in this study. Contrary to all other prescribing indicators, this study showed a decrease in prescribing from the EML in both levels of care; more in primary than secondary level of care facilities; an effect that could have been due to the introduction and use of CMIS. Tests for statistical significance were not conducted for analyses by level of care due to the small sample of secondary level facilities. Bigger studies need to be conducted to ascertain significant differences in prescribing by level of care.

Overall, this study showed a significant increase in generic prescribing over time and a non-significant decrease in the use of antibiotics in both intervention and control arms. However, there was no evidence of the effect of the intervention on antibiotics use over time. Study findings showed improvement in all WHO/INRUD prescribing indicators except prescribing of medicines from the EML. The positive changes observed in this study could have been due to the small group education aspect of the intervention, where facility staff came together to discuss their prescribing practices as a facility and the monitoring that happened during the visits. Literature has shown that peer education on rational use of medicines potentially increases knowledge (Ross-Degnan et al., 1997). Furthermore, this study combined educational and managerial interventions to try and reduce the use of antibiotics for chronic conditions. Though the overall reduction in use of antibiotics was statistically insignificant, the desired result i.e., a reduction in antibiotics use seems to have been possible due to the use of a combination of interventions (supervision coupled with small group education in this study). Literature shows that a combination of these interventions is effective in improving prescribing patterns post intervention (Pérez-Cuevas et al., 1996). Improvements in indicators were shown during the intervention visits, though the sample sizes were small. However, to make valid conclusions on positive effects of combining intervention, similar processes followed during intervention visits, using larger sample sizes of prescriptions reviewed and analyzed during the visits should be conducted. Systematically organised continued education programmes with repeated seminars have been shown to improve prescribing (Bexell et al., 1996).

This study seems to have yielded positive results of a combination of interventions similar to a systematic review studying effects of intervention measures on irrational antibiotics/antibacterial drug use in developing countries which showed that multifaceted interventions were more successful than individual interventions (Bbosa et al., 2014; Ross-Degnan et al., 1997; Rowe et al., 2018). Some aspects of the reduction in the use of antibiotics were sustained at the end of the follow up period. The use of multi-interventions in this study could have resulted in some of the desired results being sustained, as literature shows that multiple interventions tend to produce desired, sustained results (Ibrahim, Wertheimer, & Babar, 2017; Trap et al., 2001). Educational interventions alone have been shown to improve prescribing practices, however, their effects are not sustained post intervention (Pérez-Cuevas et al., 1996). Though some effects were sustained post the intervention for some indicators, the effect of combined educational and managerial interventions was shown not to last at the end of the follow-up period for other indicators. Reports of intervention effects not being sustained post intervention are evident in literature (Ibrahim et al., 2017; Pérez-Cuevas et al., 1996; Trap et al., 2001).

Findings from the regression analyses to assess the effect of the intervention showed that the intervention had no effect on prescribing indicators after controlling for independent variables and confounders. Changes in the health systems that investigators had no control over could have had negative effects on the intervention. These changes include stock-outs of medicines, changes in the pharmaceutical structure, and introduction of CMIS.

Effect of using participatory approach in conducting the study

Findings from this study show that, though statistically insignificant, information disseminated during the first feedback meeting had a positive impact in improving healthcare workers' prescribing attitudes. Effectiveness of once-off educational meetings and seminars has been proven in other settings similar to Eswatini such as Indonesia (Santoso, 1996) and Zambia (Bexell et al., 1996).

Though statistically significant changes were not evident in this study, participants reported to have enjoyed processes followed in the study. Their involvement in the study made them want to implement study procedures in their facilities. Participatory approaches to implementing interventions have been reported to build a strong sense of ownership of interventions in participants. Furthermore, participants tend to translate research findings to action (Cargo & Mercer, 2008; Israel et al., 1998; O'Fallon & Dearry, 2002). Ownership of research and translating it to action was evidenced in this study as one facility went on to implement activities in their facility.

7.2.2 Qualitative Component

Qualitative data collected at the end of the follow-up period provided some suggestions as to why the intervention was not more successful. At the end of the study, though there was positive feedback on the study exposing staff in facilities to RMU, which some staff were not aware of, most of the issues highlighted to influence prescribing at baseline were reported to have remained the same. These included staff rotations, where participants enrolled in the study transferred between facilities (intervention and control) hence diluting the effect of the intervention. This could be true as at the end of the study over 90% of staff initially interviewed had been transferred out of the facilities. Stock-out of essential medicines, as highlighted during the baseline survey, was again cited to affect rational prescribing and adherence to the STG/EML. Other factors reported to have affected rational prescribing were the introduction of CMIS, appointment of regional pharmacists, and removal of Zimbabwean pharmacy technicians from the health system all of which potentially affected the effect of the intervention. Based on the analyses of post quantitative data we believe that introduction of CMIS was the most important confounding factor as CMIS has pull down menus that force healthcare workers to use generic names but does not require them to follow the standard treatment guidelines. This allowed unrestricted use of antibiotics irrespective of the diagnosis. If CMIS did not allow antibiotic use for NCDs, this could have reduced the inappropriate use of antibiotics in NCDs where they are not indicated.

7.3 Processes followed in conducting the study

7.3.1 First consultative meeting (sharing baseline findings and intervention selection)

Though this step is relatively unusual in an intervention study, this was a health system strengthening study that aimed to involve all health actors at different stages of the study. The process of meeting with all study participants (from both intervention and control facilities) created an interest in participants from the different levels of care to utilise baseline findings and support the study. However, involvement of facilities in the control arm during this consultative meeting could have introduced bias to the study as evidence by one facility in the control that went on to implement measures to monitor medicine use patterns in their facility. Group work conducted during this meeting allowed participants to deeply engage and debate the different interventions available to promote rational use of medicines and ultimately decide on an intervention that was feasible and affordable for the country. Hence by the end of the meeting there was wide acceptance of the chosen and tested intervention - prescription audit coupled with small group education. One effect of this workshop was to sensitise all participants to the problem of irrational use of medicines. This did result in at least one facility undertaking an activity to address this problem - this facility turned out to be in the control group!

7.3.2 Allocation of facilities to the intervention and control arms

Based on antibiotics use, facilities that had the highest use were paired with one to be in the intervention or control arms. If we had used a composite indicator, the IRDP (Zhang & Zhi, 1995), we would have had a different allocation of facilities to intervention and control arms. However, the focus of our intervention was on antibiotics use, particularly for non-communicable chronic conditions, and that was the reason we chose to use antibiotics to pair facilities.

7.3.3 Intervention design and implementation

A participatory approach was used, where both investigators and participants deliberated and decided on the intervention to be implemented to promote rational prescribing and ultimately rational use of medicines in Eswatini.

7.3.4 Final consultative meeting

As described in the methods section, this meeting was an important opportunity for researchers to discuss results of the study with participants and receive feedback from participants who came from the most remote facilities in the country all the way to the Deputy Director of Pharmaceutical Services. Key insights that were shared during this meeting included appreciation by participants of the skill of conducting audits and feedback that will enable them to monitor how medicines are being used in facilities, across regions and in the country as a whole. Participants highlighted that since there is one regional pharmacist per region, they could use these audits to focus on facilities with problems to supportively supervise and monitor them to improve rational use of medicines. Participants highlighted the importance of orienting all healthcare workers on the STG/EML and educating patients in appropriate language on rational use of medicines. Value of having the consultative meetings was acknowledged as investigators witnessed the benefits of using a participatory approach in deciding on and implementing the intervention. Participants seemed to have owned the study processes, an advantage highlighted for participatory approaches in literature (Cargo & Mercer, 2008; Israel et al., 1998; Jagosh et al., 2012; O'Fallon & Dearry, 2002). An outstanding statement made by one of the meeting attendants was:

> "*The research processes have helped the country to translate research to policy – I like the nature of this study, how collaborative it has been to include the Ministry of Health at all levels (facility, CMS, policy making). This involvement makes it easy to implement research*" [NN_P_CL_M].

A question asked that could potentially be answered with the existing datasets was to assess the effect of pharmacy technicians being posted to facilities to see whether their availability in facilities improved rational use of medicines. While this was not the objective of the current study, the methods used and data sources exist to answer this question.

7.4 Strengths and Limitations of the study

Study strengths include its participatory approach including consultative meetings which allowed participants to fully engage with study procedures. Also using a mixed methods study design allowed us to see whether medicines were prescribed rationally or not and further explore reasons behind rational/irrational use of medicines. The study was inclusive of facilities by level of care and geographical location; hence it was a representative sample of healthcare facilities in the country. Furthermore, using a combination of interventions (prescription audit coupled with small group education) and having facilities allocated to intervention and control arms enabled us to assess the effect of the intervention as opposed to just doing a pre- and post-intervention study for the same facilities.

The limitations of the study are that it happened in the natural world and some factors could not be controlled for. The protocol for this study proposed to conduct three visits to intervention facilities, two months apart. The PI (NBQN) injured her ankle after conducting the third intervention visit to two facilities and could not visit the other 14 facilities in the intervention arm. Hence two intervention visits rather than three were used to undertake the intervention. Similar challenges (though their challenge was fuel shortages), where two instead of four visits were conducted to test the effect of an intervention, were experienced in a Zimbabwean study, yet the researchers were able to make meaningful conclusions (Trap et al., 2001). This study is similar to Trap et al's study but goes beyond measuring the effect of the intervention post intervention to include a follow-up period which allowed us to assess if the effects of the intervention were sustained 6-months after the intervention.

Also, the effect of the intervention could have been diluted by the fact that participants from control facilities were part of the first consultative meeting before random allocation to intervention and control arms occurred, thus control facilities were aware of the high usage of antibiotics and other problems highlighted by the baseline study. The small sample size limited analyses especially to allow us to differentiate by level of care, diagnosis, and regions. The WHO/INRUD indicators are general so it is a challenge to tailor intervention towards specific issues such as use of antibiotics in the management of NCDs. Another limitation is that our study did not measure availability of essential medicines to allow us to make concrete conclusions on prescribing practices.

Staff rotations within departments in the facility and out of the facility could have diluted the effect of the intervention as staff could have been transferred from intervention arm facilities to control arm facilities and the other way around. Since data for this study was collected retrospectively, only information on prescribing indicators could be obtained. It would have been good to do analyses of prescribing from the STG to assess if prescribing practices in Eswatini adhere to the STGs. This assessment was difficult to perform because it was difficult to link diagnoses recorded in CMIS with those in the STGs. Alignment of diagnoses in CMIS with those in the STG will allow for future assessment of adherence to STGs.

Other healthcare system factors that could have diluted the effect of the intervention include stock-outs, staff rotations, pharmaceutical human resource restructuring including appointment of regional pharmacists, change in the calibre of pharmacy technicians (most pharmacy technicians of Zimbabwean origin and trained in Zimbabwe were removed and replaced with pharmacy technicians trained in Eswatini), and introduction of CMIS.

CHAPTER 8: CONCLUSION AND RECOMMENDATIONS

8.1 Conclusions

Rational use of medicines is essential to ensure that appropriate, safe, cost-effective, and good quality services are afforded to all members of the Eswatini population. This study's baseline findings showed that prescribing indicators were higher than WHO/INRUD recommended standards; the percentage of prescriptions with one or more injections prescribed was the only indicator that conformed to the WHO/INRUD standards. Irrational medicine use was observed in the average number of medicines prescribed (indicating polypharmacy); medicines were prescribed by brand names; antibiotics were over-prescribed, and were prescribed for managing chronic diseases; and prescribing medicines from the EML was below the recommended 100%. The intervention implemented (supervision coupled with small group education) to promote rational medicine use using prescribing indicators, and mainly focusing on reducing prescribing of antibiotics for NCDs, improved prescribing practices from baseline though these improvements were not statistically significant. The intervention was rolled out in two visits, two months apart to intervention facilities while control facilities were left to continue functioning as they normally do. By the end of the study all prescribing indicators, except prescribing of medicines from the EML which decreased, had improved. The only indicators that had statistically significant changes were generic prescribing and medicines prescribed from the EML, though it was difficult to attribute these changes to the effect of the intervention. Uncontrollable changes such as human resource, prescribing systems, medicine availability was perceived to affect the intervention in this study.

Study findings showed that the educational intervention implemented positively impacted prescribing practices though this effect was not sustained. Supportive supervisory visits were also reported to have worked as constant reminders about appropriate prescribing and to provide guidance where necessary. Exposure to this study motivated facility staff to implement facility-based interventions to monitor prescribing practices and appropriate use of medicine. Frontline managers perceived that the appointment of regional pharmacists who helped to train facilities on appropriate use of medicines and stock management practices improved prescribing practices. Challenges such as stock-outs of essential medicines, staff rotations, unavailability of medicines in certain levels of care, lack of pharmacy personnel in clinics, patient demands, high patient volumes, and introduction of the electronic prescribing and dispensing system were said to make it difficult for facility staff to prescribe rationally.

Study findings further highlighted that in Eswatini, prescribing practices are believed to be influenced by an interaction of several factors – health system, provider, and patient – that span levels of the health system (facility level, regional level, central level and national level). Promoting rational medicines use thus goes beyond the availability of guidelines and provider training and requires concerted efforts of multiple stakeholders.

8.2 Recommendations

The Ministry of Health could potentially adopt study processes for use by regional pharmacists to assess prescribing patterns in facilities in each of the four regions. Regional pharmacists could analyse prescribing indicators, using data from CMIS, and use results from these analyses to target interventions (e.g., supportive supervision) by individual facility. Individual facilities could also adopt this study's procedures and analyse by prescriber and facility to analyse facility's prescribing practices and give feedback to facility PTCs as they work to improve rational use of medicines in facilities. Analyses could also be done at national level and results used to plan for the country. Also training on RMU, incorporating orientation to standard treatment guidelines should be used in orientation of newly recruited frontline managers, supervisors, and policy makers. Multipronged interventions to study appropriate medicine use such as Supervision, Performance Assessment, and Recognition Strategy (SPARS) could also be tested in Eswatini (Trap et al., 2020). Material for continuing medical education (CME) should also be developed and used. Some frontline managers highlighted that they were not involved in the development of the current guidelines nor oriented on them. Future plans of rolling out of STG/EML should incorporate training of guideline users to improve rational use of medicines. In addition, the CMIS system should be adapted to be consistent with EML/STG and to link the pull-down menus to the stated diagnosis. In this way a diagnosis of an NCD would not include an antibiotic among therapeutic choices.

Frontline managers highlighted that unavailability of pharmacy personnel in clinics (primary healthcare) negatively impacted stock management practices ultimately affecting rational use as.

Future studies, with pharmacy personnel available in all levels of care, in similar settings, need to be conducted to show the effect of availability of pharmacy personnel and stock management practices on rational use of medicines.

Future studies in settings like Eswatini need to be conducted to assess if changing from paper-based prescribing and dispensing systems to electronic systems impact prescribing practices. The pharmaceutical administrative structure also changed during this study; other studies need to be conducted to assess if such changes influence prescribing practices. Also, stock out of essential medicines was cited as a factor that contributed to irrational use of medicines; further studies where there is adequate stock or overstock of medicines need to be conducted to assess if stock shortages impact prescribing practices. Methods employed in this study could be used by authorities such as the Ministry of Health and other policy makers to monitor and evaluate appropriate use of medicines in Eswatini.

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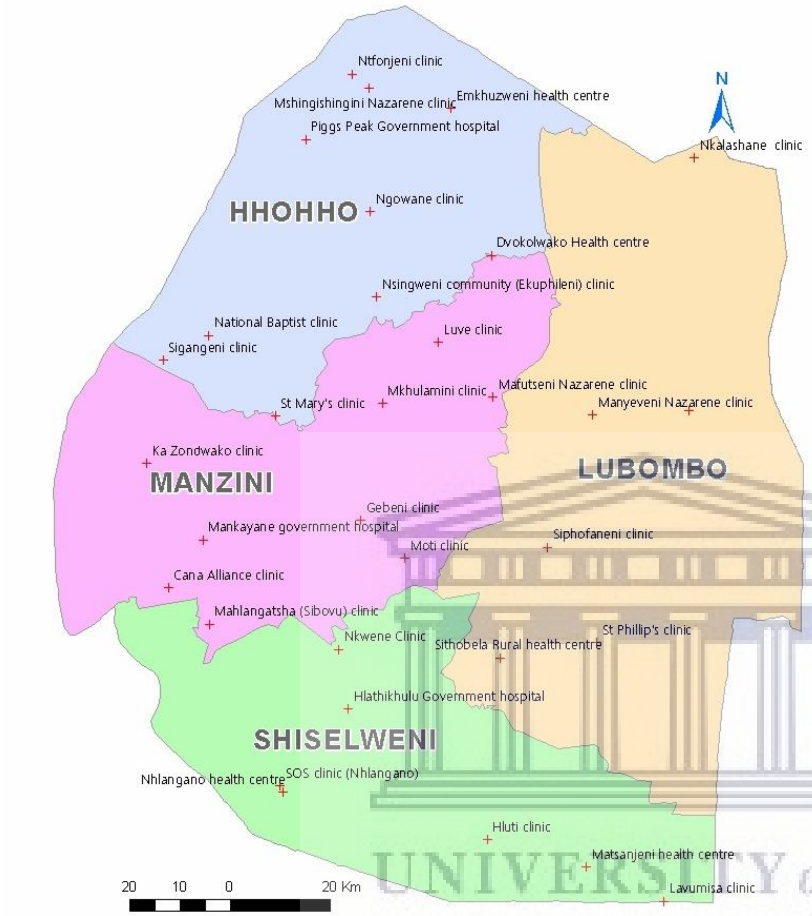
APPENDICES

Appendix 1: Map of Eswatini



Appendix 2: Prescribing Indicator Form

Location: ______________________ Investigator: ___________________

Date: _________________

Rx Number	Type *(R/P)	Date of Rx	Age (yrs)	No. of Drugs	No. of Generics	Antibiotic ¹(0/1)	Injection ¹(0/1)	Availability of EML ¹(0/1)	No. on EML	EML Date
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100										
Total										
Average										
Percentage										

*Retrospective !0 = No 1= Yes

Appendix 3: Documents reviewed to ascertain the state of RMU in Eswatini

Title	Author (Year)	Document Type	Description
The National Health Sector Strategic Plan II (NHSSPII: 2014-2018)	Kingdom of Eswatini Ministry of Health (2018)	Report	The document gives information on how to improve access and availability of quality pharmaceutical services. It advocates for implementation of guiding pharmaceutical documents decentralization of pharmaceutical services. The document further states that rational medicine use should be promoted among health care workers and at community level.
National Health Policy	Kingdom of Swaziland Ministry of Health (2007)	Report	The document states that all health practitioners in all sectors in Eswatini (government, private, industrial or mission) should comply with the established essential medicines list according to WHO standards. Furthermore, the document proposes that the national referral hospital and regional hospitals be accessed through a referral process, and for an additional fee to be charged for patients who choose not to follow the referral system.
National Pharmaceutical Policy	Kingdom of Swaziland Ministry of Health (2011)	Report	The document gives information on pharmaceutical services in the country including management of the pharmaceutical sector, regulations and legislation operational in the country, medicines access and supply, human resources within the pharmaceutical sector, production of medicines, medicine donations, pharmaceutical quality assurance, financing of medicines, RMU,

			and traditional/complementary medicines.
Swaziland Pharmaceutical Strategic Plan (2012-2016)	Kunene, K., Fakudze, F., Mndzebele, S., Magagula, F., Shongwe, K., & Vilane, M. (2013)	Baseline Survey	The document provides information on the organization of the health system in Swaziland and how the pharmaceutical sector fits within the system. It also details the specific functions performed within the pharmaceutical sector and identifies underperformances within the sector.
Standard Treatment Guidelines and Essential Medicines List of Common Medical Conditions in the Kingdom of Swaziland	Government of the Kingdom of Swaziland Ministry of Health, the US President's Emergency Plan for AIDS Relief, USAID, and SPS (2012)	Guideline	The document provides a list of common conditions in the Kingdom of Eswatini and advice on how these conditions should be managed and at what level of care. The document also lists all medicines that are supposed to be available in Eswatini.
Report of the Prime Minister's inter-ministerial task team on health service delivery: An Assessment of the Status Regarding the Supply of Medicines & Medical Supplies in Swaziland	The Government of the Kingdom of Swaziland, Ministry of Health (2017)	Report	The document gives information on the status of health care delivery in Eswatini. It also advocates for the revitalization and operationalization of Pharmaceutical and Therapeutics Committees (PTCs) in health facilities as well as the monitoring of prescribing of pharmaceuticals in order to ensure adherence to STGs and avoid irrational use of medicines.

Appendix 4: Published paper on baseline qualitative findings

Ncube, N.B.Q., Knight, L., Bradley, H.A., Schneider, H., Laing, R. (2020). Health system actors' perspectives of prescribing practices in public health facilities in Eswatini: A Qualitative Study. PLoS ONE. https://doi.org/10.1371/journal.pone.0235513

Short Title: Prescribing practices and rational use of medicines

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Abstract

Background: Rational medicines use (RMU) is the prescribing/dispensing of good quality medicines to meet individual patient's clinical needs. Policy-makers, managers and frontline providers play critical roles in safeguarding medicine usage thus ensuring their rational use. This study investigated perspectives of key health system actors on prescribing practices and factors influencing these in Eswatini. Public sector healthcare service delivery is through health facilities (public sector, not-for-profit faith-based, industrial) and community-based care.

Methods: A qualitative, exploratory study using semi-structured in-depth interviews with seven policymakers and managers, and 32 facility-based actors was conducted. Drawing on Social Practice Theory, material (health system context), competence (provider) and cultural (patient and provider) factors influencing prescribing practices were explored.

Results: Participants were aged between 21-57years, had been practicing for 1-30 years, and were a mix of doctors, nurses, pharmacists and pharmacy-technicians. Factors contributing to irrational medicines use included: poor use of treatment guidelines, lack of RMU policies, poorly-functioning pharmaceutical and therapeutics committees, stock-outs of medicines, lack of pharmacy personnel in primary healthcare facilities, and restrictions of medicines by level of care. Provider-related factors included: knowledge, experience and practice ethic, symptomatic prescribing, high patient numbers. Patient-related factors included late presentation, language, and the need to be prescribed many medicines.

Conclusion: In Eswatini, prescribing practices are influenced by the interaction of factors (health system, provider and patient) that span levels (facility, region, and policy-making) of the health system. Promoting RMU thus goes beyond the availability of guidelines and provider training and requires concerted efforts of multiple stakeholders.

Introduction

Rational use of medicines is crucial to well-functioning health systems. The World Health Organization (WHO) considers that medicines are used rationally when individual patients are prescribed and dispensed correct medicines, of good quality, in appropriate doses to meet their clinical needs, at a minimal cost to them and their community, and for an appropriate duration of treatment [1]. Health system actors, including policymakers, essential medicines lists/formulary committee members, prescribers, and pharmacists, play critical roles in safeguarding the use of medicines, from procurement until they reach the end-user [2]. In healthcare facilities, frontline providers (prescribers and pharmacy personnel) ensure that medicines are ordered from the central medical stores (CMS), stored correctly, and used rationally.

Prescribing practices, also referred to as prescribing behaviours, are key to understanding patterns of medicines use. This research draws on the Social Practice Theory (SPT) to study prescribing practices in public sector and not-for-profit faith-based facilities in the Kingdom of Eswatini (formerly Swaziland, and hereafter referred to as Eswatini). The SPT seeks to explore the relationship between available resources, the nature of practice, and contexts within which individuals function; and suggests that practices, and changes in practice, are shaped not only by individual competence but also by the social (shared meanings) and material (resources) contexts [3, 4] as illustrated in Fig 1.

The SPT is a socially oriented approach to analysing behaviour that is useful in gaining insights into the processes and structures that generate behaviour [5]. It is based on the understanding that individualist approaches have not been effective in creating expected changes as they tend to ignore the wider context of practice and function as specific “corrective” action. Socially orientated approaches, on the other hand, help to develop new strategies for changing behaviour involving multiple stakeholders, and may require all these stakeholders to do their daily activities in a different manner [5].

Literature on prescribing behaviour highlights a range of provider, patient and health system factors that can be mapped onto the domains of the SPT (Table 1).

In Eswatini, guides to prescribing include The Standard Treatment Guidelines and Essential Medicines List (STG/EML) of Common Medical Conditions in the Kingdom of

Swaziland, published in 2012 [17]. The STG gives guidance on how conditions should be managed pharmacologically and non-pharmacologically as well as the level of care at which the pharmacological treatment can be available. The EML gives a list of medicines (including its strength, dosage form) approved for use in Eswatini; the vital, essential, non-essential (VEN) allocation of the medicine; and the level of care (A= all health facilities; B = Health centers; C = Hospitals; S = prescribed by specialist doctors) at which the medicine can be used. Though literature shows that availability of guides such as essential medicines lists may improve prescribing practices [18], there is no evidence on whether the Eswatini STG/EML has influenced the use of medicines in the country. At the time of data collection, an implementing partner (Management Sciences for Health/ Systems for Improved Access to Pharmaceuticals and Services (MSH/SIAPS)) was providing support for strengthening pharmaceutical systems in the country. A survey conducted by MSH/SIAPS in 2013 revealed that there was no continuous professional development training available on rational medicines use (RMU), although small-scale facility-based RMU training was taking place [19]. This is in line with statements in the National Pharmaceutical Policy (NPP) (2011), which highlight that the country does not have mechanisms for monitoring medicine use by health workers and the public, mainly due to lack of the necessary tools, staff and resources [20]. The NPP further recommends that existing prescribing and dispensing practices need to be rationalized and streamlined through the development of various RMU tools and staff training.

Studies on prescribing practices have mainly been quantitative using the WHO/INRUD prescribing indicators, which assess the following: average number of medicines per patient encounter, percentage of medicines prescribed by generic name, percentage of prescriptions with one or more antibiotic prescribed, percentage of prescriptions with one or more injection prescribed, and percentage of medicines prescribed from the essential medicines list or formulary [21, 22]. Literature on reasons behind certain prescribing practices using qualitative approaches is scant. Minimal work has been done on prescribing practices in Eswatini and this study seeks to fill this gap.

The aim of this study was to explore policy-maker, manager and frontline healthcare providers' perspectives on existing prescribing practices and the factors influencing these in Eswatini. Specifically, it investigated the perspectives of policymakers in medicine management (senior pharmaceutical staff in the Ministry of Health (MoH) including CMS and regional level staff), implementing partners supporting pharmaceutical services, and frontline healthcare providers (prescribers (doctors and nurses), pharmacists and pharmacy technicians in the MoH) on prescribing practices in Eswatini.

METHODS

Study setting

Eswatini is a landlocked country in Southern Africa sharing its borders with South Africa and Mozambique. The country has an estimated surface area of 17,364 square kilometres and a population of about 1.2 million [23]. Most of the population resides in rural areas with only 22% in urban areas [24]. The country is divided into four administrative regions: Hhohho, Manzini, Shiselweni and Lubombo. In the health sector, healthcare services are delivered in both private and public sectors. The public sector provides services through public, not-for-profit faith-based, and industrial health facilities (clinics and outreaches, public health units, health centres and hospitals), and community based care (faith-based healthcare providers, rural health motivators and volunteers) [25]. While clinics only provide primary healthcare services, health centres and hospitals provide both primary and secondary healthcare services. Clinics are manned by nurses who are responsible for prescribing and dispensing medicines; health centers have nurses and doctors responsible for prescribing while pharmacy technicians dispense medicines; and hospitals have nurses and doctors responsible for prescribing while pharmacists and pharmacy technicians dispense medicines. Previously, the government did not have posts for pharmacy assistants. Posts for pharmacy assistants to be employed in all levels of care, particularly clinics where there were no pharmacy personnel as part of human resource, were approved in 2017. [26].

The MoH is responsible for ensuring that national health-related administrative and executive functions are performed adequately in the country. It also provides guidance on essential health care package delivery to all levels of healthcare countrywide. The MoH decentralises its activities to regional health offices (RHO) in the four regions, and the RHOs are responsible for the implementation of national health plans and policies. At the regional level, the regional health management team (RHMT) provides technical leadership in the implementation processes. The

RHMT comprises of the regional health administrator (overall in-charge), a senior matron from the regional health office, senior medical officers and matrons from hospitals and health centres, clinic sisters (senior nurses based in the different clinics in the country), a pharmacist, and other health professionals stationed at the RHO depending on their availability.

Conceptual framework

To study rational medicine use practices among policy makers at the national department of health (NDoH) and frontline medicine managers (prescribers (doctors and nurses), and pharmacy personnel (pharmacists, pharmacy technicians and pharmacy assistants)) in Eswatini, this study used a theory informed approach.

The bigger study was conducted in three phases; this paper focuses on the qualitative aspect of Phase I using the SPT. Phase I was a situational analysis to establish practices and processes in place regarding RMU in the country. Elements of the SPT were used to develop the data collection tools for assessing medicine prescribing practices among health actors in Eswatini.

Study design and sampling

A qualitative exploratory study design was used to conduct this study. A qualitative exploratory study is defined as a study that allows researchers to investigate topics that have received minimal attention in the past and are not well defined [27]. Further, qualitative exploratory study designs allow study participants to contribute information towards building knowledge in the area under study [28].

This research is part of a baseline survey conducted for a larger study aimed at improving RMU in Eswatini. Facilities were randomly sampled for the bigger study. Sampling for facilities has been thoroughly investigated by the INRUD group which recommends a minimum of 20 facilities to allow researchers to draw meaningful conclusions (Hogerzeil et al., 1993). A sampling frame of 325 public and faith-based facilities that receive essential medicines from the central medical stores (CMS) was obtained from CMS. Faith-based facilities are public sector facilities that also receive support from faith-based organizations such as churches. The CMS codes facilities by region and these codes were used to assign facilities to the four regions (Hhohho, Manzini, Lubombo, and Shiselweni) in the country. Specialized facilities (i.e. national referral hospital, psychiatric hospital, tuberculosis (TB) hospital and those facilities governed by other bodies such as the police services and the army) were excluded from the sampling frame, leaving 286 eligible facilities. Clinics only provide primary healthcare and are staffed with nurses. Health centres and hospitals provide primary and secondary healthcare and are staffed with nurses, doctors, pharmacists (hospitals only), and pharmacy technicians (hospitals and health centers). A patient can choose to attend at any level of care they want to go to regardless of presenting condition. Very ill patients are referred from clinics to health centres or hospital depending on the proximity.

From the 286 facilities, one hospital per region (4) and all health centres in the country (5) were purposively included leaving 277 clinics to sample from. To sample clinics, a random sequence was used to select five clinics per region. To allow for non-response, the sample of clinics was inflated by 20% per region (making six clinics per region). A total of 24 clinics (six per region) were included in the sample, making the overall sample size 33. One facility (a clinic) in the Shiselweni region was closed on the day the principal investigator (PI) went to collect data. Efforts were made to find out on the functioning of this facility and reasons that were beyond the research team were given. Since the sample of clinics had been inflated by 20%, the research team decided to drop this facility leaving the total number of facilities at 32. Table 2 provides characteristics of respondents by cadre and level of care.

Key informants (7) were purposively selected based on their involvement in RMU policy decisions, while frontline managers (32) were from the different levels of care available in the country, as randomly sampled for the bigger study. Frontline managers were recruited into the study based on their presence at work on the day of data collection and their willingness to participate in the study. Only frontline managers involved in medicine use such as prescribers (doctors and nurses) and dispensers (pharmacists and pharmacy technicians) were approached for recruitment into the study.

Data collection

A semi-structured interview guide informed by the SPT and covering themes such as knowledge of RMU, prescribing practices, enablers and barriers to the rational use of medicine, and interventions available to promote RMU was used to conduct one-on-one interviews with key informants. A similar interview guide, but focusing on RMU activities and functioning in facilities, was used to conduct one-on-one interviews with frontline healthcare providers. Interviews were conducted between April and September 2017. Semi-structured in-depth interviews were used to collect data on medicine use practices in public sector and faith-based facilities in Eswatini. Semi-structured in-depth interviews were used as they employ the use of an interview guide with open ended questions to allow a range of responses from participants in a comprehensive and systematic manner to obtain the desired information [30]. Interview guides were piloted on healthcare professionals from facilities that were not in the sample (for frontline managers) and the CMS (for KIs). All interviews were conducted in English and the interviews lasted between 20 and 60 minutes. No repeat interviews were carried out.

The principal investigator (NN, a female PhD student) approached KIs and requested them to participate in the study after giving verbal and written information on the study. In facilities, the principal investigator (PI) introduced herself to management using the permission letter from the MoH and management guided on participants to be approached. NN conducted key informant interviews in offices in the MoH headquarters, implementing partner's office, and CMS; while a quiet office with minimal disturbance was used in health facilities. Interviews were audio recorded (all except one non-consenting participant), and were supplemented by field notes using a reflexive journal by NN. Some of the participants were people that NN previously worked with while practicing as a pharmacist in Eswatini, while others were not known to the PI. For frontline managers, data saturation, a phenomenon achieved when the data gathered no longer brings out new information [31], was achieved by the 15th interview. However, since the PI was collecting quantitative data from 32 facilities, she continued conducting interviews in all facilities. A research assistant transcribed the interviews and saved transcripts onto a password-protected laptop. Some participants (3 key informants) were interested to review transcripts and they were given the opportunity to do so (member-checking) before finalization of the transcripts. Frontline managers were not keen on reviewing their transcripts.

Ethical considerations

Ethics approval to conduct the study was obtained from the Biomedical Science Research Ethics Committee of the University of the Western Cape (Ref: BM/16/4/2) and the National Health Research Review Board in Eswatini. Permission to access healthcare facilities was granted by the office of the Deputy Director Pharmaceutical Services in the MoH. Consenting participants were given verbal and written information (information leaflet) on the study and were assured that they were free to refuse participation with no repercussions. No incentives were provided for being part of this study. Written consent was obtained from all participants.

Data Management

Data were anonymized and securely stored on a password protected computer. A research assistant transcribed the audio recordings verbatim. The first author (NN) re-checked all the transcripts for completeness and correctness. Two of the authors (NN, LK) read through the transcripts thoroughly for familiarization. Two transcripts were randomly selected from the lot and independently coded by NN and LK on Atlas.ti. Notes and memos were made from the selected transcripts to inductively generate the initial codes. NN and LK discussed their independent codes identifying similarities and differences through a discursive process. Using the initial codes, NN and LK developed a codebook. Codes with similar ideas were clustered to form sub-themes. Sub-themes with identical concepts were grouped deductively into final themes provided by the SPT framework. NN used the codebook to analyse the remaining transcripts. The reorganizing of codes was achieved in a discursive process with all the authors.

The Framework Method [32], which is part of the thematic analysis family [33] was used to analyze the data. Thematic analysis is defined as a method in qualitative research that is used to identify, analyse and report themes or patterns within data; prescribing patterns in this study [33]. Using the Framework Method, we applied a hybrid of inductive and deductive thematic analysis. The initial coding was done inductively and the themes emanating from the coding were then classified deductively using the SPT framework. Thematic analysis was chosen for this study because it is a flexible method that allows researchers to produce a rich and detailed account of data [33].

RESULTS

Study participants consisted of a mix of doctors, nurses, pharmacists and pharmacy technicians. Their ages ranged from 21 – 57 years, and they had been practicing for periods ranging from 1-30 years (median = 12.7 years).

Key themes that emerged from the data included contextual, healthcare provider, and patient-oriented factors. Themes were organized around the SPT elements (material, meaning and competence), factors identified in literature to affect prescribing practices, and factors emerging from the data.

Health system context factors (Material)

This section will highlight factors that participants reported to affect prescribing practices in line with how literature suggests that the context within which practice happens affect rational use of medicines. Availability of policy to guide RMU practices, availability and use of the STG/EML, availability of essential medicines, lack of pharmacy personnel in primary levels of care, restrictions of medicines by level of care, and active Pharmaceutical and Therapeutics Committees (PTCs) in hospitals and health centres were reported as health system factors (material) that affect prescribing and rational use of medicines.

Availability of policies to guide RMU practices:

Frontline healthcare providers mentioned that the country had no policies to guide RMU, and this made it difficult for healthcare professionals to practice RMU without guiding policies. One frontline healthcare provider mentioned that due to lack of policies there was no guidance on who in the nursing cadre can and cannot prescribe, and this resulted in irrational prescribing.

Availability and use of the STG/EML:

Information from key informants highlighted that public sector prescribing practices were influenced by the current STG/EML; with the STG having been mainly targeted at primary health care (though they can still be used at secondary and tertiary levels of healthcare), and the EML covering all levels of care. Until the latest guidelines published in 2012, Eswatini did not have country-specific guidelines. The current STG was a starting point to mainly guide clinics which provide primary healthcare and are only managed by nurses with no doctors and pharmacists;

though the EML is comprehensive and includes all medicines available in the country at the different levels of care. The Ministry of Health had planned to then develop a more comprehensive guideline at a later stage. However, key informants highlighted that targeting the STG at primary level of care resulted in secondary and tertiary level facilities prescribing outside the guidelines.

> "At tertiary level they say our STG is skewed a lot towards primary health care and doesn't provide for their guidance. And of course it is a little bit true… there is some truth to it because you know at tertiary level we can do with a little bit of a revision and we do both tertiary level and primary health care level [guideline needs to be revised for both primary and tertiary level], because at primary health care level we know that we do not have medical practitioners so we thought those are the ones that needed the guidance the most that's why we started with them (KI_P_N_H)."

Key informants also reported that though the STG/EML was outdated as they were published in 2012. However, KIs reported that availability of the STG/EML positively influenced rational use of medicine as some facilities used the STG/EML to develop their own (facility-specific) formularies. Though the STG/EML was seen to promote rational use of medicines, key informants reported that adherence to these guidelines seemed poor.

> "We have put in place some contingency measures to try and guide or to try and coerce people to use medicines rationally by putting in place standard treatment guidelines. But when we follow with our facilities, we have realised that it is not used as such because some of them when you visit facilities, they have to look for the STG within their cabinets and stuff, yet you'd expect it on the desk where they are working with it (KI_P_N_H)."

A reason that was cited by key informants to possibly result in poor adherence to guidelines was that frontline healthcare providers were not comfortable to use the guidelines in front of patients.

> "Because people think that [pause] I don't know it has not been proven so I want to believe it's a perception of the health care workers, because they tend to think that if they flip through their STG the patient will think they do not know, each time they are treating them they have to be checking but maybe with a mobile app on their smart phone the fears will be allayed (KI_P_IP_H)."

Key informants further reported that poor adherence to the STG/EML resulted in overuse of antibiotics which will in the near future contribute to the global problem of antimicrobial resistance. On the contrary, frontline healthcare providers validated overuse of antibiotics by reporting that most of the conditions that patients presented with required management with antibiotics.

Restrictions of medicines by level of care:

Frontline healthcare providers highlighted the difficulty for them to adhere to the STGs due to restrictions on availability of medicines at certain levels of care. An example cited was the unavailability of ceftriaxone and azithromycin at primary healthcare levels yet the latest guidelines for managing sexually transmitted infections (STIs), published in June 2018, recommend these medicines as first line therapy and for them to be available at primary healthcare level. According to the EML, these medicines are not available for use in primary healthcare. This finding showed that delays in the revision of the STG/EML resulted in the development of newer guidelines, e.g. the STI guidelines, which make recommendations not in line with the national STG/EML. Furthermore, frontline healthcare providers, particularly in clinics and health centres aired their frustration on certain medicines that were, according to the EML, not available at these levels of care yet they see a lot of patients who need such medicines. Health centre level frontline providers questioned restriction of some medicines to hospital level, yet there were doctors in health centres who could manage patients the same way they would be managed in hospitals.

> "I want to believe that the ministry of health has got the presentation on power point made by Facility Y in which we are asking the ministry to revise some parts that are in the guideline to make more drugs available for health centres and clinics. We know that in Swaziland there are drugs that you can't find in clinics. There are drugs that you can't find in health centre though those drugs are available in the country (FM_MO_Sec_L)."

In such cases frontline healthcare providers from clinics and health centres mentioned that they referred patients to hospitals and it is often geographically difficult for patients to access these. Most medicines for managing NCDs were reported to not be allocated for use in primary healthcare facilities in the STG and hence not available at primary level facilities. The following are medicines for management of NCDs available at primary level of care: for hypertension - only hydrochlorthiazide; for diabetes – none of the medicines are available at primary level; for arthritis – indomethacin, colchicine, allopurinol, acetylsalicylic acid, and procaine penicillin/erythromycin [for osteomyelitis] are indicated for primary level use). Antibiotics were also reported as medicines that are not available at primary level of care; these were: penicillins (amoxicillin + clavulanic acid, flucloxacillin) all cephalosporins, sulphonamides (trimethoprim/sulphamethoxazole (400/80) injection), Macrolides /lincosamides/streptogramins (clarithromycin, clindamycin), aminoglycoside (streptomycin and vancomycin injections), quinolones (ciprofloxacin 250mg tablet, while the 500mg tablet is indicated for primary level use), and nitrofurantoin.

Availability of essential medicines:

Frontline healthcare providers reported that essential medicines were constantly out of stock at the CMS and in health facilities. Stock-outs were reported as barriers that affect adherence to the STG/EML and rational use of medicines. Due to frequent unavailability of medicines, frontline healthcare providers reported that they often find themselves out of options on what to prescribe for the patients, and at the same time, found it difficult to send patients home with no medicines to alleviate their suffering. In such instances, frontline healthcare providers reported that they send patients to private sector facilities and sometimes prescribe out of the STG/EML and give medicines that might not be appropriate for the condition. Frontline healthcare providers stated that patients needed to have money to buy medicines and for transport to get to private sector facilities. Medicines that were reported to constantly be out-of-stock were those for managing NCDs. Often, patients would report to not have money to travel and buy medicines and such patients then discontinue taking their NCD medicines, compromising their management.

Some reasons that were cited for stock-outs of essential medicines were poor stock management practices which result in inadequate amounts ordered from the CMS.

> "I think there are challenges with stock ordering from the facilities. You find that they run out because they haven't ordered the right quantities due to poor stock management practices (KI_P_C_M)."

Delayed ordering by facilities, long lead times for CMS to deliver in facilities, inconsistent/inadequate supply of medicines by the CMS, and poor communication on stock availability between the CMS and facilities were also reported to affect stock availability and ultimately RMU.

> "We only hear about stock shortages from facilities when they now are complaining that they are not getting their order, so there is no transparent communication between the central medical stores and the facility or at least the region (KI_P_C_M)."

Lack of pharmacy personnel in primary levels of care:

Frontline healthcare providers reported that clinics do not have pharmacy personnel, and this made it difficult for nurses to manage facility stocks of medicines (monitoring average monthly consumptions, quantities to order, and share slow-moving stock with other facilities to minimize expiries) as their professional qualification does not equip them to do this work. Though frontline healthcare providers reported that they receive off-and-on-site intermittent trainings on stock management from the CMS and implementing partners, they highlighted that not all nurses in a facility would receive the training. Furthermore, rotations of nurses between facilities resulted in some facilities having no nurses trained on stock management.

Inactive PTCs:

Key informants and frontline healthcare providers reported that health centres and hospitals had PTCs, however, most were reported to not function adequately. Information gathered from some participants highlighted that monitoring of activities of PTCs was through meeting minutes that are submitted to the MoH headquarters. On probing on activities performed by PTCs, participants mentioned that meetings mainly discussed errors in prescribing; and due to prescribers feeling as if they were targeted during these, they often did not attend meetings. This resulted in committee members not forming a quorum and hence cancelling most meetings, ultimately rendering PTCs inactive in facilities. Clinics reported that they have monthly/weekly meetings which they used to discuss all issues pertaining their facilities – including prescribing patterns.

Patient Factors (Meaning)

This section reports on the effects of cultural conventions, expectations, and socially shared meaning on rational use of medicines. Themes reported to affect prescribing were mainly patient factors. Frontline healthcare providers reported that patients took too long to present to facilities. By the time they did, ailments would have progressed to complications, making it difficult for providers to treat these patients according to the STG/EML. Frontline providers also reported that patients demanded more medicines (an issue resulting in polypharmacy) and were not comfortable to leave the healthcare facility with no or few medicines.

> "There also is also pressure from the patient that require a lot of variety of medicine. Patients are not satisfied if they are going away with maybe three types of medicines when they leave the facility, ah maybe they have a flu or headache or maybe a simple injury, you discover that they are not satisfied once they give, if you just give them one or two medicines, they want many (FM_PT_Sec_S)."

To increase the number of medicines, frontline providers mentioned that prescribers end up prescribing medicines with no or little proven effectiveness. Frontline providers also mentioned that they sometimes prescribe and dispense a lot of medication to try and cover all ailments that the patients could be suffering from.

> "uhm, yah we can benefit but once we had, we want to give the best care to our clients, we want to give extra actually if I can say so we don't want the client to come back with such a case that you gave me this drug what, what, what (FM_N_Prim_L)".

On probing, the medicines that were reported to be mostly prescribed to increase medicine numbers were multivitamins, vitamin B complex, methyl salicylate and low doses of calcium gluconate. Key informants highlighted that polypharmacy was not just as a result of patients demanding many medicines from healthcare providers. They reported that polypharmacy for NCDs was very high, due to poor consulting practices by some healthcare providers.

> "When it comes to chronic medications - that is where we have observed the worst case the most because you find that the prescriber, before even the chronic patient comes in for their diabetes or hypertension, the prescriber has started writing something on their prescription book the first two being a pain killer or even some multivite without assessing the patient and not knowing what is wrong with them. I mean does it mean everyone who

leaves the hospital must have a pain killer, does it mean everyone is in pain - so that's why we say we have picked up elements of irrational use which we need to tell people to solve… Evidence of that is that at times when they [patients] are given some of these [medicines], because they know their core medicines that they need to take, and then the others [medicines] they will tell you "oh I still have that at home", so it shows that they are keeping it they're not taking it they are just taking their BP medication because that is their basic medication so they know that the others are just for pain if I may call them that […Laughs…](KI_P_N_H)."

Possible reasons for polypharmacy as stated by one frontline healthcare provider were poor adherence to the STG/EML, ignorance and poor knowledge

"I think it's ignorance, lack of knowledge, not following the standard treatment guideline or even trying to please the patient (FM_P_Sec_H)".

Language was also cited as a patient factor that affected rational use of medicines. In facilities that were close to the border, frontline providers mentioned that they had patients that came to access healthcare from Mozambique and it was difficult to communicate with them. Also, providers reported that the elderly often struggled to understand instructions on how to use the medicine they were prescribed which left frontline providers uncertain if such patients used the medicines correctly.

Provider factors (Competence)

Provider-oriented factors that were reported to affect rational prescribing were: symptomatic prescribing, high patient volumes, competence, individual prescriber practice ethic, poor teamwork in patient management, and poor documentation practices. Frontline healthcare providers reported that irrational use of medicines is sometimes driven by symptomatic prescribing; whereby prescribers treat symptoms and not the diagnosis.

"The treatment is according to symptoms, so if you are sneezing you get items for sneezing, if you are coughing you get something for coughing and if you have an itchy eye you get something for the itchy eye. Itchy nose you get something for the itchy nose, if you have irritating throat, they give you something for irritating throat, list continuous like that, instead of making a proper diagnosis: what is the proper diagnosis, maybe the person has got one diagnosis which is flu, or which is respiratory tract infection. Just treat the disease, what do they do, treat each symptom with each medication (FM_PT_Sec_L)."

Regarding patient volumes, frontline healthcare providers reported that they sometimes prescribe as many medicines as possible to cover symptoms reported by patients and ensure that they do not come back to the facility the following day and increase patient numbers.

In this study, healthcare provider knowledge and embodied skills, as highlighted by the SPT, were reported to affect prescribing practices. Health system actors reported that actors at all levels of care in the country were poorly trained on rational use of medicines, and this resulted in inappropriate use of medicines in health facilities. Though some RMU training for frontline healthcare providers was happening, key informants reported that this training was not streamlined and policy makers were not privy to information on who has and has not been trained as they were not receiving training reports from facilitators.

Frontline healthcare providers reported that Eswatini did not have pre-service orientation of foreign-qualified healthcare professionals on RMU and use of the STG/EML.

"Their competence is not tested, in terms of prescribing or their knowledge on the disease patterns that are affecting the Southern region as well as the patterns again that affect the local region. They struggle in the early days to uh to understand the disease pattern that we do have so at the end of the day they just prescribe anything maybe according to whatever they have been trained, so there is also a general problem of not following the treatment guideline of which they are there (FM_PT_Sec_H)".

Different practice ethics by prescribers were reported to also affect rational use of medicines in Eswatini. One key informant mentioned that some prescribers were not comfortable to consult guidelines in front of patients.

"Because people think that […pause…] I don't know it has not been proven so I want to believe it's a perception of the health care workers because they tend to think that if they flip through their STG the patient will think they do not know, each time they are treating them they have to be checking but maybe with a mobile app on their smart phone the fears will be allayed (KI_P_IP_H)."

On probing to find how the issue of frontline healthcare providers not being comfortable to consult guidelines in front of patients could be solved, health system actors suggested the use of a mobile application.

Poor teamwork in the management of patients was also reported to result in irrational use of medicines. Pharmacy staff mentioned that prescribers were not comfortable with suggestions made by pharmacy personnel on adjusting prescriptions to meet the patients' needs and often felt undermined.

"The pharmacy personnel call that prescriber when they receive a prescription and feel there is some irrational use of medicines to discuss the issues. However, a lot of times the pharmacy staff come across challenges when they do this as some of the prescribers then feel undermined, offended, and most of the time they refuse to change the prescription (FM_PT_Sec_H)."

If pharmacy staff changed the prescription, the patient often went back to the prescriber to question the change. This caused disputes between pharmacy staff and prescribers which resulted in disciplinary meetings being called for pharmacy staff.

"It's like they really don't want to be corrected and so they called a meeting against pharmacy so our challenge is tight, but now we don't call them now you look at the prescription and you see what you can do (FM_PT_Sec_S)."

Furthermore, frontline providers reported that "being used to doing things in a certain way" resulted in inappropriate use of medicines.

"So, the weakness there is training, and not only training it's again changing the culture and the practice and culture … The tendency is, you see if we have a problem, we talk maybe in a therapeutic committee today and hope that people will bring sort of change, then after that the graph just goes down. People change into their old practices that's why I said it's a culture, a culture is difficult to change for someone who is, maybe, they have been taught at school that this is what they are supposed to do and so you know trying to change that culture is a long process (FM_P_Sec_M)."

Poor/no documentation of prescribing information in some facilities was reported as another factor affecting rational use of medicines. Key informants highlighted that they were not sure if facilities with no records of prescribing information did this due to lack of knowledge on the importance of documentation and record keeping. On probing as to how it was possible for a facility to not have such records, key informants reported that in such facilities the doctor/nurse writes a prescription on a notepad that the patient takes it to the pharmacy and no record of the prescription remains in the prescriber's room. Once the prescription has been filled in the pharmacy, the patient takes the original prescription with them leaving the facility with no record of what was prescribed and dispensed for the patient.

Contrary to information from key informants on record keeping, frontline healthcare providers reported that they knew and understood the importance of keeping patient records in facilities. However, the government was constantly stocked out on prescription booklets in which each prescription is triplicate. Once the prescription has been written, the first and second copies are given to the patient to take to the pharmacy for dispensing of medicine – one copy stays in the pharmacy after dispensing while one copy leaves with the patient. The third copy remains with the prescriber, hence, there then is a record of each patient that stays with the prescriber and another with the pharmacy which are kept in the facility.

Beyond identifying factors that affect rational use of medicine, health system actors had recommendations on how RMU can be promoted in the country. Such recommendations included: functional PTCs; on- and off-site training of prescribers on appropriate use of medicines and inventory management; pre-service training for healthcare providers who qualify outside Eswatini; review and update of the STG/EML; supervision and mentorship of facility staff on medicines; widening the list of medicines available at primary health care level; development, implementation and monitoring of RMU policies; and availability of nurses trained on RMU in all facilities.

Discussion

Findings of this study show that there is inappropriate use of medicines in Eswatini. An interaction of health system context factors, provider factors and patient factors were found to affect rational use of medicines. Reported health system factors such as poor adherence to guidelines, stock outs of essential medicines, unavailability of RMU policies, lack of RMU training for healthcare professionals, and poor functioning of PTCs negatively affected prescribing practices. Poor adherence to treatment guidelines is not peculiar to Eswatini as similar findings have been reported in Sierra Leone [34], Botswana [35], and China [18]. The importance of adhering to national treatment guidelines cannot be over emphasized as national guidelines are developed as a strategy to improve rational use of medicines.

Poor inventory management and poor communication on stock availability both resulting in stock outs of essential medicines were reported to affect rational use of medicines in the country. Unavailability of essential medicines compromises prescribing in line with national guidelines. In Eswatini, the Ministry of Health receives its financial budget from the Ministry of Finance. Unavailability of essential medicines could be due to lack of funds by the Ministry of Finance, delays in the release of the budget by the Ministry of Finance for health commodities, and poor stock management by the CMS and facilities. Negative effects on stock levels due to limited financing of health commodities from the government are not unique to Eswatini. In China, limited financing from local governments was reported to influence reduction of medicine stocks and negatively affect service delivery to local consumers [36]. To improve medicine availability and promote RMU in Eswatini, concerted efforts to ensure timely availability of funds for health commodities between the Ministries of Health and Finance, and inventory management, need to be strengthened.

Pharmaceutics and therapeutics committees were reported to be in place in health centres and hospitals. However, informants reported that these PTCs were not as active as they expected them to be. Poor performance of PTCs has also been reported in rural Thailand where they reported that, among other factors, the performance of hospital PTCs was compromised by professional and personal prejudices and conflicts, poor performance monitoring, poor communication, lack of a standardized way of selecting medicines and over-stretched committee members [37]. Efforts to ensure that PTCs, as custodians of medicines in health facilities, are actively performing their duties need to be strengthened in order to improve the rational use of medicines in Eswatini.

Prescriber-oriented factors that result in irrational use of medicines reported in this study included: the prescriber's knowledge, personal preference and experience in clinical management of patients, and prescribers not being comfortable to consult guidelines in front of patients. Irrational use of medicines due to prescriber-oriented factors is not unique to Eswatini as literature shows that insufficient prescriber knowledge, their personal beliefs, and their fear that not giving certain medicines lead to patient complications contribute to irrational prescribing of medicines [6, 11, 12, 38–41]. Availability of national policies on RMU and a standardized orientation programme for recently qualified healthcare professionals could help address these prescriber-oriented factors.

This study also found that patient factors, where patients influence prescribers to prescribe certain medicines for them, affect prescribing practices and rational use of medicines. Similar findings have been reported in Tanzania [42]. Literature further shows that in the private sector patients are thought to negatively influence prescribers' prescribing practices since prescribers are likely to lose patients if they do not give in to their demands [13].

Engagement of stakeholders in the different Ministries responsible for availability of medicines, capacitation of healthcare professionals, up-to-date STG/EMLs, functioning PTCs, patient education, and supportive supervision on rational use of medicines could potentially improve RMU in Eswatini.

Trustworthiness and rigour

We acknowledge that some respondents may have provided thin descriptions of prescribing practices in relation to rational use of medicines as rational medicine use was an abstract topic to them. Lincoln and Guba's criteria for generating trustworthy results were applied in conducting this study [43]. Trustworthiness and study rigour were improved by applying the following principles. The interview guides were piloted to assess the information that would likely be produced. After piloting, questions that were poorly understood by the respondent were rephrased. Other questions were added to explore other aspects that came up during piloting. The revised interview guides were then applied to conduct the main study. Also, during interviews, the PI guarded against leading participants and allowed them to freely share information. Credibility of study findings was further improved through member checks (recapping key messages emanating from the interview) at the end of each interview to check if theories formulated captured participants' views.

To ensure credibility, the audio recordings were transcribed verbatim in English. After the transcription by the research assistant, the first author rechecked to ensure that the transcriptions were accurate by re-listening to the tapes and reading the transcripts. During the entire study, a reflexive journal – forming part of an audit trail - that captured discussions and decisions of the investigators was kept. To improve dependability, two members of the research team (NN and LK) independently coded transcripts. Agreement was used to reach consensus. The research team had no relationship with the participants though the PI had previously worked with some of the KIs. Finally, in reporting study findings, relevant elements for reporting qualitative research (COREQ) outlined by Tong, Sainsbury, and Craig [44] were followed. Quotes obtained from the original transcripts were provided as evidence of the identified themes and subthemes.

Study limitations

The limitation of using an exploratory study design is that it predominantly provides descriptive findings rather than explanatory (how and why things happen).

Though the SPT was a starting point in analyzing practice and helped in gaining insight into how practice can change; it has limitations in that it provides contextual analyses that cannot be generalized [45]. Hence findings from this study only apply to the facilities assessed in Eswatini. Furthermore, adapting the SPT for this study meant that we utilized it to meet our needs in order to answer questions relating to prescribing practices in Eswatini. By so doing, we could have missed other aspects that could have emanated from the data. Another limitation to this study is that most respondents were from the pharmacy cadre; hence reported findings could mainly be views from this cadre.

Conclusion

Availability of the STG/EML to guide medicine use in public sector, not-for-profit faith-based and industrial health facilities has promoted rational use of medicines. Findings of this study highlight that in Eswatini, prescribing practices are influenced by the interaction of a number of factors – health system, provider and patient – that span levels (facility, region, and policy-making) of the health system. Promoting rational medicines use thus goes beyond the availability of guidelines and provider training and requires concerted efforts of multiple stakeholders.

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Supporting information

S1 Fig 1. **The social practice theory**. This is the S1 Fig legend.

S2 Table 1. **Factors affecting prescribing behaviours and how they link to the SPT**. This is the S2 Table legend.

S3 Fig 2. **Study theories and procedures**. This is the S3 Fig legend.

S4 Table 2. **Study participants' characteristics**. This is the S4 Table legend.

S5 **COREQ 32 Checklist**.

S6 **Key informants interview guide**.

S7 **Frontline managers interview guide**.

S8 **Key informants study data**.

S9 **Key informants quotes**.

S10 **Frontline managers study data**.

S11 **Frontline managers quotes**.

Appendix 5: Semi-structured Interview Guide for National Department of Health, Implementing partner, and Central Medical Stores Medicine Managers

1. What in your opinion is rational medicine use (RMU)?
2. How do you think RMU applies to consumers/patients?
3. What is the interaction between the NDoH/ CMS and prescribers in facilities with regard to RMU?
4. Are you aware of any interventions that the country has in place to promote RMU?
5. Please describe any interventions that the country has in place to promote RMU:

   Prompts:
   - Standard treatment guidelines?
     - Who has been involved?
     - How satisfactory was the intervention?
     - Could you please describe what happened?
   - Pharmaceutics and Therapeutics Committees?
     - Who has been involved?
     - How satisfactory was the intervention?
     - Could you please describe what happened?
   - Training?
     - Who has been involved?
     - How satisfactory was the intervention?
     - Could you please describe what happened?
6. What do you think are the benefits of using medicines rationally?

Appendix 6: Semi-structured Interview Guide for Facility Frontline Managers

1. What in your opinion is rational medicine use (RMU)?
2. How do you think RMU applies to consumers/patients?
3. Are there any challenges regarding the rational use of medicines in your facility?
4. Are you aware of any interventions in place in your facility to promote RMU?
5. Describe any interventions that your facility has been involved in promoting RMU:

   Prompts:

   - Standard treatment guidelines?
     - Who has been involved?
     - How satisfactory was the intervention?
     - Could you please describe what happened?
   - Pharmaceutics and Therapeutics Committees?
     - Who has been involved?
     - How satisfactory was the intervention?
     - Could you please describe what happened?
   - Training?
     - Who has been involved?
     - How satisfactory was the intervention?
     - Could you please describe what happened?
6. How do you think your facility would benefit if medicines were used rationally?

Appendix 7: Allocation of Facilities to Intervention and Control arms

Facility	%Antibiotics	Random Number	Intervention/Control
Gebeni Clinic	73	0.527759374	C
St. Mary's Clinic	73	0.949320706	I
Nhlangano Health Centre	72	0.888795252	C
Zondwako Clinic	69	0.937956501	I
Mkhulamini Clinic	68	0.326398346	I
National Baptist Clinic	67	0.237078706	C
Manyeveni Clinic	65	0.820450436	I
Moti Clinic	63	0.043930515	C
Sigangeni Clinic	63	0.19381204	C
Mahlangatsha Clinic	60	0.603256939	I
Mshingishingini Clinic	60	0.6271888	I
Mafutseni Clinic	57	0.094706287	C
Nkwene Clinic	56	0.694664245	I
Hluti Clinic	56	0.245045596	C
Mkhuzweni Health Centre	55	0.444697725	I
Sithobela Health Centre	54	0.293723258	C
Ngowane Clinic	53	0.289787275	C
Lubombo Ref Hospital	52	0.525619937	I
Hlatikulu Gvt Hospital	52	0.000724845	C
Piggs Peak Gvt Hospital	52	0.57203735	I
Cana Clinic	51	0.657189268	I
Siphofaneni Clinic	50	0.542322837	C
Dvokolwako Health Centre	50	0.968663657	I
Ekufikeni Clinic	50	0.94971238	C
Nkalashane Clinic	49	0.631544592	I
Lavumisa Clinic	47	0.615050972	C
Ntfonjeni Clinic	46	0.563156205	I
Nhlangunjani Clinic	45	0.128752406	C
Mankayane Gvt Hospital	43	0.084415325	C
St. Philipp's Clinic	40	0.139579885	I
Matsanjeni Health Centre	37	0.205084264	C
Luke Commission Clinic	31	0.254397272	I

Appendix 8: Educational material for intervention visits

Management of Arthritis

Gouty Arthritis

Type	Acute	Chronic
Signs & Symptoms	• Recurrent acute pain in joints • One joint (usually big toe) • Extreme pain, swelling and very hot • Increased serum uric acid concentration (above 0.5mmol/L)	• Many acute attacks (more than 4 per yr) • Serum uric acid above 0.5mmol/L
Non-Pharmacological management	• Bed rest • Increase fluid intake • Avoid alcohol and use of aspirin	• Controlled weight loss • Avoidance of alcohol, aspirin, and red meat
Pharmacological management	• Indomethacin 800mg PO immediately • Then 200-400mg every 6-8 hours for 2-3 days • Thereafter, if need be, 200-400mg every 8 hours until the pain subsides *No response to indomethacin* • Colchicine 0.5-1mg PO immediately • Then 0.5mg every 2-3hours until pain is relieved or gastrointestinal distress develops	REFER

Osteoarthritis – disease of people over 50 years

Signs & Symptoms	• Joint pain stiffness, relieved with rest, worse with movement, worse during cold/rainy weather
Pharmacological management	• Acetylsalicylic acid 600mg PO QID, as needed • Advise patients to keep joints warm

Osteomyelitis

Definition – acute or chronic infection of the bone	
Signs & Symptoms	• Fever, pain on moving affected area • Chills, weakness, elevated temperature (39 degrees Celsius or higher) • Redness, temperature, and swelling over area of affected bone or in the nearby joint
Non-Pharmacological Management	• Immobilize the affected area with splints
Pharmacological Management	• REFER • If referral delayed, give Procaine penicillin 900 000 IU IM BD • For patients allergic to penicillin, give erythromycin (500mg PO every 6 hours adults; 15mg/kg PO every 6 hours)

Management of Hypertension

Table 1.1B Stepwise Pharmacological Management of Hypertension

Step 1		
Entry to Step 1	**Treatment**	**Target**
Mild hypertension ▪ Without existing cardiovascular disease, major risk factors, and co-morbidities	Lifestyle modification	BP <140/90 mm Hg within 2 months
Step 2		
Entry to Step 2	**Treatment**	**Target**
Moderate hypertension ▪ Without existing cardiovascular diseases, major risk factors and co-morbidities ▪ Failure of lifestyle modification	Lifestyle modification **—PLUS—** **Hydrochlorothiazide** 12.5 mg PO daily **(A)**	BP <140/90 mm Hg within 3 months
REFER to hospital. ⚠		
Step 3		
Entry to Step 3	**Treatment**	**Target**
Failure to achieve target in steps 1 and 2 **—OR—** Severe hypertension	Lifestyle modification **—PLUS—** **Hydrochlorothiazide** 12.5–25 mg PO daily **(A)** **—PLUS—** ACE inhibitor [e.g., **captopril** 12.5 mg PO twice daily titrate up wto 50 mg three times daily **(B)**] **—OR—** Beta-adrenergic blocker: **atenolol** 50 mg PO daily **(B)**	BP <140/90 mm Hg within 3 months
Step 4		
Entry to Step 4	**Treatment**	**Target**
Failure of step 3 after 1 month of compliance	Lifestyle modification **—PLUS—** **Hydrochlorothiazide** 12.5–25 mg PO daily **(A)** **—PLUS—** ACE inhibitor [e.g., **captopril** 12.5 mg PO twice daily titrate up to 50 mg three times daily **(B)**] **—PLUS—** Beta-adrenergic blocker: **atenolol** 50 mg PO daily **(B)**	BP <140/90 mm Hg within 3 months
Step 5. REFER to specialist or expert panel. ⚠		

****NB: HCTZ stated as Level B medicine in the EML and Level A medicine in the STG (Eswatini STG/EML).**

Management of Diabetes

<table>
<tr><td>Notes</td><td>Type1</td><td>Type 2</td></tr>
<tr><td>Signs and Symptoms</td><td colspan="2">Thirst, tiredness, hunger, unexplained weight loss or gain, ketoacidosis, polyuria, pins-and-pricks sensation in the feet or hands, impaired visual acuity</td></tr>
<tr><td>Non-Pharmacological Management</td><td>NA</td><td>Lifestyle modification
• Maintain healthy diet (regular meals, high fibre, low GI, low fat)
• Maintain ideal BMI (18.5 – 25)
• Regular 30 minutes' exercise thrice a week
• Regular home glucose monitoring</td></tr>
<tr><td>Pharmacological Management</td><td>Insulin injections [B]: Adults starting dose = 0.6units/kg/day; Children = 0.5 – 1unit/kg/da</td><td>Table 5.1.2 Stepwise Management of Type 2 DM
<table>
<tr><th>Entry to Step 1</th><th>Management and Duration</th><th>Target</th></tr>
<tr><td>Typical symptoms:
▪ Thirst
▪ Urinary frequency
▪ Polyuria
▪ RBG >11 mmol/L</td><td>▪ Lifestyle modification for life
▪ Appropriate diet (see 5.1.1)</td><td>▪ RBG <10 mmol/L
▪ FBG 6–8 mmol/L
▪ HbA_{1AC} <6.5%</td></tr>
<tr><th>Entry to Step 2</th><th>Management and Duration</th><th>Target</th></tr>
<tr><td>▪ FBG >10 mmol/L
—OR—
▪ Urine glucose >0.5% (++)
—PLUS—
▪ After 3 months of compliance with treatment plan (e.g., weight loss)</td><td>▪ Lifestyle modification
—PLUS—
▪ Initiate pharmacotherapy with sulphonylurea (glibenclamide [B] or gliclazide [B]) if underweight
—OR—
▪ Metformin (B) if severely overweight</td><td>▪ RBG <10 mmol/L
—OR—
▪ FBG 6–7 mmol/L
—OR—
▪ Urine glucose 0–0.5% (negative to +)
—PLUS—
▪ Ideal body weight (weight reduction may be a lengthy process)</td></tr>
</table></td></tr>
</table>

****NB: Mix-up in labelling of section 5.1.1 and reference for this in management of type 2 diabetes melitus in the Eswatini STG.**

Management of Asthma

Nonpharmacological management

- Advise patient to avoid—
  - Known allergens
  - Smoking and polluted environment
  - Strenuous exercise

Pharmacological management

Adults—

- Inhaled **salbutamol** (short acting) 200 micrograms every 4–6 hours **(A)**
  —OR—
- **Salbutamol** 4 mg PO up to 4 times a day **(A)**
- Low-dose steroid: **beclomethasone** inhaler 200–400 micrograms 2 times a day **(B)**
- High-dose steroid: **beclomethasone** 400 micrograms 2–4 times a day **(B)**
- Oral steroid: **prednisolone** 2.5–10 mg 1–3 times a day **(A)** and reduce dose gradually over 7 days.
- **Theophylline anhydrous** 200 mg PO 2–3 times a day **(A)**

Children—

- Inhaled **salbutamol** (short acting) 200 micrograms via spacer every 4–6 hours **(A)**
- Low-dose steroid: **beclomethasone** inhaler 200–400 micrograms 2 times a day **(B)**
- High-dose steroid: **beclomethasone** 400 micrograms 2–4 times a day **(B)**

Management of acute attack

Adults—

- Give **oxygen** 8 L per minute via mask (40%) **(B)**.
- Ensure hydration.
- Nebulise with **salbutamol (A)**.
- Give **hydrocortisone** 100–200 mg/mL IM/IV **(B)**.
  —OR—
- Give **dexamethasone** 8 mg PO **(B)**.
- Give **prednisolone** 20 mg stat **(A)**.
- **REFER** urgently if no response in 3 hours.

Appendix 9: Intervention roll out Visit 1 notes
1. LUBOMBO REFERAL HOSPITAL

DATE: 12 March 2018

Total no. of February prescriptions = 1274

Randomly selected prescriptions = 20. Paper based prescriptions from the triplicate prescription book.

Length of meeting = 20 minutes

Present	Designation	Age	Years of Practice	Gender
1. Rejoice Dladla	Pharm Tech	58	30+	Female
2. Linda Chester	Nurse	29	5	Female
3. Sihle Zwane	Pharmacist	29	3	Female

Notes:

- Collected 20 prescriptions and analysed. Presented baseline findings and findings for February prescriptions and compared medicine use patterns between the 2 periods.
- Polypharmacy (4.1 meds/prescription)
- Overuse of antibiotics an issue (45%)
- Use of antibiotics for chronic conditions observed, particularly for peptic ulcer disease (flagyl); Gastritis (Bactrim).

Reasons for medicine use patterns

- STG/EML does not cater for this level of care
- STG/EML needs to be updated and in this update include stepped care in management of patients as well as categorise conditions by severity
- Poor recording of diagnoses because the diagnoses must be in line with the tally record book. Most of the conditions that the facility treats are not listed in the tally record book, so they find themselves only capturing the main diagnoses. This results in the audit reflecting improper use of medicines yet this is due to poor documentation of diagnoses. Tally record book needs to be updated.
- Facility uses antibiotics in the management of peptic ulcer disease because a doctor in Hlathikhulu government hospital conducted a study which showed that antibiotics should be added for this condition.
- *Staff was enthusiastic, grateful for findings and eager to present to the rest of the staff.*

2. NKALASHANE COMMUNITY CLINIC

DATE: 12 March 2018 (all staff attended meeting)

Total no. of February prescriptions = 137

Randomly selected prescriptions = 20. Register used to collect prescriptions.

Length of meeting = 30 minutes

Present	Designation	Age	Years of Practice	Gender
1. Thandi Mawelela	Nurse	48	8	Female
2. Ncamsile Simelane	Nurse	31	6	Female
3. Precious Shongwe	Nurse	37	12	Female

Notes:

- Collected 20 prescriptions and analysed. Presented baseline findings and findings for February prescriptions and compared medicine use patterns between the 2 periods.
- Overuse of antibiotics an issue (45%)
- Polypharmacy an issue (avg 4.5 meds/prescription)

Reasons for medicine use patterns

- Staff does polypharmacy to try and cover all conditions that the patient might be suffering from
- It is difficult for patients to access the facility so once they are there the staff prescribes everything that can possibly help
- Staff always gives amoxyl for most prescriptions to cover as much illnesses as possible
- Use of injections is low due to stock outs/unavailability of injections. Staff particularly prescribes a lot of Vit BCO injection. Patients pressurise staff to give BCO injection as they believe it is good for their libido.
- The only injection available in stock at the moment is benzathine penicillin – staff sometimes prescribes this injection even if not necessary because patients believe they feel better after getting an injection. Also, benzathine penicillin is sometimes prescribed if the patient really looks ill, even if giving this injection is not warranted
- Staff find it difficult to decide on antibiotics to prescribe since they cannot perform sensitivity tests

- Currently there are no medicines for URTI for children so staff end up giving amoxyl to all patients as they cannot send patients away with paracetamol only when the patients are coughing
- Staff does polypharmacy because if they give little medicines or refer patients to bigger facilities, patients complain of not having money to travel to bigger facilities. Patients' failure to go to bigger facilities makes them come back to Nkalashane in a few days. So the staff give many medicines and tell the patients that they have given them all they can possibly give for their complaints.
- *Staff was eager to know findings and very engaging*

3. MANYEVENI CLINIC (all staff attended meeting)

DATE: 13 March 2018

Total no. of February prescriptions = 929 (including ART and TB, ANC, Child welfare): Facility using electronic system (CMIS)

Randomly selected prescriptions = 20

Length of meeting = 60 minutes

Present	**Designation**	**Age**	**Years of Practice**	**Gender**
1. Nonhlanhla Shongwe	Nurse	30	10	Female
2. Goodwill Dlamini	Nurse	37	13	Male
3. Thelma Tsabedze	Nurse	50	20+	Female
4. Yolanda Dlamini	Nurse	25	1	Female

Notes:

- Polypharmacy an issue (avg 4.2 meds/prescription)
- Overuse of antibiotics (70%)

Reasons for medicine use patterns

- Polypharmacy due to unavailability of stock therefore prescribe as many medicines as possible to try and cater for illnesses
- STG/EML does not cover most of the conditions that facility needs to treat

- It is pointless to regulate medicines in public sector where there is no regulation in the private pharmacies. By the time the patient comes to the public sector facility they are already failing on the treatment they received from private pharmacies particularly for STIs. One patient with a non-resolving STI had a drug sensitivity test done – the patient was resistant to benzathine penicillin and ceftriaxone.
- Facility sees a lot of patients with STIs
- The ministry needs to look at other options to treat syphilis. Patients do not finish the once weekly IM Benzathine penicillin for 3 weeks
- *Goodwill dominated the discussion. Efforts were made to allow other staff to comment but they seemed to rely a lot on Goodwill and his decisions as a facility.*

4. St PHILLIP'S CLINIC

DATE: 13 March 2018 (all staff attended meeting)

Total no. of February prescriptions = 1134 (including ART and TB, ANC, Child welfare): Facility using electronic system (CMIS)

Randomly selected prescriptions = 20

Length of meeting = 35 minutes

Present	**Designation**	**Age**	**Years of Practice**	**Gender**
1. Sarah Tshuma	Nurse Manager	40	16	Female
2. Thandiwe Mathunjwa	Nurse	55	30	Female
3. Velaphi Msibi	Nurse	34	8	Male
4. Mbonisi Siziba	Nurse	35	13	Male
5. David Hlophe	Nurse	44	20	Male

Notes:

- Average no of medicines/prescription = 3.82
- Use of antibiotics = 88%
- Use of injections = 12%

Comments from staff

- Clinics do not initiate medicines for chronic conditions but refill for down-referred patients.
- Use of antibiotics for chronic conditions is not a big challenge but there is overuse of antibiotics in general
- STG/EML is old and does not cater for currently prevalent conditions
- The STG/EML defines diseases very well but the pharmacological management is not very clear
- Facility sees a lot of patients with STIs during the first quarter of the year (Jan- Mar) due to the buganu (amarula) season. Hence high usage of antibiotics.
- Most of the medicines listed by the STG/EML for use at primary health care clinics are never available from CMS
- *Staff appreciated information as they buy their own medicines so being aware of how they are using their meds helps for budgeting purposes. Staff requested help for the government to start supplying them with essential medicines*

5. MAHLANGATSHA CLINIC

DATE: 14 March 2018 (all staff attended meeting)

Total no. of February prescriptions = 342. Facility using electronic system (CMIS) and register. Prescriptions collected from the register.

Randomly selected prescriptions = 20

Length of meeting = 40 minutes

Present	**Designation**	**Age**	**Years of Practice**	**Gender**
1. Velaphi Simelane	Nurse	36	8	Male
2. Mduduzi Dlamini	Nurse	31	10	Male
3. Philsiwe Dlamini	Nurse	40	12	Female
4. Mavis Mndzebele	Nursing Sister	56	20+	Female

Notes:

- Avg no of medicines/prescription = 3.8
- Use of antibiotics = 40%

Comments from staff

- STG/EML needs to be updated - Herpes zoster management: facility can't access acyclovir (not available at their level of care) yet they see a lot of patients with the condition
- Facility using aldomet to manage HTN – this is not in the guideline but aldomet is available at CMS. Why is CMS supplying it if they are not supposed to give this to patients?
- In the management of asthma, they use salbutamol all the time because beclomethasone is never available. They do give oral short course prednisone for adults with severe attacks but cannot give this to children
- *Staff interested in their findings and looking forward to next meeting*

6. CANA CLINIC

DATE: 14 March 2018 (all staff attended meeting)

Total no. of February prescriptions = 2329 (ALL). Facility using electronic system (CMIS)

Randomly selected prescriptions = 20

Length of meeting = 20 minutes

Present	Designation	Age	Years of Practice	Gender
1. Faith Mkhatshwa	Nursing Sister	40	15+	Female
2. Thandi Pheya	Nurse	50	30	Female
3. Lindiwe Dlamini	Nurse	23	2 months	Female
4. Samkeliso Magagula	Pharm assistant	32	8	Male

Notes:

- Avg no of medicines/prescription = 4.35
- Use of antibiotics = 85%
- *Staff very reserved and not forthcoming with information. Note: the gentleman enrolled into the study has moved facilities*

Comments from staff

- Antipsychotics are out of stock
- Comment on use of antibiotics for chronic conditions (NCDs): Facility does not initiate but refill down-referrals
- Patients on injectable antidiabetics are referred to Mankayane hospital

7. DVOKOLWAKO HEALTH CENTRE

DATE: 15 March 2018 (most staff attended meeting)

Total no. of 14 February – 14 March prescriptions = 4336 (ALL). Facility using electronic system (CMIS)

Randomly selected prescriptions = 20

Length of meeting = 60 minutes

Present	Designation	Age	Years of Practice	Gender
1. John Mubhambati	Pharm tech	41	14	Male
2. Tachiyiwa Mbengo	Pharm tech	37	12	Male
3. Mthandazo Moyo	Doctor	32	7	Male
4. Gaethan Kibwe	Doctor	32	7	Male
5. Nkosinathi Vilakati	Nurse	33	10	Male
6. Musa Zwane	Nurse	38	13	Male
7. Tiny Dlamini	Nursing Sister	50	20+	Female
8. Wendy Surtee	Nurse	22	1 month	Female

Notes:

- Avg no of medicines/prescription = 4.1
- Use of antibiotics = 65%
- *There seems to be a silent war between the pharm techs and the doctors particularly Dr Moyo who was quite pompous and felt the meeting was quite negative in the beginning. By the time we finished the meeting he was quite humble and realized that there he also needed to check if his prescribing was appropriate*
- *Staff was very engaging and admitting that their prescribing was inappropriate most of the time*

Comments from staff

- Facility is using the electronic system to manage patients but there are conditions that have not been pre-loaded on the system

- CMIS is too slow and shuts down around 4pm. Patients seen after hours cannot be entered onto the system
- STG/EML is ok for primary health centres but not for health centres
- Guideline needs to be reviewed to cater for higher levels of care

8. MKHUZWENI HEALTH CENTRE

DATE: 15 March 2018 (most staff attended meeting)

Total no. of 14 February – 14 March prescriptions = 4336 (ALL). Difficult to count, no electronic register, only triplicate prescription books but could not get hold of all the books. Record keeping quite bad. The data clerk gave information that on average they see +/- 5000 patients

Randomly selected prescriptions = 20

Length of meeting = 45 minutes

Present	**Designation**	**Age**	**Years of Practice**	**Gender**
1. James Moyo	Pharm tech	35	13	Male
2. Cosmas Jereka	Pharm tech	47	18	Male
3. Lubi Kasai	Doctor	40	6	Male
4. Cynthia Dlamini	Nursing sister	45	22	Female
5. Zodwa Dlamini	Nurse	51	25+	Female

Notes

- The senior medical officer was going to join us but then had an emergency
- *Staff was eager to know how they are performing and very engaging. The pharm techs were a bit quiet and started talking once the rest of the staff had left. Meeting was held in the pharmacy.*

Comments from staff

- Staff mentioned that NCDs are poorly managed reason being that they hardly ever have stock of the necessary medicines. This facility does not fully rely on the STG/EML as they feel it does not cater for their level of care. Also, there are challenges with patients who never come for review.
- The nurses do not refill NCDs, all patients with NCDs are referred to the doctor
- Not all conditions are listed in the EML

- Pharm tech made a comment about the use of Ca for patients on Nifedipine who also have MSD. The patients receive 300mg daily of Ca, what about the interaction with the Nifedipine? Also, is this dose of Ca effective? Is the Ca is given with Mg to increase absorption? Basically the feeling in the room was that it's an ineffective dose of Ca and reduces the effectiveness of the Nidfedipine. All the Ca does is give the patient constipation.
- Pharm tech recommended that it would be interesting to find out the amount of money CMS spends on supplying medicines which may seem cheap like the MVT, BCO, PCM which happen to be on every patient's prescription. These medicines may seem cheap to buy but the amounts that are dispensed to patients add up.
- BCO was again mentioned as a fast moving medicine particularly for diabetic male patients who mention that it helps them get an erection and increases their libido
- The facility manages type II diabetes with Glibenclamide, Actraphane, Metformin – question raised was if this combination was effective?
- Another question raised by the pharm tech was the use of cotrimoxazole for life in patients on ART as prophylaxis for TB and pneumonia – is this appropriate and how much money are we spending as a country on the use of CTX? What about the side effects?

9. THE LUKE COMMISSION CLINIC

DATE: 20 March 2018

Total no. of 14 February – 14 March prescriptions = 230 (ALL). Randomly selected prescriptions = 20

Length of meeting = 2 hours

Present	Designation	Age	Years of Practice	Gender
1. Rebekah Sartori	Pharmacy Manager			Female

Notes

- Rebekah was initially interviewed and she is a participant in the study. Initially they were not comfortable having me there as they were not sure what my agenda is – which is the reason they also could not come to the feedback meeting. They go to the communities (mobile clinics) set up for the day and see as many patients as they can. They normally set up in a school or a church
- For them it is key to attend to patients and not spending a lot of time in meetings
- They do their outreach in all 4 regions in the country and they go out on Mondays to Thursdays. On Fridays they have a pastor coming on site and they have fellowship and get a chance to do paper work which cannot be done on the other days.

- They also have a clinic on site where they only attend to patients who are really sick. If the patient is not too sick they are sent to a primary health care facility nearby
- They help their patients with transport to get to their facility or any facility they refer to.
- They help them cancer patients obtain passports (which have gone from E80 to E500-and most patients cannot afford this) so they can be able to go for treatment in South Africa through the Phalala fund
- A doctor comes from America every month or second month for a week to remove cataracts for patients on site
- The facility also farms and give vegetable packs to patients
- They have overnight facilities (10 beds) where they keep patients who are really ill and have no one to look after them as well as those who have psychosocial problems in addition to the illnesses they have
- Facility is using an electronic app – slack – for patient management. With this app they are able to even communicate with doctors not based at the facility all the way to the States.
- *Rebekah sat and collected the prescriptions with me, we did the analyses together and finally discussed the findings*

Comments from staff

- The reason their average number of medicines per prescription is high is because they do outreaches and their outreaches are not necessarily repeated – it is a different venue and new people every time. So when they see the patient they give as many medicines as possible to cater for all their complaints
- Though the use of antibiotics seems low and below the WHO recommendation, as a facility they actually use a lot of antibiotics for the same reason given in point 1 above
- She appreciated the information and wanted to use the INRUD indicators to conduct her own surveys in the facility
- Facility requested me to mentor and supervise them on regular basis

10. PIGGS PEAK GOVERNMENT HOSPITAL

DATE: 12 April 2018 (most if not all prescribers attended meeting)

Total no. of March prescriptions = 288 x 6 = 1728

Randomly selected prescriptions = 15 (time constraints – I got to the facility just after 9am and the meeting had been scheduled for 9, so had about 15 minutes to collect prescriptions before the meeting without keeping staff away from their duties for too long)

Length of meeting = 2 hours

Present	Designation	Age	Years of Practice	Gender
1. Bongiwe Magagula	Staff nurse	34	7	F
2. Nontobeko Ndlangamandla	Nursing assistant	42	15	F
3. Maria Makhanya	Nursing sister	47	22	F
4. Mpendulo Malamba	NS	42	20	M
5. Ernest Mabuza	NS	51	27	M
6. M.J. Kemkwende	MO	70	12	M
7. Leidip Sardvy Sauchez	MO	30	6	F
8. Victoria Leme	Obs&Gynae	35	10	F
9. Dr Mukoke	MO	30	18	F
10. Hels Nkunku	MO	30	6	F
11. Ncamiso Dlamini	Staff Nurse	26	2	M
12. Brian Munro	MO	30	5	M
13. Mzwakhe Shelembe	Staff Nurse	26	1	M
14. Alfred Gamedze	Staff Nurse	28	5	M
15. Senzo Khoza	Staff Nurse	32	6	M
16. Aline Nkweh	Staff Nurse	40	18	F
17. Princess Gwebu	Staff Nurse	44	22	F
18. Philile Phiri	Staff Nurse	37	10	F
19. Desmond	Pharm Tech			M
20. Dr Gwebu	MO			M

Notes:

- Staff was super engaging particularly the MOs, Desmond and nurse Princess but generally everyone was contributing to the discussions.
- Staff is using manual system

Comments

	AVG No of Drugs	% Generics	% Antibiotics	% Injections
Baseline	3.44	79%	52%	35%
Intervention	3.85	86%	62%	46%

Issues: polypharmacy, overuse of antibiotics, overuse of injections

Discussions:

- Issues identified are due to poor documentation not necessarily irrational prescribing.
- The outpatients register is limiting in terms of the amount of information that can be captured (i.e. there is no space) particularly the diagnoses. Due to space constraints in the register, staff just captures the main diagnoses which ends up looking like improper use of medicines in the analyses
- High use of antibiotics and injections: the pharm tech stated that he attests to this as he sees a lot of prescriptions for diclofenac IM in the pharmacy. The rest of the staff was adamant that they are not overusing injections until we went through the 100 baseline prescriptions and ProcPen was the injectable overly prescribed.
    - ProcPen is readily available at OPD especially after hours. One doctor commented that the even if the doctor is called to attend to the patient, by the time they get there the patient has already been given ProcPen
- Dr Gwebu was adamant that there is nothing wrong with injections use shooting to 35% and topping all facilities in the sample if the medicines were being prescribed rationally. However, scrutiny of the individual baseline and intervention prescriptions showed that there was irrational prescribing. The Doctor still tried to defend the use of antibiotics for URTIs but I challenged him using evidence stating that these are most of the time viral and self-limiting. Unless if the facility is able to send specimens to the lab for testing then they cannot give antibiotics for URTIs
- Reasons for giving a lot of ProcPen at OPD after hours:
    - Pharmacy staff does not like to be called to come and dispense medicines after hours so nurses just give the ProcPen which is readily available
    - The calibre of patients they see is not the type that will complete the course of antibiotics. So is an injectable is given, one is assured that the patient will be covered for some time
    - Patient pressure; particularly those who come after hours really demand the injections. Staff agreed that patients need education on the medicines that they are not always useful but could potentially cause harm. However, their

argument was it is difficult to explain to patients who do not even understand why they cannot be given an injection. I then used Prof's example of the mothers with children receiving injections – very interesting discussion!
  - Prescriber satisfaction – the nurse feels that the patient will be covered with the antibiotic until they can access services from the pharmacy during normal working hours. This particularly applies if the patient comes to the facility after hours on a day before the weekend or holidays
- Dr Gwebu was disappointed that my intervention was not targeting the problems they face as a facility. As an example he expected me to correct pharmacy for not willing to attend to patients after hours as this would curb the overuse of injections and antibiotics. I responded to clarify that I am just a researcher but as a facility they should be raising such issues in their PTC and ensuring that their meeting minutes are sent to the office of the DDPS, so that the DDPS is aware of the challenges they are facing as a facility.
- Use of Guidelines in prescribing: staff commented that the guideline was not very helpful to them for most of the conditions they see as it tends to advise them to "refer the patient to the hospital". Question is which hospital because they are already a hospital. Staff ends up prescribing according to experience or culture of how they normally managed certain conditions. I assured them that the guideline mainly targets primary health care.
- A male nurse really thanked me and requested continued support to this facility. He stated that it was evident that there were issues to be addressed and change in prescribing needs to happen though people are never willing to change.

Recommendations:

- Development of a hospital guideline
- Re-evaluation and updating of the outpatient register. The register does not have skin conditions.

11. Mshingishingini Clinic

Date of Visit: 12 April 2018

Total number of prescriptions for March 2018: 987 prescriptions (collected from CMIS)

Sampled prescriptions: 21

Staff Complement: 3 (all were present in the meeting)

Length of meeting: 30 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Thoko Mathunjwa	Staff Nurse	42	7	F	7626 2065
Bongani Dlamini	Nursing Sr	43	16	M	76222588
Bongekile Tsabedze	Staff Nurse	24	16 mths	F	7653 8331

Comments:

The lady initially recruited into the study has since left and unfortunately the rest of the staff did not know about the study. The staff was very reserved but they agreed to talk to me. The ladies did not contribute much to the discussions. Bongani was the one trying to contribute though it seemed as though they all felt as if I was grading their performance as a facility.

Findings

	Avg No Drugs	**% Generics**	**% Antibiotics**	**% Injections**
Baseline survey	3.71	78%	60%	10%
Visit 1	3.48	76%	81%	29%

Notes:

- Refreshments were a selling point in staff allowing me to do the work and have the feedback meeting
- Staff viewed the meeting as a “corrective” measure and really clammed up.
- Efforts were made to encourage staff to talk but they either were scared or really not interested

Valuable inputs

- STG/EML needs to be updated
- Facility doesn’t receive stock directly from CMS but from Raleigh Fitkin Memorial Hospital. Stock outs are not a problem but they sometimes experience them.

12. Zondwako Clinic visit 1 notes

Date of Visit: 2 May 2018

Total number of prescriptions for April 2018: 660 prescriptions (collected from patient register. CMIS is also installed but staff has no confidence in the system and doing double entry on the register and CMIS)

Sampled prescriptions: 20

Staff Complement: 4 – Sister in charge (Patricia Nkhambule – 7608 0337)

Length of meeting: 20 minutes

Present	Designation	Age	Years of practice	Gender	Contact Details
Gugu Hlatshwayo	Nurse	40	13	F	7812 7848
Peggy Thwala	Nurse	54	25	F	7633 1220
Nokwanda Maduna	Nurse	23	2	F	7810 9608

Comments:

The nurse who was initially enrolled into the study has since left. The staff was willing to listen to and work with me.

Findings:

	AVG No of Drugs	**% Generics**	**% Antibiotics**	**% Injections**
Baseline Survey	3.82	68%	69%	6%
Visit 1	4.25	63%	70%	10%

Issues identified and highlighted in meeting:

- High average number of drugs per prescription
- Overuse of antibiotics
- Injection use was good during baseline survey but needs some monitoring as it has increased

Notes:

- Staff mentioned that most of the patients they see are co-infected with HIV and most of the conditions they present with require antibiotics.
- Patients presenting to the facility are not always able to go to bigger facilities or to private pharmacies to buy medicines stocked out at the facility. So the staff ends up giving antibiotics for most conditions. Staff felt that the antibiotics they prescribed even for the common cold were warranted. Education on appropriate use of antibiotics was then given. Overuse of antibiotics for asthma was also an issue discussed with the staff.
- The STG/EML needs to be updated to include certain medicines that the clinic needs such as adrenaline for asthma
- The dosing regimens for paediatric formulations need to be updated
- The clinic sees a lot of patients who present with snakebites. The guideline does not have dosing information for antivenom
- Staff is unable to properly manage asthma as they are almost always out of stock of nebulising solution. CMS does not supply nebulizing solution for clinics. The updated guideline needs to recommend for nebulizing solution to be available in clinics
- Staff needs support/education on how to manage asthma and diabetes.
- The new guideline should advocate for NSAIDs to be available in clinics.
- Staff uses a lot of antibiotics

13. Mkhulamini Clinic visit 1 notes

Date of Visit: 2 May 2018

Total number of prescriptions for April 2018: 240

Sampled prescriptions: 20 from the patient register. Facility has CMIS but doing double entry

Sister in charge: Ncamsile Thwala

Staff Complement: 7

Length of meeting: 45 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Matilda Ndzimandze	Nurse	40	13	F	7627 7589
Mavis Dlamini	Nurse	56	30	F	7603 6564
Furtunate Sibiya	Nurse	26	2	F	7814 4741
Zandile Dlamini	Nurse	34	9	F	7643 9167
Nokuthula Simelane	Nurse	32	10	F	7612 9766

Comments: the nurse initially enrolled into the study has since left.

Findings:

	AVG No of Drugs	**% Generics**	**%Antibiotics**	**% Injections**
Baseline Survey	3.64	51%	68%	4%
Visit 1	4.10	59%	70%	0%

Notes:

- Facility has overuse of antibiotics. Staff mentioned that they appropriately use the antibiotics – challenge was they were unable to document appropriately due to either space issues in the patient register or pre-loaded conditions on CMIS. CMIS functions in such a way that the conditions are pre-loaded. One therefore cannot edit the information entered; you just pick the closest option. This is the case particularly for skin conditions.
- Staff also uses chlorpheniramine as prophylaxis for asthma. When asked why they were doing this as this is not what the guideline recommends, the staff mentioned that they do this because they feel the allergens trigger asthma attacks hence the need for the chlorpheniramine prophylaxis.

14. Ntfonjeni Clinic

Date of Visit: 15 May 2018

Total number of prescriptions for April 2018: 287

Sampled prescriptions: 3 from CMIS

Sister in charge: Nokuthula Mabuza

Staff Complement: 3 (all present in meeting)

Length of meeting: 30 minutes

Present	Designation	Age	Years of practice	Gender	Contact Details
Nokuthula Mabuza	Sister	49	25	F	76159313
Nozizwe Zwane	Nurse	37	5+	F	
Ruth Mohlala	Nursing assistant	53	28	F	76044159

Comments:

There was a power cut after I had collected three prescriptions. I waited from 9am to 12 noon and power was not coming back. The staff prescribes on pieces of paper when there is power outage and enter the scripts electronically once the power is back. So there was no other source of information with the power cut. We still had the meeting and discussed their baseline findings as they did not have representative come to the feedback meeting.

Discussions:

- They had a high usage of antibiotics. Reasons for this were that they are not able to properly document patient complaints at the time as they were using the patient register which did not have enough space for documentation.
- Stock-outs were mentioned as contributing factors to misaligned diagnoses and treatment. Staff ends up prescribing whatever they have to try and treat patients. Staff also felt that there was poor communication between CMS and the facility on stock availability. If they place an order for a commodity, the only way they will know that it is out of stock is when CMS does not deliver it. Even when the commodities are then available at CMS, CMS does not communicate to tell them that they can place their orders.
- Some conditions like the urinary tract infection (UTI) are not listed as an option on CMIS – this then comes across as irrational prescribing because staff ends up choosing the closest option.
- Staff is using aldomet for HTN. Reason is that patients do not respond to only HCTZ, and CMS does not supply the facility with ACE inhibitiors like enalapril. Staff however is aware that other facilities at same level of care as they are get supplied with ACE inhibitors. When probed on why they do not follow up with CMS to find out why they were not supplied, staff revealed that they did not know the proper channels to be followed – even when they call CMS they wouldn't know who to speak to. I encouraged the staff to get in touch with their regional pharmacist – whom they said they did not know and were

currently relying on the pharmacist at Piggs Peak hospital. On the issue of using aldomet - the staff was aware that they should be using it for pregnant mothers but mentioned that they were using it as they had no other option with CMS only supplying HCTZ as well as the aldomet.

- Staff orders diclofenac from CMS but it is never supplied.

15. St Mary's Clinic

Date of Visit: 15 May 2018

Total number of prescriptions for April 2018: 93 – facility using the register

Sampled prescriptions: 20

Staff Complement: 3 (all present in meeting)

Length of meeting: 45 minutes

Present	Designation	Age	Years of practice	Gender	Contact Details
Nhlanhla Msweli	Pharm assistant	46	12	M	76089583
Shirley Chamunorwa	Nurse	34	11	F	76226432
Banele Ndlovu	Nurse	24	1	M	76723832

Comments:

- Facility has a pharmacy assistant who has learnt on the job (i.e. not qualified as a pharm assistant)
- Patients pay a minimum of E20 for consultation, then they pay for each medicine prescribed. The facility gets some medicines from CMS and buys some.

Findings:

	AVG No of Drugs	% Generics	% Antibiotics	% Injections
Baseline	2.94	72%	73%	25%
Visit 1	3.20	75%	55%	10%

Discussions:

- There was over-use of antibiotics. Reasons for this were patient pressure – patients pay for consultation and medicines at this facility. Hence you find that a patient goes to a different facility and they are not given antibiotics – they then come to St Mary's and they will tell the care giver that they have been to another facility and specifically want to get an injection or antibiotic from St. Mary's. The staff mentioned that it becomes difficult for them to refuse because the patient will complain that they are paying both for the service and the medicine. Staff was encouraged to practice their right of knowing about the medicine more than the patient and actually educating patients on both the benefits and harm of improper use of medicines.
- Staff mentioned that they hardly use the STG/EML as a guideline because they find it shallow. Even if they wanted to use it, the Min of Health did not provide enough copies for the facility. The facility only has one copy which must be share among all of them – this becomes difficulty especially on busy days.
- Injections use was also high though not as high as baseline results. The staff mentioned that patients request vit BCO injection as they believe that it increases their libido.

16. Nkwene Clinic

Date of Visit: 21 May 2018

Total number of prescriptions for April 2018: 1356 – facility using CMIS

Sampled prescriptions: 20

Staff Complement: 4 (Nursing sister, Rose Ndlangamandla absent)

Length of meeting: 45 minutes

Present	**Designation**	**Age**	**Years of practice**	**Gender**	**Contact Details**
Thabsile Ntshangase	Nurse	45	17	F	76242782
Menzi Nkomo	Nurse	35	6	M	76246948
Sgayoyo Maseko	Nurse	28	2+	M	76623535

Findings:

	AVG No of Drugs	% Generics	% Antibiotics	% Injections
Baseline	3.05	81%	56%	9%
Visit 1	4.05	91%	80%	15%

Discussions:

- Facility has overuse of antibiotics. Visit one results show an increased use compared to baseline findings. Reasons for this were:
    - Some prescribers refuse to change their prescribing patterns even if their attention is drawn to errors in prescribing. They will argue that their experience has shown that certain prescribing tendencies (as opposed to guidelines) are more effective.
    - Medicines for treating URTI in children are not available at CMS or if they are CMS never supplies orders. The staff find themselves prescribing amoxyl (which is the one antibiotic that is always available) to children even if it is not warranted, but just because it is very difficult for them to send hoe a very sick child with only paracetamol.
    - Also, for URTI in children, staff prescribes a lot of salbutamol because there is nothing else to use. *This was evident in the prescriptions collected and analysed.*
    - Staff highlighted that an "oversight" during prescribing results in inappropriate use of medicines. This oversight is due to high patient volumes, so one ends up prescribing without checking their prescribing against the guideline.
- STG/EML was said to be confusing and not user-friendly. Previously, there were printed A4 papers for managing conditions which the staff found user friendly. One didn't have to flip through pages looking for diagnosis and treatment nor look through the contents/indices of the book – conditions were grouped and all pertaining a condition was found on the one page.
- Stock-outs are a major cause of inappropriate prescribing. At the moment there are no zinc tablets that staff normally uses to manage diarrhea. Staff then find themselves using metronidazole and ORS even if there was no reason to use the metronidazole.
- On the issue of generic prescribing staff mentioned that some medicines were loaded in trade names on CMIS. They have taken this issue up with the CMIS team and medicines have then been loaded in generic names, and the ones initially loaded with trade names have not been deleted. Staff then noted that they need to make sure they choose the right name when they prescribe.
- Staff was really thankful for the information and mentioned that they have never had someone doing such for them – they were happy to sit with me and reflect on their prescribing practices as they end up being habits. On the issue of addressing improper prescribing they really asked me to speak to the sister – who apparently is the most difficult to address even if someone in the pharmacy picks that she has prescribed incorrectly, sister

will refuse to change the prescription and argue that her experience has taught her to prescribe the way she does.

Appendix 10: Intervention roll out Visit 2 notes
Mkhuzweni Health Centre **31st May 2018**

- Sampled April and May 2018 prescriptions from Dr's and nurses' prescribing books. 50 books with 100 pages each
- 20 prescriptions sampled
- Staff Complement = +/- 30 (4 doctors, 2 matrons, 6 sisters, staff nurses, 2 pharm techs)
- Length of meeting: 2 hours

Present	Designation	Age	Years of Practice	Gender	Contact Details
Dr Mahlalela	SMO	51	10	M	76401644
Zodwa	Nurse			F	
James Moyo	Pharm Tech			M	
Satis Khumalo	Nurse	30	8	M	76241480
Phumzile Mkhonta	Nursing Sr	48	25	F	76148853
Cosmas Jereka	Pharm Tech				

Summary of findings:

	No. of Drugs	**%Generics**	**Antibiotics**	**Injections**
Baseline	3.2	80%	55%	21%
Visit 1	3	75%	50%	15%
Visit 2	3.45	73%	50%	5%

Discussions:

- Antibiotics use is not changing much; still high. Staff encouraged to try and reduce the use of antibiotics. As a team we went through the prescriptions collected on the day, one by one and discussed whether the medicines prescribed were appropriate.
- Staff was over-excited with the drop in usage of injections from baseline to first and second visits. The SMO requested me to come and present to the whole staff the following week Wednesday at 2pm. Unfortunately I had transport issues on the day and was not able to go.

Comments from staff:

- DM is not managed appropriately. Clear guidelines and availability of medicines are the contributing factors.
- On the use of vitamins, staff commented that there was overuse of multivitamins and BCO – suggestion from staff was that there is need to link supplements to BMI, MVT (which are claimed to increase appetite) should then be given to patients with lower BMIs.

- There was a comment that iron gets prescribed for patients complaining of dizziness – way forward was that there is need to do lab investigations (which can be done quite quickly on site and results available immediately) before prescribing iron.
- The issues of using fluoroquinolones for patients with TB was also discussed. The pharmacy staff felt that fluoroquinolones should not be used generously for all patients but rather reserved for patients with TB.
- Staff complained about a radio talk show that aired on certain mornings of the week. They said inappropriate information was given to the public particularly promoting the use of injectable antibiotics. It then becomes difficult for staff in facilities to do their job properly without being pressurized into giving injectable antibiotics.
- Staff agreed that their prescribing culture needed to change; and they emphasized the importance of patient education.
- Staff felt that patients perceived BCO, MVT, M/S as vital items. The facility was out of these for a while and patients were complaining saying that they are not being managed properly after spending hours in the facility. Again, patient education was highlighted to be important in resolving this issue.

Piggs Peak Hospital **12th June 2018**

- Sampled April and May 2018 prescriptions (3207) from the curative register in the data room
- 20 prescriptions collected
- Length of meeting: 30 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Sifundo Zwane	Pharmacist				
Noel	Pharm Tech				
Desmond	Pharm Tech				
Dr Dube	Doctor				

- Not enough people were mobilized to attend the meeting. The sisters were uncomfortable to come to the meeting as they felt the sample size was too small and a few prescriptions particularly for skin conditions were included in the sample. I explained that I am following a method and mainly monitoring the general use of medicines and not particularly focusing on the conditions. Of course for me to make sense of the use of medicines I am aligning the diagnosis with the treatment. So I assured the staff that attended the meeting that I will be collecting a bigger sample during my final data collection.

Summary of findings:

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	3.44	79%	52%	35%
Visit 1	3.85	86%	62%	46%
Visit 2	3.8	79%	40%	10%

Discussions:

- The use of antibiotics is considerably dropping as well as the use of injections
- The staff that attended the meeting was ecstatic and looking forward to the next visit to see if their indicators are improving even more.
- The pharmacist asked for a copy of the findings so she can present to the rest of the group.

Dvokolwako Health Centre

Prescriptions from 12 April - 12 June 2018 from CMIS. 9573 prescriptions including blank ones pulled out from that period and collected 20 random prescriptions.

Staff Complement: +/- 33 prescribing and dispensing staff

Length of meeting: 1hr30minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Sr Tiny					
Dr Nyandoro	Medical officer	32	6	Male	
Dr Kibwe	Medical officer	32	7	Male	
Wendy Surtee					
Musa Zwane					
Mzweleni Dlamini	Staff Nurse	29	4	Male	
Kazembe Banza	SMO	48	14	Male	

Summary of Findings

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	5.14	77%	29%	13%
Visit 1	4.1	95%	65%	0%
Visit 2	3.65	93%	75%	0%

Notes:

Use of antibiotics has increased considerably, while the use of injections has dropped to 0. The use of injections – these are not getting captured into CMIS, because the treatment room does not have CMIS. So the staff mentioned that they are actually using a lot of injections but these are written on a piece of paper that the patient has to take to the treatment room. I encouraged staff to find a way of making sure that these are captured onto CMIS. The following were mentioned as reasons for the overuse of antibiotics.

- Poor documentation - CMIS does not have enough space for clinicians to write clinical examination notes and add extra information to diagnoses. The system has diagnoses that are preloaded which makes it difficult for staff to choose the appropriate diagnosis if it is not preloaded.
- Prescribers use their own discretion to decide how they will manage patients based on their observations and experience without necessarily following guidelines. Staff was encouraged to use the STG/EML as it helps to standardize management of common conditions in the country. Also, the guidelines are evidence informed, hence the reason to adhere to them.
- A lot of patients present to the facility with pneumonia and cellulitis. We then went over individual prescriptions that I captured on the day and in the sampled prescriptions there was no cellulitis or pneumonia yet the use of antibiotics was 75%.

Nkalashane Community Clinic

20 prescriptions between April and June 2018. The total sampling frame was 187.

Length of meeting: 45 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Ncamsile	Nurse				
Mawelela	Nurse				

Summary of Findings

	No. of Drugs	**%Generics**	**Antibiotics**	**Injections**
Baseline	3.99	82%	49%	6%
Visit 1	4.5	74%	45%	0%
Visit 2	4.5	79%	50%	5%

- There isn't much change on the use of antibiotics in this facility – usage is still high

- Injections use is consistently low

Reasons for indicators:

- Staff mentioned that they give in to patient demands most times and prescribe medicines even when they are not warranted particularly antibiotics, multivitamins, BCO, and M/S. They mentioned that patients discuss their ailments among themselves and what they were prescribed whether from this facility or a different one. So by the time the patient comes into the consultation room they already know what they want the nurse to prescribe. I asked if staff believed that patients had enough knowledge on medicines for them to be able to make those decisions. We had a lengthy discussion and even discussed the use of antibiotics for URTIs and staff confessed that they themselves do not take antibiotics when they have the common cold yet they were ok prescribing them for patients. Staff was encouraged to educate patients on inappropriate use of medicines and explain to patients that there is nothing wrong with them coming to the facility and leaving without medicine or one packet of medicine. In the end staff agreed and really felt that they need to go back to basics and spend more time doing group health education in the mornings before consulting the patients.
- Staff is looking forward to my next visit as they felt it was encouraging that I come and support them every now and then.
- My take on the staff prescribing patterns is that they are just demotivated and doing the best they can under the circumstances they work in. They just prescribe whatever the feel like prescribing or whatever the patient asks for. The facility is geographically difficult to access so not many people come to support the facility. Also, once the patient is at the facility the staff feels they should prescribe as many medicines to make sure the patient doesn’t come back with symptoms that are not responding to treatment.

Lubombo Referal Hospital

20 prescriptions between March and June 2018 were collected. On average the facility sees 250 patients per month. Length of meeting 2h15minutes.

Present	Designation	Age	Years of Practice	Gender	Contact Details
Mwamba E	Doctor	48	10	M	
Joyce Dladla	Pharm Tech	57	30+	F	
Nomsa Makhanya	Matron 1	54	31	F	
Nontobeko Sikhondze	Nurse	28	2	F	
Linda Chester	Nurse	29	5	F	
Sihle Zwane	Pharmacist	30	4	F	
Lawrence Sithole	Matron II	59	30	M	
Solomon Dlamini	Nurse	53	24	M	
Didier Mpata	Doctor	51	18	M	

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	4.01	79%	52%	15%
Visit 1	4.1	68%	45%	5%
Visit 2	4.25	78%	55%	25%

- Polypharmacy, overuse of injections and overuse of antibiotics are problematic in this facility.
- We looked at individual sampled prescriptions to see what the diagnoses were and what treatment was given for the different diagnoses.
- There was a patient who had HTN and was prescribed and dispensed digoxin. When questioned why this was the case, staff mentioned that patients come with prescriptions from private doctors (specialists) though it was difficult to ascertain if these private doctors were real specialists. Staff stated that it was difficult for them to then change those prescriptions as patients come with them and say they could not afford to buy the medicines from private pharmacies hence they come to the facility to refill.
- Use of BCO and B6 on the same patient was discussed. There is no need to give someone B6 if they are already prescribed BCO.
- This exercise of going through the individual sampled prescriptions is interesting because the prescribers get to discuss the prescribing and question improper use of medicines themselves.
- There were a number of prescriptions that had albendazole yet the diagnosis was not helminthiasis. Staff mentioned that albendazole is given as prophylaxis and sometimes patients ask for it as they walk out of the consultation room. In such cases it gets written on the prescription but it is not recorded in the record that remains in the facility.
- Staff complained that CMIS has restricted diagnoses which can be inaccurate/inappropriate at times. Staff then find themselves choosing an option close to the diagnosis. However when someone audits that prescription they might conclude that treatment was not aligned with diagnosis.

St Phillips Clinic

20 prescriptions between April and June sampled from CMIS. Sampling frame was 2150.

Length of meeting: 30 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Sarah Tshuma	Nurse				
Velaphi	Nurse				

- There was another community meeting that the other members of staff had to attend which unfortunately popped up last minute and could not be moved.

Summary of Findings

	No. of Drugs	**%Generics**	**Antibiotics**	**Injections**
Baseline	4.04	55%	40%	3%
Visit 1	3.82	88%	88%	12%
Visit 2	3.75	89%	65%	15%

- The findings show that there has been a reduction in the average number of medicines from baseline to 1st and 2nd visits.
- Prescribing by generic name is increasing
- Antibiotics usage increased between baseline and 1st visit and a 23% reduction was observed during the 2nd visit.
- Injections use on the other hand keeps increasing

Discussions:

- Staff complained about student nurses who are placed in the facility to do their internship. As much as staff mentioned that they supervise and mentor the junior staff, the reality is that they cannot do it 100%. They have been having these student nurses in the last 2 months and staff mentioned that the students do not have their own login details into CMIS and use the senior staff credentials. Hence it ends being difficult to see if it is the students making the mistakes or the senior staff prescribing practices need attention.

Cana Clinic **3 July 2018**

20 prescriptions sampled between May and July 2018; sampling frame = 4127

Length of Meeting: 45 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Samkeliso Magagula	Pharm assistant	32	8	M	

Summary of Findings

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	2.99	94%	51%	9%
Visit 1	4.35	87%	85%	0%
Visit 2	3.55	86%	65%	0%

Notes

- No of drugs per prescription increased from baseline to 1st visit, and there was a decrease from 1st to 2nd visit
- Percentage of prescriptions with generically prescribed medicines dropped from baseline to 1st and to 2nd visit
- Percentage of prescriptions with one or more antibiotics increased from baseline to 1st visit and has decreased from 1st to 2nd visit
- Percentage of prescriptions with one or more injections dropped from 9% to 0% from baseline to 1st visit and stayed at 0% during 2nd visit.
- The sister in charge was away attending a meeting offsite. The older nurse as well – it was only the junior staff on duty. The staff was much more relaxed and engaging compared to the last visit.

Comments:

- Stock outs impact on improper prescribing
- Staff believes in unevidenced/undocumented use of certain medicines e.g.
    - Multivitamins for appetite
    - Calcium gluconate 300mg OD for bone pain
- Experience, and not guidelines, is used a lot in prescribing
- Polypharmacy and use of injections decreased from 1st to 2nd visit. Staff commented that after my visit most of them were cautious when prescribing antibiotics but after a while people just reverted to what they were doing before. They commented that it was a bit more difficult to call the senior staff to order and correct their prescribing as they argue that they have been doing what they do for the longest time.
- Staff was free to talk and express their concerns as the sister in charge and the senior nurse were absent.

Mahlangatsha Clinic

20 prescriptions sampled from 4622 prescriptions on CMIS – sampled between 15 March and 3 July 2018.

Length of meeting: 30 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Velaphi					
Mduduzi					
Tengetile Masuku	Nurse	10	33	F	

Summary	**No. of Drugs**	**%Generics**	**Antibiotics**	**Injections**
Baseline	3.8	76%	40%	0%
Visit 1	3.83	72%	60%	3%
Visit 2	2.7	78%	80%	0%

Notes:

- No of drugs has decreased from baseline to visit 2
- Use of generic names in prescribing is increasing – challenge is that some of the medicines are preloaded in trade names on CMIS
- Use of antibiotics has increased steadily from baseline to visit 2 – we had discussions on the use of antibiotics which were mainly used for URTIs
- Injections use is below 5% for all visits.

Zondwako Clinic

20 prescriptions sampled from 43 pages (30 prescriptions per page) of the curative registers.

Length of meeting: 20 minutes (staff was overwhelmed as only 2 nurses were on duty)

Present	Designation	Age	Years of Practice	Gender	Contact Details
Gugu Hlatshwayo					
Nokwanda Maduma					

Summary of Findings

No. of Drugs		**%Generics**	**Antibiotics**	**Injections**
Baseline	3.82	68%	69%	6%
Visit 1	4.25	63%	70%	10%
Visit 2	2.9	70%	45%	5%

Notes:

- Staff was very excited to see their indicators improving! Even browsing through all the prescriptions I noticed the decrease in the use of antibiotics. We really had a good meeting and it was exciting to have the staff more engaging than it was the last time.
- Staff encouraged me to come on the 2nd week of September when the sister will definitely be around – 1st week of every month clinic sisters have their meetings. Staff mentioned that the sister was the one who mainly prescribed antibiotics unnecessarily and mainly because she hasn't been part of the discussions we have had. All three times when I visited the facility, the sister was away.

St Mary's Clinic

20 prescriptions sampled from 10 pages (30 prescriptions per page) of the curative register.

Length of meeting: 45 minutes

Present	Designation	Age	Years of Practice	Gender	Contact Details
Shirley					
Nhlanhla Msweli					
Banele					

Summary of Findings

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	2.94	73%	72%	25%
Visit 1	3.2	75%	55%	10%
Visit 2	2.4	86%	65%	10%

Notes:

- The one indicator that is greatly improving is the average number of drugs per prescription.
- Antibiotics use on the other hand keeps increasing. Staff mentioned that patients first go to government facilities before coming to them. By the time they come to this facility they say they didn't get all the medicines they wanted from the government facility and they particularly demand antibiotics. When the staff tries to reason with them and explain why they should not get antibiotics – patients demand and say that they particularly paid to come to this facility, hence they should be given all that they want as the fact that they paid should be considered.

The Luke Commission Clinic

20 prescriptions sampled from an electronic system – Slack.

Talked to Rebekah Sartori

Summary of Findings

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	7.19	59%	31%	1%
Visit 1	3.45	77%	20%	0%
Visit 2	4.3	81%	15%	0%

Notes:

- There is improvement on all indicators from baseline to visit 2

Mkhulamini Clinic

20 prescriptions sampled from CMIS (sampling frame 2300)

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	3.44	79%	52%	35%
Visit 1	3.85	86%	62%	46%
Visit 2	3.8	79%	40%	10%

Notes:

- Reduction in the average no. of drugs and the use of antibiotics and injections.
- Staff was excited to see improvement in their indicators and appreciated my coming to do the analyses and reporting back on their performance.

Nkwene Clinic

20 prescriptions sampled from CMIS (sampling frame 3894)

	No. of Drugs	%Generics	Antibiotics	Injections
Baseline	4.01	79%	52%	15%
Visit 1	4.1	68%	45%	5%
Visit 2	4.25	78%	55%	25%
Visit 3	3.35	86%	55%	25%

Notes:

- Reduction in the average no of drugs, increased generic prescribing, no change in use of antibiotics and injections between visits 1 and 2.

Appendix 11: Ethics approval from the University of the Western Cape

UNIVERSITY of the WESTERN CAPE

OFFICE OF THE DIRECTOR: RESEARCH
RESEARCH AND INNOVATION DIVISION

Private Bag X17, Bellville 7535
South Africa
T: +27 21 959 2988/2948
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E: research-ethics@uwc.ac.za
www.uwc.ac.za

27 October 2016

Mrs NBQ Ncube
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM/16/4/2

Project Title: A systematic approach to improve rational medicine use in Swaziland.

Approval Period: 28 September 2016 to 28 September 2017

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval. Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

PROVISIONAL REC NUMBER -130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

Appendix 12: Eswatini ethics approval

Research Protocol clearance certificate

Type of review	Expedited	X		Full Board	
Name of Organization	**STUDENT**				
Title of study	**A SYSTEMATIC APPROACH TO IMPROVE RATIONAL MEDICINE USE IN SWAZILAND**				
Protocol version	**1.0**				
Nature of protocol	New	X		Amendment	
List of study sites	**SEE ATTACHED LIST**				
Name of Principal Investigator	**NONDUMISO BQ NCUBE**				
Names of Co- Investigators	**N/A**				
Names of steering committee members in the case of clinical trials	**N/A**				
Names of Data and Safety Committee members in the case of clinical trials	**N/A**				
Level of risk (Tick appropriate box)	Minimal X			High	
Clearance status (Tick appropriate box)	Approved	X		Disapproved	
Clearance validity period	Start date	**27/03/2017**		End date	**27/03/2018**
Signature of Chairperson					
Date of signing	**28/03/2017**				
Secretariat Contact Details	Name of contact officers			**Ms Simangele Masilela**	
	Email address	kaluamasi@gmail.com			
	Telephone no.	**(00268) 24040865/24044905**			

MINISTRY OF HEALTH
28 MAR 2017
HEALTH RESEARCH REVIEW BOARD
SWAZILAND

Page **1** of **2**

List of Public Health Facilities to be sampled for RMU in Swaziland Project

Region	Facility Name	Type
Manzini	Mankayane Hospital	Hospital
	Zondwako Clinic	Clinic
	Luke Commission	Clinic
	Cana Mission	Clinic
	Mahlangatsha Clinic	Clinic
	Mkhulamini Clinic	Clinic
	Gebeni Clinic	Clinic
Shiselweni	Hlathikhulu Hospital	Hospital
	Nhlangano Health Centre	Health Centre
	Matsanjeni Health Centre	Health Centre
	Moti Clinic	Clinic
	Nhlangunjani Clinic	Clinic
	Nkwene Clinic	Clinic
	Nhletsheni Clinic	Clinic
	Lavumisa Clinic	Clinic
	Hluti Clinic	Clinic
Lubombo	Lubombo Referral Hospital	Hospital
	Sithobela Health Centre	Health Centre
	Mshingishingini Nazarene Clinic	Clinic
	Manyeveni Nazarene Clinic	Clinic
	Mafutseni Nazarene Clinic	Clinic
	St. Phillip's Clinic	Clinic
	Siphofaneni Clinic	Clinic
	Nkalashane Community Clinic	Clinic
Hhohho	Piggs Peak Hospital	Hospital
	Dvokolwako Health Centre	Health Centre
	Mkhuzweni Health Centre	Health Centre
	St. Mary's Clinic	Clinic
	Sigangeni Clinic	Clinic
	Ekufikeni Clinic	Clinic
	National Baptist Mission Clinic	Clinic
	Ntfonjeni Clinic	Clinic
	Ngowane Clinic	Clinic
Total Number of Facilities	33	

Appendix 13: Permission to access facilities

Telephone: (+268 2404 2431)
Fax: (+268 2404 2092)

SIYINQABA

MINISTRY OF HEALTH
P.O. BOX 5
MBABANE
SWAZILAND

THE KINGDOM OF SWAZILAND

Date: 3rd April 2017

The Regional Health Administrator (Manzini)
The Regional Health Office
Manzini

Dear Sir/Madam

Re: REQUEST FOR YOU TO SUPPORT NONDUMISO NCUBE TO CONDUCT STUDY ON RATIONAL MEDICNE USE AND PRESCRIBING PRACTICES AT SELECTED HEALTH CARE FACILITIES IN THE REGION

As the Ministry of Health under the office of the Chief Pharmacist, we are requesting you to support the principal investigator, Nondumiso, in conducting the above-mentioned study that will help gather information on whether facilities have essential medicines and if these medicines are used rationally. The following facilities in the Manzini region have randomly been sampled to be in the study:

1. Mankayane Hospital
2. Zondwako Clinic
3. Luke Commission
4. Cana Mission
5. Mahlangatsha Clinic
6. Mkhulamini Clinic
7. Gebeni Clinic

The study involves accessing and collecting data from facility prescribing records, and some interviews with frontline medicine managers (doctors/ nurses/ pharmacists/ pharmacy technicians) on prescribing practices. The following information will be collected anonymously from prescription records: the number of medicines prescribed and dispensed, number of generics prescribed and dispensed, number of antibiotics prescribed and dispensed, number of injections prescribed and dispensed, and medicines prescribed from the Essential Medicines List. Furthermore, data on patient care indicators (consulting, dispensing, consulting-dispensing times, and labelling of medication (medicine name, dosing frequency and duration, the number of tablets/capsules or millilitres of medicine dispensed))will be collected from random patients at the facility. Personal identifying features such as names and addresses will not be collected from both medicine managers and patients.

The study has been reviewed and approved by the University of the Western Cape Senate Research Committee (reference number: BM16/14/2) and the Ministry of Health (Health Research Review Board).

Should you have any questions, please do not hesitate to contact my office.

Yours Faithfully,

Bhembe

Fortunate Ntombi Bhembe
Chief Pharmacist
Ministry of Health
Kingdom of Swaziland
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MINISTRY OF HEALTH
CHIEF PHARMACIST
03 APR 2017
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MBABANE H100
SWAZILAND

Appendix 14: Information Leaflet for participants

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa
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E-mail: soph-comm@uwc.ac.za

Information Leaflet for Medicine Managers

Title of Research Project: A systematic approach to improve rational medicine use in Eswatini

My name is Nondumiso Ncube, a Ph.D. student at the School of Public Health, University of the Western Cape, Cape Town, South Africa. I am inviting you to participate in a research project to study the use of medicines in Swaziland. Please take some time and read this information leaflet which gives you the details of the research project. After reading the information leaflet, please make sure that you clearly understand what the research is about and how you will be involved. Participation in this research is completely voluntary, and you are free to decline participation or withdraw from the project at any time during the research with no repercussions.

The research protocol for this study was approved by the University of the Western Cape Senate Research Committee (Reference: BM/16/4/2) and the National Health Research Review Board in Eswatini. Permission to conduct research activities in health facilities was granted by the Deputy Director Pharmaceutical Services in the Ministry of Health. Research processes will be conducted in accordance with the ethical guidelines and principles of the International Declaration of Helsinki (2013), the South African Guidelines for Good Clinical Practice, and the Kingdom of Eswatini's Ministry of Health Ethical Guidelines for Research.

What is this research study about?

This study is being conducted on Medicine managers at the National Department of Health, Central Medical Stores and a random sample of 32 health facilities across the four regions in Eswatini. The study aims to investigate if Rational Medicine Use (RMU) is being practiced, and to design and implement an intervention to improve RMU practices in the country. You will be

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asked questions on your perspectives on medicine use in the country through an interview conducted by the Principal Investigator (PI), which will take about an hour. Interview proceedings will be audio recorded (you have the right to refuse to be audio recorded) but your name, or any feature that identifies you will not be recorded. All recordings will be kept in a lockable cabinet that can only be accessed by the PI, and will be deleted five years after the end of the study. Recordings will be transcribed onto a password-protected computer. The PI and her supervisors will have access to the transcript, and you will have an opportunity to read and correct it before any manuscript is produced.

Why have you been invited to participate?

As a healthcare professional involved in managing medicines, you have a good understanding of how medicines are used in your facility or the country. By giving your honest insight, you will assist the study team to gather information that could improve the availability of, access to, and use of medicines in the country.

What will your responsibilities be?

Your responsibility will be to read and understand the information leaflet, complete and sign the consent form, and be interviewed at a time and place convenient to you.

Who will benefit from taking part in the research?

The Ministry of Health in Eswatini and any person in the country who will need medicines in the future.

Are there risks involved in your participation in this research?

There is some risk involved in your participation. Some questions in the interview may cause discomfort. You have the right to decline to answer any question that you are uncomfortable with. Also, your privacy, anonymity, and confidentiality will be maintained at all times.

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What might happen if you do not agree to participate?

If you decide not to participate in the study or change your mind and withdraw from study proceedings, nothing will happen to you.

Will you be paid to take part and are there any costs involved?

You will not be paid to participate in the study. However, you will be reimbursed if you travel to be part of study proceedings.

What if you have questions?

If you are not clear on what the study entails or anything is not clear during the study proceedings, please contact Nondumiso Ncube, the Deputy Director Pharmaceutical Services in the Ministry of Health, or the project supervisors.

Contact Details:

Principal Investigator: Nondumiso Ncube, School of Public Health, University of the Western Cape, Robert Sobukwe Road, Bellville, 7535

Tel: +2721 959 9390 Mobile: +268 7664 0888 Email: nncube@uwc.ac.za

Deputy Director Pharmaceutical Services: Ms. Fortunate Bhembe, 2nd Floor, Ministry of Justice & Constitutional Affairs Building, Mhlambanyatsi Road, Mbabane, Swaziland

Tel: +268 2404 5514 / 2404 2431 Email: fortunatebhembe@gmail.com

Supervisors:

1. Dr. Hazel Bradley, School of Public Health, University of the Western Cape, Robert Sobukwe Road, Bellville, 7535

   Tel: +2721 959 2630 Email: hbradley@uwc.ac.za

2. Prof Richard Laing, Boston University School of Public Health, 801 Massachusetts Avenue Boston MA 02118/ School of Public Health, University of the Western Cape

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   Tel: +2721 959 Email: hschneider@uwc.ac.za

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Appendix 15: INFORMED CONSENT FORM

Title of Research Project: **Rational Medicines Use (RMU) in selected public sector facilities in Swaziland**

The study has been described to me in language that I understand. My questions about the study have been answered. I understand what my participation will involve and I agree to participate of my own choice and free will. I agree for information shared during this workshop to be recorded for study purposes only. I understand that my identity will not be disclosed to anyone, and that I may withdraw from the study at any time without giving a reason and without fear of negative consequences or loss of benefits.

___ I agree to be photographed during my participation in this study.

___ I do not agree to be photographed during my participation in this study.

Participant's name……………………….

Participant's signature……………………………….

Date………………………

School of Public Health
University of the Western Cape
Private Bag X17
Bellville 7535

Appendix 16: Quantitative Analyses

Both acute and chronic together

Table 1 a and b

Intra-group baselines and changes (mean (SD)) across 3 difference measures* with paired t tests

Intervention group (n=16)	Base line	Difference 1	p value (paired t-test)	Difference 2	p value (paired t-test)	Difference 3	p value (paired t-test)
No of Drugs	3.9 (1)	-0.36 (0.99)	0.165	-0.41 (0.96)	0.110	-0.04 (0.21)	0.410
%Generics	73 (11)	5.38 (14.49)	0.159	8.38 (13.14)	0.022	3 (4.65)	0.021
%Antibiotics	54 (13)	-1.62 (12.36)	0.607	1.62 (11.28)	0.573	3.25 (8.11)	0.130
%Injections	11 (10)	-2.37 (8.55)	0.284	-1.31 (11.34)	0.650	1.06 (6.05)	0.493
%EML	94 (3)	-5.69 (2.8)	<0.001	-3.56 (3.35)	0.001	2.13 (2.96)	0.012

Control group (n=16)	Baseline	Difference 1	p value (paired t-test)	Difference 2	p value (paired t-test)	Difference 3	p value (paired t-test)
No of Drugs	3.5 (0.6)	-0.14 (0.79)	0.497	-0.21 (0.87)	0.347	-0.08 (0.37)	0.425
%Generics	75 (8)	9.75 (11.29)	0.004	11.75 (10.21)	<0.001	2.00 (5.74)	0.184
%Antibiotics	55 (10)	-8.69 (21.23)	0.123	2.88 (12.74)	0.381	11.56 (12.07)	0.002
%Injections	9 (5)	-1.44 (5.24)	0.290	4.06 (13.74)	0.255	5.50 (12.79)	0.106
%EML	95 (3)	-2.94 (3.38)	0.003	-1.50 (2.58)	0.035	1.44 (2.73)	0.053

* Note: Difference 1 = post intervention – baseline

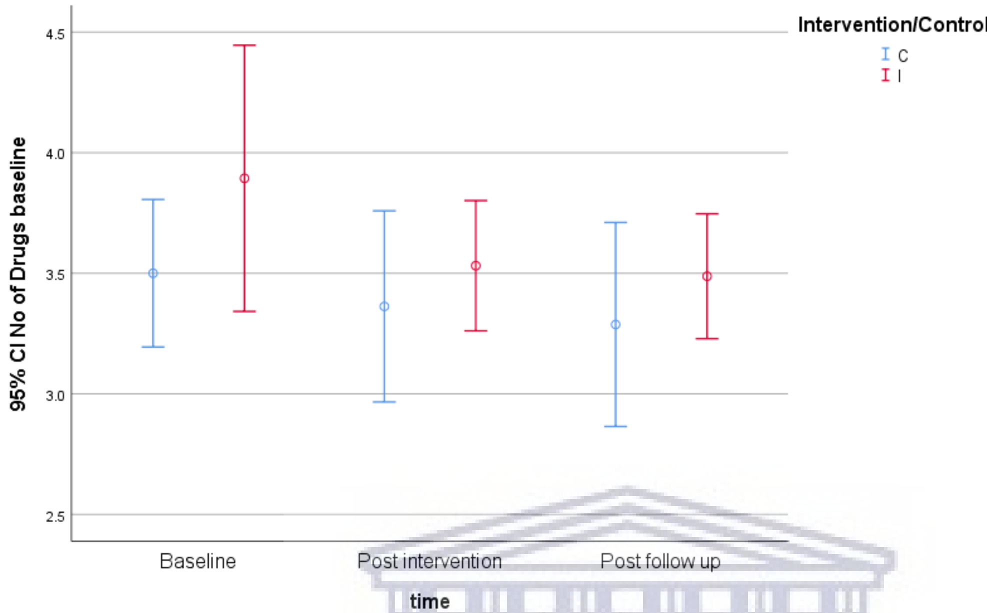
Difference 2 = post follow up – baseline

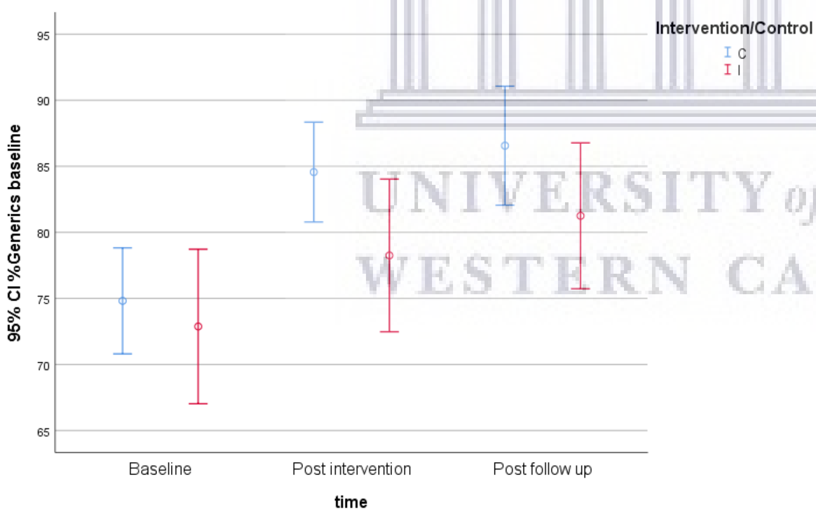
Difference 3 = post follow up – post intervention

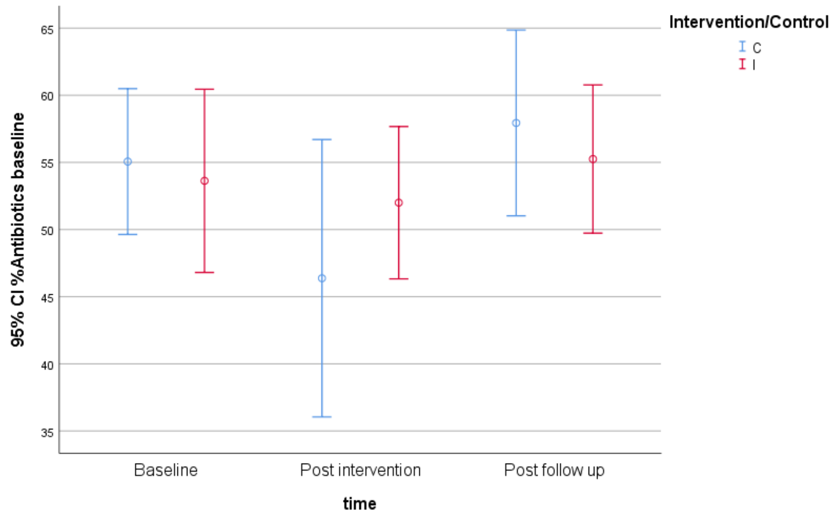
Table 2: Difference between intervention and control groups. Mean difference is a difference of differences calculated as intervention minus control. Negative difference means control increased more than intervention. Positive difference means intervention increased more than control.

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in number of drugs between baseline and post intervention	-.709	30	.484	-.22500	.31738	-.8732	.42317
Difference in number of drugs between baseline and post follow up	-.598	30	.554	-.19375	.32382	-.8551	.46759
Difference in number of drugs between post intervention and post follow up	.297	30	.768	.03125	.10507	-.1833	.24583
Difference in percent of generics between baseline and post intervention	-.953	30	.348	-4.37500	4.59291	-13.76	5.00497
Difference in percent of generics between baseline and post follow up	-.811	30	.424	-3.37500	4.15970	-11.87	5.12025
Difference in percent of generics between post intervention and post follow up	.542	30	.592	1.0000	1.84617	-2.770	4.77038
Difference in percent antiobiotics between baseline and post intervention	1.150	30	.259	7.06250	6.14179	-5.481	19.60571
Difference in percent antibiotis between baseline and post follow up	-.294	30	.771	-1.25000	4.25319	-9.936	7.43616
Difference in percent antibiotics between post intervention and post follow up	-2.29	30	.029	-8.31250	3.63601	-15.74	-.88678
Difference in percent injections between baseline and post intervention	-.374	30	.711	-.93750	2.50640	-6.056	4.18125
Difference in percent injections between baseline and post follow up	-1.21	30	.237	-5.37500	4.45270	-14.47	3.71863
Difference in percent injections between post intervention and post follow up	-1.26	30	.219	-4.43750	3.53609	-11.66	2.78415
Difference in percent EML between baseline and post intervention	-2.51	30	.018	-2.75000	1.09616	-4.989	-.51135
Difference in percent EML between baseline and post follow up	-1.95	30	.060	-2.06250	1.05660	-4.220	.09537
Difference in percent EML between post intervention and post follow up	.682	30	.500	.68750	1.00765	-1.370	2.74540

The difference was significantly larger than zero in percent antibiotics between post intervention and post follow up (p=0.029). The difference was -8.31 which meant that the control group experienced a greater increase between these time points than the intervention. Percent EML was also significantly different between the groups between baseline and post intervention (p=0.018). The difference was -2.75 which meant that the intervention decreased more than the control.







Intervention/Control
C
I
95% CI %Antibiotics baseline
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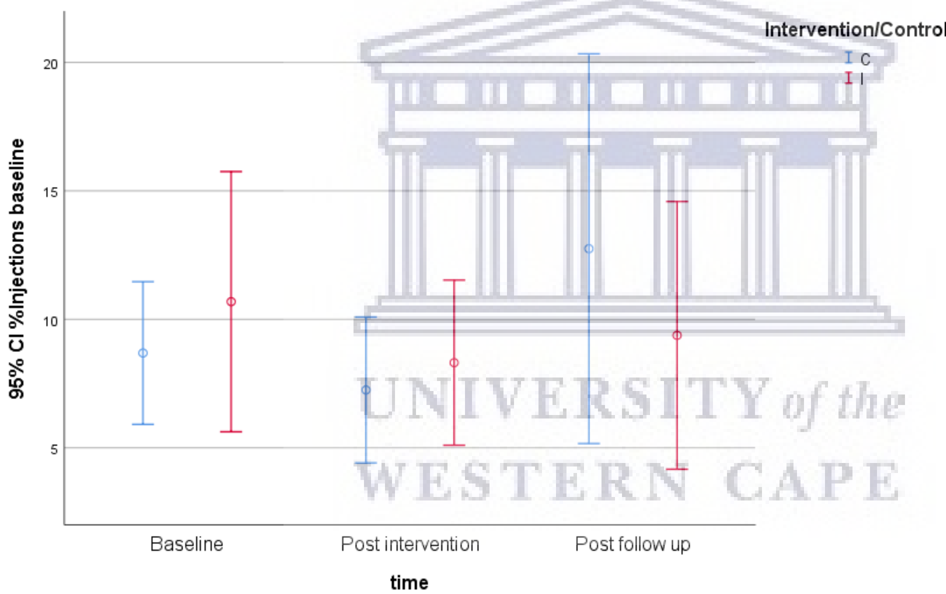
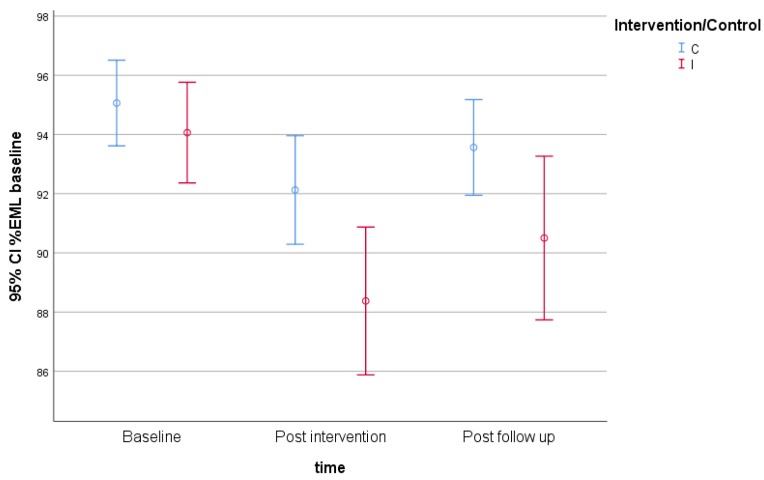
60
55
50
45
40
35
Baseline
Post intervention
Post follow up
time



Intervention/Control
C
I
95% CI %Injections baseline
20
15
10
5
Baseline
Post intervention
Post follow up
time



Acute only

Table 4 a and b

Intra-group baselines and changes (mean (SD)) across 3 difference measures* with paired t tests in acute prescriptions

Intervention group (n=15)	Baseline	Difference 1	p value (paired t-test)	Difference 2	p value (paired t-test)	Difference 3
No of Drugs	3.68 (0.99)	0.34	0.138	-0.43(0.80)	0.055	-0.99(0.23
%Generics	67.37 (10.91)	9.25	0.054	12.92(15.73)	0.007	3.61(5.09
%Antibiotics	74.28 (14.93)	13.97	0.004	-10.23(12.95)	0.009	1.97(9.76
%Injections	14.73 (13.52)	-5.72	0.089	-4.76(13.17)	0.183	0.65(5.54
%EML	92.97 (3.82)	-6.59	<0.001	-4.07(4.56)	0.004	2.84 (4.04

Control group (n=16)	Baseline	Difference 1	p value (paired t-test)	Difference 2	p value (paired t-test)	Difference 3	p value (paired t-test)
No of Drugs	3.29 (0.5)	-0.08 (0.68)	0.631	-0.13 (0.80)	0.511	-0.05 (0.38)	0.605
%Generics	70.44 (8.97)	13.22 (12.09)	0.001	15.72 (10.42)	<0.001	2.51 (6.67)	0.153

%Antibiotics	75.44 (8.76)	-15.22 (17.82)	0.004	-6.29 (11.23)	0.041	8.93 (10.10)	0.003
%Injections	10.89 (7.22)	-2.99 (7.05)	0.111	2.88 (14.93)	0.452	5.87 (12.11)	0.071
%EML	93.88 (2.80)	-3.74 (4.27)	0.003	-1.35 (3.33)	0.125	2.39 (4.71)	0.061

* Note: Difference 1 = post intervention – baseline

Difference 2 = post follow up – baseline

Difference 3 = post follow up – post intervention

Table 5 Difference between intervention and control groups in acute prescriptions.

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in number of drugs between baseline and post intervention	-.935	29	.358	-.25561	.27346	-.81491	.30369
Difference in number of drugs between baseline and post follow up	-1.043	29	.306	-.29976	.28745	-.88765	.28813
Difference in number of drugs between post intervention and post follow up	-.372	30	.712	-.04141	.11126	-.26863	.18580
Difference in percent of generics between baseline and post intervention	-.754	29	.457	-3.97092	5.26909	-14.74741	6.80557
Difference in percent of generics between baseline and post follow up	-.589	29	.560	-2.80450	4.76229	-12.54447	6.93548
Difference in percent of generics between post intervention and post follow up	.527	30	.602	1.10502	2.09671	-3.17702	5.38707

Difference in percent antiobiotics between baseline and post intervention	.523	29	.605	3.02301	5.77858	-8.79552	14.84153
Difference in percent antibiotis between baseline and post follow up	-.906	29	.372	-3.93771	4.34512	-12.82447	4.94906
Difference in percent antibiotics between post intervention and post follow up	-1.981	30	.057	-6.95694	3.51146	-14.12830	.21442
Difference in percent injections between baseline and post intervention	-.774	29	.445	-2.73067	3.52964	-9.94958	4.48825
Difference in percent injections between baseline and post follow up	-1.507	29	.143	-7.64308	5.07017	-18.01273	2.72658
Difference in percent injections between post intervention and post follow up	-1.569	30	.127	-5.22592	3.33021	-12.02712	1.57528
Difference in percent EML between baseline and post intervention	-2.095	29	.045	-2.85133	1.36131	-5.63553	-.06714
Difference in percent EML between baseline and post follow up	-1.904	29	.067	-2.71610	1.42683	-5.63430	.20209
Difference in percent EML between post intervention and post follow up	.289	30	.775	.44772	1.55174	-2.72137	3.61680

Chronic only

Table 6 a and b

Intra-group baselines and changes (mean (SD)) across 3 difference measures* with paired t tests in chronic prescriptions

Intervention group (n=15)	Baseline	Difference 1	p value (paired t-test)	Difference 2	p value (paired t-test)	Difference 3
No of Drugs	4.32 (1.21)	0.47 (1.00)	0.087	-0.42 (1.07)	0.150	0.16(0.51
%Generics	75.60 (10.51)	7.06(17.04)	0.131	5.76(14.07)	0.135	-1.25(6.64
%Antibiotics	25.67 (11.35)	-4.01(17.89)	0.400	-3.60(12.31)	0.277	1.12(12.61
%Injections	5.93 (8.04)	-0.75 (10.16)	0.779	5.41(12.80)	0.124	5.77(11.23

%EML	95.80 (3.21)	-1.35 (2.83)	0.087	-0.87(3.49)	0.352	0.32(4.08

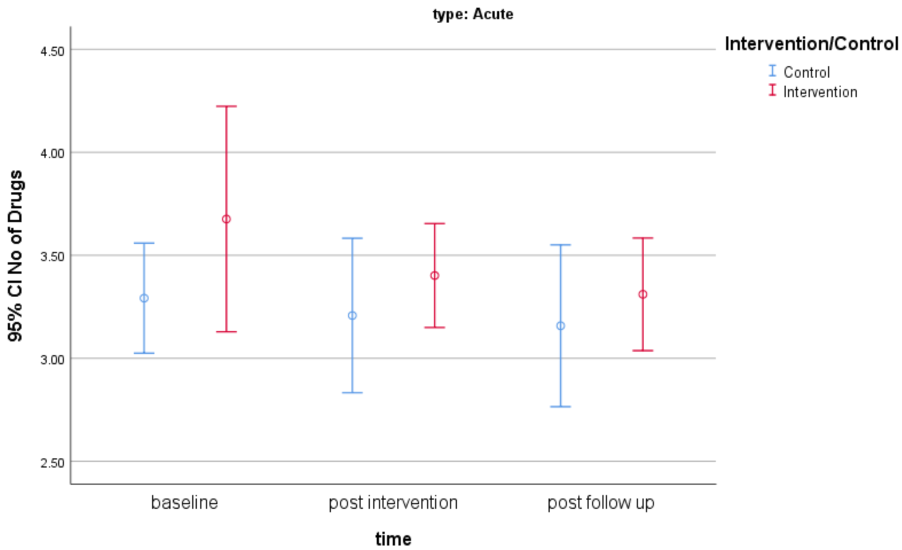
Control group (n=16)	Baseline	Difference 1	p value (paired t-test)	Difference 2	p value (paired t-test)	Difference 3
No of Drugs	3.83 (0.70)	-0.06 (1.09)	0.842	-0.21 (0.1.16)	0.483	-0.15 (0.5
%Generics	80.94 (6.94)	5.66 (12.69)	0.094	5.91 (10.87)	0.046	0.25(5.6
%Antibiotics	24.84 (11.21)	-5.57(16.96)	0.209	-2.81(10.31)	0.293	2.76(11.5
%Injections	5.00 (5.72)	1.33(8.84)	0.556	3.35 (12.14)	0.274	2.12(9.4
%EML	96.74 (1.90)	-0.33(2.11)	0.541	-0.72 (3.53)	0.429	-0.39(3.9

Table 7 Difference between intervention and control groups in chronic prescriptions.

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Difference in number of drugs between baseline and post intervention	-1.111	29	.276	-.41865	.37687	-1.18944	.35215
Difference in number of drugs between baseline and post follow up	-.529	29	.601	-.21214	.40128	-1.03285	.60857
Difference in number of drugs between post intervention and post follow up	.876	30	.388	.16865	.19251	-.22451	.56181
Difference in percent of generics between baseline and post intervention	.259	29	.797	1.39173	5.37380	-9.59892	12.38237
Difference in percent of generics between baseline and post follow up	-.033	29	.974	-.15006	4.49957	-9.35272	9.05259
Difference in percent of generics between post intervention and post follow up	-.687	30	.497	-1.49621	2.17711	-5.94247	2.95005

Difference in percent antiobiotics between baseline and post intervention	.249	29	.805	1.55622	6.25873	-11.24431	14.35675
Difference in percent antibiotis between baseline and post follow up	-.192	29	.849	-.78334	4.06970	-9.10681	7.54013
Difference in percent antibiotics between post intervention and post follow up	-.382	30	.705	-1.63506	4.27710	-10.37008	7.09995
Difference in percent injections between baseline and post intervention	-.609	29	.547	-2.08063	3.41440	-9.06386	4.90260
Difference in percent injections between baseline and post follow up	.438	29	.665	1.96223	4.47851	-7.19735	11.12180
Difference in percent injections between post intervention and post follow up	.996	30	.327	3.65789	3.67112	-3.83953	11.15531
Difference in percent EML between baseline and post intervention	-1.136	29	.265	-1.01592	.89407	-2.84450	.81266
Difference in percent EML between baseline and post follow up	-.121	29	.905	-.15212	1.26213	-2.73348	2.42923
Difference in percent EML between post intervention and post follow up	.494	30	.625	.70230	1.42178	-2.20136	3.60596

Graphs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Intervention/Control
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Intervention
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3.00
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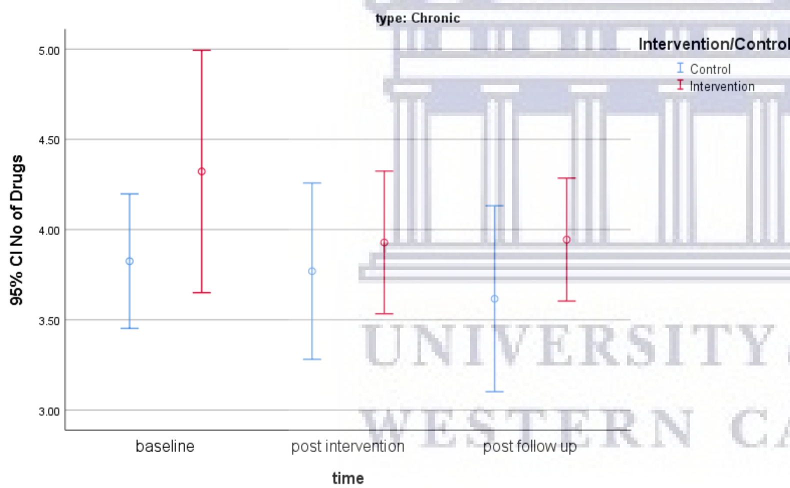
95% CI No of Drugs
baseline
post intervention
post follow up
time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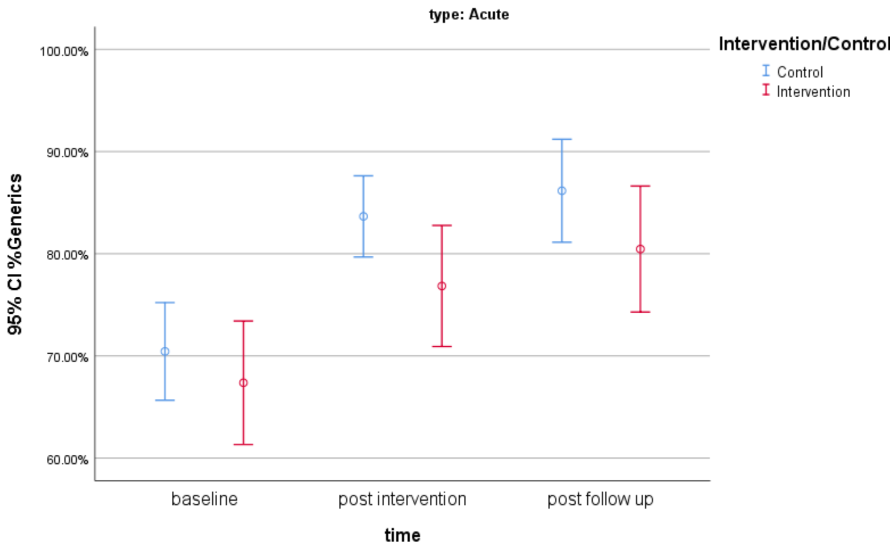
Intervention/Control
Control
Intervention
5.00
4.50
4.00
3.50
3.00
95% CI No of Drugs
baseline
post intervention
post follow up
time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Intervention/Control
Control
Intervention
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90.00%
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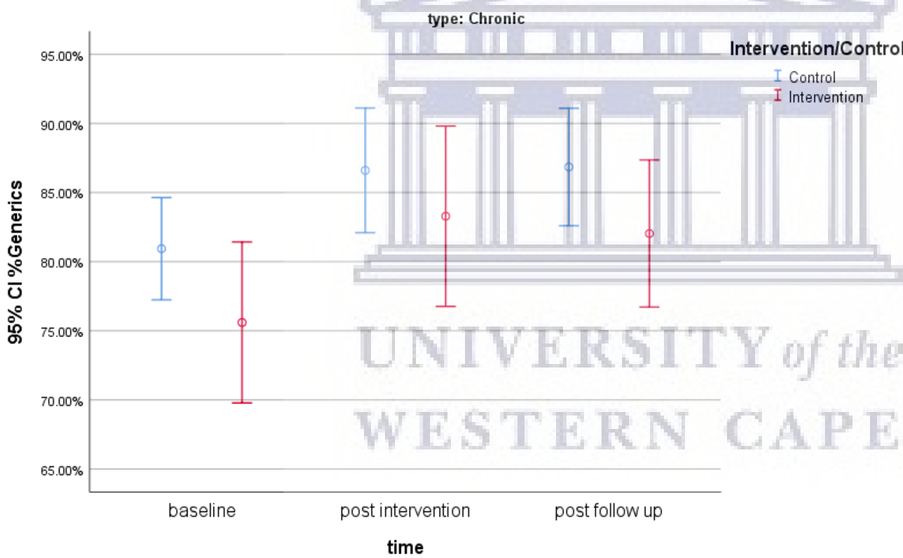
95% CI %Generics
baseline
post intervention
post follow up
time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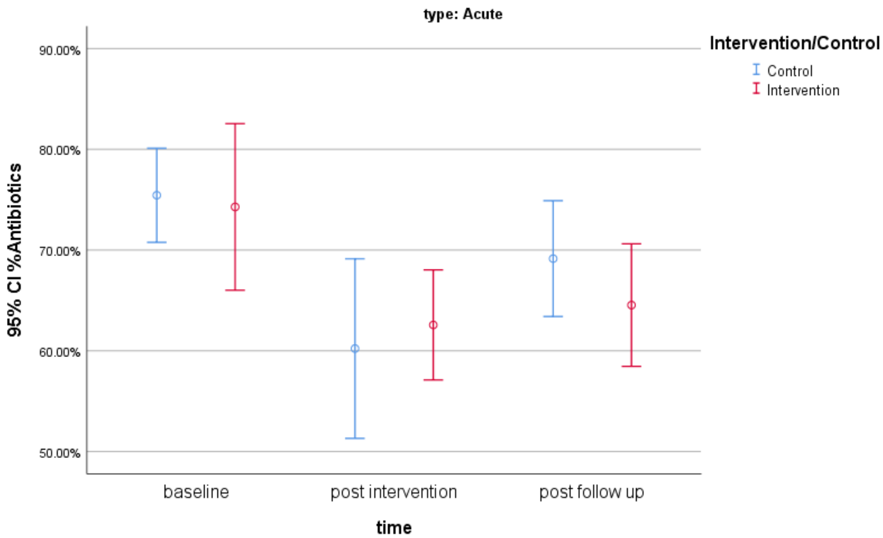
baseline
post intervention
post follow up
time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baseline
post intervention
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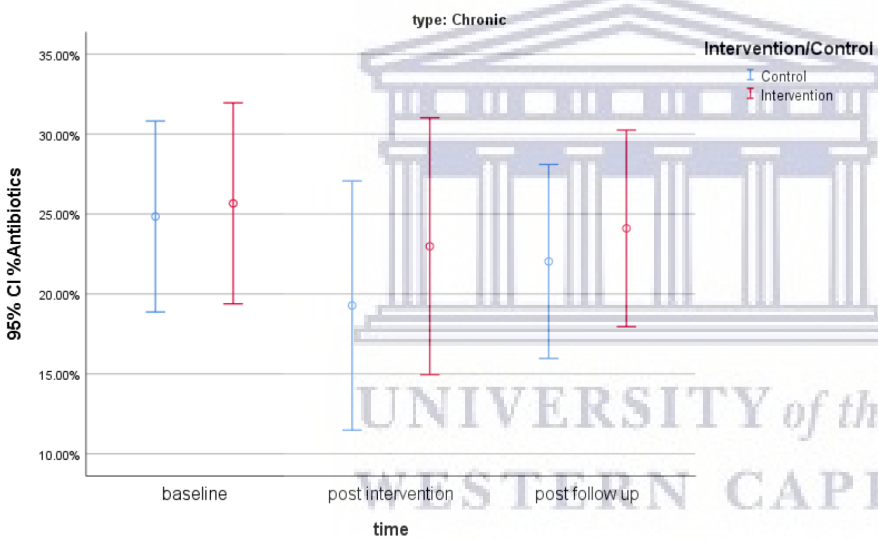
time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Intervention/Control
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Intervention
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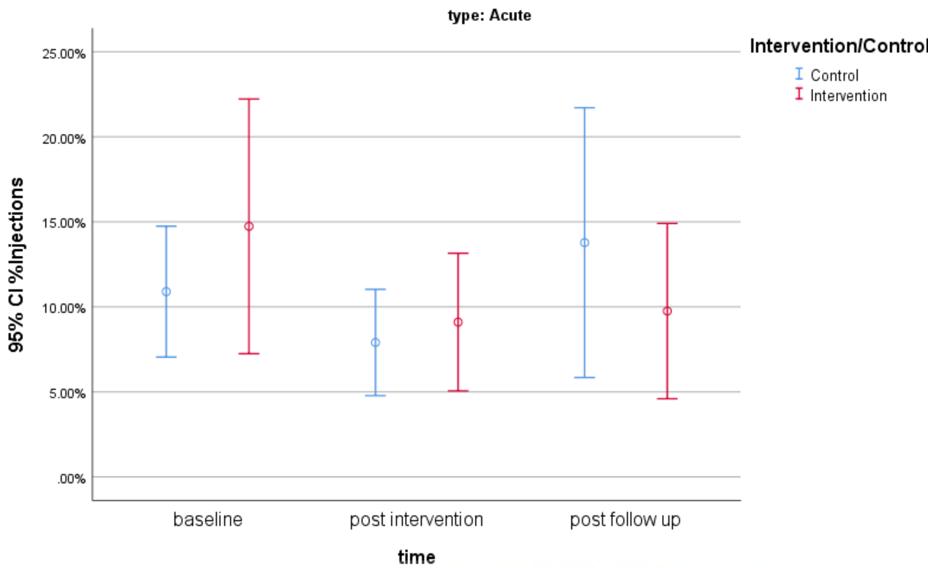
30.00%
25.00%
20.00%
15.00%
10.00%
95% CI %Antibiotics
baseline
post intervention
post follow up
time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Intervention/Control
Control
Intervention
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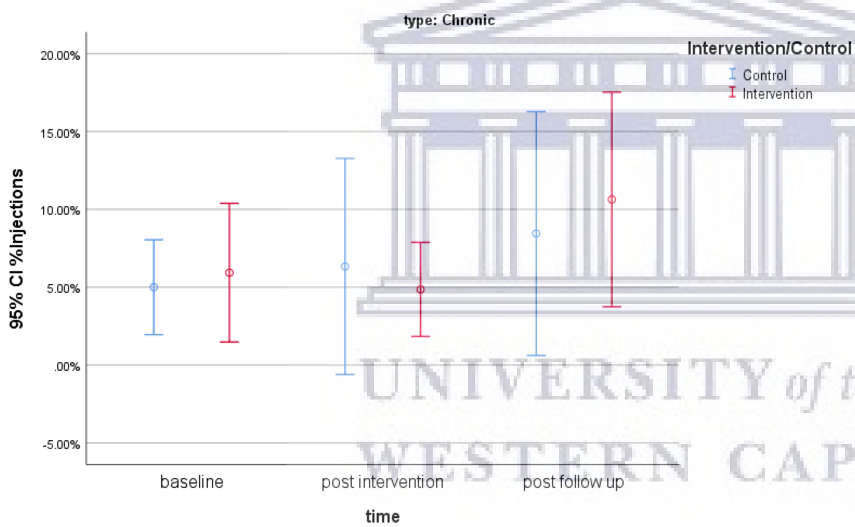
baseline
post intervention
post follow up
time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Intervention/Control
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Intervention
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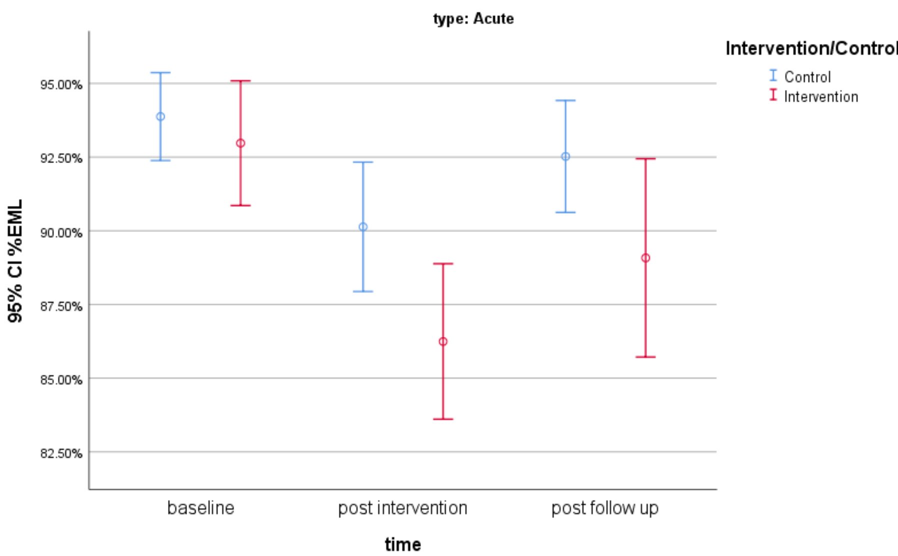
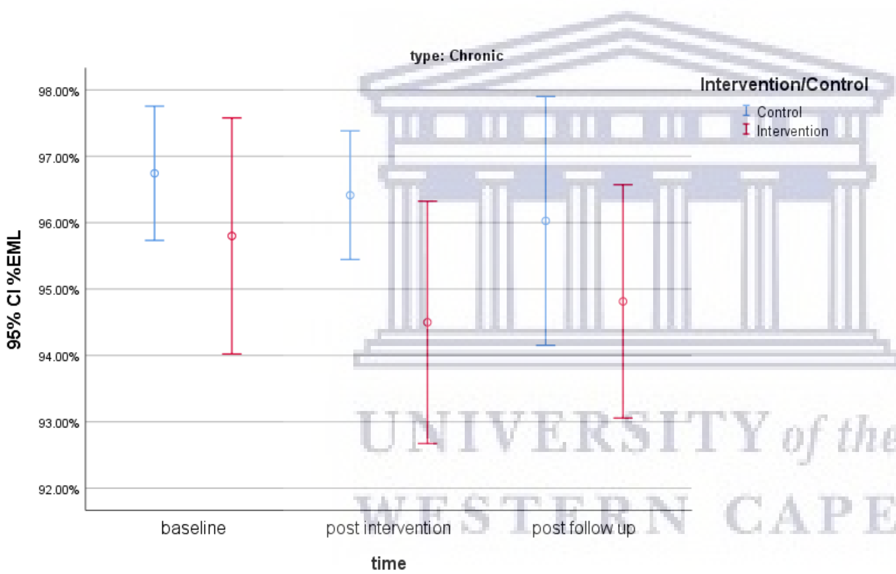
baseline
post intervention
post follow up
time





The effect of intervention on the outcomes over time, while controlling for confounders

Analysis was done at the facility level. Within subjects effect of time (3 time points: baseline, post intervention, post follow up) and type (chronic or acute) were specified as well as between subjects effects of level of care (1 or 2), region (4 regions), and group (intervention or control). Repeated measures ANOVA testing was used with a full factorial model. The model was y = intercept + region + level + group + (region*level)+ (region*group)+ (level*group)+ (region*level*group). The within-subjects design was time +type+ (time*type). Time * group interaction effects (effect of the intervention) were plotted on profile plots with adjusted marginal means. The analysis was used for the outcomes which were relatively normally distributed ie number of drugs, percent generics, and percent antibiotics.

Number of Drugs:

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.
time	Pillai's Trace	.071	.653[b]	2.000	17.000	.533
	Wilks' Lambda	.929	.653[b]	2.000	17.000	.533
	Hotelling's Trace	.077	.653[b]	2.000	17.000	.533
	Roy's Largest Root	.077	.653[b]	2.000	17.000	.533
time * Region	Pillai's Trace	.146	.471	6.000	36.000	.825
	Wilks' Lambda	.858	.449[b]	6.000	34.000	.840
	Hotelling's Trace	.160	.427	6.000	32.000	.855
	Roy's Largest Root	.122	.734[c]	3.000	18.000	.545
time * LevelofCare	Pillai's Trace	.030	.265[b]	2.000	17.000	.770
	Wilks' Lambda	.970	.265[b]	2.000	17.000	.770
	Hotelling's Trace	.031	.265[b]	2.000	17.000	.770
	Roy's Largest Root	.031	.265[b]	2.000	17.000	.770
time * group	Pillai's Trace	.034	.298[b]	2.000	17.000	.746
	Wilks' Lambda	.966	.298[b]	2.000	17.000	.746
	Hotelling's Trace	.035	.298[b]	2.000	17.000	.746
	Roy's Largest Root	.035	.298[b]	2.000	17.000	.746
time * Region * LevelofCare	Pillai's Trace	.131	.422	6.000	36.000	.860
	Wilks' Lambda	.872	.403[b]	6.000	34.000	.872
	Hotelling's Trace	.144	.383	6.000	32.000	.884
	Roy's Largest Root	.112	.671[c]	3.000	18.000	.581
time * Region * group	Pillai's Trace	.242	.826	6.000	36.000	.558
	Wilks' Lambda	.762	.825[b]	6.000	34.000	.558
	Hotelling's Trace	.307	.820	6.000	32.000	.563
	Roy's Largest Root	.290	1.741[c]	3.000	18.000	.194
time * LevelofCare * group	Pillai's Trace	.059	.529[b]	2.000	17.000	.599
	Wilks' Lambda	.941	.529[b]	2.000	17.000	.599
	Hotelling's Trace	.062	.529[b]	2.000	17.000	.599
	Roy's Largest Root	.062	.529[b]	2.000	17.000	.599
type	Pillai's Trace	.832	89.235[b]	1.000	18.000	.000

	Wilks' Lambda	.168	89.235[b]	1.000	18.000	.000
	Hotelling's Trace	4.958	89.235[b]	1.000	18.000	.000
	Roy's Largest Root	4.958	89.235[b]	1.000	18.000	.000
type * Region	Pillai's Trace	.291	2.468[b]	3.000	18.000	.095
	Wilks' Lambda	.709	2.468[b]	3.000	18.000	.095
	Hotelling's Trace	.411	2.468[b]	3.000	18.000	.095
	Roy's Largest Root	.411	2.468[b]	3.000	18.000	.095
type * LevelofCare	Pillai's Trace	.363	10.248[b]	1.000	18.000	.005
	Wilks' Lambda	.637	10.248[b]	1.000	18.000	.005
	Hotelling's Trace	.569	10.248[b]	1.000	18.000	.005
	Roy's Largest Root	.569	10.248[b]	1.000	18.000	.005
type * group	Pillai's Trace	.089	1.761[b]	1.000	18.000	.201
	Wilks' Lambda	.911	1.761[b]	1.000	18.000	.201
	Hotelling's Trace	.098	1.761[b]	1.000	18.000	.201
	Roy's Largest Root	.098	1.761[b]	1.000	18.000	.201
type * Region * LevelofCare	Pillai's Trace	.219	1.686[b]	3.000	18.000	.206
	Wilks' Lambda	.781	1.686[b]	3.000	18.000	.206
	Hotelling's Trace	.281	1.686[b]	3.000	18.000	.206
	Roy's Largest Root	.281	1.686[b]	3.000	18.000	.206
type * Region * group	Pillai's Trace	.051	.324[b]	3.000	18.000	.808
	Wilks' Lambda	.949	.324[b]	3.000	18.000	.808
	Hotelling's Trace	.054	.324[b]	3.000	18.000	.808
	Roy's Largest Root	.054	.324[b]	3.000	18.000	.808
type * LevelofCare * group	Pillai's Trace	.042	.788[b]	1.000	18.000	.386
	Wilks' Lambda	.958	.788[b]	1.000	18.000	.386
	Hotelling's Trace	.044	.788[b]	1.000	18.000	.386
	Roy's Largest Root	.044	.788[b]	1.000	18.000	.386
time * type	Pillai's Trace	.009	.077[b]	2.000	17.000	.926
	Wilks' Lambda	.991	.077[b]	2.000	17.000	.926
	Hotelling's Trace	.009	.077[b]	2.000	17.000	.926
	Roy's Largest Root	.009	.077[b]	2.000	17.000	.926
time * type * Region	Pillai's Trace	.288	1.008	6.000	36.000	.435
	Wilks' Lambda	.716	1.029[b]	6.000	34.000	.423
	Hotelling's Trace	.391	1.042	6.000	32.000	.417
	Roy's Largest Root	.376	2.257[c]	3.000	18.000	.117
time * type * LevelofCare	Pillai's Trace	.135	1.327[b]	2.000	17.000	.291
	Wilks' Lambda	.865	1.327[b]	2.000	17.000	.291
	Hotelling's Trace	.156	1.327[b]	2.000	17.000	.291

	Roy's Largest Root	.156	1.327[b]	2.000	17.000	.291
time * type * group	Pillai's Trace	.064	.583[b]	2.000	17.000	.569
	Wilks' Lambda	.936	.583[b]	2.000	17.000	.569
	Hotelling's Trace	.069	.583[b]	2.000	17.000	.569
	Roy's Largest Root	.069	.583[b]	2.000	17.000	.569
time * type * Region * LevelofCare	Pillai's Trace	.633	2.779	6.000	36.000	.025
	Wilks' Lambda	.465	2.644[b]	6.000	34.000	.033
	Hotelling's Trace	.940	2.506	6.000	32.000	.042
	Roy's Largest Root	.570	3.419[c]	3.000	18.000	.040
time * type * Region * group	Pillai's Trace	.396	1.482	6.000	36.000	.212
	Wilks' Lambda	.612	1.579[b]	6.000	34.000	.183
	Hotelling's Trace	.622	1.658	6.000	32.000	.164
	Roy's Largest Root	.600	3.603[c]	3.000	18.000	.034
time * type * LevelofCare * group	Pillai's Trace	.179	1.859[b]	2.000	17.000	.186
	Wilks' Lambda	.821	1.859[b]	2.000	17.000	.186
	Hotelling's Trace	.219	1.859[b]	2.000	17.000	.186
	Roy's Largest Root	.219	1.859[b]	2.000	17.000	.186

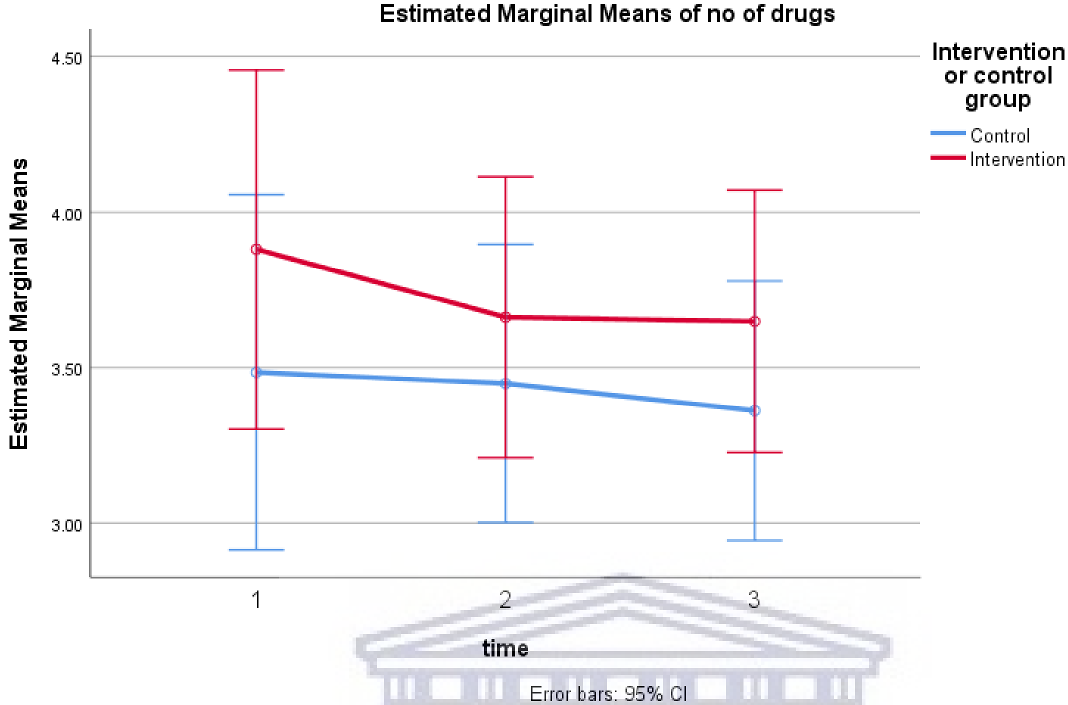
a. Design: Intercept + Region + LevelofCare + group + Region * LevelofCare + Region * group + LevelofCare * group + Region * LevelofCare * group

Within Subjects Design: time + type + time * type

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

There was no interaction between time and group for number of drugs even after adjusting for all other coviariates (p=0.746). The plot below shows that the intervention group had slightly higher mean number of drugs throughout the three time periods and that there was a slight decrease over time in both groups.



Percent generics

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.
time	Pillai's Trace	.390	5.428[b]	2.000	17.000	.015
	Wilks' Lambda	.610	5.428[b]	2.000	17.000	.015
	Hotelling's Trace	.639	5.428[b]	2.000	17.000	.015
	Roy's Largest Root	.639	5.428[b]	2.000	17.000	.015
time * Region	Pillai's Trace	.176	.581	6.000	36.000	.743
	Wilks' Lambda	.831	.551[b]	6.000	34.000	.765
	Hotelling's Trace	.196	.522	6.000	32.000	.787
	Roy's Largest Root	.132	.793[c]	3.000	18.000	.514
time * LevelofCare	Pillai's Trace	.062	.559[b]	2.000	17.000	.582
	Wilks' Lambda	.938	.559[b]	2.000	17.000	.582
	Hotelling's Trace	.066	.559[b]	2.000	17.000	.582
	Roy's Largest Root	.066	.559[b]	2.000	17.000	.582
time * group	Pillai's Trace	.020	.174[b]	2.000	17.000	.842
	Wilks' Lambda	.980	.174[b]	2.000	17.000	.842

	Hotelling's Trace	.020	.174[b]	2.000	17.000	.842
	Roy's Largest Root	.020	.174[b]	2.000	17.000	.842
time * Region * LevelofCare	Pillai's Trace	.155	.502	6.000	36.000	.802
	Wilks' Lambda	.850	.481[b]	6.000	34.000	.818
	Hotelling's Trace	.172	.458	6.000	32.000	.834
	Roy's Largest Root	.135	.809[c]	3.000	18.000	.505
time * Region * group	Pillai's Trace	.132	.426	6.000	36.000	.857
	Wilks' Lambda	.868	.416[b]	6.000	34.000	.863
	Hotelling's Trace	.152	.405	6.000	32.000	.870
	Roy's Largest Root	.149	.895[c]	3.000	18.000	.463
time * LevelofCare * group	Pillai's Trace	.008	.072[b]	2.000	17.000	.931
	Wilks' Lambda	.992	.072[b]	2.000	17.000	.931
	Hotelling's Trace	.008	.072[b]	2.000	17.000	.931
	Roy's Largest Root	.008	.072[b]	2.000	17.000	.931
time * Region * LevelofCare * group	Pillai's Trace	.000	.[b]	.000	.000	.
	Wilks' Lambda	1.000	.[b]	.000	17.500	.
	Hotelling's Trace	.000	.[b]	.000	2.000	.
	Roy's Largest Root	.000	.000[b]	2.000	16.000	1.000
type	Pillai's Trace	.125	2.562[b]	1.000	18.000	.127
	Wilks' Lambda	.875	2.562[b]	1.000	18.000	.127
	Hotelling's Trace	.142	2.562[b]	1.000	18.000	.127
	Roy's Largest Root	.142	2.562[b]	1.000	18.000	.127
type * Region	Pillai's Trace	.024	.145[b]	3.000	18.000	.931
	Wilks' Lambda	.976	.145[b]	3.000	18.000	.931
	Hotelling's Trace	.024	.145[b]	3.000	18.000	.931
	Roy's Largest Root	.024	.145[b]	3.000	18.000	.931
type * LevelofCare	Pillai's Trace	.018	.327[b]	1.000	18.000	.574
	Wilks' Lambda	.982	.327[b]	1.000	18.000	.574
	Hotelling's Trace	.018	.327[b]	1.000	18.000	.574
	Roy's Largest Root	.018	.327[b]	1.000	18.000	.574
type * group	Pillai's Trace	.032	.587[b]	1.000	18.000	.453
	Wilks' Lambda	.968	.587[b]	1.000	18.000	.453
	Hotelling's Trace	.033	.587[b]	1.000	18.000	.453
	Roy's Largest Root	.033	.587[b]	1.000	18.000	.453
type * Region * LevelofCare	Pillai's Trace	.086	.562[b]	3.000	18.000	.647
	Wilks' Lambda	.914	.562[b]	3.000	18.000	.647
	Hotelling's Trace	.094	.562[b]	3.000	18.000	.647
	Roy's Largest Root	.094	.562[b]	3.000	18.000	.647

type * Region * group	Pillai's Trace	.177	1.291[b]	3.000	18.000	.308
	Wilks' Lambda	.823	1.291[b]	3.000	18.000	.308
	Hotelling's Trace	.215	1.291[b]	3.000	18.000	.308
	Roy's Largest Root	.215	1.291[b]	3.000	18.000	.308
type * LevelofCare * group	Pillai's Trace	.018	.332[b]	1.000	18.000	.571
	Wilks' Lambda	.982	.332[b]	1.000	18.000	.571
	Hotelling's Trace	.018	.332[b]	1.000	18.000	.571
	Roy's Largest Root	.018	.332[b]	1.000	18.000	.571
type * Region * LevelofCare * group	Pillai's Trace	.000	.[b]	.000	.000	.
	Wilks' Lambda	1.000	.[b]	.000	18.000	.
	Hotelling's Trace	.000	.[b]	.000	2.000	.
	Roy's Largest Root	.000	.000[b]	1.000	17.000	1.000
time * type	Pillai's Trace	.441	6.704[b]	2.000	17.000	.007
	Wilks' Lambda	.559	6.704[b]	2.000	17.000	.007
	Hotelling's Trace	.789	6.704[b]	2.000	17.000	.007
	Roy's Largest Root	.789	6.704[b]	2.000	17.000	.007
time * type * Region	Pillai's Trace	.135	.433	6.000	36.000	.852
	Wilks' Lambda	.866	.424[b]	6.000	34.000	.858
	Hotelling's Trace	.155	.413	6.000	32.000	.865
	Roy's Largest Root	.153	.916[c]	3.000	18.000	.453
time * type * LevelofCare	Pillai's Trace	.067	.612[b]	2.000	17.000	.554
	Wilks' Lambda	.933	.612[b]	2.000	17.000	.554
	Hotelling's Trace	.072	.612[b]	2.000	17.000	.554
	Roy's Largest Root	.072	.612[b]	2.000	17.000	.554
time * type * group	Pillai's Trace	.072	.657[b]	2.000	17.000	.531
	Wilks' Lambda	.928	.657[b]	2.000	17.000	.531
	Hotelling's Trace	.077	.657[b]	2.000	17.000	.531
	Roy's Largest Root	.077	.657[b]	2.000	17.000	.531
time * type * Region * LevelofCare	Pillai's Trace	.182	.602	6.000	36.000	.726
	Wilks' Lambda	.826	.569[b]	6.000	34.000	.752
	Hotelling's Trace	.201	.536	6.000	32.000	.777
	Roy's Largest Root	.113	.678[c]	3.000	18.000	.577
time * type * Region * group	Pillai's Trace	.330	1.185	6.000	36.000	.336
	Wilks' Lambda	.694	1.134[b]	6.000	34.000	.364
	Hotelling's Trace	.405	1.081	6.000	32.000	.394
	Roy's Largest Root	.281	1.687[c]	3.000	18.000	.205
time * type * LevelofCare * group	Pillai's Trace	.139	1.372[b]	2.000	17.000	.280
	Wilks' Lambda	.861	1.372[b]	2.000	17.000	.280

	Hotelling's Trace	.161	1.372[b]	2.000	17.000	.280
	Roy's Largest Root	.161	1.372[b]	2.000	17.000	.280
time * type * Region * LevelofCare * group	Pillai's Trace	.000	.[b]	.000	.000	.
	Wilks' Lambda	1.000	.[b]	.000	17.500	.
	Hotelling's Trace	.000	.[b]	.000	2.000	.
	Roy's Largest Root	.000	.000[b]	2.000	16.000	1.000

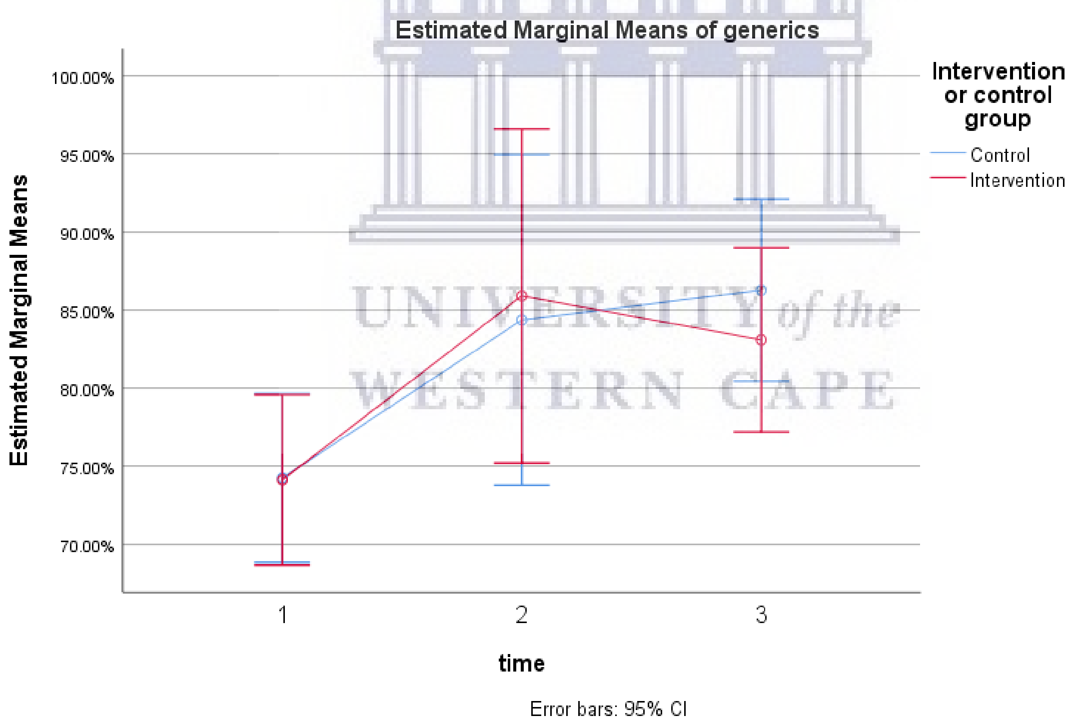
a. Design: Intercept + Region + LevelofCare + group + Region * LevelofCare + Region * group + LevelofCare * group + Region * LevelofCare * group

Within Subjects Design: time + type + time * type

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

For percent generics the time effect was significant (p=0.015) indicating that both groups increased significantly over time. There was no significant effect of the intervention over time (p=0.453).



Percent antibiotics

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.
time	Pillai's Trace	.306	3.742[b]	2.000	17.000	.045
	Wilks' Lambda	.694	3.742[b]	2.000	17.000	.045
	Hotelling's Trace	.440	3.742[b]	2.000	17.000	.045
	Roy's Largest Root	.440	3.742[b]	2.000	17.000	.045
time * Region	Pillai's Trace	.159	.519	6.000	36.000	.790
	Wilks' Lambda	.844	.501[b]	6.000	34.000	.803
	Hotelling's Trace	.181	.482	6.000	32.000	.817
	Roy's Largest Root	.154	.926[c]	3.000	18.000	.448
time * LevelofCare	Pillai's Trace	.074	.684[b]	2.000	17.000	.518
	Wilks' Lambda	.926	.684[b]	2.000	17.000	.518
	Hotelling's Trace	.080	.684[b]	2.000	17.000	.518
	Roy's Largest Root	.080	.684[b]	2.000	17.000	.518
time * group	Pillai's Trace	.090	.842[b]	2.000	17.000	.448
	Wilks' Lambda	.910	.842[b]	2.000	17.000	.448
	Hotelling's Trace	.099	.842[b]	2.000	17.000	.448
	Roy's Largest Root	.099	.842[b]	2.000	17.000	.448
time * Region * LevelofCare	Pillai's Trace	.155	.502	6.000	36.000	.802
	Wilks' Lambda	.846	.495[b]	6.000	34.000	.808
	Hotelling's Trace	.182	.485	6.000	32.000	.815
	Roy's Largest Root	.179	1.075[c]	3.000	18.000	.385
time * Region * group	Pillai's Trace	.117	.374	6.000	36.000	.891
	Wilks' Lambda	.883	.364[b]	6.000	34.000	.896
	Hotelling's Trace	.132	.353	6.000	32.000	.903
	Roy's Largest Root	.130	.783[c]	3.000	18.000	.519
time * LevelofCare * group	Pillai's Trace	.068	.617[b]	2.000	17.000	.551
	Wilks' Lambda	.932	.617[b]	2.000	17.000	.551
	Hotelling's Trace	.073	.617[b]	2.000	17.000	.551
	Roy's Largest Root	.073	.617[b]	2.000	17.000	.551
time * Region * LevelofCare * group	Pillai's Trace	.000	.[b]	.000	.000	.
	Wilks' Lambda	1.000	.[b]	.000	17.500	.
	Hotelling's Trace	.000	.[b]	.000	2.000	.
	Roy's Largest Root	.000	.000[b]	2.000	16.000	1.000
type	Pillai's Trace	.952	359.206[b]	1.000	18.000	.000
	Wilks' Lambda	.048	359.206[b]	1.000	18.000	.000
	Hotelling's Trace	19.956	359.206[b]	1.000	18.000	.000
	Roy's Largest Root	19.956	359.206[b]	1.000	18.000	.000
type * Region	Pillai's Trace	.325	2.890[b]	3.000	18.000	.064

	Wilks' Lambda	.675	2.890[b]	3.000	18.000	.064
	Hotelling's Trace	.482	2.890[b]	3.000	18.000	.064
	Roy's Largest Root	.482	2.890[b]	3.000	18.000	.064
type * LevelofCare	Pillai's Trace	.044	.825[b]	1.000	18.000	.376
	Wilks' Lambda	.956	.825[b]	1.000	18.000	.376
	Hotelling's Trace	.046	.825[b]	1.000	18.000	.376
	Roy's Largest Root	.046	.825[b]	1.000	18.000	.376
type * group	Pillai's Trace	.227	5.282[b]	1.000	18.000	.034
	Wilks' Lambda	.773	5.282[b]	1.000	18.000	.034
	Hotelling's Trace	.293	5.282[b]	1.000	18.000	.034
	Roy's Largest Root	.293	5.282[b]	1.000	18.000	.034
type * Region * LevelofCare	Pillai's Trace	.323	2.863[b]	3.000	18.000	.066
	Wilks' Lambda	.677	2.863[b]	3.000	18.000	.066
	Hotelling's Trace	.477	2.863[b]	3.000	18.000	.066
	Roy's Largest Root	.477	2.863[b]	3.000	18.000	.066
type * Region * group	Pillai's Trace	.266	2.170[b]	3.000	18.000	.127
	Wilks' Lambda	.734	2.170[b]	3.000	18.000	.127
	Hotelling's Trace	.362	2.170[b]	3.000	18.000	.127
	Roy's Largest Root	.362	2.170[b]	3.000	18.000	.127
type * LevelofCare * group	Pillai's Trace	.260	6.321[b]	1.000	18.000	.022
	Wilks' Lambda	.740	6.321[b]	1.000	18.000	.022
	Hotelling's Trace	.351	6.321[b]	1.000	18.000	.022
	Roy's Largest Root	.351	6.321[b]	1.000	18.000	.022
type * Region * LevelofCare * group	Pillai's Trace	.000	.[b]	.000	.000	.
	Wilks' Lambda	1.000	.[b]	.000	18.000	.
	Hotelling's Trace	.000	.[b]	.000	2.000	.
	Roy's Largest Root	.000	.000[b]	1.000	17.000	1.000
time * type	Pillai's Trace	.352	4.609[b]	2.000	17.000	.025
	Wilks' Lambda	.648	4.609[b]	2.000	17.000	.025
	Hotelling's Trace	.542	4.609[b]	2.000	17.000	.025
	Roy's Largest Root	.542	4.609[b]	2.000	17.000	.025
time * type * Region	Pillai's Trace	.536	2.198	6.000	36.000	.066
	Wilks' Lambda	.507	2.295[b]	6.000	34.000	.057
	Hotelling's Trace	.889	2.372	6.000	32.000	.052
	Roy's Largest Root	.781	4.687[c]	3.000	18.000	.014
time * type * LevelofCare	Pillai's Trace	.050	.446[b]	2.000	17.000	.647
	Wilks' Lambda	.950	.446[b]	2.000	17.000	.647
	Hotelling's Trace	.053	.446[b]	2.000	17.000	.647

	Roy's Largest Root	.053	.446[b]	2.000	17.000	.647
time * type * group	Pillai's Trace	.030	.262[b]	2.000	17.000	.773
	Wilks' Lambda	.970	.262[b]	2.000	17.000	.773
	Hotelling's Trace	.031	.262[b]	2.000	17.000	.773
	Roy's Largest Root	.031	.262[b]	2.000	17.000	.773
time * type * Region * LevelofCare	Pillai's Trace	.238	.811	6.000	36.000	.569
	Wilks' Lambda	.775	.770[b]	6.000	34.000	.599
	Hotelling's Trace	.273	.729	6.000	32.000	.630
	Roy's Largest Root	.178	1.066[c]	3.000	18.000	.388
time * type * Region * group	Pillai's Trace	.438	1.681	6.000	36.000	.154
	Wilks' Lambda	.609	1.596[b]	6.000	34.000	.178
	Hotelling's Trace	.566	1.510	6.000	32.000	.207
	Roy's Largest Root	.345	2.067[c]	3.000	18.000	.140
time * type * LevelofCare * group	Pillai's Trace	.131	1.285[b]	2.000	17.000	.302
	Wilks' Lambda	.869	1.285[b]	2.000	17.000	.302
	Hotelling's Trace	.151	1.285[b]	2.000	17.000	.302
	Roy's Largest Root	.151	1.285[b]	2.000	17.000	.302
time * type * Region * LevelofCare * group	Pillai's Trace	.000	.[b]	.000	.000	.
	Wilks' Lambda	1.000	.[b]	.000	17.500	.
	Hotelling's Trace	.000	.[b]	.000	2.000	.
	Roy's Largest Root	.000	.000[b]	2.000	16.000	1.000

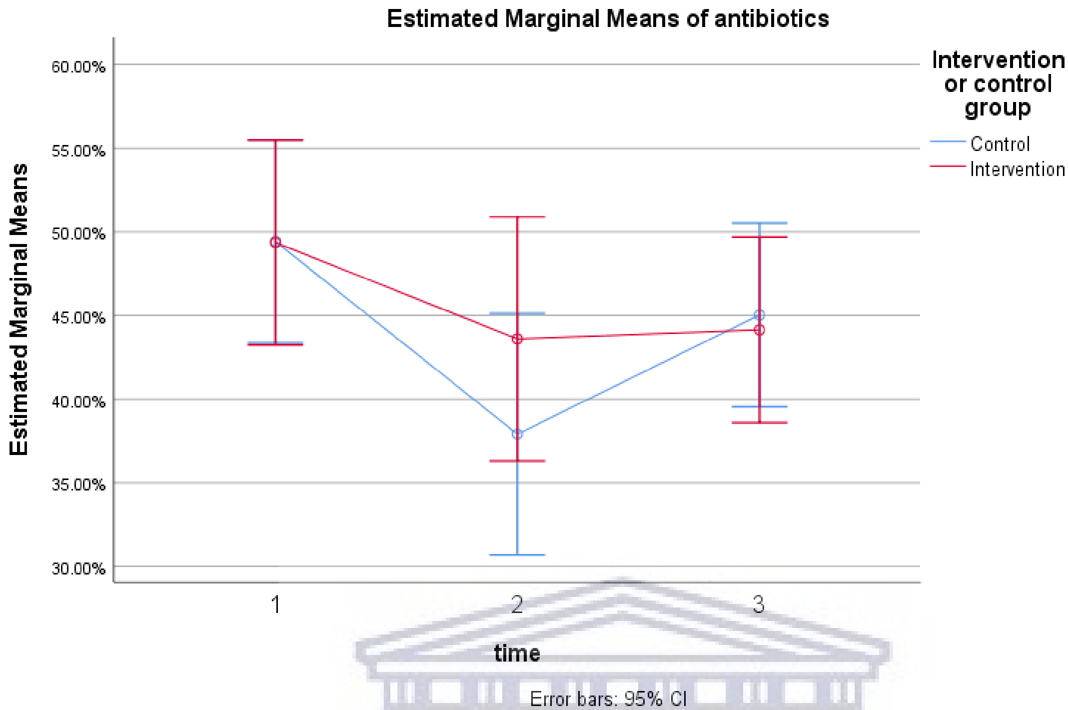
a. Design: Intercept + Region + LevelofCare + group + Region * LevelofCare + Region * group + LevelofCare * group + Region * LevelofCare * group

Within Subjects Design: time + type + time * type

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

There was a general decrease in the percentage of antibiotics used irrespective of intervention (p=0.045). There was no evidence of an intervention effect over time (p=0.448). The profile plot confirms that both groups showed similar trajectories over time.



Percent injections

Acute

Hypothesis Test Summary

Intervention or control group		Null Hypothesis	Test	Sig.	Decision
Control	1	The distributions of Injections.acute: %Injections baseline, Injections_A.acute: %Injections post intervention and Injections_B.acute: %Injections post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.538	Retain the null hypothesis.
Intervention	1	The distributions of Injections.acute: %Injections baseline, Injections_A.acute: %Injections post intervention and Injections_B.acute: %Injections post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.025	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .050.

Chronic

Hypothesis Test Summary

Intervention or control group		Null Hypothesis	Test	Sig.
Control	1	The distributions of Injections.chronic: %Injections baseline, Injections_A.chronic: %Injections post intervention and Injections_B.chronic: %Injections post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.
Intervention	1	The distributions of Injections.chronic: %Injections baseline, Injections_A.chronic: %Injections post intervention and Injections_B.chronic: %Injections post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.

Asymptotic significances are displayed. The significance level is .050.

EML

Acute

Hypothesis Test Summary

Intervention or control group		Null Hypothesis	Test	Sig.
Control	1	The distributions of EML.acute: %EML baseline, EML_A.acute: %EML post intervention and EML_B.acute: %EML post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.
Intervention	1	The distributions of EML.acute: %EML baseline, EML_A.acute: %EML post intervention and EML_B.acute: %EML post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.

Asymptotic significances are displayed. The significance level is .050.

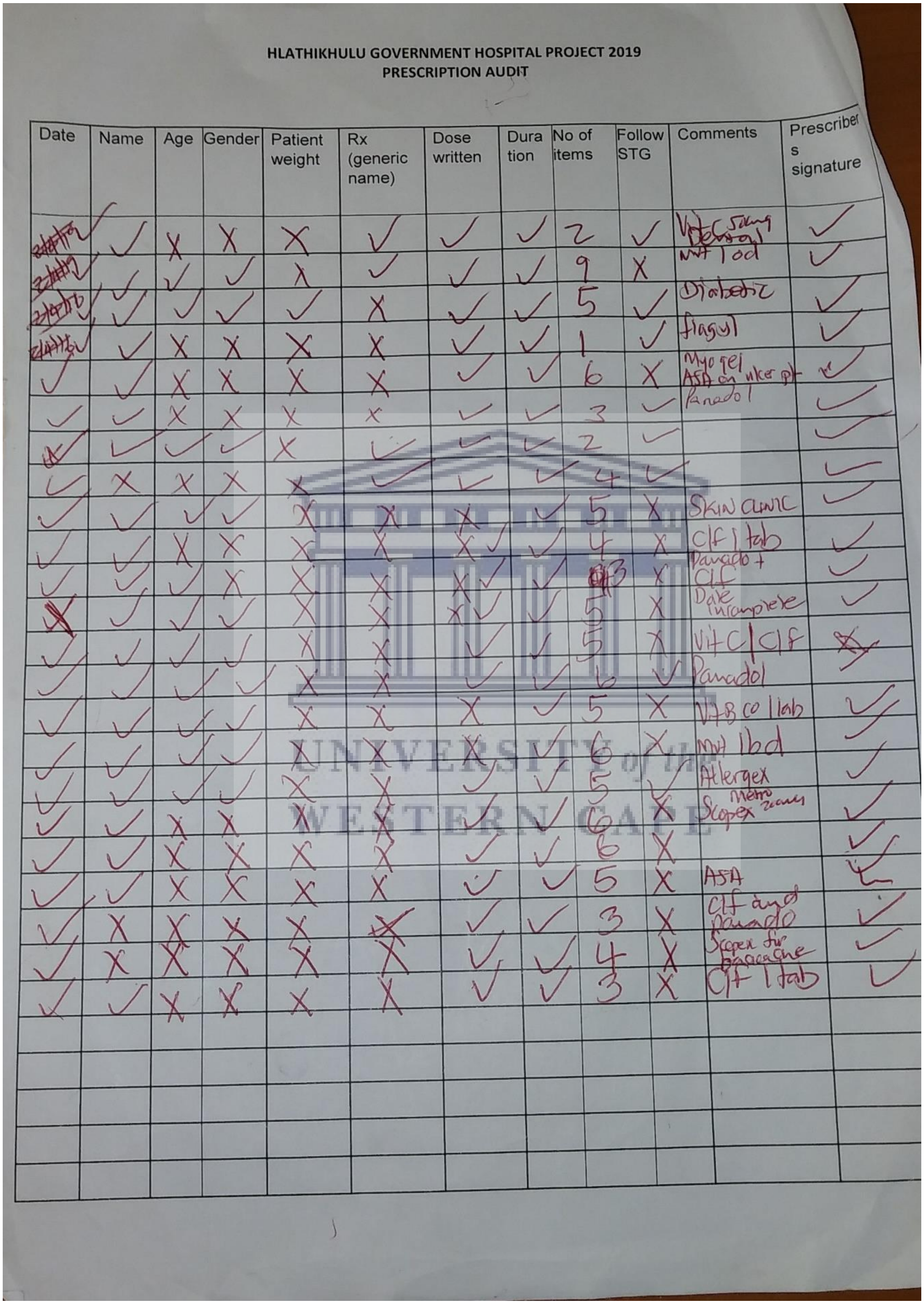
Chronic

Hypothesis Test Summary

Intervention or control group		Null Hypothesis	Test	Sig.
Control	1	The distributions of EML.chronic: %EML baseline, EML_A.chronic: %EML post intervention and EML_B.chronic: %EML post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.
Intervention	1	The distributions of EML.chronic: %EML baseline, EML_A.chronic: %EML post intervention and EML_B.chronic: %EML post followup are the same.	Related-Samples Friedman's Two-Way Analysis of Variance by Ranks	.

Asymptotic significances are displayed. The significance level is .050.

Appendix 17: Data collection tool developed by one of the study facilities



HLATHIKHULU GOVERNMENT HOSPITAL PROJECT 2019
PRESCRIPTION AUDIT

Date	Name	Age	Gender	Patient weight	Rx (generic name)	Dose written	Duration	No of items	Follow STG	Comments	Prescribers signature
2/4/19	✓	X	X	X	✓	✓	✓	2	✓	Vit C 500mg Debrox	✓
2/4/19	✓	✓	✓	X	✓	✓	✓	9	X	MVT 1od	✓
2/4/19	✓	✓	✓	✓	X	✓	✓	5	✓	Diabetic	✓
2/4/19	✓	X	X	X	X	✓	✓	1	✓	Flagyl	✓
✓	✓	X	X	X	X	✓	✓	6	X	Myogel ASA on ulcer pt	✓
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X	✓	✓	✓	X	X	X ✓	✓	5	X	Date incomplete	✓
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✓	✓	X	X	X	X	✓	✓	3	X	C/F 1 tab	✓

Appendix 18: Feedback Meeting 1 Agenda

Rational Medicines Use in Selected Public sector Facilities in Swaziland Programme – 20 February 2018

8: 15am – Registration

8:30am – Introductions and Ice breaker: Ms Sibongile Mabuza

8:45am – Welcome Remarks: Deputy Director Pharmaceutical Services (DDPS): Ms Fortunate Bhembe

9:00am – RMU Study Findings Presentation: Nondumiso Ncube

10:30am -10:45am – Tea break

10:45am – 11:15am – Interventions to promote RMU: Prof Richard Laing

11:15am – 12:15pm – Group work- Priority setting and intervention selection: Dr Hazel Bradley

12:15pm – 12:45pm – Group Feedback & Discussion: Dr Hazel Bradley

12:45pm – Wrap up & Closing Remarks

1:15pm – Lunch

Appendix 19: Feedback meeting 1 participant list

School of Public Health

University of the Western Cape

Private Bag X17

Bellville

Rational Medicine Use Feedback Meeting: 20 February 2018

Name &Surname	Facility	Region	Designation	Phone number	Email address	Signature
~~Thandiwe Mathunjwa~~	~~Cabrini ministries~~	~~Lubombo~~	~~Pharmacy Tech~~	~~23434947~~		Mathunjwa
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Rational Medicine Use Feedback Meeting: 20 February 2018

Name &Surname	Facility	Region	Designation	Phone number	Email address	Signature
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Appendix 20: Feedback meeting 2 agenda

RMU Feedback Meeting Program **4 February 2020**

Program Director: **Ms. Sibongile Mabuza**

1. Introductions
2. Program overview: **Dr. Hazel Bradley**
3. Welcome remarks: **Ms. Fortunate Bhembe (Deputy Director Pharmaceutical Services)**
4. Presentation: **Nondumiso Ncube**
    a. Recap of Baseline Results
    b. Intervention description
    c. Presentation of Post-intervention Results
        i. Quantitative
        ii. Qualitative
    d. Question for clarification
5. Group work: **Prof Richard Laing**
    i. Discuss the key results of the study
    ii. Identify key issues to be addressed in thesis discussion and conclusion sections
6. Vote of thanks: Ms Sibongile Mabuza

Refreshments and follow up discussions

Appendix 21: Feedback meeting 2 participant list

RMU Post Intervention MOH Feedback Meeting
Tuesday 4 February 2020, Mbabane, Eswatini

Name	Designation	Facility	Email	Phone	Signature
Thandiwe Mathunjwa	Pharmacy Technician	St Philips Cabonini		76263075	Tmathunjwa
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RMU Post Intervention MOH Feedback Meeting
Tuesday 4 February 2020, Mbabane, Eswatini

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(2)