Trends in antibiotic consumption in the Namibian Public Health Sector 2010-2016

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KEYWORDS

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Consumption

Distribution

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Patterns

Daily Defined Dose

Resistance patterns

Retrospective study

DEFINITIONS OF KEY TERMS

Anatomic Therapeutic Class (ATC) – is a classification system that uses active pharmaceutical ingredients to classify medicines into a system consisting of five different levels

Antibiotics – substances which inhibit the growth of bacteria or directly destroy the bacteria with the aim of resolving infection

Antibiotic resistance – when bacteria continues to grow in the presence of antibiotic substance which would ordinarily inhibit its growth or destroy it this will mean that the bacteria has become resistant to the antibiotic substance

Antimicrobials – substances which destroying or inhibit the growth of microorganisms which include antibiotics, antivirals, antiprotozoals and antifungals

Antimicrobial resistance – when microorganisms continue to grow in the presence of antimicrobial substance which would ordinarily inhibit its growth or destroy it this will mean that the microorganism has become resistant to the antibiotic substance

Daily Defined Dose – is the assumed average maintenance dose per day for a drug used for its main indication in adults

Daily Defined Dose per 1000 inhabitants per day (DID) – represents the proportion of the selected population using a particular medicine per day

Namibia Essential Medicines List (NEMList) – The NEMList is a list of essential medicines which can be ordered, stored and prescribed at public sector health facilities in Namibia

ABSTRACT

Background Antibiotic resistance is a phenomenon that occurs naturally and is accelerated by use. There have been no studies looking at trends in antibiotic consumption in the public health sector in Namibia, which provides services to 85% of the population.

Aim This study described the pattern of antibiotic consumption in the Namibian public health sector based on distribution of antibiotics from Central Medical Stores (CMS) to the 13 regions in the country.

Methodology Antibiotic consumption data from distribution records at the Central Medical Store (CMS), public health sector wholesaler, between 1 January 2010 and 31 December 2016 was collated and analysed to describe trends and usage patterns in the public health sector of Namibia. For the purpose of this study DDD per 1000 inhabitants per day (DID) was used as an indicator so as to be comparable with previously conducted studies. DIDs provide information about the proportion of the selected population using a particular medicine per day. The World Health Organization (WHO) recommended anatomical therapeutic classification (ATC)/daily defined dose (DDD) methodology be used to analyse the data and evaluate the consumption. Data was presented using stacked bar charts to demonstrate the variation in consumption by ATC classes in each region and over time.

Ethical Considerations Ethical clearance was obtained from the University of the Western Cape Biomedical Research Ethics Committee and permission to access and use the data was provided by the Ministry of Health and Social Services. As the study used retrospective data from the CMS there were no direct interactions with patients or health services staff.

Results and Discussion A total of 227,068 items were issued from the CMS and multi-regional medical stores (MRMS) to the public health facilities in Namibia, during the period under review. Of those items 41,025 (18%) were antibiotics as defined by anatomical therapeutic

classification (ATC) class J01 of the World Health Organization (WHO) classification. Namibia's antibiotic consumption for the public sector increased by 13.2% from 38.31 DID in 2010 to 43.37 DID in 2016, with an average of 41.81 DID during the study period. The antibiotic class with the highest consumption in the public sector was sulphonamide and trimethoprim which made up 51% of the total antibiotic consumption in 2010 and again in 2016. In the sulphonamide and trimethoprim class the co-trimoxazole 80 + 400 mg tablets were the highest consumed item during the period under review, making co-trimoxazole 80 + 400 mg tablets the highest consumed antibiotic formulation in the Namibian public sector. Beta lactam penicillins were the second highest antibiotic class. Among the regions, the lowest consumption was found in Ohangwena region which contributed 6% to the national total, with Zambezi having the highest consumption making up about 13% of national total. The largest increase in consumption within the regions was for Zambezi region which increased by 73% from 2010 to 2016; this increase was followed by 57% in Ohangwena region and 47% in Omaheke.

Conclusion The total national antibiotic consumption for Namibia is classified as high according to the European Surveillance of Antimicrobial Consumption (ESAC) 2010 classification system. The high consumption of sulphonamides and trimethoprim was attributed to the wide use of co-trimoxazole prophylaxis for HIV/AIDS related opportunistic infections. It is therefore imperative that one of the consumption reduction strategies be targeted at reducing the burden of HIV/AIDS with the aim of reducing the requirement for the antibiotic co-trimoxazole. The high consumption of beta lactam penicillins class is ascribed to the fact that beta lactam penicillins are first line treatment in the majority of the cases needing antibiotics in Namibia according to the national Standard Treatment Guidelines.

Recommendations Several recommendations have been formulated. They include: That this study be carried out on an annual basis by each Regional Pharmacist in each region in Namibia. The differences in consumption rates between regions should be further investigated in order to determine the cause of the differences. It was also recommended that all countries use this methodology to determine the consumption of antibiotics with the aim of gathering data to inform interventions to reduce or rationalise the use of antibiotics.

DECLARATION

I hereby declare that this study "**Trends in antibiotic consumption in the Namibian Public Health Sector 2010-2016**" is my own work and it has not been submitted for any degree or examination to any other university, and that all sources I have used or quoted have been indicated and acknowledged by referencing.

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CHAPTER 1: INTRODUCTION

1.1 Introduction

Antibiotic resistance is a phenomenon that occurs naturally, however it is accelerated by overuse or misuse of antibiotics (Centre for Disease Dynamics, Economics & Policy, 2015, 2009; Goossens, 2009; Pereko, et al., 2016; Santa-Ana-Tellez, et al., 2015). This means that the larger the volume of antibiotics used the higher the risk of resistance developing. This is an issue of growing concern for all countries including Namibia and others in Sub-Saharan Africa. Evidence of resistance to antibiotics from the Namibian Institute for Pathology (NIP) indicates that there is an increase in drug resistance in humans in Namibia (MoHSS Namibia, 2017). One of the concerns highlighted by the NIP database is the significant resistance to amoxicillin which is currently the first line treatment for most bacterial infections as per National Standard Treatment Guidelines (STGs). However, insufficiencies in surveillance of drug resistance hampers the process required to understand the challenges and magnitude of issues related to antimicrobial resistance (AMR). In addition, a study conducted on antibiotic usage in the private health sector revealed an increase in the use of antibiotics which was disproportionate to the increase in the population size (Pereko, et al., 2016). The situation in the public health sector, which provides care to 85% of population, is unknown (MoHSS, 2014).

The Centre for Disease Dynamics, Economics & Policy (2015) claims that increased use can also be attributed to rising income levels which provides increased financial means to access antibiotics as well as the increase of antibiotic use in aqua- and agriculture. This is due to increased demand for animal production which leads producers to use antibiotics for growth enhancement (Centre for Disease Dynamics, Economics & Policy, 2015).

Resistance has six main causative pathways (Yap, 2013; WHO, 2017).
These include:

- over-prescribing,
- under-dosing,
- non-therapeutic and sub-therapeutic use of antibiotics in livestock and aquaculture for the purposes of metaphylaxis, prophylaxis as well as growth enhancement,
- poor infection control in hospitals which allows for the spread of ‘superbugs” from patient to patient as nosocomial infections,

- lack of hygiene coupled with poor sanitation among the general public which leads to infections that require treatment with antibiotics further increasing the consumption of antibiotics
- lag in discovery and development of new antibiotic classes (Santa-Ana-Tellez, et al., 2015).

1.2 Problem Statement

Antimicrobial resistance negatively impacts health outcomes and health care costs, driven by the fact that patients with resistant strains are likely to be hospitalized for longer and that the medicines used to treat resistant strains are more expensive than those used to treat susceptible strains (Mohulatsi, 2016). There is also the risk of reversing the gains made possible by the effective treatment of previously curable infections. There is also strong evidence that high consumption of antibiotics translates to high levels of resistance (Wirtz, et al., 2010; Yap, 2013; Pereko, et al., 2015; Centre for Disease Dynamics, Economics & Policy, 2015; Pereko, et al., 2016).

There is evidence of growing resistance to antimicrobials used in the public sector of Namibia (Kibuule, et al., 2017). Resistance to antimicrobials used in the treatment of urinary tract infections (Mengistu, et al., 2014) as well as meningitis (Mengistu, et al., 2013) prompted a change in treatment protocols in Namibia following analysis of antimicrobial sensitivity data that showed growing resistance to the recommended first line therapy. Pereko, et al., (2016) analysed utilization of antibiotics in the Namibian private health sector, however, there have been no studies analysing trends in antibiotic consumption for the public sector which provides health services to 85% of the population of Namibia (MoHSS, 2014). This study addressed this data gap by analysing antibiotic consumption in the public health sector, disaggregated by region and over time.

1.3 Study Setting

Namibia is a country in south-western Africa with an area of about 824,000 square kilometres and a population of 2,113,077 in 2011 (MoHSS Namibia, 2013). The public health sector is divided into 13 Regional Health Directorates which oversee service delivery to 34 health districts. Public health services are provided through one national referral hospital, four intermediate hospitals, 30 district hospitals, 44 health centres, and 269 clinics including mission

hospitals. Due to the vastness of the country, the sparse distribution of the population, and the lack of access to permanent health facilities in some communities, outreach (mobile clinic) services are provided at about 1,150 outreach points across the country (MoHSS Namibia, 2013). The Namibian public health system serves about 85% of the total population with the rest being catered for by the private sector (MoHSS, 2014).

The Namibian Medicines Regulatory Authority (NMRA) is the statutory body that controls medicines intended for humans and animals in both the public and private sectors. A pharmacist or other pharmacy staff may not sell antibiotics without a written prescription from a registered/licensed doctor or veterinarian (MoHSS Namibia, 2017). In line with the World Health Organisation (WHO) recommendations, Namibia's first Essential Medicines List (NEMList) was developed in 1995. It was developed and updated through an evidence-based process conducted by the National Essential Medicines List Committee (MoHSS, 2016). Medicines are classified according to the level of the health care system where they should be available at and may be prescribed at, in line with the Namibian Standard Treatment Guidelines (STGs) (MoHSS, 2016). This classifications means that some medicines are available at all levels of care whilst some are only available at district-, intermediate and tertiary health care hospitals see Appendix 2. The guidelines indicate the treatment protocols to be followed in the country and guide the use of the medicines which are in the NEMList. These guidelines were launched in 2011 and they are the same for all regions. They have not been revised since 2011.

Public sector medicines are procured by the government tender board and distributed to hospitals every six weeks via the Central Medical Stores (CMS). Distribution is via the pull method in which health facility staff determine their needs based on previous consumption data and place orders with their supplier. The CMS Distribution Network is depicted in Appendix 1 for easy reference. Medicines are procured and distributed to the different health facility levels according to their classification in the NEMList (MoHSS, 2016) see Appendix 2.

1.4 Purpose

The purpose of this study was to describe the patterns of antibiotic consumption in the Namibian public health sector over seven years, between 2010 and 2016, desegregated by region, antibiotic class and antibiotic. This study helped identify regions where the rate of consumption of antibiotics per person was changing and those where consumption was stable.

In addition, the pattern of antibiotic use by class of antibiotic was be characterized. This information serves as baseline data for measuring the impact of Namibia's soon to be finalized National Action Plan on Antimicrobial Resistance (Namibia MoHSS, 2017) and for interventions to be developed and implemented through the newly revived antimicrobial stewardship programme. This study highlighted some of the key problem areas of antibiotic use, including areas for further investigation, which will guide future interventions.

CHAPTER 2: LITERATURE REVIEW

2.1 Global

The world's antibiotic consumption increased by 30% from 50 billion to 70 billion units between the years 2000 to 2010 with the highest increase reported in lower middle-income countries (Center for Disease Dynamics, Economics & Policy, 2015). According to Klein, et al., (2018) global antibiotic consumption increased by 39% between 2000 and 2015 from 11.3 to 15.7 DID. This is a concern since an increase in use is associated with an increase in resistance. There are two major contributors to this global increase in consumption. One is the increasing access to antibiotics through increased income which is evidenced by the higher consumption noted in higher income countries. The second is the increasing demand for animal proteins which leads to high use of antibiotics in agriculture to optimize production (Centre for Disease Dynamics, Economics & Policy, 2015).

A study looking at antibiotic usage trends in Latin American countries found there to be substantial variation in antibiotic usage patterns between the countries studied (Wirtz, et al., 2010). In this study consumption was measured using the unit defined daily dose per 1 000 inhabitants per day (DID). The average utilization among the eight countries included increased from 10.92 DID in 1997 to 11.99 in 2007 with Venezuela having a high of 15.99 DID in 2007 and Uruguay a low of 3.93 DID in 1997 (Wirtz, et al., 2010). These differences could be ascribed to socioeconomic factors such as economic crises, which leads to decreased income, as well as policy changes such as prohibition of over the counter antibiotic sales and interventions such as awareness campaigns that can decrease antibiotic consumption as was the case for Chile in 1999 (Wirtz, et al., 2010). Utilization data such as large changes in consumption could also be used to inform further research with the aim of finding out the causes of the change and use that information to strengthen interventions (Wirtz, et al., 2010).

The study by Klein, et al., (2018) used the same ATC/DDD classification system that was used for the above-mentioned study making the results comparable. Klein, et al., (2018) noted an increase of 4%, from 26.8 DID in 2000 to 25.7 DID in 2015, for high income countries (HIC) and an increase of 77%, from 7.6 DID in 2000 to 13.5 DID in 2015, for low and middle income countries (LMICs), leading to the conclusion that global increase of consumption was mostly attributable to high rates of consumption in LMICs. Although the rates for LMICs have

increased faster than that of the HICs the data shows that consumption in HICs is still higher than that in LMICs (Klein, et al., 2018). Klein, et al., (2018) results show that antibiotic consumption for UMICs increased by 78% from 12.0 DID in 2000 to 21.3 DID in 2015.

2.2 Africa and the Southern African Development Community

Literature on public sector consumption data in sub-Saharan African countries is rare as indicated in the recently published report on Surveillance of Antibiotic Consumption 2016-2018 (World Health Organization, 2018). According to WHO (2018) based on 2015 sales data submitted by Burkina Faso, Cote d'Ivore and Burundi as well as 2016 import data provided by Tanzania. The report recorded a total antibiotic consumption of 27.3 DID for Tanzania, Burkina Faso 13.8 DID, Côte d'Ivoire 10.7 DID and Burundi with 4.4 DID. The report also stated that whilst data from other countries were national figures including both public and private sector Burundi only provided data from the public sector (World Health Organization, 2018). When looking at consumption per pharmacological group penicillins were the highest consumed groups taking up 40% of the total consumption in Burkina Faso and Côte d'Ivoire, 27% in Tanzania and 78% in Burundi. For Burkina Faso and Côte d'Ivoire the penicillins were followed by sulfonamides and trimethoprim which were 24% and 31% in Burkina Faso and and Côte d'Ivoire respectively. In Tanzania, the penicillins were followed by tetracyclines which took up 18% of the total consumption and quinolones 14%.

The Resistance Map is a web based data collection tool supported by the Center for Disease Dynamics Economics and Policy which includes antibiotic consumption data from 75 countries from years 2000 to 2014 as obtained from IMSHealth's MIDAS and Xponent databases (The Center for Disease Dynamics Economics and Policy, 2017). The data on this website is reported in daily defined doses (DDDs) per 1,000 population, this unit was then divided by 365 in order for it to become comparable to other data using DID unit. According to this source the antibiotic consumption for South Africa was reported to be on a steady increase from 16.08 DID (2000), 17.35 DID (2004), 27.62 DID (2010), 24.89 DID (2011), 27.62 DID (2012), 29.67 DID (2013), 23.92 DID (2014) to 25.14 DID in 2015 (The Center for Disease Dynamics Economics and Policy, 2017). The South African private health sector also reported an increasing trend in the use of broad-spectrum antibiotics such as penicillins, fluoroquinolones, carbapenems and penems, carbacephems and glycopeptides with annual increases evident from 2008 to 2011 (Essack, et al., 2011). This increase is similar to global trends. A study looking

at antimicrobial prescribing and cost in a South African private sector patient population noted that penicillins accounted for 26.43% of all antimicrobial products prescribed (Truter, 2015). Both of these studies looked at antibiotic consumption in humans.

2.3 Namibia

The total population for Namibia was projected at 2,143,411 million in 2010 and 2,399,057.00 in 2016 (Central Bureau of Statistics, 2006). Its variations per region and over time are indicated in below Table 1 and Figure 1 extracted from Central Bureau of Statistics data (2006).

Table 1: Population by region, Namibia, 2010-2016

Year	Erongo	Hardap	Karas	Kavango	Khomas	Kunene	Ohangwena	Omaheke	Omusati	Oshana	Oshikoto	Otjozondjupa	Zambezi	National
2010	113,573	71,995	73,135	265,373	336,617	76,598	265,992	79,959	245,788	178,665	184,175	163,457	88,084	2,143,411
2011	114,342	72,483	73,630	273,659	348,171	77,581	270,755	81,473	247,948	180,777	187,098	167,051	89,125	2,184,092
2012	115,114	72,972	74,127	282,199	360,116	78,574	275,598	83,013	250,122	182,910	190,065	170,721	90,176	2,225,707
2013	115,882	73,459	74,622	290,984	372,441	79,574	280,507	84,576	252,295	185,054	193,063	174,458	91,233	2,268,150
2014	116,640	73,940	75,110	300,000	385,135	80,577	285,463	86,157	254,453	187,197	196,082	178,252	92,290	2,311,294
2015	117,378	74,407	75,585	309,232	398,179	81,576	290,447	87,748	256,576	189,326	199,107	182,091	93,339	2,354,992
2016	118,087	74,857	76,042	318,657	411,548	82,564	295,434	89,344	258,643	191,425	202,121	185,960	94,374	2,399,057

Source: Central Bureau of Statistics, 2006

As can be seen in Table 1 and Figure 1 Kavango (265,373-2010; 318,657 -2016) and Khomas (336,617-2010; 411,548-2016) regions had the highest population from 2010 to 2016. Hardap (71,995-2010; 74,857 -2016) and Karas (76,042 -2010; 73,135-2016) regions have had the lowest populations from 2010 to 2016.

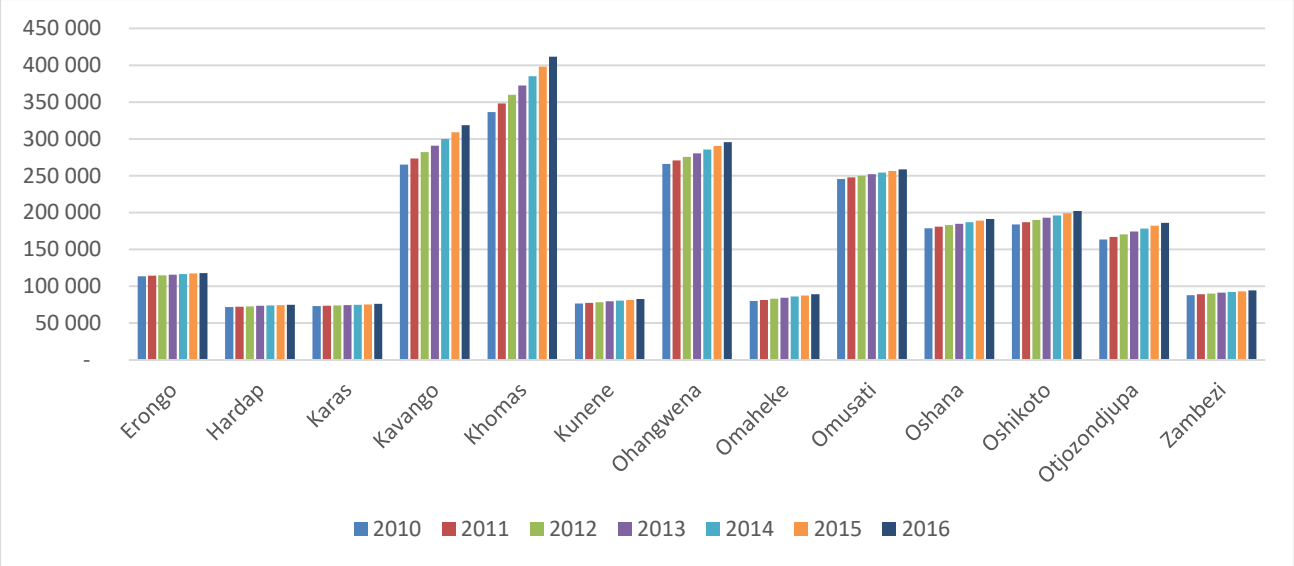
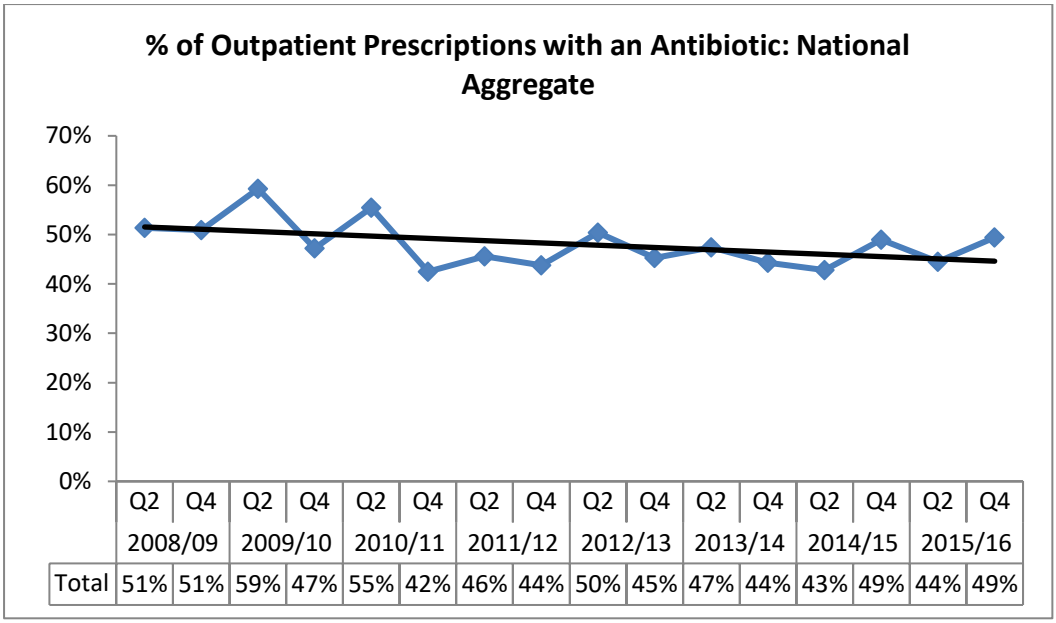


Figure 1: Population by region, Namibia, 2010-2016

In the Namibian public health sector antibiotic use is monitored through an indicator-based system that uses data from the Pharmacy Management Information System (PMIS) which is a data collection system that belongs to the Ministry of Health and Social Services and is adopted from the World Health Organization (WHO). This tool monitors the number of prescriptions with antibiotics in the public health sector but is silent on the actual quantity of antibiotics being consumed (MoHSS, 2012). According to this tool the percentage of outpatient prescriptions containing antibiotics in the Namibian public health sector is well above the WHO acceptable range of 35% (MoHSS, 2012), with figures as high as 55% in 2012 and 49% in 2016 (MoHSS, 2016). The data from these indicators shows that much needs to be done in terms of reducing anti-microbial use in the country (Kibuule, et al., 2017).



Source: (MoHSS, 2016:22)

Figure 2: Percentage of outpatient department prescriptions with an antibiotic, Namibia

The Medicines and Related Substances Control Act of 2003 which regulates medicines distribution in Namibia prohibits the sale of antibiotics without prescription (MoHSS Namibia, 2015). However, there is as yet no system in place to enforce prescription only antibiotic sales since the Namibian Medicines Regulatory Council does not compare dispensing records to prescriptions at the dispensing site. What is in place is that the dispensing records must be retained for at least five years, meaning that if the medicines regulatory body were to inspect, the records would be available to carry out the requisite cross checking between the antibiotics dispensed and the prescriptions presented for those antibiotics in retrospect (MoHSS Namibia, 2015).

Although Namibia has STGs and a NEMList, in place since 2011 and 2002 respectively, aimed at ensuring access to and rational use of medicines, these documents lack "concurrence" in terms of antibiotics. Kibuule, et al., (2017) suggests that this lack of "concurrence" between the treatment guidelines and the essential medicines list may lead to inappropriate use for the items on essential list and not in the guidelines, and possible lack of access for those in the guidelines and not in the list since the list is what determines what is to be procured by the central medical stores (CMS).

A study by Pereko et, al. (2016) looked at antibiotic consumption in the private sector of Namibia and analysed wholesale and prescription data from 2008 to 2011. The results of this study showed a 57% increase in unit sales of antibiotics over the four years using wholesale data (Pereko , et al., 2016). Pereko et, al. (2016) further showed increases in antibiotic consumption from 19.0 to 22.11, 29.05, and 35.41 DID in each of the years 2008 to 2011, respectively. This makes the overall average antibiotic consumption over the total study period in the Namibian private sector to 26.4 DID. According to the European Surveillance of Antimicrobial Consumption (ESAC) classification 2010, consumption figures of >22.38 DIDs are considered high consumers. The Pereko study also found a worrying increase in the use of broad spectrum vs. narrow spectrum antibiotics (Pereko , et al., 2016).. Additionally the study showed penicillins to be the most used antibiotic class, accounting for 39% of all antibiotic use for wholesale data (Pereko et, al 2016). Data for antibiotic consumption in the public human health sector has not yet been analysed in DIDs.

This finding is consistent with the findings in the study conducted in South Africa (Essack, et al., 2011). In the Namibia private sector penicillins were followed by cephalosporins, macrolides, tetracyclines, and quinolones in terms of frequency of use (Pereko et, al 2016). These usage patterns indicated a shift in preference from narrow-spectrum in favour of broad-spectrum antibiotics; this is of concern since broad spectrum antibiotic use accelerates resistance through cross resistance (Pereko et, al 2016).

According to Centre for Disease Dynamics, Economics & Policy (2015) a decrease in consumption of antibiotics could translate in to a decrease in resistance and even a return of potency of some antibiotics to previously resistant strains. This is evidenced by some high-income countries with good stewardship programmes that have led to not only a decline in resistance patterns but also a decrease in the actual quantities consumed (Centre for Disease Dynamics, Economics & Policy, 2015).

2.4 Namibia's National Antimicrobial Resistance Action Plan (NAAP)

The Global Action Plan (GAP) to tackle AMR was endorsed at the 68th World Health Assembly in May 2015 (WHO, 2015). All WHO member states including Namibia agreed to prepare a National AMR Action Plan (NAAP) in line with the GAP. The NAAP was preceded by a situation analysis that was conducted from February 2017 to March 2017 through a highly

consultative process. Key stakeholders from the Ministry of Agriculture, Water and Forestry, Ministry of Health and Social Services, Ministry of Environment and Tourism, Training Institutions, private healthcare facilities and development partners, actively participated in the development process (MoHSS Namibia, 2017).

The NAAP which was based on the findings from the situation analysis had the following key objectives (Namibia MoHSS, 2017):

1. Surveillance – to achieve monitoring capacity through surveillance to capture essential information on AMR and inform decision making
2. Prevention – to reduce the incidence of infection through effective hygiene and Infection Prevention and Control (IPC) measures
3. Antimicrobial use – to optimize the use of antimicrobial medicines in human and animal health
4. Awareness, Collaboration and Communication - to improve awareness, collaboration and communication regarding AMR
5. Education and Training - to improve understanding of AMR through education and training
6. Research and Development – to promote research and development in prevention, medicine use, indigenous knowledge systems and medicinal plants

As can be seen in the NAAP Namibia has adopted the "one health" approach to tackling AMR by ensuring that all key stakeholders have objectives addressed to them to tackle AMR across all sectors (Namibia MoHSS, 2017). This document will therefore serve as a guide for Namibia's anti-microbial stewardship program.

2.5 Consumption of antibiotics measured using WHO ATC classification system and the defined daily dose system

The World Health Organization Anatomic Therapeutic Classification and Daily Defined Dose (WHO ATC/DDD) system is used to analyse and present medicine use information for the purpose of improving use (WHO, 2018). The ATC/DDD system standardizes the unit of measurement and therefore makes medicine use data comparable within and across countries as well as between different health care settings and over time. Within countries the standardised unit makes it possible to compare medicine use over different periods of time and allows for trend analysis (WHO, 2018).

According to WHO (2018) medicine use data based on ATC and DDDs can be used to provide medicine consumption profiles nationally, regionally or for individual health facilities. Data can also be used by health systems to identify medicine use patterns and develop interventions to correct incorrect medicine use practices.

The ATC/DDD system can use data from many sources e.g. sales data, dispensing data, patient encounter based data, patient survey data- which is collected at patient level as well as health facility data (WHO, 2018). The data is reported in units that take into account differences in population size such as DDDs per 1000 inhabitants per day, DDD per inhabitant per year, or as DDDs per 100 bed days (WHO, 2018). This provision allows for comparisons across various time periods and population groups and is good for identifying trends in consumption.

The denominator used during the analysis of medicine use data must be chosen carefully and should depend on the selected health context. WHO (2018) recommends the following denominators:

1. DDD per 1000 inhabitants per day (DID) gives us information about the proportion of the selected population using a particular medicine per day. In an example provided by WHO (2018): The figure 10 DDDs per 1000 inhabitants means that an average of 10 DDDs of medicine are utilized on any given day of the time period under review out of a population of 1000 individuals. Thus 10/1000 (1%) of the population are receiving this drug each day in that year. This denominator is useful when comparing data between regions in a country or between countries.

2. The DDD per 100 bed days is an ideal denominator for studying hospital consumption. A bed day in this case is defined by WHO (2018) as a day when the patient is confined to a bed and stays overnight in that hospital. When using this denominator it is important to ensure that the same definition for bed days is used for any study that you use for comparison purposes. In an example provided by WHO (2018): The figure 70 DDDs per 100 bed days means that 70% of the inpatients receive one DDD of the medicine under review every day.

3. DDD/patient: when the denominator is the patient then treatment intensity is measured (WHO, 2018).

4. DDDs per inhabitant per year: According to WHO (2018) this indicator is ideal for medicines that are used for short durations such as antibiotics. It provides information about how long each inhabitant was treated per year. In an example provided by WHO (2018) 5 DDDs/inhabitant/year indicates that on average each inhabitant consumed 5 days of medicine during the year under review.

For the purpose of this study DID as an indicator was used so as to be comparable with previously conducted studies (Pereko, et al., 2016;Wirtz, et al., 2010). It is important to note that the DDDs only provide for a rough estimate of consumption this is due in part to the fact that the actual dose prescribed is not always equal to the DDD as the actual doses can differ depending on the indication, the age of the patient and the severity of the infection (WHO, 2018).

The anatomic therapeutic class (ATC) classification system uses active pharmaceutical ingredients to classify medicines into a system consisting of five different levels. The first level classifies medicines according to the part of the human system that they work on e.g. group J which consists of anti-infectives. From level two (2) to level four (4) medicines are further broken down into levels based on chemical, pharmacological or therapeutic sub-groups and the fifth (5^{th}) and final level has the codes for the actual chemical substance (WHO, 2018). This concept is tabulated below in an excerpt from Mohulatsi (2016:21). In the below table amoxicillin is used as an example from the anatomical group of anti-infectives for systemic use.

Table 2: An example of ATC classification

Level	Definition	Example
1	Main anatomical group	J- Anti-infectives for systemic use
2	Pharmacological /therapeutic subgroup	J01- Antibacterials for systemic use
3	Pharmacological subgroup	J01C- beta-lactam anti-bacterials, penicillins
4	Chemical sub group	J01CA penicillins with extended spectrum
5	Chemical substance	J01CA04- amoxicillin

Source: Mohulatsi, 2016:21

ATC and DDDs are updated annually and therefore differences can occur between versions of the ATC index. It is therefore important to indicate which index version was used for data compared over time as well as when comparisons are made between different countries at different times (WHO, 2018).

The use of the ATC/DDD classification system fast becoming the tool of choice when it comes to measuring consumption of antibiotics. This is great since it allows one to do comparisons in usage within and between countries when a standard unit is used for analysis. There seems to be an increase in antibiotic consumption worldwide with the pharmaceutical group consisting of penicillins being the biggest contributor to consumption. There is also an increase in preference for broad spectrum antibiotics over the narrow spectrum antibiotics.

CHAPTER 3: METHODOLOGY

3.1. Aim and Objectives

3.1.1 Aim

To describe the pattern of antibiotic consumption in the Namibian public sector based on distribution of antibiotics from Central Medical Stores (CMS) to the 13 Regions between 2010 and 2016.

3.1.2. Objectives

1. To describe antibiotic consumption by volume according to each WHO ATC class between 2010 and 2016.
2. To describe the consumption of selected antibiotics by volume between 2010 and 2016.
3. To describe antibiotic class consumption per region in the Namibian public health sector between 2010 and 2016.

3.2 Study Design

The study used consumption data from distribution records which was collated and analysed to describe trends and usage patterns in the public health sector of Namibia as a trend analysis over a period of seven years. This study utilized the medicine issues data from the central medical stores (CMS) as well as that from the Oshakati multi-regional medical stores, which constitute the public health sector wholesalers in Namibia. Antibiotic usage for the period 1 January 2010 through to 31 December 2016 was investigated.

All medicines and health commodities for the public sector are centrally received by the CMS in Windhoek and distributed either directly to hospitals or through Rundu regional store which caters to the Kavango region and the Oshakati regional medical store which caters to a number of regions as depicted in the CMS distribution network (Appendix 1). This single distribution system ensures optimal reliability, efficiency, and security to support the implementation of health programmes (MoHSS, 2016). This CMS Distribution Network covers all public health facilities in the country which include 36 district hospitals and more than 250 health centres and clinics; this translates to 100 percent coverage of the public health sector. The CMS fleet

delivers supplies to designated sites every six weeks, according to a delivery schedule (MoHSS, 2016).

3.3 Data Sources

Distribution/issues data is data which is generated during distribution of medicines, including antibiotics, to the health facilities, is considered suitable data to use in medicines use reviews (Pereko, et al., 2016; WHO, 2003). The advantage of this data source is that it is readily available and easy to access. For this study, issues data from CMS as well as from Oshakati multi-regional store was used.

The data from CMS and the Oshakati multi-regional store contained the following data elements:

- Stock code – this code is unique to each product strength as well as pack size, this means that each pack size has a different code
- Product description containing generic name
- Total distributed units per year per facility in a region with the exception of those in the region covered by the Rundu Regional medical store

Population information was sourced from Republic of Namibia Population Projections (Central Bureau of Statistics, 2006). Medium variant projection was used due to the fact that there was no reason to expect substantial variations.

3.4 Data Extraction

The population was the units of all antibiotics distributed in the public health sector in the period between 1 January 2010 and 31 December 2016 stratified by year. The NEMList currently contains 146 antimicrobial formulations as listed in the attached Appendix 3. Due to the high burden of tuberculosis and HIV/AIDS, in Namibia (MoHSS Namibia, 2013), it was proposed that these specific groups of antibiotics were not included in this assessment as they may distort the results (WHO, 2003). Consequently, all antibiotics distributed were included in the study. Additionally, only data related to antibiotics for systemic use and belonging to WHO anatomical therapeutic classification (ATC) J01 was collected and analysed (WHO Collaborating Centre for Drug Statistics Methodology, 2018). This means that antibiotics formulated as topicals or eye drops were also excluded.

Data was extracted using all six digits of the ATC code which allowed for analysis by antibiotic group and by individual antibiotics as per the WHO (2017) recommended method for determining DID. The WHO ATC classification and DDD list from WHO 2018 were used (WHO, 2018). Data from 2010 to 2016 was extracted from CMS and Oshakati multi-regional medical store records by the senior pharmacists at these facilities. The data was received in Microsoft Excel® 2010 format.

The researcher compiled a list of the antibiotics that would be included in the study by listing all the medicines in the WHO J01 class that were distributed by CMS between January 2010 and December 2016. This list consisted of 128 different stock items and these items were arranged according to their ATC classification up to level 4 - the description of the medicine, the strength, pack size, specific DDD, route of administration, as well as its unique stock code allocated by the CMS. This unique list of items is attached as Appendix 4. The researcher then provided this list to a statistician to use to extract the data needed from the distribution data from CMS and collate the number of packs issued per item and per region. The data required to complete the data collection tool (Appendix 5) was extracted and collated by the statistician using R (Version 3.2.3, The R Foundation for Statistical Computing) and RStudio (Version 1.1.423, Integrated Development for R, RStudio Inc.). The output of this was a region specific listing of the total volumes issued of each antibiotic per year. The statistician was also able to provide a listing of the total number of items issued by CMS during the period under review, including the proportions that were antibiotics, those used in the analysis and the fraction of items discarded due to missing data or incompatible values –as was the case for negative quantities shipped. This was the extent of the involvement of the statistician.

The senior pharmacist at CMS indicated that these negative values represented credit notes but due to the fact that they only represented 0.29% of the total entries included in the study they were left out of the calculation as it was difficult to determine which year they stemmed from, as some were written up to two years after the date of incorrect issue.

The study variable location and time was identified for analysis to see how geographic location as well as time affected or changed the results of the study through stratification.

3.5 Data Analysis

All of the data analysis was carried out by the researcher using Microsoft Excel®. The WHO recommended ATC/daily defined dose (DDD) methodology was used to evaluate the consumption (WHO Collaborating Centre for Drug Statistics Methodology, 2018). DID, a consumption indicator reported as defined daily dose (DDD) per 1 000 population per day, was used to compare antibiotic use across settings and is a standard measure recommended by WHO (2017) which allows comparisons between countries, regions and over time. Data was presented using stacked bar charts and trend lines which demonstrated the variation in consumption by ATC classes in each region and over time as was done by Wirtz, et al. (2010).

Each antibiotic was assigned a DDD obtained from the WHO Collaborating Centre for Drug Statistics Methodology (WHO, 2018). The DDD is calculated as unit strength × pack size × quantity sold/ DDD assigned. The data source used was kilograms of issues per year aggregated by region which were then converted to DDD per 1000 inhabitants per day (DID) as the unit of analysis. The issues data was then expressed as DDD/1,000 population/day using the following formula:

DDD/1,000/day = (Total consumption in DDDs/Total population covered × 365) × 1,000.

The population used for the issues data was 85% of the Namibian population per region, which is the population estimated to be serviced by the CMS (MoHSS, 2014). The number of days used was 365 days. Results were presented in DDD/1000/day of antibiotics consumed which identified the WHO ATC classes with the highest consumption nationally as well as per region and within the ATC class the specific antibiotic with the highest consumption trend was identified.

3.6 Validity and Reliability

To address validity of this study the WHO guidelines from the Collaborating Centre for Drug Statistics Methodology (2018) was followed throughout the process (WHO Collaborating Centre for Drug Statistics Methodology, 2018). In order to improve reliability all the data on the selected antibiotics was used and data over a large period (7 years) was extracted by the researcher. This minimized the risk to validity since the larger the sample, the more likely it is to be representative of the evaluation population (Chopra & Coveney, 2003) and in this case the "sample" is the whole population. The senior pharmacist at CMS was asked to review the

extracted data to ensure consistency and all queries that arose during data cleaning were discussed with the senior pharmacist at both CMS and the Oshakati Multi-regional store.

3.7 Limitations

DDD is an average unit measure and does not account for actual doses used per individual patients and is also based on average adult dose and not that of a child which means that the DID might have been higher or lower depending on the age distribution of the population consuming that antibiotic (Wirtz, et al., 2010).

In this study secondary data was used which were the issues data from the country's CMS to the public health service facilities. This data was originally recorded for administrative and billing purposes only. From this source, data can be broken down into two components namely cost and volume of antibiotics consumed per given time period per geographical or administrative area. The limitation with using issues data is that not all medicines issued to the facilities are consumed as losses occur from expiries, theft as well as breakage (Wirtz, et al., 2010). However, these losses are likely to be consistent over time and as such changes in issued volumes are likely to reflect real changes in consumption trends. An additional threat to external validity is that some antibiotics were sourced directly by the health facilities during this period from a supplier other than CMS. This form of procurement, known as 'buyouts', is only utilised in very few exceptional cases and was therefore not included in this study since this data is not routinely collected nor readily available and is expected to be minimal (MoHSS, 2016). Another possible limitation with retrospective data is that the data is designed for the purpose of billing and not necessarily for research purposes so there is a chance for inaccuracy and perhaps some data losses. The positive benefit of this data source is that this data is subject to financial audit.

From the total number of items issued by CMS during the period under review, a fraction of items were discarded due to missing data such as negative quantities shipped. The senior pharmacist at CMS indicated that these values represented credit notes but due to the fact that they only represented 0.29% of the total entries included in the study they were left out of the calculation as it was difficult to determine which year they stemmed from, as some were written up to two years after the data of incorrect issue.

3.8. Ethical statement

Ethical clearance for this study was obtained from the University of the Western Cape Biomedical Research Ethics Committee. Permission for access and use of the data for the study was provided by MoHSS. These letters are attached as Appendix 6. As the study involved the use of retrospective data on medicines issues from the CMS, there were direct interactions with patients or health services staff and no risk of direct harm to patients or staff. All the data received from CMS was kept safe and was only accessed by the researcher and the bio statistical consultant. All hard copies of data were stored in a locked cabinet with only the researcher having access. Both electronic data and hard copies will be stored for a period of five years.

The results of this study will be shared with all health professionals at management level in MoHSS and then cascaded down through the official communication channels in order for it to reach all health care workers in the health sector including those involved in anti-microbial stewardship programme.

CHAPTER 4: RESULTS

4.1 Introduction

This chapter describes the findings of the study, which described the pattern of antibiotic consumption in the Namibian public sector between 2010 and 2016 based on distribution of antibiotics from Central Medical Stores (CMS) to the 13 Regions between 2010 and 2016.

A total of 227,068 items were issued from the CMS and multi-regional medical stores (MRMS), to the public health facilities in Namibia, during the period under review. Of those items 41,025 (18%) were antibiotics as defined by anatomical therapeutic classification (ATC) class J01 of the WHO classification (WHO, 2018). Of those 41,025 a total of 120 (0.29%) items were found to have negative issued quantities. According to the senior pharmacist at CMS these were credits issued to the facilities and cannot be allocated to a particular year as these credits could overlap in years. The researcher then decided to exclude these 120 (0.29%) entries from the study thus 40,905 items were included in the analysis.

The results are presented as follows for the years 2010 to 2016:

4.2 National trend of antibiotic consumption by total volume

4.3 National trend of antibiotic consumption by total volume per antibiotic class

4.4 National consumption trends for selected antibiotics by volume

4.5 Regional trends of antibiotic consumption by total volume

4.6 Regional consumption by antibiotic class

Since the public health sector was estimated to serve 85% of the population (MoHSS, 2014), the national and regional DIDs were determined using 85% of the national and regional population figures respectively.

4.2 National trend of antibiotic consumption by total volume

The national antibiotic consumption for the Namibian public sector for the period between 2010 and 2016 is presented in Figure 3. During the period under review the DDD per 1000 inhabitants per day (DID) for the public sector had a steep rise from 38.31 DID in 2010 to 41.48 DID in 2011 from where it dipped slightly to 39.36 DID (2012). From there it rose to 42.70 DID (2013) and 43.31 DID (2014) to a peak of 43.86 DID in 2015 and thereafter there was a slight decrease to 43.37 DID in 2016.

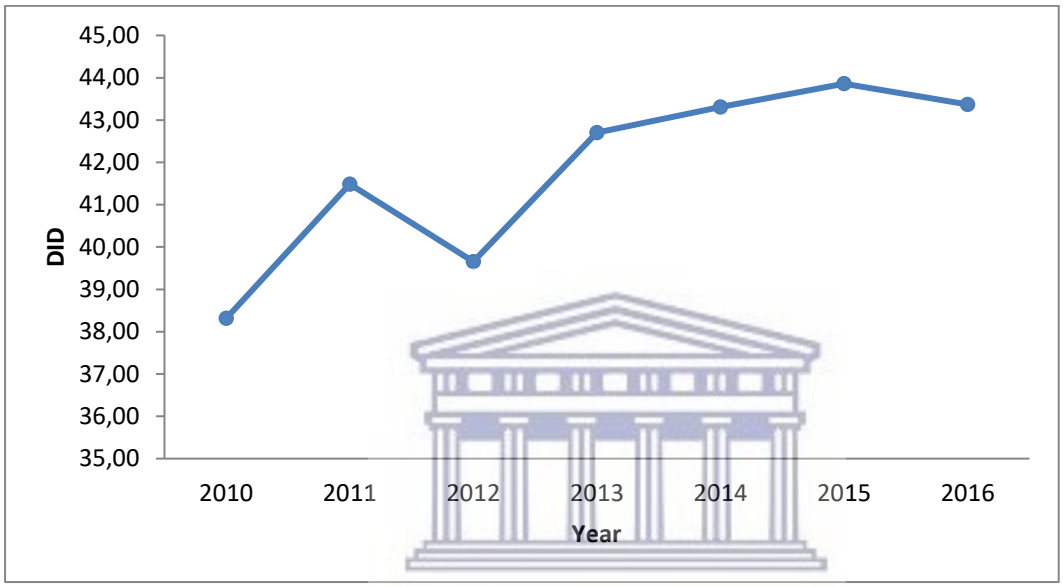


Figure 3: National Antibiotic consumption trend, Namibia, 2010-2016

4.3 National trend of antibiotic consumption per antibiotic class

The consumption per antibiotic class consumed in Namibia was analyzed per year and is presented in Table 3.

Table 3: Trends of national antibiotic consumption in Namibia by antibiotic class, 2010-2016

	Total DID's							% of total consumption 2010	% of total consumption 2016
	2010	2011	2012	2013	2014	2015	2016		
Aminoglycoside antibacterials	0.35	0.31	0.32	0.28	0.45	0.24	0.26	0,91%	0,61%
Amphenicols	0.04	0.03	0.02	0.02	0.01	0.01	0.01	0,11%	0,02%
Beta lactam antibiotics, penicillins	12.39	13.39	10.94	13.13	12.76	12.95	14.17	32,33%	32,66%
Macrolides, lincosamides and streptogramins	1.91	2.25	2.04	2.02	2.24	2.11	2.52	4,99%	5,81%
Other antibacterials	0.18	0.15	0.26	0.32	0.12	0.38	0.37	0,47%	0,86%
Other beta lactam antibacterials	0.78	1.02	1.02	1.13	1.28	1.39	1.10	2,03%	2,54%
Quinolone antibacterials	1.21	1.49	1.22	1.28	1.15	1.04	1.30	3,16%	3,00%
Sulphonamides and trimethoprim	19.40	21.00	22.04	23.22	23.17	24.30	21.99	50,65%	50,69%
Tetracyclines	2.05	1.83	1.79	1.32	2.14	1.44	1.65	5,36%	3,80%
Total	38.31	41.48	39.65	42.70	43.31	43.86	43.37	100,00%	100,00%

**other beta lactam antibacterials include cephalosporins and carbapenems*

**other antibacterials include vancomycin, nitrofurantoin, fusidic acid and linezolid*

In 2010 as presented in Table 3 and depicted in Figure 4, sulphonamides and trimethoprim (51%) had the highest percentage of the total consumption followed by beta-lactam penicillins (32%) and then tetracyclines (5%) macrolides, lincosamides and streptogramins (5%) with and amphenicols and other antibacterials (0%) having the lowest consumption figures. For 2016 the highest consumed antibiotic class was still sulphonamides and trimethoprim (51%) followed by beta lactam penicillins (33%) and then macrolides, lincosamides and streptogramins (6%) as well as tetracyclines (4%). In 2016, amphenicols (0%) had the lowest consumption figures.

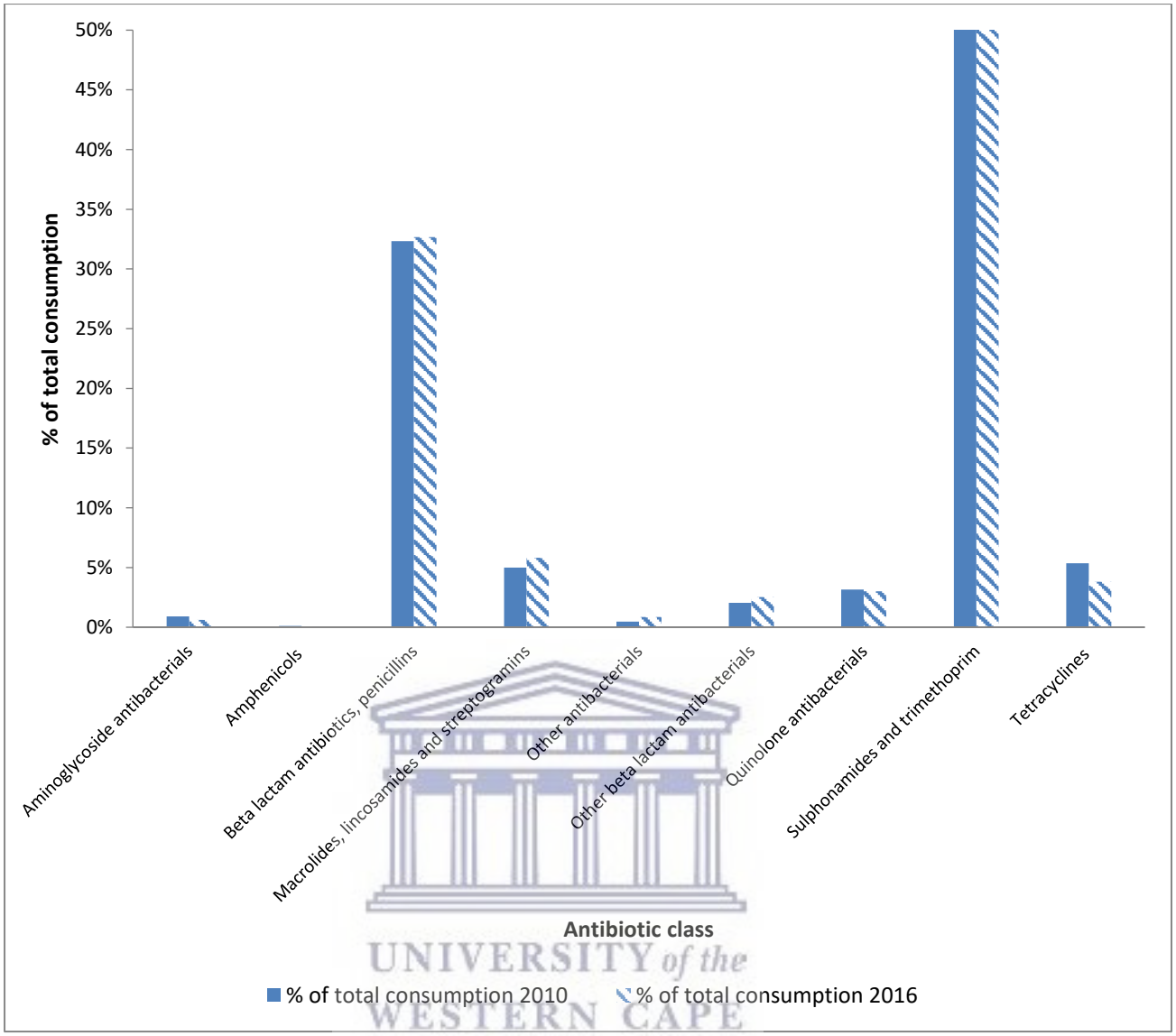


Figure 4: Proportion of total consumption per antibiotic class, Namibia, 2010 & 2016

Table 3 and Figure 5 and show the consumption per antibiotic class. The trend for sulphonamides and trimethoprim had a DID of 19.40 in 2010 followed by a rise to 21.00 in 2011 followed by a steep rise to 22.04 in 2012 and 23.22 in 2013 from where a near steady level was maintained up to 24.30 DID in 2015 which was followed by a drop to 21.99 DID in 2016.The trend for the beta lactam (penicillin) class of antibiotics showed a steep rise from year 2010 12.39 to 13.13 DID in 2013 where after it dropped to 12.76 DID in 2014 and further increased steadily to reach 14.17 DID in 2016.

The trend for the amphenicol class of antibiotics was the lowest consumed of all the classes. It started off at 0.04 DID in 2010 followed by a drop to 0.03 in 2011 where after it further decreased to 0.02 in 2012 and 2013 followed by a decrease to 0.01 DID from 2014 to 2016. The trend for the other beta lactam antibacterials indicated a low consumption of this class as well. The trend showed a DID of 0.78 in 2010 followed by an increase to 1.02 in 2011, there was a rise from 2012 (1.02 DID) to 2013 (1.13 DID) and 1.28 DID in 2014 from where it rose to 1.39 DID in 2015. It then dropped back down to 1.10 DID in 2016.

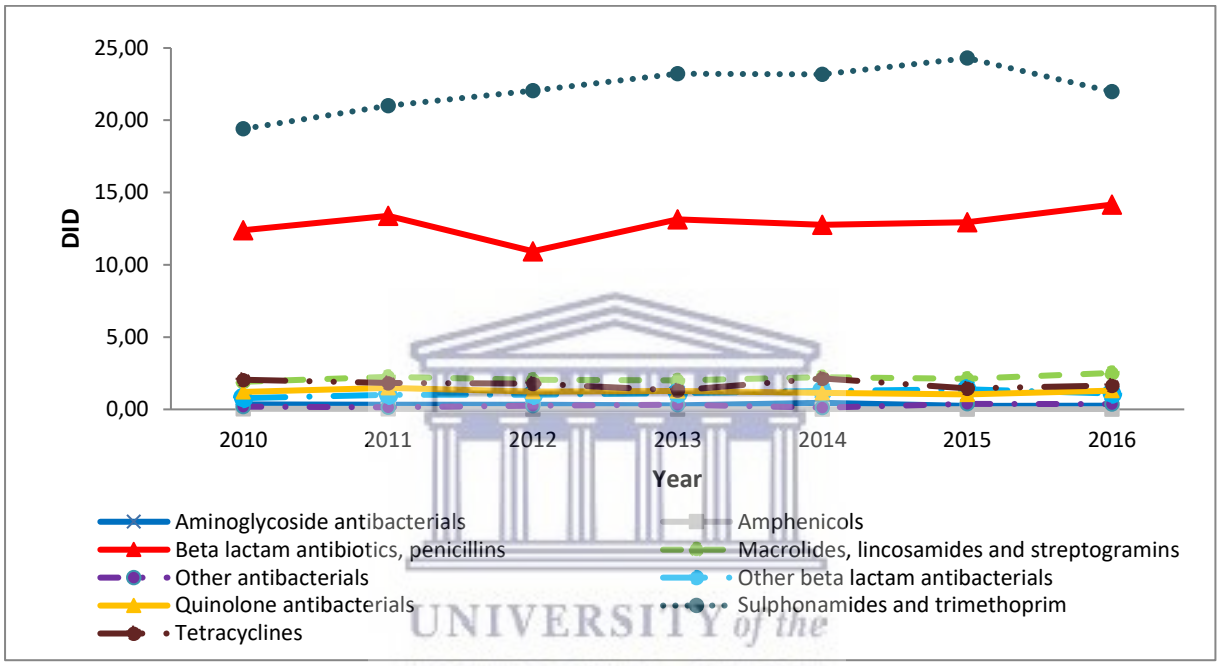


Figure 5: National antibiotic consumption trends per antibiotic classification, Namibia, 2010-2016

4.4 National consumption trends for selected antibiotics by volume between 2010 and 2016

The distribution of the two antibiotic classes with the highest consumption was further analyzed and the results are shown in Tables 4 & 5 and Figure 6 & 7.

Table 4 and Figure 6 show that of all the antibiotics in the sulphonamide and trimethoprim class the co-trimoxazole 80+400mg tabs have the highest consumption in the Namibian public health sector. According to Table 4 co-trimoxazole 80+400mg tabs constituted 83% of the total sulphonamide and trimethoprim antibiotics consumed in 2010 and 86% in 2016. Co-trimoxazole 40/200mg/5ml syrup was the second highest consumed formulation in the class with 11% (2010) and 14% (2016) of the consumption within the group being attributed to this formulation.

Table 4: Consumption trends of sulphonamides and trimethoprim, Namibia, 2010-2016 in DID

	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**% of total 2010**	**% of total 2016**
Co-trimoxazole 160+800mg tabs	1.161	0.214	0	0	0	0	0	5,98%	0,00%
Co-trimoxazole 40/200mg/5ml	2.162	3.389	2.891	3.142	3.406	2.92	3.09	11,14%	14,05%
Co-trimoxazole 80+400mg tabs	16.07	17.4	19.14	20.08	19.76	21.37	18.89	82,84%	85,93%
Co-trimoxazole 80mg/400mg inj	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0,04%	0,02%
Total	**19.40**	**21.00**	**22.04**	**23.22**	**23.17**	**24.30**	**21.99**	**100,00 %**	**100,00 %**

Figure 6 indicates that the consumption for co-trimoxazole 80 + 400 mg tabs was, in line with the national consumption patterns, rose from 16.07 DID (2010) to 17.4 DID (2011) and then to 19.14 DID (2012). From there it rose steadily to 20.08 DID (2013) and to its peak of 21.37 DID in 2015. This rise was followed a slight decrease to 18.89 DID in 2016.

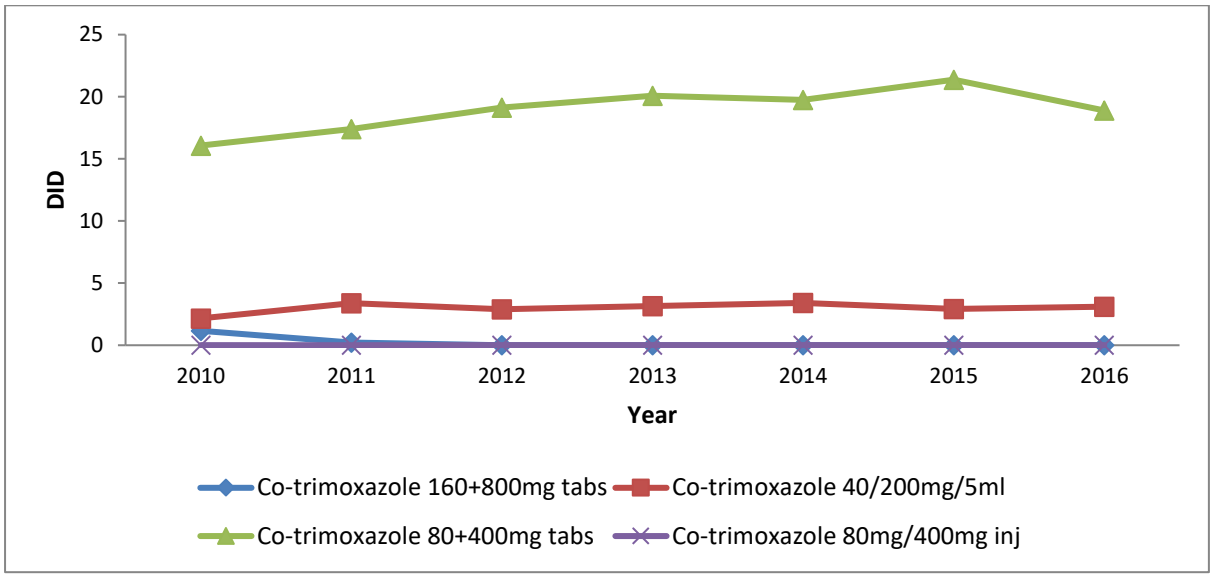


Figure 6: Consumption trends of sulphonamides and trimethoprim, Namibia, 2010-2016

Table 5 and Figure 7 show that of all the antibiotics in the penicillins class, amoxicillin-based formulations have the highest consumption in the Namibian public health sector. According to Table 5, amoxicillin-based formulations constituted 70.75% of the total penicillin class antibiotics consumed in 2010 and 73.04% in 2016, this was followed by pen V K, which constituted 19.87% of the penicillins class consumption in 2010 and 16.27% in 2016. Cloxacillin constituted 7.01% in 2010 and 8.66% in 2016 of the total consumption within this class.

Table 5: Consumption trends of penicillins, Namibia, 2010 to 2016 in DID

	2010	2011	2012	2013	2014	2015	2016	% of total 2010	% of total 2016
Amoxicillin	8.76	9.07	7.31	9.93	9.62	9.85	10.35	70.75%	73.04%
Cloxacillin	0.87	1.09	1.22	0.99	1.00	1.18	1.23	7.01%	8.66%
Benzathine penicillin	0.15	0.07	0.07	0.09	0.08	0.06	0.07	1.21%	0.46%
Pen V K	2.46	3.00	2.11	1.92	1.89	1.74	2.30	19.87%	16.27%
Ampicillin	0.13	0.12	0.18	0.18	0.16	0.11	0.21	1.03%	1.46%
Piperacillin/tazobactam & Procaine	0.02	0.05	0.05	0.03	0.02	0.02	0.02	0.13%	0.12%
Total	**12.39**	**13.39**	**10.94**	**13.13**	**12.76**	**12.95**	**14.17**	**100.00%**	**100.00%**

In line with the national consumption trends, the DID for amoxicillin rose from 8.76 DID (2010) to 9.07 DID (2011) from where it dipped slightly to 7.31 DID (2012). Thereafter, it rose steadily to 9.93 DID (2013) and to 9.85 DID in 2015. This rise continued to a high of 10.35 DID in 2016.

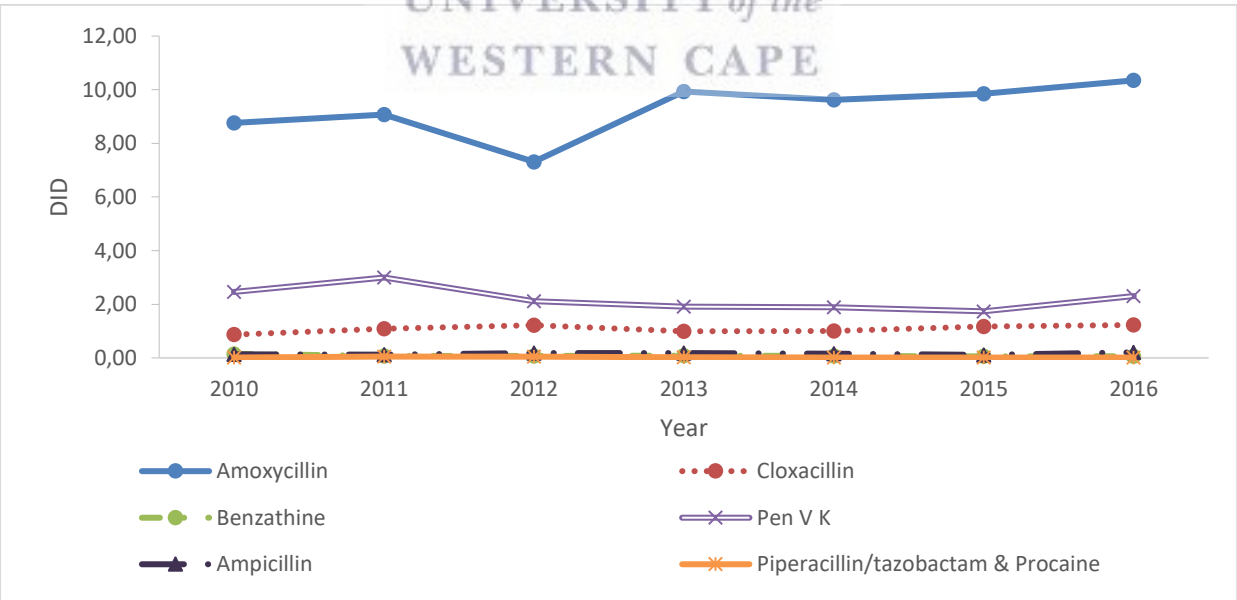


Figure 7: Consumption trends of Penicillins, Namibia, 2010 to 2016

4.5 Trends of antibiotic consumption per region in Namibia

Table 6 shows the antibiotic consumptions rates varied by region and over time and ranged from a low of 22.32 DID in Omaheke region in 2010 and a high of 84.79 DID in the Zambezi region in 2016. In 2010 Zambezi (10%), Erongo (10%) and Kavango (10%) regions were responsible for a combined total of 30% of the total antibiotic consumption; whilst in 2016, Hardap (9%), Karas (9%), Kavango (9%) and Zambezi (14%) contributed 41%. The regions Ohangwena (4%, 2010 and 6%, 2016), Omaheke (4%, 2010 and 5%, 2016), and Otjozondjupa (6%, 2010 and 6%, 2016) had the lowest consumption figures in the country.

Table 6: Trends of antibiotic consumption by region in Namibia, 2010-2016 in DID

	2010	2011	2012	2013	2014	2015	2016	Min	Max	% of total consumption 2010	% of total consumption 2016
Erongo	49.68	58.75	55.69	57.25	58.47	60.41	44.91	44.91	60.41	9,80%	7,52%
Hardap	39.83	38.73	44.47	52.33	47.77	49.83	54.69	38.73	54.69	7,86%	9,15%
Karas	43.24	37.42	42.63	50.89	45.79	58.91	51.33	37.42	58.91	8,53%	8,59%
Kavango	50.98	43.10	43.47	46.03	47.01	43.24	52.03	43.10	52.03	10,06%	8,71%
Khomas	36.07	44.70	44.03	37.68	41.05	35.04	36.18	35.04	44.70	7,12%	6,05%
Kunene	41.67	47.10	43.47	36.64	46.51	50.37	43.49	36.64	50.37	8,22%	7,28%
Ohangwena	22.48	29.84	29.10	38.91	31.46	32.07	35.19	22.48	38.91	4,43%	5,89%
Omaheke	22.32	31.72	24.50	33.45	34.85	29.54	32.81	22.32	34.85	4,40%	5,49%
Omusati	40.54	38.78	35.21	39.64	44.07	48.19	47.02	35.21	48.19	8,00%	7,87%
Oshana	34.69	39.96	37.48	38.07	33.22	41.73	35.36	33.22	41.73	6,84%	5,92%
Oshikoto	45.99	42.55	38.09	50.59	48.16	49.52	43.35	38.09	50.59	9,07%	7,26%
Otjozondjupa	30.36	39.56	34.28	35.34	39.18	43.59	36.41	30.36	43.59	5,99%	6,09%
Zambezi	49.05	59.87	57.47	61.57	74.92	72.21	84.79	49.05	84.79	9,68%	14,19%
National	38.31	41.48	39.65	42.70	43.31	43.86	43.37	38.31	43.86		

Figure 8 depicts the trend of consumption by region. The trend indicates that Karas, Kavango, Oshikoto, Hardap, Erongo and Zambezi regions have consumption trends that are higher than the national DID. The highest consumption was recorded for the Zambezi region and the trend line showed a steep rise from a low of 49.05 DID (2010) to 59.87 DID (2011) where after it decreased to 57.47 DID (2012) and then rose again to 61.57 DID (2013) and 74.92 DID (2014). It fell slightly to 72.21 DID in 2015 and the reached a peak of 84.79 DID in 2016. Kavango region had a DID of 50.98 in 2010 which dropped to 43.10 DID in 2011 and 43.47 DID in

2012. From there the trend continued its rise to 46.03 DID in 2013 and 47.01 in 2014 and this was followed by a drop to 43.24 DID in 2015 and a peak of 52.03 DID in 2016.

According to Figure 8, Omaheke region had the lowest consumption of antibiotics in the country. The trend started off at 22.32 DID in 2010 followed by a steep rise to 31.72 DID in 2011 where after it decreased drastically to 24.50 DID in 2012 and rose to 33.45 DID in 2013. In 2014 the trend increased slightly to 34.85 DID and went back down to 29.54 DID in 2015 and then continued steadily upwards to reach 32.81 DID in 2016. Figure 8 indicates that the Ohangwena region had the second lowest consumption of antibiotics in the country following Ohangwena. The trend started off at 22.48 DID in 2010, followed by an increase to 29.84 DID in 2011 where after it dipped to 29.10 in 2012. In 2013 it rose to 38.91 DID and dropped again to 31.46 DID in 2014. In 2015 the trend increased slightly to 32.07 DID and 35.19 DID in 2016.

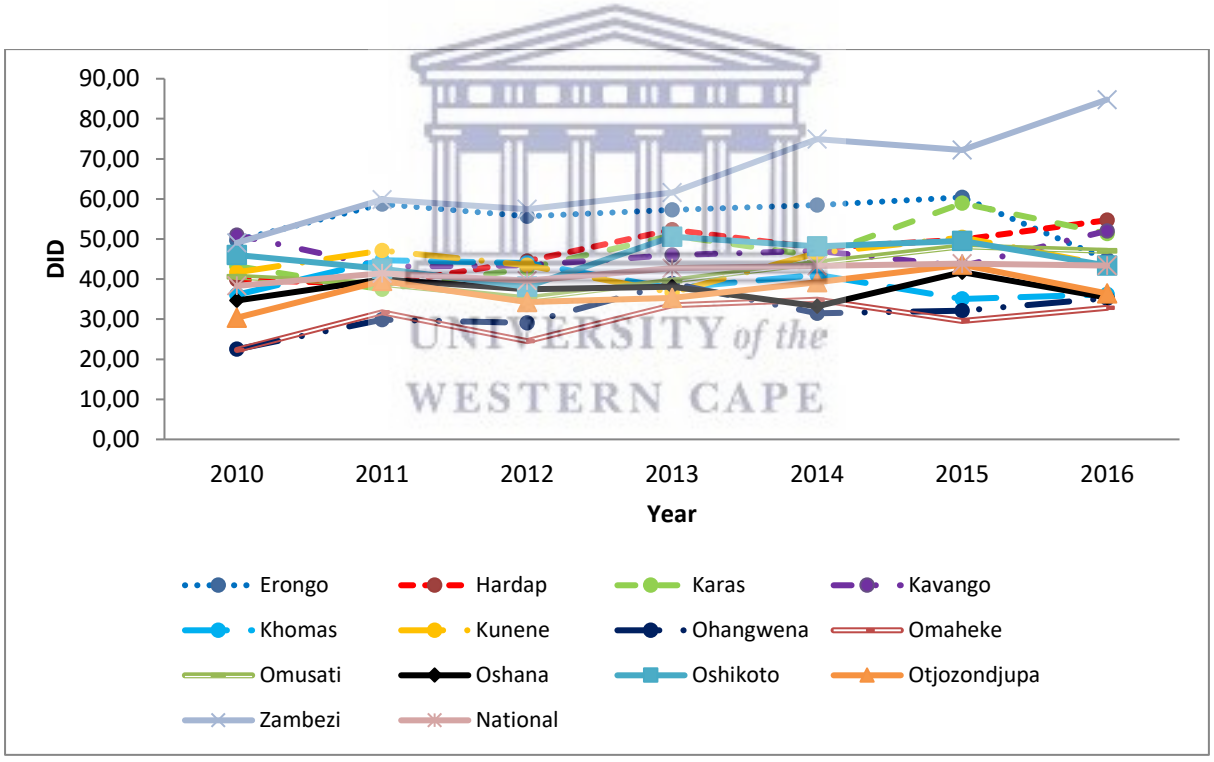


Figure 8: Trends of antibiotic consumption by region in Namibia, 2010-2016

Table 7 shows that in terms of relative change, with 2010 as a baseline, consumption of antibiotics increased in all the regions, except for Erongo and Oshikoto where there a decrease was observed. The largest percentage increase was in Zambezi region, with an increase of 72.85%, followed by Ohangwena with an increase of 56.53%.

Table 7: Changes in antibiotic consumption by region in Namibia, 2010-2016

	Antibiotic consumption, 2010 (DID)	Antibiotic consumption, 2016 (DID)	Change in consumption 2010-2016 (DID)	Percent change within regions	Minimum annual consumption 2010-2016 (DID)	Maximum annual consumption 2010-2016 (DID)
Erongo	49.68	44.91	-4.77	-9.60	44.91	60.41
Hardap	39.83	54.69	14.85	+37.29	38.73	54.69
Karas	43.24	51.33	8.08	+18.69	37.42	58.91
Kavango	50.98	52.03	1.06	+2.08	43.10	52.03
Khomas	36.07	36.18	0.11	+0.30	35.04	44.70
Kunene	41.67	43.49	1.82	+4.37	36.64	50.37
Ohangwena	22.48	35.19	12.71	+56.53	22.48	38.91
Omaheke	22.32	32.81	10.49	+46.99	22.32	34.85
Omusati	40.54	47.02	6.48	+15.99	35.21	48.19
Oshana	34.69	35.36	0.67	+1.92	33.22	41.73
Oshikoto	45.99	43.35	-2.63	-5.72	38.09	50.59
Otjozondjupa	30.36	36.41	6.05	+19.93	30.36	43.59
Zambezi	49.05	84.79	35.74	+72.85	49.05	84.79
Regional average	38.31	43.37	5.06			

4.6 Regional consumption by antibiotic class 2010 and 2016

Looking at the antibiotic consumption by region and by antibiotic class Figure 9 & 10 indicates sulphonamides and trimethoprim as the highest consumed class across all the regions for both 2010 and 2016. This examination was conducted for the years 2011 to 2015 and is available in Appendix 7.

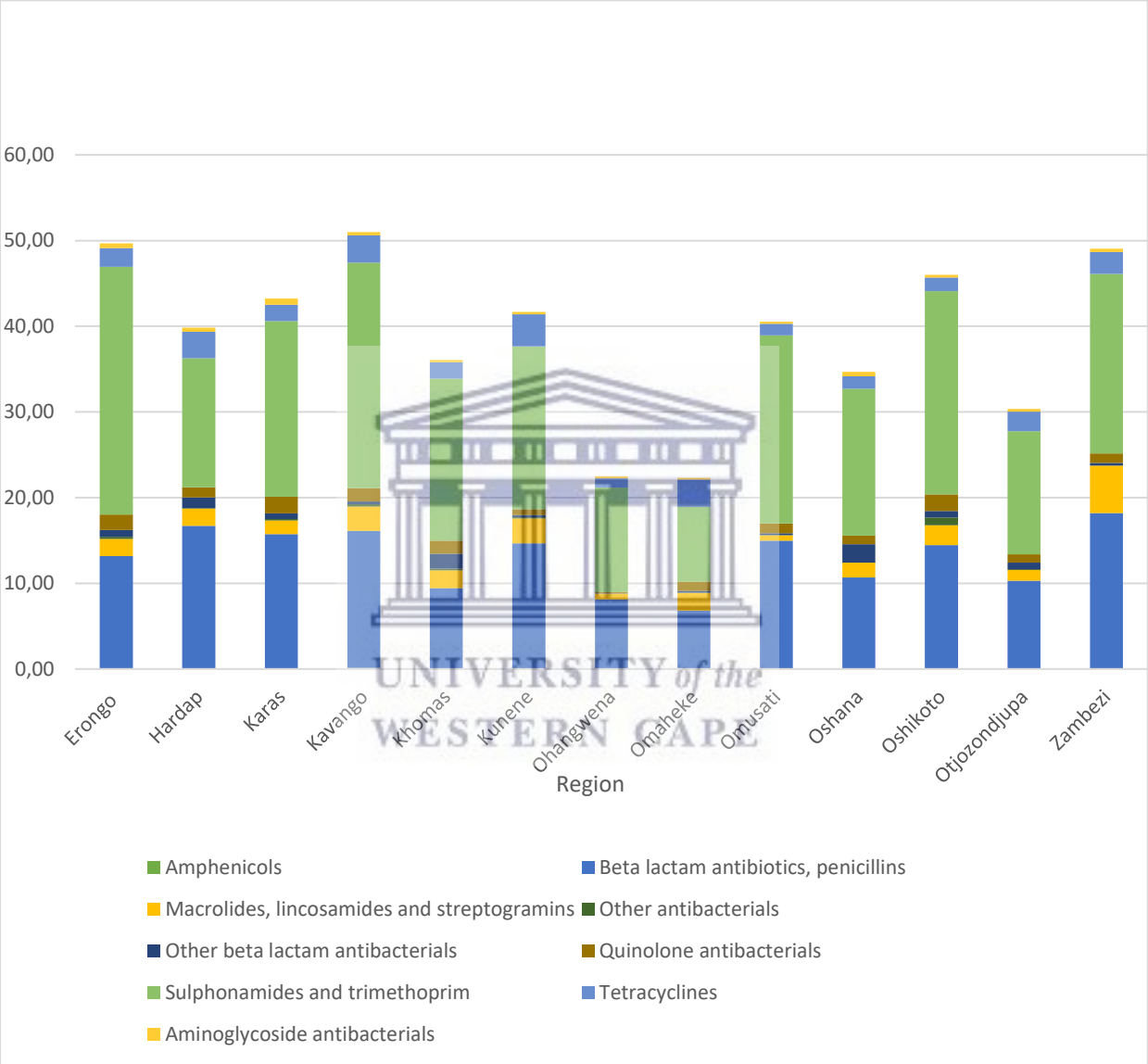


Figure 9: **Antibiotic consumption by region by antibiotic class, Namibia, 2010**

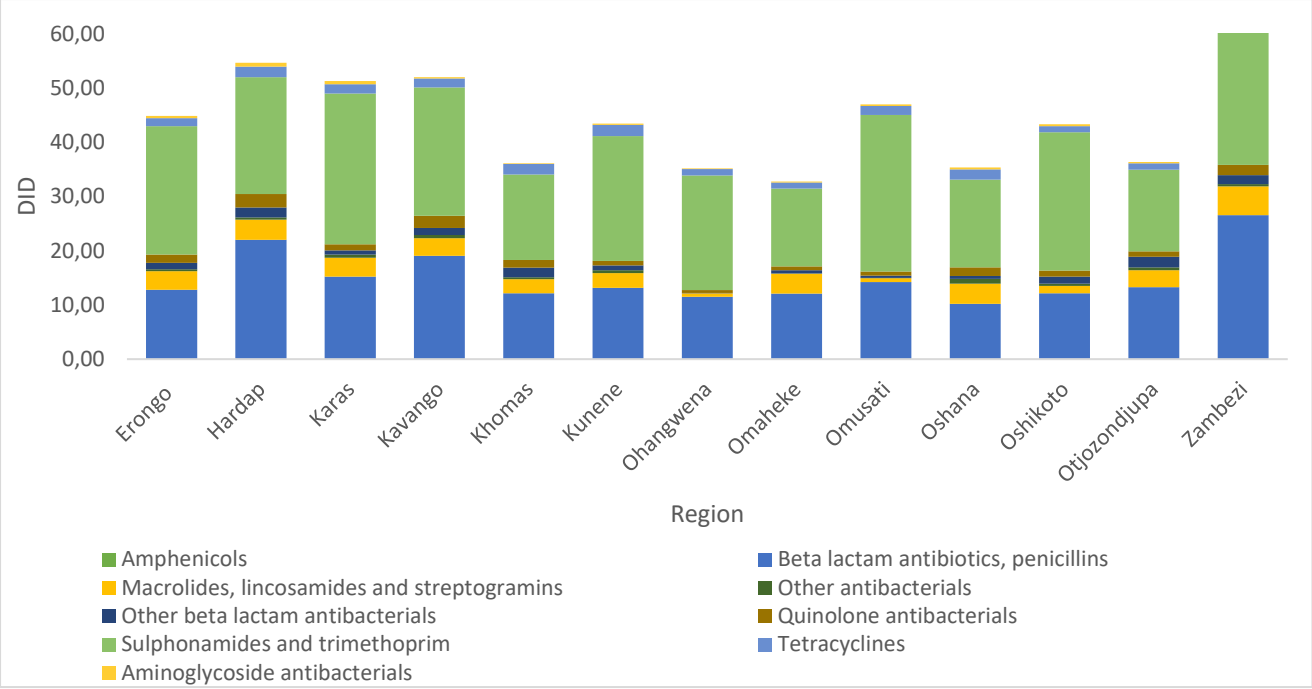


Figure 10: **Antibiotic consumption by region by antibiotic class, Namibia, 2016**

Table 8: Antibiotic consumption in the Zambezi region and national total, by antibiotic class, 2010 & 2016

ATC 3 class	Zambezi				National			
	2010 DID	% of total consumption 2010	2016 DID	% of total consumption 2016	2010 DID	% of total consumption 2010	2016 DID	% of total consumption 2016
Aminoglycoside antibacterials	0.39	0,80%	0.43	0,50%	0.35	0,91%	0.26	0,61%
Amphenicols	0.04	0,07%	0.01	0,01%	0.04	0,11%	0.01	0,02%
Beta lactam antibiotics, penicillins	18.15	37,00%	26.60	31,37%	12.39	32,33%	14.17	32,66%
Macrolides, lincosamides and streptogramins	5.54	11,29%	5.28	6,23%	1.91	4,99%	2.52	5,81%
Other antibacterials	0.00	0,00%	0.45	0,53%	0.18	0,47%	0.37	0,86%
Other beta lactam antibacterials	0.33	0,67%	1.63	1,92%	0.78	2,03%	1.10	2,54%
Quinolone antibacterials	1.10	2,23%	1.87	2,21%	1.21	3,16%	1.30	3,00%
Sulphonamides and trimethoprim	20.94	42,69%	45.06	53,14%	19.40	50,65%	21.99	50,69%
Tetracyclines	2.57	5,24%	3.46	4,08%	2.05	5,36%	1.65	3,80%
Total	49.05	100%	84.79	100%	38.31	100,00%	43.37	100%

Antibiotic consumption per antibiotic class per region are shown in Table 8 and Figures 9 and 10. The classes with the highest consumption in Zambezi for both 2010 and 2016 were sulphonamides and trimethoprim (43%, 2010 and 53%, 2016) followed by penicillins (37%, 2010 and 31%, 2016), which were in line with the national picture.

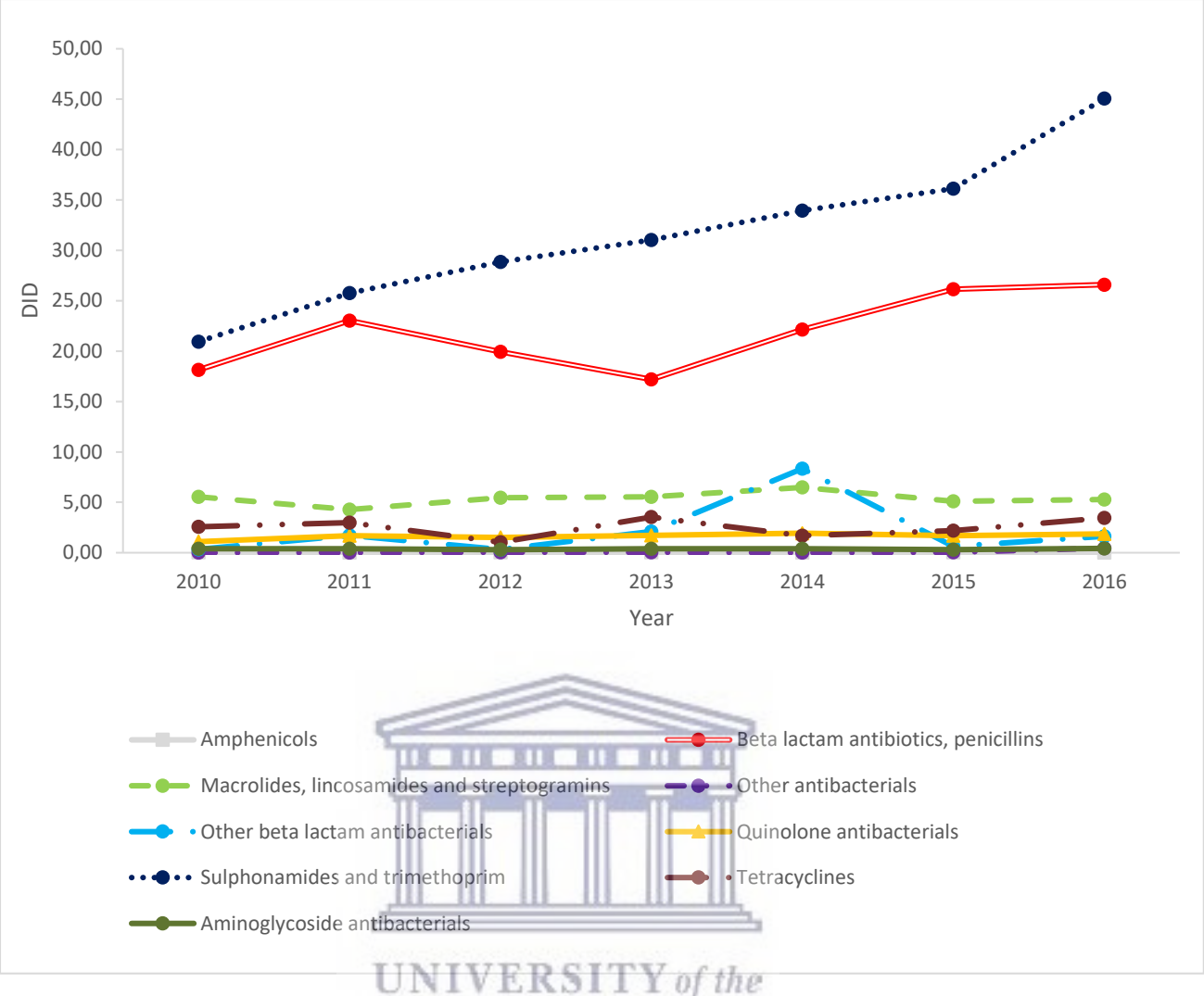


Figure 11: **Regional antibiotic consumption trends per antibiotic classification, Zambezi, 2010-2016**

The trend line for the consumption of the antibiotics consumed in Zambezi is presented in Figure 11 and depicts a steady increase in consumption of sulphonamide and trimethoprim from 2010 to 2016. The consumption of penicillins show an initial rise from 2010 to 2011 followed by a decline up to 2013 where after it increases steadily up to its peak in 2015 and slight decrease to its 2016 value. The consumption of macrolides, lincosamides and streptogramin class showed a steady near linear progression from 2010 to 2016. Trend lines for the other regions are available in Appendix 8.

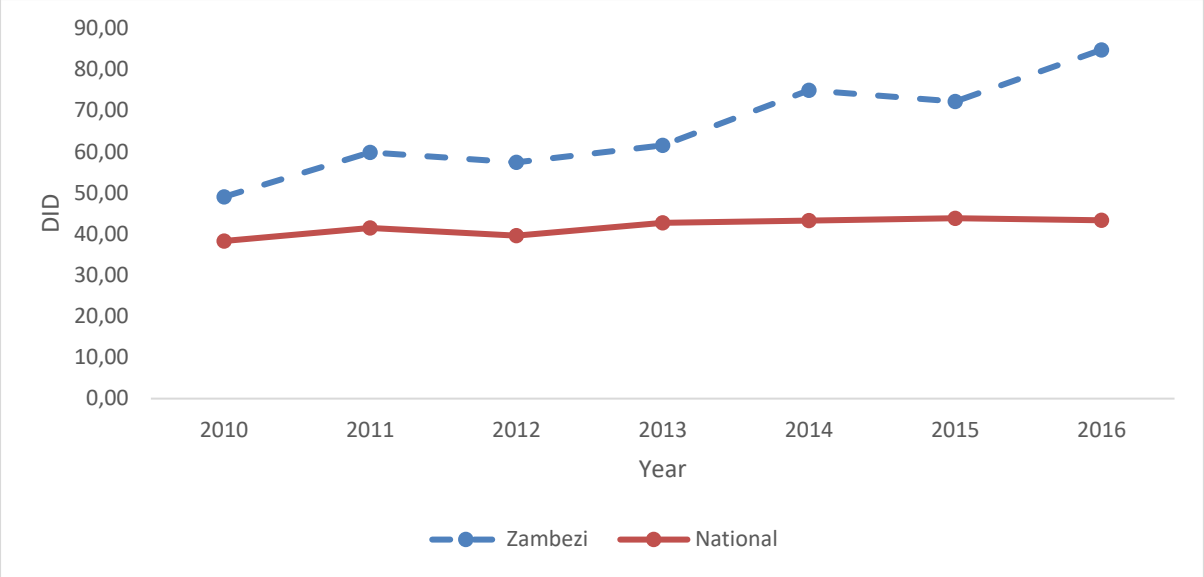


Figure 12: **Antibiotic consumption trend, Zambezi vs national average, and 2010-2016**

Figure 12 shows a comparison of the trend line for consumption of antibiotics in Zambezi with that of the national average between 2010 and 2016. It was clear that consumption in Zambezi was much higher than the national DID, and that the Zambezi region showed a steady rise during the period whilst national trend line maintained a near linear progression.

CHAPTER 5: DISCUSSION

5.1 Introduction

As antibiotic resistance is driven by the volume of consumption, understanding how consumption works over time and between countries or regions could serve as a baseline measurement for AMR stewardship initiatives. This study assessed the pattern of antibiotic consumption in the Namibian public sector between 2010 and 2016 based on distribution of antibiotics from Central Medical Stores (CMS) to each of the 13 Regions between 2010 and 2016. The WHO recommended ATC/daily defined dose (DDD) methodology was used to evaluate the consumption (WHO, 2018). The study analyzed a total of 24,110 antibiotic distributions issued from the Central Medical Store (CMS), with antibiotics as defined by anatomical therapeutic classification (ATC) class J01 of the WHO classification (WHO, 2018).

The discussion is presented as follows:

- National trend of antibiotic consumption by total volume versus international trends
- National trend of antibiotic consumption by total volume per antibiotic class
- National consumption trends for selected antibiotics by volume
- Regional trends of antibiotic consumption by total volume
- Regional consumption by antibiotic class

5.2 National trend of antibiotic consumption by total volume versus international trends

Namibia's antibiotic consumption for the public sector increased by 13.2% from 38.31 DID in 2010 to 43.37 DID in 2016, with an average of 41.81 DID during the study period. Namibia is classified by the World Bank as an upper middle income country (UMIC) (World Bank Group, 2018). Although the increase in antibiotic consumption in Namibia was lower in percentage terms when compared to other UMICs as well as South Africa in Klein, et al., (2018), the absolute numbers are still twice as high as other UMICs in 2016. The DID for Namibia is comparable to countries such as Turkey, Tunisia, Greece and Spain which had similar DIDs in 2015 (Klein, et al., 2018). South Africa's consumption increased by 56% from 16.08 DID in 2000 to 25.14 DID in 2015 (Klein, et al., 2018).

The differences could be partially attributed to the methodology of the studies as the study conducted by Klein, et al., (2018) used the 2016 WHO ATC/DDD classification, whilst Pereko,

et al., (2015) used the 2013 version and this study used the 2018 version. As DDD are revised and added to over the years this could provide for some slight differences in the results. However, the trend and percentage change should still be comparable. The Klein, et al., (2018) study also indicated that molecules not included in the ATC/DDD 2016 classification were provided for through estimates from other sources whilst this study only used those that were already allocated DDDs by the ATC/DDD system. This could mean that more molecules were included in the Klein, et al., (2018) study than for the other studies which could increase the DID reported. For this public sector study all the required data was available and was used so no sampling was done. However, the data for the Klein, et al., (2018) study used sampling and extrapolated where no data was available which would make the Namibia public sector study more accurate since no sampling was done.

The Pereko, et al., (2015) study only had wholesale data from one of the two main wholesalers in the private sector for Namibia, meaning that not all the data was available. The Pereko, et al., (2015) study only covered the private sector and this study the public sector whilst the Klein et al., (2018) study looked at whole countries for the most part. However Klein et al., (2018) does depend on IQVIA® data which in some cases only collects private sector data and does not collect public sector data. In some countries like South Africa they do collect both but not all. So their figures may also be an underestimate where products are procured by both the public and private sectors. It is therefore possible that the figures from this study could have been lower had they been a combination of both private (lower) and public (higher) sector consumption instead of sector specific. This also means that the Namibia data from each study cannot be generalized to the whole population since neither of the studies covered both sectors. Other than that, all the methodologies were the same as the reccomended WHO ATC/DDD methodology.The sources for the population data also differed as for this study projections from the Central Bureau of Statistics, (2006) were used whilst Klein et al., (2018) used the World Bank data bank population data.

According to the European Surveillance of Antimicrobial Consumption (ESAC) classification (Mohulatsi, 2016), Namibia is a high antibiotic consumer based on the fact that both the private and public sector consumption figures are well above 22.38 DIDs. Namibia's public sector consumption rate is higher than that of the Namibian private sector which showed an increase of 25% from 19 DID in 2008 to 35.41 DID in 2011 (Mohulatsi, 2016). It is also higher than

that of even the high income countries' consumption as reported by Klein, et al., (2018) and Wirtz, et al.,(2010). The difference between private and public sector consumption in Namibia could be attributed to many factors one of them being that the public sector medicines are provided at a very low cost about USD 0.50 inclusive of consultation and screening. As of 2017 only about 200,000 out of a total of 2, 5 million Namibians are covered by medical aid, translating to only 8% of Namibians having medical aid (NAMAF, 2017). In the private sector a patient is charged per item out of pocket and those that have medical aid still have to pay 5% to 30% per item co-payment when using insurance which is higher than the USD 0.50 paid in the public sector. This economic element might have played a role in reducing the consumption in the private sector.

Klein, et al., (2018) proposed that high consumption is attributable to high income as well as high burdens of infectious diseases. This scenario is typical for an UMIC such as Namibia with high burden of infectious diseases, such as tuberculosis, HIV and malaria, prevailing poor socio-economic conditions, such as poor sanitation (MoHSS Namibia, 2013) which leads to increased exposure to disease causing agents. These diseases are then in turn treated with antibiotics and this leads to an increase in the use of antibiotics. Namibia's gross domestic product (GDP) has been on the rise for most of the period under review (tradingeconomics, 2018). According to Klein, et al., (2018) an increase in GDP provides for access to more goods and services including antibiotics leading to increase in access to antibiotics and therefore an increase in consumption. Rising GDP, as is the case for Namibia, is also associated with urbanization, which involves people from rural areas moving to more economically active urban areas in search for jobs (Klein, et al., 2018). Many of these people live in poor conditions as the urban areas that they move to are usually unable to provide sufficient services for the rapid influx of people that usually occurs. The poor living conditions in turn lead to further rise in infectious diseases and other illnesses that, although not infectious, may still lead to irrational use of antibiotics (Klein, et al., 2018).

According to Pereko, et al., (2015) one of the strategies that can be used to improve rational use of antibiotics is the provision and use of treatment guidelines/antibiotic protocols. The Namibian standard treatment guidelines (STGs) were launched in 2011 (MoHSS, 2011). The launch was accompanied by training aimed at educating the prescribers (Akpabio, et al., 2014). Before Namibia had the STGs there were several guidelines in place but none as

comprehensive as the STGs (MoHSS, 2011). One would have expected that the launch of the guidelines would have some influence on prescribing practices and reflect on the consumption of antibiotics. However, Akpabio, et al., (2014) in a study carried out between 2012 and 2013 found a low compliance level of about 27% to the STGs. This meant that the effect of the STG was not as pronounced as expected.

The lack of concurence between the STGs and NEMList could also have negatively affected the prescribing practices. This negative effect stems from lack of access for the items in the STGs and not in the NEMList , since the public sector procurement system relies mostly on the NEMList for procurement. Innapropriate use would be expected for the items in the NEMList and not in the guidelines due to lack of guidance for their use.

Although the STGs compliance rate does not allow one to make a direct correllation, it was noted that the total consumption of antibiotics did take a slight dip in 2012 which was be the first year in which the guidelines were used. This dip was from 41.48 DID in 2011 to 39.65 DID in 2012. However, there is a need to further analyse the use of antibiotics in order to determine other causes of this high use and find ways to reduce it (Mohulatsi, 2016). This data shows how much antibiotic are being consumed and that the rate is higher than average. However, it does not say whether the use is warranted vis-à-vis the disease burden or socio-economic conditions within which the population lives. To answer this question one would need to conduct another study. What the increasing DID tells us however is that the consumption is increasing faster than the population growth since the DID unit measures per inhabitant (Mohulatsi, 2016).

5.3 National trend of antibiotic consumption by total volume per antibiotic class

Within the antibiotic classes, the class with the highest consumption in the public sector was sulphonamide and trimethoprim which made up 51% of the total antibiotic consumption in 2010 and again in 2016. The reason for the high consumption of the sulphonamide and trimethoprim class is due to the fact that co-trimoxazole was used as prophylaxis for opportunistic infections in HIV positive patients during the period under review. As at March 2016 Namibia had about 220 000 HIV positive people of which there were 148 920 patients on antiretroviral treatment. (Namibia MoHSS, 2016; MOHSS, 2016). The antiretroviral treatment guidelines in Namibia recommends co-trimoxazole prophylaxis for all adults with

HIV with a CD4 cell count of ≤ 350 or in WHO Clinical Stage 3 or 4 disease (MOHSS, 2016).The results of this study indicate that many of these patients are taking co-trimoxazole as a daily dose (MoHSS, 2011;MoHSS, 2017). Beta lactam penicillins were the second highest consumed antibiotic class. This is to be expected as they are the first line treatment in the majority of the cases needing antibiotics in Namibia (MoHSS, 2011). However, according to Klein, et al., (2018) the consumption of penicillins could be exaggerated due to the fact that the assigned DDD is much lower than the actual prescibed dose. Macrolides, lincosamide and streptogramin classes only contributed 6% to consumption. The private sector for Namibia had a similar affinity for the use of beta lactam antibiotics, penicillins, cephalosporins and macrolides, lincosamide and streptogramins as these are the highest consumed antibiotics in the private sector (Pereko , et al., 2016). However, sulphonamides did not appear in their top 9 highest consumed antibiotics (Mohulatsi, 2016). This would suggest that patients being treated for HIV either receive their prophylaxis in the public sector or the private sector does not make use of co-trimoxazole as prophylaxis.

Klein, et al., (2018) further reported a global increase in consumption of last resort antibiotics such as carbapenems as well as an increase in cephalosporins. For the Namibian public sector the consumption in the class containing carbapenems and cephalosporins which is the class called other beta-lactam antibiotics showed a 40% increase in consumption from 2010 to 2016 from a low level. This increase in last line of defence would mean fewer options for severly ill patients This increase has been attributed to rising in resistance to penicillins and quinolones which are now being replaced by cephalosporins in countries like India (Klein, et al., 2018). One would need to do more in terms of resistance mapping in order to determine if this is the cause of the shift in the Namibia situation. If we can get this local resistance data we will then have sceintific basis (Klein, et al., 2018) for efforts towards reducing the consumption.

5.4 National consumption trends for selected antibiotics by volume

In the sulphonamide and trimethoprim class the co-trimoxazole 80 + 400 mg tablets were the highest consumed item during the period under review. This implies that co-trimoxazole 80 + 400 mg tablets is the highest consumed antibiotic formulation in the Namibian public sector even outside its class. This is to be expected as these were the formulation of choice for prophylaxis for opportunistic infections in HIV positive patients in Namibia, given the

prevalence of HIV (14% in adults age 15 to 49) in Namibia during the period under review (MoHSS Namibia, 2013).

In the beta lactam, penicillin antibiotic class the highest consumed antibiotic was amoxicillin which was responsible for about 70% of the beta lactam, penicillin antibiotics consumed in the Namibia public sector. Amoxicillin and is indicated for the treatment of a wide variety of conditions (Joint Formulary, 2015; MoHSS, 2011). It is therefore acceptable for it to be the highest consumed medicine in its class. What the data can't tell us is if this use is rational. For us to find out if the use of amoxicillin is in line with guidelines is outside the scope of this study.

The study also found that in 2012 when there was a reduction in the consumption of amoxicillin, there was a compensatory increase in the consumption of the other beta lactam penicillins ampicillin and cloxacillin. One can assume that there might have been a stock out of amoxicillin which lead to substitution with the other broad spectrum antibiotics within the same class, since the consumption pattern was reversed again in 2013 and onwards.

5.5 Regional trends of antibiotic consumption by total volume

The study found substantial variation in regional antibiotic consumption trends. The lowest consumption was in Ohangwena region which contributed 6% to the total national consumption, with Zambezi having the highest regional consumption making up about 13% of total consumption, more than double that of Ohangwena. The reasons for these variances were outside the scope of this study but need to be investigated.

The regions Karas, Kavango, Oshikoto, Hardap, Erongo and Zambezi had a higher consumption than the national average for most of the period under review. These regions are spread out all over the country with no obvious similarities. Figure 1 tells us that Khomas, Kavango and Ohangwena had the highest population figures for the period under review. In 2016, 14% of the national antibiotic consumption was attributable to Zambezi region which according to Table 1 only accommodated 3.9% of the national population in the same year. One would have expected that Khomas region have the highest consumption since that is where urbanization is high and where people are living in the poorest of conditions on the outskirts of the city.

The largest increase in consumption within the regions was in Zambezi region which increased by 73% from 2010 to 2016, this increase was followed by a 57% increase in Ohangwena region and a 47% increase in Omaheke. These large increases would need to be investigated further in order to determine whether the increases were appropriate and if not to recommend appropriate action.

5.6 Regional consumption by antibiotic class

The beta lactam antibiotics, penicillin class and sulphonamide and trimethoprim antibiotics were the highest consumed classes across all the different regions. For the Zambezi region, which is the region with the highest consumption, the above classes were closely followed by an increasing consumption in macrolides, lincosamides and streptogramins, as well as the tetracycline classes of antibiotics.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This study described the patterns of antibiotic consumption in the Namibian public health sector over seven years between 2010 and 2016 by region, antibiotic class and antibiotic. It has provided trend and regional data that can serve as a baseline for the Namibian AMR stewardship program. The total national antibiotic consumption for Namibia, 38.31 DID in 2010 and 43.37 DID in 2016, is classified as high according to the European Surveillance of Antimicrobial Consumption (ESAC) 2010 classification system.

When looking at consumption at the regional level, Karas, Kavango, Oshikoto, Hardap, Erongo and Zambezi regions contributed significantly to the national consumption. The largest increase in consumption within the regions was for Zambezi region which increased by 73% from 2010 to 2016; this increase was followed by an increase of 57% in the Ohangwena region and a 47% increase in the Omaheke region. These large increases would need to be investigated further in order to determine whether the increases were appropriate and if not appropriate actions should be recommended.

The study found that the highest class of antibiotics consumed in Namibia were sulphonamides and trimethoprim, which contributed 51% of the total consumption in 2016 followed by beta lactam penicillins responsible for 32% of consumption. The high consumption of sulphonamides and trimethoprim could be attributed to the use of co-trimoxazole prophylaxis for HIV/AIDS related opportunistic infections. It is therefore imperative that one of the consumption reduction strategies should be targeted at reducing the burden of HIV/AIDS with the aim of reducing the requirement for the antibiotic co-trimoxazole (Klein, et al., 2018).The high consumption of beta lactam penicillins class is ascribed to the fact that beta lactam penicillins are first line treatment in the majority of the cases needing antibiotics in Namibia according to the national STGs (MoHSS, 2011).

The important data gathered during this study could serve as baseline data for monitoring and measuring the impact of Namibia's recently finalized National Action Plan on Antimicrobial Resistance (Namibia MoHSS, 2017). It could also serve as baseline data for different interventions to be developed and implemented through the newly revived antimicrobial

stewardship program. While some of these interventions may be national others could be targeted at high volume consuming regions or randomized regions to learn which interventions are effective. Such an approach of testing interventions would allow the AMR stewardship committee to learn which interventions were most effective in the Namibian context.

In conclusion, this study has highlighted some of the key problem areas in antimicrobial use, including areas for further investigation, which can guide future interventions. Regular monitoring of consumption is important and annual updates of the consumption data for 2017 and 2018 should be under taken early in 2019.

6.2. Recommendations

The following recommendations are proposed:

1. This study should be carried out on an annual basis by each Regional Pharmacist in each region in Namibia. The differences in consumption rates between regions should be further investigated in order to determine the cause of the differences. The discussion of the results should be a standing agenda point at the Annual National Pharmacists' Forum. The main aim would be to assist in devising interventions towards rationalization of antibiotic use and for sharing best practices from the regions that are performing better than others. Regular monitoring and evaluation of the implementation of the devised interventions would also be required in order to ensure that they are efficient and effective.

2. All countries should use this methodology to determine the consumption of antibiotics in their countries. This would increase the pool of data on the consumption of antibiotics in order to enable benchmarking.

3. In future, primary consumption data should be used for assessing antibiotic use. This is to avoid having to assume that all medicines issued to the facilities are consumed and not take into account that losses occur from expiries, theft as well as breakage, as is the case when secondary data is used. This data is already available for the private sector and will be possible in Namibia in the near future as MoHSS is working on an electronic

dispensing tool which will enable the country to collect this data for the public sector as well.

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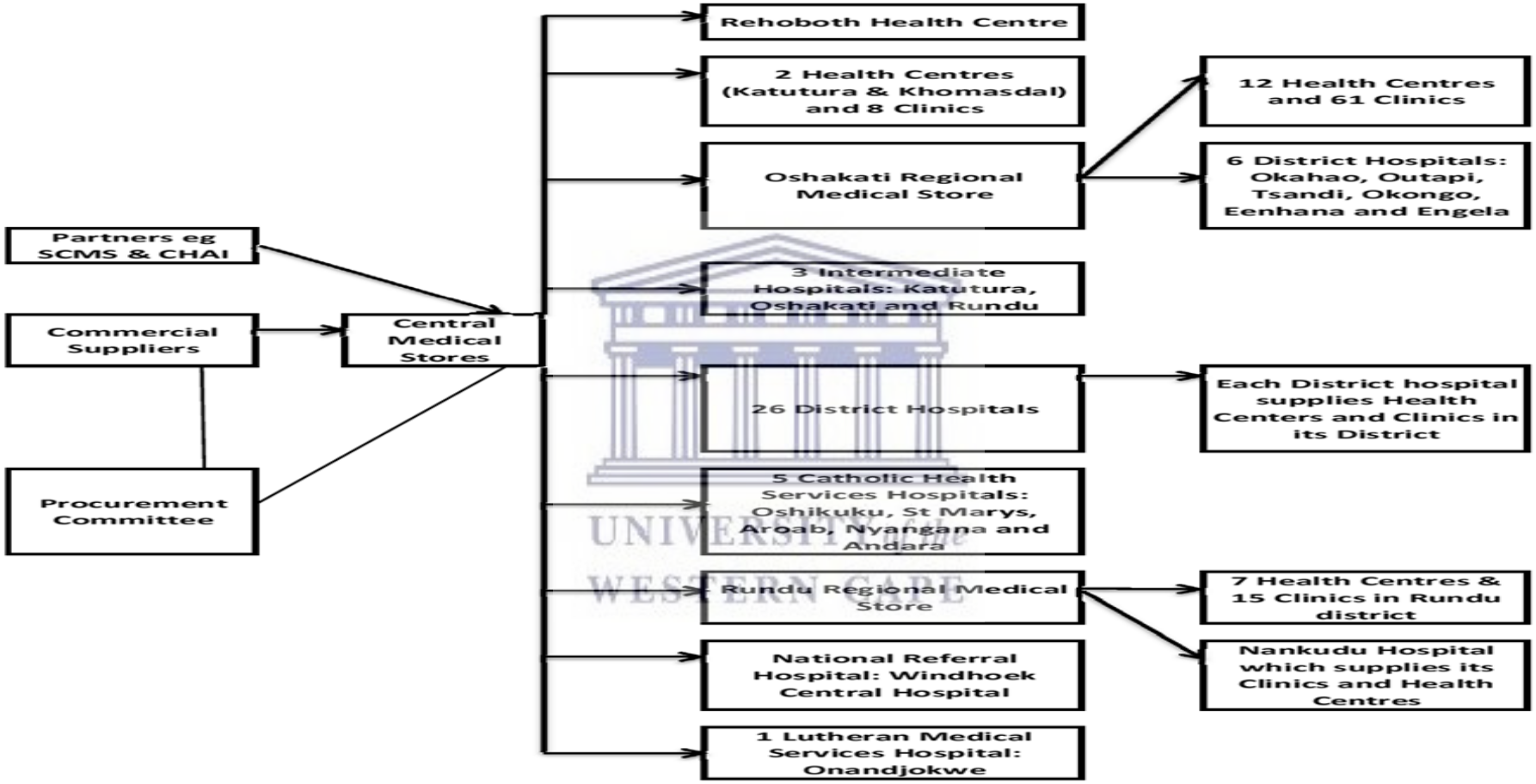
Appendix 1: CMS Distribution Network.



Appendix 2: NEMList Classification according to level of availability and prescribing restrictions

ABC	The preparation can be ordered and prescribed at all levels of care by any competent prescriber.
ABC#	The treatment must be initiated by a Medical Officer, but the preparation can be available at health centres and clinics for follow-up treatment of chronic patients only.
ABC-R	The preparation will be available at PHC facilities to be used ONLY according to conditions specified in the NEMList. The inventory of these medicines must be controlled with the appropriate registers
AB	The preparation will be available for prescription by any Medical Officer and for ordering at district hospital (Class C) or higher levels
AB*	As for AB but the preparation will also be available at clinics and health centres conducting deliveries.
A	The preparation will be available for ordering and prescription at regional hospitals (Class B) or higher levels
S	The preparation will be available for prescription by designated Specialists only
R	The preparation will be available for use ONLY for specific conditions and/or in restricted circumstances, as specified in Chapter 2 of this document.
IMAI-R	These items are to be made available at clinics and health centres that have staff that have been trained in IMAI. Refer to Chapter 2 for more details They can also be stocked at District Hospital levels and above, and used as normal AB class items in these facilities

Appendix 3: List of General Anti-infectives (excerpt from MoHSS (2016))

G	**GENERAL ANTI - INFECTIVES. SYSTEMIC**				
	Cephalosporins				
	MEDICINE	STRENGTH	DOSAGE FORM	LEVEL	VEN
021	Cefazolin	1 gram	Powder for Injection	AB	E
061	Cefixime	200mg	Tablets	R	V
051	Cefradine	500mg	Capsules	AB	E
061	Cefradine	125mg/5ml	Suspension	A	E
021	Ceftriaxone	250mg	Powder for Injection	R	V
021	Ceftriaxone	1g	Powder for Injection	A	E

021	Cefuroxime	750mg	Powder for Injection	AB	E
051	Cefuroxime	250mg	Tablets	AB	E
061	Cefuroxime	125mg/5ml	Suspension	AB	E
	Penicillins				
061	Amoxycillin	125mg/5ml	Syrup	ABC	V
051	Amoxycillin	250mg	Capsules	ABC	V
061	Amoxycillin + Clavulanic Acid	125mg/31mg	Suspension	AB	E
	Amoxycillin + Clavulanic Acid	1000/200 mg	Injection	AB	V
051	Amoxycillin + Clavulanic Acid	875/125mg	Tablets	AB	E
021	Ampicillin	250mg	Powder for Injection	AB	V
021	Ampicillin	500mg	Powder for Injection	AB	V
021	Benzathine Benzylpenicillin	2.4 million IU	Powder for Injection	ABC	V

021	Benzyl-, + Benzathine + Procaine Penicillin	1.2 million IU	Powder for Injection	ABC	N
021	Benzylpenicillin	1 million IU	Powder for Injection	AB	E
051	Cloxacillin	250mg	Capsules	AB	E
061	Cloxacillin	125mg/5ml	Syrup	AB	E
021	Cloxacillin	250mg	Powder for Injection	AB	E
021	Cloxacillin	500mg	Powder for Injection	AB	E
051	Phenoxymethylpenicillin	250mg	Tablets	ABC	V
061	Phenoxymethylpenicillin	250mg/5ml	Syrup	ABC	V
021	Piperacillin + Tazobactam	4g + 500mg	Powder for Injection	S	E
021	Procaine Benzyl Penicillin	3g (3 million IU) or 300mg/ml	Powder for Injection (10ml)	ABC	V

	All other Antibiotics				
021	Amikacin	250mg/ml	Injection (2ml)	A	V
051	Azithromycin	1g	Tablets	ABC	V
061	Azithromycin	200mg/5ml	Suspension	ABC	V
051	Chloramphenicol	250mg	Capsules	AB	E
061	Chloramphenicol	125mg/5ml	Suspension	AB	E
021	Chloramphenicol	1g	Powder for Injection	AB	E
051	Ciprofloxacin	500mg	Tablets	R	V
021	Ciprofloxacin	2mg/ml	Infusion (200ml)	R	V
051	Clindamycin	150mg	Capsules	A	E
021	Clindamycin	150mg/ml	Injection (4ml)	S	E
051	Doxycycline	100mg	Capsules	ABC	V
061	Erythromycin	125mg/5ml	Suspension	R	E
051	Erythromycin	250mg	Tablets	ABC	V

021	Erythromycin	1g	Powder for Injection	A	E
051	Fusidic Acid	250mg	Capsules	AB	N
061	Fusidic Acid	250mg/5ml	Syrup	S	N
021	Fusidic Acid	500mg	Powder for Injection	S	E
021	Gentamicin	10mg/ml	Injection (2ml)	AB	V
021	Gentamicin	40mg/ml	Injection (2ml)	AB	V
051	Hydroxychloroquine	200mg	Tablets	AB	E
021	Linezolid	2mg/ml	Infusion (300ml)	R	V
051	Linezolid	400mg	Tablets	R	V
051	Linezolid	600mg	Tablets	R	V
021	Meropenem	500mg	Injection	S	V
021	Meropenem	1g	Injection	S	V
051	Nalidixic Acid	500mg	Tablets	ABC	V
061	Nalidixic Acid	250mg/5ml	Suspension	ABC	V

051	Nitrofurantoin	100mg	Capsules	AB	E
021	Streptomycin	1g	Powder for Injection	ABC#	V
021	Vancomycin	500mg	Injection	S	V
021	Vancomycin	1g	Injection	S	V
	Systemic Antimycotics excluding Griseofulvin				
041	Amphotericin B	50mg	Powder for Injection	AB	V
021	Fluconazole	2mg/ml	Solution for Infusion	R	N
051	Fluconazole	200mg	Tablets	R	E
051	Itraconazole	100mg	Capsules	AB	E
051	Ketoconazole	200mg	Tablets	A	E
021	Voriconazole	200mg/ml	Injection	R	E
	Sulphonamides with Anti-Infectives in Combination				

051	Co-trimoxazole	80mg/400mg	Tablets	ABC	E
061	Co-trimoxazole	40mg/200mg/5ml	Suspension	ABC	E
021	Co-trimoxazole	80mg/400mg/5ml	Injection	AB	E
051	Metronidazole	400mg	Tablets	ABC	V
061	Metronidazole	200mg/5ml	Syrup	ABC	E
052	Metronidazole	1g	Suppositories	AB	E
021	Metronidazole	5mg/ml	Injection (100ml)	S	V
	Tuberculostatics, excluding Streptomycin				
051	Bedaquiline	100mg	Tablets	R	V
021	Capreomycin	1g	Injection	S	V
021	Cefoxitin	100mg	Injection	S	V
051	Clarithromycin	500mg	Tablets	S	V
051	Cycloserine	250mg	Tablets	AB	V
051	Delamanid	50mg	Tablets	R	V
051	Ethambutol	100mg	Tablets	ABC#	V

051	Ethambutol	400mg	Tablets	ABC#	V
051	Ethionamide	250mg	Tablets	AB	V
051	Isoniazid	100mg	Tablets	ABC#	V
021	Kanamycin	1g	Injection	AB	V
051	Levofloxacin	250mg	Tablets	AB	V
051	Moxifloxacin	400mg	Tablets	R	V
021	Moxifloxacin	400mg/250ml	Infusion	S	V
001	*p*-Amino Salicylic Acid	4g	Sachet	S	V
051	Pyrazinamide	500mg	Tablets	ABC#	V
051	Rifampicin	150mg	Capsules	ABC#	V
051	Rifampicin	450mg	Tablets	ABC#	V
061	Rifampicin	100mg/5ml	Syrup	ABC#	V
061	Rifampicin + Isoniazid	60mg +30mg	Tablets	ABC#	V
061	Rifampicin + Isoniazid	150mg +75mg	Tablets	ABC	V
061	Rifampicin + Isoniazid + Pyrazinamide	60mg +30mg +150mg	Tablets	ABC#	V

061	Rifampicin + Isoniazid + Ethambutol	150mg + 75mg + 275mg	Tablets	ABC#	V
061	Rifampicin + Isoniazid + Pyrazinamide + Ethambutol	150mg + 75mg + 400mg + 275mg	Tablets	ABC	V
	Leprostatics				
051	Clofazimine	100mg	Tablets	A	V
051	Dapsone	100mg	Tablets	A	V
051	Rifampicin	450 mg	Tablets	ABC#	V
	Antivirals for Systemic Use				
051	Acyclovir (Aciclovir)	400mg	Tablets	R	E
051	Acyclovir (Aciclovir)	800mg	Tablets	R	E
	Antiretrovirals				
012	Abacavir	300mg	Tablets	AB	V
012	Abacavir	20mg/ml	Liquid	AB	V

012	Abacavir	60mg	Tablets	AB	V
012	Didanosine	025mg	Capsules/Tablets	AB	V
012	Didanosine	050mg	Capsules/Tablets	AB	V
012	Didanosine	100mg	Capsules/Tablets	AB	V
012	Didanosine	200mg	Capsules/Tablets	AB	V
012	Didanosine	250mg	Capsules/Tablets	AB	V
012	Didanosine	400mg	Capsules/Tablets	AB	V
012	Efavirenz	050mg	Capsules/Tablets	AB	V
012	Efavirenz	100mg	Capsules/Tablets	AB	V
012	Efavirenz	200mg	Capsules/Tablets	AB	V
012	Efavirenz	600mg	Tablets	IMAI-R	V
012	Efavirenz	30mg/ml	Syrup	AB	V
012	Indinavir	400mg	Capsules	AB	V
012	Lamivudine	50mg/5ml	Oral Solution	AB	V
012	Lamivudine	150mg	Tablets	IMAI-R	V
012	Lamivudine + Abacavir	30mg + 60mg	Tablets	AB	V

012	Lamivudine + Stavudine	030mg + 06mg	Tablets	AB	V
012	Lamivudine + Stavudine	060mg + 12mg	Tablets	AB	V
012	Lamivudine + Stavudine	150mg + 30mg	Tablets	IMAI-R	V
012	Lamivudine + Stavudine + Abacavir	150mg + 300mg + 300mg	Tablets	IMAI-R	V
012	Lamivudine + Stavudine + Nevirapine	030mg + 06mg + 050mg	Tablets	AB	V
012	Lamivudine + Stavudine + Nevirapine	060mg + 12mg + 100mg	Tablets	AB	V
012	Lamivudine + Stavudine + Nevirapine	150mg + 30mg + 200mg	Tablets	IMAI-R	V
012	Lamivudine + Tenofovir	300mg + 300mg	Tablets	IMAI-R	V
012	Lamivudine + Zidovudine	30mg + 60mg	Tablets	AB	V
012	Lamivudine + Zidovudine	150mg + 300mg	Tablets	IMAI-R	V
012	Lamivudine + Zidovudine + Nevirapine	150mg + 300mg + 200mg	Tablets	IMAI-R	V
012	Lamivudine + Zidovudine + Nevirapine	30mg + 60mg + 50mg	Tablets	AB	V

012	Lopinavir + Ritonavir	(400 + 100)mg/5ml	Oral Solution	AB	V
012	Lopinavir + Ritonavir	200mg + 50mg	Tablets	AB	V
012	Lopinavir + Ritonavir	100mg + 25mg	Tablets	AB	V
012	Nevirapine	200mg	Tablets	IMAI-R	V
012	Nevirapine	50mg/5ml	Suspension	AB	V
012	Ritonavir	100mg	Capsules	AB	V
012	Stavudine	15mg	Capsules	AB	V
012	Stavudine	20mg	Capsules	AB	V
012	Stavudine	30mg	Capsules	AB	V
012	Stavudine	1mg/ml	Liquid	AB	V
012	Tenofovir	300mg	Tablets	IMAI-R	V
012	Tenofovir + Emtricitabine	300mg+200mg	Tablets	IMAI-R	V
012	Tenofovir + Emtricitabine + Efavirenz	300mg+200mg+600mg	Tablets	IMAI-R	V
012	Zidovudine	50mg/5ml	Syrup	AB	V
012	Zidovudine	100mg	Tablets	AB	V

012	Zidovudine	300mg	Tablets	IMAI-R	V

Appendix 4: Unique list of items

	ATC 1st level	ATC 2nd level	ATC 5th level	DDD in grams	Adm.Route	ATC 3rd level	ATC4thlevel	item description	pack size	strength
1	Anti-infectives for systemic use	Antibacterial drugs	J01AA02	0.1	O	Tetracyclines	Tetracyclines	Doxycycline 100mg tabs	100	100
2	Anti-infectives for systemic use	Antibacterial drugs	J01AA02	0.1	O	Tetracyclines	Tetracyclines	Doxycycline 100mg tabs	1000	100
3	Anti-infectives for systemic use	Antibacterial drugs	J01AA06	1	O	Tetracyclines	Tetracyclines	Oxytetracycline 250mg caps	1000	250
4	Anti-infectives for systemic use	Antibacterial drugs	J01BA01	3	P	Amphenicols	Amphenicols	Chloramphenicol 1gm inj	50	1000
5	Anti-infectives for systemic use	Antibacterial drugs	J01BA01	3	O	Amphenicols	Amphenicols	Chloramphenicol 250mg caps	1000	250
6	Anti-infectives for systemic use	Antibacterial drugs	J01BA01	3	O	Amphenicols	Amphenicols	Chloramphenicol 125mg/5ml susp	20	125

7	Anti-infectives for systemic use	Antibacterial drugs	J01BA01	3	P	Amphenicols	Amphenicols	Chloramphenicol 1gm inj	1	1000
8	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 500mg pfi	5	500
9	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 500mg pfi	50	500
10	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 250mg pfi	5	250
11	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 500mg pfi	100	500
12	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 250mg pfi	50	250
13	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 500mg pfi	10	500

14	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 250mg pfi	10	250
15	Anti-infectives for systemic use	Antibacterial drugs	J01CA01	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Ampicillin 250mg pfi	100	250
16	Anti-infectives for systemic use	Antibacterial drugs	J01CA12	14	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Piperacillin/tazobactam pfi	1	4500
17	Anti-infectives for systemic use	Antibacterial drugs	J01CA12	14	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Piperacillin/tazobactam pfi	12	4500
18	Anti-infectives for systemic use	Antibacterial drugs	J01CE08	3.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Benzathine penicillin 2.4mu	50	1500
19	Anti-infectives for systemic use	Antibacterial drugs	J01CE08	3.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Benzathine penicillin 2.4mu	10	1500
20	Anti-infectives for systemic use	Antibacterial drugs	J01CE09	0.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Procaine penicillin g 3miu inj	50	3000

21	Anti-infectives for systemic use	Antibacterial drugs	J01CE09	0.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Procaine penicillin g 3miu inj	10	3000
22	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 250mg pfi	10	250
23	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 250mg pfi	50	250
24	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 500mg pfi	10	500
25	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 500mg pfi	50	500
26	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 250mg caps	100	250
27	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 125mg/5ml syr	20	125

28	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 250mg caps	1000	250
29	Anti-infectives for systemic use	Antibacterial drugs	J01CF02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Cloxacillin 250mg caps	500	250
30	Anti-infectives for systemic use	Antibacterial drugs	J01DB04	3	P	first-generation cephalosporins	other beta-lactam antibacterials	Cefazoline 1g inj	1	1000
31	Anti-infectives for systemic use	Antibacterial drugs	J01DB04	3	P	first-generation cephalosporins	other beta-lactam antibacterials	Cefazoline 500mg inj	1	500
32	Anti-infectives for systemic use	Antibacterial drugs	J01DB09	2	O	first-generation cephalosporins	other beta-lactam antibacterials	Cefradine 125mg/5ml suspn	20	125
33	Anti-infectives for systemic use	Antibacterial drugs	J01DB09	2	O	first-generation cephalosporins	other beta-lactam antibacterials	Cefradine 500mg caps	100	500
34	Anti-infectives for systemic use	Antibacterial drugs	J01DB09	2	O	first-generation cephalosporins	other beta-lactam antibacterials	Cefradine 500mg caps	20	500

35	Anti-infectives for systemic use	Antibacterial drugs	J01DC01	6	P	second-generation cephalosporins	other beta-lactam antibacterials	Cefoxitin 1g inj	50	1000
36	Anti-infectives for systemic use	Antibacterial drugs	J01DC01	6	P	second-generation cephalosporins	other beta-lactam antibacterials	Cefoxitin 1g inj	1	1000
37	Anti-infectives for systemic use	Antibacterial drugs	J01DC02	3	P	second-generation cephalosporins	other beta-lactam antibacterials	Cefuroxime 750mg pfi	1	750
38	Anti-infectives for systemic use	Antibacterial drugs	J01DC02	3	P	second-generation cephalosporins	other beta-lactam antibacterials	Cefuroxime 750mg pfi	50	750
39	Anti-infectives for systemic use	Antibacterial drugs	J01DC02	0.5	O	second-generation cephalosporins	other beta-lactam antibacterials	Cefuroxime 250mgtabs	10	250
40	Anti-infectives for systemic use	Antibacterial drugs	J01DC02	0.5	O	second-generation cephalosporins	other beta-lactam antibacterials	Cefuroxime 125mg/5ml suspn	20	125
41	Anti-infectives for systemic use	Antibacterial drugs	J01DC02	0.5	O	second-generation cephalosporins	other beta-lactam antibacterials	Cefuroxime tabs 250mg	100	250

42	Anti-infectives for systemic use	Antibacterial drugs	J01DC02	3	P	second-generation cephalosporins	other beta-lactam antibacterials	Cefuroxime 750mg pfi	10	750
43	Anti-infectives for systemic use	Antibacterial drugs	J01DD02	4	P	third-generation cephalosporins	other beta-lactam antibacterials	Ceftazidime 1g inj	1	1000
44	Anti-infectives for systemic use	Antibacterial drugs	J01DD04	2	P	third-generation cephalosporins	other beta-lactam antibacterials	Ceftriaxone 250mg pfi	1	250
45	Anti-infectives for systemic use	Antibacterial drugs	J01DD04	2	P	third-generation cephalosporins	other beta-lactam antibacterials	Ceftriaxone 1gm pfi	1	1000
46	Anti-infectives for systemic use	Antibacterial drugs	J01DD08	0.4	O	third-generation cephalosporins	other beta-lactam antibacterials	Cefixime 200mg tabs	100	200
47	Anti-infectives for systemic use	Antibacterial drugs	J01DD08	0.4	O	third-generation cephalosporins	other beta-lactam antibacterials	Cefixime 200mg tabs	20	200
48	Anti-infectives for systemic use	Antibacterial drugs	J01DH02	2	P	carbapenems	other beta-lactam antibacterials	Meropenem 1g inj	1	1000

49	Anti-infectives for systemic use	Antibacterial drugs	J01DH02	2	P	carbapenems	other beta-lactam antibacterials	Meropenem 500mg inj	1	500
50	Anti-infectives for systemic use	Antibacterial drugs	J01DH51	2	P	carbapenems	other beta-lactam antibacterials	Imipenem 500 mg + cilastatin	1	500
51	Anti-infectives for systemic use	Antibacterial drugs	J01DH51	2	P	carbapenems	other beta-lactam antibacterials	Imipenem 500mg inj	1	500
52	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 80+400mg tabs	500	480
53	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 80+400mg tabs	100	480
54	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 80+400mg tabs	1000	480

55	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	3.36	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 40/200mg/5ml	20	240
56	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	3.36	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 40/200mg/5ml	20	240
57	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	P	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 80mg/400mg inj	10	480
58	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 160+800mg tabs	500	960
59	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	O	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 80+400mg tabs	1000	480

60	Anti-infectives for systemic use	Antibacterial drugs	J01EE01	1.92	P	combinations of sulfonamides and trimethoprim, incl. derivatives	sulfonamides and trimethoprim	Co-trimoxazole 80mg/400mg inj	5	480
61	Anti-infectives for systemic use	Antibacterial drugs	J01FA01	1	O	macrolides	macrolides, lincosamides and streptogramins	Erythromycin 250mg tabs	100	250
62	Anti-infectives for systemic use	Antibacterial drugs	J01FA01	1	P	macrolides	macrolides, lincosamides and streptogramins	Erythromycin 1g pfi	1	1000
63	Anti-infectives for systemic use	Antibacterial drugs	J01FA01	1	O	macrolides	macrolides, lincosamides and streptogramins	Erythromycin 125mg/5ml suspn	20	125
64	Anti-infectives for systemic use	Antibacterial drugs	J01FA09	0.5	O	macrolides	macrolides, lincosamides and streptogramins	Clarithromycin 500mg tabs	14	500
65	Anti-infectives for systemic use	Antibacterial drugs	J01FA10	0.3	O	macrolides	macrolides, lincosamides	Azithromycin 500mg tabs	3	500

							and streptogramins			
66	Anti-infectives for systemic use	Antibacterial drugs	J01FA10	0.3	O	macrolides	macrolides, lincosamides and streptogramins	Azithromycin 200mg/5ml suspn	20	200
67	Anti-infectives for systemic use	Antibacterial drugs	J01FA10	0.3	O	macrolides	macrolides, lincosamides and streptogramins	Azithromycin 1000mg tabs	30	1000
68	Anti-infectives for systemic use	Antibacterial drugs	J01FF01	1.2	O	lincosamides	macrolides, lincosamides and streptogramins	Clindamycin 150mg caps	100	150
69	Anti-infectives for systemic use	Antibacterial drugs	J01FF01	1.8	P	lincosamides	macrolides, lincosamides and streptogramins	Clindamycin 150mg/ml inj 4ml	1	600
70	Anti-infectives for systemic use	Antibacterial drugs	J01FF01	1.8	P	lincosamides	macrolides, lincosamides and streptogramins	Clindamycin 150mg/ml inj 4ml	10	600

71	Anti-infectives for systemic use	Antibacterial drugs	J01GA01	1	P	streptomycins	aminoglycoside antibacterials	Streptomycin sulphate 1gm pfi	50	1000
72	Anti-infectives for systemic use	Antibacterial drugs	J01GB04	1	P	other aminoglycosides	aminoglycoside antibacterials	Kanamycin 1g inj	50	1000
73	Anti-infectives for systemic use	Antibacterial drugs	J01GB04	1	P	other aminoglycosides	aminoglycoside antibacterials	Kanamycin 1g inj	10	1000
74	Anti-infectives for systemic use	Antibacterial drugs	J01GB06	1	P	other aminoglycosides	aminoglycoside antibacterials	Amikacin 250mg/ml inj 2ml	10	500
75	Anti-infectives for systemic use	Antibacterial drugs	J01GB06	1	P	other aminoglycosides	aminoglycoside antibacterials	Amikacin 250mg/ml inj 2ml	1	250
76	Anti-infectives for systemic use	Antibacterial drugs	J01MA01	0.4	O	fluoroquinolones	quinolone antibacterials	Ofloxacin 400mg tabs	1000	400
77	Anti-infectives for systemic use	Antibacterial drugs	J01MA02	1	O	fluoroquinolones	quinolone antibacterials	Ciprofloxacin 500mg tabs	10	500
78	Anti-infectives for systemic use	Antibacterial drugs	J01MA02	1	O	fluoroquinolones	quinolone antibacterials	Ciprofloxacin 2mg/ml 200ml	1	400
79	Anti-infectives for systemic use	Antibacterial drugs	J01MA02	1	O	fluoroquinolones	quinolone antibacterials	Ciprofloxacin 500mg tabs	10	500

80	Anti-infectives for systemic use	Antibacterial drugs	J01MA02	1	O	fluoroquinolones	quinolone antibacterials	Ciprofloxacin 250mg/5ml susp	20	250
81	Anti-infectives for systemic use	Antibacterial drugs	J01MA12	0.5	O	fluoroquinolones	quinolone antibacterials	Levofloxacin 250mg tabs	672	250
82	Anti-infectives for systemic use	Antibacterial drugs	J01MA12	0.5	O	fluoroquinolones	quinolone antibacterials	Levofloxaciin 250mg tabs	100	250
83	Anti-infectives for systemic use	Antibacterial drugs	J01MA12	0.5	O	fluoroquinolones	quinolone antibacterials	Levofloxacin 500mg tabs	5	500
84	Anti-infectives for systemic use	Antibacterial drugs	J01MA12	0.5	O	fluoroquinolones	quinolone antibacterials	Levofloxacin 500mg tabs	10	500
85	Anti-infectives for systemic use	Antibacterial drugs	J01MA12	0.5	O	fluoroquinolones	quinolone antibacterials	Levofloxacin 250mg tabs	5	250
86	Anti-infectives for systemic use	Antibacterial drugs	J01MA12	0.5	O	fluoroquinolones	quinolone antibacterials	Levofloxacin 250mg tabs	50	250
87	Anti-infectives for systemic use	Antibacterial drugs	J01MA14	0.4	O	fluoroquinolones	quinolone antibacterials	Moxifloxacin 400mg tabs	5	400
88	Anti-infectives for systemic use	Antibacterial drugs	J01MA14	0.4	O	fluoroquinolones	quinolone antibacterials	Moxifloxacin 400mg/250ml inj	1	400

89	Anti-infectives for systemic use	Antibacterial drugs	J01MB02	4	O	other quinolones	quinolone antibacterials	Nalidixic acid 500mg tabs	100	500
90	Anti-infectives for systemic use	Antibacterial drugs	J01MB02	4	O	other quinolones	quinolone antibacterials	Nalidixic acid 250mg/5ml suspn	20	250
91	Anti-infectives for systemic use	Antibacterial drugs	J01MB02	4	O	other quinolones	quinolone antibacterials	Nalidixic acid 500mg tabs	1000	500
92	Anti-infectives for systemic use	Antibacterial drugs	J01XA01	2	P	glycopeptide antibacterials	other antibacterials	Vancomycin hcl 500mg pfi	10	500
93	Anti-infectives for systemic use	Antibacterial drugs	J01XA01	2	P	glycopeptide antibacterials	other antibacterials	Vancomycin hcl 1g pfi	10	1000
94	Anti-infectives for systemic use	Antibacterial drugs	J01XA02	0.4	P	glycopeptide antibacterials	other antibacterials	Teicoplanin 400mg inj	1	400
95	Anti-infectives for systemic use	Antibacterial drugs	J01XC01	1.5	P	steroid antibacterials	other antibacterials	Fusidic acid 500mg pfi	1	500
96	Anti-infectives for systemic use	Antibacterial drugs	J01XC01	1.5	O	steroid antibacterials	other antibacterials	Fusidic acid 250mg/5ml suspn	20	500
97	Anti-infectives for systemic use	Antibacterial drugs	J01XE01	0.2	O	nitrofuran derivatives	other antibacterials	Nitrofurantoin 100mg caps	250	100

98	Anti-infectives for systemic use	Antibacterial drugs	J01XE01	0.2	O	nitrofuran derivatives	other antibacterials	Nitrofurantoin 100mg caps	1000	100
99	Anti-infectives for systemic use	Antibacterial drugs	J01XE01	0.2	O	nitrofuran derivatives	other antibacterials	Nitrofurantoin 100mg caps	50	100
100	Anti-infectives for systemic use	Antibacterial drugs	J01XE01	0.2	O	nitrofuran derivatives	other antibacterials	Nitrofurantoin 100mg caps	30	100
101	Anti-infectives for systemic use	Antibacterial drugs	J01XX08	1.2	P	other antibacterials	other antibacterials	Linezolid 600mg/300ml infusion	1	600
102	Anti-infectives for systemic use	Antibacterial drugs	J01XX08	1.2	P	other antibacterials	other antibacterials	Linezolid 600mg/300ml iv infus	10	600
103	Anti-infectives for systemic use	Antibacterial drugs	J01XX08	1.2	O	other antibacterials	other antibacterials	Linezolid 600mg tabs	10	600
104	Anti-infectives for systemic use	Antibacterial drugs	J01XX08	1.2	O	other antibacterials	other antibacterials	Linezolid 400mg tabs	10	400
105	Anti-infectives for systemic use	Antibacterial drugs	J01CE01	3.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Benzyl penicillin g 5mu pfi	50	5000

106	Anti-infectives for systemic use	Antibacterial drugs	J01CE01	3.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Benzyl penicillin g 1mu pfi	50	1000
107	Anti-infectives for systemic use	Antibacterial drugs	J01CE01	3.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Benzyl penicillin g 1mu pfi	100	1000
108	Anti-infectives for systemic use	Antibacterial drugs	J01GB03	0.24	P	other aminoglycosides	aminoglycoside antibacterials	Gentamycin 40mg/ml inj 2ml	10	80
109	Anti-infectives for systemic use	Antibacterial drugs	J01GB03	0.24	P	other aminoglycosides	aminoglycoside antibacterials	Gentamycin 10mg/ml inj 2ml	10	20
110	Anti-infectives for systemic use	Antibacterial drugs	J01GB03	0.24	P	other aminoglycosides	aminoglycoside antibacterials	Gentamycin 10mg/ml inj 2ml	100	20
111	Anti-infectives for systemic use	Antibacterial drugs	J01GB03	0.24	P	other aminoglycosides	aminoglycoside antibacterials	Gentamycin 40mg/ml inj 2ml	100	80
112	Anti-infectives for systemic use	Antibacterial drugs	J01CA04	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 250mg caps	100	250
113	Anti-infectives for systemic use	Antibacterial drugs	J01CA04	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 250mg caps	500	250

114	Anti-infectives for systemic use	Antibacterial drugs	J01CR02	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 875mg+clavulanic	10	875
115	Anti-infectives for systemic use	Antibacterial drugs	J01CA04	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 125mg/5ml suspn	20	125
116	Anti-infectives for systemic use	Antibacterial drugs	J01CA04	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 250mg caps	1000	250
117	Anti-infectives for systemic use	Antibacterial drugs	J01CR02	3	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 500mg + clavulanic	5	500
118	Anti-infectives for systemic use	Antibacterial drugs	J01CR02	3	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 1000mg +clavulanic	5	1000
119	Anti-infectives for systemic use	Antibacterial drugs	J01CA04	3	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 500mg + clavulanic	10	500
120	Anti-infectives for systemic use	Antibacterial drugs	J01CA04	3	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 1000mg +clavulanic	10	1000

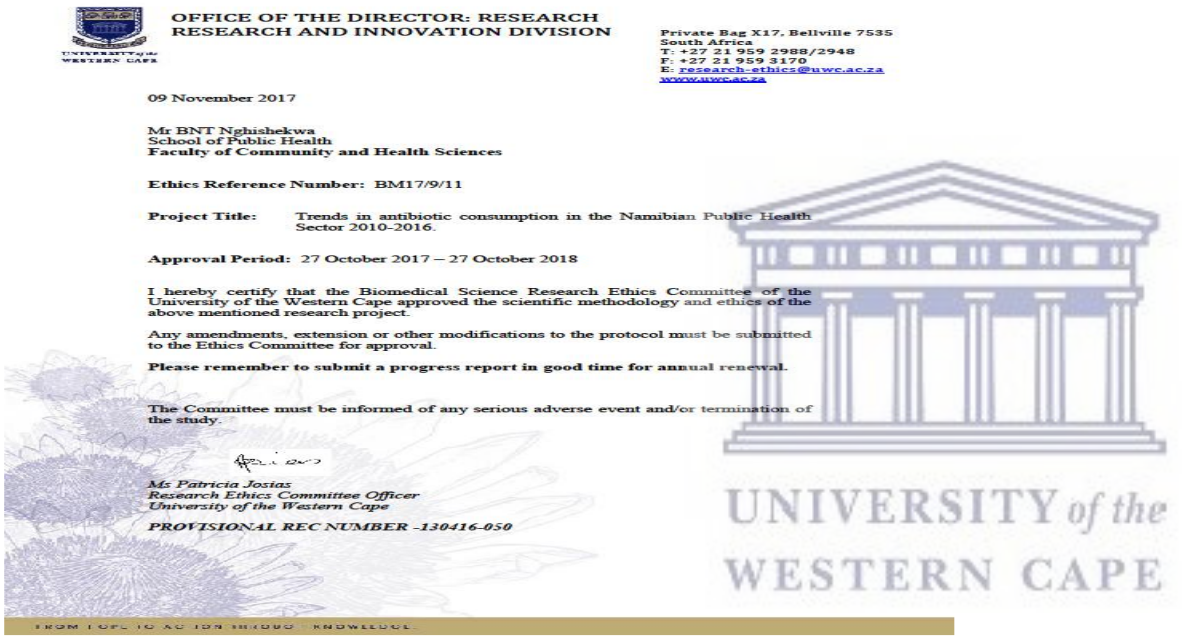
121	Anti-infectives for systemic use	Antibacterial drugs	J01CR02	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 875mg + clavulanic	10	875
122	Anti-infectives for systemic use	Antibacterial drugs	J01CR02	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 250mg + clavulanic	15	250
123	Anti-infectives for systemic use	Antibacterial drugs	J01CR02	1	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Amoxycillin 125mg + clavulanic	20	125
124	Anti-infectives for systemic use	Antibacterial drugs	J01CE02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Pen v k 250mg tabs	500	250
125	Anti-infectives for systemic use	Antibacterial drugs	J01CE02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Pen v k 250mg tabs	1000	250
126	Anti-infectives for systemic use	Antibacterial drugs	J01CE02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Pen v k 250mg/5ml suspn	20	250
127	Anti-infectives for systemic use	Antibacterial drugs	J01CE02	2	O	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Pen v k 125mg/5ml suspn	20	125

128	Anti-infectives for systemic use	Antibacterial drugs	J01CE01	3.6	P	beta-lactam antibacterials, penicillins	beta-lactam antibacterials, penicillins	Penicillin 1.2miu pfi	50	750

Appendix 5: Data Collection Tool

Anatomical Therapeutic Class (ATC) 1	ATC2	ATC3	ATC4	ATC5	Stock code	Pack size	item	DDD miligrams	strength miligrams	DDD per pack	region	number of packs issued 2010	85% pop2010	DDD issued 2010	2010 DID

Appendix 6: Ethical clearance from the University of the Western Cape Biomedical Research Ethics Committee & permission for access and use of the data for the study provided by MoHSS



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09 November 2017

Mr BNT Nghishekwa
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM17/9/11

Project Title: Trends in antibiotic consumption in the Namibian Public Health Sector 2010-2016.

Approval Period: 27 October 2017 – 27 October 2018

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

UNIVERSITY of the WESTERN CAPE

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198
Windhoek
Namibia

Ministerial Building
Harvey Street
Windhoek

Tel: 061 – 2032150
Fax: 061 – 222558
Email: shimenghipangelwa71@gmail.com

OFFICE OF THE PERMANENT SECRETARY

Ref: 17/3/3 BN
Enquiries: Mr. J. Nghipangelwa

Date: 07 December 2017

Ms. B N Nghishekwa
University of Western Cape
Cape Town

Dear Ms. Nghishekwa

Re: Trends in Antibiotic consumption in the Namibian Public Health Sector 2010-2016

1. Reference is made to your application to conduct the above-mentioned study.
2. The proposal has been evaluated and found to have merit.
3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for academic purposes;
3.2 No other data should be collected other than the data stated in the proposal;
3.3 Stipulated ethical considerations in the protocol related to the protection of Human Subjects' should be observed and adhered to, any violation thereof will lead to termination of the study at any stage;
3.4 A quarterly report to be submitted to the Ministry's Research Unit;
3.5 Preliminary findings to be submitted upon completion of the study;

3.6 Final report to be submitted upon completion of the study;

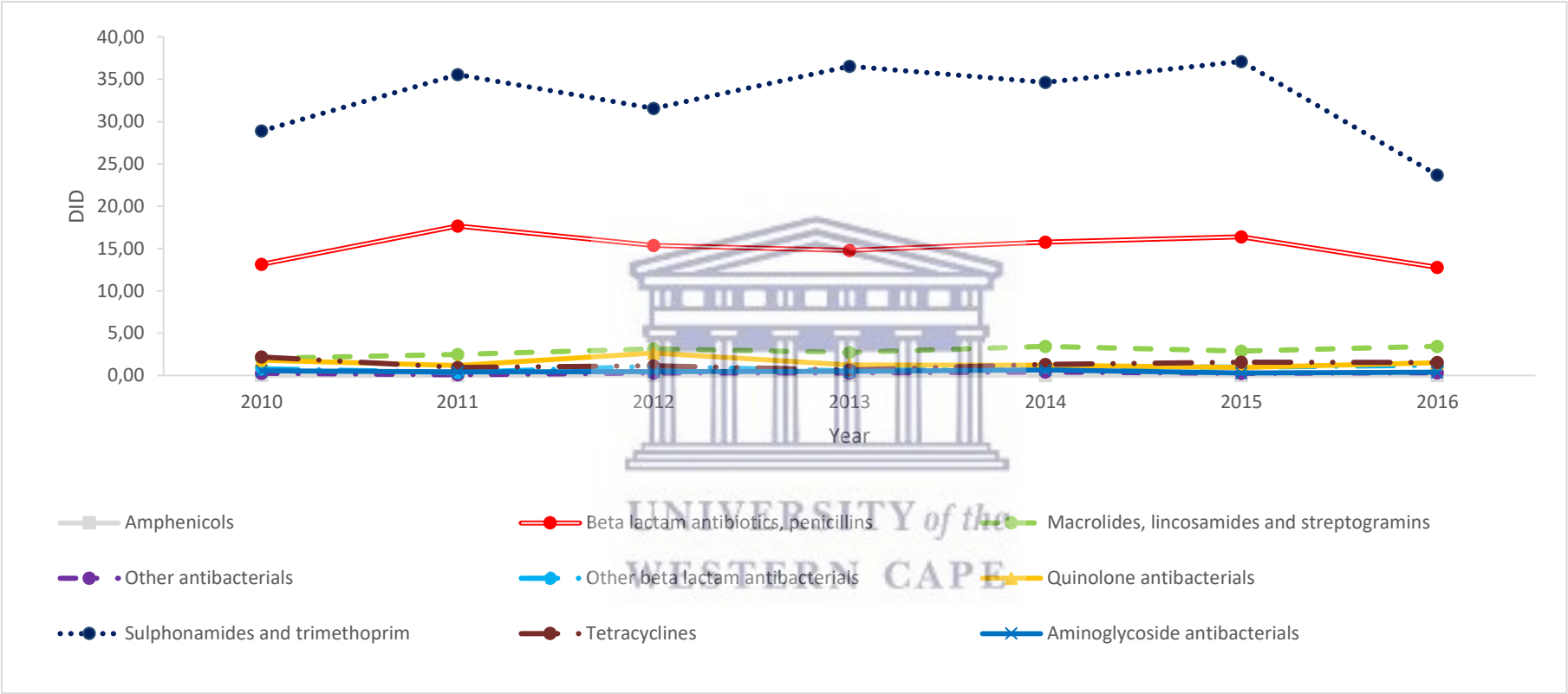
3.7 Separate permission should be sought from the Ministry of Health and Social Services for the publication of the findings.

Yours sincerely,

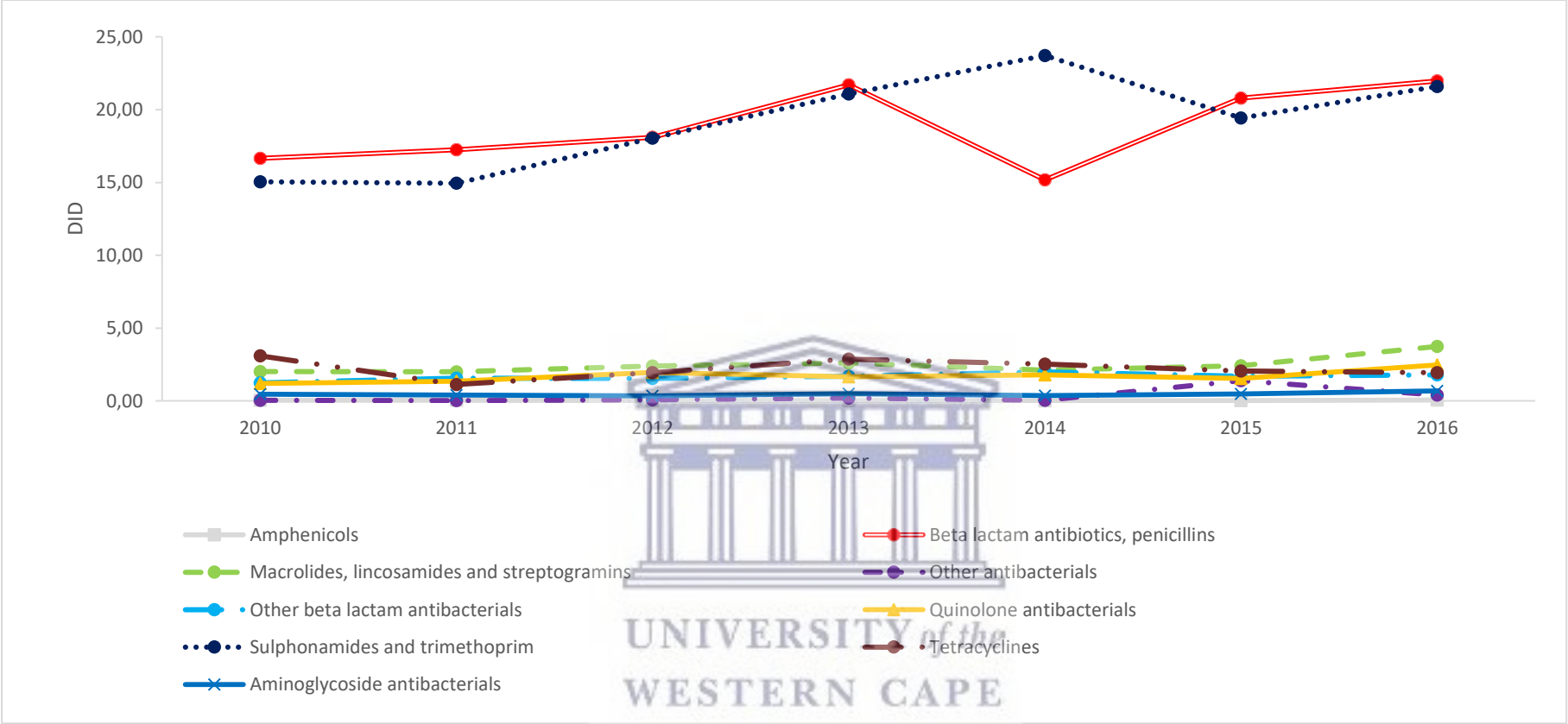
PERMANENT SECRETARY
MINISTRY OF HEALTH & SOCIAL SERVICES

Andreas Mwoombola (Dr.)
Permanent Secretary

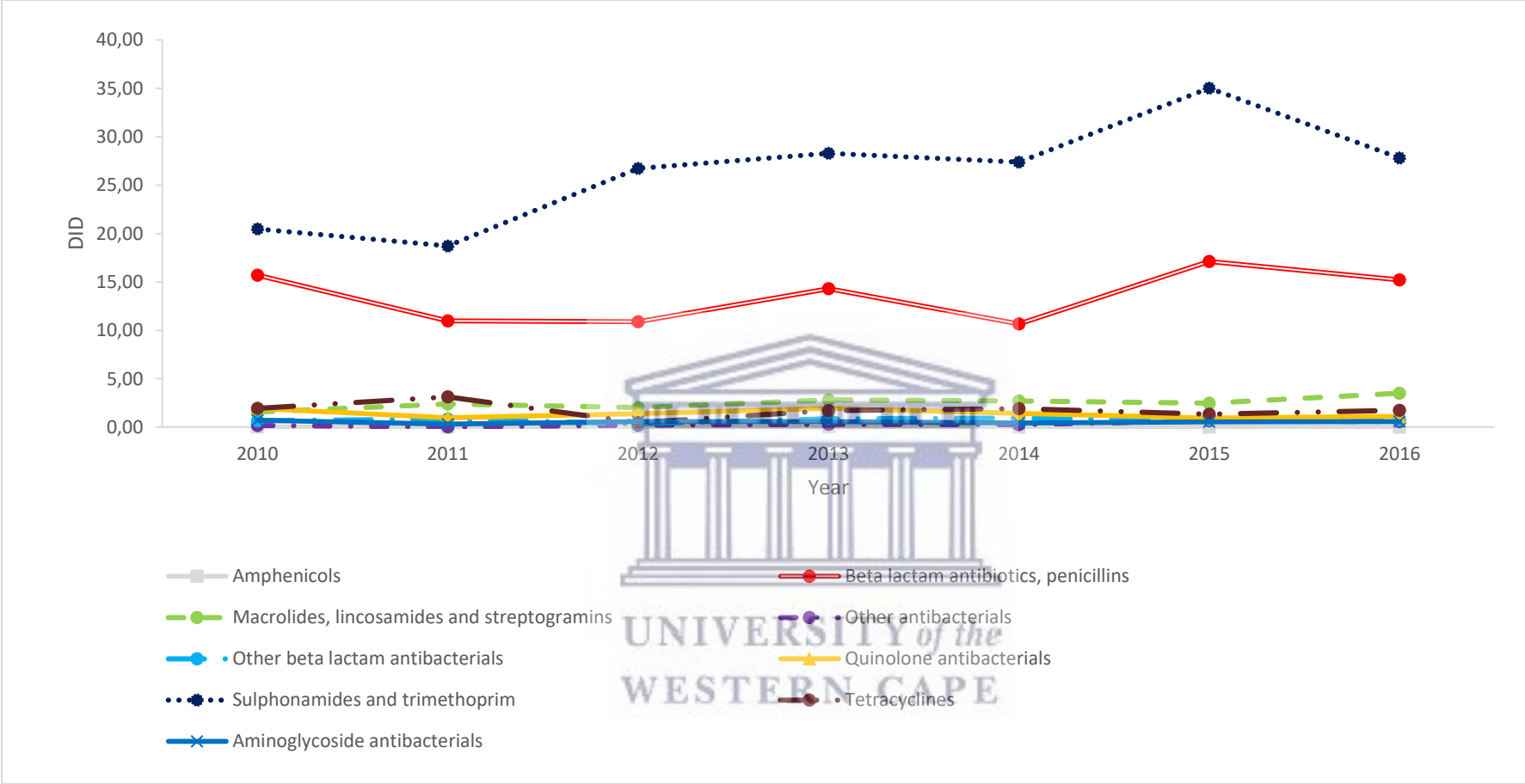
Appendix 7: National antibiotic consumption trends per antibiotic classification



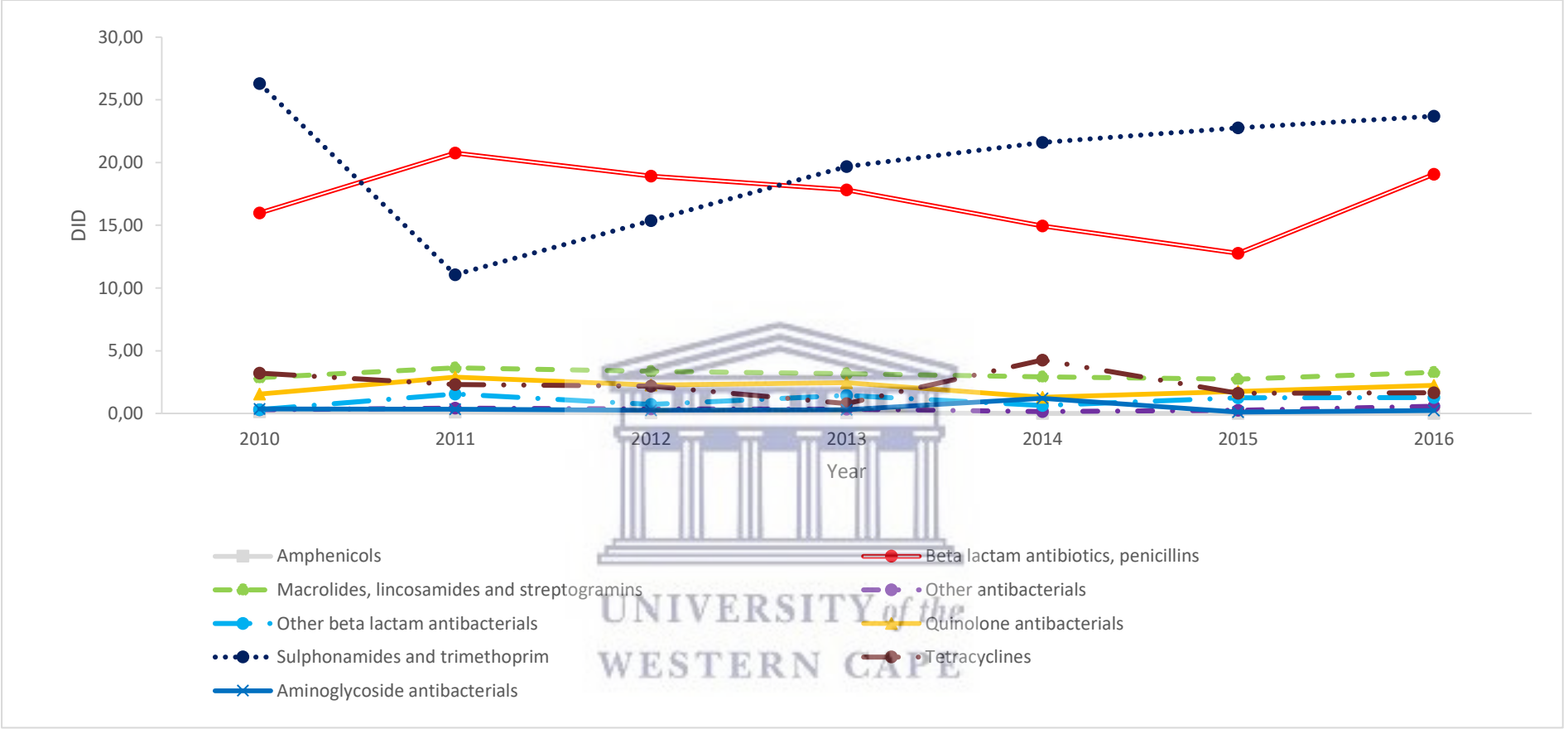
National antibiotic consumption trends per antibiotic classification, Erongo, 2010-2016



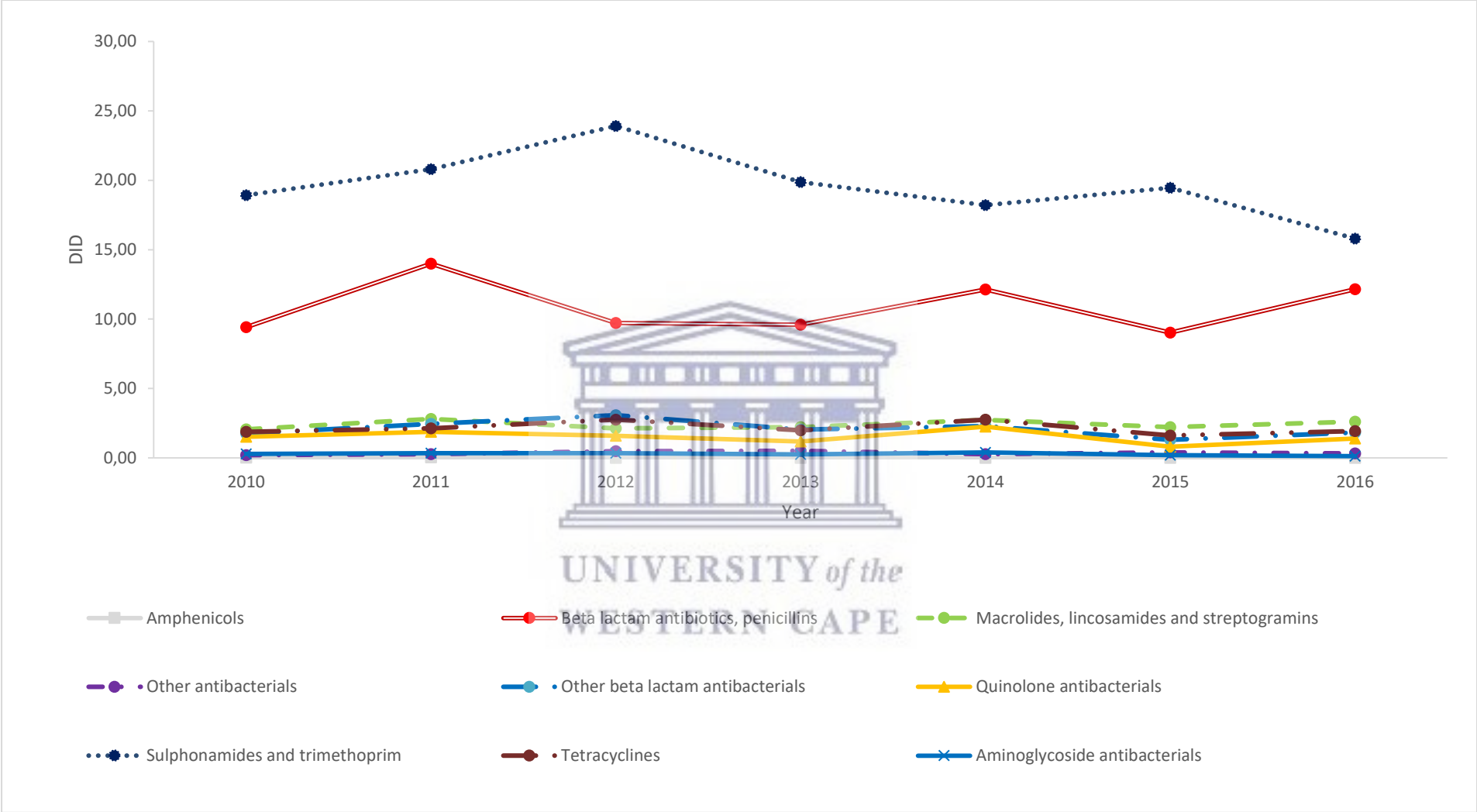
National antibiotic consumption trends per antibiotic classification, Hardap, 2010-2016



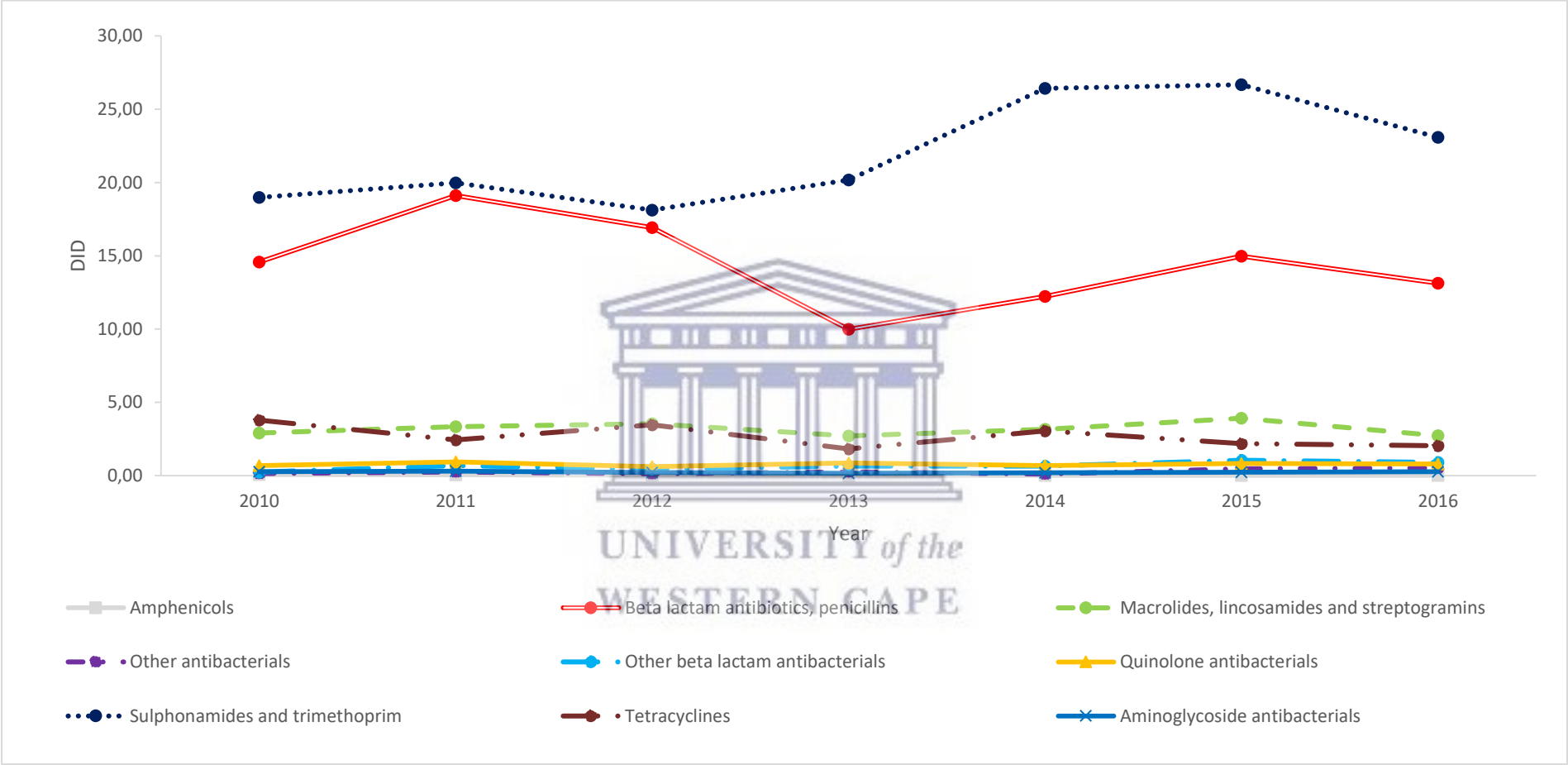
National antibiotic consumption trends per antibiotic classification, Karas, 2010-2016



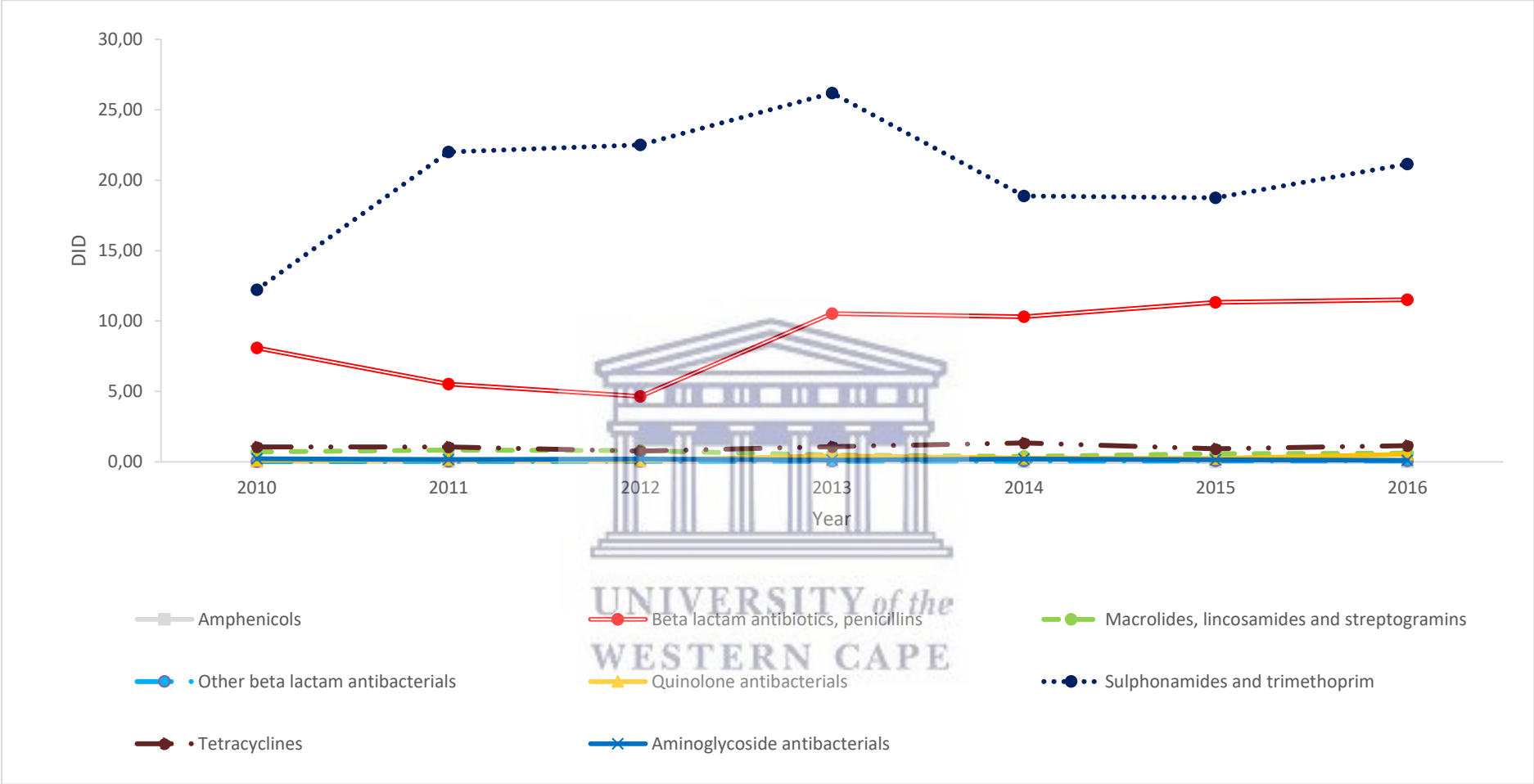
National antibiotic consumption trends per antibiotic classification, Kavango, 2010-2016



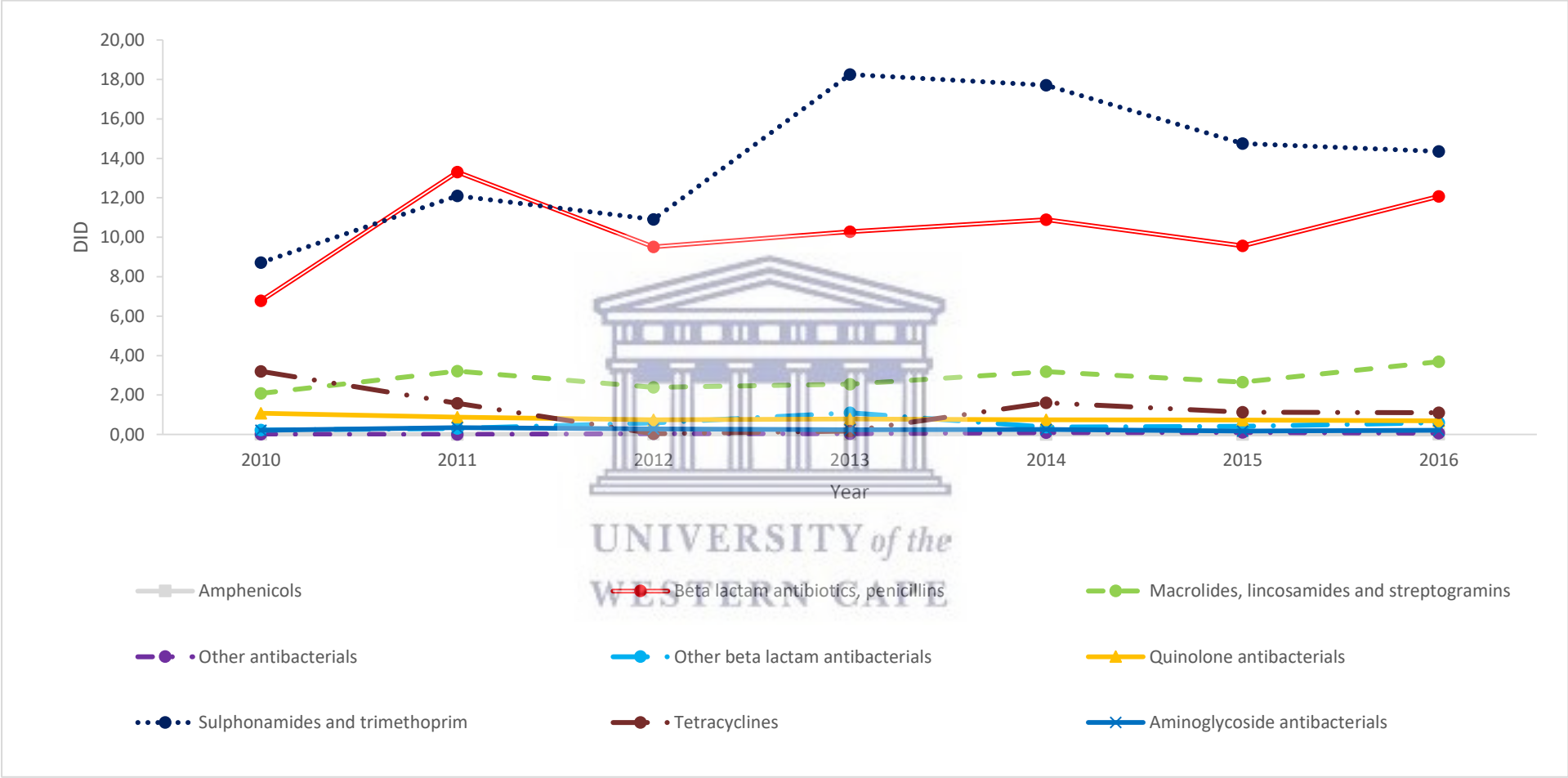
National antibiotic consumption trends per antibiotic classification, Khomas, 2010-2016



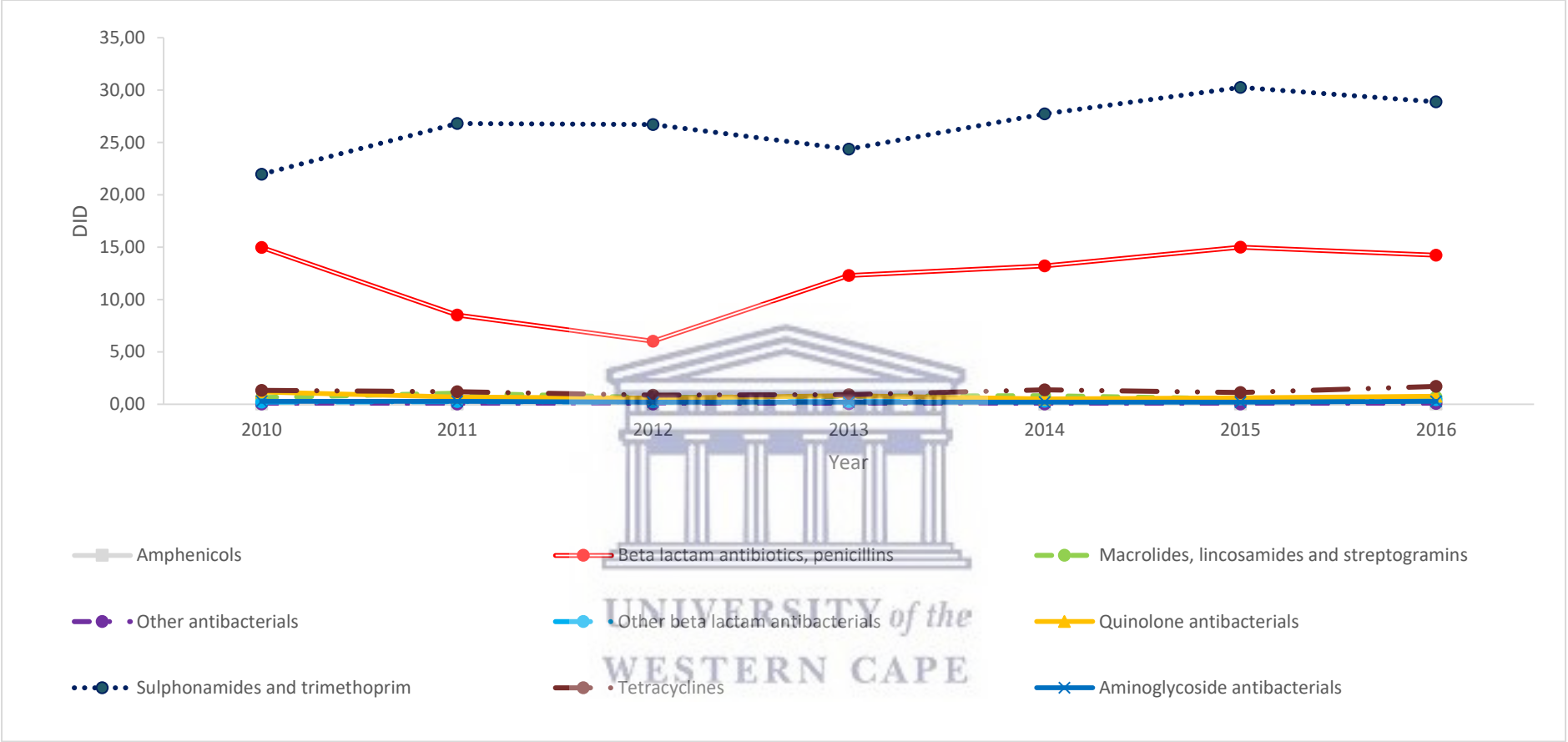
National antibiotic consumption trends per antibiotic classification, Kunene, 2010-2016



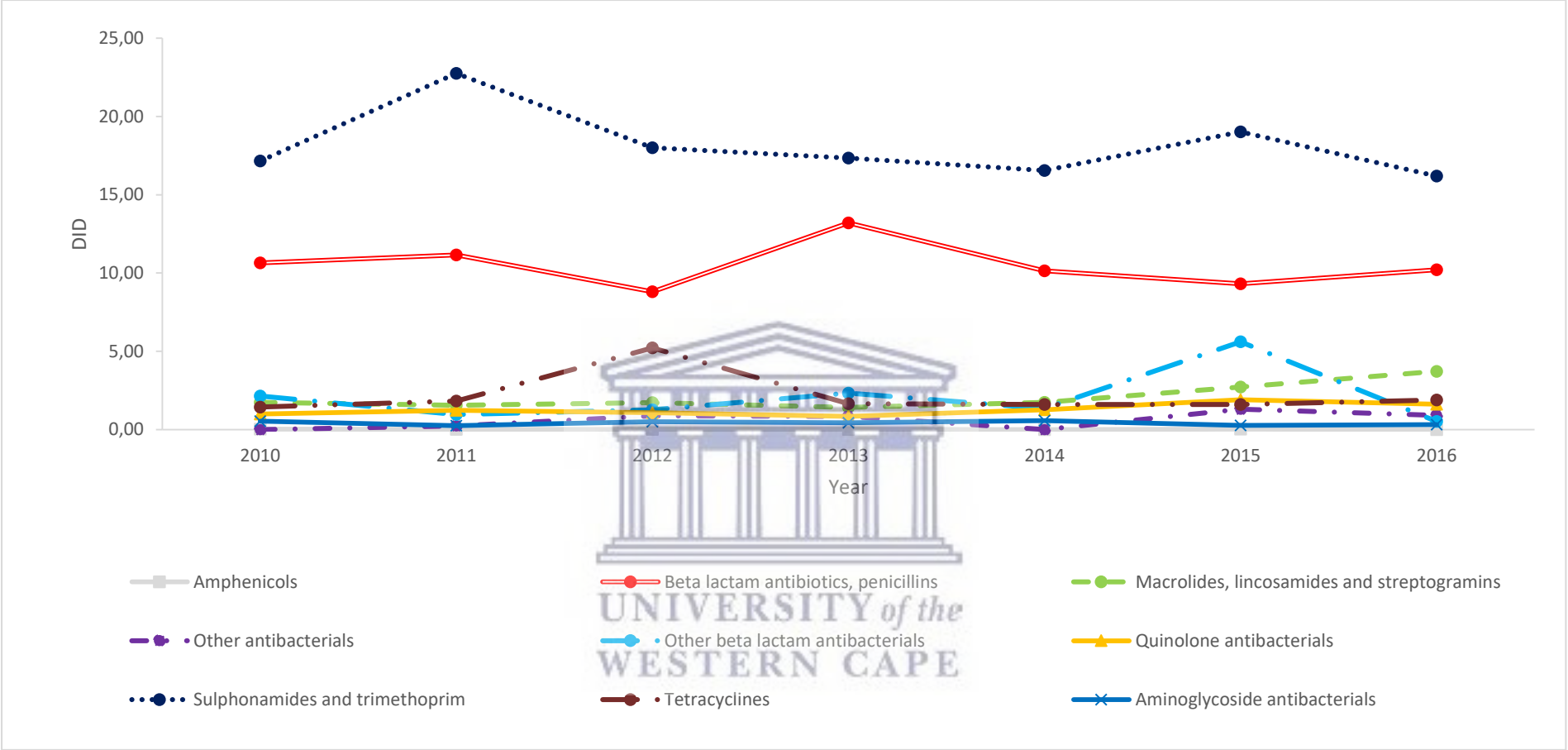
National antibiotic consumption trends per antibiotic classification, Ohangwena, 2010-2016



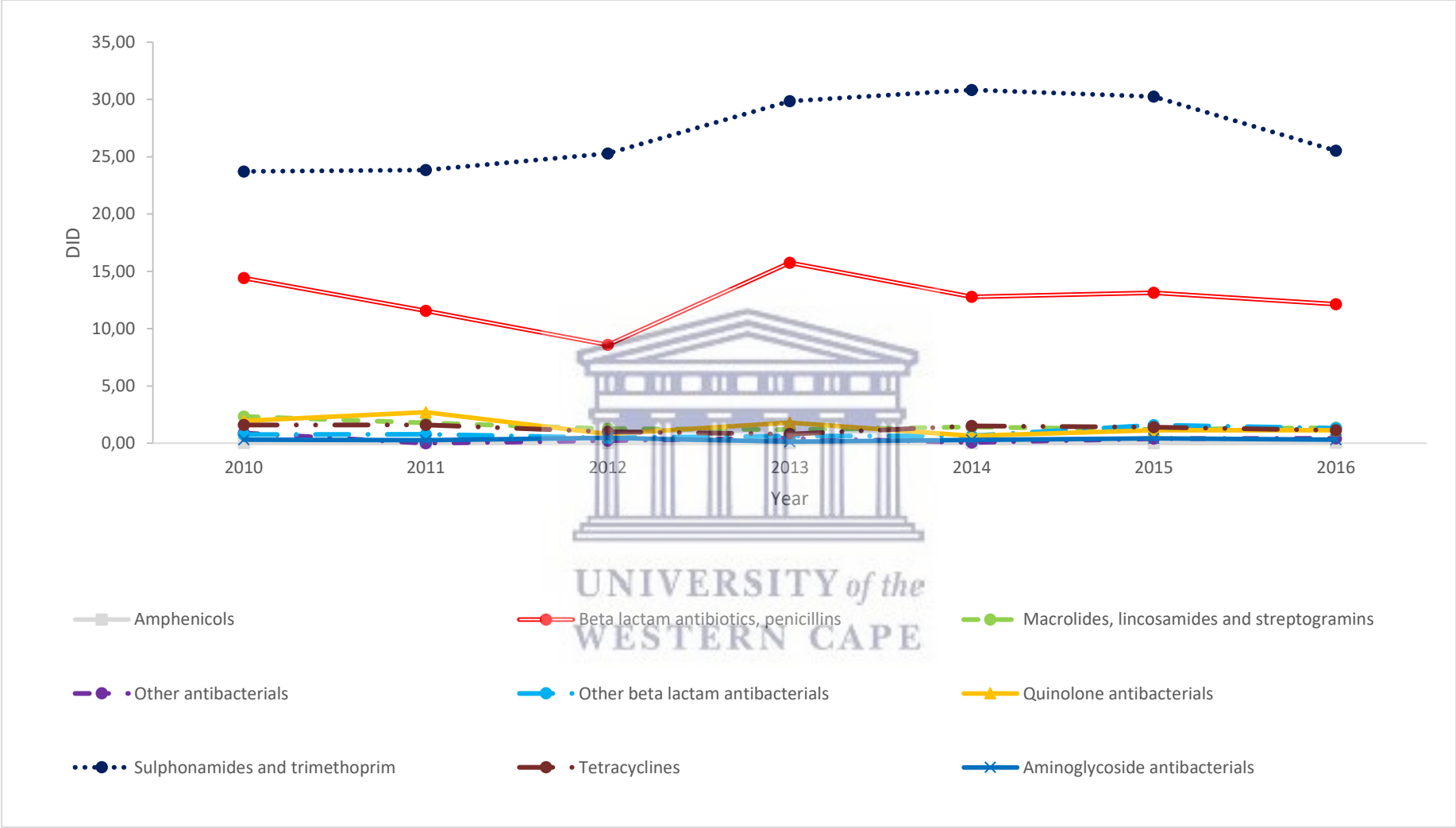
National antibiotic consumption trends per antibiotic classification, Omaheke, 2010-2016



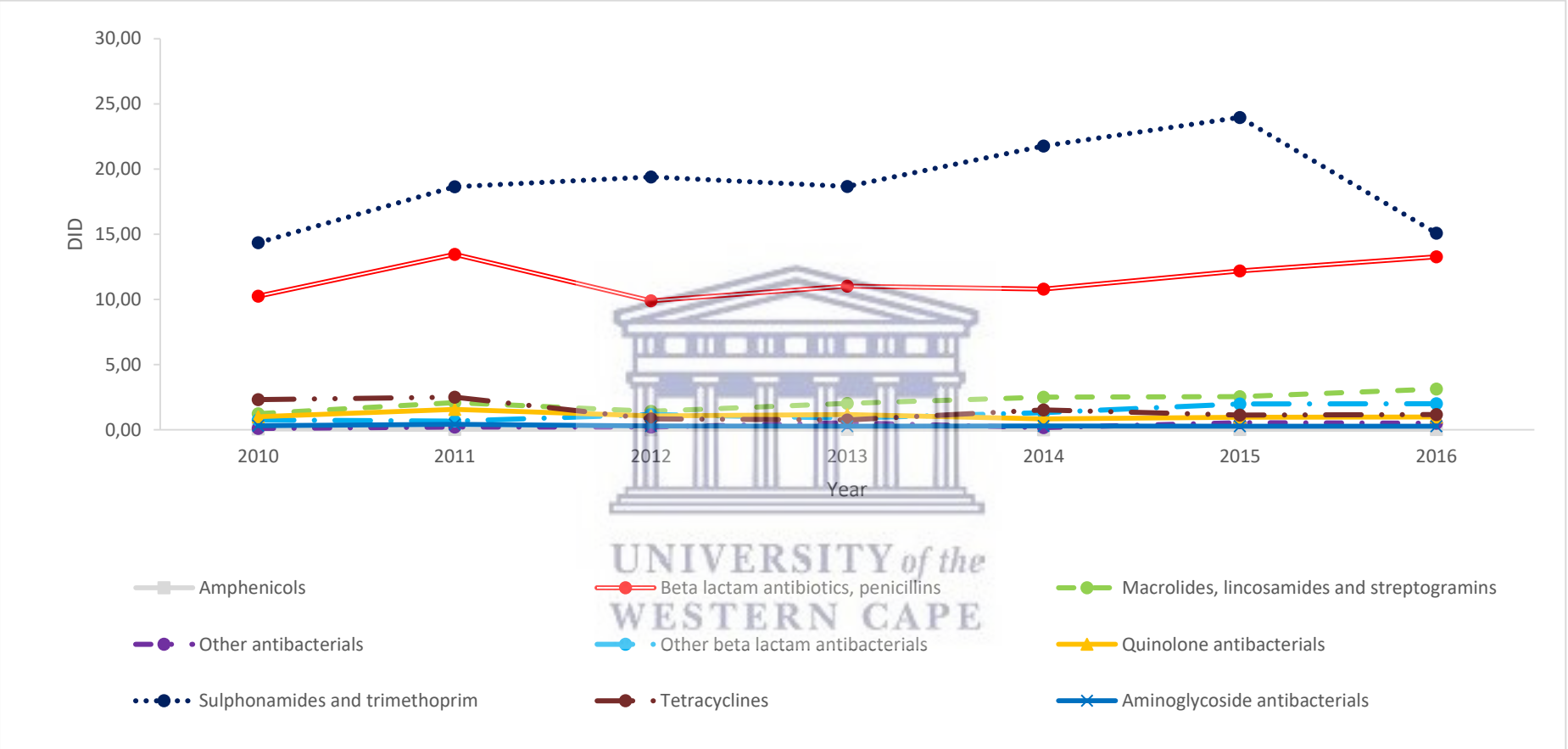
National antibiotic consumption trends per antibiotic classification, Omusati, 2010-2016



National antibiotic consumption trends per antibiotic classification, Oshana, 2010-2016

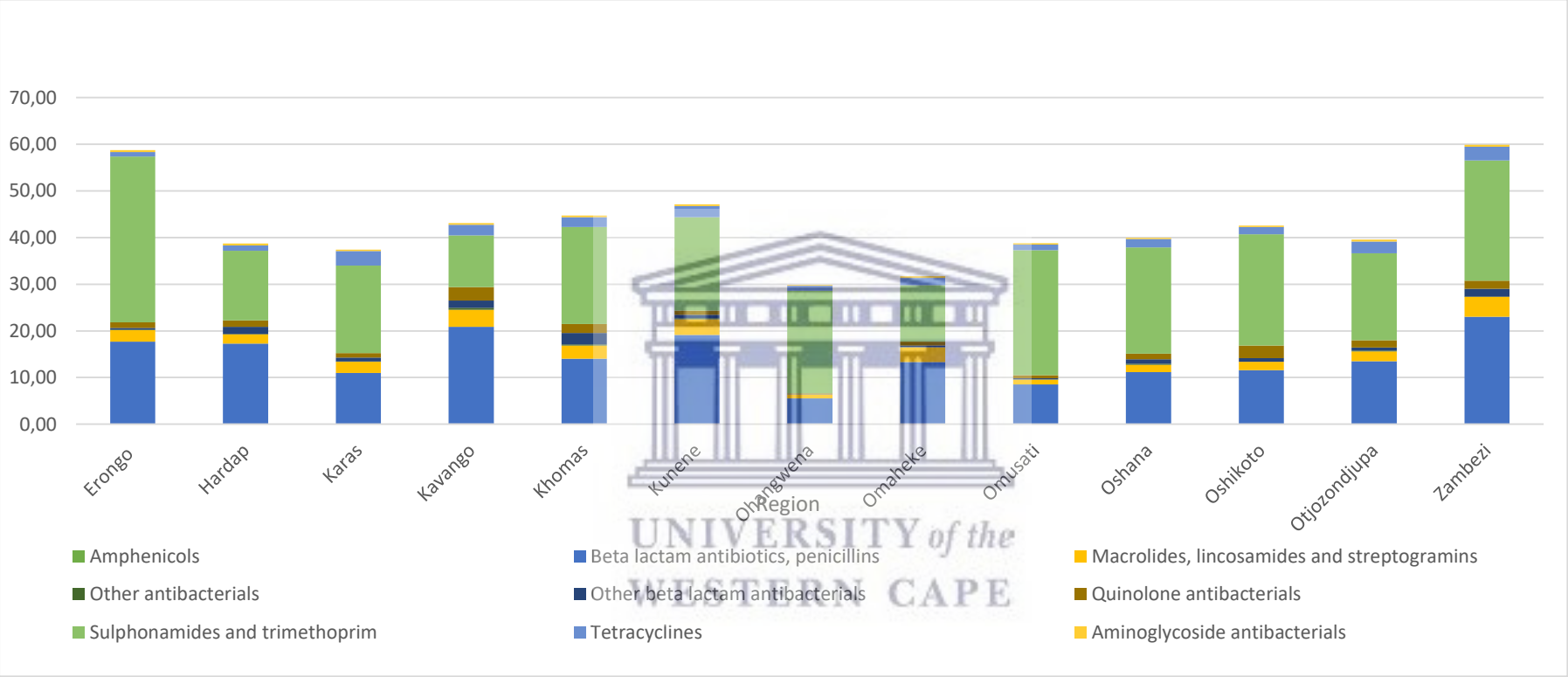


National antibiotic consumption trends per antibiotic classification, Oshikoto, 2010-2016

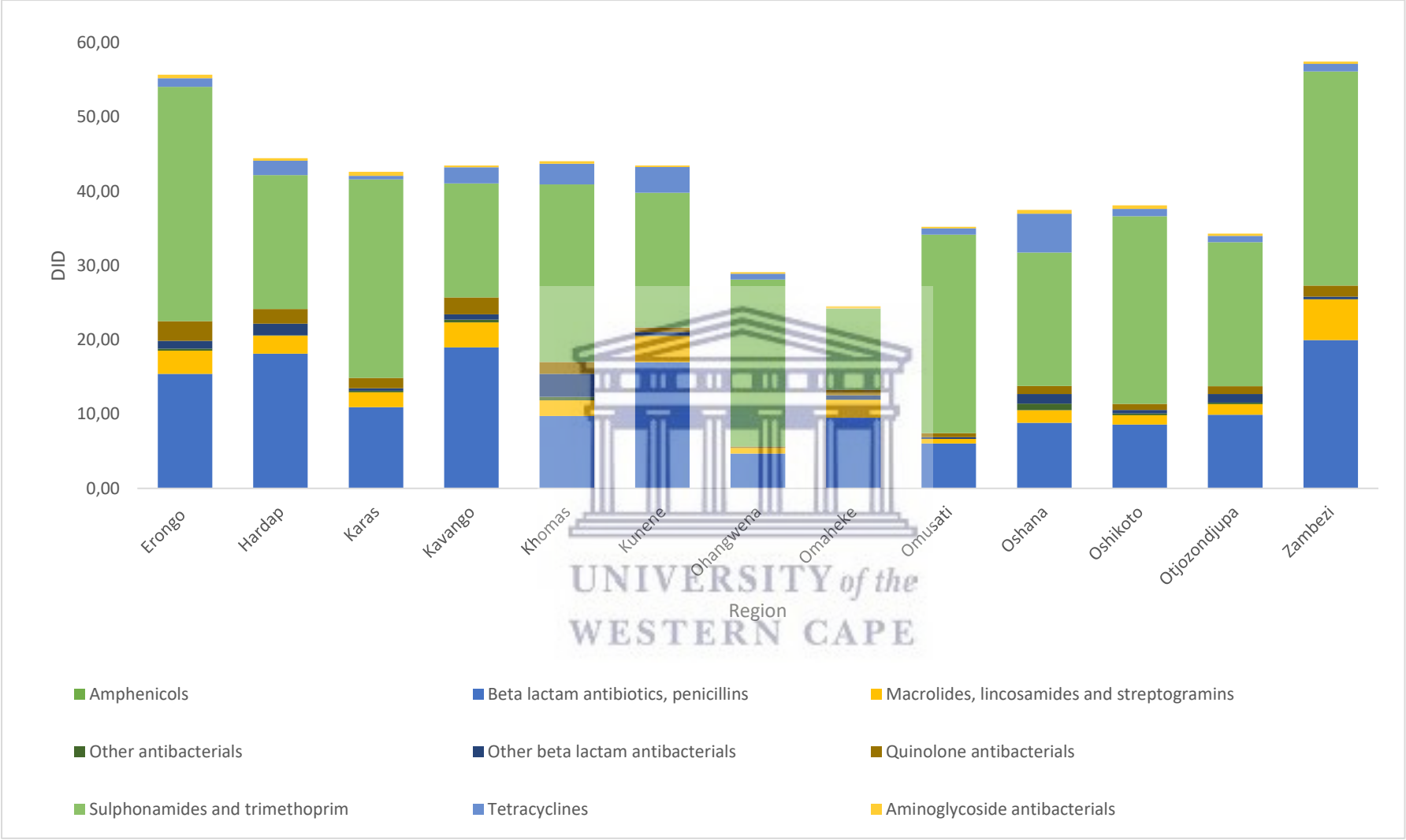


National antibiotic consumption trends per antibiotic classification, Otjozondjupa, 2010-2016

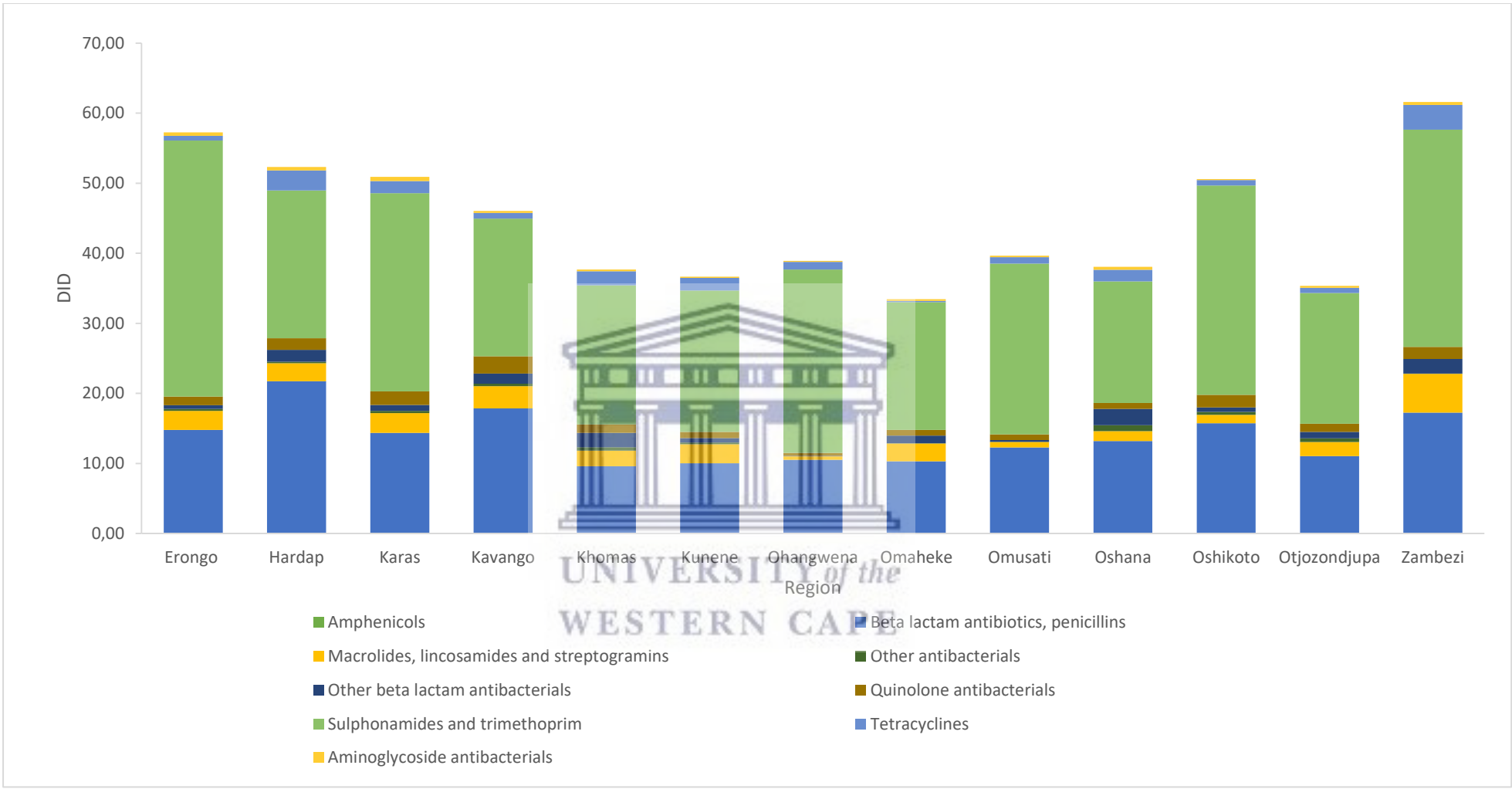
Appendix 8: Antibiotic consumption by region by antibiotic classification



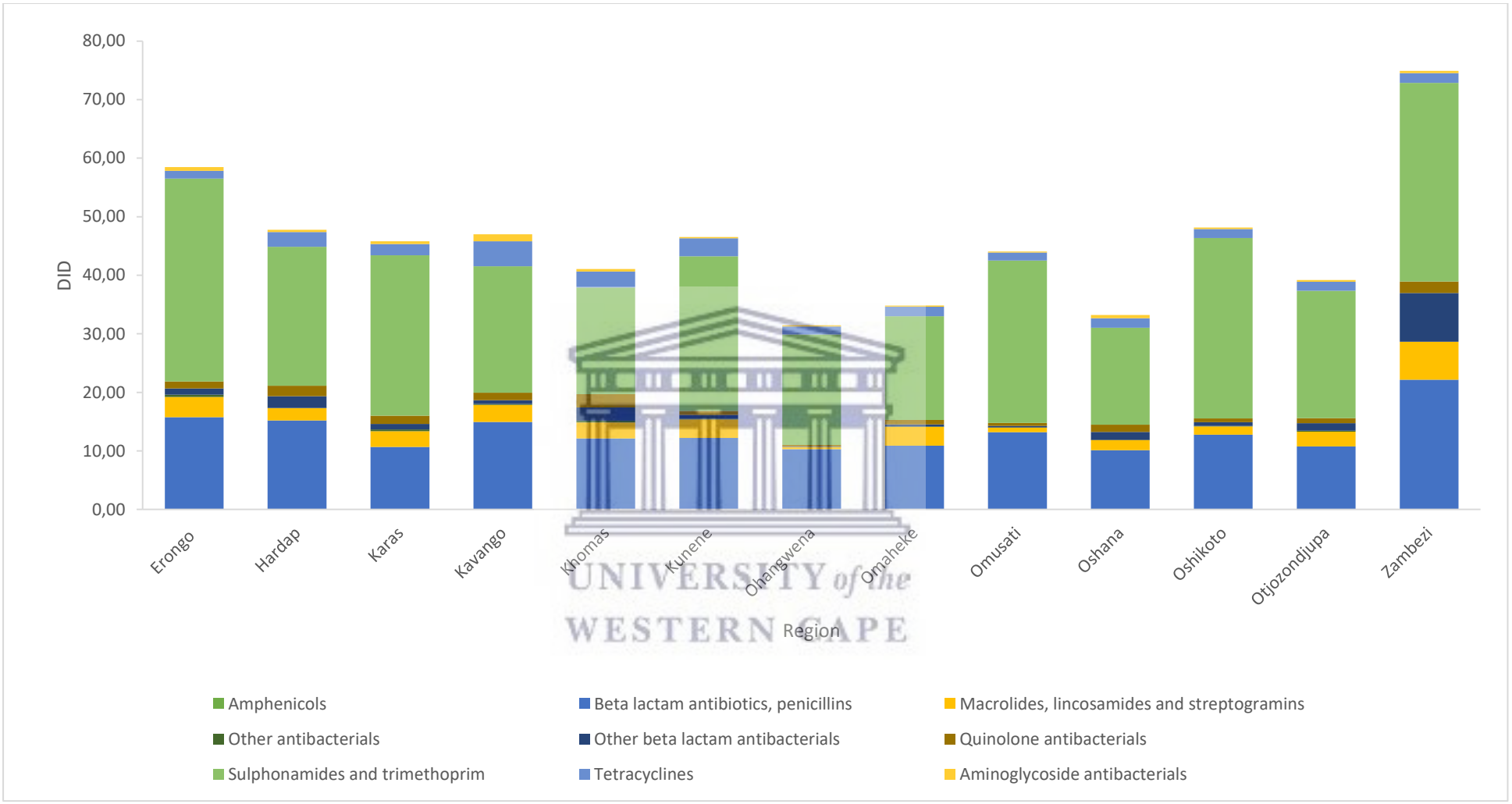
Antibiotic consumption by region by antibiotic classification, Namibia, 2011



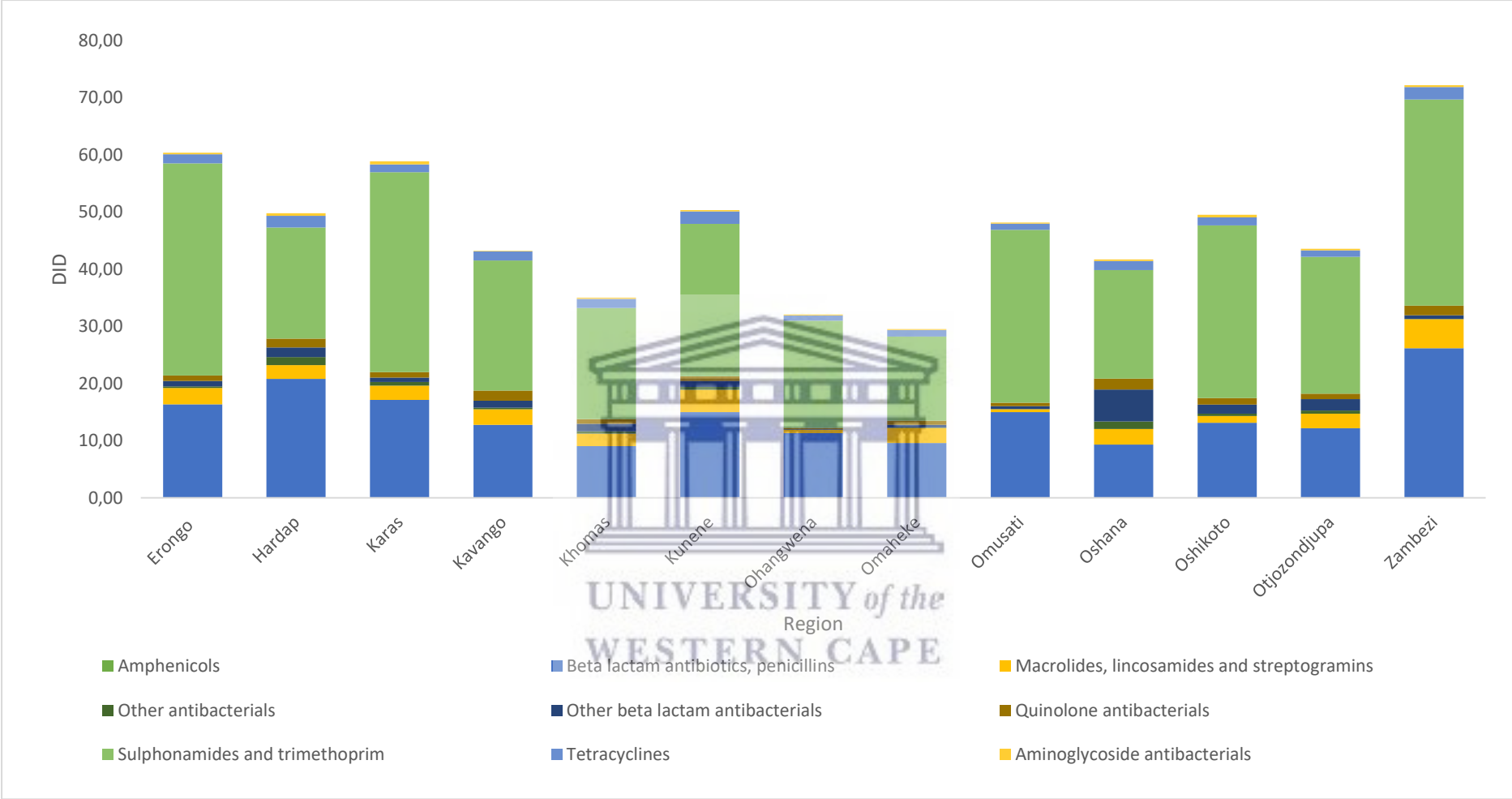
Antibiotic consumption by region by antibiotic classification, Namibia, 2012



Antibiotic consumption by region by antibiotic classification, Namibia, 2013



Antibiotic consumption by region by antibiotic classification, Namibia, 2014



Antibiotic consumption by region by antibiotic classification, Namibia, 2015