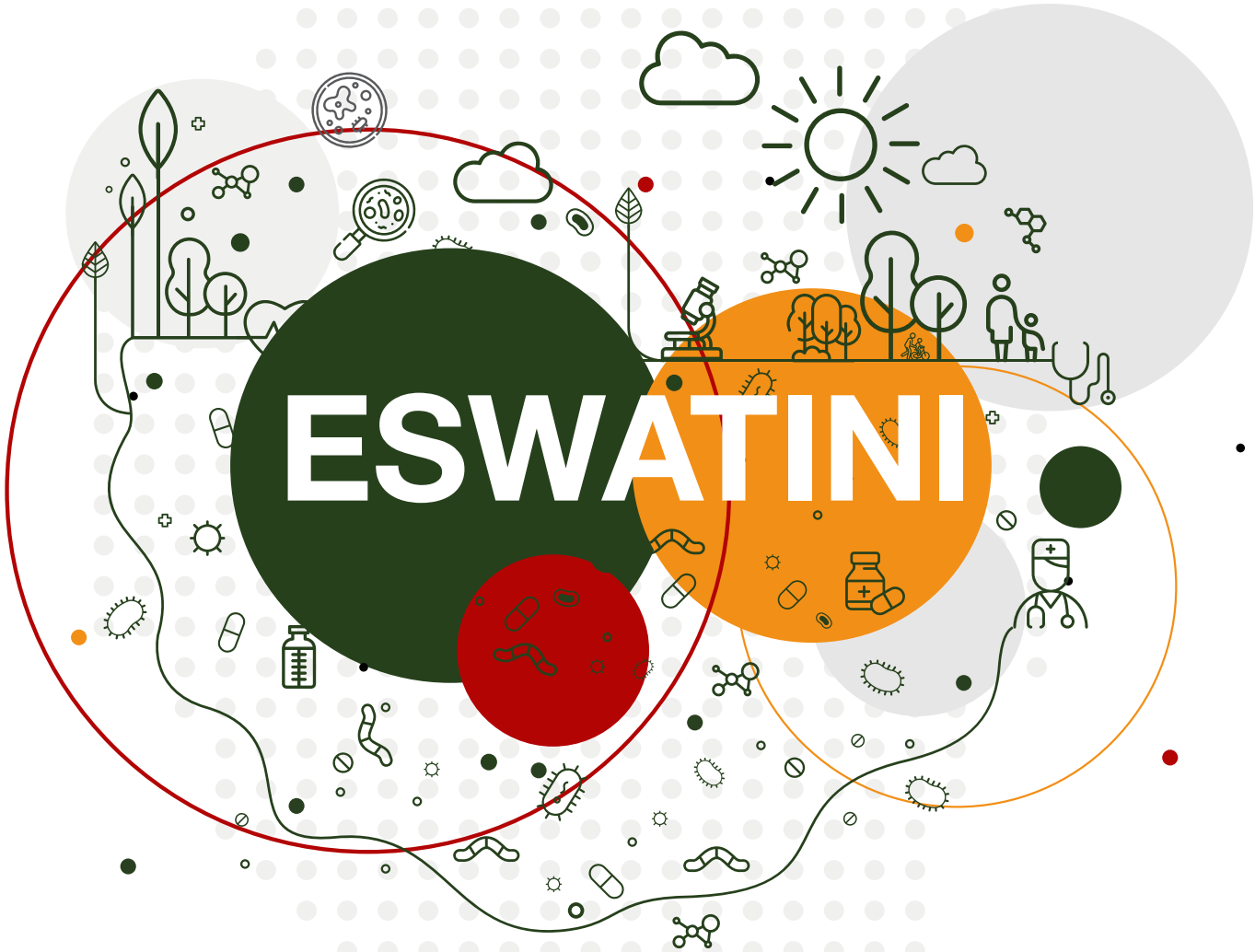
MAAP
Mapping AMR & AMU Partnership

Annual Report

National Situation of Antimicrobial Resistance and Consumption Analysis from 2016-2018



The Fleming Fund Regional Grants
UKaid from the British people
African Union
AFRICA CDC Centres for Disease Control and Prevention Safeguarding Africa's Health
ASLM African Society for Laboratory Medicine
ECOWAS
InSTEDD Innovative Support To Emergencies Diseases and Disasters
IQVIA
ONEHEALTH TRUST

Year: 2022

Eswatini (2016-2018)

ESWATINI

Fleming Fund Regional Grant (Round 1)

Mapping Antimicrobial Resistance and Antimicrobial Use Partnership

African Society for Laboratory Medicine
Africa CDC
WAHO
ECSA-HC
Center for Disease Dynamics, Economics and Policy
IQVIA
InSTEDD

The country report summarises the analysis of retrospective data on AMR and AMC commissioned in the context for Fleming Fund Regional Grant (Round 1) programme.

Table of Contents

Abbreviations

AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMRCC	Antimicrobial Resistance Coordinating Committee
AMS	Antimicrobial Stewardship
AMU	Antimicrobial Use
ASLM	African Society for Laboratory Medicine
ASP	antimicrobial stewardship programme
AST	antibiotic susceptibility testing
ATC	Anatomical Therapeutic Chemical
AWaRe	Access, Watch and Reserve
CDDEP	Center for Disease Dynamics, Economics and Policy
CI	Confidence Interval
CLSI	Clinical and Laboratory Standards Institute
CMS	Central Medical Store
CSF	Cerebrospinal Fluid
DDD	Defined Daily Dose
DID	DDD per 1 000 inhabitants per day
DRI	Drug Resistance Index
ECSA-HC	East, Central and Southern Africa Health Community
EML	Essential Medicines List
EQA	External Quality Assessment
EUCAST	European Committee on Antibiotic Susceptibility Testing
GLASS	Global Antimicrobial Resistance Surveillance System
HIS	Hospital Information System
InSTEDD	Innovative Support to Emergencies, Diseases and Disasters
KIIs	Key Informant Interviews
LIS	Laboratory Information System
LMIC	Low-or Middle-Income Country
LQMS	Laboratory Quality Management System
MAAP	Mapping Antimicrobial resistance and Antimicrobial use Partnership
MoH	Ministry of Health
MTC	Medical Therapeutics Committee
NGO	Non-Governmental Organisation
ODDPS	Office of the Deputy Director for Pharmaceutical Services
OR	Odds Ratio
QA	Quality Assessment
QC	Quality Control
QMS	Quality Management System
RFM	Raleigh Fitkin Memorial
RSN	ResistanceMap Surveillance Network
SLIPTA	Stepwise Laboratory Improvement Process Towards Accreditation
SLMTA	Strengthening Laboratory Management Towards Accreditation
SOP	Standard Operating Procedure
WHO	World Health Organisation

Executive Summary

Antimicrobial resistance (AMR) is a major public health concern that needs to be urgently addressed to avoid needless suffering and the reversal of medical advancement in fighting infectious diseases. A clear link has been shown between the misuse of antimicrobials and the emergence of AMR. However, owing to the limited capacity of health systems and technological hurdles, the availability of comprehensive and robust AMR, antimicrobial use (AMU) and antimicrobial consumption (AMC) data in many low- and middle-income countries (LMICs), is generally lacking and there remains significant uncertainty as to the burden of drug resistance.

The Fleming Fund, a 265-million-pound United Kingdom aid, supports a range of initiatives to increase the quantity and quality of AMR data in LMICs. Regional Grant (Round 1) activities in Africa are led by The African Society for Laboratory Medicine (ASLM) and implemented by the 'Mapping Antimicrobial resistance and Antimicrobial use Partnership' (MAAP) consortium.

This report summarises the activities undertaken by MAAP during the implementation of the Regional Grant and aims to determine national AMR, AMC and AMU surveillance capacity, resistance rates and trends, and assess the antimicrobial flow in Eswatini during 2016-2018.

Three laboratories in the national laboratory network of Eswatini reported to have capacity for bacteriology testing. Based on self-reported information from the three laboratories, functioning and quality compliance were assessed to understand the laboratory preparedness for AMR surveillance. AMR rates presented are based on the analysis of antimicrobial susceptibility results 0f 5 247 positive cultures obtained from three laboratories. Moderate to high resistance was observed for methicillin-resistant Staphylococcus aureus (21-58%) and 3rd-generation cephalosporin-resistant Enterobacterales (25-41%). Rates for carbapenem-resistant Enterobacterales were lower (<6%). Antimicrobial-resistant infections were found to be more common in males and infants. All results should be interpreted with caution as the participating laboratories were at different levels of service and had variable testing capacity.

AMC is measured as the quantity of antimicrobials sold or dispensed whereas AMU reviews whether antimicrobials are used appropriately based on additional data such as clinical indicators. Only AMC data were retrievable at selected sentinel pharmacies. AMU data were not obtained due to lack of a unique patient identifier and tracking systems across hospital departments. The average national total AMC levels in Eswatini between 2016-2018 were 46.6 defined daily doses (DDD) per 1000 inhabitants per day, ranging from 17 in 2016, 21 in 2017 and 102 in 2018. Antimicrobial utilisation by the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) classification was highest for combinations of sulfonamides and trimethoprim, including derivatives (range 0.0% to 64.9%), followed by penicillins with extended spectrum (range 6.3% to 32.1%) and by tetracyclines (range 7.1% to 27.6%). The top five most consumed antimicrobials were sulfamethoxazole/trimethoprim, amoxicillin, doxycycline, metronidazole and erythromycin. Together they accounted for 88% of total consumption share thus suggesting lack of variation. This consumption trend could potentially increase AMR. The total AMC came from 86.8% 'Access', 13.2% of 'Watch' and <0.1% of 'Reserve' antibiotics. Between 2016-2018, the use of 'Access' category antibiotics exceeded the WHO minimum recommended consumption threshold of 60%.

The drug resistance index (DRI) is a simple metric based on aggregate rates of resistance and measured on a scale of 0-100, where 0 indicates fully susceptible and 100 indicates fully resistant. The DRI estimate was found to be high at 64.8% (95% CI, 54.3–75.2%) implying low antibiotic effectiveness. This is a threat to effective infectious disease management and calls for urgent policy intervention. A weak positive correlation was noted between AMR and AMC, implying that the latter may not be a significant driver of AMR in Eswatini.

The report includes recommendations for policy makers and healthcare providers, to further strengthen AMR and AMC surveillance for AMR mitigation in the country.

Overview

The Fleming Fund Grants Programme

The Fleming Fund Grants Programme, a United Kingdom-sponsored initiative aimed to address the critical gaps in surveillance of AMR in LMICs in Asia and sub-Saharan Africa.[1] The programme included Regional Grants, Country Grants and the Fleming Fellowship Scheme. Mott MacDonald was the authority for grant management.

The Fleming Fund Regional Grants Round 1 Programme

The Fleming Fund Regional Grant Round 1 covered four regions (West Africa, East and Southern Africa, South Asia, and Southeast Asia) and aimed to expand the volume of data available on AMR and AMU.

Problem Statement

AMR is a global health priority. However, the quantum and quality of surveillance data are sub-optimal in LMICs where AMR rates are typically lacking.[2] This hinders the assessment of the current treatment efficacy and understanding of the drivers of resistance. Additionally it impacts the adoption of appropriate policies to improve antimicrobial use, which has a downstream impact on patient care. However, in most LMICs, there are institutions (academic, research, public and private health facilities, etc.) which have been collecting data on AMR for decades.

While the 'hidden treasure' is simply inaccessible for use in large-scale analytics, collecting and, where necessary, digitising data from these institutions has the potential to establish baselines of AMR across a wide range of pathogen/drug combinations and assess spatiotemporal trends. Likewise, retrieving information through prescriptions or sales in healthcare facilities, should provide a wealth of information on the potential drivers of AMR. Linking susceptibility data with patient information can further provide a valuable understanding of the current treatment efficacy, which can inform evidence-based policy and stewardship actions.

MAAP

Against this background, the Regional Grant Round 1 aimed to increase the volume of Against this background, the Regional Grant Round 1 aimed to increase the volume of data available to improve spatiotemporal mapping of AMR and AMU across countries in each region and establish baselines. The programme was implemented by MAAP, a multi-organisational consortium of strategic and technical partners. ASLM was the Lead Grantee for the programme.[3]

MAAP's strategic partners included ASLM, the Africa Centres for Disease Control and Prevention, West African Health Organisation, the East Central and Southern Africa Health Community (ECSA-HC). The technical partners were the Center for Disease Dynamics, Economics and Policy (CDDEP), IQVIA, and Innovative Support to Emergencies, Diseases and Disasters (InSTEDD). ASLM oversaw consortium activities and ensured fulfilment of ethical considerations and completion of data sharing agreements with the participating countries.

MAAP was set up to collect and analyse historical antimicrobial susceptibility and consumption/usage data collected for the period 2016-2018, in each country and understand the regional landscape. MAAP's primary focus was to determine the levels of resistance of the bacterial priority pathogens that were listed by WHO, and other clinically important pathogens. Through standardised data collection and analytical tools, MAAP gathered, digitised, and collated the available AMR and AMC data between 2016 and 2018. Based on feasibility, MAAP set out to collect information on AMC instead of AMU.

The results of this analysis contribute to the determination of baselines and trends for AMR and AMC, AMR drivers as well as critical gaps in surveillance. The study recommendations aim to increase country capacity for future collection, analysis and reporting of AMR and AMC OR AMU data.

Fourteen African countries across West Africa (Burkina Faso, Ghana, Nigeria, Senegal snd Sierra Leone), East Africa (Kenya, Tanzania and Uganda), Central Africa (Cameroon and Gabon) as well as Southern Africa (Eswatini, Malawi, Zambia and Zimbabwe) were included in MAAP activities.

Aim

To determine the spatiotemporal baselines and trends of AMR and AMC in Eswatini using the available historical data

Specific Objectives

- To assess the sources and quality of historical AMR data generated routinely by the national laboratory network of Eswatini, including the public and private human healthcare sector
- To collect, digitise and analyse retrospective data from selected facilities using standardised electronic tools; to describe the completeness and validity of AMR data in selected facilities

- To estimate the country-level AMR prevalence and trends for WHO priority pathogens other clinically important and frequently isolated pathogens, as well as comparing countries on spatiotemporal maps.
- To describe the in-country antimicrobial flow and highlight the status of the in-country AMC and AMU surveillance system
- To quantify and evaluate the trends of AMC and AMU at national and pharmacy level.
- To assess the relationship between AMC and AMR through the DRI
- To assess the drivers of AMR

Outcome measures

- Number of laboratories from the national network generating AMR data and proportion of laboratories reporting compliance to standards of quality and bacteriology testing
- Level of AMR data completeness and validity among laboratories selected for AMR data collection
- AMR prevalence and trends for the WHO priority pathogens, other clinically important and frequently isolated pathogens
- A semi-quantitative analysis of the in-country status in AMC and AMU surveillance
- Total consumption of antimicrobials (defined daily dose) in addition to AMC and AMU trends over time at national and pharmacy levels
- Country-level DRI
- Association between patient factors and AMR

The results are intended to serve as a baseline for prospective AMR, AMC and AMU surveillance, highlight gaps and recommend measures for surveillance strengthening.

Key engagements and activities

The Regional Grants Round 1 engagement commenced with a kick-off meeting with representatives from Mott MacDonald (Grant Managers), MAAP consortium (for Africa Region) and CAPTURA ('Capturing Data on AMR Patterns and Trends in Use in Regions of Asia') consortium for Asia Region. The meeting was held in Brighton, England, in February 2019. In April 2019, MAAP convened a stakeholder consultation in Addis Ababa, Ethiopia with representatives from the 14 participating countries in Africa to discuss continental efforts on AMR control and the implications of the Regional Grant. Over the next year and a half, workshops were held in each country to finalise data sharing agreements and methodologies. The workshops brought together representatives from MAAP and the countries, including representatives from the ministries of health (MoH), AMR coordinating committees, health facilities, laboratories and pharmacies. This was followed by site selection and data collection in each country. Data analysis was conducted by the technical partners. The final results were shared through dissemination meetings (Figure 1).

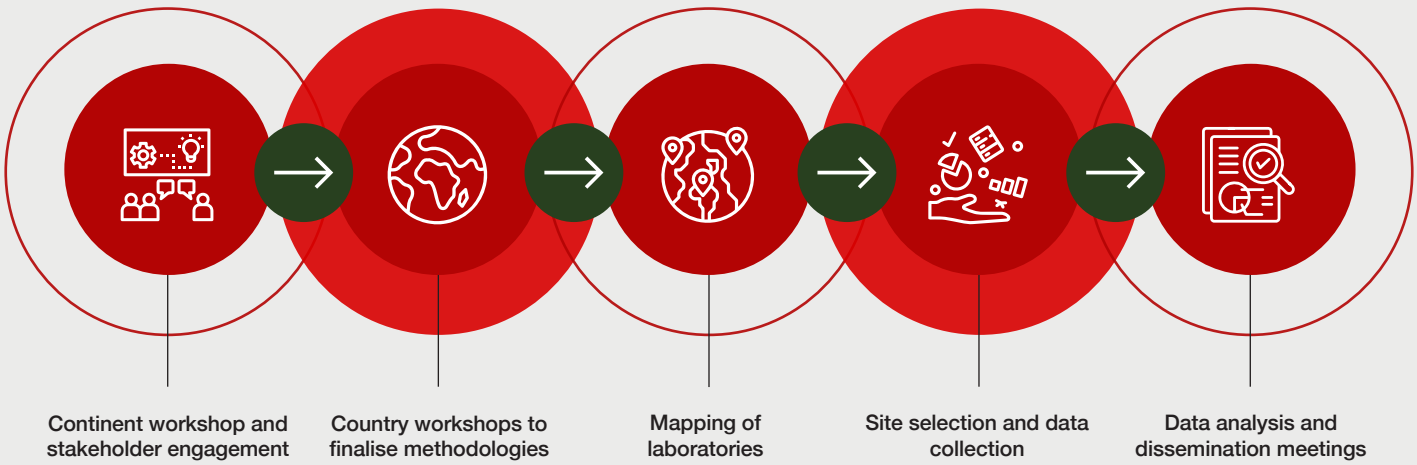


Figure 1: Key engagements and activities

Ethical issues and data sharing agreements

To ensure that ethical concerns, confidentiality, use and ownership of the data are regulated and adhered to during the project, a data-sharing agreement (DSA) was signed with the ministry of health. The DSA facilitated clear communication and established additional safeguards to the management of the collected data (see Appendix 1).

Country Profile

Health and demographic profile

As of 2020, Eswatini was estimated to have a population of 1.1 million inhabitants with a life expectancy of 60 years. The country has a very high infectious disease burden with a TB incidence of 319 per 100 000 and an HIV prevalence of 26.8%. The country has a physician density rate of 0.09 per 1 000 inhabitants and nurses density rate of 4.14 per 1 000 inhabitants. With a universal health coverage index of 58, Eswatini appears to have an above-average coverage of essential services (Table 1).

Table 1: Health and demographic profile of Eswatini

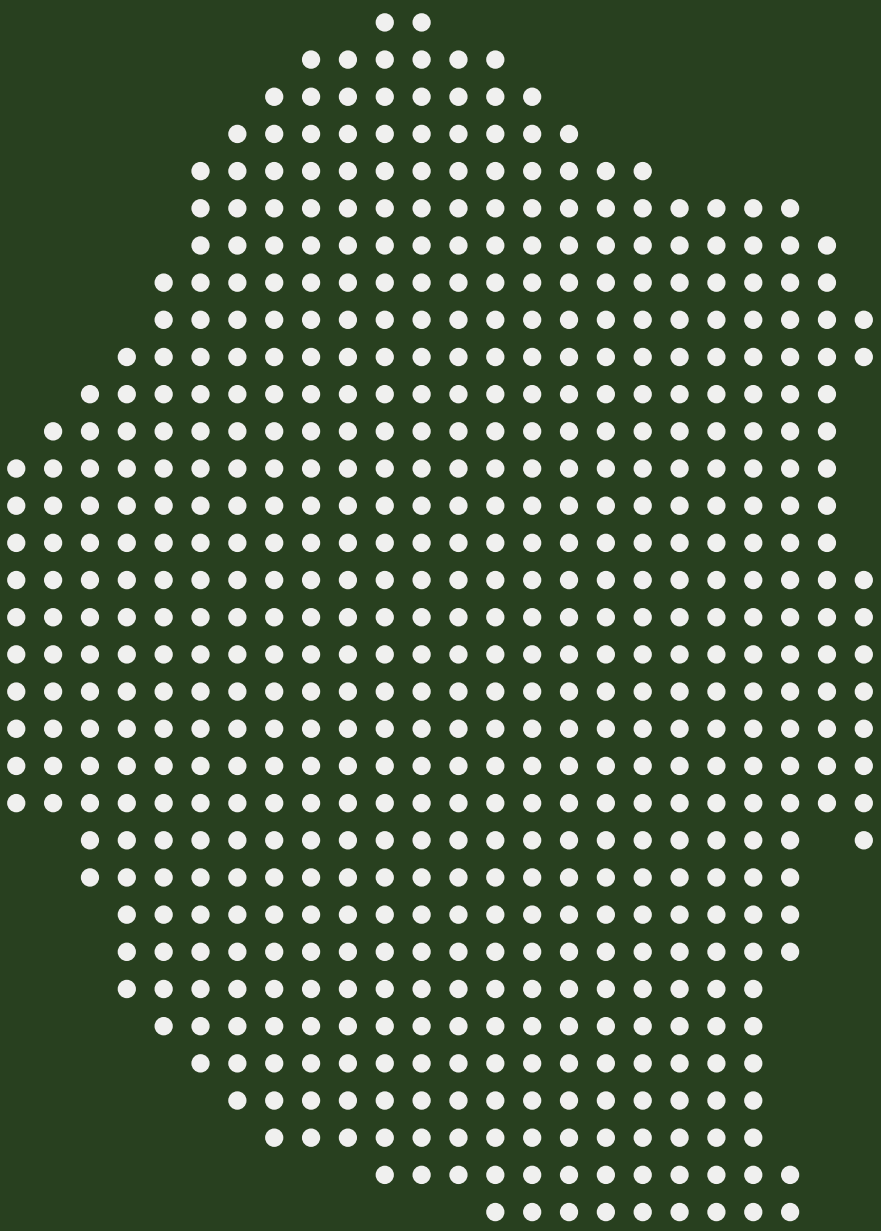
	Eswatini		Comparator values (most recent year)*		
	Year	Value	India	Argentina	United States
Population	2020	1 160 164	1 380 004390	45 376 763	329 484 123
Life expectancy during the study period, total (years)	2019	60	70	77	79
Universal health coverage service index (0-100)	2019	58	61	67	83
GDP per capita (current US$)	2020	3 424.28	1 927.7	8 579.0	63 593.4
Immunisation, DPT (% of children ages 12-23 months)	2019	90	91.0	86.0	94.0
Incidence of tuberculosis (per 100 000 people)	2020	319	188.0	31.0	2.4
Prevalence of HIV, total (% of population ages 15-49)#	2020	26.8	0.2*	0.4 2020	0.4 2019
Primary education (%)#	2019	88.6	94.6	98.6	100
Physicians density (physicians per 1 000)#	2016	0.09	0.93	4.0	2.6
Nurses density (nurses and midwives per 1 000)#	2018	4.14	2.39	2.60	15.69

Sourced from World Bank[4,5 6] and *National AIDS Control Organisation[7]
Data for some country parameters may not necessarily be of the same year (but sourced from the most recently available information between 2017-2020).

Policy frameworks

Eswatini has developed a multisectoral National AMR Containment Strategic Plan for Antimicrobial Resistance (2018-2022).[10] This document details how AMR will be prevented and monitored using a One Health approach in Eswatini. National AMR strategic plans are intended to align with the AMR Global action plan.[8] The Global Antimicrobial Resistance Surveillance System (GLASS) launched by the WHO is an initiative intended to support the implementation of the Global Action Plan on Antimicrobial Resistance and strengthen AMR surveillance and research.[9] GLASS provides standardised methodologies for AMR data collection and analysis and encourages countries to share their data on the global surveillance platform. GLASS has various modules and tools including emerging AMR events, AMC and promotes integration with surveillance in the animal and environment sectors. At the data of Eswatini was not enrolled in GLASS yet.

Part A: Antimicrobial Resistance



Section I: Laboratory assessment

Objective

To assess the sources and quality of historical data on AMR generated routinely by the national laboratory network of Eswatini, including the public and private healthcare sectors.

Methodology

Initially, up to 16 laboratories (two reference, four private, and 10 public) were expected to be included in the study for the purpose of AMR data collection. Ultimately, only those laboratories most likely to guarantee the highest level of data quality were selected. Country-specific circumstances, the actual number of selected laboratories, and their affiliations and levels necessitated some adjustments in the study protocol.

During the initial stages of in-country work, the laboratory network was mapped with support from the country's MoH. An inventory of laboratories in the tiered network was created and laboratories capable of conducting antimicrobial susceptibility testing (AST) were identified. A survey was administered to the identified laboratories, with the aim of obtaining site-specific details and assessing the laboratories on five aspects: status of commodities and equipment, quality management systems (QMS), personnel and training, specimen management, and laboratory information systems (AMR Appendix 2). Based on self-reported information on the above parameters, each laboratory was assigned a readiness score for AMR surveillance (AMR Appendix 3). The scoring scheme was standardised across all participating countries. The final selection of laboratories for data collection was made by the MoH and was not necessarily based on laboratory rankings.

Results

Mapping and selection of laboratories

During the initial stages of in-country work in Eswatini, three laboratories were mapped to the national laboratory network. An eligibility questionnaire was sent to assess capacity for bacteriology testing. Each laboratory had a different affiliation: Lancet was private; Mbabane Government Hospital Laboratory was public and Raleigh Fitkin Memorial (RFM) Hospital was founded by the Church of the Nazarene (Table 2, Supplementary Table 1). The laboratory readiness scores of the surveyed laboratories ranged between 81.6% and 84.2%. All three laboratories were selected for data collection. The laboratories named in the tables are listed in order of decreasing laboratory readiness scores.

Table 2: Laboratory readiness scores

Surveyed laboratories*	Laboratory readiness score (%)	Level of service	Affiliation
Selected			
Lancet Laboratories (Lancet)	84.2	Other	Private
Mbabane Government Hospital Laboratory (Mbabane)	81.6	Reference	Government
Raleigh Fitkin Memorial Hospital Laboratory (RFM)	81.6	Regional/intermediate	Other

** Laboratory names are abbreviated.*

Surveillance preparedness of surveyed laboratories

Based on self-reported information from the three laboratories, laboratory functioning and quality compliance were assessed to understand preparedness for AMR surveillance. All laboratories had implemented QMS, used automated methods for pathogen identification and had at least one qualified microbiologist on board. However, only one laboratory was accredited (Figure 3, Supplementary Table 2). Since these findings may affect the quality of laboratory data, caution in interpreting the AMR rates presented in this report is warranted.

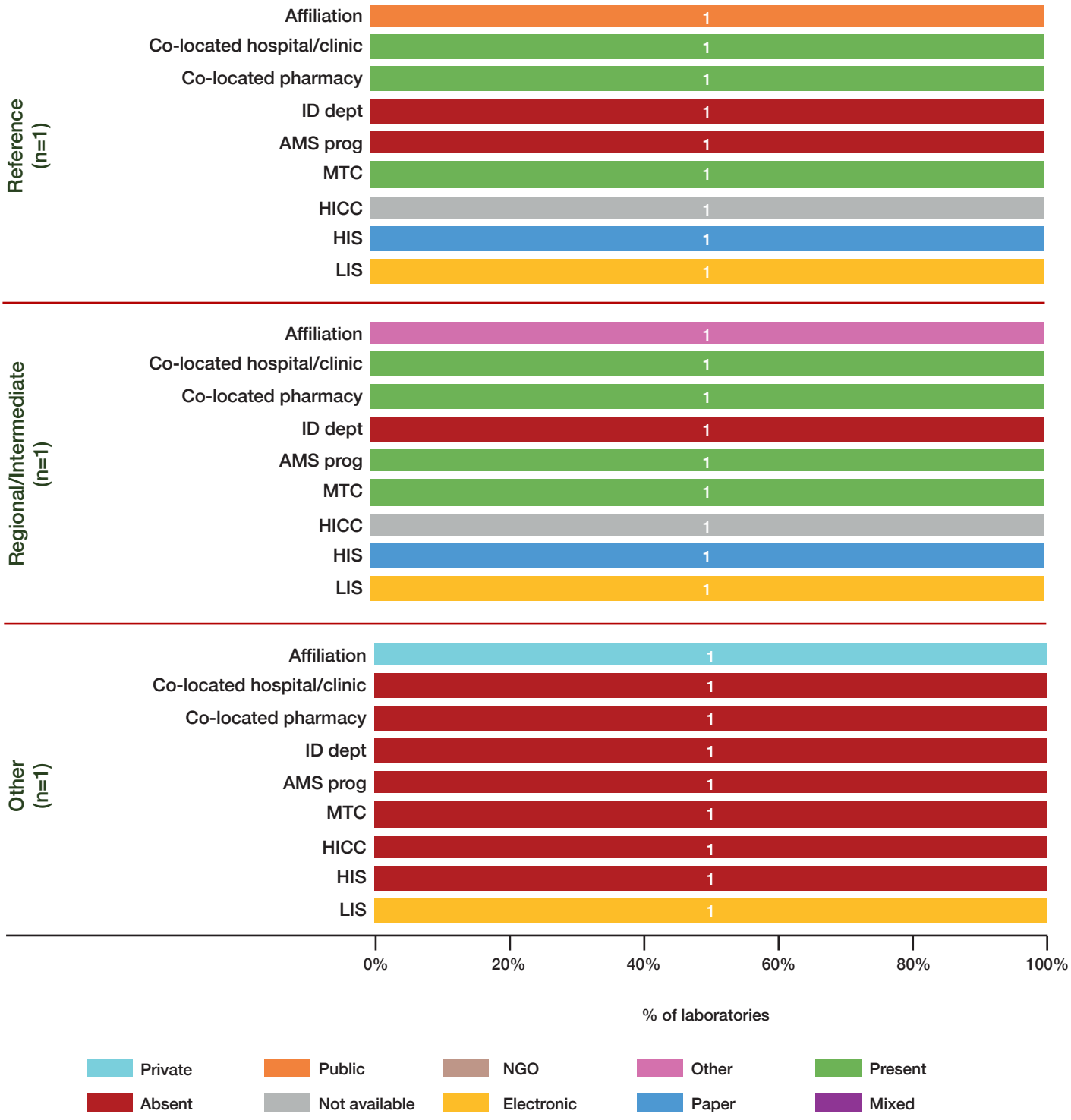
	Parameters			N (%)
Commodity and equipment status	Regular power supply and functional back up			3 (100.0)
	Continuous water supply)			3 (100.0)
	Certified and functional biosafety cabinets			3 (100.0)
	Automated methods for pathogen identification			3 (100.0)
	Automated methods for AST			3 (100.0)
	Methods for testing AMR mechanisms			3 (100.0)
QMS implementation	Reported QMS Implementation			3 (100.0)
		Types of QMS	LQMS	1 (33.3)
			SLIPTA	0
			SLMTA	2 (67.7)
			Mentoring	0
			Combination‡	0
			Others	0
	Quality Certification			3 (100.0)
		Types of Quality certification	SLIPTA	2 (67.7)
			Col. of Am. Path	0
			Others	1 (33.3)
	Accreditation			1 (33.3)
	Participation in proficiency testing			3 (100.0)
	Utilization of reference strains			3 (100.0)
	Reported consistent maintenance of QC records			3 (100.0)
	Designated focal quality person			3 (100.0)
	Reported compliance to standard operating procedures			3 (100.0)
	Reported compliance to AST standards			3 (100.0)
Personnel and training status	Presence of at least one qualified microbiologist			3 (100.0)
	Presence of an experienced laboratory scientist/technologist			3 (100.0)
	Up-to-date and complete records on staff training and competence			3 (100.0)
Specimen Management status	Reported compliance to SOPs on specimen collection and testing			3 (100.0)
	Reported compliance to SOPs on specimen rejection			3 (100.0)
	Average number of specimens processed for AST in 2018			-
LIS and Linkage to Clinical Data	Assigned specimen (laboratory) identification number			3 (100.0)
	Availability of system/database to store patient data			3 (100.0)
		Database format	Paper-based	0
			Electronic	3 (100.0)
			Mixed	0
	Captured patients' records on test request forms			3 (100.0)
			Retrievable	3 (100.0)

‡ Combination refers to more than one option presented in the questionnaire (laboratory quality management system, stepwise laboratory improvement process towards accreditation, strengthening laboratory management towards accreditation and mentoring).

Figure 3: Laboratory preparedness for AMR surveillance

Profile of Selected Laboratories

Two laboratories were co-located with clinical facilities and pharmacies. Of these two, only one had a running antimicrobial stewardship programme (ASP) and a medical therapeutic committee. Information systems were electronic at all the three laboratories (Figure 4).



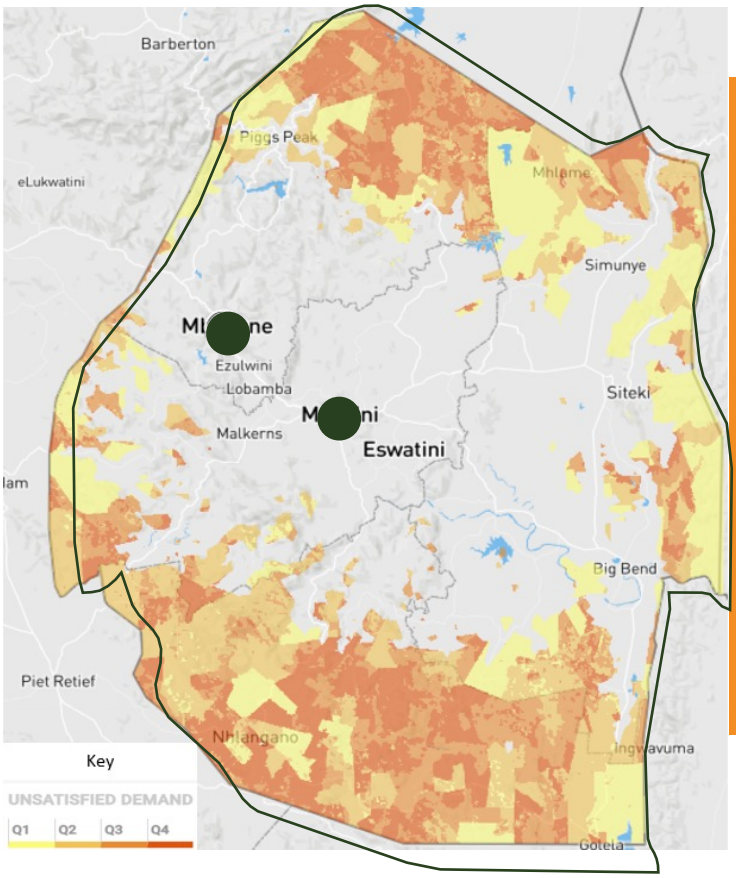
Abbreviations: AMS=antimicrobial stewardship; HICC=hospital infection control committee; HIS=hospital information system; IDD=infectious diseases department; LIS=laboratory information system; MTC=medical therapeutics committee

Figure 4: Profile of selected laboratories

Population coverage of laboratories

We analysed the data using the PlanWise® solution. PlanWise incorporates data on the population, road network, and other variables and applies an algorithm and geospatial optimisation techniques to show unmet needs. We evaluated the proportion of the population covered by the laboratories participating in the study. We evaluated the proportion of population covered by mapped laboratories within a two hours' drive (Supplementary Figure 1).

As of 2020, Eswatini had an estimated population of 1.16 million.



Population coverage of laboratory services is defined as the catchment population living within one-hour travel (by car or foot) from the testing laboratory. It is represented in grey on the map. The analysis uses the assumption that the laboratory has sufficient testing capacity to serve the entire population within the catchment area. The population outside the catchment area of the facilities is, by definition, representative of the overall unmet need. For ease of use, the unit of unmet need is represented on the map as 'pixels', i.e., the lowest base unit of a raster image. To visualise the geographical areas with the most critical unmet needs, each base component is ranked from the lowest to the highest, according to the number of the population living in the 'pixel'. The ranking is then divided into quartiles made of equal population fractions (from Q1 _lowest density of population to Q4 highest density) also corresponding to different colours (from yellow to dark red, see the legend).

Supplementary Figure 1: Population coverage of AST laboratories in Eswatini

Therefore, colour on the map relates to the level of unmet need (people nor in the reach of a facility) relative to the whole population.

In Eswatini, the catchment population living within one-hour travel time from the three participating AMR surveillance sites covers **62%** of the population. Hence, 38% of the population is not covered at all by the existing facilities. To increase the population coverage, new capacity should be introduced (either by upgrading an existing laboratory to start providing services or by constructing a new laboratory) in regions in dark red (Q3) and thus prioritising regions with the highest absolute unmet need.

Section II: Collection, analysis and interpretation of AMR data

Objective

1. To collect, digitise and analyse retrospective data from selected facilities using standardised electronic data collection and analysis tools
2. To describe the completeness and validity of AMR data in selected facilities

Methodology

Data collection

The main variables were the patient's culture (laboratory) results, clinical information and antimicrobial usage (AMR Appendix 4). For all positive blood and cerebrospinal fluid (CSF) cultures, information on the patient's demographics, clinical profile and antimicrobial usage was also collected from clinics and hospitals. However, this was possible only where patient records could be tracked between the laboratories and hospitals (Figure 5). Additionally, data were collected on AMC at the facility and national level.

For laboratories with paper-based records, at least 5 000 records per laboratory per year were to be collected. However, no such limit was imposed for digitised data. The goal was to obtain at least 240 000 records from the three laboratories across three years.

As a first step, the MoH and IQVIA were jointly involved in recruiting local field data collectors. A capacity-building workshop was conducted as part of the MAAP to train the field staff on data collection, including the use of WHONET[12] and the specially developed MAAP tool for secure transfer of collected data.

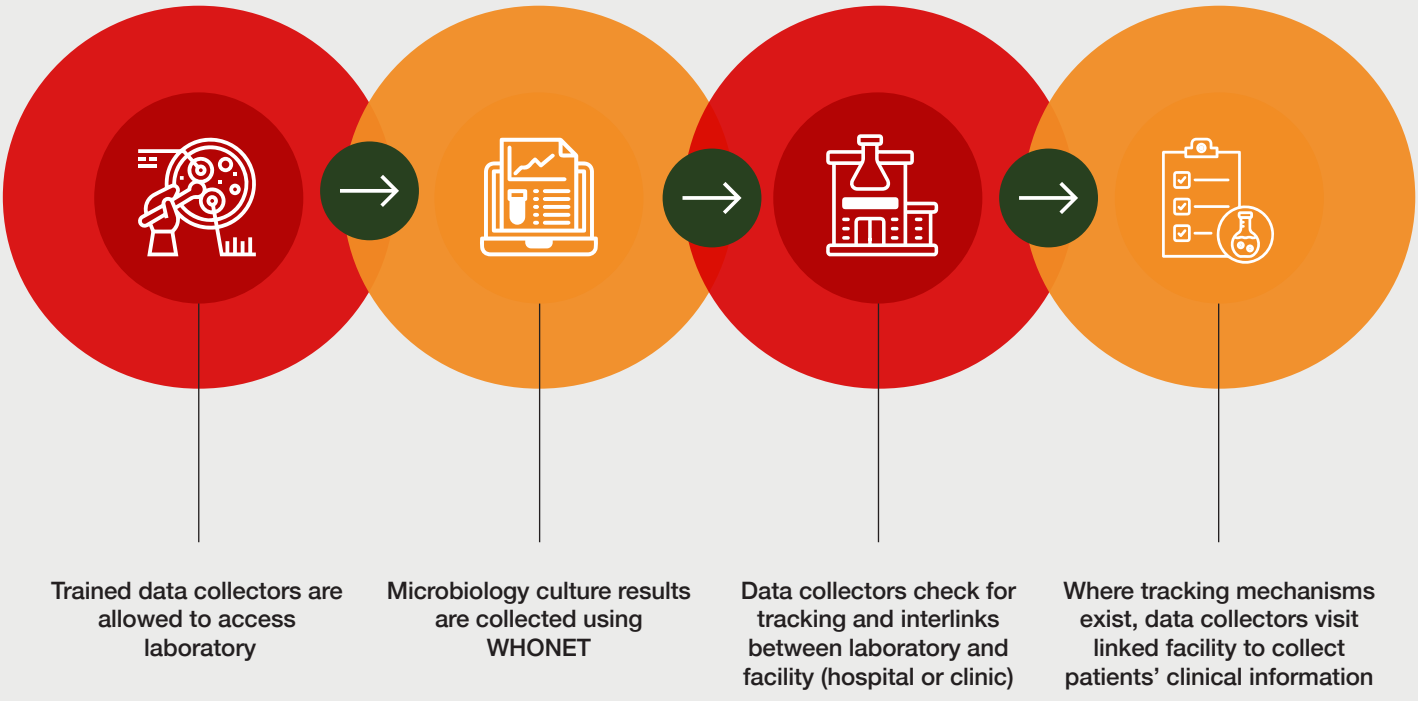


Figure 5: Steps of AMR data collection

Historical data were collected for the period January 1, 2016, through to December 31, 2018. The AMR data were initially captured through WHONET, a free Windows-based database software programme developed for the management and analysis of microbiology laboratory data. The software allowed data entry of clinical and microbiological information from routine diagnostic testing or research studies. WHONET has a simple data file structure and output formats compatible with major database, spreadsheet, statistical and word-processing software. It permits customisation to include variables of interest and has several alert features that highlight unlikely or important results. From WHONET, data were transferred into an online application (repository) for further analysis. Each row of the database represented an individual patient's results. Where the laboratory or hospital issued unique patient identification numbers, it was also possible to track a patient along multiple visits.

Figure 6: Data collection at a Eswatini facility

Data analysis

A preliminary data review was conducted to check for data completeness, accuracy, and redundancy. Data summarisation was based on the following parameters: quantum of cultures (total cultures, valid cultures, positive cultures or positive cultures with AST results), level of pathogen identification, inappropriate testing, clinical information; culture characteristics, specimen characteristics and identified pathogens. Each parameter is described below.

- **Quantum of cultures:** Total cultures were the number of patient rows in the database received from the laboratories. Valid cultures were a subset of total cultures which had complete information on the specimen type, collection date and pathogen name. Positive cultures were valid cultures for which pathogen growth was reported, irrespective of AST results. Total cultures were quantified for each laboratory and over the entire study period. Valid cultures and positive cultures were stratified for each laboratory as well as for each study year (Figure 7).
- **Level of pathogen identification:** Positive cultures with AST results were summarised based on the level of pathogen identification. Gram identification and genus-level identification were considered incomplete where reporting at a species level indicated complete pathogen identification. Data were stratified for each laborator, and assessment was conducted over the entire study period (Figure 7).

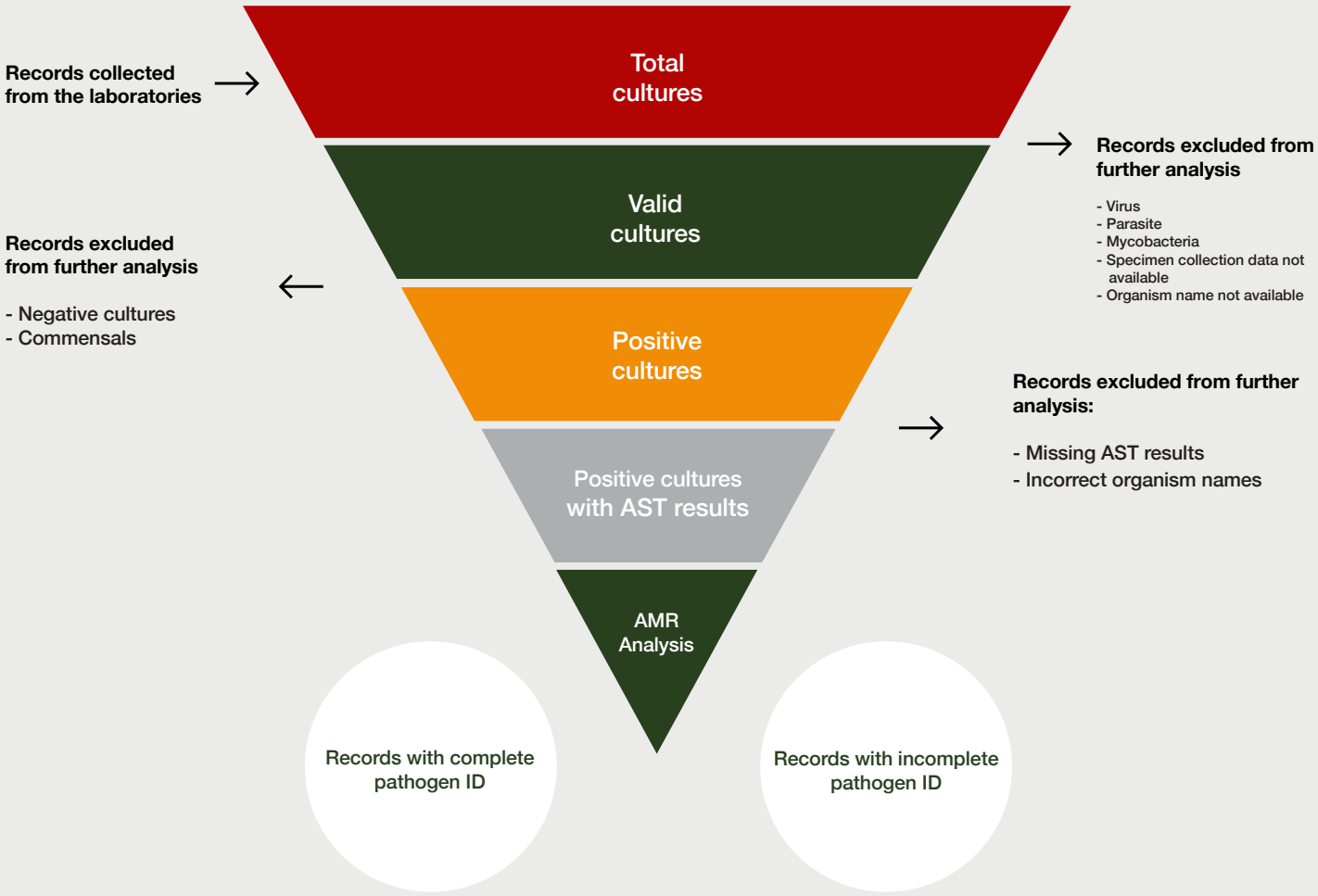


Figure 7: Conceptual framework for deriving quantum of cultures

- **Culture characteristics:** Cultures were characterised across gender, age group and pathogen type (bacteria or fungi). Data were pooled across all laboratories and assessment was conducted for each study year.
- **Inappropriate testing:** Positive cultures with AST results were assessed for compliance to AST standards. However, comprehensive assessment of validity of AST results was beyond the study scope. Data were pooled across laboratories and assessed for each study year. The conventional AST standards are Clinical and Laboratory Standards Institute (CLSI), European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Comité de l'antibiogramme de la Société Française de Microbiologie, the European Committee on Antimicrobial Susceptibility Testing.
- **Clinical information:** Positive cultures with AST results were summarised based on information available for the patient's clinical profile: diagnosis, origin of infection (whether hospital-acquired, or community-acquired), presence of indwelling device and antimicrobial use. Data were quantified for each laboratory and assessed over the entire study period.
- **Specimen characteristics:** Positive cultures with AST results were summarised based on information on specimen types. Data were pooled across all laboratories and assessed for each study year.
- **Quality of data:** We used the level of pathogen identification as a parameter to evaluate the data quality from each laboratory seeing as the complete identification of pathogens is key in AMR surveillance and implies the quality of the laboratory's testing practices. Scoring was based on quartiles of the proportion of completely identified pathogens. The laboratories with >75% of pathogens identified at the species level were awarded the highest score (4). Laboratories with <25% identification received the lowest score (1), (Table 3). Firstly, the scoring was performed per year (i.e., 2016–2018). Thereafter, the average was assigned as the laboratory data quality score for each laboratory.

Table 3: Data scoring scheme

Level of pathogen identification	Score
<25%	1
25-50%	2
51-75%	3
>75%	4

Seeing as we pooled all the data to obtain AMR rates at a national level, we computed a single metric to estimate the overall quality of data received from a country. This metric is referred to as the 'country data quality score' and weights the laboratory data quality score with the quantum of valid cultures contributed by each laboratory, as shown in the formula below. The maximum attainable score is 4. Table 4 below shows how the country data quality score was rated.

Table 4: Data quality rating

Score	Rating
4	Excellent
3-3.9	Good
2-2.9	Average
1-1.9	Poor

$$\text{Country data quality score} = \sum_{i=1}^{n} \frac{(\text{Laboratory data quality score}_{(i)} \times \text{Quantum of valid cultures}_{(i)}}{\sum \text{Quantum of valid cultures}_{(1\ldots n)}}$$

Where *n* is the total number of contributing labs and *i* represents individual laboratories.

Results

Retrospective data for 2016–18 was collected from three laboratories and corresponding facilities of Eswatini.

1. Quantum of cultures and level of pathogen identification

Data were retrieved for 9 445 total cultures, of which 9 386 were valid and 5 290 were positive. Of the positive cultures, AST results were available for 5 247 cultures, maximum (n=2 896) coming from Mbabane Hospital and the least (n=576) from RFM Hospital (Figure 8 and 9). Not all pathogens were identified completely (i.e., at species level). Complete identifications were highest for Lancet (85.1%) and lowest for RFM Hospital (45.0%) (Table 5).

Table 5: Data summary

Variable (Columns) / Laboratory (Rows)	Total Cultures N=9 445	Valid Cultures N=9 386	Positive Cultures N=5 290	Positive Cultures with AST Results N=5 247	Incomplete Identity* N=1 445	Complete Identity* N=3 802
Lancet	5 952	5 893 (99.0)	1 814 (30.8)	1 775 (97.9)	265 (14.9)	1 510 (85.1)
Mbabane Hospital	2 909	2 909 (100.0)	2 900 (99.7)	2 896 (99.9)	863 (29.8)	2 033 (70.2)
RFM Hospital	584	584 (100.0)	576 (98.6)	576 (100.0)	317 (55.0)	259 (45.0)

* Subsets of the category 'Positive cultures with AST results' where 'incomplete' includes cultures with only Gram or genus-level identification; 'complete' includes cultures with species-level identification; — information not available

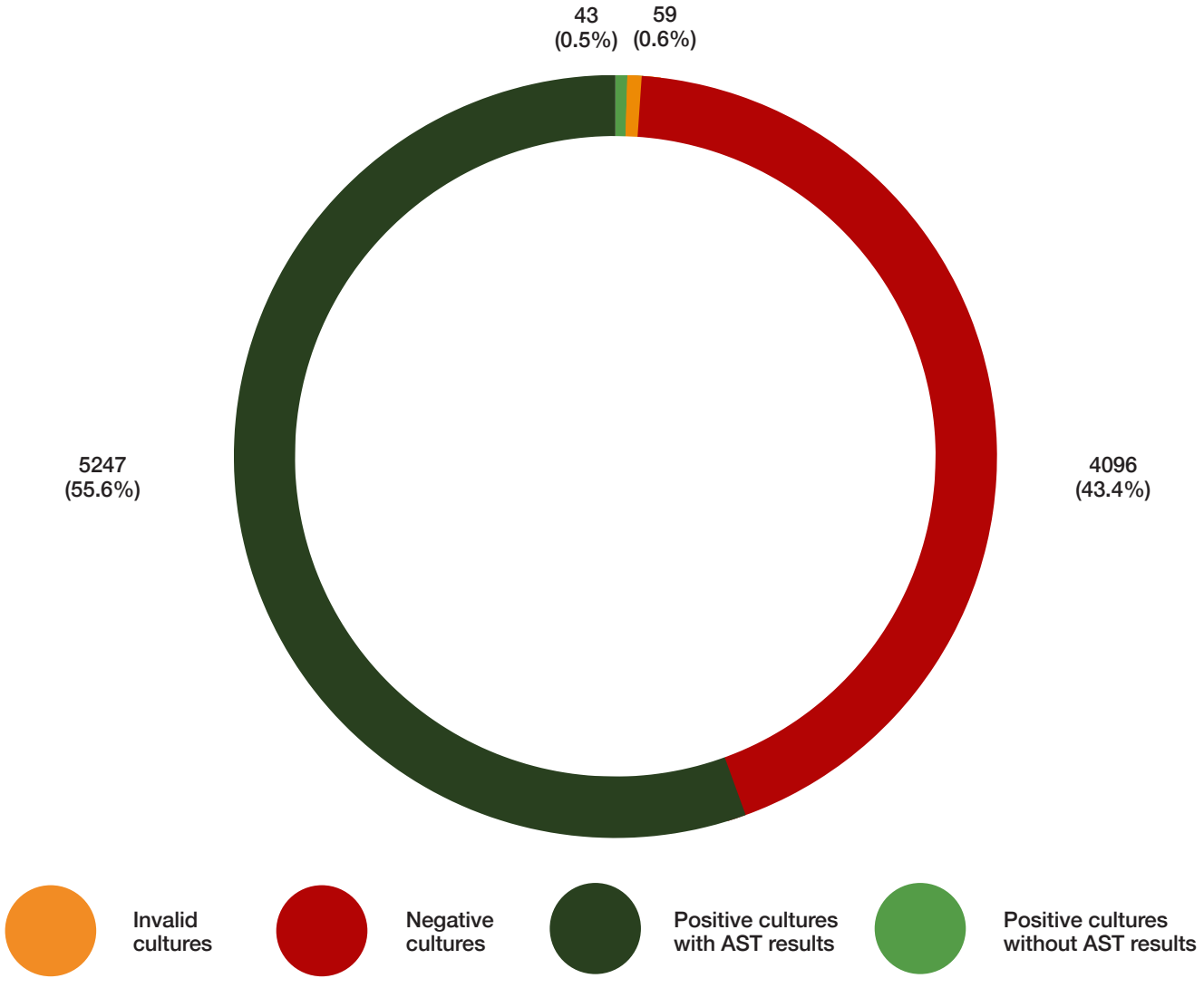


Figure 8: Quantum of cultures across all selected laboratories

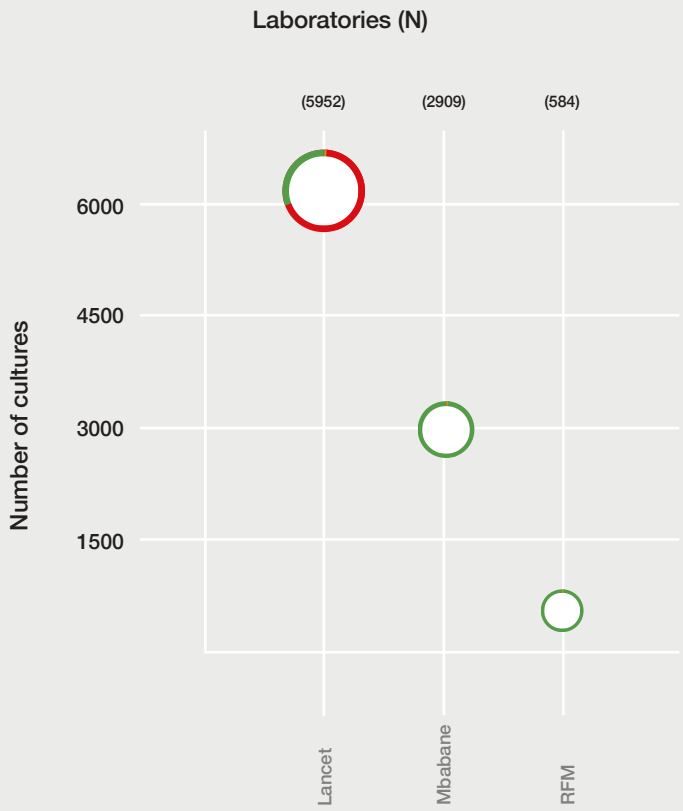


Figure 9: Quantum of cultures in each selected laboratory

2. Culture characteristics

Bacterial pathogens (5 202) were more commonly isolated from positive cultures than fungal pathogens. Information on age was missing from 5.6% of cultures, but where available, data showed a median age of 35 years (range 0–90 years) with most cultures (2 504) obtained from patients 18–49 years old. Males (2 023) contributed more to the quantum of positive cultures with AST results. More data came from 2017 (2 231) than other years (Table 6, Supplementary Table 3).

Table 6: Culture characteristics

Characteristics	Positive cultures with AST results n=5 247 n (%)
Gender	
Male	3 224 (61.4)
Female	2 023 (38.6)
Age, years	
Less than 1	472 (8.9)
1 to 17	772 (14.7)
18 to 49	2 504 (47.7)
50 to 65	718 (13.6)
Above 65	484 (9.2)
Unknown age	297 (5.6)
Years	
2016	1 339 (25.5)
2017	2 231 (42.5)
2018	1677 (31.9)
Pathogen	
Bacteria	5202 (99.1)
Fungi	45 (0.9)

3. Inappropriate testing

During the review of AST results, the following instances of inappropriate testing were noted:

Fungi tested against antibiotics (Supplementary Figure 2a). Enterobacterales were tested against inappropriate agents such as vancomycin, penicillin G or oxacillin and S.taphylococcus aureus was tested against vancomycin using disk diffusion method (Supplementary Figure 2b).

4. Clinical information

Patient metadata, particularly clinical information, were sparse (Table 7).

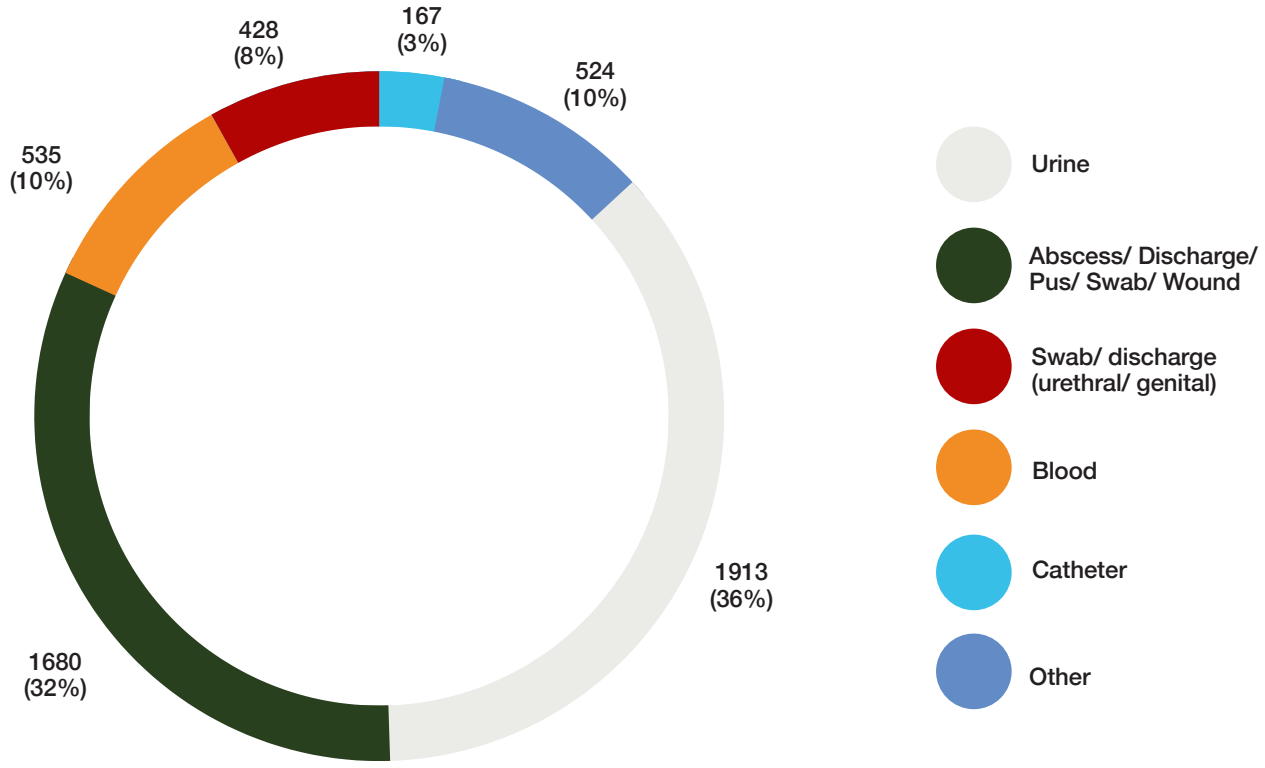
Table 7: Clinical information

Laboratory	Positive cultures with AST results n=5 247	Diagnosis data	Infection origin data*	Indwelling device data	AMU data
Lancet	1 775	0	0	0	0
Mbabane	2 896	11	6	3	9
RFM	576	0	0	0	0

- information not available; * hospital acquired, or community acquired; AMU=antimicrobial use; AST=antibiotic susceptibility testing.

5. Specimen characteristics

Urine, purulent discharge and blood accounted for most of the positive cultures in each study year (Figure 10, Supplementary Table 4).



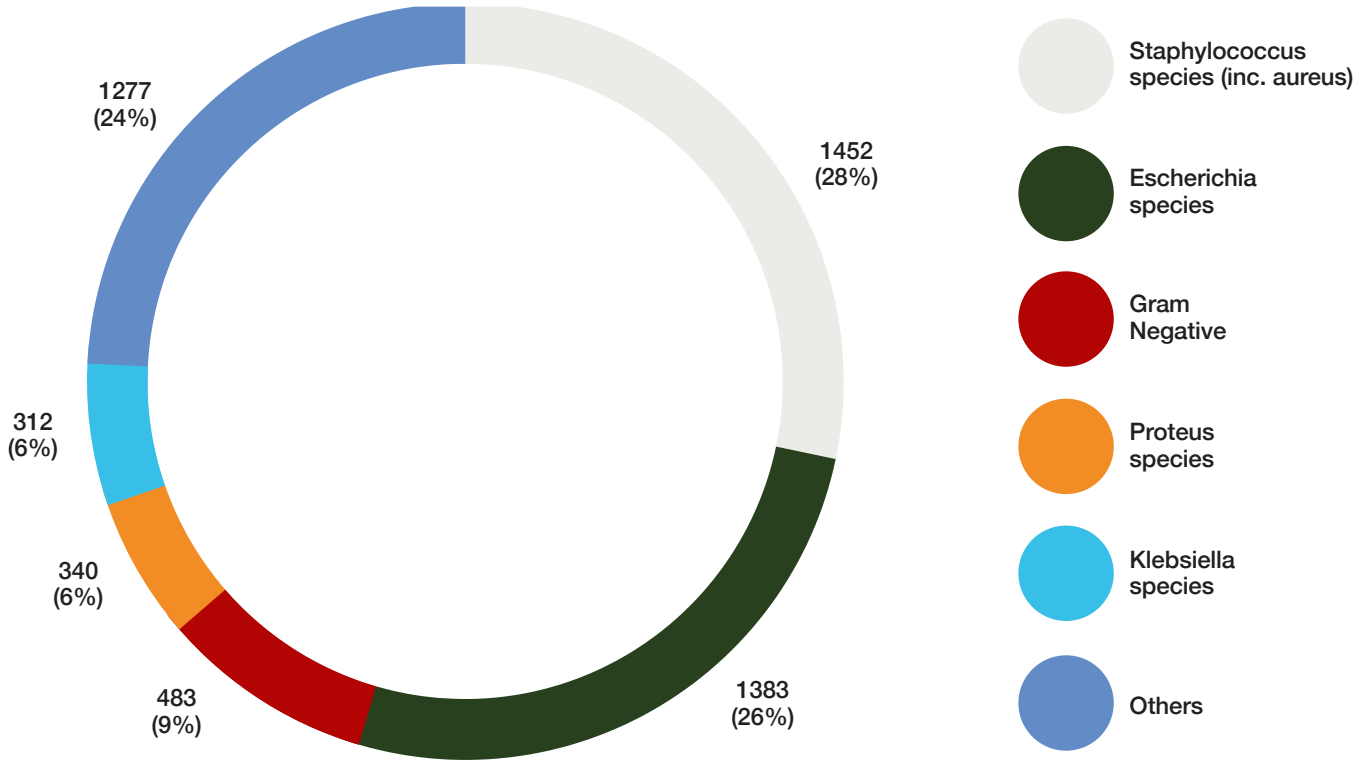
* Others include all other specimens excluding the top 5 mentioned here

Figure 10: Specimen characteristics

6. Identified pathogens

Staphylococcus species (28%), Escherichia species (26%), Proteus species (6%) and Klebsiella species (6%) largely contributed to the quantum of positive cultures (Figure 11).

In 2016, of the 1 339 positive cultures with AST results, Escherichia species (32.1%), Staphylococcus species (26%) and Klebsiella species (7.5%) were the most reported. In 2017, of the 2 231 positive cultures with AST results, Staphylococcus species (27.1%), Escherichia species (24.8%), and Proteus species (7.2%) were the most reported. In 2018, of the 1 677 positive cultures, Staphylococcus species (29.8%), Escherichia species (23.8%), and Proteus species (5.1%) were the again the most reported (Supplementary Table 5).



* Others include all other pathogens excluding the top 5 mentioned here

Figure 11: Pathogens identified

7. Quality of data

The country data quality score of the 9 386 valid culture records obtained from the three laboratories in Eswatini was 3.7 and was rated as good for AMR analysis. For individual laboratory data quality scores from each contributing laboratory, see Supplementary Table 6.

Section III: AMR rates

Objective

To estimate the country-level AMR prevalence and trends for WHO priority pathogens and other clinically important and frequently isolated pathogens as well as to enable the comparison of countries on spatiotemporal maps.

Methodology

Data from positive cultures with AST results was analysed to estimate the country-level AMR prevalence of pathogens and identify the drivers of resistance.

Estimation of AMR rates

In this report, the AMR rate is the extent to which a pathogen is resistant to a particular antimicrobial agent or class as is determined by the proportion of isolates that are non-susceptible (i.e., either intermediate or resistant) over a one-year period:

$$\text{AMR rate} = \frac{\text{No. of non-susceptible isolates}}{\text{No. of tested isolates}} \times 100 \ (\text{CI } 95\%)$$

AMR rates were estimated for the WHO priority pathogens[13] where the number of tested isolates exceeded 30 regardless of the specimen type (AMR Appendix 5). AMR trends were mapped for the WHO priority pathogens depending on data availability.

In addition, AMR rates were estimated for:

1. Clinically important pathogens isolated from blood and cerebrospinal fluid (AMR Appendix 6)
2. Top three highly resistant bug-drug combinations (regardless of the specimen type)
3. Pathogens tested against the most and least consumed antimicrobial classes (regardless of the specimen type, please refer to part C)

Data were analysed as per resistance interpretation submitted by the laboratories. Where laboratories provided quantitative results (i.e., diameter measurements or minimum inhibitory concentrations), data were adjusted based on the updated breakpoints available on WHONET. Although nonsusceptibility interpretations were based on results from the tested antimicrobials, they are represented at the antimicrobial class level wherever possible (AMR Appendix 7). Analysis was limited to bacterial and fungal pathogens.

Removal of duplicate records

Before AMR rates were calculated, duplicate AST results were removed such that only the results of the first pathogen isolate per patient per year, irrespective of AST profile (and body site or specimen type in the case of WHO priority pathogens), were included; this approach follows the CLSI M39A4 criteria.[14,15] Duplicate removal was based on the availability of unique patient identifiers. When no patient identifiers were available, the results of all isolates were included. The AST data from all laboratories were then aggregated and rates were calculated as the proportion of non-susceptible isolates.

AMR estimates statistics

Confidence intervals (CIs) at the 95% level of confidence were calculated to quantify the uncertainty in the estimated resistance rates. Typically, CIs for AST data have been constructed using the Wilson score method. This is a binomial calculation that assumes that all samples are independent.[16] However, there are likely correlations between data within each laboratory and between laboratories that draw from similar populations. Thus, where appropriate, the Wilson cluster robust CI method was employed to account for a lack of data independence such that each laboratory represented a cluster.[17]

Estimated AMR rates should be interpreted with caution because they were derived from aggregated data from laboratories with varying testing capabilities and not all selected laboratories contributed to the AST results. The validation of AST results was beyond the study scope; data were taken at face value for assessment of resistance rates.

Online data visualisation

AMR data were aggregated to the national level and definitions of resistance were harmonised across countries to enable comparisons. Data were uploaded to a private and secure portal for countries and laboratories to permit analysis of their data at the patient level (CDDEP's ResistanceMap Surveillance Network [RSN], surveillance.cddep.org). RSN provides a simple approach to analysing AMR data. Point-and-click editing tools allow the user to mine the data to answer complex questions where the resulting analyses can be displayed as bar charts representing resistance over a time period or line graphs showing changes over time by month or year. RSN will be made available for at least one year, following completion of the study, to each participating country.

Data were also uploaded to CDDEP's ResistanceMap platform, a publicly available repository for aggregated country-level data (resistancemap.cddep.org).[18] Spatiotemporal analysis for the combined AMR and AMC-AMU datasets were built on the ResistanceMap framework. Current capabilities include maps, trend line charts and frequency bar charts.

Results

(i) AMR rates and trends for WHO priority pathogens

AMR rates for the WHO priority pathogens were calculated as the proportion of isolates that were non-susceptible over each one-year interval. Across 2016–18, AMR rates for some organisms remained consistent; the rates for others varied. Moderate to high resistance was noted for methicillin-resistant S. aureus (21-58%) and 3rd-generation cephalosporin-resistant Enterobacterales (25-41%). Rates for carbapenem-resistant Enterobacterales were lower (<6%) (Table 8, Figures 12 and 13). Statistics for vancomycin-resistant and intermediate Staphylococcus species and S. aureus are not included.

Table 8: AMR rate estimates for WHO priority pathogens

Pathogen	Antibiotic, class	2016				2017				2018			
		N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)
A. baumannii	Carbapenems	3	1	-	2 (1 - 2)	1	0	-	1 (1)	8	4	-	2 (1 - 7)
P. aeruginosa	Carbapenems	18	2	-	2 (8 - 10)	11	0	-	2 (1 - 10)	25	1	-	2 (6 - 19)
Enterobacter ales	Carbapenems	435	5 (1.1)	0 - 23.4	3 (4 - 328)	344	12 (3.5)	0.1- 63.5	3 (1 - 302)	366	21 (5.7)	0.1 - 73.4	3 (6 - 319)
Enterobacter ales	Cephalosporins (3rd generation)	584	147 (25.2)	4 - 72.9	3 (49 - 350)	905	373 (41.2)	10.3 - 81.1	3 (118 - 473)	545	196 (36)	4.7 - 86.4	3 (22 - 336)
E. faecium	Vancomycin	5	1	-	2 (2 - 3)	10	2	-	2 (3 - 7)	-	-	-	-
H. influenzae	Ampicillin	-	-	-	-	1	1	-	1 (1)	1	0	-	1 (1)
H. pylori	Clarithromycin	-	-	-	-	-	-	-	-	-	-	-	-
N. gonorrhoeae	Cephalosporins (3rd generation)	9	0	-	1 (9)	14	0	-	1 (14)	5	1	-	2 (1 - 4)
N. gonorrhoeae	Fluoroquinolones	9	1	-	1 (9)	14	7	-	1 (14)	5	3	-	2 (1 - 4)
Campylobacter species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolones	7	3	-	2 (3 - 4)	5	1	-	2 (1 - 4)	3	1	-	2 (1 - 2)
Shigella species	Fluoroquinolones	1	0	-	1 (1)	3	0	-	2 (1 - 2)	3	1	-	2 (1 - 2)
S. aureus	Methicillin	147	31 (21.1)	0.8 - 89.3	3 (1 - 86)	282	100 (35.5)	3.3 - 89.9	3 (7 - 178)	174	101 (58)	2.8 - 98.5	3 (11 - 93)
S. pneumoniae	Beta-lactam combinations	1	0	-	1 (1)	3	0	-	1 (3)	-	-	-	-
S. pneumoniae	Penicillins	2	0	-	1 (2)	6	3	-	2 (2 - 4)	2	2	-	2 (1 - 1)

N = number of tested isolates; n = number of non-susceptible isolates; n% and 95%CI are shown only if >30 isolates/ year; — information not available; # contributing laboratories and range of tested isolates; where the pathogen is suffixed as species, all isolates of same genus are grouped as one entity.

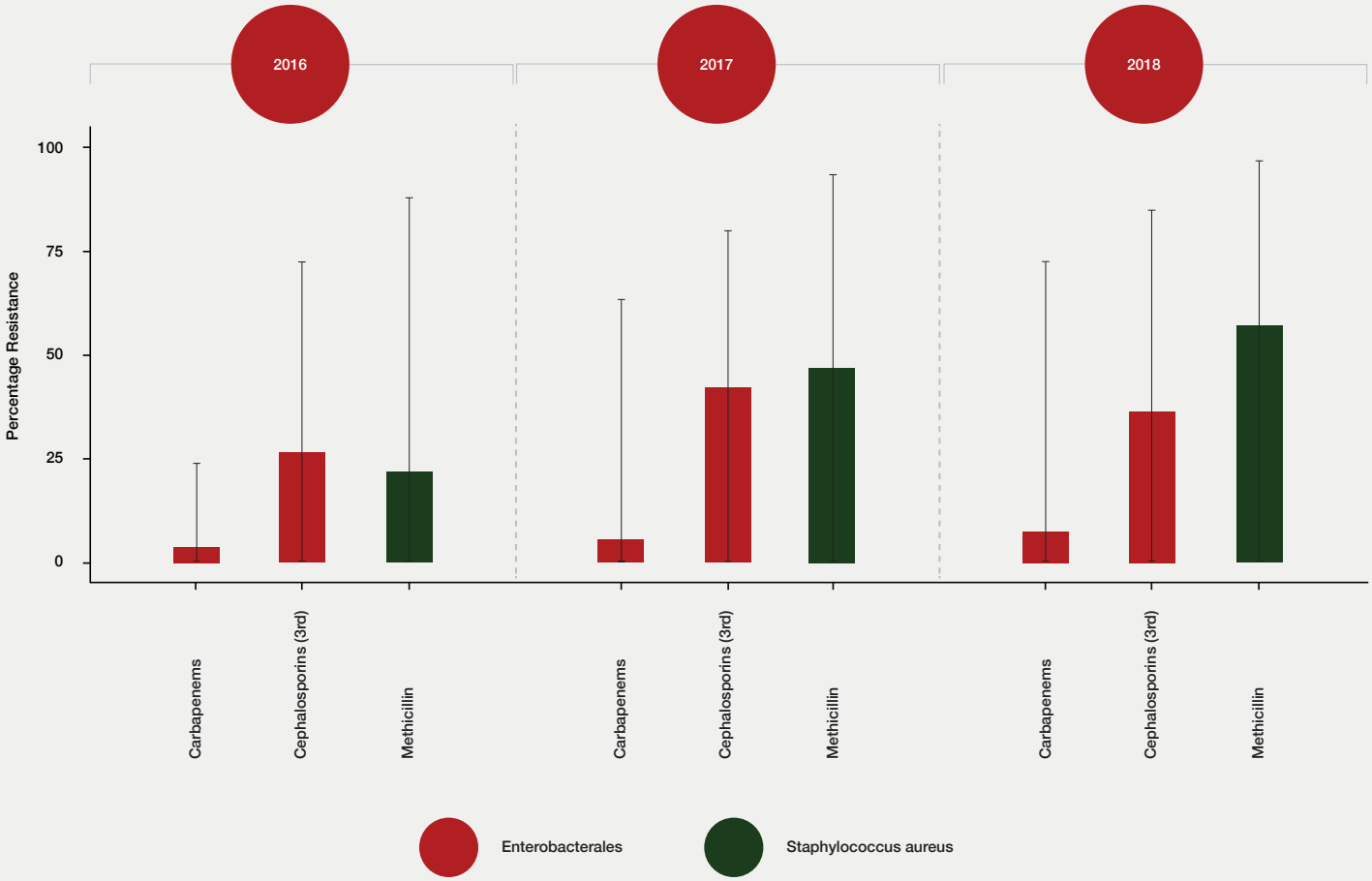


Figure 12: AMR rate estimates for WHO priority pathogens

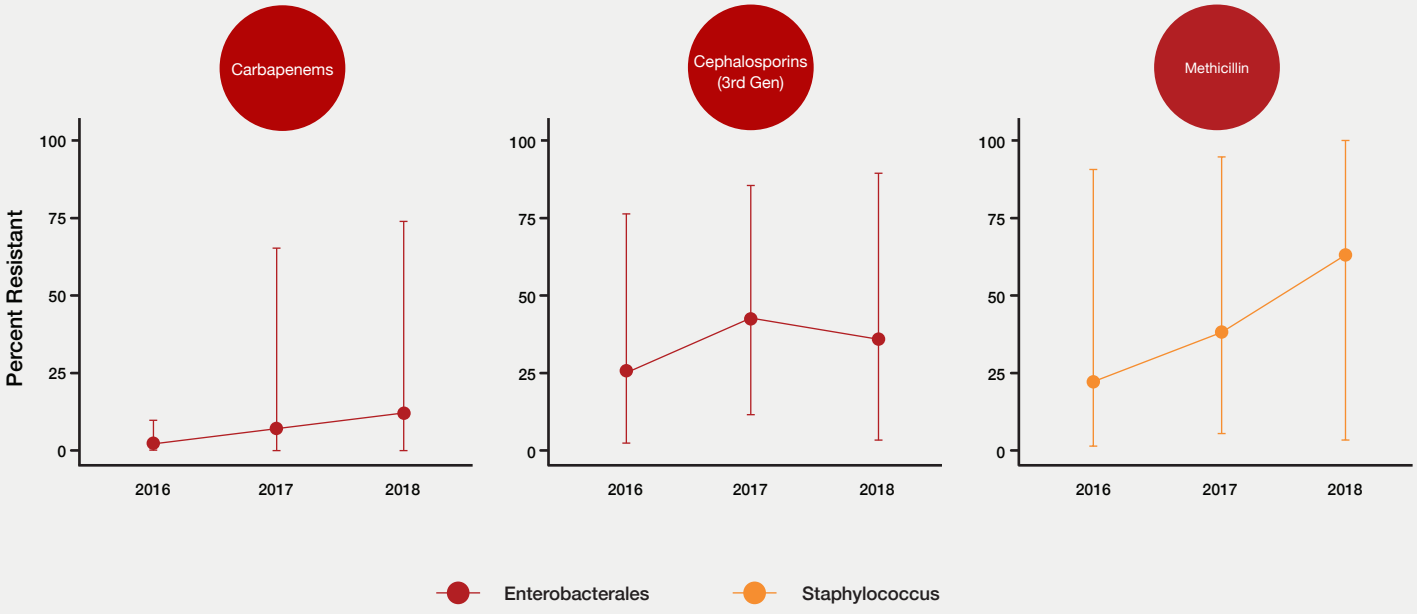


Figure 13: AMR trends for WHO priority pathogens

(ii) AMR rates for other pathogens of clinical importance

AST data from blood and CSF isolates were largely insufficient for further analysis and interpretation. The AMR rate for methicillin-resistant Staphylococcus species (excluding aureus) was 14.8% (61 tested isolates) and 31.8% (44 tested isolates) in 2016 and 2017, respectively (Table 9).

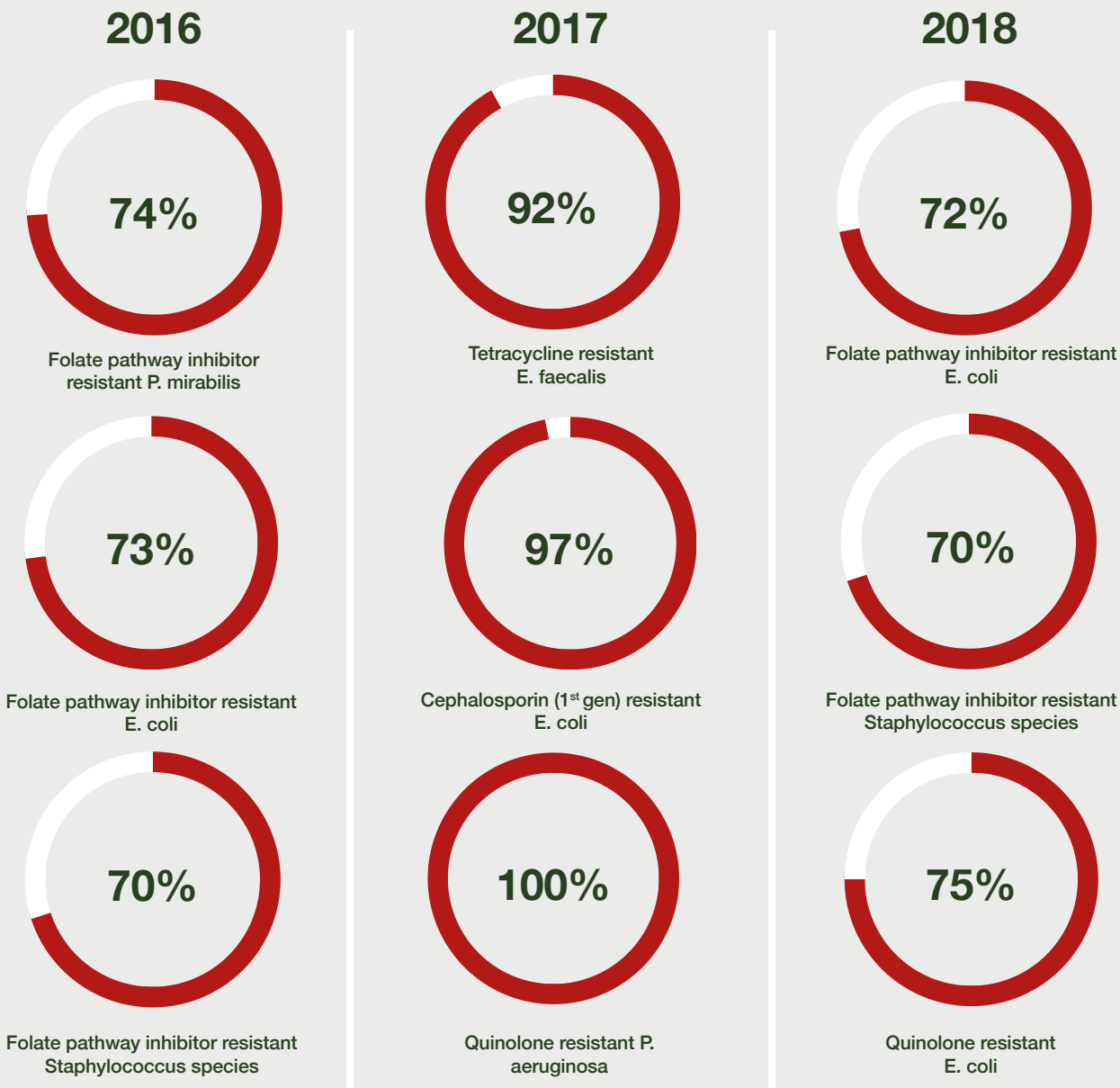
*Table 9: AMR rate estimates for other clinically important pathogens**

		2016				2017				2018			
Pathogen	Antibiotic, class	N	n (%)	95% CI	Labs# (range)	N	n (%)	95% CI	Labs# (range)	N	n (%)	95% CI	Labs# (range)
Acinetobacter species	Carbapenems	1	0	-	1 (1)	2	0	-	1 (2)	1	0	-	1 (1)
Acinetobacter species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Aminoglycosides (high level)	-	-	-	-	-	-	-	-	1	1	-	1 (1)
Enterococcus species	Vancomycin	5	0	-	2 (1 - 4)	10	0	-	2 (3 - 7)	1	0	-	1 (1)
H. influenzae	Ampicillin	-	-	-	-	-	-	-	-	-	-	-	-
H. influenzae	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Klebsiella species	Carbapenems	4	0	-	2 (1 - 3)	4	0	-	1 (4)	6	1	-	2 (1 - 5)
Klebsiella species	Cephalosporins (3rd generation)	11	9	-	3 (1 - 7)	12	6	-	3 (1 - 7)	8	7	-	2 (3 - 5)
N. meningitidis	Ampicillin	-	-		-	1	1	-	1 (1)	-	-	-	-
N. meningitidis	Cephalosporins (3rd generation)	-	-	-	-	1	0	-	1 (1)	-	-	-	-
Pseudomonas species	Carbapenems	3	0	-	3 (1 - 1)	1	0	-	1 (1)	-	-	-	-
Pseudomonas species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	
Salmonella species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Macrolides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	Methicillin	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus species (Excluding aureus)	Methicillin	61	9 (14.8)	0.4 - 89.3	3 (1 - 50)	44	14 (31.8)	0.1- 99.5	2 (19 - 25)	29	10	-	2 (1 - 28)
S. pneumoniae	Penicillins	2	0		1 (2)	3	2	-	2 (1 - 2)	1	1	-	1 (1)
S. pneumoniae	Beta-lactam combinations	1	0	-	1 (1)	1	0	-	1 (1)	-	-	-	
S. pneumoniae	Macrolides	2	0	-	2 (1 - 1)	2	0	-	2 (1 - 1)	-	-	-	-
S. pneumoniae	Vancomycin	3	0	-	2 (1 - 2)	1	0	-	1 (1)	-	-	-	-

* From blood and CSF; N = number of tested isolates; n = number of non-susceptible isolates; %n and %CI are shown only if >30 isolates/year; # contributing laboratories and range of tested isolates; — information not available; where the pathogen is suffixed as species, all isolates of same genus are grouped as one entity.

(iii) AMR rates for highly resistant pathogens

Based on the available data, very high (~100%) resistance was estimated for clinically important pathogens like Pseudomonas aeroginosa (vs. quinolones) and E. coli (vs. cephalosporin 1st generation) (Figure 14).



Pathogen nomenclature is shown as reported by laboratories; antimicrobials are reported at class level

Figure 14: Top five highly resistant pathogens

(iv) AMR rates for fungal pathogens

Available AST data on fungal isolates were insufficient for further analysis.

Section IV: Drivers of antimicrobial resistance

Objective

To assess the drivers of AMR

Methodology

AMR drivers are factors that could predispose patients to AMR. To determine the association between AMR and its potential drivers, the following patient and country-level factors were considered:

- Patient-level factors: demographics (age and gender), diagnosis, comorbidities, antimicrobial usage, presence of device (catheter, central line, ventilator) and origin of infection (hospital or community)
- Country-level factors: Global Health Security index scores on AMR prevention, primary education, GDP per capita, physician and nurse density, disease prevalence and antibiotic consumption in DDD per 1 000 inhabitants (the country-level associations are presented separately at a regional or continental level)

To identify the drivers of resistance, a composite AMR rate for select groups of pathogens (Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, P. aeruginosa, S. aureus, Enterococcus faecium and Enterococcus faecalis) and antibiotics or antibiotic classes (aminoglycosides, broad-spectrum penicillins, carbapenems, cephalosporins, glycopeptides, narrow spectrum penicillins and quinolones) was estimated (AMR Appendix 8). The choice of pathogens and antimicrobials was guided by the DRI methodology (Part C).

Statistical analysis

An initial exploration of the data was done to identify missing information and any collinearity between the patient-level factors (drivers). Logistic regression analyses (univariate and multiple) were performed to determine the association with AMR. The analyses were adjusted for the number of contributing laboratories to account for the variation in the respective laboratory datasets. Crude odds ratios (ORs) were estimated in the univariate logistic regression analysis to describe the association between AMR and the investigated variables. Only those with $p<0.2$ were evaluated in a multiple logistic regression analysis (statistical significance was set at $p<0.05$). The Wilson score method with robust standard error was used to construct CIs for the AMR rates.

To explore the association between country factors (continuous variables) and AMR, correlation analysis (Pearson's) was performed with reporting at a continental level.

All results should be interpreted with caution as they were derived from data aggregated from facilities with varying capabilities in addition to the data from the laboratories being varied.

Results

Three variables namely, age, and gender were evaluated for possible association with AMR. The data availability for these variables was age: 96.6% and gender: 98.9%. The univariate logistic regression results showed that males were more likely to have a resistant infection (OR 1.51, 95% CI 1.31 – 1.74). Patients in the following age groups: <1 year (OR 1.91, 95% CI 1.07 – 3.41), and 50 – 65 years (OR 1.22, 95% CI 1.01 – 1.49), were also more likely to have resistant infections (Supplementary Table 7).

Gender and age were included in the multiple logistic regression model based on the set inclusion criteria. When controlling for the effect of age, males were more likely to have resistant infections (OR 1.43, 95% CI 1.20 – 1.70). However, when controlling for the effect of gender, only patients aged below one year (OR 1.67, 95% CI 1.02 – 2.74) were more likely to have resistant infections (Table 10).

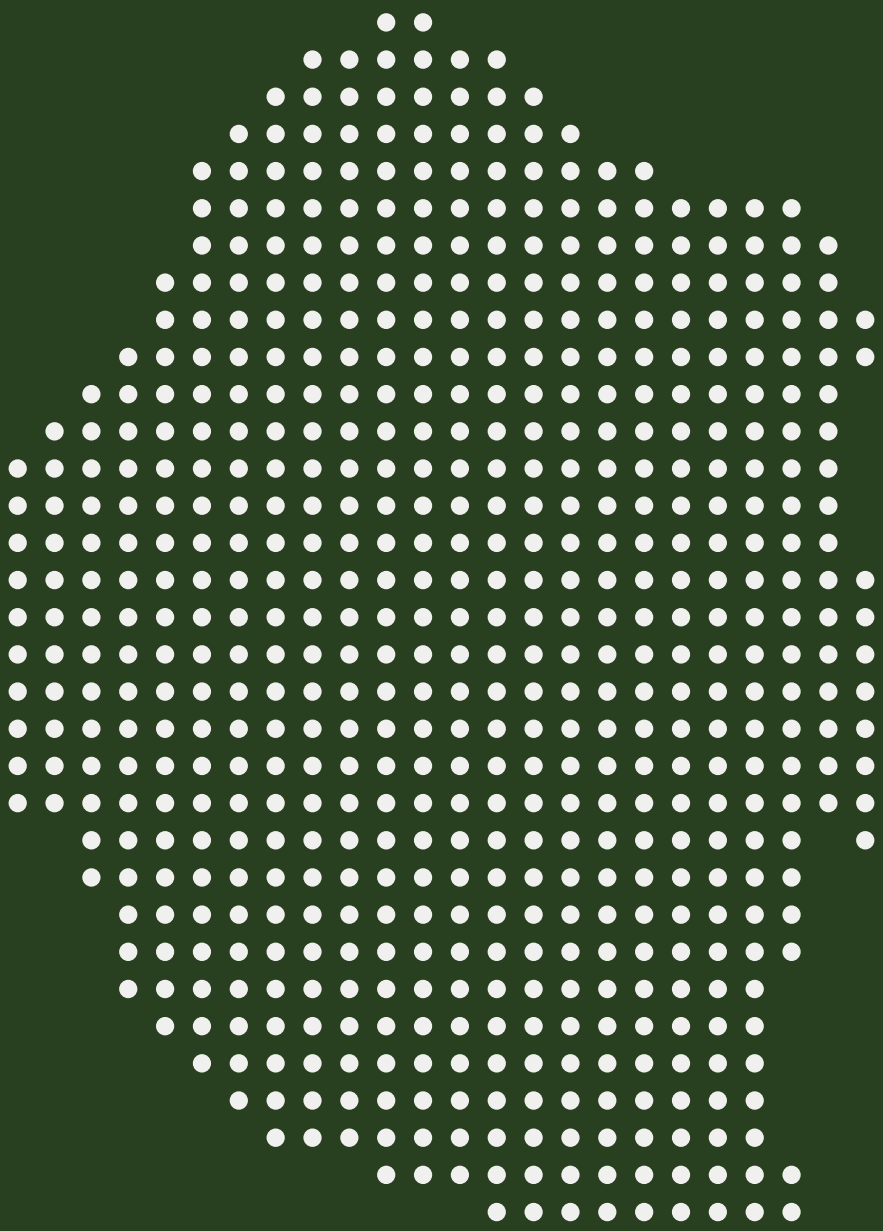
Table 10: Multiple logistic regression analysis

Variable	Options	N	NS (%)	Adjusted OR (95% CI)	P-value
Gender	Female	5 305	30.7	**Reference category**	
	Male	2 117	39.9	1.43 (1.20 – 1.70)	0.000
Age	<1	375	45.1	1.67 (1.02 – 2.74)	0.039
	1-17	906	36.9	1.30 (0.92 – 1.81)	0.132
	18-49	3 981	30.6	**Ref**	
	50-65	1 277	35.1	1.18 (1.00 – 1.38)	0.048
	>65	883	34.4	1.11 (0.87 – 1.42)	0.390

N=number of tested isolates; NS (%)=proportion of non-susceptible isolates.

Information on other patient factors was unavailable or inadequate for analysis.

Part B: Antimicrobial (antibiotic) Consumption



Section I: Background of antimicrobial consumption (AMC) and antimicrobial use (AMU)

Overuse and misuse of antimicrobials are crucial factors in the complex web of causation of AMR. Widespread and unregulated antimicrobials usage exert a selective pressure by reducing the reproductive success of some of the microorganisms and consequently accelerating the development of AMR.[19,20] Therefore, close surveillance on how the antimicrobials are utilised is a key step for stewardship programs in order to stem AMR. The surveillance mechanisms recommended by WHO include the monitoring of AMC and AMU. This aligns with the MAAP's aim to expand the volume of data presently available on AMR and AMC or AMU across Africa and the country's National AMR Containment Strategic Plan (2018-2022).[21]

Definition of AMC and AMU

AMC is defined as the quantification of antimicrobials used within a specified setting (e.g., national-level, hospital, or community healthcare-level) over a specified period. AMC is calculated from aggregated data, such as import, wholesalers, insurance, or facility dispensing or procurement data sources. AMU tracks whether antimicrobials are prescribed appropriately, for the right infections and according to treatment guidelines. AMC and AMU are terminologies that are sometimes used interchangeably and incorrectly so. It is therefore prudent to delineate these definitions further through clarification that AMC data describes quantities of antimicrobials dispensed (e.g., at national stores or pharmacies) whereas AMU data describe how and why antimicrobials are used (e.g., whether required laboratory tests and clinical assessments were conducted prior to issuing a prescription, whether the right antimicrobial was prescribed at the correct strength and frequency over an appropriate duration to treat the right indication as per country guidelines, and if the patient correctly and/or completely consumed the prescribed antimicrobial).[22]

Link between the antimicrobial usage and AMR

The unwarranted use of antimicrobials contributes to the emergence of AMR. This association implies that a reduction in the unnecessary consumption of antimicrobials could in turn reduce AMR levels.[19] The inappropriate use of antimicrobials refers to the use of the wrong type of antimicrobial, and/or at the wrong dose, frequencies or duration, and/or for the wrong indication. For the past few decades, there has been a global increase in the consumption of antimicrobials and a shift in consumption towards the use of both broad-spectrum and last-resort antimicrobials, particularly in LMICs. These shifts are because of improved access and increased economic strength within some of these countries. However, AMR can also develop as a result of a lack of access to antimicrobials, leading to the prolonged use of particular antimicrobial over a long time and thus permitting selective pressure to favour microbes that evade these predominantly used antimicrobials. This is often the picture in several LMICs where inequities in access to antimicrobials still persist.[23] This complicated picture demonstrates the need for the research and development of new agents that counteract emerging AMR, but also strongly indicates the need to use the available antimicrobials appropriately and ensure their accessibility.

In view of obtaining an elaborate and complete picture of the link between AMC or AMU and AMR in Eswatini, the identification of prevalent gaps, as well as areas for targeted intervention to encourage rational use of antimicrobials and a surveillance system for consumption, is of paramount importance. In this regard, one of the MAAP's key objectives was to evaluate the ability to conduct AMC and AMU surveillance (data collection and analysis) in Eswatini that would equip the country with valuable information to support the appropriate use of antimicrobials. The objective was to identify gaps that may exist in establishing a comprehensive surveillance system and provide the country with the needed information to support the setup of such a monitoring system.

AMC and AMU surveillance impact

In an effort to ensure successful treatment of infectious diseases in patients, optimising the correct usage of antimicrobials is one of the strategic objectives within the WHO Global Action Plan (World Health Organization, 2015). For the successful implementation of the above objective, there is a need to understand country's pattern of antimicrobials use and quantification of their consumption. At present, there are only few published reports on AMC surveillance and AMU in Africa,[24-28] including one report on AMU in Eswatini.[29] The process of obtaining AMC or AMU data for a country equips the country with local information on various problems that exist with antimicrobials use and allows for monitoring the accessibility of antimicrobials. Furthermore, obtaining of AMC or AMU data permits the continuous local assessment of correlations between antimicrobial usage to emerging local AMR, which in turn allows for proper mitigation policies and activities to be planned using the relevant data. Data obtained from local surveillance exercises also presents the opportunity to better inform stewardship programmes.

Therefore, MAAP set out to quantify consumption and analyse AMC and AMU trends at selected facilities as well as at the national level, in order to better inform the design of future ASP and policies which will optimise the use of antimicrobials in Eswatini. In addition, this will provide the country with a reference point to measure the impact and success of future implemented interventions.

The aim of this work

1. To describe the antimicrobial flow in-country and highlight the status of the AMC and AMU surveillance system in Eswatini

2. To quantify and evaluate the trends of AMC and AMU at national and pharmacy level

Section II: AMC or AMU surveillance status

Objective

To describe the antimicrobial flow in-country and highlight current status of the AMC and AMU surveillance system in Eswatini

Methodology

AMC and AMU data sources

Through open-structured key informant interviews (KIIs) (AMC Appendix 1), the Antimicrobial Resistance Coordinating Committee (AMRCC) contacts shared their insights about the current landscape of AMC surveillance in the country as well as from where national AMC data can best be surveilled. Consequently, the central medical store (CMS), the public-sector procurement mechanism, was identified as potential source for national AMC data in Eswatini.

Under the guidance of the Eswatini's AMRCC, MAAP also targeted to recruit and obtain data from twice as many pharmacies as the selected AST laboratories (i.e., a total of 32 pharmacies) to obtain aggregated pharmacy-level AMC data. Here, AMC data was targeted for collection from pharmacies that were co-located in the same facility with AST laboratories (n=3) (AMC Appendix 2 for tool used). Additionally, community pharmacies (n=16) were also targeted and were nominated by the co-located pharmacies based on their proximity to the AST laboratories. Community pharmacies were also selected based on serving as the preferred patient purchase source or as a backup prescription fulfilment source in case of stock outs in the main hospital pharmacy. In addition to this, availability of retrospective data from 2016-2018 and willingness to share data were key criteria considered for selection. However, 10 facilities (1 hospital pharmacy and 9 community pharmacies) dropped out during the data collection process of the study. The only hospital facility excluded had a standalone laboratory without an in-house pharmacy and 9 community pharmacies dropped out due to unwillingness to share data with an appropriate replacement not being able to be found.

Besides AMC data collection, AMU data was targeted for collection from the hospital pharmacies (n=3) and this was to be provided from the facilities' prescription or patient medical records. To clarify, community pharmacies, also known as retail pharmacies, are licensed commercial pharmaceutical stores that provide medicinal products (prescription only and over-the-counter medicines) to a specific community group or region and excludes unregulated and informal medicine dispensers. Hospital pharmacies, on the other hand, are pharmacies located within a hospital for the provision of medicinal products to inpatients and outpatients who visit the hospital.

Data collection scope

MAAP purposively selected data collection on J01 (antibiotics for systemic use) consumption trends. J01 medicines are one of the WHO core monitoring Anatomical Therapeutic and Chemical (ATC) medicine categories for AMC surveillance. In addition, as per the country's request, selected P01AB (nitroimidazole derivates) and selected J02 (Antimycotics for systemic use) were also included in the scope for AMC data collection (See Appendix 3 for full list of selected antimicrobials in Eswatini). P01AB and J02 ATC antimicrobials are part of the WHO core and optional monitored medicine classes respectively for AMC surveillance.[30] AMC data from the above medicine categories was collected from January 2016 to December 2018.

Data collection

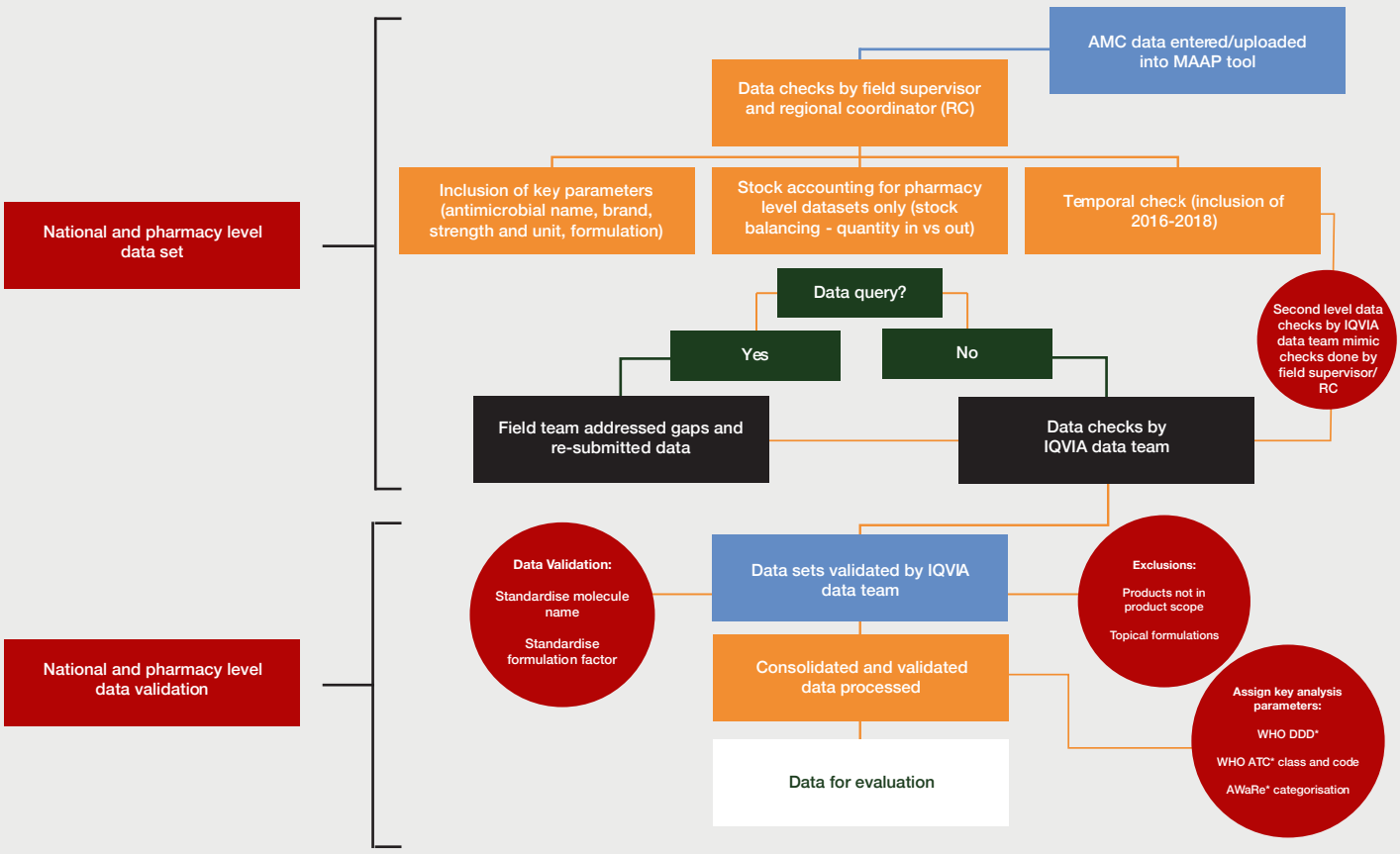
The CMS datasets were provided directly to the MAAP data collectors electronically in the form of a Microsoft Excel™ sheet (for the period 2016-2018). The datasets were reviewed and cleaned by the data collection teams using Excel™. The datasets were then transferred securely through the MAAP tool that captured all the antimicrobials by their standard molecular name and/or product brand, pack size, strength and formulation (e.g., tablets or capsules, suspensions or syrups). Appendix 4 captures the full list of data variables collected to tally national- and pharmacy-level AMC.

For the pharmacy-level data, the trained MAAP data collectors extracted the consumption data from the facility's Health Information System (HIS) into an Excel™ sheet where data were available electronically. Alternatively, abstracted data from stock record cards were manually entered into the MAAP tool within facilities that held manual records. The electronic datasets were reviewed and cleaned by the data teams and then transferred securely through the MAAP tool to the central data processing and analysis team. AMC Appendix 5 details the data collection process.

MAAP also planned to collect the AMU data in pharmacies that were co-located within the facilities also housing AST laboratories and clinical services to assess the appropriateness of consumed antimicrobials. Data to be captured included patient characteristics, indication for which the antimicrobial is being used and the appropriateness of the prescription in relation to national guidelines (including conducting of any relevant laboratory testing and clinical assessment done prior to prescribing, assessment of dose, strength, frequency and duration of prescription).

Data cleaning and validation

The national-level AMC datasets were categorised in this report as generally representing the public sector as they were sourced from the CMS datasets. Once the datasets were received by MAAP, both the national- and pharmacy-level AMC data were then subjected to a series of data validation checks to ensure accuracy and consistency. (Data checks and the validation process for national AMC data are detailed in AMC Appendix 6). Here, the pharmacy and national AMC data were subjected to secondary and tertiary checks by field supervisors, the IQVIA regional coordinator and data team, as outlined in Figure 15.



*WHO World Health Organisation - *DDD Defined Daily Dose - * AWaRe Access, Watch, and Reserve

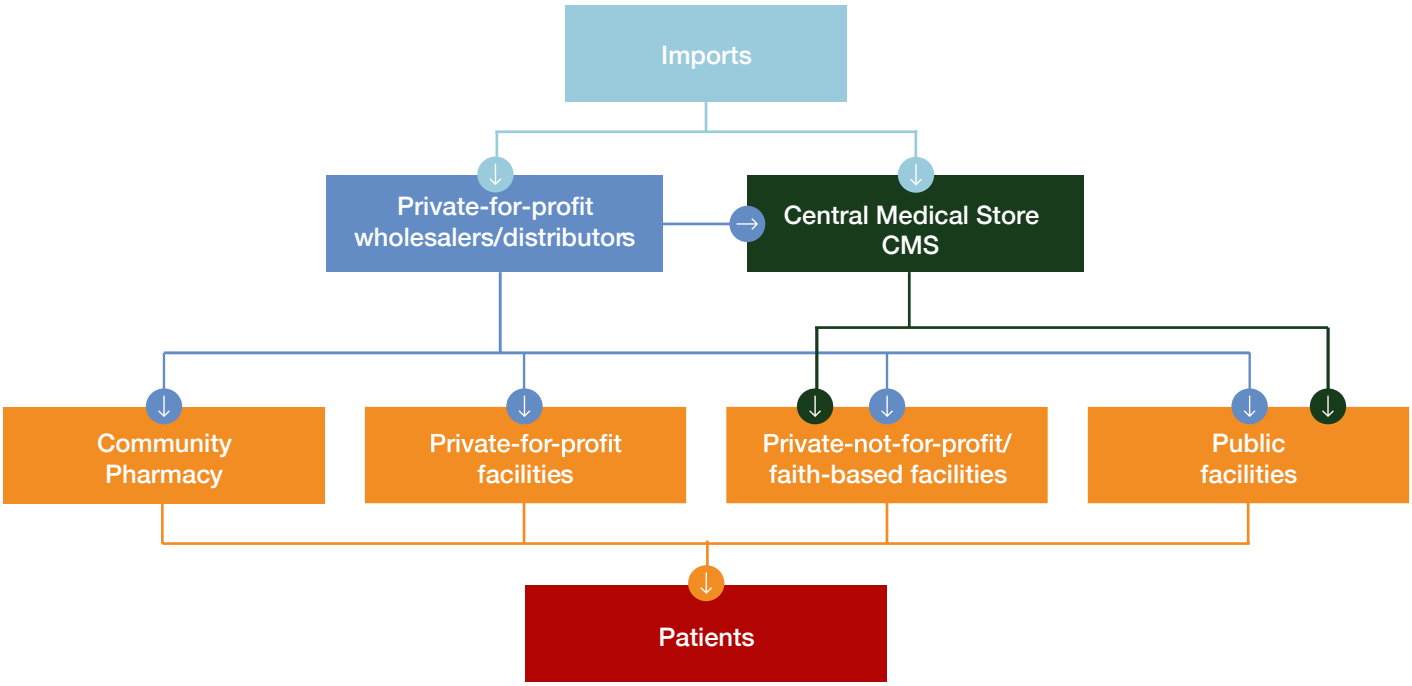
Figure 15: Flow chart explains the data checks procedures and validation process for the national and pharmacy level AMC data collected in Eswatini

Results

Flow of antimicrobials in the country

To characterise the pathway through which antimicrobials get to patients in the country, a total of three KIIs were conducted with stakeholders in the national AMRCC, the Office of the Deputy Director for Pharmaceutical Services (ODDPS) and the CMS. ODDPS controls all imports of medicines, including antimicrobials, into Eswatini and each importer must first obtain an import permit before medicines are allowed into the country. Additionally, ODDPS governs the medicines regulation as well as acts as the pharmaceutical licensing agency of the country.

There were no local medicine manufacturers in the country during the reviewed period (i.e., 2016-2018). Therefore, all medicines including the antimicrobials, are purchased by the public-sector facilities through imports which are managed by the CMS while the private sector facilities purchase imported medicines mainly through the private for-profit wholesalers or distributors. Following purchase, private for-profit wholesalers or distributors and the national CMS then pass along the antimicrobials to the community pharmacies, private (both for-profit and non-profit) facilities and public facilities who eventually issue the antimicrobials to patients. The flow chart below (Figure 16) illustrates the route through which antimicrobials get to the patients in Eswatini.



*JMS: Joint Mecial Store; **NMS: National Medical Store

Figure 16: Flow chart explaining the circulation of antimicrobials within the country to the patients in Eswatini. A dotted line indicates supplies are not mainstream

Regulation of antimicrobials consumption

In Eswatini, antimicrobials for human consumption are regulated by the Medicine and Related Substances Control Act, 2016, which also reviews the registration of suppliers of antimicrobials and other medicines for human consumption.[11] This law stipulates that requisite antimicrobials can only be sourced from registered suppliers and dispensed upon issuance of a valid prescription. The overuse and misuse of antimicrobials are significant contributors towards the emergence of AMR. Therefore, to address the above issues and other prevalent gaps, Eswatini developed a National AMR Containment Strategic Plan (2018-2022) that seeks to further build regulations around AMC to curb the growth or emergence of AMR.

Availability of data for AMU surveillance

Attempts were made to obtain AMU data from the participating pharmacies that were co-located in the AST laboratories that also offered clinical services (n=11). No AMU data were obtained during MAAP data collection. The inability to collect AMU data was due to the nature of the data sources at the participating pharmacies (i.e., stock issuance record cards), which did not allow for retrieval of AMU variables (i.e., patient characteristics and indication for which the antimicrobial is being used, appropriateness of prescription in relation to national guidelines including conducting of any relevant laboratory testing and clinical assessment done prior to prescribing, assessment of dose, strength, frequency and duration of prescription) as stock issuance records do not track specific patients and the medicines they received. As a result, MAAP was unable to collect AMU data in Eswatini from the selected health facilities.

Availability of data for AMC surveillance

National-level data

National AMC data were obtained from the CMS for the years 2016 to 2018. The resultant national AMC data that was collected and analysed represented approximately 90% of the total antimicrobials consumed in public health facilities during the reviewed period (2016-2018). However, due to a lack of participation by the private sector, the national-level analysis excludes private sector representation. The CMS data (national level) had all the variables required to conduct AMC analysis (including date of transaction, antibiotic name, pack size, strength and formulation (e.g., tablets or capsules, suspensions or syrups and injections). MAAP was able to collect CMS data from January 2016 – December 2018 as planned within the scope of the study.

Facility-level data

Pharmacy data collection was successfully conducted in 18 pharmacies out of 32 targeted pharmacies including hospital pharmacies (n=11) and community pharmacies (n=7). A total of 12 AST laboratories were recruited for data collection, however, one was a stand-alone national microbiology reference laboratory i.e., without a co-located hospital pharmacy. Therefore, for (n=1) this stand-alone laboratory, we were unable to adhere to the protocol and the subsequent enrolment of a community pharmacy (n=1). Of the participating hospital pharmacies (n=11) that were co-located with the AST laboratories, nine were in public government hospitals. The remaining recruited pharmacies (n=7) were stand-alone community pharmacies. Additional targeted community pharmacies (n=9) declined to share their AMC data for the reviewed years (2016-2018) and were therefore excluded from the data collection. As the total number of hospital or community pharmacies in Uganda could not be established, data representativeness at facility level could not be assessed.

In the case of pharmacy-level data, necessary variables were available in stock cards or electronic records of 18 pharmacies where the data was collected. However, there were instances in each of the visited facilities wherein strength or pack size information for few line items or transactions were missing from the stock cards. These information gaps were addressed by re-visiting the facilities and gathering information from the facility staff or through secondary desk research using the available product details. Of the 11 hospital pharmacies, MAAP was able to collect data across the three years in 10 pharmacies. Only one participating hospital pharmacy did not have archived data for the 2016-2017 period. The remaining seven recruited community pharmacies did not provide data for the years 2016-2017 as they either declined to share their data or did not have archived data between 2016-2017 in their systems.

Due to the lack of any national AMC surveillance policy or structured AMC surveillance system during the reviewed period, none of the recruited pharmacies actively reported AMC data regionally or centrally. Table 11 below summarises the core characteristics of the hospital pharmacies from which AMC data was collected.

Table 11: Characteristics of the recruited hospital pharmacies adjoined with the antimicrobial susceptibility testing (AST) laboratories in Eswatini

	Pharmacy Name	Level of Service#	Affiliation	Region	Record keeping*	Pharmacy system directly linked to patient records *†	AMC reporting*
Hospital Pharmacies (co-located with AST laboratories) ~	Dvokolwako Health Centre	Secondary	Public	Manzini	Manual	No	No
	Emkhuzweni Health Centre	Secondary	Public	Hhohho	Manual	No	No
	Good Shepherd Hospital	Tertiary	Private, faith based	Lubombo	Manual	No	No
	Hlatikhulu Government Hospital	Tertiary	Public	Shiselweni	Manual	No	No
	Mankayane Government Hospital	Tertiary	Public	Manzini	Manual	No	No
	Matsanjeni Health Centre	Secondary	Public	Shiselweni	Manual	No	No
	Mbabane Government Hospital	Tertiary	Public	Hhohho	Manual	No	No
	Nhlangano Health	Regional referral	Public	Kabarole/ Western region	Manual	No	No
	Piggs Peak Hospital	Tertiary	Public	Hhohho	Manual	No	No
	RFM Hospital	Tertiary	Private/Faith Based	Manzini	Manual	No	No
	Sithobela Health Centre	Secondary	Public	Lubombo	Manual	No	No
Community pharmacies~	Clicks Pharmacy Ezulwini	Dispensing	Private	Hhohho	Electronic	N/A	No
	Clicks Pharmacy Manzini	Dispensing	Private	Manzini	Electronic	N/A	No
	Clicks Pharmacy Mbabane	Dispensing	Private	Hhohho	Electronic	N/A	No
	LinkMed Pharmacy Matsapha	Dispensing	Private	Manzini	Electronic	N/A	No
	LinkMed Pharmacy Mbabane	Dispensing	Private	Hhohho	Electronic	N/A	No
	LinkMed Pharmacy Riverstone Mall Manzini	Dispensing	Private	Manzini	Electronic	N/A	No
	LinkMed Spar Manzini	Dispensing	Private	Manzini	Electronic	N/A	No

*For the review period i.e. 2018. AMC: Antimicrobial consumption.

† Refers to ability for pharmacy to link dispensing records with the patient's hospital records to obtain patient diagnostic and characteristic information.

#Secondary care services are delivered at government district and private hospitals and provide primary care services for the local population along with outpatient (for patient refereed from peripheral health units) and inpatient services i.e. admission facilities, diagnostic services, management of accident and emergencies. Tertiary care services are delivered at government regional level and at some private hospital and are involved in specialist surgeries such as internal medicine, obstetrics and gynaecology and paediatrics.

Section III: AMC or AMU analysis trends over time at national and pharmacy levels

Objective

To quantify and evaluate the trends of AMC and AMU at national and pharmacy level

Methodology

Statistical analysis

Data analysis for MAAP was conducted according to WHO's protocol for conducting AMC analysis using the DDD-ATC-AwaRe methodology.[30,31] Figure 17 provides a high-level summary of the AMC analysis that was conducted. Each of these WHO methodologies are described below as well as the additional analysis conducted. In addition, and where possible, associations were drawn between AMC and AMR. Details of this analysis can be found in Part C.

i. Defined Daily Dose (DDD)

DDDs or related metrics are utilised to study AMC analysis. Considering different doses (in milligram) for each antibiotic for managing infections, the DDD metric helps in standardizing for easy comparison. Additionally, it is recommended to use drug utilisation figures such as DDD using a relevant denominator for the health context e.g., DDDs/1000 inhabitants/day, DDD/ inhabitant/year or as DDDs/100 bed days. Studying DDDs or associated metrics over time helps to understand the consumption pattern or determine whether any national- or facility-level interventions have led to change (+/-) in the consumption patterns over the study period or pre-defined base period.

Using WHO 2020 DDD guide, the total DDDs were the quotient of the total consumed milligrams per antimicrobial divided by the standard DDD value issued by WHO.[32] The total DDDs were then adjusted for the country population size in the year of data collection, 2016-2018,[33] and presented as DDDs/1000 inhabitants/day (DID). Pharmacy-level AMC data were to be adjusted as DDD per the number of inpatients and presented as DDD/100 patient bed days. However, the use of WHO DDD per 100 patient bed days presented limitations at the point of analysis as patient bed days were not an appropriate denominator to use across the pharmacy-level AMC datasets. In addition, for most of the hospital facilities, patient bed days and patient days information was not easily accessible. Secondly, this metric would not allow for comparison between hospital pharmacy consumption and community pharmacy consumption, as in the latter, the patient bed days metric is not applicable. Therefore, the pharmacy-level AMC data is presented as absolute DDD to aid comparison between the hospital and community pharmacies. Detailed DDD calculations can be found in Appendix 7. All calculations were conducted in Excel ™.

ii. Anatomic Therapeutic Chemical (ATC) Classification

Using the standard list of antimicrobial names, data collected was coded in the Excel analysis database in accordance with the 2020 WHO ATC codes and then analysed to characterise the macro (above-molecule) AMC trends. The description of ATC codes is presented in AMC Appendix 7. Furthermore, an attempt was made to conduct statistical testing to determine the year-on-year differences within each ATC class, however, this was not possible as some of the datasets were missing core components for analysis i.e., month of transaction.

iii. WHO Access, Watch and Reserve (AWaRe)

The WHO AwaRe categorisation classifies antibiotics under the Access, Watch, and Reserve groups. 'Access' group includes antibiotics of choice for the 25 most common infections and these should be affordable and available at all times as well as the quality assured in the country or facilities. 'Watch' includes antibiotics indicated for specific and limited infective syndromes (since they are prone to be a target of antibiotic resistance). Hence, their use is controlled through stewardship programmes and monitoring). Lastly, 'Reserve' antibiotics are considered as a "last resort" treatment option. They are indicated in case of life-threatening infections due to multi-drug resistance (closely monitored and prioritised in stewardship programmes to ensure their continued effectiveness).

Through WHO AwaRe analysis, the total AMC by DDDs per antibiotic molecule were labelled as either Access, Watch or Reserve in accordance with the 2019 WHO AwaRe list[34] in Excel. Total DDDs per each WHO AwaRe category were then analysed to determine the proportion of AMC per category and over time i.e., yearly and monthly (where possible). WHO recommends that at least 60% of a country's total AMC should come from the 'Access' category of antibiotics (threshold defined in WHO's 13th General Program of Work). Finally, an analysis was conducted to identify the top five antibiotics consumed in each WHO AwaRe category.

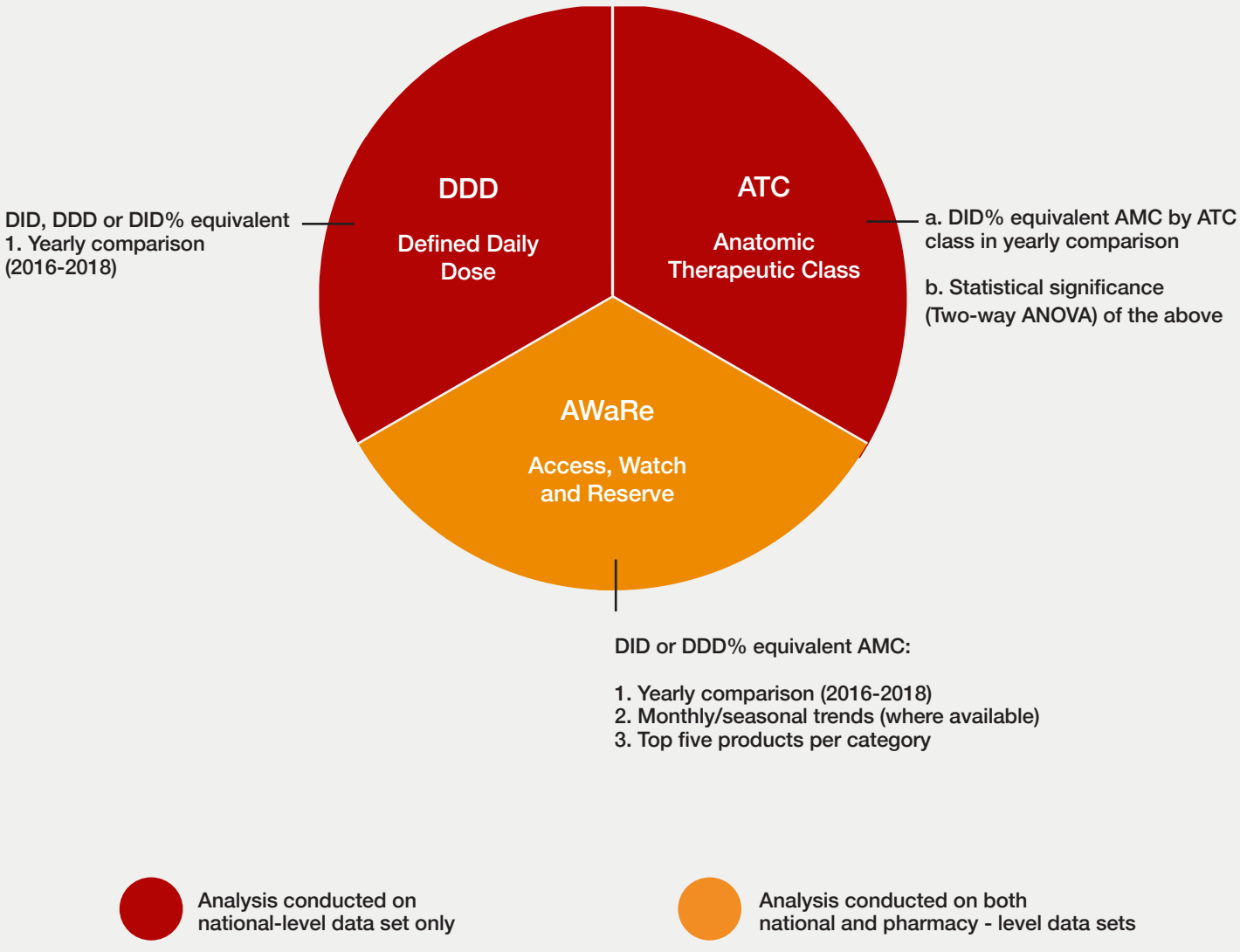


Figure 17: Methods and indicators used for the analysis of the data collected in Eswatini. Defined Daily Dose (DDD) indicators utilised for volume metric standardisation was sourced from WHOCC 2020, ATC Classification utilised to categorise the antibiotics according to the organ or system on which they act, and their therapeutic, pharmacological and chemical properties sourced from WHOCCC ATC database. The Access, Watch and Reserved categorisation was sourced from 2019 WHO AwaRe classification [34]

iv. Review of Essential Medicines List (EML)

According to WHO, essential medicines are those that satisfy the priority healthcare needs of a population. They are selected with regard to disease prevalence and public health relevance, evidence of efficacy and safety and comparative cost-effectiveness. They are intended to be always available in functioning health systems, in appropriate dosage forms, of assured quality and at prices individuals and health systems can afford. A document analysis was conducted in which the antimicrobials listed in the WHO EML were compared with the antimicrobials listed in the Eswatini EML and against the documented antimicrobials from the national- and pharmacy-level data collection. The comparison was conducted using WHO defined AwaRe categories.

Results

National AMC datasets analysed by DDD per year

The average total in-country AMC between 2016 and 2018 was 46.6 DDD per 1 000 inhabitants per day (DID). The total AMC noted in the country in 2016 was 17 DID, 21 DID in 2017 and 102 DID in 2018. The disparity between 2017 and 2018 AMC data consumption represented a notable increase of 391% (81 DID) which when further investigated, was largely attributable to the consumption of the sulfamethoxazole/trimethoprim combination (Figure 17). In order to determine the impact on annual AMC trends in the absence of this outlier, aggregated national-level data were represented without the consumption data of the sulfamethoxazole/trimethoprim combination. Following the outlier removal, overall, the results revealed a notable increase of 91% (17 DID) between 2016-2018 (Figure 18).

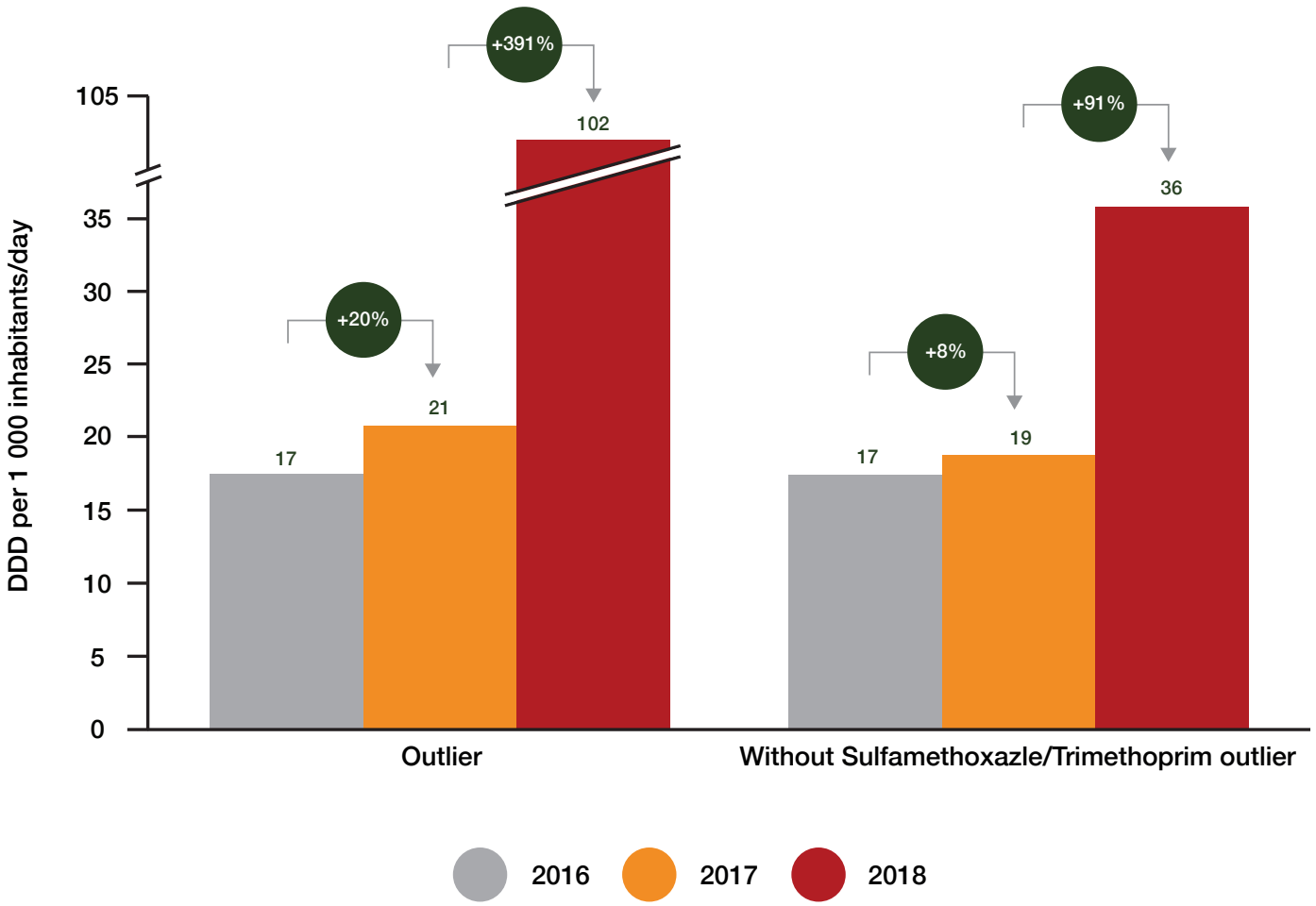


Figure 18: Bar graphs represents the total DID and percentage variation from the year 2016 to 2018 for the national level AMC data analysed in Eswatini. In the above figure the data represents with (left three bar graphs) and without (right three bar graphs) the consumption of sulfamethoxazole/trimethoprim combination from the years 2016 to 2018

National AMC analysed by ATC classification

The top five most consumed antimicrobials were sulfamethoxazole/trimethoprim, amoxicillin, doxycycline, metronidazole and erythromycin (Figure 19). Together, they accounted for 88% of the total consumption share. Combinations of sulfonamides and trimethoprim, including derivatives (J01EE), were the most frequently consumed ATC class overall in Eswatini across the review period at 0.0% in 2016, 9.8% in 2017 and 64.9% in 2018. The sulfamethoxazole/trimethoprim combination mostly accounted for the increase in consumption of antimicrobials between 2017 and 2018 (81.2 DID). However, penicillins with extended spectrum (J01CA) revealed a higher consumption when compared to combinations of sulfonamides and trimethoprim, including derivatives for the years 2016 at 32.1% and 2017 at 22.9%. Amoxicillin was the most frequently consumed antibiotic within this class. In addition, across the reviewed period, tetracyclines (J01AA) were the third-leading ATC classes overall, with doxycycline leading the consumption within these ATC classes. A detailed list of national AMC by antimicrobial molecule and by ATC class are mentioned in AMC Appendix 8 and Appendix 9, respectively.

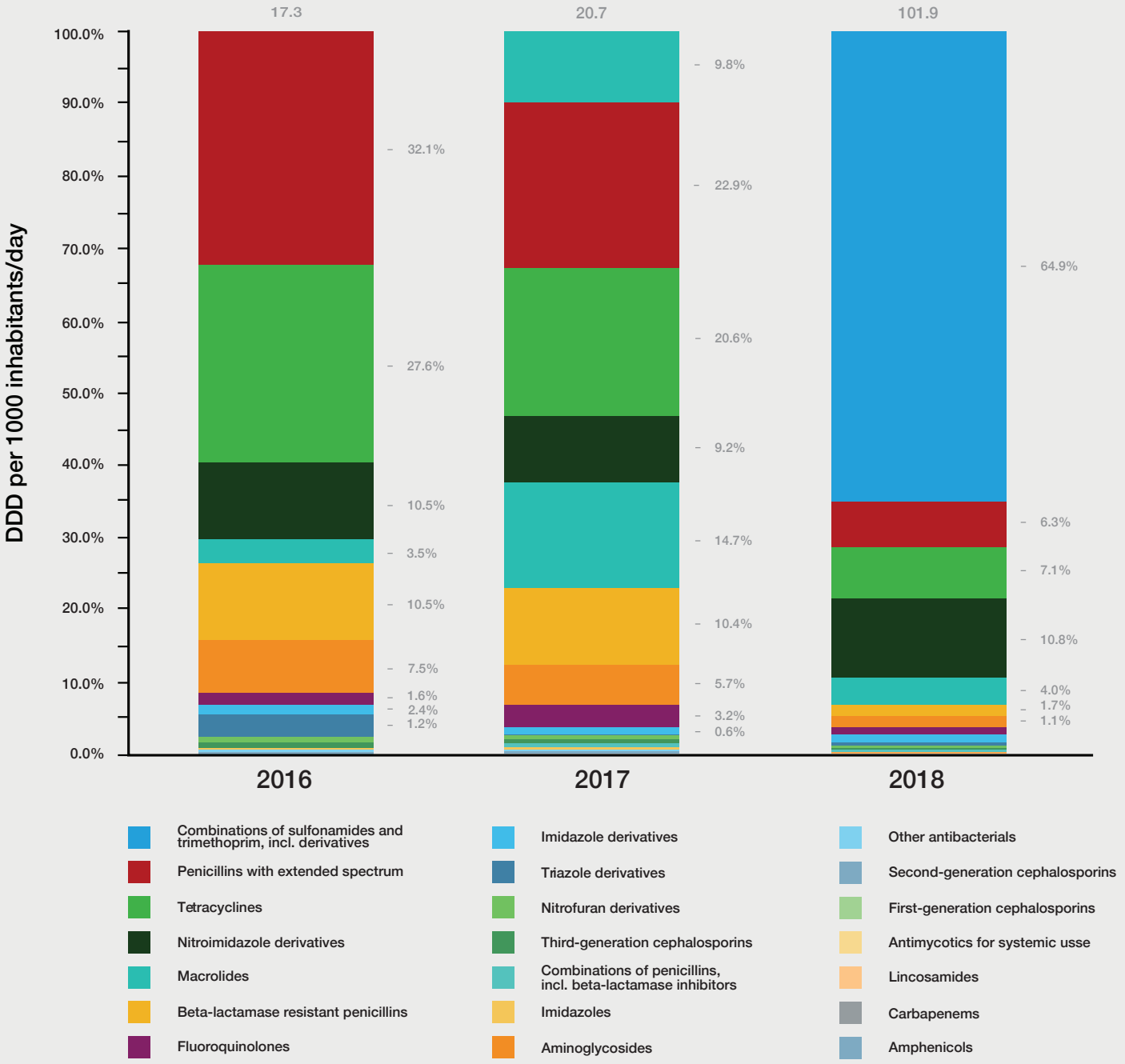


Figure 19: Results of national level AMC data analysed in Eswatini are presented by the total DID and percentage of antimicrobials consumed by ATC classes from the years 2016 to 2018. Combinations of sulfonamides and trimethoprim, including derivatives were the highest consumed antimicrobials overall. However, penicillins with extended spectrum class of molecules were the highest consumed antimicrobials in the year 2016 and 2017. Statistical testing was not carried out due to the nature of the data obtained. See Appendix 8 for a more detailed breakdown of AMC by ATC classes

National and pharmacy AMC analysed by WHO AwaRe categorization

The average national consumption of antibiotics across the three years analysed was 86.8% 'Access', 13.2% 'Watch' and <0.1% 'Reserve'. Annual AMC trends indicated an increase of 8.8% in consumption share of 'Access' antibiotics between 2016 and 2017 and a further increase of 7.2% between 2017 and 2018. This is against a corresponding proportional decrease 8.7% in consumption share of 'Watch' antibiotics between 2016 and 2017 that was followed by a decrease of 7.3% between 2017 and 2018 (Figure 18). Both overall (for three years) and within-each-year consumption of 'Access' category antibiotics in Eswatini well exceeded the 60% minimum consumption threshold set by WHO. The below analysis depicting WHO AwaRe proportions of antibiotics consumed, omits 4.2% (0.9 DID) of the total AMC that is not categorised within the WHO AwaRe classification list of 2019.

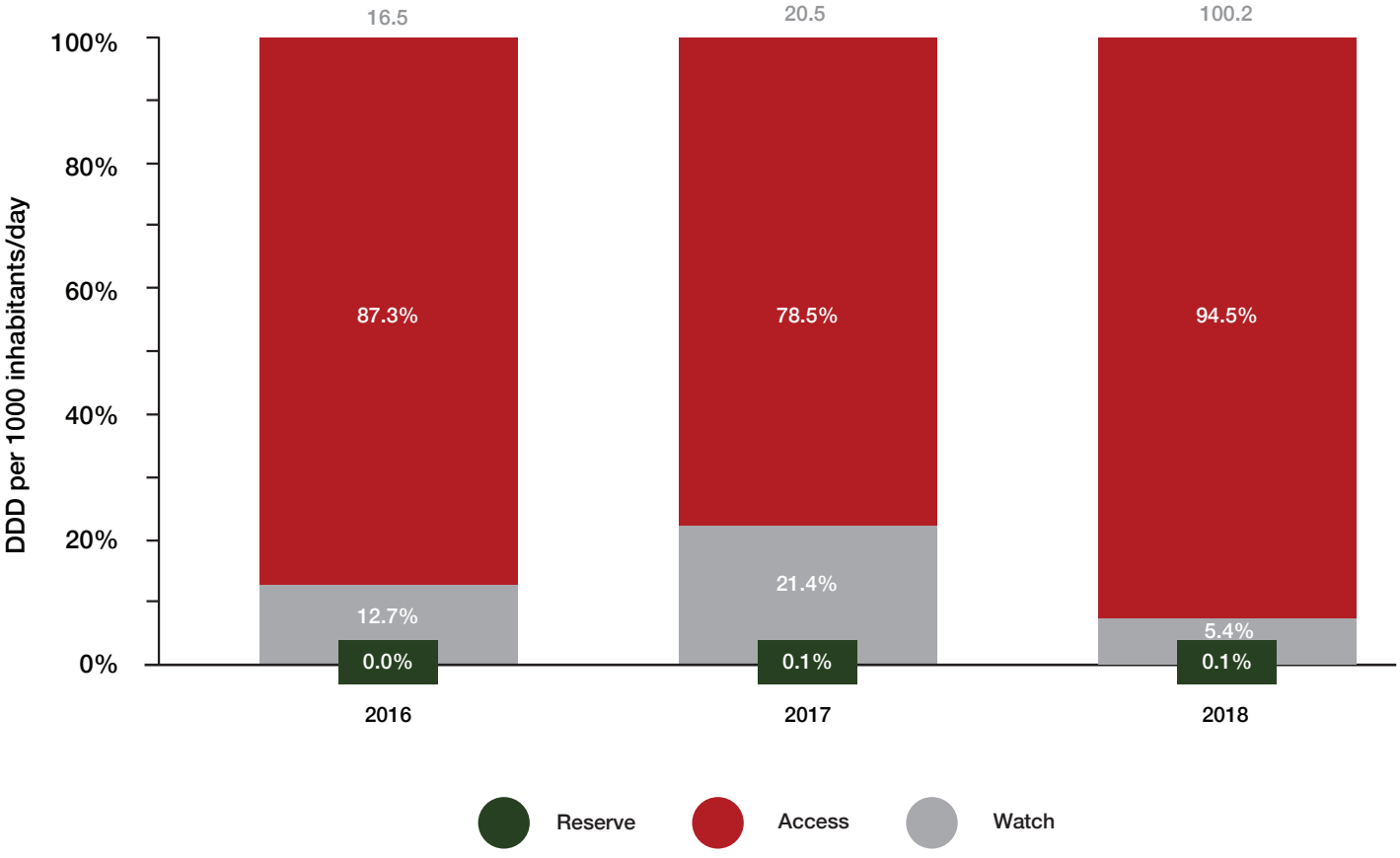
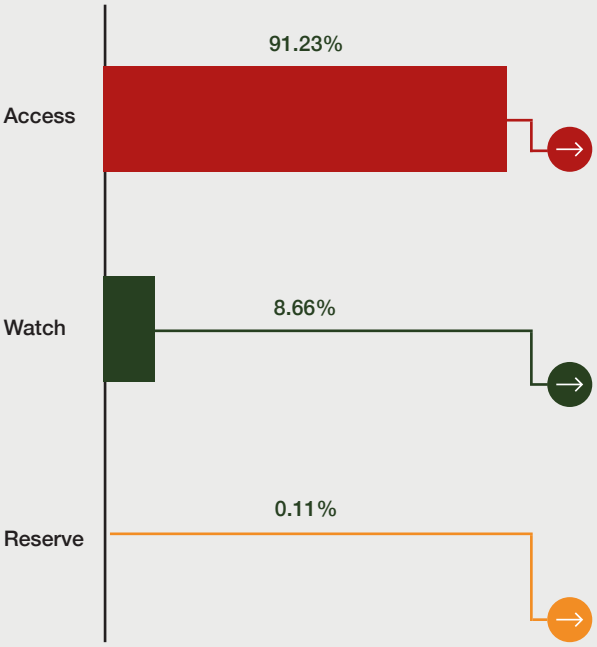


Figure 20: Results for the AMC data analysed in Eswatini are presented by the total DID and percentage of antibiotics consumed by WHO AwaRe categories from the years 2016 to 2018. Also, it shows the percentage change in consumption share of Access and Watch category antibiotics from the years 2016 to 2018

Further analysis was conducted to identify the most frequently consumed antibiotics nationally, within each WHO AwaRe category (Figure 21). In the 'Access' category, the top five most frequently consumed antibiotics accounted for 96.3% of all AMC within this group (Figure 19). In the 'Watch' category, however, the top five consumed antibiotics accounted for 96.9% of all the consumption within this group. Lastly, national consumption was only recorded for one antibiotic, Linezolid, within the 'Reserve' category.



Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Sulfamethoazole/Trimethoprim	54.4%	22.7
Amoxicillin	13.4%	5.6
Doxycycline	13.0%	5.4
Metronidazole	12.0%	5.0
Phenoxymethylpenicillin	3.5%	1.4

Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Erythromycin	62.4%	2.5
Levofloxacin	14.8%	0.6
Ciprofloxacin	14.6%	0.6
Ceftriaxone	3.3%	0.1
Clarithromycin	1.8%	0.1

Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Linezolid	100%	<0.1

Figure 21: Breakdown of the Access, Watch and Reserve categories of antibiotics consumed at the national level by percentage and total DID from the years 2016 to 2018 in Eswatini. It also shows, the top five consumed antibiotics in their respective categories

Aggregated pharmacy-level data was analysed from the (n=18) participating pharmacies and examined by the type of pharmacy (hospital against community pharmacies), the hospital service level (secondary care against tertiary care) and by their proportional consumption of WHO AwaRe category antibiotics. Here, hospital pharmacies (both public and private or faith-based) far exceeded the WHO threshold of 60% consumption of antibiotics represented within the 'Access' category at 94.6%. In contrast, community pharmacies failed to meet this minimum WHO Access category threshold and were observed to only have consumed 38.4% of total medicines from this category.

Further analysis was made to identify the reasons for the relatively high overall consumption of 'Access' antibiotics within the recruited pharmacies. The analysis revealed that (n=11) public hospital pharmacies recorded high consumption of the sulfamethoxazole/trimethoprim combination (accounting for up to 90% of the 'Access' group consumption). The high proportion of sulfamethoxazole or trimethoprim contributed to skewing the data towards the 'Access' category and rendered observations of consumption of other antibiotics difficult to interpret. Therefore, to ensure a clearer representation of consumption of other 'Access' antibiotics, consumption data of sulfamethoxazole or trimethoprim was excluded. Following this exclusion, hospital pharmacies (both public and private or faith-based) still maintained an average consumption of greater than 60% for the 'Access' category antibiotics consumption at 79.6% (Table 12).

There was no significant change for the community pharmacies in the consumption of sulfamethoxazole or trimethoprim. Community pharmacies consumed considerably more (43%) 'Watch' category antibiotics compared to hospital pharmacies. Within the hospital-based pharmacies, of which (n=11) met the WHO threshold, both the secondary and tertiary care facilities consumed almost a similar amount of 'Access' category antibiotics while within the community pharmacies, there were (n=4) pharmacies which failed to meet the minimum threshold of consuming >60% 'Access' category antibiotics. 'Reserve' category antibiotics (n=1) consumption was only recorded within the (n=5) public hospital pharmacies (among which two were secondary care facilities, (n=3) were in tertiary care facilities) and just (n=1) private or faith-based hospital pharmacy (located within a tertiary care facility).

Table 12: Percentage share in the consumption of antibiotics by WHO AwaRe categories for the recruited hospital and community pharmacies (public and private/faith-based) for the reviewed year (2018) in Eswatini. Also presents the consumption excluding outlier sulfamethoxazole or trimethoprim

	AWaRe Categorisation		
	Access	Watch	Reserve
Pharmacy Type	Percentage share	(Absolute DDD)	
Community pharmacies (7/18)	38.4% (48 705)	61.6% (78 115)	0.0% (0)
Hospital pharmacies (11/18)	94.6% (216 654 03)	5.4% (122 60 43)	<0.1% (4140)
Public hospital pharmacies (9/11)	95.3% (173 780 96)	4.7% (86 39 13)	<0.1% (3245)
Secondary care hospitals (5/11)	94.3% (835 442 5)	5.7% (50 17 75)	<0.1% (1280)
Tertiary care hospitals (4/11)	96.1% (902 367 0)	3.9% (36 21 38)	<0.1% (1965)
Private faith-based hospital pharmacies (2/11)	92.2% (428 730 7)	7.8% (36 21 30)	<0.1% (895)
Grand Total	94.3% (217 141 07)	5.7% (130 415 7)	<0.1% (4 140)
Excluding sulfamethoxazole or trimethoprim			
Community pharmacies (7/18)	36.6% (45,109)	63.4% (78,115)	0.0% (0)
Hospital pharmacies (11/18)	79.6% (478,449,9)	20.4% (122,604,3)	<0.1% (4140)
Public hospital pharmacies (9/11)	80.9% (369,283,9)	19.0% (86,39,13)	<0.1% (3245)
Secondary care hospitals (5/11)	77.5% (173,471,3)	22.4% (50,17,76)	<0.1% (1280)
Tertiary care hospitals (4/11)	84.3% (195,812,7)	15.6% (36,21,38)	<0.1% (1965)
Private faith-based hospital pharmacy (2/11)	75.0% (109,165,9)	24.9% (36,21,30)	<0.1% (895)
Grand Total	78.7% (482,960,8)	21.3% (130,415,8)	<0.1% (4140)

Comparison of the WHO EML and Eswatini EML with documented antibiotics by WHO AwaRe categorisation

The WHO EML includes 39 antibiotics across the AwaRe categories. A total of 60 antibiotics were documented during national- and pharmacy-level data collection. Figure 22 shows the number of antibiotics in the WHO and Eswatini EMLs for each AwaRe category, thereby indicating whether the antibiotic was documented during data collection.

It was determined that two antibiotics in the 'Access' category, three in the 'Watch' category and one in the 'Reserve' category are listed in the WHO EML and were documented during data collection although they are not part of the Eswatini EML. In addition, one 'Access' category, one 'Watch' category and seven 'Reserve' category antibiotics are part of the WHO EML, yet they are not listed in the Eswatini EML nor were documented during data collection. For each AwaRe category, including the uncategorised, antibiotics which are neither part of the WHO or Eswatini EMLs were documented during data collection. The detailed breakdown of antibiotics documented and their inclusion in the WHO and Eswatini EMLs is provided in AMC Appendix 10.

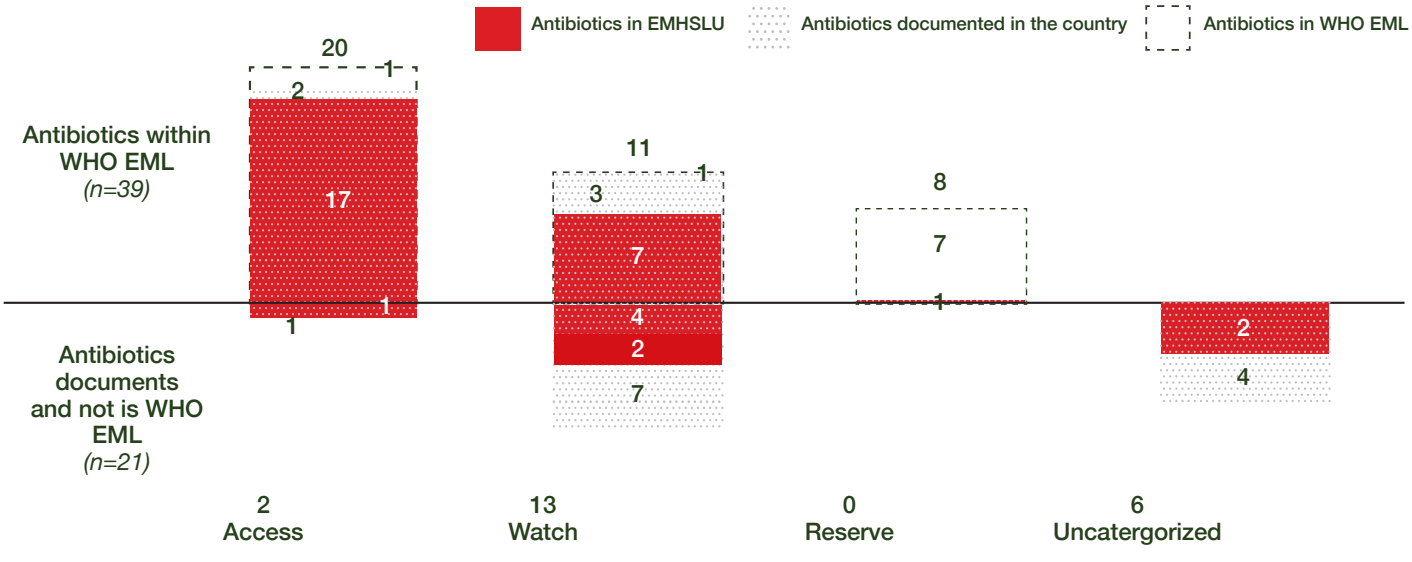
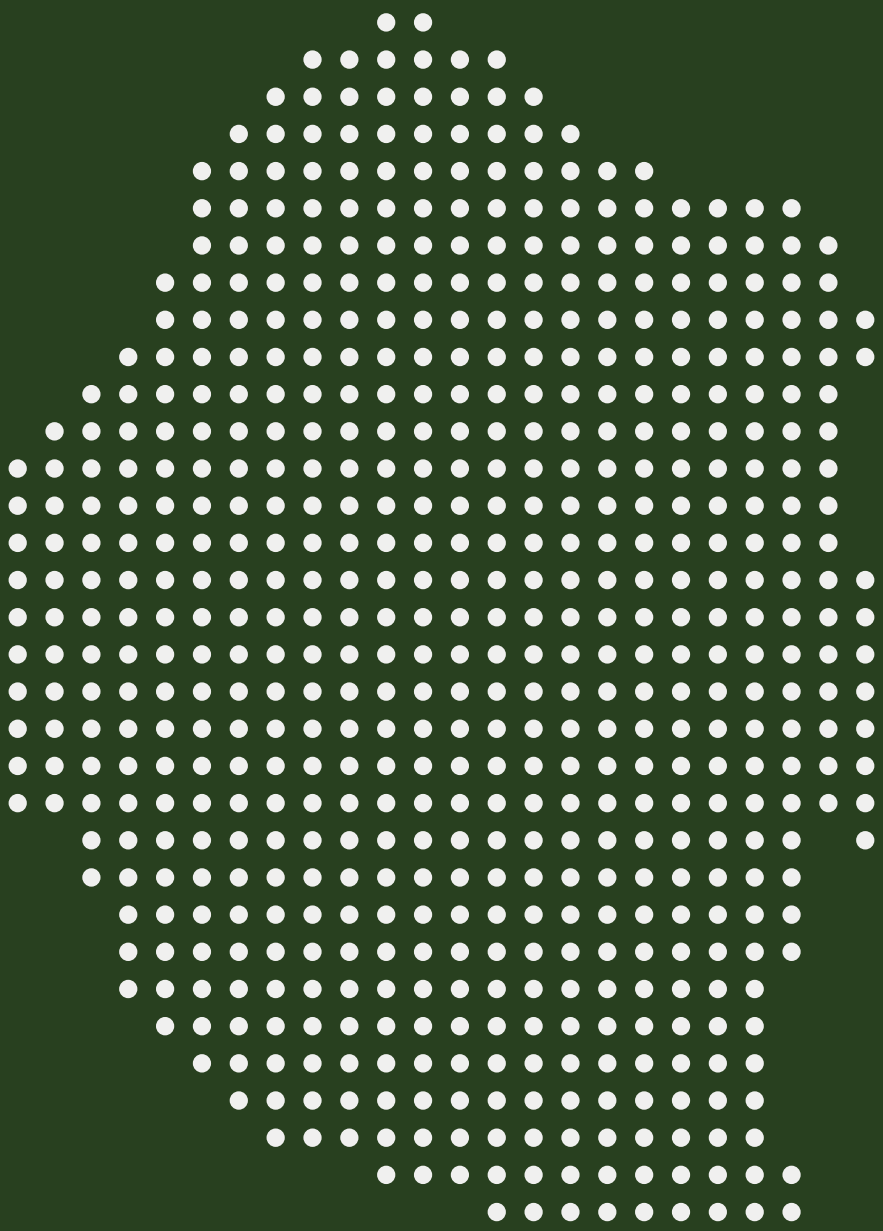


Figure 22: AwaRe analysis of documented antibiotics in national- and pharmacy-level data for the years 2016 to 2018 compared to WHO and Eswatini EML definitions

Part C: Resistance and Consumption Interlinkages



Objective

To assess the relationship between antimicrobial consumption and antimicrobial resistance

Methodology

The DRI was estimated to convey aggregate rates of resistance as well as measurements of AMC (at a national level since AMU data were not available) across select pathogen-antimicrobial combinations (Pathogens: A. baumannii, E. coli, K. pneumoniae, P. aeruginosa, S. aureus, E. faecium and E. faecalis; Antibiotics: aminoglycosides, broad-spectrum penicillins, carbapenems, cephalosporins, glycopeptides, narrow-spectrum penicillins and quinolones). The DRI estimates were generated using a previously published methodology[35,36](AMR Appendix 8) and help communicate the effectiveness of antibiotic therapy to decision makers. DRI values range from 0 (100% susceptibility) to 100 (100% resistance). Available AST results for at least 30 tested isolates and for at least 15 of the 25 combinations were prerequisites for the estimation of the DRI. To generate CIs for the DRI as the variance of the product of variables, the variance of the proportions of non-susceptible isolates was combined with a uniform standard deviation based on the estimated DDD.[37,39]

Apart from the DRI, correlation between AMC and AMR was conducted. Data on AMC were obtained from facilities and based on the total DDD over the entire study period. The AMC of a particular antimicrobial class was correlated with a composite resistance rate (covering all pathogens tested against the same antimicrobial class, as reported by the laboratories). Pearson's correlation analysis was performed between the two variables (AMR rate [%] and total DDD). Antibiotic classes contributing less than 0.05% to the total antibiotics consumed were excluded from the analysis.

Based on previously described methodology, the resistance of all pathogens tested against most and least consumed antimicrobial classes, is reported by the laboratories and based on data availability, in each study year.

Results

Drug Resistance Index

The DRI estimate was found to be high at 64.8% (95% CI, 54.3-75.2%) implying low antibiotic effectiveness, which is a threat to effective infectious disease management and calls for urgent policy intervention (Figure 23).

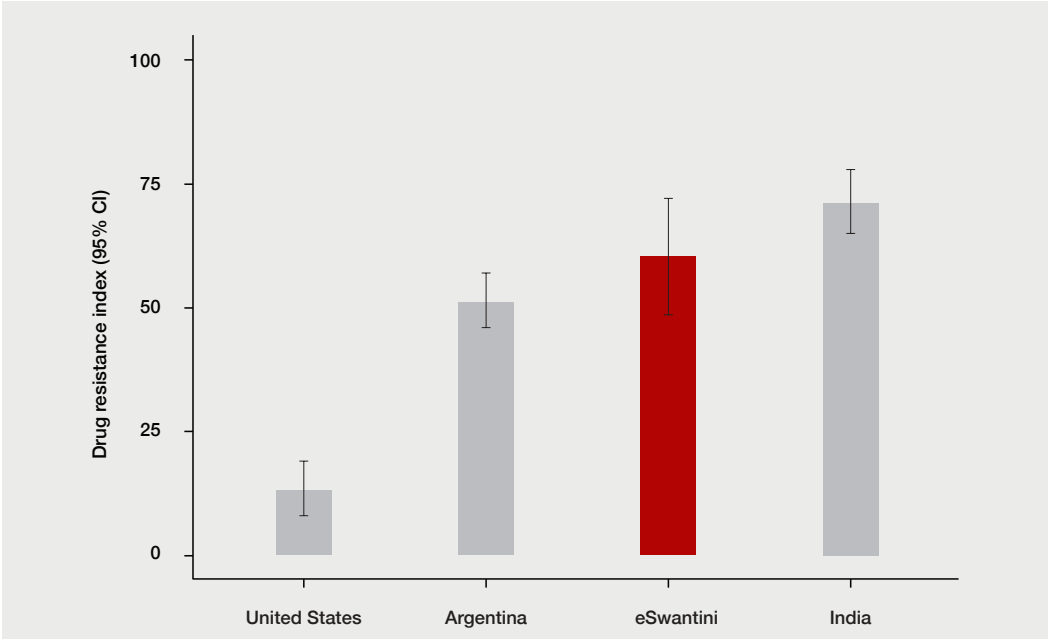


Figure 24: Drug Resistance Index

AMC and AMR correlation

The top three highly consumed antibiotic classes at facility level were macrolides, folate pathway inhibitors and aminopenicillins. The AMR rates were highest for penicillins (93.1%), aminopenicillins (73.4%) and folate pathway inhibitors (66.6%) (Table 13). Pearson's correlation analysis revealed a weak positive correlation (r2=0.04) between AMR and AMC, implying that antibiotic consumption is not a significant driver of AMR in Eswatini (Figure 24).

Table 13: AMC and AMR rates across antibiotic classes

Antibiotic class	Year	Total DDD in thousands	Resistance rate (%)
Macrolides	2016-18	99.15	51.4
Folate pathway inhibitors	2016-18	71.59	66.6
Aminopenicillins	2016-18	4.26	73.4
Tetracyclines	2016-18	3.35	49.7
Methicillin	2016-18	1.21	44.9
Fluoroquinolones	2016-18	1.18	30.6
Nitrofurans	2016-18	1.04	14.5
Penicillins	2016-18	0.3	93.1
Beta-lactam combinations	2016-18	0.41	36.1
Fluoroquinolones	2016-18	0.21	36.4

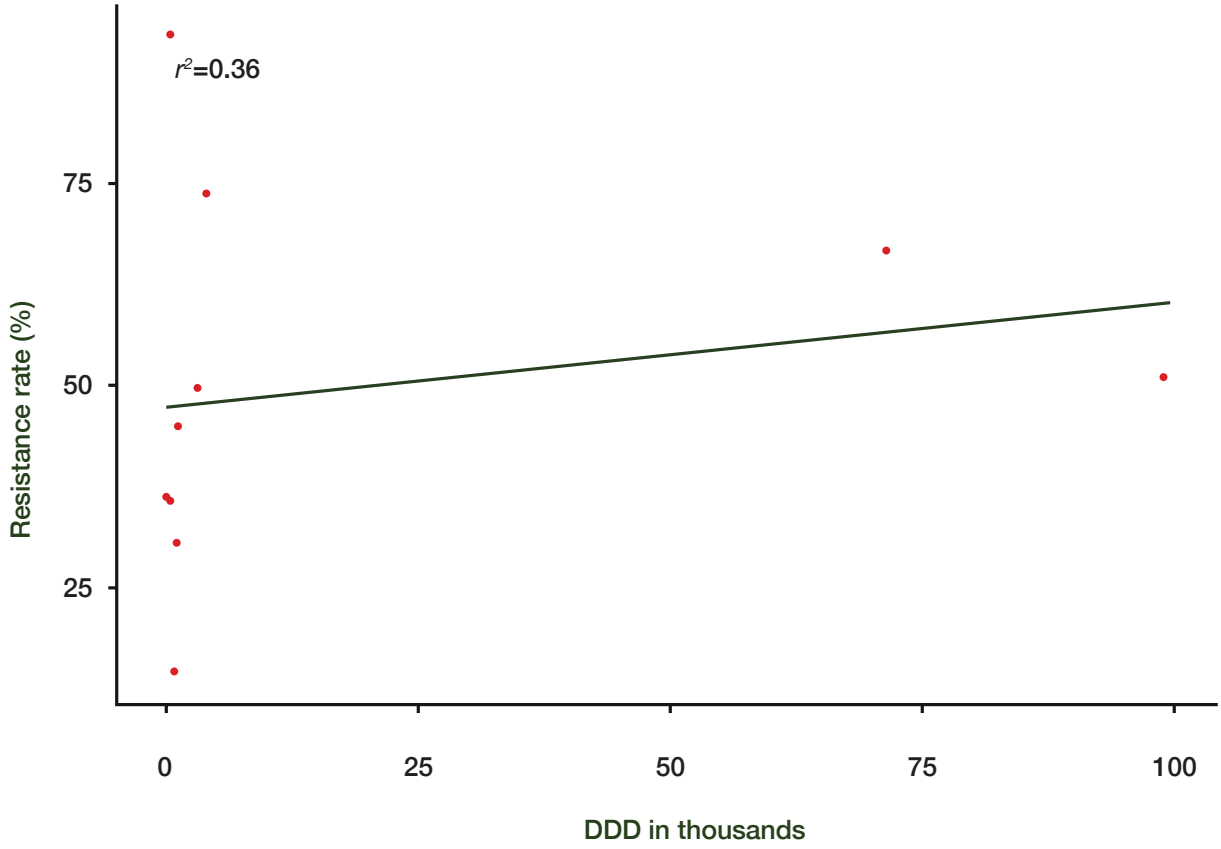


Figure 24: Correlation between AMR and AMC

Resistance profiles of most and least consumed antimicrobial classes

The most consumed antimicrobial classes across the study years were aminopenicilins, tetracyclines, macrolides and nitroimidazoles. In 2016, resistance rates were more than >75% for aminopenicillin-resistant Pseudomonas species, Klebsiella species and Escherichia species. In 2017, high resistance rates (>75%) were observed for aminopenicillin-resistant Pseudomonas species, Klebsiella species, Escherichia species and Staphylococcus species, macrolide-resistant Enterococcus species, tetracylcine-resistant Enterococus species and Escherichia species. In 2018, the highest resistance rates (>50%) were observed for folate pathway inhibitor-resistant Klebsiella species, Escherichia species, Proteus species, Serratia species and Staphylococcus species (Figure 23, 24 and 25).

The least consumed antimicrobial classes across the study years were cephalosporin (1st generation), lincosamides and polyenes. Although the consumption of these antimicrobial classes was low, high resistance rates were observed across many pathogen-antimicrobial class combinations. In 2016, resistance rates were more than >25% for cephalosporin- (1st-generation) resistant Escherichia species and lincosamide-resistant Staphylococcus species. In 2017, extremely high resistance (>90%) was observed in cephalosporin- (1st-generation) resistant Escherichia species. In 2018, resistance rates were more than >25% for lincosamide-resistant Staphylococcus species (Figures 25, 26 and 27).

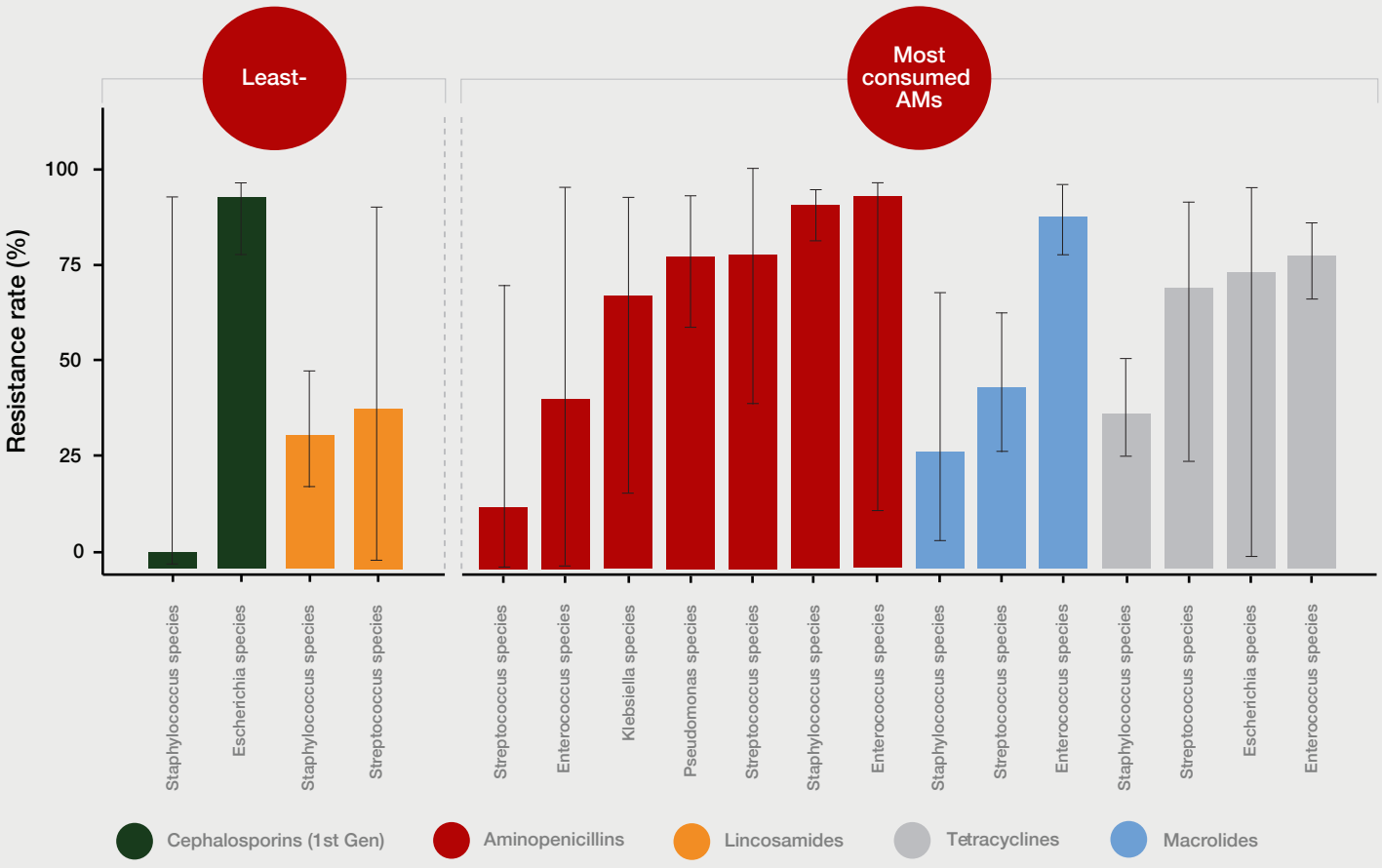


Figure 25: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2016

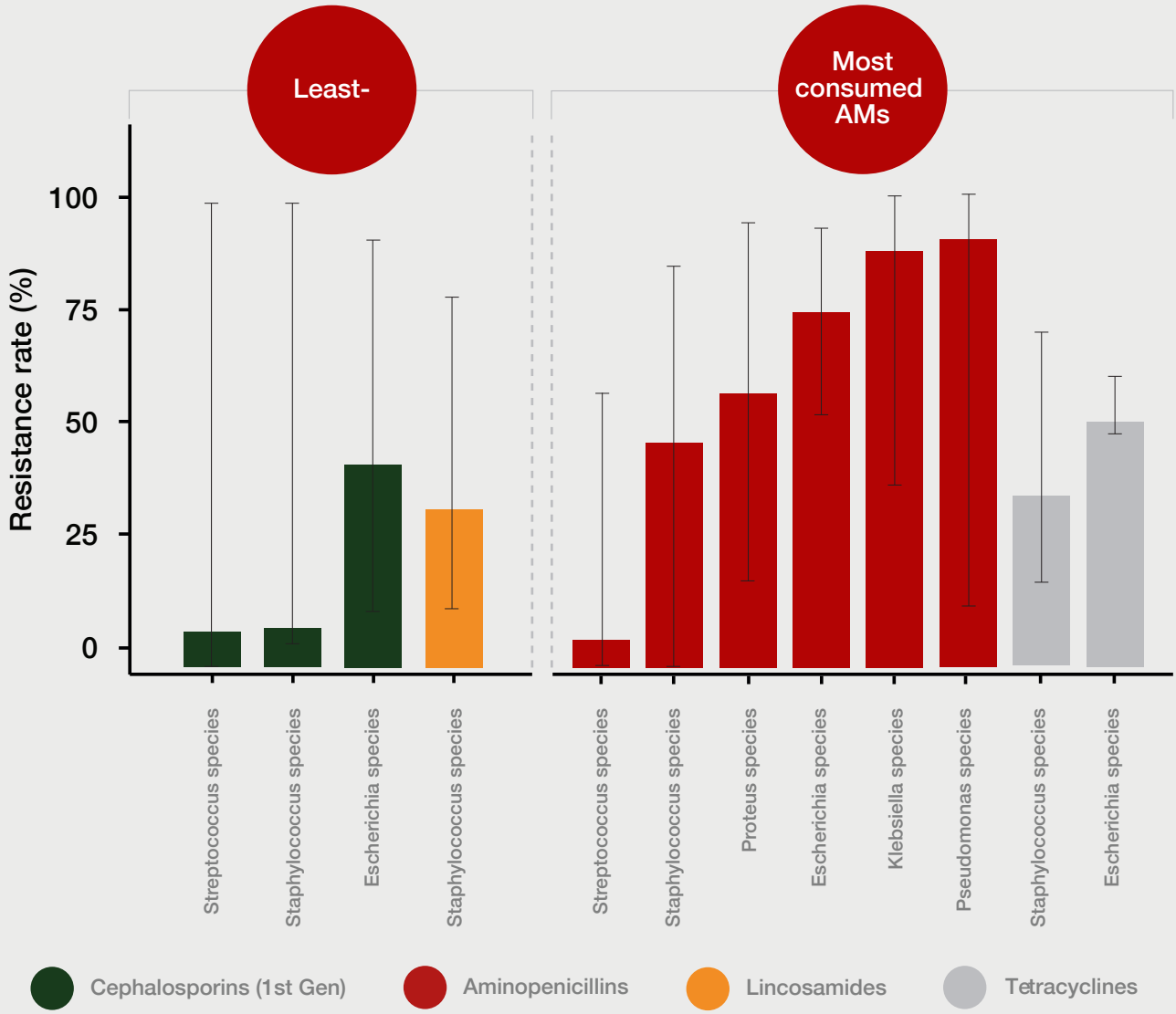


Figure 26: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2017

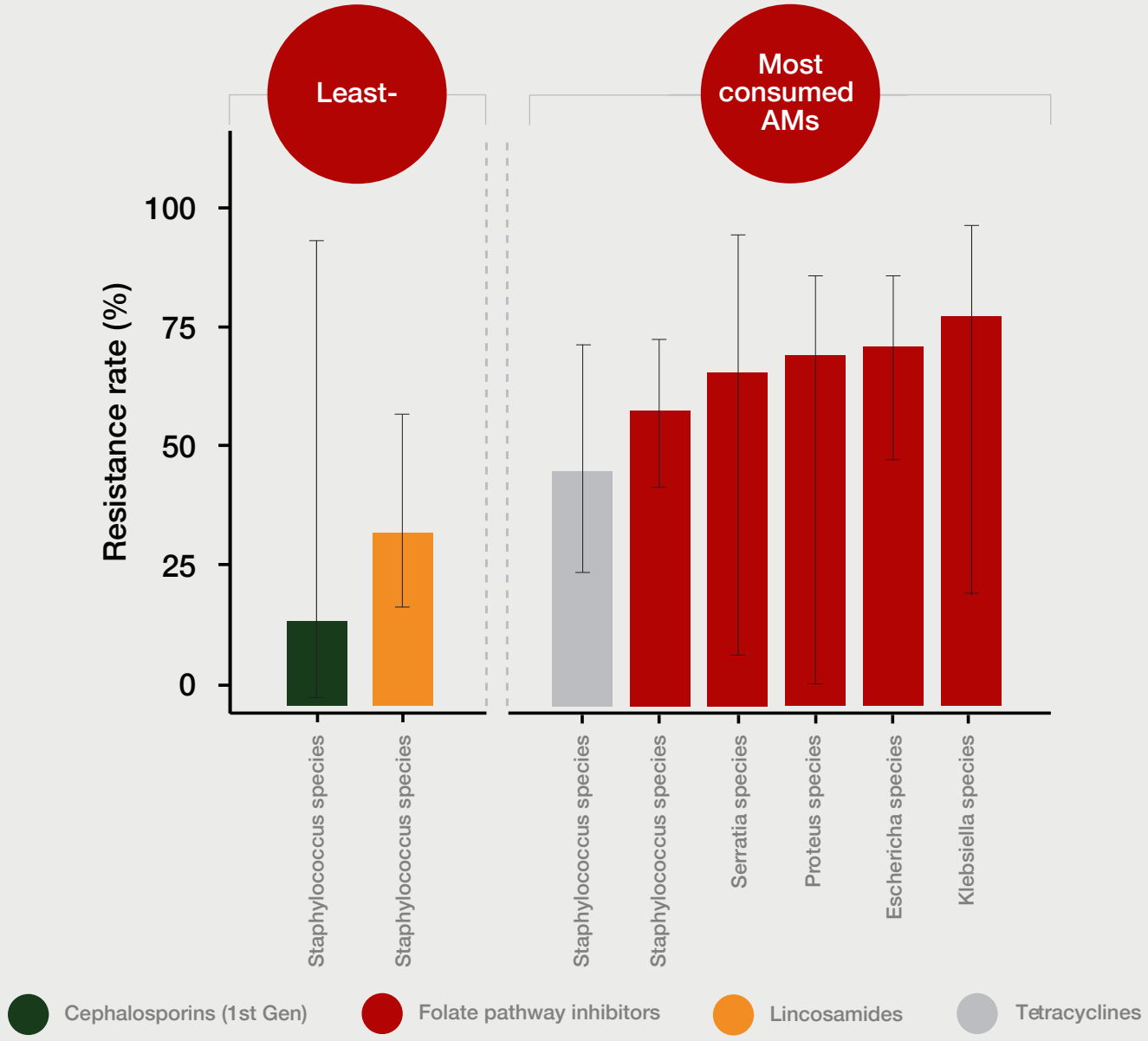
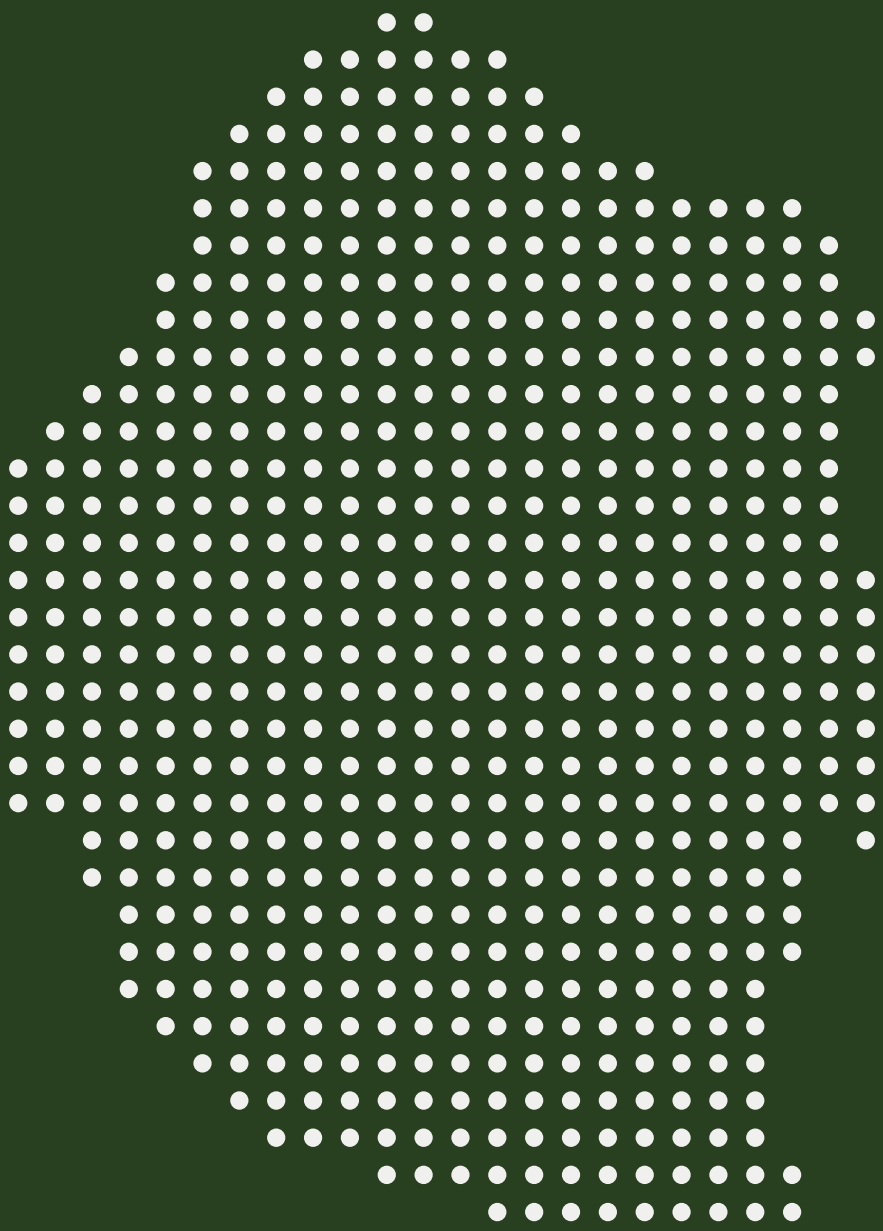


Figure 27: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2018

Part D: Recommendations



AMR is a major threat to medical advancements and has drawn global attention over the past few years and more so recently, due to the COVID-19 pandemic. Unfortunately, owing to inconsistent surveillance data, the AMR burden is not well quantified in most countries. A recent review reported nonavailability of AMR data for more than 40% of African countries and expressed concerns about the quality of the microbiology data that did exist.[39]

The mitigation of AMR calls for a multipronged approach including building resilient health and laboratory systems as well as improving ASP (diagnostic, antimicrobial use, and infection prevention). Based on our study findings, we propose the following recommendations to strengthen AMR surveillance in Eswatini.

Significance of AMR and DRI data and recommendations

Analysis of available AMR data from Eswatini revealed moderate to high levels of resistance for MRSA (21-58%) and 3rd-generation cephalosporin-resistant Enterobacterales (25-41%).

S. aureus (methicillin-resistant or sensitive) is a common cause of many skin and soft tissue infections (SSTI) in both community and healthcare settings. It can also cause invasive infections like endocarditis, osteomyelitis, pneumonia, visceral abscess, brain abscess, shunt infections and bacteraemia. Risk factors for MRSA infections include high prevalence, past infections/colonisation/close contact, trauma, invasive devices (catheters, shunts, implants and prosthesis), prior-antibiotic use, neutropenia, other underlying conditions, post-surgical status, dialysis and admission to long-term care facilities. While antimicrobial therapy and source control (drainage or catheter removal) are essential for the treatment modalities, it is as important to prevent and control the spread of MRSA infections. Use of catheters and invasive devices must be minimised, and stewardship principles practised (culture taken prior to initiating antibiotics and prompt de-escalation from empirical to targeted therapy). High-risk and pre-operative patients must be screened for MRSA carriage and decolonised. Patients and caregivers should be educated on the importance of handwashing and contact precautions.

Enterobacterales can be asymptomatic colonisers or result in community- and healthcare- associated infections (commonly affecting the urinary tract, bloodstream, lower respiratory tract and surgical sites). Various risk factors predispose to resistance against 3rd-generation cephalosporins and carbapenems. These risk factors are prior use of cephalosporins and/or carbapenems, indwelling catheters, mechanical ventilation, underlying comorbidities (such as diabetes, malignancy, severe illness etc.), injuries, transplantation etc. To limit the spread of resistant Enterobacterales, compliance to standard and contact precautions (including hand hygiene), minimal use of catheters and invasive devices, compliance to infection prevention bundles, and antimicrobial stewardship, is essential. Additionally, high-risk patients should be screened for rectal colonisation.

The estimated DRI for Eswatini was also high and indicates decreasing effectiveness of antimicrobials. Evidently, this calls for targeted interventions including improved stewardship and infection prevention as well as regulations on the use of high-end antibiotics. We observed that males and the elderly were prone to resistant infections, although further studies are necessary to establish an association.

Service delivery

During the initial stages of in-country work in Eswatini, three laboratories were mapped to the national laboratory network and were identified as bacteriological laboratories with AST capabilities. While all three laboratories reported implementing QMS, not all were accredited. Considering a country population of over 1.1 million, the laboratories did not equitably cover the country's population. The testing load (quantum of cultures) at most participating laboratories was found to be less and suggested the lack of routine microbiology testing. hence, this risks overestimating the AMR rates as the majority of tests would have been conducted on special patient categories (such as failure of first-line therapy or admission to intensive care).

To strengthen the delivery of services by the laboratories, we recommend that all laboratories are mapped across a range of indicators including population coverage, infectious disease burden, testing capabilities and quality compliance. This would inform decision makers on unmet needs and decide way forward for expansion of the laboratory network. A larger network also provides a richer sampling frame for better representation and generalisation of results.

Health workforce

As reported by the survey, all laboratories had an experienced laboratory scientist or technologist, up-to-date records on training and competence, and at least one qualified microbiologist. For high quality microbiology testing and reporting, staff training on laboratory standards, ability to identify common pathogens, and data management skills are essential.[40] Capacity-building of staff may be completed through in-house expertise or outsourced to external organisations or tertiary facilities.

Information systems

The Regional Grant was a step towards the collection and digitisation of data. We observed that most of the surveyed laboratories relied on electronic records but very few had linkages to patients' clinical records. In the current study involving three laboratories over a three-year period, susceptibility results could be collected for just 5 247 positive cultures. In order to strengthen AMR surveillance, it is essential to curate the right data and generate evidence. We recommend data collection through standardised formats at all levels (laboratories, clinics and pharmacies) as well as the use of automation for data analyses. For the current study, we used WHONET for data digitisation. Empirical guidelines for management of infectious diseases should be based on epidemiology specific to patient settings, and resistance data should be shared on national and supra-national platforms. We also recommend establishing a system of assigning permanent identification numbers for patient tracking over time. This would help to collect data on a patient's clinical profile, antimicrobial history as well as pathogen's molecular profile (where available), thus offering more context to the AMR epidemiology than stand-alone antimicrobial susceptibility data.

Medicines and technologies

While there are various determinants of patient care, the importance of quality diagnostics can never be undermined. Even though laboratory audit was not the scope of the current study, we noted instances of inappropriate testing and hence data unfit for analysis. Such results can be misleading and impact patient care.

In order to strengthen AMR surveillance, it is imperative to generate reliable laboratory results through appropriate testing methods, using authorised surrogates and ensuring an uninterrupted availability of reagents including antibiotics for susceptibility testing. Improving supply chains for essential reagents, should be a country priority and interruptions in routine testing must be minimal. Standardisation of testing methods across laboratories, can aid in this process as then the purchases can be pooled and coordinated by the MoH. All laboratories and testing centres must conform to AST quality standards and aim for accreditation and quality certification status.

Finally, we recommend increasing the community awareness on the importance of public health interventions (vaccinations, clean water, sanitation and hand hygiene) as well as compliance to physicians' medical advice. The strengthening of health and laboratory systems must be prioritised at national level and complemented with the right investment.

Significance of AMC and AMU data including recommendations

This section discusses the significance of our AMC and AMU findings and puts forth suggested recommendations for Eswatini to possibly consider in order to optimise the observed trends in consumption of antimicrobials and thus facilitate future surveillance activities.

Feasibility of obtaining AMC and AMU data in Eswatini and recommendations

MAAP successfully collected and analysed national and pharmacy-level AMC data for Eswatini. This implies that surveillance of AMC data is possible and that Eswatini can respond to WHO's call to participate in GLASS, which now has an AMC reporting component. However, the AMC data collected excluded the private-for-profit wholesalers or distributors as they were unwilling to share their data. MAAP was unable to quantify this gap in data coverage which represents the consumption of the private sector facilities. Therefore, as the national AMC data analysed excluded the private for-profit sector, efforts should be made by relevant regulatory authorities and the AMRCC to identify and recruit the country's private for-profit wholesalers or distributors to bridge this gap in surveillance. This approach would also offer the added benefits of allowing an examination of AMC trends within the private and public sector.

Furthermore, as the AMC data received from the CMS was subjected to a series of data cleaning and validation checks, a comprehensive guiding policy for routine AMC data surveillance is required in the country. This will give guidance to, at the minimum, reporting AMC data variables and routine data cleaning and reporting practices to minimise the amount of time spent standardising and cleaning the data before routine surveillance exercises. This guiding policy will help ensure that the data used is accurate and usable for informing country policies. Pharmacy-level AMC data from the hospitals was collected from manual records. To make future AMC surveillance more time and cost-efficient, hospitals could consider converting to electronic systems and ensure such systems have the capabilities to transfer data across systems and/or produce user-friendly reports on AMC.

MAAP was unable to obtain AMU data in Eswatini which would have helped to characterise the appropriateness of antimicrobials use at the facility level, as per country's guidelines, as well as in line with WHO's drug use research methodology.[41] This inability to collect AMU data from participating pharmacies that were co-located in health facilities with AST laboratories was due to the fact that AMC data sources (i.e., stock record cards at the pharmacy) did not allow back-tracing to individual patients to whom antimicrobials were issued as prescription chits were not archived. A single centre study which reported AMU data collection retrospectively in Eswatini has been documented.[29] However, as this study was conducted at a single HIV clinic facility, where presumably, records are better kept for chronic care patients and there are perhaps separate data systems with compartmentalised patient clinical care pathways that allow better AMU tracking, conclusions drawn from it cannot be assumed to represent national AMU or the sampled MAAP pharmacies.

MAAP attempted to conduct retrospective data collection across multiple sites for all prescriptions given to the patients. Thus, the study approach might not be feasible and scalable if conducted outside of an HIV clinic setting. Therefore, MAAP in alignment with the WHO guide on facility AMU assessment, would recommend that future AMU surveillance attempts in the country be conducted through point prevalence surveys on a larger scale in order to give a nationally representative portrait of antimicrobials use in the country.[31] However, this approach recommended by WHO is admittedly time-consuming, unlike retrospective data collection, and often requires specialised data collection teams, making it expensive and challenging to undertake in resource-limited settings. Retrospective AMU data collection can, however, still be an option if facilities targeted for data collection are selected based on the existence of electronic patient records, presence of cross-department unique patient identifiers and a functional and efficient patient record retention system.

Overview of AMC consumption trends and recommendations

The total AMC levels documented in this report offer a useful benchmark to be compared against future country consumption levels following implementation of stewardship programmes. Compared to studies from other countries in the region, the observed AMC levels in Eswatini exceed levels observed in Burundi, Burkina Faso, Cote d'Ivoire[19] and Sierra Leone[24] but were lower than the levels observed in Tanzania.[42] The data for Eswatini included public data that include hospitals and lower-level care facilities in comparison to Burundi, which only used data from public hospitals. For Tanzania, import data was used to calculate the DDD for the population, even though data on local production was lacking. This could be a reason why Eswatini AMC levels appear lower than those of Tanzania. Another reason could be that in Eswatini, there is a relatively higher rate of HIV burden (approximately 20%) compared to other countries which can be an imparting factor in driving the consumption of the sulfamethoxazole or trimethoprim combination and thus, resulting in higher AMC trends.

The disparities in AMC within the compared countries might be due to the different relative burden of infectious diseases within the countries and limited availability of laboratory or point-of-care diagnostics at the health facility level. This may lead to presumptive treatment and unnecessary prescriptions of antimicrobials. Widespread availability of antimicrobials over-the-counter and the unexplained use of some antimicrobials in the animal health sector may be additional contributing factors.[19] Due to the relatively higher rates of AMC in Eswatini, AMU point prevalence surveys are recommended to better understand the country's AMC levels and eventually guide any future national action plans to optimise the antimicrobials consumption if any overuse or misuse is detected.

During the period of AMC analysis, an overall increase in the national AMC was observed. It is difficult to comprehensively assess and characterise all the possible reasons for this increase. However, increase in the consumption of the sulfamethoxazole or trimethoprim combination from the year 2017 to 2018, can be attributed to the overall increase in the AMC levels. Nevertheless, the reason for an increase in the consumption of this combination was not clear. The establishment of regular AMC surveillance will allow for the examination of AMC trends against baseline results presented here.

The evaluation of antibiotics consumption according to the WHO AWaRe categories, demonstrated that the proportion of narrow spectrum antibiotics in the 'Access' category well exceeded the minimum WHO recommended consumption threshold[34] and minimal consumption of broader spectrum 'Watch' category antibiotics. This finding is quite commendable as it implies that any emerging AMR trends due to misuse or overuse will likely be restricted to a narrow spectrum of antibiotics; sparing the lesser used broader-spectrum and last-resort antibiotics in the 'Watch' and 'Reserve' categories. However, a closer examination of the spectrum of antibiotics used within each AWaRe category revealed that an overwhelming majority of antibiotics consumed within the 'Access' and 'Watch' categories came only from the top five antibiotics in each category. Such a consumption pattern could be postulated to be sub-optimal as evolutionary pressure driving resistance would be focused only amongst the narrow band of antibiotics consumed.[43] This narrow consumption of antibiotics within the 'Access' and 'Watch' categories of antibiotics can also make the country susceptible to stockouts if manufacturing and supply chain issues are encountered for these antibiotics. It is therefore recommended that the country's ASP explores ways to ensure a wider spread in consumption of the antibiotics within each WHO AWaRe category. This includes interventions including offering incentives for the importation and distribution of other antibiotics in the WHO AWaRe categories, in line with the country's EML.

Interestingly, on reviewing the pharmacy-level usage of 'Access' category antibiotics, hospital pharmacies showed a high consumption of 'Access' antibiotics compared to the community pharmacies due to the high consumption of sulfamethoxazole or trimethoprim. The sulfamethoxazole or trimethoprim combination is used for prophylaxis against opportunistic infections among people living with HIV and as a routine intervention in HIV treatment programmes in Eswatini with its procurement largely through donation. This prophylactic use of sulfamethoxazole or trimethoprim contributed to the high use observed of this fixed-dose combination in the country, well above the minimum recommended consumption threshold, i.e., that 60% of all antibiotics consumed should come from the 'Access' category antibiotics.

The consumption of 'Access' group antibiotics remained above WHO recommended minimum of 60% even after exclusion of sulfamethoxazole or trimethoprim. This consumption trend of 'Access' category antibiotics in Eswatini is commendable and indicated that narrow spectrum antibiotics are typically the first line of antibiotics used in Eswatini, further lowering the potential for widespread AMR in case of antibiotic overuse or misuse. This finding also suggests that Eswatini's EML comprises mostly of 'Access' category antibiotics which are widely available in the country.[44]

Despite this overall good performance, it is important to note that community pharmacies failed to meet the WHO Access category consumption threshold. Furthermore, despite meeting the minimum WHO Access antibiotics consumption threshold, as a whole, it was found that the community pharmacies consumed nearly triple the amount of 'Watch' category antibiotics when compared to hospital-based pharmacies. The reason for the higher consumption of 'Watch' category antibiotics in community pharmacies is unknown but could possibly imply that there is less oversight when dispensing broader-spectrum prescription antibiotics in this category of pharmacies. This observation would therefore require AMRCCs to target their oversight, regulatory and sensitisation roles to community retail pharmacies to correct this consumption trend and have narrower spectrum ('Access' category) antibiotics offered to patients. To better understand the consumption pattern, targeted AMU studies might be best placed to investigate whether prescriptions were appropriate and antibiotics consumed according to national treatment guidelines. The high consumption trend of 'Watch' category antibiotics by the community pharmacies further highlights the importance of including all healthcare sectors into the country's ASPs.

The consumption of WHO 'Reserve' category antibiotics was observed only within the sampled hospital pharmacies (public and private or faith-based hospital pharmacies). Interestingly, the country's EML does not include any of the seven WHO 'Reserve' antibiotics listed as vital medicines within the WHO EML. The absence of this category of antibiotics within the country's EML cannot be assumed to be as a result of an absence of their clinical need. Therefore, it is possible that other conditions requiring treatment with 'Reserve' category antibiotics exist in Eswatini that may be sub-optimally treated due to the unavailability of the remaining 'Reserve' category antibiotics as they were not detected in-country by MAAP. Therefore, MAAP recommends an urgent review be conducted by the MoH and AMRCC in an effort to assess the availability of the 'Reserve' category antibiotics in the country. Where deemed necessary, that may subsequently lead to the revision of the country's EML and treatment guidelines to include these vital antibiotics. This approach will ensure that the most vital antibiotics are available for all patients.

AMC and AMU summary and way forward

Data generated from AMC and AMU surveillance trends can provide unique insights for national stewardship programmes and for the formulation of policies to stem the emergence of AMR. Eswatini should be commended for far exceeding the minimum threshold of consumption of at least 60% of antibiotics coming from the WHO 'Access' (narrow spectrum, first-choice antibiotics) category. Yet, only five antibiotics make up for 88% of the consumption which indicates the opportunity for more diversification. Table 14 describes the next steps for AMC and AMU surveillance.

Table 15: Next steps for AMC and AMU surveillance

A.

Leadership and Governance

The country will require an AMC surveillance policy and address by whom, how and when national AMC datasets should be reported. This activity could be led by the AMRCC.

- Such a policy should provide guidance on the minimum required reporting variables, data quality appraisals, data analysis and reporting pathways to both the ministry and the WHO GLASS system, in order to ensure a continuous stream of localised AMC data beyond MAAP that will help inform or assess future policy decisions by the national antimicrobial stewardship programme.
- Lessons learned from the ongoing Fleming Fund Country Grants and MoH surveillance programs could be taken into consideration in the development of the policy.

The national stewardship programmes could work to review the Eswatini EML and national treatment guidelines for inclusion of essential 'Reserve' antibiotics.

B.

Service Delivery

Future attempts to collect AMU data in the country should seek to identify facilities that have unique patient identifiers and fully electronic medical records capabilities, or, as a limited number of facilities have such systems in place, the country could aim to prospectively collect this data as guided by WHO methodology for point prevalence surveys.[31]

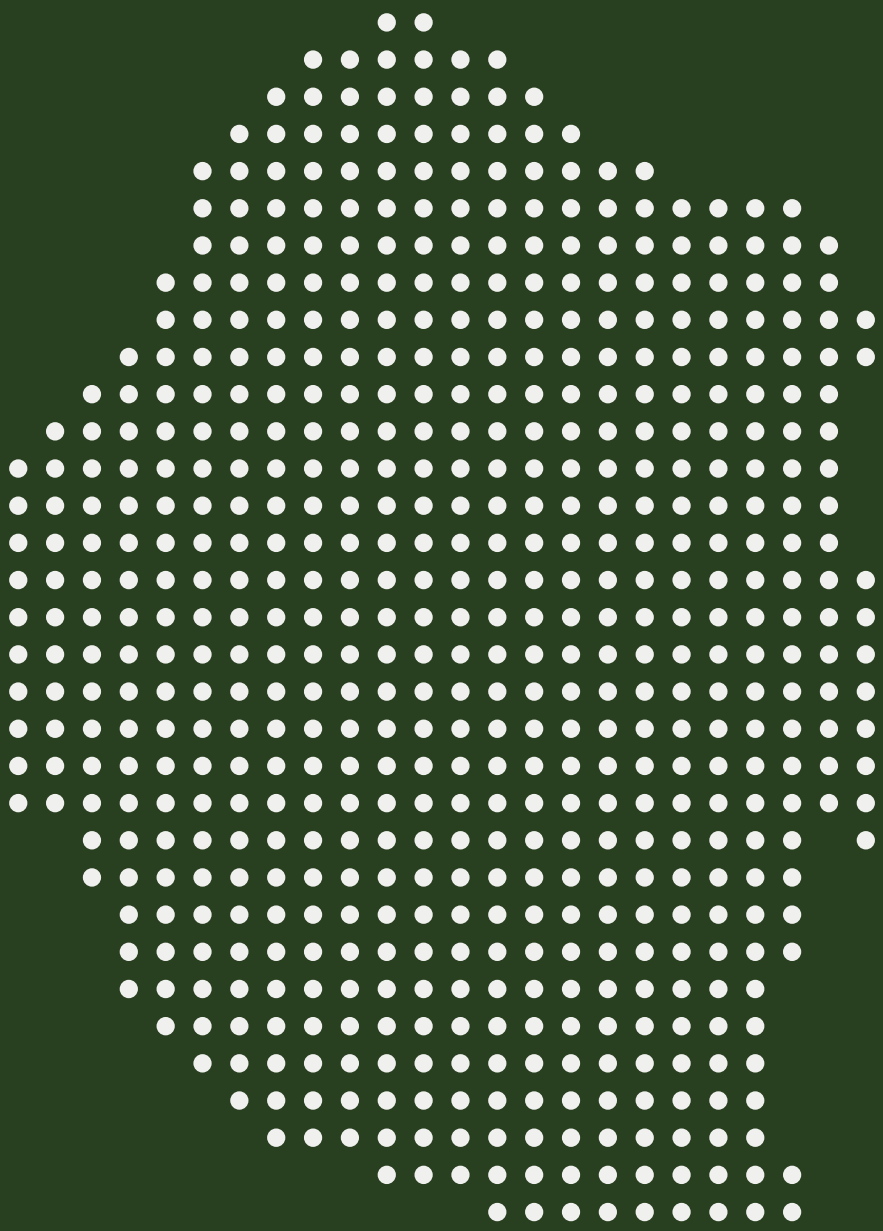
National stewardship programmes led by the AMRCC could conduct educational campaigns for healthcare practitioners to ensure that they are aware of the full spectrum of antimicrobials available in the country's EML.

C.

Medical products and technologies

National stewardship programmes to collaborate with pharmacists and medicine importers to increase importation of more varieties of antibiotics, including 'Reserve' category antibiotics in selected facilities, as per the revised country's EML.

Part E: Limitations



Since the participating laboratories were at different levels of service and had variable testing capacity, all results in this report should be interpreted with caution. We encountered a few limitations during the conducting of the current study, as summarised below:

1. It was often difficult to obtain patients' hospital identifiers from laboratory records, thus impacting the collection of demographic and clinical information from medical archives. Where identifiers could be matched, it was found that hospital records were paper based, thus requiring manual retrieval. This was often compounded by issues of illegibility and/or incomplete demographics and clinical information.

2. The laboratories had varying levels of quality and testing practices. Consequently, data contributions were uneven, and it proved challenging to consolidate data to provide robust analyses of resistance and clinical impact.

3. The participating laboratories, three, may not fully represent the true resistance rates in the country as they only encompassed a small proportion of the country's population (over 1.1 million). Furthermore, as routine testing does not appear to be the norm in most hospitals and laboratories, the data may overestimate the resistance rates as infections that fail therapy may be more likely to be tested.

4. Clinical data and antimicrobial usage information were not sufficient to provide robust analysis of drivers of resistance.

5. In relation to the national-level datasets, the private for-profit market was not covered. Thus, the gap in obtaining this (private for-profit wholesalers or distributors) data means that total medicine consumption levels reported for Eswatini in this report are an underestimate of the country's total AMC.

6. To better understand whether the national AMC trends were mirrored by pharmacy-level AMC trends, a sample of 18 pharmacies were purposively selected for data collection. This sample size was a relatively small proportion compared to the total number of pharmacies in Eswatini. This sample did not geographically represent all regions and health zones in Eswatini, unlike the national AMC datasets which represented consumption across the country. Therefore, a more systematic sampling strategy that factors in populations serviced and geographical locations, will be required to make conclusions from pharmacy-level data more representative.

7. MAAP was only successful in collecting AMC data for the reviewed year (2018) and also only from (n=7) community pharmacies. This was mainly due to either their unwillingness to share data, the inability to access the data from their systems or as a result of them not meeting the inclusion criteria.

8. MAAP was unable to obtain AMU data from the participating pharmacies co-located with AST laboratories and clinics. Therefore a better understanding of how and why antimicrobials are prescribed as well as dispensed (i.e., the appropriateness of prescriptions and antimicrobials consumed) was not achieved. This information is important as it would help better inform the country on where they would need to focus their stewardship programmes.

References

1. Fleming Fund. Accessed April 2, 2020. https://www.flemingfund.org/.
2. World Health Organisation. Worldwide Country Situation Analysis: Response to Antimicrobial Resistance. Accessed June 15, 2021. http://apps.who.int/iris/bitstream/handle/10665/163468/9789241564946_eng.pdf;jsessionid=040F003DCA2DE23A0E1484CFCF-967D32?sequence=1.
3. African Society for Laboratory Medicine. MAAP. Accessed April 16, 2020. https://aslm.org/what-we-do/maap/.
4. DataBank | The World Bank. Accessed December 26, 2021. https://databank.worldbank.org/home.aspx
5. Education Statistics - All Indicators | DataBank. Accessed December 26, 2021. https://databank.worldbank.org/source/education-statistics-%5E-all-indicators
6. UHC service coverage index | Data. World Bank. Published 2019. Accessed April 14, 2022. https://data.worldbank.org/indicator/SH.UHC.SRVS.CV.XD
7. HIV Facts and Figures | National AIDS Control Organisation | MoHFW | GoI. Accessed May 24, 2022. http://naco.gov.in/hiv-facts-figures
8. World Health Organisation. Global Action Plan on Antimicrobial Resistance.; 2015. Accessed April 16, 2019. https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1.
9. World Health Organisation. Global Antimicrobial Resistance Surveillance System (GLASS). Published 2021. Accessed April 16, 2021. https://www.who.int/glass/en/.
10. Eswatini: National Antimicrobial Resistance Containment Strategic Plan 2018-2022. Accessed June 9, 2022. https://www.who.int/publications/m/item/Eswatini-national-antimicrobial-resistance-containment-strategic-plan-2018-2022
11. Medicines and Related Substances Control Act. (2016). Medicines Regulatory Authority, King and Parliement of Swaziland. Retrieved from http://www.rrfa.co.za/wp-content/uploads/2012/11/Swaziland-Medicines-Related-Substances-Control-Act-9-2016.pdf
12. WHONET | Welcome to the WHONET Community website! Accessed December 23, 2021. https://whonet.org/
13. World Health Organisation. Prioritization of Pathogens to Guide Discovery, Research and Development of New Antibiotics for Drug-Resistant Bacterial Infections, Including Tuberculosis.; 2017.
14. Clinical and Laboratory Standards Institute. CLSI. Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition. CLSI Document M39-A4.; 2014.
15. Li F, Ayers TL, Park SY, et al. Isolate removal methods and methicillin-resistant Staphylococcus aureus surveillance. Emerging Infectious Diseases. 2005;11(10):1552-1557. doi:10.3201/eid1110.050162.
16. Brown Lawrence D. CTTDA. Interval Estimation for a Binomial Proportion. Stats Sci. 2001;16(2):101-133.
17. Kalanxhi E, Osena G, Kapoor G, Klein E. Confidence interval methods for antimicrobial resistance surveillance data. Antimicrobial Resistance and Infection Control. 2021;10(1). doi:10.1186/s13756-021-00960-5.
18. The Center for Disease Dynamics Economics and Policy. ResistanceMap: Antibiotic resistance. 2018. Accessed June 15, 2021. https://resistancemap.cddep.org/About.php.
19. World Health Organisation. (2018). WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation. Retrieved December 23, 2020, from https://apps.who.int/iris/bitstream/handle/10665/277359/9789241514880-eng.pdf?ua=1
20. Van Boeckel, T. P., Gandra, S., Ashok, A., Caudron, Q., Grenfell, B. T., Levin, S. A., and al., e. (2014). Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. The Lancet Infectious Diseases, 14(8), 742-750.
21. Kingdom of Eswatini. (2018). THE NATIONAL ANTIMICROBIAL RESISTANCE CONTAINMENT STRATEGIC PLAN 2018 – 2022. Retrieved from https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-spc-npm/nap-library/Eswatini_final-signed-amr-strategy-implementation-plan-10june2021.pdf?sfvrsn=1fab5cbb_3anddownload=true
22. Gordon, C. (2020, April). Technical Bulletin: Surveillance and AMU. Retrieved June 01, 2021, from https://www.flemingfund.org/wp-content/uploads/29e140d66670221b9d95aaaa108ef03e.pdf

23.	Martinez, E. M., Klein, E. Y., Van Boeckel, T. P., Pant, S., Gandra, S., Levin, S. A., . . . Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proceedings of the National Academy of Sciences, 115(15), E3463-E3470.
24.	Kanu, J. S., Khogali, M., Hann, K., Tao, W., Barlatt, S., Komeh, J., . . . al., e. (2021). National Antibiotic Consumption for Human Use in Sierra Leone (2017–2019): A Cross-Sectional Study. Tropical Medicine and Infectious Disease, 6(2), 77.
25.	Namugambe JS, D. A. (2021). National Antimicrobial Consumption: Analysis of Central Warehouses Supplies to In-Patient Care Health Facilities from 2017 to 2019 in Uganda. Tropical Medicine and Infectious Disease, 6(2), 83.
26.	Okoth, C., Opanga, S., Okalebo, F., Oluka, M., Kurdi, A. B., and Godman, B. (2018). Point prevalence survey of antibiotic use and resistance at a referral hospital in Kenya: findings and implications. Hospital Practice, 46(3), 128-136.
27.	Maina, M., Mwaniki, P., Odira, E., Kiko, N., McKnight, J., Schultsz, C., . . . Tosas-Auguete, O. (2020). Antibiotic use in Kenyan public hospitals: Prevalence, appropriateness and link to guideline availability. International Journal of Infectious Diseases, 99, 10-18.
28.	Mukokinya, M. M., Opanga, S., Oluka, M., and Godman, B. (2018). Dispensing of Antimicrobials in Kenya: A Cross-sectional Pilot Study and Its Implications. Journal of Researc in Pharmacy Practice, 7(2), 77-82.
29.	Ness TE, S. A. (2021). Evaluating antibiotic use and developing a tool to optimize prescribing in a family-centered HIV clinic in Eswatini. PLOS ONE, 1-10.
30.	World Health Organisation. (2016). WHO methodology for a global programme on surveillance of antimicrobial consumption. Version 1.0. Retrieved December 23, 2020, from https://www.who.int/medicines/areas/rational_use/WHO_AMCsurveillance_1.0.pdf
31.	World Health Organisation. (2019). WHO Methodology for Point Prevalence Survey on Antibiotic Use in Hospitals. Version 1.1. Retrieved June 21, 2021, from https://www.who.int/publications/i/item/WHO-EMP-IAU-2018.01
32.	World Health Organisation. (2020). WHOCC - ATC/DDD Index. Retrieved December 21, 2020, from https://www.whocc.no/atc_ddd_index/
33.	Worldometer. (2020). Eswatini population (2020 and historical) - Worldometer. Retrieved December 21, 2020, from https://www.worldometers.info/world-population/Eswatini-population/
34.	World Health Organisation. (2019). Essential medicines and health products: WHO releases the 2019 AWaRe Classification Antibiotics. Retrieved December 21, 2020, from https://www.who.int/medicines/news/2019/WHO_releases2019AWaRe_classification_antibiotics/en/
35.	Klein EY, Tseng KK, Pant S, Laxminarayan R. Tracking global trends in the effectiveness of antibiotic therapy using the Drug Resistance Index. BMJ Global Health. 2019;4(2):1315. doi:10.1136/bmjgh-2018-001315.
36.	Laxminarayan R, Klugman KP. Communicating trends in resistance using a drug resistance index. BMJ Open. 2011;1(2):e000135. doi:10.1136/bmjopen-2011-000135.
37.	Barnett HAR. The Variance of the Product of Two Independent Variables and Its Application to an Investigation Based on Sample Data. J Inst Actuar. 1955;81(2):190-190. doi:10.1017/S0020268100035915
38.	Goodman LA. The Variance of the Product of K Random Variables. Journal of the American Statistical Association. 2012;57(297):54-60. doi:10.1080/01621459.1962.10482151
39.	Tadesse BT, Ashley EA, Ongarello S, et al. Antimicrobial resistance in Africa: a systematic review. BMC Infectious Diseases 2017 17:1. 2017;17(1):1-17. doi:10.1186/S12879-017-2713-1
40.	Carey RB, Bhattacharyy S, Kehl SC, et al. Implementing a quality management system in the medical microbiology laboratory. Clinical Microbiology Reviews. 2018;31(3). doi:10.1128/CMR.00062-17
41.	World Health Organisation. (2003). Introduction to Drug Utilization Research. Retrieved May 19, 2021, from https://www.who.int/medicines/areas/quality_safety/safety_efficacy/Drug%20utilization%20research.pdf?ua=1
42.	Mbwasi, R., Mapunjo, S., Wittenauer, R., Valimba, R., Msovela, K., Werth, B. J., . . . Konduri, N. (2020). National Consumption of Antimicrobials in Tanzania: 2017–2019. Frontiers in Pharmacology, 11, 1667
43.	Laxminarayan, R., Matsoso, P., Pant, S., Brower, C., Røttingen, J.-A., Klugman, K., and al., e. (2016). Access to effective antimicrobials: a worldwide challenge. The Lancet, 387(10014), 168-175.
44.	Eswatini Essential Medicines List. (2012). Standard Treatment Guidelines and Essential Medicines List of Common Medical Conditions in the Kingdom of Swaziland. Retrieved from https://www.medbox.org/pdf/5e148832db60a2044c2d2d3e

Glossary

Accreditation:
According to the National Accreditation Board for Testing and Calibration Laboratories, accreditation is a procedure by which an authoritative body gives formal recognition of technical competence for specific tests or measurements, based on third-party assessment and following international standards.

Antimicrobial consumption:
According to the WHO, antimicrobial consumption is defined as quantities of antimicrobials used in a specific setting (total, community, hospital) during a specific period of time (e.g., days, months and year).

Antimicrobial resistance:
According to the WHO, antimicrobial resistance occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines, making infections more difficult to treat and thus increasing the risk of disease spread, severe illness and death. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become increasingly difficult or impossible to treat.

Antimicrobial resistance rate:
The extent to which a pathogen is resistant to a particular antimicrobial agent or class, determined by the proportion of isolates that are non-susceptible (i.e., either intermediate or resistant) over a one-year period:
AMR rate = No. of non-susceptible isolates / No. of tested isolates [CI 95%]

Antimicrobial susceptibility testing:
Tests used to determine the specific antibiotics and extent to which a particular bacteria or fungus is sensitive.

Antimicrobial susceptibility testing standards:
A number of internationally recognised agencies that produce the standards to be followed by laboratories while performing antimicrobial susceptibility testing e.g., Clinical Laboratory Standards Institute, European Committee on Antimicrobial Susceptibility Testing, etc. It is essential that laboratories comply with at least one of these standards while performing AST.

Country data quality score:
A metric computed to estimate the overall quality of AMR data received from a country. Firstly, each laboratory was assigned a data score based on their level of pathogen identification. Scoring was based on quartiles of the proportion of completely identified pathogens where laboratories with >75% of pathogens identified at the species level were awarded the highest score (4) and those with <25% identification received the lowest score (1). Scoring was performed per year and thereafter the average of all years assigned as the laboratory data quality score for each laboratory. Secondly, the country data quality score was computed by weighting the laboratory data quality score with the quantum of valid cultures contributed by each laboratory. The maximum country data quality score was 4.

Eligibility questionnaire:
A questionnaire to be answered by laboratories in the country's laboratory network. It comprised questions on site information, commodity and equipment, quality assurance, accreditation and certification, personnel and training, specimen management and laboratory information systems. Laboratories were scored on their response.

GLASS:
According to the WHO, the Global Antimicrobial Resistance Surveillance System provides a standardised approach to the collection, analysis and sharing of AMR data by countries and seeks to support capacity development and monitor the status of existing or newly developed national AMR surveillance systems.

Laboratory readiness assessment:
It is the process of scoring the responses on the laboratory eligibility questionnaire to assess the laboratory's readiness or preparedness for AMR surveillance.

Laboratory readiness score:
The score obtained by the laboratory based on the laboratory readiness assessment. The maximum possible score was 38.

MAAP:
The Mapping Antimicrobial resistance and Antimicrobial use Partnership is a multi-organisational consortium of strategic and technical partners. It was set up to collect and analyse historical antimicrobial susceptibility and consumption or usage data collected for the period 2016-2018 in each country as well as understand the regional landscape.

Positive cultures:
Positive cultures are valid cultures for which pathogen growth was reported irrespective of AST results.

Positive cultures with AST:
Positive cultures with AST are a subset of positive cultures for which pathogen growth was reported and AST results were also available.

Proficiency testing:
According to the National Accreditation Board for Testing and Calibration Laboratories, proficiency testing is the evaluation of participant performance against pre-established criteria by means of inter-laboratory comparisons.

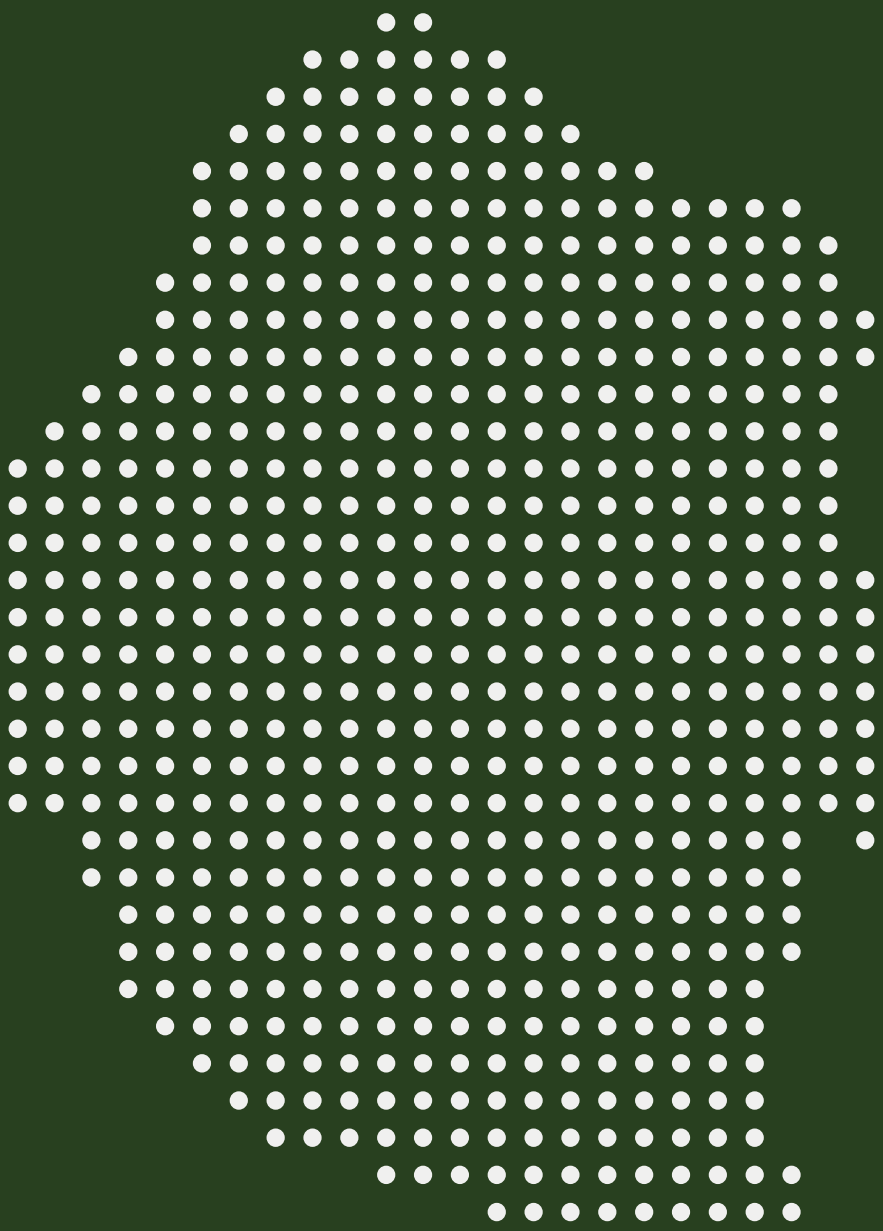
Quality Certification:
Certification is used for verifying that laboratory personnel have adequate credentials to practise certain disciplines as well as verifying that products meet certain requirements.

Quality Management Systems:
These are systematic and integrated sets of activities to establish and control the work processes from pre-analytical to post-analytical processes, manage resources, conduct evaluations and make continued improvements to ensure consistent quality results.

Total cultures:
The number of patient rows in the database received from the laboratories.

Valid cultures:
Valid cultures are a subset of total cultures and include information on the specimen type, collection date and the laboratory's testing volume.

AMR Appendices and Supplementary Tables



Appendix 1: Data Sharing Agreement

Data-Sharing Agreement

Between

Ministry of Health

(The Provider)

And

The African Society for Laboratory Medicine (ASLM)

(Recipient)

1. Purpose of Agreement.

This agreement establishes the terms and conditions put in place to facilitate the sharing of antimicrobial resistance (AMR) and antimicrobial use (AMU) associated data between the parties. As such, the Provider agrees to share the data with the Mapping Antimicrobial Resistance & Antimicrobial Use Partnership (MAAP) consortium hereby represented by the African Society for Laboratory Medicine (ASLM), the lead grantee for the Fleming Fund Regional Grant (East, South and West Africa) on the terms set out in this agreement. MAAP agrees to use the data on the terms set out in this Agreement.

2. Description of Data.

2.1 Pursuant to the terms of this agreement, the Ministry of Health hereafter referred to as the Provider, shall grant permission to ASLM and the MAAP consortium partners to access data elements as set forth in the MAAP methodology which include:

- AMR data linked to patient demographics and information on clinical syndrome
- AMU (procurement, sales and distribution) of antibiotics

AMR data will be collected in laboratory facilities conducting antibiotic susceptibility testing and in clinical facilities linked to those laboratories. AMU data will also be collected in pharmacies and the central medical stores as described by the MAAP methodology and as per prior agreement with the Ministry of Health. Data will be collected from selected public and private facilities. The parties shall take any reasonable steps necessary to facilitate the principle of data sharing to strengthen AMR and AMU data publication and usage in line with the objectives of the Fleming Fund and the Eswatini eHealth strategy and related data security guidelines.

3. Confidentiality, use and storage of data

3.1 The confidentiality of data pertaining to individuals will be protected as follows:

3.1.1 The Recipient will not release the names of individuals, or information that could be linked to an individual, nor will the Recipient present the results of data analysis (including maps) in any manner that would reveal the identity of individuals.

3.1.2 The Recipient will not release individual addresses, nor will the Recipient present the results of data analysis (including maps) in any manner that would reveal individual addresses.

3.1.3 Both parties shall comply with all Country laws and regulations governing the confidentiality of the information that is the subject of this Agreement.

3.1.4 The Recipient will not release data to a third party without prior approval from the Provider.

3.1.5 The Recipient will not share, publish, or otherwise release any findings or conclusions derived from analysis of data obtained from the data provider without prior approval from the Provider.

3.2 Data Storage and Management

3.2.1 The Recipient shall be responsible for the storage of the data in appropriate secure medium and location agreed upon with the provider ensuring that Provider has unlimited access to their data.

3.2.2 The Provider shall be responsible for the storage and management of the data in the Ministry of Health Data Centre

3. Representatives

3.1 In witness whereof, The Recipient and The Provider have caused this agreement to be signed and delivered by their authorized representatives as of the date set forth below.

ASLM's representatives to represent ASLM for the purpose of this Agreement shall be Nqobile Ndlovu (nndlovu@aslm.org), Acting CEO of ASLM. The daily management of the grant will be conducted by Pascale Ondoa (pondoa@aslm.org), ASLM Director of Science and New Initiatives, on behalf of Mr. Nqobile Ndlovu.

For and on behalf of ASLM: _____

Name: _____

Position: _____

Signature: _____

Date: _____

"PROVIDER's Representative" to represent the PROVIDER for the purpose of this Agreement shall be the Principal Secretary, Dr. Simon M. Zwane (smz1157@gmail.com) who may be represented by the Director of Health Services, Dr. Vusi Magagula (magmu@realnet.co.sz):

For and on behalf of Provider: Ministry of Health.

Name: DR SIMON ZWANE

Position: PRINCIPAL SECRETARY

Signature: _____

Date: 18/11/19.

MINISTRY OF HEALTH PRINCIPAL SECRETARY'S OFFICE 18 NOV 2019 P. O. BOX 5 MBABANE-H100 ESWATINI ESWATINI

Appendix 2: Laboratory Eligibility Questionnaire

Question	Response
Part 1: Site Information	
1.1 What is the name of the laboratory?	

1.2	Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing?	Yes		No	
1.3	Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium?	Yes		No	

1.4 What is the address of the laboratory?

1.5 What is the laboratory's level of service?

Reference- tier 3 or 4	Regional/Intermediate	District or community	Other

1.6 What is the laboratory's affiliation?

Government/Ministry of Health	Private	Non-government organisation	Other

1.7	Is the laboratory co-located in a clinical facility?	Yes		No	
1.8	Is a pharmacy co-located with the laboratory?	Yes		No	
1.9	Did the laboratory serve as a national AMR surveillance site at any time between 2016 and 2018?	Yes		No	
1.10	Is your country participating in the World Health Organisation's Global Antimicrobial Resistance Surveillance System (WHO GLASS)?	Yes		No	
Part 2: Commodity and Equipment					
2.1	Did the laboratory have regular power supply with functional back up, in place at any time between 2016-18?	Yes		No	
2.2	Did the laboratory have continuous water supply, in place at any time between 2016-18?	Yes		No	
2.3	Did the laboratory have certified and functional biosafety cabinet, in place at any time between 2016-18?	Yes		No	
2.4	Did the laboratory have automated methods for bacterial identification, in place at any time between 2016-18?	Yes		No	
2.5	Did the laboratory have automated methods for antimicrobial susceptibility testing, in place at any time between 2016-18?	Yes		No	
2.6	Did the laboratory test for mechanisms of antimicrobial resistance at any time between 2016-2018?	Yes		No	
Part 3. Quality Assurance (QA), Accreditation and Certification					
3.1A	Was the laboratory implementing quality management systems at any time between 2016-2018?	Yes		No	
3.1B	If you answered 'yes' to question 1A: What quality management tools did the laboratory utilize? (e.g., LQMS, SLIPTA, SLMTA, mentoring, others)				
3.2A	Did the laboratory receive a quality certification at any time between 2016-2018?	Yes		No	
3.2B	If you answered 'yes' to question 2A: What kind of quality certification did the laboratory receive? (e.g., SLIPTA, College of American pathologists)				
3.2C	If you answered 'yes' to question 2A: What was the laboratory's level of quality certification (e.g., star rating for SLIPTA certified laboratories)?				
3.3A	Was the laboratory accredited by a national or international body at any time between 2016-2018?	Yes		No	
3.3B	If you answered 'yes' to question 3A: What was the name of the accreditation body/bodies?				

3.4	Did the laboratory participate in an inter laboratory comparison or external quality assessment (EQA) scheme for pathogen identification and AST at any time between 2016-18?	Yes		No	
3.5	Did the laboratory utilize reference strains to verify that stains, reagents, and media are working correctly at any time between 2016-18?	Yes		No	
3.6	Did the laboratory maintain records of QC results, at any time between 2016-18?	Yes		No	
3.7	Was there a quality focal person in your laboratory at any time between 2016-2018?	Yes		No	
3.8	Did the laboratory follow standard operating procedures (SOPs) on pathogen identification and AST methodology at any time between 2016-18?	Yes		No	
3.9	Did the laboratory comply with any standards (e.g., CLSI, EUCAST, others) for reporting AST results at any time between 2016-18?	Yes		No	

Part 4. Personnel and Training

4.1	Did the laboratory have at least one qualified microbiologist, in place at any time between 2016-18?	Yes		No	
4.2	Did the laboratory have a laboratory scientist/technologist /technician experienced in microbiology with skill set in bacteriology, in place at any time between 2016-18?	Yes		No	
4.3	Did the laboratory have up to date complete records on staff training and competence record for the microbiology tests they perform, in place at any time between 2016-18?	Yes		No	

Part 5. Specimen Management

5.1	Did the laboratory follow a defined standard operating procedure (SOP) for specimen collection and testing, at any time between 2016-18?	Yes		No	
5.2	Did the laboratory comply with specimen rejection criteria for rejecting inadequate specimens, at any time between 2016-18?	Yes		No	
5.3A	Does the laboratory have information on the average number of specimens processed for culture and sensitivity in 2018?	Yes		No	
5.3B	If you answered 'yes' to question 3A: What was the average number of specimens processed for bacterial culture in 2018?				
5.3C	If you answered 'yes' to question 3A: What was the average number of specimens that yielded bacterial growth and were processed for susceptibility tests, in 2018?				

<200	200-1000	1000-3000	>3000

Part 6. Laboratory Information System and Linkage to Clinical Data

6.1	Was a specimen (laboratory) identification number assigned to patient specimens received between 2016-18?	Yes		No	
6.2A	Was there a system/database to store patient data (demographic, clinical and specimen) at any time between 2016-18?	Yes		No	
6.2B	If you answered 'yes' to question 2A: What type of data was captured in the system/database?				
6.2C	If you answered 'yes' to question 2A: What was the format for storage of information?	Yes		No	
6.2D	If you answered 'yes' to question 2A: What is the location of this database, or where can this database be accessed from?				
6.3A	Were patient demographics and clinical information captured on test request forms at any time between 2016-18?	Yes		No	
6.3B	If you answered 'yes' to question 3A: Were test request forms submitted between 2016 and 2018 stored and retrievable?	Yes		No	

Note: For question 1.4, the exact address was preferred, however, the nearest landmark or street intersection was acceptable, where applicable; for questions 1.5 and 1.6, more than one response was possible and for the option 'other', the response was entered as plain text; for question 2.2 mechanisms of antimicrobial resistance can vary: common mechanisms are production of enzymes (extended spectrum beta lactamase, carbapenemase, etc.) and resistance genes (mecA gene in MRSA, etc.); for question 4.a, the qualified microbiologist should possess a postgraduate degree in microbiology (medical or non-medical); for question 6.2c, more than one response was possible and for the option 'other', responses were entered as plain text (i)

Of note, some countries received a version of the EQ which did not have the following two questions from part I: (i) Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing? (ii) Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium? However, AST capabilities were confirmed before the EQ evaluation, and the data sharing aspect of the process was already in place in agreements with the MoH.

Appendix 3: Laboratory Readiness Assessment

The EQ questions were scored for laboratory readiness as follows:

Part 1: Site Information (Maximum score=0)

	Question	Response				Scoring
1.1	What is the name of the laboratory?					None
1.2	Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing?	Yes		No		None
1.3	Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium?	Yes		No		None
1.4	What is the address of the laboratory?					None
1.5	What is the laboratory's level of service?					None
	Reference- tier 3 or 4	Regional/Intermediate	District or community	Other		
1.6	What is the laboratory's affiliation?					None
	Government/Ministry of Health	Private	Non-government organisation	Other		
1.7	Is the laboratory co-located in a clinical facility?	Yes		No		None
1.8	Is a pharmacy co-located with the laboratory?	Yes		No		None
1.9	Did the laboratory serve as a national AMR surveillance site at any time between 2016 and 2018	Yes		No		None
1.10	Is your country participating in the World Health Organisation's Global Antimicrobial Resistance Surveillance System (WHO GLASS)?	Yes		No		None

Part 2: Commodity and Equipment (Maximum score=6)

2.1	Did the laboratory have regular power supply with functional back up, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.2	Did the laboratory have continuous water supply, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.3	Did the laboratory have certified and functional biosafety cabinet, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.4	Did the laboratory have automated methods for bacterial identification, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.5	Did the laboratory have automated methods for antimicrobial susceptibility testing, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.6	Did the laboratory test for mechanisms of antimicrobial resistance at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No

Part 3. Quality Assurance (QA), Accreditation and Certification (Maximum score=10)

3.1A	Was the laboratory implementing quality management systems at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.1B	If you answered 'yes' to question 1A: What quality management tools did the laboratory utilize? (e.g., LQMS, SLIPTA, SLMTA, mentoring, others)					Score 1 for "Yes" and 0 for "No
3.2A	Did the laboratory receive a quality certification at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.2B	If you answered 'yes' to question 2A: What kind of quality certification did the laboratory receive? (e.g., SLIPTA, College of American pathologists)					None
3.2C	If you answered 'yes' to question 2A: What was the laboratory's level of quality certification (e.g., star rating for SLIPTA certified laboratories)?					None
3.3A	Was the laboratory accredited by a national or international body at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.3B	If you answered 'yes' to question 3A: What was the name of the accreditation body/bodies?					None
3.4	Did the laboratory participate in an inter laboratory comparison or external quality assessment (EQA) scheme for pathogen identification and AST at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
3.5	Did the laboratory utilize reference strains to verify that stains, reagents, and media are working correctly at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No

3.6	Did the laboratory maintain records of QC results, at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
3.7	Was there a quality focal person in your laboratory at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.8	Did the laboratory follow standard operating procedures (SOPs) on pathogen identification and AST methodology at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
3.9	Did the laboratory comply with any standards (e.g., CLSI, EUCAST, others) for reporting AST results at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No

Part 4. Personnel and Training (Maximum Score=3)

4.1	Did the laboratory have at least one qualified microbiologist, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
4.2	Did the laboratory have a laboratory scientist/technologist /technician experienced in microbiology with skill set in bacteriology, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
4.3	Did the laboratory have up to date complete records on staff training and competence record for the microbiology tests they perform, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No

Part 5. Specimen Management (Maximum Score=3)

5.1	Did the laboratory follow a defined standard operating procedure (SOP) for specimen collection and testing, at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
5.2	Did the laboratory comply with specimen rejection criteria for rejecting inadequate specimens, at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
5.3A	Does the laboratory have information on the average number of specimens processed for culture and sensitivity in 2018?	Yes		No		Score 1 for "Yes" and 0 for "No
5.3B	If you answered 'yes' to question 3A: What was the average number of specimens processed for bacterial culture in 2018?					None
5.3C	If you answered 'yes' to question 3A: What was the average number of specimens that yielded bacterial growth and were processed for susceptibility tests, in 2018?					None

<200	200-1000	1000-3000	>3000

Part 6. Laboratory Information System and Linkage to Clinical Data (Maximum Score=16)

6.1	Was a specimen (laboratory) identification number assigned to patient specimens received between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
6.2A	Was there a system/database to store patient data (demographic, clinical and specimen) at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
6.2B	If you answered 'yes' to question 2A: What type of data was captured in the system/database?	Yes		No		Score 1 for "Yes" and 0 for "No

Patient demographic data (i.e., age, date of birth, gender, location)	Patient clinical data (i.e., primary/chief diagnosis, comorbidities, current antibiotic treatment)	Patient outcome

6.2C	If you answered 'yes' to question 2A: What was the format for storage of information?	Score 1 for paper; 2 for mixed (E/P; E/P/O; others; mixed) and 3 for electronic (max score being 3)

Paper-based	Electronic (laboratory information system, hospital information system, other databases e.g., WHONET)	Other

6.2D	If you answered 'yes' to question 2A: What is the location of this database, or where can this database be accessed from?	Score 1 for other; 2 for clinic and 3 for lab (max score being 6)

Laboratory	Clinical facility	Other

6.3A	Were patient demographics and clinical information captured on test request forms at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No"
6.3B	If you answered 'yes' to question 3A: Were test request forms submitted between 2016 and 2018 stored and retrievable?	Yes		No		Score 1 for "Yes" and 0 for "No"

Appendix 4: Key AMR Variables

	Variables	Mandatory/ Optional
Patient laboratory variables		
1	Patient code	Mandatory
2	Specimen type (name)	Mandatory
3	Specimen site	Mandatory
4	Date of specimen collection	Mandatory
5	Culture results – (no growth/contaminated/pathogen name)	Mandatory
6	AST Results	Mandatory
7	AST Standard	Mandatory
8	Resistance mechanism - if available	Optional
Patient demographic variables		
1	Patient code	Mandatory
2	Patient gender	Mandatory
3	Patient age or date of birth	Mandatory
4	Patient location	Mandatory
5	Patient department/specialty	Mandatory
6	Patient admission date	Optional
7	Patient discharge date	Optional
8	Patient level of education	Optional
9	Patient weight and height	Optional
10	Pregnancy status	Optional
11	Premature birth	Optional
12	Whether the patient was transferred from another clinical set-up?	Optional
Patient clinical/health variables		
1	Chief complaint	Mandatory
2	Primary diagnosis at admission	Mandatory
3	ICD code	Mandatory
4	Comorbidities	Optional
5	Whether antibiotics were prescribed to patient prior to sampling; antibiotic(s) name and duration	Optional
6	Was the patient on an indwelling medical device at time of sampling; type of device	Optional
7	Origin of infection - community acquired or hospital acquired	Optional
8	Patient outcome at discharge (recovered/deteriorated/dead/others)	Optional

Laboratory-specific variables		
1	Laboratory's level of service (Reference- tier 3 or 4/ Regional/ Intermediate/ District/ Community/ Other	Mandatory
2	Laboratory's affiliation (Government/Ministry of Health/ Private/Non-government organisation/ Other)	Mandatory
3	Laboratory co-location with clinic/hospital/pharmacy	Mandatory
4	If laboratory served as a national AMR surveillance site at any time between 2016 and 2018?	Mandatory
5	Facility and Equipment related variables	Mandatory
6	Quality Assurance (QA), accreditation and certification related variables	Mandatory
7	Personnel and training related variables	Mandatory
8	Specimen management related variables	Mandatory
9	Laboratory information system and linkage to clinical data	Mandatory
Facility-specific variables (facility denotes co-located clinic/hospital or even from stand-alone laboratory as applicable; this information is obtained during phase of data collection)		
1	Ownership of facility (public/private/partnership/mission/military etc.)	Optional
2	Level of facility (primary, secondary, tertiary)	Optional
3	Facility co-location with pharmacy/lab	Optional
4	Number of inpatient beds in 2018 (and prior years as applicable)	Optional
5	Admissions in 2018 (and prior years as applicable)	Optional
6	Outpatients in 2018 (and prior years as applicable)	Optional
7	Presence of ID Department	Optional
8	No of ID physicians	Optional
9	No of ID nurses	Optional
10	Presence of AMS program	Optional
11	Frequency of AMS meetings	Optional
12	Presence of Medical therapeutic committee (MTC)	Optional
13	Frequency of MTC meet	Optional
14	Presence of HIC committee	Optional
15	Frequency of HIC meet	Optional
16	Number of bacterial cultures processed in 2018 (and prior years as applicable)	Optional
17	Number of fungal cultures processed in 2018 (and prior years as applicable)	Optional
18	Number of positive cerebrospinal fluid cultures in 2018 (and prior years as applicable)	Optional
19	Number of positive blood cultures in 2018 (and prior years as applicable)	Optional
20	Format for storing patient laboratory records	Optional
21	Format for storing patient clinical records	Optional

Appendix 5: WHO Priority Pathogens

Pathogen	Resistance	Priority
Acinetobacter baumannii	Carbapenem-resistant	Critical
Pseudomonas aeruginosa	Carbapenem-resistant	Critical
Enterobacterales*	Carbapenem-resistant, ESBL-producing	Critical
Enterococcus faecium	Vancomycin-resistant	High
Staphylococcus aureus	Methicillin-resistant, Vancomycin-intermediate and resistant	High
Helicobacter pylori	Clarithromycin-resistant	High
Campylobacter species	Fluoroquinolone-resistant	High
Neisseria gonorrhoeae	3rd generation Cephalosporin-resistant, Fluoroquinolone-resistant	High
Salmonellae	Fluoroquinolone-resistant	High
Shigella species	Fluoroquinolone-resistant	Medium
Streptococcus pneumoniae	Penicillin-non-susceptible	Medium
Hemophilus influenzae	Ampicillin-resistant	Medium

**Previously known as Enterobacteriaceae.*

Appendix 6: Other clinically important pathogens

Pathogen	Antimicrobial
Acinetobacter species*	Carbapenems Lipopeptides
Enterococcus species*	Aminoglycosides (high level) Vancomycin
E coli*	Carbapenems 3rd generation cephalosporins
H. influenzae*	Ampicillin 3rd generation cephalosporins
Klebsiella species*	Carbapenems 3rd generation cephalosporins
N. meningitidis*	Ampicillin 3rd generation cephalosporins
Pseudomonas species*	Carbapenems Lipopeptides
Salmonella species*	Fluoroquinolones Macrolides 3rd generation cephalosporins
Shigella species*	Fluoroquinolones Macrolides 3rd generation cephalosporins
Staphylococcus aureus*	Methicillin
Staphylococcus species* (other than S. aureus)	Methicillin
S. pneumoniae*	Penicillins Beta-lactam combinations Vancomycin Macrolides
Fungal pathogens**	(As per information available from countries)

*(ii) * from blood and CSF only; ** from all specimens*

Appendix 7: Pathogen Phenotype Definitions

Pathogen	Antimicrobial agent	Numerator	Denominator
Acinetobacter species	Lipopeptides (Colistin and Polymyxin B)	Any isolate that tested non-susceptible to colistin and polymyxin B	Any isolate that tested susceptible or non-susceptible to colistin and polymyxin B
Acinetobacter species	Carbapenems	Any isolate that tested non-susceptible to carbapenems	Any isolate that tested susceptible or non-susceptible to carbapenems
Campylobacter species	Fluoroquinolones	Any isolate that tested non-susceptible to fluoroquinolones	Any isolate that tested susceptible or non-susceptible to fluoroquinolones
Enterobacterales	3rd generation cephalosporins	Any isolate that tested non-susceptible to 3rd generation cephalosporins	Any isolate that tested susceptible or non-susceptible to 3rd generation cephalosporins
Enterobacterales	Carbapenems	Any isolate that tested non-susceptible to carbapenems	Any isolate that tested susceptible or non-susceptible to carbapenems
Enterobacterales	Fluoroquinolones	Any isolate that tested non-susceptible to fluoroquinolones	Any isolate that tested susceptible or non-susceptible to fluoroquinolones
Enterobacterales	Aminoglycosides	Any isolate that tested non-susceptible to aminoglycosides	Any isolate that tested susceptible or non-susceptible to aminoglycosides
Enterobacterales	Beta-lactam combinations including anti-pseudomonals	Any isolate that tested non-susceptible to beta-lactam combinations including anti-pseudomonals	Any isolate that tested susceptible or non-susceptible to beta-lactam combinations including anti-pseudomonals
Enterobacterales	Lipopeptides (Colistin and Polymyxin B)	Any isolate that tested non-susceptible to lipopeptides	Any isolate that tested susceptible or non-susceptible to lipopeptides
Enterobacterales	Ampicillin	Any isolate that tested non-susceptible to ampicillin	Any isolate that tested susceptible or non-susceptible to ampicillin
Enterobacterales	Sulfamethoxazole-Trimethoprim	Any isolate that tested non-susceptible to Sulfamethoxazole-Trimethoprim	Any isolate that tested susceptible or non-susceptible to Sulfamethoxazole-Trimethoprim
Enterobacterales	Macrolides	Any isolate that tested non-susceptible to macrolides	Any isolate that tested susceptible or non-susceptible to macrolides
Enterobacterales	Chloramphenicol	Any isolate that tested non-susceptible to chloramphenicol	Any isolate that tested susceptible or non-susceptible to chloramphenicol
Enterococcus species	Aminoglycosides (high level)	Any isolate that tested non-susceptible to aminoglycosides (high level)	Any isolate that tested susceptible or non-susceptible aminoglycosides (high level)
Enterococcus species	Quinopristin dalfopristin	Any isolate that tested non-susceptible to quinopristin dalfopristin	Any isolate that tested susceptible or non-susceptible to quinopristin dalfopristin
Enterococcus species	Vancomycin	Any isolate that tested non-susceptible to vancomycin	Any isolate that tested susceptible or non-susceptible to vancomycin
Enterococcus species	Ampicillin	Any isolate that tested non-susceptible to ampicillin	Any isolate that tested susceptible or non-susceptible to ampicillin
Haemophilus influenzae	Ampicillin	Any isolate that tested non-susceptible to ampicillin	Any isolate that tested susceptible or non-susceptible to ampicillin

Helicobacter pylori	Clarithromycin	Any isolate that tested non-susceptible to clarithromycin	Any isolate that tested susceptible or non-susceptible to clarithromycin
Neisseria gonorrhoeae	3rd generation cephalosporins	Any isolate that tested non-susceptible to 3rd generation cephalosporins	Any isolate that tested susceptible or non-susceptible to 3rd generation cephalosporins
Neisseria gonorrhoeae	Fluoroquinolones	Any isolate that tested non-susceptible to fluoroquinolones	Any isolate that tested susceptible or non-susceptible to fluoroquinolones
Pseudomonas species	Carbapenems	Any isolate that tested non-susceptible to carbapenems	Any isolate that tested susceptible or non-susceptible to carbapenems
Pseudomonas species	Aminoglycosides	Any isolate that tested non-susceptible to aminoglycosides	Any isolate that tested susceptible or non-susceptible to aminoglycosides
Pseudomonas species	Beta-lactam combinations (anti-pseudomonals)	Any isolate that tested non-susceptible to beta-lactam combinations (anti-pseudomonals)	Any isolate that tested susceptible or non-susceptible to beta-lactam combinations (anti-pseudomonals)
Pseudomonas species	Lipopeptides (Colistin and Polymyxin B)	Any isolate that tested non-susceptible to Colistin and Polymyxin B	Any isolate that tested susceptible or non-susceptible to Colistin and Polymyxin B
Pseudomonas species	Carbapenems	Any isolate that tested non-susceptible to carbapenems	Any isolate that tested susceptible or non-susceptible to carbapenems
Staphylococcus species	Methicillin	Any isolate that tested non-susceptible to penicillins (anti-staphylococcal) or cephamycins	Any isolate that tested susceptible or non-susceptible to penicillins (anti-staphylococcal) or cephamycins
Staphylococcus species (iii)	Vancomycin resistant (iv)	Any isolate that tested resistant to vancomycin (v)	Any isolate that tested susceptible or non-susceptible to vancomycin (vi)
Staphylococcus species	Vancomycin intermediate	Any isolate that tested intermediate to vancomycin	Any isolate that tested susceptible or non-susceptible to vancomycin
Staphylococcus species	Penicillins	Any isolate that tested non-susceptible to penicillins	Any isolate that tested susceptible or non-susceptible to penicillins
Staphylococcus species	Linezolid	Any isolate that tested non-susceptible to linezolids	Any isolate that tested susceptible or non-susceptible to linezolids
Streptococcus pneumoniae	Penicillins	Any isolate that tested non-susceptible to penicillins	Any isolate that tested susceptible or non-susceptible to penicillins
Gram-negatives*	3rd generation cephalosporins	Any isolate that tested non-susceptible to 3rd generation cephalosporins	Any isolate that tested susceptible or non-susceptible to 3rd generation cephalosporins
Gram-negatives*	Carbapenems	Any isolate that tested non-susceptible to carbapenems	Any isolate that tested susceptible or non-susceptible to carbapenems
Gram-negatives*	Lipopeptides (Colistin and Polymyxin B)	Any isolate that tested non-susceptible to Colistin and Polymyxin B.	Any isolate that tested susceptible or non-susceptible to Colistin and Polymyxin B.
Gram-positives*	Vancomycin	Any isolate that tested non-susceptible to vancomycin	Any isolate that tested susceptible or non-susceptible to vancomycin
Gram-positives*	Linezolid	Any isolate that tested non-susceptible to linezolids	Any isolate that tested susceptible or non-susceptible to linezolids

Note: Non-susceptible isolates include isolates which tested resistant or intermediate.

* Reflects pathogens for which only Gram stain identification was available (the number is exclusive of other pathogens identified at genus/species level).

Appendix 8: Pathogens and antimicrobials for AMR drivers and DRI

Pathogen	Antimicrobial
Acinetobacter baumannii	Aminoglycosides
Escherichia coli	Aminoglycosides
Klebsiella pneumoniae	Aminoglycosides
Pseudomonas aeruginosa	Aminoglycosides
Enterococcus faecalis	Aminoglycosides (High)
Enterococcus faecium	Aminoglycosides (High)
Enterococcus faecalis	Aminopenicillins
Enterococcus faecium	Aminopenicillins
Escherichia coli	Aminopenicillins
Acinetobacter baumannii	Carbapenems
Escherichia coli	Carbapenems
Klebsiella pneumoniae	Carbapenems
Pseudomonas aeruginosa	Carbapenems
Acinetobacter baumannii	Cephalosporins (3rd generation)
Escherichia coli	Cephalosporins (3rd generation)
Klebsiella pneumoniae	Cephalosporins (3rd generation)
Pseudomonas aeruginosa	Cephalosporins (3rd generation)
Acinetobacter baumannii	Fluoroquinolone
Escherichia coli	Fluoroquinolones
Klebsiella pneumoniae	Fluoroquinolones
Pseudomonas aeruginosa	Fluoroquinolones
Staphylococcus aureus	Methicillin
Pseudomonas aeruginosa	Beta-lactam combinations
Enterococcus faecalis	Vancomycin
Enterococcus faecium	Vancomycin

AMR Supplementary Tables

Supplementary Table 1: Level of service and affiliation of surveyed laboratories

Affiliation	Surveyed N=20 n (%)	Reference N = 4 n (%)	Regional/ Intermediate N =9 n (%)	District/ Community N = 3 n (%)	Unspecified N = 4 n (%)
Government	1 (33.33)	1 (100.0)	0	0	0
Private	1 (33.33)	0	0	0	1 (100.0)
NGO	0	0	0	0	0
Others	1 (33.33)	0	1 (100.0)	0	0

Supplementary Table 2: Assessment of preparedness for AMR surveillance

Parameters	Surveyed laboratories N=20 n (%)
Commodity and equipment status	
Regular power supply and functional back up	3 (100.0)
Continuous water supply	3 (100.0)
Certified and functional biosafety cabinets	3 (100.0)
Automated methods for pathogen identification	3 (100.0)
Automated methods for antimicrobial susceptibility testing	3 (100.0)
Methods for testing antimicrobial resistance mechanisms	3 (100.0)
QMS implementation	
Reported QMS Implementation	**3 (100.0)**
• Reported QMS tool (n=18)	
• LQMS	**1 (33.3)**
• SLIPTA	**0**
• SLMTA	**2 (67.7)**
• Mentoring	**0**
• Combination‡	**0**
• Others	**0**
Quality Certification	**3 (100.0)**
• Reported certification type (n=16)	
• SLIPTA	**2 (67.6)**
• College of American Pathologists	**0**
• Others	**1 (33.3)**
Accreditation	1 (33.3)
Participation in proficiency testing	3 (100.0)
Utilization of reference strains	3 (100.0)
Reported consistent maintenance of QC records	3 (100.0)
Designated focal quality person	3 (100.0)
Reported compliance to standard operating procedures	3 (100.0)
Reported compliance to antimicrobial susceptibility testing standards	3 (100.0)
Personnel and training status	
Presence of at least one qualified microbiologist	3 (100.0)
Presence of an experienced laboratory scientist/technologist	3 (100.0)
Up-to-date and complete records on staff training and competence	3 (100.0)
Specimen Management status	
Reported compliance to standard operating procedures on specimen collection and testing	3 (100.0)
Reported compliance to standard operating procedures on specimen rejection	3 (100.0)
Availability on average number of specimens processed for culture and sensitivity in year 2018	-
Laboratory Information System and Linkage to Clinical Data	
Assigned specimen (laboratory) identification number	3 (100.0)
Availability of system/database to store patient data	3 (100.0)
• System/database format (n=19)	
• Paper-based	0
• Electronic	3 (100.0)
• Mixed	0
Captured patients' demographics and clinical information on test request forms	3 (100.0)
• Retrievable test request forms (n=20)	3 (100.0)

*Data reflect laboratory functions between years 2016 - 2018; ‡ Combination refers to more than one option presented in the questionnaire (LQMS, SLIPTA, SLMTA and mentoring).

Supplementary Table 3: Culture characteristics (yearly)

Variable		Valid			Positive			Positive with AS		
		2016	2017	2018	2016	2017	2018	2016	2017	2018
Annual Totals		1343	2236	5807	1340	2233	1717	1339	2231	1677
Pathogen type	bacteria				1327 (99.0)	2218 (99.3)	1686 (98.2)	1326 (99.0)	2216 (99.3)	1660 (99.0)
	fungi				13 (1.0)	15 (0.7)	31 (1.8)	13 (1.0)	15 (0.7)	17 (1.0)
Age, years	Less than 1	154 (11.5)	195 (8.7)	320 (5.5)	154 (11.5)	195 (8.7)	126 (7.3)	154 (11.5)	194 (8.7)	124 (7.4)
	1 to 17	171 (12.7)	345 (15.4)	754 (13.0)	170 (12.7)	344 (15.4)	263 (15.3)	169 (12.6)	344 (15.4)	259 (15.4)
	18 to 49	633 (47.1)	1045 (46.7)	2863 (49.3)	631 (47.1)	1044 (46.8)	851 (49.6)	631 (47.1)	1044 (46.8)	829 (49.4)
	50 to 65	196 (14.6)	292 (13.1)	850 (14.6)	196 (14.6)	291 (13.0)	235 (13.7)	196 (14.6)	291 (13.0)	231 (13.8)
	Above 65	106 (7.9)	207 (9.3)	460 (7.9)	106 (7.9)	207 (9.3)	175 (10.2)	106 (7.9)	207 (9.3)	171 (10.2)
	Unknown Age	83 (6.2)	152 (6.8)	560 (9.6)	83 (6.2)	152 (6.8)	67 (3.9)	83 (6.2)	151 (6.8)	63 (3.8)
Gender	Male	489 (36.4)	854 (38.2)	2315 (39.9)	488 (36.4)	851 (38.1)	699 (40.7)	488 (36.4)	850 (38.1)	685 (40.8)
	Female	854 (63.6)	1382 (61.8)	3492 (60.1)	852 (63.6)	1382 (61.9)	1018 (59.3)	851 (63.6)	1381 (61.9)	992 (59.2)
Laboratory	Lancet	625 (46.5)	586 (26.2)	4682 (80.6)	625 (46.6)	586 (26.2)	603 (35.1)	624 (46.6)	586 (26.3)	565 (33.7)
	Mbabane	511 (38.0)	1431 (64.0)	967 (16.7)	511 (38.1)	1429 (64.0)	960 (55.9)	511 (38.2)	1427 (64.0)	958 (57.1)
	RFM	207 (15.4)	219 (9.8)	158 (2.7)	204 (15.2)	218 (9.8)	154 (9.0)	204 (15.2)	218 (9.8)	154 (9.2)

Supplementary Table 4: Specimen characteristics

Specimen Type	All years* N= 5247 n (%)	2016 N = 1339 n (%)	2017 N = 2231 n (%)	2018 N = 1677 n (%)
Abscess/Discharge/Pus/Swab/Wound	1651 (31.5)	284 (21.2)	745 (33.4)	622 (37.1)
Aspirate/discharge	29 (0.6)	5 (0.4)	11 (0.5)	13 (0.8)
Blood	535 (10.2)	188 (14)	235 (10.5)	112 (6.7)
Catheter (central line)	1 (0)	-	-	1 (0.1)
Catheter (umbilical)	1 (0)	-	1 (0)	-
Catheter (unspecified)	167 (3.2)	49 (3.7)	69 (3.1)	49 (2.9)
Catheter (urinary)	4 (0.1)	-	1 (0)	3 (0.2)
CSF	47 (0.9)	16 (1.2)	20 (0.9)	11 (0.7)
Drain	1 (0)	1 (0.1)	-	-
Fluid (abdominal/peritoneal)	4 (0.1)	1 (0.1)	2 (0.1)	1 (0.1)
Fluid (Gastric)	7 (0.1)	1 (0.1)	5 (0.2)	1 (0.1)
Fluid (joint/synovial)	3 (0.1)	-	1 (0)	2 (0.1)
Fluid (pleural)	17 (0.3)	3 (0.2)	7 (0.3)	7 (0.4)
Fluid (scrotal)	2 (0)	1 (0.1)	1 (0)	-
Fluid (unspecified)	38 (0.7)	4 (0.3)	21 (0.9)	13 (0.8)
Genitourinary	11 (0.2)	1 (0.1)	8 (0.4)	2 (0.1)
Other	17 (0.3)	-	-	17 (1)
Respiratory-Lower	11 (0.2)	6 (0.4)	4 (0.2)	1 (0.1)
Respiratory-Upper	149 (2.8)	35 (2.6)	63 (2.8)	51 (3)
Semen	11 (0.2)	-	7 (0.3)	4 (0.2)
Stool	132 (2.5)	42 (3.1)	66 (3)	24 (1.4)
Swab (cervical)	1 (0)	-	1 (0)	-
Swab (rectal)	2 (0)	1 (0.1)	-	1 (0.1)
Swab (urethral)	28 (0.5)	9 (0.7)	9 (0.4)	10 (0.6)
Swab (vaginal)	399 (7.6)	96 (7.2)	181 (8.1)	122 (7.3)
Tissue/biopsy	14 (0.3)	3 (0.2)	8 (0.4)	3 (0.2)
Ulcer	6 (0.1)	2 (0.1)	-	4 (0.2)
Unknown	46 (0.9)	20 (1.5)	26 (1.2)	-
Urine	1913 (36.5)	571 (42.6)	739 (33.1)	603 (36)

**Indicates positive cultures with AST results*

Supplementary Table 5: Pathogen identification

Pathogen	All years* N= 5247 n (%)	2016 N = 1339 n (%)	2017 N = 2231 n (%)	2018 N = 1677 n (%)
Positive cultures with specific pathogen name	**3802 (72.5)**	**988 (73.8)**	**1641 (73.6)**	**1173 (69.9)**
Acinetobacter baumannii	48 (0.9)	5 (0.4)	24 (1.1)	19 (1.1)
Acinetobacter haemolyticus	1 (0)	1 (0.1)	-	-
Acinetobacter lwoffii	2 (0)	1 (0.1)	1 (0)	-
Aeromonas hydrophila	23 (0.4)	3 (0.2)	4 (0.2)	16 (1)
Aeromonas salmonicida	1 (0)	-	1 (0)	-
Alcaligenes faecalis	1 (0)	-	1 (0)	-
Burkholderia cepacia	14 (0.3)	1 (0.1)	1 (0)	12 (0.7)
Burkholderia pseudomallei	1 (0)	-	1 (0)	-
Campylobacter coli	1 (0)	-	-	1 (0.1)
Campylobacter jejuni	1 (0)	-	-	1 (0.1)
Candida albicans	17 (0.3)	6 (0.4)	2 (0.1)	9 (0.5)
Candida glabrata	1 (0)	-	1 (0)	-
Candida lusitaniae	1 (0)	1 (0.1)	-	-
Candida parapsilosis	6 (0.1)	1 (0.1)	2 (0.1)	3 (0.2)
Chryseomonas luteola	4 (0.1)	1 (0.1)	3 (0.1)	-
Citrobacter freundii	29 (0.6)	3 (0.2)	13 (0.6)	13 (0.8)
Citrobacter koseri	20 (0.4)	2 (0.1)	9 (0.4)	9 (0.5)
Clostridium bifermentans	2 (0)	1 (0.1)	1 (0)	-
Clostridium difficile	4 (0.1)	-	4 (0.2)	-
Clostridium innocuum	1 (0)	-	1 (0)	-
Clostridium subterminale	1 (0)	-	1 (0)	-
Corynebacterium jeikeium	2 (0)	-	2 (0.1)	-
Corynebacterium striatum	1 (0)	-	1 (0)	-
Cronobacter sakazakii	3 (0.1)	-	-	3 (0.2)
Cryptococcus laurentii	1 (0)	-	-	1 (0.1)
Cryptococcus neoformans	16 (0.3)	4 (0.3)	8 (0.4)	4 (0.2)
Enterobacter cloacae	51 (1)	8 (0.6)	29 (1.3)	14 (0.8)
Enterobacter gergoviae	2 (0)	1 (0.1)	-	1 (0.1)
Enterococcus faecalis	116 (2.2)	21 (1.6)	72 (3.2)	23 (1.4)
Enterococcus faecium	19 (0.4)	7 (0.5)	12 (0.5)	-
Enterococcus gallinarum	3 (0.1)	1 (0.1)	-	2 (0.1)
Escherichia coli	1376 (26.2)	430 (32.1)	554 (24.8)	392 (23.4)

Escherichia vulneris	7 (0.1)	-	-	7 (0.4)
Haemophilus influenzae	2 (0)	-	1 (0)	1 (0.1)
Haemophilus parainfluenzae	3 (0.1)	2 (0.1)	-	1 (0.1)
Kingella denitrificans	1 (0)	-	1 (0)	-
Klebsiella aerogenes	56 (1.1)	31 (2.3)	14 (0.6)	11 (0.7)
Klebsiella oxytoca	44 (0.8)	10 (0.7)	23 (1)	11 (0.7)
Klebsiella pneumoniae	171 (3.3)	48 (3.6)	90 (4)	33 (2)
Kocuria kristinae	1 (0)	-	-	1 (0.1)
Leuconostoc pseudomesenteriodes	1 (0)	-	-	1 (0.1)
Micrococcus luteus	1 (0)	-	-	1 (0.1)
Moraxella catarrhalis	6 (0.1)	2 (0.1)	4 (0.2)	-
Morganella morganii	13 (0.2)	2 (0.1)	7 (0.3)	4 (0.2)
Neisseria cinerea	3 (0.1)	-	2 (0.1)	1 (0.1)
Neisseria gonorrhoeae	30 (0.6)	9 (0.7)	14 (0.6)	7 (0.4)
Neisseria meningitidis	1 (0)	-	1 (0)	-
Pantoea (Enterobacter) agglomerans	6 (0.1)	-	-	6 (0.4)
Pasteurella pneumotropica	1 (0)	-	-	1 (0.1)
Propionibacterium acnes	1 (0)	-	1 (0)	-
Proteus mirabilis	224 (4.3)	71 (5.3)	111 (5)	42 (2.5)
Proteus penneri	11 (0.2)	3 (0.2)	4 (0.2)	4 (0.2)
Proteus vulgaris	20 (0.4)	3 (0.2)	11 (0.5)	6 (0.4)
Providencia rettgeri	5 (0.1)	-	3 (0.1)	2 (0.1)
Providencia stuartii	2 (0)	-	-	2 (0.1)
Pseudomonas aeruginosa	142 (2.7)	34 (2.5)	70 (3.1)	38 (2.3)
Pseudomonas alcaligenes	1 (0)	-	1 (0)	-
Pseudomonas fluorescens	12 (0.2)	4 (0.3)	8 (0.4)	-
Pseudomonas putida	3 (0.1)	-	3 (0.1)	-
Ralstonia pickettii	1 (0)	1 (0.1)	-	-
Raoultella ornithinolytica	2 (0)	2 (0.1)	-	-
Rhizobium radiobacter	2 (0)	-	1 (0)	1 (0.1)
Salmonella enterica	9 (0.2)	4 (0.3)	2 (0.1)	3 (0.2)
Serratia ficaria	1 (0)	-	-	1 (0.1)
Serratia fonticola	8 (0.2)	1 (0.1)	6 (0.3)	1 (0.1)
Serratia liquefaciens	6 (0.1)	1 (0.1)	-	5 (0.3)
Serratia marcescens	22 (0.4)	4 (0.3)	8 (0.4)	10 (0.6)
Serratia odorifera	54 (1)	3 (0.2)	10 (0.4)	41 (2.4)

Serratia plymuthica	1 (0)	-	1 (0)	-
Shigella sonnei	7 (0.1)	-	4 (0.2)	3 (0.2)
Sphingomonas paucimobilis	3 (0.1)	1 (0.1)	2 (0.1)	-
Staphylococcus aureus	914 (17.4)	198 (14.8)	396 (17.7)	320 (19.1)
Staphylococcus epidermidis	56 (1.1)	25 (1.9)	16 (0.7)	15 (0.9)
Staphylococcus haemolyticus	43 (0.8)	3 (0.2)	26 (1.2)	14 (0.8)
Staphylococcus intermedius	2 (0)	2 (0.1)	-	-
Staphylococcus lugdunensis	9 (0.2)	1 (0.1)	5 (0.2)	3 (0.2)
Staphylococcus pseudintermedius	1 (0)	-	-	1 (0.1)
Staphylococcus saprophyticus	58 (1.1)	9 (0.7)	15 (0.7)	34 (2)
Staphylococcus xylosus	1 (0)	-	-	1 (0.1)
Stenotrophomonas (Xanthomonas) maltophilia	2 (0)	-	2 (0.1)	-
Streptococcus agalactiae	12 (0.2)	1 (0.1)	7 (0.3)	4 (0.2)
Streptococcus alactolyticus	1 (0)	-	-	1 (0.1)
Streptococcus anginosus	1 (0)	-	1 (0)	-
Streptococcus bovis	1 (0)	1 (0.1)	-	-
Streptococcus milleri	3 (0.1)	1 (0.1)	1 (0)	1 (0.1)
Streptococcus mitis	1 (0)	-	1 (0)	-
Streptococcus pneumoniae	16 (0.3)	4 (0.3)	8 (0.4)	4 (0.2)
Streptococcus pyogenes	13 (0.2)	6 (0.4)	7 (0.3)	-
Streptococcus salivarius	1 (0)	-	-	1 (0.1)
Streptococcus viridans	8 (0.2)	2 (0.1)	2 (0.1)	4 (0.2)
Vibrio parahaemolyticus	2 (0)	-	1 (0)	1 (0.1)
Yersinia enterocolitica	4 (0.1)	1 (0.1)	2 (0.1)	1 (0.1)
Positive cultures with non-specific pathogen name	**1445 (27.5)**	**351 (26.2)**	**590 (26.4)**	**504 (30.1)**
Achromobacter Species	3 (0.1)	1 (0.1)	2 (0.1)	-
Acinetobacter Species	7 (0.1)	-	6 (0.3)	1 (0.1)
Actinobacillus Species	1 (0)	-	1 (0)	-
Aerococcus Species	3 (0.1)	1 (0.1)	2 (0.1)	-
Aeromonas Species	1 (0)	-	1 (0)	-
Bacillus Species	2 (0)	-	-	2 (0.1)
Campylobacter Species	2 (0)	-	-	2 (0.1)
Candida Species	1 (0)	-	1 (0)	-
Citrobacter Species	6 (0.1)	-	1 (0)	5 (0.3)
Clostridium Species	2 (0)	-	1 (0)	1 (0.1)

Corynebacterium Species	3 (0.1)	3 (0.2)	-	-
Enterobacter Species	5 (0.1)	-	3 (0.1)	2 (0.1)
Enterococcus Species	20 (0.4)	2 (0.1)	11 (0.5)	7 (0.4)
Erwinia Species	2 (0)	-	-	2 (0.1)
Granulicatella Species	1 (0)	-	-	1 (0.1)
Haemophilus Species	1 (0)	1 (0.1)	-	-
Hafnia Species	3 (0.1)	1 (0.1)	-	2 (0.1)
Klebsiella Species	41 (0.8)	12 (0.9)	15 (0.7)	14 (0.8)
Leuconostoc Species	1 (0)	-	1 (0)	-
Micrococcus Species	4 (0.1)	-	2 (0.1)	2 (0.1)
Moraxella Species	1 (0)	-	-	1 (0.1)
Neisseria Species	2 (0)	1 (0.1)	1 (0)	-
Non fermenting gram negative bacilli	30 (0.6)	-	12 (0.5)	18 (1.1)
Proteus Species	85 (1.6)	17 (1.3)	35 (1.6)	33 (2)
Pseudomonas Species	66 (1.3)	22 (1.6)	19 (0.9)	25 (1.5)
Rhizopus Species	1 (0)	1 (0.1)	-	-
Salmonella Species	9 (0.2)	3 (0.2)	4 (0.2)	2 (0.1)
Serratia Species	3 (0.1)	1 (0.1)	1 (0)	1 (0.1)
Shigella Species	5 (0.1)	1 (0.1)	1 (0)	3 (0.2)
Staphylococcus Species	368 (7)	110 (8.2)	147 (6.6)	111 (6.6)
Stemphylium Species	1 (0)	-	1 (0)	-
Streptococcus Species	128 (2.4)	57 (4.3)	44 (2)	27 (1.6)
Unspecified (Gram negative bacteria)	479 (9.1)	85 (6.3)	194 (8.7)	200 (11.9)
Unspecified (Gram negative cocci)	4 (0.1)	2 (0.1)	1 (0)	1 (0.1)
Unspecified (Gram positive bacteria)	11 (0.2)	6 (0.4)	3 (0.1)	2 (0.1)
Unspecified (Gram positive cocci)	139 (2.6)	24 (1.8)	79 (3.5)	36 (2.1)
Unspecified (Gram positive coccobacilli)	1 (0)	-	1 (0)	-
Yersinia Species	3 (0.1)	-	-	3 (0.2)

*Note: * indicates positive cultures with AST results; '-' means information was not available.*

Supplementary Table 6: Laboratory data scoring

Laboratory name	Laboratory data score (out of 4)			
	2016	2017	2018	Average
Lancet	4	4	4	4
Mbabane	4	3	3	3.3
RFM	2	3	2	2.3

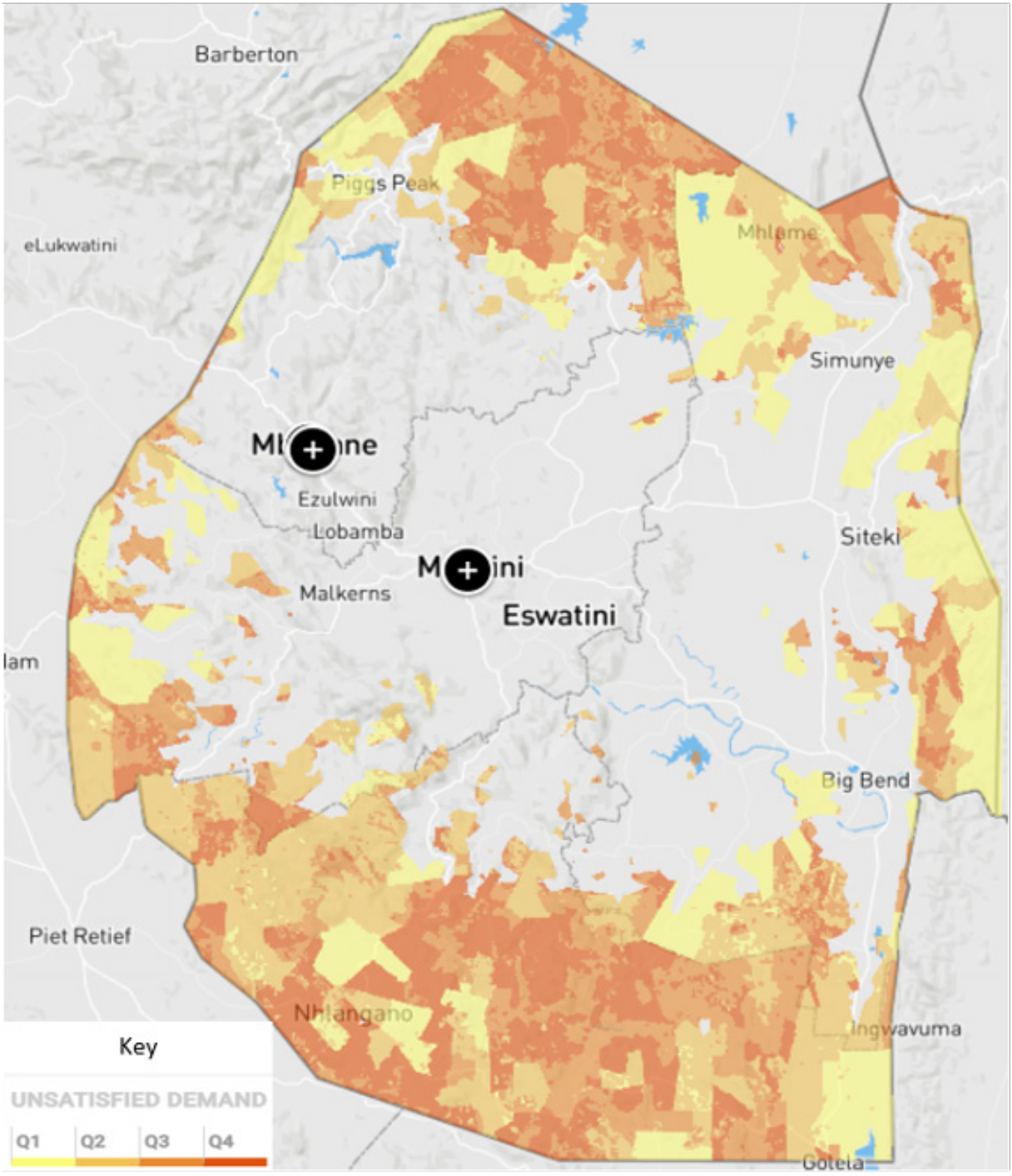
Supplementary Table 7: Univariate logistic regression analysis

Variable	Options	N	NS (%)	Crude OR (95% CI)	P-value
Gender	Female	5470	30.5	Ref	0.000
	Male	2204	40.0	1.51 (1.31 - 1.74)	
Age, years	<1	407	45.7	1.91 (1.07 - 3.41)	0.004
	1-17	929	36.4	1.29 (0.93 - 1.82)	
	18-49	3989	30.6	Ref	
	50-65	1277	35.1	1.22 (1.01 - 1.49)	
	>65	888	34.4	1.19 (0.97 - 1.46)	

N-number of tested isolates; NS (%)-Proportion of non-susceptible isolates; Ref: Reference category

AMR Supplementary Figures

Supplementary Figure 1: Population coverage of laboratories



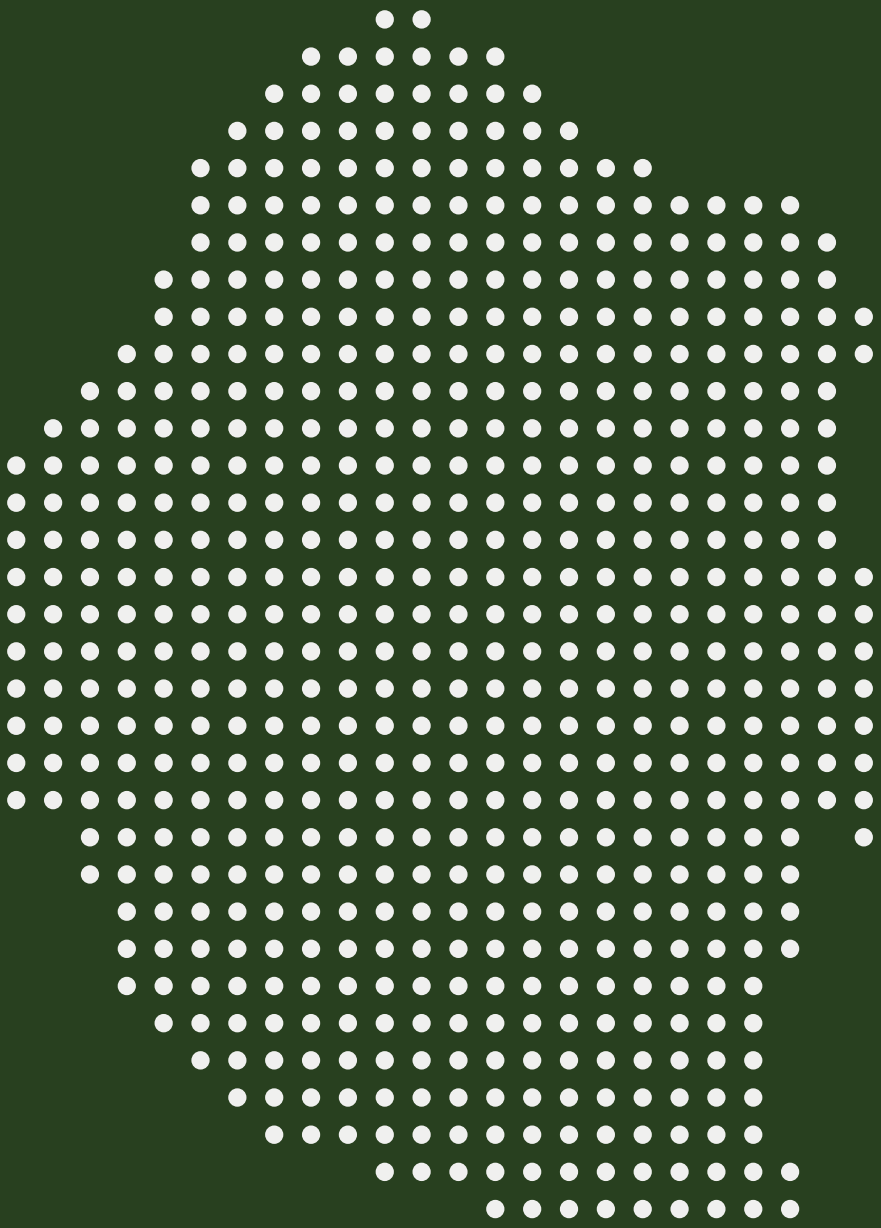
Supplementary Figure 2a: Inappropriate testing A

Organism Name	Antimicrobial Agent	Agent Code	Interpreted Results	Antimicrobial Susceptibility Method	Year
Rhizopus sp.	Ampicillin	AMB_ND10	R	Disk	2016
Rhizopus sp.	Nalidixic acid	NAL_ND30	R	Disk	2016
Candida albicans	Amikacin	AMK_ND30	S	Disk	2016
Candida albicans	Ampicillin	AMP_ND10	S	Disk	2016
Candida albicans	Imipenem	IPM_ND10	S	Disk	2016
Candida albicans	Nitrofurantoin	NIT_ND300	S	Disk	2016
Candida albicans	Tigecycline	TGC_ND15	S	Disk	2016
Candida sp.	Ampicillin	AMP_ND10	R	Disk	2017
Candida sp.	Doxycycline	DOX_ND30	R	Disk	2017
Candida sp.	Gentamicin	GEN_ND10	R	Disk	2017
Candida sp.	Nalidixic acid	NAL_ND30	R	Disk	2017
Candida albicans	Tetracyclines	TCY_ND30	R	Disk	2017
Candida albicans	Ciprofloxacin	CIP_ND5	S	Disk	2017
Stemphylium	Ciprofloxacin	CIP_ND5	S	Disk	2017
Cryptococcus laurentii	Ceftriaxone	CRO_ND30	R	Disk	2018
Cryptococcus laurentii	Cefotaxime	CTX_30	R	Disk	2018
Candida albicans	Tetracyclines	TCY_ND30	R	Disk	2018
Cryptococcus laurentii	Imipenem	IPM_ND10	S	Disk	2018
Candida albicans	Ciprofloxacin	CIP_ND5	S	Disk	2018

Supplementary Figure 2b: Inappropriate testing B

Organism Name	Antimicrobial Agent	Agent Code	Interpreted Results	Antimicrobial Susceptibility Method	Year
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Proteus mirabilis	Oxacillin	OXA_ND1	R	Disk	2016
Proteus mirabilis	Oxacillin	OXA_ND1	I	Disk	2016
Proteus mirabilis	Oxacillin	OXA_ND1	S	Disk	2016
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	S	Disk	2017
Proteus mirabilis	Oxacillin	OXA_ND1	R	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2018
Proteus sp.	Oxacillin	OXA_ND1	R	Disk	2018
Proteus sp.	Penicillin G	PEN_ND10	R	Disk	2018
Klebsiella oxytoca	Penicillin G	PEN_ND10	R	Disk	2018
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2016
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2016
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2016
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	I	Disk	2016
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2016
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	I	Disk	2017
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2017
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2017
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2017
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2018
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	I	Disk	2018
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2018
Staphylococcus aureus ss aureus	Vancomycin	VAN_ND30	R	Disk	2018

AMC Appendices



Appendix 1: Key Informant Interview (KII) tool

(Contains ALL questions: However, during implementation, only specific questions were asked to suitable stakeholders)

Domestic Producers and Importers

1.1	What quantity/proportion of antibiotics are produced/manufactured (if any) within the country?	N/A
1.2	If domestically produced what manufactured quantity is later exported?	
1.3	What quantity/proportion of antibiotics are imported?	
1.4	What proportion (if any) are then re-exported?	

Procurement, Storage and Distribution

1.5	Are there any specific regulations regarding Procurement and/or storage of antibiotics?	Yes		No	

Public Sector

1.6	Who supplies to the public sector (names of the companies/organisations)?
1.7	What role (if any) does the Central Medical Stores play in the procurement, storage and distribution of antibiotics in the country?
1.8	What quantity/proportion of antibiotics is purchased by public healthcare facilities from central medical stores and what quantity/ proportion from wholesalers/other suppliers? (specify who these other suppliers are)
1.9	How do public facilities procure and receive their antibiotic supplies?

Private Sector

1.10	Who supplies to the private sector (names of the companies/organisations)?
1.11	What quantity/proportion of antibiotics is purchased by Private healthcare facilities from central medical stores and what quantity/ proportion from wholesalers/other suppliers? (specify who these other suppliers are)
1.12	How do private facilities procure and receive their antibiotic supplies?

Donor Funded Supply

1.13	Is there any donor support for procurement of antibiotics in the country?	Yes		No	
1.14	If yes to above, who are the donors and what are the procedures regarding import and distribution of donated antibiotics?				
1.15	Which sector(s) is supported with supplies procured through donor agencies?				
	Public Sector		Private		
1.16	If there is donor support, are antibiotics sourced locally or imported?				
1.17	Does the available donor data indicate specific country antibiotic consumption? Do these procurement mechanisms fit in with the countries regulatory systems and WHOs recommended surveillance practices? or are there challenges?				
1.18	What proportion/quantity of antibiotics are procured/supplied from donor programs; and using which mechanisms are such products procured e.g., WAMBO for The Global Fund, pooled procurement mechanisms etc.				
1.19	What are the requirements and procedures for suppliers to import/export antibiotics in the country?				

2. Data and Information Systems

2.1	What information systems are currently in use at **national level** for managing data on antibiotics?						
2.2	Are the systems manual or electronic?						
Manual				Electronic			
2.3	What type of information is captured using these systems? (e.g. generic names, dose strengths, formulations, pack size, brand names and volumes)						
Generic names		Dose strengths		Formulations		Pack size/ Volumes	
Brand names		Other:					
2.4	Does the country have a centralised data source for all antibiotics that are imported/exported?						
No		Yes, manual data system		Yes, electronic data system			
2.5	What are the available data sources to quantify antibiotic consumption at **facility level** (records from pharmacies, data from health insurance programs, prescribing records of physicians, dispensing records of pharmacists etc.)?						
2.6	What are the available data sources to quantify antibiotic consumption at **sub – national level** (records from pharmacies, data from health insurance programs, prescribing records of physicians, dispensing records of pharmacists etc.)?						
2.7	What are the available data sources to quantify antibiotic consumption at **the national level** (records from pharmacies, data from health insurance programs, prescribing records of physicians, dispensing records of pharmacists etc.)?						
2.8	What challenges (if any) are faced in terms of data availability on antibiotics?						
2.9	Do public sector healthcare providers have LMIS to monitor and retrieve data of logistics of antibiotics? How is it managed and what data does it gather and for what use?				Yes		No

3. Informal Supply Chains

3.1	Is there an estimate of the antibiotic black-market size in the country?
3.2	Are there any mechanisms utilized by relevant authorities to track and trace illegally imported antibiotics in the country?

Appendix 2: Eligibility questionnaire for pharmacies

Purpose:
To determine eligibility of community pharmacies for data collection Antimicrobial Consumption (AMC)

Instructions

Pre-requisite for administering the Questionnaire:
List of public hospitals/ private facilities where the laboratories are situated/ where eligibility of laboratories is being tested
Contact details of pharmacy situated within/ connected to the above public/ private hospital
Mode of administering the Questionnaire:
Administered over email and/ or over the phone

Eligibility questionnaire for Community Pharmacies:

A. General information				
1. What is the name and complete address of your pharmacy?				
2. Does the pharmacy house a laboratory?	Yes		No	
3. Does the pharmacy have relevant certification/ accreditation (in example by the pharmacy and poison board etc.)	Yes		No	
4. Did the pharmacy have the following in place at any time between 2016-18?				
4.1 At least one Pharmacist	Yes		No	
4.2 At least one pharmacy technician	Yes		No	
4.3 Are there SOPs in place for entering issues / sales of antibiotics?	Yes		No	
B. Antibiotic Consumption Data				
1. Are the following data at the pharmacy stored electronically? (State Y/N for each)				
2. Sales of antibiotics to patients/customers	Yes		No	
3. Purchases (from wholesalers/distributors/open markets etc.)	Yes		No	
4. Current stock in hand of antibiotics (at end of month)	Yes		No	
5. No electronic records are maintained	Yes		No	
6. If answer is YES to Q5, how far back in time do the electronic records exist (indicate start month and year – for 2018, 2017 and 2016 for each of the below)?				
7. Sales to patients/customers	Month:			
	Year:			
8. Purchases (from wholesalers/distributors/open markets etc.)	Month:			
	Year:			
9. Current stock in hand of medicines (at end of each month)	Month:			
	Year:			
10. As a follow up to Q6, is it possible to extract historical data (for 2018, 2017, 2016 or part thereof) in excel, CSV or any other format from electronic pharmacy system? (State Y/N for each)				
11. Sales to patients, customers and/ or Prescriptions	Yes		No	
12. Purchases (from wholesalers/distributors/open markets etc.)	Yes		No	
13. Current stock of medicines (at end of each month)	Yes		No	
14. If answer is NO to Q5, does the pharmacy manually hold paper-based data for medicines? (State Y/N for each)				
15. Sales to patients/customers	Yes		No	

16. Purchases from wholesalers/distributors etc.	Yes		No	
17. Current stock in hand of medicines	Yes		No	
18. How far back in time do the manual/ paper-based records exist for the following (indicate start month and year – for 2018, 2017 and 2016 for each of the below)?				
19. Sales to patients/customers	Month:			
	Year:			
20. Purchases (from wholesalers/distributors/open markets etc.)	Month:			
	Year:			
21. Current stock in hand of medicines	Month:			
	Year:			
22. What records can be used for historical data extraction for antibiotic sales? (State Y/N for each option)				
23. Sales invoices / prescriptions to customers/patients (sell-out)	Yes		No	
24. Supplier invoices received by pharmacy (sell-in)	Yes		No	
25. Any other (please state)	Yes		No	
26. What kind of stock control system does the pharmacy store maintain? (State Y/N for each option)				
27. Issues/ sales book	Yes		No	
28. Stock card/Bin Card	Yes		No	
29. Electronic	Yes		No	
30. Any other (please state)	Yes		No	
31. In case of dispensing antibiotics to patients, can the pharmacy trace if there was a prescription?	Yes		No	

Based on historical data, will it be possible to obtain month-wise disaggregated data for the following fields for 2018, 2017 and 2016?	In the table below just indicate Y/N to understand availability of the kind of data – DO NOT fill actual data for now

Antibiotic Name	Form* (Tablets, Vials, Capsules, Syrup etc.)	Strength* (in MG)	Pack* size	Manufacturer	Data available for- No. of units DISPENSED in a month	Data available for- No. of units PURCHASED in a month	Data available for- Stock in Hand end of each month
AMOXICILLIN	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N

* A single antibiotic may come in different forms, with different strength and in different pack sizes. Idea here is to understand whether consumption / purchase data can be made available at the pharmacy for each of the different form-strength-pack size combinations. For instance, Amoxicillin 'Capsules' (form) '250 mg' (strength) '100' (pack size) will be one row, and so on.

Stock out status of antibiotics (State Y/N to each of the below statements)				
a. Is there often a stock-out of antibiotics at the pharmacy?	Yes		No	
b. If yes to a, is a record of the stocked-out antibiotics maintained?	Yes		No	
c. In case some antibiotic is out of stock or not available, how do patients purchase that medicine generally?	Yes		No	
d. Purchase from the public hospital pharmacy	Yes		No	
e. Purchase from nearby other private pharmacy	Yes		No	
f. Purchase from private pharmacy near their residence	Yes		No	
g. Purchase from the market	Yes		No	

Appendix 3: Harmonised list of antimicrobials to be included in data collection

Antimicrobial name	WHO ATC Index	A/W/R/U category
Acetyl Kitasamycin	J01	U
Acetylspiramycin	J01	W
Alatrofloxacin	J01	U
Amoxicillin/Ampicillin	J01	U
Amoxicillin/Cloxacillin	J01	U
Amoxicillin/Dicloxacillin	J01	U
Amoxicillin/Flucloxacillin	J01	U
Amoxicillin/Metronidazole	J01	U
Amoxicillin/Sulbactam	J01	A
Ampicillin/Cloxacillin	J01	U
Ampicillin/Dicloxacillin	J01	U
Ampicillin/Flucloxacillin	J01	U
Ampicillin/Oxacillin	J01	U
Ampicillin/Sulbactam	J01	A
Ampicillin/Sultamicillin	J01	A
Antofloxacin	J01	W
Astromicin	J01	W
Balofloxacin	J01	W
Benzylpenicillin/Phenoxymethylpenicillin	J01	A
Benzylpenicillin/Phenoxymethylpenicillin/Streptomycin	J01	U
Benzylpenicillin/Streptomycin	J01	U
Bleomycin A5	J01	U
Cefadroxil/Clavulanic Acid	J01	A
Cefathiamidine	J01	A
Cefepime/Sulbactam	J01	U
Cefepime/Tazobactam	J01	U
Cefixime/Azithromycin	J01	U
Cefixime/Cefpodoxime	J01	U
Cefixime/Clavulanic Acid	J01	W
Cefixime/Cloxacillin	J01	U
Cefixime/Dicloxacillin	J01	U
Cefixime/Levofloxacin	J01	U
Cefixime/Linezolid	J01	U
Cefixime/Moxifloxacin	J01	U
Cefixime/Ofloxacin	J01	U
Cefixime/Sulbactam	J01	U
Cefoperazone/Sulbactam	J01	U
Cefoperazone/Tazobactam	J01	U
Cefoselis	J01	R

Cefotaxime/Sulbactam	J01	U
Cefpodoxime/Azithromycin	J01	U
Cefpodoxime/Cloxacillin	J01	U
Cefpodoxime/Dicloxacillin	J01	U
Cefpodoxime/Levofloxacin	J01	W
Cefpodoxime/Ofloxacin	J01	W
Ceftazidime/Avibactam	J01	R
Ceftazidime/Sulbactam	J01	U
Ceftazidime/Tazobactam	J01	U
Ceftazidime/Tobramycin	J01	U
Ceftizoxime/Tazobactam	J01	U
Ceftolozane	J01	R
Ceftriaxone/Sulbactam	J01	U
Ceftriaxone/Tazobactam	J01	U
Ceftriaxone/Vancomycin	J01	U
Cefuroxime/Clavulanic Acid	J01	W
Cefuroxime/Linezolid	J01	U
Cefuroxime/Sulbactam	J01	U
Cephalosporin C	J01	U
Ciclacillin	J01	U
Erythromycin Stearate	J01	U
Erythromycin Stinoprate	J01	U
Etimicin	J01	W
Furbenicillin	J01	W
Guamecycline	J01	U
Imipenem	J01	U
Kitasamycin	J01	U
Lenampicillin	J01	U
Levofloxacin/Azithromycin	J01	W
Levofloxacin/Metronidazole	J01	U
Meleumycin	J01	U
Meropenem/Sulbactam	J01	U
Norvancomycin	J01	W
Novobiocin	J01	U
Ofloxacin/Azithromycin	J01	U
Panipenem	J01	W
Piperacillin/Sulbactam	J01	U
Piperacillin/Tazobactam	J01	W
Pivampicillin/Pivmecillinam	J01	U
Polymyxin M	J01	R
Sulfadoxine/Trimethoprim	J01	U

Sulfalene/Trimethoprim	J01	U
Sulfamethizole/Trimethoprim	J01	A
Sulfamethoxypyridazine/Trimethoprim	J01	U
Demeclocycline	J01AA01	U
Doxycycline	J01AA02	A
Chlortetracycline	J01AA03	W
Lymecycline	J01AA04	W
Metacycline	J01AA05	W
Oxytetracycline	J01AA06	W
Tetracycline	J01AA07	A
Minocycline	J01AA08	W, R (IV)
Rolitetracycline	J01AA09	U
Penimepicycline	J01AA10	U
Clomocycline	J01AA11	U
Tigecycline	J01AA12	R
Eravacycline	J01AA13	R
Chloramphenicol	J01BA01	A
Thiamphenicol	J01BA02	A
Ampicillin	J01CA01	A
Pivampicillin	J01CA02	A
Carbenicillin	J01CA03	W
Amoxicillin	J01CA04	A
Carindacillin	J01CA05	U
Bacampicillin	J01CA06	A
Epicillin	J01CA07	U
Pivmecillinam	J01CA08	A
Azlocillin	J01CA09	W
Mezlocillin	J01CA10	W
Mecillinam	J01CA11	A
Piperacillin	J01CA12	W
Ticarcillin	J01CA13	W
Metampicillin	J01CA14	U
Talampicillin	J01CA15	U
Sulbenicillin	J01CA16	W
Temocillin	J01CA17	W
Hetacillin	J01CA18	U
Aspoxicillin	J01CA19	U
Benzylpenicillin	J01CE01	A
Phenoxymethylpenicillin	J01CE02	A
Propicillin	J01CE03	U
Azidocillin	J01CE04	U

Pheneticillin	J01CE05	W
Penamecillin	J01CE06	A
Clometocillin	J01CE07	A
Benzathine phenoxymethylpenicillin	J01CE10	U
Dicloxacillin	J01CF01	A
Cloxacillin	J01CF02	A
Meticillin	J01CF03	U
Oxacillin	J01CF04	A
Flucloxacillin	J01CF05	A
Nafcillin	J01CF06	A
Sulbactam	J01CG01	U
Tazobactam	J01CG02	U
Ampicillin/Clavulanic Acid	J01CR01	A
Amoxicillin/Clavulanic Acid	J01CR02	A
Ticarcillin/Clavulanic Acid	J01CR03	W
Sultamicillin	J01CR04	A
Cefalexin	J01DB01	A
Cefaloridine	J01DB02	U
Cefalotin	J01DB03	A
Cefazolin	J01DB04	A
Cefadroxil	J01DB05	A
Cefazedone	J01DB06	A
Cefatrizine	J01DB07	A
Cefapirin	J01DB08	A
Cefradine	J01DB09	A
Cefacetrile	J01DB10	A
Cefroxadine	J01DB11	A
Ceftezole	J01DB12	A
Cefoxitin	J01DC01	W
Cefuroxime	J01DC02	W
Cefamandole	J01DC03	W
Cefaclor	J01DC04	W
Cefotetan	J01DC05	W
Cefonicid	J01DC06	W
Cefotiam	J01DC07	W
Loracarbef	J01DC08	U
Cefmetazole	J01DC09	W
Cefprozil	J01DC10	W
Ceforanide	J01DC11	W
Cefminox	J01DC12	W
Cefbuperazone	J01DC13	W

Flomoxef	J01DC14	W
Cefotaxime	J01DD01	W
Ceftazidime	J01DD02	W
Cefsulodin	J01DD03	U
Ceftriaxone	J01DD04	W
Cefmenoxime	J01DD05	W
Latamoxef	J01DD06	W
Ceftizoxime	J01DD07	W
Cefixime	J01DD08	W
Cefodizime	J01DD09	W
Cefetamet	J01DD10	W
Cefpiramide	J01DD11	W
Cefoperazone	J01DD12	W
Cefpodoxime	J01DD13	W
Ceftibuten	J01DD14	W
Cefdinir	J01DD15	W
Cefditoren	J01DD16	W
Cefcapene	J01DD17	W
Cefteram	J01DD18	W
Cefotaxime/Clavulanic Acid	J01DD51	W
Ceftazidime/Clavulanic Acid	J01DD52	W
Ceftazidime/Clavulanic Acid	J01DD52	W
Cefoperazone/Clavulanic Acid	J01DD62	W
Ceftriaxone/Clavulanic Acid	J01DD63	W
Cefpodoxime/Clavulanic Acid	J01DD64	W
Cefepime	J01DE01	W
Cefpirome	J01DE02	R
Cefozopran	J01DE03	R
Aztreonam	J01DF01	R
Carumonam	J01DF02	U
Meropenem	J01DH02	W
Ertapenem	J01DH03	W
Doripenem	J01DH04	W
Biapenem	J01DH05	W
Tebipenem Pivoxil	J01DH06	W
Imipenem/Cilastatin	J01DH51	W
Meropenem/Vaborbactam	J01DH52	R
Panipenem/Betamipron	J01DH55	U
Ceftobiprole Medocaril	J01DI01	R
Ceftaroline Fosamil	J01DI02	R
Faropenem	J01DI03	W

Ceftolozane/Tazobactam	J01DI54	U
Ceftolozane/Clavulanic Acid	J01DI54	R
Trimethoprim	J01EA01	A
Brodimoprim	J01EA02	U
Iclaprim	J01EA03	U
Sulfaisodimidine	J01EB01	U
Sulfamethizole	J01EB02	U
Sulfadimidine	J01EB03	U
Sulfapyridine	J01EB04	U
Sulfafurazole	J01EB05	U
Sulfanilamide	J01EB06	U
Sulfathiazole	J01EB07	U
Sulfathiourea	J01EB08	U
Sulfamethoxazole	J01EC01	U
Sulfadiazine	J01EC02	U
Sulfamoxole	J01EC03	U
Sulfadimethoxine	J01ED01	U
Sulfalene	J01ED02	U
Sulfametomidine	J01ED03	U
Sulfametoxydiazine	J01ED04	U
Sulfamethoxypyridazine	J01ED05	U
Sulfaperin	J01ED06	U
Sulfamerazine	J01ED07	U
Sulfaphenazole	J01ED08	U
Sulfamazone	J01ED09	U
Trimethoprim/Sulfamethoxazole	J01EE01	A
Sulfadiazine/Trimethoprim	J01EE02	A
Sulfametrole/Trimethoprim	J01EE03	A
Sulfamoxole/Trimethoprim	J01EE04	A
Sulfadimidine/Trimethoprim	J01EE05	U
Sulfadiazine/Tetroxoprim	J01EE06	U
Sulfamerazine/Trimethoprim	J01EE07	U
Erythromycin	J01FA01	W
Spiramycin	J01FA02	W
Midecamycin	J01FA03	W
Oleandomycin	J01FA05	W
Roxithromycin	J01FA06	W
Josamycin	J01FA07	W
Troleandomycin	J01FA08	U
Clarithromycin	J01FA09	W
Azithromycin	J01FA10	W

Miocamycin	J01FA11	U
Rokitamycin	J01FA12	U
Dirithromycin	J01FA13	W
Flurithromycin	J01FA14	U
Telithromycin	J01FA15	W
Solithromycin	J01FA16	U
Clindamycin	J01FF01	A
Lincomycin	J01FF02	W
Pristinamycin	J01FG01	W
Quinupristin/Dalfopristin	J01FG02	R
Streptomycin	J01GA01	A
Streptoduocin	J01GA02	U
Tobramycin	J01GB01	W
Gentamicin	J01GB03	A
Kanamycin	J01GB04	A
Neomycin	J01GB05	W
Amikacin	J01GB06	A
Netilmicin	J01GB07	W
Sisomicin	J01GB08	W
Dibekacin	J01GB09	W
Ribostamycin	J01GB10	W
Isepamicin	J01GB11	W
Arbekacin	J01GB12	W
Bekanamycin	J01GB13	U
Ofloxacin	J01MA01	W
Ciprofloxacin	J01MA02	W
Pefloxacin	J01MA03	W
Enoxacin	J01MA04	W
Temafloxacin	J01MA05	U
Norfloxacin	J01MA06	W
Lomefloxacin	J01MA07	W
Fleroxacin	J01MA08	W
Sparfloxacin	J01MA09	W
Rufloxacin	J01MA10	W
Grepafloxacin	J01MA11	U
Levofloxacin	J01MA12	W
Trovafloxacin	J01MA13	U
Moxifloxacin	J01MA14	W
Gemifloxacin	J01MA15	W
Gatifloxacin	J01MA16	W
Prulifloxacin	J01MA17	W

Pazufloxacin	J01MA18	W
Garenoxacin	J01MA19	W
Sitafloxacin	J01MA21	W
Tosufloxacin	J01MA22	W
Delafloxacin	J01MA23	W
Rosoxacin	J01MB01	U
Nalidixic acid	J01MB02	U
Piromidic Acid	J01MB03	U
Pipemidic Acid	J01MB04	U
Oxolinic Acid	J01MB05	U
Cinoxacin	J01MB06	U
Flumequine	J01MB07	W
Nemonoxacin	J01MB08	U
Cefuroxime/Metronidazole	J01RA03	U
Spiramycin/Metronidazole	J01RA04	W
Levofloxacin/Ornidazole	J01RA05	U
Cefepime/Amikacin	J01RA06	U
Azithromycin/Fluconazole/Secnidazole	J01RA07	U
Tetracycline/Oleandomycin	J01RA08	U
Ofloxacin/Ornidazole	J01RA09	U
Ciprofloxacin/Metronidazole	J01RA10	U
Ciprofloxacin/Tinidazole	J01RA11	U
Ciprofloxacin/Ornidazole	J01RA12	U
Norfloxacin/Tinidazole	J01RA13	U
Vancomycin	J01XA01	W
Teicoplanin	J01XA02	W
Telavancin	J01XA03	R
Dalbavancin	J01XA04	R
Oritavancin	J01XA05	R
Colistin	J01XB01	R
Polymyxin B	J01XB02	R
Fusidic Acid	J01XC01	W
Metronidazole	J01XD01	A
Tinidazole	J01XD02	U
Ornidazole	J01XD03	U
Nitrofurantoin	J01XE01	U
Nifurtoinol	J01XE02	U
Furazidin	J01XE03	U
Fosfomycin	J01XX01	R
Xibornol	J01XX02	U
Clofoctol	J01XX03	W

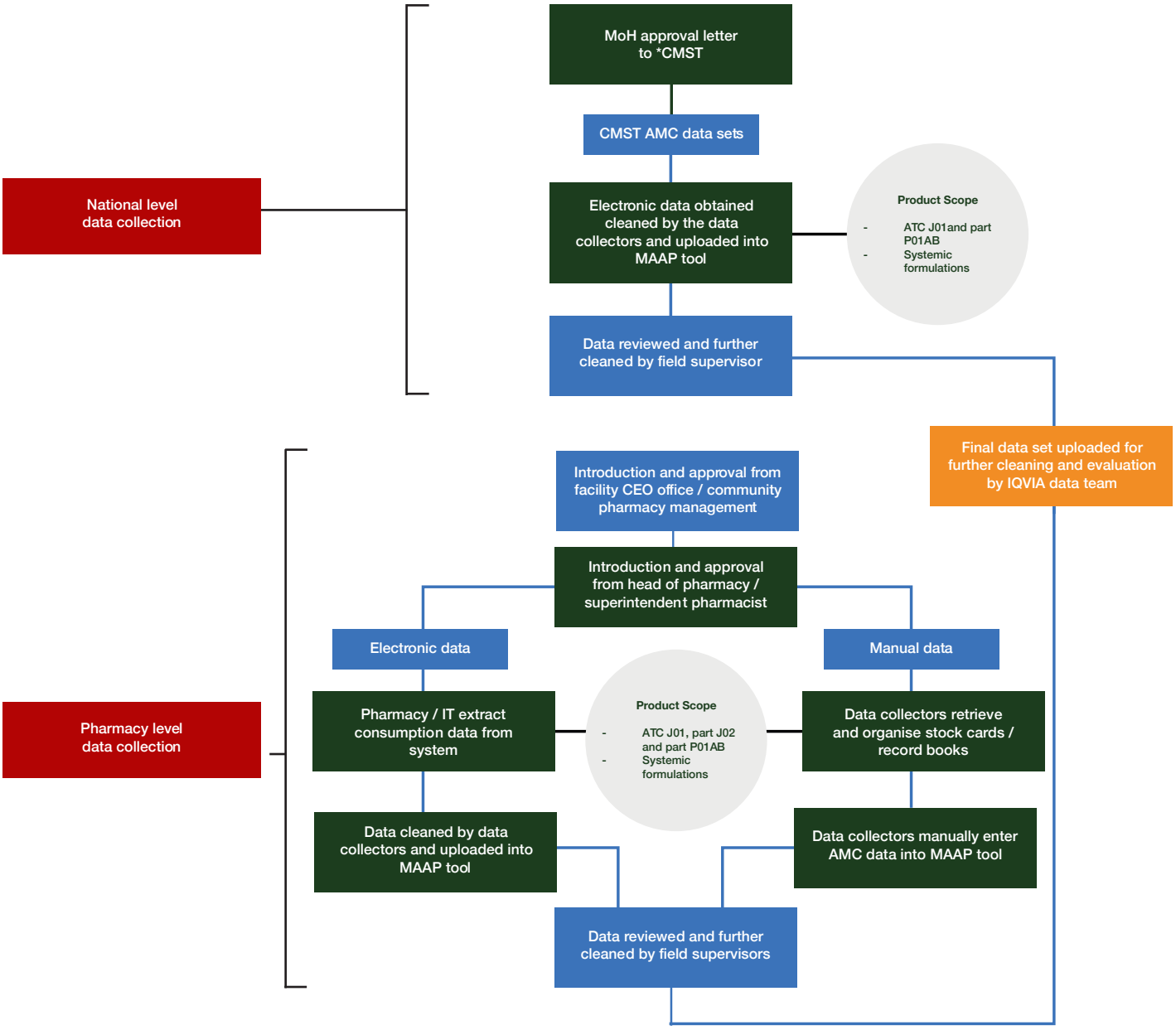
Spectinomycin	J01XX04	A
Linezolid	J01XX08	R
Daptomycin	J01XX09	R
Bacitracin	J01XX10	U
Tedizolid	J01XX11	R
Amphotericin B	J02AA01	N/A
Fluconazole	J02AC01	N/A
Itraconazole	J02AC02	N/A
Voriconazole	J02AC03	N/A
Posaconazole	J02AC04	N/A
Isavuconazole	J02AC05	N/A
Flucytosine	J02AX01	N/A
Caspofungin	J02AX04	N/A
Micafungin	J02AX05	N/A
Anidulafungin	J02AX06	N/A

Key - A: Access W: Watch R: Reserve U: Uncategorised

Appendix 4: Key AMC specific variables

	Variables	Mandatory or Optional
	Antimicrobial consumption specific	
1	Site Name /Pharmacy name	Mandatory
2	Date of transaction	Mandatory
3	Antibiotic Name	Mandatory
4	Antibiotic Identification Number	Optional
5	Antibiotic strength	Mandatory
6	Antibiotic Strength Units	Mandatory
7	Form	Mandatory
8	Pack size	Mandatory
10	Brand	Mandatory
11	Quantity Issued IN/OUT	Mandatory
12	Balance (after a transaction is complete)	Mandatory
13	Date of data entry (data capture date by data collectors)	Optional
14	Date of data review (data review date by data manager or regional coordinator)	Optional
15	Recipient facility	Optional
16	Recipient unit	Optional

Appendix 5: Data collection process flowchart



*DDD - Defined Daily Dose *ATC - Anatomic Therapeutic Chemical *AwaRe - Access, Watch and Reserve

Figure 15: Flow chart explains the data checks procedures and validation process for the national and pharmacy level AMC data collected in Eswatini

Appendix 6: Description of AMC analysis methodology

Defined Daily Dose (DDD) AMC Analysis:
DDD's were calculated as follows:

$$\text{Number of DDDs} = \frac{\text{Total milligrams used}}{\text{DDD value in milligrams*}}$$

***WHO approved DDDs for antibiotics:**

Where total grams of the antimicrobial used is determined by summing the amount of active ingredient across the various formulations (different strengths of tablets, or capsules, syrup formulations) and pack sizes.

Once AMC is converted to standard DDDs, the data is further analysed into the below standard units: DDDs/1000 inhabitants/day (DID): used to calculate total AMC for the Eswatini population at a national level; includes all age and gender groups and used the known population numbers as the denominator (obtained from the Worldometer Population Database). The below formula summarizes how this calculation was done:

The below formula summarizes how this calculation was done:

DDD/1000 Inhabitants/day =

$$\frac{\text{Utilization in DDDs} \times 1000}{\text{(Number of inhabitants*)} \times \text{(Number of days in the period of data collection)}}$$

*Eswatini population estimated for 2016-2018 obtained from:
https://www.worldometers.info/world-population/Eswatini-population/

DDD equivalent: used to calculate AMC at site level (presented as a percentage) and used WHO DDD as the denominator. The below formulas indicate how this was done:

DDD equivalent (%) =

$$\frac{\text{Total milligrams consumed/purchased} \times 100}{\text{WHO DDD*}}$$

*WHO approved DDDs for antibiotics:

WHO Anatomical Therapeutic Chemical (ATC) classification

Definition of the classification of the medicines in groups at five different levels:

Level 1: Indicates the anatomical main group, it is represented by a letter. For antimicrobials, the main group is 'J', which represented Anti-infectives for systemic use. It should be noted that there are antimicrobials that are classified in other main groups.

Level 2: Indicates the therapeutic subgroups and is represented by a number. For example: J01 groups together Antibacterial for systemic use.

Level 3: Classifies the pharmacological subgroup, e.g., J01C is Beta (β)-lactam antibacterial, Penicillins and J01F lists Macrolides, Lincosamides and Streptogramins

Level 4: Further defines the group by pharmacological subgroup, e.g., J01CA is Penicillins with extended spectrum and J01FA is Macrolides

Level 5: Is the chemical substance, e.g., J01CA01 is ampicillin and J01FA10 s azithromycin

WHO Access, Watch and Reserve (AWaRe) AMC Analysis:

Description of the AWaRe categories below:

'Access': This group includes antibiotics that generally have a narrow spectrum of activity against microbes and are active against a wide range of common infections. The 'Access' group represents first- and second-choice antibiotics for the empiric treatment of the most common infectious syndromes. They offer the best therapeutic value, while minimizing the potential for resistance. The distribution of antibiotics in this group includes Beta (β)–lactam (52.63%), followed by aminoglycosides (15.78%), macrolides (5.26%) and tetracyclines (5.26%). The 'Access' group compromises of 48 antibiotics; 19 of which are included in the WHO's EML.

'Watch': These antibiotics generally have a broader spectrum of activity against microbes and are to be used sparingly as first- or second-choice treatment options for specified infectious syndromes; they are indicated for specific, limited number of infective syndromes or patient groups. These medicines are also preferred over access antibiotics in serious infections. β-lactams (54.54%) constitute the larger share of the 'Watch' group antibiotics followed by macrolides (18.18%), aminoglycosides (9.09%) and carbapenems (9.09%). 'Watch' group compromises of 110 antibiotics; 11 of which are included in the WHO's EML. 'Watch' group antibiotics should be prioritised as key targets of stewardship programmes and monitoring.

'Reserve' group antibiotics: These should strictly be considered as the last-resort option. They should be used only in the most severe circumstances when all other alternatives have failed i.e., in life-threatening infections due to multi-drug resistant bacteria. The 'Reserve' group is majorly constituted of polymyxin (28.57%) followed by β-lactams (14.28%) and aminoglycosides (14.28%). 'Reserve' group compromises of 22 antibiotics; 7 of which are included in the WHO's EML. The use of antibiotics in this group should be closely monitored and prioritised as targets for AMS to ensure their continued effectiveness.

Appendix 7: National AMC by Antimicrobial molecules

ATC Class Rank	AWaRe category	Molecule	2016	2017	2018	Mean DDD/1000 inhabitant-days
			DDD/1000 inhabitant-days (%*)			
J01 Class		**Total**	**14.73 (100)**	**89.21 (100)**	**89.21 (100)**	**40.85**
1	Access	Sulfamethoxazole or trimethoprim	0 (0)	2.03 (10.9)	66.13 (74.1)	22.72
2	Access	Amoxicillin	5.54 (37.6)	4.75 (25.5)	6.47 (7.2)	5.59
3	Access	Doxycycline	4.76 (32.3)	4.27 (22.9)	7.21 (8.1)	5.41
4	Watch	Erythromycin	0.45 (3.1)	2.97 (15.9)	4.00 (4.5)	2.47
5	Access	Phenoxymethylpenicillin	1.38 (9.4)	1.67 (9)	1.29 (1.4)	1.45
6	Access	Cloxacillin	0.28 (1.9)	0.65 (3.5)	1.23 (1.4)	0.72
7	Watch	Levofloxacin	0.80 (5.4)	0.55 (3)	0.41 (0.5)	0.59
8	Watch	Ciprofloxacin	0.43 (2.9)	0.61 (3.3)	0.69 (0.8)	0.58
9	Access	Nitrofurantoin	0.15 (1)	0.13 (0.7)	0.43 (0.5)	0.23
10	Access	Procaine benzylpenicillin	0.34 (2.3)	0.32 (1.7)	0.002 (0)	0.22
11	Watch	Ceftriaxone	0.14 (1)	0.12 (0.6)	0.14 (0.2)	0.13
12	Access	Benzathine benzylpenicillin	0.02 (0.2)	0.06 (0.3)	0.26 (0.3)	0.11
13	Access	Benzylpenicillin	0.07 (0.5)	0.10 (0.5)	0.14 (0.2)	0.10
14	Access	Amoxicillin/Clavulanic Acid	0.02 (0.1)	0.10 (0.5)	0.18 (0.2)	0.1
15	Access	Metronidazole	0.05 (0.3)	0.06 (0.3)	0.12 (0.1)	0.08
16	Watch	Clarithromycin	0.13 (0.9)	0.06 (0.3)	0.03 (0)	0.07
17	Access	Gentamicin	0 (0)	0.02 (0.1)	0.16 (0.2)	0.06
18	Reserve	Linezolid	0 (0)	0.02 (0.1)	0.13 (0.1)	0.05
19	Watch	Cefaclor	0.06 (0.4)	0.05 (0.2)	0.04 (0)	0.05
20	Watch	Moxifloxacin	0.06 (0.4)	0.02 (0.1)	0.05 (0.1)	0.05
21	Watch	Azithromycin	0.02 (0.1)	0.02 (0.1)	0.05 (0.1)	0.03
22	Access	Cefazolin	0.01 (0.1)	0.02 (0.1)	0.01 (0)	0.01
23	Access	Spectinomycin	0.01 (0.1)	0.01 (0.1)	0.01 (0)	0.01
24	Access	Flucloxacillin	0.005 (0)	0.01 (0)	0.01 (0)	0.006
25	Access	Clindamycin	0.01 (0)	0 (0)	0.005 (0)	0.003
26	Watch	Imipenem/Cilastatin	0.002 (0)	0.002 (0)	0.001 (0)	0.002
27	Access	Chloramphenicol	0.001 (0)	0.001 (0)	0.002 (0)	0.001
28	Access	Amikacin	0 (0)	0 (0)	0.002 (0)	0.001
J02 Class		**Total**	**0.72 (100)**	**0.22 (100)**	**1.62 (100)**	**0.85**
1	Uncategorised	Ketoconazole	0.42 (57.6)	0.13 (59.5)	1.01 (62.5)	0.52
2	Uncategorised	Fluconazole	0.3 (41.6)	0.08 (36.7)	0.6 (37)	0.33
3	Uncategorised	Amphotericin-B	0.006 (0.8)	0.01 (3.8)	0.007 (0.4)	0.007
P01AB Class		**Total**	**1.81 (100)**	**1.92 (100)**	**11.04 (100)**	**4.92**
1	Access	Metronidazole	1.81 (100)	1.92 (100)	11.04 (100)	4.92

***Antibiotics marked as 'uncategorised' have not been awarded a category within the 2019 WHO AWaRe database, including not being placed within the 'not recommended' list.*

Appendix 8: Breakdown of national AMC by ATC classes

	% consumption		
ATC class	2016	2017	2018
Combinations of sulfonamides and trimethoprim, incl. derivatives	0.0%	9.8%	64.9%
Penicillins with extended spectrum	32.1%	22.9%	6.3%
Tetracyclines	27.6%	20.6%	7.1%
Nitroimidazole derivatives	10.5%	9.2%	10.8%
Macrolides	3.5%	14.7%	4.0%
Beta-lactamase sensitive penicillins	10.5%	10.4%	1.7%
Fluoroquinolones	7.5%	5.7%	1.1%
Beta-lactamase resistant penicillins	1.6%	3.2%	1.2%
Imidazole derivatives	2.4%	0.6%	1.0%
Triazole derivatives	1.7%	0.4%	0.6%
Nitrofuran derivatives	0.8%	0.6%	0.4%
Third-generation cephalosporins	0.8%	0.6%	0.1%
Combinations of penicillins, incl. beta-lactamase inhibitors	0.1%	0.5%	0.2%
Imidazoles	0.3%	0.3%	0.1%
Aminoglycosides	0.0%	0.1%	0.2%
Other antibacterials	0.1%	0.2%	0.1%
Second-generation cephalosporins	0.3%	0.2%	<0.1%
First-generation cephalosporins	0.1%	0.1%	<0.1%
Antimycotics for systemic use	<0.1%	<0.1%	<0.1%
Lincosamides	<0.1%	0.0%	<0.1%
Carbapenems	<0.1%	<0.1%	<0.1%
Amphenicols	<0.1%	<0.1%	<0.1%

**Consumption was recorded for the last four classes; however, rates were below 0.1% of the total AMC.*

Appendix 9: Breakdown of antibiotic documented and their inclusion in the WHO EML and National EML

Standardised Molecule Name	WHO AWaRe Categorisation	WHO ATC Code	WHO EML	National EML	Documented Data
Amikacin	Access	J01GB06	Y	Y	Y
Amoxicillin	Access	J01CA04	Y	Y	Y
Amoxicillin/Clavulanic Acid	Access	J01CR02	Y	Y	Y
Amoxicillin/Flucloxacillin		J01CR50	N	N	Y
Amphotericin-B		J02AA01	N	Y	Y
Ampicillin	Access	J01CA01	Y	Y	Y
Ampicillin/Cloxacillin		J01CR50	N	N	Y
Azithromycin	Watch	J01FA10	Y	Y	Y
Benzathine benzylpenicillin	Access	J01CE08	Y	Y	Y
Benzylpenicillin	Access	J01CE01	Y	Y	Y
Cefaclor	Watch	J01DC04	N	Y	Y
Cefadroxil	Access	J01DB05	N	N	Y
Cefalexin	Access	J01DB01	Y	N	Y
Cefazolin	Access	J01DB04	Y	Y	Y
Cefepime	Watch	J01DE01	N	N	Y
Cefiderocol	Reserve	J01DI04	Y	N	N
Cefixime	Watch	J01DD08	Y	Y	Y
Cefotaxime	Watch	J01DD01	Y	N	Y
Cefpodoxime proxetil	Watch	J01DD13	N	N	Y
Ceftazidime	Watch	J01DD02	Y	N	N
Ceftazidime/avibactam	Reserve	J01DD52	Y	N	N
Ceftriaxone	Watch	J01DD04	Y	Y	Y
Cefuroxime	Watch	J01DC02	Y	Y	Y
Cefuroxime/Clavulanic Acid		J01DC--	N	N	Y
Chloramphenicol	Access	J01BA01	Y	Y	Y
Ciprofloxacin	Watch	J01MA02	Y	Y	Y
Clarithromycin	Watch	J01FA09	Y	Y	Y
Clindamycin	Access	J01FF01	Y	Y	Y
Cloxacillin	Access	J01CF02	Y	Y	Y
Colistin	Reserve	J01XB01	Y	N	N

Doxycycline	Access	J01AA02	Y	Y	Y
Erythromycin	Watch	J01FA01	N	Y	Y
Flucloxacillin	Access	J01CF05	N	Y	Y
Fluconazole		J02AC01	N	Y	Y
Fosfomycin (IV)	Reserve	J01XX01	Y	N	N
Fosfomycin (oral)	Watch	J01XX01	Y	N	Y
Gentamicin	Access	J01GB03	Y	Y	Y
Imipenem/Cilastatin	Watch	J01DH51	N	N	Y
Kanamycin	Watch	J01GB04	N	Y	N
Ketoconazole		J02AB02	N	N	Y
Levofloxacin	Watch	J01MA12	N	Y	Y
Linezolid	Reserve	J01XX08	Y	N	Y
Lymecycline	Watch	J01AA04	N	N	Y
Meropenem	Watch	J01DH02	Y	N	Y
Meropenem/vaborbactam	Reserve	J01DH52	Y	N	N
Metronidazole	Access	P01AB01, J01XD01	Y	N	Y
Minocycline	Watch	J01AA08	N	N	Y
Moxifloxacin	Watch	J01MA14	N	Y	Y
Nitrofurantoin	Access	J01XE01	Y	Y	Y
Norfloxacin	Watch	J01MA06	N	N	Y
Ofloxacin	Watch	J01MA01	N	Y	N
Phenoxymethylpenicillin	Access	J01CE02	Y	Y	Y
Piperacillin/Tazobactam	Watch	J01CR05	Y	N	Y
Plazomicin	Reserve	J01GB14	Y	N	N
Polymyxin-B	Reserve	J01XB02	Y	N	N
Procaine benzylpenicillin	Access	J01CE09	Y	Y	Y
Spectinomycin	Access	J01XX04	Y	Y	Y
Sulfamethoxazole/ Trimethoprim	Access	J01EE01	Y	Y	Y
Trimethoprim	Access	J01EA01	Y	N	N
Vancomycin	Watch	J01XA01	Y	Y	Y

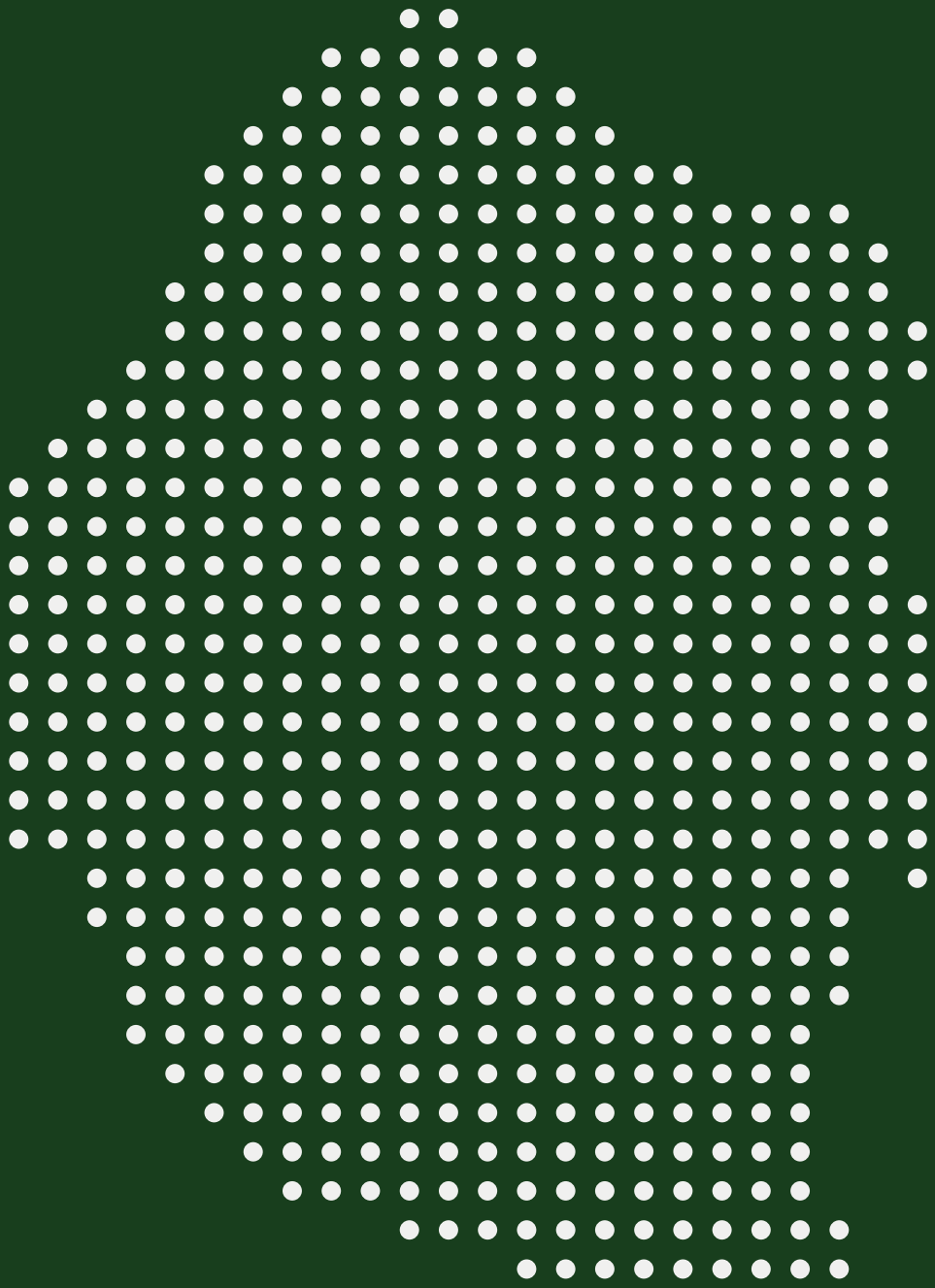
Appendix 10: AMC data collection and expired drug and losses tool

AMC Data Collection Tool

Product Name
Pack Size_Value
Pack Size_Unit
Strength Num_Value
Strength Num_Unit
Strength Denom_Value
Strength Denom_Unit
ATC5
Combi-nation
Route
Salt
Volume

Expired Drug and Losses Tool

Country
Pharmacy Name
Date of Transaction
Antibiotic Name
Strength Value
Strength Unit
Form
Pack Size
Brand
Quantity



MAAP
Mapping AMR & AMU Partnership

The Fleming Fund
Regional Grants

UKaid
from the British people

African Union

AFRICA CDC
Centres for Disease Control and Prevention
Safeguarding Africa's Health

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

ECOWAS

ECSA Health Community

InSTEDD
Innovative Support To Emergencies Diseases and Disasters

IQVIA

ONEHEALTH TRUST