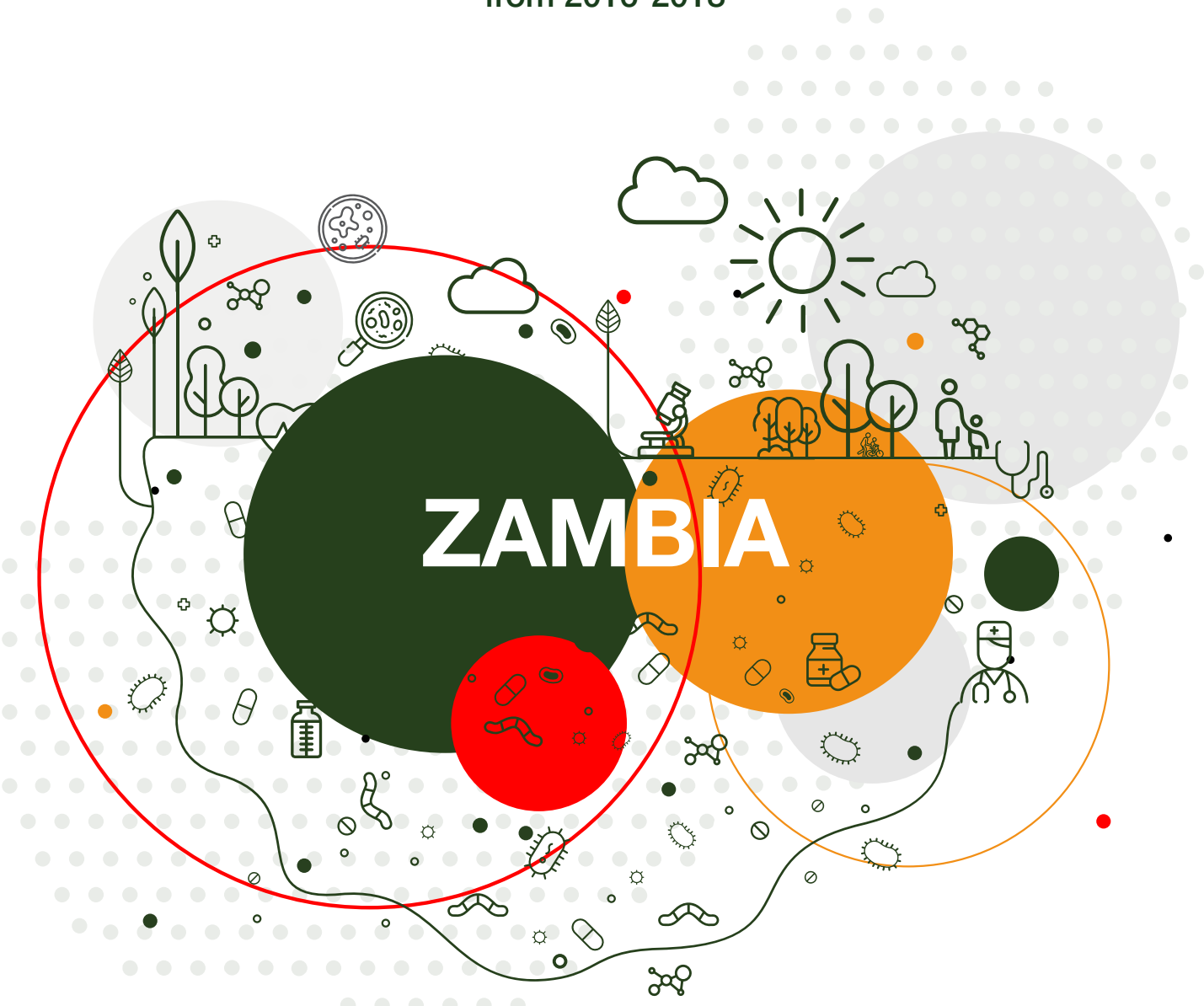
MAAP
Mapping AMR & AMU Partnership

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

Zambia (2016-2018)

ZAMBIA

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.

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Abbreviations

ACDC	Africa Centres for Disease Control
AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMRCC	Antimicrobial Resistance Coordinating Committee
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
CAPTURA	Capturing Data on AMR Patterns and Trends in Use in Regions of Asia
CASFM	Comité de l'antibiogramme de la Société Française de Microbiologie
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
FDC	Fixed Dose Combinations
GAP	Global Action Plan
GHSI	Global Health Security
GLASS	Global Antimicrobial Resistance Surveillance System
GDP	Gross Domestic Product
HICC	Hospital Infection Control Committee
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
MSL	Medical Store Limited
MRSA	Methicillin-resistant Staphylococcus aureus
MRSA	Methicillin-resistant Staphylococcus aureus
MTC	Medical Therapeutics Committee
NAP	National Action Plan
OR	Odds Ratio
QA	Quality Assessment
QC	Quality Control
QMS	Quality Management System
RSN	ResistanceMap Surveillance Network
SLIPTA	Stepwise Laboratory Improvement Process Towards Accreditation
SLMTA	Strengthening Laboratory Management Towards Accreditation
SOP	Standard Operating Procedure
STG	Standard Treatment Guidelines
WAHO	West African Health Organisation
WHA	World Health Assembly
WHO	World Health Organisation
ZAMRA	Zambia Medicines Regulatory Authority
ZEML	Zambia Essential Medicines List

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, comprehensive and robust AMR, antimicrobial use (AMU) and antimicrobial consumption (AMC) data is lacking in many low- and middle- income countries (LMICs), 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. The 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 the MAAP consortium to implement the Regional Grant and aims to determine national AMR, AMC and AMU surveillance capacity, rates and trends and to assess the antimicrobial flow in Zambia during 2016-2018.

Zambia had approximately 1 608 laboratories in the national laboratory network during the study period, of which 23 reported bacteriology testing capacity. Self-reported functioning and quality compliance information from 22 laboratories were assessed to determine laboratory AMR surveillance preparedness.

The presented AMR rates are based on antimicrobial susceptibility results 0f 22 343 positive culture isolates obtained from 14 laboratories. High levels of resistance were noted for third-generation cephalosporin in Enterobacterales (~65%), fluoroquinolone in Salmonella species (65-73%) and methicillin in Staphylococcus aureus (30-63%). Antimicrobial-resistant infections were found to be more common in persons below 18 years and those with renal conditions. All results should be interpreted cautiously because the participating laboratories were at different service levels of service and had varying testing capacities.

AMC is the number of antimicrobials sold or dispensed, whereas AMU reviews the appropriateness of antimicrobials prescription using additional data, such as clinical indicators. Only AMC data were retrieved from the selected sentinel pharmacies; AMU data were not obtained due to the lack of a unique patient identifier and tracking systems across hospital departments. The data collected from Medical Stores Limited (MSL), which would have served as national AMC, was not analysed as the datasets missed key information, such as pack size and strength information. Thus, the MAAP could not calculate the defined daily doses (DDDs) consumed; the DDD is a primary requirement for AMC analysis. Henceforth, the findings reported here result from aggregated pharmacy-level AMC datasets. The average total AMC consumption levels in the sampled pharmacies between 2016-2018 were 10 946 812.1 defined daily doses (DDDs). Antimicrobial utilisation by Anatomical Therapeutic Chemical (ATC) medicine classification was highest for combinations of penicillins, including beta-lactamase inhibitors (range 4.8% to 48.5%), followed by fluoroquinolone (range 16.3% to 33.2%) and by tetracyclines (6.6% to 12.7%). The top five most consumed antimicrobials were amoxicillin/clavulanic acid, ciprofloxacin, doxycycline, metronidazole and sulfamethoxazole/trimethoprim. Together they account for >72% of the total consumption share suggesting a lack of variation. This consumption trend could potentially increase AMR.

The pharmacy-level AMC included antimicrobials from the 'Access' 66.7%, 'Watch' 33.3% and 'Reserve' 0% antibiotics. This data indicated that the use of 'Access' antibiotics exceeded the WHO minimum recommended consumption threshold of 60%. The 'Reserve' category antibiotics were not consumed possibly because they were unavailability within the sampled pharmacies. The consumption of five combinations of two or more broad-spectrum fixed-dose combinations (FDCs) of antimicrobials was documented in the selected pharmacies. However, these identified combinations of FDCs were not recommended for clinical utility. Of those, ampicillin/cloxacillin was most commonly consumed (mean DDD of 16 189.2).

The drug resistance index (DRI) aggregates and measures resistance rates on a scale of 0-100, where 0 indicates fully susceptible while 100 indicates fully resistant. The DRI estimate was found to be high at 60.9% (95% CI, 53.8–69.7%) implying low antibiotic effectiveness, which threatens effective infectious disease management and calls for urgent policy intervention.

The following recommendations aim to strengthen AMR and AMC surveillance to mitigate AMR in the country and should be noted by policymakers and healthcare providers.

- We recommend that all laboratories are mapped across a range of indicators, including population coverage, infectious disease burden, testing capabilities, and quality compliance. This mapping exposes unmet needs and informs laboratory network expansion plan to strengthen laboratory service delivery.
- Staff training on laboratory standards, common pathogen identification and data management skills are essential for high-quality microbiology testing and reporting. staff capacity building could be achieved by leveraging in-house expertise or outsourcing to external organisations or tertiary facilities.
- Curating the right data and generating evidence is essential for strengthening AMR surveillance. We recommend standardised data collection formats at all levels (laboratories, clinics and pharmacies) and automated data analyses. Also, we recommend establishing a system of assigning permanent identification numbers for tracking patients.
- Due to the limited number of facilities assessed, the MAAP, per the WHO facility AMU assessment guide, recommends that future AMU and AMC surveillance attempts in the country be through large-scale point prevalence surveys to give a nationally representative portrait of antimicrobials use in the country.
- The consortium recommends that a comprehensive routine AMC data surveillance policy be developed. The policy should, at the minimum, stipulate the AMC data variables to be reported and routine data cleaning and reporting practices to minimise the time spent standardising and cleaning data before routine surveillance exercises.
- Hospitals should switch to electronic medical record systems to make future AMC surveillance more time and cost-efficient. These systems should be interoperable and user-friendly.
- The consortium recommends that the country's Antimicrobial Resistance Coordinating Committee (AMRCC) should introduce facility-level Antimicrobial Stewardship Programs (ASPs) to regulate the use of broader spectrum antibiotics and educate prescribers on the importance of reserving these to maintain their efficacy.
- From the assessment, the top five antibiotics consumed within the 'Access' and 'Watch' categories were the majority of antibiotics consumed in each category. Such a consumption pattern could be postulated to be sub-optimal as evolutionary pressure driving resistance would be focused only on the narrow-band antibiotics consumed. 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.
- The consortium recommends an urgent review of the 'Reserve' category antibiotics list by the Ministry of Health (MoH), AMRCC to assess their availability in the country. This survey may inform a subsequent review of the country's EML and treatment guidelines to include these vital antibiotics, if necessary. This approach will ensure that the most vital antibiotics are available for all patients.

Overview

The Fleming Fund Grants Programme

The Fleming Fund Grants Programme is a United Kingdom-sponsored initiative aimed to address the critical gaps in the 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 available data on AMR and AMU.

Problem Statement

The quantum and quality of surveillance data are suboptimal in LMICs where AMR rates are typically lacking.[2] This data paucity hinders the assessment of the current treatment efficacy and understanding of the drivers of resistance. It also impacts the adoption of appropriate policies to improve AMU, which impacts patient care. However, in most LMICs, some institutions (academic, research, public and private health facilities) have been collecting AMR data 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 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 data available to improve the spatiotemporal mapping of AMR and AMU across countries in each region and establish baselines. The programme was implemented by the 'Mapping Antimicrobial resistance and Antimicrobial use Partnership' (MAAP), a multi-organisational consortium of strategic and technical partners. ASLM was the lead grantee for the programme.[3]

The MAAP's strategic partners included the ASLM, the Africa Centres for Disease Control and Prevention (ACDC), West African Health Organisation and 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). The ASLM oversaw the consortium's ensured the fulfilment of the ethical process and completed the data-sharing agreements with the participating countries.

The MAAP collected and analysed each country's historical antimicrobial susceptibility and consumption and usage data for 2016-2018 to understand the country and regional AMR landscape. The MAAP's primary focus was to determine the AMR levels of the WHO-priority bacterial pathogens and other clinically important pathogens. The MAAP collected, digitised and collated the available AMR and AMC data between 2016 and 2018 using standardised data collection and analytical tools. The MAAP could only collect AMC information instead of AMC and AMU data.

The results of this analysis contribute to determining AMR and AMC baselines and trends, drivers and surveillance gaps. The study recommendations aim to increase the country's capacity for future AMR, AMC and AMU data collection, analysis and reporting.

Fourteen African countries across Western (Burkina Faso, Ghana, Nigeria, Senegal and Sierra Leone), Eastern (Kenya, Tanzania and Uganda), Central (Cameroon, Gabon), and 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 Zambia 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 Zambia, 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 and 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 AMC and AMU surveillance system in-country status
- To quantify and evaluate the trends of AMC and AMU at the national and pharmacy-level
- To assess the relationship between AMC and AMR through the DRI
- To assess the AMR drivers

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 in-country analysis of the current AMC and AMU surveillance status
- Total consumption of antimicrobials (defined daily dose), plus AMC and AMU trends over time at national and pharmacy levels
- Country-level Drug Resistance Index (DRI)
- Association between patient factors and AMR

The results could 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 the representatives from Mott MacDonald (Grant Managers), the MAAP consortium (for Africa Region) and the Capturing Data on AMR Patterns and Trends in Use in Regions of Asia (CAPTURA) consortium for Asia Region. The meeting was held in Brighton, England, in February 2019. In April 2019, the MAAP convened a stakeholder consultation in Addis Ababa, Ethiopia with representatives from the 14 participating African countries, 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 of the consortium and the countries, including representatives from the MoH, AMR coordinating committees, health facilities, laboratories, and pharmacies. These workshops were followed by site selection and data collection in each country. The technical partners analysed the data and the final results were shared at dissemination meetings (Figure 1).

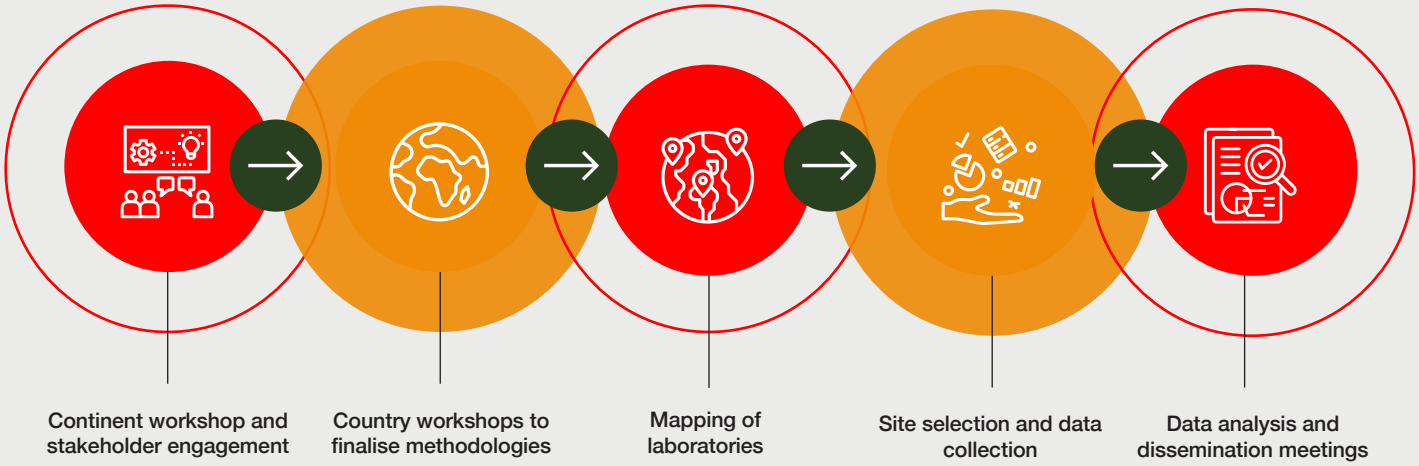


Figure 1: Key engagements and activities

Ethical issues and data sharing agreements

To ensure ethical conduct, confidentiality, regulated use and ownership of the data, a data-sharing agreement (DSA) was signed with the Ministry of Health and adhered to during the project. The DSA facilitated clear communication and established additional safeguards for managing the collected data (AMR Appendix 1).

Country Profile

Health and demographic profile

As of 2020, Zambia had an estimated population of 18.4 million inhabitants with a life expectancy of 64 years. The country has a high infectious disease burden with a TB incidence of 319 per 100 000 and an HIV prevalence of 11.1%. The country has a physicians density rate of 0.09 per 1 000 inhabitants and a nurses density rate of 1.02 per 1 000 inhabitants. With a universal health coverage index of 55, Zambia appears to have above-average coverage of essential medical services (Table 1).

Table 1: Health and demographic profile of Zambia

	Zambia		Comparator values (most recent year)*		
	Year	Value	India	Argentina	United States
Population	2020	18 383 956	1 380 004 390	45 376 763	329 484 123
Life expectancy during the study period, total (years)	2019	64	70	77	79
Universal health coverage service index (0-100)	2019	55	61	67	83
GDP per capita (current US$)	2020	985.13	1 927.7	8 579.0	63 593.4
Immunisation, DPT (% of children ages 12-23 months)	2019	88	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	11.1	0.2*	0.4 2020	0.4 2019
Primary education (%)#	2010	98.0	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	1.02	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 (sourced from the most recently available information between 2017-2020). GDP=Gross domestic product; DPT=Diphtheria, Pertussis and Tetanus

Policy frameworks

In May 2015, the World Health Assembly (WHA) approved the Global Action Plan on Antimicrobial Resistance.[8] Later that year, the WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS)[9] to support the implementation of the Global Action Plan on Antimicrobial Resistance and strengthen AMR surveillance and research.[9] The GLASS provides standardised AMR data collection and analysis methodologies and encourages countries to share their data on the global surveillance platform. The GLASS has various modules and tools covering emerging AMR and AMC events and promotes the integration of animal and environment sectors' AMR surveillance data.

Zambia enrolled in the GLASS in May 2016 and has participated in the data calls.[10-12] Zambia has a multisectoral National Action Plan(NAP) on antimicrobial resistance (2017-2027)[13]. The Zambia NAP provides a coherent "One Health" framework for combating AMR by including the Zambia human, animal, agricultural and environmental health sectors. Zambia has a system to report AMR data to national authorities.

Part A: Antimicrobial Resistance

Section I: Laboratory assessment

Objective

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

Methodology

Initially, up to 16 laboratories, two reference, four private, and 10 public laboratories, were to be included in the study for 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 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 questionnaire was administered to the identified laboratories, to obtain site-specific details and assess 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 MoH and was not necessarily based on laboratory rankings.

Results

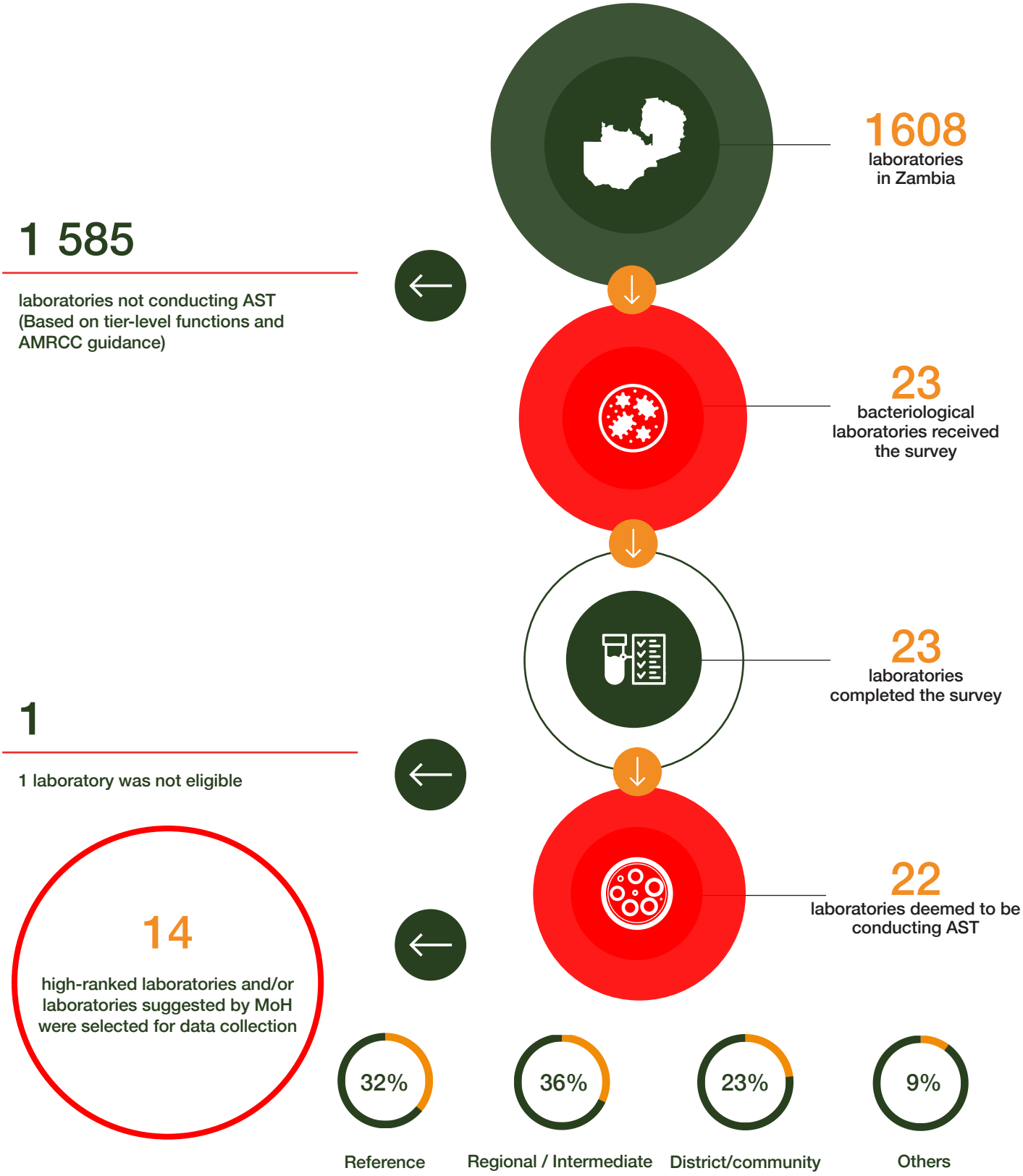
Mapping and selection of laboratories

During the initial stages of in-country work in Zambia, 1 608 laboratories were mapped to the national laboratory network. An eligibility questionnaire was sent to 23 laboratories identified as having bacteriology testing capacity. Of the 22 laboratories that responded to the questionnaire and had AST capacity, most were affiliated with the government (Table 2, AMR Supplementary Table 1). The laboratory readiness scores of the surveyed laboratories varied widely (range: 39.5–81.6%). From the 22 laboratories, 14 were selected for AMR data collection (Figure 2). The laboratories named in the tables are listed in order of decreasing laboratory readiness scores.

Table 2: Laboratory readiness scores of 23 laboratories with bacteriology testing capacity in Zambia

Surveyed laboratories*	Laboratory readiness score (%)	Level of service	Affiliation
Selected			
Arthur Davison Hospital (Arthur)	78.9	Reference	Government
Nchanga North General Hospital (Nchanga)	73.7	Regional/Intermediate	Government
Bacteriology laboratory, University Teaching Hospital (UTH)	65.8	Reference	Government
Ndola Teaching Hospital (Ndola)	63.2	Reference	Government
Livingstone Teaching Hospital (Livingstone)	63.2	Reference	Government
Chilonga Mission General Hospital (Chilonga)	60.5	Regional/Intermediate	Government
Lewanika General Hospital Laboratory (Lewanika)	60.5	Regional/Intermediate	Government
Microbiology laboratory, Mansa General Hospital (Mansa)	57.9	Regional/Intermediate	Government
Bacteriology laboratory, Chipata Central Hospital (Chipata)	57.9	Other	Government
Levy Mwanawasa University Teaching Hospital Laboratory (Levy)	55.3	Regional/Intermediate	Government
St. Francis Hospital Laboratory (St. Francis)	55.3	Reference	Government
Bacteriology laboratory, Kasama Central Hospital (Kasama)	52.6	Regional/Intermediate	Government
Kabwe Central Hospital Laboratory (Kabwe)	52.6	Regional/Intermediate	Government
Solwezi General Laboratory (Solwezi)	50	Regional/Intermediate	Government
Not selected			
Bacteriology laboratory at the Petauke District Hospital	81.6	Other	NGO
Lancet Laboratory Limited (Lancet)	68.4	Reference	Private
Microbiology Laboratory Nyanje Mission Hospital	63.2	Reference	Government
Mwami Adventist hospital	55.3	District/Community	Government
Lusaka Trust Hospital Pathology Laboratory (Lusaka)	52.6	District/Community	Government
Kamoto Mission Hospital	50	District/Community	Government
Bacteriology laboratory at Chadiza District Hospital	39.5	District/Community	Government
Centre for Infectious Disease Research in Zambia – Central Laboratory	39.5	District/Community	Government

** Laboratory names are abbreviated.*



Abbreviations: AST=antibiotic susceptibility testing; AMRCC=antimicrobial resistance coordinating committee; MoH=Ministry of Health

Figure 2: Selection of laboratories in Zambia

Surveillance preparedness of surveyed laboratories

Based on self-reported information from the 22 laboratories, laboratory function, and quality compliance were assessed to understand their preparedness for AMR surveillance. Twenty laboratories had implemented QMS and 12 laboratories had at least one qualified microbiologist on board. Four laboratories were accredited and used automated methods for pathogen identification (Figure 3, AMR Supplementary Table 2). Since these findings may affect the laboratory data quality, the AMR rates presented in this report should be cautiously interpreted.

	Parameters			N (%)
Commodity and equipment status	Regular power supply and functional back up			27 (100)
	Continuous water supply)			27 (100)
	Certified and functional biosafety cabinets			23 (85.2)
	Automated methods for pathogen identification			1 (3.7)
	Automated methods for AST			2 (7.4)
	Methods for testing AMR mechanisms			12 (44.4)
QMS implementation	Reported QMS Implementation			27 (100)
		Types of QMS	LQMS	2 (7.4)
			SLIPTA	11 (40.7)
			SLMTA	2 (7.4)
			Mentoring	-
			Combination‡	2 (7.4)
			Others	10 (37.0)
	Quality Certification			19 (70.4)
		Types of Quality certification	SLIPTA	11 (57.9)
			Col. of Am. Path	-
			Others	8 (42.1)
	Accreditation			6 (22.2)
	Participation in proficiency testing			25 (92.6)
	Utilisation of reference strains			25 (92.6)
	Reported consistent maintenance of QC records			26 (96.3)
	Designated focal quality person			25 (92.6)
	Reported compliance to standard operating procedures			27 (100.0)
	Reported compliance to AST standards			25 (92.6)
Personnel and training status	Presence of at least one qualified microbiologist			6 (22.2)
	Presence of an experienced laboratory scientist/technologist			27 (100.0)
	Up-to-date and complete records on staff training and competence			25 (92.6)
Specimen Management status	Reported compliance to SOPs on specimen collection and testing			27 (100.0)
	Reported compliance to SOPs on specimen rejection			27 (100.0)
	Average number of specimens processed for AST in 2018			25 (92.6)
LIS and Linkage to Clinical Data	Assigned specimen (laboratory) identification number			27 (100.0)
	Availability of system/database to store patient data			25 (92.6)
		Database format	Paper-based	4 (16.0)
			Electronic	-
			Mixed	21 (84.0)
	Captured patients' records on test request forms			25 (92.6)
			Retrievable	19 (76.0)

‡ Combination refers to more than one option presented in the questionnaire (laboratory quality management system (LQMS), stepwise laboratory improvement process towards accreditation (SLIPTA), strengthening laboratory management towards accreditation (SLMTA), and mentoring).
Abbreviations: AMR=antimicrobial resistance; AST=antibiotic susceptibility testing; LIS=laboratory information system; LQMS=laboratory quality management system; QMS=quality management system; QC=quality control; QMS=quality management system; SOP=standard operating procedure; College of American Pathology=

Figure 3: Laboratory preparedness for AMR surveillance assessment of the 22 selected laboratories with bacteriology testing capacity in Zambia

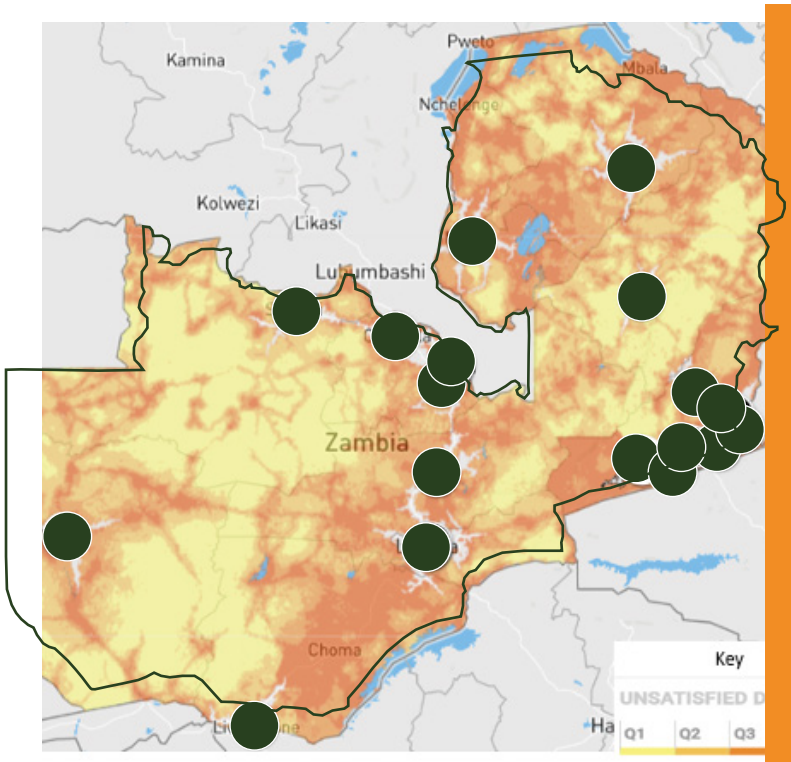
Profile of Selected Laboratories

Facility data were largely unavailable. Eight laboratories had paper-based laboratory information systems (LIS), while five had mixed (paper and electronic) LIS.

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 mapped laboratories within a two-hour drive (Supplementary Figure 1).

As of 2020, Zambia had an estimated population of 18.38 million.



The laboratory population coverage 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 assumes that the laboratory has sufficient testing capacity to serve the entire population within its catchment area.

The population outside the catchment area of the facilities is, by this definition, 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. Each base component is ranked from the lowest to the highest, per the number of population living in the 'pixel' to visualise the geographical areas with the most critical unmet needs. The ranking is then divided into quartiles made of equal population fractions (from Q1 –lowest population density to Q4 –highest population density) corresponding to the different colours (from yellow (Q1) to dark red (Q4) (Supplementary Figure 1)). Therefore, the colour on the map relates to the level of unmet need (people nor in the reach of a facility) relative to the whole population.

Supplementary Figure 1: Population coverage of AST laboratories in Zambia

In Zambia, the catchment population living within a one-hour travel time from the 22 participating AMR surveillance sites covers 42% of the population. Hence, the existing facilities do not cover 58% of the population. Regions with the highest absolute unmet need should be prioritised for capacity building to increase population coverage. New capacity should be introduced by upgrading an existing laboratory to start providing services or by constructing a new laboratory.

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). In clinics and hospitals where patient records are tracked between the laboratories and hospitals, patient demographics, clinical profile and antimicrobial usage data for all positive blood and cerebrospinal fluid (CSF) cultures were collected (Figure 4). Additionally, facility- and national-level antimicrobial consumption (AMC) data were collected.

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 16 laboratories across three years.

The MoH and IQVIA jointly recruited local field data collectors. The consortium conducted a capacity-building workshop to train the field staff on data collection, including the use of WHONET[17] and the specially developed MAAP tool for the secure transfer of collected data was conducted.

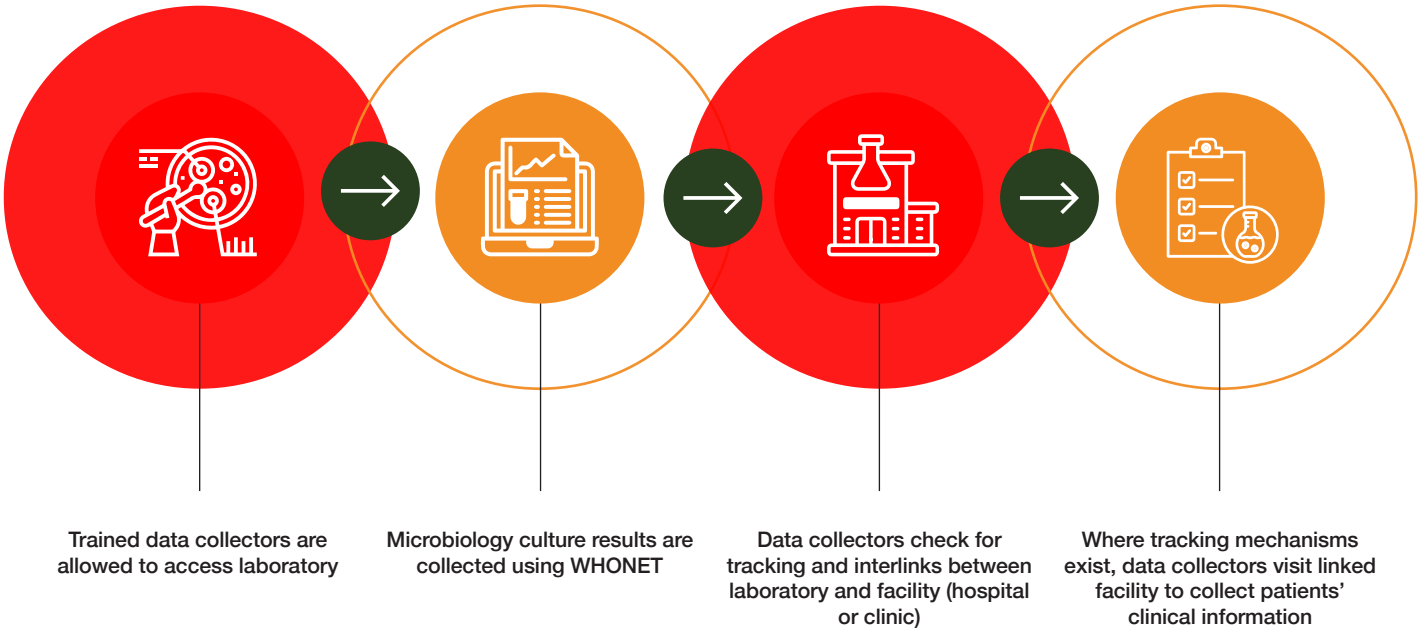


Figure 4: Steps of AMR data collection

Historical data from January 1, 2016, to December 31, 2018, were collected. The AMR data were initially captured through the WHONET, a free Windows-based database software programme developed for the management and analysis of microbiology laboratory data. The software allowed the entry of clinical and microbiological data from routine diagnostic testing or research studies. The WHONET has a simple data file structure and output formats compatible with major databases, spreadsheets and statistical and word-processing softwares. It permits customisation to include variables of interest and has several alert features that highlight unlikely or important results. From the 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, patients were tracked across multiple visits (Figure 5).

Figure 5: Data collection at a Zambia facility

Data analysis

A preliminary data review was conducted to check for data completeness, accuracy, and redundancy. Data were summarised by 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 the subset of total cultures that had complete information on the specimen type, collection date and pathogen name. Valid positive cultures were cultures with pathogen growth reported, irrespective of the 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 6).
- **Level of pathogen identification:** Positive cultures with AST results were summarised based on the level of pathogen identification. Gram and genus-level identification were considered incomplete; reporting at a species level indicated complete pathogen identification. Each laboratory data were stratified and assessed over the entire study period (Figure 6).

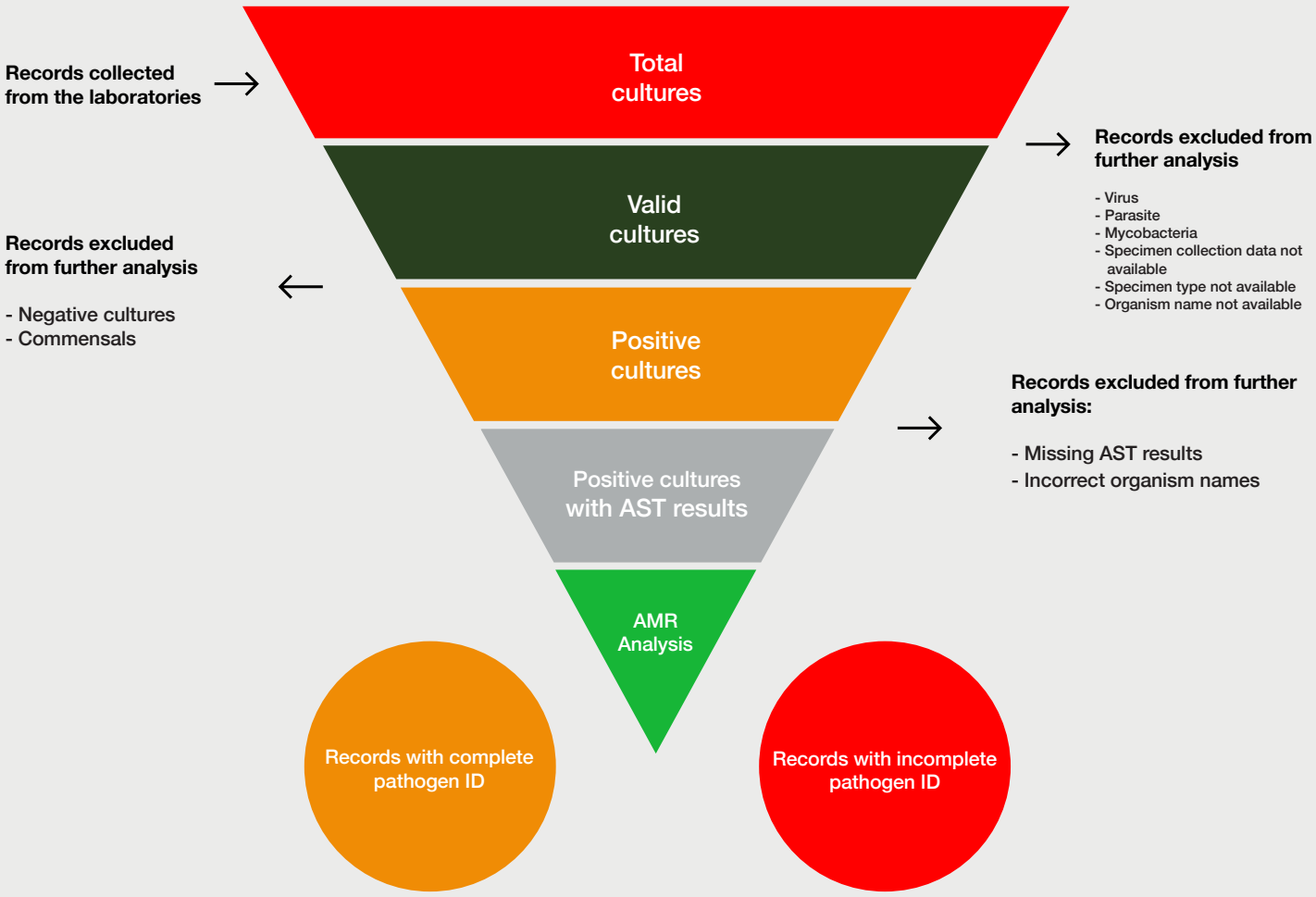


Figure 6: Conceptual framework for deriving quantum of cultures

- **Culture characteristics:** Cultures were characterised across gender, age group, and pathogen type (bacteria or fungi). Data were pooled across all laboratories, and assessment was done for each study year.
- **Inappropriate testing:** Positive cultures with AST results were assessed for compliance with AST standards. However, a comprehensive validity assessment of AST results was beyond the study's scope. Data were pooled across laboratories and assessed for each study year. The conventional AST standards are Clinical and Laboratory Standards Institute (CLSI), the European Committee on Antimicrobial Susceptibility Testing (EUCAST), and Comité de l'antibiogramme de la Société Française de Microbiologie-European Committee on Antimicrobial Susceptibility Testing (CASFM-EUCAST).
- **Clinical information:** Positive cultures with AST results were summarised based on available clinical information, including diagnosis, infection origin (either hospital- or community-acquired), presence of an indwelling device, and antimicrobial use. Data was 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 since 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 more than 75% species-level pathogens identification were awarded the highest score (4). Laboratories with less than 25% identification received the lowest score (1), (Table 3). First, the scoring was performed per year (i.e., 2016–2018), and then 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

Since 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. Therefore, the maximum attainable data quality score was 4, corresponding to an 'Excellent' rating (Table 4).

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 laboratories and i represents individual laboratories.

Results

Retrospective data from 2016–2018 were collected from 14 laboratories and their healthcare facilities in Zambia.

1. Quantum of cultures and level of pathogen identification

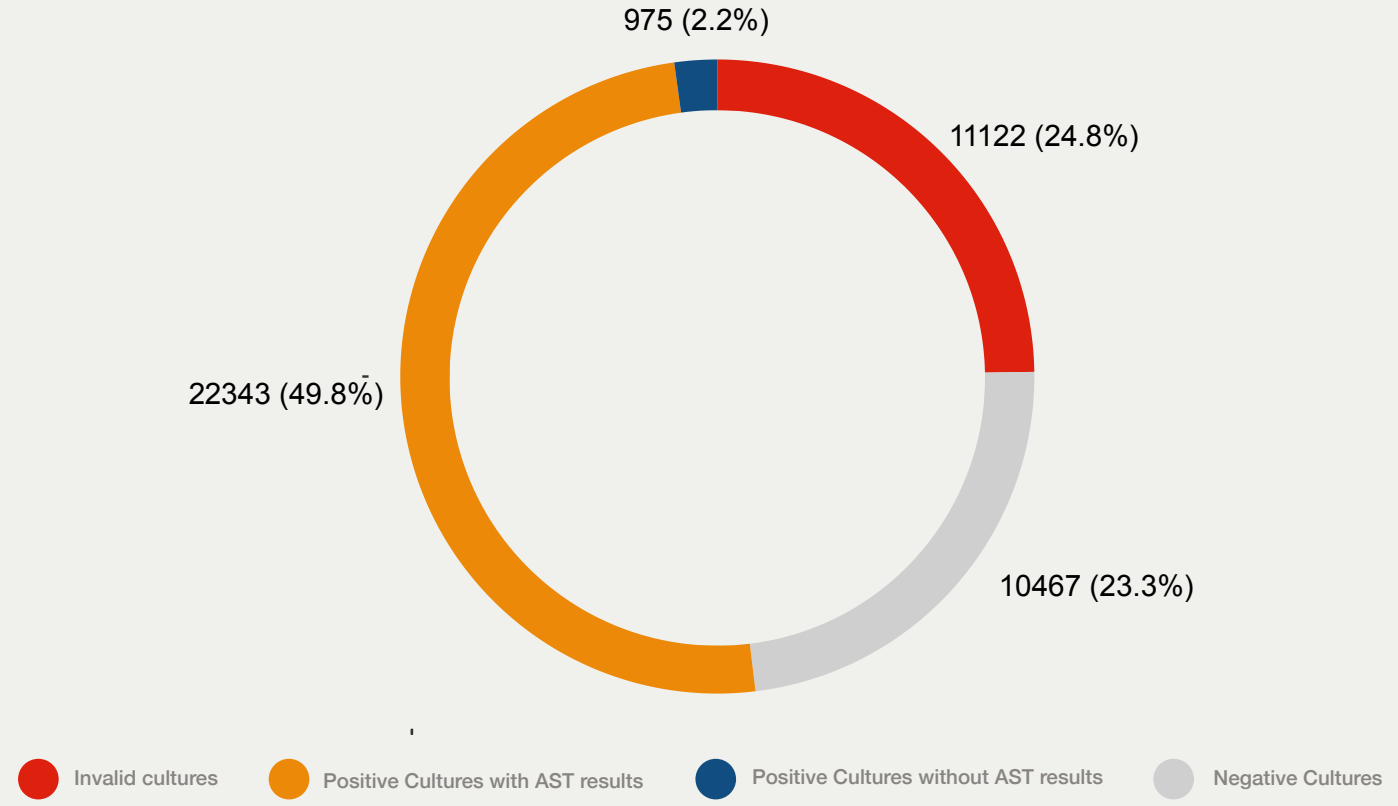
Data were retrieved for 44 912 total cultures, of which 33 790 were valid and 23 318 were positive. Of the positive cultures, AST results were available for 22 343 positive cultures, with the highest (n=19 336) coming from University Teaching Hospital and the least (n=28) from Lewanika (Figures 7 and 8). Not all pathogens were identified completely (i.e., at the species level). Complete identifications were highest at the Livingstone laboratory (73%) and lowest for Arthur Davidson (8%) (Table 5).

Table 5: Culture and AST data retrieved from 14 selected laboratories in Zambia, 2016-2018

Variable (Columns) / Laboratory (Rows)	Total Cultures N = 44 912	Valid Cultures N = 33 790	Positive cultures N = 23 318	Positive cultures with AST results N = 22 343	Incomplete identity* N = 7 712	Complete identity* N = 14 631
Arthur	2 120	2 062.0 (97.3)	695 (33.7)	686 (98.7)	629 (91.7)	57 (8.3)
Nchanga	1 264	1 261.0 (99.8)	215 (17.0)	185 (86.0)	114 (61.6)	71 (38.4)
UTH	31 880	21 083.0 (66.1)	20 149 (95.6)	19 336 (96.0)	5 936 (30.7)	13 400 (69.3)
Ndola	118	116.0 (98.3)	113 (97.4)	113 (100.0)	50 (44.2)	63 (55.8)
Livingstone	295	256.0 (86.8)	243 (94.9)	229 (94.2)	62 (27.1)	167 (72.9)
Chilonga	548	532.0 (97.1)	233 (43.8)	182 (78.1)	56 (30.8)	126 (69.2)
Lewanika	350	346.0 (98.9)	28 (8.1)	28 (100.0)	10 (35.7)	18 (64.3)
Mansa	1 026	898.0 (87.5)	288 (32.1)	284 (98.6)	192 (67.6)	92 (32.4)
Chipata	744	719.0 (96.6)	302 (42.0)	300 (99.3)	131 (43.7)	169 (56.3)
Levy	1 808	1 796.0 (99.3)	168 (9.4)	159 (94.6)	91 (57.2)	68 (42.8)
St. Francis	1 315	1 294.0 (98.4)	94 (7.3)	90 (95.7)	36 (40.0)	54 (60.0)
Kasama	291	286.0 (98.3)	138 (48.3)	131 (94.9)	42 (32.1)	89 (67.9)
Kabwe	2 466	2 458.0 (99.7)	484 (19.7)	479 (99.0)	325 (67.8)	154 (32.2)
Solwezi	687	683.0 (99.4)	168 (24.6)	141 (83.9)	38 (27.0)	103 (73.0)

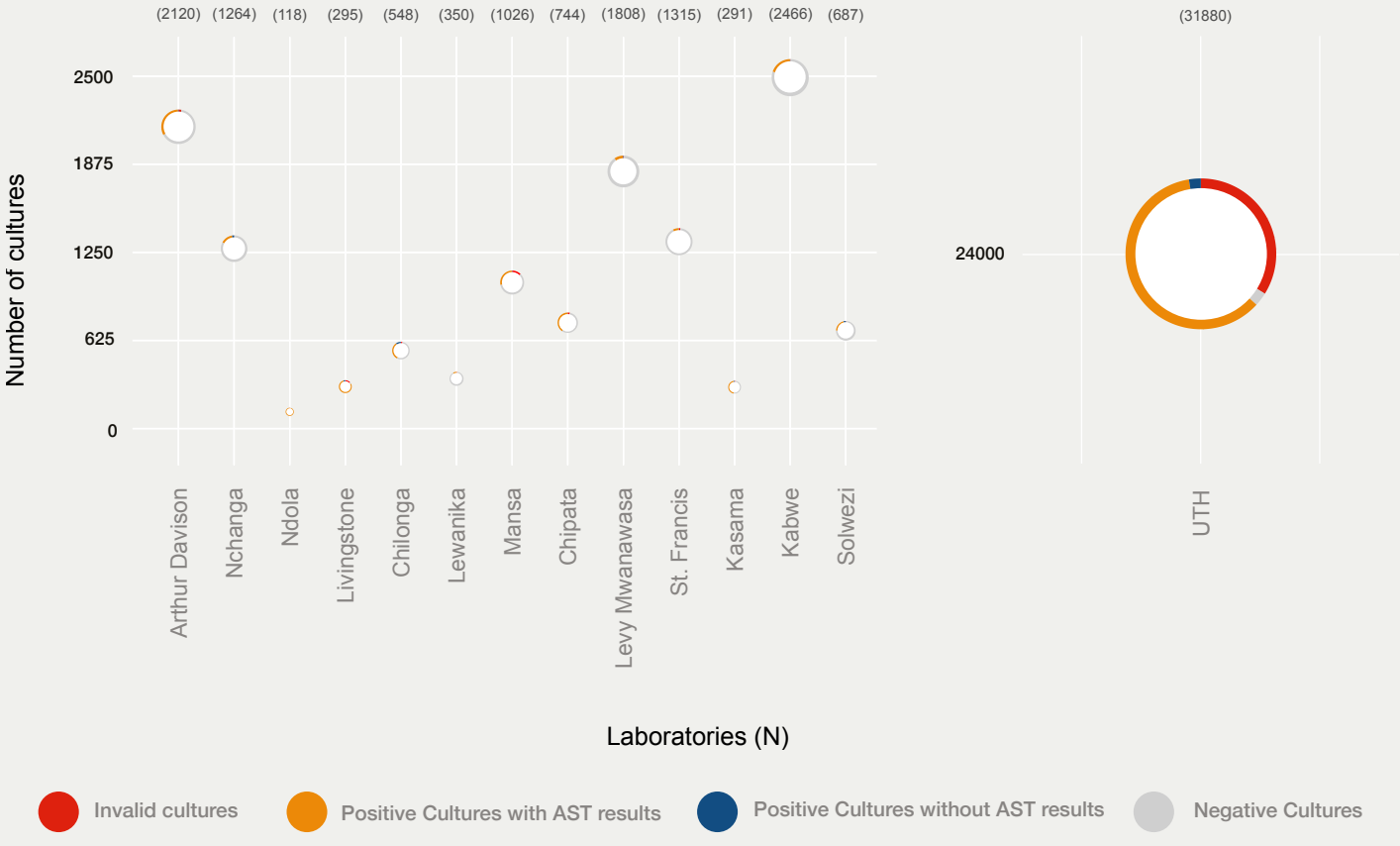
* Subsets of the category 'Positive cultures with AST results' where 'incomplete', it includes cultures with only Gram or genus-level identification; 'complete' includes cultures with species-level identification; — information not available

AST=Antibiotic Susceptibility Testing



Abbreviations: AST=antibiotic susceptibility testing

Figure 7: Quantum of cultures from all 14 selected AST laboratories in Zambia, 2016-2018



AST=Antibiotic Susceptibility Testing

Figure 8: Quantum of cultures in each selected laboratory in Zambia, 2016-2018

2. Culture characteristics

Bacterial pathogens (22 308) were more commonly isolated from positive cultures than fungal pathogens. Information on age was missing from 13.1% of cultures, but where available, the data showed a patient-median age of 29 years (range: 0–90 years), with most of the cultures (9 979) obtained from patients 18–49 years old. Females (20 923) contributed more to the quantum of positive cultures with AST results. More data came from the year, 2018 (8 833) than in other years (Table 6, Supplementary Table 3).

Table 6: Socio-demographic characteristics of positive cultures with AST results retrieved from 14 selected laboratories in Zambia, 2016 -2018 characteristics

Characteristics	Positive cultures with AST results n=22 343 n (%)
Gender	
Male	1 420 (6.4)
Female	20 923 (93.6)
Age, years	
Less than 1	1 774 (7.9)
1 to 17	4 231 (18.9)
18 to 49	9 979 (44.7)
50 to 65	1 827 (8.2)
Above 65	1 615 (7.2)
Unknown age	2 917 (13.1)
Years	
2016	6 546 (29.3)
2017	6 964 (31.2)
2018	8 833 (39.5)
Pathogen	
Bacteria	22 308 (99.8)
Fungi	35 (0.2)

3. Inappropriate testing

Ten laboratories reported compliance with CLSI AST standards, while the others did not provide this information. However, a review of AST results revealed instances of inappropriate testing.

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

4. Clinical information

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

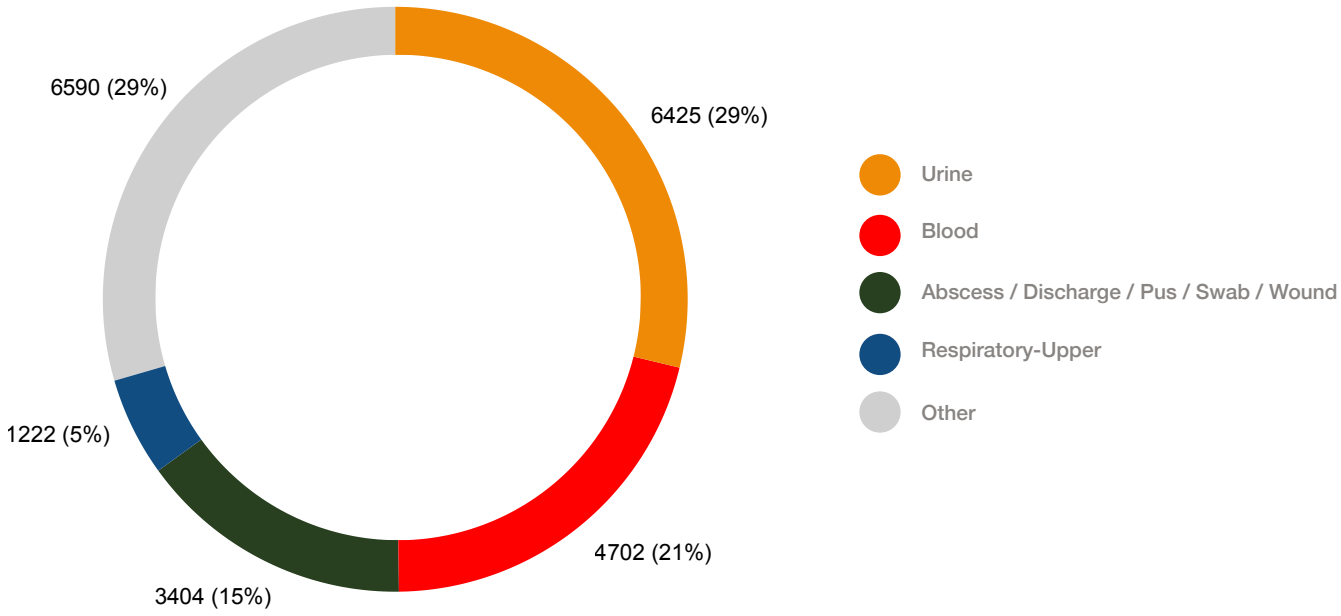
Table 7: Clinical characteristics of positive cultures with AST results retrieved from the 14 selected laboratories in Zambia, 2016-2018

Laboratory	Positive cultures with AST results N=22 343	Diagnosis data	Infection origin data*	Indwelling device data	AMU data
Arthur	686	-	-	-	-
Nchanga	185	-	-	-	-
UTH	19 336	11 184	-	-	-
Ndola	113	-	-	-	-
Livingstone	229	-	-	-	-
Chilonga	182	-	-	-	-
Lewanika	28	-	-	-	-
Mansa	284	-	-	-	-
Chipata	300	-	-	-	-
Levy	159	-	-	-	-
St. Francis	90	-	-	-	-
Kasama	131	-	-	-	-
Kabwe	479	-	-	-	-
Solwezi	141	-	-	-	-

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

5. Specimen characteristics

Urine, blood, and purulent discharge accounted for most of the positive cultures in each study year (Figure 9, AMR Supplementary table 4).



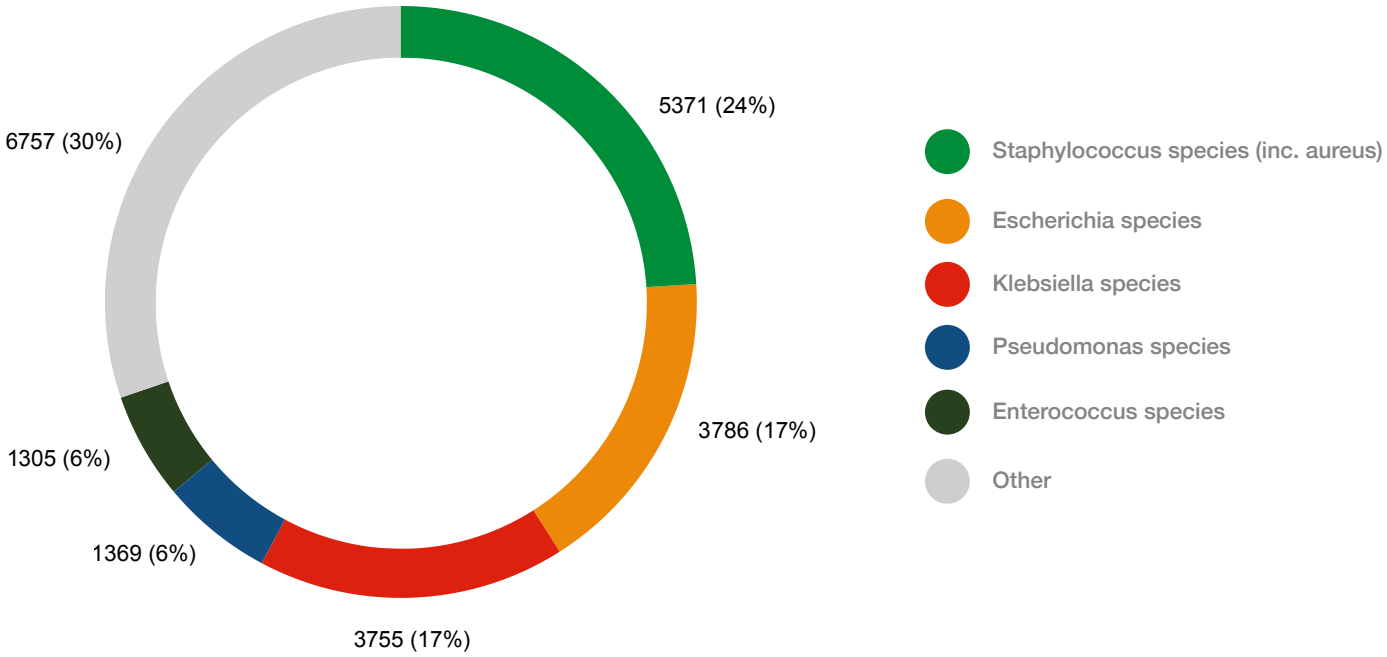
* Others include all other specimens excluding the top five mentioned here

Figure 9: Specimen-type distribution of positive cultures retrieved from 14 selected laboratories in Zambia, 2016-2018

6. Identified pathogens

Staphylococcus species (24%), Escherichia species (17%), and Klebsiella species (17%) largely contributed to the quantum of positive cultures (Figure 10).

In 2016, of the 6 546 positive cultures with AST results, Staphylococcus species (22.2%), Escherichia species (19.7%), and Klebsiella species (18.9%) were the most reported. In 2017, of the 6 964 positive cultures with AST results, Staphylococcus species (22.4%), Escherichia species (17.2%), and Klebsiella species (19%) were again the most reported. In 2018, information was available for a greater number of cultures (8 833), though pathogen distribution remained similar to prior years (Supplementary Table 5).



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

Figure 10: Pathogens identified at the 14 selected laboratories in Zambia, 2016-2018

7. Quality of data

The country data quality score of the 33 790 valid culture records obtained from the 14 laboratories in Zambia was 2.9, which is an 'average data quality' 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 the WHO priority pathogens and other clinically important and frequently isolated pathogens
To enable spatiotemporal mapping of AMR and AMU data across countries

Methodology

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

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, determined by the proportion of non-susceptible isolates (i.e., either intermediate or resistant) per year:

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

AMR rates were estimated for the WHO priority pathogens[15] with more than 30 tested isolates regardless of the specimen type (AMR Appendix 5). The AMR trends for the WHO priority pathogens were mapped, 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 interpreted using the updated breakpoints available on the WHONET. Although non-susceptibility interpretations were based on results from the tested antimicrobials, they are represented at the antimicrobial class level wherever possible (AMR Appendix 7). the 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 isolated per patient per year, irrespective of AST profile and specimen characteristics (specimen site or type in the case of WHO priority pathogens) were included; this approach follows the CLSI M39A4 criteria.[16,17] Duplicates were removed 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 AMR rates were calculated as the proportion of non-susceptible isolates.

AMR estimates statistics

Confidence intervals (CIs) were calculated to quantify the uncertainty in the estimated resistance rates, at the 95% level of confidence. Typically, AST CIs data have been constructed using the Wilson score method, a binomial calculation that assumes that all samples are independent.[18] However, there are likely correlations between data within each laboratory and between laboratories that draw from similar populations. Thus, the Wilson cluster robust CI method was employed where appropriate to account for the lack of data independence, such that each laboratory represented a cluster.[19]

There 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. AST result validation was beyond the study's scope; thus, data were taken at face value to assess resistance rates.

Online data visualisation

The AMR data were aggregated at 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]). The RSN provides a simple approach for analysing AMR data: point-and-click editing tools allow the user to mine the data to answer complex questions and the resulting analyses can be displayed as bar charts representing resistance over a period or line graphs showing changes over time(e.g., by month or year). The RSN will be made available to each participating country for at least one year, following the end of the study.

Data were also uploaded to the CDDEP's ResistanceMap platform, a publicly available repository of aggregated country-level data.[20] Spatiotemporal analyses of 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 non-susceptible isolates per year interval. From 2016–2018, the AMR rates for some organisms remained consistent; the rates for others varied. The highest AMR rates were observed for third-generation cephalosporin in the Enterobacterales (~65%), fluoroquinolone in the Salmonella species (65-73%%) and methicillin in S. aureus (MRSA) (30–63%). Rates for carbapenem-resistant Acinetobacter baumannii (10-18%), P. aeruginosa (7-16%) and Enterobacterales (4-9%) were lower (Table 8, Figures 11 and 12). Statistics for vancomycin-resistant and intermediate Staphylococcus species and Staphylococcus aureus are not included.

Table 8: AMR rate estimates for WHO priority pathogens in Zambia, 2016-2018

Pathogen	Antibiotic, class	2016				2017				2018			
		N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)
Acinetobacter baumannii	Carbapenems	51	9 (17.6)	9.4-30.6	1 (51)	51	5 (9.8)	3.9-21.5	1 (51)	12	0	-	1 (12)
Pseudomonas aeruginosa	Carbapenems	70	5 (7.1)	2.8-16.1	1 (70)	67	11 (16.4)	9.3-27.3	1 (67)	62	4 (6.5)	0.2-74.5	2 (1 - 61)
Enterobacter ales	Carbapenems	810	32 (4)	2.8-5.6	1 (810)	679	61 (9)	5.7-14	4 (1 - 671)	397	34 (8.6)	6-12	3 (1 - 395)
Enterobacter ales	Cephalosporins (3rd generation)	1 583	1 011 (63.9)	58.4-69	6 (1 – 1 414)	1 763	1 139 (64.6)	60.2-68.8	8 (1 - 1613)	1 722	1 127 (65.4)	51.2-77.4	12 (6 – 1 135)
Enterococcus faecium	Vancomycin	45	1 (2.2)	0-12.8	1 (45)	28	0	-	1 (28)	3	0	-	1 (3)
Haemophilus influenzae	Ampicillin	15	3	-	1 (15)	2	0	-	1 (2)	8	3	-	1 (8)
H. pylori	Clarithromycin	-	-	-	-	-	-	-	-	-	-	-	-
Neisseria gonorrhoeae	Cephalosporins (3rd generation)	1	1	-	1 (1)	-	-	-	-	2	1	-	1 (2)
Neisseria gonorrhoeae	Fluoroquinolones	-	-	-	-	1	1	-	1 (1)	1	0	-	1 (1)
Campylobacter species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolones	70	51 (72.9)	62.1-81.5	2 (1 - 69)	68	44 (64.7)	55.3-73.1	3 (1 - 64)	80	53 (66.2)	48.3-80.5	5 (1 - 65)
Shigella species	Fluoroquinolones	36	5 (13.9)	5.7-29.3	1 (36)	18	5	-	2 (1 - 17)	14	6	-	3 (2 - 9)
Staphylococcus aureus	Methicillin	495	149 (30.1)	26.3-34.2	3 (1 - 490)	417	176 (42.2)	33.2-51.7	4 (1 - 402)	376	237 (63)	56.7-68.9	7 (1 - 345)
Streptococuus pneumoniae	Beta-lactam combinations	-	-	-	-	7	0	-	1 (7)	-	-	-	-
S. pneumoniae	Penicillins	23	4	-	1 (23)	10	0	-	1 (10)	19	11	-	6 (1 - 9)

N=the number of tested isolates; n=the 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 the same genus are grouped as one entity.

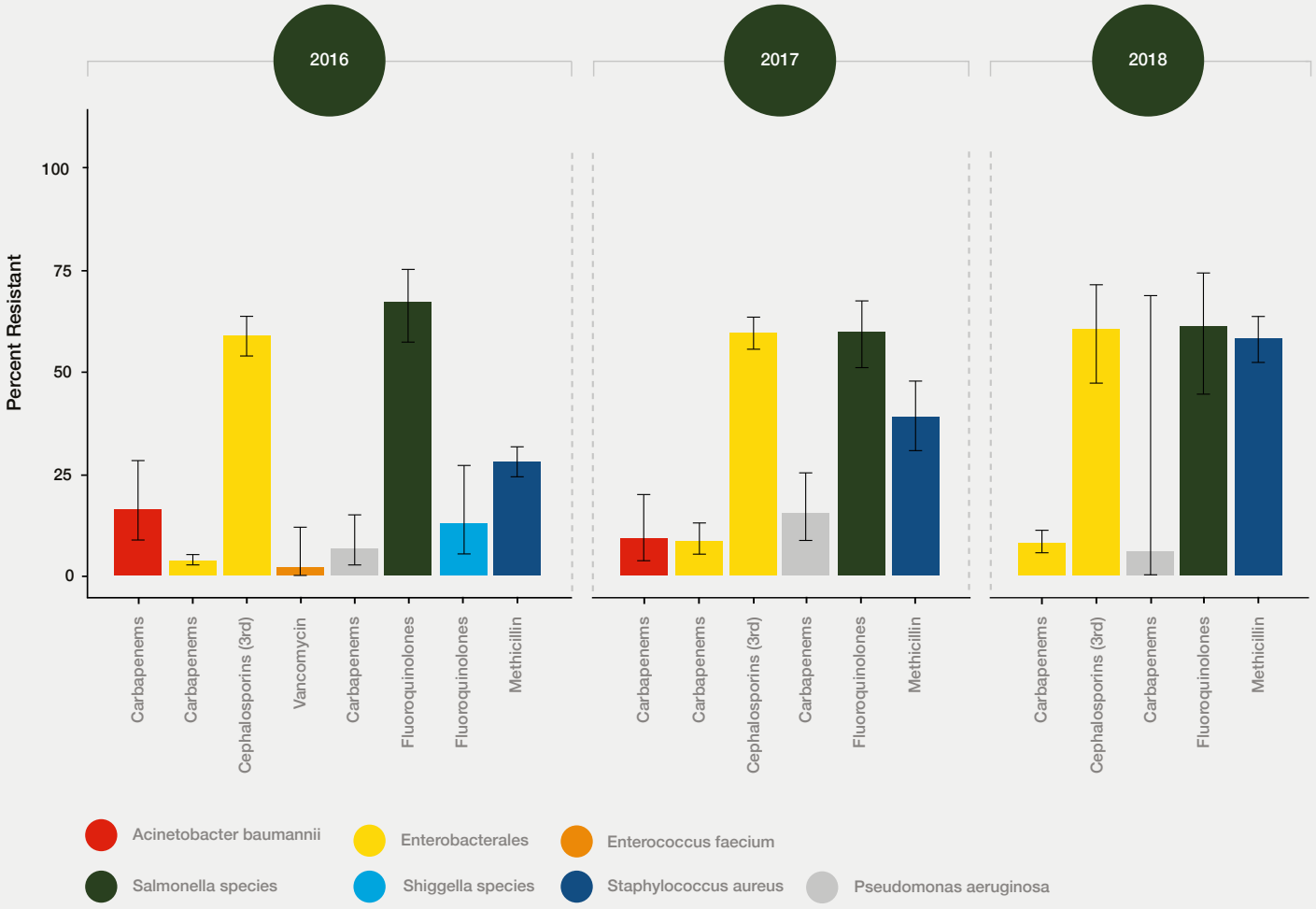
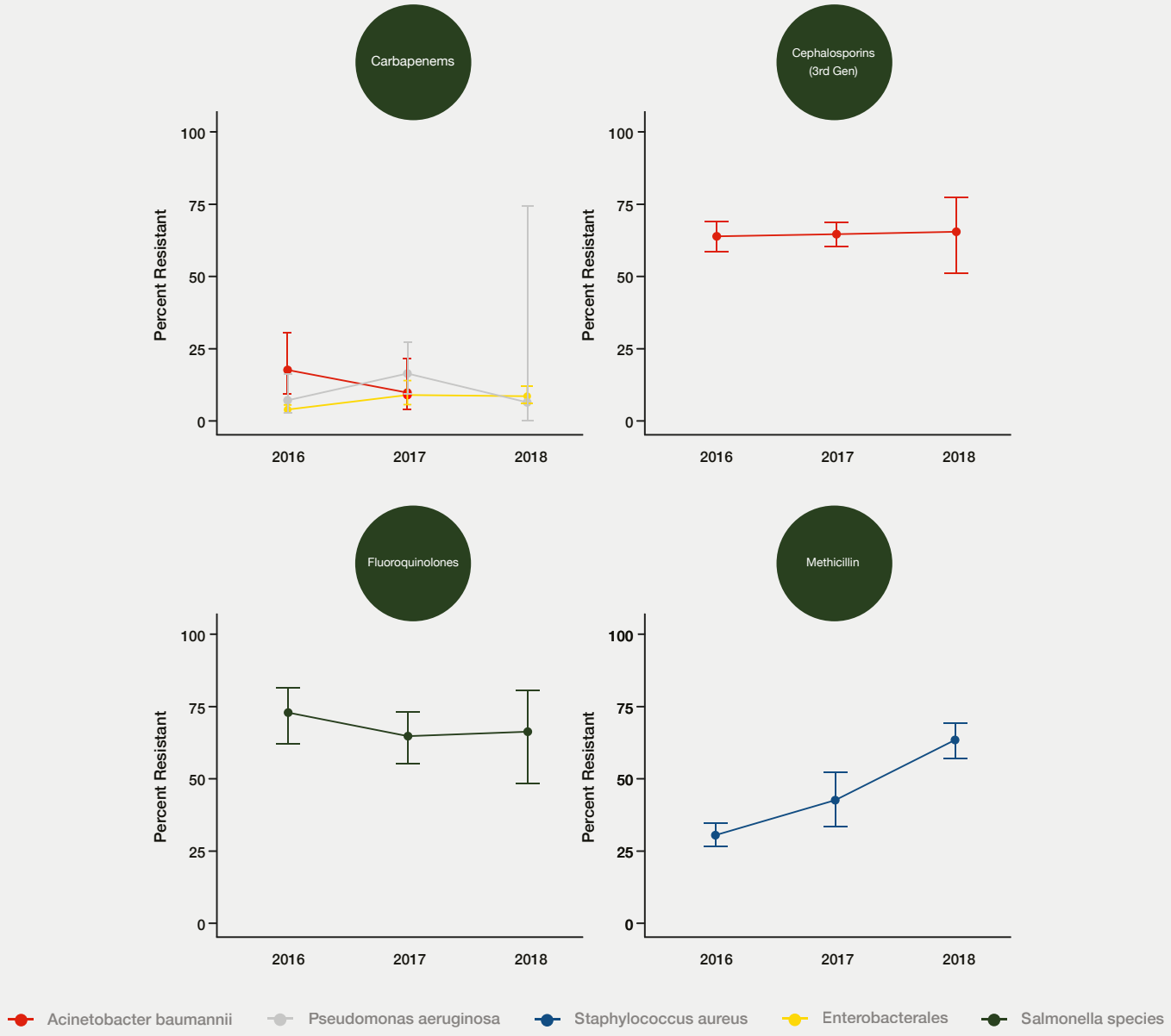


Figure 11: AMR rate estimates for selected WHO priority pathogens isolated by 14 selected facilities in Zambia, 2016-2018



3rd Gen=Third generation

Figure 12: AMR trends of selected WHO priority pathogens isolated by the 14 selected laboratories in Zambia, 2016 -2018

(ii) AMR rates for other pathogens of clinical importance

Analysis of the AST data from blood and CSF isolates revealed very high rates of third-generation cephalosporin-resistant Klebsiella species (~80-95%) and MRSA (79-82%). The AMR rate for carbapenem-resistant Klebsiella species was low (<5%), while it was variable for vancomycin-resistant Enterococci species (Table 9).

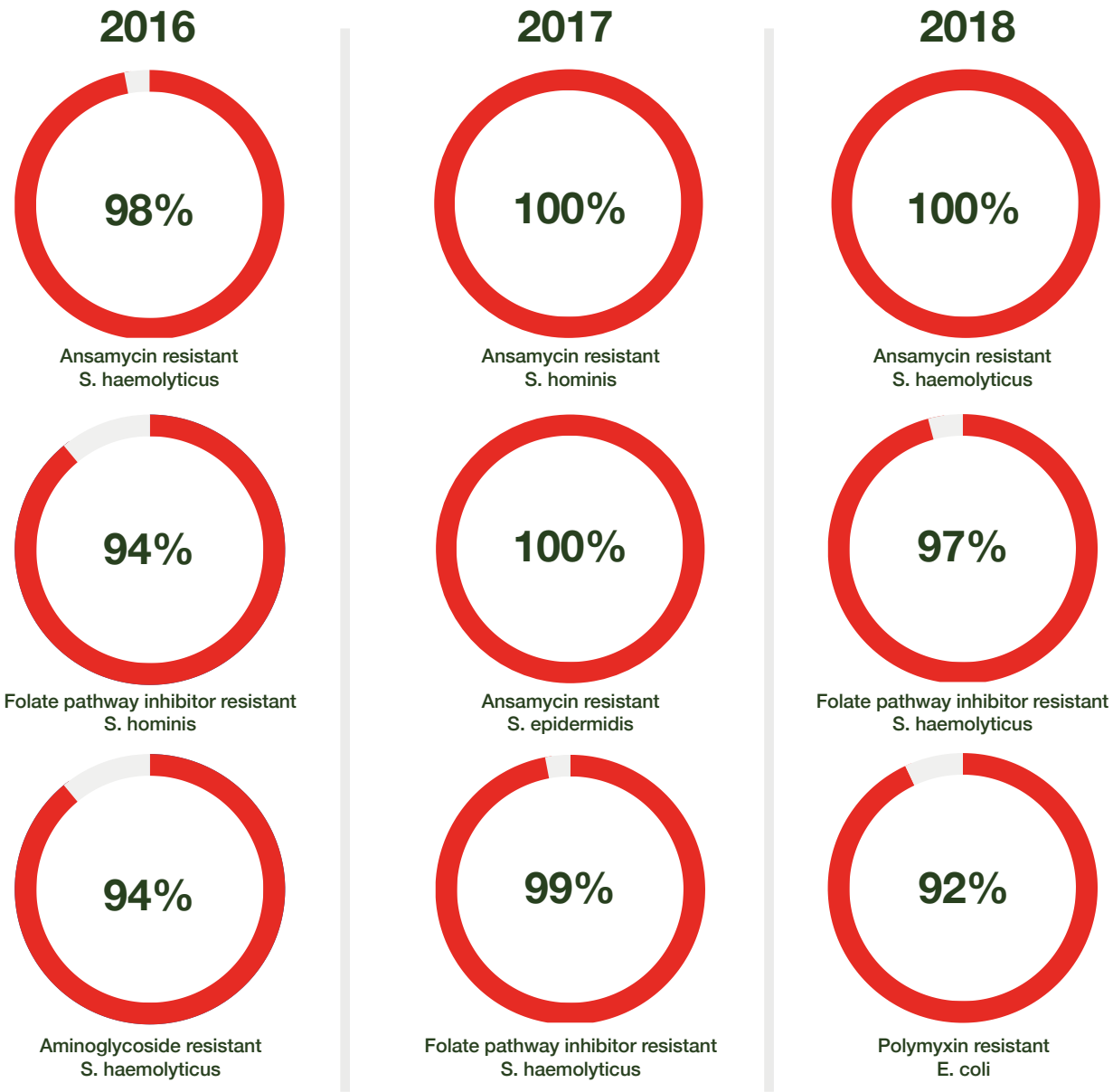
*Table 9: AMR rate estimates for other clinically important pathogens*identified at 14 selected laboratories in Zambia, 2016-2018*

		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	20	2	-	1 (20)	9	1	-	1 (9)	24	3	-	1 (24)
Acinetobacter species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Aminoglycosides (high level)	12	12	-	1 (12)	1	0	-	1 (1)	4	3	-	1 (4)
Enterococcus species	Vancomycin	110	6 (5.5)	2.3-11.7	1 (110)	56	16 (28.6)	8.5-63.2	2 (1 - 55)	47	5 (10.6)	4.3-23.2	1 (47)
H. influenzae	Ampicillin	2	0	-	1 (2)	-	-	-	-	-	-	-	-
H. influenzae	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Klebsiella species	Carbapenems	257	4 (1.6)	0.5-4.1	1 (257)	44	2 (4.5)	0.5-16.2	1 (44)	127	3 (2.4)	0.5-7.1	1 (127)
Klebsiella species	Cephalosporins (3rd generation)	291	279 (95.9)	92.8-97.7	1 (291)	118	92 (78)	60.4-89.1	4 (1-108)	199	187 (94)	93.2-94.7	2 (1-198)
N. meningitidis	Ampicillin	-	-	-	-	1	1	-	1 (1)	-	-	-	-
N. meningitidis	Cephalosporins (3rd generation)	-	-	-	-	3	3	-	1 (3)	-	-	-	-
Pseudomonas species	Carbapenems	20	2	-	1 (20)	14	5	-	2 (1 - 13)	11	2	-	1 (11)
Pseudomonas species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Macrolides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	Methicillin	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus species (excluding aureus)	Methicillin	318	254 (79.9)	78.2-81.4	2 (1-317)	396	323 (81.6)	79.3-83.6	4 (1-386)	201	158 (78.6)	72.4-83.7	1 (201)
S. pneumoniae	Penicillins	4	2	-	1 (4)	10	6	-	4 (1 - 5)	3	0	-	1 (3)
S. pneumoniae	Beta-lactam combinations	-	-	-	-	-	-	-	-	1	0	-	1 (1)
S. pneumoniae	Macrolides	6	3	-	1 (6)	5	4	-	4 (1 - 2)	3	0	-	1 (3)
S. pneumoniae	Vancomycin	5	0	-	1 (5)	6	1	-	2 (1 - 5)	-	-	-	-

* Isolates were from blood and cerebrospinal fluid; N = number of tested isolates; n = number of non-susceptible isolates; 95% CI are shown only if there are >30 isolates per year; # contributing laboratories and range of tested isolates; — information not available; for pathogens with the suffix 'species', all isolates of the same genus are grouped as one entity

(iii) AMR rates for highly resistant pathogens

Based on available data, very high resistance (100%) was estimated for clinically important pathogens like Staphylococcus hominis (vs. ansamycins), S. haemolyticus (vs. ansamycins) and S. epidermidis (vs. ansamycins) (Figure 13).



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

Figure 13: Top five highly resistant pathogens isolated by the 14 selected laboratories in Zambia, 2016 -2018

(iv) AMR rates for fungal pathogens

The 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. The association of the following patient and country-level factors with AMR were assessed to identify potential AMR drivers.

- Patient-level factors: demographics (age, gender), diagnosis, comorbidities, antimicrobial usage, presence of an indwelling medical 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, gross domestic product (GDP) per capita, physicians and nurses densities, disease prevalence, and antibiotic consumption in DDD per 1 000 inhabitants (the country-level associations are presented separately at a regional/ continental level)

To identify the drivers of resistance, a composite AMR rate for select groups of pathogens (Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus 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 DRI methodology guided the choice of pathogens and antimicrobials (see Part C).

Statistical analysis

An initial data exploration was conducted 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 ratio (ORs) were estimated in the univariate logistic regression analysis to describe the association between AMR and the investigated variables, and 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 the robust standard error was used to construct CIs for the AMR rates.

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

All results should be interpreted with caution because they were derived from data aggregated from facilities and laboratories with varying capabilities.

Results

Information on patient factors was unavailable or inadequate for analysis, except for age, gender and diagnosis. The possible association of these three variables with AMR was evaluated. The data availability of the selected variables was: gender, 7.8%; diagnosis, 55.3%; and age, 89.1%. The univariate analysis revealed that patients aged above 50 years were more likely to have resistant infections (50-65: OR 1.12, 95% CI 1.06 – 1.18; >65 OR 1.32, 95% CI 1.17 – 1.48). In addition, renal and respiratory diagnoses were significantly associated with AMR, with patients with a renal diagnosis more likely to have resistant infections (OR 1.47, 95% CI 1.15 – 1.90) and those with respiratory diagnosis less likely to have resistant infections (OR 0.64, 95% CI 0.45 – 0.92) (AMR Supplementary Table 7).

Age and diagnosis were included in the multiple logistic regression analysis based on the set criteria. When controlling for the effect of age, patients with the renal diagnosis were more likely to have resistant infections (OR 1.44, 95% CI 1.11 – 1.87) while those with the respiratory diagnosis were less likely to have resistant infections (OR 0.65, 95% CI 0.45 – 0.95). When adjusting for the diagnosis, age groups below 18 years i.e., <1 year (OR 1.14, 95% CI 1.01 – 1.27) and 1 - 17 years (OR 1.13, 95% CI 1.01 – 1.27), were more likely to have resistant infections (Table 10).

Table 10: Demographic drivers of AMR in Zambia, 2016 - 2018

Variable	Options	N	NS (%)	Crude OR (95% CI)	P-value
Age	<1	1 709	57.5	1.14 (1.01 – 1.27)	0.039
	1-17	1 995	58.0	1.13 (1.01 - 1.27)	0.040
	18-49	3 796	55.1	Ref	
	50-65	866	55.8	1.04 (0.89 - 1.21)	0.626
	>65	558	58.1	1.13 (0.94 - 1.35)	0.194
Diagnosis	Infection/Inflammation	4 738	56.1	Ref	
	Cardiovascular	77	58.4	1.11 (0.70 – 1.76)	0.650
	Diabetes	105	60.0	1.20 (0.81 – 1.79)	0.361
	Haematological	105	60.0	1.16 (0.78 – 1.72)	0.472
	Injuries	578	57.3	1.01 (0.85 – 1.22)	0.874
	Neoplasm	196	62.2	1.29 (0.96 – 1.73)	0.095
	Nonspecific	2 035	55.4	0.98 (0.88 -1.09)	0.704
	Nutritional	490	56.5	0.95 (0.78 - 1.16)	0.636
	Obs/Gynaecological	99	62.6	1.39 (0.92 – 2.09)	0.123
	Renal	259	64.5	1.44 (1.11 – 1.87)	0.006
	Respiratory	113	45.1	0.65 (0.45 – 0.95)	0.028
	Surgical/Orthopaedic	129	55.8	1.02 (0.72 – 1.45)	0.914

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

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 AMR causation. Widespread and unregulated antimicrobials use exerts a selective pressure by inhibiting the growth of susceptible microorganisms, consequently favouring the overgrowth of resistant strains, exacerbating AMR.[21,22] Therefore, close surveillance on how the antimicrobials are utilised is a key step for stewardship programmes to stem AMR. The surveillance mechanisms recommended by the WHO include monitoring AMC and AMU and are in line with the MAAP's aim to expand the volume of AMR and AMC/AMU data available across Africa and Zambia's multi-sectoral NAP on AMR (2017-2027).[13]

Definition of AMC and AMU

AMC is defined as the number of antimicrobials used within a specified setting (e.g., national-, hospital-, or community healthcare levels) over a specified period. The AMC is calculated from aggregated data such as import, wholesalers, insurance, 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 incorrectly used interchangeably. It is therefore prudent to further clarify that AMC data describe quantities of antimicrobials dispensed (e.g., at national stores or pharmacies), whereas AMU data describes how and why antimicrobials are used (i.e., whether the required laboratory tests and clinical assessments were conducted before prescription, whether the right antimicrobial was prescribed at the correct strength and frequency, for the appropriate duration, to treat the right indication as per country guidelines and whether the patient correctly and completely consumed the prescribed antimicrobial).[23]

Link between the antimicrobial usage and AMR

TThe unwarranted use of antimicrobials is in part attributable to the emergence of AMR. This association implies that a reduction in the unnecessary consumption of antimicrobials could, in turn, reduce AMR levels.[21] Inappropriate antimicrobial use refers to the use of the wrong type of antimicrobial and or at the wrong dose, frequency or duration and or for the wrong indication. Recent decades have seen a global increase in the consumption of antimicrobials and a consumption shift towards 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 increase due to lack of access to antimicrobials, leading to the prolonged use of a particular antimicrobial over a long time and thus selective pressure favours microbes that evade these predominantly used antimicrobials. This is often the picture in several LMICs where inequities in antimicrobial access persist.[24]

This complicated picture demonstrates the need for the research and development of new agents that counteract emerging AMR, and also strongly supports the need for appropriate use of and access to available antimicrobials. In this regard, one of the MAAP's key objectives was to evaluate the ability to conduct AMC and AMU surveillances (data collection and analysis) in Zambia, which would equip the country with valuable information to support the appropriate use of antimicrobials. The objective was also to identify gaps that may exist in setting up 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

Optimising the correct usage of antimicrobials is one of the strategic objectives of the WHO GAP to ensure the successful treatment of infectious diseases in patients.[8] For the successful implementation of the above objective, there is a need to understand a country's pattern of AMU and quantify their consumption. At present, there are only a few published reports on AMC surveillance and AMU in Africa.[25-29] The process of obtaining AMC/AMU data equips the country with local information on various problems that exist with AMU and allows for monitoring the accessibility of antimicrobials. Further, obtaining AMC/AMU data permits the continuous local assessment of correlations between antimicrobial usage to emerging local AMR that informs proper mitigation policies and activities. Data obtained from local surveillance exercises will also better inform stewardship programmes. Therefore, the MAAP set out to quantify consumption and analyse AMC and AMU trends at selected facilities and the national-level.

The aim of this work

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

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

Section II: AMC or AMU surveillance status

Objective

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

Methodology

Through open-structured Key Informant Interviews (KIIs) (AMC Appendix 1), the AMRCC contacts shared their insights about the country's current AMC surveillance landscape and where national AMC and AMU data can best be surveilled from. From this, Zambia Medicines Regulatory Authority (ZAMRA) was identified as a potential source for national AMC data as they were the sole entity involved in approving and regulating all medicines imported into or manufactured in the country. The MSL was also identified as another national AMC source, which is Zambia's medicine procurement, storage and distribution agency.

Under the guidance of the Zambia AMRCC, the MAAP intended to recruit and obtain data from twice as many pharmacies as the selected AST laboratories (i.e., a total of 32 pharmacies). Pharmacy-level AMC data were collected from the pharmacies that were co-located in the same facility with AST laboratories (n=16) (AMC Appendix 2 for the tool used). Additionally, AMC data were collected from sixteen community pharmacies nominated by the AST laboratory-co-located-pharmacies because of their proximity to the AST laboratories and or their status as the preferred patient medicine purchase sites or backup prescription fulfilment source during stock-outs in the main hospital pharmacy. Additionally, the availability of retrospective data from 2016-2018 and willingness to share data were key selection criteria.

Besides AMC data collection, AMU data were collected from sixteen hospital pharmacies; AMU data were abstracted 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 exclude unregulated and informal medicine dispensers. While hospital pharmacies are the pharmacies located within a hospital that provides medicinal products to the hospital's in and outpatients.

Data collection scope

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

Data collection

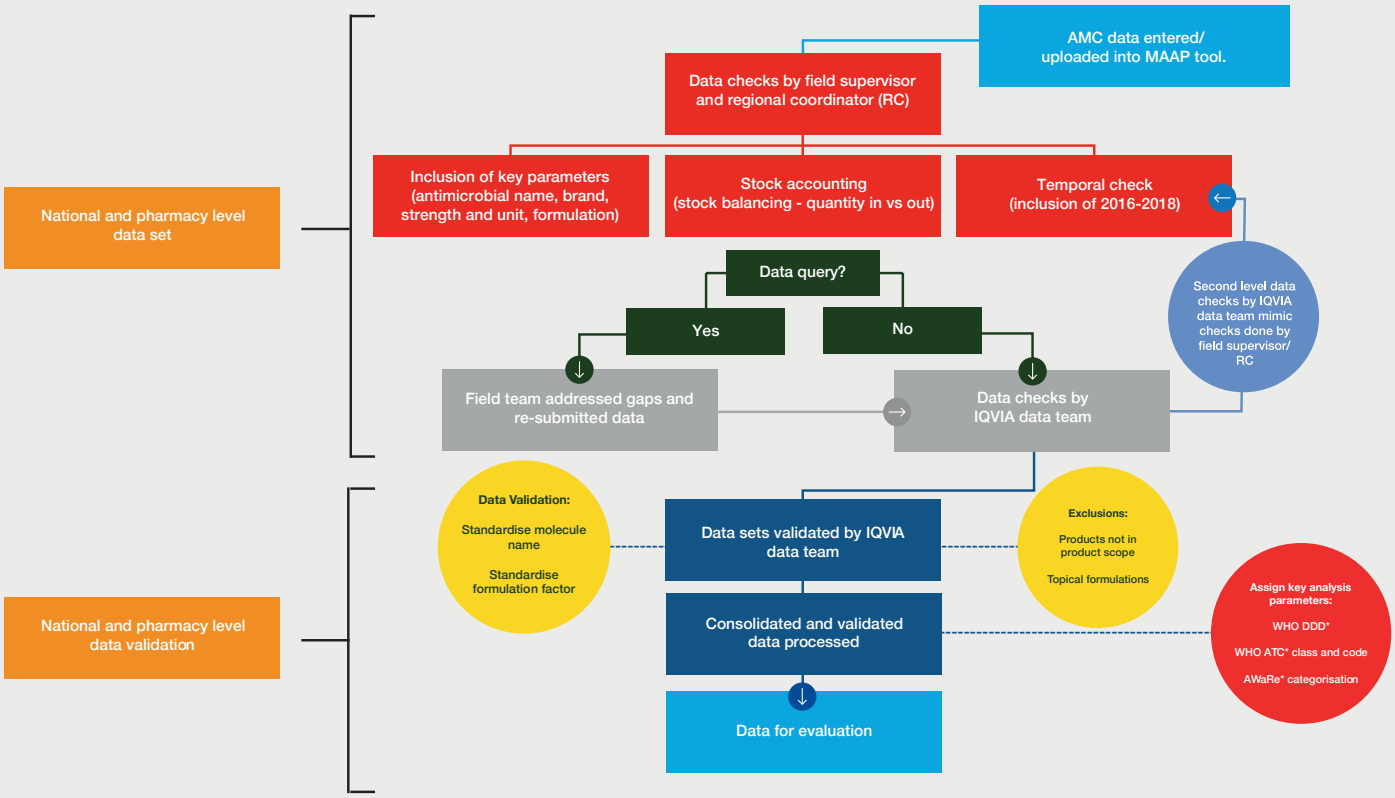
Electronic MSL datasets were provided directly to the MAAP field data collectors in Microsoft Excel™ sheet. Following multiple unsuccessful attempts, MAAP was unable to access data from the ZAMRA. The MSL datasets were sorted to filter out the products within scope. The datasets were then reviewed and cleaned by the data collection teams on Microsoft Excel™ software, which were then transferred securely through the MAAP tool. The MAAP tool captured all of the antimicrobials by their standard molecule name and/or product brand, pack size, strength, and formulation (e.g., tablets/capsules, suspensions/ syrups). The AMC Appendix 4 captures the full list of data variables collected to tally national- and pharmacy-level AMC.

In facilities with Health Information Systems (HIS), the trained MAAP data collectors electronically extracted consumption data into a Microsoft Excel™ sheet. However, consumption data were manually abstracted data from stock record cards and entered into the MAAP tool in 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).

The MAAP also planned to collect AMU data in pharmacies co-located with AST Laboratories in the same facility to assess the appropriateness of consumed antimicrobials. Data to be captured included, patient characteristics and prescription indication, prescription appropriateness per national guidelines, including conducting relevant laboratory tests and clinical assessments before prescribing and assessing dose, strength, frequency, and duration of the prescription.

Data cleaning and validation

Once the national-level antimicrobial datasets from MSL were received by the MAAP, the national-and pharmacy-level AMC datasets were then validated to ensure accuracy and consistency (AMC Appendix 6). Here, the pharmacy and national AMC datasets were subjected to secondary and tertiary checks by field supervisors, the regional coordinator and the IQVIA data team as outlined in Figure 14.



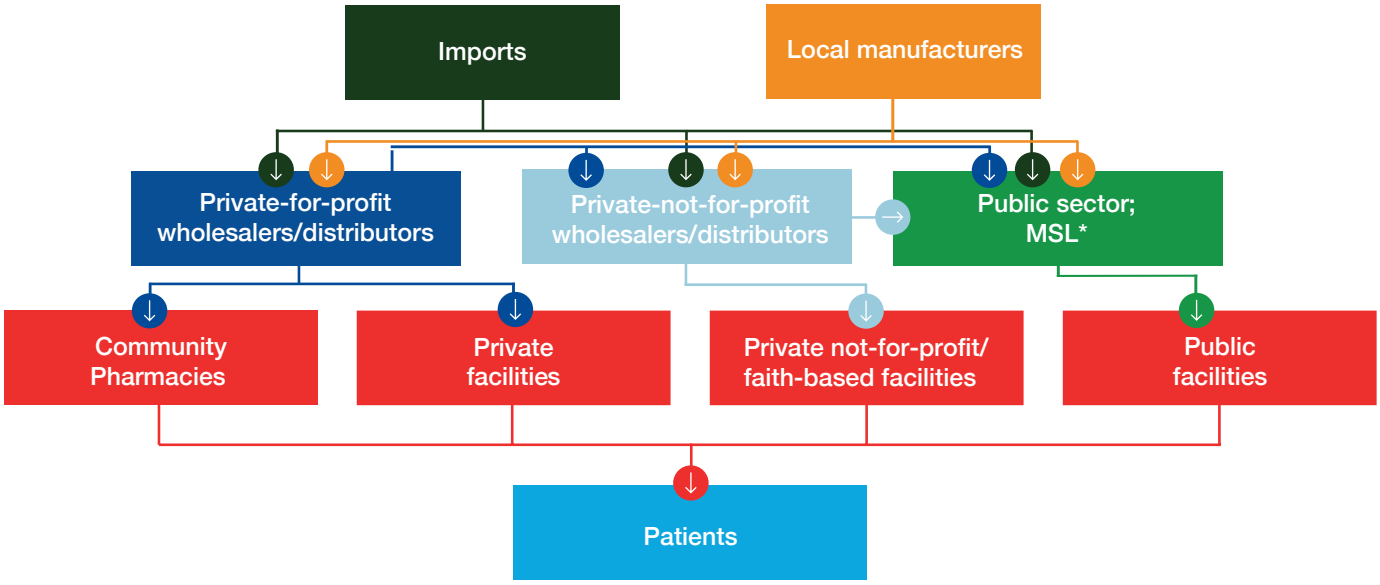
*DDD Defined Daily Dose - *ATC - Anatomical Therapeutic Chemical *AWaRe - Access, Watch and Reserve

Figure 14: Data checks and validation procedures for the national- and pharmacy-level AMC datasets collected in Zambia, 2016-2018

Results

Flow of antimicrobials in the country

Three KIIs were conducted with stakeholders in the national Antimicrobial Resistance Coordinating Committee (AMRCC), the public sector procurement mechanism – Medical Stores Limited (MSL) and representatives from MoH to characterise antimicrobials flow to patients. In Zambia, medicines including antimicrobials are imported and locally manufactured. The ZAMRA regulates and licenses all pharmaceutical products (imported or locally manufactured). After importation or local production, private (for-profit and not-for-profit) wholesalers and public-sector central medical store –MSL, then pass along the antimicrobials to the community pharmacies, private (both for- and non-profit) facilities and public facilities, which eventually dispenses the antimicrobials to patients. The flow chart below (Figure 15) illustrates the route through which antimicrobials get to the patients in Zambia.



*MSL: Medical Store Limited

Figure 15: Antimicrobial circulation to patients in Zambia, 2016-2018

Regulation of antimicrobials consumption

In Zambia, antimicrobials for human consumption are regulated under the Medicines and Allied Substances Act No. 3 of 2013. This Act stipulates that requisite antimicrobials can only be sourced from registered suppliers and can only be dispensed upon issuance of a valid prescription. Despite this antimicrobial dispensing regulation, there is still poor enforcement, leading to the widespread availability of over-the-counter antimicrobials without a prescription in Zambia.[13] This non-authorised over-the-counter retail of prescription antimicrobials, may lead to their overuse and or misuse. The overuse and misuse of antimicrobials significantly contribute towards the emergence of AMR. Therefore, to address the above issues and other prevalent gaps, the country developed the Zambia Multi-sectoral NAP on AMR (2017-2027) that seeks to further build AMC regulations to curb the growth or emergence of AMR.

Availability of data for AMU surveillance

Attempts were made to obtain AMU data from fourteen participating pharmacies that were co-located with the AST laboratories in facilities offering clinical services. However, no AMU data were obtained during MAAP data collection because of the nature of the data sources. The participating pharmacies used stock issuance record cards that did not track the specific medicines received by each person, hindering the retrieval of AMU variables, including patient characteristics and indication for which the antimicrobial is being used and appropriateness of prescription per national guidelines. Variables for assessing prescription appropriateness were also not retrieved, including, determining the conduct of any relevant laboratory tests and clinical assessment before prescribing and assessing prescription dose, strength, frequency, and duration. As a result, the MAAP was unable to collect AMU data in Zambia from the selected health facilities.

Availability of data for AMC surveillance

National-level data

The national AMC data were obtained from MSL for the years 2016 to 2018. However, these datasets had key information missing which is critical for AMC data analysis, particularly the antimicrobials pack size and strength information. Thus, the MAAP data team were unable to calculate DDDs consumed, which is a primary requirement for AMC analysis, from collected MSL national datasets. Subsequently, the MAAP, together with the country's AMRCC, attempted to retrieve national AMC data from ZAMRA using import manifest records. However, the datasets from ZAMRA were inaccessible to MAAP after several attempts. Therefore, this report analyses and presents results from aggregated pharmacy-level AMC datasets only.

Facility-level data

Pharmacy data were collected from 28 pharmacies out of 32 targeted pharmacies, and this included hospital pharmacies (n=14) and community pharmacies (n=14). Fifteen AST laboratories were recruited for data collection; however, one was a stand-alone laboratory i.e., not a hospital pharmacy and was subsequently excluded from the study. Pharmacy data were successfully collected from fourteen targeted hospital-based pharmacies. Furthermore, pharmacy data were collected from Fourteen targeted community pharmacies. Two targeted community pharmacies were unwilling to share data and thus were excluded. The total number of hospital/community pharmacies in Zambia is unknown, thus representativeness of facility-level data could not have been assessed.

The necessary variables for pharmacy-level data were collected from stock cards or electronic records of 28 pharmacies. However, there were instances where strength or pack size information was missing from the stock cards for a few line items/transactions in each of the visited facilities. These information gaps were filled by revisiting the facilities and gathering information from the facility staff or through secondary desk research using the available product details. Of the 14 hospital pharmacies, the MAAP collected data for the three years in 11 pharmacies. Three participating hospital pharmacies did not have archived data for the 2016-2017 period. Of the 14 recruited community pharmacies, 8 pharmacies did not provide data for one or more of the study years for lack of archived data or unwillingness to share the data.

Of the participating hospital pharmacies (n=14) that were co-located with the AST laboratories, (n=12) were in public government hospitals (two co-located within tertiary care facilities and ten co-located in secondary care facilities). The remaining (n=2) AST-co-located hospital pharmacies were within secondary care private, faith-based facilities. In Zambia, all the recruited hospital pharmacies actively reported AMC data for stock received from MSL directly to MSL, as per the MoH's directives (Table 11).

Table 11: Characteristics of the recruited hospital and community pharmacies in Zambia

	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)	Kasama General Hospital Pharmacy	Secondary	Public	Kasama	Mixed*	No	Yes- partially^
	Mansa General Hospital Pharmacy	Secondary	Public	Mansa	Mixed*	No	Yes- partially^
	Lewanika General Hospital	Secondary	Public	Mongu	Mixed*	No	Yes- partially^
	Kabwe Central Hospital Pharmacy	Secondary	Public	Kabwe	Mixed*	No	Yes- partially^
	Solwezi General Hospital Pharmacy	Secondary	Public	Solwezi	Mixed*	No	Yes- partially^
	Nchanga North General Hospital Pharmacy	Secondary	Public	Chingola	Mixed*	No	Yes- partially^
	Ndola Central Hospital Pharmacy	Secondary	Public	Ndola	Mixed*	No	Yes- partially^
	Arthur Davison Children's Hospital Pharmacy	Secondary	Public	Ndola	Mixed*	No	Yes- partially^
	Chipata Central Hospital Pharmacy	Secondary	Public	Chipata	Mixed*	No	Yes- partially^
	St. Francis Mission Hospital Pharmacy	Secondary	Private, faith-based	Katete	Mixed*	No	Yes- partially^
	Livingstone Central Hospital Pharmacy	Secondary	Public	Livingstone	Mixed*	No	Yes- partially^
	University Teaching Hospital Pharmacy	Tertiary	Public	Lusaka	Mixed*	No	Yes- partially^
	Levy Mwanawasa Teaching Hospital Pharmacy	Tertiary	Public	Lusaka	Mixed*	No	Yes- partially^
	Chilonga Mission Hospital	Secondary	Private, faith-based	Mpika	Mixed*	No	Yes- partially^
Community pharmacies ~	Broken Hill Pharmacy, Kabwe	Dispensing	Private	Kabwe	Manual	N/A	No
	Chipata Chemist	Dispensing	Private	Chipata	Manual	N/A	No
	Choice Pharmacy, Chilonga	Dispensing	Private	Chingola	Manual	N/A	No
	Edma Pharmacy Kasama	Dispensing	Private	Kasama	Manual	N/A	No
	Kansenshi Chemist	Dispensing	Private	Ndola	Manual	N/A	No
	Katete Pharmacy	Dispensing	Private	Katete	Manual	N/A	No
	Life Pharmacy Mongu	Dispensing	Private	Mongu	Manual	N/A	No
	Livingstone Pharmacy	Dispensing	Private	Livingstone	Manual	N/A	No
	Pharmaking Chingola Pharmacy	Dispensing	Private	Chingola	Manual	N/A	No
	Pharmaking Solwezi Pharmacy	Dispensing	Private	Solwezi	Manual	N/A	No
	Ridgeway Chemist, Lusaka	Dispensing	Private	Lusaka	Manual	N/A	No
	Sisters of Mercy Pharmacy	Dispensing	Private	Mpika	Manual	N/A	No
	Stalilo Pharmacy, Lusaka	Dispensing	Private	Lusaka	Manual	N/A	No
	Westgate Pharmacy Chipata	Dispensing	Private	Chipata	Manual	N/A	No

#Tertiary care facilities are central hospitals and provide mainly specialised healthcare services, such as psychiatry, surgery, paediatrics, obstetrics, gynaecology services, training and research. Patients are usually referred from secondary care facilities. Secondary care facilities refer to provisional general hospitals and are referral centres for patients from district hospitals. They offer internal medicines, general surgery, paediatrics and obstetric acute care services, among other non-specialised services. These secondary care facilities are intended to provide services to up to 800 000 people, including referral patients from primary care facilities (district hospitals).

*Mixed recording keeping refers to pharmacy dispensing and recording systems that exist partially in electronic and manual forms.

**For the review period i.e., 2016-2018. AMC: Antimicrobial consumption

^ For hospital pharmacies that receive antimicrobial stock from the MSL, the MoH directs them to report AMC data directly to the MSL.

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

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 the national and pharmacy levels

Methodology

Statistical analysis

Data analysis for MAAP was conducted according to the WHO's protocol for conducting AMC analysis using the DDD-ATC-AWaRe methodology (Figure 16)[30,31] Each of the WHO methodologies used and additional analysis done are described briefly below. In addition, and where possible, associations were drawn between AMC and AMR (Part A, Section II:3c).

i. Defined Daily Dose (DDD)

DDDs and related metrics are utilised to analyse AMC data. The DDD metric allows for easy comparison by standardising different doses (in milligrams) for each antibiotic used in managing infections. Also, it is recommended to use drug utilisation figures, such as DDD, with a relevant denominator for the health context, such as numbers of DDDs/1 000 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 positive or negative change(s) in the consumption patterns over the studied period or a pre-defined base period.

Using the WHO 2020 DDD guide, the total consumed milligrams per antimicrobial was to be divided against the standard DDD value issued by the WHO to obtain total DDDs.[32] The total DDDs were then to be adjusted for the country's population[33] in the studied years (2016-2018) and presented as DDDs/1 000 inhabitants/day (DID). However, due to missing pack size information within the datasets received, analysis of the national-level AMC was not possible. Furthermore, pharmacy-level AMC datasets were to be adjusted as DDD per the number of inpatients and presented as DDD/100 patient bed days. However, the WHO DDD per 100 patient bed days was not computed because patient bed days and patient days information was not easily accessible in most hospital facilities. Secondly, the lack of DDD per bed days hindered comparing hospital- and community-pharmacy consumptions, as in the latter the patient bed days metric is not applicable. Therefore, the pharmacy-level AMC datasets are presented as absolute DDD to aid comparison between hospital and community pharmacies for downstream analysis. Detailed DDD calculations can be found in AMC Appendix 7. All calculations were done in Microsoft Excel™ software.

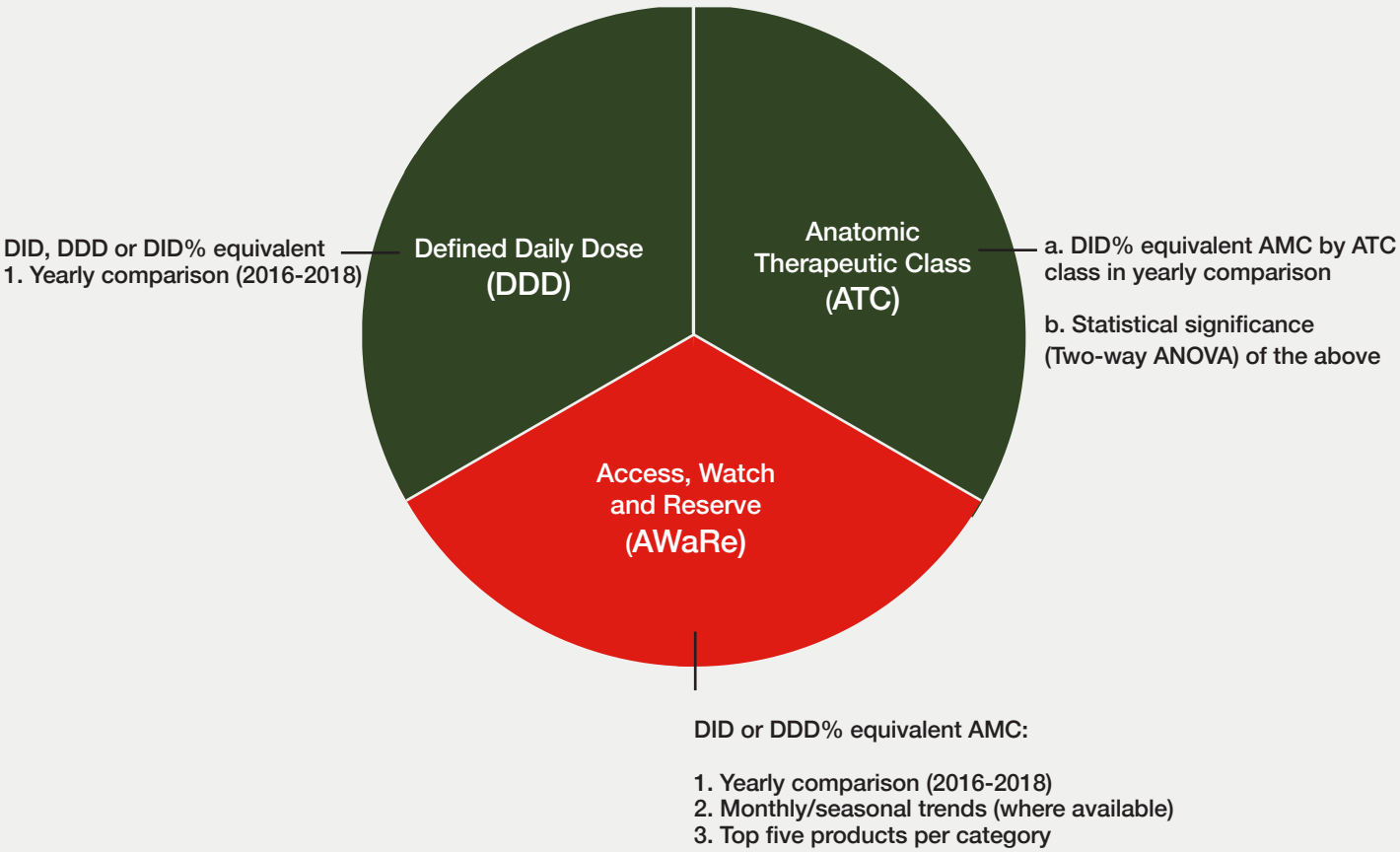
ii. Anatomic Therapeutic Chemical (ATC) Classification

The antimicrobials documented in the pharmacy-level datasets were coded by their standard antimicrobial names per the 2020 WHO ATC codes AMC Appendix 7 in Microsoft Excel TM sheet and then analysed to characterise the macro (above-molecule) AMC trends. The MAAP was unable to compute the year-on-year differences within each ATC class because the aggregated pharmacy-level dataset included AMC datasets from nine pharmacies that did not provide data for all three years reviewed.

iii. WHO Access, Watch and Reserve (AWaRe)

The WHO AWaRe categorises antibiotics under 'Access', 'Watch' and 'Reserve' groups. The 'Access' group includes antibiotics of choice for the 25 most common infections, and these antibiotics should be affordable, available at all times, and quality-assured in the country or facilities. The 'Watch' group antibiotics are those indicated for only a specific, limited number of infective syndromes since organisms easily develop resistance to these. Hence, their use is controlled via stewardship programmes and monitoring. Lastly, the 'Reserve' group antibiotics are considered as the "last resort" treatment options. They are indicated in life-threatening infections due to multi-drug resistance and are closely monitored and prioritised in stewardship programmes to ensure their continued effectiveness.

We stratified the total AMC by DDDs per antibiotic molecule per 2019 WHO AWaRe categories, 'Access', 'Watch' or 'Reserve'[34] in Microsoft Excel™ sheet. The total DDDs per each WHO AWaRe category was then analysed to determine the proportion of consumption per category and over time, yearly and monthly (where possible). The WHO recommends that at least 60% of a country's total AMC should come from the 'Access' category of antibiotics. Finally, we identified the top five antibiotics consumed in each WHO AWaRe category.



Defined Daily Dose (DDD) indicators utilised for volume metric standardisation were sourced from the WHOCC 2020. The ATC classification used to categorise the antibiotics according to the organ or system on which they act, and their therapeutic, pharmacological and chemical properties were sourced from the WHOCCC ATC database, and the 'Access', 'Watch' and 'Reserve' categorisation was sourced from 2019 WHO AWaRe classification.[35]

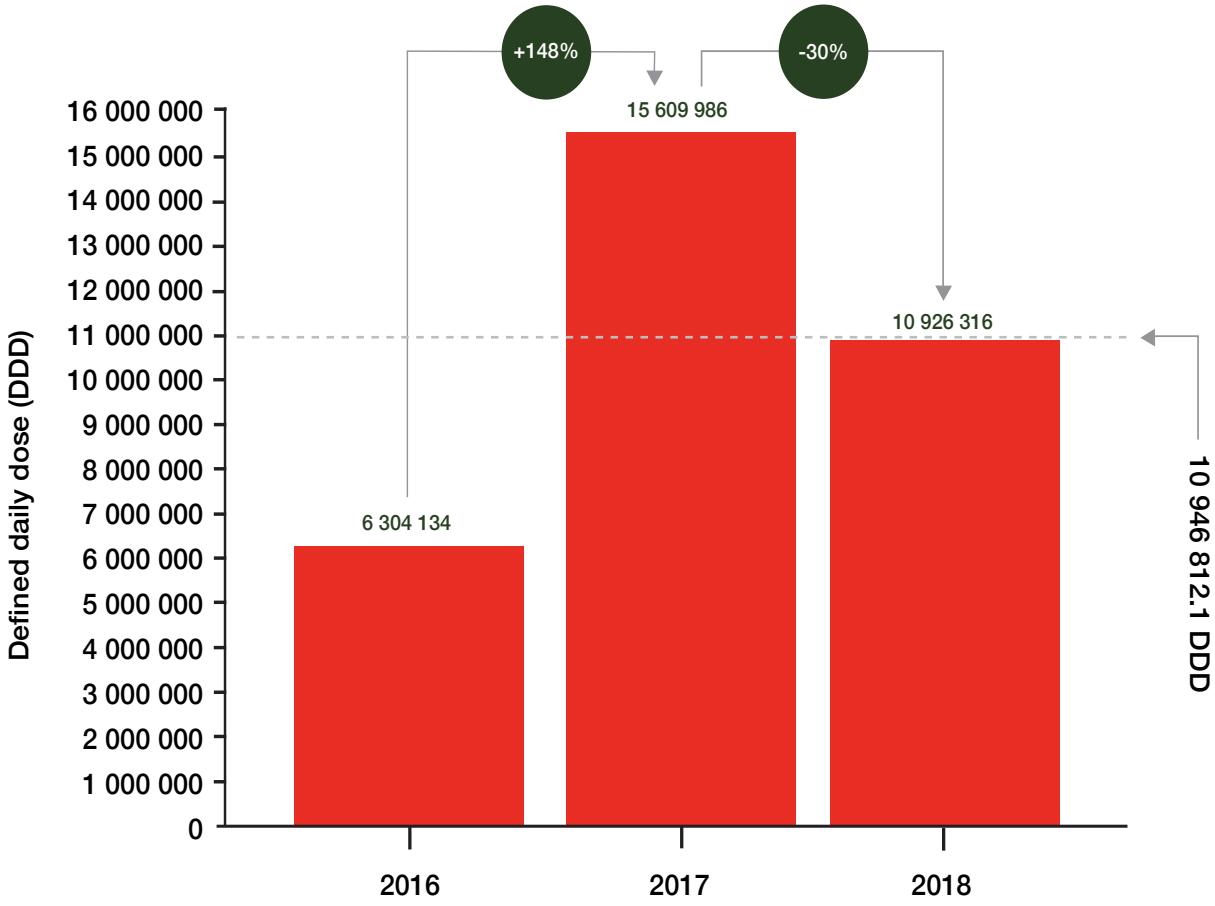
Figure 16: Methods and indicators used for the analysis of the datasets collected in Zambia

iv. Review of Essential Medicines List (EML)

According to the WHO, essential medicines are those that satisfy the priority health care needs of a population. They are selected with due regard to disease prevalence and public health relevance, evidence of efficacy and safety and comparative cost-effectiveness. They should be readily available in functioning health systems, in appropriate dosage forms, in assured quality and at affordable prices for individuals and health systems. A document analysis comparing the antimicrobials listed in the WHO EML to those listed in the Zambia Essential Medicines List (ZEML) and against antimicrobials documented in the national- and pharmacy-level data was done. The comparison was conducted per the WHO AWaRe categories.

Results

The average AMC of the sampled pharmacies between 2016 to 2018 was 10 946 812.1. A 148% increase in total antimicrobial consumption was observed between 2016 and 2017, followed by a reduction of 30% in 2018 (Figure 17).

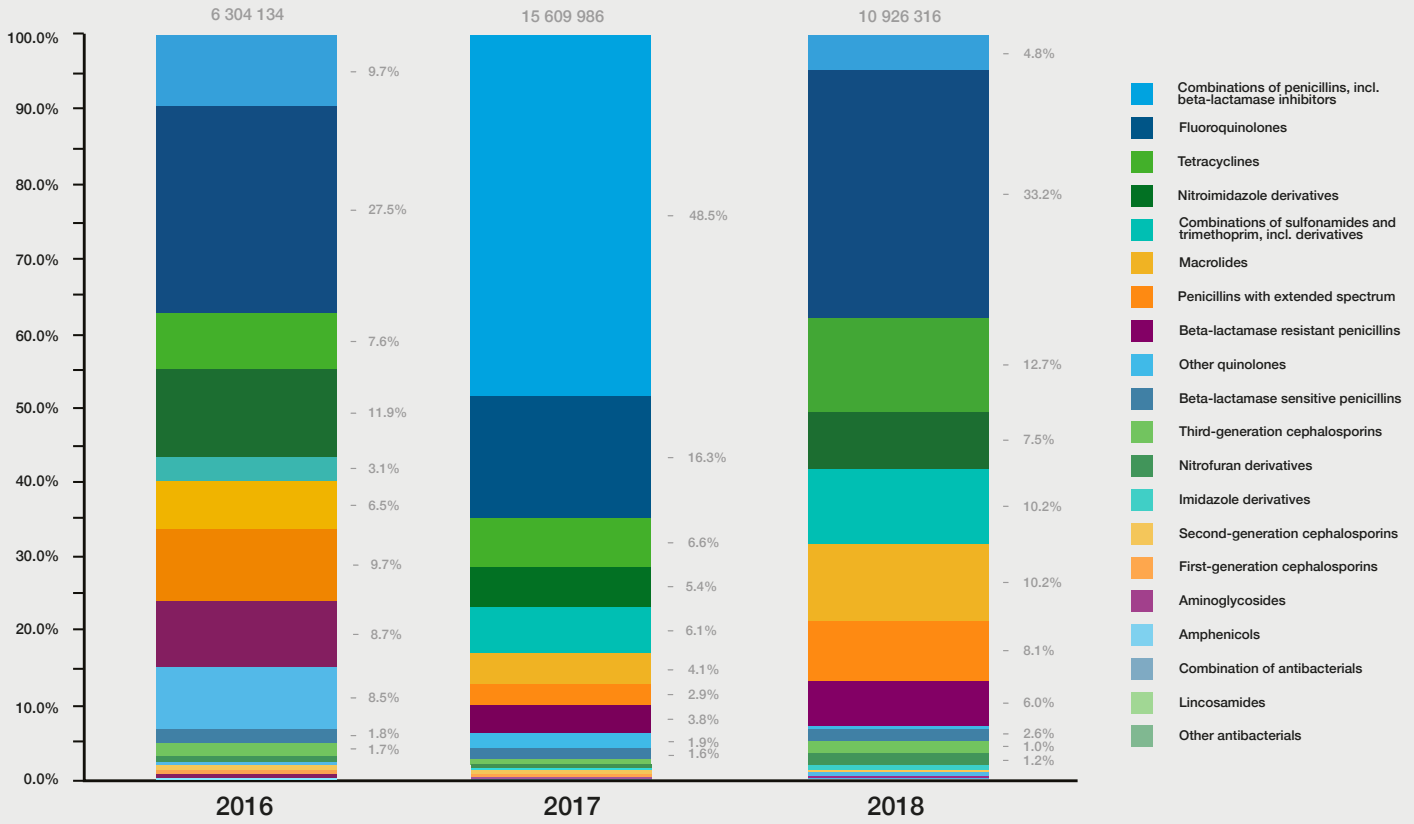


*=DDDs shown here are not normalised to the country population levels or facility catchment population; -DDD=defined daily dose

Figure 17: Variation in the total yearly DDD of sampled pharmacies in Zambia from 2016-2018*

Pharmacy AMC analysed by ATC classification

Penicillins combined with beta-lactamase inhibitors (J01CR) were the most frequently consumed ATC class in the pharmacies sampled in Zambia across the reviewed period. Their consumption was 9.7% in 2016, 48.5% in 2017 and 4.8% in 2018 (Figure 18). Amoxicillin/clavulanic acid was the most frequently consumed antibiotic within this class. Fluoroquinolones (J01MA) and tetracyclines (J01AA) were the second and third most consumed ATC classes, with ciprofloxacin and doxycycline leading consumption within these ATC classes respectively. The top five most consumed antimicrobials were amoxicillin/clavulanic acid, ciprofloxacin, doxycycline, metronidazole and sulfamethoxazole/trimethoprim. Together they accounted for >72% of the total AMC. A detailed breakdown of the pharmacy-level AMC by antimicrobial molecule and ATC class are presented in AMC Appendix 8 and AMC Appendix 9, respectively.



Penicillin combinations, including beta-lactamase inhibitors ATC class of molecules, were on average the highest consumed antimicrobials for the reviewed period (2016 to 2018). Statistical testing was not carried out due to the nature of the data obtained. See AMC Appendix 9 for a more detailed breakdown of AMC by ATC classes.

Figure 18: AMC of selected pharmacies in Zambia, 2016-2018

Pharmacy AMC analysed by WHO AWaRe categorisation

The average consumption of antibiotics for the sampled pharmacies across the three years analysed was 66.7%, 'Access'; 33.3%, 'Watch'; and 0.0% 'Reserve'. The annual AMC trends indicated an increase of 18.1% in the consumption of 'Access' antibiotics between 2016 and 2017 and a reduction of 22.8% between 2017 and 2018. This observed 'Access' category consumption trend is against a corresponding reduction of 18.1% in the 'Watch' antibiotics between 2016 and 2017 and a 22.8% increase in consumption between 2017 and 2018 (Figure 19). No 'Reserve' antibiotics were consumed in the sampled pharmacies in Zambia during the reviewed period. On average, consumption of 'Access' category antibiotics within the pharmacies sampled in Zambia meets the 60% minimum consumption threshold set by the WHO. However, the sampled pharmacies failed to meet the target in 2016 and 2018. This analysis of pharmacy-level AMC per the WHO AWaRe categories omits 3.2% (354 061.1 DDDs) of total AMC that are not categorised within the WHO AWaRe list of 2019.

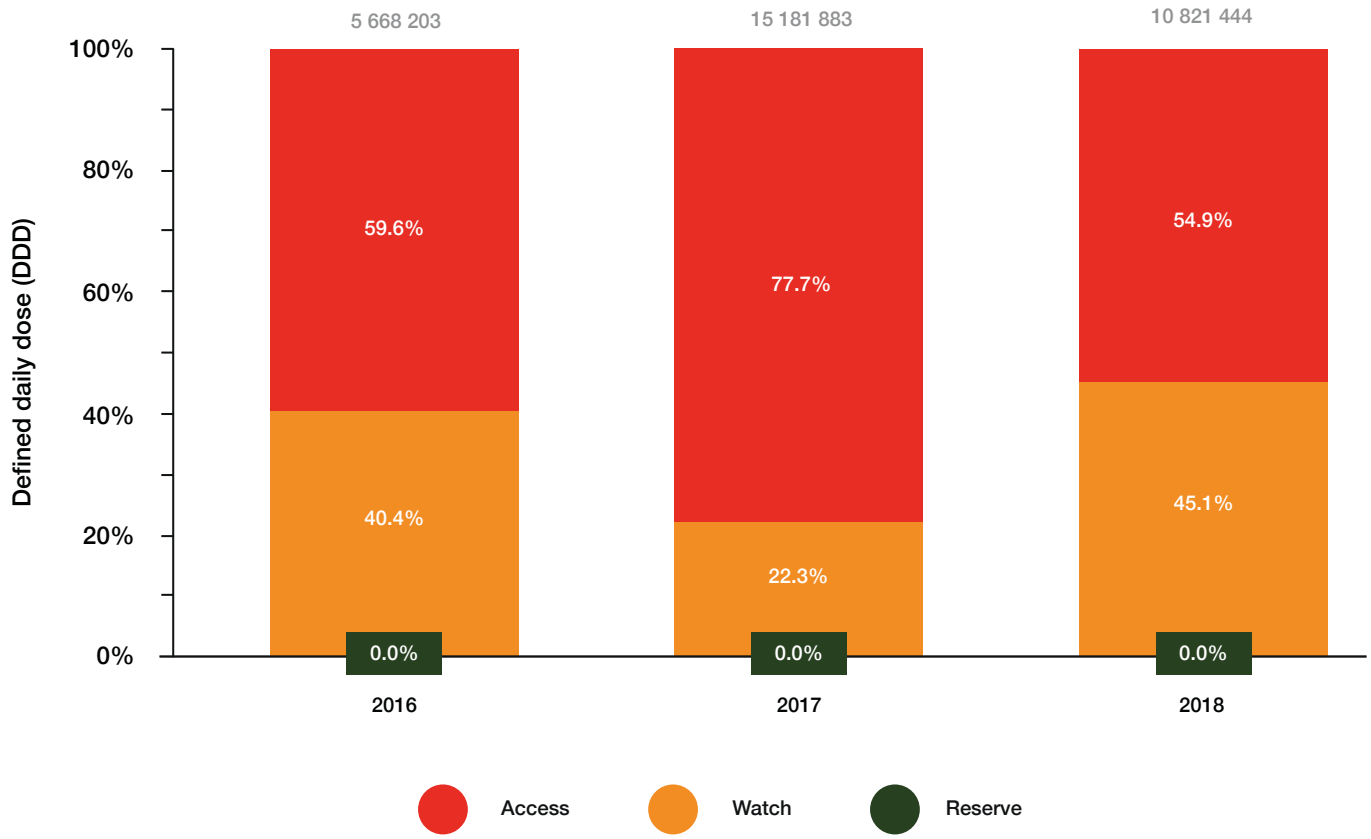
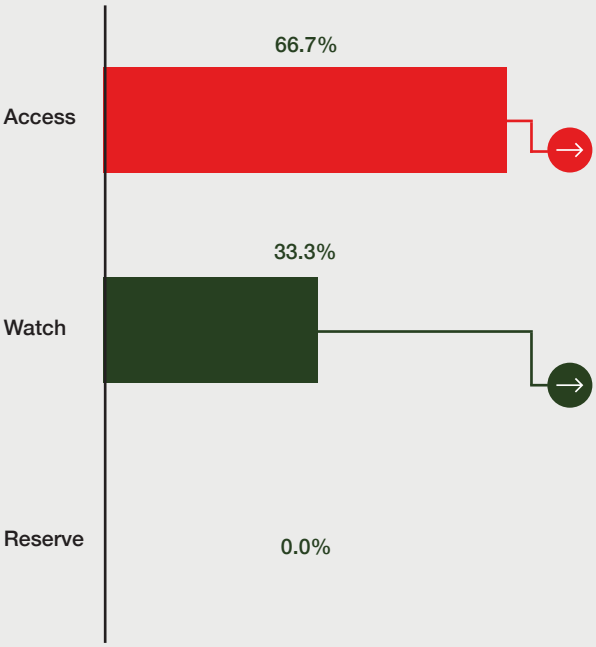


Figure 19: AMC by WHO AWaRe categories for the sampled pharmacies in Zambia, 2016 to 2018

Further analysis was done to identify the most frequently consumed antibiotics within the sampled pharmacies, within each WHO AWaRe category (Figure 20). In the 'Access' category, the top five consumed antibiotics accounted for 85.6% of all AMC within this group, while in the 'Watch' category, the top five antibiotics accounted for 97.6% of all 'Watch' antibiotics consumption.



Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Amoxicillin/Clavulanic Acid	40.8%	2 886 744
Doxycycline	13.5%	953 990
Metronidazole	11.5%	812 250
Sulfamethoazole/Trimethoprim	10.7%	753 274
Amoxicillins	9.1%	645 124

Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Ciprofloxacin	74.2%	2 615 478
Erythromycin	18.0%	633 308
Clarithromycin	2.2%	76 248
Cefotaxime	1.7%	61 372
Cefuroxime	1.5%	52 885

Abbreviations: DDD=defined daily dose

Figure 20: The top five most consumed 'Access' and 'Watch' category antibiotics consumed at the sampled pharmacies in Zambia, 2016-2018

Within the WHO AWaRe database, there exists a list of 'antibiotics not recommended'. This group of antibiotics consists of FDCs of multiple broad-spectrum antibiotics that are not recommended in high-quality international guidelines. Thus, the WHO does not recommend their use in clinical practice and the MAAP presents these as 'uncategorised' and excludes them from the WHO AWaRe analysis results presented above. The MAAP analysed the pharmacy AMC data to identify the consumption rate of these 'uncategorised' antibiotics in the country. Four of these antibiotics were consumed, representing 0.2% of the total pharmacy AMC (Table 12). Among them, the FDC of ampicillin/cloxacillin was the most frequently consumed, accounting for 91.4% 'uncategorised' FDC antibiotics consumption (Table 12), with a mean DDD 16 189.2.

Table 12: AMC rank of the WHO AWaRe 'uncategorised' antimicrobials in Zambia, 2016-2018*

AMC rank*	Molecule
21	Ampicillin/Cloxacillin
32	Ciprofloxacin/Tinidazole
33	Norfloxacin/Metronidazole
35	Ofloxacin/Ornidazole

**AMC rank reports the position of antibiotics consumed (in terms of the total DDD and percentage share) from the reviewed list of antimicrobials for the sampled pharmacies in Zambia (see AMC Appendix 8 for the consumption rate of each listed antibiotic).*

The pharmacy-level datasets from the 28 participating pharmacies were disaggregated by pharmacy type (community or hospital) and hospital service level (secondary versus tertiary care and private versus public). Afterwards, their proportional consumption of WHO AWaRe category antibiotics was examined (Table 13). The hospital and community pharmacies, on average, met the WHO threshold of 60% consumption of antibiotics represented within the 'Access' category at 66.9% and 64.6% respectively. Community pharmacies consumed 2.3% more 'Watch' category antibiotics compared to the hospital pharmacies (community pharmacies, 35.4%; hospital pharmacies, 33.1% 'Watch' antibiotics consumption). Within the hospital pharmacies, the public hospital pharmacies consumed 31.1% more 'Watch' category antibiotics compared to the private faith-based hospital pharmacies. Furthermore, within the public hospital pharmacies, tertiary care hospital pharmacies, which failed to meet the 'Access' consumption threshold of >60%, consumed 22.8% more 'Watch' category antibiotics compared to the secondary care hospital pharmacies. A closer look at the pharmacies found that 50% (n=7) of the hospital pharmacies and only 7% (n=1) of the community pharmacies failed to meet the WHO 'Access' category antibiotics consumption threshold.

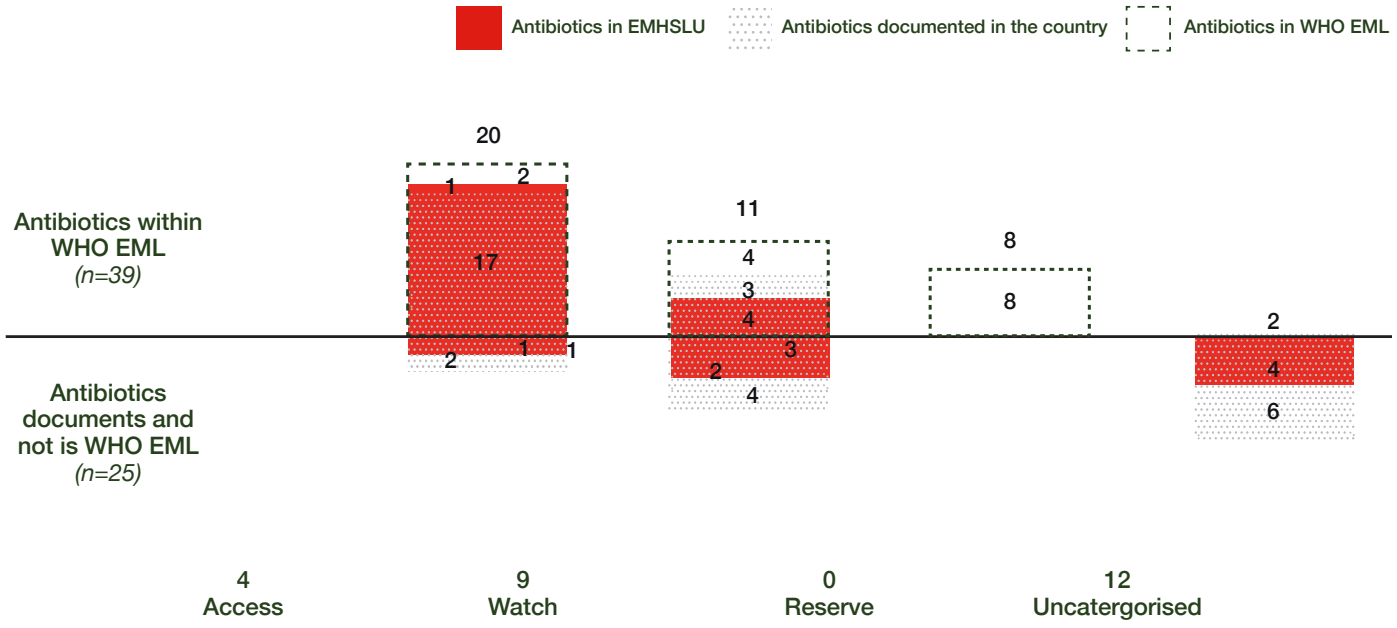
Table 13: Hospital and community pharmacies' percentage consumption of the WHO AWaRe categories in Zambia, 2016-2018

	AWaRe Categorisation	
	Access	Watch
Pharmacy Type	Percentage share	(Absolute DDD)
Community pharmacies (14/28)	64.6% (1.7 million)	35.4% (958 811)
Hospital Pharmacies (14/28)	66.9% (19.4 million)	33.1% (9.6 million)
Public hospital pharmacies (12/14)	65.9% (18.5 million)	34.1% (9.5 million)
Secondary care hospitals (10/12)	70.4% (15.8 million)	29.6% (6.6 million)
Tertiary care hospital (2/12)	47.7% (2.6 million)	52.4% (2.9 million)
Private, faith-based hospital pharmacy (2/14)	96.9% (930 713)	3.0% (29,191)
Grand Total	66.7% (21.2 million)	33.3% (10.5 million)

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. 64 antimicrobials were documented in the pharmacy-level data spreading across the WHO AWaRe category the number of antibiotics documented during data collection and whether they were in the WHO EML, ZEML or both (Figure 21).

Three 'Watch' category antibiotics were listed in the WHO EML and documented by the pharmacies, yet they were not part of the ZEML. In addition, two 'Access' categories, four 'Watch' categories and eight 'Reserve' category antibiotics are part of the WHO EML, yet they are not listed in the ZEML nor were they documented during data collection. Interestingly, one 'Access' category antibiotic is listed in the WHO EML and the ZEML but was not documented during data collection. For each AWaRe category, including the uncategorised, an antimicrobial was documented which was neither part of the WHO EML nor ZEML (AMC Appendix 10).



Abbreviations: WHO=World Health Organisation; EML=Essential Medicines List, ZEML=Zambia Essential Medicines List

Figure 21: Documented antibiotics in national- and pharmacy-level data in Zambia, 2016-2018 compared to WHO- and Zambia EML

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 communicated the effectiveness of antibiotic therapy to decision-makers. The DRI values range from 0 (100% susceptibility) to 100 (100% resistance). Available AST results for at least 30 tested isolates and 15 of the 25 combinations were prerequisites for estimating the DRI. 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 to generate CIs for the DRI as the variance of the product of variables.[37,38]

Apart from the DRI, the correlation between AMC and AMR was determined. Facility antimicrobial consumption was obtained from facilities 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). A Pearson's correlation analysis was performed to determine the correlation 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 the previously described methodology, the resistance of all pathogens tested against the 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 60.9% (95% CI, 53.8–69.7%) implying low antibiotic effectiveness, which is a threat to effective infectious disease management and calls for urgent policy intervention (Figure 22).

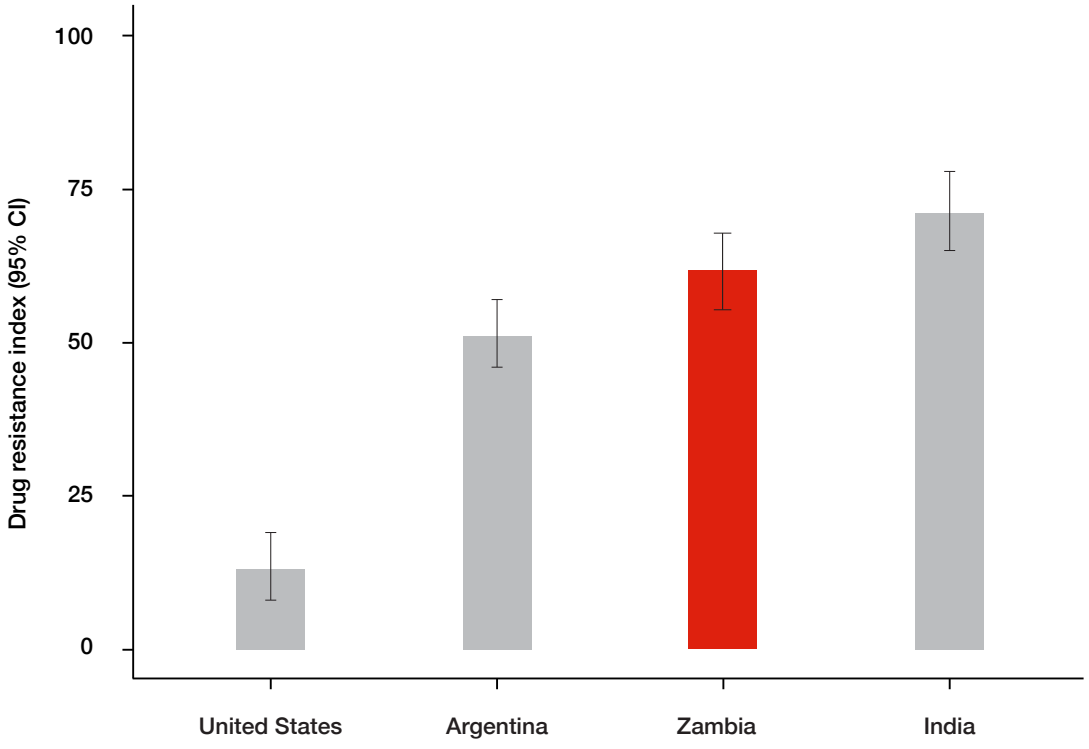


Figure 22: Drug Resistance Index of Zambia 2016-2018, compared to the drug resistance index estimates for the United States, Argentina and India

AMC and AMR correlation

The top three highly consumed antibiotic classes at the facility level were aminopenicillins, macrolides and folate pathway inhibitors. The AMR rates were highest for penicillins (94.3%), folate pathway inhibitors (87.1%) and tetracyclines (85.9%) (Table 12). Pearson's correlation analysis revealed a weak positive correlation (r^2=0.08) between AMR and AMC, implying that AMC is not a significant driver of AMR in Sierra Leone (Figure 20).

Table 14: AMC and AMR rates across antibiotic classes

Antibiotic class	Year	Total DDD in thousands	Resistance rate (%)
Beta-lactam combinations	2016-18	8.7	37.8
Fluoroquinolones	2016-18	79.1	57.0
Tetracyclines	2016-18	2.90	56.5
Folate pathway inhibitors	2016-18	2.26	77.8
Macrolides	2016-18	2.17	62.8
Aminopenicillins	2016-18	1.94	79.1
Methicillin	2016-18	17.9	62.0
Quinolones	2016-18	0.86	77.2
Penicillins	2016-18	0.70	73.1
Cephalosporins (3rd generation)	2016-18	0.32	61.7
Nitrofurans	2016-18	0.25	38.9
Cephalosporins (2nd generation)	2016-18	0.16	67.0
Cephalosporins (1st generation)	2016-18	0.15	77.1
Aminoglycosides	2016-18	0.10	49.0
Lincosamides	2016-18	0.00	38.6

Abbreviations: DDD=defined daily dose

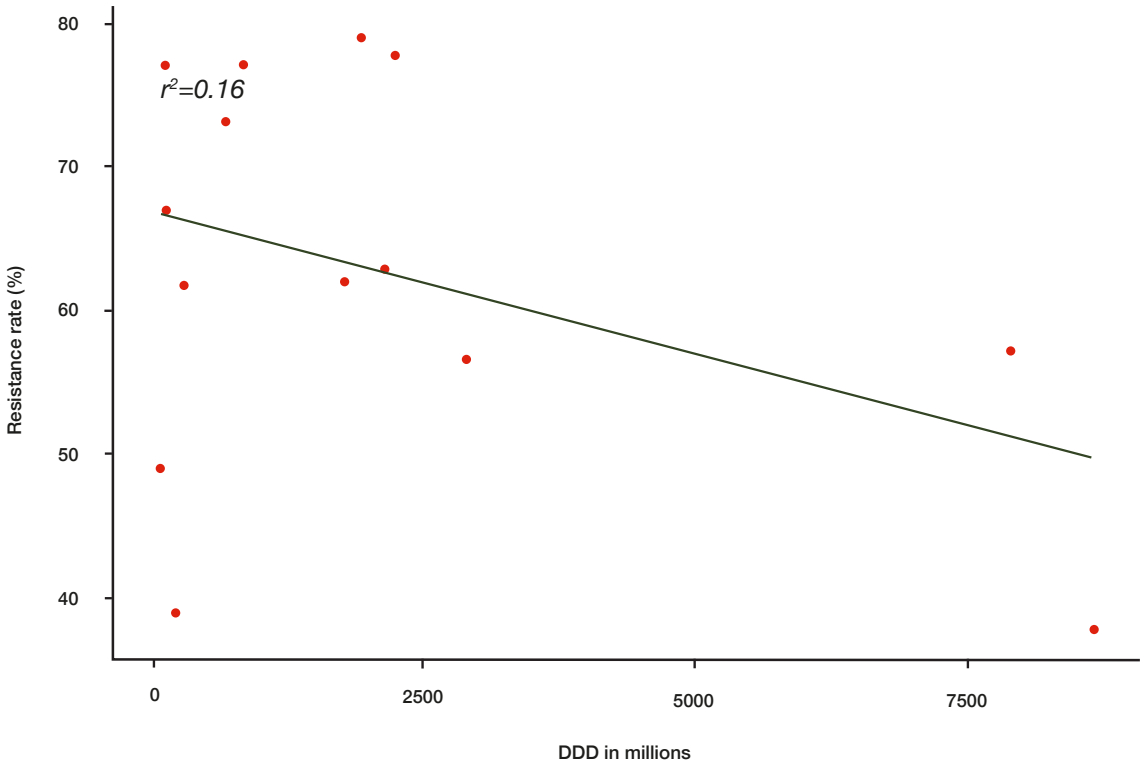
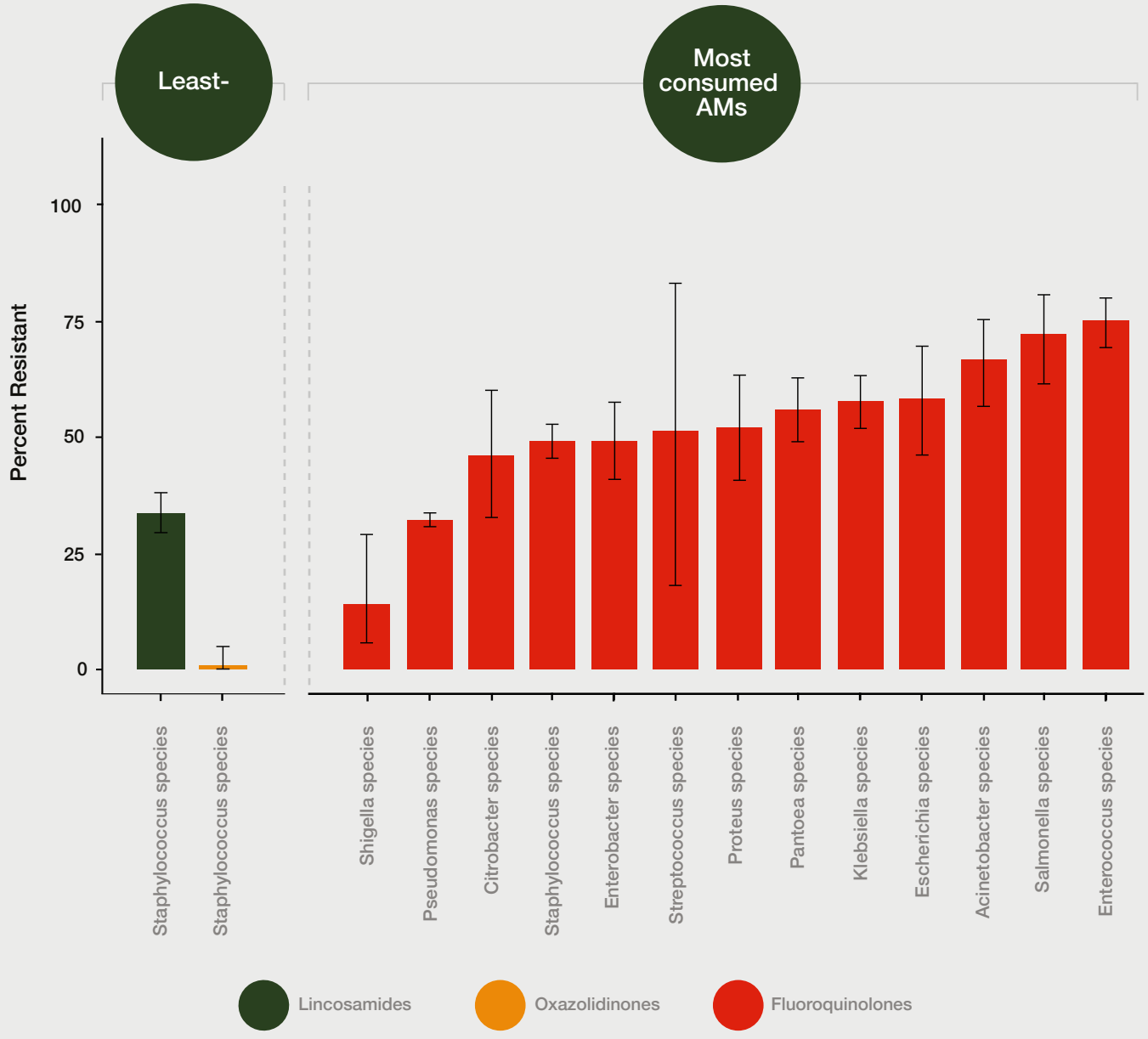


Figure 23: Correlation between AMR and AMC in Zambia, 2016-2018

Resistance profiles of most and least consumed antimicrobial classes

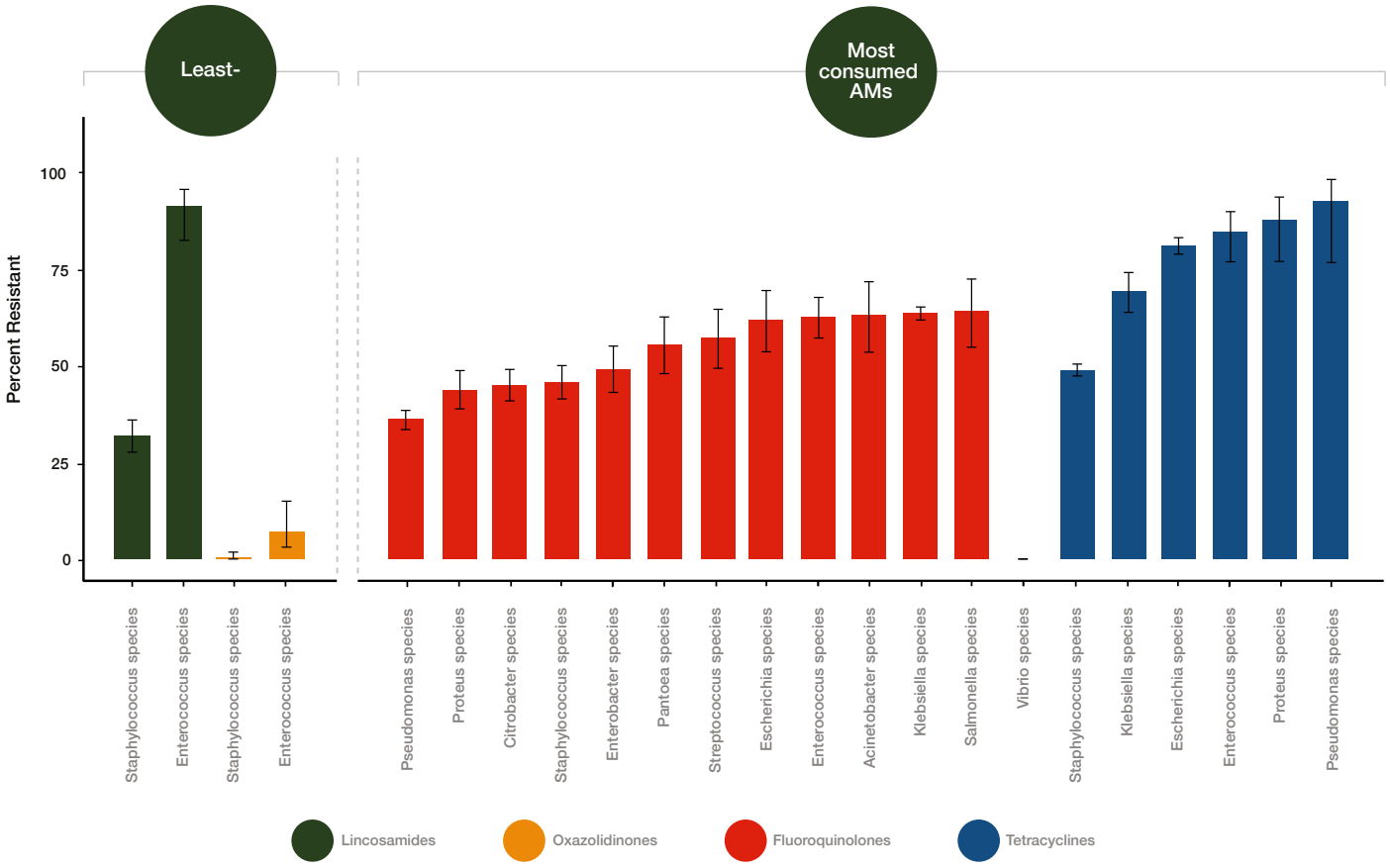
The most consumed antimicrobial classes across the study years were beta-lactam combinations, fluoroquinolones, tetracyclines, and folate pathway inhibitors. In 2016, resistance rates were ~75% for fluoroquinolone in Enterococcus species and Salmonella species. In 2017, high resistance rates (>75%) were noted for tetracycline in Pseudomonas species, Proteus species, Enterococcus species and Escherichia species. 2018 had high rates (>75%) of fluoroquinolone-resistant Enterococcus species, tetracycline-resistant Escherichia species and folate pathway inhibitor-resistant Enterococcus species, Klebsiella species, Citrobacter species, Pantoea species, Escherichia species, Staphylococcus species, Enterobacter species and Proteus species (Figures 24, 25 and 26).

The least consumed antimicrobial classes across the study years were lincosamides and oxazolidinones. Even though the consumption of these antimicrobial classes was low, high resistance rates were noted across many pathogen-antimicrobial class combinations. In 2016 resistance rates were more than >25% for lincosamide in Staphylococcus species. In 2017, resistance rates were more than >75% for lincosamide in Enterococcus species. In 2018, lincosamide resistance rates were more than >25% in Staphylococcus species and Streptococcus species (Figures 24, 25 and 26).



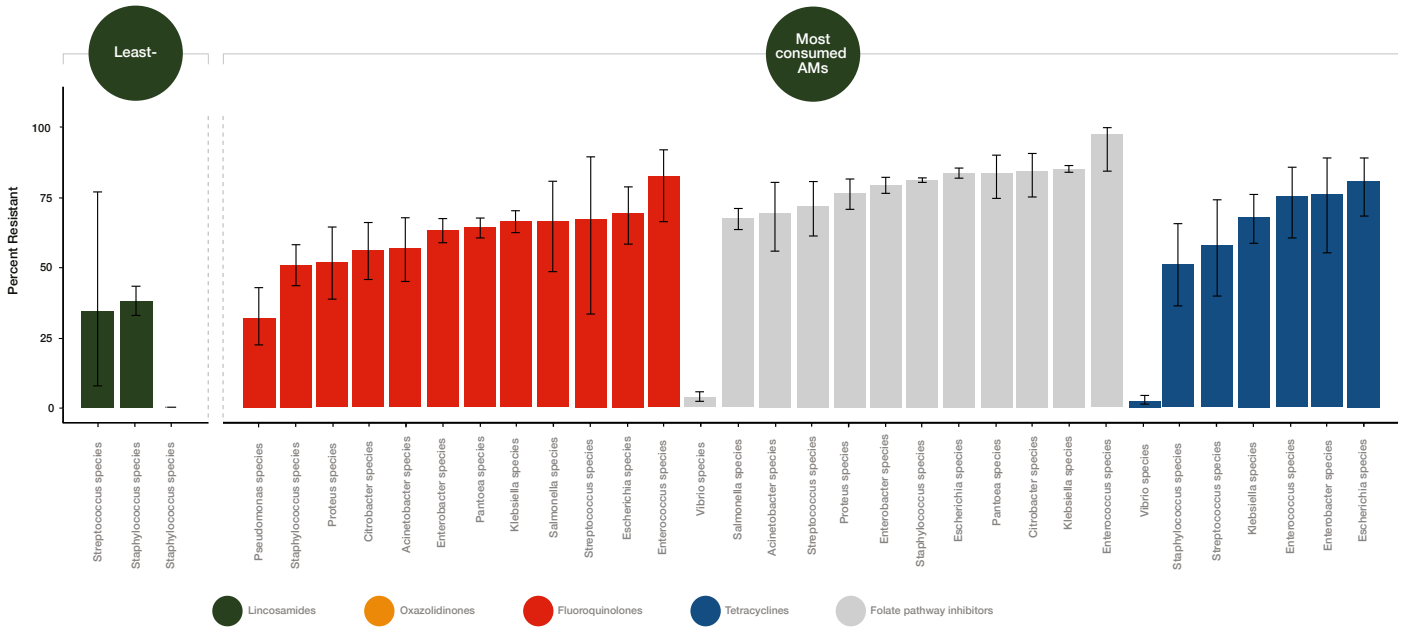
Abbreviations: AMs= antimicrobials; Least-=Least consumed antimicrobials

Figure 24: AMR rates for the least (left) and the most (right) consumed antimicrobial classes in Zambia in 2016



Abbreviations: AMs= antimicrobials; Least-=Least consumed antimicrobials

Figure 25: AMR rates for the least (left) and the most (right) consumed antimicrobial classes in Zambia in 2017



Abbreviations: AMs= antimicrobials; Least-=Least consumed antimicrobials

Figure 26: AMR rates for the least (left) and the most (right) consumed antimicrobial classes in Zambia in 2018

Part D: Recommendations

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

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

Significance of AMR and DRI data including recommendations

Analysis of available AMR data from Zambia revealed high levels of third-generation cephalosporin-resistant Enterobacterales (~65%), fluoroquinolone-resistant Salmonella species (65-73%) and MRSA (30–63%).

Enterobacterales can be asymptomatic colonisers and cause community and healthcare-associated infections (commonly affecting the urinary tract, bloodstream, lower respiratory tract, and surgical sites). Various risk factors predispose to resistance against third-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 and severe illness), injuries and transplantation. Compliance with standard and contact precautions (e.g., hand hygiene), minimal use of catheters and invasive devices, compliance with infection prevention bundles and antimicrobial stewardship is essential to limit the spread of resistant Enterobacterales. Additionally, high-risk patients should be screened for rectal colonisation.

Salmonella (also a member of Enterobacterales) strains are known causes of enteric fever, food-borne gastroenteritis and invasive infections. Salmonella infections are acquired through the oro-faecal route, and various risk factors (such as extremes of age, malaria, schistosomiasis, hemoglobinopathies, immunocompromised state and chronic liver disease) predispose one to nontyphoidal Salmonella bacteraemia. While earlier simple antibiotics, like ampicillin, trimethoprim-sulfamethoxazole, and chloramphenicol, were effective, multidrug resistance has rapidly spread and fluoroquinolone non-susceptibility is a current global concern. Food and water safety, screening food handlers for chronic carrier state and typhoid vaccination of susceptible vulnerable populations must be ensured to control Salmonella infections. Patients must complete their full antibiotic course and be monitored for Salmonella carriage and relapse. The use of fluoroquinolones in hospitals and animal husbandry must be restricted, and surveillance of AMR patterns is essential.

Staphylococcus aureus (methicillin-resistant or sensitive) is a common cause of many skin and soft tissue infections, 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 a high prevalence, past infections/colonisation/close contact, trauma, use of invasive devices (catheters, shunts, implants, 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 treatment modalities, it is also important to prevent and control the spread of MRSA infections. The use of catheters and invasive devices must be minimised, and stewardship principles should be practised, including taking culture specimens before initiating antibiotics therapy, 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.

Service delivery

The Zambia laboratory network consisted of 1 608 laboratories, of which only 22 of the 23 bacteriological laboratories confirmed their AST capabilities. While most of the surveyed laboratories reported implementing QMS, not all were certified or accredited. The laboratories did not equitably cover the country's population of over 18.4 million. The testing load (quantum of cultures) at most participating laboratories was low and suggested lack of a routine microbiology testing. There is also the risk of overestimating the AMR rates as most 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 get mapped across a range of indicators including population coverage, infectious disease burden, testing capabilities and quality compliance. This would inform decision-makers of unmet needs and inform laboratory network expansion approaches. An extensive network also provides a richer sampling frame for better representation and generalisation of results.

Health workforce

As reported by the surveyed laboratories, all of them had an experienced laboratory scientist or technologist, 54% had at least one qualified microbiologist and only 45% had up-to-date records on training and competence. For high-quality microbiology testing and reporting, staff training on laboratory standards, identification of common pathogens and data management are essential.[40] Staff capacity building may be achieved by leveraging in-house expertise or outsourcing to external organisations or tertiary facilities.

Information systems

The Regional Grant was a step towards AMR data collection and digitisation. Most surveyed laboratories relied on paper-based records or a combination of electronic and paper-based records, and very few linked patients' clinical records. In the current study, involving 14 laboratories over three years, susceptibility results could be collected for just 22 343 positive cultures.

It is essential to curate the right data and generate evidence to strengthen AMR surveillance. We recommend data collection through standardised formats at all levels (laboratories, clinics and pharmacies), and automation of data analysis. For the current study, we used the WHONET for data digitisation. Empirical guidelines for infectious disease management should be based on the epidemiology specific to the patient's setting, and AMR data should be shared with national and supra-national platforms. We also recommend establishing a system of assigning permanent identification numbers for tracking patients over time. Permanent patient identification numbers would help to collect data on the patients 'clinical profile, antimicrobial history as well as pathogen's molecular profile (where available).

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 observed instances of inappropriate testing that made the data unfit for analysis as results of such inappropriate tests can be misleading and impact patient care.

It is imperative to generate reliable laboratory results using appropriate testing methods and authorised surrogates and ensure an uninterrupted supply of reagents, including antibiotics for susceptibility testing. Improving supply chains for essential reagents should be a country's priority and interruptions in routine testing must be minimal. Standardising testing methods across laboratories can ensure reagent supply through pooled purchasing coordinated by the MoH. All laboratories and testing centres must conform to AST quality standards and aim for accreditation and quality certification status.

Lastly, we recommend increasing community awareness of the importance of public health interventions (vaccinations, clean water, sanitation and hand hygiene) and compliance with physician's advice. Also, strengthening health and laboratory systems must be prioritised at the 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 suggests recommendations to improve future surveillance and AMS activities in Zambia.

a) Feasibility of obtaining AMC and AMU data in Zambia and recommendations

The MAAP successfully collected and analysed pharmacy-level AMC datasets for Zambia for the years reviewed i.e., 2016 to 2018. MAAP was unable to analyse national-level AMC datasets due to gaps in the package contents of the datasets provided by MSL. Thus, we recommend that Zambia develops an AMC surveillance policy to guide routine AMC surveillance and report to GLASS. This policy should stipulate the minimum AMC data variables to be reported. For instance, it should explicitly state the required package content and antimicrobial strength and routine data cleaning and reporting practices. These detailed policy requirements will inform agencies supplying AMC datasets on the minimum data recording and quality requirements for surveillance exercises.

The MSL datasets used provided only partial coverage of Zambia's AMC. Thus, relevant regulatory authorities should identify and recruit private sector (both for and not-for-profit) wholesalers or distributors or large volume health facilities to serve as sub-national points for AMC surveillance to ensure complete coverage of the country's AMC. This approach would also allow examination of AMC trends of the private and public sector and end-user institutions. It is commendable that pharmacy-level AMC data from the hospitals were collected from mixed record systems (i.e., simultaneous use of manual and electronic records in a facility). Future AMC surveillance will be time and cost-efficient if hospitals switch fully to electronic record systems capable of transferring data across systems and producing user-friendly AMC reports.

The MAAP did not obtain AMU data in Zambia; thus, per the WHO's drug use research methodology, the MAAP was unable to determine reasons for the antimicrobials used and whether their consumption per the country's guidelines.[41] AMU data was not collected from participating AST-co-located pharmacies because the AMC data sources (i.e., stock record cards at the pharmacy) did not allow tracing back to individual patients to whom antimicrobials were dispensed. Hence, retrospective retrieval of the relevant clinical and laboratory files for any patients who received antimicrobials was impossible. Nevertheless, a cross-sectional survey which reported AMU data in Zambia has been documented.[42] This study took place at a single location and sampled only non-critically ill patients admitted to one of the six general medicine wards. Therefore, conclusions drawn from it cannot be assumed to represent national AMU or any of the sampled MAAP pharmacies. Nonetheless, the success of this AMU study implies that retrieval of AMU data, where sub-optimal data systems exist, can only be achieved through the set-up of prospective studies for which collection procedures are intentionally set up to assess the patient in real-time through the cascade of care. Retrospective studies, such as this MAAP study, may not be ideal for collecting AMU data.

Therefore, the MAAP, in alignment with the WHO guide on facility AMU assessment, recommends that future AMU surveillance attempts in the country be conducted through larger, representative prospective data collection approaches.[31] Compared to retrospective data collection, the prospective approach is time-consuming and often requires engaging trained data collection teams for prolonged durations, ultimately making prospective studies expensive and challenging to undertake in resource-limited settings. Retrospective AMU data collection remains an option if targeted facilities have electronic patient records and cross-department unique patient identifiers.

Overview of AMC consumption trends and recommendations

The pharmacy-level AMC trends documented in this report provide a useful benchmark for comparing future consumption trends after implementing the country's ASPs. The MAAP was unable to estimate Zambia's national AMC levels using data received from the MSL due to the missing product strength and packaging information. Despite the absence of nationally representative AMC datasets, this report details the AMC trends within sampled pharmacies in Zambia. There was an overall increase in the consumption of antimicrobials from 2016 to 2018. However, not much insight can be drawn from total AMC consumption in DDDs as MAAP was not able to normalise the datasets per facility catchment population. Furthermore, a few pharmacies provided data for only part of the reviewed years. However, as the majority of the consumption is represented as a percentage share within each year, observations provided within a given year are an accurate reflection of a trend. This section, therefore, focuses on the relative comparison of consumption within pharmacies as per WHO AWaRe proportion analysis.

Evaluation of antibiotics relative consumption according to the WHO AWaRe categories revealed that the consumption of narrow-spectrum antibiotics in the 'Access' category exceeded the minimum WHO recommended consumption threshold.[34] This consumption is quite commendable as it implies that any emerging AMR trends due to misuse or overuse will likely be restricted to narrow-spectrum antibiotics, sparing the less used broad-spectrum and last-resort antibiotics in the 'Watch' and 'Reserve' categories, respectively.

Ciprofloxacin, which is one of the antimicrobials in the Several interesting trends were also observed when AMC was examined by pharmacy type. First, the average consumption of 'Access' category antibiotics within the community pharmacies was comparable to that in the hospital pharmacies. Furthermore, the consumption of 'Access' category antibiotics within the private, faith-based hospital pharmacies was larger than that in the public hospital pharmacies. Therefore, this consumption trend implies that the ZEML[43] antibiotics that comprise mostly of 'Access' category antibiotics are widely available in the public and private (not-for-profit and for-profit) community pharmacies in Zambia.

Second, within the public hospital pharmacies, the tertiary care hospital pharmacies failed to meet the 'Access' category consumption threshold and consumed more 'Watch' category antibiotics compared to the secondary care hospital pharmacies. Higher consumption of the 'Watch' category antibiotics at the tertiary care hospital pharmacies could be attributed to the fact that these facilities deal with complex infection cases requiring treatment regimens with second and third-line antimicrobial agents. The inability to meet the minimum consumption threshold of 'Access' category antibiotics, implies that the broader spectrum antibiotics (Watch category) may be used more regularly as first or second-line antimicrobials than recommended. In addition, it implies that antimicrobial stewardship activities may not be active within these facilities or may be sub-optimal in regulating the use of the 'Watch' category antibiotics that have a higher resistance potential. The MAAP would therefore recommend that the country's AMRCC consider introducing facility-level ASPs to regulate the use of broad-spectrum antibiotics and educate prescribers on the importance of preserving these antibiotics to maintain their efficacy.

Lastly, none of the seven 'Reserve' category antibiotics listed in the WHO EML was consumed,[34] probably due to the absence of these antibiotics in the ZEML rather than a regulation of their consumption. Therefore, the MAAP recommends that the AMRCC urgently reviews the ZEML to include these agents, if required for treatment in Zambia.

A closer examination of the spectrum of the antibiotic within each WHO AWaRe category revealed that an overwhelming majority of antibiotics consumed within the 'Access' and 'Watch' categories came only from the top five antibiotics in their respective categories. Such a consumption pattern could be postulated to be sub-optimal as evolutionary pressure driving resistance would be focused only amongst the narrow-spectrum antibiotics consumed.[44] This narrow consumption can also make the facilities and the country (if this trend is mirrored country-wide) susceptible to stock-outs, if manufacturing and supply chain issues are encountered for these few consumed 'Access' and 'Watch' category antibiotics. Considering the above-mentioned observations, the MAAP, therefore recommends that the country's ASPs explore ways to encourage a wider consumption of antibiotics within each WHO AWaRe category. A few examples of such initiatives may include offering incentives for the importation and distribution of other antibiotics within each category, in line with the country's EML. There is a need to prioritise the development of sector-specific AMU treatment protocols/guidelines as outlined in the country's NAP.[13] These initiatives would in turn assist with mitigating such a limited spectrum of consumed antibiotics, and this should go hand-in-hand with ensuring appropriate use.

The WHO also terms some antibiotics as 'not recommended' for use in clinical practice due to their multiple broad-spectrum activities and lack of evidence for their clinical use.[31] In Zambia, the use of four such WHO-not-recommended FDC antibiotics was detected. Of these combinations, the use of the ampicillin/cloxacillin FDC was most prevalent. The clinical utility of using the combination of ampicillin/cloxacillin has been questioned as the two antibiotics have overlapping spectra of activity, and indications that require treatment with both these antibiotics are uncommon.[45] Therefore, as there is no recommendation for use of these FDC antibiotics, the MAAP recommends that the AMRCC identify the reasons for and exact locations that commonly prescribe or dispense the identified FDC antibiotics. This will allow the country's MoH and associated medicine regulatory bodies (e.g., ZAMRA) to embark on targeted prescriber sensitisation on correct prescribing practice (i.e., teach the appropriate treatments for each ailment).

Data generated from AMC and AMU surveillance trends can provide unique insights for national ASPs and the formulation of policies to stem AMR. Zambia should be commended for exceeding the minimum threshold of consumption of at least 60% of antibiotics from the WHO 'Access' (narrow spectrum, first choice antibiotics) category from the sampled pharmacies. Yet, only five antibiotics make up for >72% of the consumption, which indicates the opportunity to use diverse antibiotics. Table 15 describes the next steps for AMC and AMU surveillance in Zambia.

Table 15: Next steps for AMC and AMU surveillance

A.

Leadership and Governance

The country should develop an AMC surveillance policy and address who, how and when the national AMC datasets should be reported. The AMRCC could lead this activity.

- Such a policy should state the minimum required reporting variables, data quality appraisals, data analysis and reporting pathways to the MoH and the WHO GLASS system. These details will ensure a continuous stream of localised AMC data beyond the MAAP that will help inform and assess future policy decisions by the national ASP.
- Lessons learned from the ongoing Fleming Fund Country Grants and MoH surveillance programmes could be taken into consideration when developing the policy.

The national stewardship programmes, led by the AMRCC, could work to review the national treatment guidelines and the ZEML to include essential 'Reserve' category antibiotics if deemed necessary for complex case management.

B.

Service Delivery

Future attempts to collect AMU data in the country should seek to identify facilities with unique patient identifiers and fully electronic medical records capabilities. Alternatively, the country could aim to prospectively collect this data as guided by WHO methodology for point prevalence surveys[34] as the number of facilities with electronic record systems are limited.

The national ASP, 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 ZEML.

C.

Medical products and technologies

The national ASP should collaborate with pharmacists and medicine importers to increase the diversity of antibiotics as per the reviewed ZEML and availability of WHO 'Reserve' category antibiotics.

Part E: Limitations

Since the participating laboratories were at different service levels and had varying testing capacities, all results in this report should be interpreted cautiously. The limitations of the current study are summarised below.

1. Obtaining patients' hospital identifiers from laboratory records was difficult directly impeding the retrieval of demographic and clinical information from medical archives. Where patient 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, 14, may not fully represent the true resistance rates in the country as they only encompassed a small proportion of the country's population (over 18.4 million). Furthermore, routine testing appears uncommon in most hospitals and laboratories, as AST is mostly conducted in instances of failed therapy; thus, the resistance rates in this study may be overestimated.

4. Clinical data and antimicrobial usage information were insufficient to analyse AMR comprehensively.

5. National AMC records from MSL were intended to be used as a proxy national AMC data source. However, the data received from the MSL had several key information gaps that were crucial for analysis. These gaps included non-standardisation concerning the missing antimicrobial pack size and strength information. Therefore, as a result of these information gaps, it was not possible to run a national AMC analysis on these datasets.

6. The MAAP purposed to collect data from selected pharmacies in Zambia which was subsequently used to compute AMC for Zambia. However, the number of sampled pharmacies (28) was a small proportion of the total pharmacies in Zambia and did not represent all regions and health zones in Zambia. Therefore, this data cannot be assumed to represent Zambia's national consumption.

7. Lastly, the MAAP could not obtain AMU data from the participating pharmacies co-located with AST laboratories and therefore could not determine how and why antimicrobials were prescribed and dispensed (i.e., appropriateness of prescriptions and antimicrobials consumed), was not achieved. The AMU helps focus the country's ASPs.

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Glossary

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

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

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 difficult to treat and increasing the risk of disease spread, severe illness and death. Drug resistance makes antibiotics and other antimicrobial medicines ineffective and infections increasingly difficult or impossible to treat.

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

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

Antimicrobial susceptibility testing standards:
Some internationally recognised agencies produce standards to be followed by laboratories while performing antimicrobial susceptibility testing, such as CLSI and EUCAST. Laboratories must 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. First, each laboratory was assigned a data score based on the level of pathogen identification. Scoring was based on quartiles of the proportion of completely identified pathogens, 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 then the average of all years was assigned as the laboratory data quality score for each laboratory. Secondly, the country data quality score was computed to weights 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 about 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 GLASS 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:
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 and usage data collected for the period 2016-2018 in each country and 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 National Accreditation Board for Testing and Calibration Laboratories, proficiency testing evaluates participant performance against pre-established criteria using inter-laboratory comparisons.

Quality Certification:
Certification verifies that laboratory personnel have adequate credentials to practice the specific discipline and that products meet certain requirements.

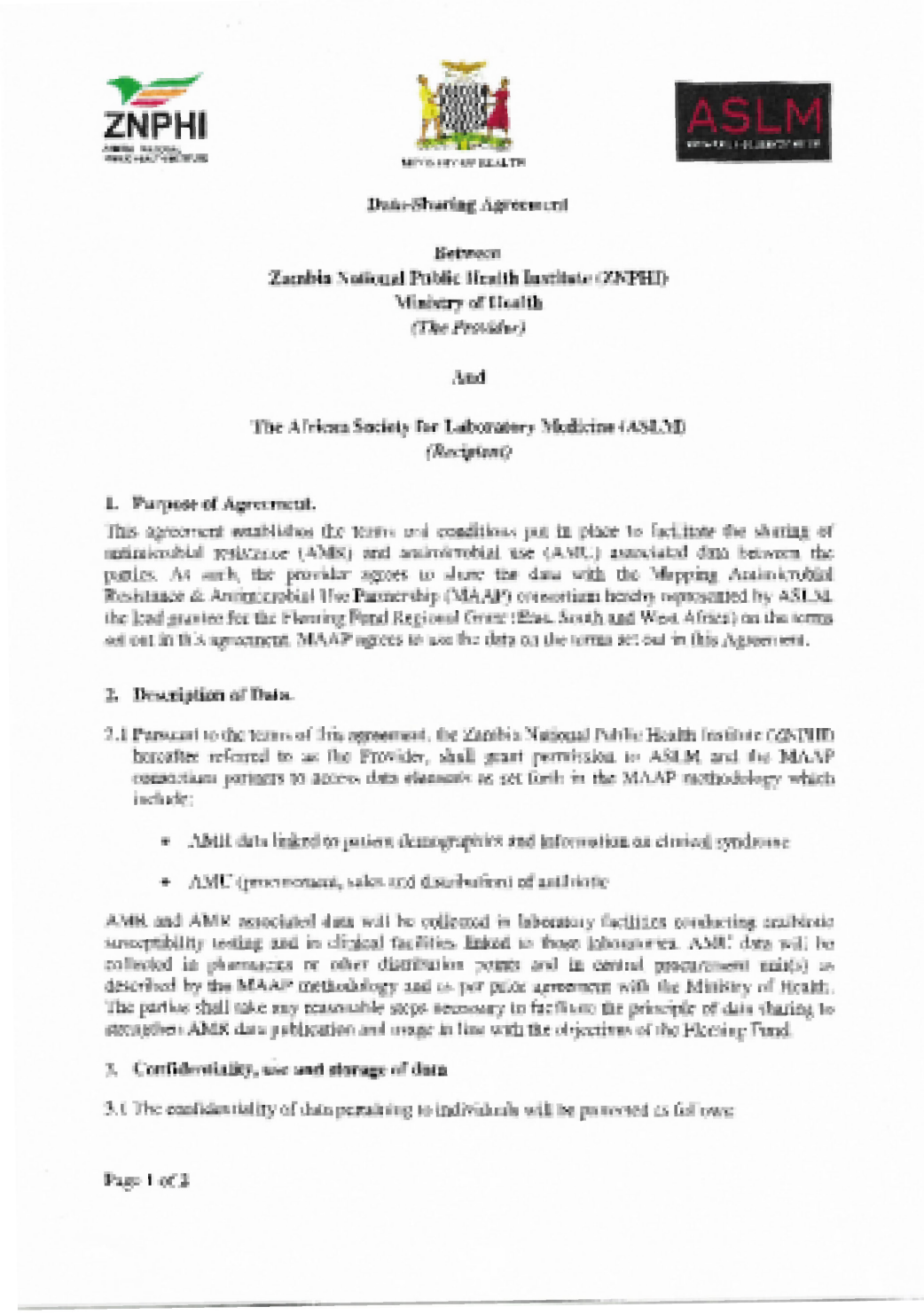
Quality Management Systems:
It is a systematic, integrated set of activities to establish and control the work processes from pre-analytical through post-analytical processes, manage resources, conduct evaluations, and make continual improvements to ensure consistent quality results.

Total cultures:
The number of patient rows retrieved from the databases of the laboratories.

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

AMR Appendices and Supplementary Tables

Appendix 1: Data Sharing Agreement



Data-Sharing Agreement

Between
Zambia National Public Health Institute (ZNPHI)
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 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 Zambia National Public Health Institute (ZNPHI) 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 antibiotic

AMR and AMR associated data will be collected in laboratory facilities conducting antibiotic susceptibility testing and in clinical facilities linked to those laboratories. AMU data will be collected in pharmacies or other distribution points and in central procurement unit(s) as described by the MAAP methodology and as per prior agreement with the Ministry of Health. The parties shall take any reasonable steps necessary to facilitate the principle of data sharing to strengthen AMR data publication and usage in line with the objectives of the Fleming Fund.

3. Confidentiality, use and storage of data

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

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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=22 n (%)	Reference N = 7 n (%)	Regional/ Intermediate N = 8 n (%)	District/ Community N = 5 n (%)	Unspecified N = 2 n (%)
Government	20 (90.91)	6 (85.7)	8 (100.0)	5 (100.0)	1 (50.0)
Private	1 (4.55)	1 (14.3)	0	0	0
NGO	1 (4.55)	0	0	0	1 (50.0)
Others	-	-	-	-	-

Supplementary Table 2: Assessment of preparedness for AMR surveillance

Parameters	Surveyed laboratories N=22 n (%)
Commodity and equipment status	
Regular power supply and functional back up	18 (81.8)
Continuous water supply	15 (68.2)
Certified and functional biosafety cabinets	8 (36.4)
Automated methods for pathogen identification	4 (18.2)
Automated methods for antimicrobial susceptibility testing	4 (18.2)
Methods for testing antimicrobial resistance mechanisms	6 (27.3)
QMS implementation	
Reported QMS Implementation	20 (90.9)
• Reported QMS tool (n=20)	
• LQMS	2 (10.0)
• SLIPTA	11 (55.0)
• SLMTA	1 (5.0)
• Mentoring	-
• Combination‡	3 (15.0)
• Others	3 (15.0)
Quality Certification	4 (18.2)
• Reported certification type (n=4)	
• SLIPTA	-
• College of American Pathologists	-
• Others	4 (100.0)
Accreditation	4 (18.2)
Participation in proficiency testing	13 (59.1)
Utilization of reference strains	16 (72.7)
Reported consistent maintenance of QC records	19 (86.4)
Designated focal quality person	20 (90.9)
Reported compliance to standard operating procedures	21 (95.5)
Reported compliance to antimicrobial susceptibility testing standards	19 (86.4)
Personnel and training status	
Presence of at least one qualified microbiologist	12 (54.5)
Presence of an experienced laboratory scientist/technologist	22 100)
Up-to-date and complete records on staff training and competence	10 (45.5)
Specimen Management status	
Reported compliance to standard operating procedures on specimen collection and testing	22 (100)
Reported compliance to standard operating procedures on specimen rejection	22 (100)
Availability on average number of specimens processed for culture and sensitivity in year 2018	22 (100)
Laboratory Information System and Linkage to Clinical Data	
Assigned specimen (laboratory) identification number	20 (90.9)
Availability of system/database to store patient data	22 (100)
• System/database format (n=22)	
• Paper-based	10 (45.5)
• Electronic	3 (13.6)
• Mixed	9 (40.9)
Captured patients' demographics and clinical information on test request forms	21 (95.5)
• Retrievable test request forms (n=21)	16 (76.2)

*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		9,279	11,246	13,265	6,880	7,238	9,200	6,546	6,964	8,833
Pathogen	bacteria	-	-	-	6,864 (99.8)	7,210 (99.6)	9,166 (99.6)	6,535 (99.8)	6,959 (99.9)	8,814 (99.8)
	fungi	-	-	-	16 (0.2)	28 (0.4)	34 (0.4)	11 (0.2)	5 (0.1)	19 (0.2)
Age, years	Less than 1	782 (8.4)	509 (4.5)	696 (5.2)	763 (11.1)	453 (6.3)	591 (6.4)	745 (11.4)	448 (6.4)	581 (6.6)
	1 to 17	1,798 (19.4)	2,658 (23.6)	2,928 (22.1)	1,223 (17.8)	1,496 (20.7)	1,772 (19.3)	1,151 (17.6)	1,415 (20.3)	1,665 (18.8)
	18 to 49	4,308 (46.4)	5,284 (47.0)	6,153 (46.4)	3,078 (44.7)	3,237 (44.7)	4,114 (44.7)	2,924 (44.7)	3,098 (44.5)	3,957 (44.8)
	50 to 65	655 (7.1)	763 (6.8)	1092 (8.2)	498 (7.2)	561 (7.8)	838 (9.1)	475 (7.3)	548 (7.9)	804 (9.1)
	Above 65	502 (5.4)	713 (6.3)	889 (6.7)	409 (5.9)	554 (7.7)	684 (7.4)	391 (6.0)	547 (7.9)	677 (7.7)
	Unknown Age	1,234 (13.3)	1,319 (11.7)	1,507 (11.4)	909 (13.2)	937 (12.9)	1,201 (13.1)	860 (13.1)	908 (13.0)	1,149 (13.0)
Gender	Male	889 (9.6)	1,967 (17.5)	2,284 (17.2)	163 (2.4)	448 (6.2)	859 (9.3)	161 (2.5)	433 (6.2)	826 (9.4)
	Female	8,390 (90.4)	9,279 (82.5)	10,980 (82.8)	6,717 (97.6)	6,790 (93.8)	8,341 (90.7)	6,385 (97.5)	6,531 (93.8)	8,007 (90.6)
	Unknown Gender	-	-	1 (0.0)	-	-	-	-	-	-
Laboratory	Arthur Davison	208 (2.2)	1,084 (9.6)	770 (5.8)	106 (1.5)	315 (4.4)	274 (3.0)	104 (1.6)	311 (4.5)	271 (3.1)
	Nchanga	-	1,259 (11.2)	2 (0.0)	-	215 (3.0)	-	-	185 (2.7)	-
	University Teaching Hos.	6,677 (72.0)	6,524 (58.0)	7,882 (59.4)	6,494 (94.4)	6,286 (86.8)	7,369 (80.1)	6,167 (94.2)	6,069 (87.1)	7,100 (80.4)
	Ndola	-	-	116 (0.9)	-	-	113 (1.2)	-	-	113 (1.3)
	Livingstone	-	-	256 (1.9)	-	-	243 (2.6)	-	-	229 (2.6)
	Chilonga	-	215 (1.9)	317 (2.4)	-	103 (1.4)	130 (1.4)	-	89 (1.3)	93 (1.1)
	Lewanika	346 (3.7)	-	-	28 (0.4)	-	-	28 (0.4)	-	-
	Mansa	-	2 (0.0)	896 (6.8)	-	2 (0.0)	286 (3.1)	-	2 (0.0)	282 (3.2)
	Chipata	2 (0.0)	361 (3.2)	356 (2.7)	1 (0.0)	158 (2.2)	143 (1.6)	1 (0.0)	157 (2.3)	142 (1.6)
	Levy Mwanawasa	1 (0.0)	1286 (11.4)	509 (3.8)	-	131 (1.8)	37 (0.4)	-	123 (1.8)	36 (0.4)
	St. Francis	512 (5.5)	505 (4.5)	277 (2.1)	33 (0.5)	27 (0.4)	34 (0.4)	29 (0.4)	27 (0.4)	34 (0.4)
	Kasama	-	-	286 (2.2)	-	-	138 (1.5)	-	-	131 (1.5)
	Kabwe	1533 (16.5)	-	925 (7.0)	218 (3.2)	-	266 (2.9)	217 (3.3)	-	262 (3.0)
	Solwezi	-	10 (0.1)	673 (5.1)	-	1 (0.0)	167 (1.8)	-	1 (0.0)	140 (1.6)

Supplementary Table 4: Specimen characteristics

Specimen Type	All years* N= 22,343 n (%)	2016 N = 6,546 n (%)	2017 N = 6,964 n (%)	2018 N = 8,833 n (%)
Abscess/Discharge/Pus/Swab/Wound	3,397 (15.2)	817 (12.5)	1,169 (16.8)	1,411 (16)
Aspirate/discharge	3 (0)	1 (0)	-	2 (0)
Blood	4,702 (21)	1,240 (18.9)	1,256 (18)	2,206 (25)
Catheter (unspecified)	4 (0)	1 (0)	1 (0)	2 (0)
CSF	22 (0.1)	2 (0)	3 (0)	17 (0.2)
Fluid (abdominal/peritoneal)	138 (0.6)	42 (0.6)	34 (0.5)	62 (0.7)
Fluid (amniotic)	6 (0)	-	3 (0)	3 (0)
Fluid (bile)	1 (0)	-	-	1 (0)
Fluid (dialysis)	1 (0)	-	-	1 (0)
Fluid (gastric)	1 (0)	1 (0)	-	-
Fluid (joint/synovial)	12 (0.1)	8 (0.1)	1 (0)	3 (0)
Fluid (pericardial)	7 (0)	-	2 (0)	5 (0.1)
Fluid (pleural)	84 (0.4)	25 (0.4)	24 (0.3)	35 (0.4)
Fluid (unspecified)	59 (0.3)	16 (0.2)	26 (0.4)	17 (0.2)
Others	4,395 (19.7)	1,484 (22.7)	1,520 (21.8)	1,391 (15.7)
Respiratory-Lower	128 (0.6)	12 (0.2)	61 (0.9)	55 (0.6)
Respiratory-Upper	1,222 (5.5)	362 (5.5)	273 (3.9)	587 (6.6)
Scraping (cornea)	40 (0.2)	14 (0.2)	11 (0.2)	15 (0.2)
Semen	223 (1)	58 (0.9)	89 (1.3)	76 (0.9)
Stool	1206 (5.4)	172 (2.6)	249 (3.6)	785 (8.9)
Swab (high vaginal)	1 (0)	-	-	1 (0)
Swab (urethral)	16 (0.1)	3 (0)	2 (0)	11 (0.1)
Swab (vaginal)	52 (0.2)	6 (0.1)	11 (0.2)	35 (0.4)
Swab/discharge	4 (0)	-	-	4 (0)
Swab/discharge (genital)	157 (0.7)	69 (1.1)	20 (0.3)	68 (0.8)
Swab/discharge (urethral)	1 (0)	-	-	1 (0)
Tissue/biopsy	34 (0.2)	19 (0.3)	12 (0.2)	3 (0)
Ulcer	1 (0)	-	1 (0)	-
Unknown	1 (0)	-	1 (0)	-
Urine	6,425 (28.8)	2,194 (33.5)	2,195 (31.5)	2,036 (23)

**Indicates positive cultures with AST results*

Supplementary Table 5: Pathogen identification

Pathogen	All years* N = 22 343 n(%)	2016 N = 6 546 n(%)	2017 N = 6 964 n(%)	2018 N = 8 833 n(%)
Positive cultures with specific pathogen name	**14,631 (65.5)**	**4,743 (72.5)**	**4,944 (71)**	**4,944 (56)**
Achromobacter xylosoxidans	3 (0)	1 (0)	2 (0)	-
Acinetobacter baumannii	145 (0.6)	60 (0.9)	58 (0.8)	27 (0.3)
Acinetobacter haemolyticus	4 (0)	1 (0)	3 (0)	-
Acinetobacter junii	7 (0)	2 (0)	5 (0.1)	-
Acinetobacter lwoffii	17 (0.1)	11 (0.2)	4 (0.1)	2 (0)
Acinetobacter ursingii	4 (0)	1 (0)	1 (0)	2 (0)
Aerococcus viridans	6 (0)	2 (0)	2 (0)	2 (0)
Aeromonas hydrophila	9 (0)	4 (0.1)	4 (0.1)	1 (0)
Alcaligenes faecalis	1 (0)	-	1 (0)	-
Bacteroides fragilis	2 (0)	-	-	2 (0)
Brucella melitensis	1 (0)	-	1 (0)	-
Burkholderia cepacia	3 (0)	1 (0)	2 (0)	-
Burkholderia pseudomallei	36 (0.2)	-	4 (0.1)	32 (0.4)
Campylobacter coli	1 (0)	-	-	1 (0)
Candida albicans	8 (0)	2 (0)	2 (0)	4 (0)
Candida famata	1 (0)	1 (0)	-	-
Cedecea lapagei	1 (0)	-	1 (0)	-
Chryseobacterium indologenes	3 (0)	2 (0)	1 (0)	-
Chryseomonas luteola	2 (0)	1 (0)	-	1 (0)
Citrobacter braakii	1 (0)	-	1 (0)	-
Citrobacter diversus	3 (0)	-	1 (0)	2 (0)
Citrobacter farmeri	1 (0)	1 (0)	-	-
Citrobacter freundii	262 (1.2)	71 (1.1)	82 (1.2)	109 (1.2)
Citrobacter koseri	265 (1.2)	55 (0.8)	81 (1.2)	129 (1.5)
Dermacoccus nishinomiyaensis	1 (0)	1 (0)	-	-
Dermatophytes	1 (0)	1 (0)	-	-
Edwardsiella tarda	1 (0)	1 (0)	-	-
Enterobacter amnigenus	1 (0)	-	-	1 (0)
Enterobacter cancerogenus	1 (0)	1 (0)	-	-

Enterobacter cloacae	390 (1.7)	106 (1.6)	120 (1.7)	164 (1.9)
Enterobacter gergoviae	1 (0)	-	-	1 (0)
Enterococcus avium	4 (0)	-	4 (0.1)	-
Enterococcus casseliflavus	8 (0)	1 (0)	7 (0.1)	-
Enterococcus faecalis	325 (1.5)	133 (2)	155 (2.2)	37 (0.4)
Enterococcus faecium	102 (0.5)	53 (0.8)	42 (0.6)	7 (0.1)
Enterococcus gallinarum	20 (0.1)	4 (0.1)	12 (0.2)	4 (0)
Enterococcus hirae	2 (0)	-	2 (0)	-
Escherichia coli	3,752 (16.8)	1,282 (19.6)	1,188 (17.1)	1,282 (14.5)
Escherichia fergusonii	1 (0)	1 (0)	-	-
Eubacterium yurii	1 (0)	-	1 (0)	-
Globicatella sanguinis	4 (0)	-	4 (0.1)	-
Haemophilus influenzae	29 (0.1)	17 (0.3)	3 (0)	9 (0.1)
Haemophilus parainfluenzae	6 (0)	3 (0)	1 (0)	2 (0)
Hafnia alvei	9 (0)	-	1 (0)	8 (0.1)
Klebsiella aerogenes	152 (0.7)	24 (0.4)	68 (1)	60 (0.7)
Klebsiella oxytoca	360 (1.6)	116 (1.8)	126 (1.8)	118 (1.3)
Klebsiella pneumoniae	2,166 (9.7)	869 (13.3)	905 (13)	392 (4.4)
Kluyvera ascorbata	1 (0)	-	1 (0)	-
Kocuria kristinae	13 (0.1)	3 (0)	8 (0.1)	2 (0)
Kocuria rosea	7 (0)	2 (0)	1 (0)	4 (0)
Kocuria varians	3 (0)	2 (0)	1 (0)	-
Leclercia adecarboxylata	2 (0)	-	1 (0)	1 (0)
Leuconostoc pseudomesenteriodes	1 (0)	-	1 (0)	-
Micrococcus luteus	17 (0.1)	6 (0.1)	3 (0)	8 (0.1)
Moraxella atlantae	1 (0)	1 (0)	-	-
Moraxella catarrhalis	59 (0.3)	18 (0.3)	12 (0.2)	29 (0.3)
Moraxella lacunata	3 (0)	3 (0)	-	-
Morganella morganii	73 (0.3)	16 (0.2)	10 (0.1)	47 (0.5)
Neisseria canis	1 (0)	-	-	1 (0)
Neisseria cinerea	2 (0)	-	1 (0)	1 (0)
Neisseria elongata	1 (0)	-	-	1 (0)

Neisseria gonorrhoeae	4 (0)	1 (0)	1 (0)	2 (0)
Neisseria meningitidis	4 (0)	-	-	4 (0)
Neisseria sicca	1 (0)	-	-	1 (0)
Pantoea (enterobacter) agglomerans	814 (3.6)	239 (3.7)	226 (3.2)	349 (4)
Pasteurella pneumotropica	3 (0)	-	2 (0)	1 (0)
Proteus hauseri	3 (0)	-	2 (0)	1 (0)
Proteus mirabilis	503 (2.3)	210 (3.2)	181 (2.6)	112 (1.3)
Proteus penneri	3 (0)	3 (0)	-	-
Proteus vulgaris	139 (0.6)	54 (0.8)	44 (0.6)	41 (0.5)
Providencia rettgeri	10 (0)	3 (0)	4 (0.1)	3 (0)
Providencia stuartii	12 (0.1)	4 (0.1)	5 (0.1)	3 (0)
Pseudomonas aeruginosa	833 (3.7)	247 (3.8)	259 (3.7)	327 (3.7)
Pseudomonas alcaligenes	3 (0)	1 (0)	1 (0)	1 (0)
Pseudomonas fluorescens	**7 (0)**	**4 (0.1)**	**3 (0)**	-
Pseudomonas mendocina	2 (0)	1 (0)	1 (0)	-
Pseudomonas putida	10 (0)	5 (0.1)	4 (0.1)	1 (0)
Pseudomonas stutzeri	8 (0)	6 (0.1)	1 (0)	1 (0)
Raoultella ornithinolytica	1 (0)	-	-	1 (0)
Raoultella planticola	1 (0)	-	1 (0)	-
Rothia mucilaginosus	1 (0)	-	-	1 (0)
Salmonella enterica	2 (0)	-	-	2 (0)
Salmonella enteritidis	1 (0)	-	-	1 (0)
Salmonella paratyphi	9 (0)	-	6 (0.1)	3 (0)
Salmonella typhi	149 (0.7)	18 (0.3)	33 (0.5)	98 (1.1)
Serratia fonticola	6 (0)	2 (0)	4 (0.1)	-
Serratia liquefaciens	2 (0)	-	2 (0)	-
Serratia marcescens	56 (0.3)	18 (0.3)	21 (0.3)	17 (0.2)
Serratia odorifera	3 (0)	-	2 (0)	1 (0)
Shewanella putrefaciens	2 (0)	2 (0)	-	-
Shigella boydii	12 (0.1)	11 (0.2)	1 (0)	-
Shigella dysenteriae	22 (0.1)	10 (0.2)	8 (0.1)	4 (0)
Shigella flexneri	46 (0.2)	18 (0.3)	12 (0.2)	16 (0.2)

Shigella sonnei	11 (0)	6 (0.1)	3 (0)	2 (0)
Sphingomonas paucimobilis	13 (0.1)	2 (0)	8 (0.1)	3 (0)
Staphylococcus arlettae	2 (0)	-	-	2 (0)
Staphylococcus aureus	2,088 (9.3)	644 (9.8)	738 (10.6)	706 (8)
Staphylococcus auricularis	4 (0)	-	1 (0)	3 (0)
Staphylococcus capitis	3 (0)	2 (0)	1 (0)	-
Staphylococcus caprae	1 (0)	-	1 (0)	-
Staphylococcus cohnii	6 (0)	1 (0)	3 (0)	2 (0)
Staphylococcus epidermidis	137 (0.6)	50 (0.8)	50 (0.7)	37 (0.4)
Staphylococcus equorum	2 (0)	-	1 (0)	1 (0)
Staphylococcus gallinarum	2 (0)	2 (0)	-	-
Staphylococcus haemolyticus	307 (1.4)	128 (2)	124 (1.8)	55 (0.6)
Staphylococcus hominis	113 (0.5)	46 (0.7)	43 (0.6)	24 (0.3)
Staphylococcus intermedius	2 (0)	-	2 (0)	-
Staphylococcus lugdunensis	16 (0.1)	1 (0)	10 (0.1)	5 (0.1)
Staphylococcus pseudintermedius	9 (0)	-	5 (0.1)	4 (0)
Staphylococcus saprophyticus	13 (0.1)	2 (0)	7 (0.1)	4 (0)
Staphylococcus sciuri	42 (0.2)	19 (0.3)	22 (0.3)	1 (0)
Staphylococcus simulans	2 (0)	-	2 (0)	-
Staphylococcus vitulinus	2 (0)	-	1 (0)	1 (0)
Staphylococcus warneri	11 (0)	2 (0)	7 (0.1)	2 (0)
Staphylococcus xylosus	7 (0)	2 (0)	5 (0.1)	-
Stenotrophomonas (xanthomonas) maltophilia	20 (0.1)	6 (0.1)	14 (0.2)	-
Streptococcus agalactiae	21 (0.1)	9 (0.1)	7 (0.1)	5 (0.1)
Streptococcus alactolyticus	1 (0)	1 (0)	-	-
Streptococcus anginosus	1 (0)	-	1 (0)	-
Streptococcus bovis	1 (0)	1 (0)	-	-
Streptococcus constellatus	1 (0)	1 (0)	-	-
Streptococcus gallolyticus	4 (0)	2 (0)	2 (0)	-
Streptococcus gordonii	1 (0)	-	-	1 (0)
Streptococcus mitis	5 (0)	2 (0)	1 (0)	2 (0)
Streptococcus oralis	2 (0)	-	2 (0)	-

Streptococcus pneumoniae	85 (0.4)	33 (0.5)	18 (0.3)	34 (0.4)
Streptococcus porcinus	2 (0)	-	2 (0)	-
Streptococcus pyogenes	55 (0.2)	18 (0.3)	24 (0.3)	13 (0.1)
Streptococcus salivarius	2 (0)	2 (0)	-	-
Streptococcus sanguinis	3 (0)	-	1 (0)	2 (0)
Streptococcus sobrinus	1 (0)	-	-	1 (0)
Streptococcus thoraltensis	7 (0)	-	4 (0.1)	3 (0)
Streptococcus viridans	105 (0.5)	22 (0.3)	23 (0.3)	60 (0.7)
Vibrio cholerae	531 (2.4)	1 (0)	52 (0.7)	478 (5.4)
Yersinia enterocolitica	10 (0)	-	1 (0)	9 (0.1)
Yersinia pestis	1 (0)	1 (0)	-	-
Positive cultures with non-specific pathogen name	**7,712 (34.5)**	**1,803 (27.5)**	**2,020 (29)**	**3,889 (44)**
Acinetobacter Sp.	191 (0.9)	48 (0.7)	60 (0.9)	83 (0.9)
Actinomyces Sp.	1 (0)	-	1 (0)	-
Aeromonas Sp.	2 (0)	-	1 (0)	1 (0)
Alcaligenes Sp.	1 (0)	-	-	1 (0)
Anaerobes	1 (0)	-	-	1 (0)
Bacillus Sp.	4 (0)	-	4 (0.1)	-
Burkholderia Sp.	4 (0)	3 (0)	-	1 (0)
Candida Sp.	20 (0.1)	5 (0.1)	3 (0)	12 (0.1)
Citrobacter Sp.	180 (0.8)	16 (0.2)	55 (0.8)	109 (1.2)
Clostridium Sp.	3 (0)	-	1 (0)	2 (0)
Cronobacter Sp.	1 (0)	-	-	1 (0)
Cryptococcus Sp.	3 (0)	-	-	3 (0)
Edwardsiella Sp.	1 (0)	-	-	1 (0)
Enterobacter Sp.	670 (3)	73 (1.1)	224 (3.2)	373 (4.2)
Enterococcus Sp.	844 (3.8)	270 (4.1)	260 (3.7)	314 (3.6)
Escherichia Sp.	33 (0.1)	6 (0.1)	7 (0.1)	20 (0.2)
Haemophilus Sp.	3 (0)	2 (0)	-	1 (0)
Klebsiella Sp.	1,077 (4.8)	229 (3.5)	223 (3.2)	625 (7.1)
Lactobacillus Sp.	1 (0)	-	1 (0)	-
Malbranchea Sp.	1 (0)	1 (0)	-	-

Micrococcus Sp.	23 (0.1)	7 (0.1)	6 (0.1)	10 (0.1)
Moraxella Sp.	36 (0.2)	13 (0.2)	9 (0.1)	14 (0.2)
Morganella Sp.	7 (0)	1 (0)	-	6 (0.1)
Neisseria Sp.	7 (0)	-	-	7 (0.1)
Non fermenting gram negative bacilli	12 (0.1)	-	-	12 (0.1)
Pantoea Sp.	4 (0)	2 (0)	2 (0)	-
Peptostreptococcus Sp.	1 (0)	-	-	1 (0)
Photobacterium Sp.	1 (0)	-	-	1 (0)
Propionibacterium Sp.	1 (0)	-	-	1 (0)
Proteus Sp.	436 (2)	87 (1.3)	126 (1.8)	223 (2.5)
Providencia Sp.	18 (0.1)	-	-	18 (0.2)
Pseudallescheria Sp.	1 (0)	1 (0)	-	-
Pseudomonas Sp.	506 (2.3)	179 (2.7)	168 (2.4)	159 (1.8)
Salmonella Sp.	224 (1)	86 (1.3)	70 (1)	68 (0.8)
Serpulina Sp.	1 (0)	-	-	1 (0)
Serratia Sp.	29 (0.1)	8 (0.1)	6 (0.1)	15 (0.2)
Shigella Sp.	18 (0.1)	1 (0)	10 (0.1)	7 (0.1)
Staphylococcus Sp.	2,602 (11.6)	555 (8.5)	539 (7.7)	1,508 (17.1)
Streptobacillus Sp.	1 (0)	-	-	1 (0)
Streptococcus Sp.	661 (3)	181 (2.8)	231 (3.3)	249 (2.8)
Unspecified (Gram negative bacilli)	9 (0)	1 (0)	2 (0)	6 (0.1)
Unspecified (Gram negative bacteria)	26 (0.1)	21 (0.3)	1 (0)	4 (0)
Unspecified (Gram negative cocci)	4 (0)	1 (0)	1 (0)	2 (0)
Unspecified (Gram negative coccobacilli)	1 (0)	-	-	1 (0)
Unspecified (Gram positive bacilli)	5 (0)	1 (0)	-	4 (0)
Unspecified (Gram positive bacteria)	2 (0)	1 (0)	1 (0)	-
Unspecified (Gram positive cocci)	23 (0.1)	3 (0)	5 (0.1)	15 (0.2)
Yersinia Sp.	12 (0.1)	1 (0)	3 (0)	8 (0.1)

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

Supplementary Table 6: Laboratory data scoring

Laboratory name	Laboratory data score (out of 4)			
	2016	2017	2018	Average
Arthur	1	1	1	1
Nchanga	-	2	-	2
UTH	3	4	3	3.3
Ndola	-	-	3	3
Livingstone	-	-	3	3
Chilonga	-	3	3	3
Lewanika	3	-	-	3
Mansa	-	-	2	2
Chipata	-	3	3	3
Levy	-	2	2	2
St. Francis	3	3	3	3
Kasama	-	-	3	3
Kabwe	2	-	2	2
Solwezi	-	4	3	3.5

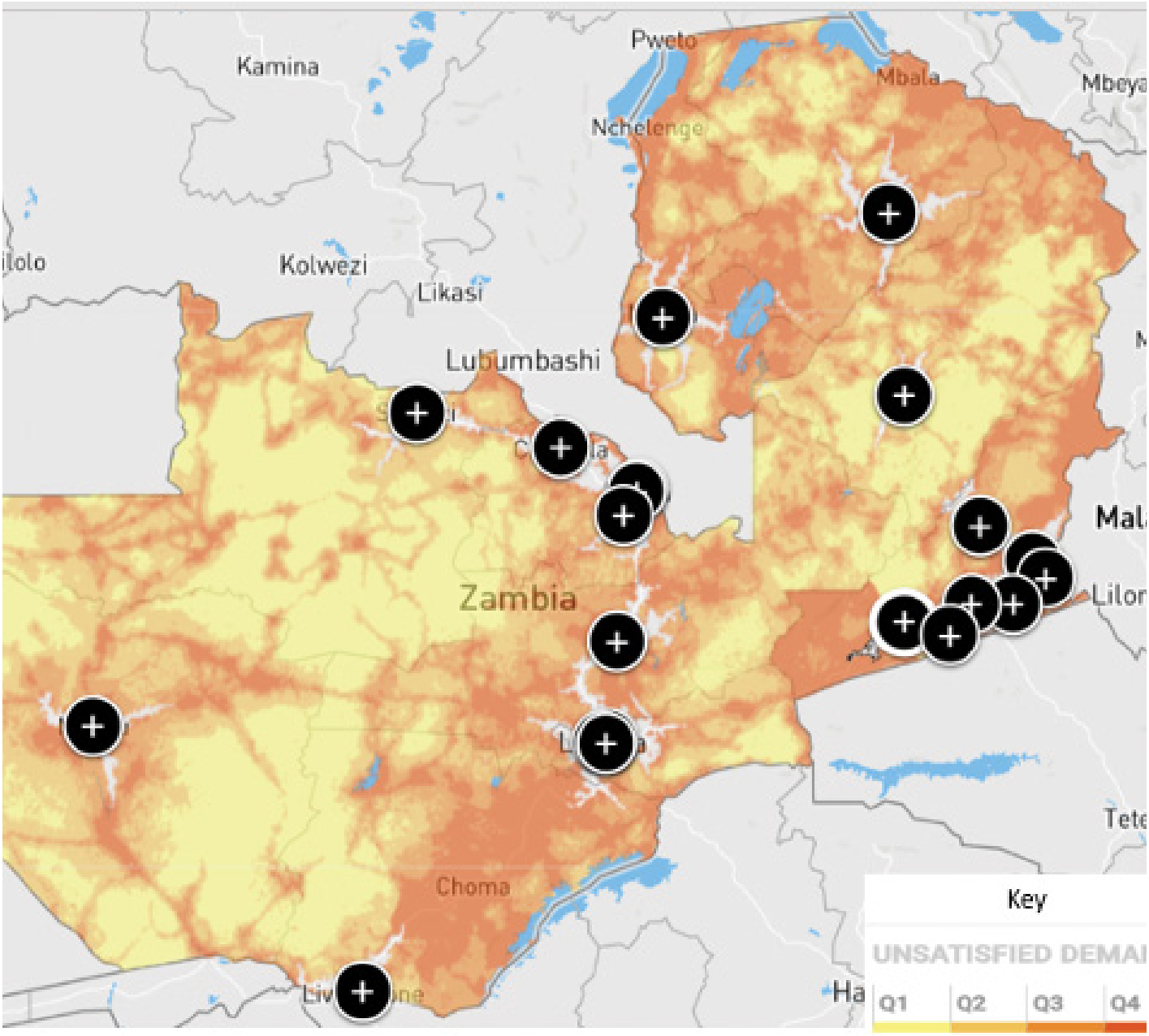
Supplementary Table 7: Univariate logistic regression analysis

Variable	Options	N	NS (%)	Crude OR (95% CI)	P-value
	Female	780	70.5	Ref	0.6199
	Male	627	71.8	1.06 (0.83 – 1.35)	
Age	<1	2,079	57.7	1.08 (0.97 – 1.21)	0.000
	1-17	3,332	56.4	1.02 (0.91 – 1.15)	
	18-49	7,790	55.5	Ref	
	50-65	1,688	58.6	1.12 (1.06 – 1.18)	
	>65	1,147	62.5	1.32 (1.17 – 1.48)	
Diagnosis	Infection/Inflammation	5,230	56.2	Ref	0.0516
	Cardiovascular	83	59.0	1.12 (0.72 – 1.75)	
	Diabetes	111	61.3	1.23 (0.84 – 1.81)	
	Hematological	107	59.8	1.16 (0.79 – 1.71)	
	Injuries	623	57.8	1.06 (0.90 – 1.26)	
	Neoplasm	203	61.1	1.22 (0.92 – 1.63)	
	Nonspecific	2,296	55.7	0.98 (0.89 – 1.08)	
	Nutritional	5,009	56.4	1.00 (0.84 – 1.21)	
	Obs/Gynaecological	101	62.4	1.29 (0.86 – 1.94)	
	Renal	278	65.5	1.47 (1.14 – 1.90)	
	Respiratory	122	45.1	0.64 (0.45 – 0.92)	
	Surgical/Orthopaedic	140	57.1	1.04 (0.74 – 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
Candida sp.	Ampicillin	AMP_ND10	R	Disk	2016
Candida sp.	Nalidixic acid	NAL_ND30	I	Disk	2016
Pseudallescheria sp.	Ampicillin	AMP_ND10	R	Disk	2016
Pseudallescheria sp.	Cefotaxime	CTX_ND30	R	Disk	2016
Candida albicans	Cefotaxime	CTX_ND30	R	Disk	2016
Candida albicans	Cefotaxime	CTX_ND30	R	Disk	2016
Candida albicans	Ampicillin	AMP_ND10	R	Disk	2017
Candida albicans	Ceftazidime	CAZ_ND30	R	Disk	2017
Candida albicans	Ciprofloxacin	CIP_ND5	R	Disk	2017
Candida sp.	Ciprofloxacin	CIP_ND5	R	Disk	2018
Candida sp.	Ciprofloxacin	CIP_ND5	I	Disk	2018
Candida sp.	Cefoxitin	FOX_ND30	R	Disk	2018
Candida sp.	Gentamicin-High	GEH_ND120	R	Disk	2018
Candida sp.	Nitrofurantoin	NIT_ND300	R	Disk	2018
Candida sp.	Oxacillin	OXA_ND1	R	Disk	2018
Candida sp.	Penicillin G	PEN_ND10	R	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
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2018
Enterobacter sp.	Penicillin G	PEN_ND10	R	Disk	2016
Escherichia coli	Penicillin G	PEN_ND10	R	Disk	2016
Proteus sp.	Penicillin G	PEN_ND10	R	Disk	2016
Enterobacter sp.	Penicillin G	PEN_ND10	R	Disk	2016
Enterobacter sp.	Penicillin G	PEN_ND10	R	Disk	2016
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2018
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2018
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2018
Staphylococcus 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

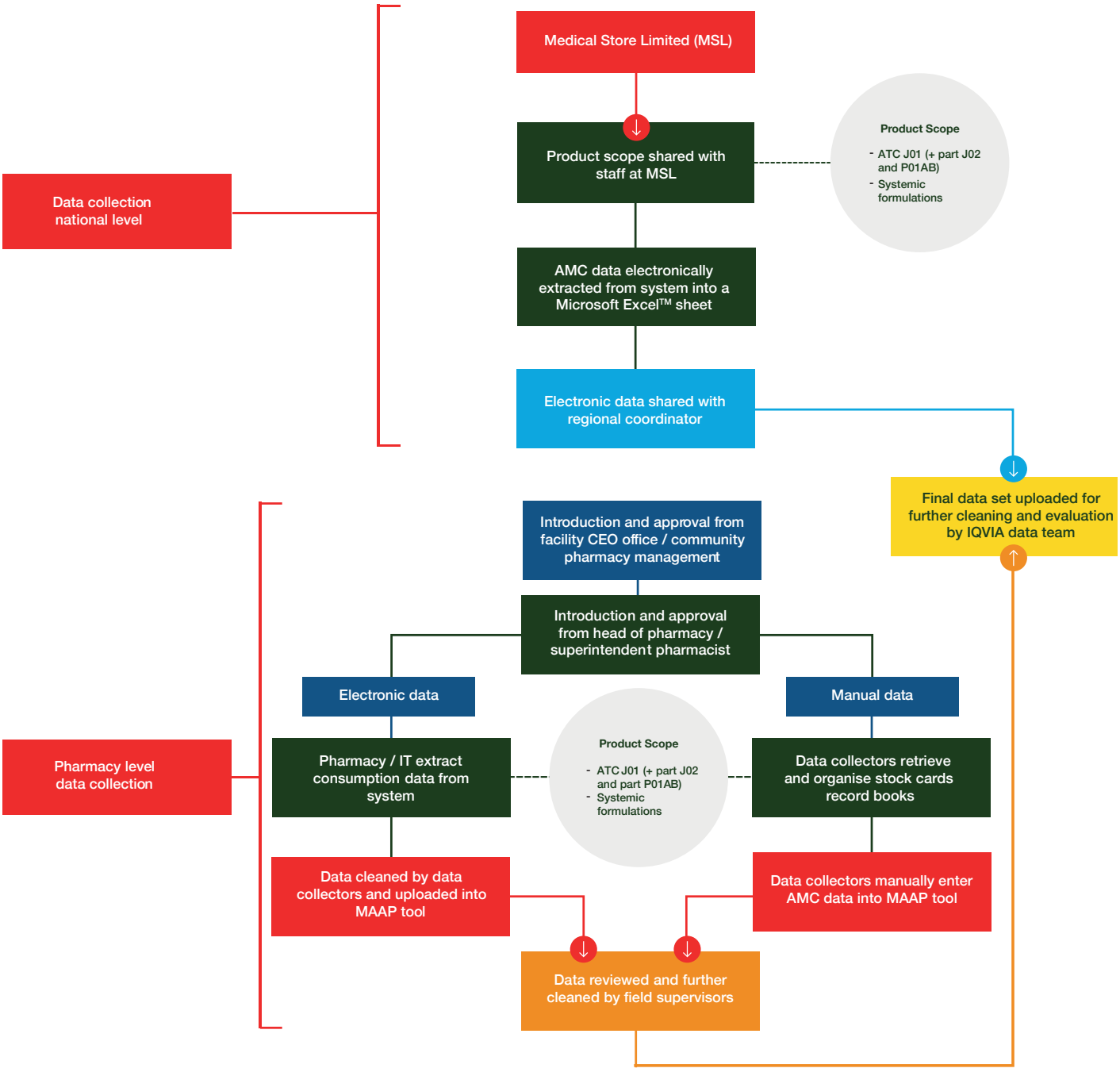
Spectinomycin	J01XX04	A
Linezolid	J01XX08	R
Daptomycin	J01XX09	R
Bacitracin	J01XX10	U
Tedizolid	J01XX11	R
Amphotericin B	J02AA01	N/A
Fluconazole	J02AC01	N/A
Itraconazole	J02AC02	N/A
Voriconazole	J02AC03	N/A
Posaconazole	J02AC04	N/A
Isavuconazole	J02AC05	N/A
Flucytosine	J02AX01	N/A
Caspofungin	J02AX04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



**Pharmacy-level AMC data is a subset of the national-level AMC data; the two datasets were analysed and presented separately*

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:
https://www.whocc.no/atc_ddd_index/

***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 the AMC is converted to standard DDDs, the data are further analysed into the below standard units:

1. **DDDs/1000 inhabitants/day (DID): used to calculate total AMC for the Zambia 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 summarises how this calculation was done:**

DDD/1000 Inhabitants/day =

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

*Zambia population estimated for 2016-2018 obtained from:
https://www.worldometers.info/world-population/zambia-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: https://www.whocc.no/atc_ddd_index/

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 represent first and second choice antibiotics for the empiric treatment of most common infectious syndromes. They offer the best therapeutic value, while minimising 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%). '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: 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; seven 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
			Defined daily dose (%*)			
J01 Class		**Total**	**5,555,163 (100)**	**14,774,186 (100)**	**10,104,932 (100)**	**10,144,760**
1	Access	Amoxicillin/Clavulanic Acid	600,934 (10.8)	7,552,424 (51.1)	506,875 (5)	2,886,744
2	Watch	Ciprofloxacin	1,724,027 (31)	2,535,835 (17.2)	3,586,573 (35.5)	2,615,478
3	Access	Doxycycline	475,240 (8.6)	1,028,290 (7)	1,358,440 (13.4)	953,990
4	Access	Sulfamethoxazole/ Trimethoprim	192,546 (3.5)	951,008 (6.4)	1,116,268 (11)	753,274
5	Access	Amoxicillin	606,988 (10.9)	446,588 (3)	881,795 (8.7)	645,124
6	Watch	Erythromycin	345,638 (6.2)	579,435 (3.9)	974,853 (9.6)	633,308
7	Access	Cloxacillin	538,648 (9.7)	590,362 (4)	650,925 (6.4)	593,311
8	Uncategorised	Nalidixic Acid	535,478 (9.6)	293,188 (2)	30,312 (0.3)	286,326
9	Access	Phenoxymethylpenicillin	98,841 (1.8)	143,650 (1)	196,249 (1.9)	146,247
10	Access	Nitrofurantoin	54,555 (1)	67,080 (0.5)	130,550 (1.3)	84,062
11	Watch	Clarithromycin	59,580 (1.1)	57,520 (0.4)	111,645 (1.1)	76,248
12	Access	Benzylpenicillin	9,914 (0.2)	97,700 (0.7)	84,842 (0.8)	64,152
13	Watch	Cefotaxime	29,727 (0.5)	80,136 (0.5)	74,255 (0.7)	61,372
14	Access	Metronidazole	28,491 (0.5)	61,029 (0.4)	86,421 (0.9)	58,647
15	Watch	Cefuroxime	38,340 (0.7)	80,826 (0.5)	39,490 (0.4)	52,885
16	Access	Cefalexin	30,245 (0.5)	57,239 (0.4)	57,649 (0.6)	48,378
17	Access	Gentamicin	23,037 (0.4)	29,492 (0.2)	37,150 (0.4)	29,893
18	Access	Chloramphenicol	24,807 (0.4)	39,766 (0.3)	19,527 (0.2)	28,033
19	Watch	Ceftriaxone	58,413 (1.1)	10,039 (0.1)	4,098 (0)	24,183
20	Watch	Cefixime	22,025 (0.4)	10,165 (0.1)	34,595 (0.3)	22,262
21	Uncategorised	Ampicillin/Cloxacillin	11,820 (0.2)	15,210 (0.1)	21,538 (0.2)	16,189
22	Watch	Azithromycin	6,583 (0.1)	9,077 (0.1)	24,945 (0.2)	13,535
23	Access	Tetracycline	3,700 (0.1)	6,730 (0)	26,220 (0.3)	12,217
24	Watch	Levofloxacin	3,310 (0.1)	10,546 (0.1)	20,822 (0.2)	11,559
25	Watch	Norfloxacin	5,000 (0.1)	5,500 (0)	15,100 (0.1)	8,533
26	Watch	Kanamycin	12,664 (0.2)	899 (0)	38 (0)	4,534
27	Access	Dicloxacillin	9,500 (0.2)	0 (0)	0 (0)	3,167
28	Access	Ampicillin	1,737 (0)	3,453 (0)	3,007 (0)	2,732
29	Access	Benzathine benzylpenicillin	921 (0)	4,257 (0)	2,468 (0)	2,549
30	Access	Procaine benzylpenicillin	1,488 (0)	3,361 (0)	2,173 (0)	2,341
31	Uncategorised	Norfloxacin/Tinidazole	200 (0)	2,150 (0)	2,360 (0)	1,570
32	Uncategorised	Ciprofloxacin/Tinidazole	350 (0)	100 (0)	2,085 (0)	845
33	Uncategorised	Norfloxacin/Metronidazole	0 (0)	733 (0)	965 (0)	566
34	Access	Clindamycin	0 (0)	300 (0)	50 (0)	117
35	Uncategorised	Ofloxacin/Ornidazole	0 (0)	0 (0)	350 (0)	117
36	Access	Spectinomycin	267 (0)	0 (0)	13 (0)	93
37	Watch	Ofloxacin	50 (0)	100 (0)	50 (0)	67
38	Access	Ampicillin/Sulbactam	100 (0)	0 (0)	50 (0)	50
39	Watch	Telithromycin	0 (0)	0 (0)	140 (0)	47
40	Watch	Cefpodoxime proxetil	0 (0)	0 (0)	50 (0)	17
P01AB Class		Total	**748,971 (100)**	**835,800 (100)**	**821,384 (100)**	**802,052**
1	Access	Metronidazole	708,855 (94.6)	749,527 (89.7)	802,426 (97.7)	753,603
2	Uncategorised	Tinidazole	39,880 (5.4)	85,745 (10.3)	17,875 (2.2)	47,833
3	Uncategorised	Secnidazole	236 (0)	528 (0.1)	1,083 (0.1)	616

**Antibiotics marked as 'uncategorised' have not been awarded a category within the 2019 WHO AWaRe database.*

Appendix 8: Breakdown of national AMC by ATC classes

	% consumption		
ATC class	2016	2017	2018
Combinations of penicillins, incl. beta-lactamase inhibitors	9.7%	48.5%	4.8%
Fluoroquinolones	27.5%	16.3%	33.2%
Tetracyclines	7.6%	6.6%	12.7%
Nitroimidazole derivatives	11.9%	5.4%	7.5%
Combinations of sulfonamides and trimethoprim, incl. derivatives	3.1%	6.1%	10.2%
Macrolides	6.5%	4.1%	10.2%
Penicillins with extended-spectrum	9.7%	2.9%	8.1%
Beta-lactamase resistant penicillins	8.7%	3.8%	6.0%
Other quinolones	8.5%	1.9%	0.3%
Beta-lactamase sensitive penicillins	1.8%	1.6%	2.6%
Third-generation cephalosporins	1.7%	0.6%	1.0%
Nitrofuran derivatives	0.9%	0.4%	1.2%
Imidazole derivatives	0.5%	0.4%	0.8%
Second-generation cephalosporins	0.6%	0.5%	0.4%
First-generation cephalosporins	0.5%	0.4%	0.5%
Aminoglycosides	0.6%	0.2%	0.3%
Amphenicols	0.4%	0.3%	0.2%
Combinations of antibacterials	0.0%	<0.1%	0.1%
Lincosamides	0.0%	0.002%	<0.1%
Other antibacterials	<0.1%	0.0%	<0.1%

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	N	N
Amoxicillin	Access	J01CA04	Y	Y	Y
Amoxicillin/ Clavulanic Acid	Access	J01CR02	Y	Y	Y
Amphotericin-B		J02AA01	N	Y	N
Ampicillin	Access	J01CA01	Y	Y	Y
Ampicillin/Cloxacillin		J01CR50	N	N	Y
Ampicillin/Sulbactam	Access	J01CR01	N	N	Y
Azithromycin	Watch	J01FA10	Y	Y	Y
Benzathine benzylpenicillin	Access	J01CE08	Y	Y	Y
Benzylpenicillin	Access	J01CE01	Y	Y	Y
Cefalexin	Access	J01DB01	Y	Y	Y
Cefazolin	Access	J01DB04	Y	N	N
Cefiderocol	Reserve	J01DI04	Y	N	N
Cefixime	Watch	J01DD08	Y	N	Y
Cefotaxime	Watch	J01DD01	Y	Y	Y
Cefoxitin	Watch	J01DC01	N	Y	N
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	N	Y
Chloramphenicol	Access	J01BA01	Y	Y	Y
Ciprofloxacin	Watch	J01MA02	Y	Y	Y
Ciprofloxacin/ Tinidazole		J01RA11	N	N	Y
Clarithromycin	Watch	J01FA09	Y	N	Y
Clindamycin	Access	J01FF01	Y	Y	Y
Cloxacillin	Access	J01CF02	Y	Y	Y
Colistin	Reserve	J01XB01	Y	N	N
Dicloxacillin	Access	J01CF01	N	N	Y
Doxycycline	Access	J01AA02	Y	Y	Y
Erythromycin	Watch	J01FA01	N	Y	Y

Flucloxacillin	Access	J01CF05	N	Y	N
Fluconazole		J02AC01	N	Y	N
Flucytosine		J02AX01	N	Y	N
Fosfomycin (IV)	Reserve	J01XX01	Y	N	N
Gentamicin	Access	J01GB03	Y	Y	Y
Kanamycin	Watch	J01GB04	N	Y	Y
Ketoconazole		J02AB02	N	Y	N
Levofloxacin	Watch	J01MA12	N	N	Y
Linezolid	Reserve	J01XX08	Y	N	N
Meropenem	Watch	J01DH02	Y	N	N
Meropenem/ Vaborbactam	Reserve	J01DH52	Y	N	N
Metronidazole	Access	P01AB01, J01XD01	Y	Y	Y
Nalidixic Acid		J01MB02	N	Y	Y
Nitrofurantoin	Access	J01XE01	Y	Y	Y
Norfloxacin	Watch	J01MA06	N	N	Y
Norfloxacin/ Metronidazole		J01RA--	N	N	Y
Norfloxacin/Tinidazole		J01RA13	N	N	Y
Ofloxacin	Watch	J01MA01	N	Y	Y
Ofloxacin/Ornidazole		J01RA09	N	N	Y
Phenoxymethylpenicillin	Access	J01CE02	Y	Y	Y
Piperacillin/tazobactam	Watch	J01CR05	Y	N	N
Plazomicin	Reserve	J01GB14	Y	N	N
Polymyxin-B	Reserve	J01XB02	Y	N	N
Procaine benzylpenicillin	Access	J01CE09	Y	Y	Y
Secnidazole		P01AB07	N	N	Y
Spectinomycin	Access	J01XX04	Y	Y	Y
Streptomycin	Watch	J01GA01	N	Y	N
Sulfamethoxazole/ Trimethoprim	Access	J01EE01	Y	Y	Y
Telithromycin	Watch	J01FA15	N	N	Y
Tetracycline	Access	J01AA07	N	Y	Y
Tinidazole		P01AB02	N	Y	Y
Trimethoprim	Access	J01EA01	Y	Y	N
Vancomycin	Watch	J01XA01	Y	N	N

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