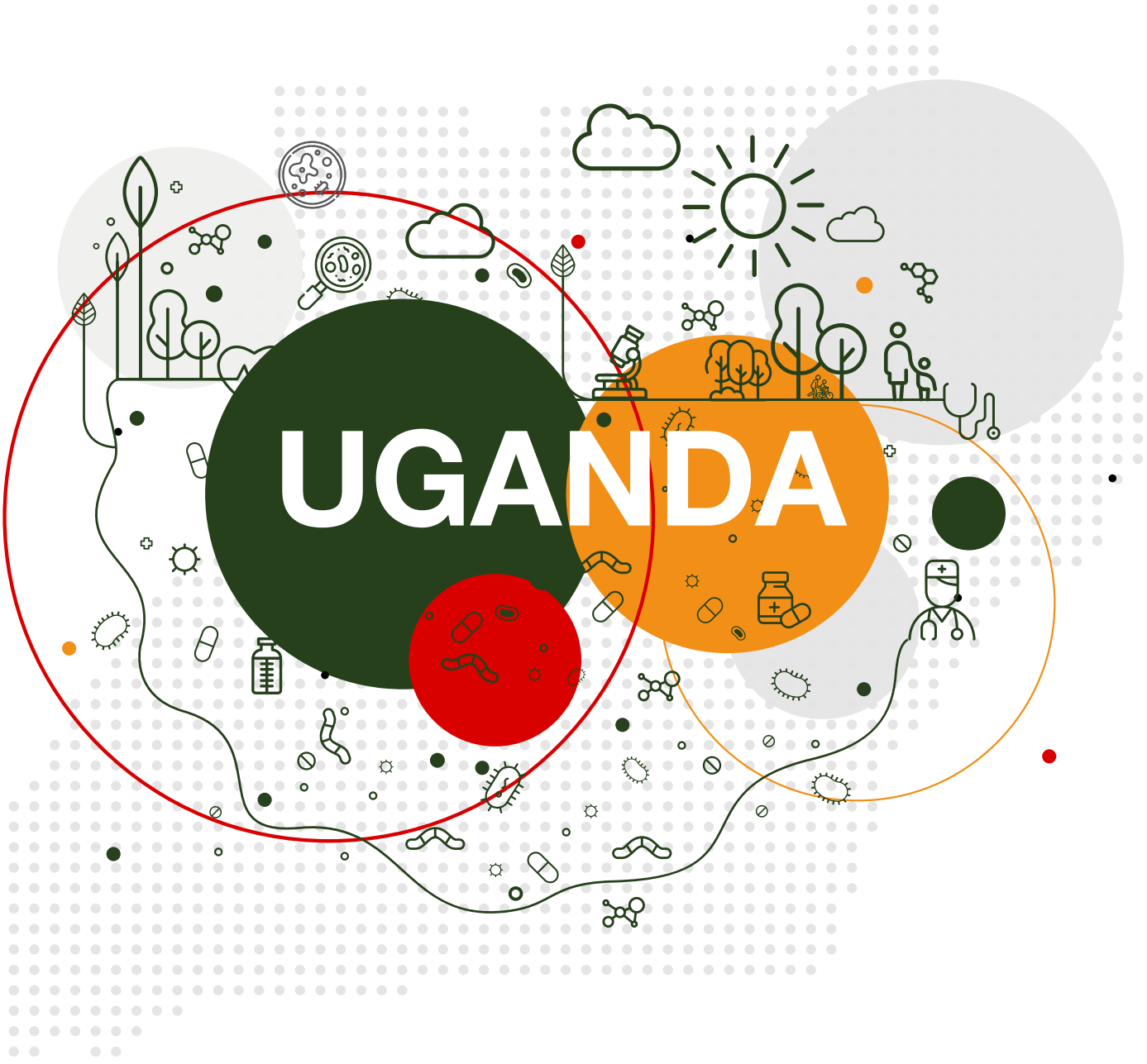
MAAP
Mapping AMR & AMU Partnership

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
EACSA
InSTEDD Innovative Support To Emergencies Diseases and Disasters
IQVIA
ONEHEALTH TRUST

Year: 2022

Uganda (2016-2018)

UGANDA

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

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
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
EMHSLU	Essential Medicines and Health Supplies List of Uganda (EMHSLU)
EML	Essential Medicines List
EQA	External Quality Assessment
EUCAST	European Committee on Antibiotic Susceptibility Testing
FDC	Fixed Dose Combinations
GLASS	Global Antimicrobial Resistance Surveillance System
HIS	Hospital Information System
InSTEDD	Innovative Support to Emergencies, Diseases and Disasters
JMS	Joint Medical Store
KIIs	Key Informant Interviews
LIS	Laboratory Information System
LMIC	Low- and Middle-Income Country
LQMS	Laboratory Quality Management System
MAAP	Mapping Antimicrobial resistance and Antimicrobial use Partnership
MoH	Ministry of Health
NCD	Non-Communicable Disease(s)
NDA	National Drug Authority
NMS	National Medical Store
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
WHO	World Health Organisation

Executive Summary

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

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

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

Uganda had approximately 1 625 laboratories in the national laboratory network during the study period, of which 30 were reported to have capacity for bacteriology testing. Based on self-reported information from 20 laboratories, functioning and quality compliance were assessed to understand the laboratory preparedness for AMR surveillance.

AMR rates presented are based on the analysis of antimicrobial susceptibility results 0f 22 349 positive cultures obtained from 16 laboratories. High levels of resistance were noted for third-generation cephalosporin-resistant Enterobacterales (49-55%), carbapenem-resistant Acinetobacter baumannii (30-54%) and methicillin-resistant Staphylococcus aureus (34-36%). Antimicrobial resistant infections were found to be more common in infants, the elderly, persons on prior antibiotics and those with hospital-acquired infections. All results should be interpreted with caution as the participating laboratories were at different levels of service and had variable testing capacity.
AMC is measured as the quantity of antimicrobials sold or dispensed, whereas AMU reviews whether antimicrobials are used appropriately based on additional data such as clinical indicators. Only AMC data were retrievable. However, AMU data were not obtained due to a lack of a unique patient identifier and tracking systems across hospital departments. AMC data collection was possible both at the national level (2017-2018) and at selected sentinel pharmacies (2016-2018) thus implying that AMC surveillance is possible in Uganda. However, national AMC data for the year 2016 were not available at the time of MAAP data collection due to a targeted national data audit of 2016 data. The average national total AMC consumption levels in Uganda annually between 2017-2018 was 7.4 defined daily doses (DDD) per 1000 inhabitants per day, ranging from 7.7 in 2017 to 7.0 in 2018.

Antimicrobial utilisation by the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) classification was highest for penicillins with extended spectrum (range 38.7% to 39.6%), followed by tetracyclines (range 14.3% to 14.9%) and finally, nitroimidazole derivatives (range 12.7% to 14.1%). The top five most consumed antimicrobials were amoxicillin, doxycycline, metronidazole, sulfamethoxazole/trimethoprim and iprofloxacin. Together, they account for >88% of the total consumption share thus suggesting a lack of variation. This consumption trend could potentially increase AMR. The total AMC came from 84.5% Access, 15.5% of Watch and <0.1% of Reserve antibiotics. Between 2017-2018, the use of Access category antibiotics exceeded the WHO minimum recommended consumption threshold of 60%. Six combinations of two or more broad-spectrum fixed-dose combinations (FDC) of antimicrobials were identified that were not recommended for clinical utility but were nevertheless consumed in Uganda. Of those, ampicillin/cloxacillin was most consumed (mean DID of 0.1).

The drug resistance index (DRI) is a simple metric based on aggregate rates of resistance and measured on a scale of 0-100, where 0 indicates fully susceptible while 100 indicates fully resistant. The DRI estimate was found to be high at 69.1% (95% CI, 64.2–74.0%) thus implying low antibiotic effectiveness which is a threat to effective infectious disease management and calls for urgent policy intervention.

The following recommendations should be noted by policy makers and healthcare providers to further strengthen AMR and AMC surveillance for AMR mitigation in the country.

- To strengthen the delivery of services by the laboratories, we recommend that all laboratories are mapped across a range of indicators, including population coverage, infectious disease burden, testing capabilities and quality compliance. This would inform decision makers on unmet needs and decide a way forward for expansion of the laboratory network.

- For high-quality microbiology testing and reporting, staff training on laboratory standards, ability to identify common pathogens and data management skills are essential. Capacity building of staff may be completed through in-house expertise or outsourced to external organisations or tertiary facilities.

- To strengthen AMR surveillance, it is essential to curate the right data and generate evidence. We recommend data collection through standardised formats at all levels (laboratories, clinics and pharmacies) as well as the use of automation for data analyses. We also recommend establishing a system of assigning permanent identification numbers for patients' tracking over time.

- Due to limitations in the number of facilities assessed, MAAP, in alignment with the WHO guide on facility AMU assessment, would recommend that future AMU and AMC surveillance attempts in the country be conducted through point prevalence surveys on a larger scale to give a nationally representative portrait of antimicrobials use in the country.

- MAAP recommends that a comprehensive guiding policy for routine AMC data surveillance be required in the country. The policy should aim to guide on, at the minimum, AMC data reporting variables, routine data cleaning and reporting practices to minimise the amount of time spent standardising and cleaning the data before routine surveillance exercises.

- To make future AMC surveillance more time- and cost-efficient, hospitals could consider converting to electronic systems and ensure such systems have the capabilities to transfer data across systems and/or produce user-friendly reports on AMC.

- MAAP recommends that the country's Antimicrobial Resistance Coordinating Committee (AMRCC) consider the introduction of facility-level Antimicrobial Stewardship Programs (ASPs) to regulate the use of these broader spectrum antibiotics and educate prescribers on the importance of reserving them to maintain efficacy.

- From the assessment, an overwhelming majority of antibiotics consumed within the Access and Watch categories were in the top five antibiotics in each category. Such a consumption pattern could be postulated to be sub-optimal as the evolutionary pressure driving resistance would be focused only on the narrow band of 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.

- MAAP recommends an urgent review be conducted by the ministry of health (MoH) and AMRCC to assess the availability of the Reserve category antibiotics in the country. This may subsequently lead to the revision of the country's essential medicines list (EML) and treatment guidelines to include these vital antibiotics, if deemed necessary. This approach will ensure that the most vital antibiotics are available for all patients.

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

Overview

The Fleming Fund Grants Programme

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

The Fleming Fund Regional Grants Round 1 Programme

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

Problem statement

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

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

MAAP

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

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

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

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

Fourteen African countries across West Africa (Burkina Faso, Ghana, Nigeria, Senegal and Sierra Leone), East Africa (Kenya, Tanzania and Uganda), Central Africa (Cameroon and 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 Uganda 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 Uganda, including the public and private human healthcare sector
- To collect, digitise and analyse retrospective data from selected facilities using standardised electronic tools; to describe the completeness and validity of AMR data in selected facilities

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

Outcome measures

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

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

Key engagements and activities

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

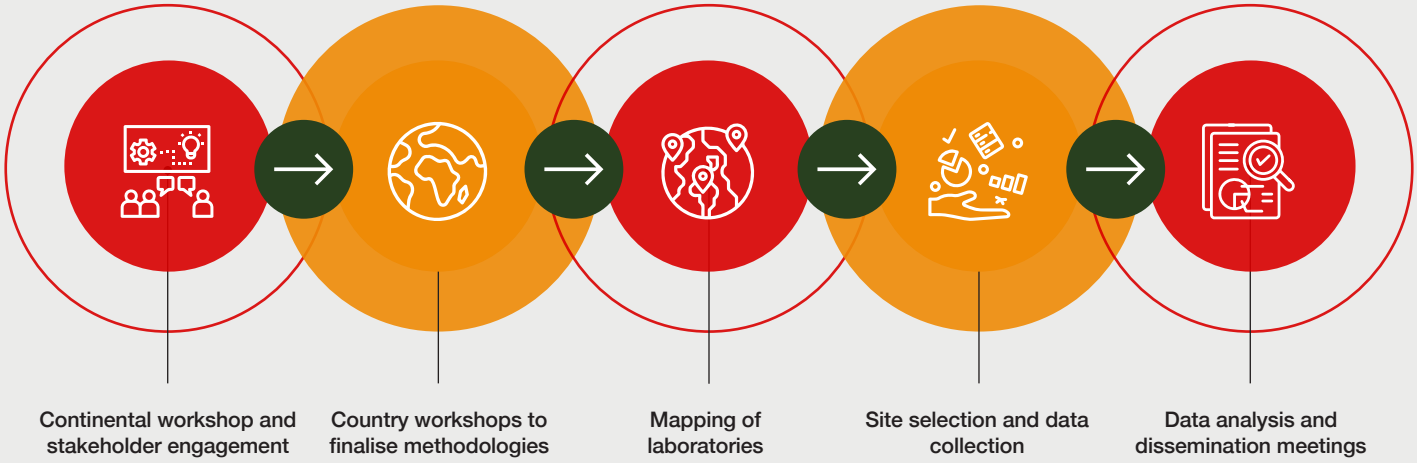


Figure 1: Key engagements and activities

Ethical issues and data sharing agreements

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

Country Profile

Health and demographic profile

As of 2020, Uganda was estimated to have a population of 45.7 million inhabitants with a life expectancy of 64 years. The country has a high infectious disease burden with a TB incidence of 127 per 100 000 and an HIV prevalence of 5.4%. The country has a physician density rate of 0.17 per 1 000 inhabitants and nurses density rate of 1.24 per 1 000 inhabitants. With a universal health coverage index of 50, Uganda appears to have an average coverage of essential services (Table 1).

Table 1: Health and demographic profile of Uganda

	Uganda		Comparator values (most recent year)*		
	Year	Value	India	Argentina	United States
Population	2020	45 741 000	1 380 004390	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	50	61	67	83
GDP per capita (current US$)	2020	822.03	1 927.7	8 579.0	63 593.4
Immunisation, DPT (% of children ages 12-23 months)	2019	85.69	91.0	86.0	94.0
Incidence of tuberculosis (per 100 000 people)	2020	127	188.0	31.0	2.4
Prevalence of HIV, total (% of population ages 15-49)#	2020	5.4	0.2*	0.4 2020	0.4 2019
Primary education (%)#	2017	52.7	94.6	98.6	100
Physicians density (physicians per 1 000)#	2017	0.17	0.93	4.0	2.6
Nurses density (nurses and midwives per 1 000)#	2018	1.24	2.39	2.60	15.69

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

Policy frameworks

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

Uganda enrolled in GLASS in 2016 and started submitting AMR data the following year. Thus far, the country has submitted its AMR data to GLASS for the last three data calls.[10-13] The Government of Uganda has also established the Antimicrobial Resistance National Action Plan (2018-2023)[14,15,] with the goal to reduce the AMR burden nationwide. Additionally, Uganda has a system for reporting AMR data to national authorities.

Part A: Antimicrobial Resistance

Section I: Laboratory assessment

Objective

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

Methodology

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

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

Results

Mapping and selection of laboratories

During the initial stages of in-country work in Uganda, 1 625 laboratories were mapped to the national laboratory network. An eligibility questionnaire was sent to 30 laboratories identified as having capacity for bacteriology testing. Twenty laboratories that responded to the questionnaire had AST capacity and the majority were affiliated with the government (Table 2, Supplementary Table 1). The laboratory readiness scores of the surveyed laboratories varied widely (range 36.8–81.6%). From the 20 laboratories with AST capacity, 16 were selected for data collection (Figure 2). The laboratories named in the tables are listed in order of decreasing laboratory readiness scores.

Table 2: Laboratory readiness scores

Surveyed laboratories*	Laboratory readiness score (%)	Level of service	Affiliation
Selected			
Lancet Laboratories (Lancet)	81.6	Other	Private
St. Francis Hospital Nsambya (St. Francis)	78.9	Reference	Private
Clinical Microbiology Lab - Makerere University (Makerere)	76.3	Reference	Other
National Microbiology Reference Laboratory (NMRL)	73.7	Reference	Government
Nakasero Hospital Laboratory (Nakasero)	71.1	Regional/Intermediate	Private
Kagando Mission Hospital (Kagando)	71.1	District/Community	NGO
Jinja Regional Referral Hospital Laboratory (Jinja)	71.1	Regional/Intermediate	Government
Fortportal Regional Referral Hospital Laboratory (Fortportal)	68.4	Regional/Intermediate	Government
Ebenezer Clinical Laboratory (Ebenezer)	68.4	Reference	Private
Mbale Regional Referral Hospital Laboratory (Mbale)	63.2	Regional/Intermediate	Government
Mengo Hospital Laboratory (Mengo)	60.5	District/Community	Private
Kabale Regional Referral Hospital Clinical Laboratory (Kabale)	60.5	Regional/Intermediate	Government
Arua Regional Referral Hospital Laboratory (Arua)	60.5	Regional/Intermediate	Government
St. Mary's Hospital Lacor- Gulu (Gulu)	57.9	Other	Private
Mulago Hospital Clinical Laboratories (Mulago)	57.9	Regional/Intermediate	Government
Department of Medical Microbiology, Mbarara University of Science and Technology (Mbarara)	52.6	Other	Government
Not selected			
MRC London School of Hygiene and Tropical Medicineand and Uvri (Uvri)	76.3	Other	NGO
Bwera General Hospital Laboratory (Bwera)	63.2	District/Community	Government
Soroti Regional Referral Hospital Laboratory (Soroti)	55.3	Regional/Intermediate	Government
Hoima Regional Referral Laboratory (Hoima)	36.8	Regional/Intermediate	Government

** Laboratory names are abbreviated.*

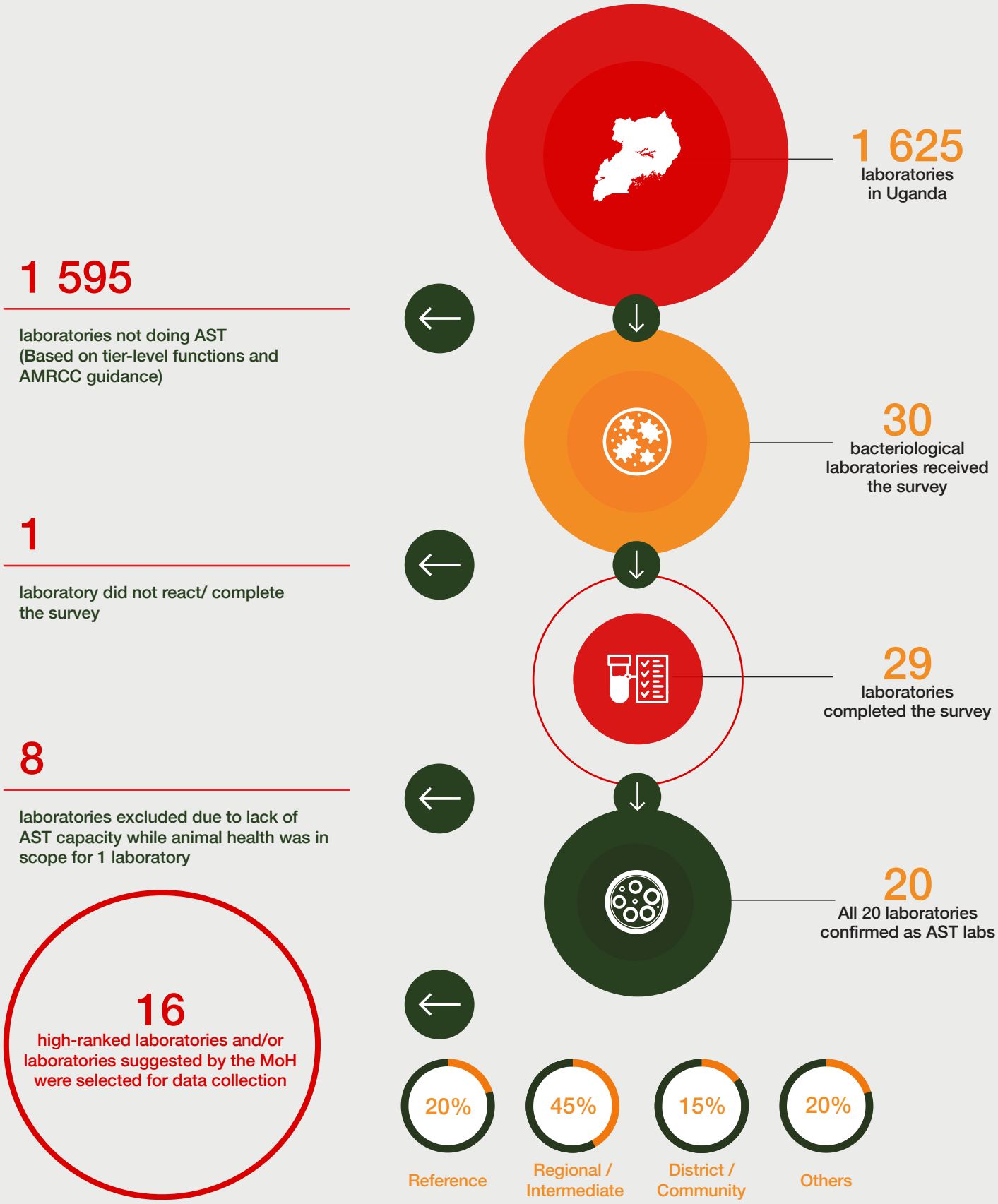


Figure 2: Selection of laboratories in Uganda

Surveillance preparedness of surveyed laboratories

Based on self-reported information from 20 laboratories, laboratory function and quality compliance were assessed to understand the preparedness for AMR surveillance. Eighteen laboratories had implemented QMS and nine laboratories had at least one qualified microbiologist on board. Few laboratories were accredited (n=5) or used automated methods for pathogen identification (n=9) (Figure 4, Supplementary Table 2). Since these findings may affect the quality of laboratory data, caution is warranted in interpreting the AMR rates presented in this report.

	Parameters			N (%)
Commodity and equipment status	Regular power supply and functional back up			18 (90.0)
	Continuous water supply			19 (95.0)
	Certified and functional biosafety cabinets			17 (85.0)
	Automated methods for pathogen identification			9 (45.0)
	Automated methods for AST			5 (25.0)
	Methods for testing AMR mechanisms			12 (60.0)
QMS implementation	Reported QMS Implementation			18 (90.0)
		Types of QMS	LQMS	3 (16.7)
			SLIPTA	1 (5.6)
			SLMTA	1 (5.6)
			Mentoring	0
			Combination‡	9 (50.0)
			Others	4 (22.2)
	Quality Certification			16 (80.0)
		Types of Quality certification	SLIPTA	7 (43.8)
			Col. of Am. Path	6.3 1 (6.3)
			Others	8 (50.0)
	Accreditation			5 (25.0)
	Participation in proficiency testing			16 (84.2)
	Utilisation of reference strains			19 (95.0)
	Reported consistent maintenance of QC records			18 (90.0)
	Designated focal quality person			19 (95.0)
	Reported compliance to standard operating procedures			19 (95.0)
	Reported compliance to AST standards			19 (95.0)
Personnel and training status	Presence of at least one qualified microbiologist			9 (45.0)
	Presence of an experienced laboratory scientist/technologist			20 (100)
	Up-to-date and complete records on staff training and competence			17 (85.0)
Specimen management status	Reported compliance to SOPs on specimen collection and testing			20 (100)
	Reported compliance to SOPs on specimen rejection			20 (100)
	Average number of specimens processed for AST in 2018			20 (100)
LIS and linkage to clinical data	Assigned specimen (laboratory) identification number			19 (95.0)
	Availability of system/database to store patient data			19 (95.0)
		Database format	Paper-based	7 (77.8)
			Electronic	1 (11.1)
			Mixed	11 (55.0)
	Captured patients' records on test request forms			20 (100.0)
			Retrievable	16 (80.0)

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

Figure 3: Laboratory preparedness for AMR surveillance

Profile of selected laboratories

Out of the 16 selected laboratories, 12 were co-located with clinical facilities. Nine clinical facilities lacked infectious disease departments and only seven had antimicrobial stewardship programmes. Medical therapeutic committees and hospital infection control committees were functional in 10 facilities. Most laboratories and hospitals had mixed (paper and electronic) information systems. (Figure 4)

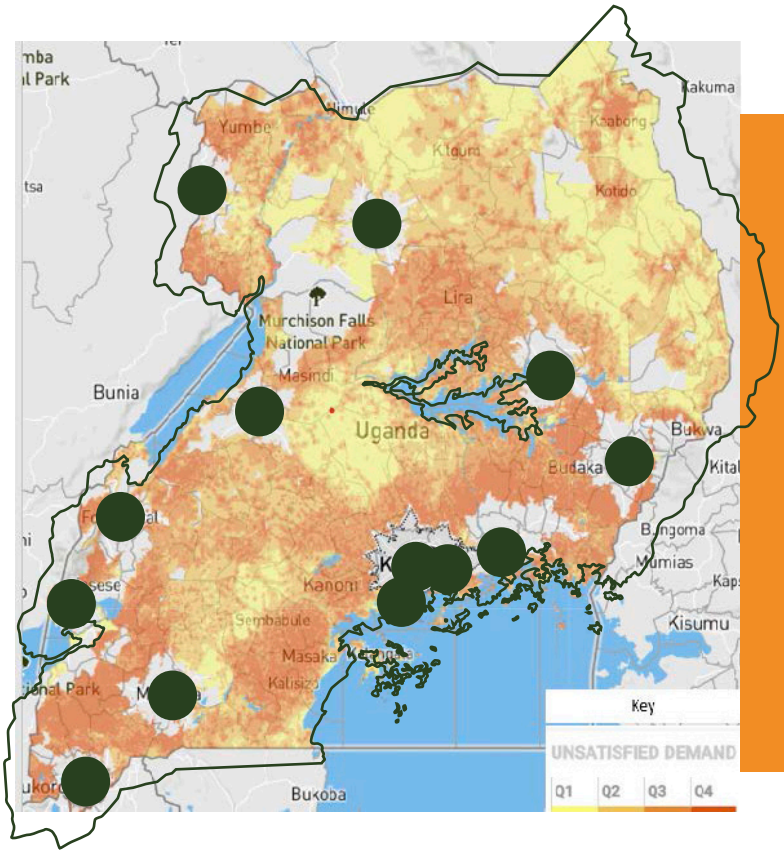
Abbreviations: AMS=antimicrobial stewardship; HICC=hospital infection control committee; HIS=hospital information system; IDD=infectious diseases department; LIS=laboratory information system; MTC=medical therapeutics committee.

Figure 4: Profile of selected laboratories

Population coverage of laboratories

We analysed the data using the PlanWise® solution. PlanWise incorporates data on the population, road network and other variables, and applies an algorithm as well as 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, Uganda had an estimated population of 45.7 million.



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

Supplementary Figure 1: Population coverage of AST laboratories in Uganda

Therefore, the colour on the map relates to the level of unmet need (people not in the reach of a facility) relative to the whole population.

In Uganda, the catchment population living within one-hour travel time from the 20 participating AMR surveillance sites covers **36%** of the population. Hence, 64% of the population is not covered at all by the existing facilities. To increase the population coverage, new capacity should be introduced (either by upgrading an existing laboratory to start providing services or by constructing a new laboratory) in regions in dark red (Q3) and thus prioritising regions with the highest absolute unmet need.

Section II: Collection, analysis and interpretation of AMR data

Objective

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

Methodology

Data collection

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

For laboratories with paper-based records, at least 5 000 records per laboratory per year were to be collected. However, no such limit was imposed for digitised data. The goal was to obtain at least 240 000 records from 16 laboratories across three years.

As a first step, the MoH and IQVIA were jointly involved in recruiting local field data collectors. A capacity-building workshop was conducted as part of the MAAP to train the field staff on data collection, including the use of WHONET[17] and the specially developed MAAP tool for secure transfer of collected data.

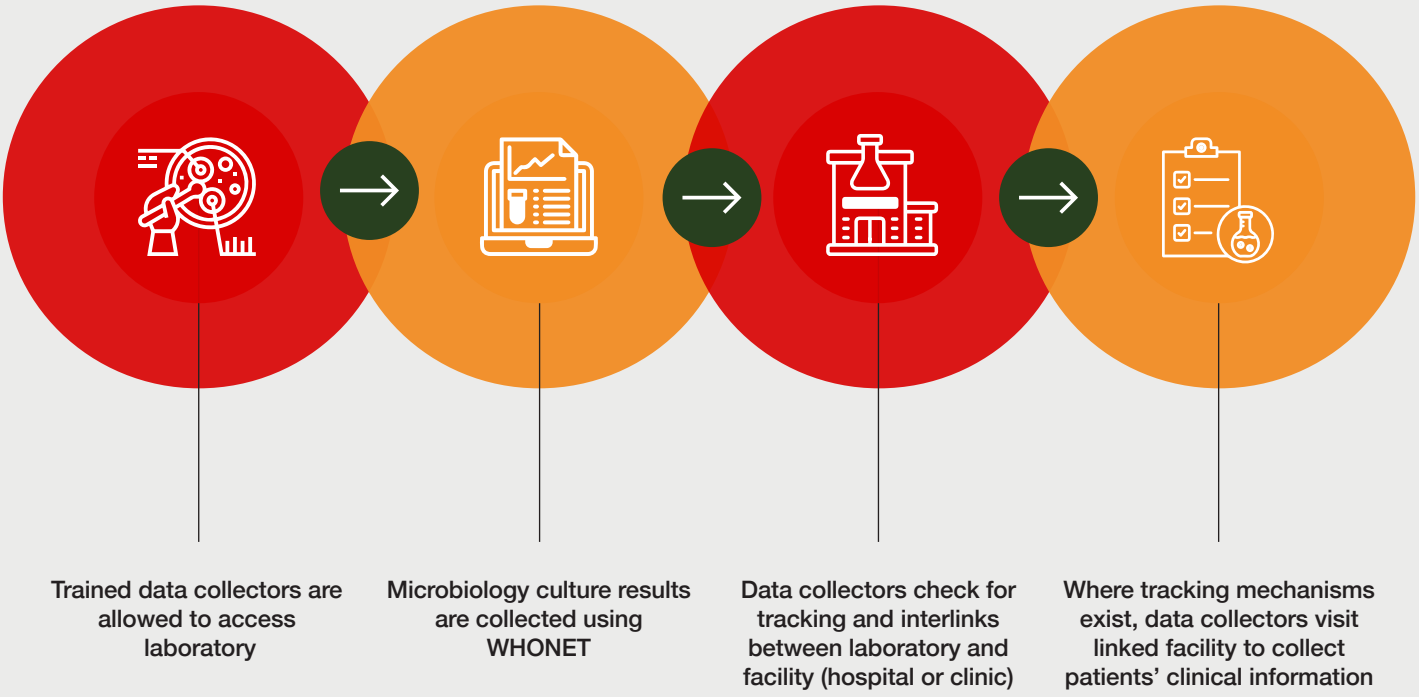


Figure 5: Steps of AMR data collection

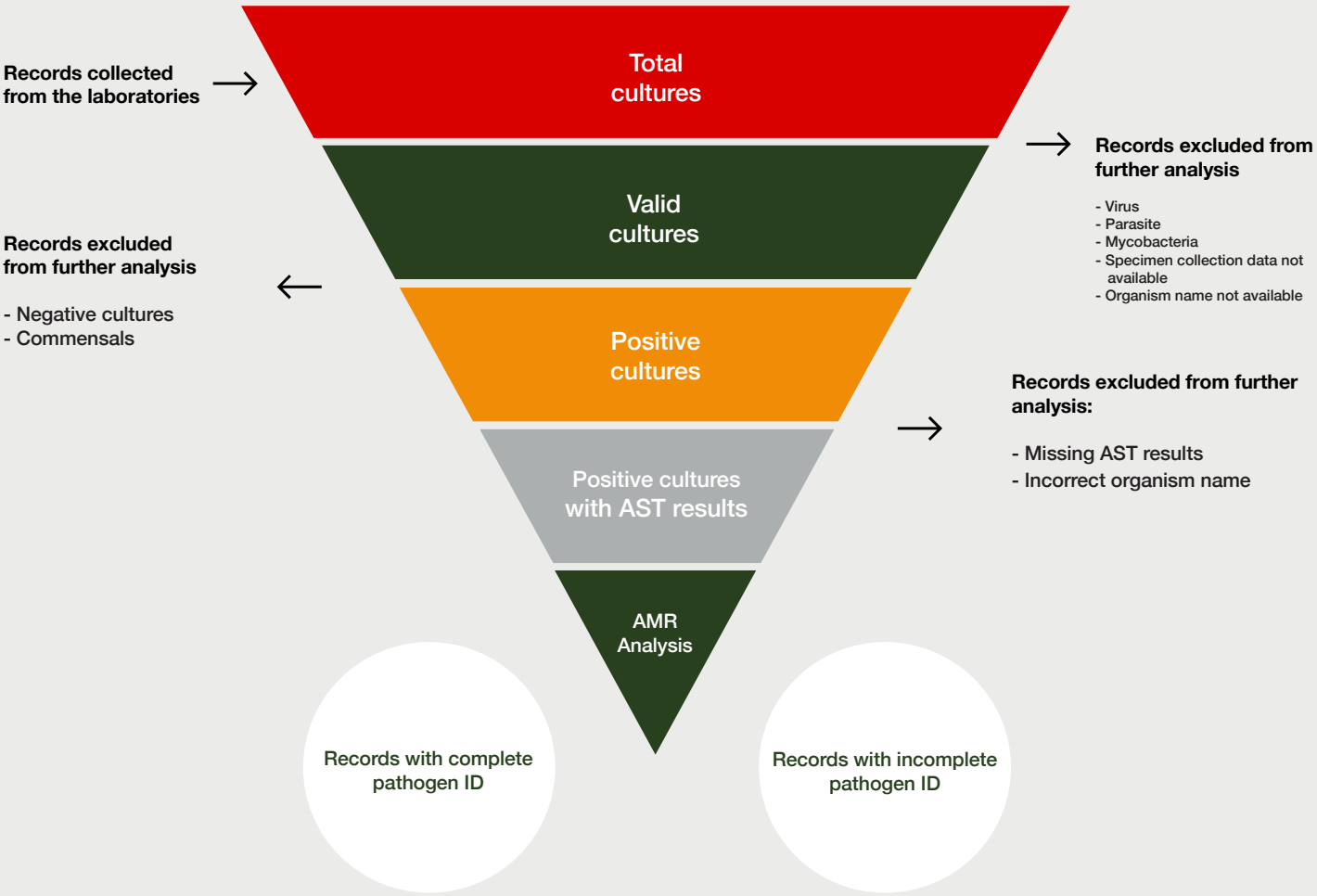
Historical data were collected for the period January 1, 2016, through to December 31, 2018. The AMR data were initially captured through WHONET, a free Windows-based database software programme developed for the management and analysis of microbiology laboratory data. The software allowed data entry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

Figure 6: Data collection at a Ugandan facility

Data analysis

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

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



- **Culture characteristics:** Cultures were characterised across gender, age group and pathogen type (bacteria or fungi). Data were pooled across all laboratories and assessment was conducted for each study year.

- **Inappropriate testing:** Positive cultures with AST results were assessed for compliance to AST standards. However, comprehensive assessment of validity of AST results was beyond the study scope. Data were pooled across laboratories and assessed for each study year. The conventional AST standards are Clinical and Laboratory Standards Institute (CLSI), European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Comité de l'antibiogramme de la Société Française de Microbiologie, the European Committee on Antimicrobial Susceptibility Testing.

- **Clinical information:** Positive cultures with AST results were summarised based on information available for the patient's clinical profile: diagnosis, origin of infection (whether hospital-acquired or community-acquired), presence of indwelling device and antimicrobial use. Data were quantified for each laboratory and assessed over the entire study period.

- **Specimen characteristics:** Positive cultures with AST results were summarised based on information on specimen types. Data were pooled across all laboratories and assessed for each study year.

- **Quality of data:** We used the level of pathogen identification as a parameter to evaluate the data quality from each laboratory seeing as the complete identification of pathogens is key in AMR surveillance and implies the quality of the laboratory's testing practices. Scoring was based on quartiles of the proportion of completely identified pathogens. The laboratories with >75% of pathogens identified at the species level were awarded the highest score (4). Laboratories with <25% identification received the lowest score (1), (Table 3). Firstly, the scoring was performed per year (i.e., 2016–2018). Thereafter, the average was assigned as the laboratory data quality score for each laboratory.

Table 3: Data scoring scheme

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

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

Table 4: Data quality rating

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

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

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

Results

Retrospective data from 2016–2018 was collected from 16 laboratories and corresponding facilities of Uganda.

1. Quantum of cultures and level of pathogen identification

Data were retrieved for 88 116 total cultures of which 85 096 were valid and 28 849 were positive. Of the positive cultures, AST results were available for 22 349 cultures, the maximum (n=8 413) coming from Lancet and the least (n=48) from Kagando (Figure 9 and 10, not all pathogens were identified completely i.e., at species level). Complete identifications were highest for St. Francis laboratory (95.8%) and lowest for Mulago laboratory (61.9%) (Table 5).

Table 5: Data summary

Variable (Columns) / Laboratory (Rows)	Total Cultures (N=88116)	Valid Cultures N=85 096	Positive Cultures N=28 849	Positive Cultures with AST Results N=22 349	Incomplete Identity* N=4370	Complete Identity* N=17 979
Lancet	28 673	27 859 (97.2)	11 140 (40.0)	8 413 (75.5)	1 282 (15.2)	7 131 (84.8)
St. Francis - Nsambya	4 258	4 258 (100.0)	2 590 (60.8)	2 200 (84.9)	93 (4.2)	2 107 (95.8)
Makerere Uni.	2 510	1 661 (66.2)	899 (54.1)	708 (78.8)	250 (35.3)	458 (64.7)
NMRL	2 613	2 585 (98.9)	1 012 (39.1)	876 (86.6)	154 (17.6)	722 (82.4)
Nakasero	1 047	1 046 (99.9)	356 (34.0)	301 (84.6)	25 (8.3)	276 (91.7)
Kagando	146	146 (100.0)	49 (33.6)	48 (98.0)	11 (22.9)	37 (77.1)
Jinja RRH	2 887	2 885 (99.9)	438 (15.2)	259 (59.1)	88 (34.0)	171 (66.0)
Fortportal	785	774 (98.6)	270 (34.9)	220 (81.5)	55 (25.0)	165 (75.0)
Ebenezer	9 751	9 745 (99.9)	2 079 (21.3)	1 589 (76.4)	323 (20.3)	1 266 (79.7)
Mbale	1 999	1 977 (98.9)	576 (29.1)	474 (82.3)	55 (11.6)	419 (88.4)
Mengo (MHL)	3 111	3 111 (100.0)	2 002 (64.4)	1 719 (85.9)	367 (21.3)	1 352 (78.7)
Kabale RRH	1 446	1 445 (99.9)	362 (25.1)	297 (82.0)	36 (12.1)	261 (87.9)
Arua Rrh	2 249	2 245 (99.8)	406 (18.1)	325 (80.0)	105 (32.3)	220 (67.7)
St. Mary's - Gulu	6 469	6 469 (100.0)	1 265 (19.6)	1 202 (95.0)	191 (15.9)	1 011 (84.1)
Mulago	14 294	13 080 (91.5)	2 589 (19.8)	2 276 (87.9)	867 (38.1)	1 409 (61.9)
Mbarara Uni.	5 878	5 810 (98.8)	2 816 (48.5)	1 442 (51.2)	454 (31.5)	988 (68.5)

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

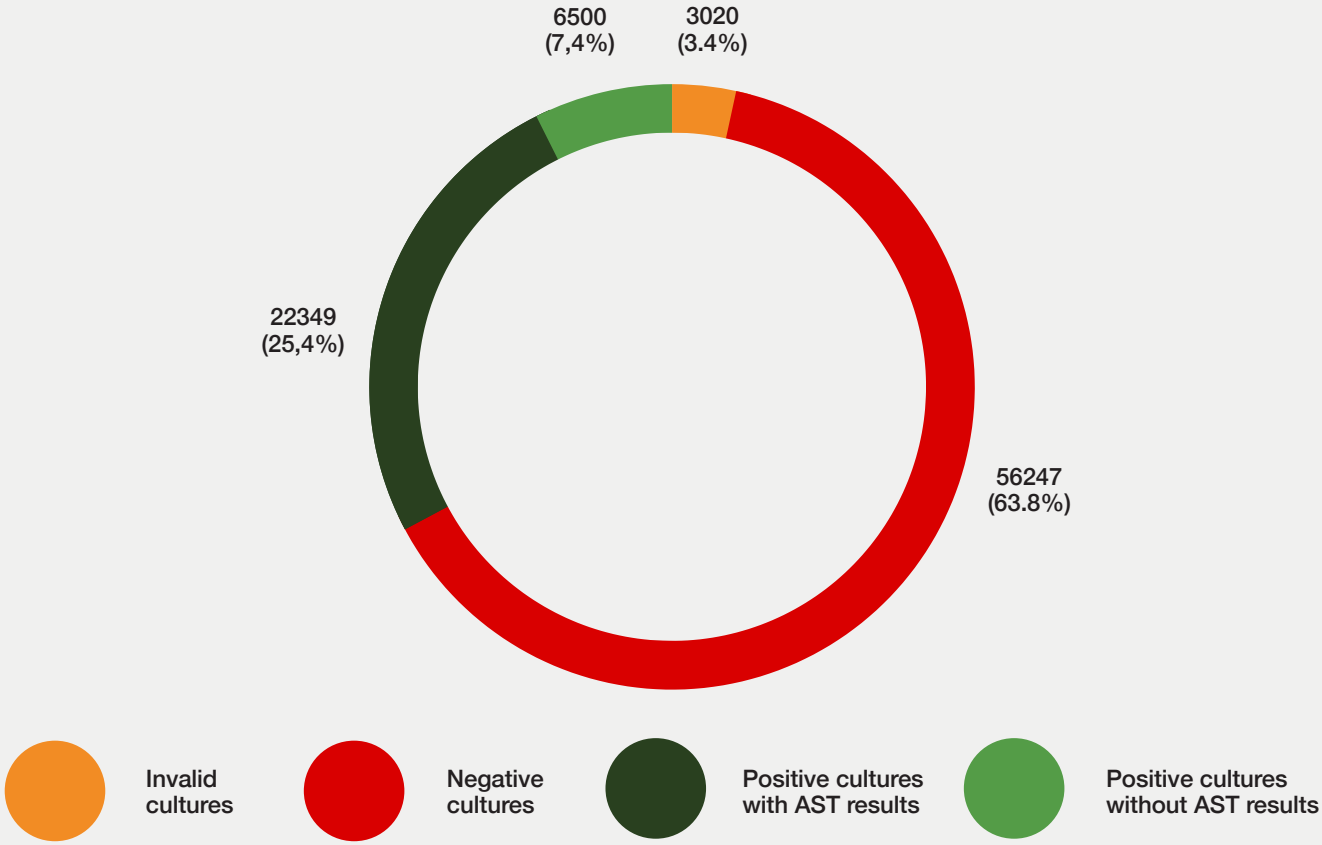


Figure 8: Quantum of cultures across all selected laboratories

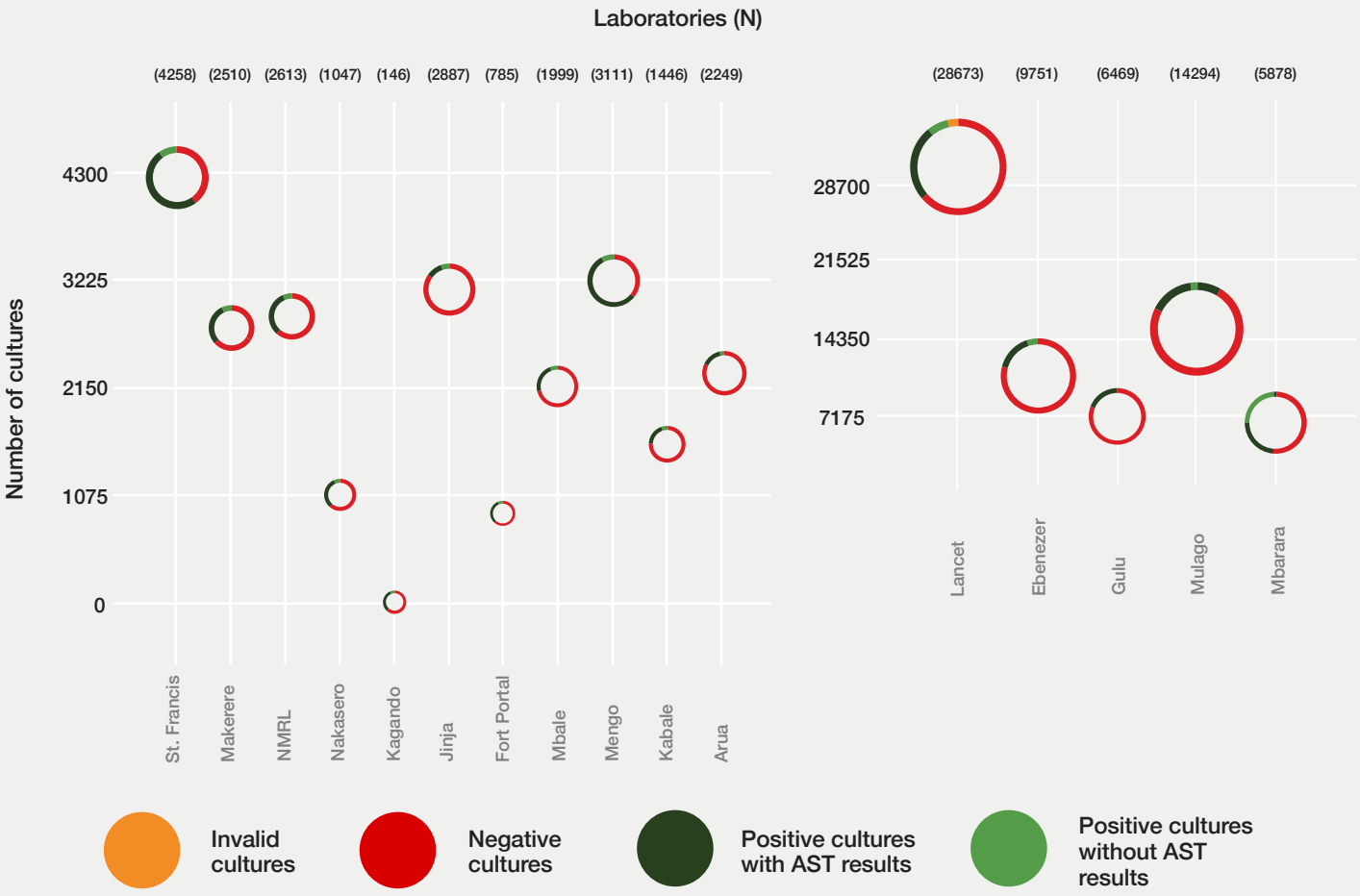


Figure 9: Quantum of cultures in each selected laboratory

2. Culture characteristics

Bacterial pathogens (22 340) were more commonly reported than fungal pathogens. Information on age was missing from 18.4% of cultures, but where available, data showed a median age of 27 years (range 0–96 years) with most cultures (9 505) obtained from patients 18–49 years old. Females (13 711) contributed more to the quantum of positive cultures with AST results. More data came from 2018 (10 967) than other years (Table 6, Supplementary Table 3).

Table 6: Culture characteristics

Characteristics	Positive cultures with AST results n=22 349 n (%)
Gender	
Male	8 638 (38.7)
Female	13 711 (61.3)
Age, years	
Less than 1	691 (3.1)
1 to 17	4 310 (19.3)
18 to 49	9 505 (42.5)
50 to 65	1 571 (7.0)
Above 65	1 284 (5.7)
Unknown age	4 988 (22.3)
Years	
2016	4 821 (21.6)
2017	6 561 (29.4)
2018	10 967 (49.1)
Pathogen	
Bacteria	22 340 (100.0)
Fungi	9 (0.0)

3. Inappropriate testing

Of the 16 selected laboratories, 14 laboratories reported using CLSI standards for AST testing; one reported compliance to the EUCAST standards and one did not comply to any standard. However, during a review of AST results, the following instances of inappropriate testing were noted:

Bacteria were tested against antifungals (Supplementary Figure 2a). S. aureus was tested against Vancomycin using the disk diffusion method. Enterobacterales were tested against oxacillin and penicillin G (Supplementary Figure 2b).

4. Clinical information

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

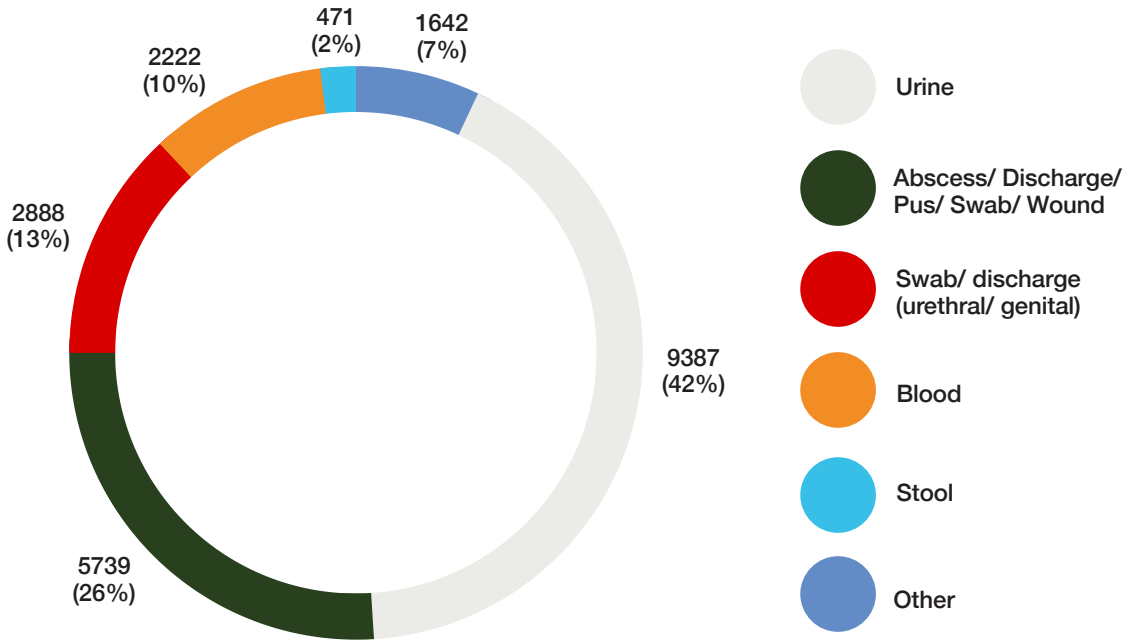
Table 7: Clinical information

Laboratory	Positive cultures with AST results N=2 2349	Diagnosis data	Infection origin data*	Indwelling device data	AMU data
Lancet	8 413	-	-	-	-
St. Francis	2 200	-	-	-	-
Makerere	708	-	-	-	-
NMRL	876	88	-	-	-
Nakasero	301	14	2	12	5
Kagando	48	1	-	-	1
Jinja	259	31	-	-	36
Fortportal	220	-	174	-	151
Ebenezer	1 589	-	-	-	-
Mbale	474	-	-	-	275
Mengo	1 719	1	-	-	-
Kabale	297	4	-	2	56
Arua	325	39	180	-	214
Gulu	1 202	-	-	-	-
Mulago	2 276	-	-	-	-
Mbarara	1 442	-	-	-	-

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

5. Specimen characteristics

Urine, purulent discharge, genito-urethral specimens and blood, accounted for most of the positive cultures in each study year (Figure 11, Supplementary Table 4).



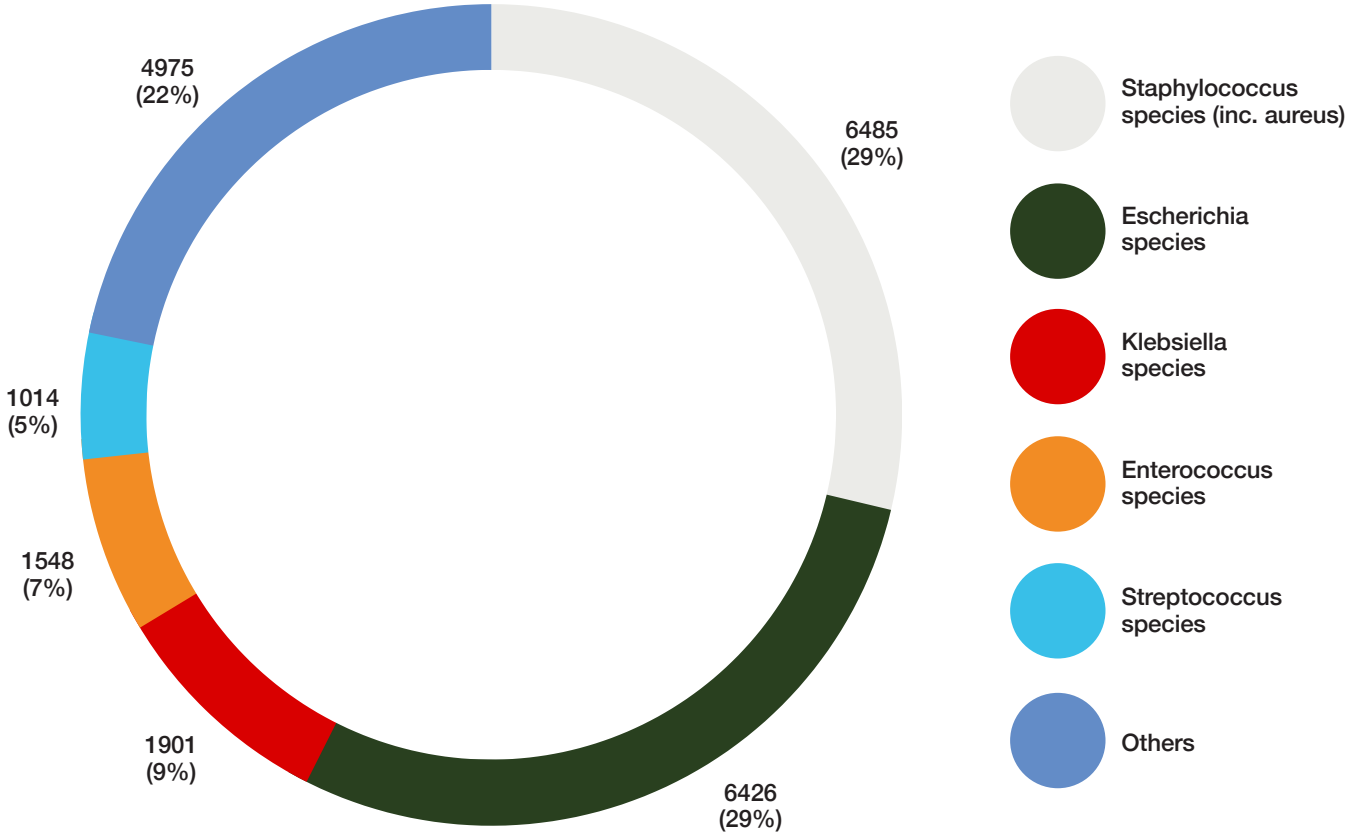
* Others include all other specimens excluding the top 5 mentioned here

Figure 10: Specimen characteristics

6. Identified pathogens

Staphylococcus species (29%) and Escherichia species (29%) largely contributed to the quantum of positive cultures (Figure 11).

In 2016, of the 4 821 positive cultures with AST results, Escherichia species (30%) and Staphylococcus species (28.5%) were the most reported. In 2017, of the 6 561 positive cultures with AST results, Escherichia species (30.9%) and Staphylococcus species (25.2%) were again the most reported. In 2018, information was available for a greater number of cultures (10 967) although pathogen distribution remained similar to prior years. (Supplementary Table 5)



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

Figure 11: Pathogens identified

7. Quality of data

The country data quality score of the 85 096 valid culture records obtained from the 16 laboratories in Uganda was 3.7 and was rated as good for AMR analysis. For individual laboratory data quality scores from each contributing laboratory, see Supplementary Table 6.

Section III: AMR rates

Objective

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

Methodology

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

Estimation of AMR rates

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

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

AMR rates were estimated for the WHO priority pathogens[18] where the number of tested isolates exceeded 30 regardless of the specimen type (AMR Appendix 5). AMR trends were mapped for the WHO priority pathogens depending on data availability.

In addition, AMR rates were estimated for:

1. Clinically important pathogens isolated from blood and cerebrospinal fluid (AMR Appendix 6)

2. Top three highly resistant bug-drug combinations (regardless of the specimen type)

3. Pathogens tested against the most and least consumed antimicrobial classes (regardless of the specimen type, please refer to part C)

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

Removal of duplicate records

Before AMR rates were calculated, duplicate AST results were removed such that only the results of the first pathogen isolate per patient per year, irrespective of AST profile (and body site or specimen type in the case of WHO priority pathogens), were included. This approach follows the CLSI M39A4 criteria.[19,20] Duplicate removal was based on the availability of unique patient identifiers. When no patient identifiers were available, the results of all isolates were included. The AST data from all laboratories were then aggregated and rates were calculated as the proportion of non-susceptible isolates.

AMR estimates statistics

Confidence intervals (CIs) at the 95% level of confidence were calculated to quantify the uncertainty in the estimated resistance rates.. Typically, CIs for AST data have been constructed using the Wilson score method. This is a binomial calculation that assumes that all samples are independent.[21] However, there are likely correlations between data within each laboratory and between laboratories that draw from similar populations. Thus, where appropriate, the Wilson cluster robust CI method was employed to account for a lack of data independence such that each laboratory represented a cluster.[22]

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

Online data visualisation

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

Data were also uploaded to CDDEP's ResistanceMap platform, a publicly available repository for aggregated country-level data.[23] Spatiotemporal analysis for the combined AMR and AMC-AMU datasets were built on the ResistanceMap framework. Current capabilities include maps, trend line charts and frequency bar charts.

Results

(i) AMR rates and trends for WHO priority pathogens

AMR rates for the WHO priority pathogens were calculated as the proportion of isolates that were non-susceptible over each one-year interval. Across 2016–2018, AMR rates for some organisms remained consistent; the rates for others varied. Moderately high AMR rates were noted for 3rd generation cephalosporin-resistant Enterobacterales (49-55%), carbapenem-resistant A. baumannii (30-54%), fluoroquinolone-resistant Neisseria gonorrhoea (34%), methicillin-resistant S. aureus (MRSA) (34-36%), and penicillin-resistant Streptococcus pneumoniae (30-41%). Rates of carbapenem-resistant Pseudomonas aeruginosa (10-22%) and fluoroquinolone-resistant Salmonella species (5-29%) were lower (Table 8, Figures 13 and 14). Statistics for vancomycin-resistant and intermediate Staphylococcus species and §are not included.

Table 8: AMR rate estimates for WHO priority pathogens

		2016				2017				2018			
Pathogen	Antibiotic, class	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)
A. baumannii	Carbapenems	50	27 (54)	39.3 - 68	3 (1 - 46)	66	20 (30.3)	22.7 - 39.1	3 (2 - 60)	60	27 (45)	25.1 -66.7	7 (2 - 33)
P. aeruginosa	Carbapenems	126	12 (9.5)	4.6 - 18.6	9 (1 - 70)	179	40 (22.3)	11.1 - 39.9	9 (1 - 68)	150	28 (18.7)	10.5 - 30	12 (1 - 69)
Enterobacter ales	Carbapenems	1 953	79 (4)	1.1 - 13.8	12 (1 - 1155)	2 545	93 (3.7)	1.2 - 10.4	13 (7 – 1 598)	2 698	112 (4.2)	1.4 - 11.6	13 (16 – 1 444)
Enterobacter ales	Cephalosporins (3rd generation)	2 395	1 170 (48.9)	35.3 - 62.6	12 (1 – 1 155)	2 903	1 587 (54.7)	47.7 - 61.5	15 (4 – 1 583)	3 21	1 662 (51.6)	44.3 - 58.9	15 (4 – 1 501)
E. faecium	Vancomycin	15	0	-	1 (15)	3	0	-	2 (1 - 2)	8	0	-	2 (1 - 7)
H. influenzae	Ampicillin	1	0	-	1 (1)	1	1	-	1 (1)	1	1	-	1 (1)
H. pylori	Clarithromycin	-	-	-	-	-	-	-	-	-	-	-	-
N. gonorrhoeae	Cephalosporins (3rd generation)	21	2	0.5 - 69.1	4 (1 - 15)	17	1	-	4 (1 - 8)	36	6 (16.7)	2.5 - 60.6	4 (1 - 17)
N. gonorrhoeae	Fluoroquinolo-nes	20	12	-	3 (1 - 15)	23	12	-	6 (1 - 8)	35	12 (34.3)	22.8 - 48	5 (1 - 13)
Campylobacter species	Fluoroquinolo-nes	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolo-nes	41	2 (4.9)	1.6 - 13.9	6 (1 - 26)	63	18 (28.6)	19.3 - 40	11 (1 - 27)	78	15 (19.2)	7 - 42.9	10 (1 - 49)
Shigella species	Fluoroquinolo-nes	3	0	-	3 (1 - 1)	15	8	-	6 (1 - 5)	27	5	-	6 (1 - 18)
S. aureus	Methicillin	727	247 (34)	12.3 - 65.4	13 (1 - 321)	622	216 (34.7)	8.4 - 75.5	11 (4 - 303)	676	243 (35.9)	15.6 - 63	13 (6 - 251)
S. pneumoniae	Beta-lactam combinations	13	2	-	3 (2 - 7)	11	1	-	3 (2 - 5)	15	2	-	6 (1 - 5)
S. pneumoniae	Penicillins	67	20 (29.9)	8.9 - 64.9	6 (1 - 42)	46	19 (41.3)	19.1 - 67.8	7 (1 - 13)	61	25 (41)	30.6 - 52.3	10 (1 - 28)

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

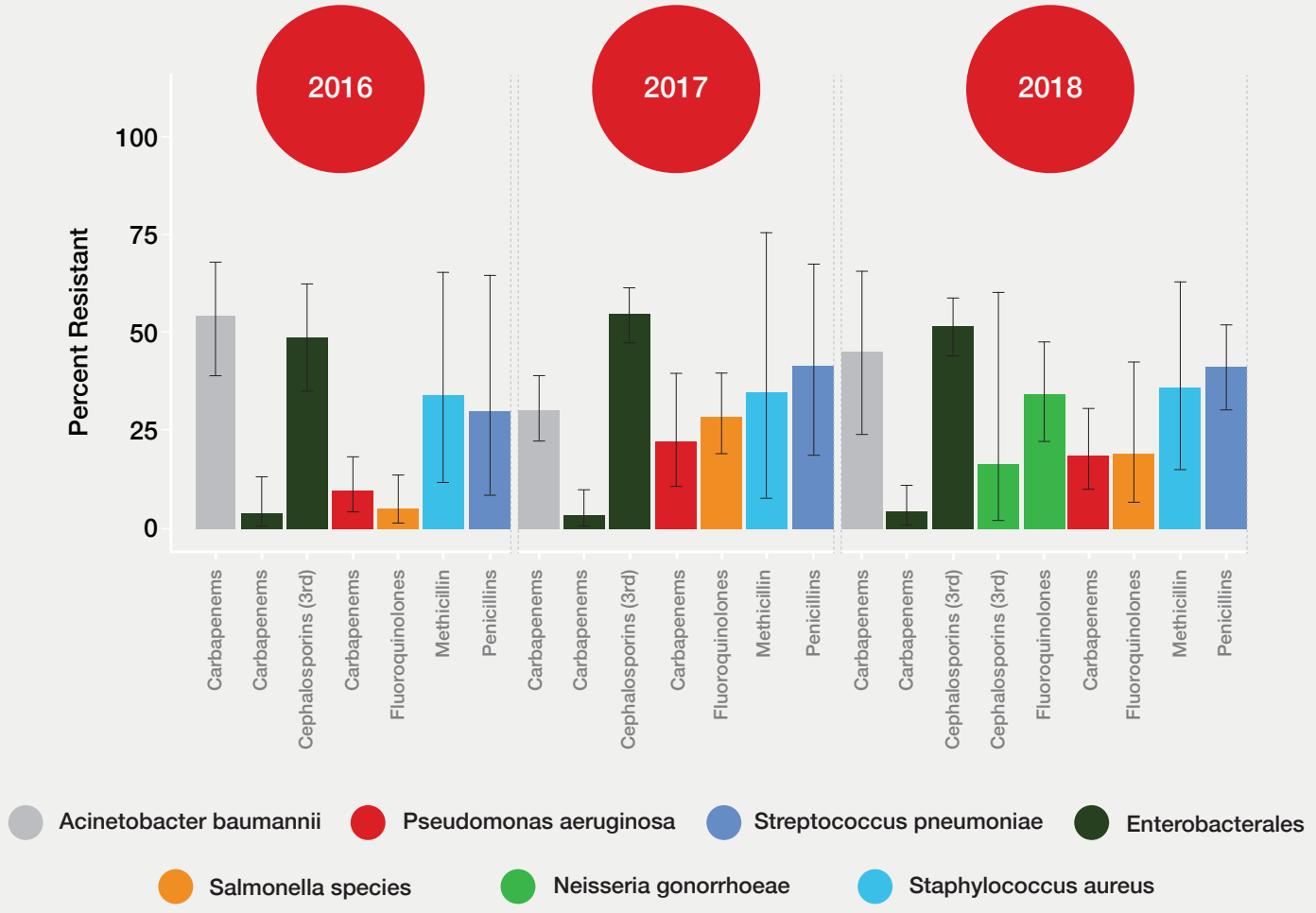


Figure 12: AMR rate estimates for WHO priority pathogens

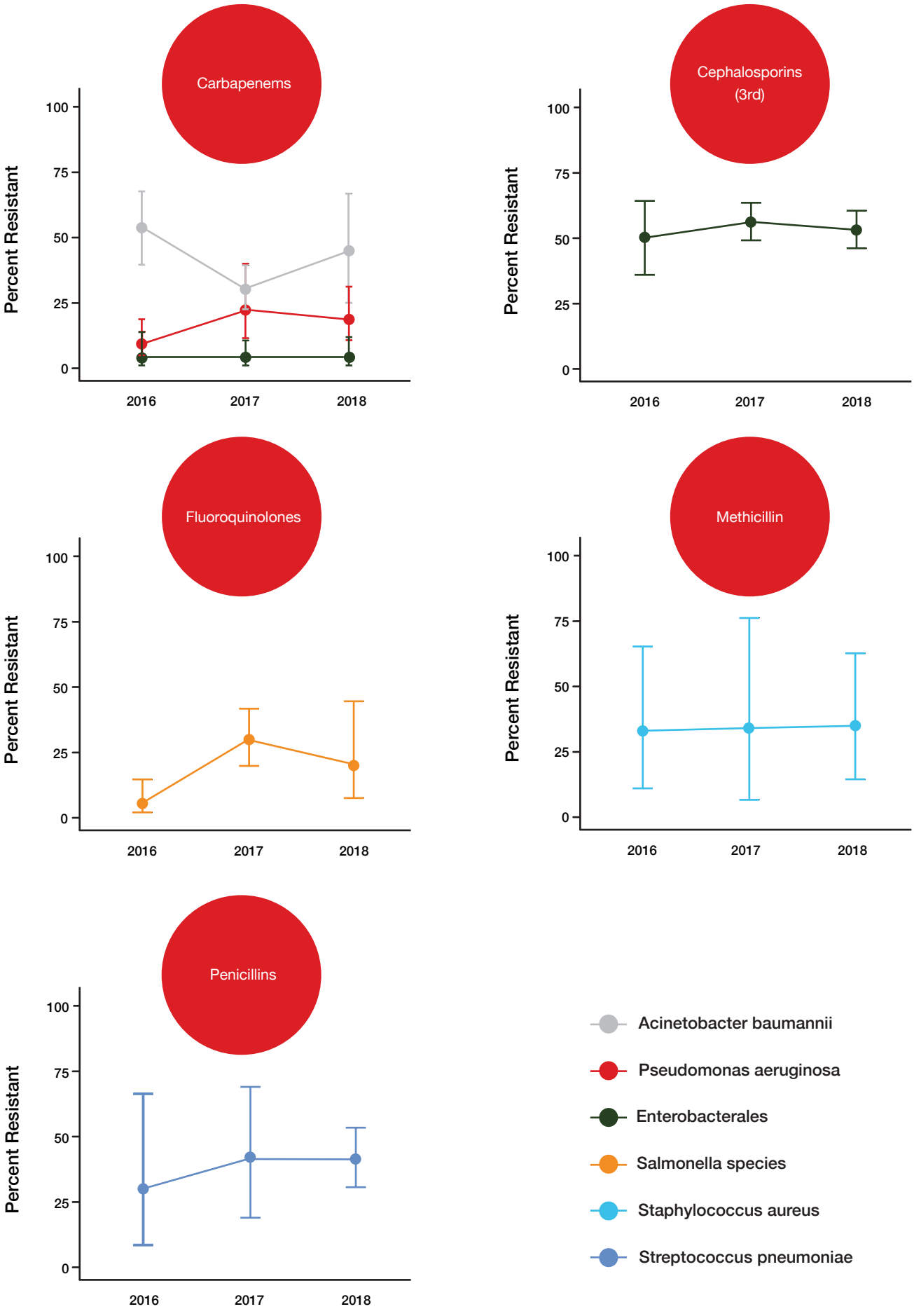


Figure 13: AMR trends for WHO priority pathogens

(ii) AMR rates for other pathogens of clinical importance

Analysis of AST data from blood and CSF isolates revealed high AMR rates for 3rd-generation cephalosporin-resistant Klebsiella species (69-78%), carbapenem-resistant Acinetobacter species (53%) and methicillin-resistant Staphylococcus species (34-39%). The AMR rate for carbapenem-resistant Klebsiella species was low (3-10%) (Table 9).

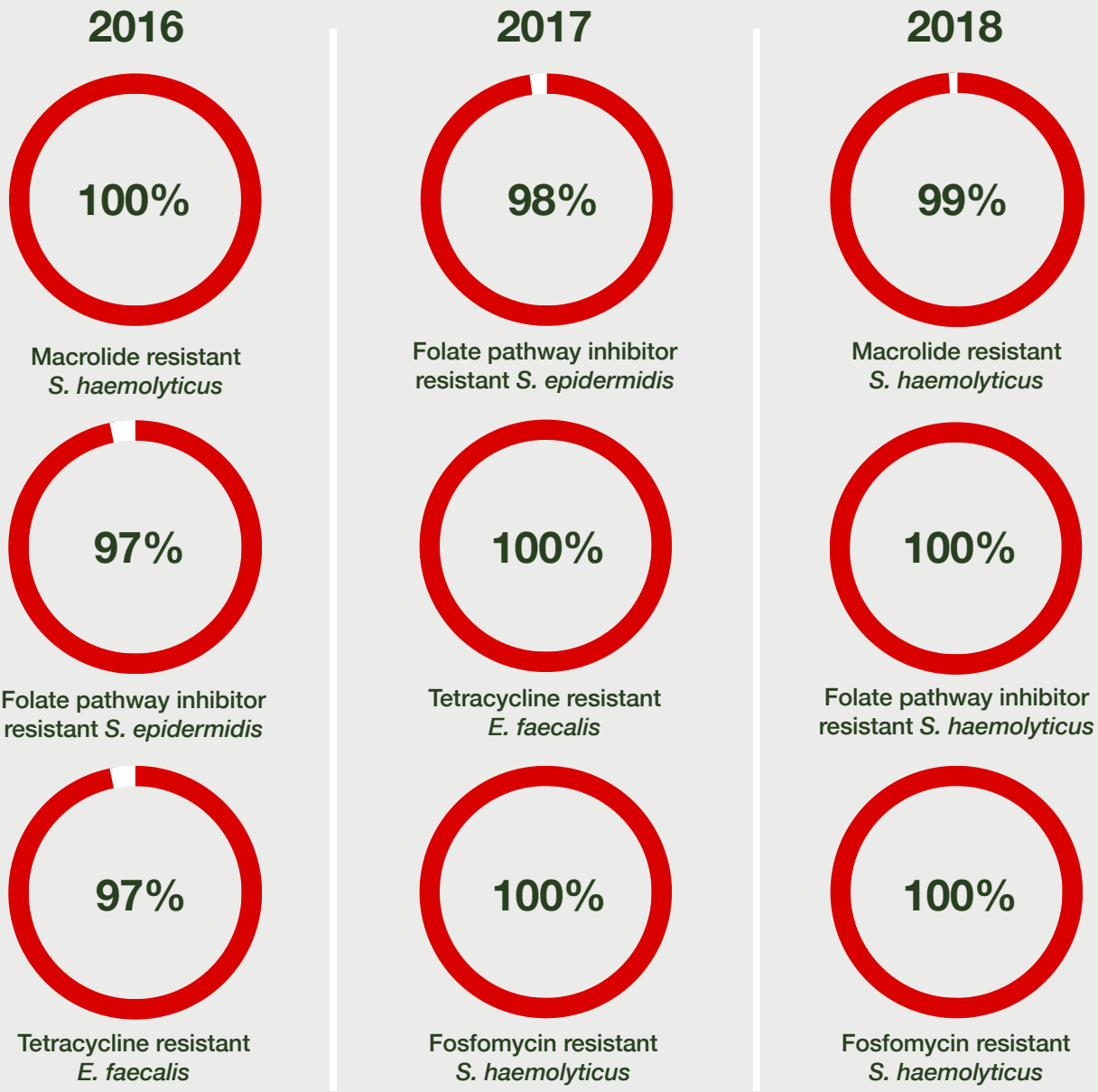
*Table 9: AMR rate estimates for other clinically important pathogens**

		2016				2017				2018			
Pathogen	Antibiotic, class	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)
Acinetobacter species	Carbapenems	30	16 (53.3)	21-83.1	3 (3 - 22)	25	5	-	3 (2 - 17)	23	6	-	4 (1 - 16)
Acinetobacter species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Aminoglycosides (high level)	11	2	-	2 (5 - 6)	17	8	-	2 (7 - 10)	6	1	-	2 (1 - 5)
Enterococcus species	Vancomycin	19	7	-	4 (1 - 12)	18	7	-	3 (1 - 10)	20	3	-	6 (1 - 10)
H. influenzae	Ampicillin	1	0	-	1 (1)	1	1	-	1 (1)	1	1	-	1 (1)
H. influenzae	3rd generation cephalosporins	1	0	-	1 (1)	1	0	-	1 (1)	-	-	-	-
Klebsiella species	Carbapenems	30	2 (6.7)	1-32.5	6 (1 - 15)	30	1 (3.3)	0.6-17.4	7 (1 - 12)	41	4 (9.8)	2.7 - 29.7	10 (1 - 13)
Klebsiella species	Cephalosporins (3rd generation)	36	25 (69.4)	37.9-89.4	8 (1 - 15)	32	23 (71.9)	33.9-92.7	7 (1 - 12)	41	32 (78)	60.4 - 89.2	10 (1 - 13)
N. meningitidis	Ampicillin	-	-	-	-	1	1	-	1 (1)	-	-	-	-
N. meningitidis	Cephalosporins (3rd generation)	7	7	-	1 (7)	2	0	-	2 (1)	-	-	-	-
Pseudomonas species	Carbapenems	17	1	-	3 (2 - 11)	14	3	-	3 (1 - 10)	14	2	-	4 (1 - 10)
Pseudomonas species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Macrolides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	Methicillin	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus species (Excluding aureus)	Methicillin	156	55 (35.3)	11.1-70.5	6 (1 - 124)	222	75 (33.8)	12.2-65.2	7 (1 - 179)	204	80 (39.2)	13.2 - 73.3	6 (1 - 157)
S. pneumoniae	Penicillins	23	13	-	6 (1 - 13)	27	8	-	5 (1 - 11)	14	4	-	6 (1 - 7)
S. pneumoniae	Beta-lactam combinations	7	1	-	2 (1 - 6)	6	1	-	2 (2 - 4)	7	2	-	3 (1 - 5)
S. pneumoniae	Macrolides	18	11	-	6 (1 - 6)	12	5	-	4 (1 - 5)	12	5	-	9 (1 - 3)
S. pneumoniae	Vancomycin	6	2	-	2 (2 - 4)	10	1	-	4 (1 - 4)	3	1	-	3 (1 - 1)

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

(iii) AMR rates for highly resistant pathogens

Based on the available data, very high (100%) resistance was estimated for clinically important pathogens like Staphylococcus haemolyticus (vs. macrolides, fosfomycines and folate pathway inhibitors) and Enterococcus faecalis (vs. tetracylines) (Figure 14).



Pathogen nomenclature is shown as reported by laboratories; antimicrobials are reported at class level.
Figure 14: Top five highly resistant pathogens

(iv) AMR rates for fungal pathogens

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

Section IV: Drivers of antimicrobial resistance

Objective

To assess the drivers of AMR

Methodology

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

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

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

Statistical analysis

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

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

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

Results

Four variables namely, age, gender, origin of infection and prior antibiotic usage were evaluated for possible association with AMR. The data availability for these variables was age: 74.5%; gender: 97.9%; origin of infection: 1.3%; and prior antibiotic usage: 2.4%. The univariate logistic regression results showed that patients in the following age groups: <1 year (OR 1.36, 95% CI 1.25 – 1.49), 50 – 65 years (OR 1.28, 95% CI 1.20 – 1.37) and >65 years (OR 1.50, 95% CI 1.28 – 1.76), were more likely to have resistant infections. In addition, patients with hospital-acquired infections (OR 1.83, 95% CI 1.77 –1.90) were more likely to have resistant infections (Supplementary Table 7).

All four variables were included in the multiple logistic regression model based on the defined inclusion criteria. When adjusting for the effect of gender, age groups <1 year (OR 1.31, 95% CI 1.20 – 1.42), 50 – 65 years (OR 1.25, 95% CI 1.15 – 1.36) and >65 years (OR 1.45, 95% CI 1.21 – 1.72), were more likely to have resistant infections. However, gender had no effect on the AMR rate when controlling for age. Furthermore, when controlling for the effects of both age and gender, patients who had hospital-acquired infections (OR 1.84, 95% CI 1.74 – 1.93) and prior antibiotic usage (OR 1.51, 95% CI 1.02 – 2.22) were more likely to have resistant infections. (Table 10)

Table 10: Multiple logistic regression analysis

Variable	Options	N	NS (%)	Adjusted OR (95% CI)	P-value
Gender	Female	18 796	41.0	Reference category	
	Male	9 161	45.2	1.13 (0.96 - 1.34)	0.146
Age, years	<1	715	49.0	**1.31 (1.20 - 1.42)**	0.000
	1-17	8 419	39.7	0.92 (0.81 - 1.04)	0.188
	18-49	14 417	41.5	Reference category	
	50-65	2 530	47.7	**1.25 (1.15 - 1.36)**	0.000
	>65	1 876	51.7	**1.45 (1.21 - 1.72)**	0.000
Origin of infection	Community	252	47.6	Ref	
	Hospital	224	62.5	**1.84 (1.74 - 1.93)**	0.000
Prior antibiotic usage	No	450	47.8	Reference category	
	Yes	433	58.0	**1.51 (1.02 – 2.22)**	0.037

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

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

Part B: Antimicrobial (antibiotic) Consumption

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

Overuse and misuse of antimicrobials are crucial factors in the complex web of ARM causation. Widespread and unregulated antimicrobials usage exert a selective pressure by reducing the reproductive success of some of the microorganisms and consequently accelerating the development of AMR.[24,25] Therefore, close surveillance on how antimicrobials are utilised is a key step for stewardship programmes in order to stem AMR. The surveillance mechanisms recommended by WHO include the monitoring of AMC and AMU. This aligns with the MAAP's aim to expand the volume of data presently available on AMR and AMC or AMU across Africa.

Definition of AMC and AMU

AMC is defined as the quantification of antimicrobials used within a specified setting (e.g., national-level, hospital or community healthcare-level) over a specified period. AMC is calculated from aggregated data such as import, wholesalers, insurance, facility dispensing or procurement data sources. AMU tracks whether antimicrobials are prescribed appropriately, for the right infections and according to treatment guidelines. AMC and AMU are terminologies that are sometimes used interchangeably and incorrectly so. It is therefore prudent to delineate these definitions further through clarification that AMC data describe quantities of antimicrobials dispensed (e.g., at national stores or pharmacies) whereas AMU data describe how and why antimicrobials are used (e.g., whether required laboratory tests and clinical assessments were conducted prior to issuing a prescription whether the right antimicrobial was prescribed at the correct strength and frequency over an appropriate duration to treat the right indication as per country guidelines, and finally, whether the patient correctly and/or completely consumed the prescribed antimicrobial).[26]

Link between the antimicrobial usage and AMR

The unwarranted use of antimicrobials contributes to the development of AMR and explains the association between AMU and AMR. This association implies that a reduction in the unnecessary consumption of antimicrobials could, in turn, affect resistance.[24] The inappropriate use of antimicrobials refers to the use of the wrong type of antimicrobial, and/or at the wrong dose, frequencies or duration and/or for the wrong indication. For the past few decades, there has been a global increase in the consumption of antimicrobials and a shift in consumption towards the use of both broad-spectrum and last-resort antimicrobials, particularly in LMICs. These shifts are because of improved access and increased economic strength within some of these countries. However, AMR can also develop because of a lack of access to antimicrobials, leading to the prolonged use of a particular antimicrobial over a long time and thus permitting selective pressure to favour microbes that evade these predominately-used antimicrobials. This is often the picture in several LMICs where inequities in access to antimicrobials still persist.[27] This complicated picture demonstrates the need for the research and development of new agents that counteract emerging AMR, but also strongly indicates the need to use the available antimicrobials appropriately and ensure their accessibility.

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

AMC and AMU surveillance impact

To ensure the successful treatment of infectious diseases in patients, optimising the correct usage of antimicrobials is one of the strategic objectives within the WHO Global Action Plan (GAP).[8] For the successful implementation of the above objective, there is a need to understand a country's pattern of AMU and quantification of their consumption. At present, there are only few published reports on AMC surveillance and AMU in Africa.[28-32] The process of obtaining AMC or AMU data equips the country with local information on various problems that exist with antimicrobials use and allows for monitoring the accessibility of antimicrobials. Furthermore, obtaining of AMC or AMU data permits the continuous local assessment of correlations between antimicrobial usage and emerging local AMR. Data obtained from local surveillance exercises also presents the opportunity to better inform the stewardship programmes.

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

The aim of this work

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

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

Section II: AMC or AMU surveillance status

Objective

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

Methodology

AMC and AMU data sources

Through open-structured key informant interviews (KIIs) (AMC Appendix 1), the AMRCC contacts shared their insights about the current landscape of AMC surveillance in the country as well as from where national AMC and AMU data can best be surveilled. Consequently, the national medical store (NMS) mechanism for public sector procurement and the joint medical store(JMS) mechanism for private-not-for-profit procurement were identified as potential sources for the national AMC data for Uganda. In addition, import manifests held by the National Drug Authority (NDA) were also identified as an additional potential source for national AMC data in Uganda.

Under the guidance of the Uganda AMRCC, MAAP targeted 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 targeted to be collected from the pharmacies that were co-located in the same facility with AST laboratories (n=16) (AMC Appendix 2). Further AMC data were collected from the community pharmacies (n=16) that were nominated by the co-located pharmacies based on their proximity to the AST laboratories. Selection was also based on these community pharmacies serving as the preferred patient medicine purchase sites or backup prescription fulfilment sources in case of stockouts in the main hospital pharmacy. Furthermore, availability of retrospective data from 2016-2018 and willingness to share data were key criteria considered for selection.

Besides AMC data collection, AMU data were to be targeted for collection from hospital pharmacies (n=16) and this was to be abstracted from the facilities' prescription or patient medical records. To clarify, community pharmacies, which are also known as retail pharmacies, are licensed commercial pharmaceutical stores that provide medicinal products (prescription only and over-the-counter medicines) to a specific community group or region and excludes unregulated and informal medicine dispensers. Hospital pharmacies, on the other hand, are pharmacies located within a hospital for the provision of medicinal products to inpatients and outpatients who visit the hospital.

Data collection scope

MAAP purposively selected data collection on J01 (antibiotics for systemic use) consumption trends. J01 medicines are one of the WHO core monitoring Anatomical Therapeutic Chemical (ATC) medicine categories for AMC surveillance. In addition, as per the country's request, selected P01AB (nitroimidazole derivates) and/or selected J02 (antimycotics for systemic use) were also included in the scope for AMC data collection (See AMC Appendix 3 for full list of selected antimicrobials in Uganda). P01AB and J02 ATC antimicrobials are part of the WHO core and optional monitored medicine classes respectively for AMC surveillance.[33] AMC data from the above medicine categories was collected from January 2016 to December 2018.

Data collection

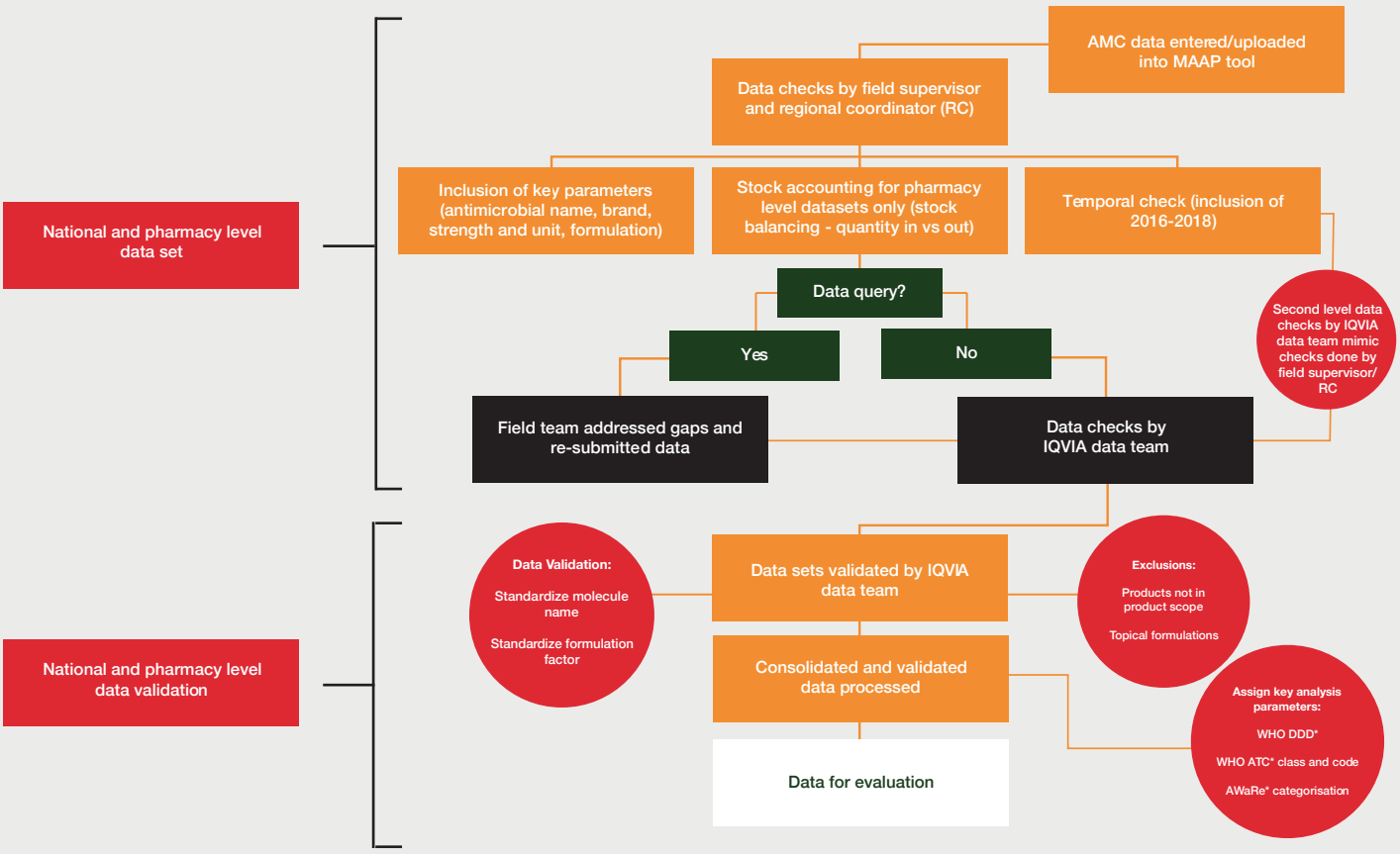
The JMS AMC datasets were obtained by the MAAP central data team from the IQVIA™ syndicated pharmaceutical consumption electronic datasets for the period 2016-2018. NMS AMC data were provided directly to the MAAP field data collectors. Both the JMS and NMS datasets were provided in electronic format (i.e., Excel™). The datasets were reviewed and cleaned by the data collection teams using Excel™ which was then transferred securely through the MAAP tool that captured all antimicrobials by their standard molecular name and/or product brand, pack size, strength and formulation (e.g., tablets or capsules, suspensions or syrups). AMC Appendix 4 captures the full list of data variables collected to tally national- and pharmacy-level AMC.

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

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

Data cleaning and validation

The national-level antimicrobial JMS datasets (as provided from the syndicated IQVIA™ dataset) were extracted from the system and provided to the regional coordinator for processing. Once the JMS (from IQVIA) and NMS datasets were received by MAAP, both the national- and pharmacy-level AMC data were then subjected to a series of data validation checks to ensure their accuracy and consistency. (Data checks and the validation process for national AMC data are detailed in AMC Appendix 6). Here, the pharmacy and national AMC data were subjected to secondary and tertiary checks by field supervisors, regional coordinators and the IQVIA data team. The validation and processing of the data were carried out by the regional coordinator and IQVIA data team, as outlined in Figure 15.



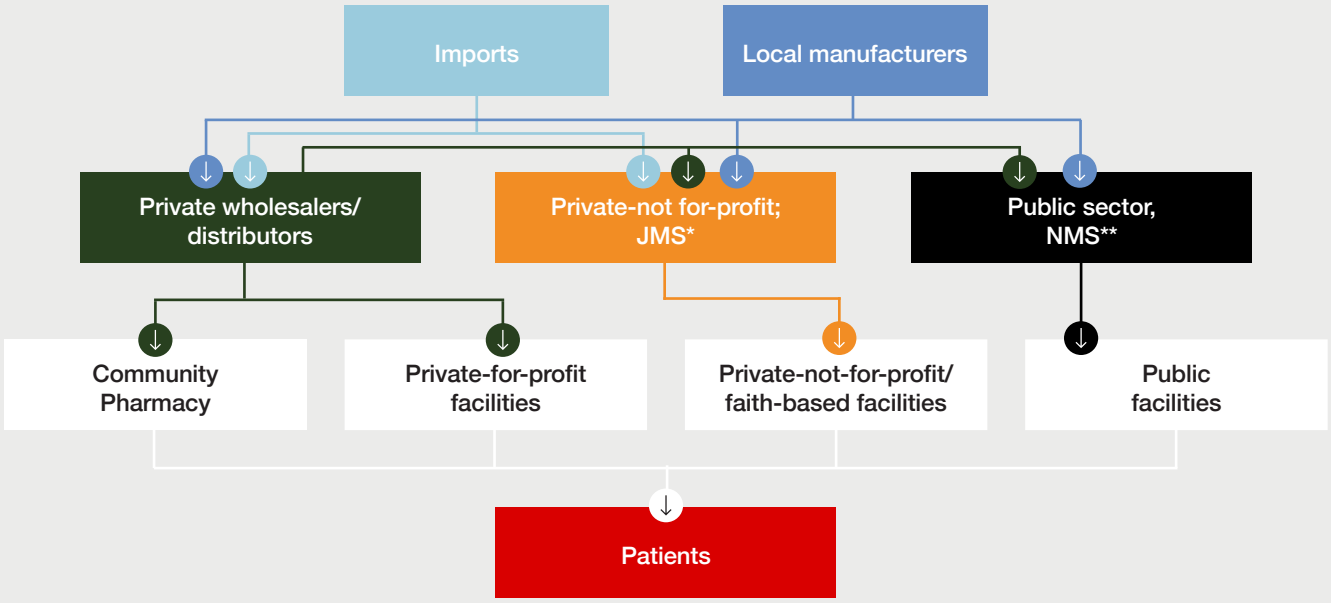
*WHO World Health Organisation - *DDD Defined Daily Dose - * AWaRe Access, Watch, and Reserve

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

Results

Flow of antimicrobials in the country

To characterise the pathway through which antimicrobials get to patients in the country, three KIIs were conducted with stakeholders in the AMRCC, the NDA, the public sector national central medical store (CMS) and the NMS. In Uganda, medicines including antimicrobials, are imported as well as manufactured in the country. After importation or local production, private for-profit wholesalers, private-not-for-profit distributors (JMS) and the national public CMS (NMS) then pass along the antimicrobials to community pharmacies, private (both for-profit and non-profit) facilities and public facilities who eventually issue the antimicrobials to patients. The flow chart below (Figure 16) illustrates the route through which antimicrobials get to patients in Uganda.



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

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

Regulation of antimicrobials consumption

In Uganda, the NDA regulates and licenses all pharmaceutical products, including those imported as well as locally manufactured. The antimicrobials for human consumption are regulated under the National Drug Policy and Authority Act Chapter 206, 1993.[16] This law stipulates that requisite antimicrobials can only be sourced from registered suppliers and dispensed with a valid prescription. The overuse and misuse of antimicrobials are significant contributors towards the emergence of AMR. Therefore, to address the above issues and other prevalent gaps, the country developed a National Action Plan on AMR (2018-2023)[14], that seeks to further build regulations around AMC in an effort to curb the growth or emergence of AMR.

Availability of data for AMU surveillance

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

Availability of data for AMC surveillance

National-level data

National AMC data were obtained from IQVIA™ as sourced from the JMS and directly obtained from the NMS for the years 2017 and 2018. The NDA datasets were not available for the period of review (2016-2018) as an internal data audit activity was underway within the NDA, which rendered the data inaccessible to MAAP. Consequently, MAAP set out to obtain AMC national data from key wholesalers or distributors identified by the AMRCC. However, the 2016 AMC datasets were not available from the NMS as they were not retrievable from their system while the JMS data were only partially available for the year 2016. Therefore, for purposes of this report, only 2017 and 2018 national AMC data are presented. Furthermore, the datasets excluded private for-profit wholesalers or distributors AMC. MAAP was unable to quantify this gap in data coverage as no information was available in relation to the private for-profit sector market share. The JMS and NMS data had all the variables required to conduct AMC analysis (including date of transaction, antibiotic name, pack size, strength and formulation (e.g., tablets or capsules, suspensions or syrups and injections).

Facility-level data

Pharmacy data collection was successfully conducted in 11 of the 16 targeted hospital pharmacies. The remaining recruited AST laboratories (n=5) were stand-alone laboratories i.e., without co-located hospital pharmacies. Consequently, MAAP set out to recruit two community pharmacies from the already successfully recruited hospital pharmacies (n=11) to reach the target pharmacy sample size (n=32). Hence, 22 community pharmacies nominated by the recruited hospital pharmacies were targeted. MAAP was unable to receive data from any of the targeted community pharmacies either due to their unwillingness to share data, as a result of not being able to access the historical data from their systems or due to the community pharmacy failing to meet the inclusion criteria. As the total number of hospital or community pharmacies in Uganda could not be established, data representativeness at facility level could not be assessed.

In the case of pharmacy-level data, necessary variables were available in stock cards or electronic records of 11 pharmacies where the data were collected. However, there were instances in each of the visited facilities wherein strength or pack size information for a few line items or transactions were missing from the stock cards. These information gaps were addressed by re-visiting the facilities and gathering information from the facility staff or through secondary desk research using the available product details. Of the 11 hospital pharmacies, MAAP was able to collect data across the three years in 9 pharmacies. Only two participating hospital pharmacies did not have archived data for the 2016-2017 period.

In relation to the recruited hospital pharmacies (n=11) that were co-located with the AST laboratories, (n=6) were in public government hospitals and the remaining (n=5) were in private or faith-based hospitals. Among the public government hospitals (n=1) was a national referral hospital, while among the remaining facilities including those private or faith-based (n=10), were regional referral hospitals. Furthermore, due to the lack of any national AMC surveillance policy or structured AMC surveillance system during the reviewed period, none of the recruited pharmacies actively reported AMC data regionally or centrally. Table 11 below summarises the core characteristics of the hospital pharmacies from which AMC data were collected.

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

Hospital Pharmacies (co-located with AST laboratories)

Pharmacy Name	Level of Service#	Affiliation	Region	Record keeping*	Pharmacy system directly linked to hospital records *†	AMC reporting*
Nakasero Hospital	Regional referral	Private	Kampala/ Central region	Electronic	Yes	No
St Francis Hospital Nsambya	Regional referral	Private faith-based	Kampala/ Central region	Manual/ Electronic	No	No
Mulago National Referral Hospital	National referral	Public	Kampala/ Central region	Manual	No	No
Mengo Hospital	Regional referral	Private faith-based	Kampala/ Central region	Manual/ Electronic	Yes	No
Mbale Regional Referral Hospital	Regional referral	Public	Mbale/ Eastern region	Manual	No	No
Jinja Regional Referral Hospital	Regional referral	Public	Jinja/ Eastern region	Manual	No	No
Kabale Regional Referral Hospital	Regional referral	Public	Kabale/ Western region	Manual	No	No
Fortportal Regional Referral Hospital	Regional referral	Public	Kabarole/ Western region	Manual	No	No
Kagando Mission Hospital	Regional referral	Private faith-based	Kasese/ Western region	Manual	No	No
St. Mary's Lacor Hospital	Regional referral	Private faith-based	Gulu/ Northern region	Manual/ Electronic	No	No
Arua Regional Referral Hospital	Regional referral	Public	Arua/ Northern region	Manual	No	No

#Regional Referral Hospitals offer specialist services such as psychiatry, ear, nose and throat (ENT), ophthalmology, dentistry, intensive care, radiology, pathology, higher level surgical and medical services than those offered in a general hospital. National Referral Hospitals provide comprehensive specialist services and in addition, are involved in teaching and research.

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

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

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

Objective

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

Methodology

Statistical analysis

Data analysis for MAAP was conducted according to WHO's protocol for conducting AMC analysis using the DDD-ATC-AWaRe methodology.[33,34] Figure 17 provides a high-level summary of the AMC analysis that was conducted. Each of these WHO methodologies are described below as well as the additional analysis conducted. In addition, and where possible, associations were drawn between AMC and AMR. Details of this analysis can be found in Part A, Section II:3c.

i. Defined Daily Dose (DDD)

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

Using the WHO 2020 DDD guide, the total DDDs were the quotient of the total consumed milligrams per antimicrobial divided by the standard DDD value issued by WHO.[35] The total DDDs were then adjusted for the country population size in the year of data collection,[36] 2016-2018, and presented as DDDs/1000 inhabitants/day (DID). Pharmacy-level AMC data were to be adjusted as DDD/number of inpatients and presented as DDD/100 patient bed days. However, the use of the WHO DDD per 100 patient bed days presented limitations at the point of analysis as patient bed days were not an appropriate denominator to use across the pharmacy-level AMC datasets. In addition, for most of the hospital facilities, patient bed days and patient days information were not easily accessible. Secondly, this metric would not allow for comparison between hospital pharmacy consumption and community pharmacy consumption as in the latter, the patient bed days metric is not applicable. Therefore, the AMC pharmacy-level data are presented as absolute DDD to aid comparison between hospital and community pharmacies. Detailed DDD calculations can be found in AMC Appendix 7. All calculations were conducted in Excel ™.

ii. Anatomic Therapeutic Chemical (ATC) Classification

Using the standard list of antimicrobial names, data collected was coded in the Excel TM analysis database in accordance with the 2020 WHO ATC codes and then analysed to characterise the macro (above-molecule) AMC trends. The description of ATC codes is presented in AMC Appendix 6. Furthermore, an attempt was made to conduct statistical testing to determine the year-on-year differences within each ATC class, however, this was not possible as the datasets were missing core components for analysis i.e., month of transaction.

iii. WHO Access, Watch and Reserve (AWaRe)

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

Through the WHO AWaRe analysis, the total AMC by DDDs per antibiotic molecule were labelled as either 'Access', 'Watch' or 'Reserve' in accordance with the 2019 WHO AWaRe list[37] in Excel ™. Total DDDs per WHO AWaRe category were then analysed to determine the proportion of AMC per category and over time i.e., 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, an analysis was conducted to identify the top five antibiotics consumed in each WHO AWaRe category.

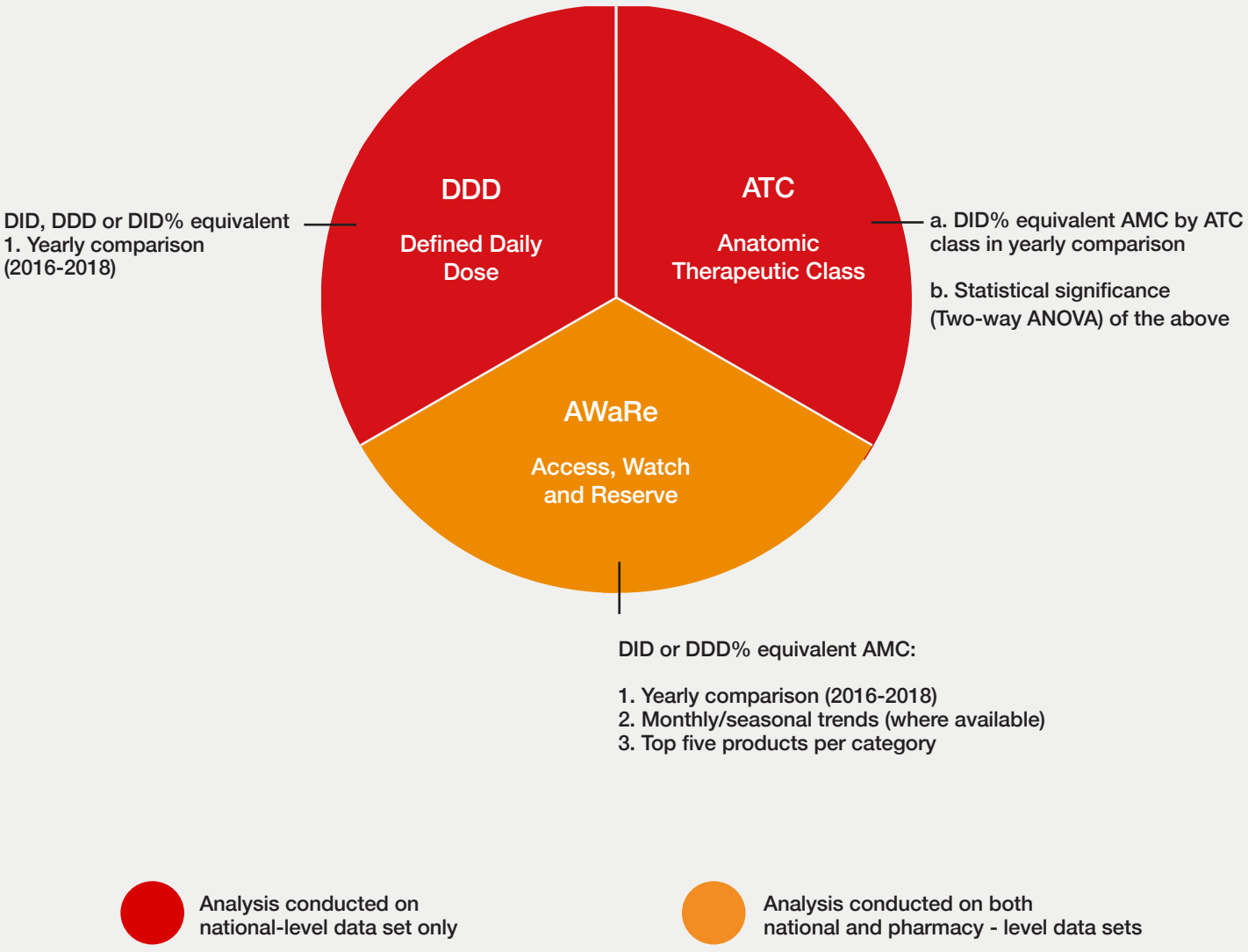


Figure 17: Methods and indicators used for the analysis of the data collected in Uganda. Defined Daily Dose (DDD) indicators utilised for volume metric standardisation was sourced from WHOCC 2020, ATC Classification utilised to categorise the antibiotics according to the organ or system on which they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

iv. Review of Essential Medicines List (EML)

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

Results

National AMC datasets analysed by DDD per year

The average total in-country AMC between 2017 and 2018 was 7.4 DDD per 1000 inhabitants per day (DID). A 9% reduction in total consumption share of the antimicrobials from the year 2017 to 2018 was documented (Figure 18). Further disaggregation of the national AMC data across the two sectors i.e., public sector (NMS) and private-not-for-profit sector (JMS), illucidated that the public sector accounted for 84.5% and the private-not-for profit-sector 15.5% of the national AMC.

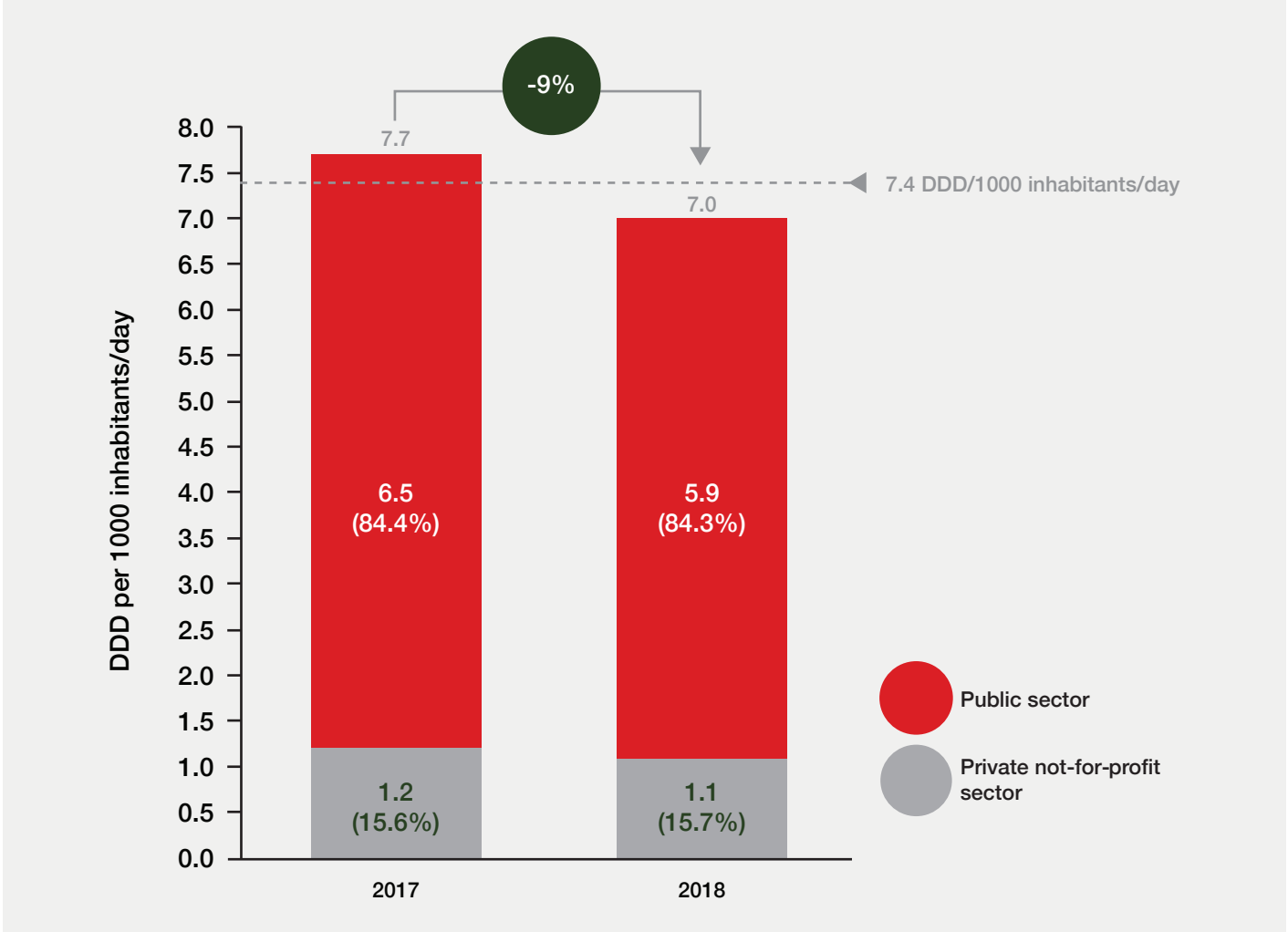


Figure 18: Bar graphs represent the total DID and percentage variation from the year 2017 to 2018 for national-level AMC data analysed in Uganda. It further describes the disaggregation of consumption of antimicrobials across the public (represented in orange) and private-not-for-profit sectors (represented in green) in Uganda, as total DID and percentage share of total consumption for each year (2017 and 2018)

National AMC analysed by ATC classification

Penicillins with extended spectrum (J01CA) were the most frequently consumed ATC class in Uganda across the review period at 38.7% in 2017 and 39.6% in 2018, with amoxicillin being the most frequently consumed antibiotic within this class (Figure 19). Tetracyclines (J01AA) and nitroimidzole derivatives (P01AB) were the second- and third-leading ATC classes, with doxycycline and metronidazole leading consumption within these ATC classes respectively. The top five most consumed antimicrobials were Amoxicillin, Doxycycline, Metronidazole sulfamethoxazole/trimethoprim and Ciprofloxacin. Together they account for >88% of total consumption share. A detailed list of national AMC by antimicrobial molecule and by ATC class is mentioned in AMC Appendix 8 and Appendix 9 respectively.

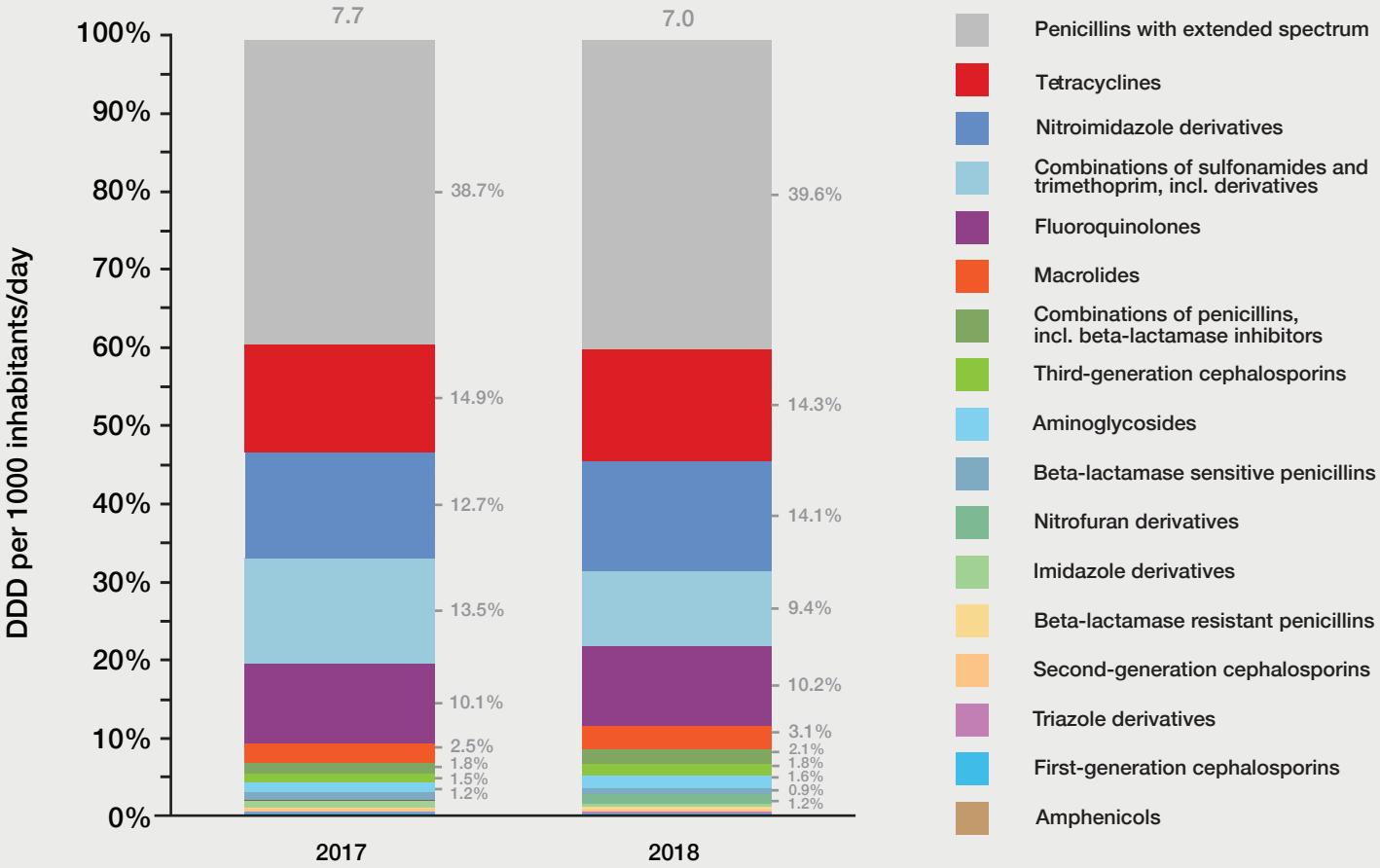


Figure 19: Results of national level AMC data analysed in Uganda are presented by total DID and percentage of antimicrobials consumed by ATC classes for the years 2017 and 2018. Penicillins with an extended spectrum class of molecules were the highest consumed antimicrobials in both 2017 and 2018. See Appendix 9 for a more detailed breakdown of AMC by ATC classes

National and pharmacy AMC analysed by WHO AWaRe categorisation

The average national consumption of antibiotics across the two years analysed was 84.5% 'Access', 15.5% 'Watch' and <0.1% 'Reserve'. Annual consumption indicated a decrease of 1.3% in the consumption share of Access antibiotics between 2017 and 2018, against a corresponding 1.3% increase in 'Watch' antibiotics between the same period (Figure 20). On average and within each year analysed, the share of consumption of 'Access' category antibiotics in Uganda exceeded the 60% minimum consumption threshold set by WHO. This analysis of national AMC by WHO AWaRe categories omits 2.3% (0.2 DID) of total AMC that are not categorised within the WHO AWaRe list of 2019.

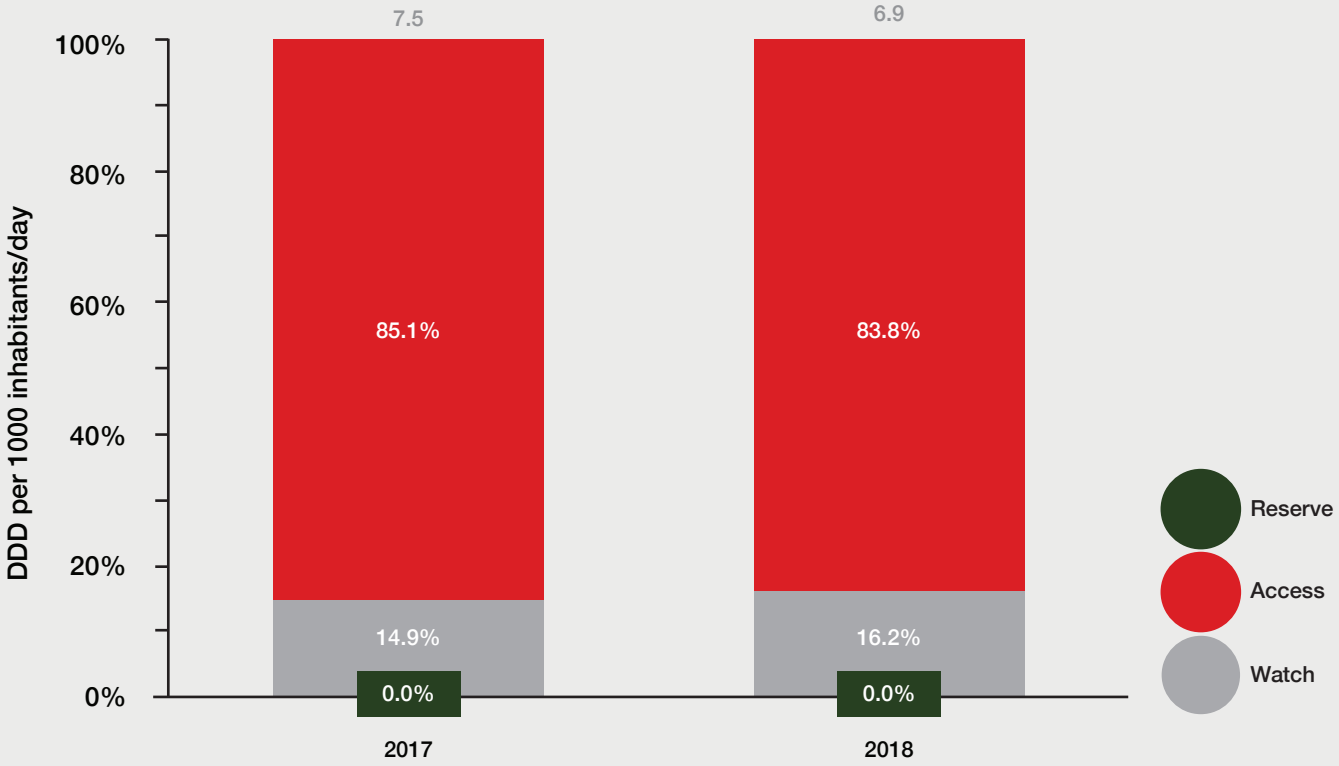


Figure 20: Results for the AMC data analysed in Uganda are presented by total DID and percentage of antibiotics consumed by WHO AWaRe categories for the years 2017 and 2018. Additionally, it shows the percentage change in consumption of 'Access' and 'Watch' category antibiotics from the year 2017 to 2018

In addition, further analysis was conducted to disaggregate the WHO AWaRe category antibiotics consumption across the two sectors represented in the national-level data i.e., public and private-not-for-profit sectors (Figure 21). The private-not-for-profit sector consumed 18% more 'Watch' category antibiotics compared to the public sector (public sector at 13% and private not-for-profit at 31%).

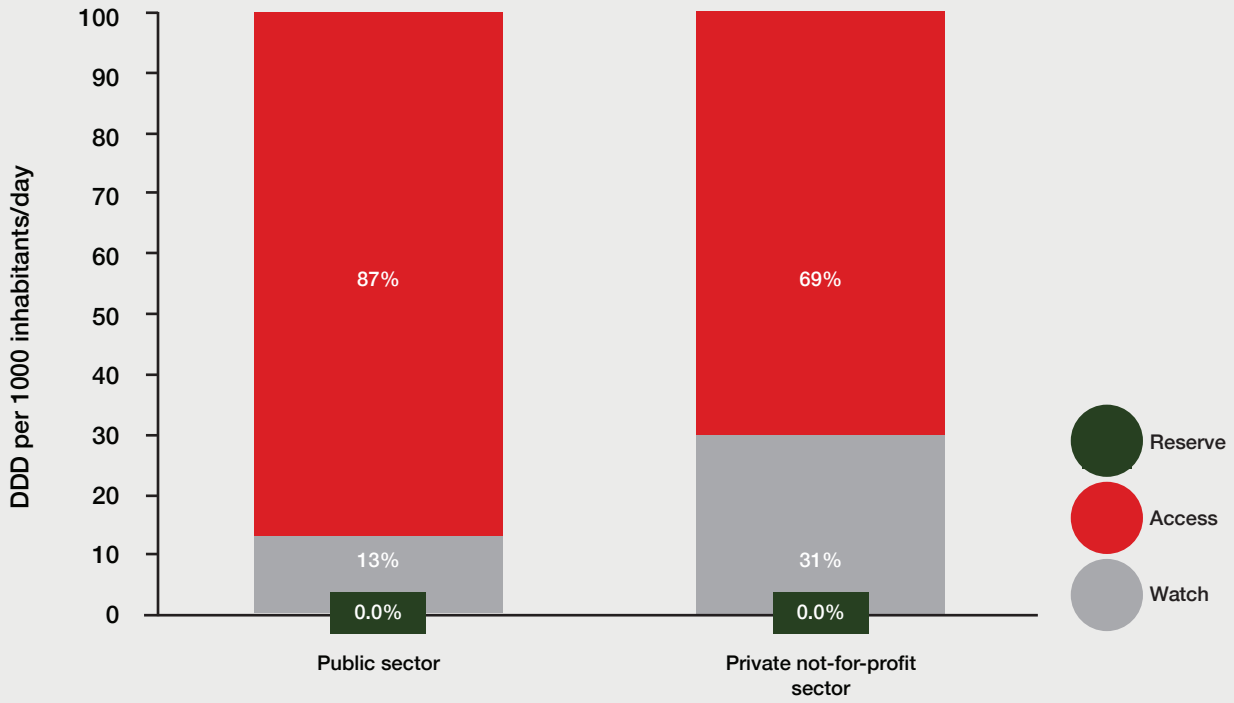
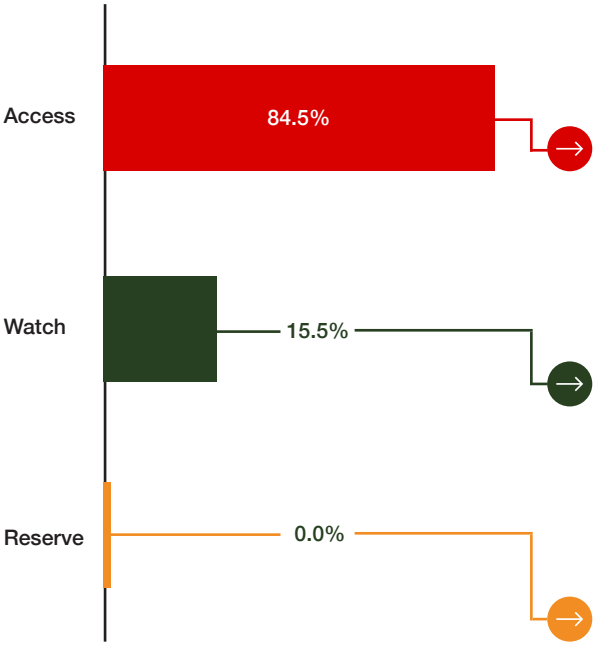


Figure 21: Disaggregation of WHO AWaRe categories antibiotics consumption by healthcare sector i.e., public and private-not-for-profit sectors. Data is presented as percentage of antibiotics consumed for the years 2017 and 2018

Further analysis was conducted to identify the most frequently consumed antibiotics nationally, within each WHO AWaRe category (Figure 22). In the 'Access' category, the top five consumed antibiotics, as listed in Figure 22, accounted for 96.7% of all AMC within this group. While in the 'Watch' category, the top five antibiotics accounted for 93.9% of all consumption within this group. In the 'Reserve category', national consumption was only recorded for one antibiotic, that is, linezolid - representing 100% of the consumption within this category. Interestingly, disaggregated AMC data by sector showed that apart from Cefixime replacing Levofloxacin within the private-not-for-profit AMC data as one of the top five 'Watch' antibiotics consumed, the remaining most-consumed antibiotics in each WHO category were the same across the two sectors.



Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Amoxicillin	47.2%	2.9
Doxycycline	17.7%	1.1
Metronidazole	16.5%	1.0
Sulfamethoazole/Trimethoprim	14.0%	0.9
Gentamicin	1.3%	0.1

Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Ciprofloxacin	64.0%	0.7
Erythromycin	12.0%	0.1
Ceftriaxone	8.9%	0.1
Azithromycin	6.4%	0.1
Levofloxacin	2.6%	0.0

Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Linezolid	100%	0.0

Figure 22: Breakdown of the 'Access', 'Watch' and 'Reserve' categories of antibiotics consumed at national level by percentage and total DID for both the years 2017 and 2018 in Uganda. It also depicts the top five consumed antibiotics in their respective categories

Within the WHO AWaRe database exists a list of 'antibiotics not recommended'. This group of antibiotics consists of FDC multiple broad-spectrum antibiotics that are neither evidence-based nor recommended by high-quality international guidelines. As a result, WHO does not recommend their use in clinical practice. Furthermore, these antibiotics are represented as 'uncategorised' by MAAP. Analysis of the national AMC data was made to identify their consumption in the country. Consumption of (n=6) of these antibiotics was observed (representing 1.6% consumption of total national AMC) and is listed in Table 12 below. Among them, the FDC of Ampicillin/Cloxacillin was the most frequently consumed (accounting for 97% of the consumption from the total consumption of the listed FDC antibiotics in Table 12), with a mean DID (0.1). This FDC antibiotic was also found to be the sixth most frequently consumed antimicrobial in the overall national AMC datasets analysed. However, disaggregation of the consumption by sector revealed that the private-not-for-profit sector contributed to 70% of the consumption of these non-recommended FDCs when compared to the public sector (which only recorded consumption of one of the six none-recommended combinations).

Table 12: List and AMC rank of antimicrobials categorised as 'not recommended' for clinical utility by WHO*

Overall AMC rank*	Not recommended combination	Percentage consumption share of total AMC for each data set	
		Public sector	Private-not-for-profit
6	Ampicillin/Cloxacillin	0.6% [10th]	7.0% [5th]
27	Cefixime/Clavulanic Acid	-	0.3% [28th]
33	Ofloxacin/Ornidazole	-	<0.1% [34th]
37	Ceftriaxone/Sulbactam	-	<0.1% [37th]
39	Cefuroxime/Clavulanic Acid	-	<0.1% [40th]
46	Azithromycin/Fluconazole/ Secnidazole	-	<0.1% [43rd]

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

(-) No consumption recorded

Aggregated pharmacy-level data were analysed from the (n=11) participating pharmacies and examined by the level of service of the hospitals (regional referral against national referral and private or faith-based versus public) and by their proportional consumption of WHO AWaRe category antibiotics. Private or faith-based hospital pharmacies consumed 34% more 'Watch' category antibiotics compared to public hospital pharmacies (public hospital pharmacies=14.8%, private or faith-based pharmacies=48.8% Watch antibiotics consumption) (Table 13). Conversely, public hospital pharmacies far exceeded the WHO threshold of 60% antibiotics consumption represented within the 'Access' category at 85.1% compared to the private or faith-based hospital pharmacies which failed to meet the threshold at 51.1%. A closer look within the public hospital pharmacies data showed that the national referral hospital pharmacy consumed 35% more 'Watch' category antibiotics compared to the (n=5) regional referral hospital pharmacies, and failed to meet the WHO Access consumption threshold. Moreover, the (n=1) private hospital pharmacy consumed 25.9% and 59.1% more 'Watch' category antibiotics when compared to the consumption of the faith-based hospital pharmacies and public hospital pharmacies, respectively. 'Reserve' category antibiotic consumption was only observed within the private or faith-based hospital pharmacies with no consumption having been recorded within the public hospital pharmacies.

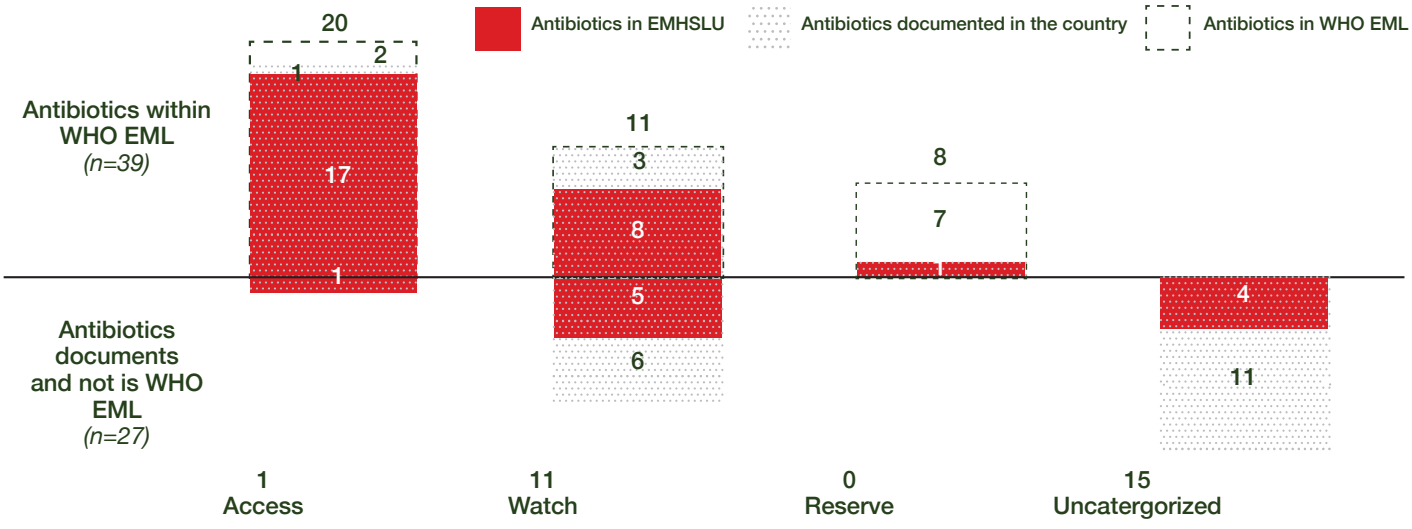
Table 13: Percentage share in the consumption of antibiotics by WHO AWaRe categories for the recruited hospital pharmacies (both public and private/faith-based) between the years (2016-2018) in Uganda

	AWaRe Categorisation		
	Access	Watch	Reserve
Pharmacy Type	Percentage share	(Absolute DDD)	
Public hospital pharmacies (6/11)	85.1% (5.9 million)	14.8% (1.0 million)	0.0% (0)
Regional Referral hospitals (5/6)	86.8% (5.7 million)	13.3% (870,738.4)	0.0% (0)
National Referral hospital (1/6)	51.4% (35,612.5)	48.6% (33,725.8)	0.0% (0)
Private or faith-based hospital pharmacies (5/11)	51.1% (1.5 million)	48.8% (1.4 million)	0.0% (2,890.0)
Faith-based hospitals (4/5)	51.9% (1.4 million)	48.0% (1.3 million)	0.0% (2268.0)
Private hospital (1/5)	25.5% (23 491.0)	73.9% (68,149.6)	0.0% (622.0)
Grand Total	**75.7% (7.2 million)**	**24.3% (2.3 million)**	**0.0% (2 890)**

Comparison of the WHO EML and the EMHSLU with documented antibiotics by WHO AWaRe categorisation

The WHO EML includes 39 antibiotics across the AWaRe categories. A total of 66 antimicrobials were documented during national- and pharmacy-level data collection. Figure 23 shows the number of antibiotics in the WHO EML and EMHSLU for each AWaRe category, thereby indicating whether the antibiotic was documented during data collection.

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



*EMHSLU – Essential Medicines and Health Supplies List of Uganda

Figure 23: AWaRe analysis of documented antibiotics in national- and pharmacy-level data for the years 2016 to 2018 compared to WHO- and EMHSLU definitions

Part C: Resistance and consumption interlinkages

Objective

To assess the relationship between antimicrobial consumption and antimicrobial resistance

Methodology

The DRI was estimated to convey aggregate rates of resistance as well as measurements of AMC (at a national level since AMU data was 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[38,39] (AMR Appendix 8) and help communicate the effectiveness of antibiotic therapy to decision makers. DRI values range from 0 (100% susceptibility) to 100 (100% resistance). Available AST results for at least 30 tested isolates and for at least 15 of the 25 combinations were prerequisites for the estimation of the DRI. To generate CIs for the DRI as the variance of the product of variables, the variance of the proportions of non-susceptible isolates was combined with a uniform standard deviation based on the estimated DDD.[40,41]

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

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

Results

Drug Resistance Index

The DRI estimate was found to be high at 69.1% (95% CI, 64.2-74.0%) implying low antibiotic effectiveness, which is a threat to effective infectious disease management and calls for urgent policy intervention (Figure 24).

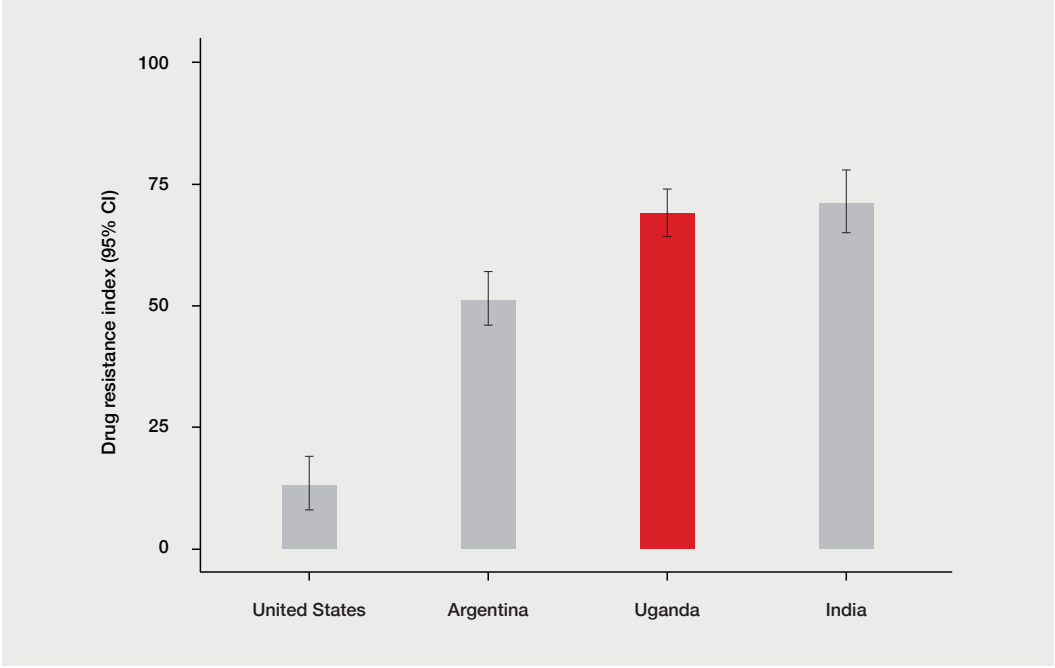


Figure 24: Drug Resistance Index

AMC and AMR correlation

The top three highly consumed antibiotic classes at facility level were folate pathway inhibitors, aminopenicillins and nitroimidazoles. The AMR rates were highest for nitroimidazoles (94.6%), folate pathway inhibitors (82%) and penicillins (78.9%) (Table 11). Pearson's correlation analysis revealed a moderate positive correlation (r^2=0.36) between AMR and AMC, implying that antibiotic consumption is a potential driver of AMR in Uganda (Figure 25).

Table 14: AMC and AMR rates across antibiotic classes

Antibiotic class	Year	Total DDD in thousands	Resistance rate (%)
Folate pathway inhibitors	2016-18	2 939.7	82.0
Aminopenicillins	2016-18	1 856.1	71.5
Nitroimidazoles	2016-18	1 351.0	94.6
Fluoroquinolones	2016-18	9 56.7	44.0
Cephalosporins (3rd generation)	2016-18	778.6	46.1
Tetracyclines	2016-18	621.3	70.3
Macrolides	2016-18	406.5	66.8
Penicillins	2016-18	335.3	79.8
Beta-lactam combinations	2016-18	194.0	63.9
Cephalosporins (2nd generation)	2016-18	160.1	50.0
Aminoglycosides	2016-18	126.1	31.8
Nitrofurans	2016-18	47 700	17.6
Methicillin	2016-18	33.9	45.3
Cephalosporins (1st generation)	2016-18	20.4	30.0

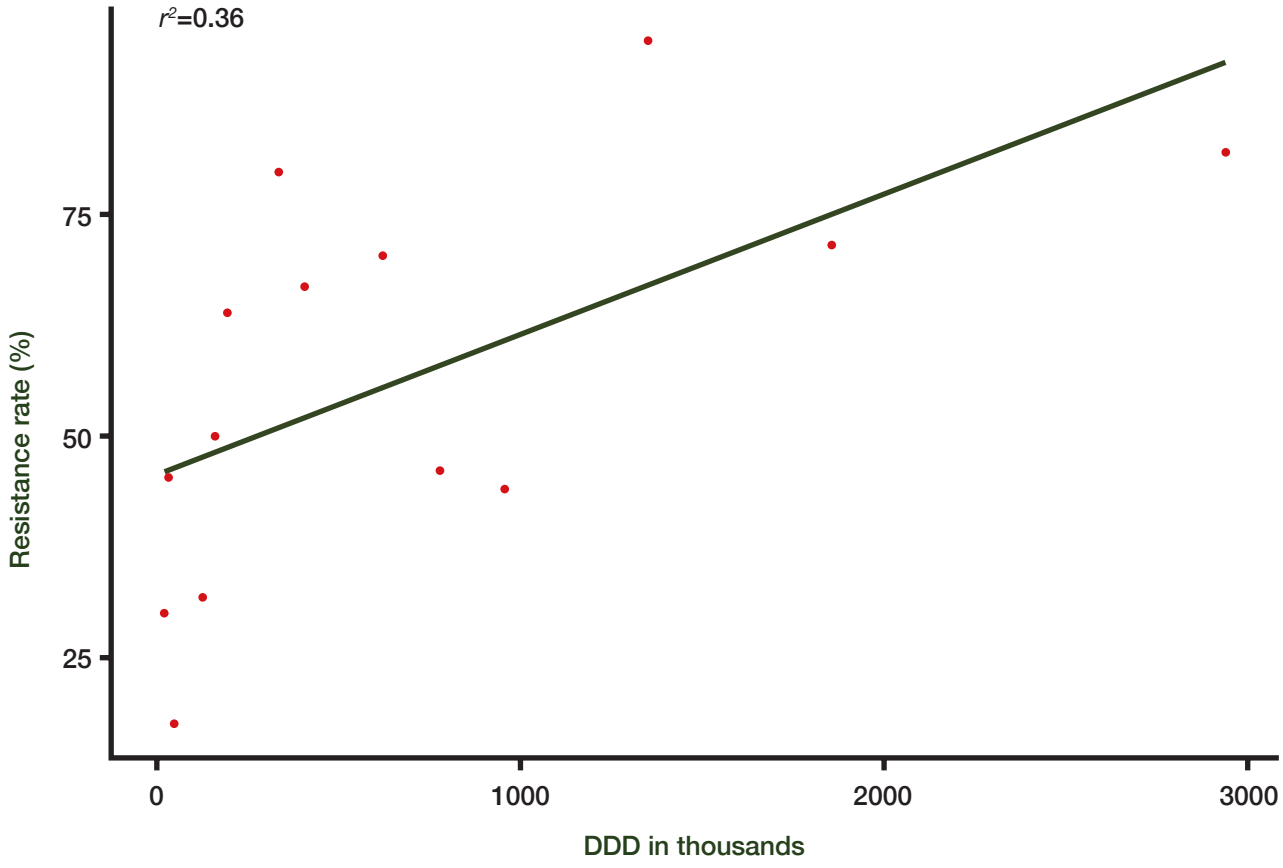


Figure 25: Correlation between AMR and AMC

Resistance profiles of most and least consumed antimicrobial classes

The most consumed antimicrobial classes across 2017 and 2018 (AMC data were not available for 2016) were folate pathway inhibitors, tetracycline and aminopenicilins (Figure 26 and 27). In 2017, high resistance rates (>85%) were observed for folate pathway inhibitor-resistant Enterococcus species and Pseudomonas species, tetracyline-resistant Enterococcus species and proteus species, and aminopenicillin-resistant Pseudomonas species and Enterobacter species. In 2018, high resistance rates (>85%) were observed for tetracycline-resistant Pseudomonas species and aminopenicillin-resistant Pseudomonas species, Klebsiella species and Citrobacter species.

The least consumed antimicrobial classes were quinolones and oxazolidinones across the study years (Figure 26 and 27). Although the consumption of these antimicrobial classes was low, high reistance rates were noted across many pathogen-antimicrobial class combinations. In 2017, resistance rates were more than 75% for quinolone-resistant Staphylococcus species and Escherichia species. In 2018, resistance rates were more than 75% for quinolone-resistant Citrobater species, Vibrio species, Staphylococcus species, Eschericia species.

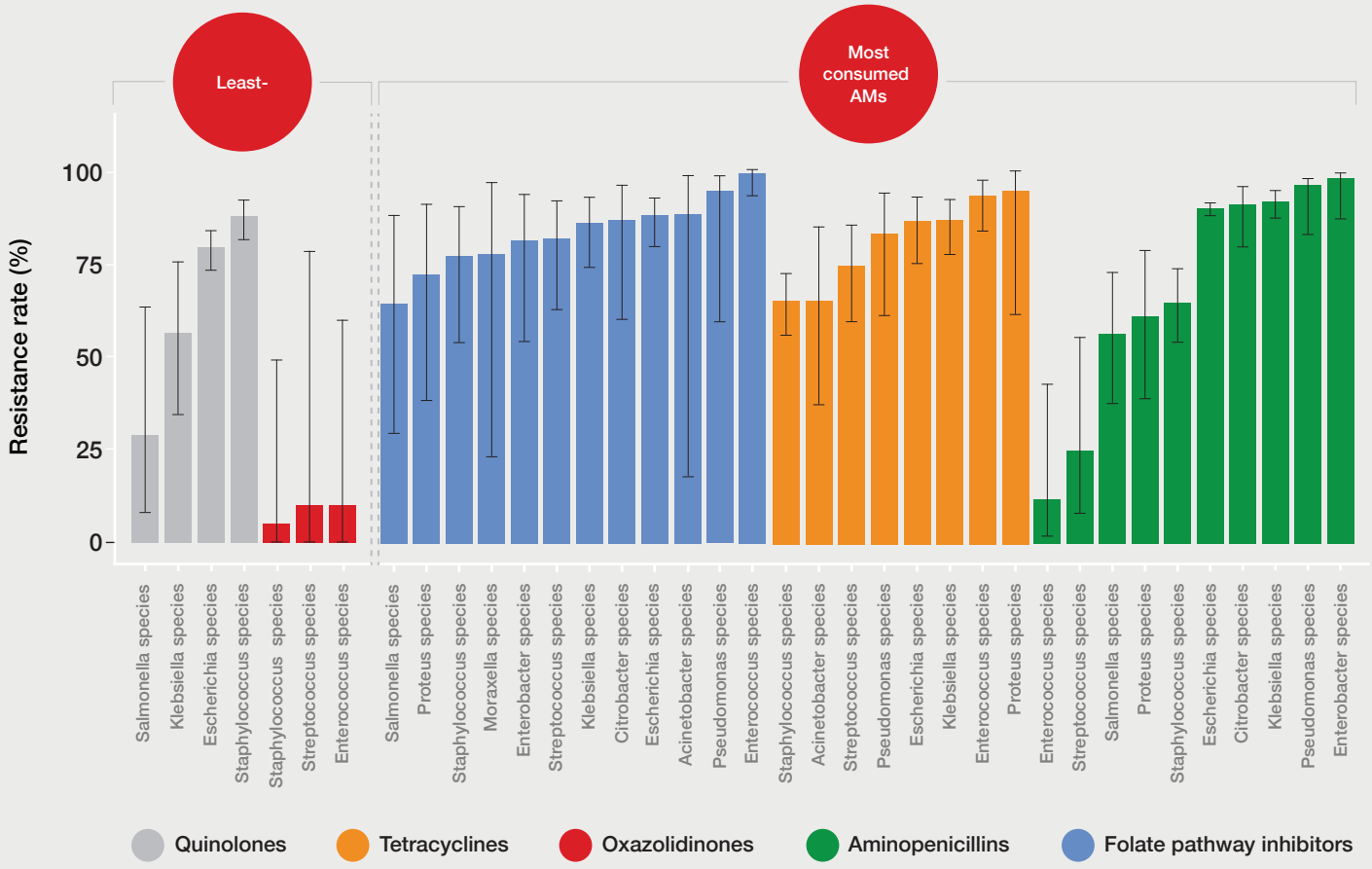


Figure 26: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2017

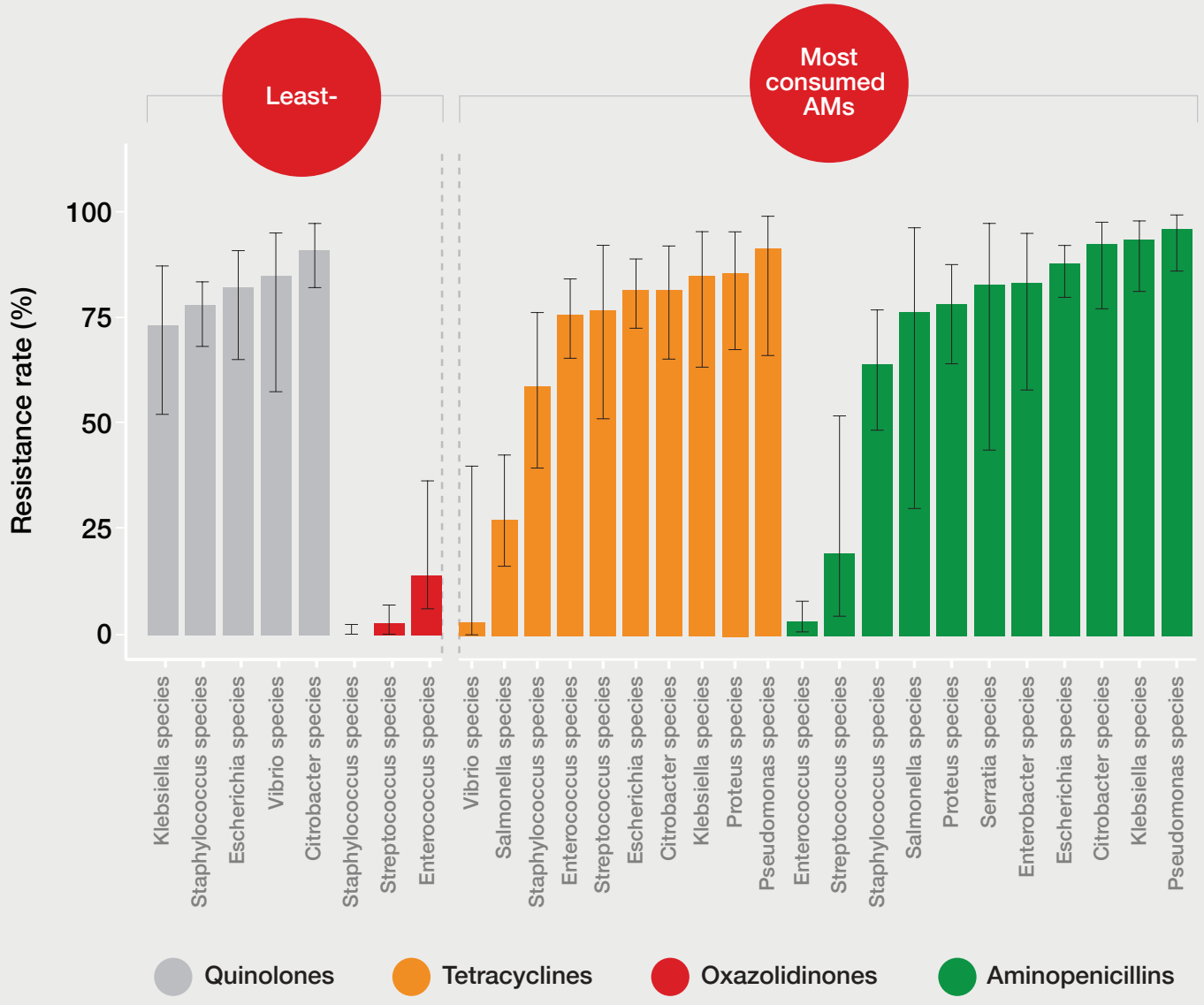


Figure 27: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2018

Part D: Recommendations

AMR is a major threat to medical advancements and has drawn global attention over the past few years and more so recently, due to the COVID-19 pandemic. Unfortunately, owing to inconsistent surveillance data, the AMR burden is not well quantified in most countries. A recent review reported 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.[42]

The mitigation of AMR 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 Uganda.

Significance of AMR and DRI data including recommendations

Analysis of available AMR data from Uganda revealed high levels of resistance for 3rd-generation cephalosporin-resistant Enterobacterales (49-55%), carbapenem-resistant A. baumannii (30-54%) and methicillin-resistant Staphylococcus aureus (34-36%).

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

A. baumannii can cause ventilator associated pneumonia, central line blood stream infection, catheter-associated urinary tract infection, meningitis, surgical site infection, community-acquired pneumonia and even eye infections. Since most infections occur in healthcare settings, it is important to recognise and control the risk factors. Commonly, stay in the ICU/dialysis/long-term care facilities, patients on devices or catheters, low birthweight, immunocompromised status, prior carbapenem use and a contaminated environment can predispose to acquiring carbapenem-resistant strains. Limiting the hospital stay, early device removal and compliance to standard precautions (including hand hygiene) are important to prevent infections and control resistance. In addition, since the pathogen can survive on surfaces, environment disinfection and sterilisation are equally critical. Empirical therapy must be de-escalated to definite therapy as soon as susceptibility results are available.

S. aureus (methicillin-resistant or sensitive) is a common cause of many skin and soft tissue infections (SSTI) in both community and healthcare settings. It can also cause invasive infections like endocarditis, osteomyelitis, pneumonia, visceral abscess, brain abscess, shunt infections and bacteraemia. Risk factors for MRSA infections include past infections/colonisation/close contact, trauma, invasive devices (catheters, shunts, implants and prosthesis), prior antibiotic use, neutropenia, other underlying conditions, post-surgical status, dialysis and admission to long-term care facilities.

While antimicrobial therapy and source control (drainage or catheter removal) are essential for the treatment modalities, it is as important to prevent and control the spread of MRSA infections. Use of catheters and invasive devices must be minimised, and stewardship principles practised (culture taken prior to initiating antibiotics and prompt de-escalation from empirical to targeted therapy). High-risk and pre-operative patients must be screened for MRSA carriage and decolonised. Patients and caregivers should be educated on the importance of handwashing and contact precautions.

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

Service delivery

The laboratory network in Uganda was found to consist of 1 625 laboratories, of which 30, were identified as bacteriological laboratories and 20 with confirmed AST capabilities. While most of the surveyed laboratories reported implementing QMS, not all were certified or accredited. Considering a country population of over 45.7 million, the laboratories did not equitably cover the country's population. The testing load (quantum of cultures) at most participating laboratories was found to be low and suggested a lack of routine microbiology testing. Hence, this risks overestimating the AMR rates as the majority of tests would have been conducted on special patient categories (such as failure of first-line therapy or admission to intensive care).

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

Health workforce

As reported by the surveyed laboratories, all of them had an experienced laboratory scientist or technologist, 85% had up-to-date records on training and competence, and only 45% had at least one qualified microbiologist. For high quality microbiology testing and reporting, staff training on laboratory standards, ability to identify common pathogens, and data management skills are essential.[43] Capacity-building of staff may be completed through in-house expertise or outsourced to external organisations or tertiary facilities.

Information systems

The Regional Grant was a step towards the collection and digitisation of data. We observed that most of the surveyed laboratories relied on a combination of electronic and paper-based records and very few had linkages to patients' clinical records. In the current study involving 16 laboratories over a three-year period, susceptibility results could be collected for just 22 349 positive cultures.

In order to strengthen AMR surveillance, it is essential to curate the right data and generate evidence. We recommend data collection through standardised formats at all levels (laboratories, clinics and pharmacies) as well as the use of automation for data analyses. For the current study, we used WHONET for data digitisation. Empirical guidelines for management of infectious diseases should be based on epidemiology specific to patient settings and resistance data should be shared on national and supra-national platforms. We also recommend establishing a system of assigning permanent identification numbers for patient tracking over time. This would help to collect data on a patient's clinical profile, antimicrobial history as well as pathogens' molecular profile (where available), thus offering more context to the AMR epidemiology than stand-alone antimicrobial susceptibility data.

Medicines and technologies

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

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

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

Significance of AMC and AMU data including recommendations

This section discusses the significance of our AMC and AMU findings and puts forth suggested recommendations for Uganda to better facilitate future surveillance activities as well as antimicrobial stewardship activities.

Feasibility of obtaining AMC and AMU data in Uganda and recommendations

MAAP successfully collected and analysed national and pharmacy-level AMC data for Uganda. This implies that surveillance of AMC data is possible and that Uganda can respond to WHO's call to participate in GLASS, which now has an AMC reporting component. However, some AMC data were missing (e.g., 2016 public sector and private-not-for-profit national AMC data). Therefore, a comprehensive guiding policy for routine AMC data surveillance is required in the country to guide on, at the minimum, reporting AMC data variables, routine data cleaning and reporting practices to minimise the amount of time spent standardising and cleaning the data. Furthermore, as the national AMC data analysed excluded the private for-profit sector, efforts should be made by relevant regulatory authorities to identify and recruit medicine wholesalers or distributors to bridge this gap in surveillance. This approach would also offer the added benefits of allowing examination of AMC trends within the private and public sector.

Policies should be put in place to outline the minimum period in which the records should be held to ensure accessibility of data for retrospective surveillance exercises (i.e., by means of establishing a clear retention and disposal schedule for essential medicine records). Efforts should also be made to address any lack of capacity, material resources, systems and infrastructure that may exist in the managing of these records. Pharmacy-level AMC data from the public hospitals was mainly collected from manual records. To make future AMC surveillance more time and cost-efficient, hospitals could consider converting to electronic systems and ensure such systems have the capabilities to transfer data across systems and/or produce user-friendly reports on AMC.

MAAP was unable to obtain AMU data in Uganda which would have helped to characterise the reasons antimicrobials were used and whether their consumption was according to country guidelines and WHO's drug use research methodology.[44] This inability to collect AMU data from participating pharmacies that were co-located in health facilities with AST laboratories was due to the fact that AMC data sources (i.e., stock record cards at the pharmacy) did not allow back-tracing to individual patients to whom antimicrobials were dispensed as prescription chits were not archived. MAAP, in alignment with the WHO guide on facility AMU assessment, would recommend that future AMU surveillance attempts in the country be conducted through prospective data collection approaches.[34] However, such an approach is time-consuming unlike retrospective data collection and often requires specialised data collection teams. This makes data collection expensive and thus challenging to undertake in resource-limited settings. Retrospective AMU data collection can, however, remain an option if facilities targeted for data collection are selected based on the existence of electronic patient records, the presence of cross-department unique patient identifiers and a functional and efficient patient record retention system.

Overview of AMC consumption trends and recommendations

The total AMC levels documented in this report offer a useful benchmark to be compared against future country consumption levels following implementation of stewardship programmes. Compared to studies from other countries in the region, the observed AMC levels in Uganda exceed those described in the literature for Burundi but were lower than the levels described in other African countries such as Burkina Faso, Cote d'Ivoire[24], Sierra Leone[28] as well as Tanzania.[45] The data in Uganda included public and private not-for-profit data compared to Burundi which only used data from the public sector. For Tanzania, import data were used to calculate the DDD for the population which was lacking local production data. This could be a reason why Uganda AMC levels appear lower than in Tanzania. The disparities in AMC within the compared countries might also be due to differences in the burden of infectious diseases within the countries as well as limited availability of laboratory and point-of-care diagnostics at the health facility-level. This may lead to presumptive treatment and the unnecessary prescription of antimicrobials.

Widespread availability of over-the-counter antimicrobials and the unexplained use of some antimicrobials in the animal health sector[24], may be additional contributing factors. Despite the lower rates of AMC in Uganda, AMU point prevalence surveys are recommended to better understand the country's AMC levels and eventually guide any future national action plans to optimise the antimicrobials consumption. It is difficult to characterise possible reasons for the overall small reduction in the national AMC observed across the reviewed years. Data for more than two years would have to be collected and examined to see if the change observed was a trend or just part of routine annual data variance in medicines consumption. However, establishment of regular AMC surveillance will allow for examination of AMC trends against baseline results presented here.

The evaluation of antibiotics consumption according to the WHO AWaRe categories showed that the proportion of narrow spectrum antibiotics in the 'Access' category well exceeded the minimum WHO recommended consumption threshold.[37] This finding is quite commendable as it implies that any emerging AMR trends due to misuse or overuse will likely be restricted to a narrow spectrum of antibiotics, sparing the lesser-used broader-spectrum antibiotics in the 'Watch' and 'Reserve' categories. Interestingly, despite meeting the minimum WHO Access antibiotics consumption threshold as a whole, it was found that the private-not-for-profit sector consumed far more 'Watch' category antibiotics when compared to the public sector. Similar observations were made by a recent AMC study carried out in Uganda.[46] This higher consumption trend of 'Watch' category antibiotics by the private-not-for-profit sector highlights the importance of including all healthcare sectors into the country's ASP, as well as inclusion of all medicine distribution sectors in future surveillance activities.

In addition, closer examination of the spectrum of antibiotics used within each WHO AWaRe category revealed that an overwhelming majority of antibiotics consumed within the 'Access' and 'Watch' categories were in the top five antibiotics in each category. Such a consumption pattern could be postulated to be sub-optimal as evolutionary pressure driving resistance would be focused only on the narrow band of antibiotics consumed.[47] This narrow consumption of antibiotics within the 'Access', 'Watch' and 'Reserve' categories of antibiotics can also make the country susceptible to stockouts if manufacturing and supply chain issues are encountered for these few antibiotics. Considering the above observations, 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 (e.g., clinician sensitisation on the country's full EML and the offering of incentives to manufacturers and importers of medicines to ensure a diverse availability of medicines).

Although, the pharmacy-level AMC data review found that, on average, the hospital pharmacies met the WHO's minimum Access consumption threshold, there was notable heterogeneity in consumption amongst them. Firstly, the public sector consumed more 'Access' antibiotics compared to the private-not-for-profit sector, and a similar trend was also observed with the national data. Secondly, private or faith-based hospital pharmacies failed to meet the WHO recommended consumption threshold unlike public hospital pharmacies who met the >60% 'Access' consumption threshold requirement from WHO. In fact, private hospital pharmacies consumed the least amount of 'Access' category antibiotics overall. The variation in consumption of 'Access' antibiotics could be due to the liberty that exists in the procurement of antimicrobials within the private or faith-based facilities compared to public-sector facilities, as the latter adhere to Uganda's EMHSLU.[48] Notably, the public-sector facilities are required to purchase medicines based of the EMHSLU and the availability of government funds. Therefore, we postulate that the public-sector facilities have more medicine procurement restrictions compared to the private or faith-based-sector facilities.

Furthermore, within these public hospital pharmacies, the national referral hospital pharmacy consumed far less 'Access' category antibiotics compared to the regional referral hospitals. In fact, the consumption level of the national referral hospital was comparable to that observed with the private or faith-based hospital pharmacies. The higher consumption of 'Watch' antibiotics at the national referral hospital could be attributed to the facility dealing with complex diseases that would require treatment using second and third-line antimicrobial agents. Finally, the consumption of 'Reserve' category antibiotics was only observed within the private or faith-based hospitals with no consumption recorded within the public hospitals. 'Reserve' category antibiotics are listed as essential medicines within the EMHSLU and their use recommended within the Ugandan treatment guidelines, 2016.[49] MAAP therefore recommends a review to be conducted by the AMRCC in an effort to assess the availability of the 'Reserve' category antibiotics within the public facilities, where deemed necessary, to ensure that the most vital antibiotics are available for patients across all healthcare sectors.

The WHO also provides guidance on antibiotics that are 'not recommended' for use in clinical practice due to their multiple broad-spectrum activity and lack of an evidence-based clinical case that advocates for their use.[37] In Uganda, six such FDCs 'not recommended' by WHO were detected, largely from the private-not-for-profit distributor. Of these antibiotic combinations, the use of Ampicillin/Cloxacillin 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.[50] As there is no recommendation for use of these FDC antimicrobials within the Uganda clinical treatment guidelines,[49] it is recommended that the AMRCC identify the reasons for prescribing or dispensing these FDCs and the exact locations that commonly prescribe or dispense these FDC antimicrobials. This will allow the country to embark through relevant bodies (MoH, healthcare training curricula, etc.) and institutions (e.g., regulatory bodies like the NDA) on sensitising the prescribers on more appropriate treatments for those ailments in order to correct the prescribing practice. The focus of these interventions should be primarily targeted towards the private-not-for-profit sector as they were identified as the major contributor in the consumption of these products.

Data generated from AMC and AMU surveillance trends can provide unique insights for national stewardship programmes for the formulation of policies to stem the emergence of AMR. Uganda should be commended for far exceeding the minimum threshold of consumption of at least 60% of antibiotics from the WHO 'Access' (narrow spectrum, first choice antibiotics) category. Yet, only five antibiotics make up for >88% of the consumption which indicates the opportunity for more diversification. Table 15 describes the next steps for AMC and AMU surveillance.

Table 15: Next steps for AMC and AMU surveillance

A.

Leadership and Governance

The country will require developing an AMC surveillance policy and address by whom, how and when national AMC datasets should be reported. This effort will ensure the successful delivery of the national surveillance plan that is currently in development. This activity could be led by the AMRCC.

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

The NDA could reconsider the registration status of unapproved fixed-dose antibiotic combinations. The national stewardship programmes, led by the AMRCC, could work to review the national treatment guidelines and the availability of the essential 'Reserve' category antibiotics within the country's essential medicines list.

B.

Service Delivery

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

National stewardship programs led by the AMRCC could conduct educational campaigns for healthcare practitioners to ensure that they are aware of the full spectrum of antimicrobials available in the country EML as well as ensure that unapproved FDC prescriptions are not used

C.

Medical products and technologies

National stewardship programmes could collaborate with pharmacists and medicine importers to increase the availability of more varieties of antibiotics as per the EMHSLU, including the availability of 'Reserve' category drugs in selected facilities.

Part E: Limitations

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

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

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

3. The 16 participating laboratories, may not fully represent the true resistance rates in the country as they only encompassed a small proportion of the country's population (over 45.7 million). Furthermore, as routine testing does not appear to be the norm in most hospitals and laboratories, the data may overestimate the resistance rates as infections that fail therapy may be more likely to be tested.

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

5. In relation to the national-level datasets, the private for-profit market was not covered although this market is estimated at roughly 30% of the total country's pharmaceutical market. This gap in data coverage (private for-profit wholesalers or distributors) may not comprehensively account for the range of antimicrobials in the country and therefore present an underestimation of their actual consumption.

6. A sample of 11 pharmacies were purposively selected for data collection. This sample size was a relatively small proportion of total pharmacies in Uganda and did not represent all districts. Therefore, a more systematic sampling strategy that factors in populations serviced and geographical locations will be required to make conclusions from pharmacy-level data more representative. Thirdly, MAAP was unable to collect AMC data from all targeted community pharmacies due to their unwillingness to share data or the inability to access the data from their systems or as a result of them not meeting the inclusion criteria.

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

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Glossary

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

AMR Appendices and Supplementary Tables

Appendix 1: Terms of Reference and Data Sharing Agreements

Data-Sharing Agreement

Between

Ministry of Health

(The Provider)

And

The African Society for Laboratory Medicine (ASLM)

(Recipient)

1. Purpose of Agreement.

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

2. Description of Data.

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

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

AMR and AMR associated data will be collected in laboratory facilities conducting antibiotic susceptibility testing and in clinical facilities linked to these 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:

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

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:

	Question	Response				Scoring
Part 1: Site Information (Maximum score=0)						
1.1	What is the name of the laboratory?					None
1.2	Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing?	Yes		No		None
1.3	Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium?	Yes		No		None
1.4	What is the address of the laboratory?					None
1.5	What is the laboratory's level of service?					None
	Reference- tier 3 or 4	Regional/Intermediate	District or community	Other		
1.6	What is the laboratory's affiliation?					None
	Government/Ministry of Health	Private	Non-government organisation	Other		
1.7	Is the laboratory co-located in a clinical facility?	Yes		No		None
1.8	Is a pharmacy co-located with the laboratory?	Yes		No		None
1.9	Did the laboratory serve as a national AMR surveillance site at any time between 2016 and 2018	Yes		No		None
1.10	Is your country participating in the World Health Organisation's Global Antimicrobial Resistance Surveillance System (WHO GLASS)?	Yes		No		None
Part 2: Commodity and Equipment (Maximum score=6)						
2.1	Did the laboratory have regular power supply with functional back up, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.2	Did the laboratory have continuous water supply, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.3	Did the laboratory have certified and functional biosafety cabinet, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.4	Did the laboratory have automated methods for bacterial identification, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.5	Did the laboratory have automated methods for antimicrobial susceptibility testing, in place at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
2.6	Did the laboratory test for mechanisms of antimicrobial resistance at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
Part 3. Quality Assurance (QA), Accreditation and Certification (Maximum score=10)						
3.1A	Was the laboratory implementing quality management systems at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.1B	If you answered 'yes' to question 1A: What quality management tools did the laboratory utilize? (e.g., LQMS, SLIPTA, SLMTA, mentoring, others)					Score 1 for "Yes" and 0 for "No
3.2A	Did the laboratory receive a quality certification at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.2B	If you answered 'yes' to question 2A: What kind of quality certification did the laboratory receive? (e.g., SLIPTA, College of American pathologists)					None
3.2C	If you answered 'yes' to question 2A: What was the laboratory's level of quality certification (e.g., star rating for SLIPTA certified laboratories)?					None
3.3A	Was the laboratory accredited by a national or international body at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.3B	If you answered 'yes' to question 3A: What was the name of the accreditation body/bodies?					None
3.4	Did the laboratory participate in an inter laboratory comparison or external quality assessment (EQA) scheme for pathogen identification and AST at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No
3.5	Did the laboratory utilize reference strains to verify that stains, reagents, and media are working correctly at any time between 2016-18?	Yes		No		Score 1 for "Yes" and 0 for "No

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

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

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

Part 5. Specimen Management (Maximum Score=3)

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

<200	200-1000	1000-3000	>3000

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

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

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

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

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

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

Laboratory	Clinical facility	Other

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

Appendix 4: Key AMR Variables

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

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

Appendix 5: WHO Priority Pathogens

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

**Previously known as Enterobacteriaceae.*

Appendix 6: Other clinically important pathogens

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

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

Appendix 7: Pathogen Phenotype Definitions

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

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

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

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

Appendix 8: Pathogens and antimicrobials for AMR drivers and DRI

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

AMR Supplementary Tables

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

Affiliation	Surveyed N = 20 n (%)	Reference N = 4 n (%)	Regional/ Intermediate N = 9 n (%)	District/ Community N = 3 n (%)	Unspecified N = 4 n (%)
Government	11 (55.0)	1 (25.0)	8 (88.9)	1 (33.3)	1 (25.0)
Private	6 (30.0)	2 (50.0)	1 (11.1)	1 (33.3)	2 (50.0)
NGO	2 (10.0)	0	0	1 (33.3)	1 (25.0)
Others	1 (5.0)	1 (25.0)	0	0	0

Supplementary Table 2: Assessment of preparedness for AMR surveillance

Parameters	Surveyed laboratories N=20 n (%)
Commodity and equipment status	
Regular power supply and functional back up	18 (90.0)
Continuous water supply	19 (95.0)
Certified and functional biosafety cabinets	17 (85.0)
Automated methods for pathogen identification	9 (45.0)
Automated methods for antimicrobial susceptibility testing	5 (25.0)
Methods for testing antimicrobial resistance mechanisms	12 (60.0)
QMS implementation	
Reported QMS Implementation	**18 (90.0)**
• Reported QMS tool (n=18)	
• LQMS	**3 (16.7)**
• SLIPTA	**1 (5.6)**
• SLMTA	**1 (5.6)**
• Mentoring	**0 (0)**
• Combination‡	**9 (50.0)**
• Others	**4 (22.2)**
Quality Certification	**16 (80.0)**
• Reported certification type (n=16)	
• SLIPTA	**7 (43.8)**
• College of American Pathologists	**1 (6.3)**
• Others	**8 (50.0)**
Accreditation	5 (25.0)
Participation in proficiency testing	16 (84.2)
Utilization of reference strains	19 (95.0)
Reported consistent maintenance of QC records	18 (90.0)
Designated focal quality person	19 (95.0)
Reported compliance to standard operating procedures	19 (95.0)
Reported compliance to antimicrobial susceptibility testing standards	19 (95.0)
Personnel and training status	
Presence of at least one qualified microbiologist	9 (45.0)
Presence of an experienced laboratory scientist/technologist	20 (100.0)
Up-to-date and complete records on staff training and competence	17 (85.0)
Specimen Management status	
Reported compliance to standard operating procedures on specimen collection and testing	20 (100.0)
Reported compliance to standard operating procedures on specimen rejection	20 (100.0)
Availability on average number of specimens processed for culture and sensitivity in year 2018	20 (100.0)
Laboratory Information System and Linkage to Clinical Data	
Assigned specimen (laboratory) identification number	19 (95.0)
Availability of system/database to store patient data	19 (95.0)
• System/database format (n=19)	
• Paper-based	7 (77.8)
• Electronic	1 (11.1)
• Mixed	11 (55.0)
Captured patients' demographics and clinical information on test request forms	20 (100.0)
• Retrievable test request forms (n=20)	16 (80.0)

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

Supplementary Table 3: Culture characteristics (yearly)

Variable		Valid			Positive			Positive with AS		
		2016	2017	2018	2016	2017	2018	2016	2017	2018
Annual Totals		19878	26672	38546	6176	8045	14628	4821	6561	10967
Pathogen type	bacteria				5091 (82.4)	6819 (84.8)	12696 (86.8)	4821 (100.0)	6561 (100.0)	10958 (99.9)
	fungi				1085 (17.6)	1226 (15.2)	1932 (13.2)	-	-	9 (0.1)
Age, years	Less than 1	834 (4.2)	930 (3.5)	1335 (3.5)	260 (4.2)	231 (2.9)	362 (2.5)	195 (4.0)	204 (3.1)	292 (2.7)
	1 to 17	3465 (17.4)	5635 (21.1)	13660 (35.4)	679 (11.0)	1188 (14.8)	4058 (27.7)	561 (11.6)	924 (14.1)	2825 (25.8)
	18 to 49	8394 (42.2)	10460 (39.2)	15746 (40.8)	2524 (40.9)	3240 (40.3)	7018 (48.0)	1688 (35.0)	2392 (36.5)	5425 (49.5)
	50 to 65	1385 (7.0)	1516 (5.7)	2349 (6.1)	352 (5.7)	437 (5.4)	1108 (7.6)	282 (5.8)	372 (5.7)	917 (8.4)
	Above 65	915 (4.6)	1163 (4.4)	1662 (4.3)	296 (4.8)	410 (5.1)	900 (6.2)	235 (4.9)	339 (5.2)	710 (6.5)
	Unknown Age	4885 (24.6)	6968 (26.1)	3794 (9.8)	2065 (33.4)	2539 (31.6)	1182 (8.1)	1860 (38.6)	2330 (35.5)	798 (7.3)
Gender	Male	8555 (43.0)	10759 (40.3)	16401 (42.5)	2155 (34.9)	2921 (36.3)	5110 (34.9)	1885 (39.1)	2593 (39.5)	4160 (37.9)
	Female	11323 (57.0)	15913 (59.7)	22145 (57.5)	4021 (65.1)	5124 (63.7)	9518 (65.1)	2936 (60.9)	3968 (60.5)	6807 (62.1)
Laboratory	Lancet	8334 (41.9)	10204 (38.3)	9321 (24.2)	3236 (52.4)	4011 (49.9)	3893 (26.6)	2408 (49.9)	3110 (47.4)	2895 (26.4)
	St. Francis	1092 (5.5)	1552 (5.8)	1614 (4.2)	622 (10.1)	904 (11.2)	1064 (7.3)	518 (10.7)	764 (11.6)	918 (8.4)
	Makerere	843 (4.2)	818 (3.1)	-	407 (6.6)	492 (6.1)	-	304 (6.3)	404 (6.2)	-
	NMRL	-	-	2585 (6.7)	-	-	1012 (6.9)	-	-	876 (8.0)
	Nakasero	-	-	1046 (2.7)	-	-	356 (2.4)	-	-	301 (2.7)
	Kagando	53 (0.3)	76 (0.3)	17 (0.0)	14 (0.2)	28 (0.3)	7 (0.0)	14 (0.3)	27 (0.4)	7 (0.1)
	Jinja	666 (3.4)	116 (0.4)	2103 (5.5)	117 (1.9)	74 (0.9)	247 (1.7)	27 (0.6)	68 (1.0)	164 (1.5)
	Fortportal	6 (0.0)	242 (0.9)	526 (1.4)	3 (0.0)	67 (0.8)	200 (1.4)	3 (0.1)	54 (0.8)	163 (1.5)
	Ebenezer	2633 (13.2)	4523 (17.0)	2589 (6.7)	590 (9.6)	854 (10.6)	635 (4.3)	475 (9.9)	700 (10.7)	414 (3.8)
	Mbale	-	-	1977 (5.1)	-	-	576 (3.9)	-	-	474 (4.3)
	Mengo	-	-	3111 (8.1)	-	-	2002 (13.7)	-	-	1719 (15.7)
	Kabale	-	-	1445 (3.7)	-	-	362 (2.5)	-	-	297 (2.7)
	Arua	467 (2.3)	865 (3.2)	913 (2.4)	79 (1.3)	78 (1.0)	249 (1.7)	62 (1.3)	43 (0.7)	220 (2.0)
	Gulu	2112 (10.6)	2278 (8.5)	2079 (5.4)	343 (5.6)	458 (5.7)	464 (3.2)	326 (6.8)	433 (6.6)	443 (4.0)
	Mulago	3672 (18.5)	5998 (22.55)	3410 (8.8)	765 (12.4)	1079 (13.4)	745 (5.1)	684 (14.2)	958 (14.6)	634 (5.8)
	Mbarara	-	-	5810 (15.1)	-	-	2816 (19.3)	-	-	1442 (13.1)

Supplementary Table 4: Specimen characteristics

Specimen Type	All years* N= 22349 n (%)	2016 N = 4821 n (%)	2017 N = 6561 n (%)	2018 N = 10967 n (%)
Abscess (brain/cerebral)	4 (0)	3 (0.1)	1 (0)	-
Abscess/Discharge/Pus/Swab/Wound	5340 (23.9)	1173 (24.3)	1610 (24.5)	2557 (23.3)
Aspirate/discharge	279 (1.2)	61 (1.3)	120 (1.8)	98 (0.9)
Blood	2222 (9.9)	653 (13.5)	655 (10)	914 (8.3)
Catheter (central line)	1 (0)	-	-	1 (0)
Catheter (umbilical)	1 (0)	-	-	1 (0)
Catheter (unspecified)	182 (0.8)	99 (2.1)	69 (1.1)	14 (0.1)
Catheter (urinary)	3 (0)	1 (0)	2 (0)	-
Catheter tip	3 (0)	-	-	3 (0)
CSF	181 (0.8)	59 (1.2)	57 (0.9)	65 (0.6)
Drain	2 (0)	-	-	2 (0)
Fluid (abdominal/peritoneal)	35 (0.2)	7 (0.1)	15 (0.2)	13 (0.1)
Fluid (Gastric)	10 (0)	2 (0)	6 (0.1)	2 (0)
Fluid (joint/synovial)	11 (0)	3 (0.1)	6 (0.1)	2 (0)
Fluid (pericardial)	1 (0)	-	-	1 (0)
Fluid (pleural)	52 (0.2)	11 (0.2)	14 (0.2)	27 (0.2)
Fluid (scrotal)	6 (0)	1 (0)	1 (0)	4 (0)
Fluid (sinus)	2 (0)	-	2 (0)	-
Fluid (unspecified)	75 (0.3)	13 (0.3)	28 (0.4)	34 (0.3)
Genitourinary	11 (0)	5 (0.1)	2 (0)	4 (0)
Respiratory-Lower	409 (1.8)	113 (2.3)	213 (3.2)	83 (0.8)
Respiratory-Upper	456 (2)	69 (1.4)	92 (1.4)	295 (2.7)
Scraping (cornea)	8 (0)	-	-	8 (0.1)
Semen	3 (0)	-	1 (0)	2 (0)
Stool	471 (2.1)	16 (0.3)	31 (0.5)	424 (3.9)
Swab (cervical)	5 (0)	-	2 (0)	3 (0)
Swab (high vaginal)	190 (0.9)	-	-	190 (1.7)
Swab (rectal)	47 (0.2)	-	20 (0.3)	27 (0.2)
Swab (urethral)	350 (1.6)	65 (1.3)	92 (1.4)	193 (1.8)
Swab (vaginal)	2299 (10.3)	408 (8.5)	436 (6.6)	1455 (13.3)
Swab/discharge	57 (0.3)	-	1 (0)	56 (0.5)
Swab/discharge (ear)	55 (0.2)	3 (0.1)	-	52 (0.5)
Swab/discharge (eye)	3 (0)	-	-	3 (0)
Swab/discharge (genital)	13 (0.1)	1 (0)	3 (0)	9 (0.1)
Swab/discharge (skin)	1 (0)	-	-	1 (0)
Swab/discharge (urethral)	31 (0.1)	-	-	31 (0.3)
Tissue/biopsy	139 (0.6)	39 (0.8)	50 (0.8)	50 (0.5)
Ulcer	4 (0)	2 (0)	-	2 (0)
Urine	9387 (42)	2014 (41.8)	3032 (46.2)	4341 (39.6)

**Indicates positive cultures with AST results*

Supplementary Table 5: Pathogen identification

Pathogen	All years* N=22349 n(%)	2016 N=4821 n(%)	2017 N=6561 n(%)	2018 N=10967 n(%)
Positive cultures with specific pathogen name	**17979 (80.4)**	**3931 (81.5)**	**5205 (79.3)**	**8857 (80.8)**
Achromobacter xylosoxidans	9 (0)	-	1 (0)	8 (0.1)
Acinetobacter baumannii	194 (0.9)	51 (1.1)	78 (1.2)	65 (0.6)
Acinetobacter calcoaceticus	11 (0)	5 (0.1)	6 (0.1)	-
Acinetobacter haemolyticus	3 (0)	1 (0)	-	2 (0)
Acinetobacter junii	2 (0)	-	1 (0)	1 (0)
Acinetobacter lwoffii	7 (0)	-	3 (0)	4 (0)
Aerococcus viridans	2 (0)	-	1 (0)	1 (0)
Aeromonas hydrophila	12 (0.1)	6 (0.1)	3 (0)	3 (0)
Aeromonas salmonicida	2 (0)	-	1 (0)	1 (0)
Aeromonas veronii	9 (0)	1 (0)	7 (0.1)	1 (0)
Bordetella bronchiseptica	1 (0)	-	-	1 (0)
Brucella melitensis	1 (0)	-	-	1 (0)
Burkholderia cepacia	29 (0.1)	14 (0.3)	6 (0.1)	9 (0.1)
Candida albicans	6 (0)	-	-	6 (0.1)
Cedecea lapagei	2 (0)	-	2 (0)	-
Chryseomonas luteola	13 (0.1)	4 (0.1)	4 (0.1)	5 (0)
Citrobacter braakii	26 (0.1)	3 (0.1)	7 (0.1)	16 (0.1)
Citrobacter farmeri	4 (0)	2 (0)	-	2 (0)
Citrobacter freundii	150 (0.7)	19 (0.4)	38 (0.6)	93 (0.8)
Citrobacter koseri	9 (0)	4 (0.1)	3 (0)	2 (0)
Citrobacter youngae	1 (0)	-	-	1 (0)
Cronobacter sakazakii	15 (0.1)	5 (0.1)	2 (0)	8 (0.1)
Cryptococcus neoformans	1 (0)	-	-	1 (0)
Enterobacter amnigenus	2 (0)	-	1 (0)	1 (0)
Enterobacter cancerogenus	1 (0)	-	1 (0)	-
Enterobacter cloacae	95 (0.4)	33 (0.7)	22 (0.3)	40 (0.4)
Enterococcus casseliflavus	27 (0.1)	-	-	27 (0.2)
Enterococcus cecorum	46 (0.2)	10 (0.2)	9 (0.1)	27 (0.2)
Enterococcus faecalis	1255 (5.6)	254 (5.3)	483 (7.4)	518 (4.7)
Enterococcus faecium	34 (0.2)	21 (0.4)	2 (0)	11 (0.1)
Enterococcus gallinarum	2 (0)	1 (0)	-	1 (0)
Escherichia coli	6424 (28.7)	1444 (30)	2029 (30.9)	2951 (26.9)
Escherichia vulneris	2 (0)	1 (0)	1 (0)	-
Flavimonas oryzihabitans	7 (0)	1 (0)	4 (0.1)	2 (0)
Granulicatella adiacens	9 (0)	2 (0)	6 (0.1)	1 (0)
Haemophilus influenzae	10 (0)	5 (0.1)	3 (0)	2 (0)
Haemophilus parainfluenzae	3 (0)	1 (0)	2 (0)	-
Hafnia alvei	3 (0)	2 (0)	1 (0)	-
Klebsiella aerogenes	35 (0.2)	7 (0.1)	9 (0.1)	19 (0.2)

Klebsiella oxytoca	78 (0.3)	22 (0.5)	25 (0.4)	31 (0.3)
Klebsiella pneumoniae	1180 (5.3)	288 (6)	409 (6.2)	483 (4.4)
Kluyvera intermedia	1 (0)	-	1 (0)	-
Kocuria kristinae	50 (0.2)	12 (0.2)	17 (0.3)	21 (0.2)
Kocuria rosea	3 (0)	-	-	3 (0)
Lactococcus garvieae	14 (0.1)	10 (0.2)	4 (0.1)	-
Leuconostoc mesenteriodes	9 (0)	3 (0.1)	3 (0)	3 (0)
Leuconostoc pseudomesenteriodes	1 (0)	-	-	1 (0)
Listeria monocytogenes	1 (0)	-	1 (0)	-
Melissococcus pluton	1 (0)	-	-	1 (0)
Micrococcus luteus	31 (0.1)	7 (0.1)	21 (0.3)	3 (0)
Moraxella catarrhalis	64 (0.3)	16 (0.3)	29 (0.4)	19 (0.2)
Moraxella nonliquefaciens	1 (0)	-	-	1 (0)
Morganella morganii	93 (0.4)	13 (0.3)	18 (0.3)	62 (0.6)
Neisseria gonorrhoeae	92 (0.4)	7 (0.1)	11 (0.2)	74 (0.7)
Neisseria meningitidis	11 (0)	-	3 (0)	8 (0.1)
Ochrobactrum anthropi	6 (0)	2 (0)	3 (0)	1 (0)
Pantoea (enterobacter) agglomerans	2 (0)	-	-	2 (0)
Pasteurella aerogenes	1 (0)	-	-	1 (0)
Pasteurella pneumotropica	1 (0)	-	1 (0)	-
Proteus mirabilis	342 (1.5)	73 (1.5)	104 (1.6)	165 (1.5)
Proteus vulgaris	128 (0.6)	10 (0.2)	20 (0.3)	98 (0.9)
Providencia rettgeri	2 (0)	-	-	2 (0)
Providencia rustigianii	1 (0)	-	1 (0)	-
Providencia stuartii	2 (0)	-	-	2 (0)
Pseudomonas aeruginosa	623 (2.8)	153 (3.2)	213 (3.2)	257 (2.3)
Pseudomonas alcaligenes	3 (0)	2 (0)	1 (0)	-
Pseudomonas fluorescens	30 (0.1)	10 (0.2)	11 (0.2)	9 (0.1)
Pseudomonas mendocina	1 (0)	1 (0)	-	-
Pseudomonas pseudoalcaligenes	1 (0)	-	-	1 (0)
Pseudomonas putida	6 (0)	5 (0.1)	1 (0)	-
Pseudomonas stutzeri	9 (0)	2 (0)	3 (0)	4 (0)
Rahnella aquatilis	2 (0)	-	-	2 (0)
Raoultella ornithinolytica	63 (0.3)	27 (0.6)	14 (0.2)	22 (0.2)
Raoultella planticola	1 (0)	-	-	1 (0)
Salmonella enterica	1 (0)	-	-	1 (0)
Salmonella paratyphi	3 (0)	1 (0)	-	2 (0)
Salmonella typhi	70 (0.3)	5 (0.1)	9 (0.1)	56 (0.5)
Serratia ficaria	6 (0)	-	3 (0)	3 (0)
Serratia fonticola	18 (0.1)	4 (0.1)	10 (0.2)	4 (0)
Serratia liquefaciens	9 (0)	2 (0)	2 (0)	5 (0)
Serratia marcescens	153 (0.7)	9 (0.2)	5 (0.1)	139 (1.3)
Serratia odorifera	15 (0.1)	2 (0)	6 (0.1)	7 (0.1)

Serratia plymuthica	2 (0)	-	-	2 (0)
Serratia rubidaea	2 (0)	2 (0)	-	-
Shigella boydii	8 (0)	-	7 (0.1)	1 (0)
Shigella dysenteriae	4 (0)	-	1 (0)	3 (0)
Shigella flexneri	5 (0)	-	-	5 (0)
Shigella sonnei	9 (0)	1 (0)	-	8 (0.1)
Sphingobacterium multivorum	2 (0)	2 (0)	-	-
Sphingomonas paucimobilis	35 (0.2)	7 (0.1)	4 (0.1)	24 (0.2)
Staphylococcus aureus	4732 (21.2)	981 (20.3)	1048 (16)	2703 (24.6)
Staphylococcus auricularis	1 (0)	-	-	1 (0)
Staphylococcus epidermidis	181 (0.8)	42 (0.9)	78 (1.2)	61 (0.6)
Staphylococcus haemolyticus	242 (1.1)	62 (1.3)	73 (1.1)	107 (1)
Staphylococcus hominis	17 (0.1)	5 (0.1)	4 (0.1)	8 (0.1)
Staphylococcus intermedius	1 (0)	1 (0)	-	-
Staphylococcus lugdunensis	6 (0)	-	3 (0)	3 (0)
Staphylococcus pseudintermedius	35 (0.2)	10 (0.2)	18 (0.3)	7 (0.1)
Staphylococcus saprophyticus	152 (0.7)	43 (0.9)	55 (0.8)	54 (0.5)
Staphylococcus sciuri	44 (0.2)	22 (0.5)	18 (0.3)	4 (0)
Staphylococcus warneri	1 (0)	-	1 (0)	-
Staphylococcus xylosus	22 (0.1)	7 (0.1)	12 (0.2)	3 (0)
Stenotrophomonas (xanthomonas) maltophilia	11 (0)	4 (0.1)	7 (0.1)	-
Streptococcus agalactiae	58 (0.3)	20 (0.4)	26 (0.4)	12 (0.1)
Streptococcus anginosus	1 (0)	-	1 (0)	-
Streptococcus bovis	7 (0)	-	2 (0)	5 (0)
Streptococcus lutetiensis	3 (0)	2 (0)	-	1 (0)
Streptococcus milleri	1 (0)	1 (0)	-	-
Streptococcus mitis	21 (0.1)	-	-	21 (0.2)
Streptococcus pleomorphus	1 (0)	-	1 (0)	-
Streptococcus pneumoniae	241 (1.1)	43 (0.9)	45 (0.7)	153 (1.4)
Streptococcus pyogenes	77 (0.3)	23 (0.5)	31 (0.5)	23 (0.2)
Streptococcus thoraltensis	2 (0)	1 (0)	-	1 (0)
Streptococcus uberis	1 (0)	-	1 (0)	-
Streptococcus viridans	183 (0.8)	63 (1.3)	71 (1.1)	49 (0.4)
Vibrio cholerae	277 (1.2)	6 (0.1)	13 (0.2)	258 (2.4)
Yersinia enterocolitica	1 (0)	-	-	1 (0)
Yersinia kristensenii	1 (0)	-	-	1 (0)
Positive cultures with non-specific pathogen name	4370 (?)	890 (18.5)	1356 (20.7)	2110 (19.2)
Abiotrophia Sp.	2 (0)	2 (0)	-	-
Acetobacterium Sp.	4 (0)	-	-	4 (0)
Achromobacter Sp.	4 (0)	-	-	4 (0)
Acinetobacter Sp.	302 (1.4)	70 (1.5)	112 (1.7)	120 (1.1)
Actinomyces Sp.	1 (0)	-	-	1 (0)
Bacillus Sp.	11 (0)	1 (0)	6 (0.1)	4 (0)

Campylobacter Sp.	1 (0)	-	-	1 (0)
Candida Sp.	2 (0)	-	-	2 (0)
Citrobacter Sp.	104 (0.5)	33 (0.7)	37 (0.6)	34 (0.3)
Corynebacterium Sp.	2 (0)	1 (0)	-	1 (0)
Enterobacter Sp.	115 (0.5)	14 (0.3)	31 (0.5)	70 (0.6)
Enterococcus Sp.	184 (0.8)	61 (1.3)	72 (1.1)	51 (0.5)
Haemophilus Sp.	2 (0)	-	1 (0)	1 (0)
Klebsiella Sp.	608 (2.7)	85 (1.8)	72 (1.1)	451 (4.1)
Kluyvera Sp.	3 (0)	-	-	3 (0)
Micrococcus Sp.	4 (0)	1 (0)	3 (0)	-
Moraxella Sp.	6 (0)	1 (0)	4 (0.1)	1 (0)
Morganella Sp.	4 (0)	1 (0)	-	3 (0)
Neisseria Sp.	7 (0)	-	2 (0)	5 (0)
Pantoea Sp.	27 (0.1)	6 (0.1)	9 (0.1)	12 (0.1)
Photobacterium Sp.	1 (0)	-	-	1 (0)
Proteus Sp.	183 (0.8)	12 (0.2)	31 (0.5)	140 (1.3)
Providencia Sp.	44 (0.2)	3 (0.1)	3 (0)	38 (0.3)
Pseudomonas Sp.	142 (0.6)	34 (0.7)	29 (0.4)	79 (0.7)
Ralstonia Sp.	6 (0)	3 (0.1)	3 (0)	-
Salmonella Sp.	170 (0.8)	34 (0.7)	47 (0.7)	89 (0.8)
Serratia Sp.	15 (0.1)	1 (0)	-	14 (0.1)
Shewanella Sp.	1 (0)	-	-	1 (0)
Shigella Sp.	24 (0.1)	1 (0)	2 (0)	21 (0.2)
Staphylococcus Sp.	1051 (4.7)	203 (4.2)	342 (5.2)	506 (4.6)
Streptococcus Sp.	418 (1.9)	116 (2.4)	125 (1.9)	177 (1.6)
Other Sp.	14 (0.1)	-	-	14 (0.1)
Unspecified (Gram negative bacilli)	888 (4)	206 (4.3)	416 (6.3)	266 (2.4)
Unspecified (Gram negative bacteria)	3 (0)	-	-	3 (0)
Unspecified (Gram negative cocci)	7 (0)	-	6 (0.1)	1 (0)
Unspecified (Gram positive bacilli)	1 (0)	-	1 (0)	-
Unspecified (Gram positive cocci)	8 (0)	1 (0)	2 (0)	5 (0)
Yersinia Species	1 (0)	-	-	1 (0)

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

Supplementary Table 6: Laboratory data scoring

Laboratory name	Laboratory data score (out of 4)			
	2016	2017	2018	Average
Lancet	4	4	4	4
St. Francis - Nsambya	4	4	4	4
Makerere Uni.	3	3	-	3
NMRL	-	-	4	4
Nakasero	-	-	4	4
Kagando	4	4	3	3.7
Jinja RRH	2	4	3	3
Fortportal	3	2	4	3
Ebenezer	4	4	3	3.7
Mbale	-	-	4	4
Mengo (MHL)	-	-	4	4
Kabale RRH	-	-	4	4
Arua Rrh	3	2	4	3
St. Mary's - Gulu	4	4	4	4
Mulago	3	3	3	3
Mbarara Uni.	-	-	3	3

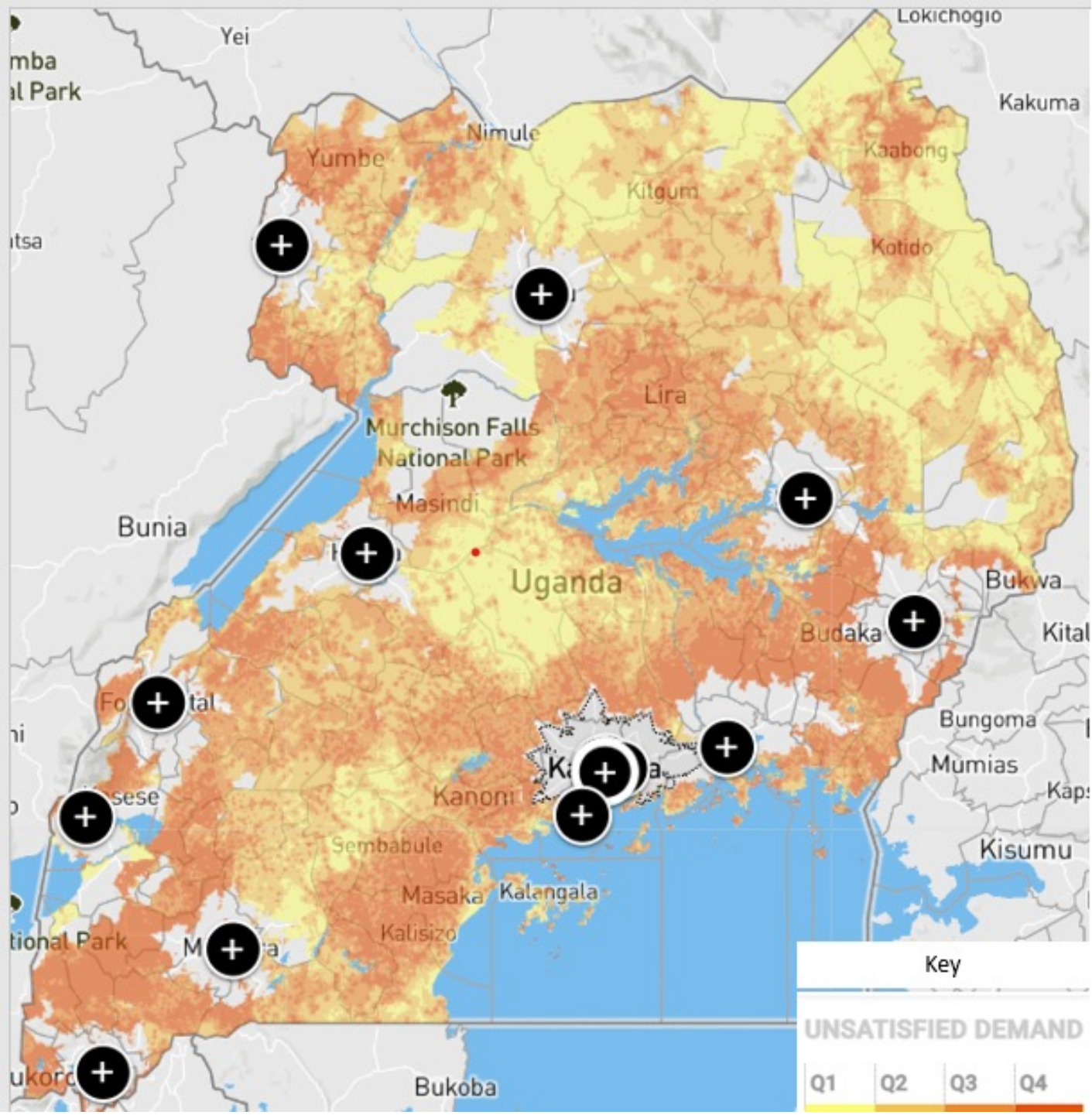
Supplementary Table 7: Univariate logistic regression analysis

Variable	Options	N	NS (%)	Crude OR (95% CI)	P-value
Gender	Female	24642	41.2	Ref	0.1062
	Male	12109	44.6	1.15 (0.97 - 1.36)	
Age, years	<1	723	49.2	1.36 (1.25 - 1.49)	0.0000
	1-17	8430	39.7	0.93 (0.82 - 1.04)	
	18-49	14436	41.6	Ref	
	50-65	2531	47.7	1.28 (1.20 - 1.37)	
	>65	1876	51.7	1.50 (1.28 - 1.76)	
Origin of infection	Community	256	47.7	Ref	0.0011
	Hospital	224	62.5	1.83 (1.77 - 1.90)	
Prior antibiotic usage	No	454	47.6	Ref	0.0547
	Yes	437	57.7	1.50 (0.99 – 2.27)	

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 Result	Antimicrobial Susceptibility Method	Year
Klebsiella pneumoniae ss. pneumoniae	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Enterococcus faecalis	Amphotericin B	AMB_ND10	R	Disk	2018
Klebsiella pneumoniae ss. pneumoniae	Amphotericin B	AMB_ND10	R	Disk	2018
Vibrio cholerae	Amphotericin B	AMB_ND10	I	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Enterococcus faecalis	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Klebsiella pneumoniae ss. pneumoniae	Amphotericin B	AMB_ND10	R	Disk	2018
Proteus mirabilis	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018
Enterococcus sp.	Amphotericin B	AMB_ND10	R	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	I	Disk	2018
Escherichia coli	Amphotericin B	AMB_ND10	R	Disk	2018

Supplementary Figure 2b: Inappropriate testing B

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

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 programmes, 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 programmes, 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 programmes, 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

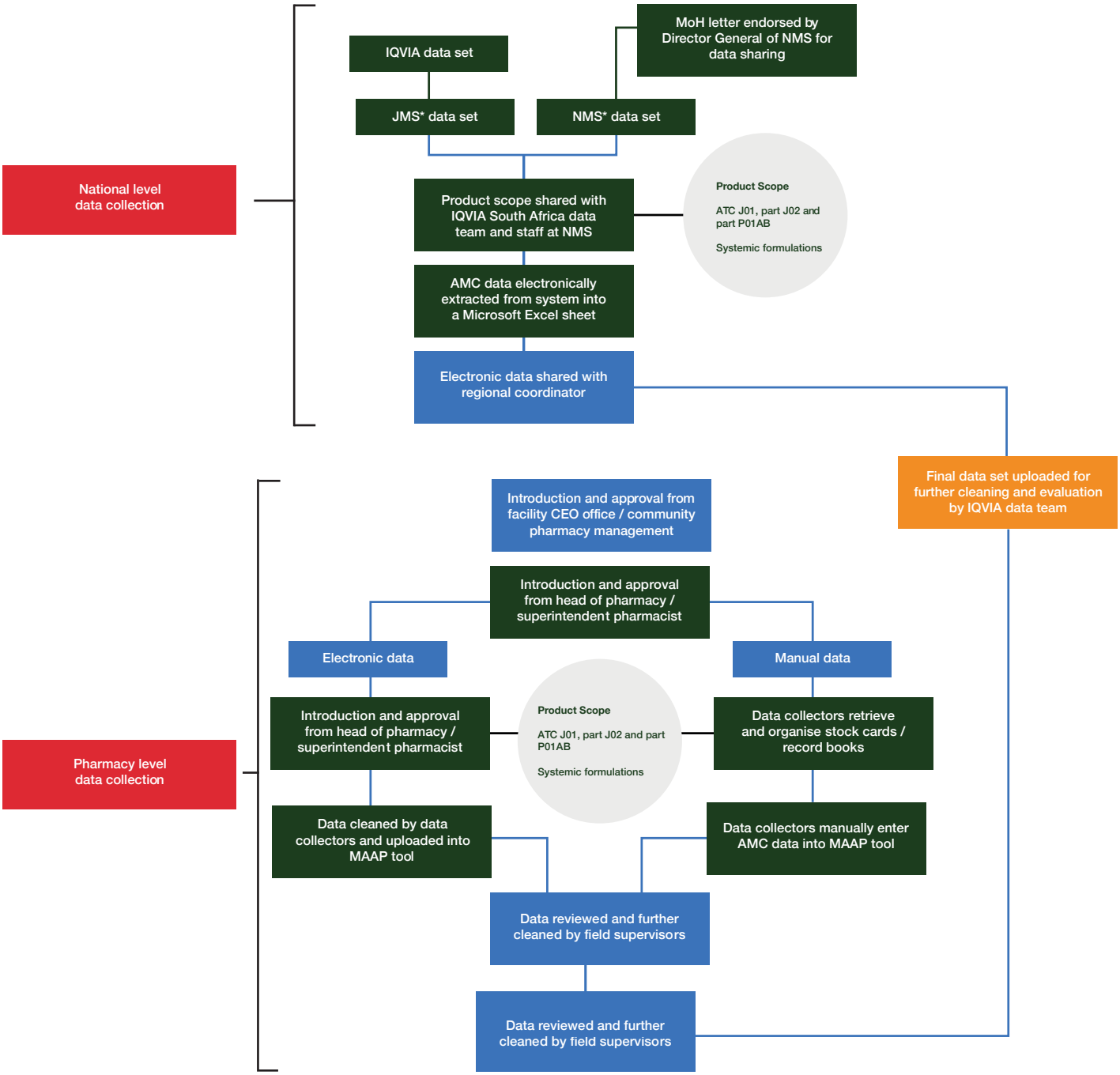
Spectinomycin	J01XX04	A
Linezolid	J01XX08	R
Daptomycin	J01XX09	R
Bacitracin	J01XX10	U
Tedizolid	J01XX11	R
Amphotericin B	J02AA01	N/A
Fluconazole	J02AC01	N/A
Itraconazole	J02AC02	N/A
Voriconazole	J02AC03	N/A
Posaconazole	J02AC04	N/A
Isavuconazole	J02AC05	N/A
Flucytosine	J02AX01	N/A
Caspofungin	J02AX04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



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

Appendix 6: Description of AMC analysis methodology

Defined Daily Dose (DDD) AMC Analysis:

DDD's were calculated as follows:

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

***WHO approved DDDs for antibiotics:**

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

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

The below formula summarizes how this calculation was done:

DDD/1000 Inhabitants/day =

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

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

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

DDD equivalent (%) =

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

*WHO approved DDDs for antibiotics:

WHO Anatomical Therapeutic Chemical (ATC) classification

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

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

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

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

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

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

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

Description of the AWaRe categories below:

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

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

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

Appendix 7: National AMC by Antimicrobial molecules

ATC Class Rank	AWaRe category	Molecule	2017	2018	Mean DDD/1000 inhabitant-days
			DDD/1000 inhabitant-days (%*)		
J01 Class		Total	6.68 (100)	6.02 (100)	6.348
1	Access	Amoxicillin	2.97 (44.5)	2.78 (46.1)	2.87
2	Access	Doxycycline	1.15 (17.2)	1.003 (16.7)	1.08
3	Access	Sulfamethoxazole/ Trimethoprim	1.04 (15.6)	0.66 (11)	0.85
4	Watch	Ciprofloxacin	0.75 (11.2)	0.68 (11.3)	0.72
5	Watch	Erythromycin	0.14 (2.1)	0.13 (2.1)	0.13
6	Uncategorised	Ampicillin/ Cloxacillin	0.11 (1.7)	0.12 (1.9)	0.11
7	Watch	Ceftriaxone	0.094 (1.4)	0.11 (1.8)	0.099
8	Access	Gentamicin	0.08 (1.2)	0.074 (1.2)	0.077
9	Watch	Azithromycin	0.06 (0.8)	0.088 (1.5)	0.072
10	Access	Nitrofurantoin	0.019 (0.3)	0.083 (1.4)	0.051
11	Access	Procaine benzylpenicillin	0.040 (0.6)	0.029 (0.5)	0.034
12	Watch	Levofloxacin	0.027 (0.4)	0.031 (0.5)	0.029
13	Access	Metronidazole	0.02 (0.3)	0.028 (0.5)	0.024
14	Access	Cloxacillin	0.017 (0.3)	0.026 (0.4)	0.022
15	Watch	Streptomycin	0.009 (0.1)	0.034 (0.6)	0.021
16	Access	Amoxicillin/ Clavulanic Acid	0.022 (0.3)	0.020 (0.3)	0.021
17	Access	Benzylpenicillin	0.02 (0.3)	0.019 (0.3)	0.020
18	Watch	Cefuroxime	0.021 (0.3)	0.016 (0.3)	0.019
19	Watch	Cefixime	0.018 (0.3)	0.015 (0.3)	0.017
20	Access	Cefalexin	0.015 (0.2)	0.012 (0.2)	0.013
21	Access	Ampicillin	0.012 (0.2)	0.0116 (0.2)	0.012
22	Access	Chloramphenicol	0.014 (0.2)	0.0098 (0.2)	0.012
23	Uncategorised	Amoxicillin/ Flucloxacillin	0.006 (0.1)	0.009 (0.2)	0.0076
24	Access	Phenoxymethylpenicillin	0.006 (0.1)	0.0077 (0.1)	0.007
25	Access	Benzathine benzylpenicillin	0.006 (0.1)	0.0059 (0.1)	0.0062
26	Watch	Moxifloxacin	0 (0)	0.0068 (0.1)	0.0034
27	Uncategorised	Cefixime/Clavulanic Acid	0.0011 (0)	0.0048 (0.1)	0.0030
28	Watch	Kanamycin	0.0021 (0)	0.0027 (0)	0.0024

29	Watch	Clarithromycin	0.00053 (0)	0.0036 (0.1)	0.0021
30	Watch	Pefloxacin	0.0017 (0)	0.0011 (0)	0.0014
31	Uncategorised	Nalidixic Acid	0.0015 (0)	0.00078 (0)	0.0012
32	Watch	Cefpodoxime proxetil	0.00061 (0)	0.0008 (0)	0.0007
33	Uncategorised	Ofloxacin/ Ornidazole	0.00019 (0)	0.00057 (0)	0.0004
34	Access	Tetracycline	0.00067 (0)	0 (0)	0.0003
35	Uncategorised	Ornidazole	0.00024 (0)	0.00027 (0)	0.0003
36	Reserve	Linezolid	0.000005 (0)	0.0004 (0)	0.0002
37	Uncategorised	Ceftriaxone/ Sulbactam	0.00006 (0)	0.0003 (0)	0.0002
38	Access	Clindamycin	0.00017 (0)	0.000098 (0)	0.0001
39	Uncategorised	Cefuroxime/ Clavulanic Acid	0 (0)	0.0002 (0)	0.0001
40	Watch	Piperacillin/ Tazobactam	0.00012 (0)	0.00009 (0)	0.0001
41	Watch	Ofloxacin	0.00007 (0)	0.00009 (0)	0.00008
42	Watch	Cefotaxime	0.00005 (0)	0.00009 (0)	0.00007
43	Watch	Meropenem	0.00007 (0)	0.00005 (0)	0.00006
44	Access	Amikacin	0.000001 (0)	0.00006 (0)	0.00003
45	Access	Cefazolin	0 (0)	0.00002 (0)	0.00001
46	Uncategorised	Azithromycin/ Fluconazole/ Secnidazole	0.000005 (0)	0.000006 (0)	0.000006
47	Watch	Imipenem/ Cilastatin	0.000001 (0)	0.000006 (0)	0.000004
48	Watch	Vancomycin	0 (0)	0.000001 (0)	0.000001
J02 Class		**Total**	**0.05 (100)**	**0.02 (100)**	**0.038**
1	Uncategorised	Ketoconazole	0.04 (75.3)	0.0073 (33.7)	0.024
2	Uncategorised	Fluconazole	0.013 (24.7)	0.014 (66.3)	0.014
P01 Class		**Total**	**0.98 (100)**	**0.99 (100)**	**0.986**
1	Access	Metronidazole	0.97 (99.4)	0.99 (99.5)	0.98
2	Uncategorised	Tinidazole	0.004 (0.4)	0.0035 (0.4)	0.0037
3	Uncategorised	Secnidazole	0.0018 (0.2)	0.0011 (0.1)	0.0014

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

Appendix 8: Breakdown of national AMC by ATC classes

	% consumption	
ATC class	2017	2018
Penicillins with extended spectrum	38.7%	39.6%
Tetracyclines	14.9%	14.3%
Nitroimidazole derivatives	12.7%	14.1%
Fluoroquinolones	10.1%	10.2%
Combinations of sulfonamides and trimethoprim, incl. Derivatives	13.5%	9.4%
Macrolides	2.5%	3.1%
Combinations of penicillins, incl. Beta-lactamase inhibitors	1.8%	2.1%
Third-generation cephalosporins	1.5%	1.8%
Aminoglycosides	1.2%	1.6%
Nitrofuran derivatives	0.2%	1.2%
Beta-lactamase sensitive penicillins	0.9%	0.9%
Imidazole derivatives	0.8%	0.5%
Beta-lactamase resistant penicillins	0.2%	0.4%
Second-generation cephalosporins	0.3%	0.2%
Triazole derivatives	0.2%	0.2%
First-generation cephalosporins	0.2%	0.2%
Amphenicols	0.2%	0.1%
Other quinolones*	0.0%	0.0%
Combinations of antibacterials*	0.0%	0.0%
Other antibacterials*	0.0%	0.0%
Lincosamides*	0.0%	0.0%
Carbapenems*	0.0%	0.0%
Glycopeptides*	0.0%	0.0%

** Consumption was recorded for the last six classes; however, rates were below 0.0% of the total AMC.*

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

Standardised Molecule Name	WHO AWaRe Categorisation	WHO ATC Code	WHO E ML	National EML	Documented Data
Amikacin	Access	J01GB06	Y	Y	Y
Amoxicillin	Access	J01CA04	Y	Y	Y
Amoxicillin/Clavulanic Acid	Access	J01CR02	Y	Y	Y
Amoxicillin/Flucloxacillin		J01CR50	N	N	Y
Amphotericin-B		J02AA01	N	Y	Y
Ampicillin	Access	J01CA01	Y	Y	Y
Ampicillin/Cloxacillin		J01CR50	N	N	Y
Azithromycin	Watch	J01FA10	Y	Y	Y
Azithromycin/Fluconazole/ Secnidazole		J01RA07	N	N	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	Y
Cefepime	Watch	J01DE01	N	N	Y
Cefiderocol	Reserve	J01DI04	Y	N	N
Cefixime	Watch	J01DD08	Y	Y	Y
Cefixime/Clavulanic Acid		J01DD--	N	N	Y
Cefoperazone/Sulbactam		J01DD62	N	N	Y
Cefotaxime	Watch	J01DD01	Y	N	Y
Cefpirome	Watch	J01DE02	N	N	Y
Cefpodoxime proxetil	Watch	J01DD13	N	N	Y
Ceftazidime	Watch	J01DD02	Y	N	Y
Ceftazidime/avibactam	Reserve	J01DD52	Y	N	N
Ceftriaxone	Watch	J01DD04	Y	Y	Y
Ceftriaxone/Sulbactam		J01DD63	N	N	Y
Cefuroxime	Watch	J01DC02	Y	Y	Y
Cefuroxime/Clavulanic Acid		J01DC--	N	N	Y
Chloramphenicol	Access	J01BA01	Y	Y	Y
Ciprofloxacin	Watch	J01MA02	Y	Y	Y
Clarithromycin	Watch	J01FA09	Y	N	Y
Clindamycin	Access	J01FF01	Y	Y	Y
Cloxacillin	Access	J01CF02	Y	Y	Y
Colistin	Reserve	J01XB01	Y	N	N
Doxycycline	Access	J01AA02	Y	Y	Y
Erythromycin	Watch	J01FA01	N	Y	Y
Fluconazole		J02AC01	N	Y	Y
Fosfomycin (IV)	Reserve	J01XX01	Y	N	N
Gentamicin	Access	J01GB03	Y	Y	Y

Imipenem/Cilastatin	Watch	J01DH51	N	Y	Y
Kanamycin	Watch	J01GB04	N	Y	Y
Ketoconazole		J02AB02	N	Y	Y
Levofloxacin	Watch	J01MA12	N	Y	Y
Linezolid	Reserve	J01XX08	Y	Y	Y
Meropenem	Watch	J01DH02	Y	Y	Y
Meropenem/Vaborbactam	Reserve	J01DH52	Y	N	N
Metronidazole	Access	P01AB01, J01XD01	Y	Y	Y
Moxifloxacin	Watch	J01MA14	N	Y	Y
Nalidixic Acid		J01MB02	N	N	Y
Nitrofurantoin	Access	J01XE01	Y	Y	Y
Ofloxacin	Watch	J01MA01	N	N	Y
Ofloxacin/Ornidazole		J01RA09	N	N	Y
Ornidazole		J01XD03	N	N	Y
Pefloxacin	Watch	J01MA03	N	N	Y
Phenoxymethylpenicillin	Access	J01CE02	Y	Y	Y
Piperacillin/Tazobactam	Watch	J01CR05	Y	Y	Y
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	N	N
Streptomycin	Watch	J01GA01	N	N	Y
Sulfamethoxazole/Trimethoprim	Access	J01EE01	Y	Y	Y
Tetracycline	Access	J01AA07	N	N	Y
Tinidazole		P01AB02	N	Y	Y
Trimethoprim	Access	J01EA01	Y	N	N
Vancomycin	Watch	J01XA01	Y	Y	Y

** Consumption was recorded for the last six classes; however, rates were below 0.0% of the total AMC.*

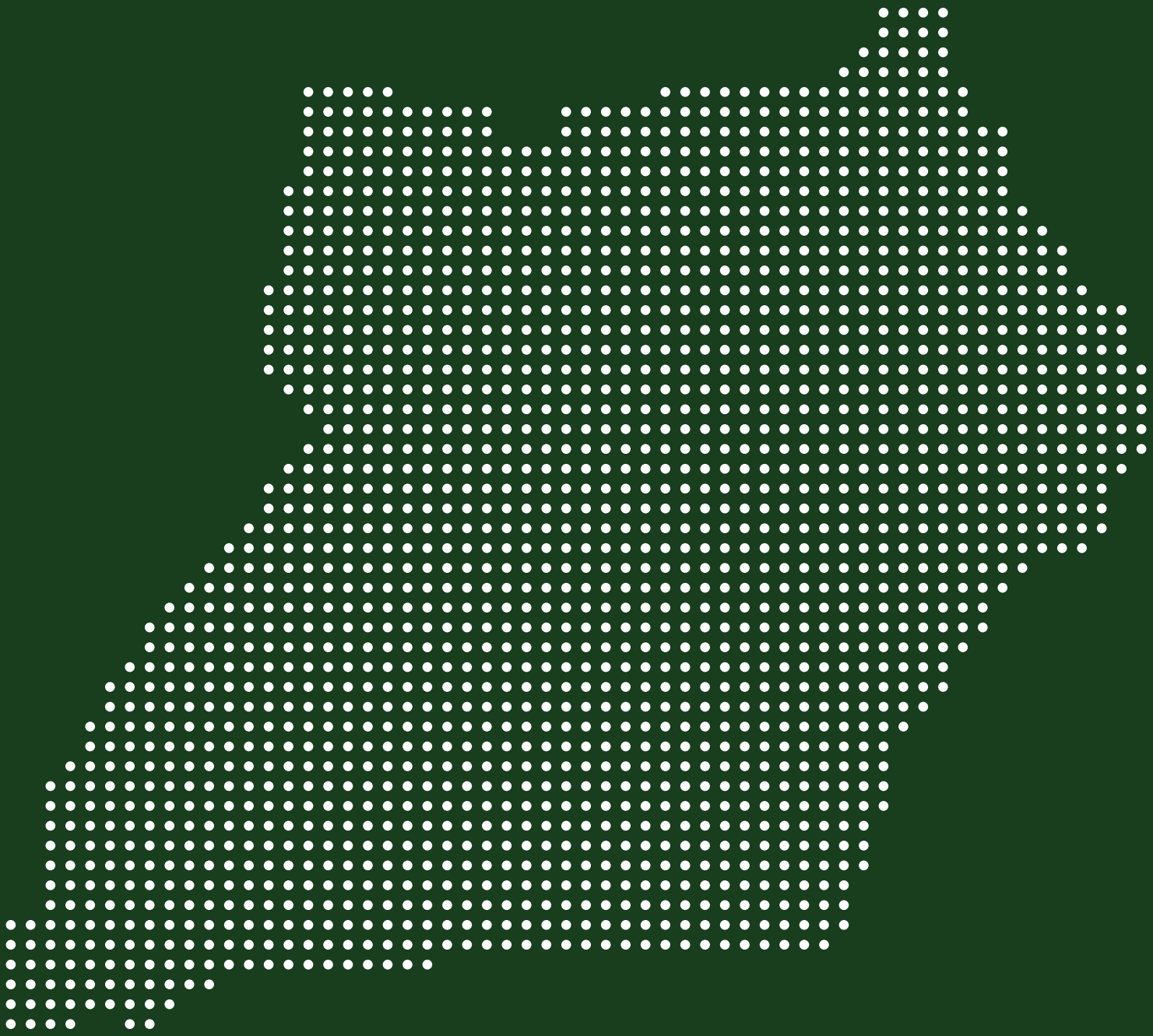
Appendix 10: AMC data collection and expired drug and losses tool

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



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