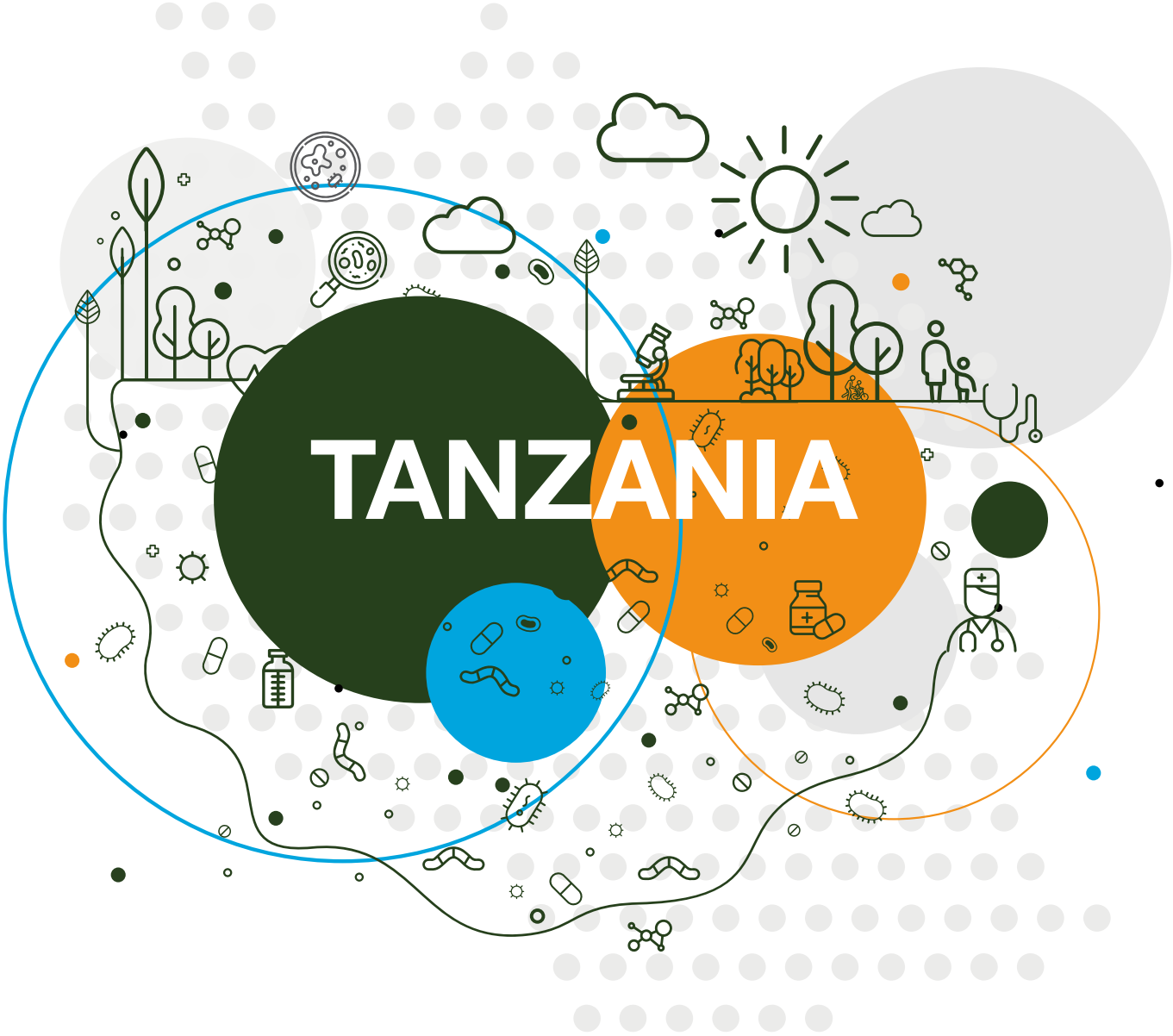
MAAP
Mapping AMR & AMU Partnership

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

Tanzania (2016-2018)

TANZANIA

Fleming Fund Regional Grant (Round 1)

Mapping Antimicrobial Resistance and Antimicrobial Use Partnership

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

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

Table of Contents

Abbreviations

AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMRCC	Antimicrobial Resistance Coordinating Committee
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	Centre for Disease Dynamics, Economics and Policy
CI	Confidence Interval
CLSI	Clinical and Laboratory Standards Institute
CMS	Central Medical Store
CSF	Cerebrospinal Fluid
DDD	Defined Daily Dose
DID	DDD per 1,000 inhabitants per day
DRI	Drug Resistance Index
ECSA-HC	East, Central and Southern Africa Health Community
EML	Essential Medicines List
EQA	External Quality Assessment
EUCAST	European Committee on Antibiotic Susceptibility Testing
FDC	Fixed Dose Combinations
GLASS	Global Antimicrobial Resistance Surveillance System
HIS	Hospital Information System
InSTEDD	Innovative Support to Emergencies, Diseases and Disasters
KIIs	Key Informant Interviews
LIS	Laboratory Information System
LMIC	Low- or Middle-Income Country
LQMS	Laboratory Quality Management System
MAAP	Mapping Antimicrobial resistance and Antimicrobial use Partnership
MEMS	Mission for Essential Medicine Supply
MSD	Medical Stores Department
MoH	Ministry of Health
NCD	Non-Communicable Disease(s)
NEMLIT	Tanzanian National Essential Medicines List
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
TSDA	Tanzania Medicines and Medical Devices Authority
WHO	World Health Organisation
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 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. The Regional Grant (Round 1) activities in Africa are led by The African Society for Laboratory Medicine (ASLM) and implemented by the 'Mapping Antimicrobial resistance and Antimicrobial use Partnership' (MAAP) consortium. This report summarises the activities undertaken by MAAP during implementation of the Regional Grant, and aims to determine national AMR, AMC and AMU surveillance capacity, resistance rates and trends as well as assess the antimicrobial flow in Tanzania during 2016-2018.

Tanzania had approximately 6 213 laboratories in the national laboratory network during the study period, of which 35 were reported to have capacity for bacteriology testing. Based on self-reported information from 27 laboratories, functioning and quality compliance were assessed to understand the laboratory preparedness for AMR surveillance.

AMR rates presented in this report are based on analysis of antimicrobial susceptibility results 0f 13,204 positive cultures obtained from 16 laboratories. High levels of resistance were noted for 3rd-generation cephalosporin-resistant Enterobacterales (54-62%), while moderate resistance was noted for methicillin-resistant Staphylococcus aureus (MRSA) (25-35%), carbapenem-resistant Pseudomonas aeruginosa (28-34%) and carbapenem-resistant Enterobacterales (18-24%). There was no association between the available patient variables and AMR. All results should be interpreted with caution because 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 was retrievable at selected sentinel pharmacies. AMU data were not obtained due to nature of the data sources used for AMC at participating pharmacies. The national AMC data for from the private (for-profit and not-for-profit) sector were inaccessible and the majority of the targeted community pharmacies didn't meet the inclusion criteria or were unable to share the data. The average national public sector AMC levels in Tanzania between 2016 and 2018 were 2.8 defined daily doses (DDD) per 1 000 inhabitants per day (DID), ranging from 2.0 for financial year 2016-2017 and 3.5 for 2017-2018.

Fluoroquinolones were found to be the most consumed antimicrobials according to the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) classification between 2016-2018 (range 14.7% to 23.1%). Combinations of sulfonamides and trimethoprim, including derivatives (range 14.2% to 18.6%) and penicillins with extended spectrum (range 13.6% and 10.3%) were the second- and third-leading ATC classes consumed. The top five most consumed antimicrobials were Ciprofloxacin, Sulfamethoxazole/trimethoprim, Amoxicillin, Doxycycline and Nitrofurantoin. Together, they accounted for 65% of the total consumption share suggesting lack of antimicrobial variation. This consumption trend could potentially increase AMR.

The total AMC came from 68.3% 'Access', 31.7% 'Watch' and 0.0% 'Reserve' antibiotics. Between July 2016-June 2018 antibiotics with narrow spectrum ('Access' category) were most used to treat common ailments and in fact exceeded the WHO minimum recommended consumption threshold of 60%. The lack of consumption of 'Reserve' category antibiotics within the public sector implied a possible unavailability of these last-resort antibiotics within this sector. However, consumption of a 'Reserve' category antibiotic (Polymyxin B) was observed only within the single private regional referral hospital pharmacy sampled. Two combinations of two or more broad-spectrum fixed-dose combinations (FDCs) of antimicrobials were identified that are not recommended for clinical utility but were nevertheless consumed in Tanzania. Of those FDCs Ampicillin/Cloxacillin was most commonly 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 59.8% (95% CI, 49.6-69.9%) 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 use of automation for data analyses. We also recommend establishing a system of assigning permanent identification numbers for patient 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 but on a larger scale in order to give a nationally representative portrait of antimicrobials use in 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 recommend that the country's Antimicrobial Resistance Coordinating Committee (AMRCC) consider the introduction of facility-level antimicrobial stewardship programmes (ASPs) in order 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 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 for an urgent review to be conducted by the Ministry of Health (MoH), AMRCC in an effort to assess the availability of the 'Reserve' category antibiotics in the country that may subsequently lead to the revision of the country's 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 essential medicines list (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 suboptimal 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 AMU, 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 or 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 'Mapping Antimicrobial resistance and Antimicrobial use Partnership' (MAAP), a multi-organisational consortium of strategic and technical partners. ASLM was the Lead Grantee for the programme.[3]

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 Centre for Disease Dynamics, Economics and Policy (CDDEP), IQVIA, and Innovative Support to Emergencies, Diseases and Disasters (InSTEDD). ASLM oversaw consortium activities and ensured fulfilment of ethical considerations and completion of data sharing agreements with the participating countries.

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

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

Fourteen African countries across West Africa (Burkina Faso, Ghana, Nigeria, Senegal and Sierra Leone), East (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 Tanzania 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 Tanzania, 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 AMC and AMU surveillance system in-country
- To quantify and evaluate the trends of AMC and AMU at national and pharmacy level.
- To assess the relationship between AMC and AMR through the DRI
- To assess the drivers of AMR

Outcome measures

- Number of laboratories from the national network generating AMR data and proportion of laboratories reporting compliance to standards of quality and bacteriology testing
- Level of AMR data completeness and validity among laboratories selected for AMR data collection
- AMR prevalence and trends for the WHO priority pathogens, other clinically important and frequently isolated pathogens
- A semi-quantitative analysis of current status in AMC and AMU surveillance in-country
- Total consumption of antimicrobials (defined daily dose), plus 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 existing 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 MoH, AMR coordinating committees, health facilities, laboratories, and pharmacies. This was followed by site selection and data collection in each country. Data analysis was done by the technical partners. The final results were then shared through dissemination meetings (Figure 1).

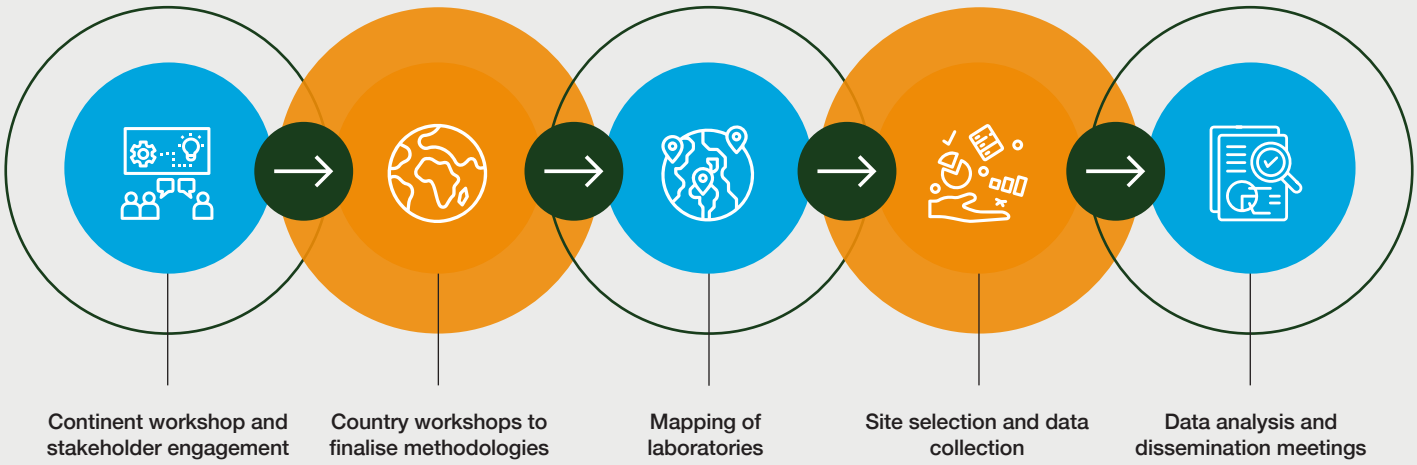


Figure 1: Key engagements and activities

Ethical issues and data sharing agreements

In order 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 AMR Appendix 1).

Country Profile

Health and demographic profile

As of 2020, Tanzania was estimated to have a population of 59.7 million inhabitants with a life expectancy of 66 years. The country has a high infectious disease burden with a TB incidence of 222 per 100 000 and an HIV prevalence of 4.7%. The country has a physician density rate of 0.06 per 1 000 inhabitants and nurse density rate of 0.58 per 1 000 inhabitants. With a universal health coverage index of 46, Tanzania appears to have an average coverage of essential services (Table 1).

Table 1: Health and demographic profile of Tanzania

	Tanzania		Comparator values (most recent year)*		
	Year	Value	India	Argentina	United States
Population	2020	59 734 213	1 380 004 390	45 376 763	329 484 123
Life expectancy during the study period, total (years)	2019	66	70	77	79
Universal health coverage service index (0-100)	2019	46	61	67	83
GDP per capita (current US$)	2020	1 076.47	1 927.7	8 579.0	63 593.4
Immunisation, DPT (% of children ages 12-23 months)	2019	89	91.0	86.0	94.0
Incidence of tuberculosis (per 100 000 people)	2020	222	188.0	31.0	2.4
Prevalence of HIV, total (% of population ages 15-49)#	2020	4.7	0.2*	0.4 2020	0.4 2019
Primary education (%)#	2020	68.74	94.6	98.6	100
Physicians density (physicians per 1 000)#	2014	0.06	0.93	4.0	2.6
Nurses density (nurses and midwives per 1 000)#	2017	0.58	2.39	2.60	15.69

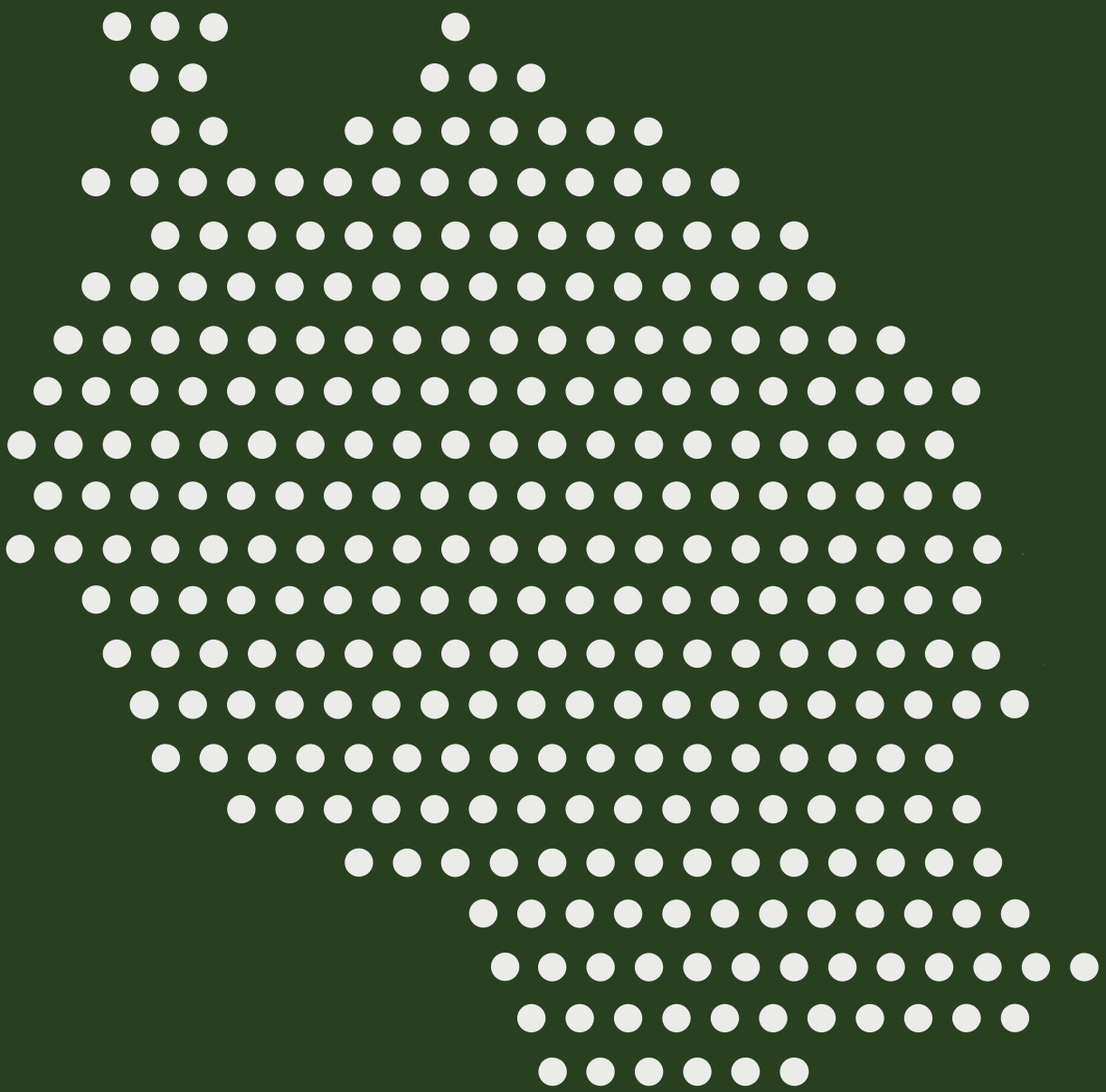
Sourced from World Bank[4,5 6] and *National AIDS Control Organisation[7]
#Data for some country parameters may not necessarily be of the same year (but sourced from the most recently available information between 2017-2020).

Policy frameworks

In May 2015, the World Health Assembly approved the Global Action Plan (GAP) on Antimicrobial Resistance.[8] Later that year, the WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS)[9] to support the implementation of the Global Action Plan on Antimicrobial Resistance and strengthen AMR surveillance and research. GLASS provides standardised methodologies for AMR data collection and analysis as well as 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.

Tanzania has documented its National Action Plan on Antimicrobial Resistance for the period of 2017-2027.[10] The document outlines the key strategic objectives, interventions and activities to slow the development and spread of AMR. The objectives are in line with the WHO Global Action Plan on AMR. Tanzania enrolled with GLASS in 2019, however, it has not started providing AMR data.[11] Tanzania has a system for reporting AMR data at the national level.

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 Tanzania, 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 Tanzania, 6 213 laboratories were mapped to the national laboratory network. An eligibility questionnaire was sent to 35 laboratories identified as having capacity for bacteriology testing. Of the 27 laboratories that responded to the questionnaire and had AST capacity, the majority were affiliated with the government (Table 2, Supplementary Table 1). The laboratory readiness scores of the surveyed laboratories varied widely (range: 76.3-39.5%). From the 27 laboratories. 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			
Central Pathology Laboratory Muhimbili National Hospital (Muhimbili)	76.3	Reference	Government
Aga Khan Hospital Dar Es Salaam (Aga Khan)	73.7	Reference	Private
St Benedict's Ndanda Referral Hospital Laboratory (St Benedict's)	71.1	Regional/Intermediate	Private
Haydom Lutheran Hosptal Clinical Laboratory (Haydom)	71.1	Reference	Private
Mawenzi Referral Regional Hospital Laboratory (Mawenzi)	68.4	Regional/Intermediate	Government
Dodoma Regional Referral Hospital Laboratory (Dodoma)	65.8	Regional/Intermediate	Government
Morogoro RRH (Morogoro)	65.8	Regional/Intermediate	Government
Sokoine RRH (Sokoine)	65.8	Regional/Intermediate	Government
Kilimanjaro Christian Medical Centre (KCMC)	65.8	Reference	Other
Central Pathology Laboratory-Bugando Medical Centre (Bugando)	65.8	Reference	Other
Sekou Toure RRH (Sekou)	63.2	Regional/Intermediate	Government
Pathology Laboratory Mnazi Mmoja Hospital (Mnazi Mmoja)	63.2	Reference	Government
Mbeya Zonal Referral Hospital (Mbeya)	63.2	Reference	Government
Iringa Regional Referral Hospital (Iringa)	63.2	Regional/Intermediate	Government
Bukoba Regional Referral Hospital Laboratory (Bukoba)	60.5	Regional/Intermediate	Government
Singida Regional Referral Hospital (Singida)	60.5	Regional/Intermediate	Government
Not selected			
Sumbawanga Regional Referral Hospital	71.1	Regional/Intermediate	Government
Musoma Regional Referral Laboratory	68.4	Regional/Intermediate	Government
St.Joseph Misson Hospital	68.4	Regional/Intermediate	NGO
Mbeya Regional Referral Hospital	63.2	Regional/Intermediate	Government
Tanga Regional Referral Hospital Laboratory	63.2	Regional/Intermediate	Government
Maweni Regional Referral Hospital	57.9	Regional/Intermediate	Government
Katavi Regional Referral Hospital Laboratory	55.3	Regional/Intermediate	Government
Temeke Regional Referral Hospital Laboratory	55.3	Regional/Intermediate	Government
Shinyanga Regional Referral Hospital	52.6	Regional/Intermediate	Government
Tumbi Regional Referral Laboratory	47.4	Regional/Intermediate	Government
Kitete Regional Referral Hospital Laboratory	39.5	Regional/Intermediate	Government

** Laboratory names are abbreviated.*

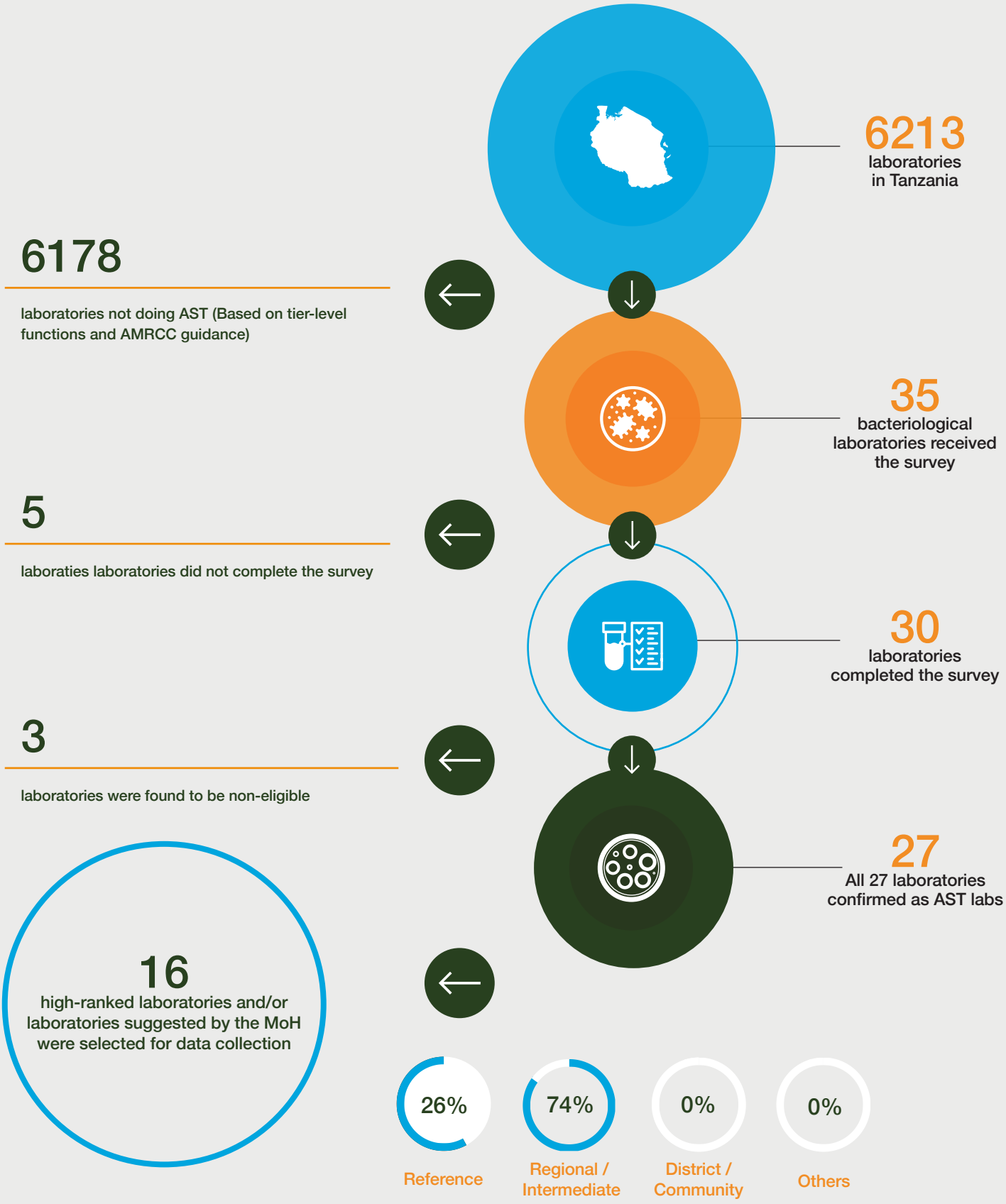


Figure 2: Selection of laboratories in Tanzania

Surveillance preparedness of surveyed laboratories

Based on self-reported information from 27 laboratories, laboratory function and quality compliance were assessed to understand the preparedness for AMR surveillance. Eleven laboratories had implemented quality management, eight used automated methods for pathogen identification while only one laboratory was accredited (Figure 3, 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.

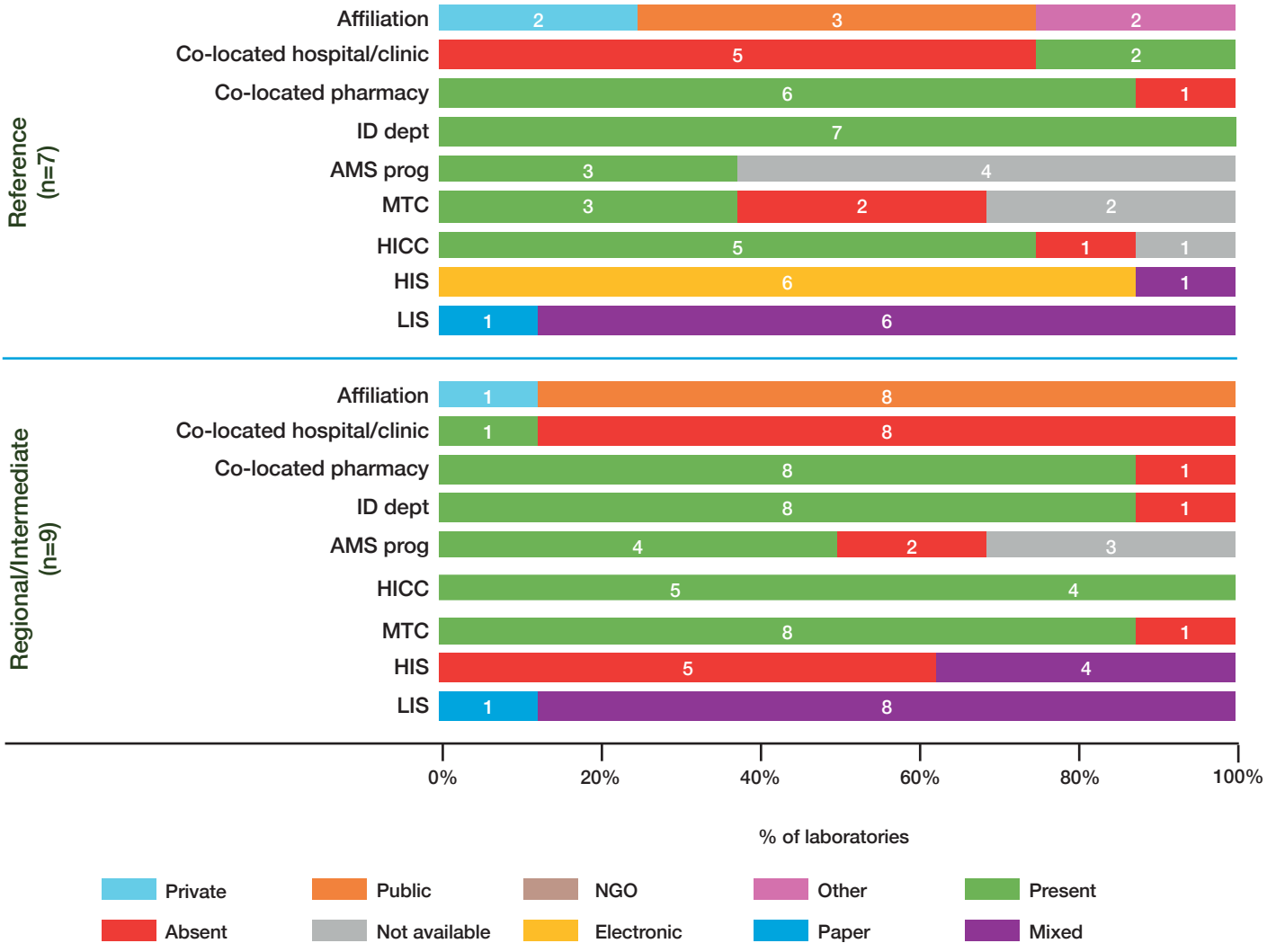
	Parameters			N (%)
Commodity and equipment status	Regular power supply and functional back up			27 (100.0)
	Continuous water supply)			27 (100.0)
	Certified and functional biosafety cabinets			23 (85.2)
	Automated methods for pathogen identification			1 (3.7)
	Automated methods for AST			2 (7.4)
	Methods for testing AMR mechanisms			12 (44.4)
QMS implementation	Reported QMS Implementation			27 (100)
		Types of QMS	LQMS	2 (7.4)
			SLIPTA	11 (40.7)
			SLMTA	2 (7.4)
			Mentoring	-
			Combination‡	2 (7.4)
			Others	10 (37.0)
	Quality Certification			19 (70.4)
		Types of Quality certification	SLIPTA	11 (57.9)
			Col. of Am. Path	-
			Others	8 (42.1)
	Accreditation			6 (22.2)
	Participation in proficiency testing			25 (92.6)
	Utilization of reference strains			25 (92.6)
	Reported consistent maintenance of QC records			25 (92.3)
	Designated focal quality person			25 (92.6)
	Reported compliance to standard operating procedures			27 (100.0)
	Reported compliance to AST standards			25 (92.6)
Personnel and training status	Presence of at least one qualified microbiologist			6 (22.2)
	Presence of an experienced laboratory scientist/technologist			27 (100.0)
	Up-to-date and complete records on staff training and competence			25 (92.6)
Specimen Management status	Reported compliance to SOPs on specimen collection and testing			27 (100.0)
	Reported compliance to SOPs on specimen rejection			27 (100.0)
	Average number of specimens processed for AST in 2018			25 (92.6)
LIS and Linkage to Clinical Data	Assigned specimen (laboratory) identification number			27 (100.0)
	Availability of system/database to store patient data			25 (92.6)
		Database format	Paper-based	4 (16.0)
			Electronic	-
			Mixed	21 (84.0)
	Captured patients' records on test request forms			25 (92.6)
			Retrievable	19 (76.0)

‡ Combination refers to more than one option presented in the questionnaire (laboratory quality management system, stepwise laboratory improvement

Figure 3: Laboratory preparedness for AMR surveillance

Profile of Selected Laboratories

Out of the 16 selected laboratories, 14 were co-located with clinical facilities. Eight clinical facilities had infectious disease departments, and only six had antimicrobial stewardship programmes. Medical therapeutic committees and hospital infection control committees were functional in 13 and 7 facilities, respectively. Most laboratories had mixed (paper and electronic) information systems, and six hospitals had electronic information systems (Figure 4).



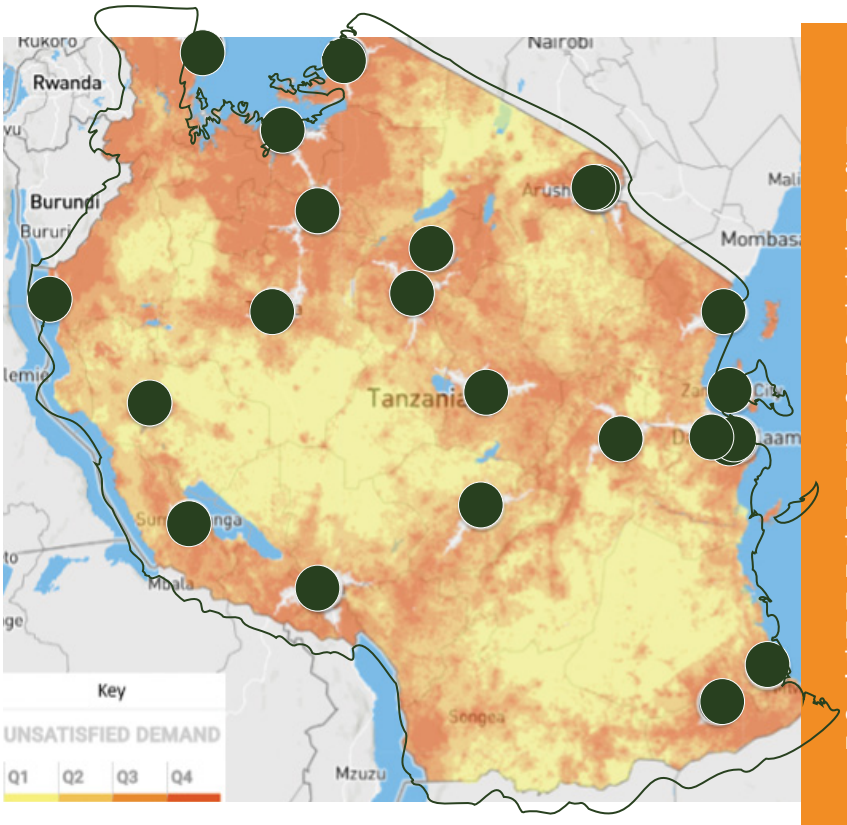
Abbreviations: AMS=antimicrobial stewardship; HICC=hospital infection control committee; HIS=hospital information system; IDD=infectious diseases department; LIS=laboratory information system; MTC=medical therapeutics committee

Figure 4: Profile of selected laboratories

Population coverage of laboratories

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

As of 2020, Tanzania had an estimated population of 59.73 million.



Supplementary Figure 1: Population coverage of AST laboratories in Tanzania

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 lab-oratory has sufficient testing capacity to serve the entire population within the catch-ment area. The population outside the catchment area of the facilities is, by definition, representative of the overall unmet need. For ease of use, the unit of unmet need is represented on the map as 'pixels', i.e., the lowest base unit of a raster image. To visualise the geographical areas with the most critical unmet needs, each base component is ranked from the lowest to the highest, according to the number of the population living in the 'pixel'. The ranking is then divided into quartiles made of equal population fractions (from Q1: lowest density of population to Q4: highest density), also corresponding to different colour (from yellow to dark red, see legend). 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 Tanzania, the catchment population living within 1 hours travel time from the 27 participating AMR surveillance sites covers **30%** of the population. Hence, 70% 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 lab to start providing services or by constructing a new lab) in regions in dark red (Q4), 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 level and national levels.

For laboratories with paper-based records, at least 5 000 records per laboratory per year were supposed 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[13] and use of the specially developed MAAP tool for secure transfer of collected data.

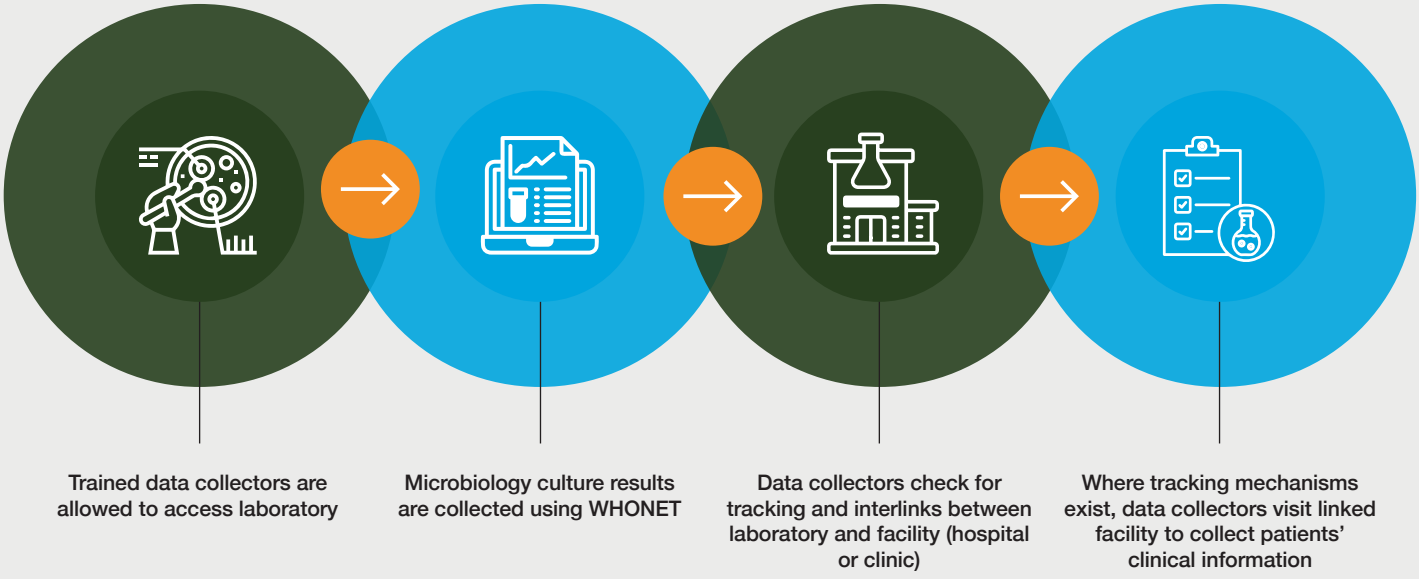


Figure 5: Steps of AMR data collection

Historical data were collected for the period January 1, 2016, through December to 31, 2018. The AMR data was 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.

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 was stratified for each laboratory and assessment was done over the entire study period (Figure 7).

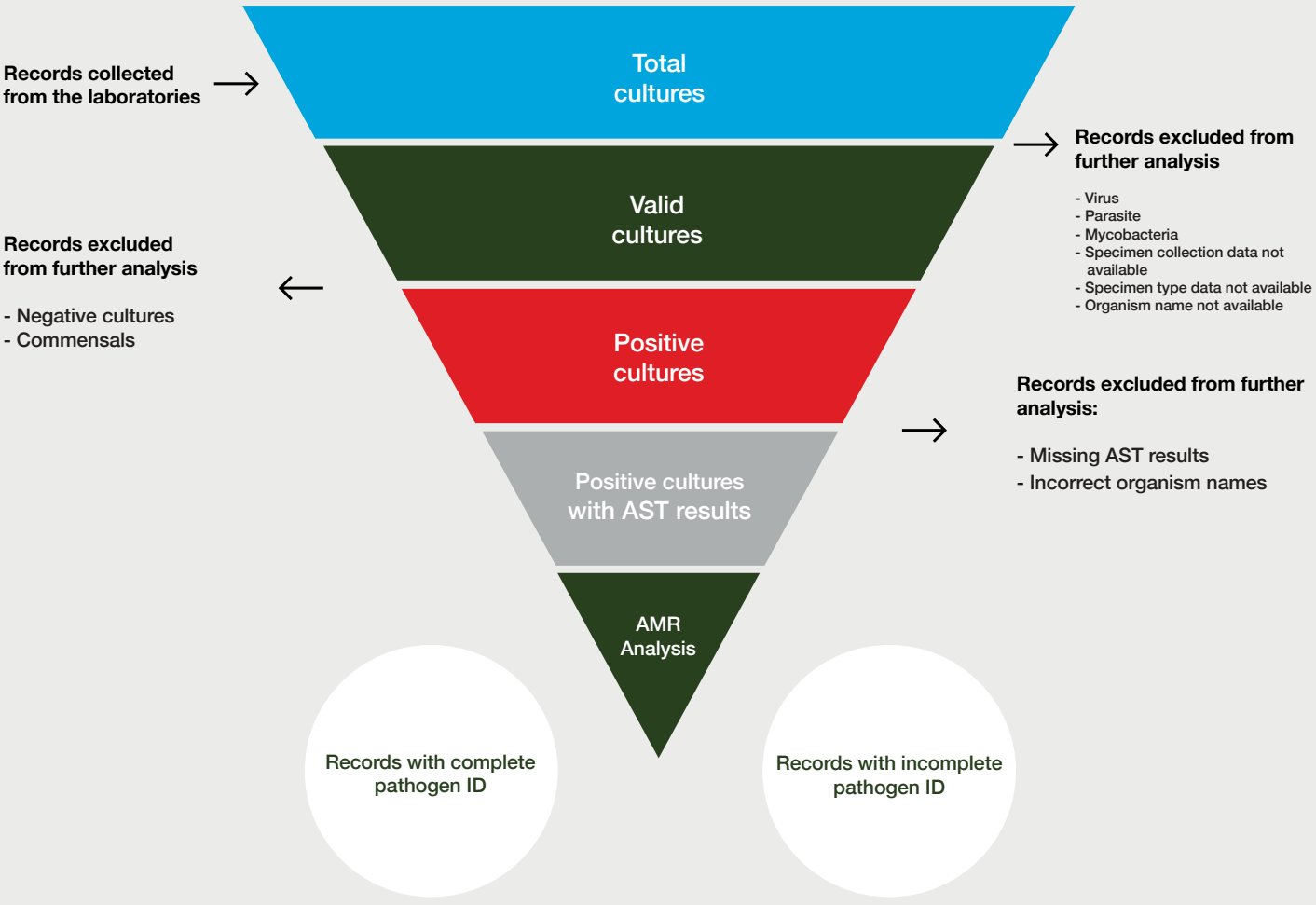


Figure 7: Conceptual framework for deriving quantum of cultures

Culture characteristics:

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

Inappropriate testing:

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

Clinical information:

Positive cultures with AST results were summarised based on information available for the patient's clinical profile: diagnosis, origin of infection (whether hospital acquired, or community acquired), presence of in-dwelling 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., 2017–2019). 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 Tanzania.

1. Quantum of cultures and level of pathogen identification

Data was retrieved for 77 550 total cultures, of which 72 587 were valid and 17 581 were positive. Of the positive cultures, AST results were available for 13 204 positive cultures, maximum (n=3 612) coming from Muhimbili and the least (n=43) from Mawenzi (Figure 7 and 8). Not all pathogens were identified completely (i.e., at species level). Complete identifications were highest for Sokoine laboratory (90.3%) and lowest for Aga Khan laboratory (27.5%) (Table 5).

Table 5: Data summary

Variable (Columns) / Laboratory (Rows)	Total Cultures N = 77 553	Valid Cultures N = 72 587	Positive cultures N = 17 581	Positive cultures with AST results N = 13 204	Incomplete identity* N = 5 625	Complete identity* N = 7 579
Muhimbili	27 565	24 427 (88.6)	3 618 (14.8)	3 612 (99.8)	1 810 (50.1)	1 802 (49.9)
Aga Khan	9 706	9 506 (97.9)	2 150 (22.6)	1 802 (83.8)	1 307 (72.5)	495 (27.5)
Ndanda	710	686 (96.6)	135 (19.7)	128 (94.8)	41 (32.0)	87 (68.0)
Haydom	412	411 (99.8)	88 (21.4)	85 (96.6)	50 (58.8)	35 (41.2)
Mawenzi	773	773 (100.0)	64 (8.3)	43 (67.2)	7 (16.3)	36 (83.7)
Dodoma	1 237	1 233 (99.7)	146 (11.8)	117 (80.1)	60 (51.3)	57 (48.7)
Morogoro	3 163	3 159 (99.9)	1 426 (45.1)	1 369 (96.0)	217 (15.9)	1 152 (84.1)
Sokoine	386	385 (99.7)	97 (25.2)	93 (95.9)	9 (9.7)	84 (90.3)
KCMC	11 163	10 514 (94.2)	3 655 (34.8)	1 486 (40.7)	646 (43.5)	840 (56.5)
Bugando	16 993	16 211 (95.4)	4 454 (27.5)	3 133 (70.3)	1 118 (35.7)	2 015 (64.3)
Sekou Toure	814	814 (100.0)	232 (28.5)	79 (34.1)	12 (15.2)	67 (84.8)
Mnazi Mmoja	891	852 (95.6)	430 (50.5)	380 (88.4)	57 (15.0)	323 (85.0)
Mbeya	2 811	2 701 (96.1)	790 (29.2)	628 (79.5)	232 (36.9)	396 (63.1)
Iringa	178	178 (100.0)	74 (41.6)	74 (100.0)	17 (23.0)	57 (77.0)
Bukoba	299	290 (97.0)	58 (20.0)	51 (87.9)	22 (43.1)	29 (56.9)
Singida	452	447 (98.9)	164 (36.7)	124 (75.6)	20 (16.1)	104 (83.9)

* 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

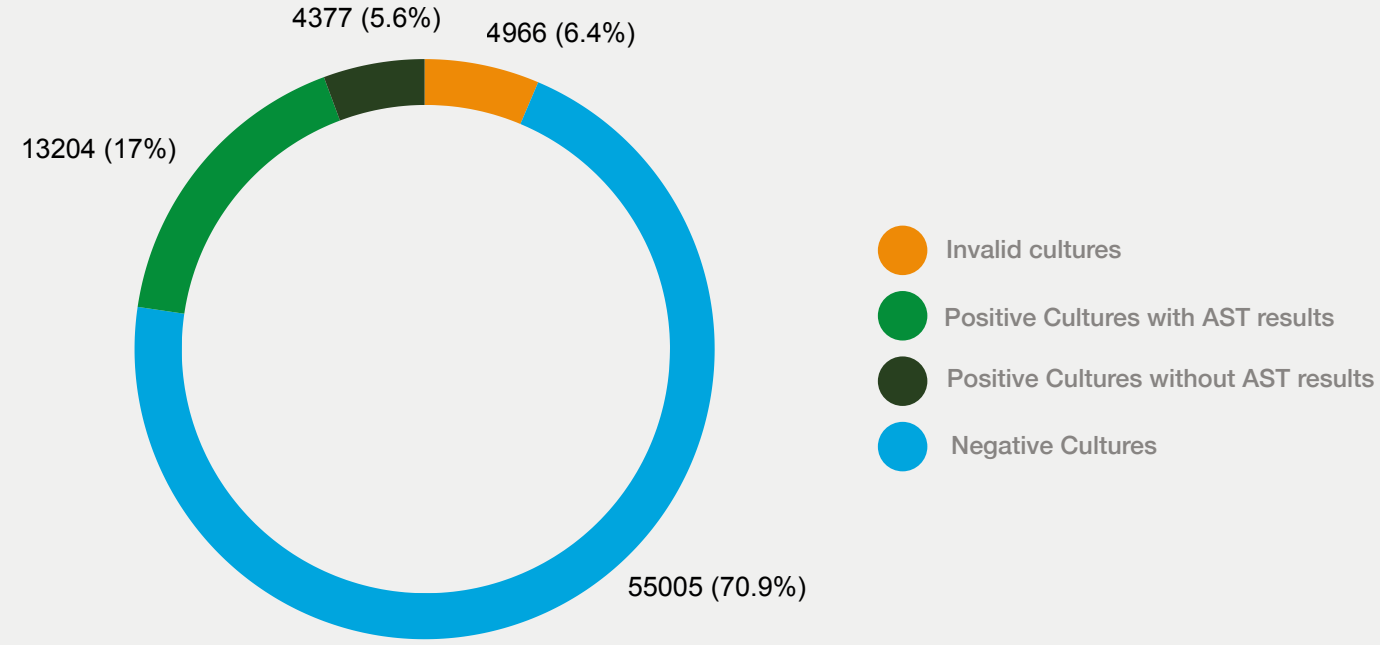


Figure 7: Quantum of cultures across all selected laboratories

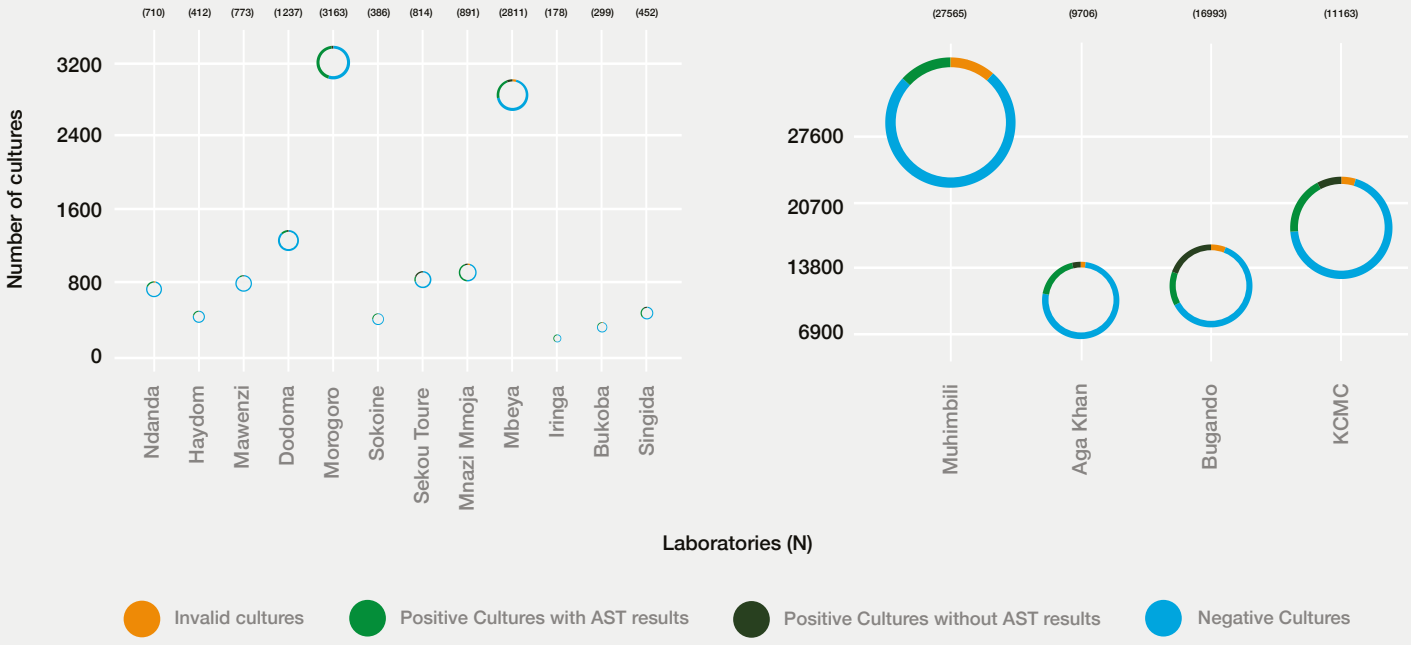


Figure 8: Quantum of cultures in each selected laboratory

2. Culture characteristics

Bacterial pathogens (13 204) were more commonly reported than fungal pathogens. Information on age was missing from 34.9% of the cultures, but where available, data showed a median age of 35 years (range: 0–101 years), with most cultures (3 259) obtained from patients 18–49 years old. Females (9 049) contributed more to the quantum of positive cultures with AST results. More data came from 2018 (8 010) than other years (Table 6, Supplementary Table 3).

Table 6: Culture characteristics

Characteristics	Positive cultures with AST results n=13 204 n (%)
Gender	
Male	4 155 (31.5)
Female	9 049 (68.5)
Age, years	
Less than 1	1 027 (7.8)
1 to 17	1 712 (13.0)
18 to 49	3 259 (24.7)
50 to 65	1 267 (9.6)
Above 65	1 335 (10.1)
Unknown age	4 604 (34.9)
Years	
2017	1 715 (13.0)
2018	3 479 (26.3)
2019	8 010 (60.7)
Pathogen	
Bacteria	13 195 (99.9)
Fungi	9 (0.1)

3. Inappropriate testing

All selected laboratories reported to be using CLSI standards for AST testing. However, during review of AST results, the following instances of inappropriate testing were noted:

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

4. Clinical information

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

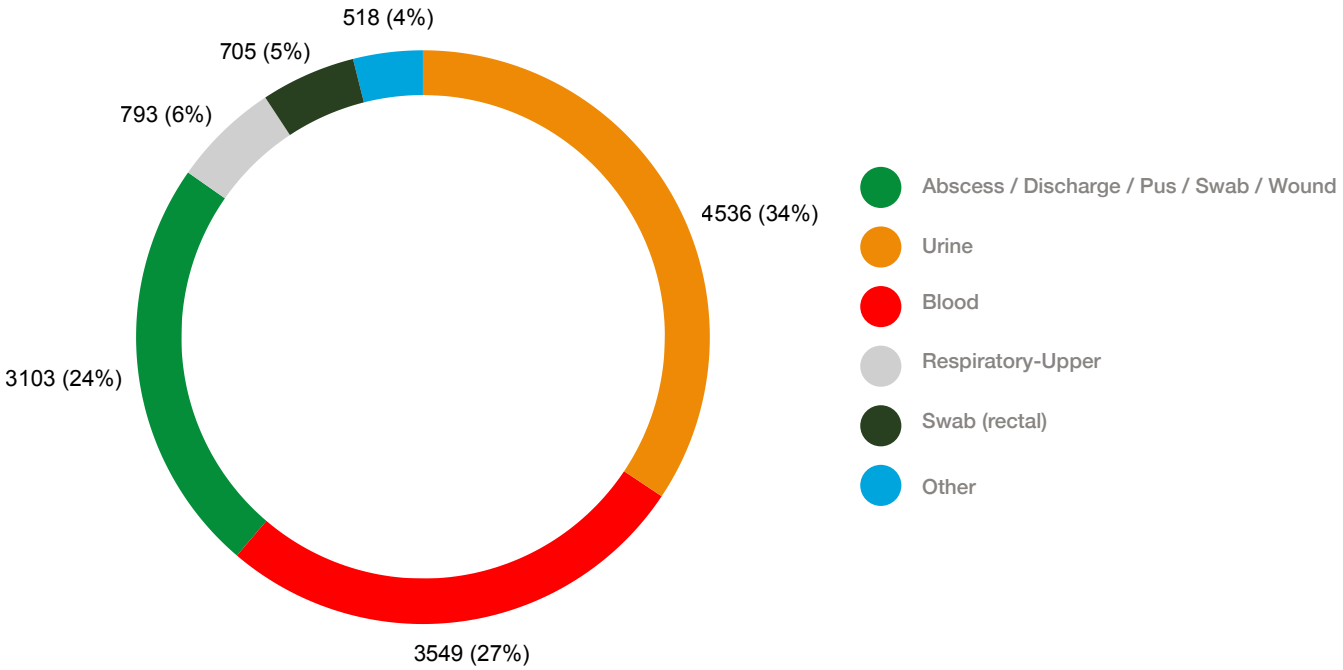
Table 7: Clinical information

Laboratory	Positive cultures with AST results N=13 204	Diagnosis data	Infection origin data*	Indwelling device data	AMU data
Muhimbili	3612	-	-	-	-
Aga Khan	1802	-	-	-	-
Ndanda	128	-	-	-	-
Haydom	85	-	-	-	-
Mawenzi	43	-	-	-	-
Dodoma	117	-	-	-	-
Morogoro	1369	-	-	-	-
Sokoine	93	-	-	-	-
KCMC	1486	-	-	-	-
Bugando	3133	-	-	-	-
Sekou Toure	79	-	-	-	-
Mnazi Mmoja	380	-	-	-	-
Mbeya	628	-	-	-	-
Iringa	74	-	-	-	-
Bukoba	51	-	-	-	-
Singida	124	-	-	-	-

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

5. Specimen characteristics

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



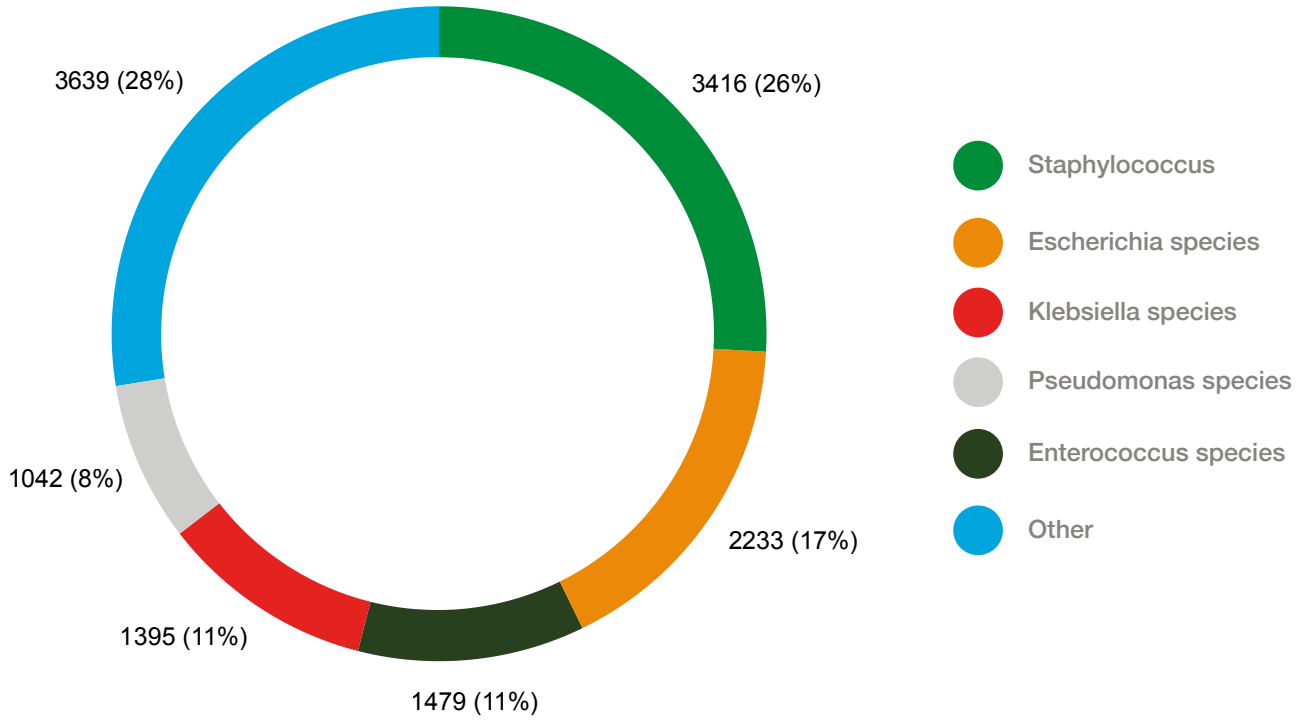
* Others include all other specimens excluding the top 5 mentioned here

Figure 9: Specimen characteristics

6. Identified pathogens

Staphylococcus species (25.9%), Escherichia species (16.9%), and Enterobacter species (11.2%) largely contributed to the quantum of positive cultures (Figure 10).

In 2016, of 1 715 positive cultures with AST results, Vibrio species (37.3%) Staphylococcus species (17%) and Escherichia species (10.3%), were the most reported. In 2017, of 3 479 positive cultures with AST results, Staphylococcus species (38.1%), Escherichia species (20.5%), and Klebsiella species (10.3%) were the most reported. In 2018, information was available for a greater number of cultures (8 010), and Staphylococcus species (22.5%), Escherichia species (16.8%), and Enterobacter species (16.7%) largely contributed to the quantum of positive cultures (Supplementary Table 5).



* Others include all other pathogens excluding the top 5 mentioned here
Figure 10: Pathogens identified

7. Quality of data

The country data quality score of the 72 587 valid culture records obtained from the 16 laboratories in Tanzania was 2.8 and was rated as average 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[14] 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.[15,16] Duplicate removal was based on 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.[17] 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 lack of data independence, such that each laboratory represented a cluster.[18]

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 and data were taken at face value for assessment of resistance rates.

Online data visualisation

AMR data were aggregated to the national level and definitions of resistance were harmonised across countries to enable comparisons. Data were uploaded to a private and secure portal for countries and laboratories to permit analysis of their data at the patient level (CDDEP's ResistanceMap Surveillance Network [RSN]). 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 of aggregated country-level data.[19] 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 nonsusceptible over each one-year interval. Across 2016–2018, AMR rates for some organisms remained consistent; the rates for others varied. High AMR rates were noted for 3rd-generation cephalosporin-resistant Enterobacterales (54-62%), while moderate resistance was noted for MRSA (25-35%), carbapenem-resistant P. aeruginosa (28-34%) and carbapenem-resistant Enterobacterales (18-24%). Resistance for fluoroquinolone-resistant Shigella species was lower (8-21%) (Table 8, Figures 11 and 12). Statistics for vancomycin-resistant and intermediate Staphylococcus species and S. aureus are not included.

Table 8: AMR rate estimates for WHO priority pathogens

Pathogen	Antibiotic, class	2016				2017				2018			
		N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)
A. baumannii	Carbapenems	-	-	-	-	1	0	-	1 (1)	2	2	-	2 (1 - 1)
P. aeruginosa	Carbapenems	4	2	-	1 (4)	83	23 (27.7)	10.7-55.1	7 (1-36)	139	47 (33.8)	14.7-60.2	8 (2-74)
Enterobacter ales	Carbapenems	74	18 (24.3)	2.1-82.9	2 (8 - 66)	614	110 (17.9)	6.6-40.2	6 (2 - 193)	1 052	191 (18.2)	6.7-40.5	8 (7 - 551)
Enterobacter ales	Cephalosporins (3rd generation)	614	333 (54.2)	42.6-65.4	12 (1 - 214)	1 374	782 (56.9)	47.4-65.9	14 (1 - 470)	1 530	951 (62.2)	57.5-66.6	14 (1 - 591)
E. faecium	Vancomycin	-	-	-	-	-	-	-	-	1	0	-	1 (1)
H. influenzae	Ampicillin	-	-	-	-	-	-	-	-	23	1	-	1 (23)
H. pylori	Clarithromycin	-	-	-	-	-	-	-	-	-	-	-	-
N. gonorrhoeae	Cephalosporins (3rd generation)	1	0	-	1 (1)	8	4	-	1 (8)	11	4	-	3 (2 - 7)
N. gonorrhoeae	Fluoroquinolones	2	1	-	1 (2)	10	5	-	1 (10)	9	8	-	4 (1 - 5)
Campylobacter species	Fluoroquinolones	1	0	-	1 (1)	1	1	-	1 (1)	-	-	-	-
Salmonella species	Fluoroquinolones	13	2	-	4 (1 - 5)	26	9	-	7 (1 - 14)	25	2	-	9 (1 - 12)
Shigella species	Fluoroquinolones	37	3 (8.1)	4.5-14.1	4 (1 - 32)	33	7 (21.2)	7.5-47.2	6 (1 - 14)	44	5 (11.4)	4.9-24.2	6 (1 - 18)
S. aureus	Methicillin	85	21 (24.7)	7.3-57.9	11 (1 - 36)	189	66 (34.9)	12.5-66.9	13 (1 - 55)	303	104 (34.3)	14.2-62.3	10 (1 - 109)
S. pneumoniae	Beta-lactam combinations	1	0	-	1 (1)	6	2	-	1 (6)	1	1	-	1 (1)
S. pneumoniae	Penicillins	2	2	-	2 (1 - 1)	14	9	-	3 (1 - 9)	25	11	-	4 (1 - 22)

N = number of tested isolates; n = number of non-susceptible isolates; 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 11: AMR rate estimates for WHO priority pathogens

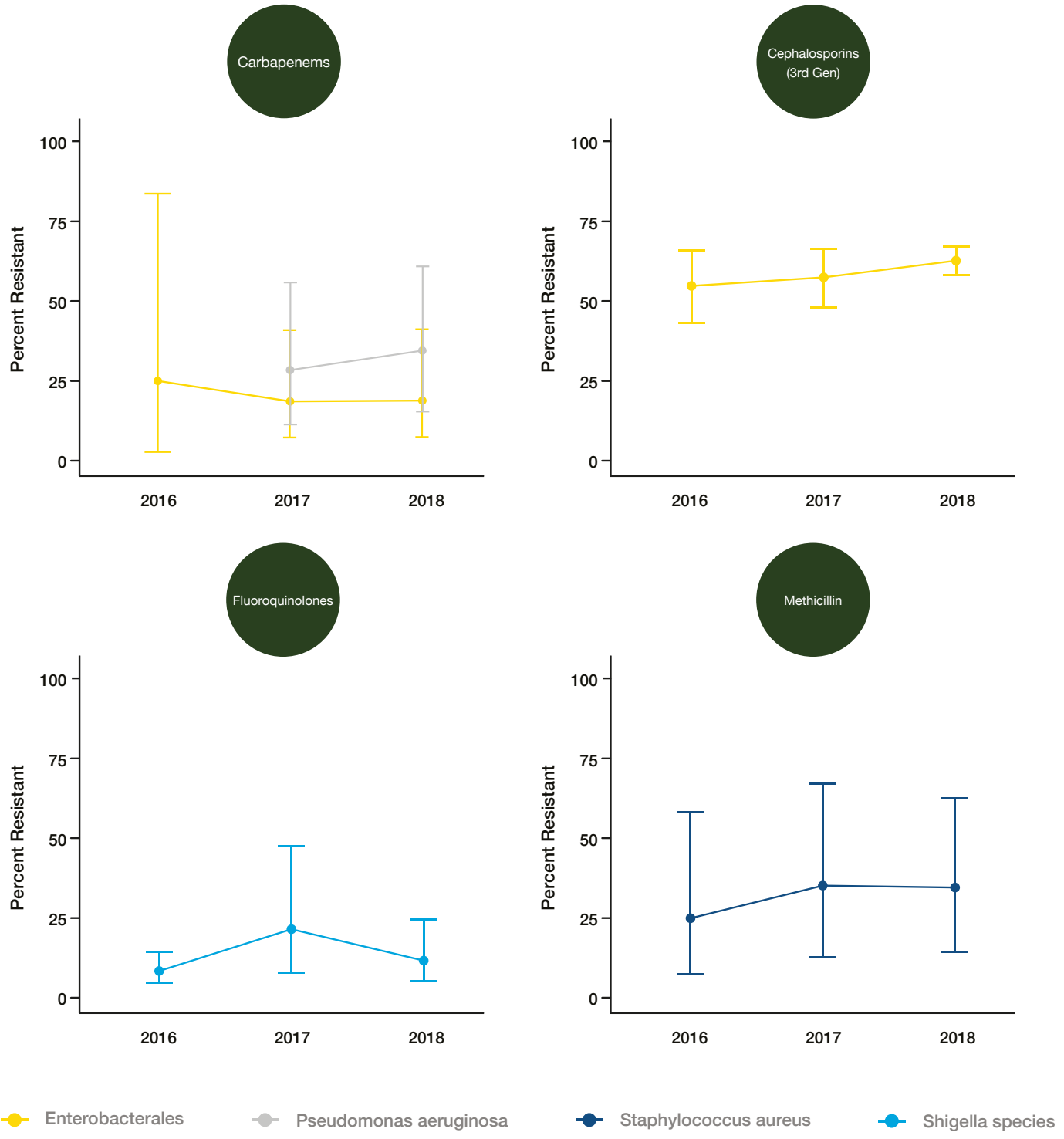


Figure 12: AMR trends for WHO priority pathogens

(ii) AMR rates for other pathogens of clinical importance

Analysis of AST data from blood and CSF isolates revealed very high AMR rates for 3rd-generation cephalosporin-resistant Klebsiella species (80-87%) and high-moderate for methicillin-resistant Staphylococcus species (53-76%) and carbapenem-resistant Pseudomonas species (34-46%). AMR rates were low for carbapenem-resistant Klebsiella species (4-15%) (Table 9).

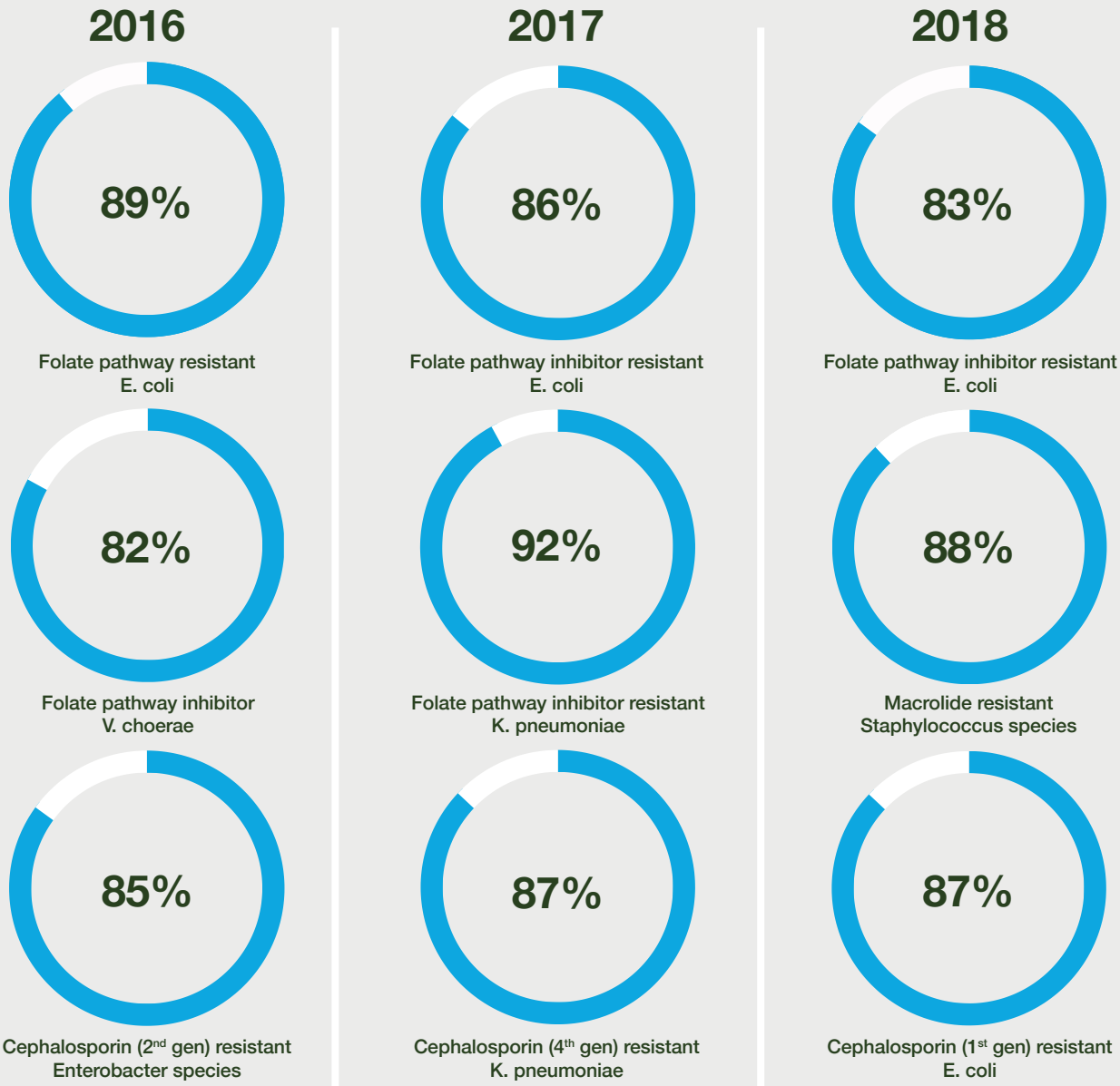
*Table 9: AMR rate estimates for other clinically important pathogens**

		2016				2017				2018			
Pathogen	Antibiotic, class	N	n (%)	95% CI	Labs# (range)	N	n (%)	95% CI	Labs# (range)	N	n (%)	95% CI	Labs# (range)
Acinetobacter species	Carbapenems	1	0	-	1 (1)	7	0	-	2 (1 - 6)	-	-	-	-
Acinetobacter species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Aminoglycosides (high level)	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Vancomycin	15	3	-	4 (1 - 10)	25	4	-	3 (3 - 16)	9	1	-	1 (9)
H. influenzae	Ampicillin	-	-	-	-	-	-	-	-	-	-	-	-
H. influenzae	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Klebsiella species	Carbapenems	56	2 (3.6)	0.3-29.1	4 (1 - 36)	101	15 (14.9)	1.8-63	4 (5 - 65)	5	2	-	1 (5)
Klebsiella species	Cephalosporins (3rd generation)	118	103 (87.3)	66.1-96	6 (2 - 64)	134	108 (80.6)	74.1-85.7	6 (1 - 66)	35	30 (85.7)	22.7-99.2	3 (4 - 27)
N. meningitidis	Ampicillin	-	-	-	-	-	-	-	-	-	-	-	-
N. meningitidis	Cephalosporins (3rd generation)	-	-	-	-	-	-	-	-	-	-	-	-
Pseudomonas species	Carbapenems	35	12 (34.3)	19.9-52.2	4 (1 - 23)	44	20 (45.5)	13.8-81.2	4 (2 - 28)	3	1	-	1 (3)
Pseudomonas species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Macrolides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	3rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	Methicillin	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus species	Methicillin	147	111 (75.5)	54.7-88.7	2 (8 - 139)	167	89 (53.3)	45.2-61.2	2 (1 - 166)	2	2	-	1 (2)
S. pneumoniae	Penicillins	2	0	-	1 (2)	1	0	-	1 (1)	-	-	-	-
S. pneumoniae	Beta-lactam combinations	-	-	-	-	-	-	-	-	-	-	-	-
S. pneumoniae	Macrolides	2	0	-	2 (1 - 1)	4	1	-	3 (1 - 2)	-	-	-	-
S. pneumoniae	Vancomycin	1	0	-	1 (1)	2	0	-	1 (2)	-	-	-	-

* From blood and CSF; N = number of tested isolates; n = number of non-susceptible isolates; 95% 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 available data, very high resistance (>90%) was estimated for clinically important pathogens like Klebsiella pneumoniae (vs. folate pathway inhibitors) (Figure 13).



Pathogen nomenclature is shown as reported by laboratories; antimicrobials are reported at class level.
Figure 13: Top five highly resistant pathogens

(iv) AMR rates for fungal pathogens

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

Section IV: Drivers of antimicrobial resistance

Objective

To assess the drivers of AMR

Methodology

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

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

To identify the drivers of resistance, a composite AMR rate for select groups of pathogens (Acinetobacter baumannii, Escherichia coli, K. pneumoniae, P. aeruginosa, S. aureus, Enterococcus faecium, and Enterococcus faecalis) and antibiotics or antibiotic classes (aminoglycosides, broad-spectrum penicillins, carbapenems, cephalosporins, glycopeptides, narrow spectrum penicillins, and quinolones) was estimated (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 and the data from the laboratories being varied.

Results

Two variables namely, age and gender were evaluated for possible association with AMR. The data availability for these variables was age: 84.7% and gender: 74.7%. The univariate logistic regression results did not reveal any significant association between the variables and AMR rates (Table 10).

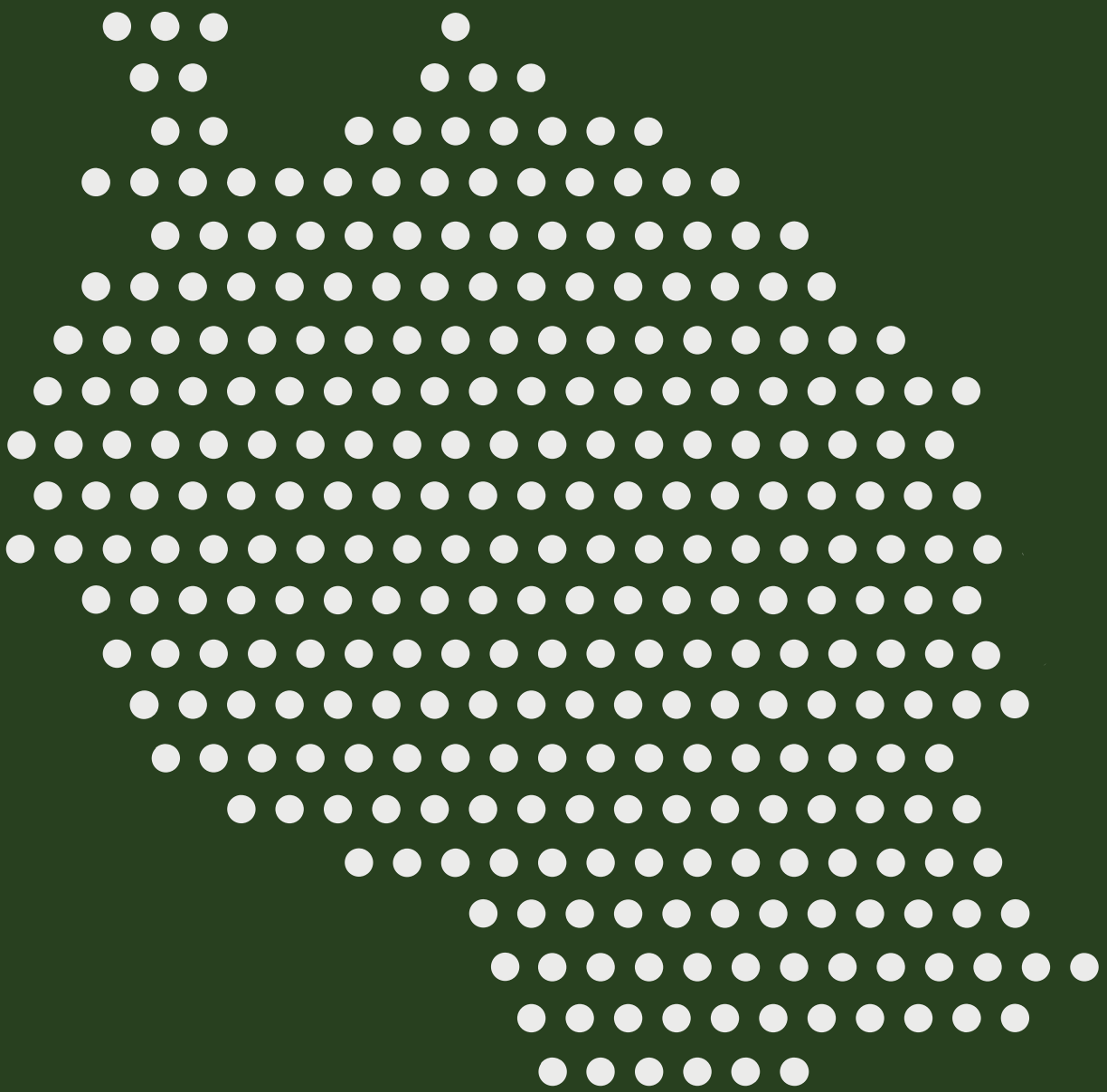
Table 10: Univariate logistic regression analysis

Variable	Options	N	NS (%)	Adjusted OR (95% CI)	P-value
Gender	Female	3 659	47.4	Ref	0.415
	Male	3 303	48.4	1.04 (0.95 - 1.14)	
Age	<1	769	52.5	1.15 (0.91 - 1.46)	0.052
	1-17	1 531	46.4	0.90 (0.68 - 1.19)	
	18-49	2 578	49.0	Ref	
	50-65	1 441	45.7	0.88 (0.77 – 1.00)	
	>65	1 287	50.4	1.06 (0.93 - 1.20)	

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

Information on other patient factors was unavailable/ 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 AMR 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.[20,21] 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 MAAP's aim to expand the volume of data presently available on AMR and AMC or AMU across Africa as well as the country's National Action Plan on Antimicrobial Resistance.[10]

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 describes quantities of antimicrobials dispensed (e.g., at national stores or pharmacies) whereas AMU data describe how and why antimicrobials are used (e.g., whether required laboratory tests and clinical assessments were conducted prior to issuing a prescription, whether the right antimicrobial was prescribed at the correct strength and frequency over an appropriate duration to treat the right indication, as per country guidelines and finally, whether the patient correctly or completely consumed the prescribed antimicrobial).[22]

Link between the antimicrobial usage and AMR

The unwarranted use of antimicrobials is in part attributable to the emergence of AMR. This association implies that a reduction in the unnecessary consumption of antimicrobials could in turn reduce AMR levels.[20] 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 particular antimicrobial over a long time and thus selective pressure favours microbes that evade these predominantly used antimicrobials. This is often the picture in a number of LMICs where inequities in antimicrobials 'Access' still persists.[21]

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 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 Tanzania that would equip the country with valuable information to support the appropriate use of antimicrobials. The objective was also to identify gaps that may exist in establishing a comprehensive surveillance system and providing the country with the required information to support the setup of such a monitoring system.

AMC and AMU surveillance impact

In an effort 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 antimicrobials use and quantification of their consumption. At present, there are only few published reports on AMC surveillance and AMU in Africa[24-28], including one report on AMU from Tanzania.[29] The process of obtaining AMC or AMU data equips the country with local information on various problems that exist with AMU and allows for the monitoring of the accessibility of antimicrobials. Furthermore, obtaining AMC or AMU data permits the continuous local assessment of correlations between antimicrobial usage to emerging local AMR, which in turn, allows for proper mitigation policies and activities to be planned using the relevant data. Data obtained from local surveillance exercises also present the opportunity to better inform stewardship programmes. Therefore, MAAP set out to quantify consumption and analyse AMC and AMU trends at selected facilities as well as at the national level.

The aim of this work

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

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

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 Tanzania

Methodology

AMC and AMU data sources

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, TMDA was identified as a potential source for medicine importation data in Tanzania as well as those locally manufactured. In addition, MSD (the country's public-sector mechanism for procurement of medicines) was identified as another potential AMC and AMU source.

Under the guidance of the Tanzania AMRCC, MAAP also targeted data from twice as many pharmacies as the selected AST laboratories (i.e., a total of 32 pharmacies) in order to obtain aggregated pharmacy-level AMC data. 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) (See AMC Appendix 2 for the tool used). Additionally, community pharmacies (n=16) were also targeted. These community pharmacies were nominated by the co-located pharmacies on the basis of their proximity to the AST laboratories and/or selected based on their serving as the preferred patient medicine purchase sites or a backup prescription fulfilment source in case of stockouts in the main hospital pharmacy. In addition to this, the 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 targeted for collection from the hospital pharmacies (n=16) and this was to be provided 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, including accredited drug dispensing outlet that provide medicines in rural and peri-urban areas 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 Tanzania). P01AB and J02 ATC antimicrobials are part of WHO's core and optional monitored medicine classes respectively for AMC surveillance.[30] AMC data from the above medicine categories were collected in financial years (i.e., July 2016 – June 2017 and July 2017 – June 2018).

Data collection

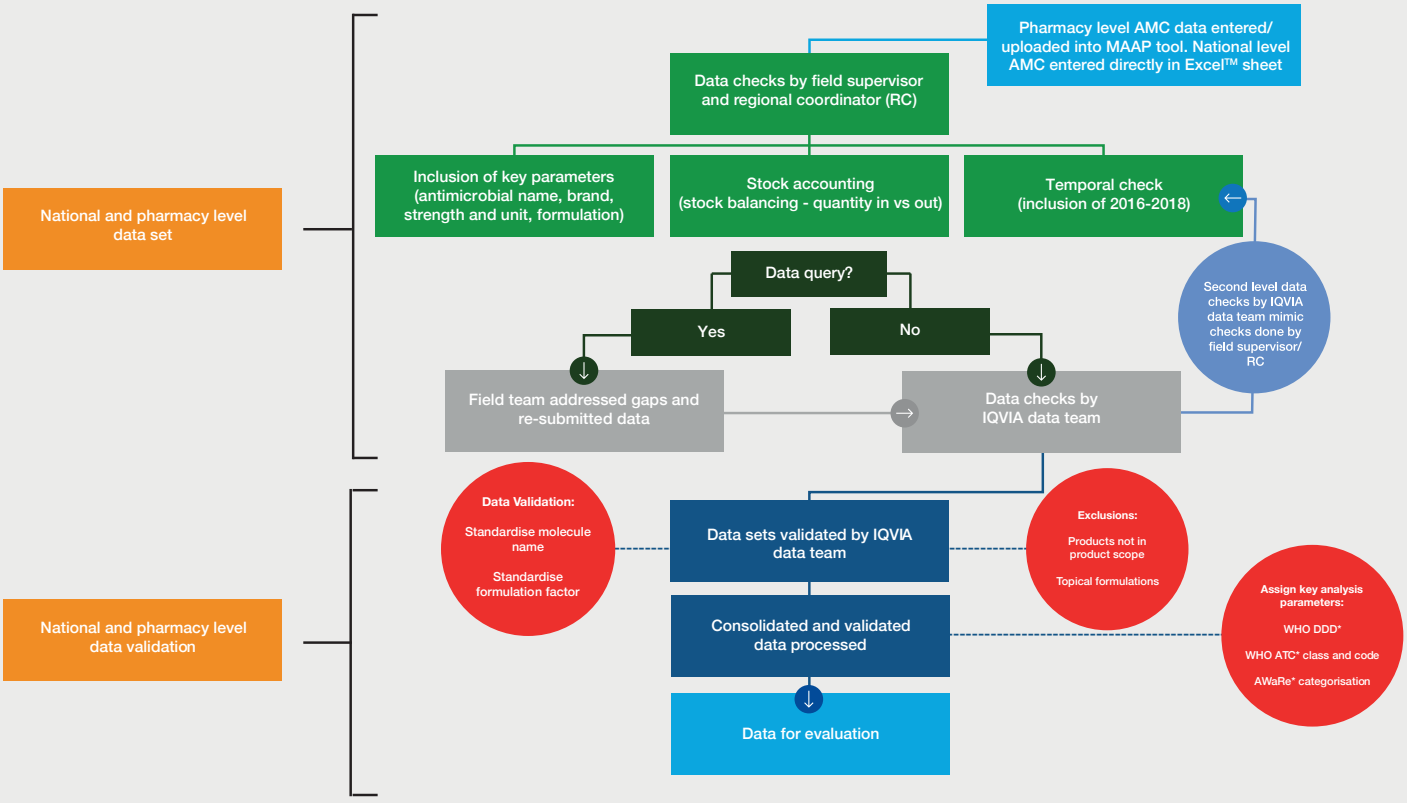
MAAP was unable to access 'the targeted TMDA data due to lengthy ethical approval procedures. However, MSD aggregated consumption data were provided through the AMRCC to MAAP data collectors for the period July 2016- June 2018. The public sector datasets from MSD were digitised by the IQVIA data analysis team and subsequently sorted to filter out the products within scope. The datasets were then reviewed and cleaned by the IQVIA data analysis team using Microsoft Excel™ software. The analysis team also ensured that all antimicrobials had their standard molecule 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 pharmacy main store Health Information System (HIS) into an Excel™ sheet where data were available electronically. Alternatively, abstracted data from stock record cards or ledger books 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 a MAAP tool to the central data processing and analysis team. AMC Appendix 5 details the data collection process.

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

Data cleaning and validation

The national-level AMC datasets were categorised in this report as generally representing the public sector as they were sourced from MSD datasets. Once the datasets were received by MAAP, both the national- and pharmacy-level AMC data were then subjected to a series of data validation checks to ensure accuracy and consistency (data checks and the validation process for national AMC data is detailed in AMC Appendix 6). Here, the pharmacy and national AMC data were subjected to secondary and tertiary checks by field supervisors, the IQVIA regional coordinator and IQVIA data team. The validation and processing of the data was carried out by IQVIA regional coordinator and IQVIA data team, as outlined in Figure 14.



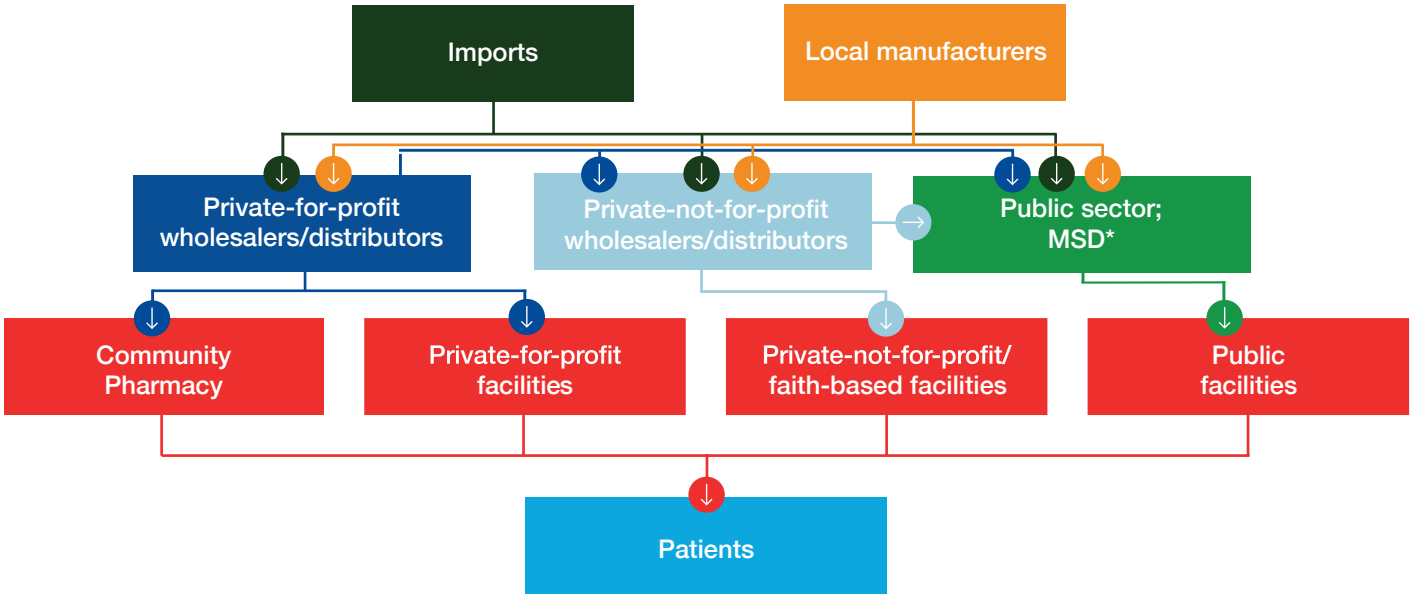
*DDD Defined Daily Dose *ATC - Anatomical Therapeutic Chemical * AWaRe Access, Watch and Reserve

Figure 14: Flow chart explains the data checks procedures and validation process for the national and pharmacy level AMC data collected in Tanzania

Results

Flow of antimicrobials in the country

To characterise the pathway through which antimicrobials get to patients in the country, a total of two key informant interviews (KIIs) were conducted with a pharmaceutical supply chain expert from the MoH and from a medicines supply organisation – Mission for Essential Medicine Supply (MEMS). The information gathered was supplemented by a literature review. In Tanzania, medicines including the antimicrobials are imported as well as manufactured in the country. After importation or local production, private (for-profit, not-for-profit) wholesalers or distributors (e.g., MEMS, Action Medeor) and the national public central store, the Medical Stores Department (MSD) then pass along the antimicrobials to the community pharmacies, private (both for-profit and non-profit) facilities and public facilities who eventually issue the antimicrobials to patients. The flowchart below (Figure 15) illustrates the route through which antimicrobials get to patients in Tanzania.



*MSD: Medical Store Department

Figure 15: Flow chart explaining the circulation of antimicrobials within the country to the patients in Tanzania. A dotted line indicates supplies are not mainstream

Regulation of antimicrobials consumption

In Tanzania, the Tanzania Medicines and Medical Devices Authority (TMDA) regulates and licenses all of the pharmaceutical and medical products, including those imported as well as locally manufactured. The antimicrobials for human consumption are regulated under the recently revised Tanzania Medicines and Medical Devices Act, Cap 219, 2021, which also reviews the registration of suppliers of antimicrobials and other medicines for human consumption.[12] This law stipulates that requisite antimicrobial can only be sourced from registered suppliers upon issuance of a valid prescription and sales are to be recorded in an antimicrobial register. Overuse and misuse of antimicrobials are significant contributors towards the emergence of AMR. Therefore, in an effort to address the above issues and other prevalent gaps, the country developed the Tanzania National Action Plan for AMR (2017-2022)[10], 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 participating pharmacies that were co-located with AST laboratories as well as also offering clinical services (n=16). Unfortunately, no AMU data were obtained during MAAP data collection due to the nature of the data sources at the participating pharmacies (i.e., patient characteristics and indication for which the antimicrobial is being used, the appropriateness of the prescription in relation to national guidelines; including conducting of any relevant laboratory testing and clinical assessment conducted prior to prescribing as well as the 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 Tanzania from the selected health facilities.

National-level data

National public sector AMC data were obtained from the MSD for the period July 2016 to June 2018. MAAP was unable to 'access TMDA data due to lengthy ethical approval procedures. Therefore, the resultant national AMC data collected and analysed represented approximately 100% of the total antimicrobials consumed in public health facilities during the reviewed financial years (July 2016- June 2018).

The MSD data (national-level public sector 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). However, data collected only represented financial years 2016-18 and excluded the January 2016 – June 2016 and July 2018 – December 2018 data

Facility-level data

Pharmacy data collection was successfully conducted in (n=16) targeted hospital-based pharmacies. Of the participating hospital pharmacies (n=16) that were co-located with the AST laboratories, (n=11) pharmacies located in public government hospitals. The remaining recruited hospital pharmacies included (n=1) private regional referral hospital and (n=4) that were in private faith-based hospitals. In addition, data was collected from seven stand-alone community pharmacies. The remaining (n=9) targeted community pharmacies were not recruited due to either their unwillingness to share their AMC data or their not meeting the inclusion criteria (i.e., either new pharmacies that did not exist during the data collection period or pharmacies that did not hold the data in an extractable format). Thus, the total sample size of successfully recruited community pharmacies was (n=7) and hospital pharmacies (n=16) out of the 32 targeted pharmacies at the beginning of the study. As the total number of hospital or community pharmacies in Tanzania 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 23 pharmacies where the data were collected. However, there were instances in each of the visited facilities wherein the 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 16 hospital pharmacies, MAAP was able to collect data across the three years in all the pharmacies. From of the remaining seven recruited community pharmacies 5 did not provide data for the years 2016 and 2017 as either they declined to share the data, or they did not have archived data between 2016-2017 in their systems.

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

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

	Pharmacy Name	Level of Service#	Affiliation	Region	Record keeping*	Pharmacy system directly linked to patient records *†	AMC reporting*
Hospital Pharmacies (co-located with AST laboratories)	Bugando Medical Centre Pharmacy	Zonal	Private faith-based	Mwanza	Manual	No	No
	Bukoba Regional Referral Hospital Pharmacy	Regional	Public	Bukoba	Manual	No	No
	Dodoma Regional Referral Hospital Pharmacy	Regional	Public	Dodoma	Manual	No	No
	Haydom Lutheran Hospital Pharmacy	Regional	Private faith-based	Haydom	Manual/ Electronic	No	No
	Iringa Regional Referral Hospital Pharmacy	Regional	Public	Iringa	Manual	No	No
	Kilimanjaro Christian Medical Centre Pharmacy	Zonal	Private faith-based	Moshi	Electronic	No	No
	Mawenzi Regional Referral Hospital Pharmacy	Regional	Public	Moshi	Manual	No	No
	Mbeya Zonal Referral Hospital Pharmacy	Zonal	Public	Mbeya	Manual	No	No
	Morogoro Regional Referral Hospital Pharmacy	Regional	Public	Morogoro	Manual	No	No
	Muhumbili National Hospital Pharmacy	National Referral	Public	Dar es Salaam	Electronic	Yes	No
	Aga Khan Hospital Pharmacy	Regional	Private	Dar es Salaam	Electronic	Yes	No
	Sekou Toure Regional Referral Hospital Pharmacy	Regional	Public	Mwanza	Manual	No	No
	Singida Regional Referral Hospital Pharmacy	Regional	Public	Singida	Manual	No	No
	Sokoine Regional Referral Hospital Pharmacy	Regional	Public	Lindi	Manual	No	No
	St. Benedict's Ndanda Referral Hospital Pharmacy	Regional	Private faith-based	Ndanda	Manual	No	No
	Mnazi Mmoja Referral Hospital Pharmacy	Regional	Public	Zanzibar	Manual	No	No
Community pharmacies~	New Bugando Pharmacy	Dispensing	Private	Mwanza	Manual	N/A	No
	ADDO	Dispensing	Private	Haydom	Manual	N/A	No
	Chooser Pharmacy	Dispensing	Private	Iringa	Electronic	N/A	No
	Kilimani Pharmacy	Dispensing	Private	Moshi	Manual	N/A	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. While, National Referral Hospitals provide comprehensive specialist services in addition are involved in teaching and research. Zonal Referral Hospitals provide the same level of services as that of National Referral hospitals. However, they are located in particular zones of the country to provide referral health services to patients coming from all regional referral hospitals located within a zone.

*For the review financial years period i.e. July 2016- June 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.[30,31] Figure 16 provides a high-level summary of 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 is 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 patient bed days. Studying DDDs or associated metrics over time helps to understand the consumption pattern or study whether any national- or facility-level interventions have led to change (+/-) in the consumption patterns over the study period or a pre-defined base period.

Using the WHO 2020 DDD guide, total consumed milligrams per antimicrobial was to be divided against the standard DDD value issued by the WHO to obtain total DDDs.[32] Total DDDs were then to be adjusted for the country population size[33] in the year of data collection (2016-2018) and presented as DDDs/1 000 inhabitants/day (DID). However, due to missing pack size information within the datasets received, analysis of the national-level AMC was not possible. Furthermore, pharmacy-level AMC datasets were to be adjusted as DDD per the number of inpatients and presented as DDD/100 patient bed days. However, the use of WHO DDD per 100 patient bed days presented limitations at the point of analysis, as patient bed days was not an appropriate denominator to use across the pharmacy-level AMC datasets. In addition, for most of the hospital facilities, patient bed days and patient days information was not easily accessible'. Secondly, this metric would not allow for the comparison between hospital pharmacy consumption and community pharmacy consumption, as in the latter, the patient bed days metric was not applicable. Therefore, the pharmacy-level AMC datasets are presented as absolute DDD to aid comparison between hospital and community pharmacies for downstream analysis. Detailed DDD calculations can be found in AMC Appendix 7. All calculations were conducted in Microsoft Excel ™ software.

ii. Anatomic Therapeutic Chemical (ATC) Classification

Using the standard list of antimicrobial names, the pharmacy-level datasets collected were coded in the Microsoft Excel™ analysis database in accordance with the 2020 WHO ATC codes and then analysed to characterise the macro (above-molecule) AMC trends. Description of ATC codes are presented in AMC Appendix 7. In addition, MAAP conducted statistical testing to see the year-on-year differences within each ATC class. However, this was not possible as the aggregated pharmacy-level dataset included AMC datasets from nine pharmacies that did not provide full coverage of the three-year review period.

iii. WHO Access, Watch and Reserve (AWaRe)

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

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

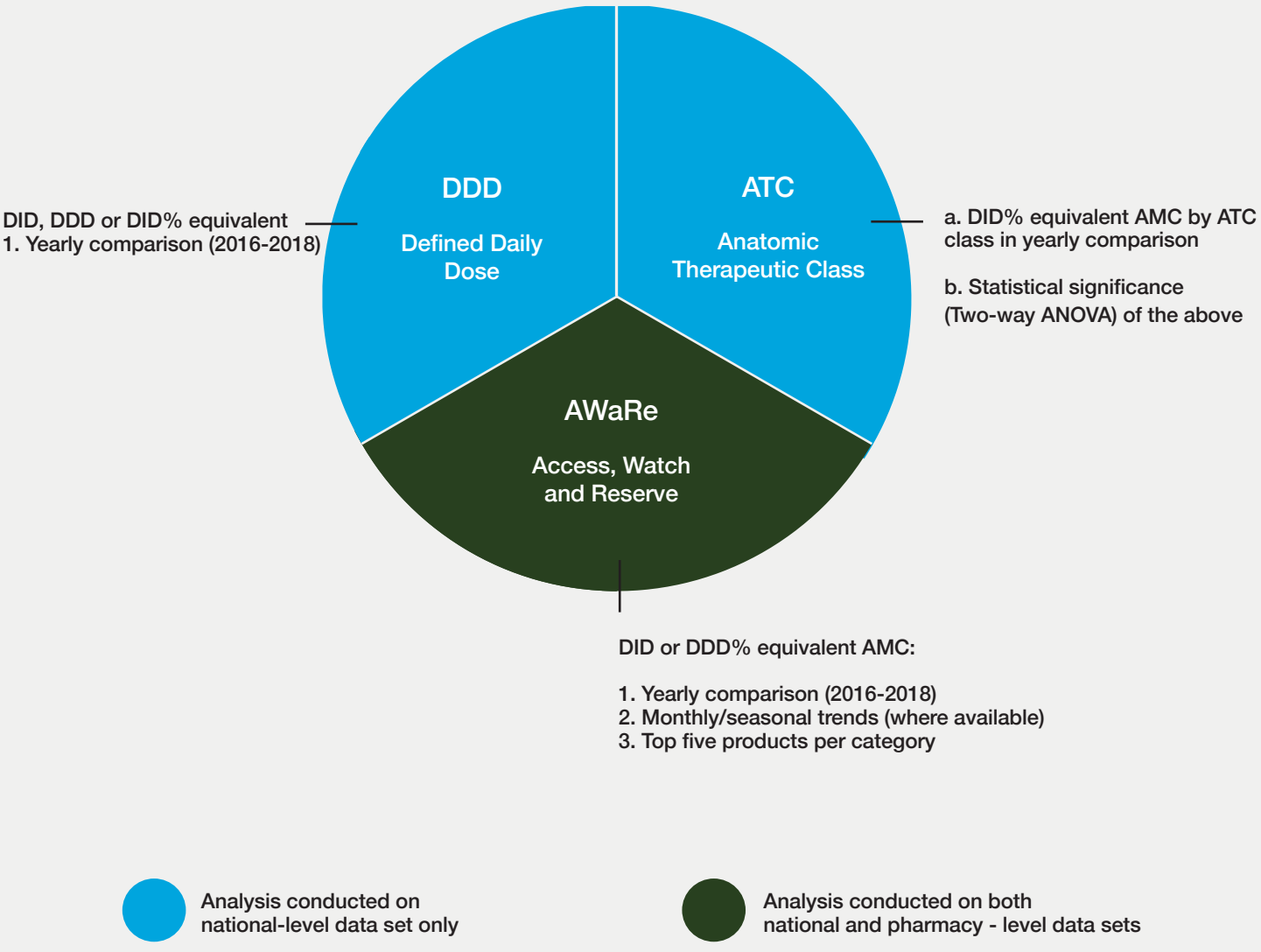


Figure 16: Methods and indicators used for the analysis of the data collected in Tanzania. Defined Daily Dose (DDD) indicators utilised for volume metric standardisation was sourced from WHOCC 2020, ATC Classification utilised to categorise the antibiotics according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties sourced from WHOCCC ATC database, and '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 Tanzanian National Essential Medicines List (NEMLIT)[35] and against the documented antimicrobials from the national- and pharmacy-level data collection. The comparison was conducted by WHO defined AWaRe categories.

Results

National AMC datasets analysed by DDD per year

The average public sector AMC in-country between July 2016-June 2017 and July 2017-June 2018 was 2.8 DDD per 1 000 inhabitants per day (DID). A 75% increase in total consumption of the antimicrobials between the financial years July 2016 to June 2018 was documented (Figure 17).

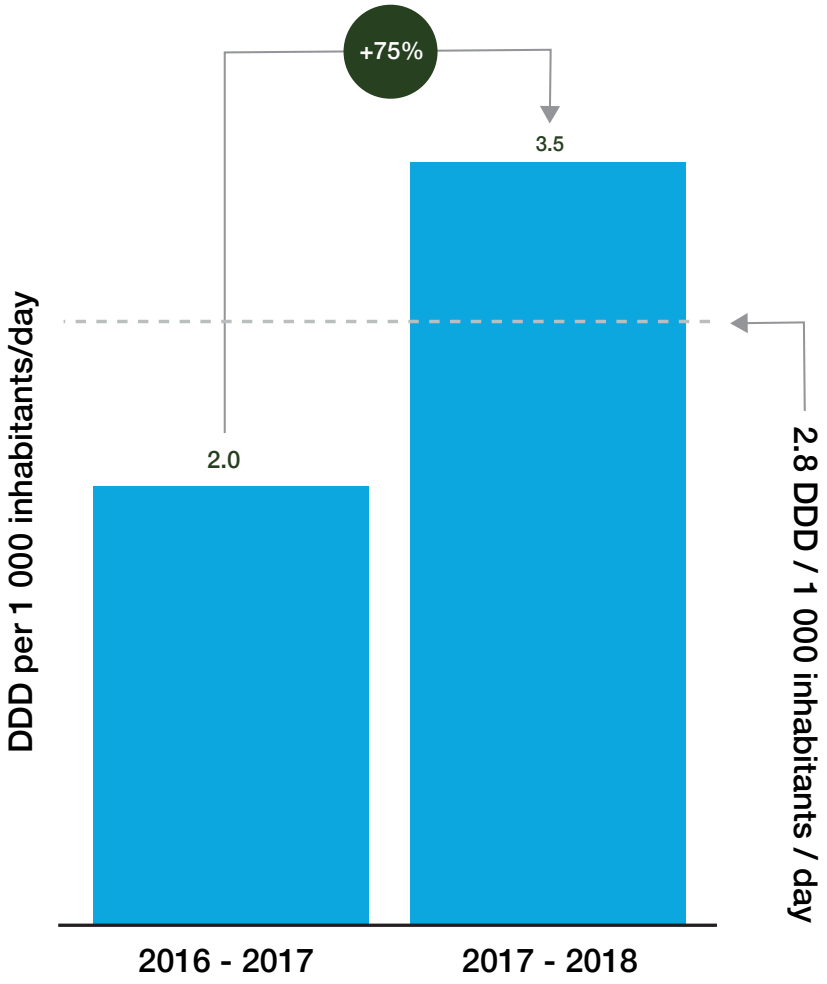


*Figure 17: Bar graphs represents the total DID and percentage variation from the financial year (2016-2017) to financial year (2017-2018) for the national public sector AMC data analysed in Tanzania. *Represents financial years (July 2016-June 2017), **Represents financial years (July 2017-June 2018)*

National AMC analysed by ATC classification

Fluoroquinolones (J01MA) were the most frequently consumed ATC class within the public sector in Tanzania across the review period at 14.7% in 2016-2017 and 23.1% in 2017-2018. Ciprofloxacin was the most frequently consumed antibiotic within this class (Figure 18). Combinations of sulfonamides and trimethoprim, including derivatives (J01EE) and penicillins with extended spectrum (J01CA), were the second- and third-leading ATC classes overall. The combination of sulfamethoxazole/trimethoprim and Amoxicillin leading the consumption within these ATC classes, respectively. The top five most consumed antimicrobials were Ciprofloxacin, sulfamethoxazole/trimethoprim, Amoxicillin, Doxycycline and Fluconazole. Together, they accounted for 65% of total consumption share. A detailed list of national public sector AMC by antimicrobial molecule and by ATC class are mentioned in AMC Appendix 8 and Appendix 9, respectively.

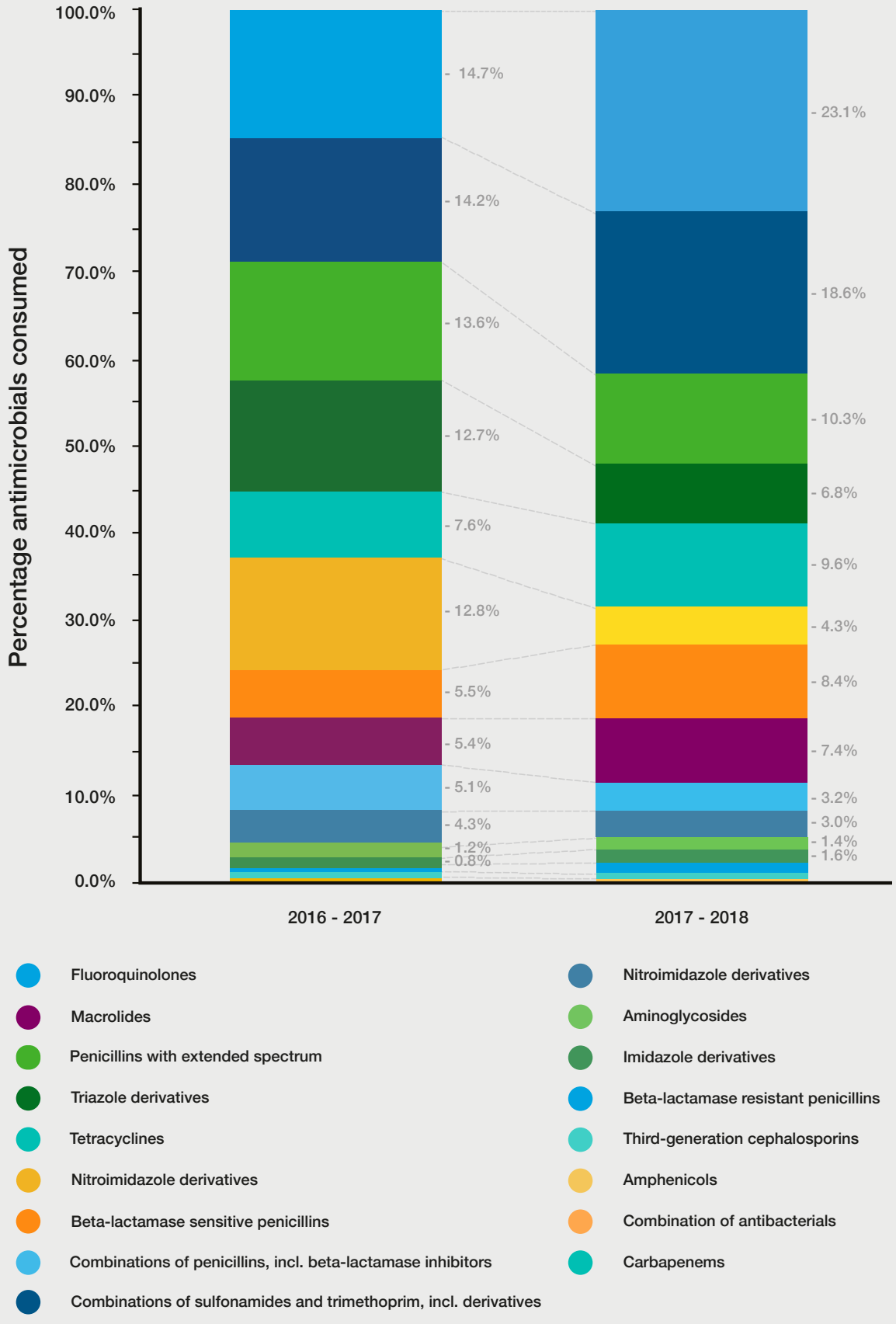


*Figure 18: Results of national public sector AMC data analysed in Tanzania are presented by the percentage of antimicrobials consumed by ATC classes for the financial years (2016-2017) and (2017-2018). Fluoroquinolones were the highest consumed antimicrobials for the financial years (2016-2017) and (2017-2018). See Appendix 9 for a more detailed breakdown of AMC by ATC classes. *Represents financial years (July 2016-June 2017), **Represents financial years (July 2017-June 2018)*

National and pharmacy AMC analysed by WHO AwaRe categorisation

The average national public sector consumption of antibiotics across the two financial years of data collected was 68.3% 'Access', 31.7% 'Watch' and 0.0% 'Reserve'. Annual AMC trends indicated a decrease of 8.9% in consumption share of 'Access' antibiotics between the financial years (2016- 2017) and (2017-2018), against a corresponding increase of 8.9% in 'Watch' antibiotics between the same period (Figure 19). There were no stocks of 'Reserve' group antibiotics consumed within the public sector during the reviewed period. Both the overall (for the two financial years) and within each year analysed consumption of 'Access' category antibiotics exceeded the 60% minimum consumption threshold set by the WHO. The above analysis, depicting WHO AWaRe proportions of antibiotics consumed, omits 13% (0.4 DID) of total AMC that are not categorised within the WHO AWaRe classification list of 2019.

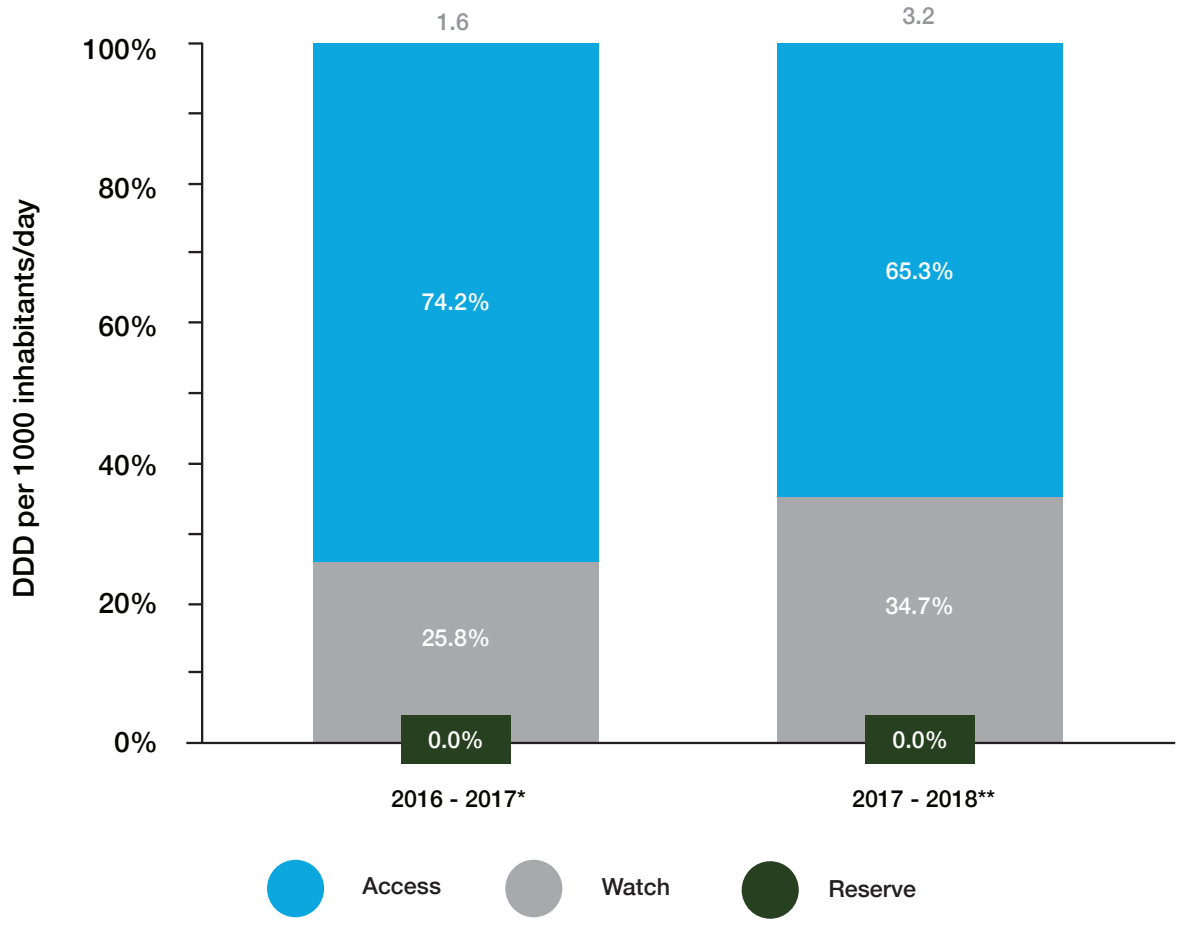
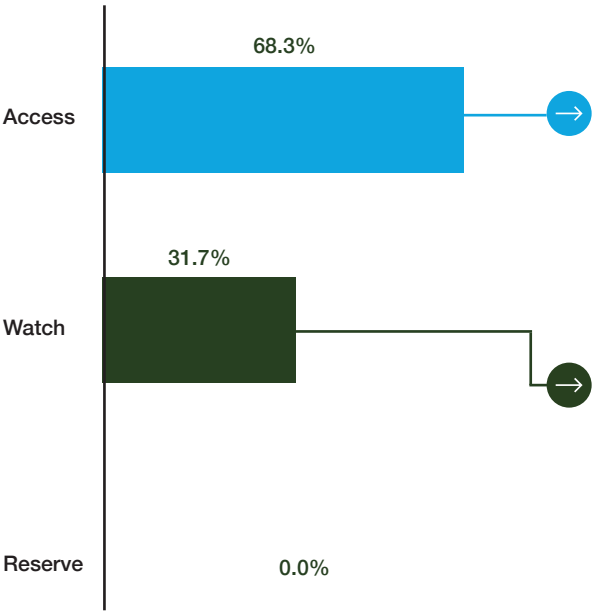


*Figure 19: Results for the public sector AMC data analysed in Tanzania are presented by the total DID and percentage of antibiotics consumed by WHO AWaRe categories for the financial years (2016-2017) and (2017-2018). Also, it shows the percentage change in consumption of 'Access' and 'Watch' category antibiotics from the year (2016-2017) to (2017-2018). *Represents financial years (July 2016-June 2017), **Represents financial years (July 2017-June 2018)*

Further analysis was conducted to identify the most frequently consumed antibiotics within each WHO AWaRe category (Figure 20). In the 'Access' category, the top five most frequently consumed antibiotics, as listed in Figure 20, accounted for 84.4% of all AMC within this group. While in the 'Watch' category, the top five consumed antibiotics accounted for approximately 100.0% of all the consumption within this category.



Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Sulfamethoazole/Trimethoprim	28.8%	0.5
Amoxicillin	18.7%	0.3
Doxycycline	15.0%	0.2
Nitrofurantion	12.5%	0.2
Benzylpenicillin	9.4%	0.2

Molecule Name	% Total	Mean DDD/1000 inhabitants/ day
Ciprofloxacin	73.1%	0.6
Erythromycin	17.6%	0.1
Azithromycin	6.7%	0.1
Ceftriaxone	2.6%	<0.1
Meropenem	<0.1%	<0.1

Figure 20: Breakdown of the 'Access', 'Watch' and 'Reserve' categories of antibiotics consumed at national public sector level by percentage and total DID for both the financial years (2016-2017) and (2017-2018) in Tanzania. It also shows, the top five consumed antibiotics in their respective categories

Within the WHO AWaRe database exists a list of 'antibiotics not recommended' for use. This group of antibiotics consists of FDCs of multiple broad-spectrum antibiotics that are neither evidence-based, nor recommended in high-quality international guidelines. As a result, the WHO does not recommend their use in clinical practice. Furthermore, these antibiotics are represented as 'uncategorised' by the MAAP project. Analysis of the national public sector AMC data was made to identify their consumption in the country. Consumption of (n=2) of these antibiotics were observed (representing 3.8% consumption of total national public sector AMC) and are listed in Table 12 below. Among them, the FDC of Ampicillin/ Cloxacillin was the most frequently consumed (accounting for 97.4% of the consumption from the total consumption of the listed FDC antibiotics in Table 12), i.e., with a mean DID of 0.1. The national datasets were analysed in accordance with the AWaRe categorisation.[34]

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

Overall AMC rank*	Not recommended combination
8	Ampicillin/Cloxacillin
19	Ceftriaxone/Sulbactam

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

Aggregated pharmacy-level data were analysed from the (n=23) participating pharmacies and examined by the type of pharmacy (community against hospital pharmacies), by the service level of the hospitals (regional and zonal referral against national referral, and private and private faith-based versus public) and by their proportional consumption of WHO AWaRe category antibiotics. On average, the community and hospital pharmacies (both public and private faith-based) maintained an average consumption of greater than 60% for the 'Access' group antibiotics consumption (Table 13). However, (n=1) private hospital (a regional referral hospital) failed to meet the 60% 'Access' antibiotics consumption target, averaging a consumption of 47.6%. In addition, this single private hospital pharmacy consumed 35.3% more 'Watch' category antibiotics compared to the public hospital pharmacies and 36% more compared to the private faith-based hospital pharmacies.

Within the hospital-based pharmacies, of which (n=12) met the WHO threshold, the single public national referral hospital consumed more 'Watch' category antibiotics when compared to the consumption of both the public regional and zonal referral hospitals (i.e., 9.7% more than the regional referral hospitals and 21.5% more than the zonal referral hospital). Furthermore, despite the private faith-based hospital pharmacies on average meeting the minimum 'Access' consumption threshold, the private faith-based regional referral hospitals failed to meet the minimum threshold of consuming at least 60% 'Access' category antibiotics. The private faith-based regional referral hospitals consumed almost five times more 'Watch' category antibiotics compared to the private faith-based zonal referral hospitals. While within the community pharmacies, one pharmacy failed to meet the minimum threshold of consuming at least 60% 'Access' category antibiotics. 'Reserve' category antibiotic consumption was only observed within the single private regional referral hospital and no consumption was recorded within the public hospitals, private faith-based hospitals, and community pharmacies.

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

Pharmacy Type	AWaRe Categorisation		
	Access	Watch	Reserve
	Percentage share (Absolute DDD)		
Community pharmacies (7/23)	74.8% (6.7 million)	25.2% (2.2 million)	0.0% (0)
Hospital pharmacies (16/23)	82.8% (469 million)	17.1% (97.2 million)	<0.1% (289)
Public hospital pharmacies (11/16)	82.9% (464 million)	17.1% (95.9 million)	0.0% (0)
Regional Referral hospitals (9/11)	82.9% (463 million)	17.1% (95.4 million)	0.0% (0)
Zonal Referral hospital (1/11)	71.2% (398,975)	28.8% (161,311)	0.0% (0)
National Referral hospital (1/11)	61.5% (584,281)	38.5% (366,082)	0.0% (0)
Private Regional Referral hospital pharmacy (1/16)	47.6% (388,175)	52.4% (427,407)	<0.1% (289)
Private faith-based hospital pharmacies (4/16)	83.6% (4.2 million)	16.4% (833,928)	0.0%(0)
Regional Referral hospitals (2/4)	53.6% (502,589)	46.4% (435,362)	0.0% (0)
Zonal Referral hospitals (2/4)	90.4% (3.7 million)	9.6% (398,566)	0.0% (0)
Grand Total	82.7% (475 million)	17.3% (99.4 million)	<0.1% (289)

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

The WHO EML includes 39 antibiotics across the AWaRe categories. A total of 68 antibiotics were documented during national- and pharmacy-level data collection. Figure 21 shows the number of antibiotics for each AWaRe category in the WHO EML and NEMLIT, thereby indicating whether the antibiotic was documented during data collection.

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

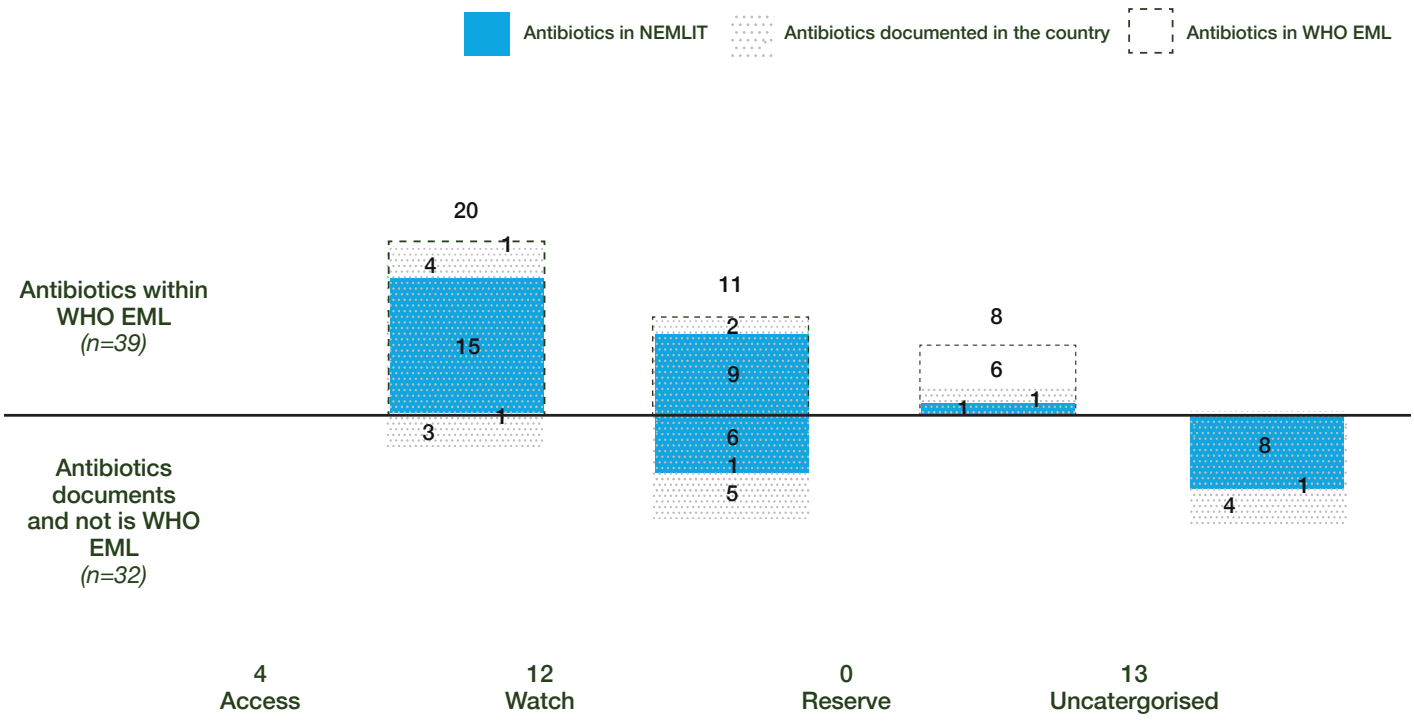
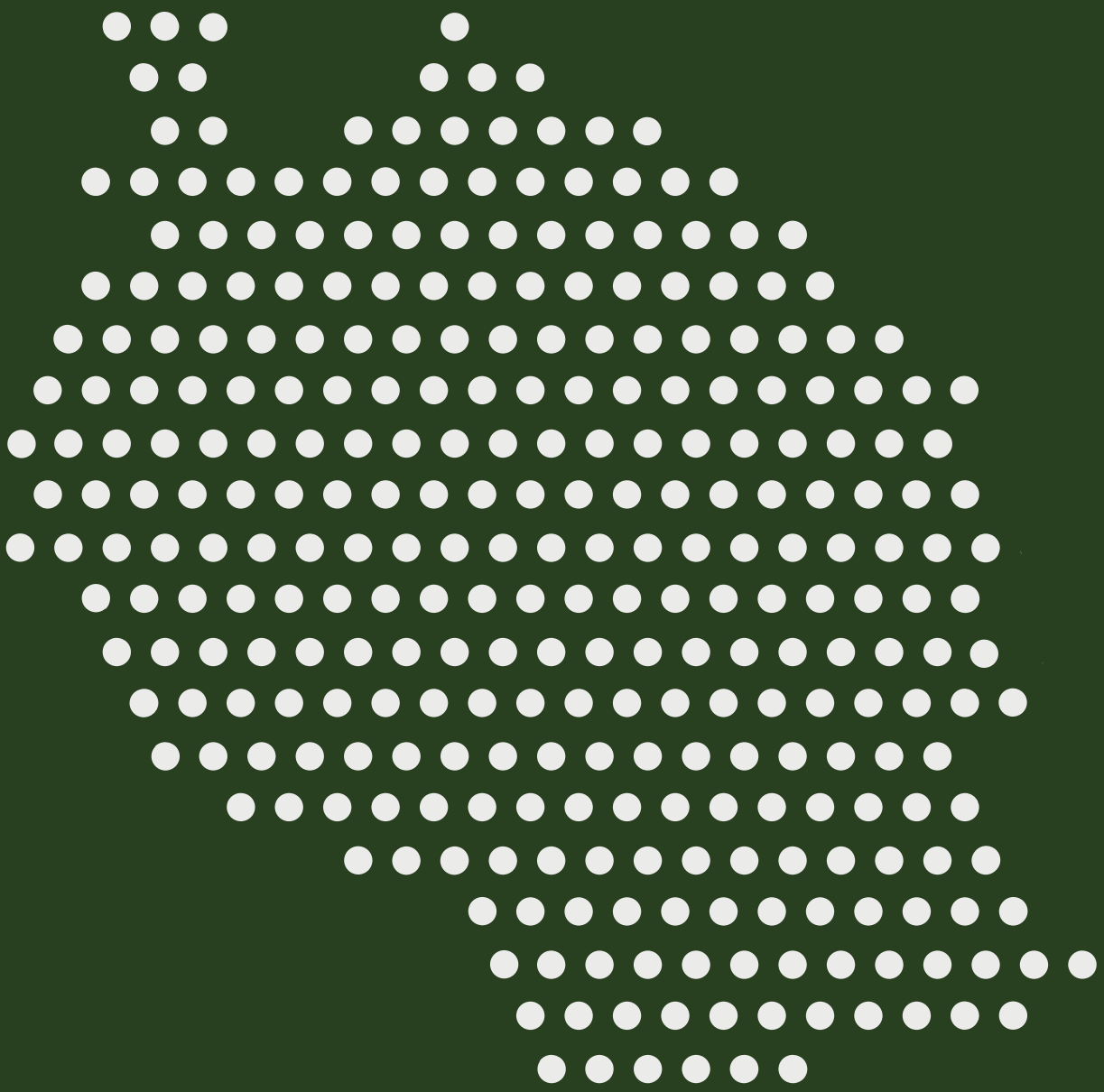


Figure 21: AWaRe analysis of documented antibiotics in national- and pharmacy-level data for the years 2016 to 2018 compared to WHO EML and NEMLIT definitions

Part C: Resistance and Consumption Interlinkages



Objective

To assess the relationship between antimicrobial consumption and antimicrobial resistance

Methodology

The DRI was estimated to convey aggregate rates of resistance as well as measurements of AMC (at a national level since AMU data were not available) across select pathogen-antimicrobial combinations (pathogens - Acinetobacter 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[36,37] (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 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. [38,39]

Apart from the DRI, correlation between AMC and AMR was conducted. Data on antimicrobial consumption 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 the most and least consumed antimicrobial classes is reported by the laboratories and based on data availability in each study year.

Results

Drug Resistance Index

The DRI estimate was found to be high at 59.8% (95% CI, 49.6-69.9%) implying low antibiotic effectiveness, which is a threat to effective infectious disease management and calls for urgent policy intervention (Figure 22).

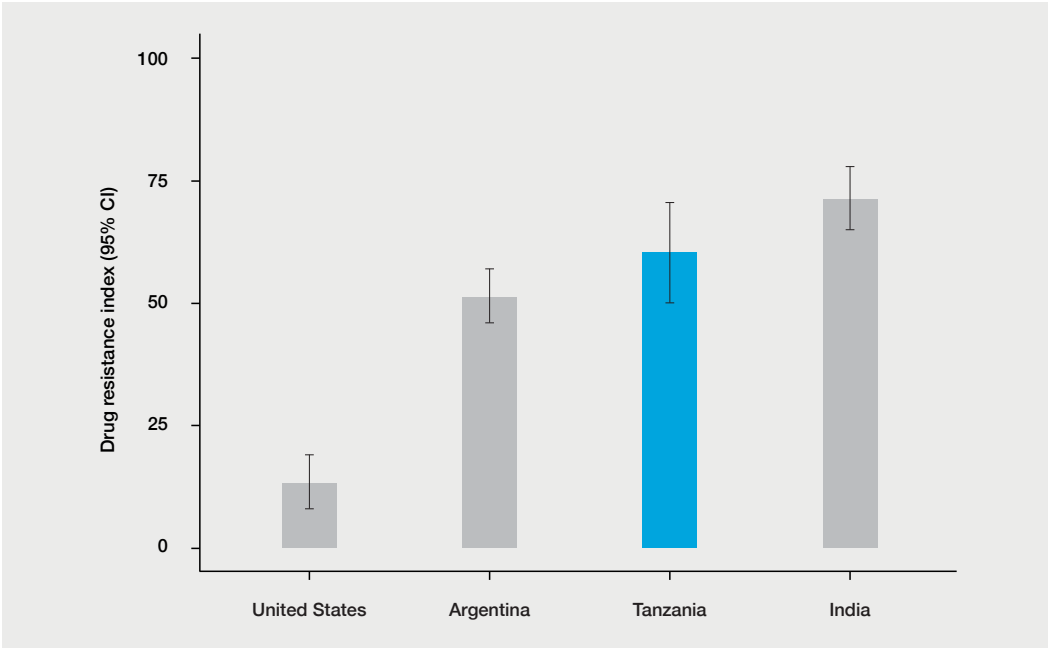


Figure 22: Drug Resistance Index

AMC and AMR correlation

The top three highly consumed antibiotic classes at facility level were aminopenicillins, nitroimidazoles, and macrolides. The AMR rates were highest for nitroimidazoles (100%), cephalosporins (1st-generation) (84%), and aminopenicillins (84%) (Table 14) Pearson's correlation analysis revealed a moderate positive correlation (r^2=0.29) between AMR and AMC, implying that the latter is a potential driver of AMR in Tanzania (Figure 23).

Table 14: AMC and AMR rates across antibiotic classes

Antibiotic class	Year	Total DDD in thousands	Resistance rate (%)
Aminopenicillins	2016-18	263.38	84.0
Nitroimidazoles	2016-18	89.45	100.0
Macrolides	2016-18	80.42	70.7
Folate pathway inhibitors	2016-18	70.07	78.4
Tetracyclines	2016-18	50.10	41.1
Fluoroquinolones	2016-18	18.37	41.8
Penicillins	2016-18	9.69	60.8
Beta-lactam combinations	2016-18	0.99	39.9
Cephalosporins (1st generation)	2016-18	0.82	84.0
Nitrofurans	2016-18	0.54	36.6
Cephalosporins (3rd generation)	2016-18	0.53	53.5

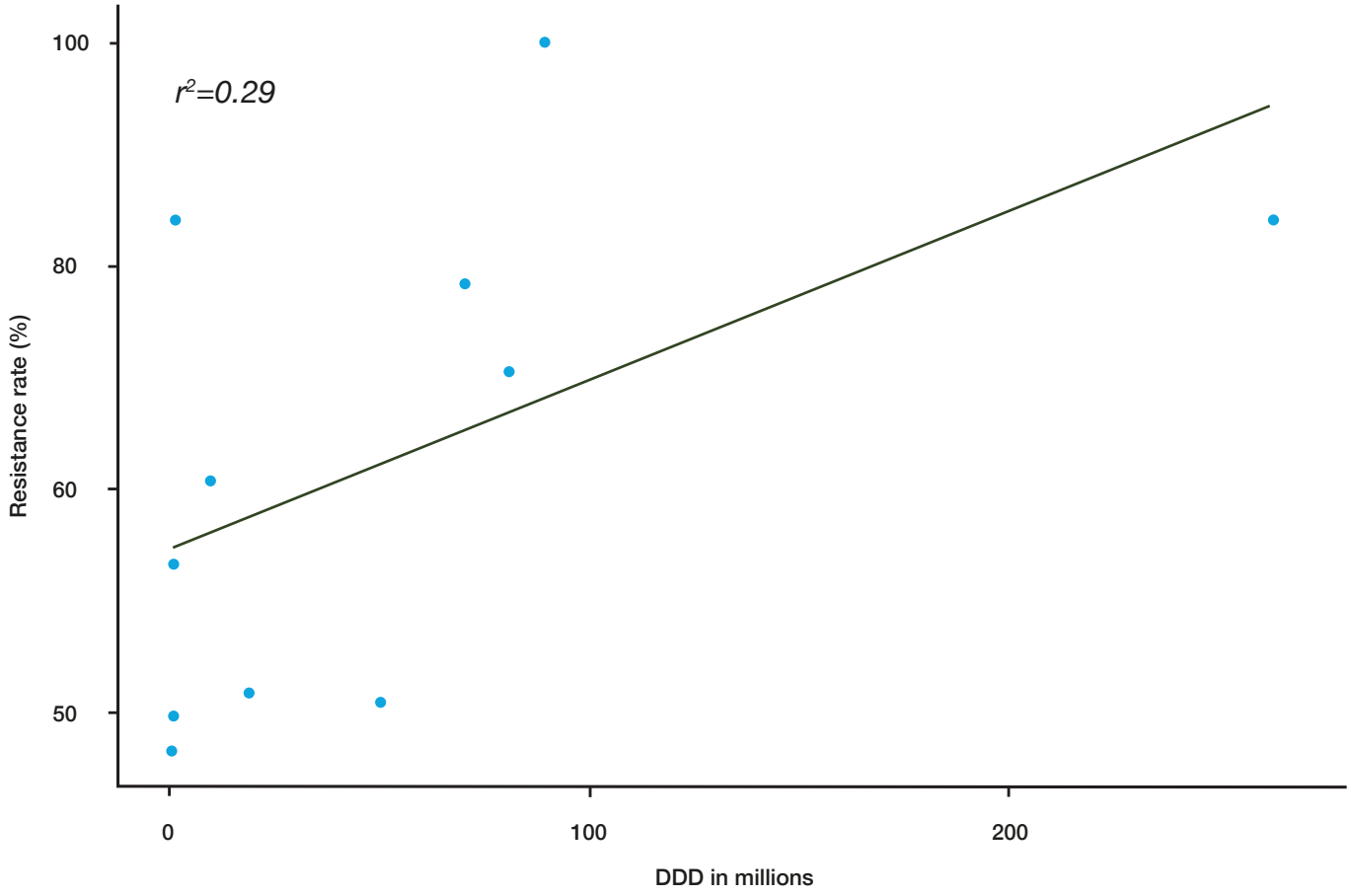


Figure 23: Correlation between AMR and AMC

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, fluoroquinolones,and nitrofurans. In 2017, high resistance rates (>75%) were noted for folate pathway inhibitor-resistant Streptococcus species, Escherichia species, Staphyloccocus species and Klebsiella species. In 2018, the highest resistance rates (>75%) were noted for folate pathway inhibitor-resistant Enterococcus species, Stretococcus species, Pseudomonas species and Escherichia species (Figure 24 and 25).

The least consumed antimicrobial classes across the study years were carbapenems and phenocols. 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 25% for carbapenem-resistant Enterbacter species, Staphylococcus species and Pseudomonas species. In 2018, resistance rates were more than 25% for carbapenem-resistant Pseudomonas species and Staphylococcus species (Figure 24 and 25).

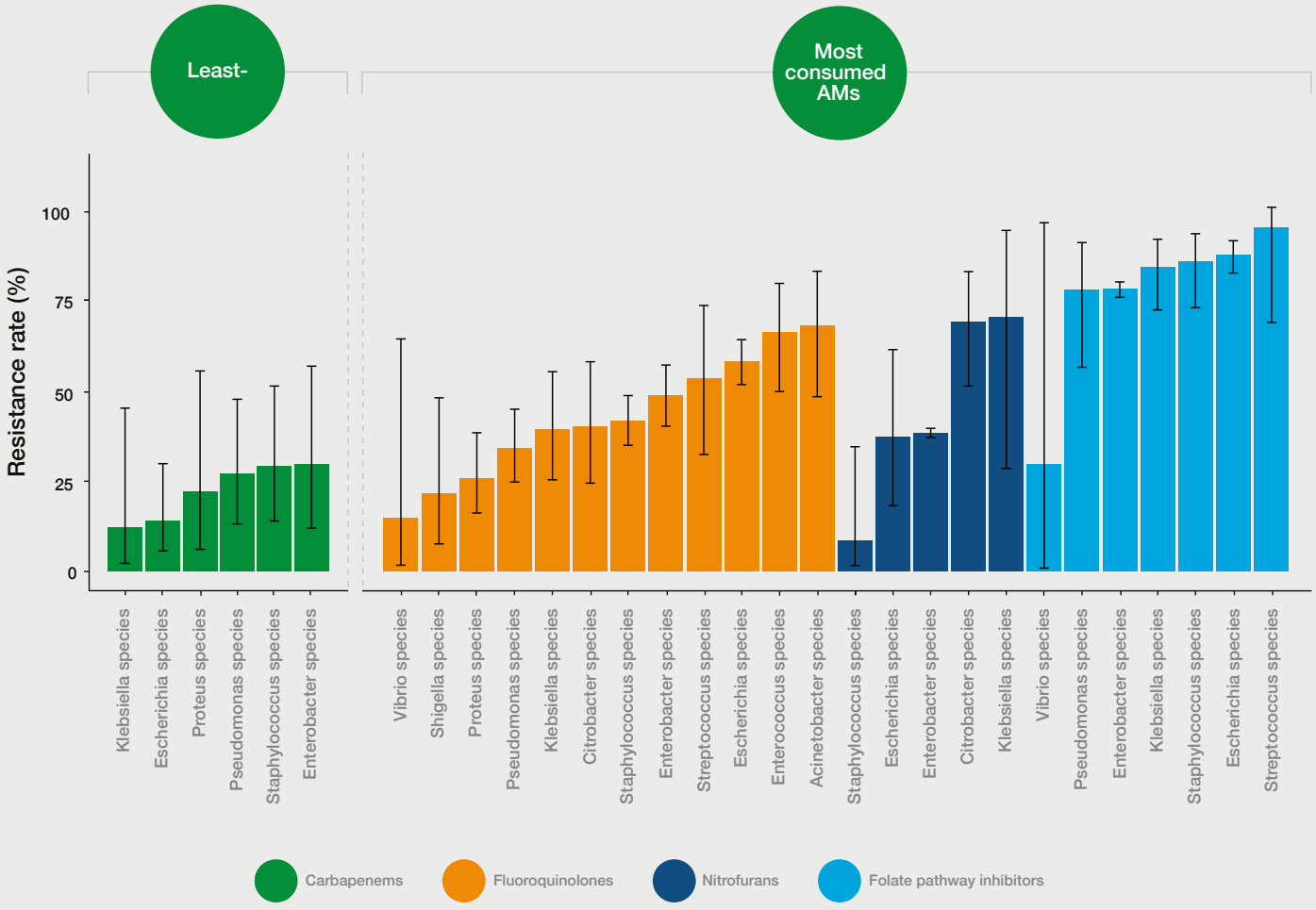


Figure 24: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2017

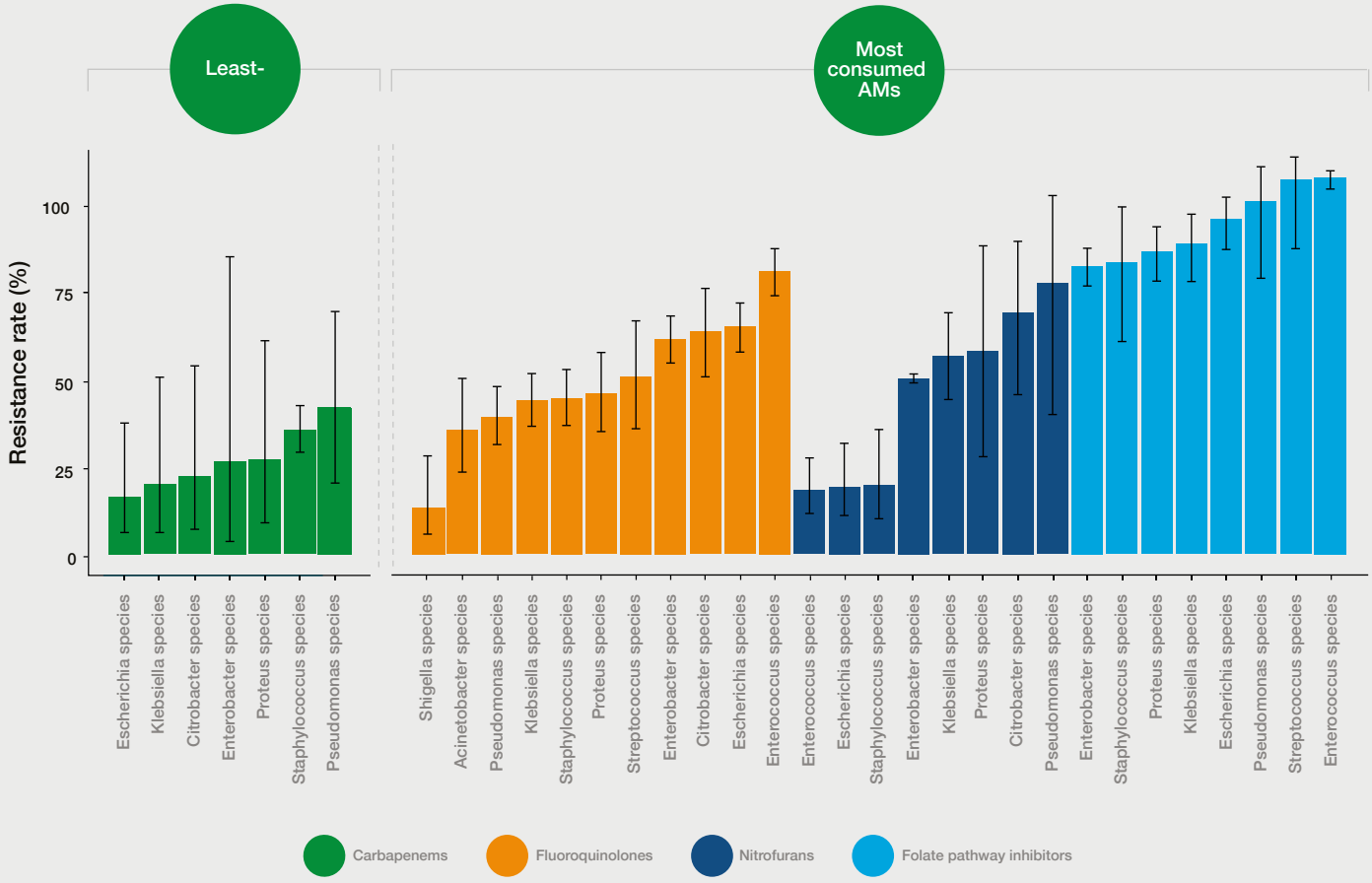
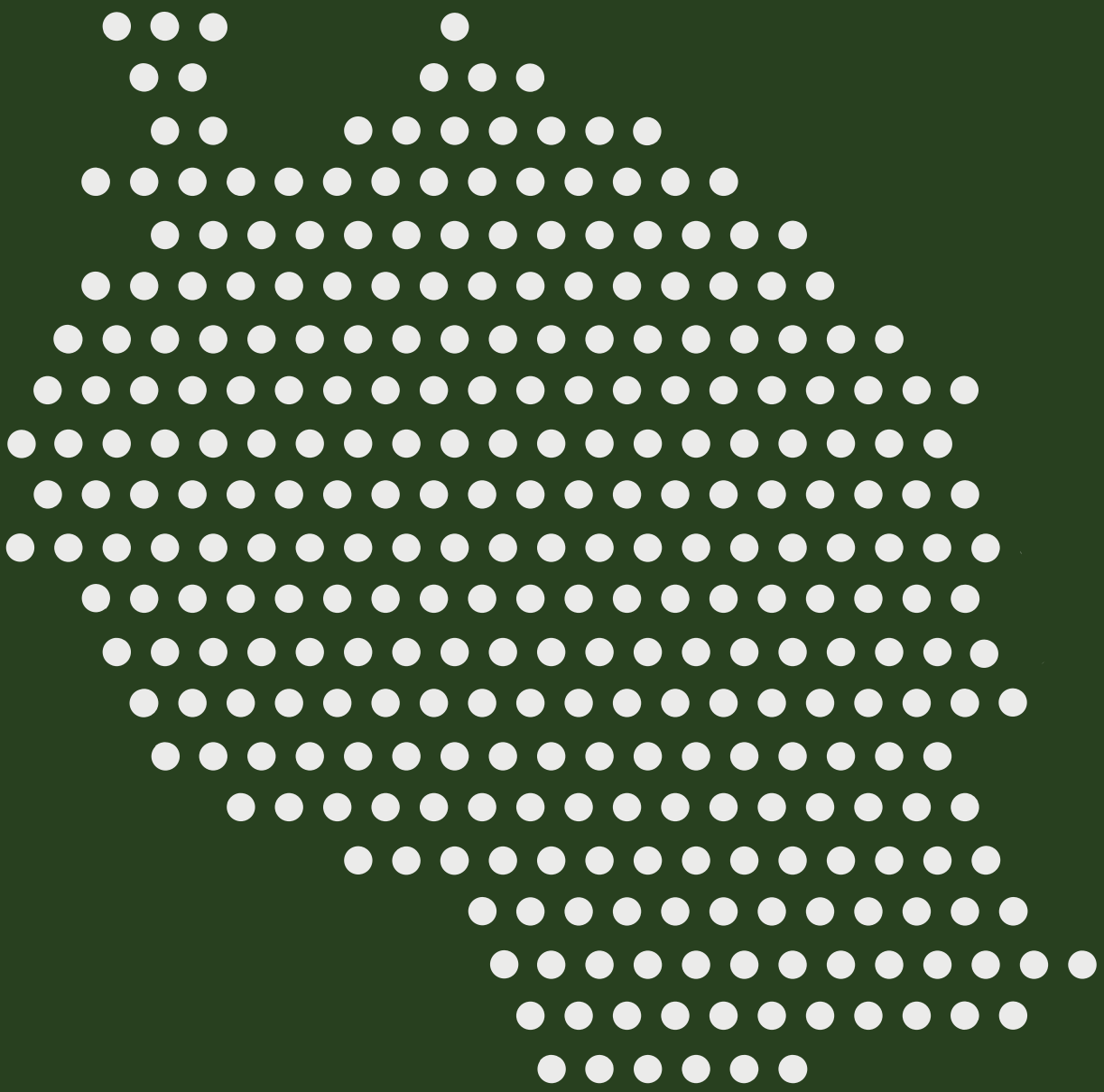


Figure 25: AMR rates for least (left) and most (right) consumed antimicrobial classes (AMs) in 2018

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.[40]

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 Tanzania.

Significance of AMR and DRI data and recommendations

Analysis of available AMR data from Tanzania revealed high levels of resistance for 3rd generation cephalosporin-resistant Enterobacterales (54-62%), while moderate resistance was noted for MRSA (25-35%), carbapenem-resistant P. aeruginosa (28-34%) and carbapenem-resistant Enterobacterales (18-24%).

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), 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.

Staphylococcus aureus (methicillin-resistant or sensitive) is a common cause of many skin and soft tissue infections in both community and healthcare settings. It can also cause invasive infections like endocarditis, osteomyelitis, pneumonia, visceral abscess, brain abscess, shunt infections and bacteraemia. Risk factors for MRSA infections include past infections/colonisation/close contact, trauma, invasive device (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 equally important to prevent and control the spread of MRSA infections. The 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.

P. aeruginosa is notorious for causing healthcare-associated infections. The organism is often multidrug resistant (either intrinsically or acquired). Prior use of carbapenems is a known risk factor for the emergence of carbapenem-resistant P. aeruginosa. Other risk factors include extended ICU stay, presence of invasive devices, prolonged bladder catheterisation, underlying comorbidities (such as diabetes and cystic fibrosis), burns and immunocompromised status. Since resistant Pseudomonas infections are often fatal, it is essential to promptly initiate the appropriate treatment as well as adopt simple source control measures such as standard precautions (including hand hygiene), catheter care, early device removal, and compliance to the infection prevention bundles. ASPs and infection control programmes must be established as they are effective efforts for AMR control.

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

Service delivery

The laboratory network in Tanzania was found to consist of 6 ,213 laboratories, of which only 35, were identified as bacteriological laboratories and with 27 confirmed their AST capabilities. While all the surveyed laboratories reported implementing QMS, not all were certified or accredited. Considering a country population of over 59.7 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. This 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, 93% had up-to-date records on training and competence and only 22% 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.[40] Capacity-building of staff may be completed through in-house expertise or outsourced to external organisations or tertiary facilities.

Information systems

The Regional Grant was a step towards the collection and digitisation of data. We noted observed that most of the surveyed laboratories relied on a combination of electronic and paper-based records and while 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 13 ,204 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 with on national and supra-national platforms. We also recommend establishing a system of assigning permanent identification numbers for patients' tracking over time. This would help to collect data on the a patient'ss' clinical profile, antimicrobial history, as well as pathogen's molecular profile (where available), thus offering more context to the AMR epidemiology than stand-alone antimicrobial susceptibility data.

Medicines and technologies

While there are various determinants of patient care, the importance of quality diagnostics can never be undermined. Even though laboratory audit was not the scope of the current study, we 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, use of authorised surrogates and ensuring the uninterrupted supply 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 physician's advice. 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 Tanzania to possibly consider in order to optimise the observed trends in consumption of antimicrobials and thus facilitate future surveillance activities.

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

In 2019, Tanzania responded to WHO's call by participating and providing national AMR data in its first global programme and reporting through the GLASS system (GLASS Report, 2020). Although the country is yet to enrol into the AMC reporting component within GLASS, Tanzania has previously participated and reported the national consumption of antimicrobials from import data for the year 2016 in WHO's first attempt to gather AMC worldwide data.20 MAAP was unsuccessful in obtaining import datasets from TMDA but was able to collect and analyse public sector consumption data from MSD. Consequently, the AMC data collected and analysed by MAAP excluded the private-for-profit and not-for-profit wholesalers or distributors data. MAAP was unable to quantify this gap in data coverage which represents consumption of the private (for-profit and not-for-profit) sector facilities and community pharmacies. Nonetheless, the historical data collected and analysed by MAAP at both the national public sector and pharmacy levels, provides the country with useful information around the trends in antimicrobial consumption. The surveillance of AMC data conducted at both the levels will further assist Tanzania's participation in GLASS-AMC reporting. However, as usage of antimicrobials datasets from MSD provides only partial coverage of AMC in Tanzania, efforts should be made by relevant regulatory authorities to identify and recruit private sector wholesalers or distributors, or large-volume health facilities to serve as sub-national points for AMC surveillance. Such an approach would also offer the added benefit of allowing the examination of AMC trends within both the private and public sectors and end-user institutions consuming the antimicrobials (i.e., national referral, zonal referral, and regional referral levels).

AMC data received from MSD required minimal cleaning and validation checks. However, better labelling of antibiotics in the system can help minimise the time required to collect the antibiotic consumption data from the data system and ensures complete data extraction. MAAP recommends the development of a comprehensive AMC surveillance policy to guide on, at the minimum, AMC data reporting variables and routine data cleaning or reporting practices to minimise the amount of time spent before routine surveillance exercises. This guiding policy will help ensure that the data used are accurate and usable for informing country policies. Pharmacy-level AMC data from the hospitals were 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 Tanzania which would have helped to characterise the reasons antimicrobials were used and whether their consumption was as according to country guidelines as well as aligned with WHO's drug use research methodology.[42] 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., ledger books at the pharmacy main store) did not allow for collection of AMU data variables. Nevertheless, a recent study successfully collected AMU data from three facilities in Tanzania through the use of the global point prevalence survey methodology.[29] This study was, however, conducted in only three hospitals and conclusions drawn from it cannot be assumed to represent national AMU or the MAAP sampled pharmacies. The success of this AMU study implies that the retrieval of AMU data where sub-optimal data systems exist can only be achieved through the establishment of point prevalence studies, and that retrospective studies, such as that which MAAP conducted in order to collect AMU data, may not be ideal.

The point prevalence studies approach would allow for data collection procedures to be intentionally set up to assess the patient in real-time through the cascade of care. Therefore, MAAP, in alignment with the WHO guide on facility AMU assessment, would recommend that future AMU surveillance attempts in the country be conducted through point prevalence surveys but on a scale that is representative of the country utilisation.[31] However, such an approach is time-consuming, unlike retrospective data collection, and often requires the engagement of trained data collection teams for prolonged durations. As a result, the approach is expensive and challenging to undertake in resource-limited settings. Retrospective AMU data collection can, however, still be an option if facilities targeted for data collection are selected based on the existence of certain systems (e.g., electronic patient records, cross-department unique patient identifiers and patient record retention systems) that will allow for the tracing of a patient through their clinical journey and utilisation of antimicrobials prescribed.

Overview of AMC consumption trends and recommendations

The total public sector AMC levels documented in this report give offer a useful benchmark to be compared against future country consumption levels following implementation of country national-level stewardship programmes. Compared to studies from other countries in the region, the observed public sector AMC levels in Tanzania are approximately equal to the levels described in literature for Burundi but was were lower than those the levels described in other African countries such as Burkina Faso, Cote d'Ivoire[20], Sierra Leone[24] as well as the levels previously reported in Tanzania[43]. The study by Mbwasi et al. (2020)[43], reported higher AMC rates in Tanzania compared to MAAP as they included both the import as well as locally manufactured records. This, which presents a comprehensive view of all antimicrobials consumed both in the public and private sectors. Conversely, the data analysed by MAAP only included public sector MSD datasets. The disparities in AMC with the other compared countries may be attributed to the limited AMC coverage by MAAP in Tanzania.

The disparities within the other countries may also be attributed to differences in relative burden of infectious diseases, limited availability of laboratory and point-of-care diagnostics at the health facility level within the countries. Widespread availability of antimicrobials over-the-counter and the unexplained use of some antimicrobials in the animal health sector may be additional contributing factors.[20] Despite the relatively lower rates of public sector AMC in Tanzania, AMU point prevalence surveys are recommended to better understand the public sector AMC levels and eventually guide any future national action plans and ASPs.

During the reviewed period, the national public sector AMC trend increased significantly. The reason(s) for this trend in the consumption of antimicrobials across the years of observation, cannot be definitively established. The private for-profit and not-for-profit wholesalers or distributors in Tanzania were not included in MAAP for the financial years July 2016 to June 2018. Future inclusion of the private for-profit, and not-for-profit wholesalers or distributors would enable the country to see whether the trends observed by MAAP were in fact a trend or whether annual data variance in AMC does in fact exist. The establishment of regular AMC surveillance will allow for the examination of AMC trends against baseline results presented here.

The evaluation relative antibiotic consumption, according to the WHO AWaRe categories, revealed that the proportion of narrow spectrum antibiotics in the 'Access' category well exceeded the minimum WHO recommended consumption threshold34 and the fair consumption of broader-spectrum 'Watch' category antibiotics was observed. This consumption trend implies that the NEMLIT antibiotics[35] that comprise mostly 'Access' category antibiotics, are widely available in the country. A similar trend of AMC was also observed when examining the consumption of 'Access' and 'Watch' category antibiotics from aggregated pharmacy-level AMC data. This finding is quite commendable as it implies that any emerging AMR trends due to misuse or overuse will likely be restricted to the narrow spectrum of antibiotics, sparing the lesser used broader-spectrum antibiotics in the 'Watch' category.

A 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 came only from the top five antibiotics in their respective 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.[44] This narrow consumption of antibiotics within the 'Access' and 'Watch' categories can also make the country susceptible to stockouts if manufacturing and supply chain issues are encountered. Considering the above-mentioned observations, it is therefore recommended that the country's ASP explores ways to encourage a wider spread in the consumption of antibiotics within each WHO AWaRe category. This may include offering incentives for the importation and distribution of other antibiotics in the WHO categories and those in-line with the country's EML. Tanzania's National EML (NEMLIT) incorrectly lists some antibiotics and FDCs 'not recommended for use' into different AWaRe categories e.g., the FDC of Ampicillin/Cloxacillin and Ceftrixazone/Sulbactum falls within the 'Access' and 'Watch' categories respectively. These combinations should instead not be recommended for use as outlined in the WHO AWaRe publication. In addition, the national EML is not exhaustive as it does not classify all MAAP reviewed antibiotics into the 'Access', 'Watch' and 'Reserve' categories. Therefore specific analysis was not made using this list. The findings from MAAP provide a useful starting point for the country AMRCC to review the current NEMLIT of antimicrobials based on the country's AMR and AMC patterns and in accordance with the WHO AWaRe categorisation of antibiotics.

Several interesting trends were observed when AMC was examined by the classification of sampled pharmacies. Firstly, within the public hospital pharmacies, the regional referral hospital pharmacies consumed lower levels of 'Watch' category antibiotics compared to the zonal referral and national referral hospital pharmacies. The higher consumption of 'Watch' category antibiotics at the national or zonal referral hospitals in comparison to regional referral hospitals could be attributed to the facilities dealing with complex diseases that would require treatment using second- and third-line antimicrobial agents. Secondly, despite the private or faith-based hospital pharmacies on average meeting the minimum WHO 'Access' category antibiotics consumption threshold as a whole, it was found that the single private regional referral hospital and the private faith-based regional referral hospitals failed to meet the 'Access' consumption threshold and consumed far more 'Watch' category antibiotics when compared to the private faith-based zonal referral hospitals.

This higher consumption trend of 'Watch' category antibiotics by the regional referral hospitals in comparison to zonal referral hospitals needs further surveillance and analysis to better understand the reasons for this occurrence. It will require AMU studies to be conducted to assess the appropriateness of these prescriptions and highlights the need for inclusion of all healthcare sectors into the country's ASP as well as the inclusion of all medicine distribution sectors in future surveillance activities by the country AMRCC. This will ensure that regulation of 'Watch' category antibiotics is conducted across all healthcare settings.

The consumption of WHO 'Reserve' category antibiotic was observed only within the pharmacy-level data, particularly from the single private regional referral hospital pharmacy. The absence of this category of antibiotics within the national AMC reported here may therefore be attributed to the absence of private sector data. Additionally, the absence of 'Reserve' antibiotics within the public sector sampled pharmacies and national public sector datasets may be attributed to the absence of these antibiotics within the NEMLIT. Here, we postulate that perhaps the public-sector facilities have more medicine procurement restrictions compared to the private sector facilities. Therefore, the absence of the consumption of 'Reserve' category antibiotics in the public sector implies a lack of 'accessibility rather than the regulation of their consumption or a lack of need for their use. It is possible that other conditions requiring treatment with 'Reserve' category antibiotics exist within the public sector that may be sub-optimally treated due to the unavailability of 'Reserve' category antibiotics in the sector.

MAAP recommends an urgent review be conducted by the MoH, AMRCC and relevant regulatory agencies in an effort to assess the availability of the 'Reserve' category antibiotics in the country, and where deemed necessary, the subsequent revision of the country's EML and treatment guidelines to include these vital antibiotics. This approach will ensure that the most vital antibiotics are available for all patients.

Finally, 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.[34] In Tanzania, within the national public sector datasets, the use of two such FDCs 'not recommended' by WHO were detected. Of these combinations, the use of the combination of Ampicillin/Cloxacillin was most prevalent. The clinical utility of using the FDC of Ampicillin/Cloxacillin has been questioned as the two antibiotics have overlapping spectra of activity, and indications that require treatment with both these antibiotics are uncommon.[45] Therefore, since this FDC and others are categorised under NEMLIT, it is recommended that the AMRCC identify the reasons for listing these 'not recommended' FDCs and determine the exact locations that commonly prescribe or dispense these FDC antibiotics. This will allow the country's MoH and associated medicine regulatory bodies to embark on sensitising prescribers on recommended treatments for those ailments to correct this prescribing practice.

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. Tanzania 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 65% of the consumption which indicates the opportunity for increased 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 be required to develop an AMC surveillance policy and address by whom, how and when national AMC datasets should be reported. This activity could be led by the AMRCC.

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

The regulatory authority, the Tanzania Medicines and Medical Devices Authority, could reconsider the registration status of unapproved FDCs.

The national stewardship programmes could work to review the EML and national treatment guidelines to anchor the availability and appropriate use of the essential 'Reserve' antibiotics.

B.

Service Delivery

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

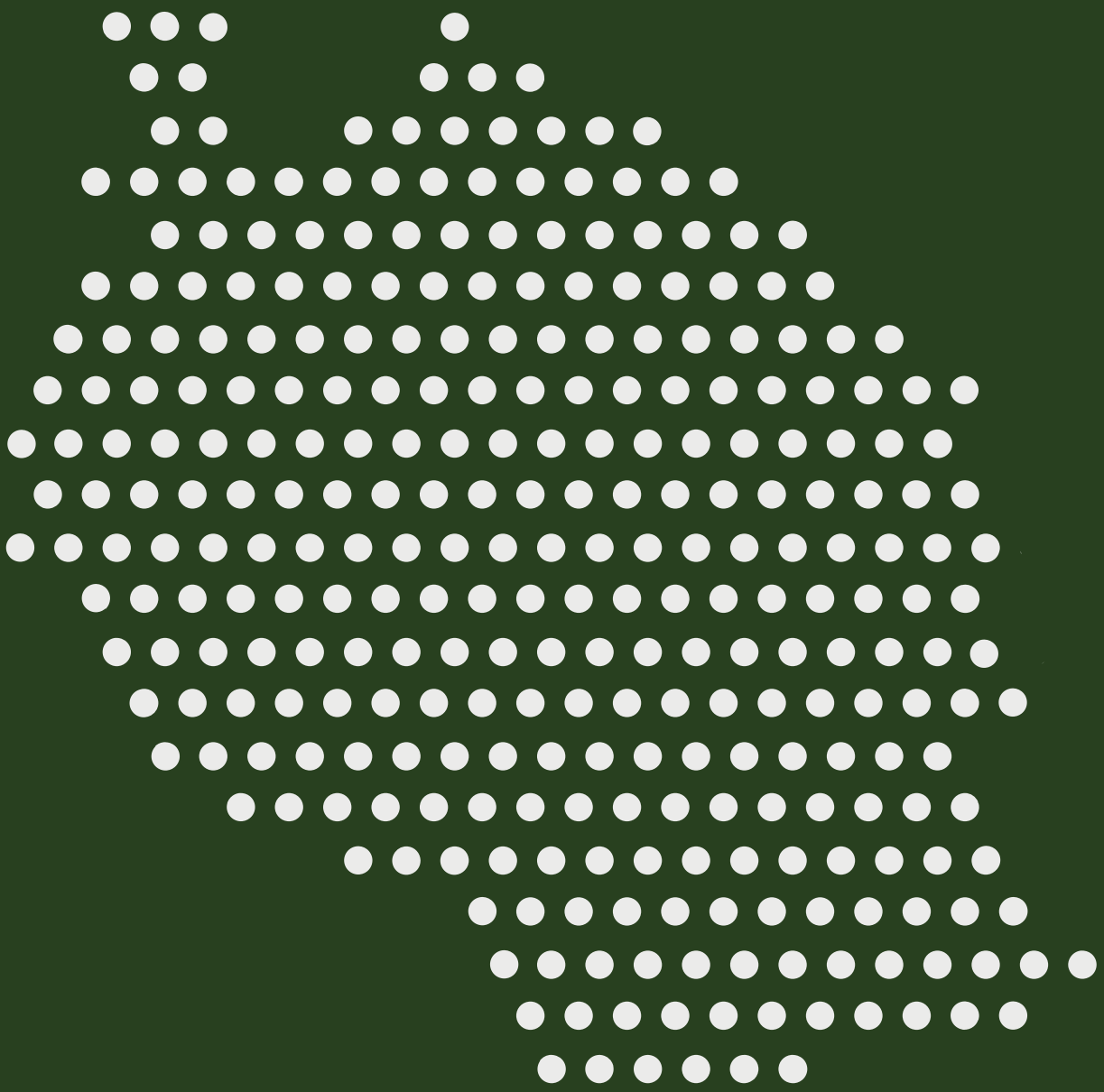
National stewardship programmes led by the AMRCC could conduct educational campaigns for healthcare practitioners to ensure that they are aware of the full spectrum of antimicrobials available in the country EML. In addition, they could investigate the use of WHO non-recommended FDC antibiotics in an effort to mitigate their use.

C.

Medical products and technologies

The country could develop national stewardship programmes and collaborate with pharmacists and medicine importers to increase the availability of 'Reserve' category antibiotics in selected facilities, as per the revised country's EML.

Part E: Limitations



Since the participating laboratories were at different levels of service and had variable testing capacity, all results in this report should be interpreted with caution. We encountered a few limitations during the conducting of the current study, as is 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 and therefore requiring manual retrieval. This was often compounded with issues of illegibility and/or incomplete demographics and clinical information.

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

3. The participating AMR laboratories (n=16) may not fully represent the true resistance rates in the country as they only encompassed a small proportion of the country's population (over 59.7 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 the drivers of resistance.

5. In relation to the national AMC level datasets, only the public sector market was covered. Thus, the lack of representation of the private (for-profit and not-for profit) wholesalers or distributors data means that the total AMC levels reported for Tanzania in this report are an underestimate of the country's total AMC.

6. To better understand whether the national public sector AMC trends were mirrored by pharmacy-level AMC trends, a sample of 23 pharmacies were purposively selected for data collection. This sample size was a relatively small proportion compared to the total number of pharmacies in Tanzania and did not geographically represent all regions and health zones in Tanzania. Therefore, a more systematic sampling strategy that factors in populations serviced as well as geographical locations will be required to make conclusions from pharmacy-level data more representative.

7. MAAP was successful in collecting AMC data from only seven community pharmacies. Other community pharmacies could not be included due to them not meeting the inclusion criteria (i.e., inability to 'access the data from their systems or the pharmacies not having data for the years of review) or due to the unwillingness to share data.

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

References

1. Fleming Fund. 'Accessed April 2, 2020. https://www.flemingfund.org/.

2. World Health Organisation. Worldwide Country Situation Analysis: Response to Antimicrobial Resistance. 'Accessed June 15, 2021. http://apps.who.int/iris/bitstream/handle/10665/163468/9789241564946_eng.pdf;jsessionid=040F003DCA2DE23A0E1484CFCF967D32?sequence=1.

3. African Society for Laboratory Medicine. MAAP. 'Accessed April 16, 2020. https://aslm.org/what-we-do/maap/.

4. DataBank | The World Bank. 'Accessed December 26, 2021. https://databank.worldbank.org/home.aspx

5. Education Statistics - All Indicators | DataBank. 'Accessed December 26, 2021. https://databank.worldbank.org/source/education-statistics-%5E-all-indicators

6. UHC service coverage index | Data. World Bank. Published 2019. 'Access'ed April 14, 2022. https://data.worldbank.org/indicator/SH.UHC.SRVS.CV.XD

7. HIV Facts and Figures | National AIDS Control Organisation | MoHFW | GoI. 'Accessed May 24, 2022. http://naco.gov.in/hiv-facts-figures

8. World Health Organisation. Global Action Plan on Antimicrobial Resistance.; 2015. 'Accessed April 16, 2019. https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1.

9. World Health Organisation. Global Antimicrobial Resistance Surveillance System (GLASS). Published 2021. 'Accessed April 16, 2021. https://www.who.int/glass/en/

10. Government of Tanzania. THE NATIONAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE, 2017 - 2022.; 2017. 'Accessed November 23, 2021. https://www.afro.who.int/sites/default/files/2017-07/NATIONAL ACTION PLAN FNL 10 May 2017.pdf

11. World Health Organisation. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report: Early Implementation 2020.; 2020. 'Accessed July 20, 2021. https://www.who.int/publications/i/item/9789240005587

12. United Republic of Tanzania, Chapter 219 . (2021, June 30). Tanzania Medicines and Medical Devices Act. Retrieved from https://www.tmda.go.tz/uploads/1630838474-CHAPTER%20219%20THE%20TANZANIA%20FOOD,%20DRUGS%20AND%20COSMETICS%20ACT.pdf

13. WHONET | Welcome to the WHONET Community website! 'Accessed December 23, 2021. https://whonet.org/

14. World Health Organisation. Prioritization of Pathogens to Guide Discovery, Research and Development of New Antibiotics for Drug-Resistant Bacterial Infections, Including Tuberculosis.; 2017.

15. Clinical and Laboratory Standards Institute. CLSI. Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition. CLSI Document M39-A4.; 2014.

16. Li F, Ayers TL, Park SY, et al. Isolate removal methods and methicillin-resistant Staphylococcus aureus surveillance. Emerging Infectious Diseases. 2005;11(10):1552-1557. doi:10.3201/eid1110.050162.

17. Brown Lawrence D. CTTDA. Interval Estimation for a Binomial Proportion. Stats Sci. 2001;16(2):101-133.

18. Kalanxhi E, Osena G, Kapoor G, Klein E. Confidence interval methods for antimicrobial resistance surveillance data. Antimicrobial Resistance and Infection Control. 2021;10(1). doi:10.1186/s13756-021-00960-5.

19. The Centre for Disease Dynamics Economics and Policy. ResistanceMap: Antibiotic resistance. 2018. 'Accessed June 15, 2021. https://resistancemap.cddep.org/About.php.

20. World Health Organisation. (2018). WHO report on surveillance of antibiotic consumption: 2016-2018 early implementation. Retrieved December 23, 2020, from https://apps.who.int/iris/bitstream/handle/10665/277359/9789241514880-eng.pdf?ua=1

21. Van Boeckel, T. P., Gandra, S., Ashok, A., Caudron, Q., Grenfell, B. T., Levin, S. A., and al., e. (2014). Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. The Lancet Infectious Diseases, 14(8), 742-750.

22. Gordon, C. (2020, April). Technical Bulletin: Surveillance and AMU. Retrieved June 01, 2021, from https://www.flemingfund.org/wp-content/uploads/29e140d66670221b9d95aaaa108ef03e.pdf

23. Martinez, E. M., Klein, E. Y., Van Boeckel, T. P., Pant, S., Gandra, S., Levin, S. A., . . . Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proceedings of the National Academy of Sciences, 115(15), E3463-E3470.

24. Kanu, J. S., Khogali, M., Hann, K., Tao, W., Barlatt, S., Komeh, J., . . . al., e. (2021). National Antibiotic Consumption for Human Use in Sierra Leone (2017–2019): A Cross-Sectional Study. Tropical Medicine and Infectious Disease, 6(2), 77.

25. Namugambe JS, D. A. (2021). National Antimicrobial Consumption: Analysis of Central Warehouses Supplies to In-Patient Care Health Facilities from 2017 to 2019 in Uganda. Tropical Medicine and Infectious Disease, 6(2), 83.

26. Okoth, C., Opanga, S., Okalebo, F., Oluka, M., Kurdi, A. B., and Godman, B. (2018). Point prevalence survey of antibiotic use and resistance at a referral hospital in Kenya: findings and implications. Hospital Practice, 46(3), 128-136.

27. Maina, M., Mwaniki, P., Odira, E., Kiko, N., McKnight, J., Schultsz, C., . . . Tosas-Auguete, O. (2020). Antibiotic use in Kenyan public hospitals: Prevalence, appropriateness and link to guideline availability. International Journal of Infectious Diseases, 99, 10-18.

28. Mukokinya, M. M., Opanga, S., Oluka, M., and Godman, B. (2018). Dispensing of Antimicrobials in Kenya: A Cross-sectional Pilot Study and Its Implications. Journal of Research in Pharmacy Practice, 7(2), 77-82.

29. Pius G. Horumpende, S. E. (2020). Point prevalence survey of antimicrobial use in three hospitals in North-Eastern Tanzania. Antimicrobial Resistance and Infection Control, 1-6, 9:149.

30. World Health Organisation. (2016). WHO methodology for a global programme on surveillance of antimicrobial consumption. Version 1.0. Retrieved December 23, 2020, from https://www.who.int/medicines/areas/rational_use/WHO_AMCsurveillance_1.0.pdf

31. World Health Organisation. (2019). WHO Methodology for Point Prevalence Survey on Antibiotic Use in Hospitals. Version 1.1. Retrieved June 21, 2021, from https://www.who.int/publications/i/item/WHO-EMP-IAU-2018.01

32.	World Health Organisation. (2020). WHOCC - ATC/DDD Index. Retrieved December 21, 2020, from https://www.whocc.no/atc_ddd_index/
33.	Worldometer. (2020). Tanzania population (2020 and historical) - Worldometer. Retrieved December 21, 2020, from https://www.worldometers.info/world-population/tanzania-population/
34.	World Health Organisation. (2019). Essential medicines and health products: WHO releases the 2019 AWaRe Classification Antibiotics. Retrieved December 21, 2020, from https://www.who.int/medicines/news/2019/WHO_releases2019AWaRe_classification_antibiotics/en/
35.	United Republic of Tanzania, Ministry of Health. (2018). Standard Treatment Guidelines and National Essential Medicines List Tanzania Mainland. Retrieved from http://www.tzdpg.or.tz/fileadmin/documents/dpg_internal/dpg_working_groups_clusters/cluster_2/health/Key_Sector_Documents/Tanzania_Key_Health_Documents/STANDARD_TREATMENT_GUIDELINES__CORRECT_FINAL_USE_THIS-1.pdf
36.	Klein EY, Tseng KK, Pant S, Laxminarayan R. Tracking global trends in the effectiveness of antibiotic therapy using the Drug Resistance Index. BMJ Global Health. 2019;4(2):1315. doi:10.1136/bmjgh-2018-001315.
37.	Laxminarayan R, Klugman KP. Communicating trends in resistance using a drug resistance index. BMJ Open. 2011;1(2): e000135. doi:10.1136/bmjopen-2011-000135.
38.	Barnett HAR. The Variance of the Product of Two Independent Variables and Its Application to an Investigation Based on Sample Data. Journal of the Institute of Actuaries. 1955;81(2):190-190. doi:10.1017/S0020268100035915
39.	Goodman LA. The Variance of the Product of K Random Variables. Journal of the American Statistical Association. 2012;57(297):54-60. doi:10.1080/01621459.1962.10482151
40.	Tadesse BT, Ashley EA, Ongarello S, et al. Antimicrobial resistance in Africa: a systematic review. BMC Infectious Diseases 2017 17:1. 2017;17(1):1-17. doi:10.1186/S12879-017-2713-1
41.	Carey RB, Bhattacharyy S, Kehl SC, et al. Implementing a quality management system in the medical microbiology laboratory. Clinical Microbiology Reviews. 2018;31(3). doi:10.1128/CMR.00062-17
42.	World Health Organisation. (2003). Introduction to Drug Utilisation Research. Retrieved May 19, 2021, from https://www.who.int/medicines/areas/quality_safety/safety_efficacy/Drug%20utilisation%20research.pdf?ua=1
43.	Mbwasi, R., Mapunjo, S., Wittenauer, R., Valimba, R., Msovela, K., Werth, B. J., . . . Konduri, N. (2020). National Consumption of Antimicrobials in Tanzania: 2017–2019. Frontiers in Pharmacology, 11, 1667.
44.	Laxminarayan, R., Matsoso, P., Pant, S., Brower, C., Røttingen, J.-A., Klugman, K., and al., e. (2016). 'Access to effective antimicrobials: a worldwide challenge. The Lancet, 387(10014), 168-175.
45.	Bortone, B. et al., 2021. High global consumption of potentially inappropriate fixed dose combination antibiotics: Analysis of data from 75 countries. PLoS ONE, 16(1), p. e0241899.

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 years).

Antimicrobial resistance:
According to the WHO, antimicrobial resistance occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines, making infections 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.

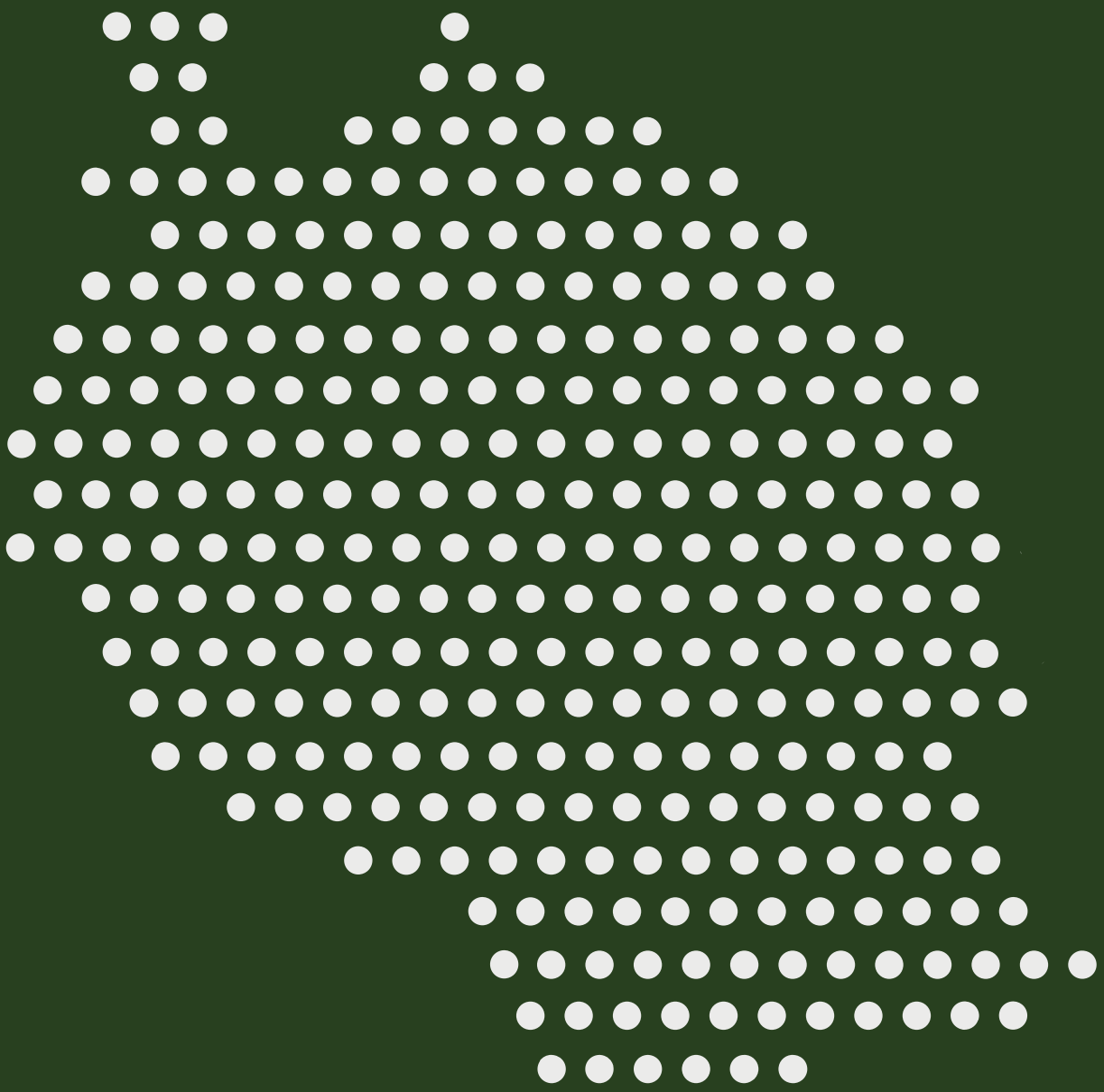
Quality Certification:
Certification is used for verifying that laboratory personnel have adequate credentials to practise certain disciplines as well as verifying that products meet certain requirements.

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

THIS DATA TRANSFER AGREEMENT FOR Researchers/Organizations (here-in-after **referred to as *the "Agreement"*)** is made this 9 Day of Oct , 2020

Between

Prof. Mabula D. Mchembe of P.O Box 743, 40478 Dodoma-Tanzania

(here-in-after referred to as the ***"PROVIDER"***);

and

Dr Yewande Alimi of P.O Box 3243, Addis Ababa, Ethiopia

(here-in-after referred to as "a person" or the ***"RECIPIENT"***).

PROVIDER and RECIPIENT may each be referred to as a "Party" or collectively as "Parties" to this Agreement.

This preamble shall be a definitive part of this Agreement

WHEREAS under this Agreement it is agreed that DATA of medical research may be transferred between Parties to this Agreement only through the conditions stipulated in this Agreement;

WHEREAS the PROVIDER retains all ownership rights on DATA procured from the study;

WHEREAS under this Agreement it is agreed that the DATA to be transferred pursuant to this Agreement are only those to be used for academic or research purposes;

WHEREAS it is hereby agreed that no transfer to third parties is allowed, except for academic or research purposes where RECIPIENT has secured the written consent of the PROVIDER;

WHEREAS it is hereby agreed that the RECIPIENT shall cooperate with the PROVIDER to facilitate capacity building in DATA management and analysis;

AND WHEREAS the parties to the Agreement undertake to be bound by any lawful order or instruction, as they will be from time to time be obliged to do by the Permit-Issuing Organization.

NOW THEREFORE in consideration of the mutual benefits to be derived and the representations, conditions and promises herein contained,

the **PARTIES HEREBY AGREE AS FOLLOWS:**

Annex I

Description of Information to be transferred under this Agreement: (**DTA**)

No 1. Antimicrobial Resistance (AMR) data linked to patient demographics and information on clinical syndrome

No 2. Antimicrobial Use/Consumption (AMU/C) (procurement, sales and distribution) of antibiotic

No 3. AMR and AMU/C information from key informant interviews (if needed)

Was the DATA described above collected under (Study Title):

MAPPING ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL USE PARTNERSHIP (MAAP)

A Research protocol Approved by Tanzania Authorities:

☑ Yes Certificate Number: NIMR/HQ/R.8a/Vol.IX/3532

☐ No

Research protocol related Grant or Contact from RECIPIENT's Government or Organization

☐ Yes Number:.....

☐ No

Provider Investigator : I declare that the above mentioned type(s) and format of Dataset areonly the one to be transferred herein.

Name: Dr. Nyanhwa Mtema

Signature: Date 24 November 2020

Seal Stamp

MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY & CHILDREN
NATIONAL HEALTH LABORATORY QUALITY ASSURANCE AND TRAINING CENTRE
P.O. Box 9083, DAR-ES-SALAAM

Authorized Official: CHAIR MRCC: **I approve ONLY ___ type (s) and format of Dataset mentioned here above to be transferred from Tanzania.**

Name: Dr. Paul. E. Kaaya

Signature: Date 27 / 22nd April / November / 2020

Seal Stamp

NATIONAL INSTITUTE FOR MEDICAL RESEARCH
NIMR
DAR ES SALAAM

Agreement No _____ Page 10 of 10

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

Part 4. Personnel and Training

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

Part 5. Specimen Management

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

<200	200-1000	1000-3000	>3000

Part 6. Laboratory Information System and Linkage to Clinical Data

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

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

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

Appendix 3: Laboratory Readiness Assessment

The EQ questions were scored for laboratory readiness as follows:

Part 1: Site Information (Maximum score=0)

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

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

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

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

3.1A	Was the laboratory implementing quality management systems at any time between 2016-2018?	Yes		No		Score 1 for "Yes" and 0 for "No
3.1B	If you answered 'yes' to question 1A: What quality management tools did the laboratory utilise? (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 utilise 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)

*(i) * 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 = 27 n (%)	Reference N = 7 n (%)	Regional/ Intermediate N = 20 n (%)	District/ Community N = 0 n (%)	Unspecified N = 0 n (%)
Government	21(77.78)	3 (42.9)	18 (90.0)	0	0
Private	3 (11.11)	2 (28.6)	1 (5.0)	0	0
NGO	1 (3.7)	0	1 (5.0)	0	0
Others	2 (7.41)	2 (28.6)	0	0	0

Supplementary Table 2: Assessment of preparedness for AMR surveillance

Parameters	Surveyed laboratories N=27 n (%)
Commodity and equipment status	
Regular power supply and functional back up	27 (100.0)
Continuous water supply	27 (100.0)
Certified and functional biosafety cabinets	23 (85.2)
Automated methods for pathogen identification	1 (3.7)
Automated methods for antimicrobial susceptibility testing	2 (7.4)
Methods for testing antimicrobial resistance mechanisms	12 (44.4)
QMS implementation	
Reported QMS Implementation	
• Reported QMS tool (n=27)	27 (100.0)
• LQMS	2 (7.4)
• SLIPTA	11 (40.7)
• SLMTA	2 (7.4)
• Mentoring	-
• Combination‡	2 (7.4)
• Others	10 (37.0)
Quality Certification	19 (70.4)
• Reported certification type (n=19)	
• SLIPTA	11 (57.9)
• College of American Pathologists	-
• Others	8 (42.1)
Accreditation	6 (22.2)
Participation in proficiency testing	25 (92.6)
Utilization of reference strains	25 (92.6)
Reported consistent maintenance of QC records	26 (96.3)
Designated focal quality person	25 (92.6)
Reported compliance to standard operating procedures	27 (100.0)
Reported compliance to antimicrobial susceptibility testing standards	25 (92.6)
Personnel and training status	
Presence of at least one qualified microbiologist	6 (22.2)
Presence of an experienced laboratory scientist/technologist	27 (100.0)
Up-to-date and complete records on staff training and competence	25 (92.6)
Specimen Management status	
Reported compliance to standard operating procedures on specimen collection and testing	27 (100.0)
Reported compliance to standard operating procedures on specimen rejection	27 (100.0)
Availability on average number of specimens processed for culture and sensitivity in year 2018	25 (92.6)
Laboratory Information System and Linkage to Clinical Data	
Assigned specimen (laboratory) identification number	27 (100.0)
Availability of system/database to store patient data	25 (92.6)
• System/database format (n=25)	
• Paper-based	4 (16.0)
• Electronic	-
• Mixed	21 (84.0)
Captured patients' demographics and clinical information on test request forms	25 (92.6)
• Retrievable test request forms (n=25)	19 (76.0)

**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		**12371**	**17493**	**42723**	**2530**	**3939**	**11112**	**1715**	**3479**	**8010**
Pathogen type	bacteria				2453 (97.0)	3862 (98.0)	10667 (96.0)	1714 (99.9)	3479 (100.0)	8002 (99.9)
	fungi				77 (3.0)	77 (2.0)	411 (3.7)	1 (0.1)		8 (0.1)
Age, years	Less than 1	379 (3.1)	874 (5.0)	2639 (6.2)	171 (6.8)	386 (9.8)	1030 (9.3)	170 (9.9)	378 (10.9)	479 (6.0)
	1 to 17	1038 (8.4)	2058 (11.8)	3638 (8.5)	390 (15.4)	567 (14.4)	1081 (9.7)	348 (20.3)	538 (15.5)	826 (10.3)
	18 to 49	2483 (20.1)	4064 (23.2)	7259 (17.0)	915 (36.2)	968 (24.6)	2152 (19.4)	780 (45.5)	869 (25.0)	1610 (20.1)
	50 to 65	545 (4.4)	1195 (6.8)	2786 (6.5)	192 (7.6)	331 (8.4)	1036 (9.3)	167 (9.7)	318 (9.1)	782 (9.8)
	Above 65	316 (2.6)	661 (3.8)	3152 (7.4)	128 (5.1)	210 (5.3)	1441 (13.0)	116 (6.8)	205 (5.9)	1014 (12.7)
	Unknown Age	7610 (61.5)	8641 (49.4)	23249 (54.4)	734 (29.0)	1477 (37.5)	4372 (39.3)	134 (7.8)	1171 (33.7)	3299 (41.2)
Gender	Male	2603 (21.0)	4618 (26.4)	5275 (12.3)	1015 (40.1)	1371 (34.8)	2007 (18.1)	903 (52.7)	1303 (37.5)	1949 (24.3)
	Female	9768 (79.0)	12875 (73.6)	37448 (87.7)	1515 (59.9)	2568 (65.2)	9105 (81.9)	812 (47.3)	2176 (62.5)	6061 (75.7)
Laboratory	Bukoba	69 (0.6)	68 (0.4)	153 (0.4)	26 (1.0)	12 (0.3)	20 (0.2)	24 (1.4)	11 (0.3)	16 (0.2)
	Dodoma	371 (3.0)	324 (1.9)	538 (1.3)	52 (2.1)	38 (1.0)	56 (0.5)	36 (2.1)	27 (0.8)	54 (0.7)
	Haydom	169 (1.4)	24 (0.1)	218 (0.5)	28 (1.1)	1 (0.0)	59 (0.5)	25 (1.5)	1 (0.0)	59 (0.7)
	Iringa	65 (0.5)	91 (0.5)	22 (0.1)	27 (1.1)	32 (0.8)	15 (0.1)	27 (1.6)	32 (0.9)	15 (0.2)
	Mawenzi	224 (1.8)	337 (1.9)	212 (0.5)	36 (1.4)	18 (0.5)	10 (0.1)	15 (0.9)	18 (0.5)	10 (0.1)
	Morogoro	1675 (13.5)	672 (3.8)	812 (1.9)	867 (34.3)	264 (6.7)	295 (2.7)	856 (49.9)	252 (7.2)	261 (3.3)
	Muhimbili	4900 (39.6)	10037 (57.4)	9490 (22.2)		1790 (45.4)	1828 (16.5)	1788 (51.4)	1824 (22.8)	
	Singida	115 (0.9)	290 (1.7)	42 (0.1)	42 (1.7)	107 (2.7)	15 (0.1)	34 (2.0)	85 (2.4)	5 (0.1)
	Sokoine	79 (0.6)	110 (0.6)	196 (0.5)	26 (1.0)	16 (0.4)	55 (0.5)	24 (1.4)	16 (0.5)	53 (0.7)
	Ndanda	112 (0.9)	178 (1.0)	396 (0.9)	26 (1.0)	39 (1.0)	70 (0.6)	23 (1.3)	36 (1.0)	69 (0.9)
	Mnazi Mmoja	22 (0.2)	281 (1.6)	549 (1.3)	5 (0.2)	127 (3.2)	298 (2.7)	5 (0.3)	93 (2.7)	282 (3.5)
	Bugando	3958 (32.0)	3749 (21.4)	8504 (19.9)	1183 (46.8)	1117 (28.4)	2154 (19.4)	595 (34.7)	827 (23.8)	1711 (21.4)
	Sekou Toure	551 (4.5)	117 (0.7)	146 (0.3)	192 (7.6)	15 (0.4)	25 (0.2)	43 (2.5)	15 (0.4)	21 (0.3)
	Aga Khan			9506 (22.3)			2150 (19.3)		1802 (22.5)	
	KCMC			10514 (24.6)			3655 (32.9)		1486 (18.6)	
	Mbeya	61 (0.5)	1215 (6.9)	1425 (3.3)	20 (0.8)	363 (9.2)	407 (3.7)	8 (0.5)	278 (8.0)	342 (4.3)

Supplementary Table 4: Specimen characteristics

Specimen Type	All years* N= 13204 n (%)	2016 N = 1715 n (%)	2017 N = 3479 n (%)	2018 N = 8010 n (%)
Abscess/Discharge/Pus/Swab/Wound	3099 (23.5)	363 (21.2)	839 (24.1)	1897 (23.7)
Aspirate/discharge	3 (0)	-	1 (0)	2 (0)
Blood	3549 (26.9)	263 (15.3)	1375 (39.5)	1911 (23.9)
Catheter (unspecified)	1 (0)	-	-	1 (0)
CSF	67 (0.5)	12 (0.7)	23 (0.7)	32 (0.4)
Fluid (abdominal/peritoneal)	22 (0.2)	2 (0.1)	11 (0.3)	9 (0.1)
Fluid (joint/synovial)	1 (0)	-	-	1 (0)
Fluid (pleural)	37 (0.3)	2 (0.1)	8 (0.2)	27 (0.3)
Fluid (unspecified)	34 (0.3)	3 (0.2)	8 (0.2)	23 (0.3)
Other	7 (0)	6 (0.3)	-	1 (0)
Respiratory-Lower	1 (0)	-	-	1 (0)
Respiratory-Upper	793 (6)	21 (1.2)	266 (7.6)	506 (6.3)
Stool	177 (1.3)	41 (2.4)	58 (1.7)	78 (1)
Swab (cervical)	3 (0)	-	1 (0)	2 (0)
Swab (rectal)	705 (5.3)	640 (37.3)	52 (1.5)	13 (0.2)
Swab (urethral)	37 (0.3)	8 (0.5)	12 (0.3)	17 (0.2)
Swab (vaginal)	126 (1)	14 (0.8)	9 (0.3)	103 (1.3)
Swab/discharge (ear)	1 (0)	-	1 (0)	-
Tissue/biopsy	4 (0)	1 (0.1)	-	3 (0)
Ulcer	1 (0)	-	-	1 (0)
Urine	4536 (34.4)	339 (19.8)	815 (23.4)	3382 (42.2)

**Indicates positive cultures with AST results*

Supplementary Table 5: Pathogen identification

Pathogen	All years* N= 13204 n (%)	2016 N = 1715 n (%)	2017 N = 3479 n (%)	2018 N = 8010 n (%)
Positive cultures with specific pathogen name	7579 (57.4)	1294 (75.5)	2122 (61)	4163 (52)
Acinetobacter baumannii	22 (0.2)	-	9 (0.3)	13 (0.2)
Aeromonas hydrophila	11 (0.1)	1 (0.1)	-	10 (0.1)
Aeromonas salmonicida	2 (0)	-	-	2 (0)
Aggregatibacter aphrophilus	1 (0)	-	-	1 (0)
Bacillus anthracis	3 (0)	-	-	3 (0)
Bacillus cereus	1 (0)	-	1 (0)	-
Bipolaris australiensis	5 (0)	-	-	5 (0.1)
Burkholderia cepacia	2 (0)	-	1 (0)	1 (0)
Burkholderia pseudomallei	1 (0)	-	-	1 (0)
Chromobacterium violaceum	2 (0)	-	-	2 (0)
Chryseomonas luteola	1 (0)	-	1 (0)	-
Citrobacter braakii	1 (0)	-	-	1 (0)
Citrobacter freundii	28 (0.2)	-	2 (0.1)	26 (0.3)
Citrobacter koseri	4 (0)	-	1 (0)	3 (0)
Corynebacterium pseudotuberculosis	1 (0)	-	-	1 (0)
Edwardsiella tarda	1 (0)	-	-	1 (0)
Ehrlichia sennetsu	1 (0)	-	-	1 (0)
Elizabethkingia meningosepticum	4 (0)	-	-	4 (0)
Enterobacter amnigenus	1 (0)	-	-	1 (0)
Enterobacter cloacae	12 (0.1)	-	1 (0)	11 (0.1)
Enterococcus faecalis	67 (0.5)	10 (0.6)	12 (0.3)	45 (0.6)
Enterococcus faecium	1 (0)	-	-	1 (0)
Escherichia coli	2211 (16.7)	176 (10.3)	710 (20.4)	1325 (16.5)
Escherichia vulneris	2 (0)	-	-	2 (0)
Haemophilus influenzae	33 (0.2)	-	3 (0.1)	30 (0.4)
Klebsiella aerogenes	11 (0.1)	-	2 (0.1)	9 (0.1)
Klebsiella oxytoca	47 (0.4)	8 (0.5)	12 (0.3)	27 (0.3)
Klebsiella pneumoniae	582 (4.4)	71 (4.1)	116 (3.3)	395 (4.9)
Moraxella catarrhalis	4 (0)	-	2 (0.1)	2 (0)
Morganella morganii	9 (0.1)	-	1 (0)	8 (0.1)
Neisseria gonorrhoeae	29 (0.2)	4 (0.2)	11 (0.3)	14 (0.2)
Ochrobactrum anthropi	3 (0)	-	-	3 (0)
Pantoea (enterobacter) agglomerans	3 (0)	-	2 (0.1)	1 (0)
Pasteurella pneumotropica	2 (0)	-	-	2 (0)

Proteus mirabilis	207 (1.6)	39 (2.3)	49 (1.4)	119 (1.5)
Proteus penneri	1 (0)	-	-	1 (0)
Proteus vulgaris	68 (0.5)	6 (0.3)	12 (0.3)	50 (0.6)
Providencia rettgeri	1 (0)	-	1 (0)	-
Providencia stuartii	4 (0)	-	1 (0)	3 (0)
Pseudomonas aeruginosa	631 (4.8)	62 (3.6)	223 (6.4)	346 (4.3)
Pseudomonas putida	5 (0)	-	-	5 (0.1)
Pseudomonas stutzeri	1 (0)	-	-	1 (0)
Raoultella ornithinolytica	9 (0.1)	-	1 (0)	8 (0.1)
Salmonella typhi	23 (0.2)	1 (0.1)	11 (0.3)	11 (0.1)
Salmonella typhimurium	1 (0)	1 (0.1)	-	-
Serratia liquefaciens	2 (0)	-	-	2 (0)
Serratia marcescens	5 (0)	-	-	5 (0.1)
Serratia odorifera	21 (0.2)	-	-	21 (0.3)
Serratia plymuthica	1 (0)	-	-	1 (0)
Shewanella putrefaciens	1 (0)	-	-	1 (0)
Shigella dysenteriae	4 (0)	-	4 (0.1)	-
Shigella flexneri	1 (0)	-	-	1 (0)
Shigella sonnei	5 (0)	-	-	5 (0.1)
Staphylococcus arlettae	2 (0)	-	2 (0.1)	-
Staphylococcus aureus	2353 (17.8)	251 (14.6)	744 (21.4)	1358 (17)
Staphylococcus auricularis	5 (0)	-	-	5 (0.1)
Staphylococcus epidermidis	64 (0.5)	1 (0.1)	30 (0.9)	33 (0.4)
Staphylococcus lugdunensis	3 (0)	-	1 (0)	2 (0)
Staphylococcus saccharolyticus	3 (0)	-	-	3 (0)
Staphylococcus saprophyticus	62 (0.5)	9 (0.5)	9 (0.3)	44 (0.5)
Stenotrophomonas (xanthomonas) maltophilia	1 (0)	-	-	1 (0)
Streptococcus agalactiae	11 (0.1)	-	4 (0.1)	7 (0.1)
Streptococcus pneumoniae	86 (0.7)	5 (0.3)	31 (0.9)	50 (0.6)
Streptococcus pyogenes	130 (1)	2 (0.1)	31 (0.9)	97 (1.2)
Streptococcus rattus	9 (0.1)	5 (0.3)	1 (0)	3 (0)
Streptococcus viridans	29 (0.2)	3 (0.2)	12 (0.3)	14 (0.2)
Vibrio cholerae	716 (5.4)	638 (37.2)	65 (1.9)	13 (0.2)
Vibrio cincinnatiensis	4 (0)	1 (0.1)	3 (0.1)	-
Vibrio fluvialis	1 (0)	-	-	1 (0)
Vibrio parahaemolyticus	1 (0)	-	-	1 (0)
Positive cultures with non-specific pathogen name	5625 (42.6)	421 (24.5)	1357 (39)	3847 (48)
Acinetobacter Sp.	66 (0.5)	7 (0.4)	21 (0.6)	38 (0.5)

Aeromonas Sp.	4 (0)	2 (0.1)	-	2 (0)
Anaerobes	1 (0)	-	-	1 (0)
Bacillus Sp.	3 (0)	-	3 (0.1)	-
Campylobacter Sp.	2 (0)	1 (0.1)	1 (0)	-
Candida Sp.	3 (0)	1 (0.1)	-	2 (0)
Chromobacterium Sp.	2 (0)	-	-	2 (0)
Citrobacter Sp.	228 (1.7)	41 (2.4)	29 (0.8)	158 (2)
Corynebacterium Sp.	5 (0)	-	3 (0.1)	2 (0)
Edwardsiella Sp.	46 (0.3)	12 (0.7)	15 (0.4)	19 (0.2)
Ehrlichia Sp.	7 (0.1)	-	1 (0)	6 (0.1)
Enterobacter Sp.	1466 (11.1)	64 (3.7)	73 (2.1)	1329 (16.6)
Enterococcus Sp.	196 (1.5)	25 (1.5)	30 (0.9)	141 (1.8)
Erwinia Sp.	1 (0)	-	1 (0)	-
Escherichia Sp.	20 (0.2)	-	4 (0.1)	16 (0.2)
Haemophilus Sp.	3 (0)	-	-	3 (0)
Kingella Sp.	7 (0.1)	-	1 (0)	6 (0.1)
Klebsiella Sp.	755 (5.7)	16 (0.9)	230 (6.6)	509 (6.4)
Micrococcus Sp.	4 (0)	-	2 (0.1)	2 (0)
Myroides Sp.	1 (0)	-	-	1 (0)
Neisseria Sp.	5 (0)	2 (0.1)	3 (0.1)	-
Non fermenting gram negative bacilli	4 (0)	-	-	4 (0)
Pantoea Sp.	1 (0)	-	-	1 (0)
Proteus Sp.	189 (1.4)	18 (1)	64 (1.8)	107 (1.3)
Prototheca Sp.	1 (0)	-	-	1 (0)
Providencia Sp.	7 (0.1)	-	-	7 (0.1)
Pseudomonas Sp.	405 (3.1)	2 (0.1)	109 (3.1)	294 (3.7)
Salmonella Sp.	56 (0.4)	11 (0.6)	20 (0.6)	25 (0.3)
Serratia Sp.	23 (0.2)	3 (0.2)	5 (0.1)	15 (0.2)
Shigella Sp.	112 (0.8)	39 (2.3)	32 (0.9)	41 (0.5)
Spirillum Sp.	8 (0.1)	-	-	8 (0.1)
Staphylococcus Sp.	924 (7)	30 (1.7)	539 (15.5)	355 (4.4)
Streptobacillus Sp.	1 (0)	-	-	1 (0)
Streptococcus Sp.	204 (1.5)	13 (0.8)	90 (2.6)	101 (1.3)
Unspecified (Gram negative bacilli)	61 (0.5)	17 (1)	4 (0.1)	40 (0.5)
Unspecified (Gram negative bacteria)	782 (5.9)	105 (6.1)	74 (2.1)	603 (7.5)
Unspecified (Gram negative cocci)	4 (0)	3 (0.2)	-	1 (0)
Unspecified (Gram positive bacilli)	3 (0)	1 (0.1)	-	2 (0)
Unspecified (Gram positive cocci)	15 (0.1)	8 (0.5)	3 (0.1)	4 (0)

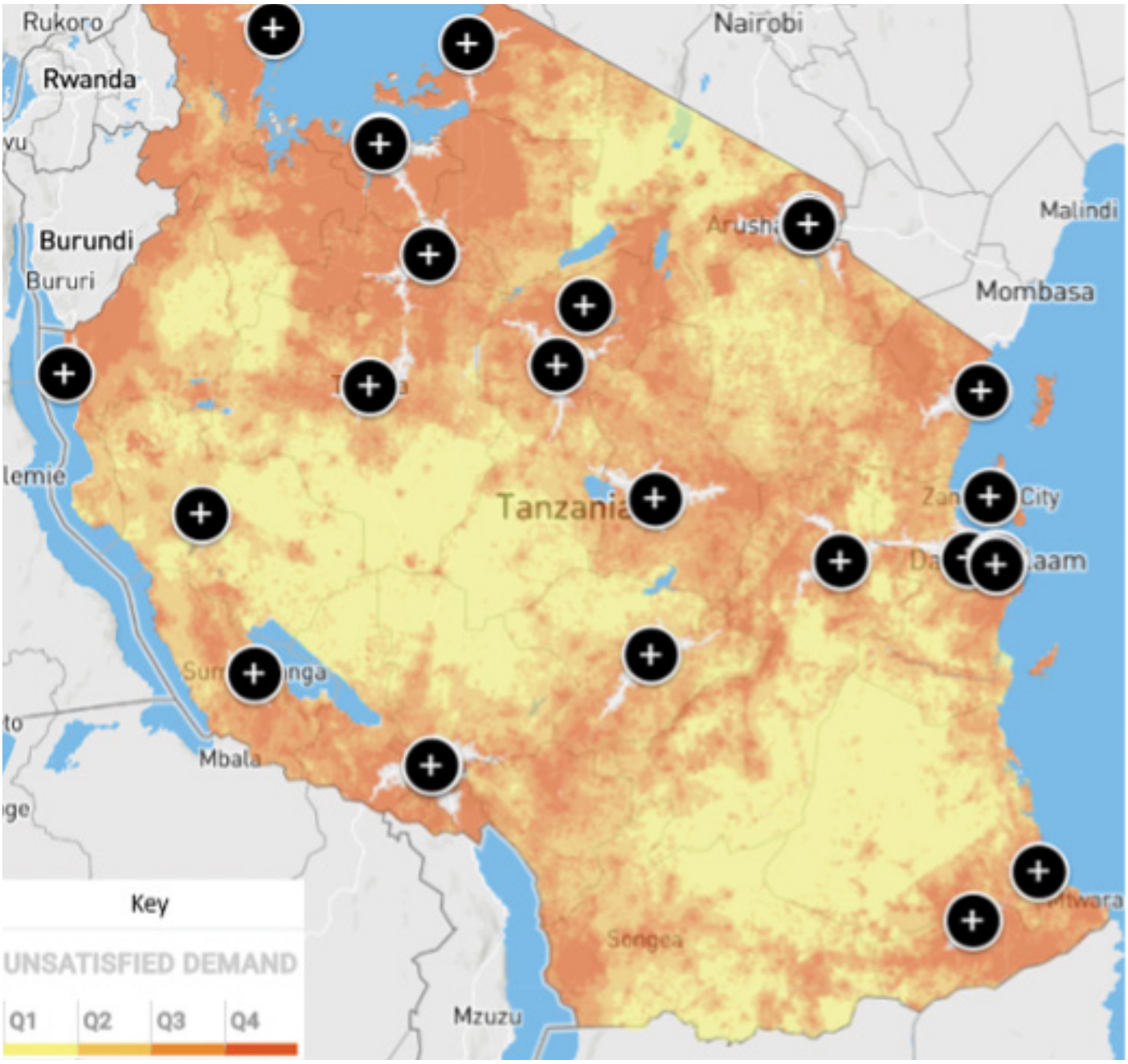
*Note: * indicates positive cultures with AST results; '-' means information was not available.*

Supplementary Table 6: Laboratory data scoring

Laboratory name	Laboratory data score (out of 4)			
	2016	2017	2018	Average
Muhimbili	-	2	3	2.5
Aga Khan	-	-	2	2
Ndanda	2	3	4	3
Haydom	-	4	3	3.5
Mawenzi	3	4	4	3.7
Dodoma	2	3	3	2.7
Morogoro	4	3	4	3.7
Sokoine	4	4	4	4
KCMC	-	-	3	3
Bugando	3	4	3	3.3
Sekou Toure	4	3	4	3.7
Mnazi Mmoja	4	4	4	4
Mbeya	3	3	3	3
Iringa	3	4	4	3.7
Bukoba	2	4	2	2.7
Singida	4	4	4	4

AMR Supplementary Figures

Supplementary Figure 1: Population coverage of laboratories



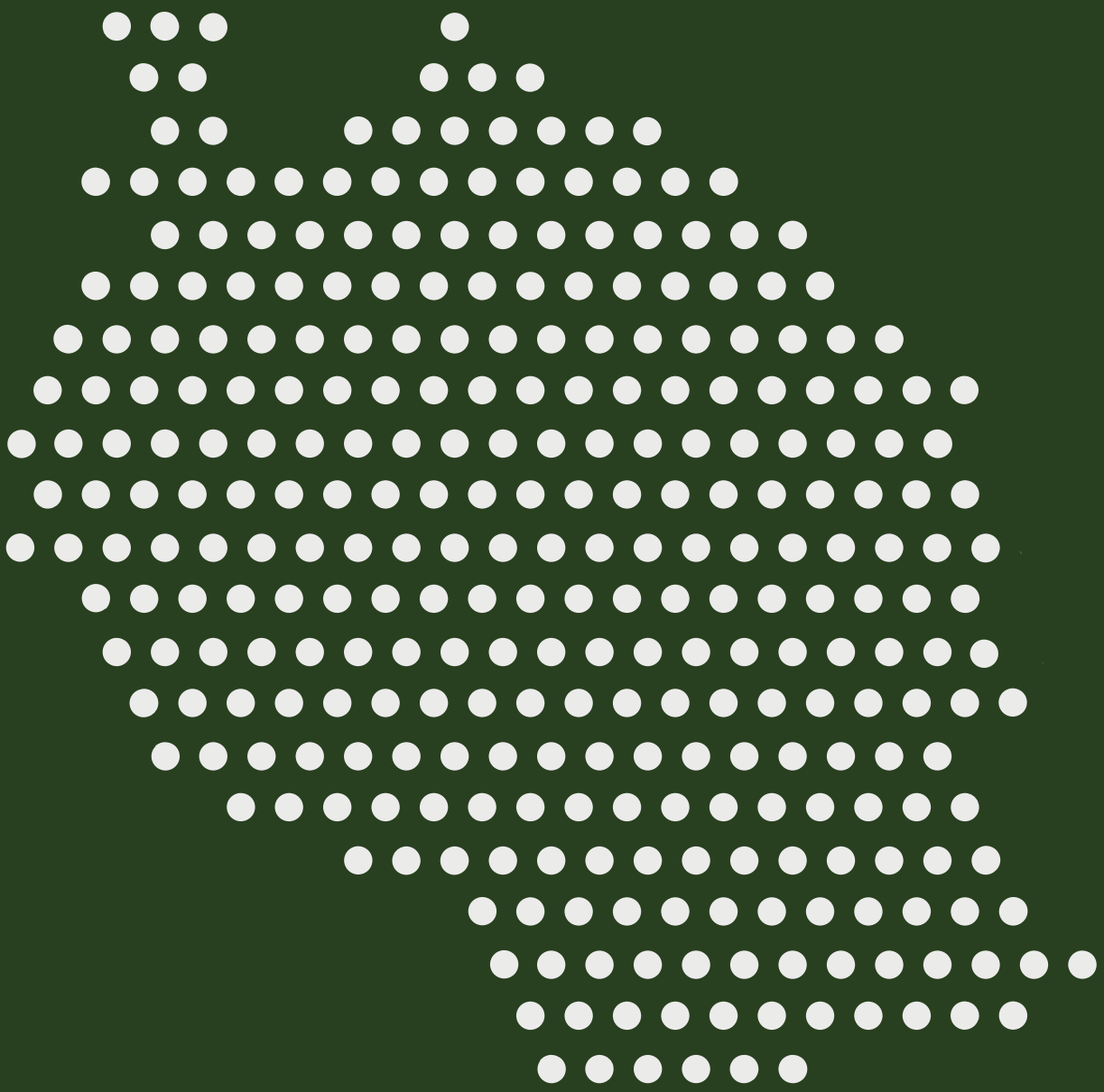
Supplementary Figure 2a: Inappropriate testing A

Organism Name	Antimicrobial Agent	Agent Code	Interpreted Results	Antimicrobial Susceptibility Method	Year
Bipolaris australiensis	Amoxicillin / Clavulanic acid	AMC_ND20	R	Disk	2016
Bipolaris australiensis	Cefuroxime	CXM_ND30	R	Disk	2016
Bipolaris australiensis	Cefepime	FEP_ND30	R	Disk	2016
Candida sp.	Gentamicin	GEN_ND10	R	Disk	2016
Candida sp.	Amoxicillin / Clavulanic acid	AMC_ND20	R	Disk	2017
Candida sp.	Ceftazidime	CAZ_ND20	R	Disk	2017
Bipolaris australiensis	Ciprofloxacin	CIP_ND5	R	Disk	2017
Bipolaris australiensis	CefuroxineCeftriaxone	CRO_ND30	R	Disk	2017
Bipolaris australiensis	Cefepime	FEP_ND30	R	Disk	2017
Bipolaris australiensis	Imipenem	IPM_ND10	R	Disk	2017
Bipolaris australiensis	Piperacillin / Tazobactam	TZP_ND100	S	Disk	2017
Candida sp.	Ciprofloxacin	CIP_ND5	S	Disk	2017
Candida sp.	Cefotaxime	CTX_ND30	S	Disk	2017
Candida sp.	Cefepime	FEP_ND30	S	Disk	2017
Candida sp.	Imipenem	IPM_ND10	S	Disk	2017
Candida sp.	Piperacillin / Tazobactam	TZP_ND100	S	Disk	2017
Candida sp.	Amikacin	AMK_ND30	S	Disk	2018
Candida sp.	Meropenem	MEM_ND10	S	Disk	2018
Candida sp.	Piperacillin	PIP_ND100	S	Disk	2018

Supplementary Figure 2b: Inappropriate testing B

Organism Name	Antimicrobial Agent	Agent Code	Interpreted Results	Antimicrobial Susceptibility Method	Year
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Enterobacter sp.	Oxacillin	OXA_ND1	R	Disk	2016
Escherichia coli	Oxacillin	OXA_ND1	R	Disk	2016
Escherichia coli	Penicillin V	PNV_ND10	R	Disk	2016
Klebsiella sp.	Penicillin V	PNV_ND10	R	Disk	2016
Enterococcus sp.	Oxacillin	OXA_ND1	R	Disk	2016
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2017
Escherichia coli	Penicillin G	PEN_ND10	R	Disk	2017
Klebsiella sp.	Penicillin V	PNV_ND10	R	Disk	2017
Klebsiella sp.	Oxacillin	OXA_ND1	R	Disk	2017
Escherichia coli	Penicillin G	PEN_ND10	S	Disk	2017
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2018
Escherichia coli	Vancomycin	VAN_ND30	I	Disk	2018
Escherichia coli	Vancomycin	VAN_ND30	S	Disk	2018
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2016
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2016
Staphylococcus aureus	Vancomycin	VAN_ND30	I	Disk	2016
Staphylococcus aureus	Vancomycin	VAN_ND30	I	Disk	2016
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2017
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2017
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2017
Staphylococcus aureus	Vancomycin	VAN_ND30	I	Disk	2017
Staphylococcus aureus	Vancomycin	VAN_ND30	R	Disk	2018

AMC Appendices



Appendix 1: Key Informant Interview (KII) tool

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

Domestic Producers and Importers

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

Procurement, Storage and Distribution

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

Public Sector

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

Private Sector

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

Donor Funded Supply

1.13	Is there any donor support for procurement of antibiotics in the country?	Yes		No	
1.14	If yes to above, who are the donors and what are the procedures regarding import and distribution of donated antibiotics?				
1.15	Which sector(s) is supported with supplies procured through donor agencies?				
	Public Sector	Private			
1.16	If there is donor support, are antibiotics sourced locally or imported?				
1.17	Does the available donor data indicate specific country antibiotic consumption? Do these procurement mechanisms fit in with the countries regulatory systems and WHOs recommended surveillance practices? or are there challenges?				
1.18	What proportion/quantity of antibiotics are procured/supplied from donor programmes; 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 utilised by relevant authorities to track and trace illegally imported antibiotics in the country?

Appendix 2: Eligibility questionnaire for pharmacies

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

Instructions

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

Eligibility questionnaire for Community Pharmacies:

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

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

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

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

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

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

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

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

Cefixime/Sulbactam	J01	U
Cefoperazone/Sulbactam	J01	U
Cefoperazone/Tazobactam	J01	U
Cefoselis	J01	R
Cefotaxime/Sulbactam	J01	U
Cefpodoxime/Azithromycin	J01	U
Cefpodoxime/Cloxacillin	J01	U
Cefpodoxime/Dicloxacillin	J01	U
Cefpodoxime/Levofloxacin	J01	W
Cefpodoxime/Ofloxacin	J01	W
Ceftazidime/Avibactam	J01	R
Ceftazidime/Sulbactam	J01	U
Ceftazidime/Tazobactam	J01	U
Ceftazidime/Tobramycin	J01	U
Ceftizoxime/Tazobactam	J01	U
Ceftolozane	J01	R
Ceftriaxone/Sulbactam	J01	U
Ceftriaxone/Tazobactam	J01	U
Ceftriaxone/Vancomycin	J01	U
Cefuroxime/Clavulanic Acid	J01	W
Cefuroxime/Linezolid	J01	U
Cefuroxime/Sulbactam	J01	U
Cephalosporin C	J01	U
Ciclacillin	J01	U
Erythromycin Stearate	J01	U
Erythromycin Stinoprate	J01	U
Etimicin	J01	W
Furbenicillin	J01	W
Guamecycline	J01	U
Imipenem	J01	U
Kitasamycin	J01	U
Lenampicillin	J01	U
Levofloxacin/Azithromycin	J01	W
Levofloxacin/Metronidazole	J01	U
Meleumycin	J01	U
Meropenem/Sulbactam	J01	U
Norvancomycin	J01	W
Novobiocin	J01	U

Ofloxacin/Azithromycin	J01	U
Panipenem	J01	W
Piperacillin/Sulbactam	J01	U
Piperacillin/Tazobactam	J01	W
Pivampicillin/Pivmecillinam	J01	U
Polymyxin M	J01	R
Sulfadoxine/Trimethoprim	J01	U
Sulfalene/Trimethoprim	J01	U
Sulfamethizole/Trimethoprim	J01	A
Sulfamethoxypyridazine/Trimethoprim	J01	U
Demeclocycline	J01AA01	U
Doxycycline	J01AA02	A
Chlortetracycline	J01AA03	W
Lymecycline	J01AA04	W
Metacycline	J01AA05	W
Oxytetracycline	J01AA06	W
Tetracycline	J01AA07	A
Minocycline	J01AA08	W, R (IV)
Rolitetracycline	J01AA09	U
Penimepicycline	J01AA10	U
Clomocycline	J01AA11	U
Tigecycline	J01AA12	R
Eravacycline	J01AA13	R
Chloramphenicol	J01BA01	A
Thiamphenicol	J01BA02	A
Ampicillin	J01CA01	A
Pivampicillin	J01CA02	A
Carbenicillin	J01CA03	W
Amoxicillin	J01CA04	A
Carindacillin	J01CA05	U
Bacampicillin	J01CA06	A
Epicillin	J01CA07	U
Pivmecillinam	J01CA08	A
Azlocillin	J01CA09	W
Mezlocillin	J01CA10	W
Mecillinam	J01CA11	A
Piperacillin	J01CA12	W
Ticarcillin	J01CA13	W
Metampicillin	J01CA14	U

Talampicillin	J01CA15	U
Sulbenicillin	J01CA16	W
Temocillin	J01CA17	W
Hetacillin	J01CA18	U
Aspoxicillin	J01CA19	U
Benzylpenicillin	J01CE01	A
Phenoxymethylpenicillin	J01CE02	A
Propicillin	J01CE03	U
Azidocillin	J01CE04	U
Pheneticillin	J01CE05	W
Penamecillin	J01CE06	A
Clometocillin	J01CE07	A
Benzathine phenoxymethylpenicillin	J01CE10	U
Dicloxacillin	J01CF01	A
Cloxacillin	J01CF02	A
Meticillin	J01CF03	U
Oxacillin	J01CF04	A
Flucloxacillin	J01CF05	A
Nafcillin	J01CF06	A
Sulbactam	J01CG01	U
Tazobactam	J01CG02	U
Ampicillin/Clavulanic Acid	J01CR01	A
Amoxicillin/Clavulanic Acid	J01CR02	A
Ticarcillin/Clavulanic Acid	J01CR03	W
Sultamicillin	J01CR04	A
Cefalexin	J01DB01	A
Cefaloridine	J01DB02	U
Cefalotin	J01DB03	A
Cefazolin	J01DB04	A
Cefadroxil	J01DB05	A
Cefazedone	J01DB06	A
Cefatrizine	J01DB07	A
Cefapirin	J01DB08	A
Cefradine	J01DB09	A
Cefacetrile	J01DB10	A
Cefroxadine	J01DB11	A
Ceftezole	J01DB12	A
Cefoxitin	J01DC01	W
Cefuroxime	J01DC02	W

Cefamandole	J01DC03	W
Cefaclor	J01DC04	W
Cefotetan	J01DC05	W
Cefonicid	J01DC06	W
Cefotiam	J01DC07	W
Loracarbef	J01DC08	U
Cefmetazole	J01DC09	W
Cefprozil	J01DC10	W
Ceforanide	J01DC11	W
Cefminox	J01DC12	W
Cefbuperazone	J01DC13	W
Flomoxef	J01DC14	W
Cefotaxime	J01DD01	W
Ceftazidime	J01DD02	W
Cefsulodin	J01DD03	U
Ceftriaxone	J01DD04	W
Cefmenoxime	J01DD05	W
Latamoxef	J01DD06	W
Ceftizoxime	J01DD07	W
Cefixime	J01DD08	W
Cefodizime	J01DD09	W
Cefetamet	J01DD10	W
Cefpiramide	J01DD11	W
Cefoperazone	J01DD12	W
Cefpodoxime	J01DD13	W
Ceftibuten	J01DD14	W
Cefdinir	J01DD15	W
Cefditoren	J01DD16	W
Cefcapene	J01DD17	W
Cefteram	J01DD18	W
Cefotaxime/Clavulanic Acid	J01DD51	W
Ceftazidime/Clavulanic Acid	J01DD52	W
Ceftazidime/Clavulanic Acid	J01DD52	W
Cefoperazone/Clavulanic Acid	J01DD62	W
Ceftriaxone/Clavulanic Acid	J01DD63	W
Cefpodoxime/Clavulanic Acid	J01DD64	W
Cefepime	J01DE01	W
Cefpirome	J01DE02	R

Cefozopran	J01DE03	R
Aztreonam	J01DF01	R
Carumonam	J01DF02	U
Meropenem	J01DH02	W
Ertapenem	J01DH03	W
Doripenem	J01DH04	W
Biapenem	J01DH05	W
Tebipenem Pivoxil	J01DH06	W
Imipenem/Cilastatin	J01DH51	W
Meropenem/Vaborbactam	J01DH52	R
Panipenem/Betamipron	J01DH55	U
Ceftobiprole Medocaril	J01DI01	R
Ceftaroline Fosamil	J01DI02	R
Faropenem	J01DI03	W
Ceftolozane/Tazobactam	J01DI54	U
Ceftolozane/Clavulanic Acid	J01DI54	R
Trimethoprim	J01EA01	A
Brodimoprim	J01EA02	U
Iclaprim	J01EA03	U
Sulfaisodimidine	J01EB01	U
Sulfamethizole	J01EB02	U
Sulfadimidine	J01EB03	U
Sulfapyridine	J01EB04	U
Sulfafurazole	J01EB05	U
Sulfanilamide	J01EB06	U
Sulfathiazole	J01EB07	U
Sulfathiourea	J01EB08	U
Sulfamethoxazole	J01EC01	U
Sulfadiazine	J01EC02	U
Sulfamoxole	J01EC03	U
Sulfadimethoxine	J01ED01	U
Sulfalene	J01ED02	U
Sulfametomidine	J01ED03	U
Sulfametoxydiazine	J01ED04	U
Sulfamethoxypyridazine	J01ED05	U
Sulfaperin	J01ED06	U
Sulfamerazine	J01ED07	U
Sulfaphenazole	J01ED08	U

Sulfamazone	J01ED09	U
Trimethoprim/Sulfamethoxazole	J01EE01	A
Sulfadiazine/Trimethoprim	J01EE02	A
Sulfametrole/Trimethoprim	J01EE03	A
Sulfamoxole/Trimethoprim	J01EE04	A
Sulfadimidine/Trimethoprim	J01EE05	U
Sulfadiazine/Tetroxoprim	J01EE06	U
Sulfamerazine/Trimethoprim	J01EE07	U
Erythromycin	J01FA01	W
Spiramycin	J01FA02	W
Midecamycin	J01FA03	W
Oleandomycin	J01FA05	W
Roxithromycin	J01FA06	W
Josamycin	J01FA07	W
Troleandomycin	J01FA08	U
Clarithromycin	J01FA09	W
Azithromycin	J01FA10	W
Miocamycin	J01FA11	U
Rokitamycin	J01FA12	U
Dirithromycin	J01FA13	W
Flurithromycin	J01FA14	U
Telithromycin	J01FA15	W
Solithromycin	J01FA16	U
Clindamycin	J01FF01	A
Lincomycin	J01FF02	W
Pristinamycin	J01FG01	W
Quinupristin/Dalfopristin	J01FG02	R
Streptomycin	J01GA01	A
Streptoduocin	J01GA02	U
Tobramycin	J01GB01	W
Gentamicin	J01GB03	A
Kanamycin	J01GB04	A
Neomycin	J01GB05	W
Amikacin	J01GB06	A
Netilmicin	J01GB07	W
Sisomicin	J01GB08	W
Dibekacin	J01GB09	W
Ribostamycin	J01GB10	W
Isepamicin	J01GB11	W

Arbekacin	J01GB12	W
Bekanamycin	J01GB13	U
Ofloxacin	J01MA01	W
Ciprofloxacin	J01MA02	W
Pefloxacin	J01MA03	W
Enoxacin	J01MA04	W
Temafloxacin	J01MA05	U
Norfloxacin	J01MA06	W
Lomefloxacin	J01MA07	W
Fleroxacin	J01MA08	W
Sparfloxacin	J01MA09	W
Rufloxacin	J01MA10	W
Grepafloxacin	J01MA11	U
Levofloxacin	J01MA12	W
Trovafloxacin	J01MA13	U
Moxifloxacin	J01MA14	W
Gemifloxacin	J01MA15	W
Gatifloxacin	J01MA16	W
Prulifloxacin	J01MA17	W
Pazufloxacin	J01MA18	W
Garenoxacin	J01MA19	W
Sitafloxacin	J01MA21	W
Tosufloxacin	J01MA22	W
Delafloxacin	J01MA23	W
Rosoxacin	J01MB01	U
Nalidixic acid	J01MB02	U
Piromidic Acid	J01MB03	U
Pipemidic Acid	J01MB04	U
Oxolinic Acid	J01MB05	U
Cinoxacin	J01MB06	U
Flumequine	J01MB07	W
Nemonoxacin	J01MB08	U
Cefuroxime/Metronidazole	J01RA03	U
Spiramycin/Metronidazole	J01RA04	W
Levofloxacin/Ornidazole	J01RA05	U
Cefepime/Amikacin	J01RA06	U
Azithromycin/Fluconazole/Secnidazole	J01RA07	U
Tetracycline/Oleandomycin	J01RA08	U
Ofloxacin/Ornidazole	J01RA09	U

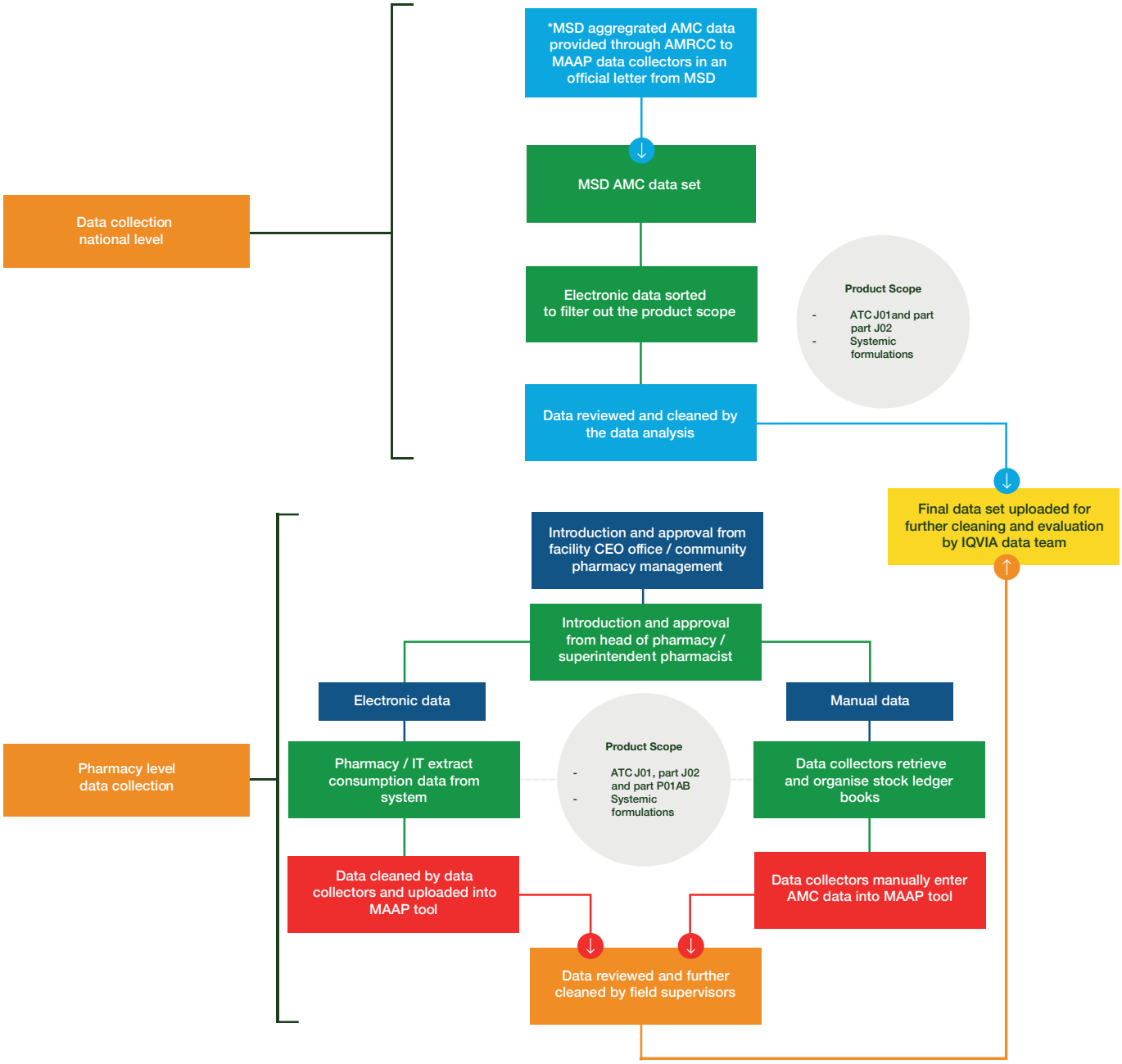
Ciprofloxacin/Metronidazole	J01RA10	U
Ciprofloxacin/Tinidazole	J01RA11	U
Ciprofloxacin/Ornidazole	J01RA12	U
Norfloxacin/Tinidazole	J01RA13	U
Vancomycin	J01XA01	W
Teicoplanin	J01XA02	W
Telavancin	J01XA03	R
Dalbavancin	J01XA04	R
Oritavancin	J01XA05	R
Colistin	J01XB01	R
Polymyxin B	J01XB02	R
Fusidic Acid	J01XC01	W
Metronidazole	J01XD01	A
Tinidazole	J01XD02	U
Ornidazole	J01XD03	U
Nitrofurantoin	J01XE01	U
Nifurtoinol	J01XE02	U
Furazidin	J01XE03	U
Fosfomycin	J01XX01	R
Xibornol	J01XX02	U
Clofoctol	J01XX03	W
Spectinomycin	J01XX04	A
Linezolid	J01XX08	R
Daptomycin	J01XX09	R
Bacitracin	J01XX10	U
Tedizolid	J01XX11	R
Amphotericin B	J02AA01	N/A
Fluconazole	J02AC01	N/A
Itraconazole	J02AC02	N/A
Voriconazole	J02AC03	N/A
Posaconazole	J02AC04	N/A
Isavuconazole	J02AC05	N/A
Flucytosine	J02AX01	N/A
Caspofungin	J02AX04	N/A
Micafungin	J02AX05	N/A
Anidulafungin	J02AX06	N/A

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

Appendix 4: Key AMC specific variables

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

Appendix 5: Data collection process flowchart



**MSD; Medical Stores Department*

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 Tanzania population at a national level; includes all age and gender groups and used the known population numbers as the denominator (obtained from the Worldometer Population Database). The below formula summarises how this calculation was done:

The below formula summarises how this calculation was done:

DDD/1000 Inhabitants/day =

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

*Tanzania population estimated for 2016-2018 obtained from:
https://www.worldometers.info/world-population/tanzania-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 represent first and second choice antibiotics for the empiric treatment of 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%). '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 prioritized as key targets of stewardship programmes and monitoring.

'Reserve': 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 prioritized as targets for AMS to ensure their continued effectiveness.

Appendix 7: National AMC by Antimicrobial molecules

ATC Class Rank	AWaRe category	Molecule	2016 - 2017 DDD/1000 inhabitant-days (%*)	2017 - 2018 DDD/1000 inhabitant-days (%*)	Mean DDD/1000 inhabitant-days
J01 Class		**Total**	**1.67 (100)**	**3.17 (100)**	**4.26**
1	'Watch'	Ciprofloxacin	0.29 (7.4)	0.81 (17.9)	0.55
2	'Access'	Sulfamethoxazole/Trimethoprim	0.29 (7.2)	0.65 (14.4)	0.47
3	'Access'	Amoxicillin	0.26 (6.6)	0.34 (7.6)	0.31
4	'Access'	Doxycycline	0.15 (3.8)	0.34 (7.4)	0.24
5	'Access'	Nitrofurantoin	0.26 (15.4)	0.15 (4.8)	0.20
6	'Access'	Benzylpenicillin	0.07 (1.9)	0.23 (5.1)	0.15
7	'Watch'	Erythromycin	0.10 (2.6)	0.16 (3.6)	0.13
8	Uncategorised	Ampicillin/Cloxacillin	0.08 (2.1)	0.1 (2.1)	0.09
9	'Watch'	Azithromycin	0.01 (0.2)	0.09 (2.1)	0.05
10	'Access'	Gentamicin	0.02 (0.6)	0.05 (1.1)	0.04
11	'Access'	Metronidazole	0.02 (0.4)	0.05 (1.2)	0.04
12	'Access'	Benzathine benzylpenicillin	0.01 (0.4)	0.04 (0.9)	0.03
13	'Access'	Cloxacillin	0.01 (0.3)	0.04 (0.9)	0.03
14	'Access'	Phenoxymethylpenicillin	0.02 (0.5)	0.03 (0.6)	0.02
15	'Watch'	Ceftriaxone	0.02 (0.4)	0.02 (0.5)	0.02
16	'Access'	Amoxicillin/Clavulanic Acid	0.02 (0.5)	0.02 (0.4)	0.02
17	'Access'	Chloramphenicol	0.01 (0.3)	0.01 (0.3)	0.03
18	'Access'	Ampicillin	0.01 (0.2)	0.02 (0.3)	0.01
19	Uncategorised	Ceftriaxone/Sulbactam	0.001 (0)	0.003 (0.1)	0.002
20	'Watch'	Meropenem	0.000003 (0)	0.000005 (0)	0.000004
J02 Class		**Total**	**0.26 (100)**	**0.24 (100)**	**0.25**
1	'Access'	Fluconazole	0.24 (95.3)	0.22 (92.1)	0.23
2	Uncategorised	Itraconazole	0.01 (4.7)	0.02 (7.9)	0.015
P01AB Class		**Total**	**0.09 (100)**	**0.11 (100)**	**0.1**
1	'Access'	Metronidazole	0.04 (52)	0.08 (74)	0.06
2	Uncategorised	Tinidazole	0.04 (46.2)	0.03 (24.3)	0.03
3	Uncategorised	Secnidazole	0.001 (1.8)	0.002 (1.8)	0.002

*Represents financial years (July 2016-June 2017), **Represents financial years (July 2017-June 2018).
#Antibiotics marked as 'uncategorised' have not been awarded a category within the 2019 WHO AWaRe database.

Appendix 8: Breakdown of national AMC by ATC classes

	% consumption	
ATC class	2016 -2017	2017 - 2018
Fluoroquinolones	14.7%	23.1%
Combinations of sulfonamides and trimethoprim, incl. derivatives	14.2%	18.6%
Penicillins with extended spectrum	13.6%	10.3%
Triazole derivatives	12.7%	6.8%
Tetracyclines	7.6%	9.6%
Nitrofuran derivatives	12.8%	4.3%
Beta-lactamase sensitive penicillins	5.5%	8.4%
Macrolides	5.4%	7.4%
Combinations of penicillins, incl. beta-lactamase inhibitors	5.1%	3.2%
Nitroimidazole derivatives	4.3%	3.0%
Aminoglycosides	1.2%	1.4%
Imidazole derivatives	0.8%	1.6%
Beta-lactamase resistant penicillins	0.6%	1.1%
Third-generation cephalosporins	0.9%	0.7%
Amphenicols	0.6%	0.4%
Combinations of antibacterials	0.1%	0.1%
Carbapenems	0.0002%	0.0001%

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

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

Standardised Molecule Name	WHO AWaRe Categorisation	WHO ATC Code	WHO EML	National EML	Documented Data
Amikacin	'Access'	J01GB06	Y	Y	Y
Amoxicillin	'Access'	J01CA04	Y	Y	Y
Amoxicillin/Clavulanic Acid	'Access'	J01CR02	Y	Y	Y
Amoxicillin/Flucloxacillin		J01CR50	N	N	Y
Amphotericin-B		J02AA01	N	Y	Y
Ampicillin	'Access'	J01CA01	Y	Y	Y
Ampicillin/Cloxacillin		J01CR50	N	Y	Y
Ampicillin/Sulbactam	'Access'	J01CR01	N	N	Y
Azithromycin	'Watch'	J01FA10	Y	Y	Y
Benzathine benzylpenicillin	'Access'	J01CE08	Y	Y	Y
Benzylpenicillin	'Access'	J01CE01	Y	Y	Y
Cefaclor	'Watch'	J01DC04	N	Y	Y
Cefadroxil	'Access'	J01DB05	N	N	Y
Cefalexin	'Access'	J01DB01	Y	Y	Y
Cefazolin	'Access'	J01DB04	Y	N	Y
Cefepime	'Watch'	J01DE01	N	Y	Y
Cefiderocol	'Reserve'	J01DI04	Y	N	N
Cefixime	'Watch'	J01DD08	Y	Y	Y
Cefotaxime	'Watch'	J01DD01	Y	Y	Y
Cefpodoxime proxetil	'Watch'	J01DD13	N	N	Y
Ceftazidime	'Watch'	J01DD02	Y	Y	Y
Ceftazidime/avibactam	'Reserve'	J01DD52	Y	N	N
Ceftriaxone	'Watch'	J01DD04	Y	Y	Y
Ceftriaxone/Sulbactam		J01DD63	N	Y	Y
Cefuroxime	'Watch'	J01DC02	Y	N	Y
Chloramphenicol	'Access'	J01BA01	Y	Y	Y
Ciprofloxacin	'Watch'	J01MA02	Y	Y	Y
Ciprofloxacin/Tinidazole	-	J01RA11	N	N	Y
Clarithromycin	'Watch'	J01FA09	Y	Y	Y
Clindamycin	'Access'	J01FF01	Y	Y	Y
Cloxacillin	'Access'	J01CF02	Y	Y	Y
Colistin	'Reserve'	J01XB01	Y	N	N
Doxycycline	'Access'	J01AA02	Y	Y	Y

Erythromycin	'Watch'	J01FA01	N	Y	Y
Flucloxacillin	'Access'	J01CF05	N	Y	Y
Fluconazole		J02AC01	N	Y	Y
Fosfomycin (IV)	'Reserve'	J01XX01	Y	N	N
Gentamicin	'Access'	J01GB03	Y	Y	Y
Imipenem/Cilastatin	'Watch'	J01DH51	N	N	Y
Itraconazole		J02AC02	N	Y	Y
Levofloxacin	'Watch'	J01MA12	N	Y	Y
Lomefloxacin	'Watch'	J01MA07	N	N	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	Y	Y
Nitrofurantoin	'Access'	J01XE01	Y	N	Y
Norfloxacin	'Watch'	J01MA06	N	N	Y
Norfloxacin/Tinidazole		J01RA13	N	N	Y
Ofloxacin	'Watch'	J01MA01	N	N	Y
Ornidazole		P01AB03	N	N	Y
Phenoxymethylpenicillin	'Access'	J01CE02	Y	Y	Y
Piperacillin/Tazobactam	'Watch'	J01CR05	Y	N	Y
Plazomicin	'Reserve'	J01GB14	Y	N	N
Polymyxin-B	'Reserve'	J01XB02	Y	N	Y
Procaine benzylpenicillin	'Access'	J01CE09	Y	N	Y
Secnidazole		P01AB07	N	Y	Y
Spectinomycin	'Access'	J01XX04	Y	N	Y
Streptomycin	'Watch'	J01GA01	N	Y	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
Kanamycin	'Watch'	J01GB04	N	Y	N
Flucytocine		J02AX01	N	Y	N
Linezolid	'Reserve'	J01XX08	Y	Y	N

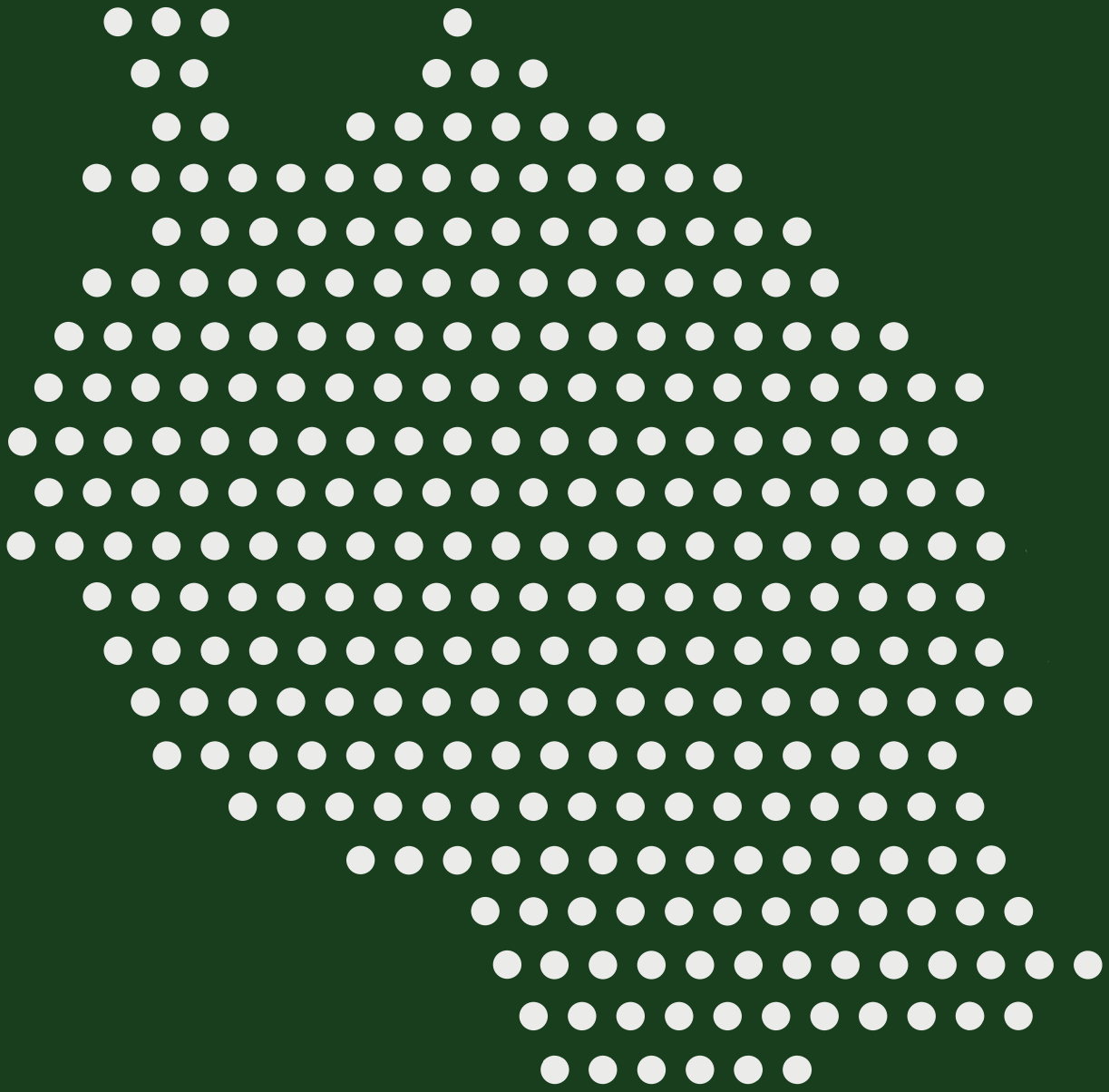
Appendix 10: AMC data collection and expired drug and losses tool

AMC Data Collection Tool

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

Expired Drug and Losses Tool

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



MAAP
Mapping AMR & AMU Partnership

The Fleming Fund
Regional Grants

UKaid
from the British people

African Union

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

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

CEDEAO
ECOWAS

ECSA
HEALTH COMMUNITY

InSTEDD
Innovative Support To Emergencies Diseases and Disasters

IQVIA

ONEHEALTH
TRUST