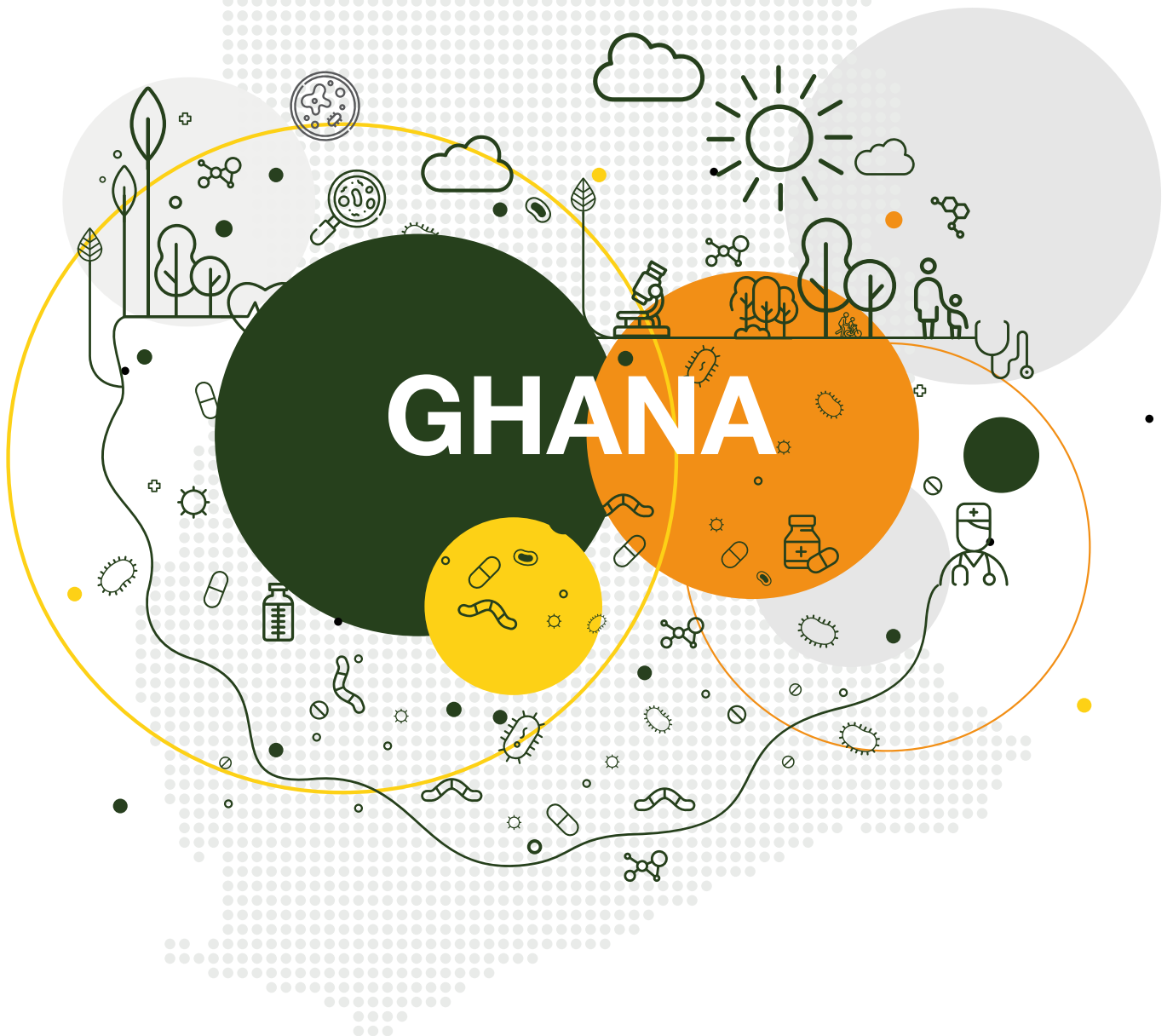
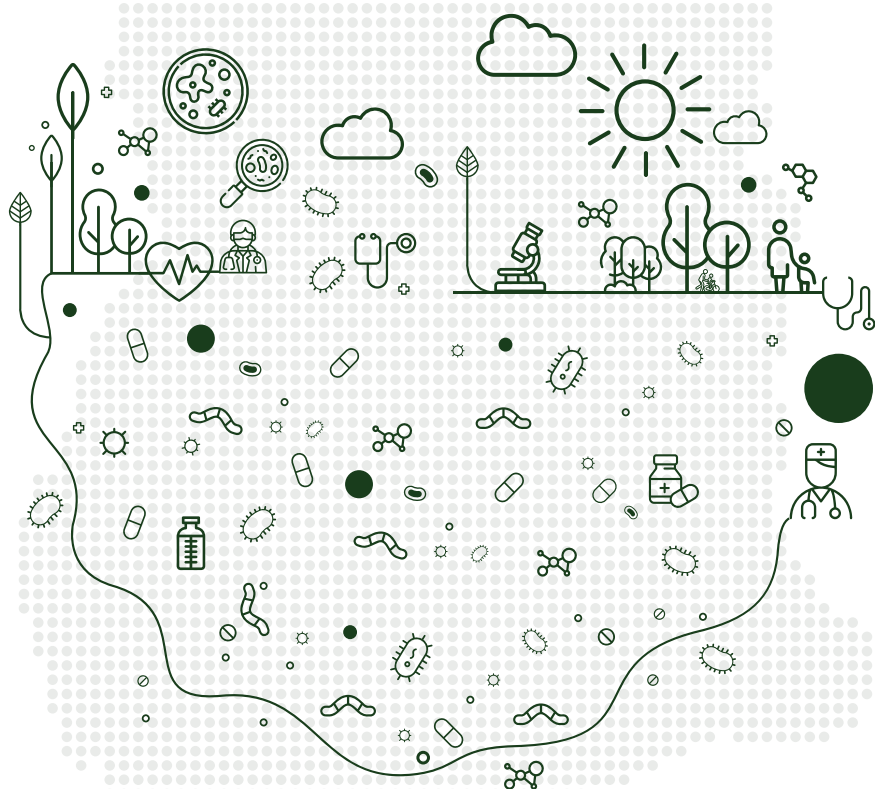


National situation of antimicrobial resistance and consumption Analysis from 2016-2018



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.

GHANA

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Abbreviations

ACDC	Africa Centres for Disease Control
AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMRCC	Antimicrobial Resistance Coordinating Committee
AMS	Antimicrobial Stewardship
AMU	Antimicrobial Use
ASLM	African Society for Laboratory Medicine
ASP	Antimicrobial Stewardship Programme
AST	Antibiotic Susceptibility Testing
ATC	Anatomical Therapeutic Chemical
AWaRe	Access, Watch, and Reserve
CAPTURA	Capturing Data on AMR Patterns and Trends in Use in Regions of Asia
CASFM	Comité de l'antibiogramme de la Société Française de Microbiologie
CDDEP	Center for Disease Dynamics, Economics and Policy
CI	Confidence Interval
CLSI	Clinical and Laboratory Standards Institute
CMS	Central Medical Store
CSF	Cerebrospinal Fluid
DDD	Defined Daily Dose
DID	DDD per 1 000 inhabitants per day
DRI	Drug Resistance Index
DSA	Data Sharing Agreement
ECSA-HC	East, Central and Southern Africa Health Community
EML	Essential Medicines List
EQA	External Quality Assessment
EUCAST	European Committee on Antibiotic Susceptibility Testing
FDA	Food and Drug Authority
FDC	Fixed Dose Combinations
GAP	Global Action Plan
GHSI	Global Health Security
GLASS	Global Antimicrobial Resistance Surveillance System
GDP	Gross Domestic Product
HIS	Hospital Information System
InSTEDD	Innovative Support to Emergencies, Diseases and Disasters
KIIs	Key Informant Interviews
LIS	Laboratory Information System
LMIC	Low- or Middle-Income Country
LQMS	Laboratory Quality Management System
MAAP	Mapping Antimicrobial resistance and Antimicrobial Use Partnership
MoH	Ministry of Health
MRSA	Methicillin-resistant Staphylococcus aureus
MTC	Medical Therapeutics Committee
NAP	National Action Plan
NGO	Non-governmental Organisation
OR	Odds Ratio
QA	Quality Assessment
QC	Quality Control
QMS	Quality Management System
RSN	ResistanceMap Surveillance Network
SLIPTA	Stepwise Laboratory Improvement Process Towards Accreditation
SLMTA	Strengthening Laboratory Management Towards Accreditation
SOP	Standard Operating Procedure
STG	Standard Treatment Guidelines
WHA	World Health Assembly
WHO	World Health Organisation

Executive Summary

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

The Fleming Fund, a 265-million-pound United Kingdom aid, supports a range of initiatives to increase the quantity and quality of AMR data in LMICs. Regional Grant (Round 1) activities in Africa are led by The African Society for Laboratory Medicine (ASLM) and implemented by the 'Mapping Antimicrobial resistance and Antimicrobial use Partnership' (MAAP) consortium. This report summarises the activities undertaken by the MAAP consortium to implement the Regional Grant and aims to determine the national AMR, AMC and AMU surveillance capacity, rates and trends and assess the antimicrobial flow in Ghana during 2016-2018.

Ghana had approximately 4 841 laboratories in the national laboratory network during the study period, of which only 93 were reported to have bacteriology testing capacity. Based on self-reported information from 64 laboratories, functioning and quality compliance were assessed to determine preparedness for AMR surveillance.

The AMR rates reported here are based on an analysis of antimicrobial susceptibility results of 4 394 positive cultures obtained from 16 laboratories. Very high AMR rates were also noted for carbapenem-resistant Enterobacterales (over 90%) during 2016 and 2017. There were high rates of third-generation cephalosporin-resistant Enterobacterales (72-78%) and methicillin-resistant *S. aureus* (MRSA) (74-85%). There was no association between the available patient variables and AMR; more studies are needed to confirm this finding. All results should be interpreted cautiously because the participating laboratories were at different service levels and had varying testing capacities.

AMC is measured as the number 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 the lack of a unique patient identifier and tracking systems across hospital departments. The data collected from Ghana Food and Drug Authority (FDA), which would have served as national AMC, was not analysed as the datasets missed essential pack size information. Consequently, the MAAP consortium could not calculate the defined daily doses (DDDs) consumed: a primary requirement for AMC analysis. Therefore, the findings reported here present results from aggregated pharmacy-level AMC datasets. The average total AMC level in the sampled pharmacies between 2016-2019 was 5 289 477.⁸ AMC was 4 521 406 in 2016, 5 692 311 in 2017, 5 345 811 in 2018 and 5 598 383 in 2019.

Antimicrobial utilisation by the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) classification was highest for penicillin and beta-lactamase inhibitor combinations (range 14.4% to 18.9%), followed by nitroimidazole derivatives (range 9.0% to 20.5%) and extended-spectrum penicillins (range 12.8% to 15.1%). The top five most consumed antimicrobials were amoxicillin/clavulanic acid, metronidazole, amoxicillin, clindamycin and cefuroxime. Together, they accounted for 64% of the total consumption share, thus suggesting a lack of variation. This consumption trend could potentially increase AMR. The total AMC came included antimicrobials in the 'Access' (75.8%), 'Watch' (24.3%), and 'Reserve' (0%) categories. This data indicated that the use of 'Access' antibiotics exceeded the WHO minimum recommended consumption threshold of 60%. The absence of 'Reserve' antibiotics consumption implied a possible unavailability of these last-resort antibiotics within the sampled pharmacies. Five combinations of two or more broad-spectrum fixed-dose combinations (FDCs) of antimicrobials were identified that were not recommended for clinical utility but were consumed in the selected pharmacies. Ampicillin/cloxacillin was most commonly consumed (mean AMC of 33 056).

Data were inadequate for estimating the country's drug resistance index (DRI). The DRI is a simple metric based on aggregate rates of resistance and measured on a scale of 0-100; higher values are suggestive of increasing bacterial resistance and antimicrobial consumption levels. Decision-makers often use the DRI to understand the level of drug resistance and the effectiveness of antibiotic therapy. Unfortunately, DRI could not be calculated for Ghana due to inadequate data.

Policymakers and healthcare providers should note the following recommendations to strengthen further AMR and AMC surveillance to mitigate AMR 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 mapping would inform decision-makers on unmet needs and decide how to expand the laboratory network.
- Staff training on laboratory standards, common pathogen identification, and data management skills are essential for high-quality microbiology testing and reporting. Staff capacity-building training may be done by leveraging in-house expertise or outsourcing to external organisations or tertiary facilities.
- Curating the right data and generating evidence is essential to strengthening AMR surveillance,. Therefore, we recommend standardised data collection standardised formats at all levels (laboratories, clinics and pharmacies) and automated data analyses. We also recommend establishing a system of assigning permanent identification numbers for patient tracking over time.
- Due to the limited number of assessed facilities, the MAAP, per the WHO facility AMU assessment guide, recommends that future AMU and AMC surveillance attempts in the country be conducted through larger-scale point prevalence surveys to give a representative portrait of the national antimicrobial use.
- A comprehensive guiding policy for routine AMC data surveillance is required in the country. The policy should stipulate the minimum country AMC, AMC data reporting variables, and routine data cleaning and reporting practices. The latter will 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 switching to electronic systems and ensure such systems have capabilities to transfer data across systems and/or produce user-friendly reports on AMC.
- MAAP recommends that the country's Antimicrobial Resistance Coordinating Committee (AMRCC) consider introducing facility-level Antimicrobial Stewardship Programs (ASPs) to regulate the use of 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 Access, Watch, and Reserve (AWaRe) category.
- The MAAP consortium recommends an urgent survey by the Ministry of Health (MoH) and AMRCC to assess the availability of the 'Reserve' category antibiotics in the country. The survey may inform the subsequent revision of the country's essential medicines list (EML) and treatment guidelines to include these vital antibiotics, if necessary. This approach will ensure that the most vital antibiotics are available for all patients.
- National stewardship programs led by the AMRCC could conduct educational campaigns for healthcare practitioners to ensure they know the full spectrum of antimicrobials available in the country's EML.

Overview

The Fleming Fund Grants Programme

The Fleming Fund Grants Programme, a United Kingdom-sponsored initiative, aims to address the critical gaps in the surveillance of AMR in LMICs in Asia and sub-Saharan Africa.¹ The programme includes regional grants, country grants, and the Fleming Fellowship Scheme. Mott MacDonald is the authority for grant management.

The Fleming Fund Regional Grants Round 1 Programme

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

Problem statement

The quantum and quality of surveillance data are suboptimal in LMICs where AMR rates are typically lacking.² This data paucity hinders the assessment of the current treatment efficacy and understanding of the drivers of resistance. It also impacts the adoption of appropriate policies to improve AMU, which impacts patient care downstream. However, in most LMICs, some institutions (academic, research, public and private health facilities) have been collecting AMR data for decades.

While the 'hidden treasure' is simply inaccessible for use in large-scale analytics, collecting and, where necessary, digitising data from these institutions has the potential to establish baselines of AMR across a wide range of pathogen/drug combinations and assess spatiotemporal trends. Likewise, retrieving information through prescriptions or sales in healthcare facilities should provide a wealth of information on potential AMR drivers. 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 the spatiotemporal mapping of AMR and AMU across countries in each region and establish baselines. The programme was implemented by the 'Mapping Antimicrobial resistance and Antimicrobial use Partnership' (MAAP), a multi-organisational consortium of strategic and technical partners. The ASLM was the Lead Grantee for the programme.³

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

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

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

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

Aim

To determine the spatiotemporal baselines and trends of AMR and AMC in Ghana 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 Ghana, including the public and private human healthcare sector.
- To collect, digitise and analyse retrospective data from selected facilities using standardised electronic tools; to describe the completeness and validity of AMR data in selected facilities.

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

Outcome measures

- Number of laboratories from the national network generating AMR data and proportion of laboratories reporting compliance to standards of quality and bacteriology testing.
- Level of AMR data completeness and validity among laboratories selected for AMR data collection.
- AMR prevalence and trends for the WHO priority pathogens, other clinically important and frequently isolated pathogens.
- A semi-quantitative in-country analysis of the 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 Drug Resistance Index (DRI).
- Association between patient factors and AMR.

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

Key engagements and activities

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

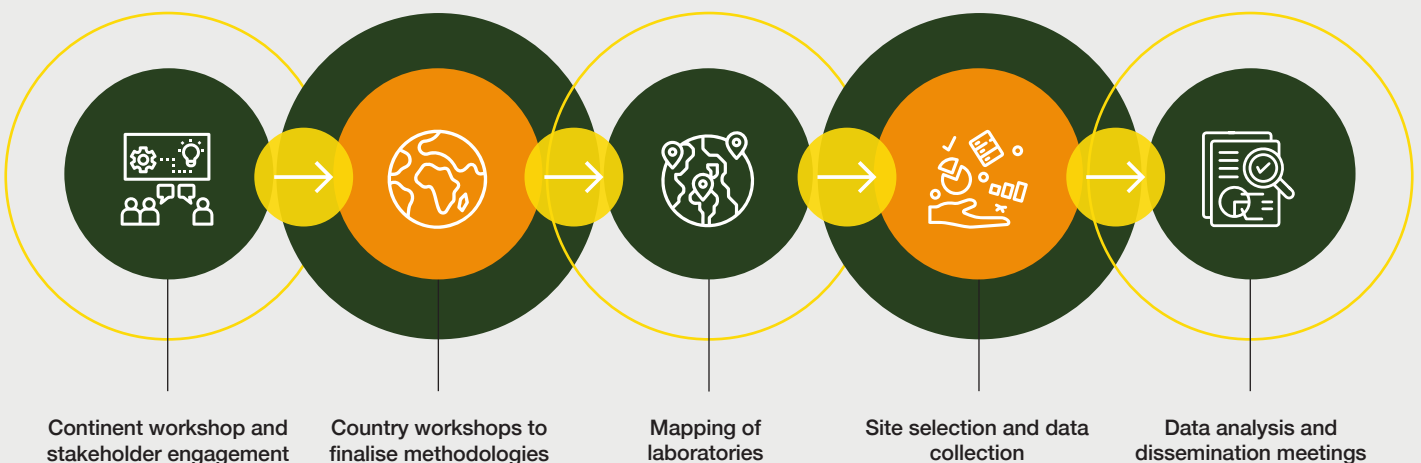


Figure 1: Key engagements and activities

Ethical issues and data sharing agreements

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

Country Profile

Health and Demographic Profile

As of 2020, Ghana had an estimated population of 31.1 million inhabitants with a life expectancy of 64 years. The country had a high infectious disease burden with a TB incidence of 143 per 100 000 and an HIV prevalence of 1.7%. The country had a physician density rate of 0.11 per 1,000 inhabitants and nurses density rate of 2.71 per 1,000 inhabitants. With a universal health coverage index of 45, Ghana had average coverage of essential services (Table 1).

Table 1: Health and demographic profile of Ghana

	Ghana		Comparator values (most recent year)*		
	Year	Value	India	Argentina	United States
Population	2020	31 072 945	1 380 004 390	45 376 763	329 484 123
Life expectancy during the study period, total (years)	2019	64	70	77	79
Universal health coverage service index (0-100)	2019	45	61	67	83
GDP per capita (current US\$)	2020	2 205.53	1 927.7	8 579.0	63 593.4
Immunisation, DPT (% of children ages 12-23 months)	2019	97	91.0	86.0	94.0
Incidence of tuberculosis (per 100 000 people)	2020	143	188.0	31.0	2.4
Prevalence of HIV, total (% of population ages 15-49)#	2020	1.7	0.2*	0.4 2020	0.4 2019
Primary education (%)#	2018	93.8	94.6	98.6	100
Physicians density (physicians per 1 000)#	2019	0.11	0.93	4.0	2.6
Nurses density (nurses and midwives per 1 000)#	2019	2.71	2.39	2.60	15.69

Sourced from World Bank^{4,5,6} and *National AIDS Control Organisation⁷

#Data for some country parameters may not necessarily be of the same year (sourced from the most recently available information between 2017-2020).

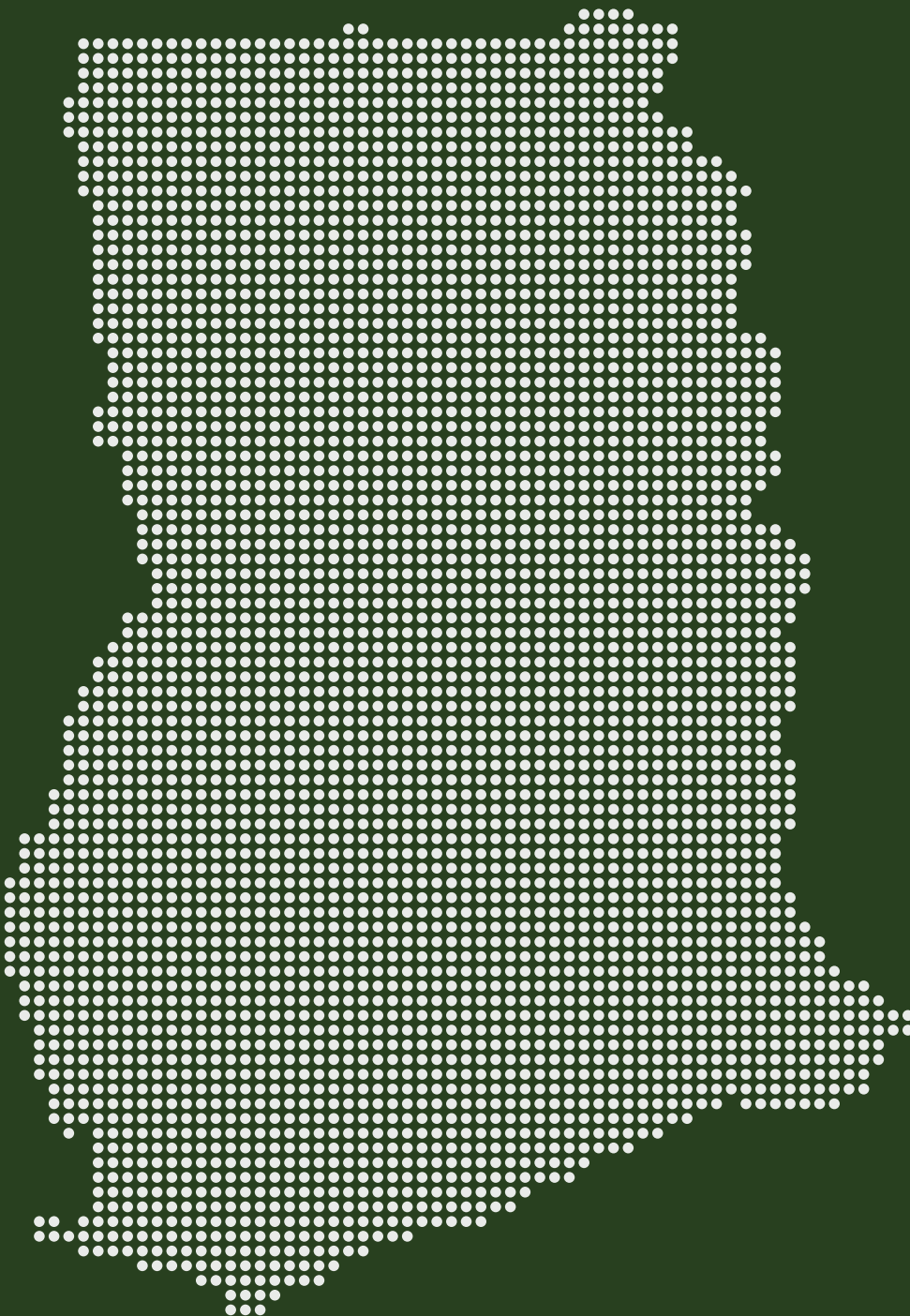
GDP=Gross domestic product; DPT=Diphtheria, Pertussis and Tetanus

Policy frameworks

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

Ghana has an Antimicrobial Resistance National Action Plan (AMR NAP) (2017-2022)¹⁰ and enrolled in GLASS in 2019.⁹ However, as of the end of 2020, Ghana has not submitted AMR data to GLASS so far and does not have a system to report AMR data to national authorities.

Part A: Antimicrobial Resistance



Section I: Laboratory assessment

Objective

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

Methodology

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

During the initial stages of in-country work, the laboratory network was mapped with support from the country's MoH. An inventory of laboratories in the tiered network was created, and laboratories capable of conducting antimicrobial susceptibility tests (AST) were identified. A questionnaire 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 (LIS) (AMR Appendix 2). Based on self-reported information on the above parameters, each laboratory was assigned a readiness score for AMR surveillance (AMR Appendix 3). The scoring scheme was standardised across all participating countries. The final selection of laboratories for data collection was made by MoH and was not necessarily based on laboratory rankings.

Results

Mapping and selection of laboratories

During the initial stages of in-country work in Ghana, 4 841 laboratories were mapped to the national laboratory network. An eligibility questionnaire was sent to 93 laboratories identified as having capacity for bacteriology testing. Of the 64 laboratories that responded to the questionnaire and had AST capacity, majority were affiliated with the government (Table 2, Supplementary Table 1). The laboratory readiness scores of the surveyed laboratories varied widely (7.9–78.9%). Sixteen laboratories 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			
Lekma Hospital Laboratory (Lekma)	78.9	District/Community	Government
Cape Coast Teaching Hospital Laboratory (Cape Coast Teaching)	73.7	Reference	Government
Public Health Reference Lab, Tamale (PHL Tamale)	71.1	Reference	Government
Tema General Hospital Laboratory (Tema)	68.4	Other	Government
St. Joseph Hospital Laboratory (St. Joseph)	68.4	District/Community	Other
Holy Family Hospital Berekum (HF Berekum)	68.4	District/Community	Government
Greater Accra Regional Hospital Laboratory (Greater Accra RH)	68.4	Regional/Intermediate	Government
Upper East Regional Hospital Laboratory (Upper-East RH)	65.8	Regional/Intermediate	Government
Patholab solutions GH Ltd. (Patholab)	65.8	Regional/Intermediate	Private
Quadushah Medical Diagnostic Centre LTD, Tema (Quadushah)	63.2	Other	Private
Paradise Diagnostic Center (Paradise)	63.2	Regional/Intermediate	Private
University of Cape Coast Hospital (University of Cape Coast)	60.5	District/Community	Government
M and G medical Laboratory Ltd (M and G)	55.3	Regional/Intermediate	Private
Holy Family Hospital, Techiman (HF Techiman)	52.6	Regional/Intermediate	Government
Nsawam Government Hospital (Nsawam)	52.6	District/Community	Government
Tamale Teaching Hospital Laboratory (Tamale Teaching)	50	Regional/Intermediate	Government
Not Selected			
37 Military Hospital Pathology Division	100	Regional/Intermediate	Government
Saint Francis Xavier Hospital	78.9	District/Community	Other
Central Laboratory Korle Bu Teaching Hospital	78.9	Other	Government
Med-Line Medical Diagnostics Service	78.9	District/Community	Private
Bono Ahafo Regional Hospital, Sunyani	76.3	Regional/Intermediate	Government
G2 Medical Laboratory Services	76.3	-	Private
Eastern Regional Hospital Laboratory Koforidua	76.3	Regional/Intermediate	Government
International Maritime Hospital Lab	76.3	Reference	Other
Sekondi Public Health Laboratory	71.1	Regional/Intermediate	Government
Gpha Clinic Laboratory	71.1	District/Community	Other
Ho Teaching Hospital (Hth)	68.4	Regional/Intermediate	Government
Stephrich Medical Diagnostic	65.8	District/Community	Private
St. Dominic's Hospital, Akwatia	65.8	District/Community	NGO
Bil Clinical Laboratory Ltd	65.8	-	Private

HandH Medical Lsaboratory Ltd.	65.8	District/Community	Private
Maternal And Child Health Hospital	63.2	District/Community	Government
Teteh Quarshie Memorial Hospital	63.2	District/Community	Government
Rokolab	63.2	Regional/Intermediate	Private
Kaara Diagnostic Services Ltd	60.5	Other	Private
Keta Municipal Hospital Laboratory Department	60.5	Regional/Intermediate	Government
Navrongo Health Centre Clinical Laboratory	60.5	Other	Government
Volta River Authority	60.5	District/Community	Other
Aga Health Foundation	57.9	District/Community	Private
Methodist Hospital Wenchi Laboratory	57.9	District/Community	Other
St. Luke Catholic Hospital Laboratory	57.9	District/Community	Other
Swedru Municipal Hospital	57.9	District/Community	Government
Amedilab Services	57.9	District/Community	Private
La General Hospital Laboratory	57.9	District/Community	Government
Medidag Diagnostic And Digital X Ray Services LTD	55.3	District/Community	Private
Bestlab Medical Diagnostic Laboratory	55.3	Other	Private
Shai-Osudoko Hospital, Dodowa	55.3	District/Community	Government
Lifesciences Medical Center	52.6		Private
Medi-Time Diagnostic Services	52.6	District/Community	Private
St. John Of God Hospital Laboratory Duayaw Nkwanta	50	District/Community	Other
Holy Family Hospital, Nkawkaw	50	District/Community	NGO
Care Diagnostic Service Ltd	50	District/Community	Private
St. Patrick's Hospital, Offinso, Ashanti	50	District/Community	Government
Topp Medical Laboratory	50	District/Community	Private
St. Elizabeth Catholic Hospital Laboratory	50	District/Community	Other
Kwahu Government Hospital	47.4	District/Community	Government
Clinilab Diagnostic Services	47.4	Other	Private
Pacesetters Medical Laboratory	44.7	Other	Private
Healthway Medical Laboratory Ltd.	44.7	Regional/Intermediate	Private
Integrated Medical Laboratory Services Ltd	44.7	Other	Private
Kath Bacteriology Lab	39.5	Other	Government
Precilab Company Limited	34.2		Private
St. Martin De Porres Hospital Laboratory	26.3	District/Community	Government
Tarkwa Municipal Hospital	7.9	District/Community	Government

* Laboratory names are abbreviated.

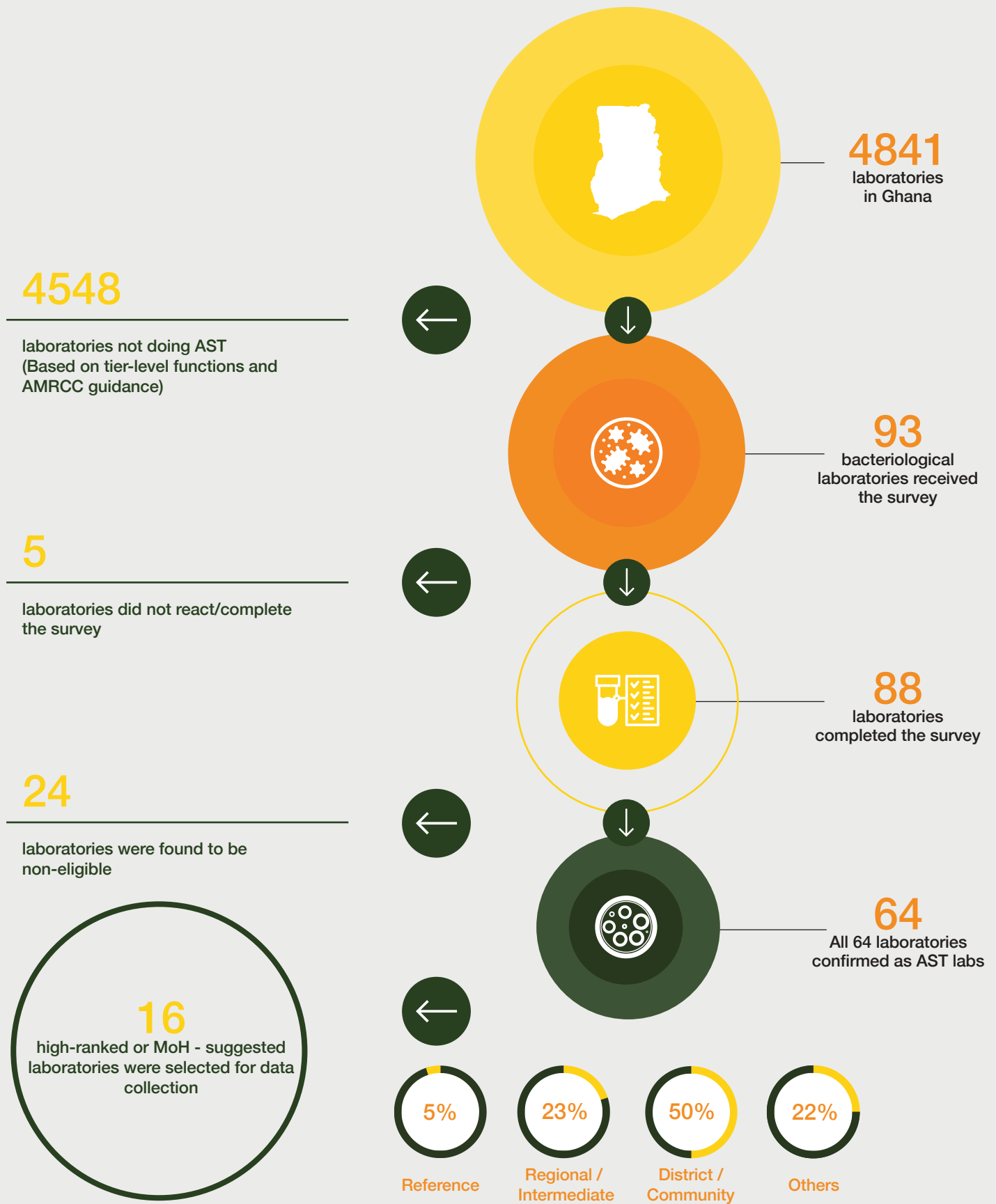
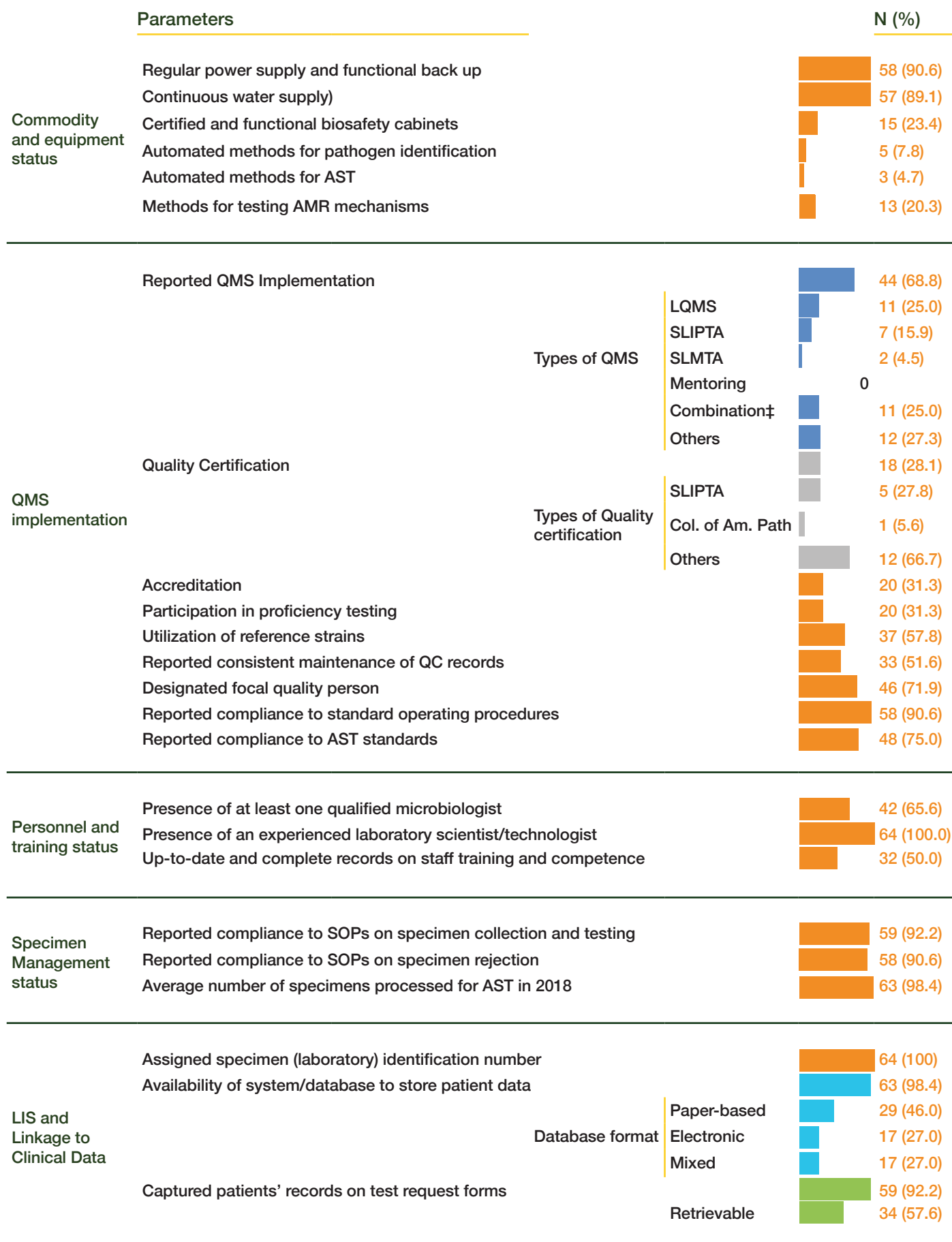


Figure 2: Selection of laboratories in Ghana

Surveillance preparedness of surveyed laboratories

Based on self-reported information from 64 laboratories, laboratory function and quality compliance were assessed to understand preparedness for AMR surveillance. Forty-four laboratories had implemented QMS, and 42 laboratories had at least one qualified microbiologist on board. Twenty laboratories were accredited, while few used automated methods for pathogen identification (n=5) (Figure 3, Supplementary Table 2). Since these findings may affect the quality of laboratory data, caution in interpreting the AMR rates presented in this report is warranted.

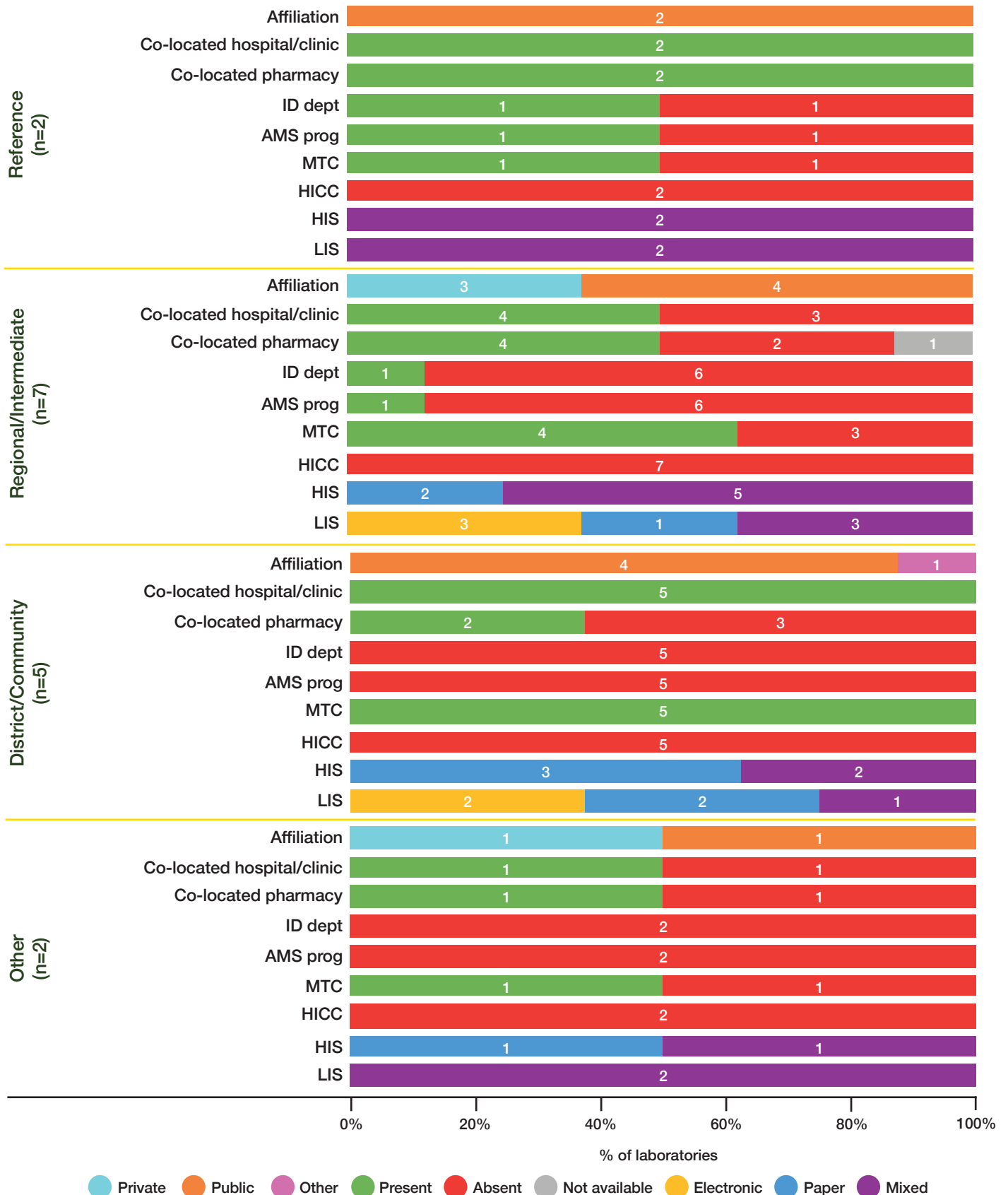


‡ Combination refers to more than one option presented in the questionnaire (laboratory quality management system (LQMS), stepwise laboratory improvement process towards accreditation (SLIPTA), strengthening laboratory management towards accreditation (SLMTA), and mentoring).

Figure 3: Laboratory preparedness for AMR surveillance

Profile of Selected Laboratories

Out of the 16 selected laboratories, 12 were co-located with clinical facilities. Nine clinical facilities lacked infectious disease departments and antimicrobial stewardship programmes (ASP). Medical therapeutic and hospital infection control committees were functional in 11 facilities. Most laboratories and hospitals had mixed (paper and electronic) information systems (Figure 4).



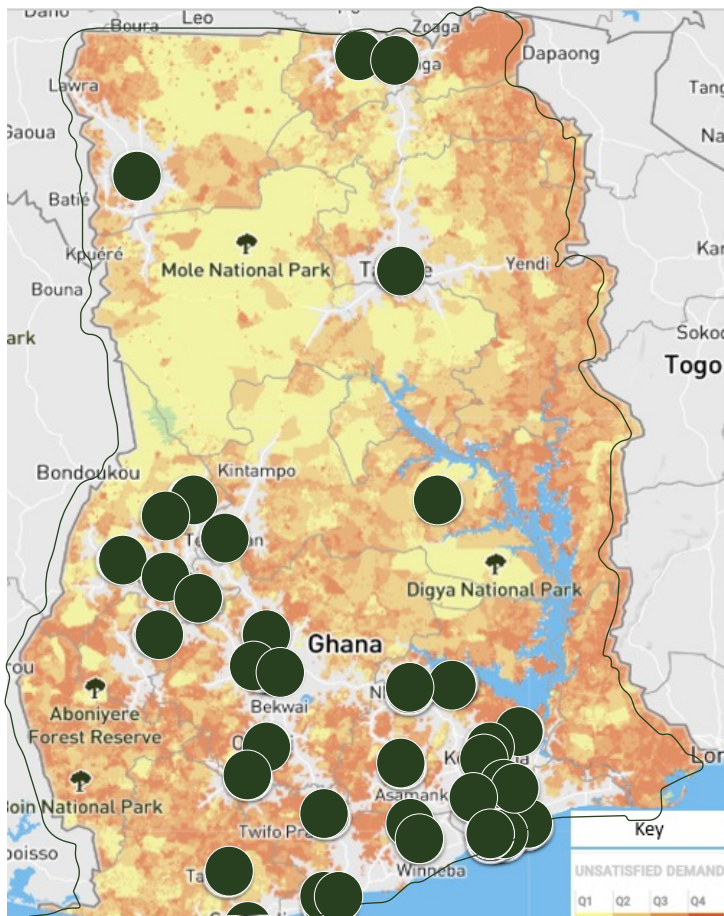
Abbreviations: AMS=antimicrobial stewardship; HICC=hospital infection control committee; HIS=hospital information system; ID Dept=infectious diseases department; LIS=laboratory information system; MTC=medical therapeutics committee

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, Ghana had an estimated population of 31.07 million.



Population coverage of laboratory services is defined as the catchment population living within one-hour travel (car, foot) from the testing lab. It is represented in grey on the map. The analysis uses the assumption that the laboratory has sufficient testing capacity to serve all the population within the catchment area

The population outside the catchment area of the facilities is, by definition, the overall unmet need. For ease of use, the unit of unmet need is represented on the map as 'pixels', i.e., the lowest base unit of a raster image. 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 population living in the 'pixel'. The ranking is then divided into quartiles made of equal population fractions (from Q1 _lowest density of population to Q4 highest density), also corresponding to different colours (from yellow to dark red, see legend). Therefore, the colours on the map relates to the level of unmet need (people far from a facility) relative to the whole population.

Supplementary Figure 1: Population coverage of AST laboratories in Ghana

In Ghana, the catchment population living within 1 hours travel time from the 64 participating AMR surveillance sites covers 65% of the population. Hence 35% of the population is not covered at all by the existing facilities. Regions in dark red (Q3), with the highest absolute unmet need, should be prioritised for testing capacity increase, either by upgrading an existing laboratory, to start providing services, or by constructing a new laboratories.

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 the positive blood and cerebrospinal fluid (CSF) cultures, patient's demographics, clinical profile, and AMU information were 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 was collected on AMC at the facility level and national level.

As a first step, the MoH and IQVIA cooperatively recruited local field data collectors. A capacity-building workshop was conducted as part of the MAAP activities to train the field staff on data collection, including the use of WHONET¹² and use of the specially developed MAAP tool for secure transfer of collected data.

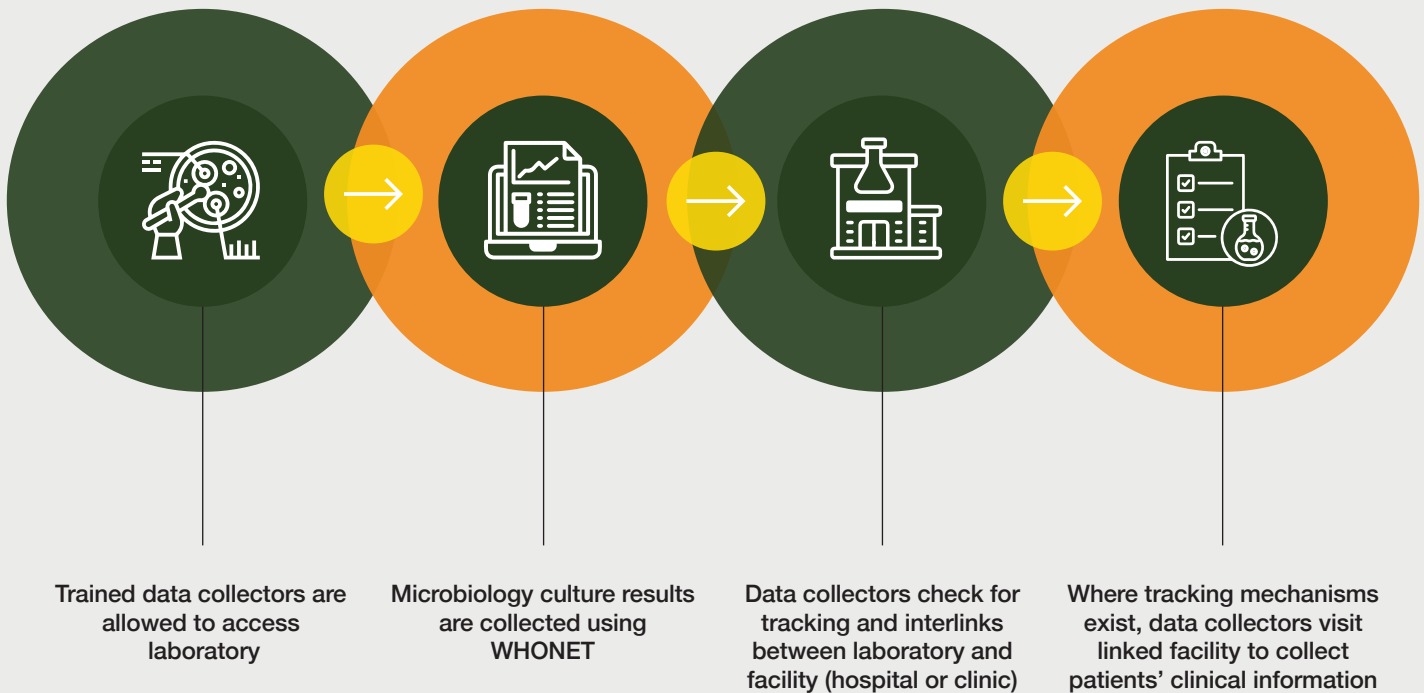


Figure 5: Steps of AMR data collection

Historical data was collected for the period from January 1, 2016, through December 31, 2018. For laboratories with paper-based records, at least 5 000 records per laboratory per year were supposed to be collected (Figure 6). However, no such limit was imposed for digitised data. The goal was to obtain at least 240 000 records from 16 laboratories across three years.

The 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 databases, spreadsheets, and 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 was transferred into an online application (repository) for further analysis. Each row of the database represented an individual patient's results. Where the laboratory or hospital issued unique patient identification numbers, it was also possible to track a patient over multiple visits.



Figure 6: Data collection at a Ghana facility

Data analysis

A preliminary data review was conducted to check for data completeness, accuracy and redundancy. Data were summarised 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 the AST results. Total cultures were quantified for each laboratory and over the entire study period. Valid cultures and positive cultures were stratified for each laboratory as well as for each study year (Figure 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. 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 8).

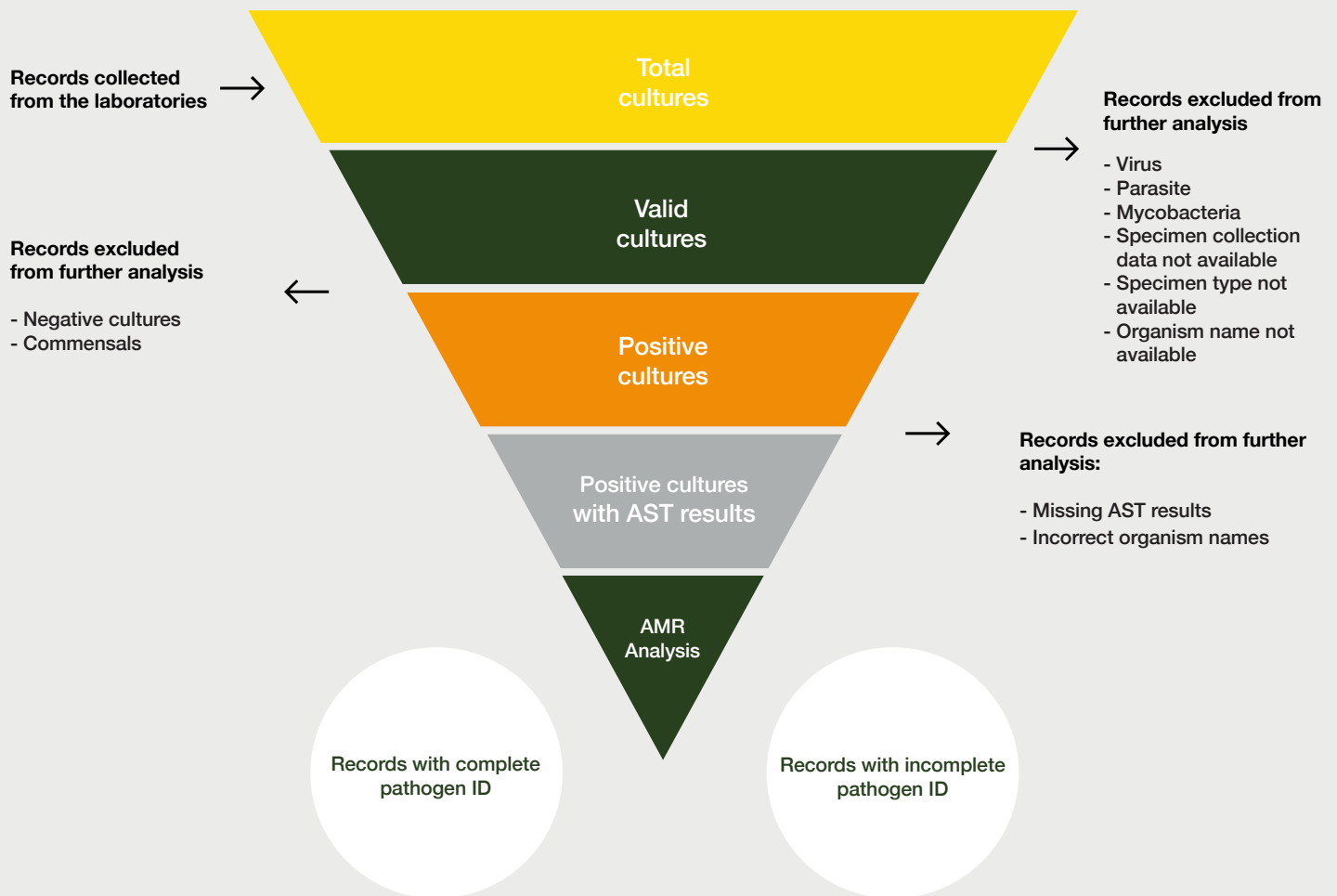


Figure 7: Conceptual framework for deriving quantum of cultures

- **Culture characteristics:** Cultures were characterised across gender, age group, and pathogen type (bacteria or fungi). Data were pooled across all laboratories, and assessment was done for each study year.
- **Inappropriate testing:** Positive cultures with AST results were assessed for compliance with AST standards. However, a comprehensive assessment of AST results validity 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 (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, the origin of infection (hospital- or community-acquired), presence of an indwelling device and antimicrobial use. Data was quantified for each laboratory and assessed over the entire study period.
- **Specimen characteristics:** Positive cultures with AST results were summarised based on specimen type. 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 for evaluating each laboratory's data quality since complete pathogen identification 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). First, the scoring was performed per year (i.e., 2016–2018), and then the average was assigned as the laboratory data quality score for each laboratory.

Table 3: Data scoring scheme

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

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

Table 4: Data quality rating

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

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

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

Results

Retrospective data from 2016–18 were collected from 16 laboratories and corresponding facilities in Ghana.

1. Quantum of cultures and level of pathogen identification

Data were retrieved for 24 427 total cultures, of which 17 096 were valid and 5 928 were positive. Of the positive cultures, AST results were available for 4 494 positive cultures, a maximum (n=1 201) coming from the Greater Accra Regional Hospital Laboratory (RH) and none from M and G (Figures 9 and 10). Not all pathogens were identified completely at the species level. Complete identifications were highest for St. Joseph (98.5%) and lowest for HF Techiman (22.1%) (Table 5).

Table 5: 2016 -2018 culture and AST data retrieved from 16 selected laboratories in Ghana

Variable (Columns)	Total Cultures N = 24 427	Valid Cultures N = 17 096	Positive cultures N = 5 928	Positive cultures with AST results N = 4 394	Incomplete identity* N = 1 533	Complete identity* N = 2 861
Laboratory (Rows)						
Lekma	2 527	1 847 (73.1)	442 (23.9)	395 (89.4)	19 (4.8)	376 (95.2)
Cape Coast Teaching	446	354 (79.4)	354 (100.0)	325 (91.8)	108 (33.2)	217 (66.8)
PHL Tamale	1 871	1 071 (57.2)	158 (14.8)	151 (95.6)	43 (28.5)	108 (71.5)
Tema	1 649	1 146 (69.5)	386 (33.7)	315 (81.6)	139 (44.1)	176 (55.9)
St. Joseph	348	209 (60.1)	73 (34.9)	66 (90.4)	1 (1.5)	65 (98.5)
HF Berekum	201	201 (100.0)	111 (55.2)	102 (91.9)	47 (46.1)	55 (53.9)
Greater Accra RH	6 117	3 332 (54.5)	1 565 (47.0)	1 201 (76.7)	388 (32.3)	813 (67.7)
Upper-East RH	1 562	1 119 (71.6)	260 (23.2)	234 (90.0)	7 (3.0)	227 (97.0)
Patholab	199	178 (89.4)	43 (24.2)	36 (83.7)	6 (16.7)	30 (83.3)
Quadushah	418	370 (88.5)	66 (17.8)	56 (84.8)	20 (35.7)	36 (64.3)
Paradise	1 776	924 (52.0)	344 (37.2)	163 (47.4)	41 (25.2)	122 (74.8)
University of Cape Coast	1 623	1 282 (79.0)	788 (61.5)	230 (29.2)	76 (33.0)	154 (67.0)
M and G	247	247(100)	-	-	-	-
HF Techiman	2 720	2 409 (88.6)	694 (28.8)	657 (94.7)	512 (77.9)	145 (22.1)
Nsawam	1 981	1 954 (98.6)	467 (23.9)	291 (62.3)	118 (40.5)	173 (59.5)
Tamale Teaching	989	700 (70.8)	177 (25.3)	172 (97.2)	8 (4.7)	164 (95.3)

* 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

AST=Antibiotic Susceptibility Testing

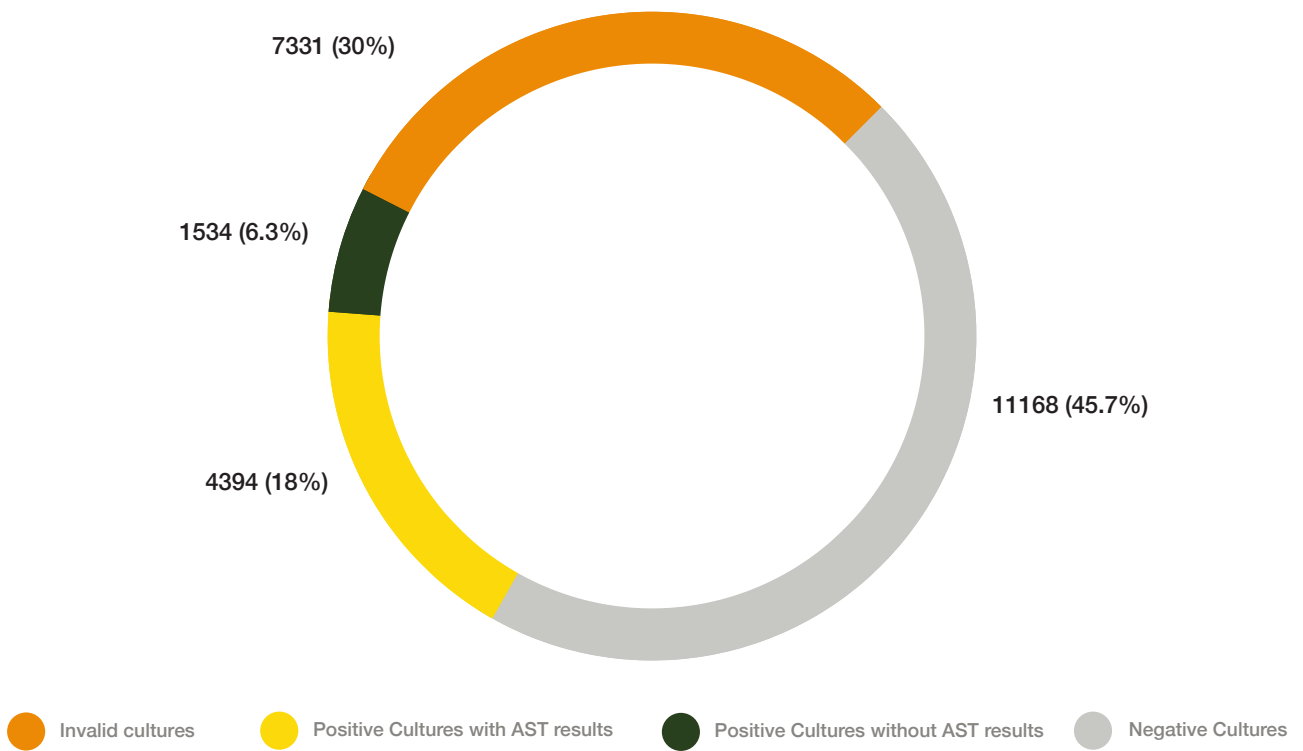


Figure 8: Quantum of cultures across all selected laboratories in Ghana from 2016-2018

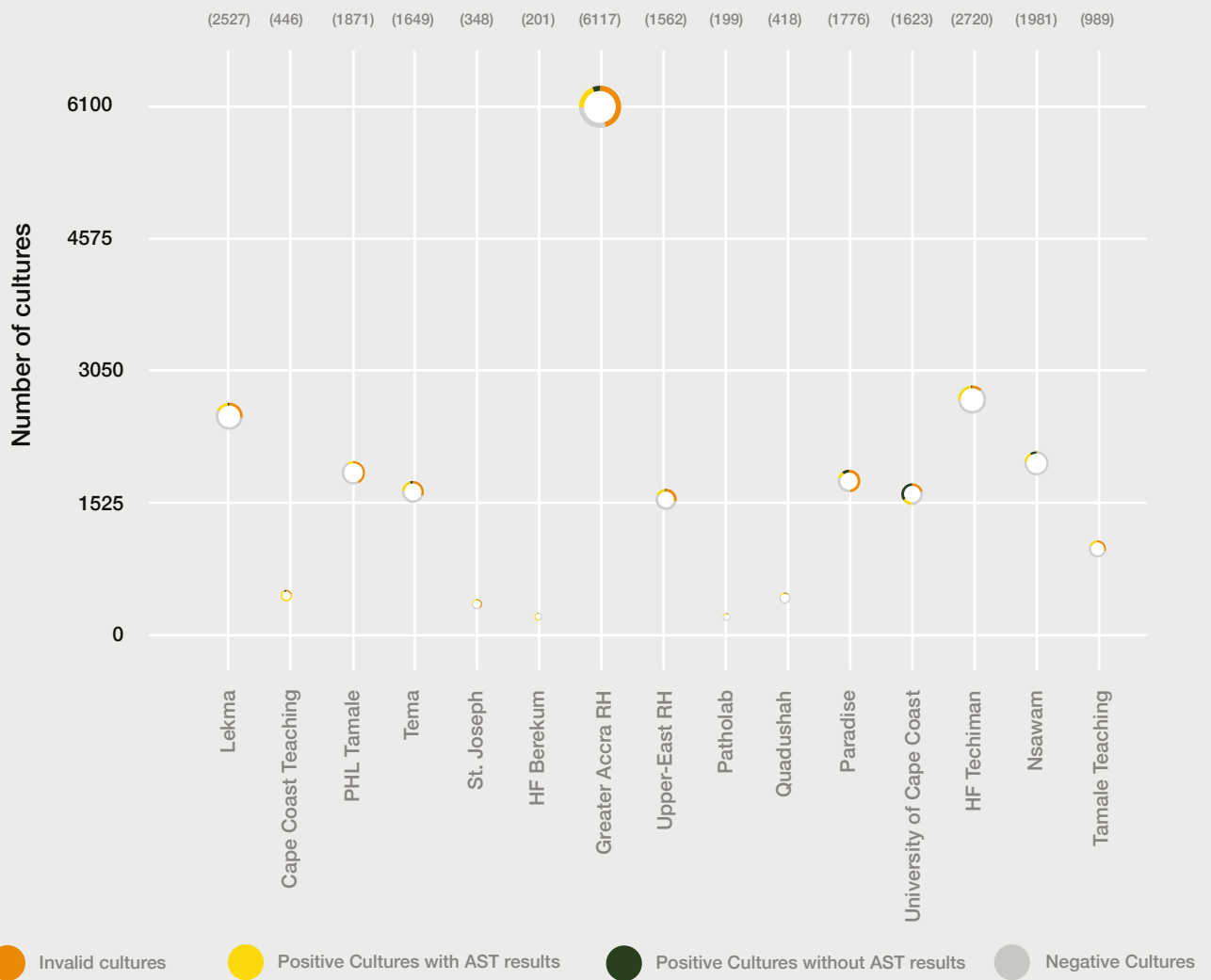


Figure 9: Quantum of cultures for each of the 16 selected laboratories in Ghana, 2016-2018

2. Culture characteristics

Bacterial pathogens (4 393) were isolated from the positive cultures. Information on age was missing from 40.7% of cultures, but where available, data showed a median age of 30 years (range: 0–90 years), with most isolates (1 084) obtained from patients 18–49 years old. Females (2 928) contributed more to the quantum of positive cultures with AST results. Additional data came from 2018 (1 784) than other years (Table 6, Supplementary Table 3).

Table 6: Socio-demographic characteristics of positive cultures with AST results retrieved from 16 selected laboratories in Ghana, 2016-2018

Characteristics	Positive cultures with AST results n = 4 394 n (%)
Gender	
Male	1 466 (33.4)
Female	2 928 (66.6)
Age, years	
Less than 1	391 (8.9)
1 to 17	652 (14.8)
18 to 49	1 084 (24.7)
50 to 65	254 (5.8)
Above 65	226 (5.1)
Unknown age	1 787 (40.7)
Years	
2016	986 (22.4)
2017	1 623 (36.9)
2018	1 785 (40.6)
Pathogen	
Bacteria	4 393 (100.0)
Fungi	(0.0)

3. Inappropriate testing

Of the 16 selected laboratories, 14 laboratories used CLSI standards for AST testing, while two reported compliance with EUCAST standards. However, during the review of AST results, the following instances of inappropriate testing were noted:

Bacteria were tested with antifungals (Supplementary Figure 2a). *Staphylococcus aureus* was tested with vancomycin using the disk diffusion method. Enterobacterales were tested with oxacillin and penicillin G (Supplementary Figure 2b).

4. Clinical information

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

Table 7: Clinical characteristics of positive cultures with AST results retrieved from 16 selected laboratories in Ghana, 2016-2018

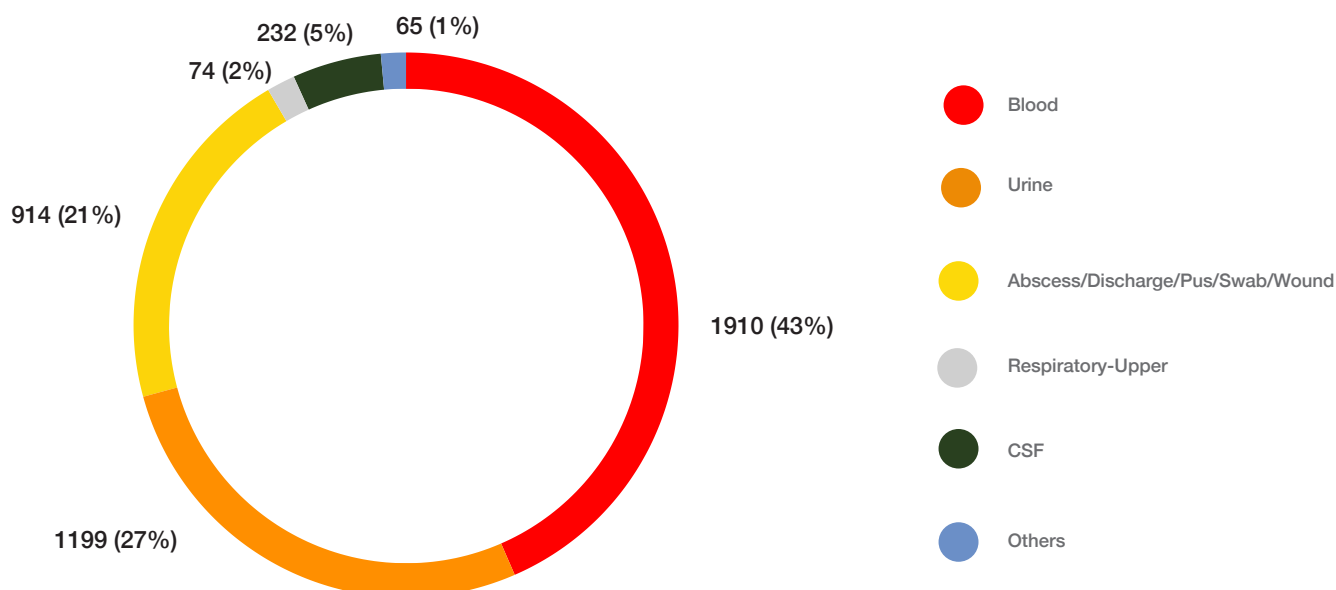
Laboratory	Positive cultures with AST results N = 4 394	Diagnosis data	Infection origin data*	Indwelling device data	AMU data
Lekma	395	0	0	0	0
Cape Coast Teaching	325	13	0	0	0
PHL Tamale	151	145	0	0	0
Tema	315	6	0	8	0
St. Joseph	66	0	0	0	0
HF Berekum	102	0	0	0	0
Greater Accra RH	1 201	0	0	0	0
Upper-East RH	234	234	0	0	0
Patholab	36	0	0	0	0
Quadushah	56	0	0	0	0
Paradise	163	0	0	0	0
University of Cape Coast	230	0	0	0	0
M and G	-	-	-	-	-
HF Techiman	657	0	0	0	0
Nsawam	291	0	0	0	0
Tamale Teaching	172	167	0	0	0

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

5. Specimen characteristics

Blood, urine and purulent discharge accounted for the most positive cultures in each study year

(Figure 10, Supplementary Table 4).



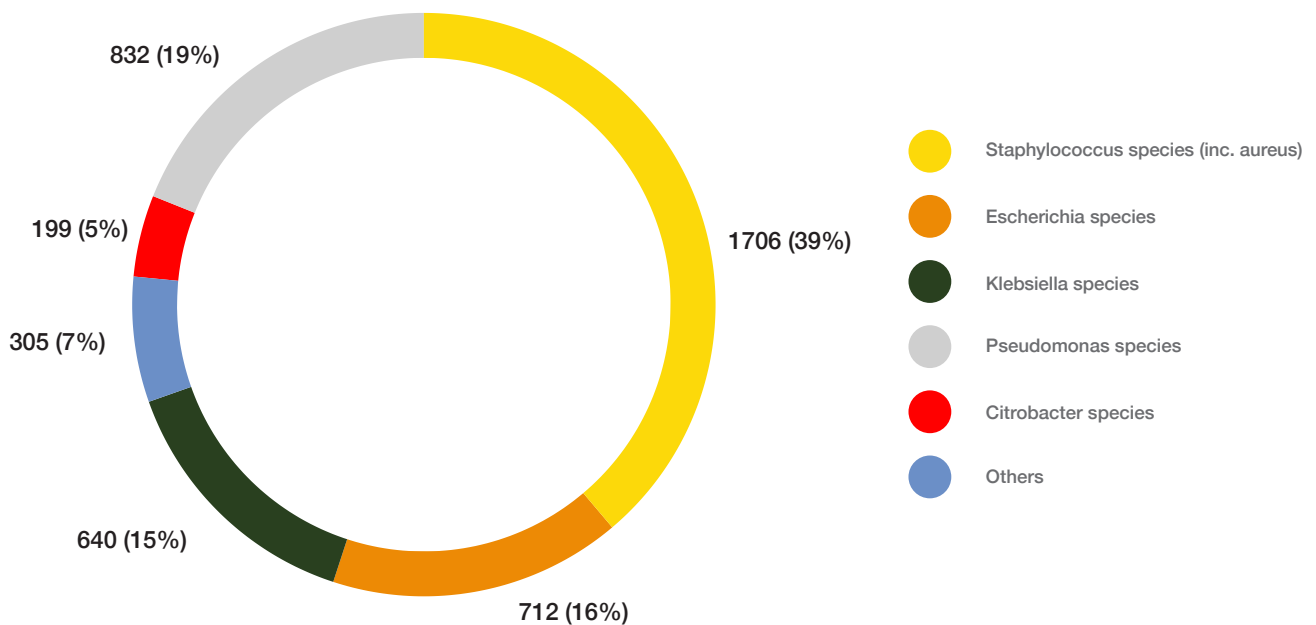
* Others include all other specimens excluding the top 5 mentioned here

Figure 10: Specimen type distribution of positive cultures retrieved from 16 selected laboratories in Ghana, 2016-2018

6. Identified pathogens

Staphylococcus species (39%), Escherichia species (16%) and Klebsiella species (15%) largely contributed to the quantum of positive cultures (Figure 12).

In 2016, of 986 positive cultures with AST results, Staphylococcus species (32.9%), Escherichia species (21.8%) and Klebsiella species (13.7%) were the most reported. In 2017, of the 1 623 positive cultures with AST results, Staphylococcus species (45%), Escherichia species (14.2%) and Klebsiella species (13.7%) were again the most reported. In 2018, information was available for a greater number of cultures (1 785), though pathogen distribution remained similar to prior years. (Supplementary Table 5).



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

Figure 11: Pathogens distribution of positive cultures with AST results retrieved from 16 selected laboratories in Ghana, 2016 -2018

7. Quality of data

The country data quality score of the 17 096 valid culture records obtained from the 16 laboratories in Ghana was 3.1 and was rated as good for AMR analysis. For individual laboratory data quality scores from each contributing laboratory, see Supplementary Table 6.

Section III: AMR rates

Objective

1. To estimate the country-level AMR prevalence and trends for the WHO priority pathogens and other clinically important and frequently isolated pathogens
2. To enable 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, determined by the proportion of isolates that are non-susceptible (i.e., either intermediate or resistant) over a one-year period:

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

The AMR rates were estimated for the WHO priority pathogens¹⁶ with more than 30 tested isolates regardless of the specimen type (AMR Appendix 5). The AMR trends for the WHO priority pathogens were mapped depending on data availability.

In addition, AMR rates were estimated for the following:

1. Clinically important pathogens isolated from blood and CSF (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 the WHONET. Although non-susceptibility interpretations were based on results from the tested antimicrobials, they are represented at the antimicrobial class level wherever possible (AMR Appendix 7). Analysis was limited to bacterial and fungal pathogens.

Removal of duplicate records

Before AMR rates were calculated, duplicate AST results were removed such that only the results of the first pathogen isolated per patient per year, irrespective of AST profile and sample characteristics (specimen source, body site, or type in the case of the WHO priority pathogens), were included; this approach follows the CLSI M39A4 criteria^{13,14}. Duplicate removal was based on the availability of unique patient identifiers. When no patient identifiers were available, the results of all isolates were included. The AST data from all laboratories were then aggregated, and rates were calculated as the proportion of non-susceptible isolates.

AMR estimates statistics

Confidence intervals (CIs) were calculated to quantify the uncertainty in the estimated resistance rates at the 95% level of confidence. Typically, CIs for AST data have been constructed using the Wilson score method. This binomial calculation assumes that all samples are independent.¹⁵ 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 the lack of data independence, such that each laboratory represented a cluster.¹⁶

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. Validation of AST results was beyond the study scope; data was taken at face value for assessment of resistance rates.

Online data visualisation

AMR data was aggregated at the national level, and definitions of resistance were harmonised across countries to enable comparisons. Data was uploaded to a private, 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 for analysing AMR data: point-and-click editing tools allow the user to mine the data to answer complex questions, and the resulting analyses can be displayed as bar charts representing resistance over a time period or line graphs showing changes over time by month or year. RSN will be made available for at least one year, following the end of the study, to each participating country.

Data was also uploaded to CDDEP's RSN platform, a publicly available repository of aggregated country-level data.¹⁷ Spatiotemporal analysis for the combined AMR and AMC-AMU datasets were built on the ResistanceMap framework. Current capabilities include maps, trend line charts, and frequency bar charts.

Results

(i) AMR rates and trends for WHO priority pathogens

AMR rates for the WHO priority pathogens were calculated as the proportion of isolates that were non-susceptible over each one-year interval. Across 2016–18, AMR rates for some organisms remained consistent; the rates for others varied. Very high AMR rates were noted for carbapenem in the Enterobacterales (over 90%) in 2016-17 though it was lower (52%) in 2018. Rates were high for 3rd generation cephalosporin in the Enterobacterales (72-78%) and methicillin in *S. aureus* (MRSA) (74-85%) (Table 8, Figures 12 and 13). Statistics for vancomycin-resistant and intermediate *Staphylococcus* species and *S. aureus* are not included.

Table 8: AMR rate estimates for WHO priority pathogens

Pathogen	Antibiotic, class	2016				2017				2018			
		N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)	N	n (%)	95% CI	Labs* (range)
<i>Acinetobacter baumannii</i>	Carbapenems	-	-	-	-	-	-	-	-	10	8	-	2 (1 - 9)
<i>Pseudomonas aeruginosa</i>	Carbapenems	14	10 (97.6)	-	2 (2 - 12)	3	3 (19.4)	-	2 (1 - 2)	23	20 (16.8)	-	4 (1 - 16)
Enterobacterales	Carbapenems	82	80 (97.6)	93.6-99.1	7 (1 - 56)	1476	286 (19.4)	10-34.2	15 (1 - 420)	1	278 (16.8)	9.2-28.8	14 (8 - 346)
Enterobacterales	Cephalosporins (3rd generation)	2	1 366 (57.3)	48.7-65.3	15 (24 - 529)	493	383 (77.7)	66.4-86	15 (1 - 133)	529	395 (74.7)	68.4-80.1	15 (1 - 190)
<i>Enterococcus faecium</i>	Vancomycin	-	-	-	-	-	-	-	-	-	-	-	-
<i>Haemophilus influenzae</i>	Ampicillin	-	-	-	-	-	-	-	-	-	-	-	-
<i>Helicobacter pylori</i>	Clarithromycin	-	-	-	-	-	-	-	-	-	-	-	-
<i>Neisseria gonorrhoeae</i>	Cephalosporins (3rd generation)	2	1	-	1 (2)	2	2	-	2 (1 - 1)	-	-	-	-
<i>N. gonorrhoeae</i>	Fluoroquinolones	3	1	-	2 (1 - 2)	3	2	-	3 (1 - 1)	-	-	-	-
<i>Campylobacter</i> species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
<i>Salmonella</i> species	Fluoroquinolones	6	1	-	4 (1 - 2)	5	1	-	2 (1 - 4)	9	1	-	5 (1 - 3)
<i>Shigella</i> species	Fluoroquinolones	1	0	-	1 (1)	2	0	-	2 (1 - 1)	3	2	-	2 (1 - 2)
<i>S. aureus</i>	Methicillin	22	17	-	5 (1 - 8)	141	120 (85.1)	77.8-90.3	8 (1 - 100)	83	61 (73.5)	48.7-89	8 (1 - 26)
<i>S. pneumoniae</i>	Beta-lactam combinations	-	-	-	-	2	1	-	1 (2)	2	0	-	2 (1 - 1)
<i>S. pneumoniae</i>	Penicillins	5	4	-	3 (1 - 2)	11	8	-	3 (2 - 5)	14	14	-	4 (1 - 9)

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

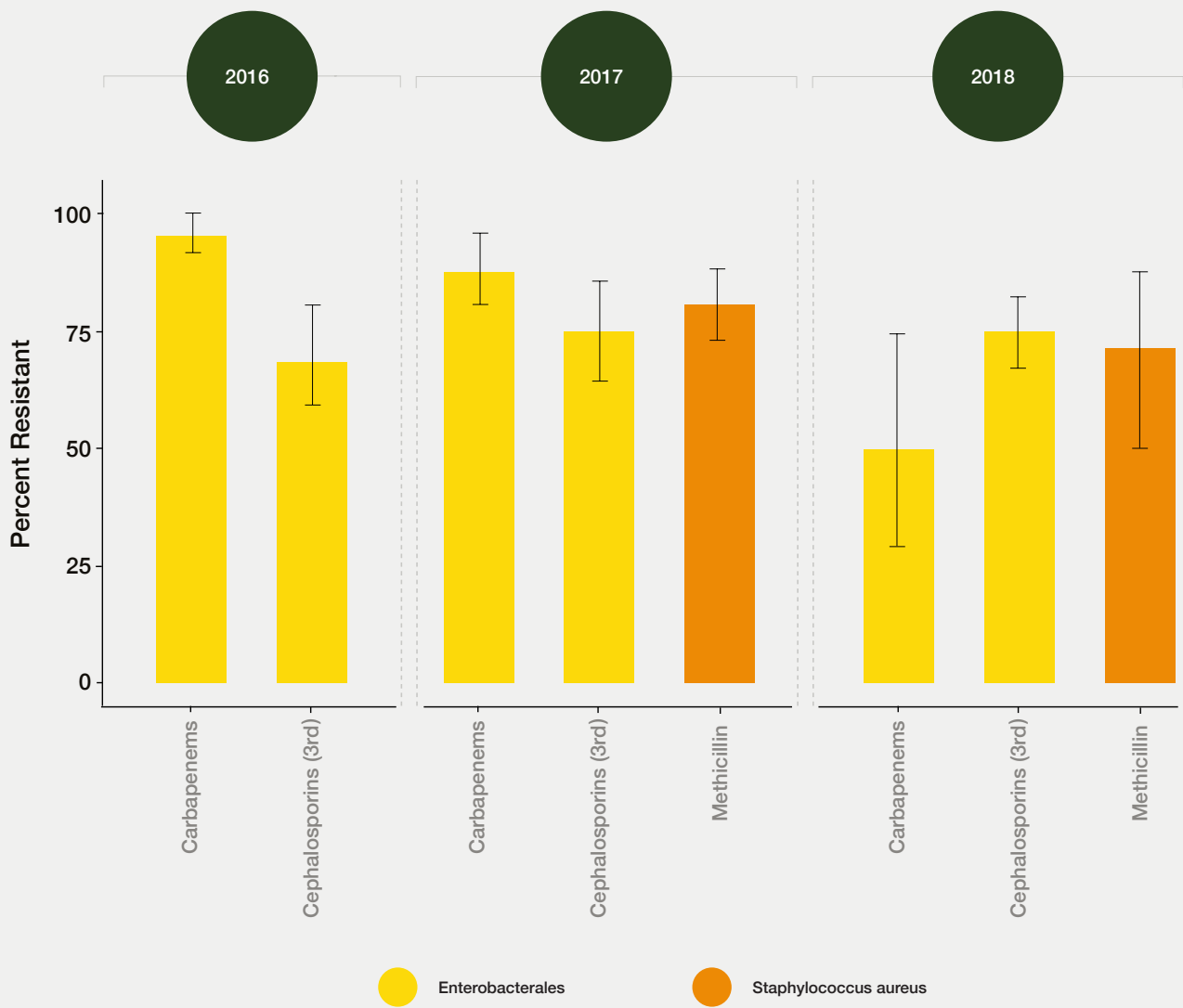
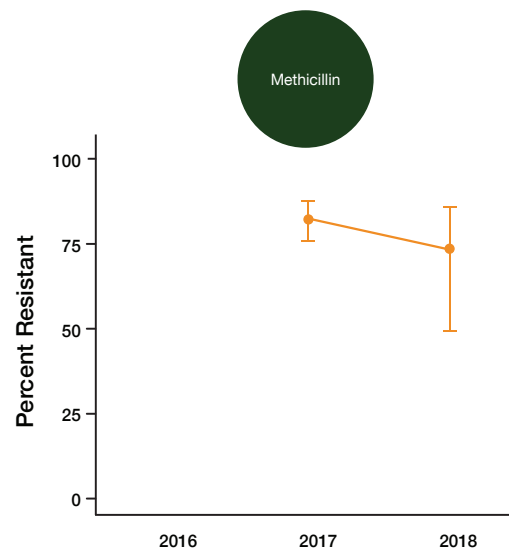
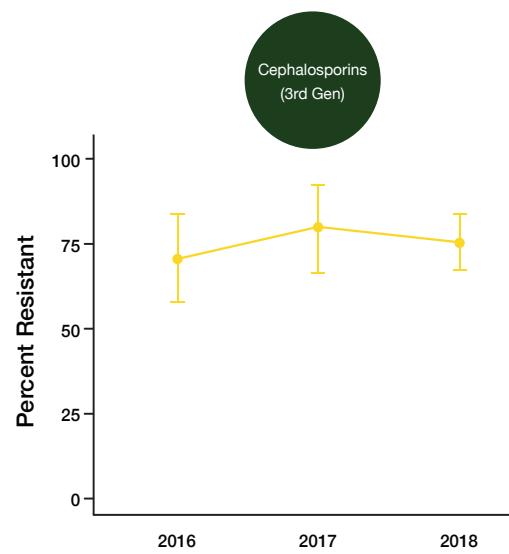
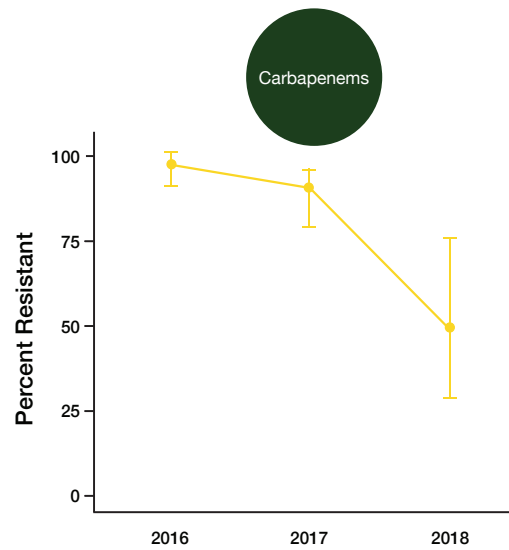


Figure 12: AMR rate estimates for selected WHO priority pathogens isolated by 16 selected laboratories in Ghana, 2016 -2018



Enterobacterales Staphylococcus aureus

3rd Gen = third generation

Figure 13: Pathogens distribution of positive cultures with AST results retrieved from 16 selected laboratories in Ghana, 2016 -2018

(ii) AMR rates for other pathogens of clinical importance

Analysis of AST data from blood and CSF isolates revealed high AMR rates for 3rd generation cephalosporin-resistant *Klebsiella* species (80-86%) and methicillin-resistant *Staphylococcus* species (73-80%). AMR rate for carbapenem-resistant *Klebsiella* species showed variable results (100% in 2017 and 48% in 2018) (Table 9).

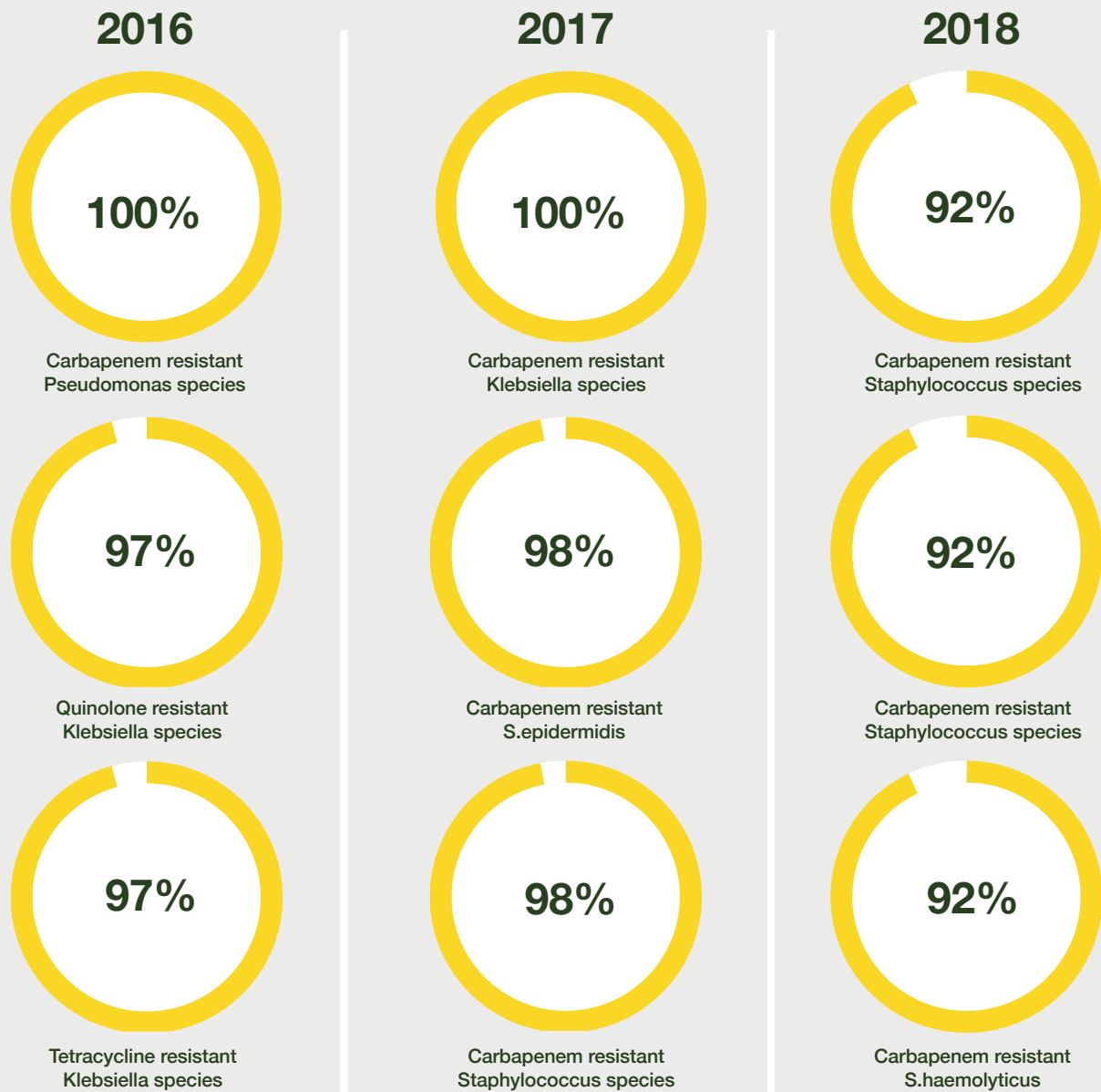
Table 9: AMR rate estimates for other clinically important pathogens* isolated by the 16 selected laboratories in Ghana, 2016-2018

Pathogen	Antibiotic, class	2016				2017				2018			
		N	n (%)	95% CI	Labs# (range)	N	n (%)	95% CI	Labs# (range)	N	n (%)	95% CI	Labs# (range)
Acinetobacter species	Carbapenems	-	-	-	-	8	8	-	1 (8)	7	7	-	2 (1-6)
Acinetobacter species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Aminoglycosides (high level)	-	-	-	-	-	-	-	-	-	-	-	-
Enterococcus species	Vancomycin	3	2	-	2 (1-2)	3	1	-	1 (3)	18	6	-	3 (2-9)
H. influenzae	Ampicillin	-	-	-	-	-	-	-	-	-	-	-	-
H. influenzae	3 rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
Klebsiella species	Carbapenems	4	4	-	2 (1-3)	30	30 (100)	86.2-102	5 (1-17)	60	29 (48.3)	27.5-69.8	6 (1-46)
Klebsiella species	Cephalosporins (3 rd generation)	13	13	-	5 (1-4)	70	56 (80)	54.5-93	8 (1-27)	81	70 (86.4)	79.6-91.2	9 (1-38)
N. meningitidis	Ampicillin	1	1	-	1 (1)	1	1	-	1 (1)	5	2	-	1 (5)
N. meningitidis	Cephalosporins (3 rd generation)	1	0	-	1 (1)	1	1	-	1 (1)	4	1	-	1 (4)
Pseudomonas species	Carbapenems	25	24	-	2 (3-22)	13	13	-	2 (1-12)	21	18	-	4 (1-10)
Pseudomonas species	Lipopeptides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Fluoroquinolones	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	Macrolides	-	-	-	-	-	-	-	-	-	-	-	-
Salmonella species	3 rd generation cephalosporins	-	-	-	-	-	-	-	-	-	-	-	-
<i>Staphylococcus aureus</i>	Methicillin	-	-	-	-	-	-	-	-	-	-	-	-
<i>Staphylococcus</i> species	Methicillin	7	6	-	2 (2-5)	125	91 (72.8)	66.6-78.2	6 (1-110)	168	134 (79.8)	67.8-88.1	5 (1-141)
<i>S. pneumoniae</i>	Penicillins	2	2	-	2 (1-1)	7	4	-	2 (3-4)	9	9	-	3 (1-7)
<i>S. pneumoniae</i>	Beta-lactam combinations	-	-	-	-	2	1	-	1 (2)	2	1	-	2 (1-1)
<i>S. pneumoniae</i>	Macrolides	1	1	-	1 (1)	3	1	-	2 (1-2)	10	3	-	4 (1-7)
<i>S. pneumoniae</i>	Vancomycin	-	-	-	-	3	1	-	1 (3)	1	1	-	1 (1)

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

(iii) AMR rates for highly resistant pathogens

Based on available data, very high resistance (~100%) was estimated in clinically important pathogens like the Pseudomonas species (to carbapenems), Klebsiella species (to carbapenems, quinolones), S. epidermidis (to carbapenems) (Figure 15).



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

Figure 14: Top five highly resistant pathogens isolated by the 16 selected laboratories in Ghana, 2016-2018

(iv) AMR rates for fungal pathogens

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

Section IV: Drivers of antimicrobial resistance

Objective To assess the drivers of AMR

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

- Patient-level factors – demographics (age, gender), diagnosis, comorbidities, antimicrobial usage, presence of an indwelling device (catheter, central line, ventilator), and origin of infection (hospital or community).
- Country-level factors – Global Health Security index (GHSI) scores on AMR prevention, primary education, gross domestic product (GDP) per capita, physicians and nurses density, disease prevalence, and antibiotic consumption in defined daily dose (DDD) per 1 000 inhabitants (the country-level associations are presented separately at a regional/continental level).

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

Statistical analysis Initial data exploration 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, and only those with $p < 0.2$ were evaluated in a multiple logistic regression analysis (statistical significance was set at $p < 0.05$). The Wilson score method with the robust standard error was used to construct CIs for the AMR rates.

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

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

Results Two variables (age and gender) were evaluated for possible association with AMR. The data availability of these variables was gender (99.9%) and age (68.4%). Both the univariate and multiple logistic regression analyses did not reveal any significant association between the variables (age and gender) and AMR (Table 10, Supplementary Table 7).

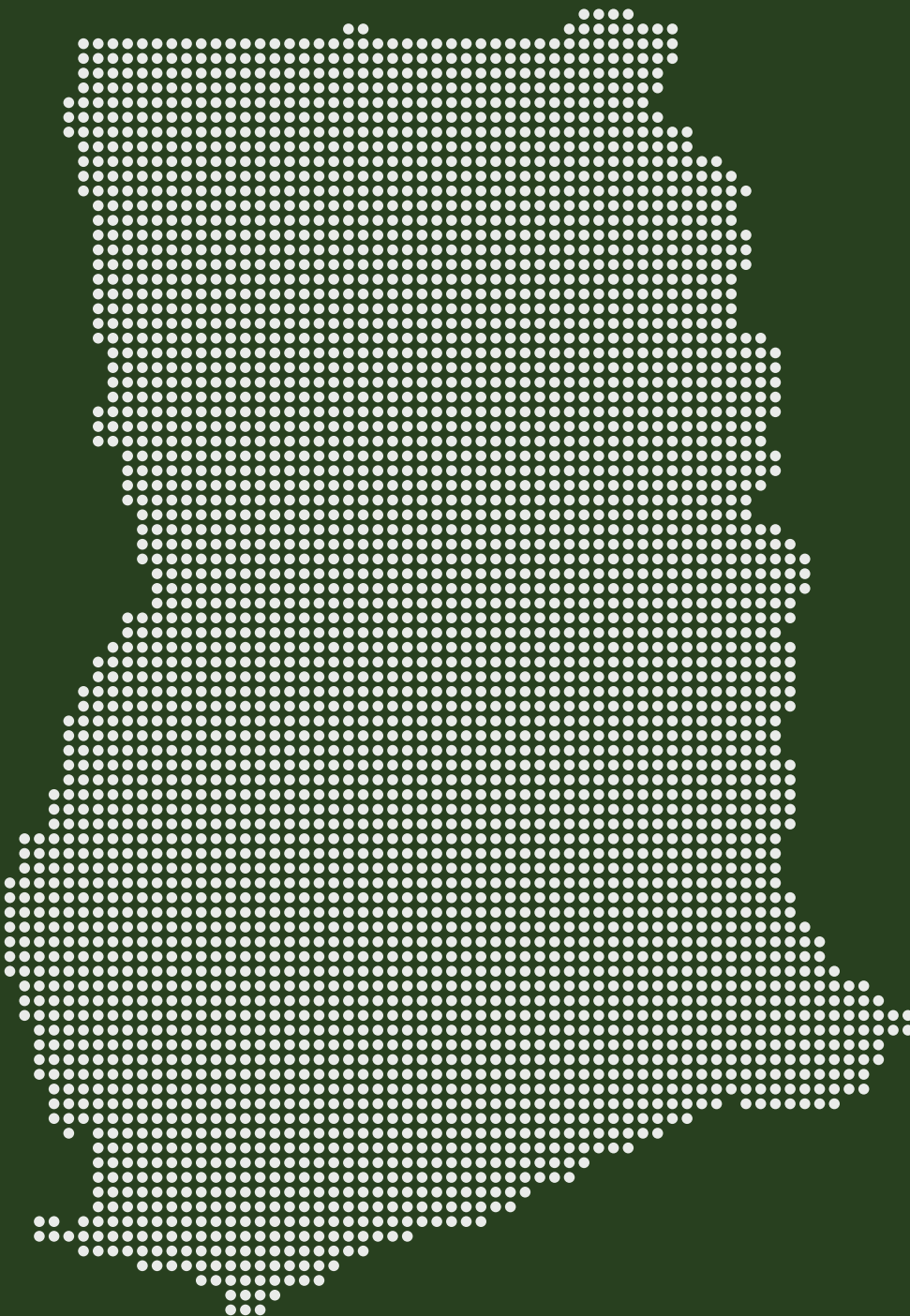
Table 10: Identification of demographic drivers of AMR in Ghana 2016 -2018

Variable	Options	N	NS (%)	Adjusted OR (95% CI)	P-value
Gender	Female	1 629	64.8	Ref	
	Male	582	62.0	0.88 (0.76 -- 1.03)	0.109
Age	<1	109	58.7	0.80 (0.59 -- 1.09)	0.156
	1-17	439	64.2	1.00 (0.65 -- 1.55)	0.991
	18-49	1 170	64.8	Ref	
	50-65	272	60.7	0.85 (0.67 -- 1.08)	0.188
	>65	221	67.0	1.15 (0.84 -- 1.57)	0.392

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

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

Part B: Antimicrobial (antibiotic) Consumption



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

Overuse and misuse of antimicrobials are crucial factors in the complex web of AMR causation. Widespread and unregulated antimicrobial usage exerts selective pressure by inhibiting the growth of some microorganisms and consequently accelerating the development of AMR.^{18,19} Therefore, close surveillance on how the antimicrobials are utilised is a key step for stewardship programs in order to stem AMR. The surveillance mechanisms recommended by WHO include the monitoring of AMC and AMU. This falls in line with the MAAP aims to expand the volume of data presently available on AMR, AMC and AMU across Africa and also in line with Ghana (2017-2022) AMR NAP.¹⁰

Definition of AMC and AMU

AMC is defined as the number of antimicrobials used within a specified setting (e.g. national-level, hospital, or community health care level) over a specified period. AMC is calculated from aggregated data such as import, wholesales, insurance, facility dispensing or procurement data sources, while AMU tracks whether antimicrobials are prescribed appropriately for the right infections and according to treatment guidelines. AMC and AMU are terminologies that are sometimes incorrectly used interchangeably. It is therefore prudent to delineate these definitions further; AMC data describe quantities of antimicrobials dispensed (e.g. at national stores or pharmacies), whereas AMU data describes how and why antimicrobials are used (e.g. if required laboratory tests and clinical assessments were done prior to issuing a prescription, and if the right antimicrobial was prescribed at the correct dose and frequency, over an appropriate duration, to treat the right indication as per country guidelines and if the patient correctly/completely consumed the prescribed antimicrobial).²⁰

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.¹⁸ 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 due to improved access and increased economic strength within some of these countries. However, AMR can also develop because of a lack of access to antimicrobials, as the prolonged use of a particular antimicrobial over a long

time selectively favours microbes that evade (are resistant to) these predominantly used antimicrobials. This selective pressure is common in a number of LMICs where inequities in antimicrobials access still persist,²¹ demonstrating the need for the research and development of new agents and the need for appropriate use and access to the available antimicrobials. An AMC surveillance system is paramount to obtain an elaborate and complete picture of the link between AMC and AMU with AMR in Ghana and identify prevalent gaps and areas for targeted intervention to encourage rational use of antimicrobials.

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 Ghana, which would equip the country with valuable information to support the appropriate use of antimicrobials.

The objective was to identify gaps that may exist in setting up a comprehensive surveillance system and provide the country with the needed information to support the setup of such a monitoring system.

AMC and AMU surveillance impact

Optimising the correct usage of antimicrobials is one of the strategic objectives of the WHO Global Action Plan (GAP) to ensure the successful treatment of infectious diseases in patients.⁸ To successfully implement the above objective, there is a need to understand the country's pattern of antimicrobial use and quantify their consumption. At present, there are only a few published reports on AMC surveillance and AMU in Africa,²²⁻²⁶ including a few reports in Ghana.^{27,28,29} The process of obtaining AMC/AMU data equips the country with local information on various problems that exist with antimicrobial use and allows for monitoring the accessibility of antimicrobials. Further, obtaining AMC/AMU data permits the continuous local assessment of correlations between antimicrobial usage and emerging local AMR, which informs proper AMR mitigation policies and activities. Data obtained from the local surveillance exercises also informs better stewardship programs.

Therefore, the MAAP set out to quantify consumption and analyse AMC and AMU trends at selected facilities and the Ghana FDA, to better inform the design of future stewardship programs and policies that will optimise the use of antimicrobials in Ghana while providing the country's reference point to measure the impact and success of future implemented interventions.

The aim of this work

1.

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

2.

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

Section II: AMC or AMU surveillance status

Objective

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

Methodology

AMC and AMU data sources

Through open-structured key informant interviews (KIIs) (AMC Appendix 1), the AMRCC contacts shared their insights about the current landscape of AMC surveillance in the country as well as where the best sources of national AMC data. From the interview, the Ghana FDA was identified as a potential source for national AMC data in Ghana as they were the sole entity involved in approving and regulating all medicine importations into the country and local medicine manufacture. The Ghana AMRCC recommended pharmacies to the MAAP to be recruited for the facility-level data.

Under the guidance of the Ghana AMRCC, the MAAP targeted to recruit and obtain data from thrice as many pharmacies as the selected AST laboratories (i.e., a total of 48 pharmacies). Pharmacy-level AMC data was collected from the pharmacies co-located in the same clinical facility with AST laboratories (n=16)(AMC Appendix 2 for pharmacy selection tool). Additionally, community pharmacies (n=32) were also targeted; these pharmacies were nominated by the co-located pharmacies on the basis of their close proximity to the AST laboratories and their status as the community-preferred patient medicine purchase sites or as the backup prescription fulfilment source in the case of stock-outs in the main hospital pharmacy. Additionally, the availability of retrospective data from 2016-2019 and willingness to share data were key criteria considered for selection.

In addition to the AMC data collected, AMU data were to be obtained from hospital pharmacies (n=16), and this was to be abstracted from the facilities' prescription or patient medical records. To clarify, community pharmacies, also known as retail pharmacies, are licensed commercial pharmaceutical stores that provide medicinal products (prescription-only and over-the-counter medicines) to a specific community group or region and exclude unregulated and informal medicine dispensers. Hospital pharmacies are pharmacies located within a hospital supplying medicinal products to inpatients and outpatients who visit the hospital.

Data collection scope

The MAAP purposively collected consumption data on J01 (antibiotics for systemic use) medicines, which are one of the WHO core monitoring ATC medicine categories for AMC surveillance. In addition, as per the country's request, selected P01AB (nitroimidazole derivatives) and J02 (antimycotics for systemic use) were also included in the scope for AMC data collection (See AMC Appendix 3 for the full list of selected antimicrobials in Ghana). P01AB and J02 ATC antimicrobials are part of WHO core and optional monitored medicine classes, respectively, for AMC surveillance.³⁰ AMC data from the above medicine categories were collected from January 2016 to December 2019.

Data collection

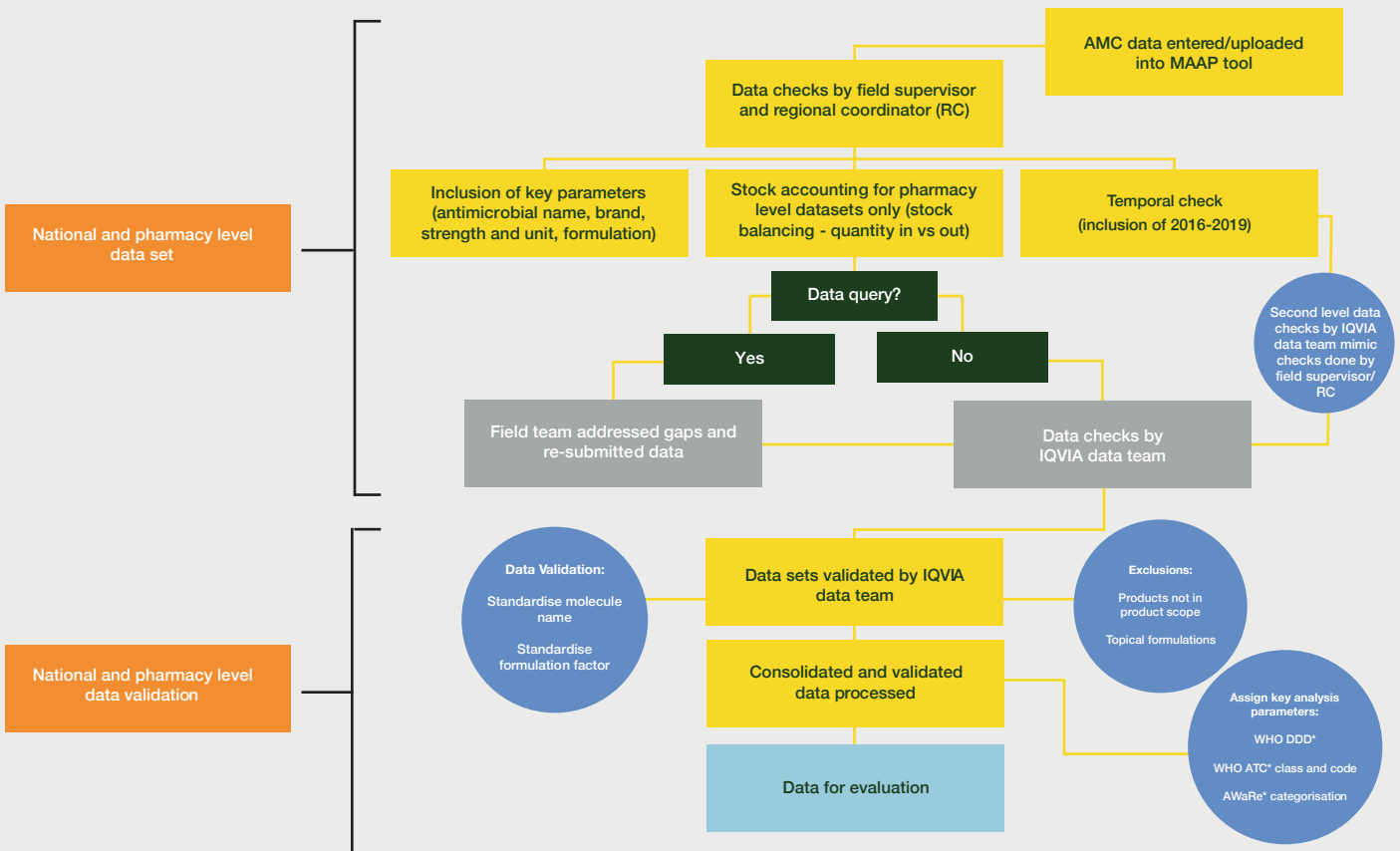
The FDA datasets were provided directly to the MAAP field data collectors electronically in the form of a Microsoft Excel™ sheet. These datasets included all commodities imported and locally manufactured in the country. Firstly, the datasets were sorted to filter out the products within scope. The dataset was then reviewed and cleaned by the data collection teams using Microsoft Excel™ software, which was then transferred securely through the MAAP tool that captured all of the antimicrobials by their standard molecule name and/or product brand, pack size, strength, and formulation (e.g., tablets/capsules, suspensions/syrups). AMC Appendix 4 captures the full list of data variables collected to determine the national and pharmacy AMC levels.

For the pharmacy-level data, the trained MAAP data collectors either extracted the consumption data from the facility’s health information system (HIS) into a Microsoft Excel™ sheet. Within facilities without electronic HIS, data were abstracted from stock record cards and manually entered into the MAAP tool. The electronic datasets were reviewed and cleaned by the data teams and then transferred securely through the MAAP tool to the central data processing and analysis team. AMC Appendix 5 details the data collection process.

The MAAP also planned to collect AMU data in pharmacies co-located in the same clinical facilities as the AST laboratories to assess the appropriateness of consumed antimicrobials. Data captured included patient characteristics and medical condition for which the antimicrobial was prescribed, and appropriateness of prescription per the national guidelines Appropriateness of prescription assessed the conduct of relevant laboratory tests and clinical assessment done prior to prescription and assessed dose, strength, frequency and duration of the prescription.

Data cleaning and validation

Once the national-level antimicrobial datasets from FDA were received by MAAP, both the national and pharmacy-level AMC data were then subjected to a series of data validation checks to ensure their accuracy and consistency (see AMC Appendix 6). The pharmacy and national AMC data were subjected to secondary and tertiary checks by field supervisors, the regional coordinator and the IQVIA data team. The IQVIA regional coordinator and IQVIA data team validated and processed the data as outlined in Figure 15.



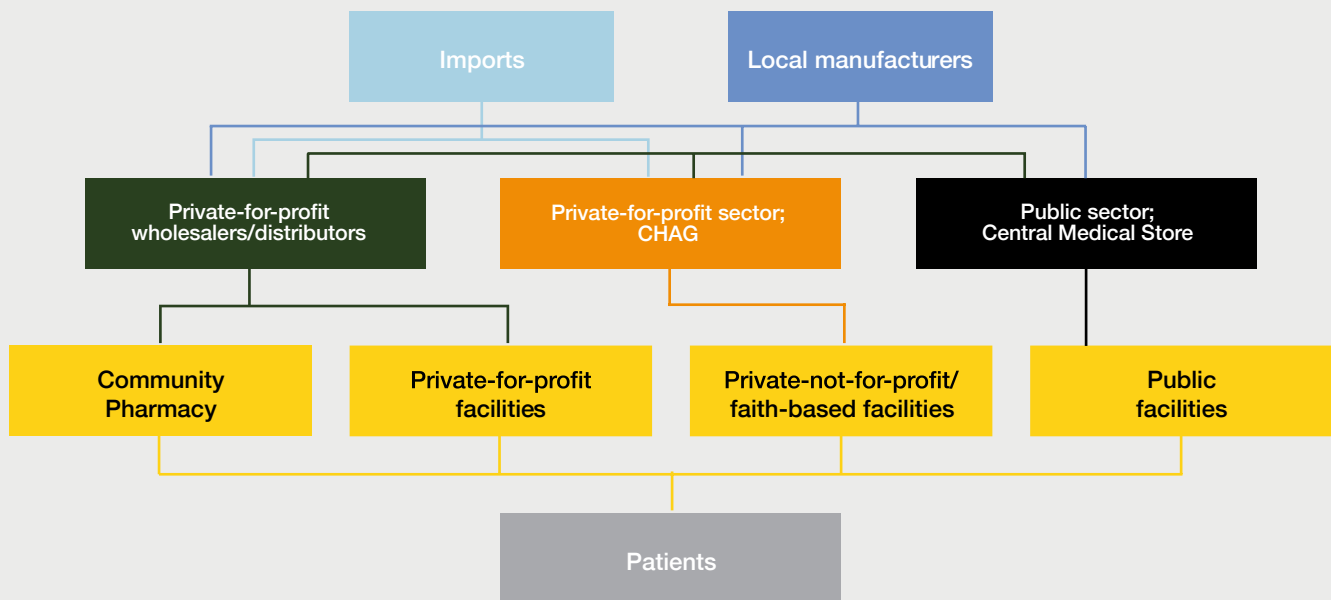
*WHO World Health Organisation - *DDD Defined Daily Dose - *AWaRe Access, Watch, and Reserve

Figure 15: : The data checks and validation process for the national- and pharmacy-level AMC data collected from 26 facilities in Ghana, 2016 -2018

Results

Flow of antimicrobials in the country

Five KIs of stakeholders in the Ghana National Antimicrobial Resistance Coordinating Committee (AMRCC), Ghana FDA, non-governmental organisations (NGO) and private community retail pharmacies to characterise the pathway through which the antimicrobials get to patients in the country using the AMC interview tool. In Ghana, medicines, including antimicrobials, are locally manufactured and imported into the country. The Ghana FDA regulates and licenses all pharmaceutical products locally manufactured or imported. After importation or local production, private (for-profit and not-for-profit) wholesalers and public-sector Central Medical Stores (CMS) then move the antimicrobials to the community pharmacies, private (both for-profit and non-profit) facilities and public facilities that eventually issue the antimicrobials to patients (Figure 16) illustrates the route through which antimicrobials get to the patients in Ghana.



CHAG: Christian Health Association of Ghana

Figure 16: The antimicrobials circulation routes to the patients in Ghana, 2016-2019

Regulation of antimicrobials consumption

In Ghana, antimicrobials for human consumption are regulated under the Food and Drugs Act, PNDCL 305B, 1996 (revised and integrated into the Public Health ACT 851 in 2012). This law stipulates that requisite antimicrobials can only be sourced from registered suppliers and can only be dispensed for a valid prescription. However, there is poor enforcement of this regulation, which has led to the widespread availability and dispensing of antimicrobials over-the-counter without a prescription and also via unauthorised persons in Ghana.¹¹ Routine over-the-counter sale of prescription-only antimicrobials is practised both in the pharmacies and by unapproved medicine vendors. This non-authorised over-the-counter retail of prescription antimicrobials, may lead to their overuse and misuse. Overuse and misuse of antimicrobials are significant drivers of AMR. Therefore, to address the above issues and other prevalent gaps, the country developed the Ghana AMR NAP (2017-2022),¹⁰ that seeks to further build regulations around AMC to curb AMR.

Availability of data for AMU surveillance

Attempts were made to obtain AMU data from the participating pharmacies that were co-located in the same clinical facility with the AST laboratories (n=11). Unfortunately, MAAP was unable to collect AMU data in Ghana from the selected health facilities due to the nature of the data sources at the participating pharmacies (i.e. stock issuance record cards). The stock issuance records do not track specific medicines received by a patient.

Availability of data for AMC surveillance

National-level data

The National AMC data were obtained from FDA for the years 2016 to 2019. However, these import manifests missed key information critical for AMC data analysis; particularly, the antimicrobials supply quantities were recorded in measurements of cartons, boxes and drums, rendering it unsuitable for estimating the number of tablets/suspensions/vials etc. Thus, the MAAP data team was unable to calculate the DDDs, the primary requirement for AMC analysis, consumed from the national FDA AMC datasets. Subsequently, the MAAP, together with the AMRCC, attempted to retrieve national AMC from another source: the health insurance data. However, the data from Ghana insurance claims offered covered approximately 5-10% of the total AMC in the country (representing mostly private insurance owners). Therefore, given the low coverage, this report only further analyses and presents results from aggregated pharmacy-level AMC datasets, as these datasets can be viewed as more representative of national AMC than the homogenous insurance data, which would represent only a small sub-group of the population.

Facility-level data

Out of the 16 targeted pharmacies co-located in the same clinical facility with AST laboratories, data was successfully collected from only (n=11) targeted hospital pharmacies. Five pharmacies (n=5) were excluded as they were stand-alone laboratories (i.e., not hospital pharmacies). Furthermore, out of the 32 targeted community pharmacies, data was successfully collected in (n=15). The remaining (n=17) targeted community pharmacies were unwilling to share their AMC data and were therefore excluded. Thus, the total sample size of successfully recruited community pharmacies was (n=15) community pharmacies and (n=11) hospital pharmacies. Due to the limited number of included hospital/community pharmacies in Ghana, the data may not be representative of facility-level AMC.

The necessary variables were available in stock cards or electronic records for the 26 pharmacies included. However, there were instances of incomplete stock card data, e.g. missing strength or pack size information. These information gaps were filled by revisiting the facilities and gathering information from the facility staff or through secondary desk research using the available product details. Of the 11 hospital pharmacies, the MAAP was able to collect data across the four years (2016 – 2019) in ten pharmacies. Only one participating hospital pharmacy did not share the 2019 complete data. Out of 15 recruited community pharmacies, only five pharmacies shared data for all four years, whereas the remaining ten pharmacies did not provide data for at least one of the study years because they either declined to share the data or did not have 2016-2018 data archives in their systems.

Of the participating hospital pharmacies (n=11) that were co-located with the AST laboratories, eight were in public government hospitals (four of these pharmacies co-located within tertiary care facilities, and the other four co-located in secondary care facilities). In Ghana, due to the lack of any national AMC surveillance policy or structured AMC surveillance system, none of the recruited pharmacies actively reported AMC data regionally or centrally. Table 11 below summarises the core characteristics of the hospital pharmacies where AMC data was collected from.

Table 11: Characteristics of the 26 recruited hospital and community pharmacies in Ghana, 2016-2019

	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)	Cape Coast Teaching Hospital Pharmacy	Tertiary	Public	Cape Coast	Electronic	No	No
	Greater Accra Regional Hospital Pharmacy, Ridge	Tertiary	Public	Greater Accra	*Mixed	No	No
	Holy Family Hospital Pharmacy	Secondary	Private, faith-based	Berekum	*Mixed	No	No
	Holy Family Hospital Pharmacy	Secondary	Private, faith-based	Techiman	*Mixed	No	No
	Lekma Hospital Pharmacy	Secondary	Public	Lekma	Manual	No	No
	Nsawam Govt. Hospital Pharmacy	Secondary	Public		Manual	No	No
	St. Joseph Hospital Pharmacy, Koforidua	Secondary	Private, faith-based	Koforidua	Manual	No	No
	Tamale Teaching Hospital Pharmacy	Tertiary	Public	Tamale	Manual	No	No
	Tema General Hospital Pharmacy	Secondary	Public	Tema	Manual	No	No
	University of Cape Coast Hospital Pharmacy	Secondary	Public	Cape Coast	Electronic	No	No
	Upper East Regional Hospital Pharmacy, Bolgatanga	Tertiary	Public	Bolgatanga	Manual	No	No
Community pharmacies	Ansu Community Pharmacy	Dispensing	Private	Accra	Manual	No	No
	Azumah Community Pharmacy	Dispensing	Private	Accra	Manual	No	No
	Cape Pill Community Pharmacy	Dispensing	Private	Cape Coast	Manual	No	No
	Gina Community Pharmacy	Dispensing	Private	Tamale	Manual	No	No
	Honsal Community Pharmacy	Dispensing	Private	Cape Coast	Manual	No	No
	Losab Community Pharmacy	Dispensing	Private	Accra	*Mixed	No	No
	Medcourt Community Pharmacy Berekum	Dispensing	Private	Berekum	Electronic	No	No
	Medcourt Community Pharmacy Techiman	Dispensing	Private	Techiman	Electronic	No	No
	Meds Community Pharmacy	Dispensing	Private	Accra	Manual	No	No
	Radiance Community Pharmacy Ghana	Dispensing	Private	Accra	Electronic	No	No
	Royal Sap Community Pharmacy	Dispensing	Private	Accra	*Mixed	No	No
	Samorak Community Pharmacy	Dispensing	Private	Bolgatanga	Manual	No	No
	Scab Community Pharmacy Berekum	Dispensing	Private	Berekum	Electronic	No	No
	Scab Community Pharmacy Techiman	Dispensing	Private	Techiman	Electronic	No	No
	Topmed Community Pharmacy	Dispensing	Private	Accra	Manual	No	No

[#]Tertiary care facilities provide mainly specialised healthcare services such as oncology, orthopaedic, trauma, geriatric etc. Patients must be referred to a tertiary care facility, from either a secondary or primary in Ghana, to receive care from these facilities. The majority of the tertiary care facilities in Ghana are owned and managed by the National Government, and they are designated as University Teaching Hospitals, Referral Hospitals and Regional Hospitals. Secondary care facilities are overseen by the respective Regional, District/Municipal Governments (where the hospital is located). The secondary care facilities are mainly designated as District Hospitals, Municipal Hospitals and General Hospitals. The majority of the private hospitals in Ghana (owned by private individuals/organisations, including faith-based facilities) provide secondary care services. Secondary care hospitals offer services such as emergency care, neonatal care, and acute obstetric care, among other non-specialised services.

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

**For the review period, i.e., 2016-2019. AMC: Antimicrobial consumption.

† Refers to the ability of the 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 the national and pharmacy levels

Methodology

Statistical analysis

The MAAP data analysis was conducted per the WHO's protocol for AMC analysis using the DDD-ATC-AWaRe methodology.^{30,31} Figure 17 summarises the AMC analysis and each of these WHO methodologies, and the additional analyses done are described in brief below. 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)

DDDDs or related metrics are required for AMC analysis. DDD metric allows for easy comparison by standardising different antibiotic doses in milligrams. Also, it is recommended to use drug utilisation figures such as DDD using a relevant denominator for the health context, such as numbers of DDDs/1 000 inhabitants/day (DID), DDD/ inhabitant/year, or as DDDs/100 bed days. Studying DDDs or associated metrics over time helps to understand the consumption pattern and measure the impact of any national- or facility-level interventions as change (increase or decrease) in the consumption patterns over the study period or a pre-defined base period.

Using the WHO 2020 DDD guide, the total consumed milligrams per antimicrobial was to be divided against the standard DDD value issued by the WHO to obtain the total DDDs.³² The total DDDs were then adjusted for the country's population³³ in the years of data collection (2016-2019) and presented as 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 data should have been adjusted as DDD per the number of inpatients and presented as DDD/100 patient bed days. However, the DDD per 100 patient bed days analysis was not computed because patient bed days and patient days' information was not easily accessible for most of the hospital facilities. Also, the lack of these data hindered the comparison between hospital pharmacy consumption and community pharmacy consumption. Therefore, the pharmacy-level AMC data are presented as absolute DDD to aid comparison between hospital and community pharmacies. Detailed DDD calculations can be found in AMC Appendix 6. All calculations were done in Microsoft Excel™ software.

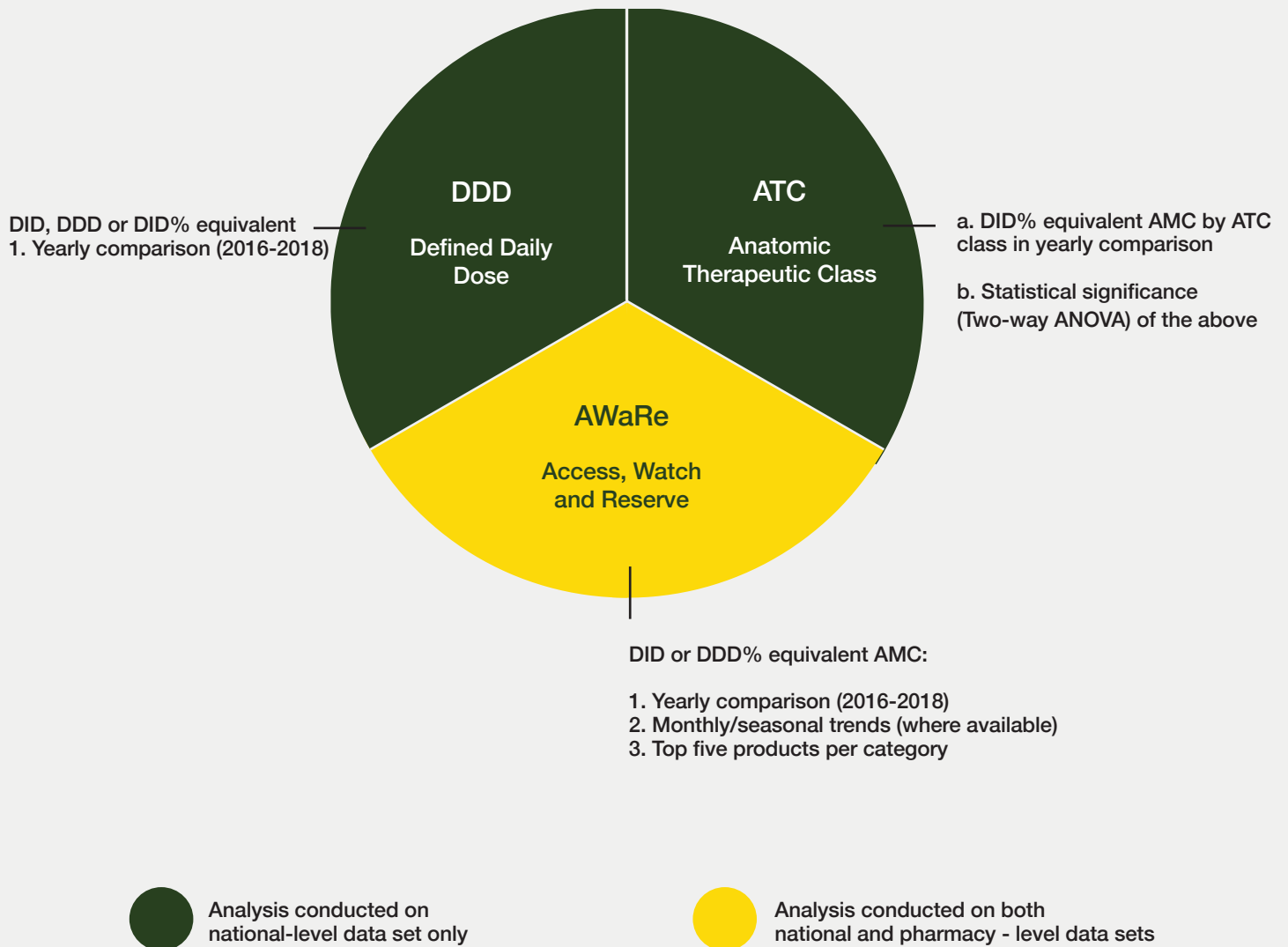
ii. Anatomic Therapeutic Chemical (ATC) Classification

The standard antimicrobial names in the pharmacy-level data collected were renamed in the Microsoft Excel™ analysis database per the 2020 WHO ATC codes (Description of ATC codes are presented in AMC Appendix 7. Analysis was then done to characterise the macro (above-molecule) AMC trends. Additional attempts to compute year-on-year differences within each ATC class were not possible as the aggregated pharmacy-level dataset included AMC datasets from ten pharmacies that did not provide full coverage of the four-year review period.

iii. WHO Access, Watch and Reserve (AWaRe)

The WHO AWaRe categorisation classifies antibiotics under 'Access', 'Watch', and 'Reserve' groups. The 'Access' group includes choice antibiotics for the 25 most common infections that should be affordable, quality-assured, and available at all times in the country or facilities. The 'Watch' group antibiotics are indicated for a specific number of infective syndromes. Since resistance to them is high, their use is controlled via stewardship programs and monitoring. Lastly, the 'Reserve' group antibiotics are considered the "last resort" treatment option. They are indicated in case of life-threatening infections due to multi-drug resistance. Thus, they are closely monitored and prioritised in stewardship programs to ensure their continued effectiveness.

Through the WHO AWaRe analysis, the total AMC by DDDs per antibiotic molecule was labelled as either 'Access', 'Watch' or 'Reserve' in accordance with the 2019 WHO AWaRe list 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). The WHO recommends that at least 60% of a country's total AMC should come from the 'Access' antibiotics. Finally, the top five antibiotics consumed in each of the WHO AWaRe categories were identified.



The defined daily dose (DDD) indicators utilised for volume metric standardisation were sourced from WHOCC 2020. The ATC Classification was utilised to categorise the antibiotics according to the organ or system on which they act, and their therapeutic, pharmacological and chemical properties were sourced from WHOCC. The ATC database and ‘Access’, ‘Watch’ and ‘Reserve’ categorisation was sourced from the 2019 WHO AWaRe classification.³⁴

Figure 17: Methods and indicators used for the analysis of the data collected in Ghana.

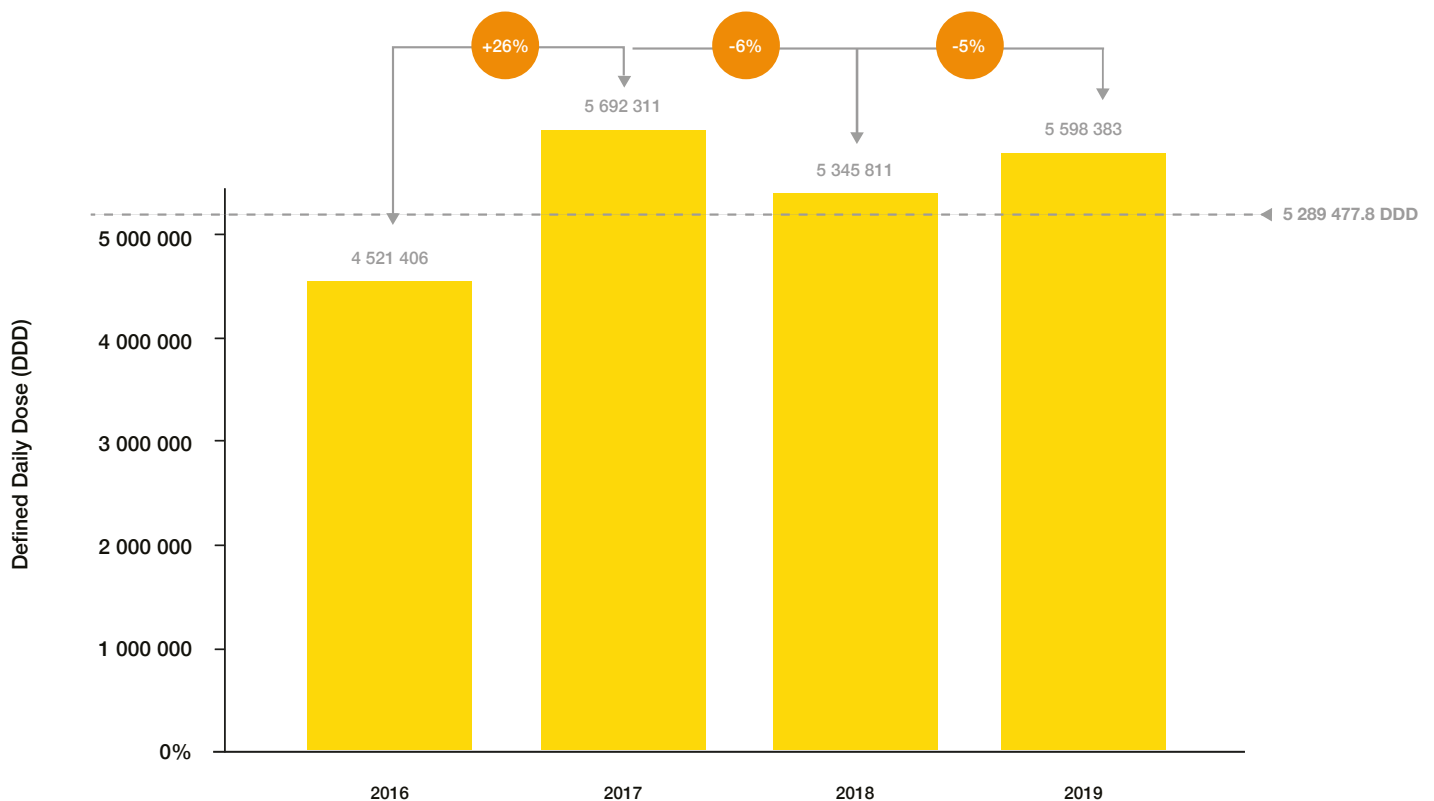
iv. Review of Essential Medicines List (EML)

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

Results

Pharmacy AMC datasets analysed by DDD per year

The average total AMC for the pharmacies sampled between 2016 to 2019 was 5 289 477.8 DDDs. A 26% increase in total antimicrobial consumption was observed from 2016 to 2017, followed by a slight reduction of 6% in 2018 and a further 5% reduction in consumption in 2019 (Figure 18).

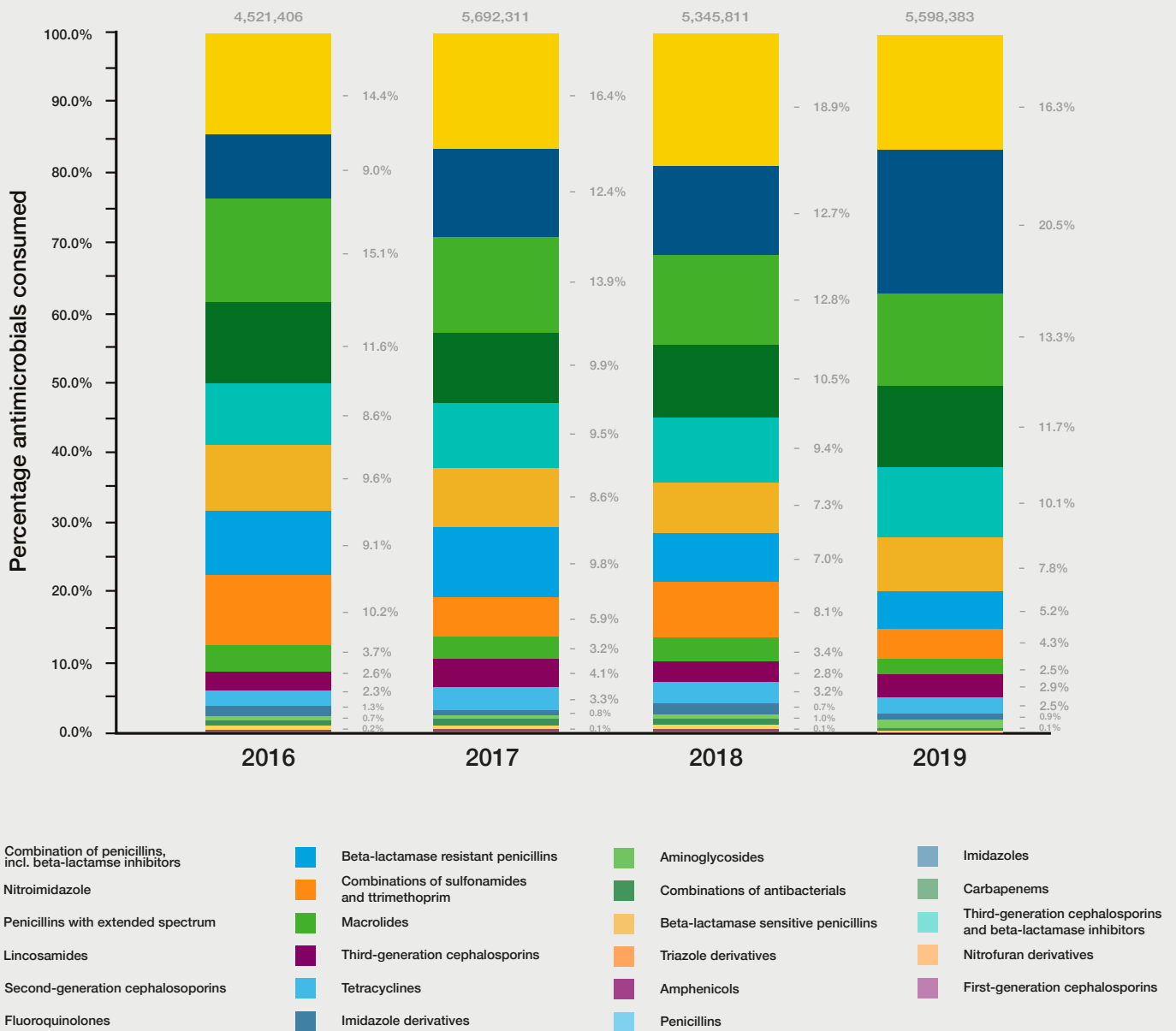


*DDDs shown here are not normalised to the country population levels or facility catchment population

Figure 18: Variation in the pharmacy-level total defined daily dose in 26 selected pharmacies in Ghana between 2016 to 2019

Pharmacy AMC analysed by ATC classification

Combinations of penicillins and beta-lactamase inhibitors (J01CR) were the overall most consumed ATC antibiotics class. Consumption for the J01CR combinations was 14.4% in 2016, 16.4% in 2017, 18.9% in 2018 and 16.3% in 2019 (Figure 19). Amoxicillin/Clavulanic acid was the most frequently consumed antibiotic within this class. Nitroimidazole derivatives (P01AB) and extended-spectrum penicillins (J01CA) were the second and third most consumed ATC classes, respectively. Metronidazole and amoxicillin led the consumption within the P01AB and J01CA ATC classes, respectively. The top five most consumed antimicrobials were amoxicillin/clavulanic acid, metronidazole, amoxicillin, clindamycin and cefuroxime. Together, they account for 64% of the total consumption share. AMC Appendix 7 lists the pharmacy-level AMC by antimicrobial molecule, and AMC Appendix 8 lists it by ATC class.



The Combinations of penicillin-beta-lactamase inhibitors ATC molecule class were, on average, the highest consumed antimicrobials across the reviewed period (2016 to 2019). Statistical testing was not carried out due to the nature of the data obtained. See AMC Appendix 8 for a more detailed breakdown of AMC by ATC classes

Figure 19: Pharmacy-level antimicrobial consumption by ATC classes in Ghana for the years 2016 to 2019

Pharmacy AMC analysed by WHO AWaRe categorization

The average consumption of antibiotics for the sampled pharmacies across the four years analysed was 75.8% 'Access', 24.3% 'Watch' and 0.0% 'Reserve'. The annual AMC trends indicated a decrease of 0.9% in the consumption of the 'Access' antibiotics between 2016 and 2017, followed by an increase of 2.6% between 2017 and 2018 and a decrease of 0.3% between 2018 and 2019. Conversely, there was an increase of 0.9% in the consumption of the 'Watch' antibiotics between 2016 and 2017, followed by a 2.6% decrease in consumption share between 2017 and 2018 and an increase of 0.3% between 2018 and 2019 (Figure 20). There were no stocks of 'Reserve' category antibiotics consumed by the sampled pharmacies in Ghana during the reviewed period. Overall and across the years analysed, consumption of the 'Access' category antibiotics met the 60% minimum consumption threshold set by the WHO. This pharmacy-level AMC analysis by the WHO AWaRe categories omits the 0.9% (47 514.3 DDDs) of total AMC that are not categorised within the 2019 WHO AWaRe list.

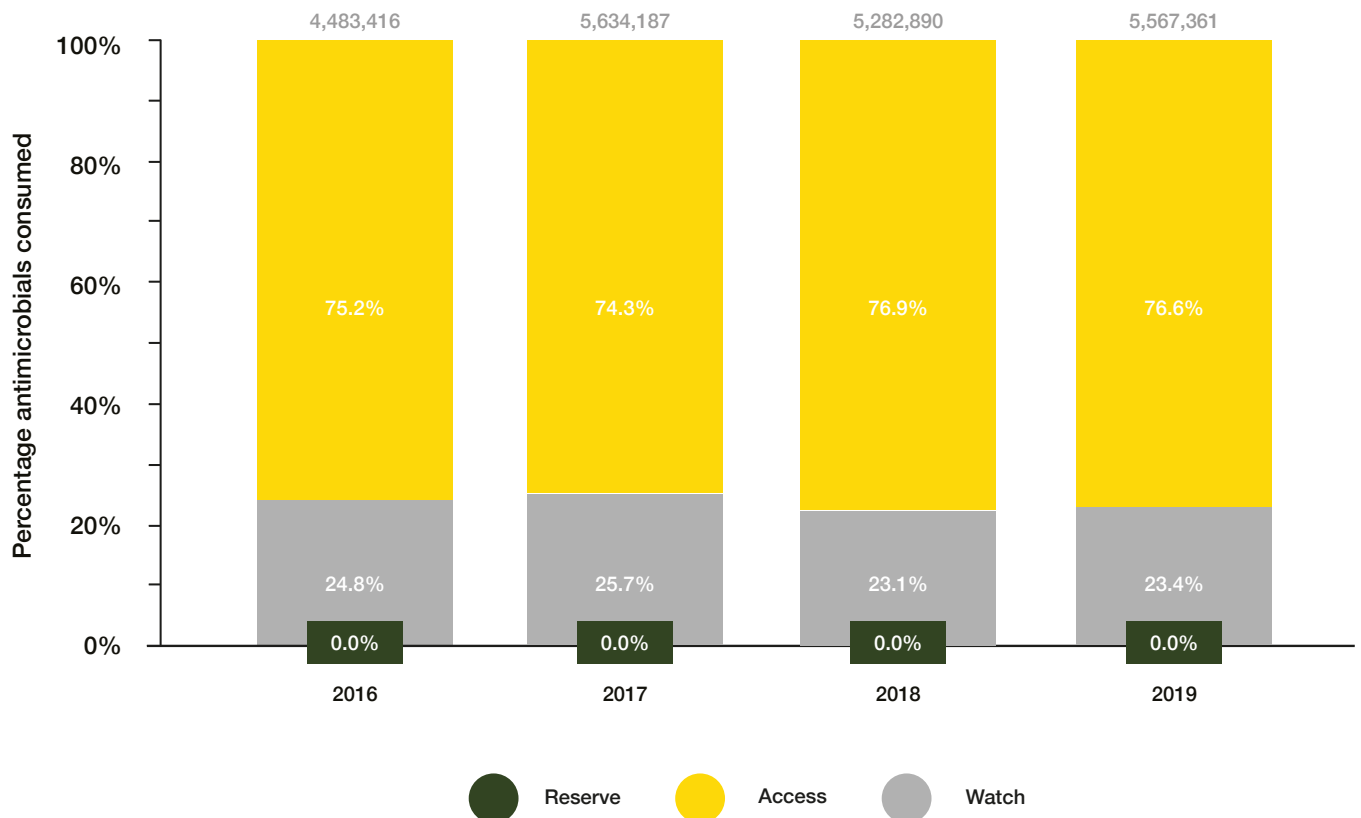


Figure 20: Consumption of WHO AWaRe category antibiotics from 26 selected pharmacies in Ghana for the years 2016 to 2019

Further analysis was done to identify the most frequently consumed antibiotics within the sampled pharmacies, within each WHO AWaRe category (Figure 21). The top five consumed antibiotics in the 'Access' category accounted for 84.8% of the category's consumption, while the top five antibiotics in the 'Watch' category accounted for 93.4% of the category's consumption.

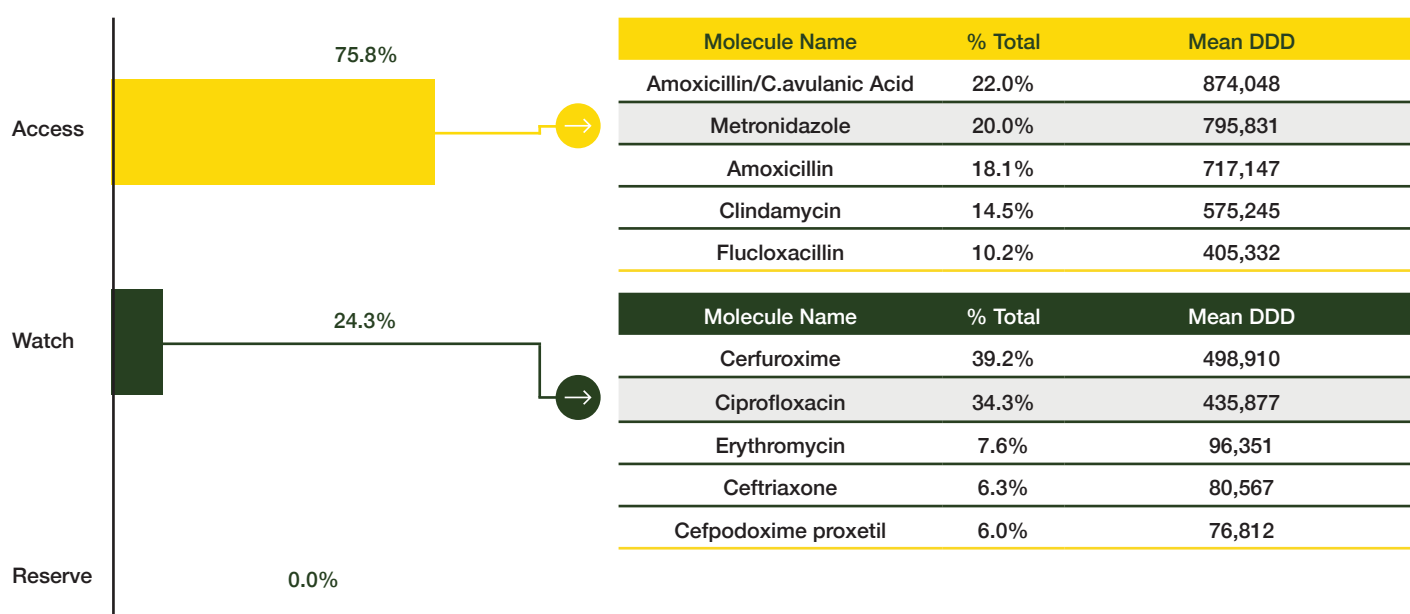


Figure 21: The top five most consumed 'Access', 'Watch' and 'Reserve' antibiotics from 26 selected pharmacies in Ghana for the years 2016 to 2019

Within the WHO AWaRe database exists a list of 'antibiotics not recommended'. This group of antibiotics consists of FDC of multiple broad-spectrum antibiotics that are neither evidence-based nor recommended by international guidelines. As a result, the WHO does not recommend their use in clinical practice. These antibiotics are represented as 'uncategorised' by MAAP and excluded from the WHO AWaRe analysis results above. Analysis of the pharmacy AMC data was made to identify their consumption in the country. Consumption of (n=5) of these antibiotics was observed (representing 0.7% consumption of total pharmacy AMC) and is listed in Table 12 below. Among them, the FDC of ciprofloxacin/tinidazole was the most frequently consumed (accounting for 88.6% of the total consumption of the listed FDC antibiotics), with a mean DDD of 33 056. This FDC antibiotic was also found to be the 15th most frequently consumed antimicrobial for the pharmacy-level dataset analysed.

Table 12: Consumption ranking* of WHO AWaRe uncategorised antimicrobials from 26 selected pharmacies in Ghana for the years 2016 to 2019

AMC rank*	Molecule
15	Ciprofloxacin/Tinidazole
23	Amoxicillin/Flucloxacillin
27	Ampicillin/Cloxacillin
29	Ceftriaxone/Sulbactam
34	Norfloxacin/Tinidazole

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

The pharmacy-level data from the (n=26) participating pharmacies were disaggregated and examined by the type of pharmacy (community against hospital), the service level of the hospitals (secondary care against tertiary care and private versus public) and proportional consumption of the WHO AWaRe category antibiotics (Table 13). Both hospital and community pharmacies, on average, met the WHO threshold of 60% consumption of antibiotics represented within the 'Access' category at 75.4% and 84.5%, respectively. Hospital pharmacies consumed, on average, 9.1% more 'Watch' category antibiotics compared to community pharmacies (hospital pharmacies consumption: 24.6%; community pharmacies: 15.5%). Also, within the hospital pharmacies, the private faith-based hospital pharmacies consumed only 2.1% more 'Watch' category antibiotics compared to the public hospital pharmacies. Within the public hospital pharmacies, the tertiary care hospital pharmacies consumed 10.8% more 'Watch' category antibiotics compared to the secondary care hospital pharmacies. A closer look at the pharmacies found that while 100% of the hospital pharmacies met the WHO 'Access' threshold, 40% (n=6) of the community pharmacies failed to meet the WHO 'Access' threshold.

Table 13: Hospital and community pharmacies' consumption of WHO AWaRe category antibiotics from 26 selected pharmacies in Ghana for the years 2016 to 2019

Pharmacy Type	AWaRe Categorisation	
	Access	Watch
Percentage share (Absolute DDD)		
Hospital pharmacies (11/26)	75.4% (15.2 million)	24.6% (4.9 million)
Public hospital pharmacies (8/11)	76.2% (11.3 million)	23.8% (3.5 million)
Secondary care hospitals (4/8)	80.9% (6.8 million)	19.1% (1.6 million)
Tertiary care hospital (4/8)	70.1% (4.5 million)	29.9% (1.9 million)
Private hospital pharmacy (3/11)	73.3% (3.9 million)	26.7% (1.4 million)
Community pharmacies (15/26)	84.5% (595 336)	15.5% (108, 853)
Grand Total	75.8% (15.8 million)	24.3% (5.0 million)

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

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

It was found that two antibiotics in the 'Watch' category are listed in the WHO EML and documented during data collection, yet they are not part of the Ghana EML. In addition, four 'Access', one 'Watch', and eight 'Reserve' category antibiotics are part of the WHO EML, yet they are not listed in the Ghana EML nor documented during data collection. Interestingly, two 'Access' category antibiotics and one 'Watch' category antibiotic is listed in the WHO EML and the Ghana EML but were not documented during data collection. There were two 'Access' category antibiotics and three 'Watch' antibiotics that were listed in the Ghana EML and documented during data collection but not listed in the WHO EML. Within the 'Watch' category and the uncategorized antibiotics were documented during data collection, which included in the WHO or Ghana EMLs. The detailed breakdown of antibiotics documented and their inclusion in the WHO EML and Ghana EML is provided in AMC Appendix 9.

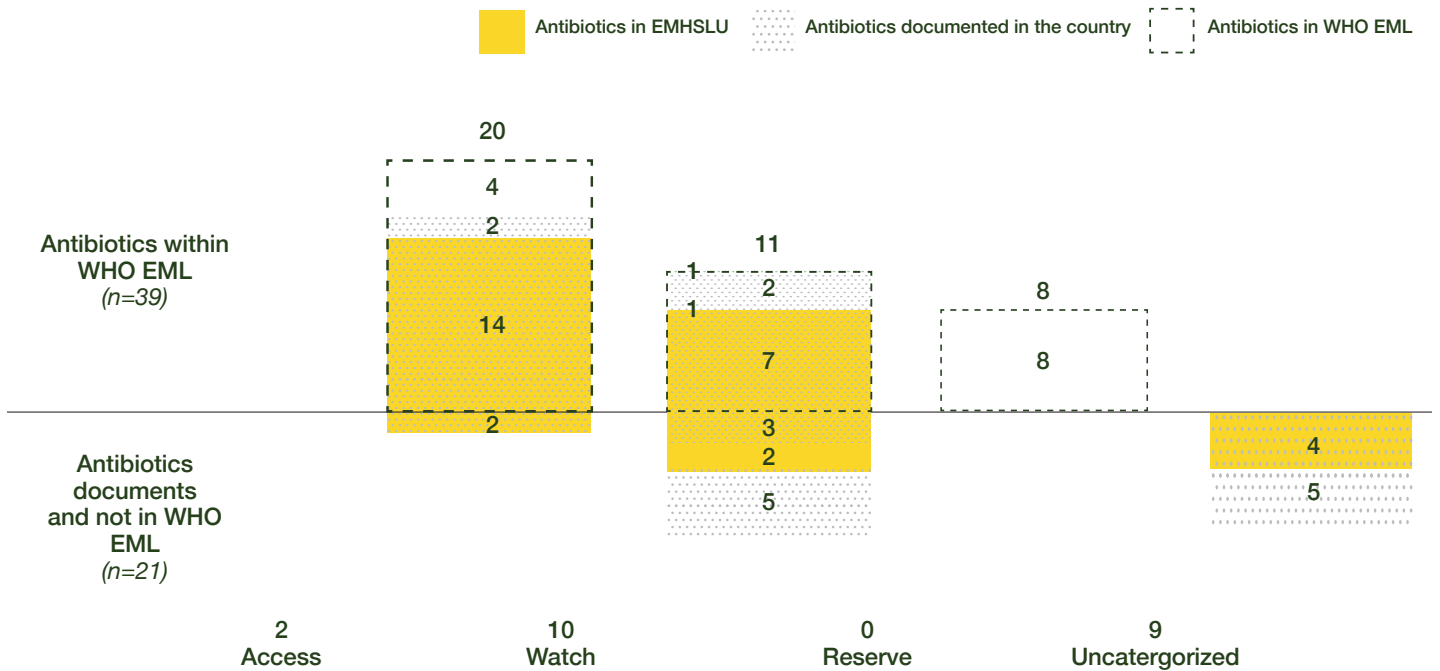
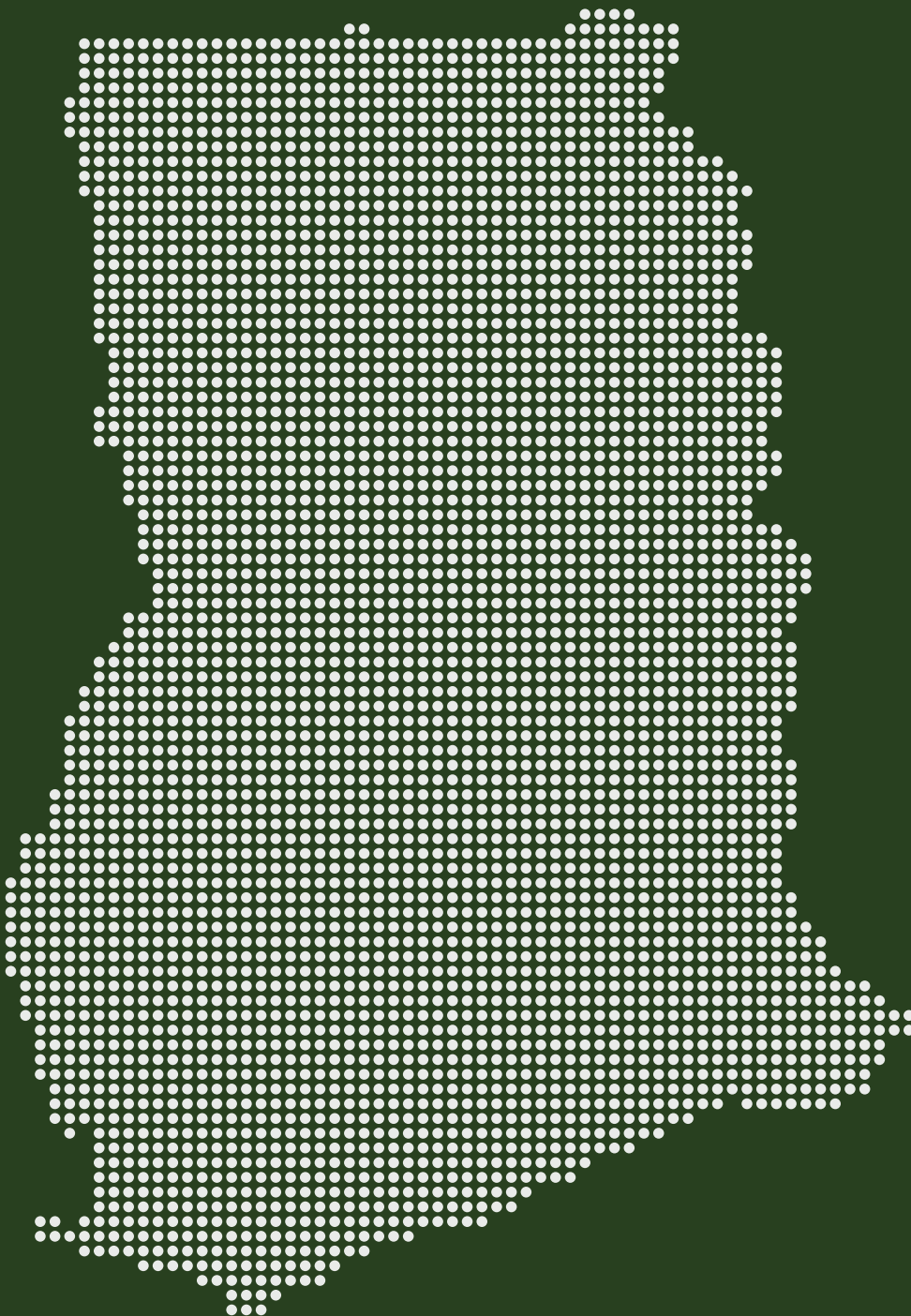


Figure 22: AWaRe analysis of documented antibiotics at the pharmacy level for the years 2016 to 2019 compared to the WHO- and Ghana EML definitions. *Data represented is based on aggregated facility data only; National data could not be retrieved and analysed for Ghana

Part C: Resistance and Consumption Interlinkages



Objective

To assess the relationship between antimicrobial consumption and antimicrobial resistance.

Methodology

The DRI was estimated to convey aggregate rates of resistance as well as measurements of AMC (at a national level since AMU data was not available) across select pathogen-antimicrobial combinations (Pathogens - *A. baumannii*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *E. faecium* and *E. faecalis*; Antibiotics - aminoglycosides, broad-spectrum penicillins, carbapenems, cephalosporins, glycopeptides, narrow-spectrum penicillins and quinolones). The DRI estimates were generated using a previously published methodology^{35,36} (AMR Appendix 8) and communicated the effectiveness of antibiotic therapy to decision-makers. The DRI values range from 0 (100% susceptibility) to 100 (100% resistance). Available AST results for at least 30 tested isolates and for at least 15 of the 25 combinations were prerequisites for estimating the DRI. The variance of the proportions of non-susceptible isolates was combined with a uniform standard deviation based on the estimated DDD to generate CIs for the DRI as the variance of the product of variables.^{37,38}

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

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

Results

Drug Resistance Index

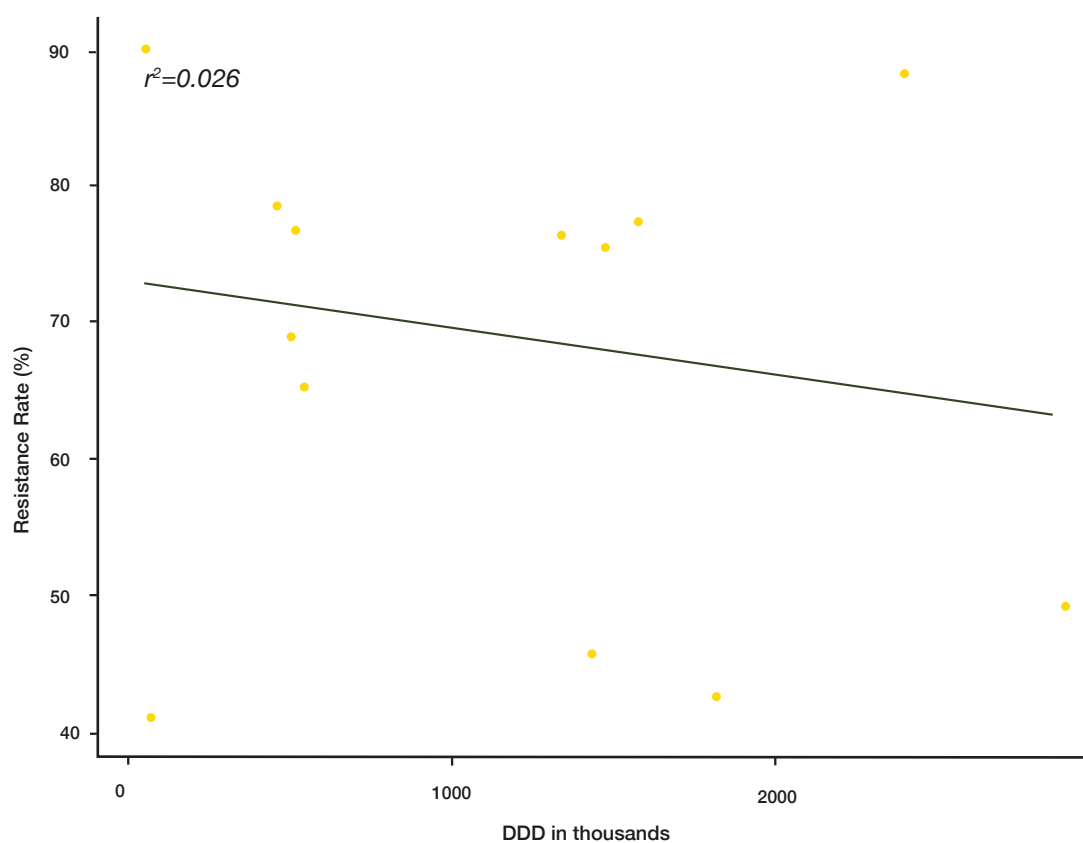
Available AST data were insufficient to estimate DRI; there were data for 11 of the 25 bug-drug combinations.

AMC and AMR correlation

The top three highly consumed antibiotic classes at the facility level were beta-lactam combinations, aminopenicillins, and lincosamides. The AMR rates were highest for penicillins (92.0%), aminopenicillins (90.0%), and tetracyclines (80.1%) (Table 14). Pearson's correlation analysis revealed a weak negative correlation ($r^2=0.03$) between AMR and AMC, implying that antibiotic consumption is not a significant driver of AMR in Ghana (Figure 23).

Table 14: AMC and AMR rates across antibiotic classes

Antibiotic class	Year	Total DDD in thousands	Resistance rate (%)
Beta-lactam combinations	2016-18	2 587.30	49.5
Aminopenicillins	2016-18	2 154.13	90.0
Lincosamides	2016-18	1 647.59	42.5
Cephalosporins (2nd generation)	2016-18	1 432.94	78.8
Methicillin	2016-18	1 339.90	76.9
Fluoroquinolones	2016-18	1 311.71	45.7
Folate pathway inhibitors	2016-18	1 228.38	77.8
Macrolides	2016-18	532.08	66.3
Cephalosporins (3rd generation)	2016-18	503.03	78.1
Tetracyclines	2016-18	456.83	80.1
Aminoglycosides	2016-18	110.35	40.9
Penicillins	2016-18	99.39	92.0



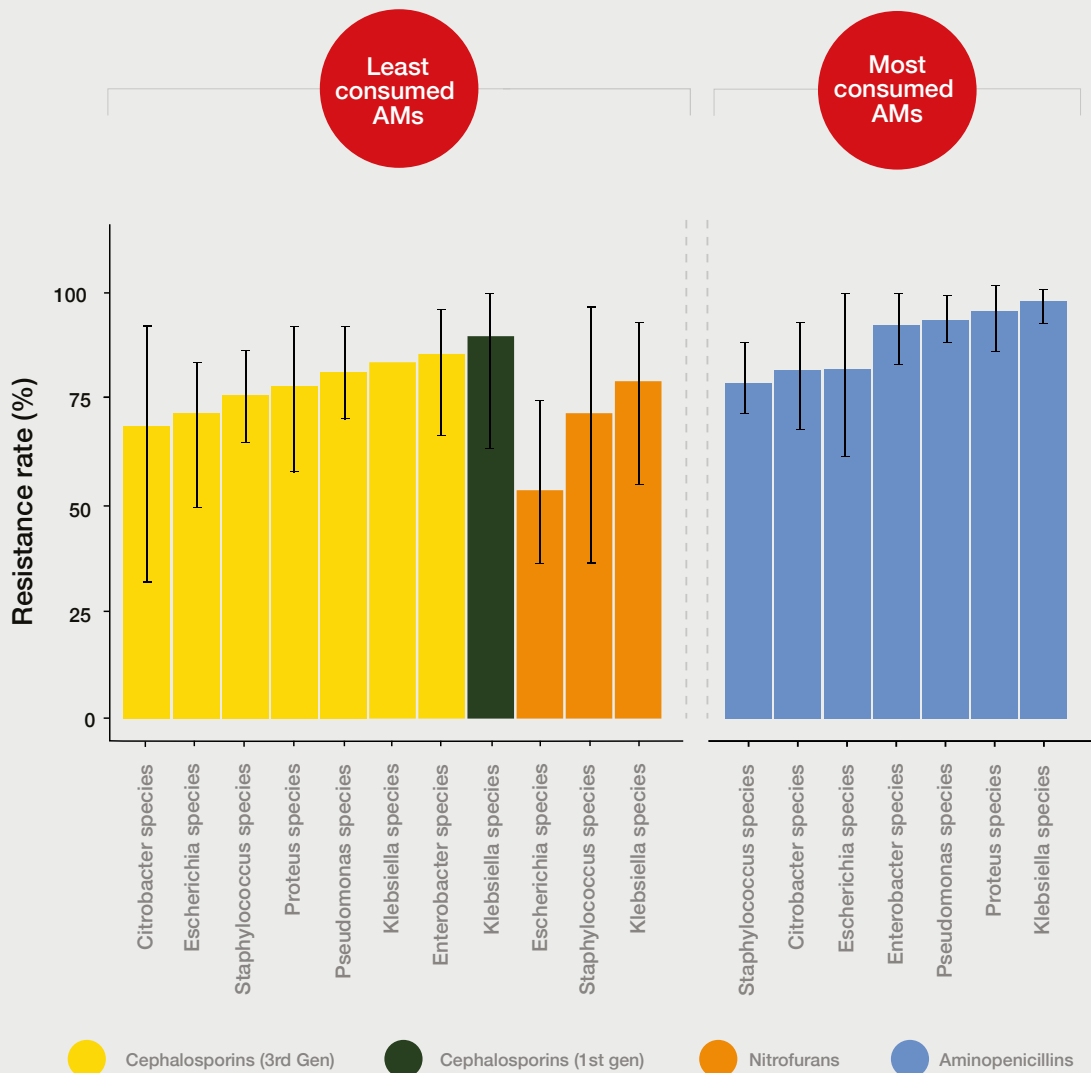
DDD=defined daily dose

Figure 23: Correlation between AMR and AMC

Resistance profiles of most and least consumed antimicrobial classes

The most consumed antimicrobial classes across the study years were aminopenicillins-beta-lactam combinations, aminopenicillins, and lincosamides. In 2016, resistance rates were more than 75% for aminopenicillin-resistant *Klebsiella* species, *Proteus* species, *Pseudomonas* species, *Enterobacter* species, *Escherichia* species, *Citrobacter* species, and *Staphylococcus* species. In 2017, there were high rates (>75%) of beta-lactam-resistant *Staphylococcus* species and *Klebsiella* species, aminopenicillin-resistant *Escherichia* species, *Proteus* species, *Enterobacter* species, *Pseudomonas* species, *Citrobacter* species, *Klebsiella* species, and *Staphylococcus* species. In 2018, the highest rates (>80%) of aminopenicillin-resistant *Enterobacter* species, *Klebsiella* species, *Pseudomonas* species, *Citrobacter* species, *Proteus* species, *Escherichia* species, *Streptococcus* species, and *Staphylococcus* species were noted (Figures 24, 25, and 26).

The least consumed antimicrobial classes across the study years were third-generation cephalosporins, carbapenems, nitrofurans and first-generation cephalosporins. Though the consumption of these antimicrobial classes was low, there were high resistance rates across many pathogen-antimicrobial class combinations. In 2016, there was more than 75% cephalosporin (3rd generation resistant)-*Enterobacter* species, *Klebsiella* species, and *Pseudomonas* species, and cephalosporin (1st generation)-resistant *Klebsiella* species. In 2017, more than 75% of *Pseudomonas* species, *Staphylococcus* species, *Enterobacter* species, *Klebsiella* species, and *Citrobacter* species were cephalosporin (3rd generation resistant)-resistant. In 2018, there was >75% for cephalosporin (3rd generation) resistance in *Enterococcus* species, *Staphylococcus* species, *Klebsiella* species, *Pseudomonas* species, *Citrobacter* species, and *Enterobacter* species (Figures 24, 25, and 26).

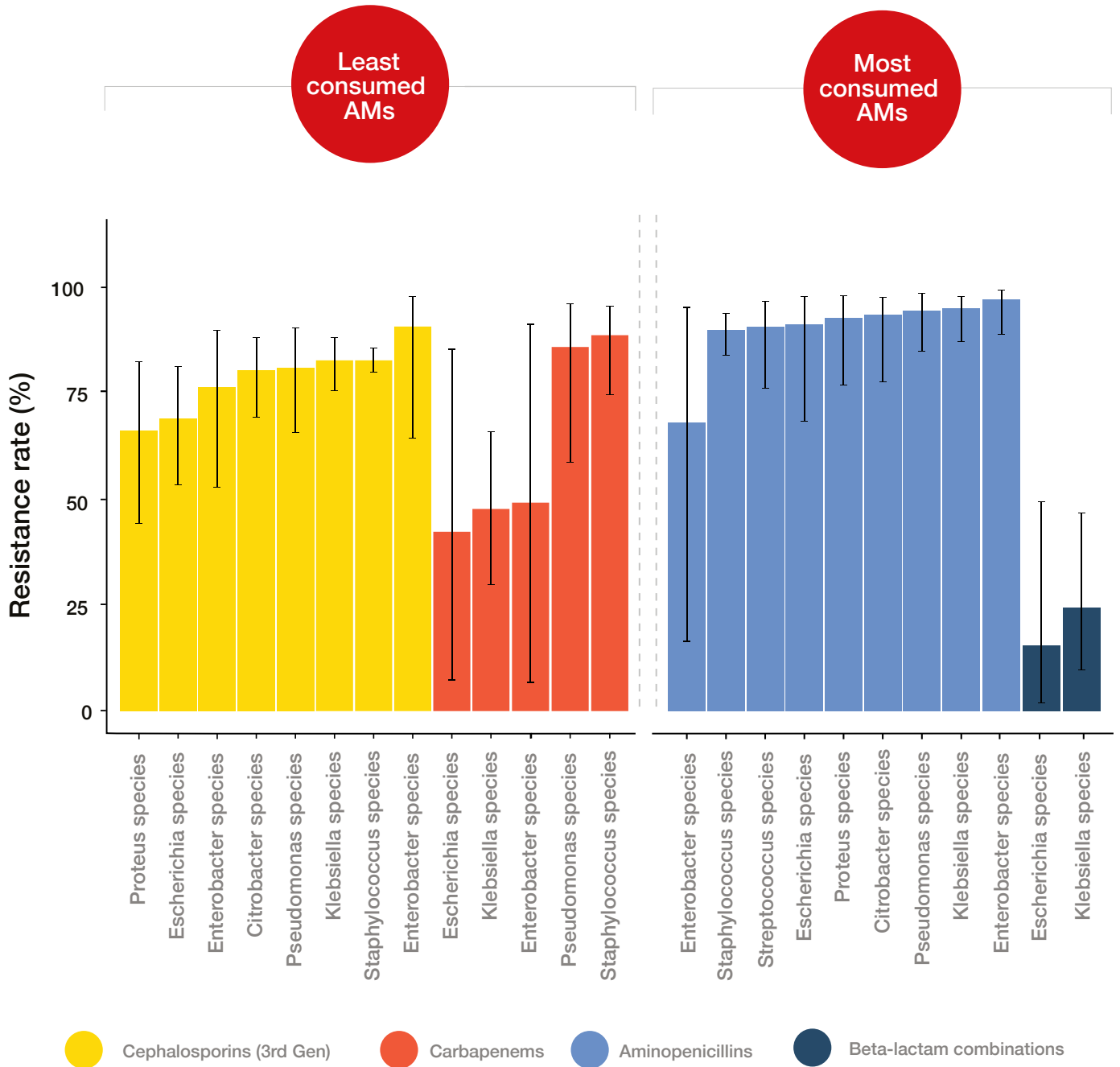


AMs=antimicrobial class; 3rd gen.=Third generation

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



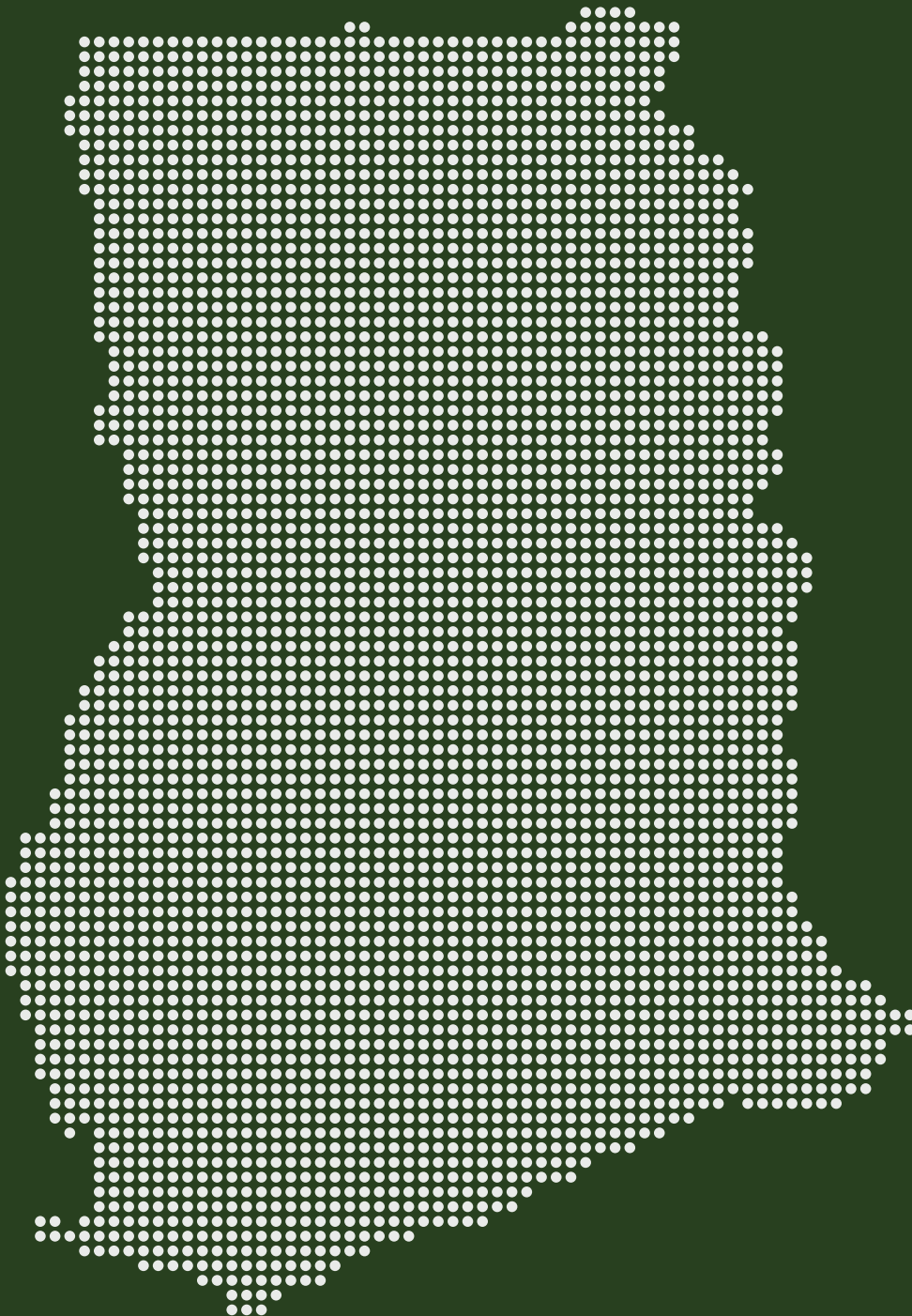
AMs=antimicrobial class; 3rd gen.=Third generation
 Figure 25: AMR rates for the least (left) and most (right) consumed antimicrobial classes in Ghana in 2017



AMs=antimicrobial class; 3rd gen.=Third generation

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

Part D: Recommendations



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

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

Significance of AMR and DRI data and recommendations

Analysis of available AMR data from Ghana revealed very high rates of carbapenem-resistant Enterobacterales (over 90%) in 2016 and 2017. High rates of third-generation cephalosporin-resistant Enterobacterales (72-78%) and methicillin-resistant MRSA (74-85%) were noted.

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

S. 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, trauma, use of an invasive device (catheters, shunts, implants, prosthesis), prior-antibiotic use, neutropenia, post-surgical status, dialysis, and admission to long-term care facilities. While antimicrobial therapy and source control (drainage or catheter removal) are essential treatment modalities, preventing and controlling the spread of MRSA infections is also important. The use of catheters and invasive devices must be minimised, and stewardship principles should be practised, including taking culture specimens before using antibiotics and prompt de-escalation from empirical to targeted therapy based on AST results. 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.

We noted that males and the elderly were more prone to resistant infections, though further studies will be needed to establish the connection.

Service delivery

The laboratory network in Ghana consisted of 4 841 laboratories, of which only 93 were identified as bacteriological laboratories, and 64 confirmed their AST capabilities. While most of the surveyed laboratories reported implementing QMS, not all were certified or accredited. The laboratories did not equitably cover the country's population of over 31.1 million. The testing load (quantum of cultures) at most participating laboratories was found to be less and suggested a lack of routine microbiology testing. There is a likelihood that the AMR rates are overestimated as the majority of tests would have been conducted on special patient categories (such as those unresponsive to first-line therapy or admitted to the intensive care unit).

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

Health workforce

All of the surveyed laboratories had an experienced laboratory scientist or technologist, with 66% of the laboratories having at least one qualified microbiologist. Only 50% had up-to-date records on training and competence. For high-quality microbiology testing and reporting, staff training on laboratory standards, the ability to identify common pathogens, and data management skills are essential.⁴⁰ Capacity building of staff may be done through in-house expertise or outsourced to external organisations or tertiary facilities.

Information systems

The Regional Grant was a step towards collecting and digitising data. We noted that most of the surveyed laboratories relied on paper-based records, and very few linked patients' clinical records. In the current study involving 16 laboratories over a four-year period, susceptibility results could be collected for just 4 394 positive cultures.

In order to strengthen AMR surveillance, it is essential to curate the right data and generate evidence. We recommend the use of standardised data collection formats at all levels (laboratories, clinics and pharmacies) and automated data analyses. For the current study, we used WHONET for data digitisation. Empirical guidelines for the management of infectious diseases should be based on the specific epidemiology of the patient's setting, and resistance data should be shared with national and supra-national platforms. We also recommend establishing a system of assigning permanent identification numbers for tracking patients over time. Permanent identification numbers would help to collect and link patients' clinical profiles to antimicrobial history, as well as the pathogen's molecular profile (where available), thus offering more context to the AMR epidemiology than stand-alone AST 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. Strengthening AMR surveillance requires generating reliable laboratory results using appropriate or surrogate testing methods and ensuring uninterrupted availability of reagents, including AST reagents. Improving supply chains for essential reagents should be a country priority, and interruptions in routine testing must be minimal. Standardising testing methods across laboratories allows pooled purchases 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 community awareness of the importance of public health interventions (vaccinations, clean water, sanitation, hand hygiene) and compliance with physicians' advice. The strengthening of health and laboratory systems must be prioritised at the national level and complemented with the right investment.

Significance of AMC and AMU data including recommendations

This section discusses the significance of our AMC and AMU findings and puts forth suggested recommendations for Ghana to better facilitate future surveillance and AMS activities.

Feasibility of obtaining AMC and AMU data in Ghana and recommendations

The MAAP successfully collected and analysed pharmacy-level AMC data for Ghana for the years reviewed, 2016 to 2019. The MAAP was unable to analyse national-level AMC data due to incomplete package content data provided by the Ghana FDA. The incomplete data could not be used to calculate the national antimicrobial consumption rate. A comprehensive national guiding policy for routine AMC data surveillance is required to ensure that Ghana reports data to the GLASS, which now has an AMC reporting component. This policy should set the minimum reportable AMC data variables (including explicit details on required package content information) and routine data cleaning and reporting practices. The policy will further serve as a guide to inform agencies supplying AMC data on the minimum required surveillance data and quality. Furthermore, antimicrobial importation and local manufacturing data assume that all antimicrobials will be consumed locally, and it does not account for expiries or losses. Therefore, obtaining national AMC data from sources close to the end user will increase the accuracy of the national AMC estimate. Efforts should be made by relevant regulatory authorities to identify and recruit medicine wholesalers or distributors and large-volume health facilities to serve as sub-national points for AMC surveillance instead of using a single national AMC data source, FDA. Such a decentralised approach would also allow the examination of AMC trends within the private/public sector and end-user institutions levels (i.e., primary, secondary, and tertiary levels). Pharmacy-level AMC data from the hospitals were collected manually and electronically. To make future AMC surveillance more time- and cost-efficient, hospitals should switch to electronic information systems and ensure such systems have capabilities to transfer data across departments and produce user-friendly AMC reports.

The MAAP was unable to obtain AMU data in Ghana, which would have identified the purpose and appropriateness of prescription and rate consumption per country guidelines.⁴¹ This inability to lack AMU data from participating pharmacies co-located within health facilities with AST laboratories was because the AMC data sources (i.e., stock record card at the pharmacy) did not link dispensed antimicrobials to individual patients as prescription chits were not archived. Hence it was not possible to retrospectively retrieve the relevant clinical and laboratory files for any patients who received antimicrobials. Nevertheless, a few studies which reported AMU data in Ghana have been documented,²⁷⁻²⁹ where AMU data was collected through the use of the global point prevalence survey methodology.³¹ Nonetheless, the success of these AMU studies implies that retrieval of AMU data, where sub-optimal data systems exist, can only be achieved through the set-up of prospective studies, for which collection procedures are intentionally set up to assess the patient data in real-time through the cascade of care.

Retrospective AMU data studies, such as this MAAP study, may not be ideal. Therefore, future AMU surveillance attempts in Ghana should involve prospective data collection on a larger scale that is representative of the country's antimicrobial use.³⁴ However, the proposed approach is time-demanding, unlike retrospective data collection and often requires engaging trained data collection teams for prolonged durations. Thus, the prospective approach is expensive and challenging to undertake in resource-limited settings. Retrospective AMU data collection remains an option if facilities targeted for data collection are selected based on the existence of electronic patient records and the presence of cross-department unique patient identifiers.

Overview of AMC consumption trends and recommendations

The pharmacy-level AMC trends are a useful benchmark for future consumption trends comparison after implementing AMP in the country. Unfortunately, the MAAP could not estimate the total national AMC levels in Ghana due to the missing product packaging information during data validation, which prevented the analysis of the national-level datasets received from the FDA. Despite the absence of nationally representative AMC data, this report provides useful insights into AMC trends based on antimicrobial consumption trends of the sampled pharmacies in Ghana. Our analysis indicated that there were some variations in the consumption of antimicrobials across the four reviewed years. However, not much insight can be drawn from total AMC consumption in DDDs as the MAAP was unable to normalise the data per facility catchment population as this data was unavailable for community pharmacies. Therefore, this section focuses on the relative comparison of consumption within pharmacies as per WHO AWaRe proportion analysis.

Evaluation of antibiotics relative consumption according to the WHO AWaRe categories showed that the proportion of narrow-spectrum antibiotics in the 'Access' category exceeded the minimum WHO recommended consumption threshold.³⁴ This finding is commendable as it implies that any emerging AMR trends due to misuse or overuse will likely be restricted to narrow-spectrum antibiotics, sparing the lesser-used broader-spectrum antibiotics in the 'Watch' and 'Reserve' categories. Several exciting trends were also observed when antimicrobial consumption was examined based on the type of pharmacy. First, the consumption of 'Access' category antibiotics within the community pharmacies was higher than that of the hospital pharmacies, while within the hospital pharmacies, the public hospitals' consumption was comparable to that of the private, faith-based hospitals. This consumption trend implies that the Ghana EML antibiotics, which comprise mostly of 'Access' antibiotics, are widely available in public and private-not-for-profit and for-profit community pharmacies.⁴² Also, it further implies that the private primary physician care sector (using community pharmacies' consumption data) also relies on the use of 'Access' category antibiotics, which is commendable.

Within the public hospital pharmacies, the tertiary care hospital pharmacies consumed more 'Watch' category antibiotics compared to the secondary care hospital pharmacies. Higher consumption of 'Watch' category antibiotics at the tertiary care hospital pharmacies could be because these facilities deal with complex infection cases requiring treatment regimens using second and third-line antimicrobials. Finally, no 'Reserve' antibiotics were consumed in the four years reviewed. This absence of 'Reserve' antibiotics consumption within the sampled pharmacies could mean the absence of these antibiotics within the country's EML and Standard Treatment Guidelines (STG) rather than a regulation of their consumption. Therefore, MAAP recommends an urgent review of the country's EML by the AMRCC to include these 'Reserve' agents for treating complex infectious diseases.

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 each category. Such a consumption pattern is sub-optimal and selective for evolutionary resistance against these most consumed antibiotics.⁴³ This narrow consumption of antibiotics within the 'Access' and 'Watch' categories of antibiotics can also make the facilities and the country (if this trend is mirrored country-wide) susceptible to stockouts of these most consumed antimicrobials if manufacturing and supply chain issues are encountered. Therefore, it is recommended that the country's ASP explores ways to encourage a wider spread in the consumption of antibiotics within each WHO AWaRe category. This could include offering incentives for importing and distributing other antibiotics in the WHO categories, in line with the country's EML, to avoid such a limited spectrum of consumed antibiotics.

WHO also provides guidance on antibiotics that are 'not recommended' in clinical practice due to their multiple broad-spectrum activities and no clinical evidence advocating for their use.³⁴ In Ghana, the use of five such FDCs of antibiotics 'not recommended' by WHO was observed. Of these combinations, the use of FDC of ciprofloxacin/tinidazole was most prevalent. Therefore, the AMRCC should identify the reasons and hotspots for prescribing or dispensing the identified FDC antibiotics listed. This information will guide targeted prescribers' sensitisation by the country's MoH and associated medicine regulatory bodies (e.g., FDA).

Data generated from AMC and AMU surveillance trends can provide unique insights for national stewardship programmes and for the formulation of policies to stem the emergence of AMR. Ghana 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 from the sampled pharmacies. Yet, only five antibiotics make up for 64% of the consumption which indicates the opportunity for more diversification. Table 15 describes the next steps for AMC and AMU surveillance.

Table 15: Next steps for AMC and AMU surveillance

Leadership and Governance

The country will require to develop an AMC surveillance policy and address by whom, how and when national AMC datasets should be reported. The AMRCC could lead this activity.

- Such a policy should guide the minimum required reporting variables, data quality appraisals, data analysis and reporting pathways to the ministry and GLASS system. This policy will ensure a continuous stream of localised AMC data beyond MAAP that will help inform/assess future policy decisions by the national ASP
- Lessons learned from the ongoing Fleming Fund Country Grants, and the MoH surveillance programs could be considered in the policy’s development.

The regulatory authority, the Ghana National Regulatory Authority, could reconsider the registration status of unapproved FDC antibiotics.

The national stewardship programs, led by the AMRCC, could work to review the national treatment guidelines, and review the Ghana EML to include essential ‘Reserve’ category antibiotics, if deemed necessary for complex case management.

A.

Service Delivery

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

National ASP led by the AMRCC could conduct educational campaigns for healthcare practitioners to ensure they know the full spectrum of antimicrobials available in the Ghana EML.

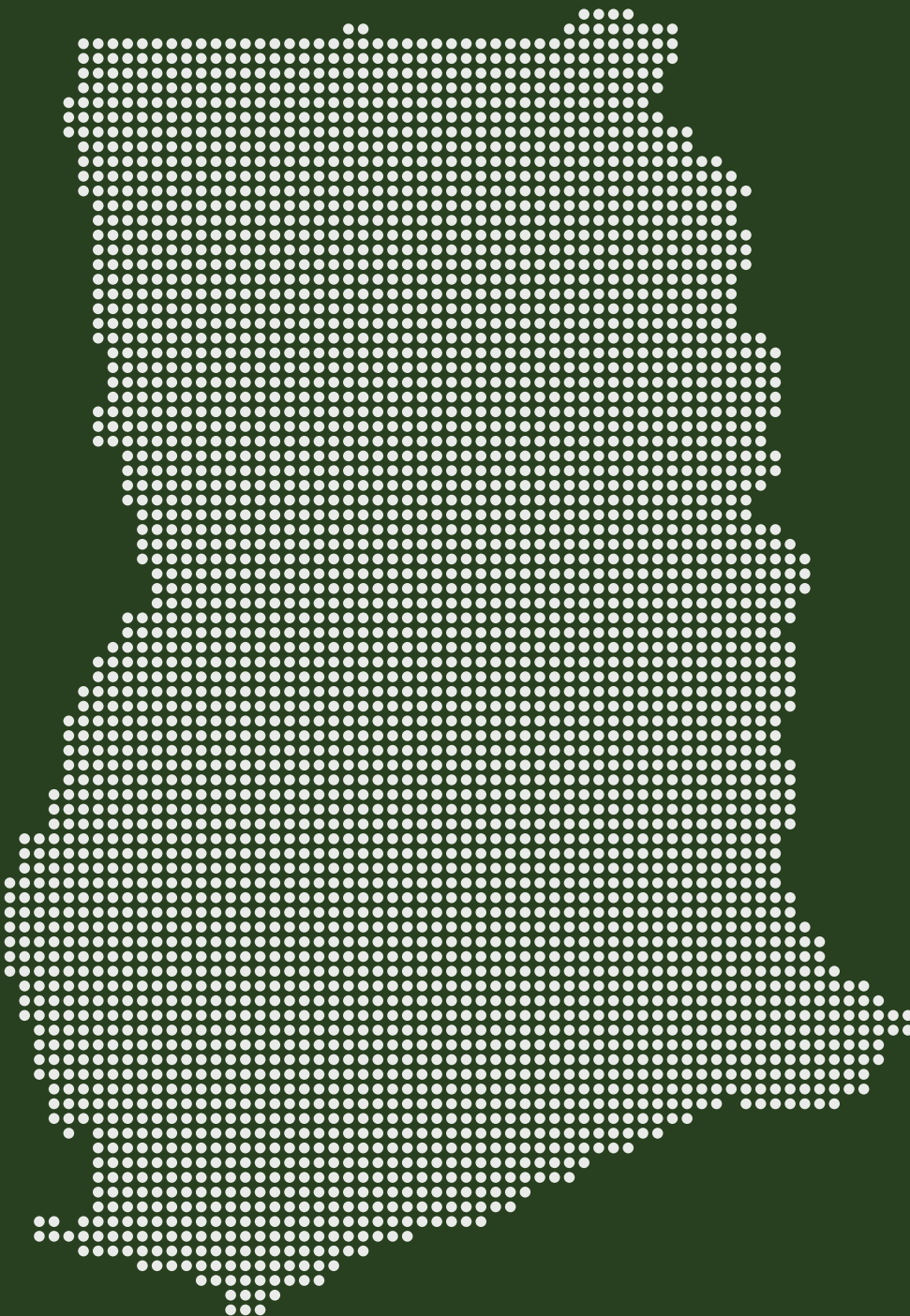
B.

Medical products and technologies

The National Stewardship programs should collaborate with to collaborate with pharmacists and medicine importers to increase the availability of more varieties of antibiotics available as per the reviewed Ghana EML, including that will include the availability of WHO ‘Reserve’ category antibiotics.

C.

Part E: Limitations



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

1.

It was often difficult to obtain patients' hospital identifiers from laboratory records, thus impacting demographic and clinical information collected from medical archives. There were instances where patient identifiers could be matched in hospitals using paper-based records; however, this required manual retrieval that was often compounded illegible and or incomplete demographics and clinical information.

2.

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

3.

The participating laboratories, 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 31.1 million). Furthermore, as routine testing does not appear to be the norm in most hospitals and laboratories, the data may overestimate the resistance rates as infections that fail therapy may be more likely to be tested.

4.

Clinical data and antimicrobial usage information were insufficient to provide a robust analysis of drivers of resistance.

5.

National AMC records from FDA were intended to be used as a proxy for consumed national AMC levels. However, the data received from FDA had several key information gaps that were crucial for analysis. These gaps included the lack of quantity standards (e.g., quantities recorded as cartons instead of numbers of tablets). Therefore, due to these information gaps, it was impossible to run a national AMC analysis on these datasets.

6.

The MAAP further purposed to collect data from selected pharmacies in Ghana which subsequently enabled AMC data analysis despite the absence of national-level data. Though the 26 included pharmacies were purposively selected for data collection, this sample size was a relatively small proportion of all the pharmacies in Ghana and did not represent all regions. Therefore, this data does not truly represent Ghana's national consumption.

7.

The MAAP could not obtain AMU data from the participating pharmacies co-located with AST laboratories. Therefore, an understanding of how and why antimicrobials are prescribed as well as dispensed (i.e., appropriateness of prescriptions and antimicrobials consumed) was not achieved. Nevertheless, this information is important as it would help better inform the country where they would focus their stewardship programs.

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Glossary

Accreditation:

According to National Accreditation Board for Testing and Calibration Laboratories, accreditation is a procedure by which an authoritative body formally recognises technical competence for specific tests/ 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 difficult to treat and increasing the risk of disease spread, severe illness and death. Drug resistance makes antibiotics and other antimicrobial medicines ineffective, making infections increasingly difficult or impossible to treat.

Antimicrobial resistance rate:

It is the extent to which a pathogen is resistant to a particular antimicrobial agent or class, determined by the proportion of non-susceptible isolates (i.e., either intermediate or resistant) over a 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 a particular bacteria or fungus is sensitive to and to what extent.

Antimicrobial susceptibility testing standards:

A number of internationally recognised agencies produce standards to be followed by laboratories while performing antimicrobial susceptibility testing, such as the 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. First, each laboratory was assigned a data score based on the level of pathogen identification. Scoring was based on quartiles of the proportion of completely identified pathogens, laboratories with >75% of pathogens identified at the species level were awarded the highest score (4), and those with <25% identification received the lowest score (1). Scoring was performed per year, and then the average of all years was assigned as the laboratory data quality score for each laboratory. Secondly, the country data quality score was computed, which weights the laboratory data quality score with the quantum of valid cultures contributed by each laboratory. The maximum country data quality score was 4

Eligibility questionnaire:

A questionnaire to be answered by laboratories in the country's laboratory network. It comprised questions on site, 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, 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/preparedness for AMR surveillance.

Laboratory readiness score:

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

MAAP:

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

Positive cultures:

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

Positive cultures with AST:

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

Proficiency testing:

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

Quality Certification:

Certification is used to verify that laboratory personnel have adequate credentials to practice certain disciplines and that products meet certain requirements.

Quality Management Systems:

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

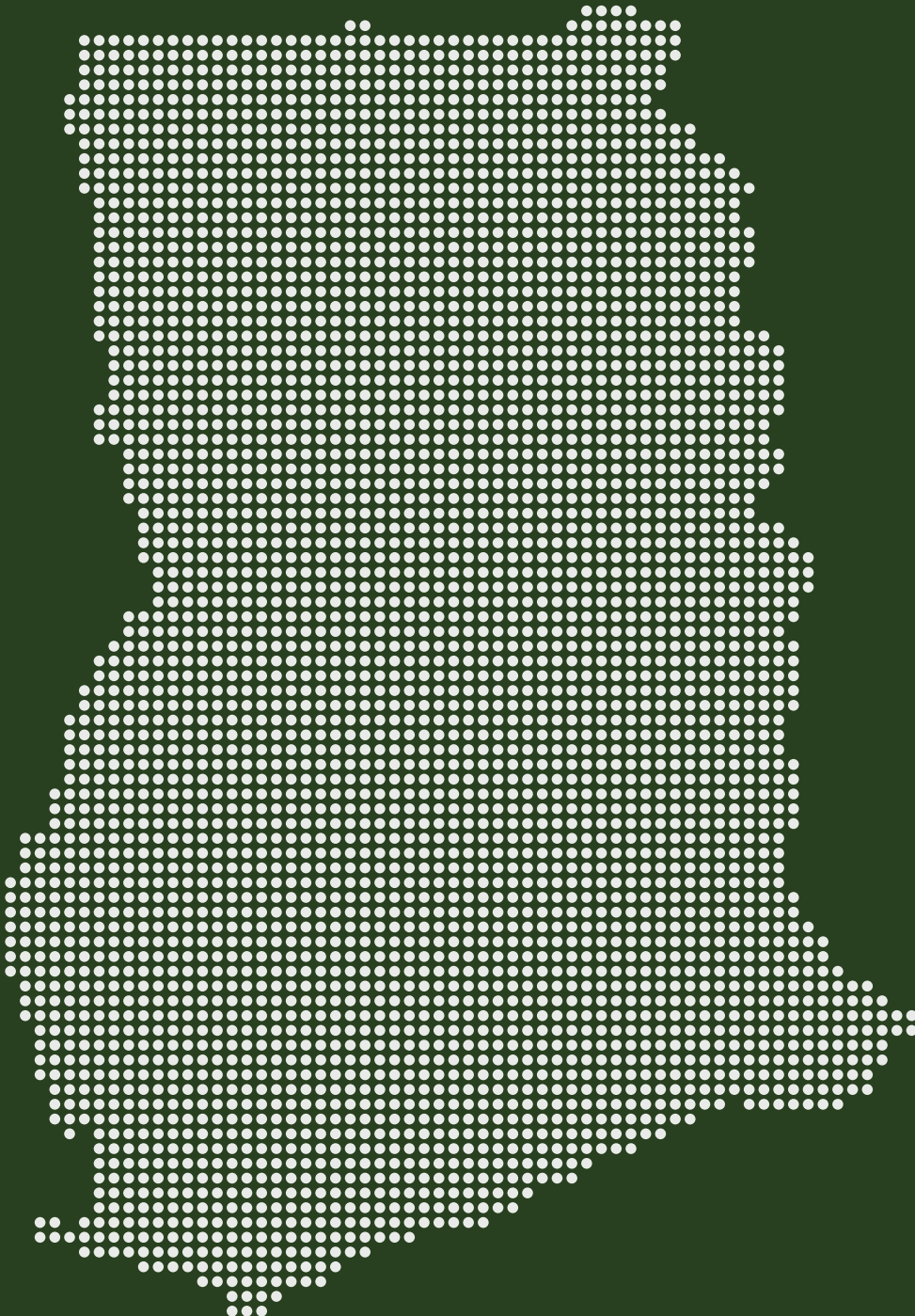
Total cultures:

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

Valid cultures:

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

AMR Appendices and Supplementary Data




Appendix 1: Terms of Reference and Data Sharing Agreements

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the number and date of this Letter should be quoted.

My Ref. GHS/RDD/ERC/Admin/App 1459
Your Ref. No.

Dr. Martha Gyansa-Lutterodt
Ministry of Health
Accra, Ghana



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Email: ethics.research@ghsmai.org
3rd December, 2020

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	GHS-ERC 001/11/20
Project Title	Mapping Antimicrobial Resistance and Antimicrobial Use Partnership (MAAP)
Approval Date	3 rd December, 2020
Expiry Date	2 nd December, 2021
GHS-ERC Decision	Approved

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report after completion of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.
- Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....*Bannerman*.....
Dr. Cynthia Bannerman
(GHS ERC Chairperson)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

Appendix 2: Laboratory Eligibility Questionnaire

Question	Response			
Part 1: Site Information				
1.1	What is the name of the laboratory?			
1.2	Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing?	Yes	No	
1.3	Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium?	Yes	No	
1.4	What is the address of the laboratory?			
1.5	What is the laboratory's level of service?			
	Reference- tier 3 or 4	Regional/Intermediate	District or community	Other
1.6	What is the laboratory's affiliation?			
	Government/Ministry of Health	Private	Non-government organisation	Other
1.7	Is the laboratory co-located in a clinical facility?	Yes	No	
1.8	Is a pharmacy co-located with the laboratory?	Yes	No	
1.9	Did the laboratory serve as a national AMR surveillance site at any time between 2016 and 2018?	Yes	No	
1.10	Is your country participating in the World Health Organisation's Global Antimicrobial Resistance Surveillance System (WHO GLASS)?	Yes	No	
Part 2: Commodity and Equipment				
2.1	Did the laboratory have regular power supply with functional back up, in place at any time between 2016-18?	Yes	No	
2.2	Did the laboratory have continuous water supply, in place at any time between 2016-18?	Yes	No	
2.3	Did the laboratory have certified and functional biosafety cabinet, in place at any time between 2016-18?	Yes	No	
2.4	Did the laboratory have automated methods for bacterial identification, in place at any time between 2016-18?	Yes	No	
2.5	Did the laboratory have automated methods for antimicrobial susceptibility testing, in place at any time between 2016-18?	Yes	No	
2.6	Did the laboratory test for mechanisms of antimicrobial resistance at any time between 2016-2018?	Yes	No	
Part 3: Quality Assurance (QA), Accreditation and Certification				
3.1A	Was the laboratory implementing quality management systems at any time between 2016-2018?	Yes	No	
3.1B	If you answered 'yes' to question 1A: What quality management tools did the laboratory utilize? (e.g., LQMS, SLIPTA, SLMTA, mentoring, others)			
3.2A	Did the laboratory receive a quality certification at any time between 2016-2018?	Yes	No	
3.2B	If you answered 'yes' to question 2A: What kind of quality certification did the laboratory receive? (e.g., SLIPTA, College of American pathologists)			
3.2C	If you answered 'yes' to question 2A: What was the laboratory's level of quality certification (e.g., star rating for SLIPTA certified laboratories)?			
3.3A	Was the laboratory accredited by a national or international body at any time between 2016-2018?	Yes	No	
3.3B	If you answered 'yes' to question 3A: What was the name of the accreditation body/bodies?			

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

Part 4. Personnel and Training

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

Part 5. Specimen Management

5.1	Did the laboratory follow a defined standard operating procedure (SOP) for specimen collection and testing, at any time between 2016-18?	Yes		No	
5.2	Did the laboratory comply with specimen rejection criteria for rejecting inadequate specimens, at any time between 2016-18?	Yes		No	
5.3A	Does the laboratory have information on the average number of specimens processed for culture and sensitivity in 2018?	Yes		No	
5.3B	If you answered 'yes' to question 3A: What was the average number of specimens processed for bacterial culture in 2018?				
5.3C	If you answered 'yes' to question 3A: What was the average number of specimens that yielded bacterial growth and were processed for susceptibility tests, in 2018?				
	<200	200-1000	1000-3000	>3000	

Part 6. Laboratory Information System and Linkage to Clinical Data

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

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

was possible and for the option 'other', responses were entered as plain text (i)

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

Appendix 3: Laboratory Readiness Assessment

The EQ questions were scored for laboratory readiness as follows:

Question	Response	Scoring
Part 1: Site Information (Maximum score=0)		
1.1	What is the name of the laboratory?	None
1.2	Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing?	Yes <input type="checkbox"/> No <input type="checkbox"/> None
1.3	Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium?	Yes <input type="checkbox"/> No <input type="checkbox"/> 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 <input type="checkbox"/> Regional/Intermediate <input type="checkbox"/> District or community <input type="checkbox"/> Other <input type="checkbox"/>	
1.6	What is the laboratory's affiliation?	None
	Government/Ministry of Health <input type="checkbox"/> Private <input type="checkbox"/> Non-government organisation <input type="checkbox"/> Other <input type="checkbox"/>	
1.7	Is the laboratory co-located in a clinical facility?	Yes <input type="checkbox"/> No <input type="checkbox"/> None
1.8	Is a pharmacy co-located with the laboratory?	Yes <input type="checkbox"/> No <input type="checkbox"/> None
1.9	Did the laboratory serve as a national AMR surveillance site at any time between 2016 and 2018?	Yes <input type="checkbox"/> No <input type="checkbox"/> None
1.10	Is your country participating in the World Health Organisation's Global Antimicrobial Resistance Surveillance System (WHO GLASS)?	Yes <input type="checkbox"/> No <input type="checkbox"/> 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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	Score 1 for "Yes" and 0 for "No"
3.1B	If you answered 'yes' to question 1A: What quality management tools did the laboratory utilize? (e.g., LQMS, SLIPTA, SLMTA, mentoring, others)		Score 1 for "Yes" and 0 for "No"
3.2A	Did the laboratory receive a quality certification at any time between 2016-2018?	Yes <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	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 <input type="checkbox"/> No <input type="checkbox"/>	Score 1 for "Yes" and 0 for "No"
3.5	Did the laboratory utilize reference strains to verify that stains, reagents, and media are working correctly at any time between 2016-18?	Yes <input type="checkbox"/> No <input type="checkbox"/>	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 laboratory (max score being 6) Score 1 for "Yes" and 0 for "No"	
	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
<i>Acinetobacter baumannii</i>	Carbapenem-resistant	Critical
<i>Pseudomonas aeruginosa</i>	Carbapenem-resistant	Critical
Enterobacterales*	Carbapenem-resistant, ESBL-producing	Critical
<i>Enterococcus faecium</i>	Vancomycin-resistant	High
<i>Staphylococcus aureus</i>	Methicillin-resistant, Vancomycin-intermediate and resistant	High
<i>Helicobacter pylori</i>	Clarithromycin-resistant	High
<i>Campylobacter</i> species	Fluoroquinolone-resistant	High
<i>Neisseria gonorrhoeae</i>	3 rd generation Cephalosporin-resistant, Fluoroquinolone-resistant	High
Salmonellae	Fluoroquinolone-resistant	High
<i>Shigella</i> species	Fluoroquinolone-resistant	Medium
<i>Streptococcus pneumoniae</i>	Penicillin-non-susceptible	Medium
<i>Hemophilus influenzae</i>	Ampicillin-resistant	Medium

*Previously known as *Enterobacteriaceae*.

Appendix 6: Other clinically important pathogens

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

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

Appendix 7: Pathogen Phenotype Definitions

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

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=64 n (%)	Reference N = 3 n (%)	Regional/ Intermediate N =15 n (%)	District/ Community N = 32 n (%)	Unspecified N = 14 n (%)
Government	29 (45.31)	2 (66.7)	10 (66.7)	13 (40.6)	4 (28.6)
Private	24 (37.5)	0	5 (33.3)	9 (28.1)	10 (71.4)
NGO	2 (3.12)	0	0	2 (6.2)	0
Others	9 (14.06)	1 (33.3)	0	8 (25.0)	0

Supplementary Table 2: Assessment of preparedness for AMR surveillance

Parameters	Surveyed laboratories N=64 n (%)
Commodity and equipment status	
Regular power supply and functional back up	58 (90.6)
Continuous water supply	57 (89.1)
Certified and functional biosafety cabinets	15 (23.4)
Automated methods for pathogen identification	5 (7.8)
Automated methods for antimicrobial susceptibility testing	3 (4.7)
Methods for testing antimicrobial resistance mechanisms	13 (20.3)
QMS implementation	
Reported QMS Implementation	44 (68.8)
• Reported QMS tool (n=44)	
• LQMS	11 (25.0)
• SLIPTA	7 (15.9)
• SLMTA	2 (4.5)
• Mentoring	0 (0.0)
• Combination‡	11 (25.0)
• Others	12 (27.3)
Quality Certification	18 (28.1)
• Reported certification type (n=18)	
• SLIPTA	5 (27.8)
• College of American Pathologists	1 (5.6)
• Others	12 (66.7)
Accreditation	20 (31.3)
Participation in proficiency testing	20 (31.3)
Utilisation of reference strains	37 (57.8)
Reported consistent maintenance of QC records	33 (51.6)
Designated focal quality person	46 (71.9)
Reported compliance to standard operating procedures	58 (90.6)
Reported compliance to antimicrobial susceptibility testing standards	48 (75.0)
Personnel and training status	
Presence of at least one qualified microbiologist	42 (65.6)
Presence of an experienced laboratory scientist/technologist	64 (100.0)
Up-to-date and complete records on staff training and competence	32 (50.0)
Specimen Management status	
Reported compliance to standard operating procedures on specimen collection and testing	59 (92.2)
Reported compliance to standard operating procedures on specimen rejection	58 (90.6)
Availability on average number of specimens processed for culture and sensitivity in year 2018	63 (98.4)
Laboratory Information System and Linkage to Clinical Data	
Assigned specimen (laboratory) identification number	64 (100.0)
Availability of system/database to store patient data	63 (98.4)
• System/database format (n=63)	
• Paper-based	29 (46.0)
• Electronic	17 (27.0)
• Mixed	17 (27.0)
Captured patients' demographics and clinical information on test request forms	59 (92.2)
• Retrievable test request forms (n=59)	34 (57.6)

*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	4012	5981	7103	1343	2303	2282	986	1623	1785	
Pathogen type	bacteria			1071 (79.7)	2117 (91.9)	2004 (87.8)	986 (100.0)	1622 (99.9)	1785 (100.0)	
	fungi			272 (20.3)	186 (8.1)	278 (12.2)	-	1 (0.1)	-	
Age, years	Less than 1	513 (12.8)	556 (9.3)	597 (8.4)	97 (7.2)	168 (7.3)	173 (7.6)	91 (9.2)	143 (8.8)	157 (8.8)
	1 to 17	767 (19.1)		1272 (17.9)	189 (14.1)	338 (14.7)	319 (14.0)	150 (15.2)	254 (15.7)	248 (13.9)
	18 to 49	1450 (36.1)	1799 (30.1)	1444 (20.3)	601 (44.8)	673 (29.2)	433 (19.0)	350 (35.5)	417 (25.7)	317 (17.8)
	50 to 65	198 (4.9)	315 (5.3)	278 (3.9)	90 (6.7)	142 (6.2)	93 (4.1)	78 (7.9)	100 (6.2)	76 (4.3)
	Above 65	185 (4.6)	214 (3.6)	231 (3.3)	91 (6.8)	81 (3.5)	73 (3.2)	85 (8.6)	76 (4.7)	65 (3.6)
	Unknown Age	899 (22.4)	1912 (32.0)	3281 (46.2)	275 (20.5)	901 (39.1)	1191 (52.2)	232 (23.5)	633 (39.0)	922 (51.7)
Gender	Male	1465 (36.5)	2159 (36.1)	2574 (36.2)	392 (29.2)	738 (32.0)	685 (30.0)	348 (35.3)	532 (32.8)	586 (32.8)
	Female	2547 (63.5)	3820 (63.9)	4527 (63.7)	951 (70.8)	1563 (67.9)	1597 (70.0)	638 (64.7)	1091 (67.2)	1199 (67.2)
	Unknown gender	-	2 (0.0)	2 (0.0)	-	2 (0.0)	-	-	-	-
Laboratory	Patholab	59 (1.5)	78 (1.3)	41 (0.6)	10 (0.7)	23 (1.0)	10 (0.4)	10 (1.0)	19 (1.2)	7 (0.4)
	Quadushah	234 (5.8)	55 (0.9)	81 (1.1)	37 (2.8)	7 (0.3)	22 (1.0)	34 (3.4)	5 (0.3)	17 (1.0)
	Upper-East RH	279 (7.0)	433 (7.2)	407 (5.7)	74 (5.5)	97 (4.2)	89 (3.9)	72 (7.3)	89 (5.5)	73 (4.1)
	Greater Accra RH	-	1358 (22.7)	1974 (27.8)	-	801 (34.8)	764 (33.5)	-	530 (32.7)	671 (37.6)
	HF Berekum	143 (3.6)	43 (0.7)	15 (0.2)	84 (6.3)	13 (0.6)	14 (0.6)	79 (8.0)	9 (0.6)	14 (0.8)
	St. Joseph	1 (0.0)	171 (2.9)	37 (0.5)	1 (0.1)	45 (2.0)	27 (1.2)	-	39 (2.4)	27 (1.5)
	Lekma	524 (13.1)	597 (10.0)	726 (10.2)	133 (9.9)	157 (6.8)	152 (6.7)	118 (12.0)	142 (8.7)	135 (7.6)
	Nsawam	1012 (25.2)	704 (11.8)	238 (3.4)	327 (24.3)	103 (4.5)	37 (1.6)	175 (17.7)	83 (5.1)	33 (1.8)
	HF Techiman	717 (17.9)	979 (16.4)	713 (10.0)	214 (15.9)	277 (12.0)	203 (8.9)	202 (20.5)	263 (16.2)	192 (10.8)
	Tema	243 (6.1)	559 (9.3)	344 (4.8)	78 (5.8)	200 (8.7)	108 (4.7)	66 (6.7)	159 (9.8)	90 (5.0)
	Paradise	100 (2.5)	111 (1.9)	713 (10.0)	31 (2.3)	28 (1.2)	285 (12.5)	13 (1.3)	19 (1.2)	131 (7.3)
	Cape Coast Teaching	98 (2.4)	139 (2.3)	117 (1.6)	98 (7.3)	139 (6.0)	117 (5.1)	93 (9.4)	129 (7.9)	103 (5.8)
	PHL Tamale	72 (1.8)	48 (0.8)	951 (13.4)	15 (1.1)	8 (0.3)	135 (5.9)	8 (0.8)	8 (0.5)	135 (7.6)
	University of Cape Coast	466 (11.6)	586 (9.8)	230 (3.2)	216 (16.1)	364 (15.8)	208 (9.1)	96 (9.7)	88 (5.4)	46 (2.6)
Tamale Teaching	64 (1.6)	120 (2.0)	516 (7.3)	25 (1.9)	41 (1.8)	111 (4.9)	20 (2.0)	41 (2.5)	111 (6.2)	

Supplementary Table 4: Specimen characteristics

Specimen Type	All years* N= 4 394 n (%)	2016 N = 986 n (%)	2017 N = 1 623 n (%)	2018 N = 1 785 n (%)
Abscess/Discharge/Pus/Swab/Wound	899 (20.5)	254 (25.8)	295 (18.2)	350 (19.6)
Aspirate/discharge	15 (0.3)	9 (0.9)	3 (0.2)	3 (0.2)
Blood	1910 (43.5)	188 (19.1)	842 (51.9)	880 (49.3)
CSF	232 (5.3)	207 (21)	15 (0.9)	10 (0.6)
Drain	3 (0.1)	-	-	3 (0.2)
Respiratory-Lower	1 (0)	-	-	1 (0.1)
Respiratory-Upper	74 (1.7)	6 (0.6)	35 (2.2)	33 (1.8)
Semen	4 (0.1)	-	4 (0.2)	-
Stool	21 (0.5)	5 (0.5)	10 (0.6)	6 (0.3)
Swab (rectal)	1 (0)	-	-	1 (0.1)
Swab (urethral)	9 (0.2)	-	1 (0.1)	8 (0.4)
Swab (vaginal)	9 (0.2)	1 (0.1)	3 (0.2)	5 (0.3)
Tissue/biopsy	17 (0.4)	-	4 (0.2)	13 (0.7)
Urine	1199 (27.3)	316 (32)	411 (25.3)	472 (26.4)

*Indicates positive cultures with AST results

Supplementary Table 5: Pathogen identification

Pathogen	All years* N= 4394 n (%)	2016 N = 986 n (%)	2017 N = 1623 n (%)	2018 N = 1785 n (%)
Positive cultures with specific pathogen name	2 861 (65.1)	626 (63.5)	963 (59.3)	1 272 (71.3)
<i>Acinetobacter baumannii</i>	15 (0.3)	-	-	15 (0.8)
<i>Actinobacillus lignieresii</i>	2 (0)	-	-	2 (0.1)
<i>Aeromonas caviae</i>	1 (0)	-	-	1 (0.1)
<i>Aeromonas hydrophila</i>	2 (0)	-	-	2 (0.1)
<i>Aeromonas salmonicida</i>	2 (0)	-	-	2 (0.1)
<i>Arcanobacterium haemolyticum</i>	2 (0)	-	-	2 (0.1)
<i>Bacillus circulans</i>	1 (0)	-	1 (0.1)	-
<i>Burkholderia cepacia</i>	2 (0)	-	-	2 (0.1)
<i>Cedecea davisae</i>	1 (0)	-	-	1 (0.1)
<i>Cedecea lapagei</i>	3 (0.1)	-	-	3 (0.2)
<i>Chromobacterium violaceum</i>	1 (0)	-	-	1 (0.1)
<i>Citrobacter diversus</i>	7 (0.2)	3 (0.3)	4 (0.2)	-
<i>Citrobacter freundii</i>	30 (0.7)	3 (0.3)	11 (0.7)	16 (0.9)
<i>Citrobacter koseri</i>	1 (0)	-	-	1 (0.1)
<i>Corynebacterium minutissimum</i>	1 (0)	-	-	1 (0.1)
<i>Corynebacterium propinquum</i>	1 (0)	-	-	1 (0.1)
<i>Corynebacterium striatum</i>	1 (0)	-	-	1 (0.1)
<i>Dermabacter hominis</i>	1 (0)	-	-	1 (0.1)
<i>Elizabethkingia meningoseptica</i>	1 (0)	-	-	1 (0.1)
<i>Enterobacter cloacae</i>	14 (0.3)	-	2 (0.1)	12 (0.7)
<i>Enterobacter nimipressuralis</i>	1 (0)	-	1 (0.1)	-
<i>Enterococcus casseliflavus</i>	1 (0)	-	-	1 (0.1)
<i>Enterococcus faecalis</i>	30 (0.7)	4 (0.4)	11 (0.7)	15 (0.8)
<i>Enterococcus seriolicida</i>	1 (0)	-	-	1 (0.1)
<i>Escherichia coli</i>	712 (16.2)	215 (21.8)	231 (14.2)	266 (14.9)
<i>Ewingella americana</i>	1 (0)	-	-	1 (0.1)
<i>Gardnerella vaginalis</i>	2 (0)	2 (0.2)	-	-
<i>Klebsiella aerogenes</i>	44 (1)	15 (1.5)	11 (0.7)	18 (1)

<i>Klebsiella oxytoca</i>	40 (0.9)	14 (1.4)	13 (0.8)	13 (0.7)
<i>Klebsiella pneumoniae</i>	253 (5.8)	27 (2.7)	72 (4.4)	154 (8.6)
<i>Kluyvera ascorbata</i>	1 (0)	-	-	1 (0.1)
<i>Kocuria kristinae</i>	2 (0)	-	-	2 (0.1)
<i>Kocuria rosea</i>	1 (0)	-	-	1 (0.1)
<i>Kocuria varians</i>	1 (0)	-	-	1 (0.1)
<i>Leifsonia aquatica</i>	1 (0)	-	-	1 (0.1)
<i>Micrococcus luteus</i>	10 (0.2)	-	-	10 (0.6)
<i>Moellerella wisconsensis</i>	3 (0.1)	-	-	3 (0.2)
<i>Moraxella catarrhalis</i>	9 (0.2)	-	9 (0.6)	-
<i>Morganella morganii</i>	8 (0.2)	1 (0.1)	3 (0.2)	4 (0.2)
<i>Neisseria gonorrhoeae</i>	6 (0.1)	3 (0.3)	3 (0.2)	-
<i>Neisseria meningitidis</i>	7 (0.2)	1 (0.1)	1 (0.1)	5 (0.3)
<i>Pantoea (enterobacter) agglomerans</i>	2 (0)	-	-	2 (0.1)
<i>Pasteurella aerogenes</i>	3 (0.1)	-	-	3 (0.2)
<i>Pasteurella multocida</i>	3 (0.1)	-	-	3 (0.2)
<i>Proteus hauseri</i>	1 (0)	1 (0.1)	-	-
<i>Proteus mirabilis</i>	93 (2.1)	21 (2.1)	33 (2)	39 (2.2)
<i>Proteus vulgaris</i>	19 (0.4)	13 (1.3)	4 (0.2)	2 (0.1)
<i>Providencia rettgeri</i>	3 (0.1)	-	-	3 (0.2)
<i>Pseudomonas aeruginosa</i>	187 (4.3)	41 (4.2)	50 (3.1)	96 (5.4)
<i>Pseudomonas fluorescens</i>	1 (0)	-	-	1 (0.1)
<i>Pseudomonas mendocina</i>	1 (0)	-	-	1 (0.1)
<i>Pseudomonas putida</i>	1 (0)	1 (0.1)	-	-
<i>Raoultella ornithinolytica</i>	2 (0)	-	-	2 (0.1)
<i>Rhizobium radiobacter</i>	2 (0)	-	-	2 (0.1)
<i>Rothia mucilaginosa</i>	2 (0)	-	-	2 (0.1)
<i>Salmonella enterica ser. Paratyphi</i>	1 (0)	1 (0.1)	-	-
<i>Salmonella enterica ser. Typhi</i>	7 (0.2)	2 (0.2)	-	5 (0.3)
<i>Serratia fonticola</i>	12 (0.3)	-	-	12 (0.7)
<i>Serratia marcescens</i>	5 (0.1)	-	-	5 (0.3)

<i>Serratia plymuthica</i>	2 (0)	-	-	2 (0.1)
<i>Shigella boydii</i>	4 (0.1)	1 (0.1)	1 (0.1)	2 (0.1)
<i>Shigella dysenteriae</i>	1 (0)	-	-	1 (0.1)
<i>Sphingomonas paucimobilis</i>	4 (0.1)	-	-	4 (0.2)
<i>Staphylococcus aureus</i>	852 (19.4)	219 (22.2)	358 (22.1)	275 (15.4)
<i>Staphylococcus capitis</i>	4 (0.1)	-	-	4 (0.2)
<i>Staphylococcus epidermidis</i>	256 (5.8)	25 (2.5)	123 (7.6)	108 (6.1)
<i>Staphylococcus gallinarum</i>	2 (0)	-	-	2 (0.1)
<i>Staphylococcus haemolyticus</i>	45 (1)	-	-	45 (2.5)
<i>Staphylococcus hominis</i>	21 (0.5)	-	-	21 (1.2)
<i>Staphylococcus intermedius</i>	1 (0)	-	-	1 (0.1)
<i>Staphylococcus kloosii</i>	1 (0)	-	-	1 (0.1)
<i>Staphylococcus pasteurii</i>	1 (0)	-	-	1 (0.1)
<i>Staphylococcus saccharolyticus</i>	1 (0)	-	-	1 (0.1)
<i>Staphylococcus saprophyticus</i>	18 (0.4)	7 (0.7)	5 (0.3)	6 (0.3)
<i>Staphylococcus schleiferi</i>	3 (0.1)	-	-	3 (0.2)
<i>Staphylococcus sciuri</i>	4 (0.1)	-	-	4 (0.2)
<i>Staphylococcus simulans</i>	2 (0)	-	-	2 (0.1)
<i>Staphylococcus warneri</i>	1 (0)	-	-	1 (0.1)
<i>Staphylococcus xylosum</i>	1 (0)	-	-	1 (0.1)
<i>Stenotrophomonas (xanthomonas) maltophilia</i>	1 (0)	-	-	1 (0.1)
<i>Streptococcus acidominimus</i>	2 (0)	-	-	2 (0.1)
<i>Streptococcus agalactiae</i>	4 (0.1)	-	-	4 (0.2)
<i>Streptococcus anginosus</i>	2 (0)	-	-	2 (0.1)
<i>Streptococcus gallolyticus</i>	1 (0)	-	-	1 (0.1)
<i>Streptococcus pneumoniae</i>	34 (0.8)	6 (0.6)	12 (0.7)	16 (0.9)
<i>Streptococcus porcinus</i>	3 (0.1)	-	-	3 (0.2)
<i>Streptococcus pyogenes</i>	9 (0.2)	-	4 (0.2)	5 (0.3)
<i>Streptococcus sanguinis</i>	1 (0)	-	-	1 (0.1)
<i>Streptococcus vestibularis</i>	1 (0)	-	-	1 (0.1)
<i>Streptococcus viridans</i>	5 (0.1)	-	-	5 (0.3)
<i>Vibrio fluvialis</i>	4 (0.1)	-	-	4 (0.2)

Yersinia intermedia	1 (0)	-	-	1 (0.1)
Yersinia pseudotuberculosis	1 (0)	-	-	1 (0.1)
Positive cultures with non-specific pathogen name	1533 (34.9)	360 (36.5)	660 (40.7)	513 (28.7)
Acetobacterium Sp.	1 (0)	-	1 (0.1)	-
Achromobacter Sp.	2 (0)	-	-	2 (0.1)
Acinetobacter Sp.	12 (0.3)	-	12 (0.7)	-
Bacillus Sp.	3 (0.1)	-	2 (0.1)	1 (0.1)
Brevibacterium Sp.	2 (0)	-	-	2 (0.1)
Candida Sp.	1 (0)	-	1 (0.1)	-
Citrobacter Sp.	161 (3.7)	50 (5.1)	65 (4)	46 (2.6)
Corynebacterium Sp.	3 (0.1)	-	3 (0.2)	-
Enterobacter Sp.	181 (4.1)	45 (4.6)	81 (5)	55 (3.1)
Enterococcus Sp.	53 (1.2)	6 (0.6)	15 (0.9)	32 (1.8)
Gardnerella Sp.	1 (0)	-	1 (0.1)	-
Haemophilus Sp.	1 (0)	-	1 (0.1)	-
Klebsiella Sp.	303 (6.9)	79 (8)	126 (7.8)	98 (5.5)
Morganella Sp.	5 (0.1)	-	4 (0.2)	1 (0.1)
Peptostreptococcus Sp.	1 (0)	-	1 (0.1)	-
Proteus Sp.	74 (1.7)	25 (2.5)	20 (1.2)	29 (1.6)
Providencia Sp.	6 (0.1)	2 (0.2)	3 (0.2)	1 (0.1)
Pseudomonas Sp.	115 (2.6)	52 (5.3)	37 (2.3)	26 (1.5)
Salmonella Sp.	15 (0.3)	3 (0.3)	5 (0.3)	7 (0.4)
Serratia Sp.	2 (0)	-	-	2 (0.1)
Shigella Sp.	1 (0)	-	1 (0.1)	-
Staphylococcus Sp.	493 (11.2)	73 (7.4)	245 (15.1)	175 (9.8)
Streptococcus Sp.	32 (0.7)	7 (0.7)	10 (0.6)	15 (0.8)
Unspecified (Gram negative bacilli)	12 (0.3)	6 (0.6)	5 (0.3)	1 (0.1)
Unspecified (Gram negative cocci)	1 (0)	1 (0.1)	-	-
Unspecified (Gram positive bacilli)	2 (0)	1 (0.1)	-	1 (0.1)
Unspecified (Gram positive cocci)	49 (1.1)	10 (1)	20 (1.2)	19 (1.1)
Yersinia Sp.	1 (0)	-	1 (0.1)	-

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
Lekma	4	4	4	4
Cape Coast Teaching	3	3	3	3
PHL Tamale	4	4	3	3.7
Tema	2	3	3	2.7
St. Joseph		4	4	4
HF Berekum	3	3	2	2.7
Greater Accra RH		3	4	3.5
Upper-East RH	4	4	4	4
Patholab	4	4	2	3.3
Quadushah	3	3	3	3
Paradise	3	4	4	3.7
University of Cape Coast	3	3	3	3
HF Techiman	2	1	1	1.3
Nsawam	3	3	3	3
Tamale Teaching	4	4	4	4
M and G	-	-	-	-

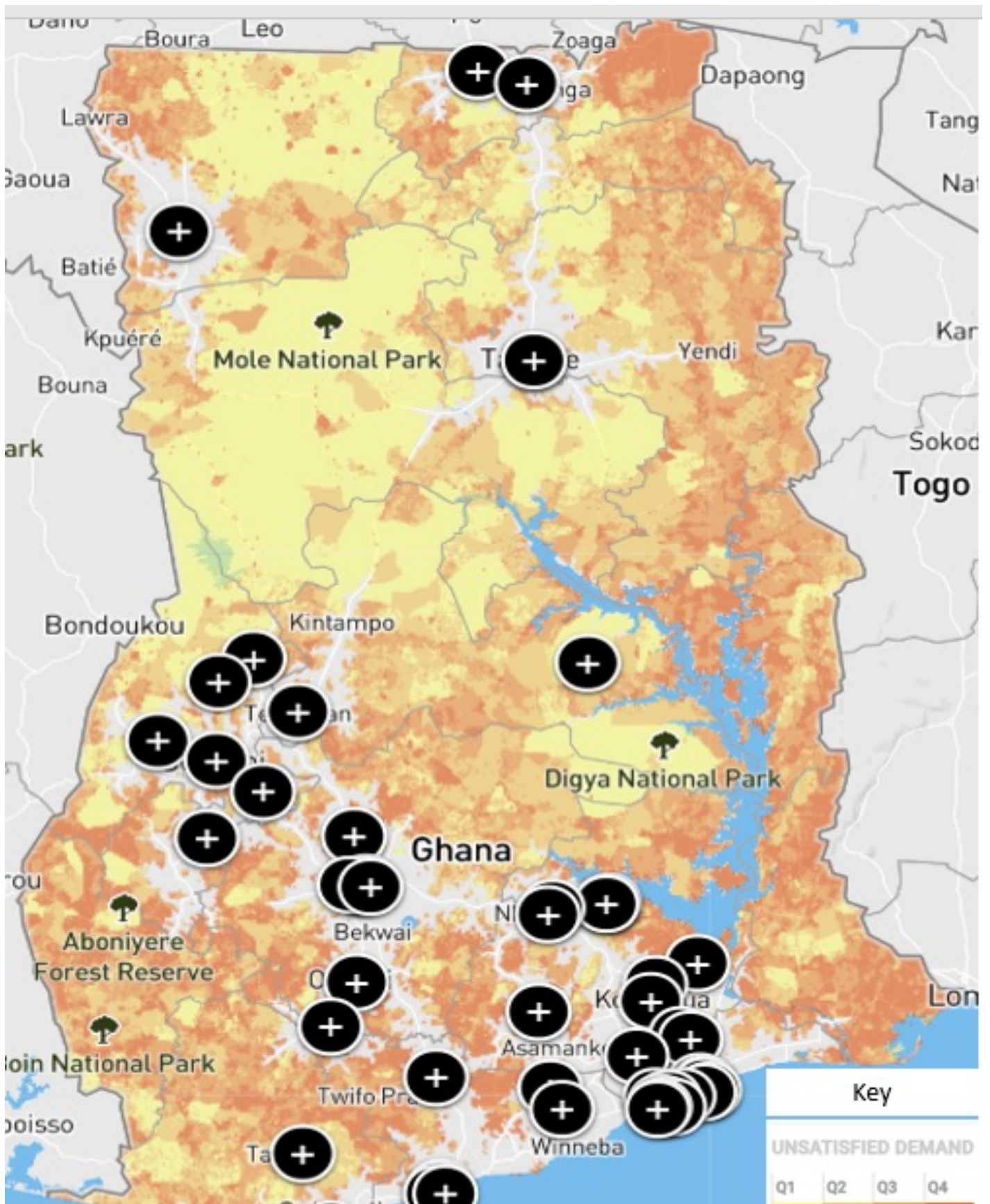
Supplementary Table 7: Univariate logistic regression analysis

Variable	Options	N	NS (%)	Crude OR (95% CI)	P-value
Gender	Female	2415	63.5	Ref	0.185
	Male	818	61.7	0.93 (0.83 – 1.04)	
Age, years	<1	109	58.7	0.77 (0.57 – 1.06)	0.1848
	1-17	439	64.2	0.98 (0.63 – 1.51)	
	18-49	1170	64.8	Ref	
	50-65	272	60.7	0.83 (0.66 – 1.07)	
	>65	221	67.0	1.10 (0.81 – 1.50)	

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

AMR Supplementary Figures

Supplementary Figure 1: Population coverage of laboratories



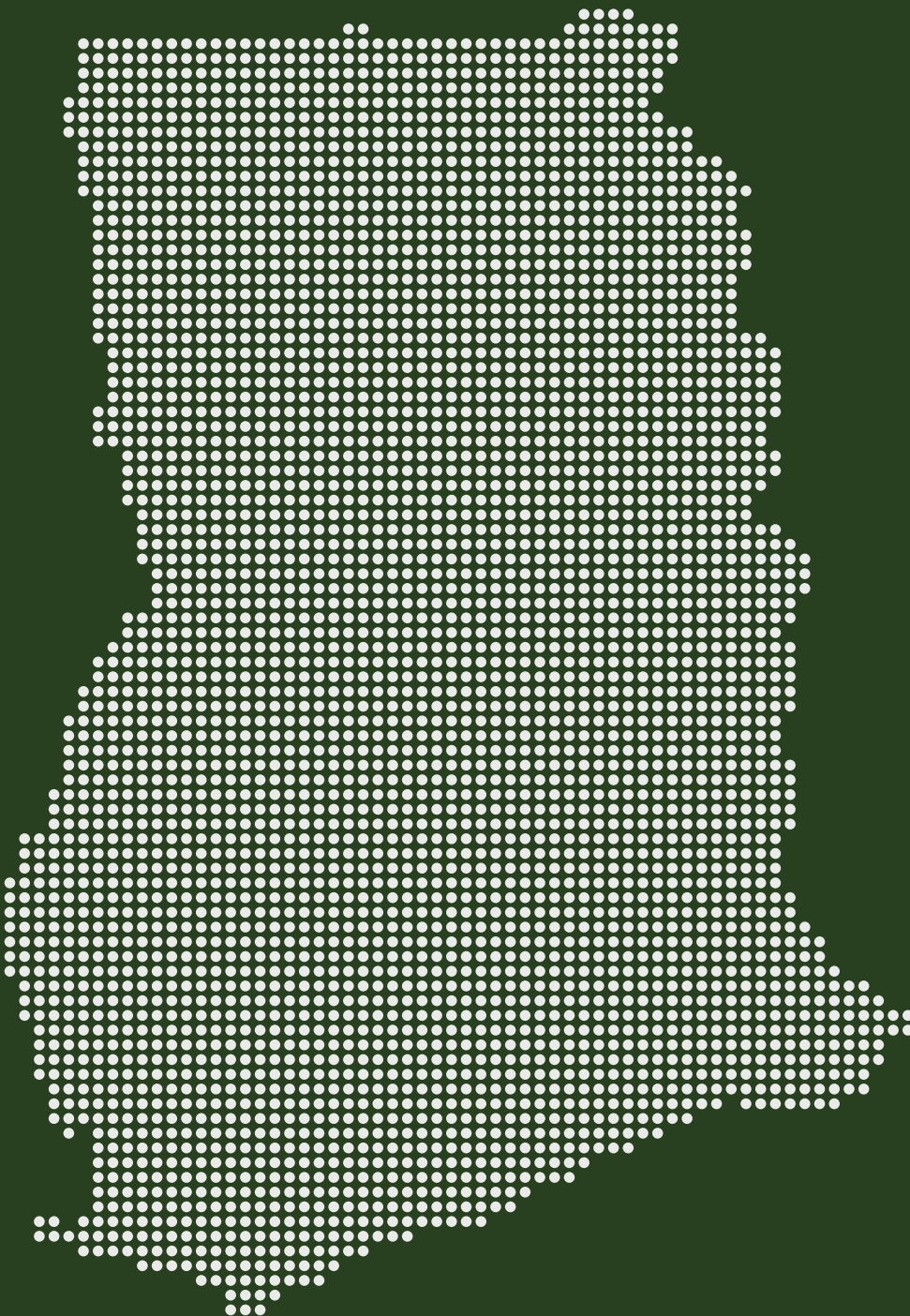
Supplementary Figure 2a: Inappropriate testing A

Organism Name	Antimicrobial Agent	Agent Code	Interpreted Results	Antimicrobial Susceptibility Method	Year
Candida sp.	Cloxacillin	CLO_NDS	R	Disk	2017
Candida sp.	Erythromycin	ERY_ND15	R	Disk	2017
Candida sp.	Penicillin G	PEN_ND10	R	Disk	2017
Candida sp.	Ciprofloxacin	CIP_ND5	S	Disk	2017
Candida sp.	Levofloxacin	LVX_ND5	S	Disk	2017
Candida sp.	Norfloxacin	NOR_D10	S	Disk	2017
Staphylococcus aureus	Fluconazole	FLU_ND25	S	Disk	2016
Staphylococcus aureus	Fluconazole	FLU_ND25	S	Disk	2016

Supplementary Figure 2b: Inappropriate testing B

Organism Name	Antimicrobial Agent	Agent Code	Interpreted Results	Antimicrobial Susceptibility Method	Year
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Escherichia coli	Vancomycin	VAN_ND30	R	Disk	2016
Klebsiella sp.	Penicillin G	PEN_ND10	R	Disk	2017
Enterobacter sp.	Penicillin G	PEN_ND10	R	Disk	2017
Escherichia coli	Penicillin G	PEN_ND10	R	Disk	2017
Enterobacter sp.	Penicillin G	PEN_ND10	R	Disk	2017
Proteus sp.	Penicillin G	PEN_ND10	R	Disk	2018
Escherichia coli	Penicillin G	PEN_ND10	I	Disk	2018
Citrobacter freundii	Penicillin G	PEN_ND10	R	Disk	2018
Escherichia coli	Penicillin G	PEN_ND10	S	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	
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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 WHO's 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
Sulfamethoxyipyridazine/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)
Rolitetraacycline	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
Methicillin	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
Ceftazole	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
Brodinoprim	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
Sulfamethoxydiazine	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

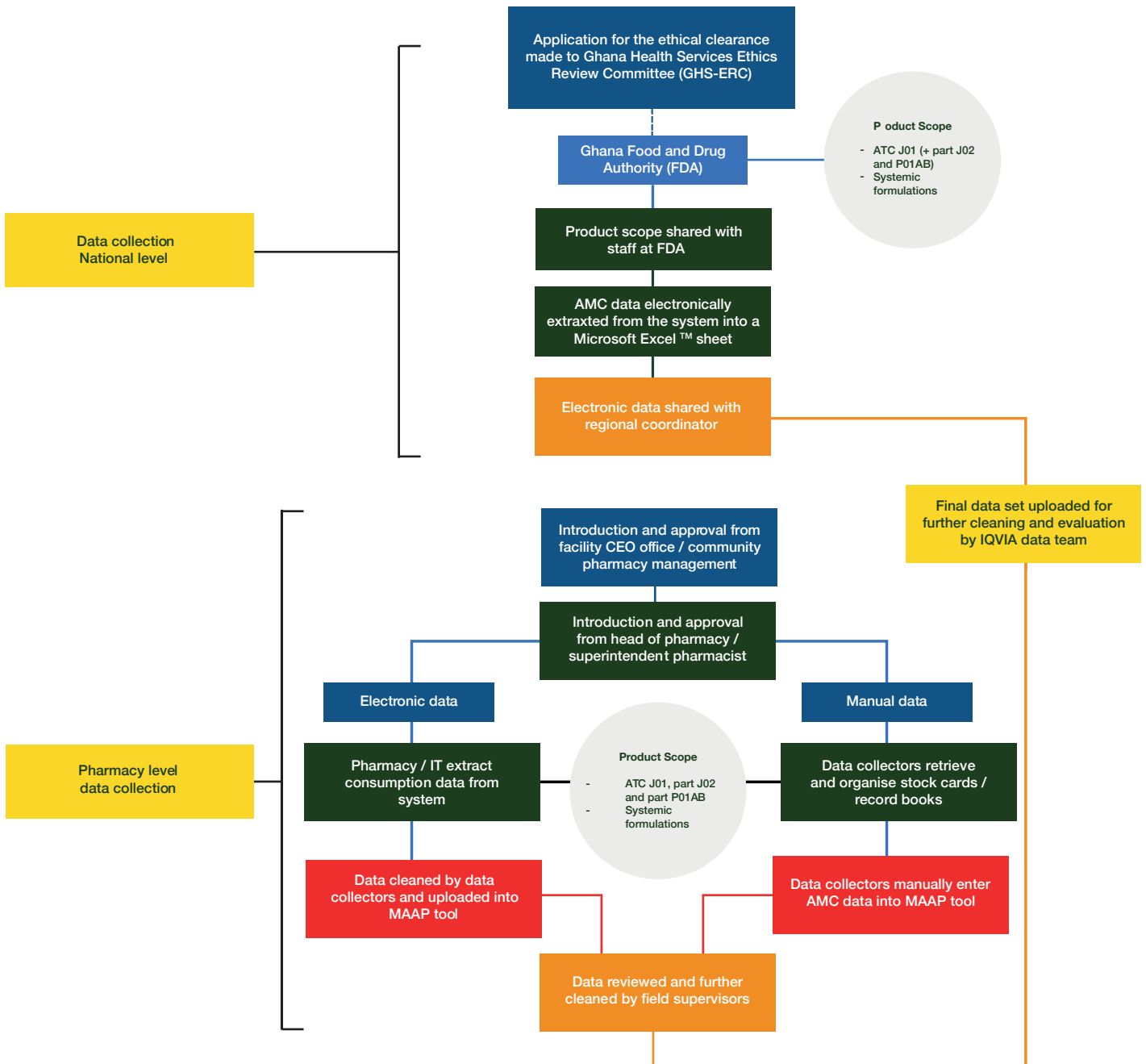
Arbekacin	J01GB12	W
Bekanamycin	J01GB13	U
Ofloxacin	J01MA01	W
Ciprofloxacin	J01MA02	W
Pefloxacin	J01MA03	W
Enoxacin	J01MA04	W
Temafloxacin	J01MA05	U
Norfloxacin	J01MA06	W
Lomefloxacin	J01MA07	W
Fleroxacin	J01MA08	W
Sparfloxacin	J01MA09	W
Rufloxacin	J01MA10	W
Grepafloxacin	J01MA11	U
Levofloxacin	J01MA12	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
Furazidone	J01XE03	U
Fosfomicin	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

Appendix 4: Key AMC specific variables

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

Appendix 5: Data collection process flowchart



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

Appendix 6: Description of AMC analysis methodology

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

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

***WHO approved DDDs for antibiotics:**

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

DDD/1000 Inhabitants/day =

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

*Ghana population estimated for 2016-2019 obtained from:
<https://www.worldometers.info/world-population/ghana-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 is 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 comprises 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 comprises of 110 antibiotics; 11 of which are included in the WHO's EML. 'Watch' group antibiotics should be prioritised as key targets of stewardship programs 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 comprises of 22 antibiotics; 7 of which are included in the WHO's EML. The use of antibiotics in this group should be closely monitored and prioritised as targets for AMS to ensure their continued effectiveness.

Appendix 7: National AMC by Antimicrobial molecules

ATC Class Rank	AWaRe category	Molecule	2016	2017	2018	2019	Mean DDD
			DDD/1000 inhabitant-days (%*)				
J01 Class		Total	4 106 646 (100)	4 974 915 (100)	4 652 916 (100)	4 436 225 (100)	4 542 676
1	Access	Amoxicillin/Clavulanic Acid	650 520 (15.8)	926 859 (18.6)	1 009 731 (21.7)	909 081 (20.5)	874 048
2	Access	Amoxicillin	678 611 (16.5)	784 171 (15.8)	677 800 (14.6)	728 004 (16.4)	717 146
3	Access	Clindamycin	525 907 (12.8)	562 931 (11.3)	558 755 (12)	653 386 (14.7)	575 245
4	Watch	Cefuroxime	389 016 (9.5)	543 415 (10.9)	500 280 (10.8)	562 930 (12.7)	498 910
5	Watch	Ciprofloxacin	435 283 (10.6)	485 859 (9.8)	386 275 (8.3)	436 091 (9.8)	435 877
6	Access	Flucloxacillin	411 547 (10)	549 522 (11)	368 284 (7.9)	291 974 (6.6)	405 332
7	Access	Sulfamethoxazole/Trimethoprim	460 866 (11.2)	334 485 (6.7)	433 025 (9.3)	238 992 (5.4)	366 842
8	Access	Doxycycline	90 308 (2.2)	164 236 (3.3)	158 843 (3.4)	134 740 (3)	137 032
9	Watch	Erythromycin	123 373 (3)	103 841 (2.1)	99 045 (2.1)	59 143 (1.3)	96 350
10	Watch	Ceftriaxone	67 518 (1.6)	78 706 (1.6)	77 834 (1.7)	98 211 (2.2)	80 567
11	Watch	Cefpodoxime proxetil	43 251 (1.1)	151 771 (3.1)	61 625 (1.3)	50 601 (1.1)	76 812
12	Access	Metronidazole	66 471 (1.6)	43 371 (0.9)	77 192 (1.7)	49 819 (1.1)	59 213
13	Watch	Azithromycin	32 542 (0.8)	60 096 (1.2)	65 618 (1.4)	58 789 (1.3)	54 261
14	Access	Gentamicin	33 417 (0.8)	38 934 (0.8)	37 366 (0.8)	67 948 (1.5)	44 416
15	Uncategorised	Ciprofloxacin/ Tinidazole	31 004 (0.8)	40 791 (0.8)	48 381 (1)	12 048 (0.3)	33 056
16	Watch	Clarithromycin	13 187 (0.3)	16 330 (0.3)	18 045 (0.4)	21 290 (0.5)	17 213
17	Access	Benzympenicillin	11 959 (0.3)	18 650 (0.4)	17 595 (0.4)	13 723 (0.3)	15 482
18	Access	Tetracycline	13 150 (0.3)	16 332 (0.3)	13 937 (0.3)	3 184 (0.1)	11 651
19	Access	Ampicillin	8 230 (0.2)	12 691 (0.3)	9 193 (0.2)	13 922 (0.3)	11 009
20	Watch	Cefixime	7 730 (0.2)	2 825 (0.1)	7 847 (0.2)	11 849 (0.3)	7 563
21	Access	Chloramphenicol	4 090 (0.1)	9 030 (0.2)	9 332 (0.2)	6 112 (0.1)	7 141
22	Access	Phenoxymethyl-penicillin	5 800 (0.1)	11 566 (0.2)	5 773 (0.1)	1 572 (0)	6 178
23	Uncategorised	Amoxicillin/ Flucloxacillin	0 (0)	7 366 (0.1)	2 321 (0)	3 854 (0.1)	3 385

24	Access	Cloxacillin	1 000 (0)	5 510 (0.1)	4 035 (0.1)	1 500 (0)	3 011
25	Watch	Cefotaxime	648 (0)	1 840 (0)	1 386 (0)	2 239 (0.1)	1 528
26	Watch	Levofloxacin	295 (0)	1 238 (0)	1 076 (0)	2 729 (0.1)	1 334
27	Uncategorised	Ampicillin/ Cloxacillin	5 (0)	1 180 (0)	600 (0)	354 (0)	535
28	Watch	Ofloxacin	415 (0)	580 (0)	550 (0)	370 (0)	479
29	Uncategorised	Ceftriaxone/ Sulbactam	0 (0)	0 (0)	190 (0)	1 070 (0)	315
30	Watch	Meropenem	138 (0)	542 (0)	335 (0)	190 (0)	301
31	Access	Amikacin	315 (0)	130 (0)	187 (0)	200 (0)	208
32	Watch	Cefaclor	0 (0)	0 (0)	225 (0)	2 (0)	57
33	Watch	Norfloxacin	50 (0)	80 (0)	5 (0)	30 (0)	41
34	Uncategorised	Norfloxacin/ Tinidazole	0 (0)	0 (0)	60 (0)	94 (0)	38
35	Watch	Ceftazidime	0 (0)	32 (0)	20 (0)	98 (0)	38
36	Access	Nitrofurantoin	0 (0)	0 (0)	100 (0)	0 (0)	25
37	Watch	Oxytetracycline	0 (0)	5 (0)	20 (0)	60 (0)	21
38	Access	Benzathine benzylpenicillin	0 (0)	0 (0)	9 (0)	20 (0)	7
39	Access	Cefalexin	0 (0)	0 (0)	21 (0)	0 (0)	5
40	Watch	Moxifloxacin	0 (0)	0 (0)	0 (0)	6 (0)	1
J02 Class		Total	6 898 (100)	7 662 (100)	6 884 (100)	8 288 (100)	7 433
1	Uncategorised	Fluconazole	7 662 (100)	7 662 (100)	6 879 (99.9)	8 288 (100)	7 432
2	Uncategorised	Itraconazole	6 884 (100)	0 (0)	5 (0.1)	0 (0)	1
P01AB Class		Total	407 862 (100)	709 734 (100)	686 011 (100)	1 153 870 (100)	739 369
1	Uncategorised	Metronidazole	407 779 (100)	708 609 (99.8)	681 526 (99.3)	1 148 556 (99.5)	736 618
2	Uncategorised	Secnidazole	83 (0)	1 121 (0.2)	4 482 (0.7)	5 314 (0.5)	2 750
3	Uncategorised	Tinidazole	0 (0)	4 (0)	3 (0)	0 (0)	2

*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

ATC class	% consumption			
	2016	2017	2018	2019
ATC class	14.4%	16.4%	18.9%	16.3%
Combinations of penicillins, incl. beta-lactamase inhibitors	9.0%	12.4%	12.7%	20.5%
Nitroimidazole derivatives	15.1%	13.9%	12.8%	13.3%
Penicillins with extended spectrum	11.6%	9.9%	10.5%	11.7%
Lincosamides	8.6%	9.5%	9.4%	10.1%
Second-generation cephalosporins	9.6%	8.6%	7.3%	7.8%
First-generation cephalosporins	9.1%	9.8%	7.0%	5.2%
Beta-lactamase resistant penicillins	10.2%	5.9%	8.1%	4.3%
Combinations of sulfonamides and trimethoprim, incl. derivatives	3.7%	3.2%	3.4%	2.5%
Macrolides	2.6%	4.1%	2.8%	2.9%
Third-generation cephalosporins	2.3%	3.2%	3.2%	2.5%
Tetracyclines	1.3%	0.8%	1.4%	0.9%
Imidazole derivatives	0.7%	0.7%	0.7%	1.2%
Aminoglycosides	0.7%	0.7%	1.0%	0.3%
Combinations of antibacterials	0.4%	0.5%	0.4%	0.3%
Beta-lactamase sensitive penicillins	0.2%	0.1%	0.1%	0.2%
Triazole derivatives	0.1%	0.2%	0.2%	0.1%
Amphenicols	0.1%	0.1%	0.1%	0.0%
Penicillins	0.2%	0.0%	0.0%	0.0%
Imidazoles	<0.1%	<0.1%	<0.1%	<0.1%
Carbapenems	0.0%	0.0%	<0.1%	0.0%
Third-generation cephalosporins and beta-lactamase inhibitors	0.0%	0.0%	<0.1%	0.0%
First-generation cephalosporins and beta-lactamase inhibitors	0.0%	0.0%	<0.1%	0.0%

*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
Linezolid	Reserve	J01XX08	Y	N	N
Amikacin	Access	J01GB06	Y	N	Y
Amoxicillin	Access	J01CA04	Y	Y	Y
Amoxicillin/Clavulanic Acid	Access	J01CR02	Y	Y	Y
Amoxicillin/Flucloxacillin		J01CR50	N	N	Y
Ampicillin	Access	J01CA01	Y	Y	Y
Ampicillin/Cloxacillin		J01CR50	N	N	Y
Azithromycin	Watch	J01FA10	Y	Y	Y
Benzathine benzylpenicillin	Access	J01CE08	Y	Y	Y
Benzylpenicillin	Access	J01CE01	Y	Y	Y
Cefaclor	Watch	J01DC04	N	N	Y
Cefalexin	Access	J01DB01	Y	N	Y
Cefazolin	Access	J01DB04	Y	N	N
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	N	Y
Ceftazidime/avibactam	Reserve	J01DD52	Y	N	N
Ceftriaxone	Watch	J01DD04	Y	Y	Y
Ceftriaxone/Sulbactam		J01DD63	N	N	Y
Cefuroxime	Watch	J01DC02	Y	Y	Y
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
Itraconazole		J02AC02	N	Y	Y
Levofloxacin	Watch	J01MA12	N	Y	Y
Meropenem	Watch	J01DH02	Y	N	Y
Meropenem/vaborbactam	Reserve	J01DH52	Y	N	N
Metronidazole	Access	P01AB01, J01XD01	Y	Y	Y
Moxifloxacin	Watch	J01MA14	N	N	Y
Nitrofurantoin	Access	J01XE01	Y	Y	Y
Norfloxacin	Watch	J01MA06	N	Y	Y
Norfloxacin/Tinidazole		J01RA13	N	N	Y
Ofloxacin	Watch	J01MA01	N	N	Y
Oxytetracycline	Watch	J01AA06	N	N	Y
Phenoxyethylpenicillin	Access	J01CE02	Y	Y	Y
Piperacillin/tazobactam	Watch	J01CR05	Y	N	N
Plazomicin	Reserve	J01GB14	Y	N	N
Polymyxin-B	Reserve	J01XB02	Y	N	N
Procaine benzylpenicillin	Access	J01CE09	Y	N	N
Secnidazole		P01AB07	N	Y	Y
Spectinomycin	Access	J01XX04	Y	N	N
Sulfamethoxazole/Trimethoprim	Access	J01EE01	Y	Y	Y
Tetracycline	Access	J01AA07	N	Y	Y
Tinidazole		P01AB02	N	Y	Y
Trimethoprim	Access	J01EA01	Y	N	N
Vancomycin	Watch	J01XA01	Y	Y	N
Kanamycin	Watch	J01GB04	N	Y	N
Streptomycin	Watch	J01GA01	N	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

