

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.

GABON

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Abbreviations

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| 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 |
| FDC | Fixed-Dose Combination |
| GLASS | Global Antimicrobial Resistance Surveillance System |
| GDP | Gross Domestic Product |
| HICC | Hospital Infection Control Committee |
| HIS | Hospital Information System |
| InSTEDD | Innovative Support to Emergencies, Diseases and Disasters |
| KIIs | Key Informant Interviews |
| LIS | Laboratory Information System |
| LMIC | Low- and Middle-Income Country |
| LQMS | Laboratory Quality Management System |
| MAAP | Mapping Antimicrobial resistance and Antimicrobial use Partnership |
| MCA | Medicine Control Agency |
| MoH | Ministry of Health |
| MRSA | Methicillin-resistant Staphylococcus aureus |
| MTC | Medical Therapeutics Committee |
| NGO | Non-Governmental Organisation |
| OPN | National Pharmaceutical Office |
| 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 |
| SSTI | Skin and Soft Tissue Infections |
| WHO | World Health Organisation |

Executive Summary

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

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

Gabon had approximately 200 laboratories in the national laboratory network during the study period, of which 31 were reported to have bacteriology testing capacity. Based on self-reported information, the functioning and quality compliance practices in 23 laboratories were assessed to understand laboratory preparedness for AMR surveillance.

AMR rates presented are based on an analysis of antimicrobial susceptibility (AST) results of 8 425 positive cultures obtained from 16 laboratories. There were high rates of methicillin-resistant *Staphylococcus aureus* (MRSA) (69-77%) and third-generation cephalosporin-resistant Enterobacterales (40-49%). Antimicrobial-resistant infections were found to be more common in male individuals and persons on prior antibiotics. All results should be interpreted with caution because the participating laboratories were at different levels of service and had variable testing capacities.

AMC is measured as the quantity of antimicrobials sold or dispensed, whereas AMU reviews whether antimicrobials are used appropriately based on additional data such as clinical indicators. Only AMC data were retrievable at the selected sentinel pharmacies. However, AMU data were not obtained due to the lack of unique patient identifiers and tracking systems across hospital departments. The average national total AMC level in Gabon between 2016-2018 was 25.8 defined daily doses (DDD) per 1 000 inhabitants per day, ranging from 26.5 in 2016 to 29.8 in 2017 and 21.0 in 2018. The World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) classification was highest for combinations of penicillins and beta-lactamase inhibitors (range 38.4% to 53.0%), followed by penicillins with extended spectrum (range 11.6% to 16.1%) and fluoroquinolones (range 5.8% to 8.0%).

The top five most consumed antimicrobials were amoxicillin/clavulanic acid, amoxicillin, doxycycline, sulfamethoxazole/trimethoprim and flucloxacillin. Together, these antimicrobials accounted for 76% of the total consumption share, suggesting a lack of variation. This consumption trend could potentially increase AMR. The total AMC included antimicrobials in the 'Access' (82.8%) and 'Watch' (17.2%) categories; none (0.0%) were in the 'Reserve' category. Between 2016-2018, the use of antibiotics in the 'Access' category exceeded the WHO minimum recommended consumption threshold of 60%. Ten combinations of two or more broad-spectrum fixed-dose combinations (FDCs) of antibiotics were identified that were not recommended for clinical utility but were nevertheless consumed in Gabon. Of those, the azithromycin/fluconazole/secnidazole combination was the most consumed (mean DDD per 1 000 inhabitants per day (DID) of 0.1).

The drug resistance index (DRI) is a simple metric based on aggregate rates of resistance and is measured on a scale of 0-100, where 0 indicates fully susceptible while 100 indicates fully resistant. The DRI estimate was found to be high at 65.2% (95% CI, 52.4-77.9%), thus implying low antibiotic effectiveness, which is a threat to effective infectious disease management and calls for urgent policy intervention.

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

- To strengthen the delivery of services by the laboratories, we recommend that all laboratories are mapped across a range of indicators, including population coverage, infectious disease burden, testing capabilities and quality compliance. This would inform decision makers on unmet needs and decide a way forward for the expansion of the laboratory network.
- For high-quality microbiology testing and reporting, it is essential to train staff on laboratory standards, identification of common pathogens and data management. Capacity building of staff may be conducted by leveraging in-house expertise or may be outsourced to external organisations or tertiary facilities.
- To strengthen AMR surveillance, it is essential to curate the right data and generate evidence. We recommend the collection of data in standardised formats at all levels (laboratories, clinics and pharmacies) as well as the use of automation for data analyses. We also recommend establishing a system of assigning permanent identification numbers for patient tracking over time.
- Due to limitations in the number of facilities assessed, MAAP, in alignment with the WHO guide on facility AMU assessment, recommends that future AMU and AMC surveillance attempts in the country be conducted through point-prevalence surveys on a larger scale to give a nationally representative portrait of antimicrobial use in the country.
- MAAP recommends that a comprehensive guiding policy for routine AMC data surveillance is required in the country. The policy should aim to guide on, at the minimum, AMC data reporting variables and routine data cleaning and reporting practices to minimise the amount of time spent standardising and cleaning the data before routine surveillance exercises.
- To make future AMC surveillance more time- and cost-efficient, hospitals could consider switching to electronic systems and ensuring that such systems have the capabilities to transfer data across systems and/or produce user-friendly reports on AMC.
- MAAP recommends that the country's Antimicrobial Resistance Coordinating Committee (AMRCC) should consider introducing facility-level Antimicrobial Stewardship Programmes (ASPs) to regulate the use of these broader spectrum antibiotics and educate prescribers on the importance of reserving them to maintain efficacy.
- From the assessment, an overwhelming majority of antibiotics consumed within the 'Access' and 'Watch' categories were among the top five antibiotics in each category. Such a consumption pattern may be sub-optimal as the evolutionary pressure driving resistance would be focused only on the narrow band of antibiotics consumed. It is therefore recommended that the country's ASP explores ways to ensure a wider spread in the consumption of the antibiotics within each WHO Access, Watch and Reserve (AWaRe) category.
- MAAP recommends an urgent review be conducted by the Ministry of Health (MoH) AMRCC to assess the availability of the 'Reserve' category antibiotics in the country. This may subsequently lead to the revision of the country's essential medicines list (EML) and treatment guidelines to include these vital antibiotics, if deemed necessary. This approach will ensure that the most vital antibiotics are available for all patients.

Overview

The Fleming Fund Grants Programme

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

The Fleming Fund Regional Grants Round 1 Programme

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

Problem Statement

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

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

Mapping Antimicrobial resistance and Antimicrobial use Partnership (MAAP)

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

MAAP's strategic partners included ASLM, the Africa Centres for Disease Control and Prevention, West African Health Organisation 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). ASLM oversaw consortium activities and ensured the fulfilment of ethical considerations and completion of data sharing agreements with the participating countries.

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

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

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

Aim

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

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

Outcome measures

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

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

Key engagements and activities

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

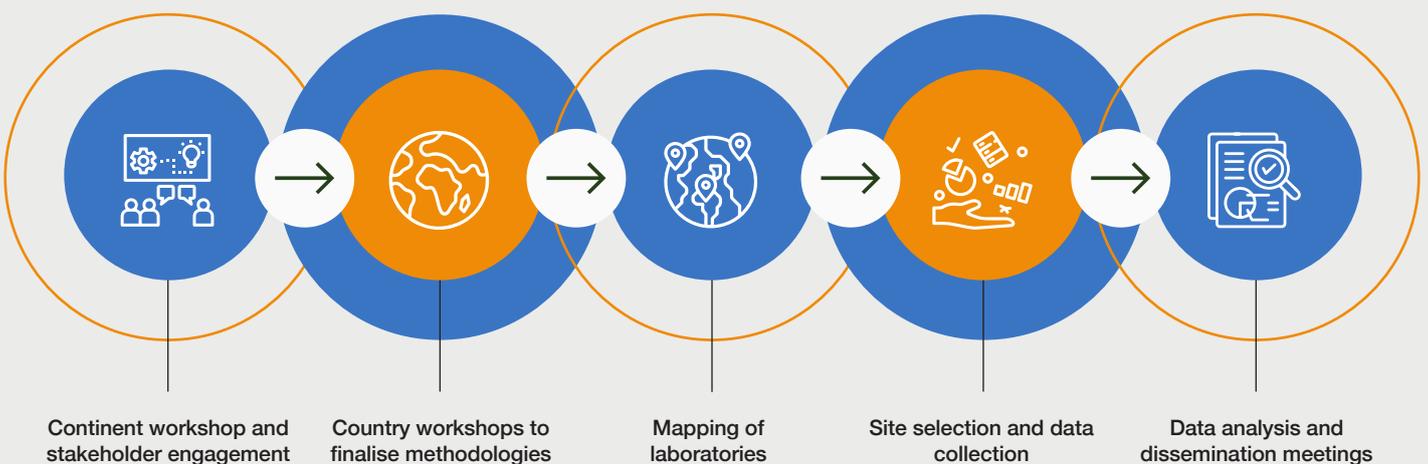


Figure 1: Key engagements and activities

Ethical issues and data sharing agreements

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

Country Profile

Health and demographic profile

As of 2020, Gabon was estimated to have a population of 2.2 million inhabitants and a life expectancy of 67 years. The country has a high infectious disease burden, with a TB incidence of 527 per 100 000 people and an HIV prevalence of 3%. The country has a physician density of 0.68 per 1 000 inhabitants and nurse density of 2.95 per 1 000 inhabitants. With a universal health coverage index of 49, Gabon appears to have an average coverage of essential services (Table 1).

Table 1: Health and demographic profile of Gabon

| Characteristic | Gabon | | Comparator values (most recent year)* | | |
|---|-------|-----------|---------------------------------------|-------------|---------------|
| | Year | Value | India | Argentina | United States |
| Population | 2020 | 2 225 728 | 1 380 004 390 | 45 376 763 | 329 484 123 |
| Life expectancy during the study period, total (years) | 2019 | 67 | 70 | 77 | 79 |
| Universal health coverage service index (0-100) | 2019 | 49 | 61 | 67 | 83 |
| GDP per capita (US dollars [\$]) | 2020 | 6 881.72 | 1 927.7 | 8 579.0 | 63 593.4 |
| Immunisation, DPT (% of children; ages 12-23 months) | 2019 | 70 | 91.0 | 86.0 | 94.0 |
| Incidence of tuberculosis (per 100 000 people) | 2020 | 527 | 188.0 | 31.0 | 2.4 |
| Prevalence of HIV, total (% of population; ages 15-49)# | 2020 | 3 | 0.2* | 0.4 2020 | 0.4 2019 |
| Primary education (%)# | 2019 | 78.43 | 94.6 | 98.6 | 100 |
| Physician density (physicians per 1 000)# | 2017 | 0.68 | 0.93 | 4.0 | 2.6 |
| Nurse density (nurses and midwives per 1 000)# | 2017 | 2.95 | 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 (but sourced from the most recently available information between 2017-2020)

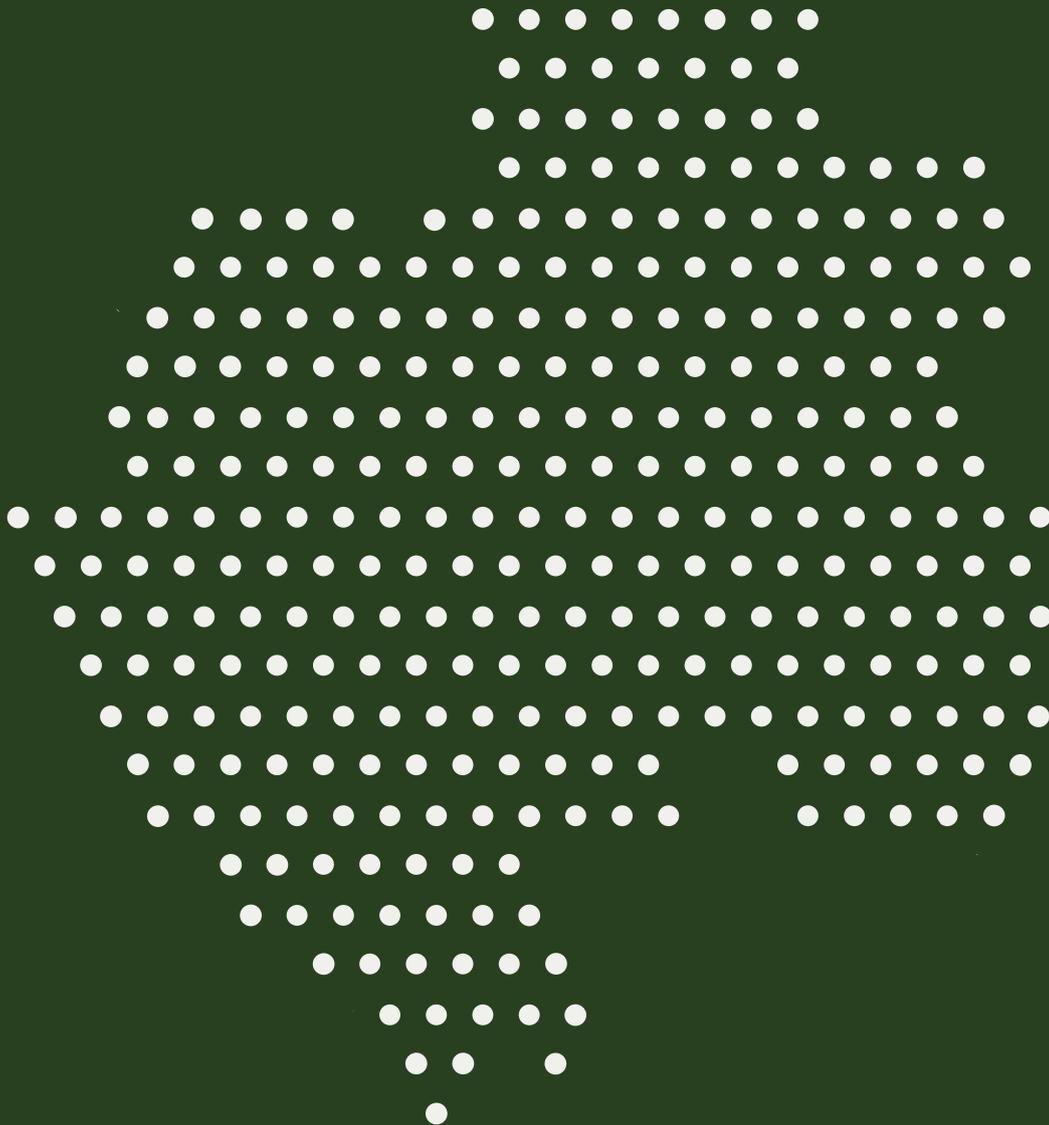
Abbreviations: GDP=gross domestic product

Policy frameworks

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

Gabon enrolled in GLASS in 2019 but has not provided information on the national surveillance to GLASS in any of the data calls.⁹ Gabon also has a national action plan on AMR.

Part A: Antimicrobial Resistance



Section I: Laboratory assessment

Objective

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

Methodology

Initially, up to 16 laboratories (two reference, four private and 10 public) were expected to be included in the study for the purpose of AMR data collection. Ultimately, only those laboratories most likely to guarantee the highest level of data quality were selected. Country-specific circumstances and 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 AST were identified. A survey 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 (AMR Appendix 2). Based on self-reported information on the above parameters, each laboratory was assigned a readiness score for AMR surveillance (AMR Appendix 3). The scoring scheme was standardised across all participating countries. The final selection of laboratories for data collection was made by the MoH and was not necessarily based on laboratory rankings.

Results

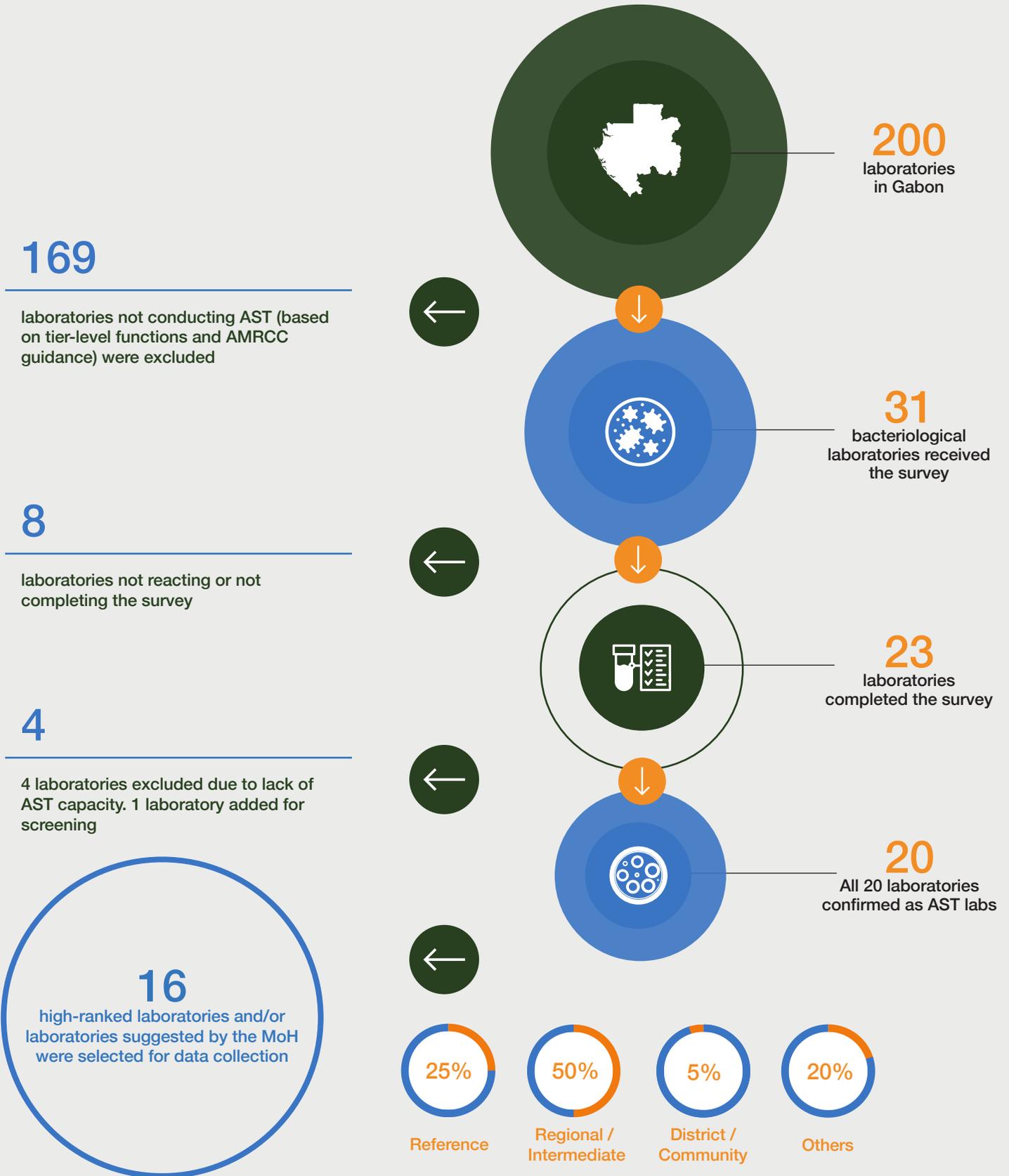
Mapping and selection of laboratories

During the initial stages of in-country work in Gabon, 200 laboratories were mapped to the national laboratory network. An eligibility questionnaire was sent to 31 laboratories identified as having capacity for bacteriology testing. Four of the 23 laboratories that submitted the completed questionnaire lacked AST capacity. 'Laboratoire Appolinaire Essono Ondo' (a large multi-patient facility with AST capability that was strategically located at the border of three countries and consented to data collection) was also included for further screening. Of the 20 laboratories that responded to the questionnaire and had AST capacity, majority were affiliated with the government (Table 2, AMR Supplementary Table 1). The laboratory readiness scores of the surveyed laboratories varied widely (range 10.5–84.2%). 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 | | | |
| Centre de Recherches Médicales de Lambarene (CERMEL) | 84.2 | Regional/Intermediate | Private |
| LAM CIRMF (LAM CIRMF) | 81.6 | Reference | Other |
| Laboratoire de Biologie Médicale (CHU Libreville) | 78.9 | Reference | Government |
| Laboratoire CHU Owendo (CHU Owendo) | 76.3 | Reference | Government |
| CHUMEF Jeanne Eboi (CHUMEF) | 65.8 | Reference | Government |
| Hôpital des Instructions des Armées Akanda (Akanda) | 65.8 | Regional/Intermediate | Government |
| Laboratoire National de Santé Publique (LNSP) | 60.5 | Reference | Government |
| Centre Hospitalier Regional de Tchibanga (CHR Tchibanga) | 57.9 | Regional/Intermediate | Government |
| Laboratoire Cabinet Medical d'Oloumé (d'Oloume) | 52.6 | Other | Private |
| Laboratoire d'analyses médicales de la clinique des Assalás (Assalás) | 52.6 | Regional/Intermediate | Private |
| Laboratoire Appolinaire Essono Ondo (Essono Ondo) | 50 | Regional/Intermediate | Private |
| Laboratoire de Bactériologie Virologie USS (USS) | 44.7 | Other | Other |
| Laboratoire d'Analyses médicales Bioclin (Bioclin) | 39.5 | Regional/Intermediate | Private |
| UNILAB (UNILAB) | 36.8 | District/Community | Private |
| Laboratoire CHR Georges Rawiri (CHR Rawiri) | 28.9 | Regional/Intermediate | Government |
| BIOLAB (BIOLAB) | 26.3 | Other | Private |
| Not selected | | | |
| Laboratoire Polyclinique Dr Chambrier | 52.6 | Other | Private |
| Laboratoire Central d'Analyses Médicales | 47.4 | Regional/Intermediate | Private |
| Laboratoire CHR Paul Moukambi | 39.5 | Regional/Intermediate | Government |
| Hôpital Jean Claude Andrault de Mounana | 10.5 | Regional/Intermediate | Government |

* Laboratory names are abbreviated.

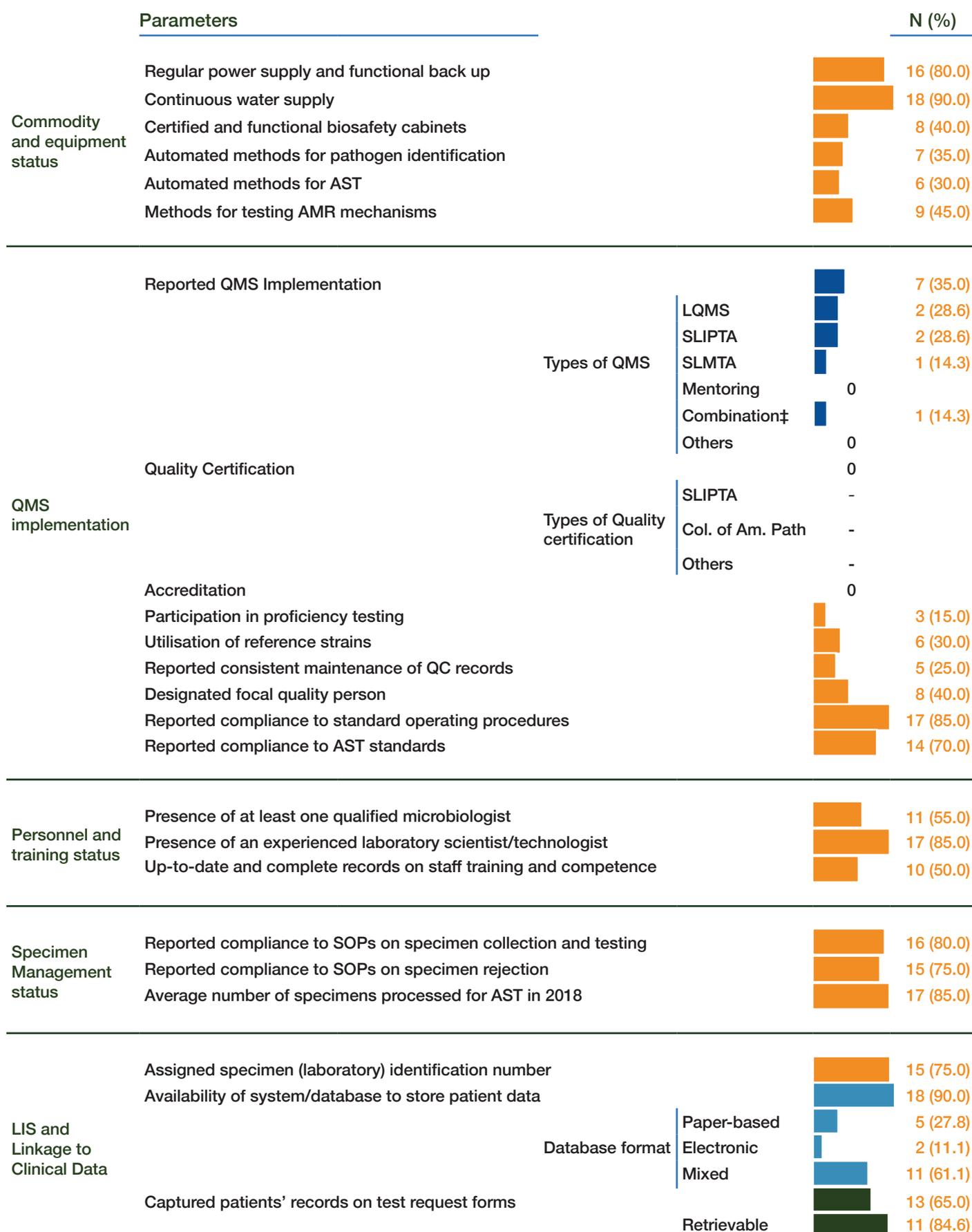


Abbreviations: AST=antibiotic susceptibility testing; AMRCC=antimicrobial resistance coordinating committee; MoH=Ministry of Health

Figure 23: Selection of laboratories in Gabon

Surveillance preparedness of surveyed laboratories

Based on self-reported information from 20 laboratories, laboratory function and quality compliance were assessed to understand their preparedness for AMR surveillance. Seven laboratories had implemented QMS and used automated methods for pathogen identification, but none of them was accredited or certified. Eleven laboratories had at least one qualified microbiologist on board (Figure 3, AMR Supplementary Table 2). Since these findings may affect the quality of laboratory data, the AMR rates presented in this report should be interpreted with caution.

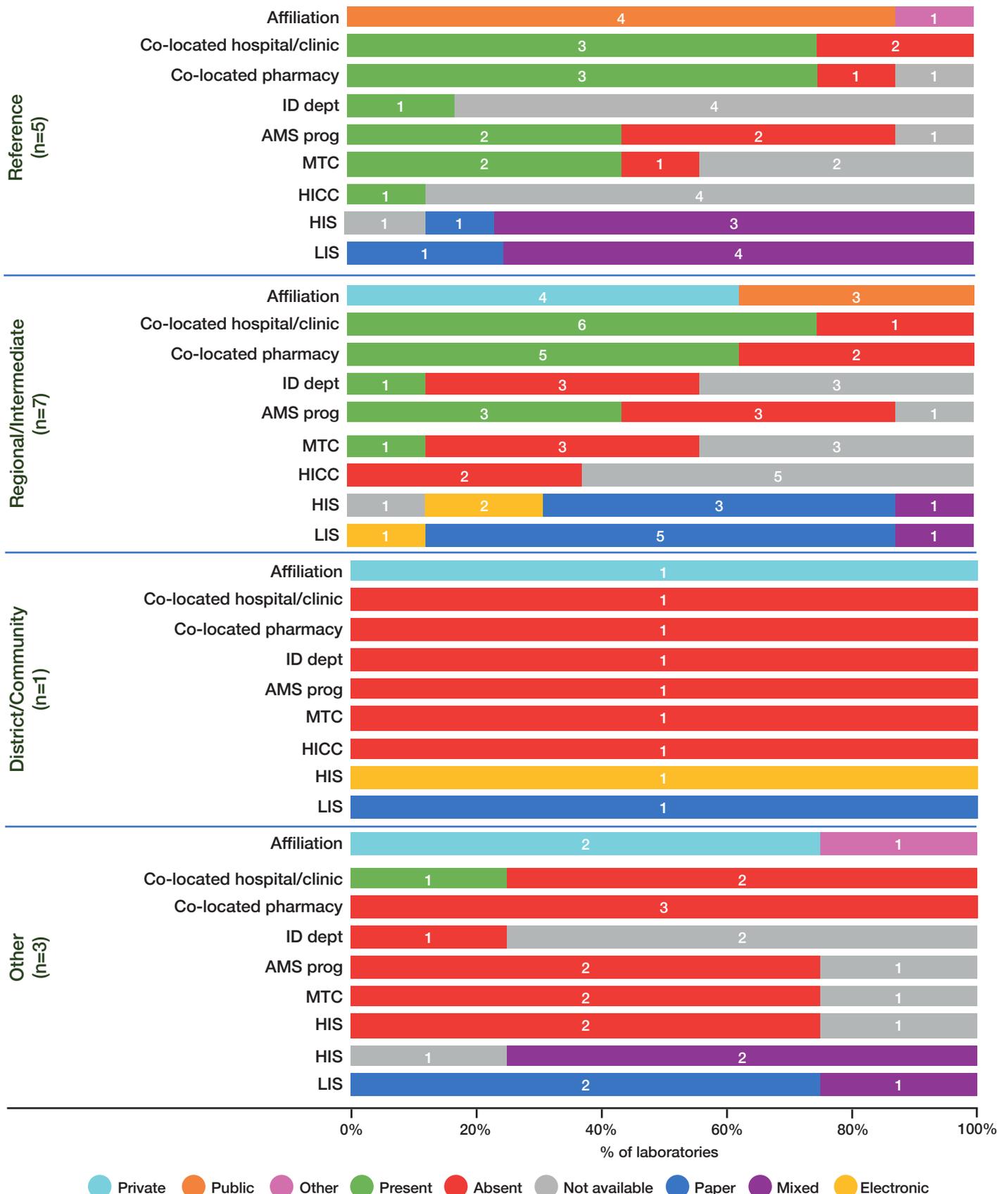


‡ Combination refers to more than one option presented in the questionnaire (laboratory quality management system, stepwise laboratory improvement process towards accreditation, strengthening laboratory management towards accreditation, and mentoring). Abbreviations: AMR=antimicrobial resistance; AST=antibiotic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

Figure 3: Laboratory preparedness for AMR surveillance

Profile of Selected Laboratories

Out of the 16 selected laboratories, 10 were co-located with clinical facilities. Information on the presence of an infectious disease department, a hospital infection control committee and a medical therapeutics committee was not available from all the facilities. Nine laboratories and four hospitals had paper-based information systems (Figure 4).



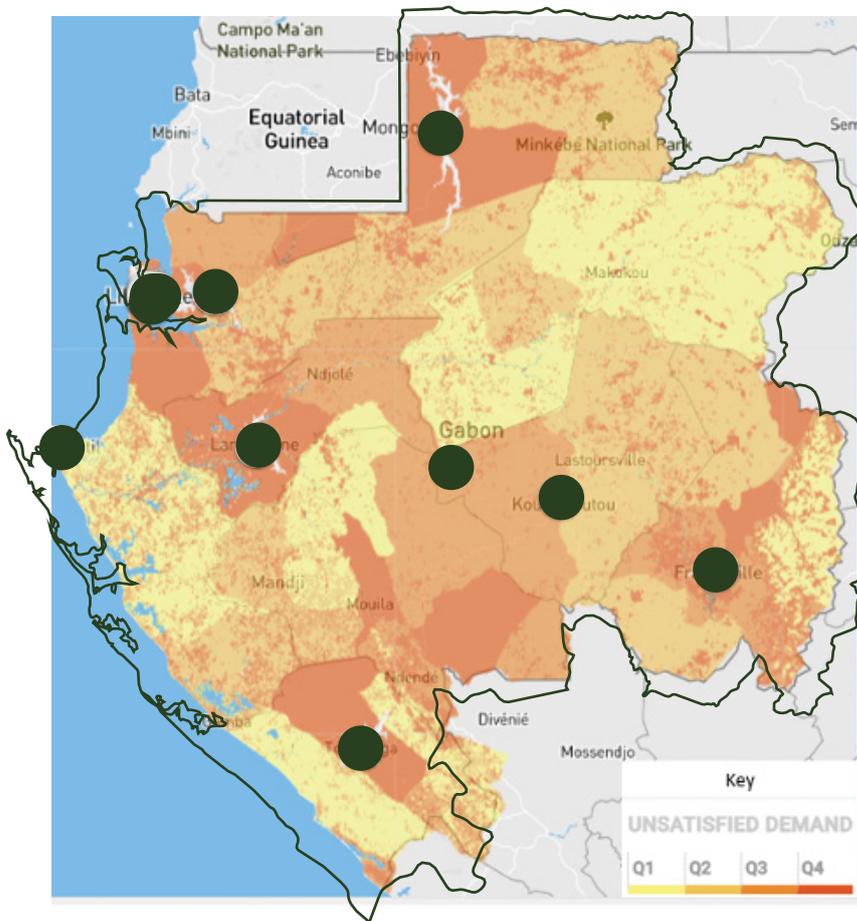
Abbreviations: AMS=antimicrobial stewardship; HICC=hospital infection control committee; HIS=hospital information system; IDD=infectious diseases department; LIS=laboratory information system; MTC=medical therapeutics committee

Figure 4: Profile of selected laboratories

Population coverage of laboratories

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

As of 2020, Gabon had an estimated population of 2.226 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, represents 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 visualize 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 colors (from yellow to dark red see legend). Therefore, color on the map relates to the level of unmet need (people nor in the reach of a facility) relative to the whole population.

Supplementary Figure 1: Population coverage of AST laboratories in Gabon

In Gabon, the catchment population living within one-hour travel time from the 20 participating AMR surveillance sites covers 65% of the population. Hence, 35% of the population is not covered at all by the existing facilities. To increase the population coverage, regions with the highest absolute unmet need (regions in dark red [Q4] should be prioritised. In these regions, new capacity should be introduced either by upgrading an existing laboratory to start providing services or by constructing a new laboratory.

Section II: Collection, analysis and interpretation of AMR data

Objective

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

Methodology

Data collection

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

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

As a first step, the MoH and IQVIA were jointly involved in recruiting local field data collectors. A capacity-building workshop was conducted as part of MAAP to train the field staff on data collection, including the use of WHONET¹⁰ and the specially developed MAAP tool for secure transfer of collected data.

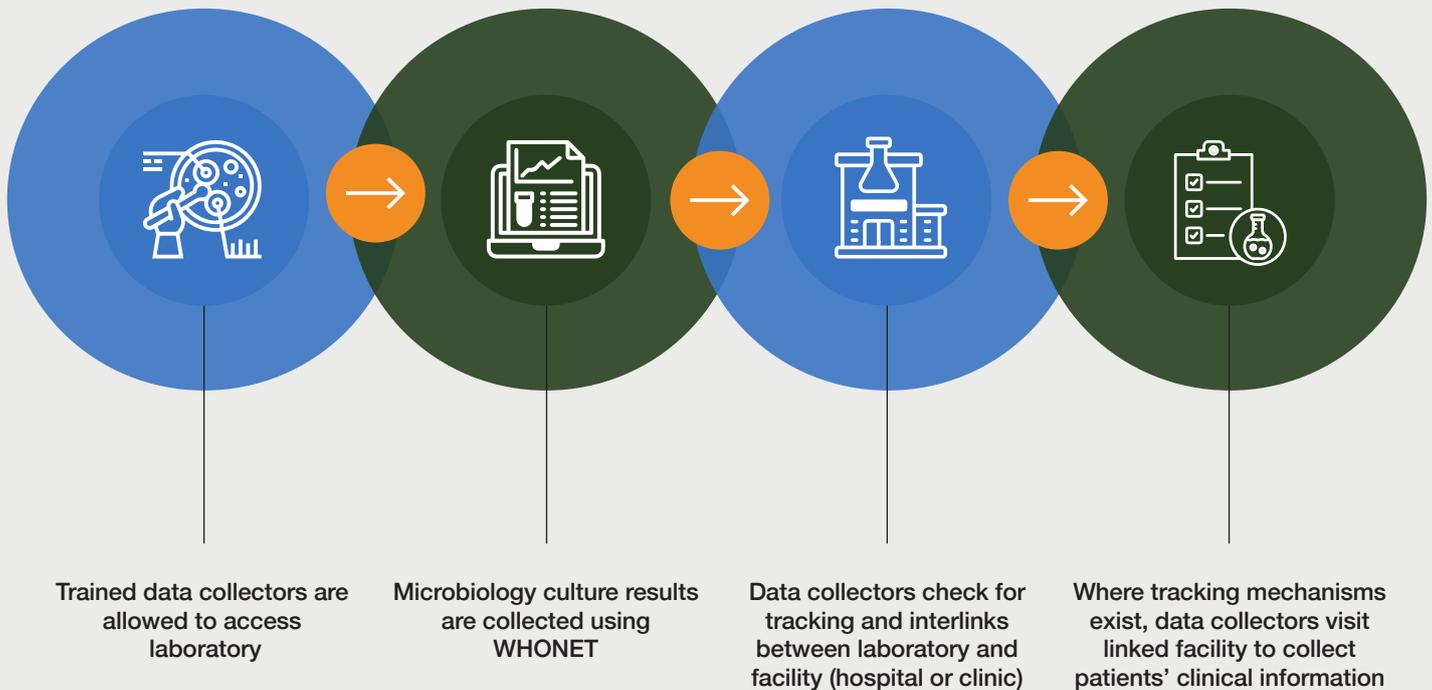


Figure 6: Steps of AMR data collection

Historical data were collected for the period between 1 January 2016 and 31 December 2018. The AMR data were initially captured using 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 that are 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 were transferred onto an online application (repository) for further analysis. Each row of the database represented an individual patient's results. Where the laboratory or hospital issued unique patient identification numbers, it was also possible to track a patient across multiple visits.

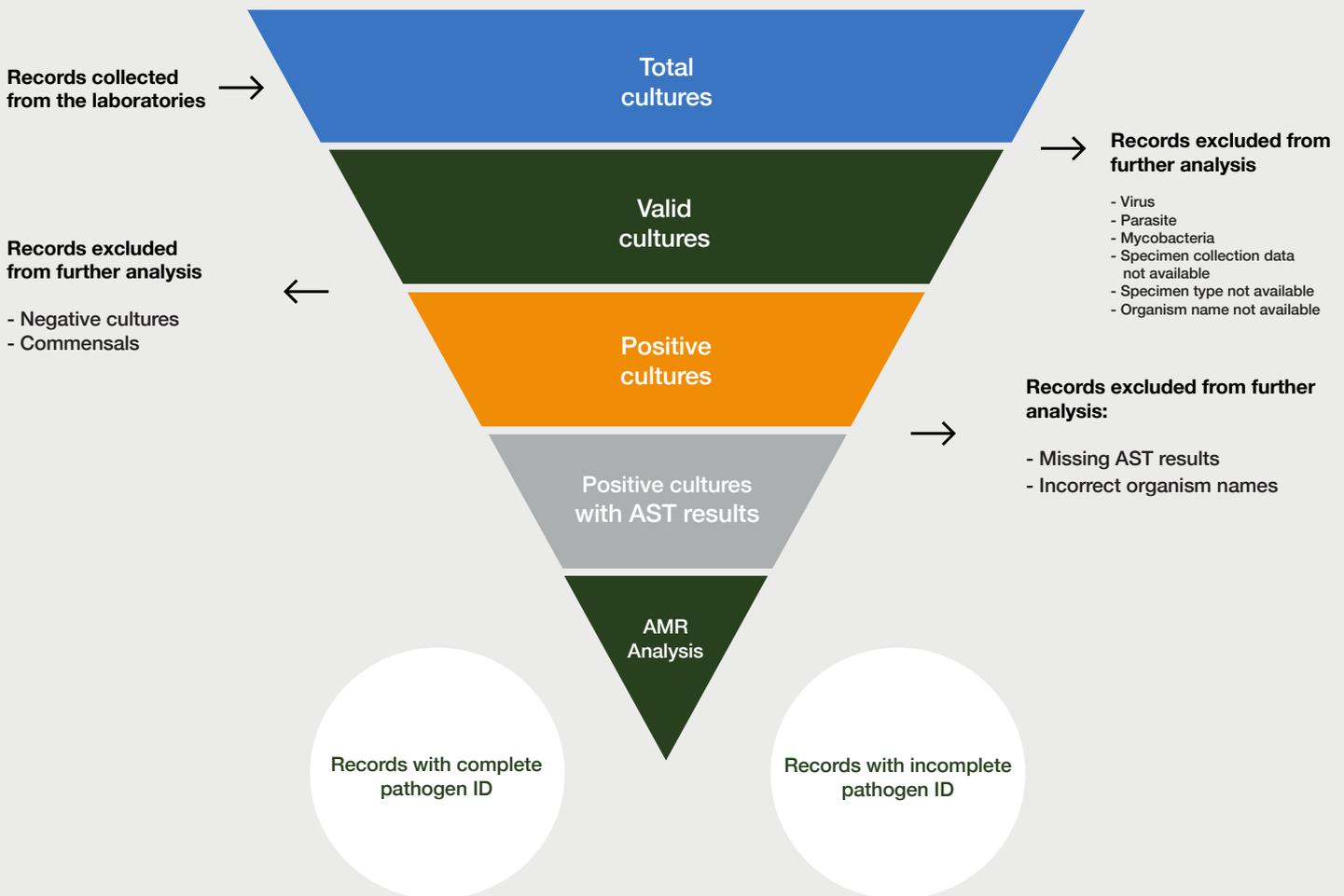


Figure 6: Data collection at a Gabonese facility

Data analysis

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

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



Abbreviations: AMR=antimicrobial resistance; AST=antibiotic susceptibility testing

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

Table 3: Data scoring scheme

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

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

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

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

The maximum attainable score was 4, which corresponds to an 'Excellent' rating (Table 4).

Table 4: Data quality rating

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

Results

Retrospective data from 2016–18 was collected from 16 laboratories and corresponding facilities of Gabon.

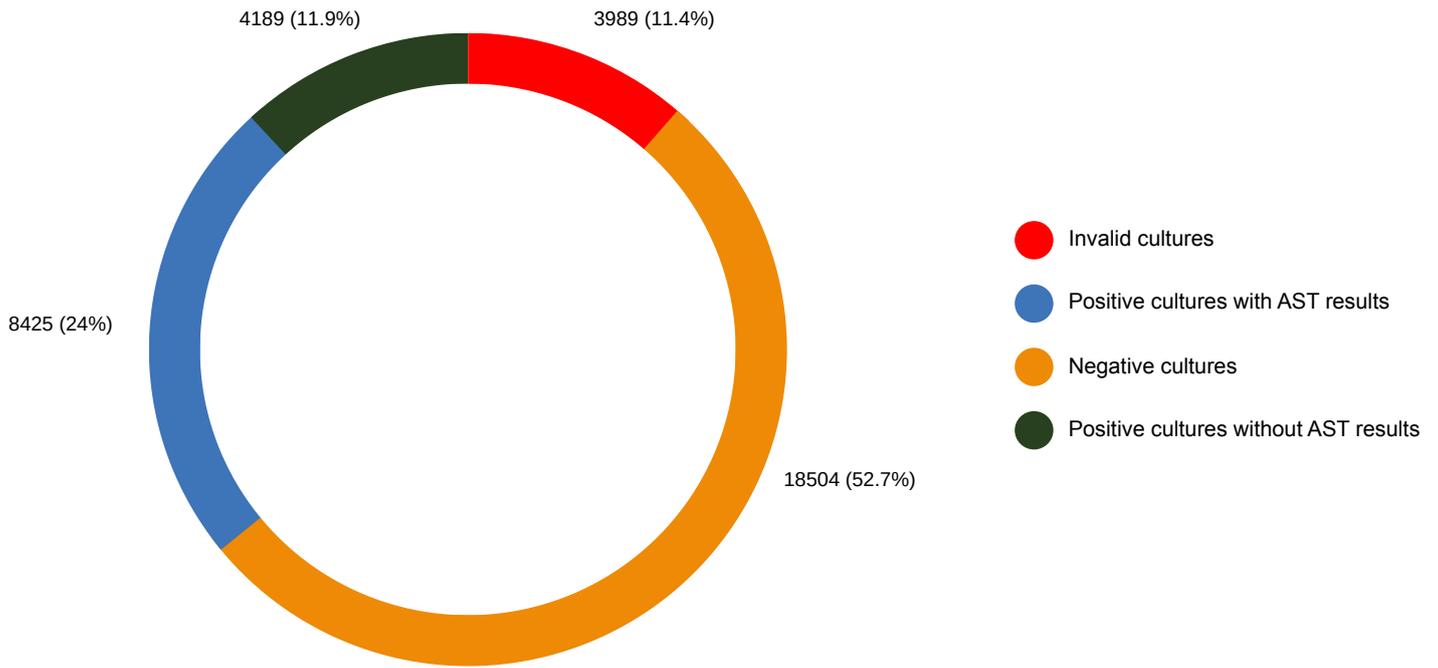
1. Quantum of cultures and level of pathogen identification

Data were retrieved for 35 119 total cultures, of which 31 152 were valid and 12 164 were positive. Of the positive cultures, AST results were available for 8 425 cultures, with the maximum (n=1 476) coming from Bioclin and the least (n=113) from Akanda (Figures 8 and 9). Not all pathogens were identified completely (i.e., at species level). Complete identifications were highest at CHR Tchibanga (99.4%) and lowest at CERMEL (66.7%) (Table 5).

Table 5: Data summary

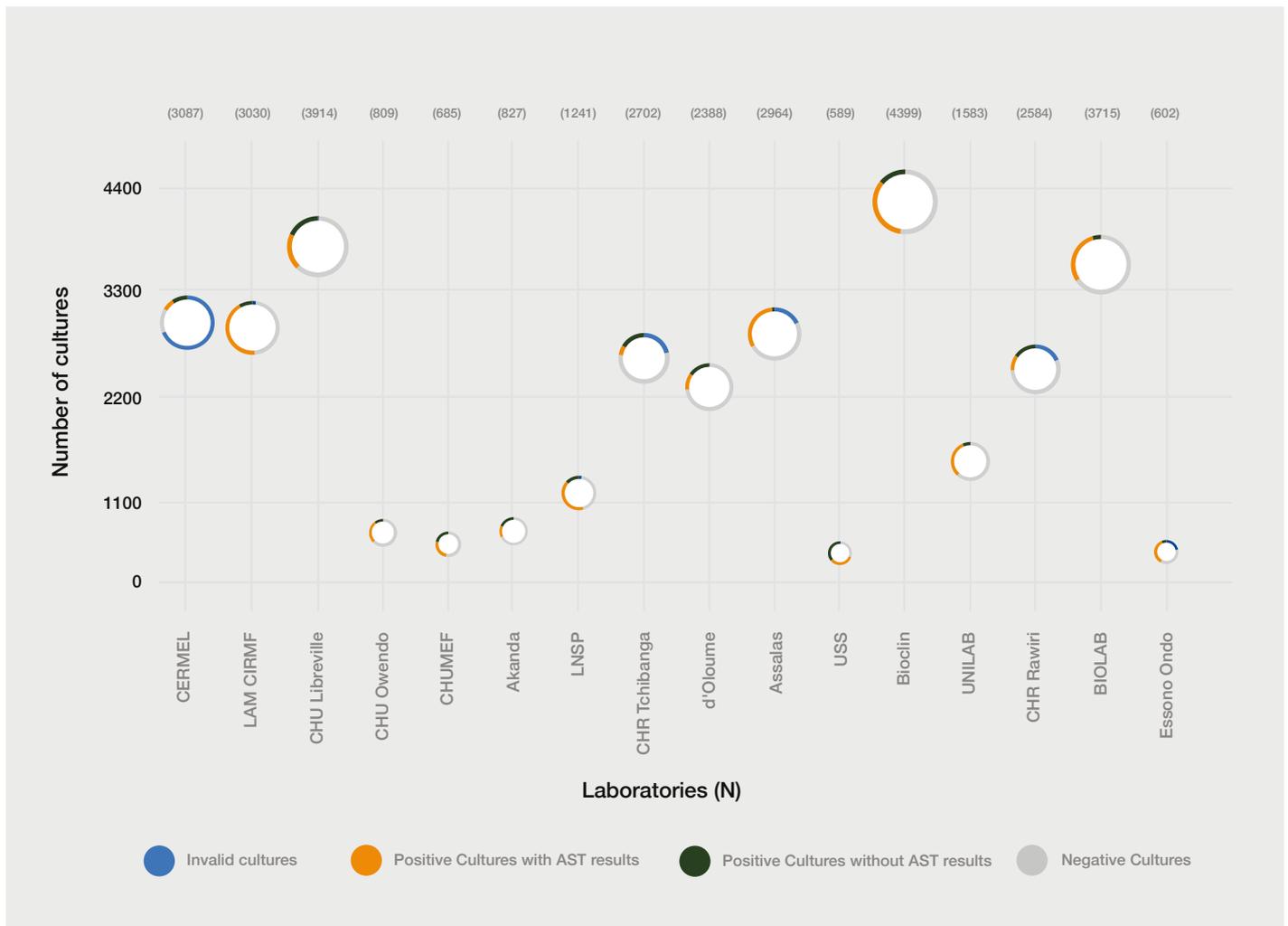
| Variable (Columns) | Total Cultures (N=35 119) | Valid Cultures N=31 152 | Positive cultures N=12 614 | Positive cultures with AST results N=8 425 | Incomplete identity* N=744 | Complete identity* N=7 681 |
|-----------------------|------------------------------|----------------------------|-------------------------------|--|----------------------------------|----------------------------------|
| Laboratory (Rows) | | | | | | |
| CERMEL | 3 087 | 961 (31.1) | 507 (52.8) | 216 (42.6) | 72 (33.3) | 144 (66.7) |
| LAM CIRMF | 3 030 | 2 968 (98.0) | 1 553 (52.3) | 1 302 (83.8) | 34 (2.6) | 1 268 (97.4) |
| CHU Libreville | 3 914 | 3 907 (99.8) | 1 474 (37.7) | 766 (52.0) | 111 (14.5) | 655 (85.5) |
| CHU Owendo | 809 | 807 (99.8) | 299 (37.1) | 216 (72.2) | 5 (2.3) | 211 (97.7) |
| CHUMEF | 685 | 685 (100.0) | 322 (47.0) | 175 (54.3) | 3 (1.7) | 172 (98.3) |
| Akanda | 827 | 827 (100.0) | 266 (32.2) | 113 (42.5) | 18 (15.9) | 95 (84.1) |
| LNSP | 1 241 | 1 207 (97.3) | 671 (55.6) | 507 (75.6) | 50 (9.9) | 457 (90.1) |
| CHR Tchibanga | 2 702 | 2 128 (78.8) | 615 (28.9) | 171 (27.8) | 1 (0.6) | 170 (99.4) |
| d'Oloume | 2 388 | 2 383 (99.8) | 637 (26.7) | 273 (42.9) | 2 (0.7) | 271 (99.3) |
| Assalas | 2 964 | 2 436 (82.2) | 983 (40.4) | 934 (95.0) | 80 (8.6) | 854 (91.4) |
| Essono Ondo | 602 | 470 (78.1) | 254 (54.0) | 217 (85.4) | 20 (9.2) | 197 (90.8) |
| USS | 589 | 583 (99.0) | 408 (70.0) | 196 (48.0) | 16 (8.2) | 180 (91.8) |
| Bioclin | 4 399 | 4 391 (99.8) | 2 091 (47.6) | 1 476 (70.6) | 30 (2.0) | 1 446 (98.0) |
| UNILAB | 1 583 | 1 578 (99.7) | 602 (38.1) | 499 (82.9) | 5 (1.0) | 494 (99.0) |
| CHR Rawiri | 2 584 | 2 108 (81.6) | 660 (31.3) | 262 (39.7) | 33 (12.6) | 229 (87.4) |
| BIOLAB | 3 715 | 3 713 (99.9) | 1 272 (34.3) | 1 102 (86.6) | 264 (24.0) | 838 (76.0) |

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



Abbreviations: AST=antibiotic susceptibility testing

Figure 8: Quantum of cultures across all selected laboratories in Gabon, 2016-2018



Abbreviations: AST=antibiotic susceptibility testing

Figure 9: Quantum of cultures in each selected laboratory in Gabon, 2016-2018

2. Culture characteristics

Bacterial pathogens (8 015) were more commonly reported than fungal pathogens. Information on age was missing from 25.7% of cultures, but where available, the data showed a median age of 32 years (range 0–90 years), with most cultures (4 701) obtained from patients aged between 18–49 years. Female patients (6 701) contributed more to the quantum of positive cultures with AST results. More data came from 2017 (3 005) and 2018 (3 119) than 2016 (2 301) (Table 6, AMR Supplementary Table 3).

Table 6: Characteristics of positive cultures in selected facilities in Gabon, 2016-2018

| Characteristics | Positive cultures with AST results n=8,425 n (%) |
|----------------------|--|
| Gender | |
| Male | 1 709 (20.3) |
| Female | 6 710 (79.6) |
| Unknown | 6 (0.1) |
| Age, years | |
| Less than 1 | 102 (1.2) |
| 1 to 17 | 664 (7.9) |
| 18 to 49 | 4 701 (55.8) |
| 50 to 65 | 499 (5.9) |
| Above 65 | 291 (3.5) |
| Unknown age | 2 168 (25.7) |
| Year of study | |
| 2016 | 2 301 (27.3) |
| 2017 | 3 005 (35.7) |
| 2018 | 3 119 (37.0) |
| Pathogen | |
| Bacteria | 8 015 (95.1) |
| Fungi | 410 (4.9) |

3. Inappropriate testing

Of the 16 selected laboratories, 12 laboratories reported using EUCAST standards for AST testing, while the rest complied with either CLSI or CASFM/EUCAST. However, during the review of AST results, the following instances of inappropriate testing were noted:

- Antifungals were tested against bacteria and antibiotics were tested against fungi (AMR Supplementary Figure 2a)
- The susceptibility of *S. aureus* to vancomycin was determined using the disk diffusion method (AMR Supplementary Figure 2b).

4. Clinical information

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

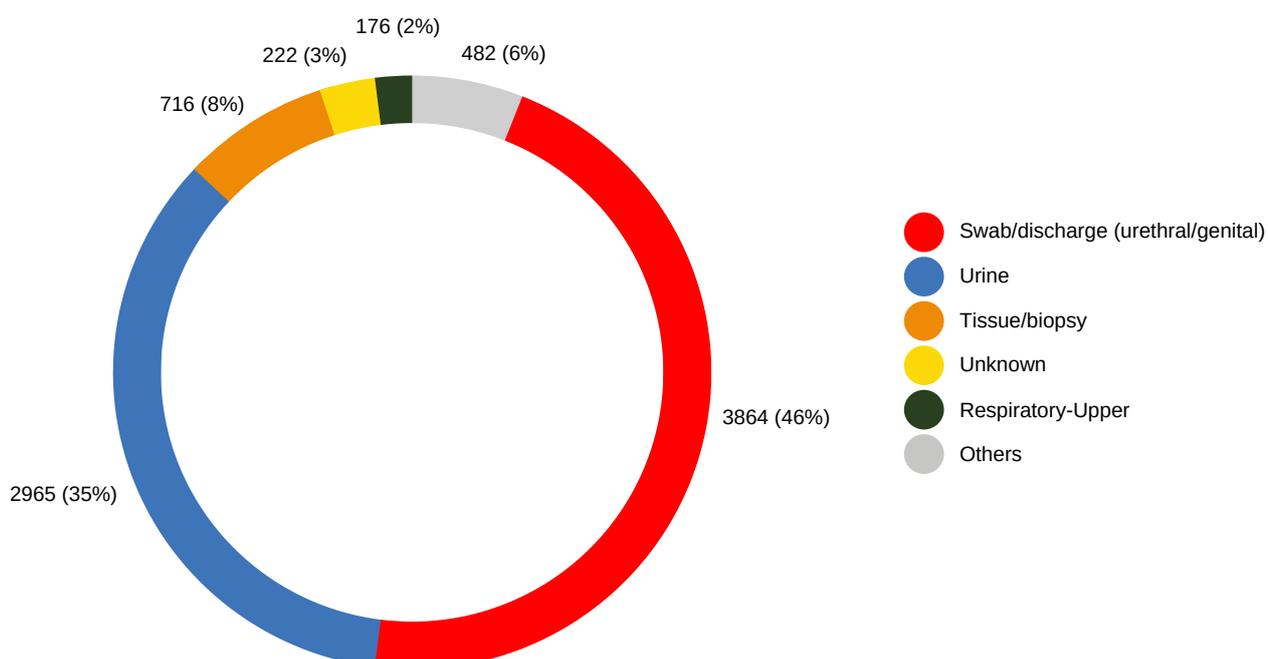
Table 7: Clinical information of patients in selected facilities in Gabon, 2016-2018

| Laboratory | Positive cultures with AST results N=8,425 | Diagnosis data | Infection origin data* | Indwelling device data | AMU data |
|----------------|---|----------------|------------------------|------------------------|----------|
| CERMEL | 507 | - | - | - | 216 |
| LAM CIRMF | 1 553 | 1 | - | - | - |
| CHU Libreville | 1 474 | 4 | - | 10 | 10 |
| CHU Owendo | 299 | - | - | - | - |
| CHUMEF | 322 | - | - | - | 14 |
| Akanda | 266 | - | - | - | - |
| LNSP | 671 | - | - | - | - |
| CHR Tchibanga | 615 | - | - | - | - |
| d'Oloume | 637 | - | - | - | - |
| Assalas | 983 | - | - | - | 21 |
| Essono Ondo | 254 | - | - | - | - |
| USS | 408 | - | - | - | 3 |
| Bioclin | 2 091 | - | - | 8 | 2 |
| UNILAB | 602 | - | - | - | 499 |
| CHR Rawiri | 660 | - | - | - | - |
| BIOLAB | 1 272 | - | - | - | - |

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

5. Specimen distribution

Urethral/genital specimens, urine, and tissue/biopsies accounted for most positive cultures in each study year (Figure 11, AMR Supplementary Table 4).



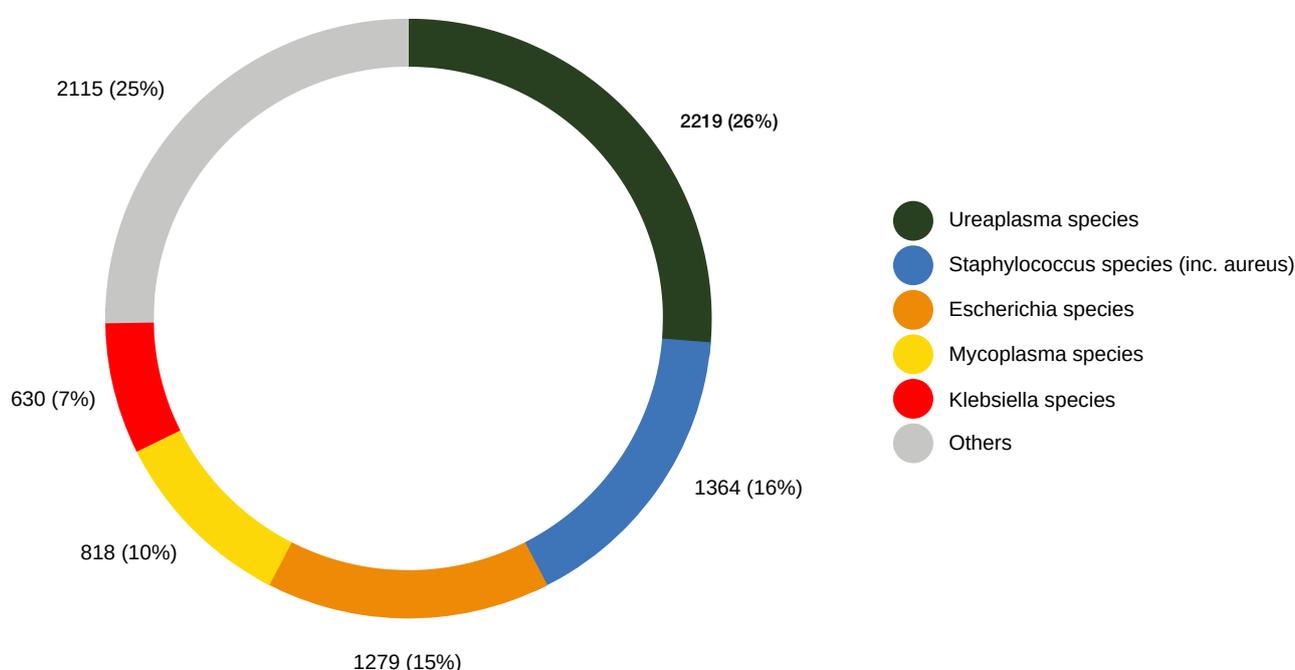
* Others include all other specimens excluding the top 5 mentioned here

Figure 10: Specimen distribution at selected facilities in Gabon, 2016-2018

6. Identified pathogens

Ureaplasma species (26%), Staphylococcus species (16%), Escherichia species (15%) and Klebsiella species (7%) made up most of the quantum of positive cultures (Figure 11).

In 2016, of the 2 301 positive cultures with AST results, Ureaplasma species (22.8%), Staphylococcus species (17.7%), Escherichia species (15.1%) and Mycoplasma species (10.1%) were the most reported. In 2017, of the 3 005 positive cultures with AST results, Ureaplasma species (24.4%), Staphylococcus species (15%), Escherichia species (16.7%), Mycoplasma species (11.6%) and Klebsiella species (8%) were again the most reported. In 2018, information was available for a greater number of cultures (3 119) but the pathogen distribution remained similar to prior years (AMR Supplementary Table 5).



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

Figure 11: Pathogens identified at selected facilities in Gabon, 2016-2018

7. Quality of data

The country data quality score of the 31 130 valid culture records obtained from the 16 laboratories in Gabon was 3.9, corresponding to a 'good' rating for AMR analysis. For individual laboratory data quality scores from each contributing laboratory, see AMR Supplementary Table 6.

Section III: AMR rates

Objective

To estimate the country-level AMR prevalence and trends for WHO priority pathogens and other clinically important and frequently isolated pathogens as well as to enable spatiotemporal mapping of AMR and AMU data across countries.

Methodology

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

Estimation of AMR rates

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

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

AMR rates were estimated for the WHO priority pathogens¹¹ where the number of tested isolates exceeded 30 regardless of the specimen type (AMR Appendix 5). AMR trends were mapped for the WHO priority pathogens depending on data availability.

In addition, AMR rates were estimated for:

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

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

Removal of duplicate records

Before AMR rates were calculated, duplicate AST results were removed such that only the results of the first pathogen isolate per patient per year, irrespective of AST profile (and body site or specimen type in the case of WHO priority pathogens), were included. This approach follows the CLSI M39A4 criteria^{12,13}. The removal of duplicates 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 the AMR rates were calculated as the proportion of non-susceptible isolates.

AMR estimates statistics

Confidence intervals (CIs) at a 95% level of confidence were calculated to quantify the uncertainty in the estimated resistance rates. Typically, CIs for AST data have been constructed using the Wilson score method, which is a binomial calculation that assumes that all samples are independent.¹⁴ However, there may be correlations between data within each laboratory and between laboratories that draw from similar populations. Thus, where appropriate, the Wilson cluster robust CI method was employed to account for a lack of data independence, such that each laboratory represented a cluster.¹⁵

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

Online data visualisation

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

Data were also uploaded to CDDEP's ResistanceMap platform, a publicly available repository of aggregated country-level data.¹⁶ The spatiotemporal analysis of the combined AMR and AMC-AMU datasets was built on the ResistanceMap framework. Current capabilities include maps, trend line charts, and frequency bar charts.

Results

(i) AMR rates and trends for WHO priority pathogens

AMR rates for the WHO priority pathogens were calculated as the proportion of isolates that were non-susceptible over each one-year interval. Across 2016–2018, AMR rates for some organisms remained consistent while the rates for others varied. There were high rates of MRSA (69-77%) and third-generation cephalosporin-resistant Enterobacterales (40-49%). In 2018, there was a high rate of carbapenem-resistant *Pseudomonas aeruginosa* (41%) but the rates of carbapenem-resistant Enterobacterales (11-15%) and carbapenem-resistant *Acinetobacter baumannii* (13%) were lower (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 in Gabon, 2016-2018

| Pathogen | Antibiotic, class | 2016 | | | | 2017 | | | | 2018 | | | |
|--------------------------|---------------------------------|------|------------|-----------|---------------|------|------------|-----------|---------------|------|------------|-----------|---------------|
| | | N | n (%) | 95% CI | Labs* (range) | N | n (%) | 95% CI | Labs* (range) | N | n (%) | 95% CI | Labs* (range) |
| Acinetobacter baumannii | Carbapenems | 24 | 4 | - | 6 (1 - 10) | 38 | 5 (13.2) | 5.8-27.1 | 9 (1 - 17) | 15 | 5 | - | 7 (1 - 5) |
| Pseudomonas aeruginosa | Carbapenems | 19 | 8 | - | 6 (1 - 8) | 27 | 9 | - | 9 (1 - 10) | 32 | 13 (40.6) | 12.5-76.6 | 7 (1 - 14) |
| Enterobacteriales | Carbapenems | 582 | 85 (14.6) | 5.3-34.2 | 13 (9 - 174) | 922 | 99 (10.7) | 5-21.6 | 15 (6 - 233) | 801 | 100 (12.5) | 5.5-25.8 | 15 (1 - 244) |
| Enterobacteriales | Cephalosporins (3rd generation) | 642 | 310 (48.3) | 30.6-66.4 | 14 (1 - 173) | 949 | 381 (40.1) | 26.1-56 | 15 (14 - 234) | 859 | 420 (48.9) | 34.7-63.2 | 15 (2 - 252) |
| Enterococcus faecium | Vancomycin | 1 | 1 | - | 1 (1) | - | - | - | - | 2 | 2 | - | 2 (1 - 1) |
| Haemophilus influenzae | Ampicillin | - | - | - | - | 1 | 0 | - | 1 (1) | 2 | 0 | - | 2 (1-1) |
| Helicobacter pylori | Clarithromycin | - | - | - | - | - | - | - | - | - | - | - | - |
| Neisseria gonorrhoeae | Cephalosporins (3rd generation) | 2 | 0 | - | 1 (2) | 4 | 0 | - | 3 (1 - 2) | 5 | 2 | - | 2 (1 - 4) |
| Neisseria gonorrhoeae | Fluoroquinolones | 2 | 0 | - | 1 (2) | 3 | 1 | - | 2 (1 - 2) | 5 | 2 | - | 2 (1 - 4) |
| Campylobacter species | Fluoroquinolones | - | - | - | - | 1 | 1 | - | 1 (1) | 7 | 6 | - | 1 (7) |
| Salmonella species | Fluoroquinolones | 9 | 3 | - | 5 (1 - 5) | 18 | 8 | - | 8 (1 - 6) | 19 | 9 | - | 7 (1-67) |
| Shigella species | Fluoroquinolones | 3 | 0 | - | 2 (1-2) | 4 | 1 | - | 3 (1 - 2) | 4 | 1 | - | 4 (1 - 1) |
| Staphylococcus aureus | Methicillin | 142 | 109 (76.8) | 44.4-93.2 | 5 (1 - 51) | 130 | 89 (68.5) | 57.5-77.7 | 7 (1 - 48) | 157 | 109 (69.4) | 39.6-88.7 | 7 (1 - 67) |
| Streptococcus pneumoniae | Beta-lactam combinations | - | - | - | - | - | - | - | - | - | - | - | - |
| Streptococcus pneumoniae | Penicillins | - | - | - | - | - | - | - | - | 3 | 3 | - | 1 (3) |

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

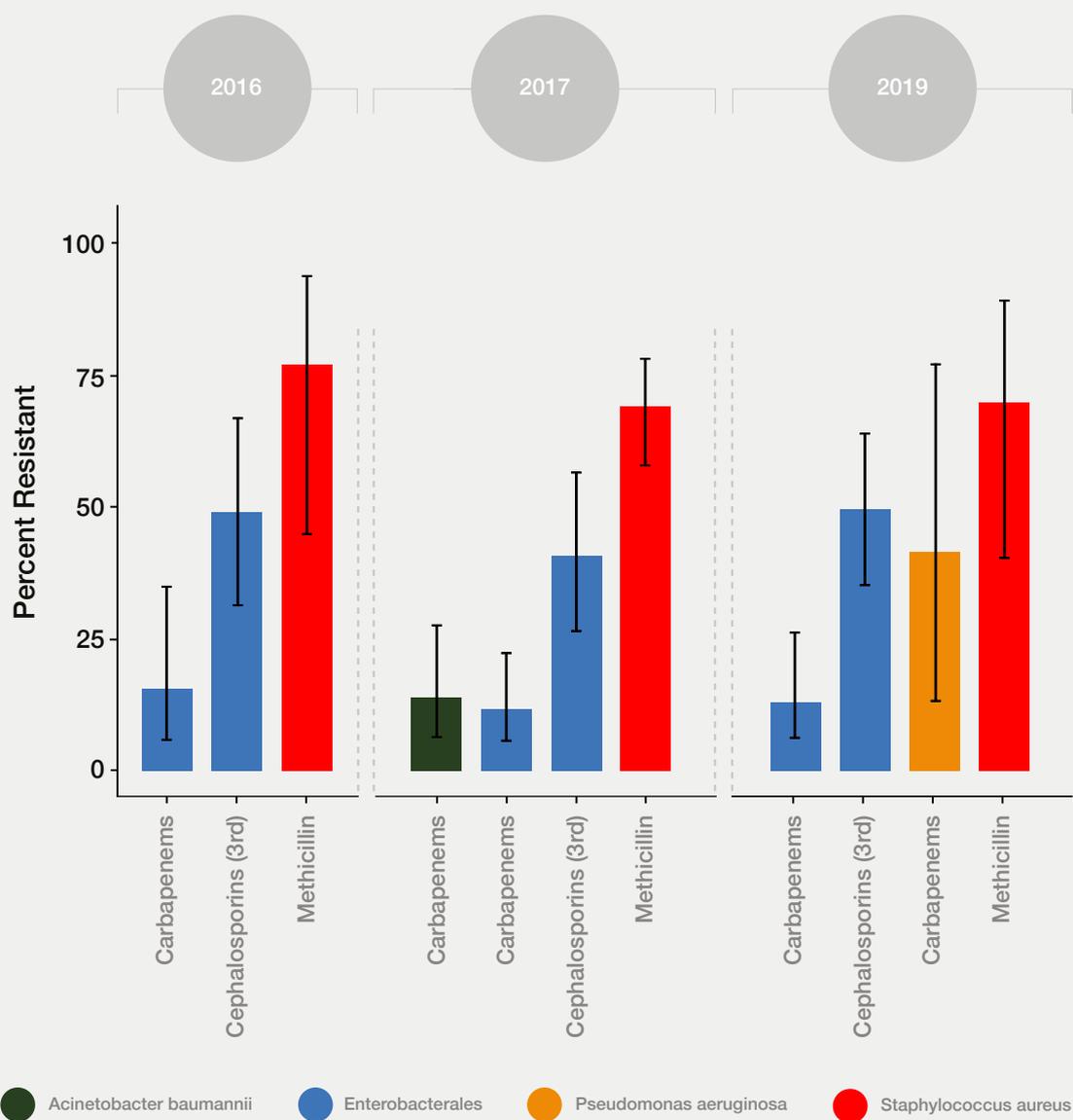


Figure 12: AMR rate estimates for WHO priority pathogens identified at selected facilities in Gabon, 2016-2018

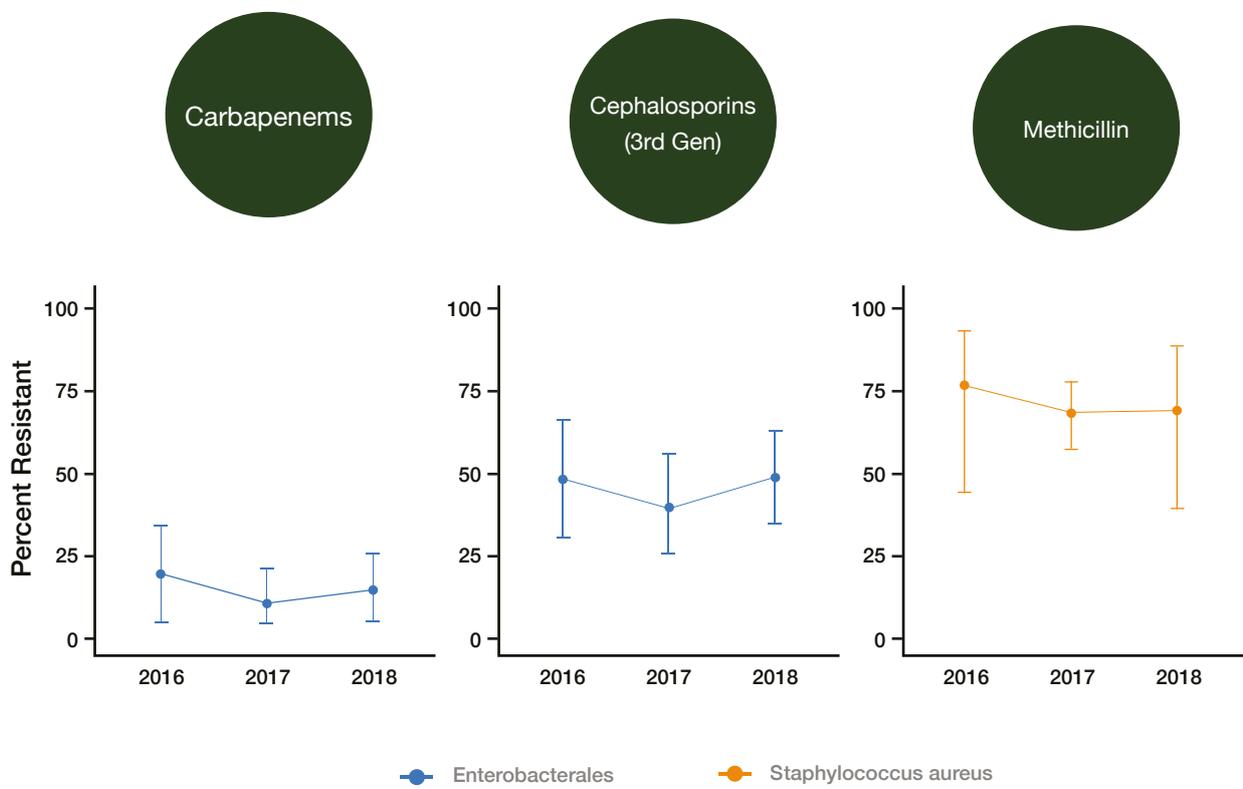


Figure 13: AMR trends for WHO priority pathogens identified at selected facilities in Gabon, 2016-2018

(ii) AMR rates for other pathogens of clinical importance

The available AST data from blood and CSF isolates were insufficient for further analysis (Table 9).

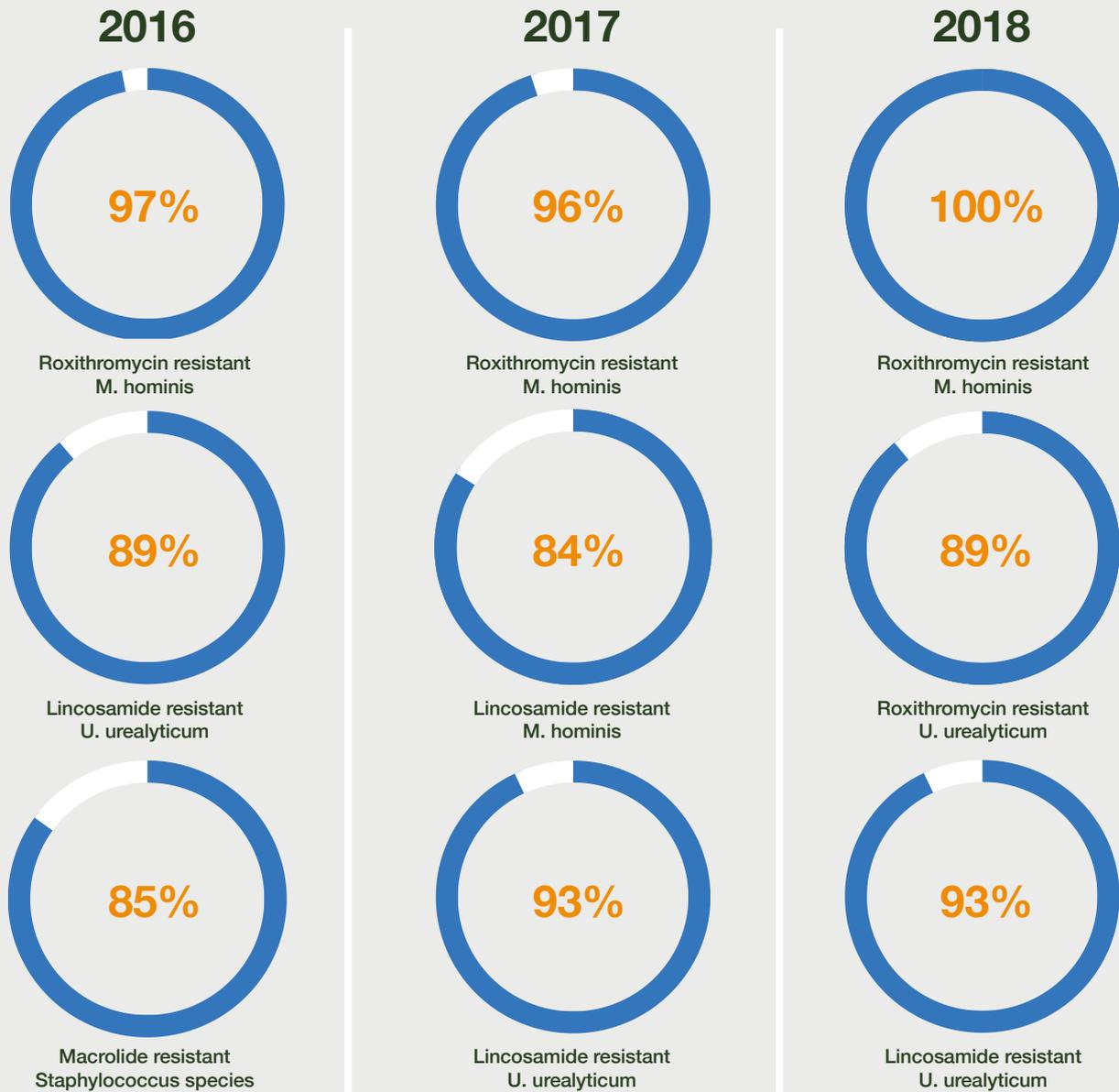
Table 9: AMR rate estimates for other clinically important pathogens* identified at selected facilities in Gabon, 2016-2018

| 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 | - | - | - | - | 1 | 0 | - | 1 (1) | 3 | 1 | - | 2 (1-2) |
| Acinetobacter species | Lipopeptides | - | - | - | - | - | - | - | - | - | - | - | - |
| Enterococcus species | Aminoglycosides (high level) | - | - | - | - | - | - | - | - | - | - | - | - |
| Enterococcus species | Vancomycin | - | - | - | - | - | - | - | - | 1 | 0 | - | 1 (1) |
| H. influenzae | Ampicillin | - | - | - | - | - | - | - | - | 2 | 0 | - | 2 (1-1) |
| H. influenzae | 3 rd generation cephalosporins | - | - | - | - | - | - | - | - | 2 | 0 | - | 2 (1-1) |
| Klebsiella species | Carbapenems | 2 | 0 | - | 1 (2) | 7 | 4 | - | 2 (1-6) | 11 | 4 | - | 2 (2-9) |
| Klebsiella species | Cephalosporins (3 rd generation) | 2 | 2 | - | 1 (2) | 7 | 7 | - | 2 (1-6) | 16 | 13 | - | 2 (3 - 13) |
| N. meningitidis | Ampicillin | - | - | - | - | - | - | - | - | - | - | - | - |
| N. meningitidis | Cephalosporins (3 rd generation) | - | - | - | - | - | - | - | - | - | - | - | - |
| Pseudomonas species | Carbapenems | - | - | - | - | - | - | - | - | 2 | 0 | - | 2 (1-1) |
| Pseudomonas species | Lipopeptides | - | - | - | - | - | - | - | - | - | - | - | - |
| Salmonella species | Fluoroquinolones | - | - | - | - | - | - | - | - | - | - | - | - |
| Salmonella species | Macrolides | - | - | - | - | - | - | - | - | - | - | - | - |
| Salmonella species | 3 rd generation cephalosporins | - | - | - | - | - | - | - | - | - | - | - | - |
| Staphylococcus aureus | Methicillin | - | - | - | - | - | - | - | - | - | - | - | - |
| Staphylococcus species | Methicillin | - | - | - | - | 6 | 2 | - | 2 (1-5) | 13 | 10 | - | 2 (1 - 12) |
| S. pneumoniae | Penicillins | - | - | - | - | - | - | - | - | - | - | - | - |
| S. pneumoniae | Beta-lactam combinations | - | - | - | - | - | - | - | - | - | - | - | - |
| S. pneumoniae | Macrolides | - | - | - | - | - | - | - | - | - | - | - | - |
| S. pneumoniae | Vancomycin | - | - | - | - | - | - | - | - | - | - | - | - |

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

(iii) AMR rates for highly resistant pathogens

Based on the available data, a very high resistance rate (>95%) was estimated for the clinically important pathogen *Mycoplasma hominis* (vs. roxithromycin) (Figure 14).



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

Figure 14: Top five highly resistant pathogens identified at selected facilities in Gabon, 2016-2018

(iv) AMR rates for fungal pathogens

The 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. To determine the association between AMR and its potential drivers, the following patient- and country-level factors were considered:

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

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

Statistical analysis

An initial exploration of the data was done to identify missing information and any collinearity between the patient-level factors (drivers). Logistic regression analyses (univariate and multiple) were performed to determine the association with AMR. The analyses were adjusted for the number of contributing laboratories to account for the variation in the respective laboratory datasets. Crude odd 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 robust standard error was used to construct CIs for the AMR rates.

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

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

Results

Three variables, namely, age, gender and prior antibiotic usage, were evaluated for possible association with AMR. Age data were available for 88.2% of patients, gender data were available for 97.1% and prior antibiotic usage data were available for 9.6%. The univariate logistic regression results showed that patients aged <1 year (OR 1.46, 95% CI 1.09 – 1.93), 50 – 65 years (OR 1.25, 95% CI 1.07 – 1.47) and >65 years (OR 1.24, 95% CI 1.01 – 1.53) were more likely to have resistant infections. In addition, patients with prior antibiotic usage (OR 2.48, 95% CI 1.08 – 5.7) were more likely to have resistant infections (AMR Supplementary Table 7).

Gender and age were included in the multiple logistic regression model based on the set inclusion criteria. When controlling for the effect of age, male patients were more likely to have resistant infections. However, age had no effect on AMR rate when controlling for gender. Furthermore, when controlling for the effects of both age and gender, patients who had prior antibiotic usage (OR 2.83, 95% CI 1.67 – 4.81) were more likely to have resistant infections (Table 10).

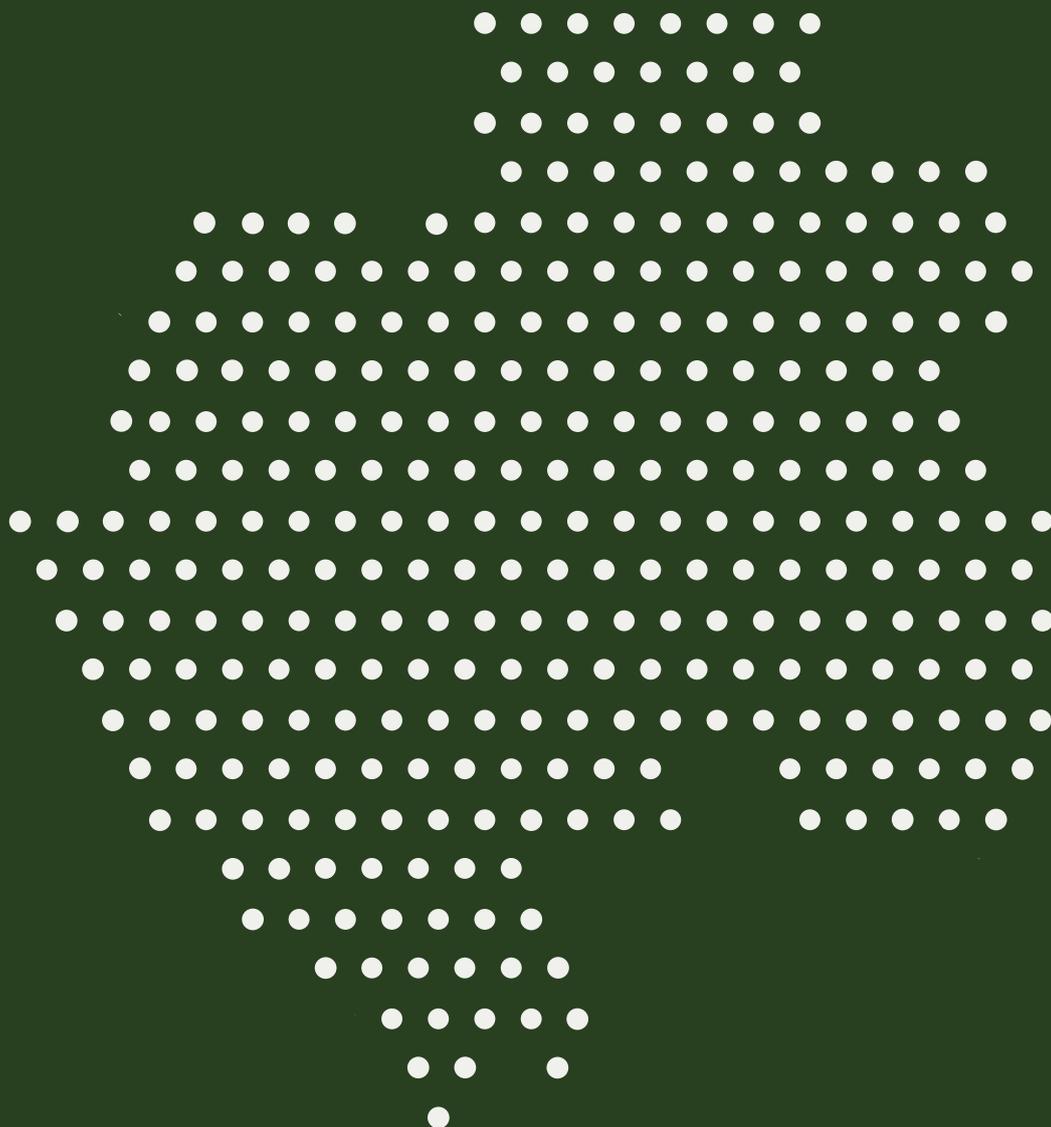
Table 10: Multiple logistic regression analysis

| Variable | Options | N | NS (%) | Adjusted OR (95% CI) | P-value |
|------------------------|---------|------|--------|----------------------|---------|
| Gender | Female | 5613 | 40.6 | Ref | |
| | Male | 1851 | 51.4 | 1.53 (1.30 – 1.79) | 0.0000 |
| Age | <1 | 160 | 50.0 | 1.17 (0.93 – 1.47) | 0.174 |
| | 1-17 | 1086 | 41.1 | 0.88 (0.65 – 1.20) | 0.418 |
| | 18-49 | 4556 | 42.0 | Ref | |
| | 50-65 | 1036 | 47.6 | 1.13 (0.95 – 1.36) | 0.165 |
| | >65 | 626 | 47.0 | 1.10 (0.92 – 1.30) | 0.400 |
| Prior antibiotic usage | No | 264 | 28.0 | Ref | |
| | Yes | 78 | 48.7 | 2.83 (1.67 – 4.81) | 0.000 |

N=number of tested isolates; NS (%)=proportion of non-susceptible isolates; OR=odds ratio; Ref=reference group

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, thus accelerating the development of AMR.^{17,18} Therefore, close surveillance on how antimicrobials are utilised is a key step for stewardship programme to stem AMR. The surveillance mechanisms recommended by the WHO include the monitoring of AMC and AMU. This is in line with MAAP's aims to expand the volume of data on AMR and AMC presently available across Africa as well as with the goals of the country's developed National Strategic Plan for Combating AMR.

Definition of AMC and AMU

AMC is defined as the quantification of antimicrobials used within a specified setting (e.g., at the national, hospital or community healthcare level) over a specified period. AMC is calculated from aggregated data such as import, wholesaler, insurance or facility dispensing or procurement data sources. On the other hand, AMU tracks whether antibiotics are prescribed appropriately, for the right infections and according to treatment guidelines. AMC and AMU are terminologies that are sometimes incorrectly used interchangeably. It is therefore prudent to further clarify that while

AMC data describe the quantities of antimicrobials dispensed (e.g., at national stores or pharmacies), AMU data describe how and why antimicrobials are used (e.g., whether the required laboratory tests and clinical assessments were done before issuing a prescription, whether the right antibiotic was prescribed at the correct strength and frequency and over an appropriate duration to treat the right indication as per country guidelines, and whether the patient correctly or completely consumed the prescribed antimicrobial).¹⁹

Link between the antimicrobial usage and AMR

The unwarranted use of antimicrobials contributes to the development of AMR and explains the link or association between antimicrobial use and AMR. This association implies that a reduction in the unnecessary consumption of antimicrobials could in turn affect resistance rates.¹⁹ The inappropriate use of antimicrobials refers to the use of the wrong type of antimicrobial and/or at the wrong dose, frequency or duration and/or for the wrong indication. 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 as a result of a lack of access to antimicrobials, particularly in LMICs where there are inequities in access to antimicrobials.²⁰ This complicated picture demonstrates the need for the research and development of new agents that counteract emerging AMR, as well as the need to ensure that the available antimicrobials are accessible and used appropriately.

To obtain a comprehensive picture of the link between AMU or AMC and AMR in Gabon, it is important to identify prevalent gaps and areas needing targeted intervention to improve AMC and AMU surveillance and encourage the rational use of antimicrobials. In this regard, one of MAAP's key objectives was to evaluate the ability to conduct AMC and AMU surveillance (data collection and analysis) in Gabon that would equip the country with valuable information to support the appropriate use of antimicrobials. The objective was to identify gaps that may exist in 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

To ensure the successful treatment of infectious diseases in patients, optimising antimicrobial usage is one of the strategic objectives of the WHO Global Action Plan (GAP).⁸ For the successful implementation of this objective, there is a need to understand the patterns of antimicrobial use and quantities of antimicrobials consumed in different countries. At present, there are only a few published reports on AMC surveillance and AMU in Africa.²¹⁻²⁵ Obtaining AMC or AMU data provides local information on the various problems that exist with antimicrobial use and allows for the monitoring of the accessibility of antimicrobials. Further, obtaining AMC or AMU data permits a continuous local assessment of correlations between antimicrobial usage and emerging local AMR, thus allowing the design of proper mitigation policies and activities using relevant data. In addition, local surveillance data can better inform stewardship programmes. Therefore, MAAP set out to analyse AMC and AMU trends at selected facilities and the national level to better inform the design of future stewardship programmes, policies and regulations with the purpose of optimising the use of antimicrobials in Gabon. In addition, this will provide the country with a reference point to measure the impact and success of these implemented interventions.

The aim of this work

1.

Describe the in-country antimicrobial flow and highlight the status of the AMC and AMU surveillance system in Gabon

2.

Quantify and evaluate the trends of AMC and AMU at the national and pharmacy levels

Section II: AMC or AMU surveillance status

Objective

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

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 the best sources of national AMC data. The national AMC data for Gabon was obtained from the public sector central purchase store (the National Pharmaceutical Office [OPN] data) and from the private sector, i.e., IQVIA™ datasets, which include data from private for-profit distributors and wholesalers.

Under the guidance of the Gabon AMRCC, MAAP aimed to recruit and obtain the data from twice as many pharmacies as the selected AST laboratories (i.e., a total of 32 pharmacies). We aimed to collect pharmacy-level AMC data from pharmacies that were co-located in the same facility with the AST laboratories (n=16) (see AMC Appendix 2 for the tool used). Additionally, we recruited community pharmacies (n=16) that were nominated by the co-located pharmacies based on their proximity to the AST laboratories and/or the fact that these community pharmacies serve as the preferred patient purchase source or a backup prescription fulfilment source in case of stock-outs in the main hospital pharmacy. Furthermore, the availability of retrospective data from 2016-2018 and willingness to share the data were key criteria considered during selection.

In addition to AMC data, AMU data were to be obtained for the (n=16) hospital pharmacies and this was to be retrieved from the prescription or patient medical records at each facility. To clarify, community pharmacies, which are also known as retail pharmacies, are licensed commercial pharmaceutical stores that provide medicinal products (prescription-only and over-the-counter medicines) to a specific community group or region; this does not include unregulated and informal medicine dispensers. Hospital pharmacies, on the other hand, are pharmacies that are located within hospitals and provide or supply medicinal products to inpatients and outpatients who visit the hospital.

Data collection scope

The MAAP scope purposively aimed to collect data on J01 (antibiotics for systemic use) consumption trends. J01 medicines are one of the WHO core monitoring anatomical therapeutic and chemical (ATC) drug categories for AMC surveillance. In addition, as per the country's request, selected P01AB (nitroimidazole derivatives) and selected J02 (antimycotics for systemic use) were also included in the scope for AMC data collection (See AMC Appendix 3 for the full list of selected antimicrobials in Gabon). P01AB and J02 ATC drugs are part of the WHO core and optional monitored drug classes respectively for AMC surveillance.²⁶ AMC data on these medicine categories were collected from January 2016 to December 2018.

Data collection

The national-level datasets from OPN and the syndicated IQVIA™ datasets were requested for the data collection period (2016-2018) from the OPN staff and the IQVIA™ Gabon data team, respectively. The datasets were provided to the local supervisor in a Microsoft Excel™ sheet. The data collection team reviewed and cleaned the datasets in an Excel™ sheet and securely transferred the datasets through the MAAP tool that captured all medicines by their standard molecule name and/or product brand, pack size, strength and formulation (e.g., tablets or capsules, suspensions or syrups). AMC Appendix 4 captures the full list of data variables collected to tally national- and pharmacy-level AMC.

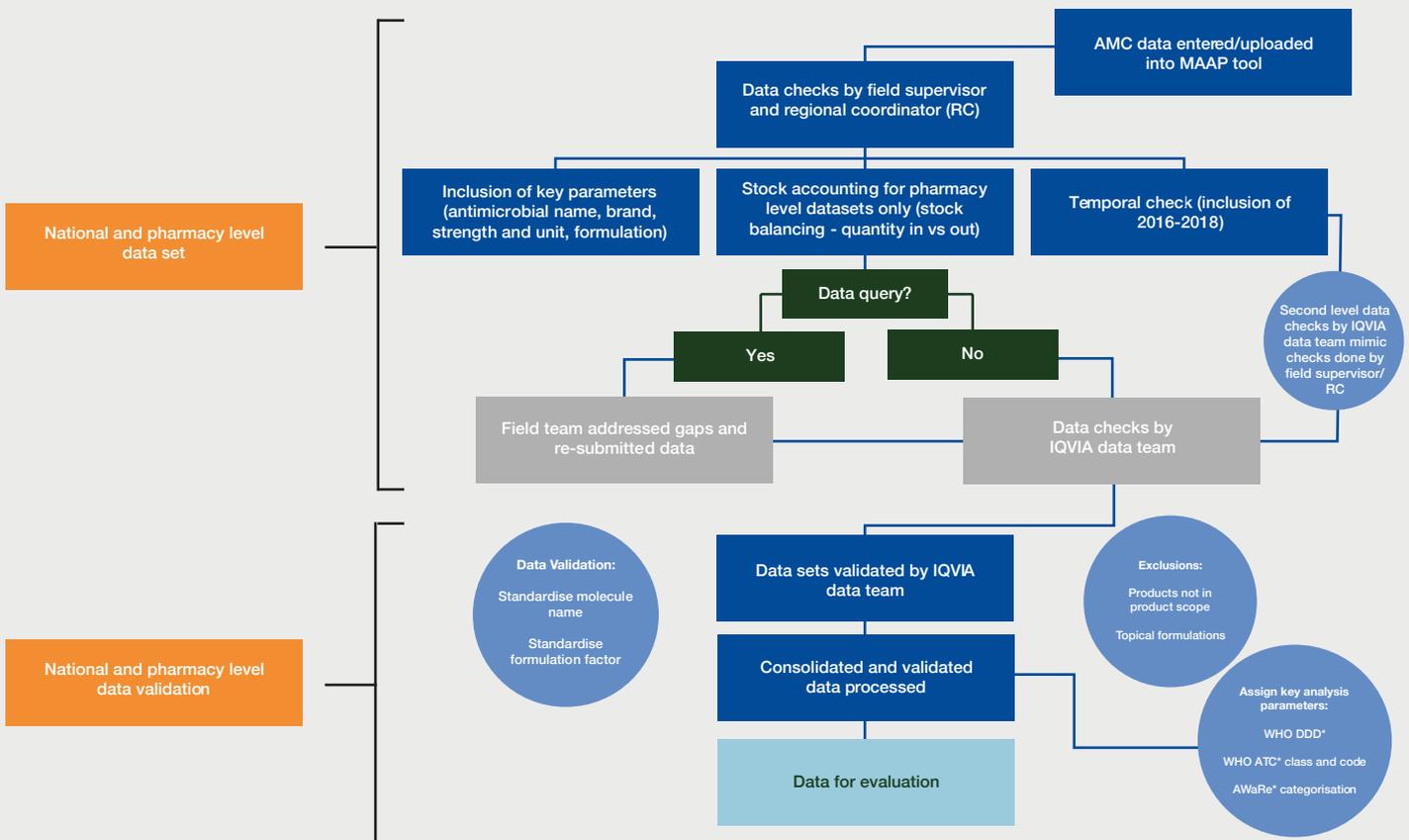
For electronic pharmacy-level data, the trained MAAP data collectors extracted the consumption data from the facility's Hospital Information System (HIS) into a Microsoft Excel™ sheet. Abstracted data from stock record cards at facilities with manual records were manually entered into the MAAP tool. 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).

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

Data cleaning and validation

The national-level antimicrobial OPN datasets (as provided from the syndicated IQVIA™ datasets) were extracted from the system and provided to the regional coordinator for processing. Once the IQVIA and OPN datasets were received by MAAP, the national- and pharmacy-level AMC data were then subjected to a series of data validation checks to ensure accuracy and consistency (Figure 15).

Here, pharmacy- and national-level AMC data were subjected to secondary and tertiary checks by field supervisors, regional coordinators and the IQVIA data team. These checks involved ensuring that key variables were complete (e.g., antimicrobial strength and formulation), that net AMC stocks consumed were accurate (i.e., stock received balanced against quantity dispensed) and that standard molecule names were used throughout different data collection sites. The validation and processing of the data were carried out by the regional coordinator and the IQVIA data team.



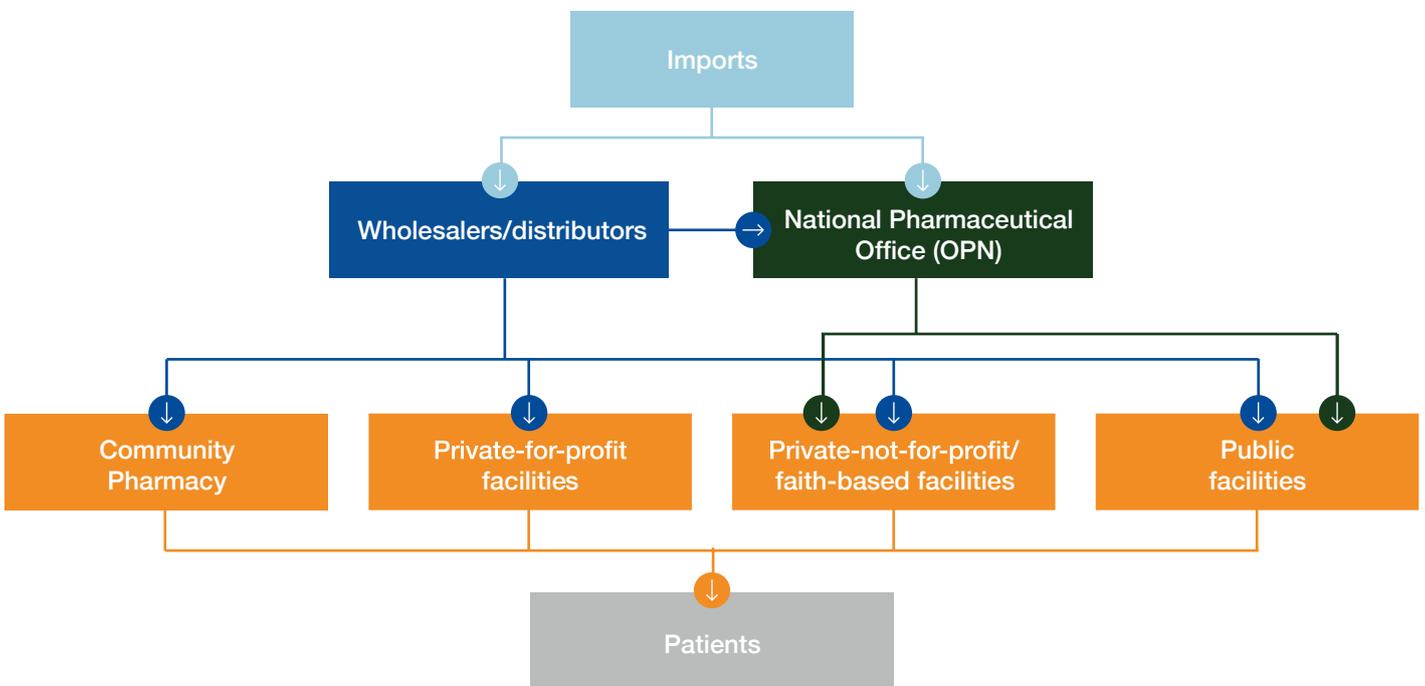
*DDD Defined Daily Dose - *ATC - Anatomical Therapeutic Chemical *AWaRe - Access, Watch and Reserve

Figure 15: Flow chart of the data checks and validation processes for national- and pharmacy-level AMC data collected in Gabon

Results

Flow of antimicrobials in the country

To characterise the pathway through which antimicrobials get to patients in the country, a total of five KIIs were conducted with stakeholders in the national AMRCC, the Directorate of Medicine and Pharmacy, the Medicine Control Agency (MCA), the OPN and the private for-profit wholesaler, UBIPHARM. The MCA is the pharmaceutical regulatory body that controls all imports of medicines, including antimicrobials, in Gabon. All importers must first obtain an import permit from the MCA before medicines are allowed into the country (AUDA-NEPAD, 2019). There were no local medicine manufacturers in the country during the reviewed period (i.e., 2016-2018). In Gabon, all medicines including antimicrobials, are purchased through imports, which is managed by the OPN. The proportion of antimicrobials purchased by public health institutions accounts for 95% of the OPN's antimicrobial stocks. On the other hand, the private sector is supplied by external central purchasing agencies and accounts for approximately 5% of the medicines consumed after purchase from the OPN. After purchase, private for-profit wholesalers and private not-for-profit distributors then pass the antimicrobials to the community pharmacies, private (both for-profit and non-profit) facilities and public facilities who eventually issue antimicrobials to the patients (Figure 16).



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

Figure 16: The flow of antimicrobials to patients in Gabon.

Regulation of antimicrobials consumption

The MCA regulates medicines in Gabon and acts as the pharmaceutical licensing agency. The overuse and misuse of antimicrobials are significant contributors to the emergence of AMR in the country. The WHO global action plan on AMR recommends that countries' ministries of health coordinate the development of policies or guidelines to optimise the use of antimicrobials.⁸ This will help prevent the emergence of AMR and, where possible, halt the rising AMR levels. However, no such policies or guidelines were existing in Gabon. Furthermore, several attempts were made to locate Gabon's National Action Plan for combating AMR.

Availability of data for AMU surveillance

Attempts were made to obtain AMU data from participating pharmacies that were co-located with AST laboratories in facilities offering clinical services (n=6). However, no AMU data were obtained during the MAAP data collection because the participating pharmacies used stock issuance record cards that do not track which patient specifically received what medicines. MAAP was thus unable to retrieve AMU variables (i.e., patient characteristics, the indication for which the antimicrobial was prescribed and the appropriateness of the prescription in relation to national guidelines) from the selected health facilities in Gabon.

Availability of data for AMC surveillance

National-level data

The national AMC data were obtained from the OPN and syndicated IQVIA™ Gabon datasets as sourced from the wholesalers/distributors and for the period of review (2016-2018). During this period, OPN was involved in the purchase of all medicines imported into the country and no medicines were manufactured locally. The resultant national data collected and analysed represented approximately 100% of the total antimicrobials market during the reviewed period (2016-2018). During data collection, it was discovered that OPN purchased medicines once every two years. Therefore, the MAAP data team only collected OPN data from 2017, as no medicines were purchased during the other years targeted for data collection (i.e., 2016 and 2018). The IQVIA datasets were available for each year targeted for data collection (i.e., 2016, 2017 and 2018).

Facility-level data

Out of the 16 targeted pharmacies co-located in the same facility with AST laboratories, data were successfully collected in only six targeted hospital pharmacies. Eight pharmacies were excluded due to being stand-alone laboratories (i.e., without a co-located hospital pharmacy) and a further two were excluded due to the unavailability of data for the study period. A total of 10 pharmacies were thus not recruited. Consequently, to approach the target sample size (n=32), MAAP set out to recruit three community pharmacies from the recruited hospital pharmacies (n=6). Hence, 26 community pharmacies nominated by the recruited hospital pharmacies were targeted. Of these, MAAP successfully recruited 18 community pharmacies and reached the saturation of community pharmacies in the country. As the total number of hospital/community pharmacies in Gabon was unknown, the representativeness of the data at the facility level could not be assessed.

In the case of pharmacy-level data, the necessary variables were available in the stock cards or electronic records of 24 pharmacies where the data were collected. However, there were instances in each of the visited facilities where the strength or pack size information for a few line items or transactions was missing from the stock cards. 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 six hospital pharmacies, MAAP was able to collect data across the three years in five pharmacies; only one participating hospital pharmacy did not have archived data for 2016. Out of the 18 community pharmacies, MAAP was able to collect data across the three years in 10 pharmacies. The remaining eight facilities did not provide data for 2016 and 2017 as they either did not have archived data in their systems or declined to share the data.

In relation to the six hospital pharmacies that were co-located with the AST laboratories, five were in public government hospitals and one was in a military hospital (Table 11). Additionally, among the public government hospitals, one was a tertiary care hospital, while the remaining five were secondary care facilities. Furthermore, due to the lack of any national AMC surveillance policy or structured AMC surveillance system during the reviewed period, none of the recruited pharmacies actively reported AMC data regionally or centrally.

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

| | Pharmacy Name | Level of Service [#] | Affiliation | Region | Record keeping* | Pharmacy system directly linked to patient records **† | AMC reporting* |
|---|--|-------------------------------|-------------|-------------|-----------------|--|----------------|
| Hospital pharmacies (colocated with AST laboratories) ~ | Centre Hospitalier Régional Georges Rawiri | Secondary care | Public | Lambaréné | Manual | No | No |
| | Centre Hospitalier Régional de Tchibanga | Secondary care | Public | Tchibanga | Manual | No | No |
| | Hôpital d'instruction des armées Omar Bongo Ondimba de Melen | Tertiary care | Military | Libreville | Manual | No | No |
| | Polyclinique Chambrier | Secondary care | Public | Libreville | Manual | No | No |
| | Centre Hospitalier Universitaire de Libreville | Secondary care | Public | Libreville | Manual | No | No |
| | Centre Hospitalier Universitaire de Owendo | Secondary care | Public | Libreville | Manual | No | No |
| | Pharmacie Privée le Menaye | Dispensing | Private | Franceville | Electronic | N/A | No |
| Community pharmacies~ | Pharmacie centrale de Port gentil | Dispensing | Private | Port-Gentil | Electronic | N/A | No |
| | Pharmacie des Batsiengui | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Akewa | Dispensing | Private | Lambaréné | Electronic | N/A | No |
| | Pharmacie Ada | Dispensing | Private | Oyem | Electronic | N/A | No |
| | Pharmacie d'Akebe | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie des Orchidées | Dispensing | Private | Libreville | Manual | N/A | No |
| | Pharmacie Razel | Dispensing | Private | Freetown | Electronic | N/A | No |
| | Pharmacie du Carrefour de la SGA | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Sotega de Truffault | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Jeanne et Leo | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Nouvelle Arambo | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie le Mais | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Mukemussialy | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie du commissariat central | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie le Forestier | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Albert Schweitzer | Dispensing | Private | Libreville | Electronic | N/A | No |
| | Pharmacie Magalie Pascal | Dispensing | Private | Libreville | Electronic | N/A | No |

* For the review period, i.e., 2016-2018; 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

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

~Hospital pharmacies refer to pharmacies located within a hospital for the provision of medicinal products to inpatients and outpatients that visit the hospital. Community pharmacies or retail pharmacies refer to commercial pharmaceutical stores that provide medicinal products (prescription-only and over-the-counter medicines) to a specific community group or region.

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

Objective

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

Methodology

Statistical analysis

Data analysis for MAAP was conducted according to the WHO's protocol for conducting AMC analysis using the DDD-ATC-AWaRe methodology (AMC Appendix 6, Figure 17).^{26,27} Each of these WHO methodologies as well as the additional analysis conducted are briefly described below. In addition, and where possible, associations were drawn between AMC and AMR. Details of this analysis can be found in Part A, Section II:3c.

i. Defined Daily Dose (DDD)

DDDs and related metrics are used to analyse AMC. The DDD metric helps in standardising the different doses (in milligrams) of different antibiotics used in managing infections to allow easy comparisons. Also, it is recommended to use drug utilisation figures such as DDD along with a relevant denominator for the health context such as numbers of DDDs per 1 000 inhabitants per day, DDD per inhabitant per year or DDDs per 100 bed days. Studying DDDs or associated metrics over time helps to understand the consumption pattern or determine if any national- or facility-level interventions have led to a change (+/-) in the consumption patterns over the study period or a pre-defined base period.

Using the 2020 DDD guide, the total consumed milligrams per antimicrobial were divided against the standard DDD value issued by the WHO to obtain total DDDs.²⁸ Total DDDs were then adjusted for the country's population size (Worldometer, 2020) and presented as DDDs per 1 000 inhabitants per day (DID). Pharmacy-level AMC data were to be adjusted as DDD per number of inpatients and presented as DDD per 100 patient bed days. However, the use of the WHO DDD per 100 patient bed days presented limitations at the point of analysis as patient bed days was not an appropriate denominator to use across the pharmacy-level AMC datasets. In addition, for most of the hospital facilities, information on patient bed days and patient days was not easily accessible. Secondly, this metric would not allow a comparison of hospital pharmacy consumption and community pharmacy consumption as in the latter, the patient bed days metric is not applicable. Therefore, the AMC pharmacy-level data were presented as absolute DDD to aid comparisons between hospital and community pharmacies. All calculations were done using the Microsoft Excel™ software.

ii. Anatomic Therapeutic Chemical (ATC) Classification

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

iii. WHO Access, Watch and Reserve (AWaRe)

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

We stratified the total DDDs per antibiotic molecule into 'Access', 'Watch' or 'Reserve' categories in accordance with the 2019 WHO AWaRe list using Microsoft Excel™. The total DDDs in each WHO AWaRe category were then analysed to determine the proportion of antimicrobials consumed per category over time (yearly and monthly), where possible. The WHO recommends that at least 60% of a country's total AMC should come from the 'Access' category of antibiotics. In addition, we determined the top five antibiotics consumed in each WHO AWaRe category.

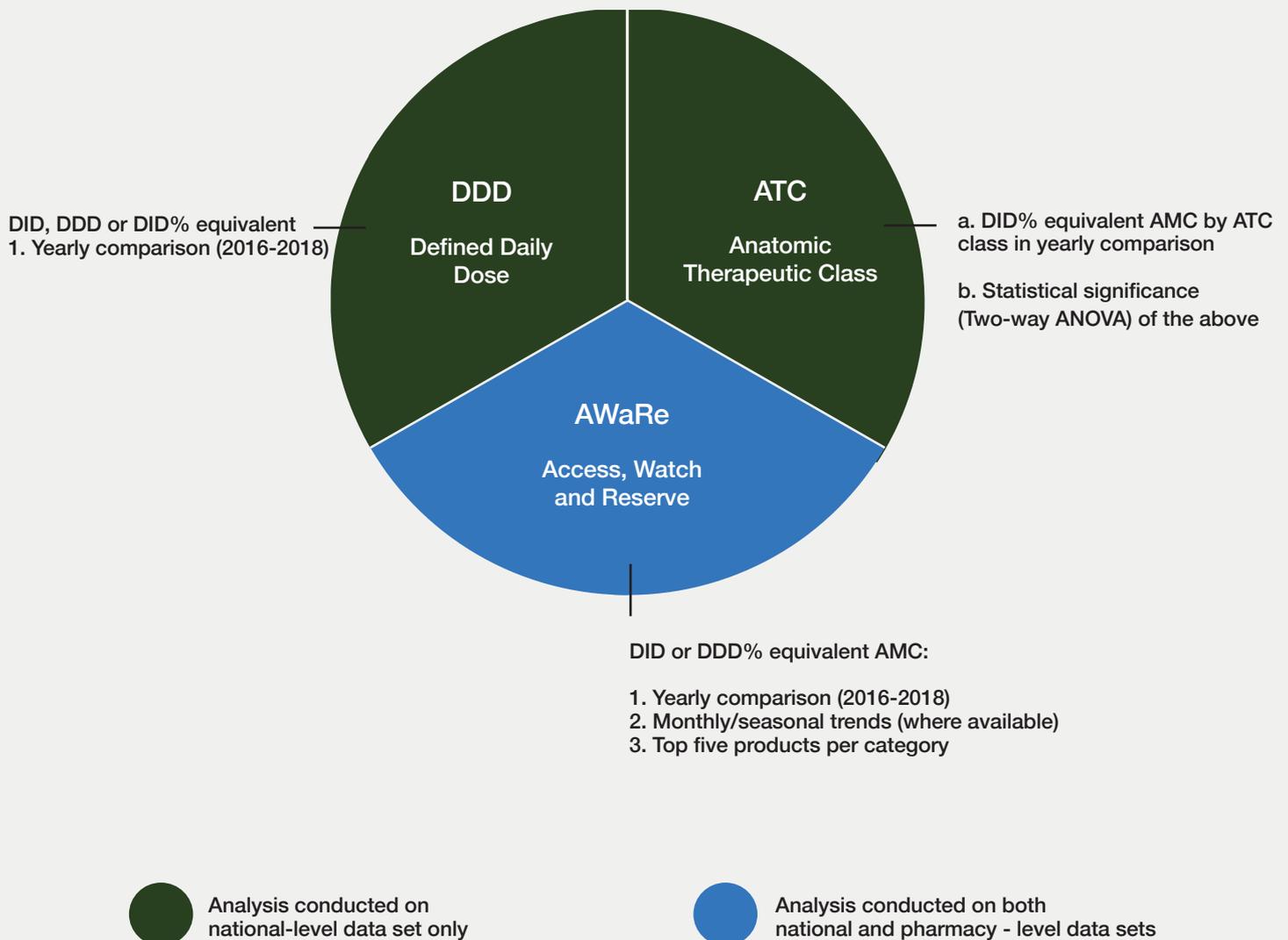


Figure 17: Methods and indicators used for the analysis of the data collected in Gabon. The defined daily dose (DDD) indicators utilised for volumetric standardisation were sourced from WHOCC 2020. The ATC Classification utilised to categorise the antibiotics according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties was sourced from the WHOCCC ATC database. The 'Access', 'Watch' and 'Reserve' categorisation was sourced from the 2019 WHO AWaRe classification²⁸

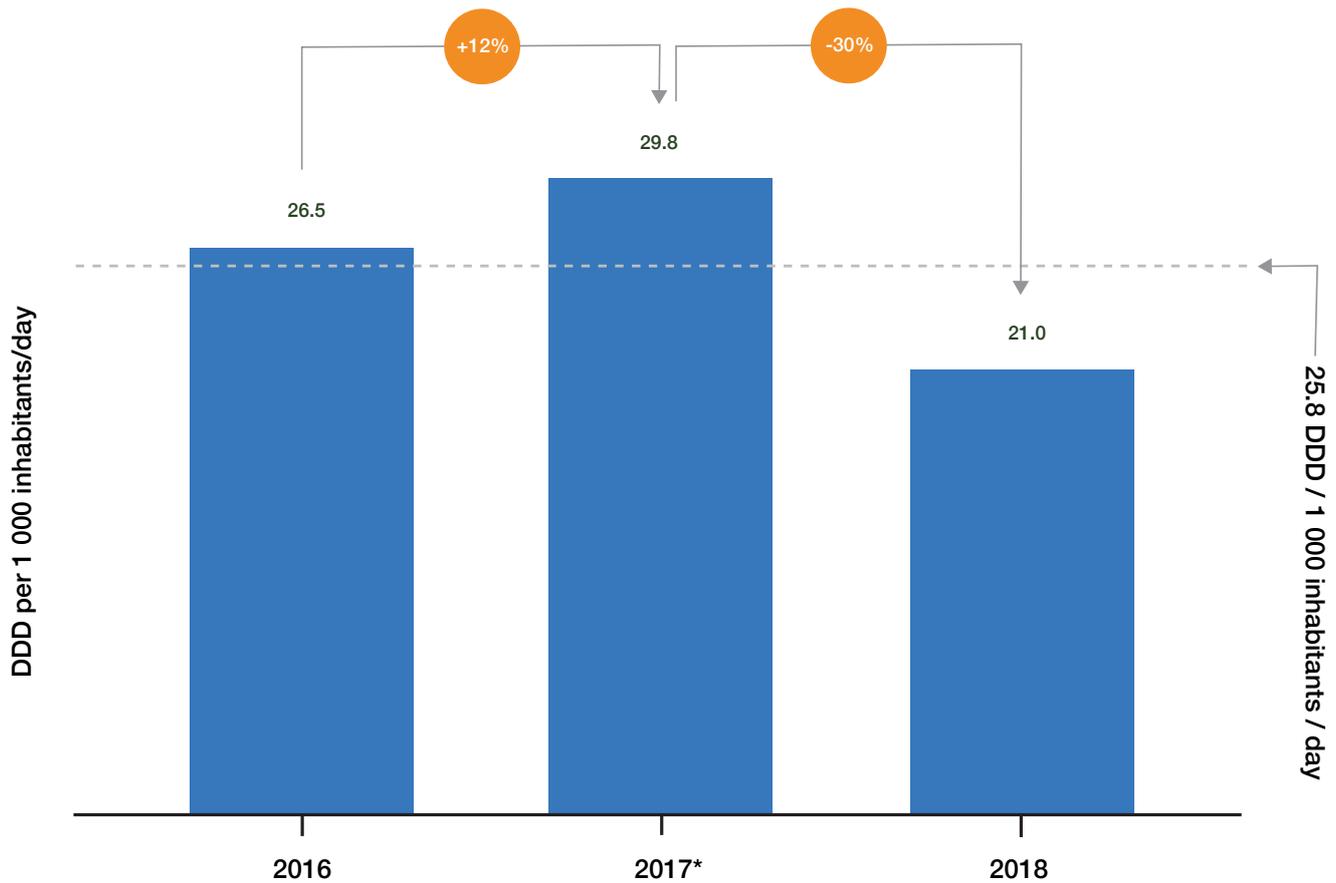
iv. Review of Essential Medicines List (EML)

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

Results

National AMC datasets analysed by DDD per year

The average total in-country AMC between 2016 and 2018 was 25.8 DDD per 1 000 inhabitants per day (DID). IQVIATM datasets were available for all three reviewed years (2016-2018), while the OPN data were only available in 2017 due to their biannual procurement procedures. Keeping this disparity in annual data availability, we noted a 12% increase in total consumption of antimicrobials from the year 2016 to 2017 and a 30% reduction in consumption from 2017 to 2018 (Figure 18). Due to the intermitted procurement trend in some AMC data, it was difficult to further explore and conclude whether overall AMC trends were changing during the period of review.



Abbreviations: DDD=defined daily dose

Figure 18: Variation in the national-level total defined daily dose per 1 000 inhabitants per day between 2016 to 2018 in Gabon. *OPN data were only available for the year 2017, which covered two years of consumption data for antimicrobials

National AMC analysed by ATC classification

Combinations of penicillins, including beta-lactamase inhibitors (J01CR), were the most frequently consumed ATC class across the years reviewed at 49.3% in 2016, 53.0% in 2017 and 38.4% in 2018. The FDC of amoxicillin/clavulanic acid was the most consumed antibiotic within this class. Penicillins with extended spectrum (J01CA) and fluoroquinolones (J01MA) were the second and third leading ATC classes, with amoxicillin and flucloxacillin being the most consumed molecules within these ATC classes, respectively (Figure 19). The top five most consumed antimicrobials were amoxicillin/clavulanic acid, amoxicillin, doxycycline, sulfamethoxazole/trimethoprim and flucloxacillin. Together they accounted for 76% of the total consumption share. Detailed breakdowns of the national AMC by antimicrobial molecules and by ATC classes are presented in AMC Appendix 7 and AMC Appendix 8.

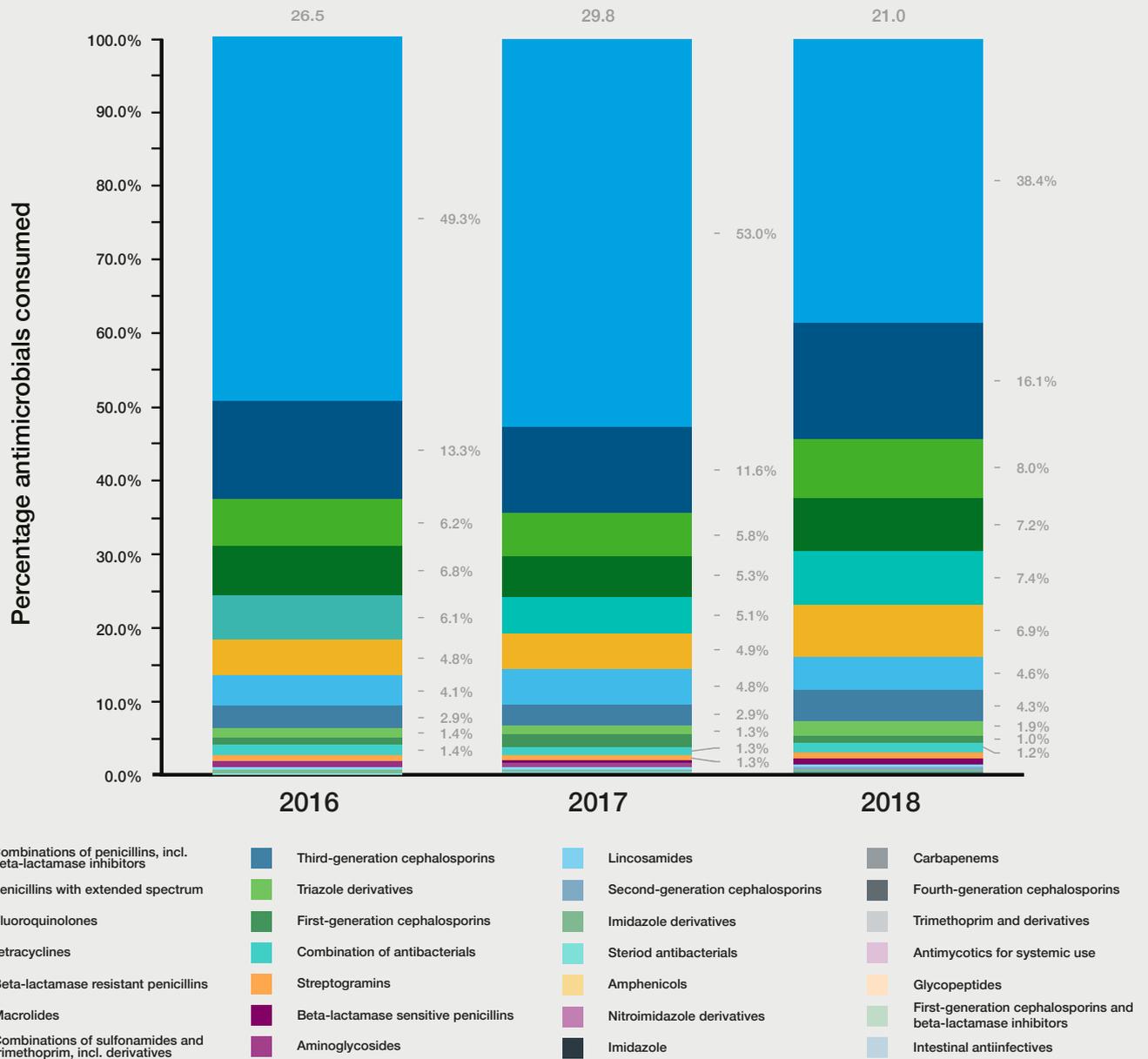


Figure 19: National-level antimicrobial consumption in Gabon between 2016-2018. The bars show the percentage of antimicrobials consumed stratified by ATC classes. The annual national-level total defined daily dose per 1 000 inhabitants per day is shown at the top of each bar. The 'Combinations of penicillins, incl. beta-lactamase inhibitors' class of molecules were the highest consumed antimicrobials across all the reviewed years 2016, 2017 and 2018. 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 class

National- and pharmacy-level AMC analysed by WHO AWaRe categorization

On average (across the three years reviewed), 82.8% of antimicrobials consumed were in the 'Access' category, 17.2% were in the 'Watch' category, and none (0.0%) were in the 'Reserve' category. Annual AMC trends indicated a minimal increase of 0.4% in the consumption share of 'Access' antibiotics in the consumption share of 'Access' antibiotics between 2016 and 2017 and a decrease of 4.4% between 2017 and 2018. This is against a corresponding proportional minimal decrease of 0.4% in the consumption share of 'Watch' antibiotics between 2016 and 2017, which was followed by an increase of 4.4% between 2017 and 2018 (Figure 20). On average (over the three years) and within each year analysed, consumption of 'Access' category antibiotics in Gabon exceeded the 60% minimum consumption threshold set by the WHO. There were no stocks of 'Reserve' group antibiotics supplied in Gabon during the reviewed period. This analysis showing the WHO AWaRe proportions of AMC medicines consumed omits 2.5% (0.6 DID) of total AMC antimicrobials that are not categorised within the WHO AWaRe list of 2019.

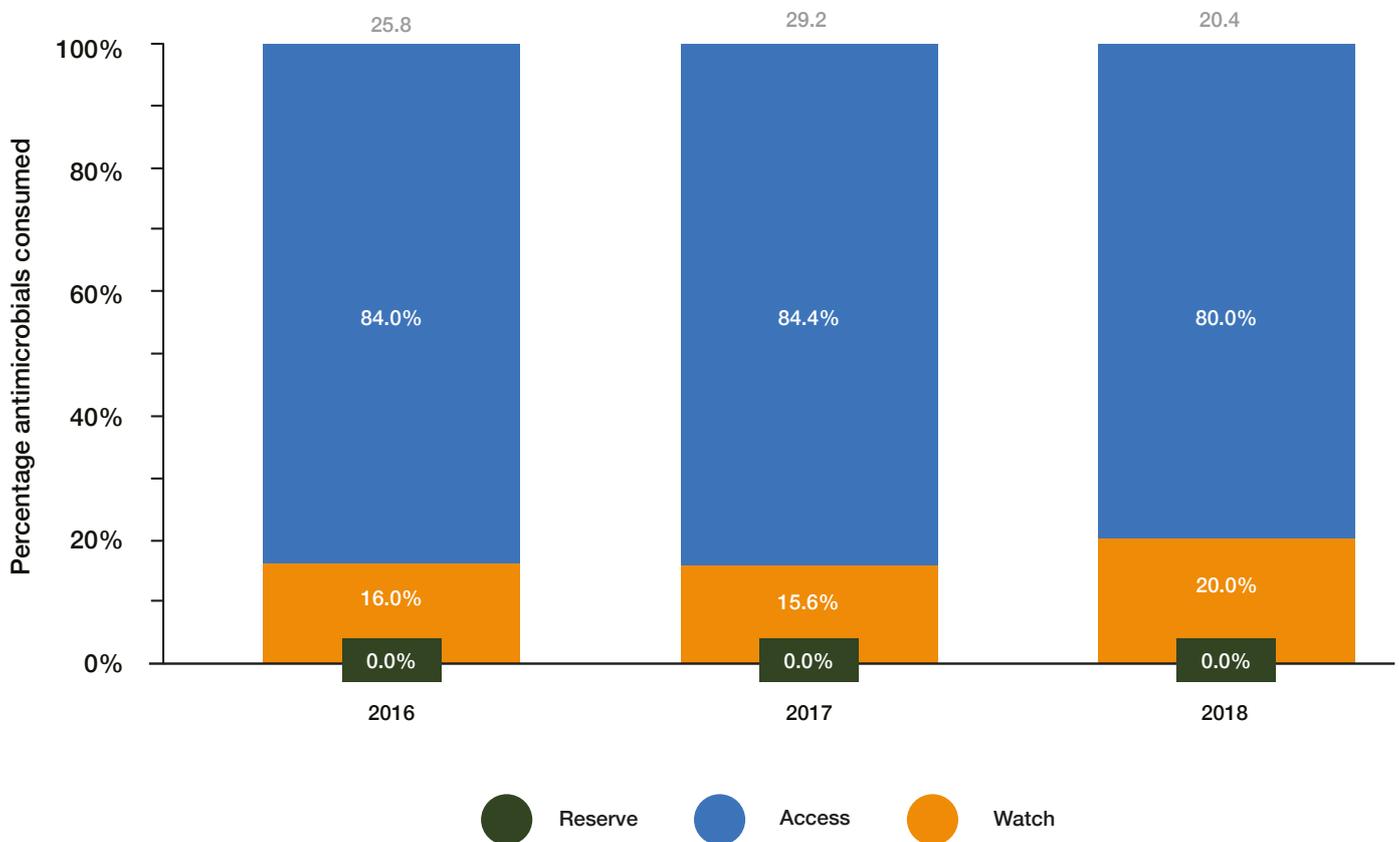
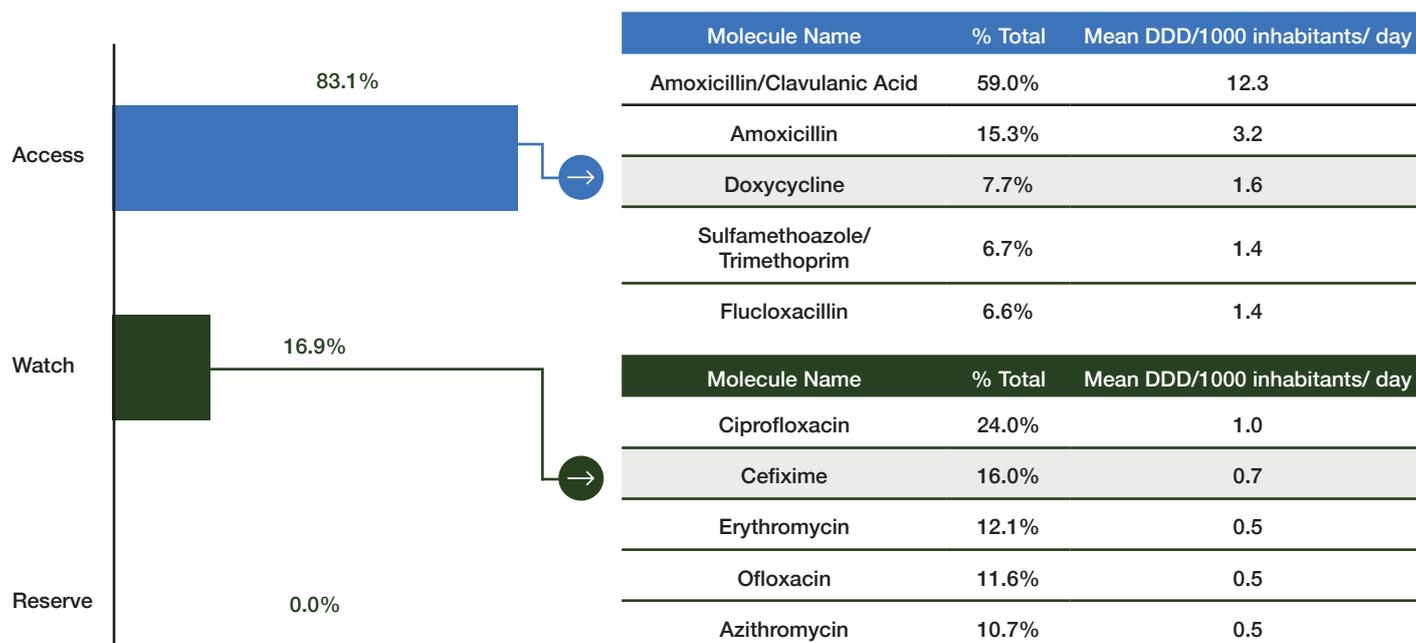


Figure 20: Antimicrobial consumption in Gabon between 2016-2018. The bars show the percentage of antibiotics consumed stratified by WHO AWaRe categories. The annual total defined daily dose per 1 000 inhabitants per day is shown at the top of each bar. Also, it shows the percentage change in consumption of 'Access', 'Watch' and 'Reserve' category antibiotics from the year 2016 to 2018

Further analysis was conducted to identify the most frequently consumed antibiotics nationally within each WHO AWaRe category. In the 'Access' category, the top five most frequently consumed antibiotics accounted for 95.2% of all AMC within this group (Figure 21). In the 'Watch' category, the top five most consumed antibiotics accounted for 74.3% of all the consumption within this group. There was no consumption of 'Reserve' category antibiotics for the reviewed period (2016-2018).



Abbreviations: DDD=defined daily dose

Figure 21: Breakdown of antibiotics consumed at the national level in Gabon by WHO AWaRe ('Access', 'Watch' and 'Reserve') category, 2016 to 2018. The inset table shows the top five consumed antibiotics in each category

Within the WHO AWaRe database, there exists a list of 'antibiotics that are not recommended' as they consist of multiple broad-spectrum antibiotics whose use is neither evidence-based nor recommended in high-quality international guidelines. As a result, the WHO does not recommend their use in clinical practice. These antibiotics are represented as 'uncategorised' by MAAP. Ten of these non-recommended FDCs were consumed during the period reviewed, representing 0.6% of the total national AMC (Table 12). Of the 10, azithromycin/fluconazole/secnidazole was the most frequently consumed (accounting for 39.4% of the consumption, with a mean DID of 0.1). AMC Appendix 9 details the full list of antibiotics categorised under each WHO AWaRe category.

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

| Overall AMC rank* | Not recommended combination |
|-------------------|--------------------------------------|
| 23 | Azithromycin/fluconazole/secnidazole |
| 24 | Amoxicillin/metronidazole |
| 32 | Ciprofloxacin/tinidazole |
| 38 | Ofloxacin/ornidazole |
| 40 | Ceftriaxone/sulbactam |
| 52 | Cefpodoxime proxetil/clavulanic acid |
| 55 | Amoxicillin/cloxacillin |
| 56 | Cefadroxil/clavulanic acid |
| 57 | Cefixime/clavulanic acid |
| 58 | Cefuroxime/clavulanic acid |

*AMC rank reports the position of antibiotics consumed (in terms of the total defined daily dose per 1 000 inhabitants per day and percentage share) from the reviewed list of antimicrobials in Gabon (see Appendix 8 for details on each listed antibiotic).

Aggregated pharmacy-level data from the 24 participating pharmacies were analysed by the type of facility (hospital-based or community-based) and by their proportional consumption of WHO AWaRe antibiotic categories. Community pharmacies consumed 24% more 'Watch' category antibiotics compared to hospital pharmacies. Both the hospital-based pharmacies (89.7%) and community pharmacies (65.1%) exceeded the WHO threshold of 60% consumption of antibiotics in the 'Access' category. All six hospital-based pharmacies met the WHO 60% consumption threshold and among these, the tertiary care facilities consumed over 14% more 'Access' category antibiotics compared to the secondary care facilities (Table 13). Within the community pharmacies, there were three who failed to meet the minimum threshold.

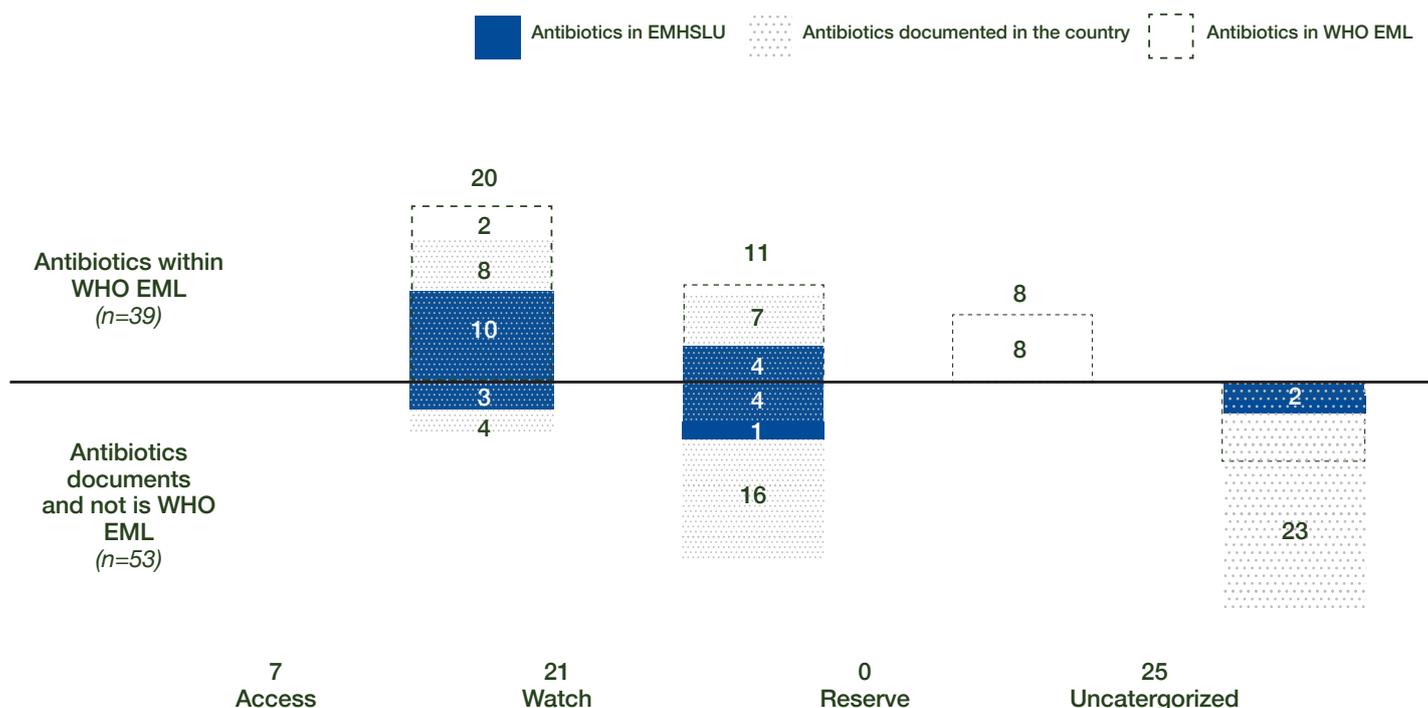
Table 13: Percentage share of total antimicrobial consumption by WHO AWaRe categories at both the hospital and community pharmacies in Gabon between 2016-2018

| Pharmacy Type | AWaRe Categorisation | |
|---------------------------------|---------------------------------|--------------------------|
| | Access | Watch |
| | Percentage share (Absolute DDD) | |
| Hospital pharmacies (6/24) | 89.7% (383 805) | 10.3% (44 034) |
| Secondary care facilities (5/6) | 85.3 % (250 981) | 14.7 % (43 114) |
| Tertiary care facilities (1/6) | 99.3 % (132 824) | 0.7 % (920) |
| Community pharmacies (18/24) | 65.1% (6 575 284) | 34.9% (3 533 145) |
| Grand Total | 66.0% (6 959 089) | 34.0% (3 577 179) |

Abbreviations: DDD=defined daily dose

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

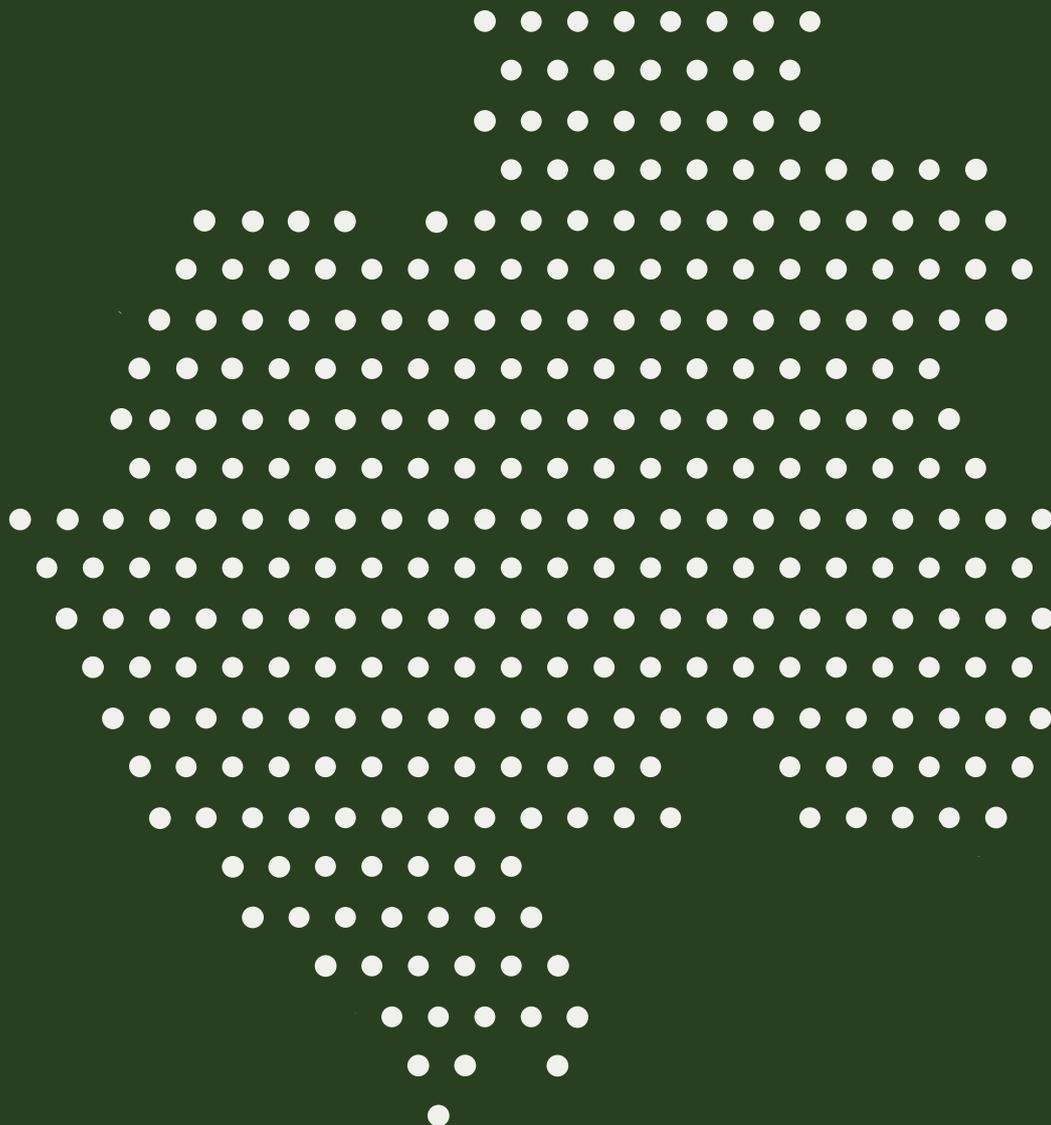
The WHO EML includes 39 antibiotics across the AWaRe categories. A total of 92 antimicrobials were documented during national- and pharmacy-level data collection (Figure 22). Unfortunately, no country-specific EML was found during desk research to facilitate further comparisons. Two 'Access' and seven 'Reserve' antibiotics that are part of the WHO EML were not documented during data collection. These antibiotics are also not part of the Gabon EML. For each AWaRe category, including the uncategorised, antimicrobials that were not part of the WHO EML were documented during data collection. The detailed breakdown of antimicrobials documented and their inclusion in the WHO EML is provided in AMC Appendix 9.



Abbreviations: WHO=World Health Organisation; EML=Emergency Medicines List

Figure 22: AWaRe analysis of documented antibiotics in national- and pharmacy-level data in Gabon (2016-2018) compared to the World Health Organisation's Emergency Medicines List definitions.

Part C: Resistance and Consumption Interlinkages



Objective

To assess the relationship between antimicrobial consumption and antimicrobial resistance

Methodology

The DRI was estimated to convey aggregate rates of resistance as well as measurements of AMC (at a national level since AMU data were not available) across select pathogen-antimicrobial combinations (AMR Appendix 8). The pathogens considered were *A. baumannii*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *E. faecium* and *E. faecalis*, while the antibiotics were the aminoglycosides, broad-spectrum penicillins, carbapenems, cephalosporins, glycopeptides, narrow-spectrum penicillins and quinolones. The DRI estimates were generated using a previously published methodology^{30,31} and helped communicate the effectiveness of antibiotic therapy to decision makers. DRI values range from 0 (100% susceptibility) to 100 (100% resistance). Available AST results for at least 30 tested isolates and at least 15 of the 25 combinations were required for the estimation of the DRI. To generate CIs for the DRI as the variance of the product of variables, the variance of the proportions of non-susceptible isolates was combined with a uniform standard deviation based on the estimated DDD.^{32,33}

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

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

Results**Drug Resistance Index**

The DRI estimate was found to be high (65.2%; 95% CI 52.4-77.9%), implying low antibiotic effectiveness, which is a threat to effective infectious disease management and calls for urgent policy intervention (Figure 23).

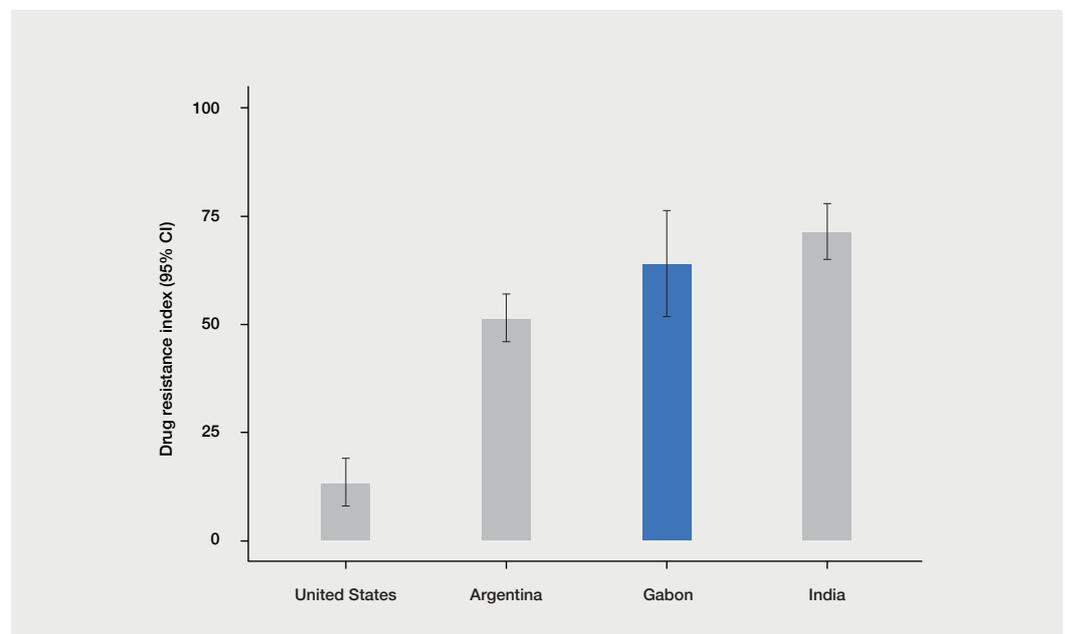


Figure 23: Drug resistance index in Gabon, 2016-2018, compared to the Drug resistance index estimates from the United States, Argentina, and India

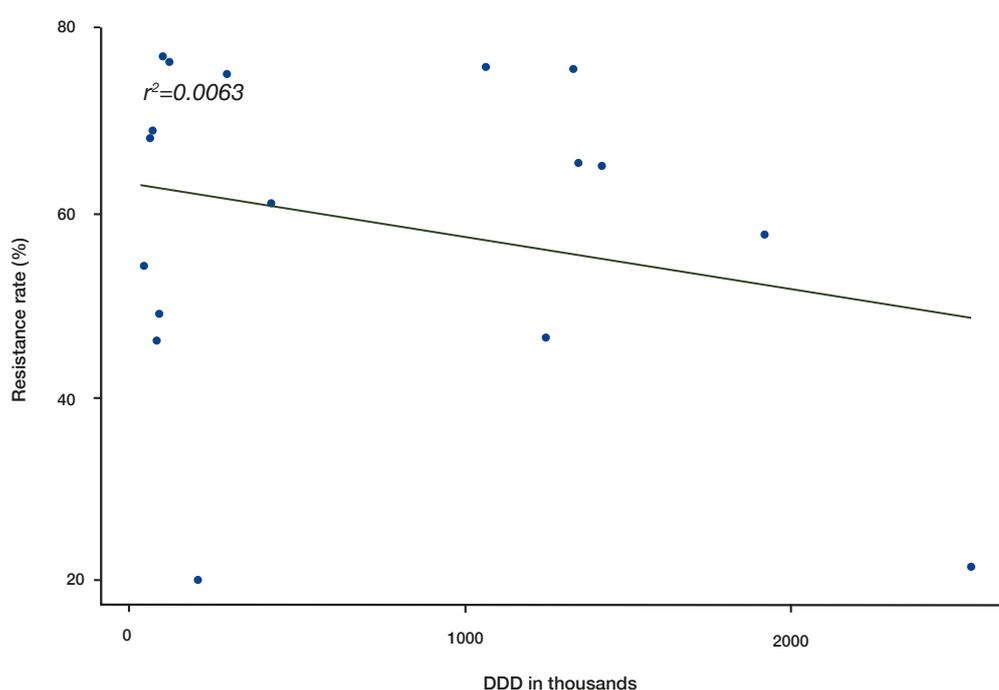
AMC and AMR correlation

The top three highly consumed antibiotic classes at the facility level were beta-lactam combinations, folate pathway inhibitors and tetracyclines. The AMR rates were highest for first-generation cephalosporins (76.8%), macrolides (76.3%) and aminopenicillins (76.2%) (Table 14). Pearson's correlation analysis revealed a weak negative correlation ($r^2=0.06$) between antimicrobial resistance and antimicrobial consumption, implying that antibiotic consumption is not a potential driver of AMR in Gabon (Figure 24).

Table 14: AMC and AMR rates across antibiotic classes

| Antibiotic class | Year | Total DDD in thousands | Resistance rate (%) |
|---------------------------------|---------|------------------------|---------------------|
| Beta-lactam combinations | 2016-18 | 2 562.9 | 22.1 |
| Folate pathway inhibitors | 2016-18 | 1 924.1 | 58.1 |
| Tetracyclines | 2016-18 | 1 425.3 | 65.4 |
| Fluoroquinolones | 2016-18 | 1 354.1 | 65.7 |
| Aminopenicillins | 2016-18 | 1 337.4 | 76.2 |
| Cephalosporins (3rd generation) | 2016-18 | 1 249.7 | 47.0 |
| Macrolides | 2016-18 | 1 065.8 | 76.3 |
| Methicillin | 2016-18 | 406.7 | 61.5 |
| Azoles (f) | 2016-18 | 266.9 | 75.7 |
| Streptogramins | 2016-18 | 183.7 | 20.6 |
| Cephalosporins (1st generation) | 2016-18 | 94.4 | 76.8 |
| Penicillins | 2016-18 | 77.2 | 77.4 |
| Cephalosporins (2nd generation) | 2016-18 | 64.9 | 49.6 |
| Aminoglycosides | 2016-18 | 56.6 | 46.6 |
| Fucidane | 2016-18 | 41.6 | 69.4 |
| Lincosamides | 2016-18 | 33.1 | 68.6 |
| Quinolones | 2016-18 | 11.6 | 54.7 |

Abbreviations: DDD=defined daily dose



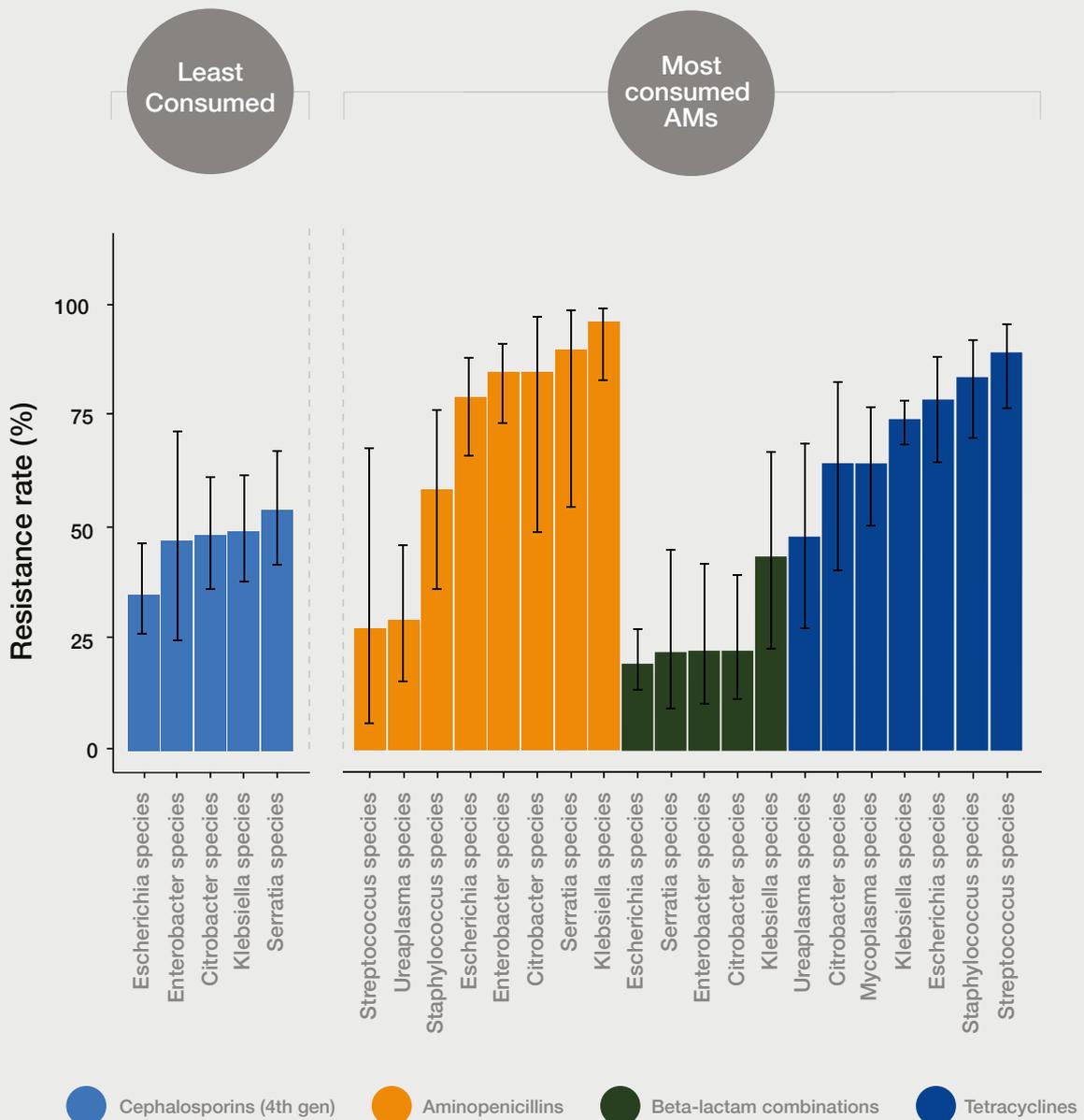
Abbreviations: DDD=defined daily dose

Figure 24: Correlation between AMR and AMC

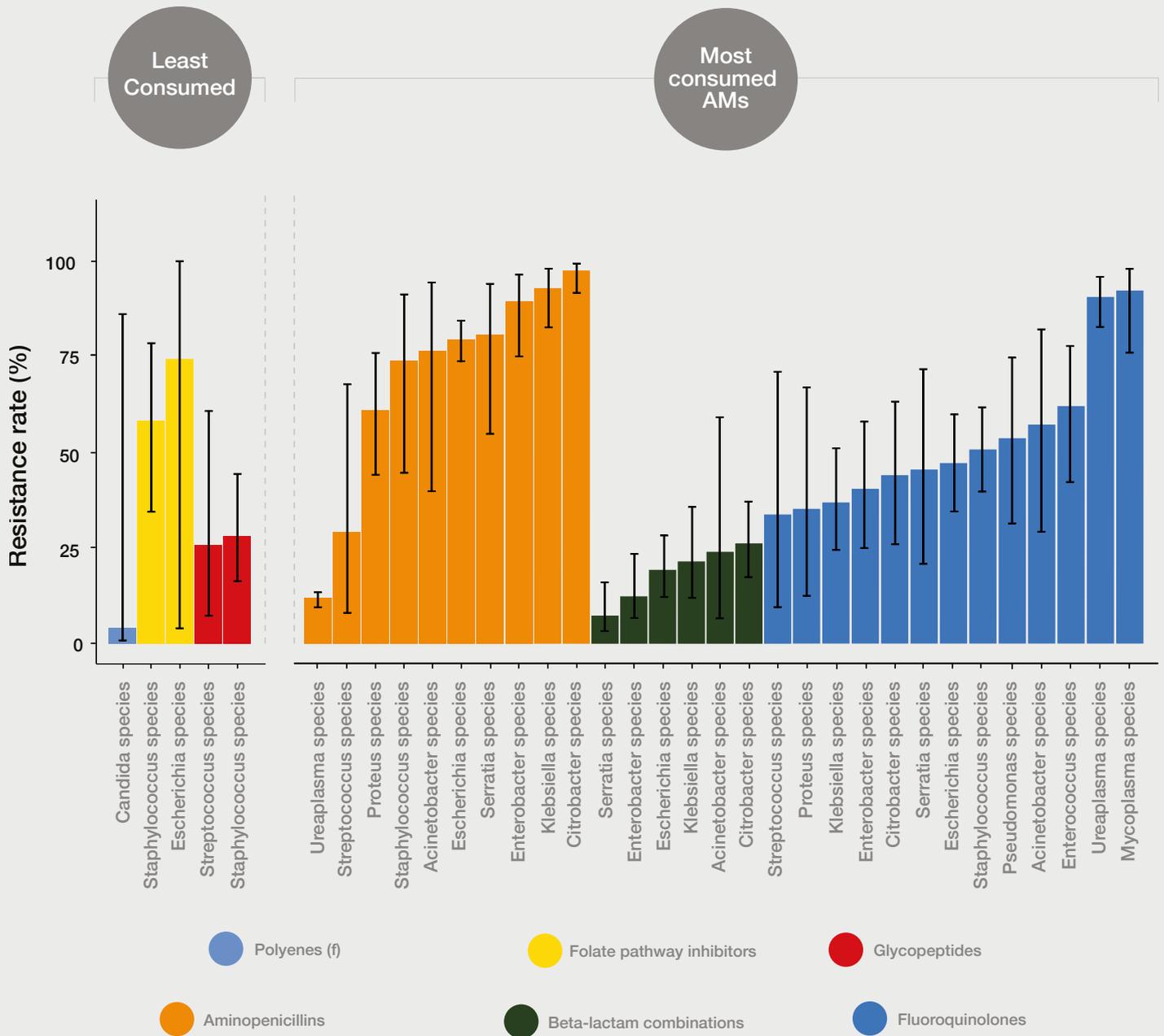
Resistance profiles of the most and least consumed antimicrobial classes

The most consumed antimicrobial classes across the study years were beta-lactam combinations, aminopenicillins and tetracyclines (Figures 25, 26 and 27). In 2016, there were high rates (>75%) of tetracycline-resistant *Streptococcus* species, *Staphylococcus* species and *Escherichia* species, as well as aminopenicillin-resistant *Klebsiella* species, *Serratia* species, *Citrobacter* species, *Enterobacter* species, and *Escherichia* species. In 2017, there were high rates (>85%) of fluoroquinolone-resistant *Mycoplasma* species and *Ureaplasma* species, as well as aminopenicillin-resistant *Citrobacter* species, *Klebsiella* species and *Enterobacter* species. In 2018, there were high rates (>75%) of fluoroquinolone-resistant *Mycoplasma* species and *Ureaplasma* species, as well as aminopenicillin-resistant *Serratia* species, *Klebsiella* species, *Enterobacter* species, *Pseudomonas* species, *Citrobacter* species and *Escherichia* species.

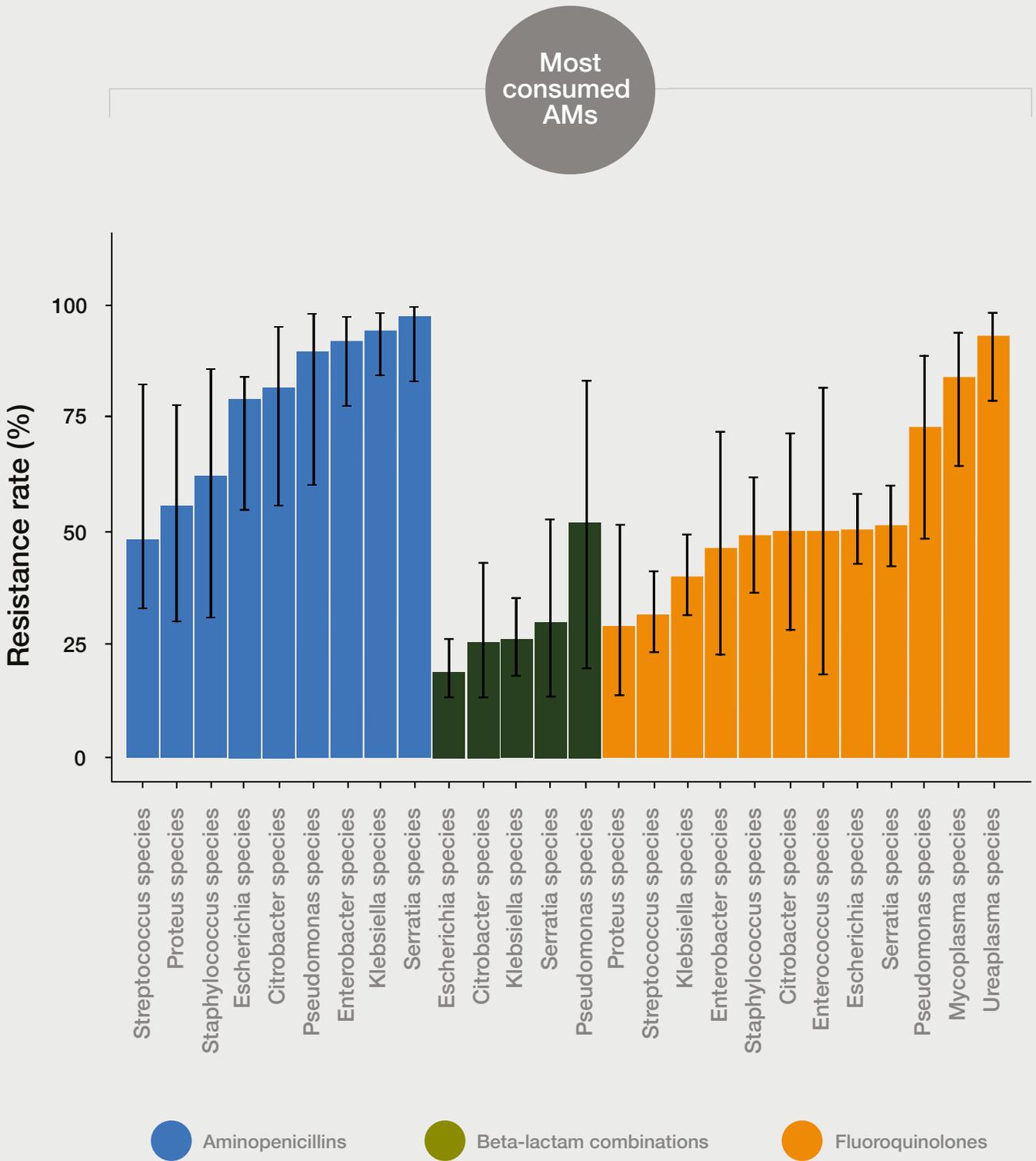
The least consumed antimicrobial classes were folate pathway inhibitors, nitroimidazoles, cephalosporins (fourth generation), glycopeptides, polyenes (f), and phenicols across the study years (Figures 25, 26 and 27). Even though the consumption of these antimicrobial classes was low, there were high resistance rates across many pathogen-antimicrobial class combinations. In 2016, >50% of *Serratia* species were cephalosporin (fourth generation)-resistant. In 2017, >50% of *Escherichia* species and *Staphylococcus* species were folate pathway inhibitor-resistant.



Abbreviations: Least cons. AMs=least consumed antimicrobials; Most cons. AMs=most consumed antimicrobials
 Figure 25: AMR rates for the least (left) and most (right) consumed antimicrobial classes in Gabon in 2016

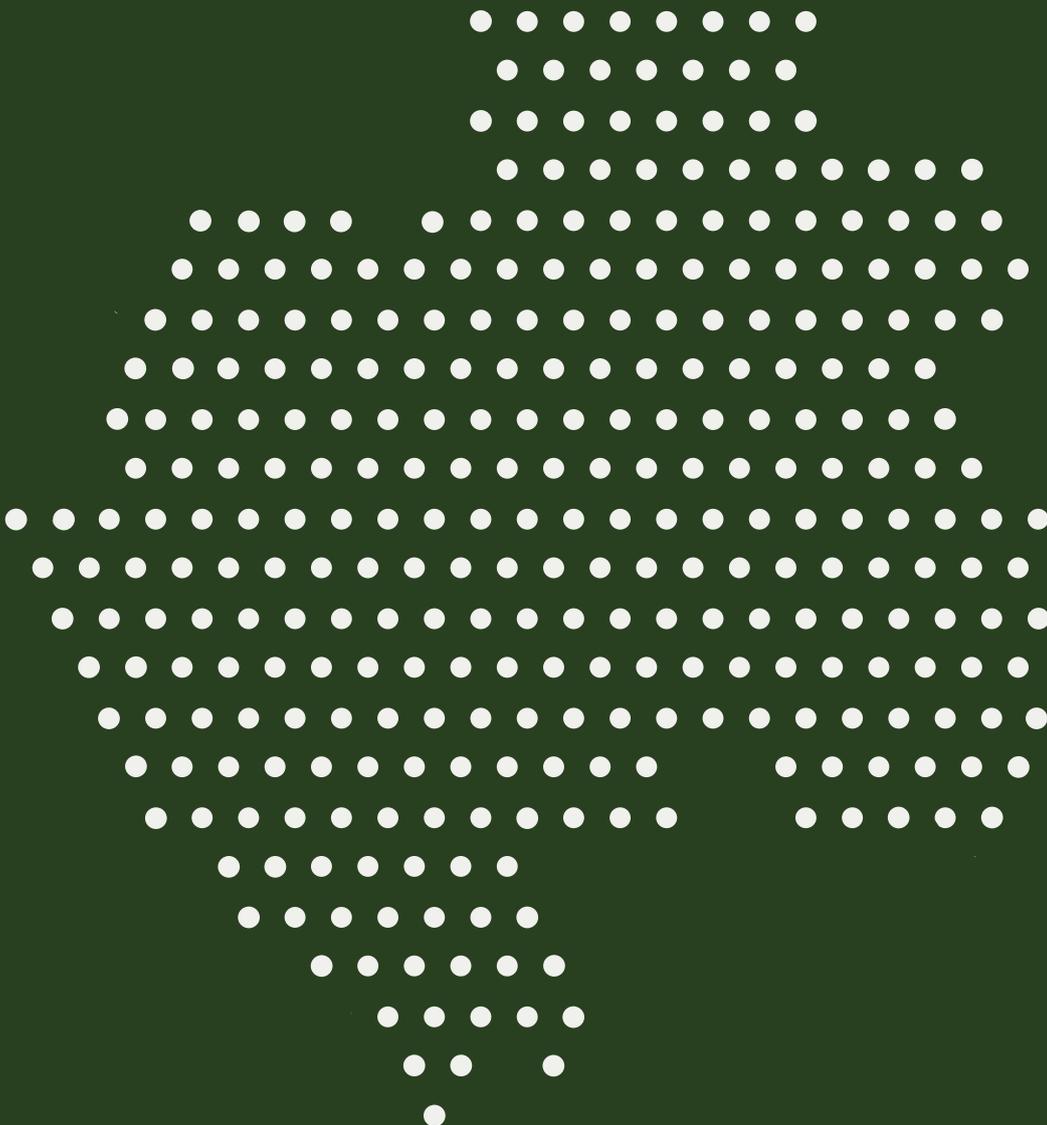


Abbreviations: Least cons. AMs=least consumed antimicrobials; Most cons. AMs=most consumed antimicrobials
 Figure 26: AMR rates for the least (left) and most (right) consumed antimicrobial classes in Gabon in 2017



Abbreviations: Most cons. AMs=most consumed antimicrobials
 Figure 27: AMR rates for the most consumed antimicrobial classes in Gabon in 2018

Part D: Recommendations



AMR is a major threat to medical advancements and has drawn global attention over the past few years and more so recently, due to the COVID-19 pandemic. Unfortunately, owing to inconsistent surveillance data, the AMR burden is not well quantified in most countries. A recent review reported 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.³⁴

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

Significance of AMR and DRI data including recommendations

Analysis of available AMR data from Gabon revealed high levels of MRSA (69-77%) and third-generation cephalosporin-resistant Enterobacterales (40-49%). *Staphylococcus aureus* (methicillin-resistant or sensitive) is a common cause of many skin and soft tissue infections (SSTI), in both community and healthcare settings. It can also cause invasive infections like endocarditis, osteomyelitis, pneumonia, visceral abscess, brain abscess, shunt infections and bacteraemia. Risk factors for MRSA infections include past infections or colonisation, trauma, invasive devices (catheters, shunts, implants, prosthesis, etc.), prior-antibiotic use, neutropenia, other underlying conditions, post-surgical status, dialysis and admission to long-term care facilities.

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

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

The estimated DRI for Gabon was also high and indicates decreasing effectiveness of antimicrobials. Clearly, this calls for targeted interventions such as improved ASP, infection prevention and regulations on the use of high-end antibiotics. We observed that male individuals and elderly patients were more prone to resistant infections, although further studies will be needed to establish the connection.

Service delivery

The laboratory network in Gabon was found to consist of 200 laboratories, of which only 31 were identified as bacteriological laboratories and 20 confirmed their AST capabilities. Only seven of the surveyed laboratories reported implementing QMS and none were accredited. Considering a country population of over 2.2 million, the laboratories did not equitably cover the country's population. The testing load (quantum of cultures) at most participating laboratories was found to be low and suggested a lack of routine microbiology testing. There is thus the increased likelihood that the AMR rates were overestimated as most tests would have been conducted on special patient categories (failure of first-line therapy or admission to intensive care).

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

Health workforce

As reported by the surveyed laboratories, 85% had an experienced laboratory scientist or technologist, 50% had up-to-date records on training and competence and only 55% had at least one qualified microbiologist. For high-quality microbiology testing and reporting, it is essential to train staff on laboratory standards, identification of common pathogens and data management.³⁵ Capacity building of staff may be conducted by leveraging in-house expertise or may be outsourced to external organisations or tertiary facilities.

Information systems

The Regional Grant was a step towards the collection and digitisation of data. Most of the surveyed laboratories relied on paper-based or a combination of electronic and paper-based records or databases, and very few had linkages to patients' clinical records. In the current study, involving 16 laboratories over a three-year period, susceptibility results could be collected for just 8 425 positive cultures. To strengthen AMR surveillance, it is essential to curate the right data and generate evidence. We recommend data collection in standardised formats at all levels (laboratories, clinics and pharmacies) as well as the use of automation for data analyses. For the current study, we used WHONET for data digitisation. Empirical guidelines for the management of infectious diseases should be based on the specific epidemiology of the patient 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. This would help to collect data on the patients' clinical profile and antimicrobial history, as well as the pathogens' 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.

To strengthen AMR surveillance, it is imperative to generate reliable laboratory results using appropriate testing methods and authorised surrogates as well as to ensure uninterrupted availability of reagents including antibiotics for susceptibility testing. Improving supply chains for essential reagents should be a country's priority and interruptions in routine testing must be minimal. Standardisation of testing methods across laboratories can aid in this process as purchases can be pooled and coordinated by ministries of health. 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 and hand hygiene) as well as 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 Gabon to facilitate future surveillance activities and inform antimicrobial stewardship activities.

Feasibility of obtaining AMC and AMU data in Gabon and recommendations

MAAP successfully collected and analysed both national and pharmacy-level AMC data in Gabon. This indicates that conducting routine in-country AMC surveillance is possible and that Gabon can respond to the WHO's call to participate in GLASS, which now has an AMC reporting component. However, the AMC data collected required verification and validation before analysis. Therefore, a comprehensive guiding policy for routine AMC data surveillance is required in the country to guide, at the minimum, the reporting of AMC data variables and routine data cleaning and reporting practices to minimise the amount of time spent in standardising and cleaning the data. This policy should be implemented before routine surveillance exercises begin to ensure that the data used are accurate and usable for informing country policy. Also, it is important to note that the OPN purchasing system involved cycles of periodic procurement, i.e., only once in two years. Therefore, the AMRCC should note that it would be difficult to assess monthly and yearly trends during future surveillance exercises using OPN datasets. Moreover, efforts should be made jointly by the OPN and AMRCC to identify ways through which yearly consumption data can be obtained from the records kept at the OPN. Such an approach would help in the smooth conductance of AMC surveillance studies and add benefits during the examination of AMC trends. Pharmacy-level AMC data from the hospitals were mainly collected from manual records. To make future AMC surveillance activities more time- and cost-efficient, hospitals could consider converting to electronic systems and ensure such systems have capabilities to transfer data across systems and/or produce user-friendly reports on AMC.

MAAP was unable to obtain AMU data in Gabon, which would have helped to characterise antimicrobial prescriptions at the facility level in line with the WHO's drug use research methodology.³⁶ This inability to collect AMU data from participating pharmacies that were co-located in health facilities with AST laboratories was due to the nature of the data that was made available to MAAP. The data sources did not allow the back-tracing of individual patients to whom antimicrobials were dispensed, as prescription chits were not archived. Nevertheless, a few studies that reported AMU data in Gabon have been documented.^{37,38} These studies, however, sampled only one facility to provide a picture of AMU, and thus the conclusions drawn from them would likely not be applicable on a national scale.

Therefore, MAAP, in alignment with the WHO guide on facility AMU assessment, would recommend that future AMU surveillance attempts in the country be conducted through prospective AMU surveillance activities (e.g., point-prevalence surveys) on a larger scale.²⁷ Such an approach would allow the design and use of cross-department patient-tracking tools and ensure continuous documentation of clinical outcomes as the patient continues to receive care. However, such an approach is time-consuming unlike retrospective data collection and often requires specialised data collection teams. This makes data collection expensive and difficult in resource-limited settings. Retrospective AMU data collection can, however, remain an option if facilities targeted for data collection are selected based on the existence of electronic patient records and the presence of cross-department unique patient identifiers.

Overview of AMC consumption trends and recommendations

The total AMC levels documented in this report provide a useful benchmark for comparing future in-country consumption levels following the implementation of in-country stewardship programmes. The observed AMC levels in Gabon far exceed the levels described in reports from other African countries such as Burkina Faso, Cote d'Ivoire¹⁷ and Sierra Leone²¹ but were lower than the AMC levels reported in Tanzania.³⁹ A potential reason for these observed differences in AMC levels could be the sources of data that were used for the AMC calculations. Burkina Faso and Cote d'Ivoire used wholesaler data, which might be less complete compared to the OPN and IQVIA data used in Gabon, which covered 100% of the antimicrobials market. Tanzania used import data, and some of these imported antimicrobials may have been exported again, thus leading to overestimated AMC levels. The observed disparities in AMC levels might also be due to relative differences in the burden of infectious diseases between the countries or limited availability of laboratory or point-of-care diagnostics at the health facility level.

These factors may lead to presumptive treatment and unnecessary prescription of antimicrobials. The widespread availability of antimicrobials over the counter and unexplained use of some antimicrobials in the animal health sector may be additional contributing factors.¹⁷ Nonetheless, given this relatively higher AMC trend in Gabon, AMU point-prevalence surveys are recommended to better understand the in-country AMC levels. This will eventually guide future national action plans to optimise AMC if any overuse or misuse is detected. The MAAP consortium was not able to assess or quantify national consumption trends due to the nature of the datasets collected and analysed, i.e., aggregated two-year datasets.

An evaluation of AMC according to the WHO AWaRe categories showed that the proportion of narrow-spectrum, 'Access' category antibiotics consumed in Gabon well exceeded the minimum WHO recommended consumption threshold.²⁸ A fair consumption of broader-spectrum 'Watch'-class antibiotics was also observed. This finding is quite commendable as it implies that any emerging AMR trends due to misuse or overuse will likely be restricted to narrow-spectrum antibiotics, thus sparing the lesser-used broader-spectrum antibiotics in the 'Watch' category. However, a closer examination of antibiotics used within each WHO AWaRe category revealed that an overwhelming majority of antibiotics consumed within the 'Access' and 'Watch' categories were among the top five antibiotics in each category. Such a consumption pattern may be sub-optimal as evolutionary pressures driving resistance would be focused mainly on the narrow band of antibiotics consumed.⁴⁰ This narrow consumption of antibiotics within the 'Access' and 'Watch' classes of antibiotics can also make the country susceptible to stock-outs in the event of manufacturing or supply chain issues. Considering the outlined observations, it is therefore recommended that the country's antimicrobial stewardship programmes explore ways to ensure a wider spread in the consumption of antibiotics within each WHO AWaRe category. This should be accompanied by measures to ensure appropriate antimicrobial use while taking in-country resistance patterns into account. Nevertheless, Gabon should also be commended for greatly exceeding the minimum threshold of consumption ($\geq 60\%$) of antibiotics in the WHO 'Access' category (narrow-spectrum and first-choice antibiotics). There is, however, room for more diversification as only five antibiotics made up 76% of the total antibiotics consumed in this category.

Given that several attempts to locate the document on national treatment guidelines were unsuccessful, MAAP recommends that the MoH make this document easily accessible to ensure that infectious diseases across the country are treated in line with the established guidelines.

Interestingly, a review of the usage of 'Access' category antibiotics revealed that the hospital pharmacies consumed higher levels of medicines in this class compared to the community pharmacies. This consumption trend was, in

part, attributable to the high consumption of the amoxicillin/clavulanic acid combination, an 'Access'-group antibiotic, in public hospital pharmacies. Despite this, both the hospital and community pharmacies met the WHO 'Access' threshold and this consumption trend is commendable as it indicates that narrow-spectrum antibiotics are typically the first line of antibiotics used in Gabon. Therefore, future antimicrobial use studies should be conducted to determine the appropriateness of consumption of this FDC combination. Such studies will highlight the instances, including the settings, where inappropriate antimicrobial use exists. In addition, these recommended studies will help direct Gabon's antimicrobial stewardship activities and provide essential information that can be used to update the country's existing EML.

Lastly, none of the seven antibiotics listed as crucial antibiotics in the WHO EML and in the 'Reserve' WHO AWaRe category was consumed in Gabon.²⁸ This finding suggests a chronic lack of access to 'Reserve' category antibiotics in Gabon between 2016 and 2018. Urgent efforts by the AMRCC are therefore required to first confirm the non-availability of 'Reserve'-type medications in Gabon. If their absence is confirmed, policies incentivising the importation, distribution and improved access to 'Reserve' drugs should be urgently implemented to ensure their availability for patients in need.

The WHO also provides guidance on antibiotics that are 'not recommended' for use in clinical practice due to their broad-spectrum activity and a lack of clinical evidence supporting their use.²⁸ Ten of such FDCs 'not recommended' for use by the WHO were used in Gabon, with azithromycin/fluconazole/secnidazole being the most common combination used. As there is no recommendation for the use of these FDC antibiotics, the AMRCC should identify the reasons for these prescriptions and the exact locations where they are commonly prescribed or dispensed. To correct this prescribing practice, prescribers should also be sensitised on more appropriate treatment options for the identified ailments.

Data generated from the 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. Table 15 describes the next steps for AMC and AMU surveillance in Gabon.

Table 15: Next steps for AMC and AMU surveillance in Gabon

Leadership and Governance

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

A.

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

The regulatory authority could reconsider the registration status of unapproved FDCs.

The MoH and national stewardship programmes, led by the AMRCC, could work to revise the current national treatment guidelines and the availability of essential 'Reserve' category antibiotics within the country's EML.

Service Delivery

B.

Future attempts to collect AMU data in the country should seek to identify facilities that have unique patient identifiers and fully electronic medical records. Alternatively, as a limited number of facilities have such systems in place, the country could aim to prospectively collect this data as guided by the WHO methodology for point-prevalence surveys.²⁸

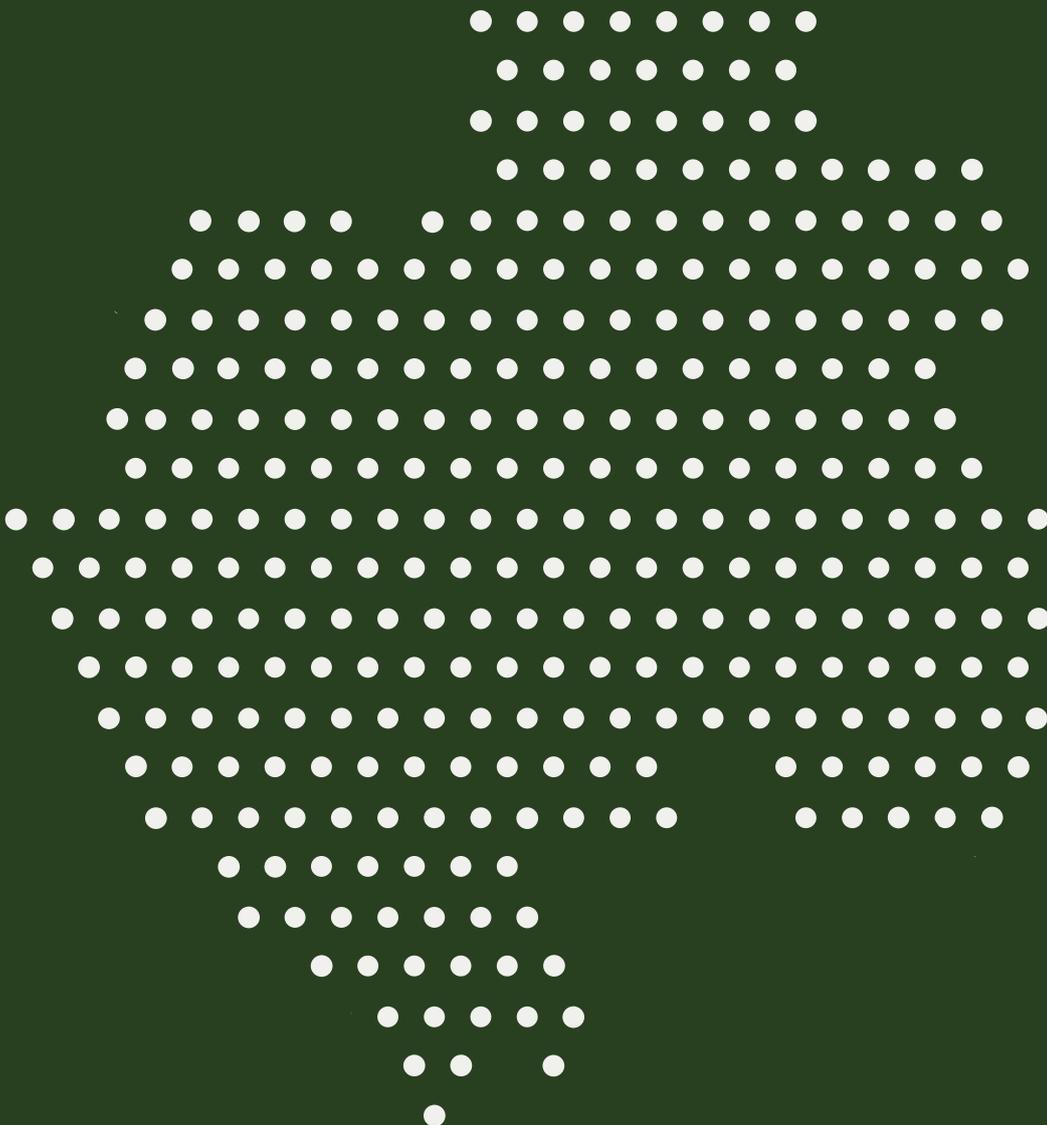
National stewardship programmes, led by the AMRCC, could educate healthcare practitioners on the full spectrum of antimicrobials available in the developing EML.

Medical products and technologies

C.

National stewardship programmes should collaborate with pharmacists and medicine importers to increase the variety of antibiotics (including 'Reserve' category antibiotics) available in selected facilities as per the developing EML.

Part E: Limitations



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

1.

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

2.

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

3.

The 16 participating laboratories may not fully represent the true resistance rates in the country as they only encompassed a small proportion of the country's population (over 2.2 million). Furthermore, as routine testing does not appear to be the norm in most hospitals and laboratories (AST is mostly conducted in instances of failed therapy), the resistance rates in this study may have been overestimated.

4.

Clinical data and antimicrobial usage information were not sufficient to allow robust analysis of AMR drivers.

5.

To better understand the national AMC trends, a sample of 24 pharmacies, mostly from within the capital, Libreville, were purposively selected for data collection. This sample size was a relatively small proportion of the total number of pharmacies in Gabon and did not represent all provinces. Therefore, a more systematic sampling strategy that factors in the populations and geographical locations served will be required to draw conclusions from pharmacy-level data.

6.

MAAP was unable to obtain AMU data from the participating pharmacies co-located with AST laboratories, therefore could not determine how and why antimicrobials were prescribed and dispensed (i.e., the appropriateness of prescriptions). This information is important to guide the country's stewardship programmes.

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Glossary

Accreditation:

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

Antimicrobial consumption:

According to the WHO, antimicrobial consumption is defined as quantities of antimicrobials used in a specific setting (total, community, hospital) during a specific period of time (e.g., days, months and 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 harder to treat and increasing the risk of disease spread, severe illness and death. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become increasingly difficult or impossible to treat.

Antimicrobial resistance rate:

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

AMR rate = No. of non-susceptible isolates / No. of tested isolates [CI 95%]

Antimicrobial susceptibility testing:

Tests used to determine the extent to which a particular bacterium or fungus is sensitive to specific antibiotics.

Antimicrobial susceptibility testing standards:

These are standards to be followed by laboratories while performing AST. The standards are produced by several internationally recognised agencies, e.g., the Clinical Laboratory Standards Institute, the European Committee on Antimicrobial Susceptibility Testing, etc. It is essential that laboratories comply with at least one of these standards while performing AST.

Country data quality score:

A metric computed to estimate the overall quality of AMR data received from a country. Firstly, each laboratory was assigned a data score based on their level of pathogen identification. Scoring was based on quartiles of the proportion of completely identified pathogens such that 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). Each laboratory was scored for each year reviewed, and the average score was assigned as the laboratory data quality score. Secondly, the country data quality score was computed by weighting the laboratory data quality score with the quantum of valid cultures contributed by each laboratory. The maximum attainable country data quality score was 4.

Eligibility questionnaire:

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

GLASS:

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

Laboratory readiness assessment:

The process of scoring the responses on the laboratory eligibility questionnaire to assess the laboratory's readiness or preparedness for AMR surveillance.

Laboratory readiness score:

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

Positive cultures:

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

Proficiency testing:

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

Quality Management Systems:

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

Valid cultures:

A subset of total cultures that include information on the specimen type, collection date and the laboratory's testing volume.

MAAP:

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

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.

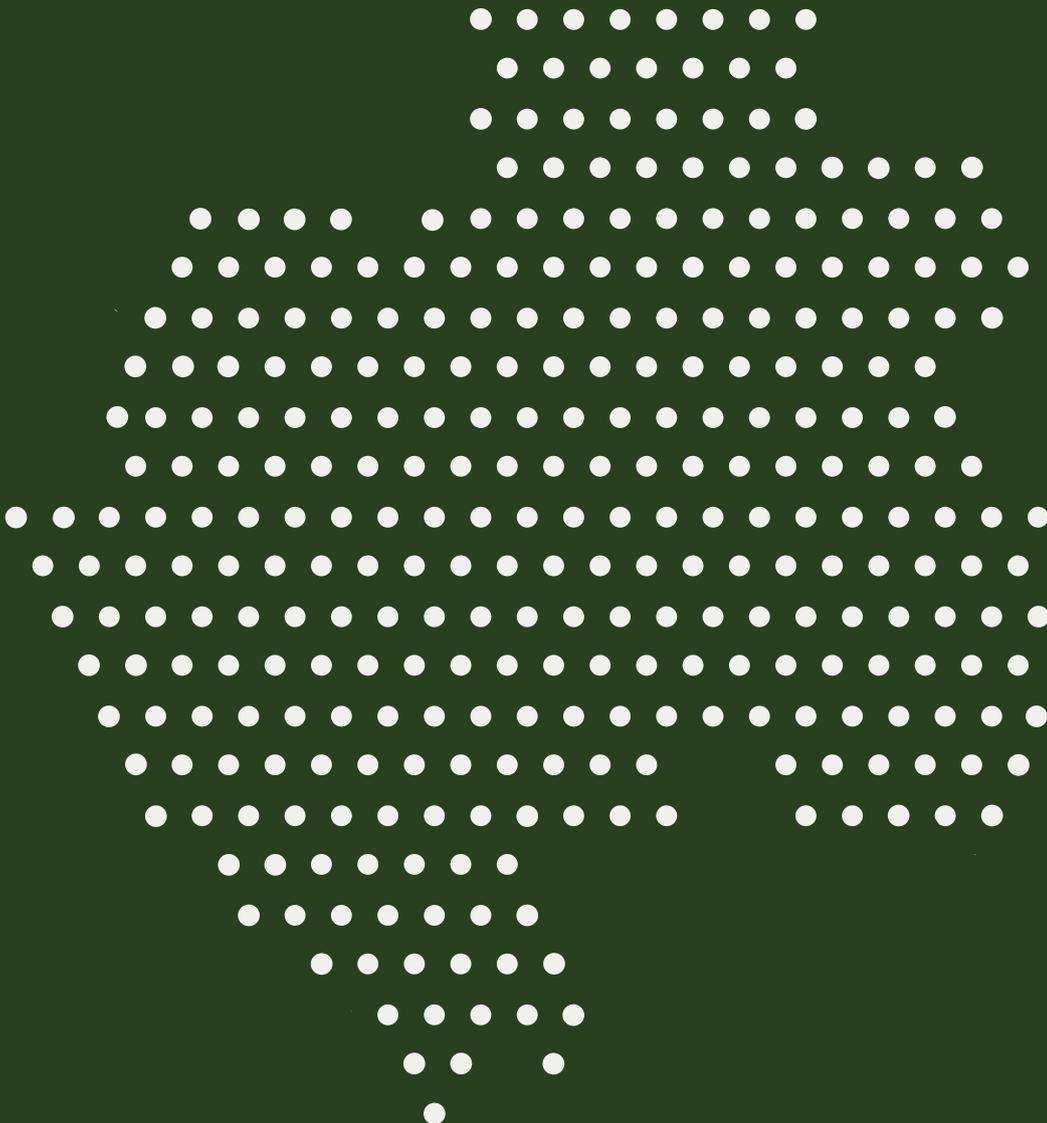
Quality Certification:

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

Total cultures:

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

AMR Appendices and Supplementary Tables



Appendix 1: Terms of Reference and Data Sharing Agreements

Data-Sharing Agreement

Between

Ministry of Health Gabon

(The Provider)

And

The African Society for Laboratory Medicine (ASLM)

(Recipient)

1. Purpose of Agreement.

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

2. Description of Data.

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

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

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

3. Confidentiality, use and storage of data

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

Appendix 2: Laboratory Eligibility Questionnaire

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

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

Part 4. Personnel and Training

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

Part 5. Specimen Management

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

Part 6. Laboratory Information System and Linkage to Clinical Data

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

Note: For question 1.4, the exact address was preferred, however, the nearest landmark or street intersection was acceptable, where applicable; for questions 1.5 and 1.6, more than one response was possible and for the option 'other', the response was entered as plain text; for question 2.2 mechanisms of antimicrobial resistance can vary: common mechanisms are production of enzymes (extended spectrum beta lactamase, carbapenemase, etc.) and resistance genes (mecA gene in MRSA, etc.); for question 4.a, the qualified microbiologist should possess a postgraduate degree in microbiology (medical or non-medical); for question 6.2c, more than one response was possible and for the option 'other', responses were entered as plain text (i) Of note, some countries received a version of the EQ which did not have the following two questions from part I: (i) Between 2016 and 2018, did the laboratory routinely conduct antimicrobial susceptibility testing? (ii) Is the laboratory willing to share 2016-2018 AST results with the MAAP consortium? However, AST capabilities were confirmed before the EQ evaluation, and the data sharing aspect of the process was already in place in agreements with the MoH.

Appendix 3: Laboratory Readiness Assessment

The EQ questions were scored for laboratory readiness as follows:

| Question | Response | Scoring |
|----------|----------|---------|
|----------|----------|---------|

Part 1: Site Information (Maximum score=0)

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

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

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

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

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

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

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

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

Part 5. Specimen Management (Maximum Score=3)

| | | | | | | |
|------|--|----------|-----------|-------|--|----------------------------------|
| 5.1 | Did the laboratory follow a defined standard operating procedure (SOP) for specimen collection and testing, at any time between 2016-18? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| 5.2 | Did the laboratory comply with specimen rejection criteria for rejecting inadequate specimens, at any time between 2016-18? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| 5.3A | Does the laboratory have information on the average number of specimens processed for culture and sensitivity in 2018? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| 5.3B | If you answered 'yes' to question 3A: What was the average number of specimens processed for bacterial culture in 2018? | | | | | None |
| 5.3C | If you answered 'yes' to question 3A: What was the average number of specimens that yielded bacterial growth and were processed for susceptibility tests, in 2018? | | | | | None |
| | <200 | 200-1000 | 1000-3000 | >3000 | | |

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

| | | | | | | |
|------|---|---|--|----|-----------------|---|
| 6.1 | Was a specimen (laboratory) identification number assigned to patient specimens received between 2016-18? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| 6.2A | Was there a system/database to store patient data (demographic, clinical and specimen) at any time between 2016-18? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| 6.2B | If you answered 'yes' to question 2A: What type of data was captured in the system/database? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| | Patient demographic data (i.e., age, date of birth, gender, location) | Patient clinical data (i.e., primary/chief diagnosis, comorbidities, current antibiotic treatment) | | | Patient outcome | |
| 6.2C | If you answered 'yes' to question 2A: What was the format for storage of information? | | | | | Score 1 for paper; 2 for mixed (E/P; E/P/O; others; mixed) and 3 for electronic (max score being 3) |
| | Paper-based | Electronic (laboratory information system, hospital information system, other databases e.g., WHONET) | | | Other | |
| 6.2D | If you answered 'yes' to question 2A: What is the location of this database, or where can this database be accessed from? | | | | | Score 1 for other; 2 for clinic and 3 for lab (max score being 6) |
| | Laboratory | Clinical facility | | | Other | |
| 6.3A | Were patient demographics and clinical information captured on test request forms at any time between 2016-18? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |
| 6.3B | If you answered 'yes' to question 3A: Were test request forms submitted between 2016 and 2018 stored and retrievable? | Yes | | No | | Score 1 for "Yes" and 0 for "No" |

Appendix 4: Key AMR Variables

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

Laboratory-specific variables

| | | |
|---|--|-----------|
| 1 | Laboratory's level of service (Reference- tier 3 or 4/ Regional/ Intermediate/ District/ Community/ Other) | Mandatory |
| 2 | Laboratory's affiliation (Government/Ministry of Health/ Private/Non-government organisation/ Other) | Mandatory |
| 3 | Laboratory co-location with clinic/hospital/pharmacy | Mandatory |
| 4 | If laboratory served as a national AMR surveillance site at any time between 2016 and 2018? | Mandatory |
| 5 | Facility and Equipment related variables | Mandatory |
| 6 | Quality Assurance (QA), accreditation and certification related variables | Mandatory |
| 7 | Personnel and training related variables | Mandatory |
| 8 | Specimen management related variables | Mandatory |
| 9 | Laboratory information system and linkage to clinical data | Mandatory |

Facility-specific variables (facility denotes co-located clinic/hospital or even from stand-alone laboratory as applicable; this information is obtained during phase of data collection)

| | | |
|----|---|----------|
| 1 | Ownership of facility (public/private/partnership/mission/military etc.) | Optional |
| 2 | Level of facility (primary, secondary, tertiary) | Optional |
| 3 | Facility co-location with pharmacy/lab | Optional |
| 4 | Number of inpatient beds in 2018 (and prior years as applicable) | Optional |
| 5 | Admissions in 2018 (and prior years as applicable) | Optional |
| 6 | Outpatients in 2018 (and prior years as applicable) | Optional |
| 7 | Presence of ID Department | Optional |
| 8 | No of ID physicians | Optional |
| 9 | No of ID nurses | Optional |
| 10 | Presence of AMS programme | 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 | Quinopristin dalfopristin | Any isolate that tested non-susceptible to quinopristin dalfopristin | Any isolate that tested susceptible or non-susceptible to quinopristin dalfopristin |
| Enterococcus species | Vancomycin | Any isolate that tested non-susceptible to vancomycin | Any isolate that tested susceptible or non-susceptible to vancomycin |
| Enterococcus species | Ampicillin | Any isolate that tested non-susceptible to ampicillin | Any isolate that tested susceptible or non-susceptible to ampicillin |
| Haemophilus influenzae | Ampicillin | Any isolate that tested non-susceptible to ampicillin | Any isolate that tested susceptible or non-susceptible to ampicillin |

| | | | |
|------------------------------|--|---|--|
| Helicobacter pylori | Clarithromycin | Any isolate that tested non-susceptible to clarithromycin | Any isolate that tested susceptible or non-susceptible to clarithromycin |
| Neisseria gonorrhoeae | 3rd generation cephalosporins | Any isolate that tested non-susceptible to 3rd generation cephalosporins | Any isolate that tested susceptible or non-susceptible to 3rd generation cephalosporins |
| Neisseria gonorrhoeae | Fluoroquinolones | Any isolate that tested non-susceptible to fluoroquinolones | Any isolate that tested susceptible or non-susceptible to fluoroquinolones |
| Pseudomonas species | Carbapenems | Any isolate that tested non-susceptible to carbapenems | Any isolate that tested susceptible or non-susceptible to carbapenems |
| Pseudomonas species | Aminoglycosides | Any isolate that tested non-susceptible to aminoglycosides | Any isolate that tested susceptible or non-susceptible to aminoglycosides |
| Pseudomonas species | Beta-lactam combinations (anti-pseudomonals) | Any isolate that tested non-susceptible to beta-lactam combinations (anti-pseudomonals) | Any isolate that tested susceptible or non-susceptible to beta-lactam combinations (anti-pseudomonals) |
| Pseudomonas species | Lipopeptides (Colistin and Polymyxin B) | Any isolate that tested non-susceptible to Colistin and Polymyxin B | Any isolate that tested susceptible or non-susceptible to Colistin and Polymyxin B |
| Pseudomonas species | Carbapenems | Any isolate that tested non-susceptible to carbapenems | Any isolate that tested susceptible or non-susceptible to carbapenems |
| Staphylococcus species | Methicillin | Any isolate that tested non-susceptible to penicillins (anti-staphylococcal) or cephamycins | Any isolate that tested susceptible or non-susceptible to penicillins (anti-staphylococcal) or cephamycins |
| Staphylococcus species (iii) | Vancomycin resistant (iv) | Any isolate that tested resistant to vancomycin (v) | Any isolate that tested susceptible or non-susceptible to vancomycin (vi) |
| Staphylococcus species | Vancomycin intermediate | Any isolate that tested intermediate to vancomycin | Any isolate that tested susceptible or non-susceptible to vancomycin |
| Staphylococcus species | Penicillins | Any isolate that tested non-susceptible to penicillins | Any isolate that tested susceptible or non-susceptible to penicillins |
| Staphylococcus species | Linezolid | Any isolate that tested non-susceptible to 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=20 n (%) | Reference N = 5 n (%) | Regional/ Intermediate N =10 n (%) | District/ Community N = 1 n (%) | Unspecified N = 4 n (%) |
|-------------|---------------------------|-----------------------------|---|--|-------------------------------|
| Government | 9 (45.0) | 4 (80.0) | 5 (50.0) | 0 | 0 |
| Private | 9 (45.0) | 0 | 5 (50.0) | 1 (100.0) | 3 (75.0) |
| NGO | 0 | 0 | 0 | 0 | 0 |
| Others | 2 (10.0) | 1 (20.0) | 0 | 0 | 1 (25.0) |

Supplementary Table 2: Assessment of preparedness for AMR surveillance

| Parameters | Surveyed laboratories N=20 n (%) |
|--|--|
| Commodity and equipment status | |
| Regular power supply and functional back up | 16 (80.0) |
| Continuous water supply | 18 (90.0) |
| Certified and functional biosafety cabinets | 8 (40.0) |
| Automated methods for pathogen identification | 7 (35.0) |
| Automated methods for antimicrobial susceptibility testing | 6 (30.0) |
| Methods for testing antimicrobial resistance mechanisms | 9 (45.0) |
| QMS implementation | |
| Reported QMS Implementation | 7 (35.0) |
| • Reported QMS tool (n=7) | |
| • LQMS | 2 (28.6) |
| • SLIPTA | 2 (28.6) |
| • SLMTA | 1 (14.3) |
| • Mentoring | 0 (0.0) |
| • Combination‡ | 1 (14.3) |
| • Others | 0 (0.0) |
| Quality Certification | 0 (0.0) |
| • Reported certification type (n=0) | |
| • SLIPTA | - |
| • College of American Pathologists | - |
| • Others | - |
| Accreditation | 0 (0.0) |
| Participation in proficiency testing | 3 (15.0) |
| Utilization of reference strains | 6 (30.0) |
| Reported consistent maintenance of QC records | 5 (25.0) |
| Designated focal quality person | 8 (40.0) |
| Reported compliance to standard operating procedures | 17 (85.0) |
| Reported compliance to antimicrobial susceptibility testing standards | 14 (70.0) |
| Personnel and training status | |
| Presence of at least one qualified microbiologist | 11 (55.0) |
| Presence of an experienced laboratory scientist/technologist | 17 (85.0) |
| Up-to-date and complete records on staff training and competence | 10 (50.0) |
| Specimen Management status | |
| Reported compliance to standard operating procedures on specimen collection and testing | 16 (80.0) |
| Reported compliance to standard operating procedures on specimen rejection | 15 (75.0) |
| Availability on average number of specimens processed for culture and sensitivity in year 2018 | 17 (85.0) |
| Laboratory Information System and Linkage to Clinical Data | |
| Assigned specimen (laboratory) identification number | 15 (75.0) |
| Availability of system/database to store patient data | 18 (90.0) |
| • System/database format (n=18) | |
| • Paper-based | 5 (27.8) |
| • Electronic | 2 (11.1) |
| • Mixed | 11 (61.1) |
| Captured patients' demographics and clinical information on test request forms | 13 (65.0) |
| • Retrievable test request forms (n=13) | 11 (84.6) |

*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 | | 7877 | 11616 | 11659 | 3284 | 4606 | 4724 | 2301 | 3005 | 3119 |
| Pathogen type | bacteria | | | | 2674 (81.4) | 3911 (84.9) | 4059 (85.9) | 2129 (92.5) | 2899 (96.5) | 2987 (95.8) |
| | fungi | | | | 610 (18.6) | 695 (15.1) | 665 (14.1) | 172 (7.5) | 106 (3.5) | 132 (4.2) |
| Age, years | Less than 1 | 83 (1.1) | 87 (0.7) | 112 (1.0) | 45 (1.4) | 43 (0.9) | 49 (1.0) | 32 (1.4) | 31 (1.0) | 39 (1.3) |
| | 1 to 17 | 783 (9.9) | 1074 (9.2) | 1082 (9.3) | 280 (8.5) | 343 (7.4) | 348 (7.4) | 191 (8.3) | 231 (7.7) | 242 (7.8) |
| | 18 to 49 | 4299 (54.6) | 6619 (57.0) | 7480 (64.2) | 1878 (57.2) | 2798 (60.7) | 3094 (65.5) | 1217 (52.9) | 1668 (55.5) | 1816 (58.2) |
| | 50 to 65 | 462 (5.9) | 736 (6.3) | 852 (7.3) | 161 (4.9) | 219 (4.8) | 275 (5.8) | 120 (5.2) | 165 (5.5) | 214 (6.9) |
| | Above 65 | 223 (2.8) | 294 (2.5) | 360 (3.1) | 88 (2.7) | 111 (2.4) | 130 (2.8) | 78 (3.4) | 103 (3.4) | 110 (3.5) |
| | Unknown Age | 2027 (25.7) | 2806 (24.2) | 1773 (15.2) | 832 (25.3) | 1092 (23.7) | 828 (17.5) | 663 (28.8) | 807 (26.9) | 698 (22.4) |
| Gender | Male | 2201 (27.9) | 2791 (24.0) | 2829 (24.3) | 654 (19.9) | 652 (14.2) | 727 (15.4) | 521 (22.6) | 552 (18.4) | 636 (20.4) |
| | Female | 5674 (72.0) | 8825 (76.0) | 8825 (75.7) | 2628 (80.0) | 3954 (85.8) | 3993 (84.5) | 1778 (77.3) | 2453 (81.6) | 2479 (79.5) |
| Laboratory | CERMEL | 2 (0.0) | | 5 (0.0) | 2 (0.1) | | 4 (0.1) | 2 (0.1) | | 4 (0.1) |
| | LAM CIRMF | 394 (5.0) | 302 (2.6) | 265 (2.3) | 231 (7.0) | 143 (3.1) | 133 (2.8) | 109 (4.7) | 60 (2.0) | 47 (1.5) |
| | CHU Libreville | 796 (10.1) | 964 (8.3) | 1208 (10.4) | 411 (12.5) | 498 (10.8) | 644 (13.6) | 301 (13.1) | 385 (12.8) | 616 (19.7) |
| | CHU Owendo | 59 (0.7) | 1512 (13.0) | 2336 (20.0) | 30 (0.9) | 580 (12.6) | 864 (18.3) | 25 (1.1) | 276 (9.2) | 465 (14.9) |
| | CHUMEF | | 219 (1.9) | 588 (5.0) | | 60 (1.3) | 239 (5.1) | | 57 (1.9) | 159 (5.1) |
| | Akanda | | 433 (3.7) | 252 (2.2) | | 204 (4.4) | 118 (2.5) | | 116 (3.9) | 59 (1.9) |
| | LNSP | 195 (2.5) | 238 (2.0) | 394 (3.4) | 55 (1.7) | 61 (1.3) | 150 (3.2) | 28 (1.2) | 37 (1.2) | 48 (1.5) |
| | CHR Tchibanga | 371 (4.7) | 741 (6.4) | 95 (0.8) | 187 (5.7) | 419 (9.1) | 65 (1.4) | 149 (6.5) | 312 (10.4) | 46 (1.5) |
| | d'Oloume | 620 (7.9) | 989 (8.5) | 519 (4.5) | 214 (6.5) | 276 (6.0) | 125 (2.6) | 45 (2.0) | 81 (2.7) | 45 (1.4) |
| | Assalas | 686 (8.7) | 879 (7.6) | 818 (7.0) | 191 (5.8) | 223 (4.8) | 223 (4.7) | 100 (4.3) | 103 (3.4) | 70 (2.2) |
| | USS | 730 (9.3) | 835 (7.2) | 871 (7.5) | 250 (7.6) | 312 (6.8) | 421 (8.9) | 228 (9.9) | 297 (9.9) | 409 (13.1) |
| | Bioclin | 249 (3.2) | 258 (2.2) | 76 (0.7) | 162 (4.9) | 185 (4.0) | 61 (1.3) | 80 (3.5) | 86 (2.9) | 30 (1.0) |
| | UNILAB | 1040 (13.2) | 1640 (14.1) | 1711 (14.7) | 487 (14.8) | 799 (17.3) | 805 (17.0) | 355 (15.4) | 539 (17.9) | 582 (18.7) |
| | CHR Rawiri | 542 (6.9) | 521 (4.5) | 515 (4.4) | 199 (6.1) | 183 (4.0) | 220 (4.7) | 162 (7.0) | 153 (5.1) | 184 (5.9) |
| | BIOLAB | 513 (6.5) | 583 (5.0) | 1012 (8.7) | 133 (4.0) | 140 (3.0) | 387 (8.2) | 70 (3.0) | 92 (3.1) | 100 (3.2) |
| Essono Ondo | 1497 (19.0) | 1330 (11.4) | 886 (7.6) | 657 (20.0) | 422 (9.2) | 193 (4.1) | 592 (25.7) | 323 (10.7) | 187 (6.0) | |

Supplementary Table 4: Specimen characteristics

| Specimen Type | All years* N= 8425 n (%) | 2016 N = 2301 n (%) | 2017 N = 3005 n (%) | 2018 N = 3119 n (%) |
|----------------------------------|--------------------------------|---------------------------|---------------------------|---------------------------|
| Abscess (brain/cerebral) | 149 (1.8) | 37 (1.6) | 50 (1.7) | 62 (2) |
| Abscess/Discharge/Pus/Swab/Wound | 1 (0) | - | 1 (0) | - |
| Aspirate/discharge | 28 (0.3) | 9 (0.4) | 11 (0.4) | 8 (0.3) |
| Blood | 3 (0) | - | 3 (0.1) | - |
| Catheter (central line) | 2 (0) | 2 (0.1) | - | - |
| Catheter (umbilical) | 10 (0.1) | 3 (0.1) | 6 (0.2) | 1 (0) |
| Catheter (unspecified) | 3 (0) | 1 (0) | - | 2 (0.1) |
| Catheter (urinary) | 10 (0.1) | 1 (0) | 1 (0) | 8 (0.3) |
| Catheter tip | 11 (0.1) | 2 (0.1) | 4 (0.1) | 5 (0.2) |
| CSF | 2 (0) | 1 (0) | - | 1 (0) |
| Drain | 1 (0) | - | 1 (0) | - |
| Fluid (abdominal/peritoneal) | 2 (0) | 2 (0.1) | - | - |
| Fluid (Gastric) | 23 (0.3) | 1 (0) | 9 (0.3) | 13 (0.4) |
| Fluid (joint/synovial) | 1 (0) | - | - | 1 (0) |
| Fluid (pericardial) | 1 (0) | - | - | 1 (0) |
| Fluid (pleural) | 1 (0) | - | 1 (0) | - |
| Fluid (scrotal) | 14 (0.2) | - | 14 (0.5) | - |
| Fluid (sinus) | 128 (1.5) | 4 (0.2) | 30 (1) | 94 (3) |
| Fluid (unspecified) | 176 (2.1) | 76 (3.3) | 30 (1) | 70 (2.2) |
| Genitourinary | 1 (0) | - | 1 (0) | - |
| Respiratory-Lower | 10 (0.1) | 3 (0.1) | 1 (0) | 6 (0.2) |
| Respiratory-Upper | 45 (0.5) | 16 (0.7) | 15 (0.5) | 14 (0.4) |
| Scraping (cornea) | 62 (0.7) | 38 (1.7) | 14 (0.5) | 10 (0.3) |
| Semen | 12 (0.1) | 7 (0.3) | 1 (0) | 4 (0.1) |
| Stool | 7 (0.1) | 2 (0.1) | - | 5 (0.2) |
| Swab (cervical) | 2040 (24.2) | 783 (34) | 632 (21) | 625 (20) |
| Swab (high vaginal) | 6 (0.1) | 4 (0.2) | 2 (0.1) | - |
| Swab (rectal) | 9 (0.1) | 2 (0.1) | 4 (0.1) | 3 (0.1) |
| Swab (urethral) | 3 (0) | 2 (0.1) | - | 1 (0) |
| Swab (vaginal) | 1638 (19.4) | 346 (15) | 554 (18.4) | 738 (23.7) |
| Swab/discharge | 6 (0.1) | 2 (0.1) | 1 (0) | 3 (0.1) |
| Swab/discharge (ear) | 117 (1.4) | 50 (2.2) | 24 (0.8) | 43 (1.4) |
| Swab/discharge (eye) | 716 (8.5) | 101 (4.4) | 237 (7.9) | 378 (12.1) |
| Swab/discharge (genital) | 222 (2.6) | 32 (1.4) | 170 (5.7) | 20 (0.6) |
| Swab/discharge (skin) | 2965 (35.2) | 774 (33.6) | 1188 (39.5) | |
| Swab/discharge (urethral) | 149 (1.8) | 37 (1.6) | 50 (1.7) | |
| Tissue/biopsy | 1 (0) | - | 1 (0) | - |
| Ulcer | 28 (0.3) | 9 (0.4) | 11 (0.4) | 8 (0.3) |
| Urine | 3 (0) | - | 3 (0.1) | - |

*Indicates positive cultures with AST results

Supplementary Table 5: Pathogen identification

| Pathogen | All years* N= 8 425 n (%) | 2016 N = 2 301 n (%) | 2017 N =3 005 n (%) | 2018 N = 3 119 n (%) |
|--|---------------------------------|----------------------------|---------------------------|----------------------------|
| Positive cultures with specific pathogen name | 7681 (91.2) | 2030 (88.2) | 2731 (90.9) | 2920 (93.6) |
| <i>Abiotrophia defectiva</i> | 1 (0) | 1 (0) | - | 2920 (93.6) |
| <i>Acinetobacter baumannii</i> | 92 (1.1) | 27 (1.2) | 45 (1.5) | - |
| <i>Acinetobacter Iwoffii</i> | 1 (0) | - | - | 20 (0.6) |
| <i>Aerococcus viridans</i> | 6 (0.1) | 5 (0.2) | 1 (0) | 1 (0) |
| <i>Aeromonas hydrophila</i> | 13 (0.2) | 5 (0.2) | 5 (0.2) | - |
| <i>Bacillus lentus</i> | 1 (0) | - | - | 3 (0.1) |
| <i>Burkholderia cepacia</i> | 8 (0.1) | - | - | 1 (0) |
| <i>Burkholderia gladioli</i> | 1 (0) | - | - | 8 (0.3) |
| <i>Candida albicans</i> | 267 (3.2) | 95 (4.1) | 63 (2.1) | 1 (0) |
| <i>Candida ciferrii</i> | 5 (0.1) | 4 (0.2) | 1 (0) | 109 (3.5) |
| <i>Candida dubliniensis</i> | 1 (0) | - | 1 (0) | - |
| <i>Candida famata</i> | 38 (0.5) | 19 (0.8) | 12 (0.4) | - |
| <i>Candida glabrata</i> | 7 (0.1) | 4 (0.2) | 3 (0.1) | 7 (0.2) |
| <i>Candida guilliermondii</i> | 1 (0) | - | 1 (0) | - |
| <i>Candida kefyr</i> | 1 (0) | - | 1 (0) | - |
| <i>Candida krusei</i> | 7 (0.1) | 4 (0.2) | 2 (0.1) | - |
| <i>Candida lusitanae</i> | 3 (0) | 2 (0.1) | 1 (0) | 1 (0) |
| <i>Candida norvegensis</i> | 2 (0) | 2 (0.1) | - | - |
| <i>Candida parapsilosis</i> | 7 (0.1) | 5 (0.2) | 1 (0) | - |
| <i>Candida rugosa</i> | 1 (0) | 1 (0) | - | 1 (0) |
| <i>Candida tropicalis</i> | 32 (0.4) | 21 (0.9) | 6 (0.2) | - |
| <i>Chryseobacterium indologenes</i> | 3 (0) | 2 (0.1) | - | 5 (0.2) |
| <i>Chryseomonas luteola</i> | 5 (0.1) | 2 (0.1) | 1 (0) | 1 (0) |
| <i>Citrobacter braakii</i> | 29 (0.3) | 13 (0.6) | 11 (0.4) | 2 (0.1) |
| <i>Citrobacter diversus</i> | 3 (0) | 2 (0.1) | 1 (0) | 5 (0.2) |
| <i>Citrobacter farmeri</i> | 8 (0.1) | 5 (0.2) | 2 (0.1) | - |
| <i>Citrobacter freundii</i> | 49 (0.6) | 15 (0.7) | 13 (0.4) | 1 (0) |
| <i>Citrobacter koseri</i> | 97 (1.2) | 38 (1.7) | 39 (1.3) | 21 (0.7) |
| <i>Citrobacter sedlakii</i> | 5 (0.1) | 5 (0.2) | - | 20 (0.6) |
| <i>Clostridium cadaveris</i> | 1 (0) | - | - | - |
| <i>Corynebacterium urealyticum</i> | 1 (0) | - | 1 (0) | 1 (0) |
| <i>Cronobacter sakazakii</i> | 6 (0.1) | 3 (0.1) | 2 (0.1) | - |
| <i>Edwardsiella tarda</i> | 1 (0) | 1 (0) | - | 1 (0) |
| <i>Elizabethkingia meningosepticum</i> | 1 (0) | - | - | - |
| <i>Enterobacter amnigenus</i> | 2 (0) | - | 2 (0.1) | 1 (0) |
| <i>Enterobacter asburiae</i> | 1 (0) | 1 (0) | - | - |
| <i>Enterobacter cloacae</i> | 138 (1.6) | 39 (1.7) | 57 (1.9) | - |
| <i>Enterobacter gergoviae</i> | 1 (0) | - | - | 42 (1.3) |
| <i>Enterococcus avium</i> | 1 (0) | 1 (0) | - | 1 (0) |

| | | | | |
|--------------------------------------|-------------|------------|------------|------------|
| <i>Enterococcus durans</i> | 1 (0) | - | - | - |
| <i>Enterococcus faecalis</i> | 107 (1.3) | 27 (1.2) | 40 (1.3) | 1 (0) |
| <i>Enterococcus faecium</i> | 4 (0) | 1 (0) | - | 40 (1.3) |
| <i>Escherichia coli</i> | 1274 (15.1) | 347 (15.1) | 503 (16.7) | 3 (0.1) |
| <i>Escherichia vulneris</i> | 4 (0) | - | - | 424 (13.6) |
| <i>Flavimonas oryzihabitans</i> | 1 (0) | 1 (0) | - | 4 (0.1) |
| <i>Gardnerella vaginalis</i> | 11 (0.1) | 2 (0.1) | 2 (0.1) | - |
| <i>Gemella morbillorum</i> | 1 (0) | - | - | 7 (0.2) |
| <i>Geotrichum candidum</i> | 1 (0) | 1 (0) | - | 1 (0) |
| <i>Haemophilus influenzae</i> | 3 (0) | - | 1 (0) | - |
| <i>Haemophilus parainfluenzae</i> | 1 (0) | - | - | 2 (0.1) |
| <i>Hafnia alvei</i> | 10 (0.1) | 1 (0) | 9 (0.3) | 1 (0) |
| <i>Klebsiella aerogenes</i> | 33 (0.4) | 9 (0.4) | 10 (0.3) | - |
| <i>Klebsiella oxytoca</i> | 160 (1.9) | 36 (1.6) | 48 (1.6) | 14 (0.4) |
| <i>Klebsiella pneumoniae</i> | 404 (4.8) | 84 (3.7) | 171 (5.7) | 76 (2.4) |
| <i>Kluyvera cryocrescens</i> | 1 (0) | - | 1 (0) | 149 (4.8) |
| <i>Kocuria kristinae</i> | 13 (0.2) | 8 (0.3) | 1 (0) | - |
| <i>Kocuria varians</i> | 4 (0) | 3 (0.1) | - | 4 (0.1) |
| <i>Lactococcus lactis</i> | 1 (0) | - | - | 1 (0) |
| <i>Morganella morgani</i> | 19 (0.2) | 5 (0.2) | 7 (0.2) | 1 (0) |
| <i>Mycoplasma hominis</i> | 808 (9.6) | 235 (10.2) | 345 (11.5) | 7 (0.2) |
| <i>Neisseria cinerea</i> | 2 (0) | 1 (0) | - | 228 (7.3) |
| <i>Neisseria gonorrhoeae</i> | 14 (0.2) | 3 (0.1) | 6 (0.2) | 1 (0) |
| <i>Ochrobactrum anthropi</i> | 1 (0) | - | - | 5 (0.2) |
| <i>Pasteurella canis</i> | 1 (0) | - | - | 1 (0) |
| <i>Pasteurella multocida</i> | 1 (0) | - | 1 (0) | 1 (0) |
| <i>Pediococcus pentosaceus</i> | 1 (0) | - | - | - |
| <i>Peptostreptococcus anaerobius</i> | 1 (0) | 1 (0) | - | 1 (0) |
| <i>Proteus hauseri</i> | 1 (0) | - | - | - |
| <i>Proteus mirabilis</i> | 103 (1.2) | 24 (1) | 35 (1.2) | 1 (0) |
| <i>Proteus vulgaris</i> | 7 (0.1) | 2 (0.1) | 2 (0.1) | 44 (1.4) |
| <i>Providencia alcalifaciens</i> | 4 (0) | - | - | 3 (0.1) |
| <i>Providencia rettgeri</i> | 3 (0) | - | 1 (0) | 4 (0.1) |
| <i>Providencia stuartii</i> | 2 (0) | - | - | 2 (0.1) |
| <i>Pseudomonas aeruginosa</i> | 90 (1.1) | 21 (0.9) | 30 (1) | 2 (0.1) |
| <i>Pseudomonas fluorescens</i> | 9 (0.1) | 3 (0.1) | 1 (0) | 39 (1.3) |
| <i>Pseudomonas putida</i> | 2 (0) | 1 (0) | - | 5 (0.2) |
| <i>Pseudomonas stutzeri</i> | 1 (0) | - | - | 1 (0) |
| <i>Rahnella aquatilis</i> | 1 (0) | 1 (0) | - | 1 (0) |
| <i>Raoultella ornithinolytica</i> | 6 (0.1) | 3 (0.1) | 1 (0) | - |
| <i>Saccharomyces cerevisiae</i> | 1 (0) | - | - | 2 (0.1) |
| <i>Salmonella choleraesuis</i> | 3 (0) | 2 (0.1) | 1 (0) | 1 (0) |
| <i>Salmonella enterica</i> | 6 (0.1) | 2 (0.1) | 2 (0.1) | - |

| | | | | |
|---|------------|-----------|-----------|------------|
| <i>Salmonella falkensee</i> | 1 (0) | - | 1 (0) | 2 (0.1) |
| <i>Salmonella typhi</i> | 3 (0) | 1 (0) | - | - |
| <i>Salmonella typhimurium</i> | 1 (0) | 1 (0) | - | 2 (0.1) |
| <i>Serratia ficaria</i> | 2 (0) | 1 (0) | - | - |
| <i>Serratia fonticola</i> | 8 (0.1) | 2 (0.1) | 6 (0.2) | 1 (0) |
| <i>Serratia liquefaciens</i> | 26 (0.3) | 9 (0.4) | 10 (0.3) | - |
| <i>Serratia marcescens</i> | 60 (0.7) | 12 (0.5) | 27 (0.9) | 7 (0.2) |
| <i>Serratia odorifera</i> | 143 (1.7) | 29 (1.3) | 62 (2.1) | 21 (0.7) |
| <i>Serratia plymuthica</i> | 2 (0) | - | 1 (0) | 52 (1.7) |
| <i>Serratia rubidaea</i> | 1 (0) | 1 (0) | - | 1 (0) |
| <i>Shigella sonnei</i> | 5 (0.1) | 4 (0.2) | - | - |
| <i>Sphingobacterium multivorum</i> | 1 (0) | - | 1 (0) | 1 (0) |
| <i>Sphingomonas paucimobilis</i> | 25 (0.3) | 4 (0.2) | 7 (0.2) | - |
| <i>Staphylococcus arlettae</i> | 3 (0) | 1 (0) | - | 14 (0.4) |
| <i>Staphylococcus aureus</i> | 884 (10.5) | 226 (9.8) | 294 (9.8) | 2 (0.1) |
| <i>Staphylococcus capitis</i> | 6 (0.1) | 4 (0.2) | 2 (0.1) | 364 (11.7) |
| <i>Staphylococcus caprae</i> | 3 (0) | - | 2 (0.1) | - |
| <i>Staphylococcus epidermidis</i> | 65 (0.8) | 8 (0.3) | 20 (0.7) | 1 (0) |
| <i>Staphylococcus haemolyticus</i> | 41 (0.5) | 11 (0.5) | 13 (0.4) | 37 (1.2) |
| <i>Staphylococcus hominis</i> | 11 (0.1) | 1 (0) | 1 (0) | 17 (0.5) |
| <i>Staphylococcus intermedius</i> | 1 (0) | 1 (0) | - | 9 (0.3) |
| <i>Staphylococcus lugdunensis</i> | 1 (0) | - | 1 (0) | - |
| <i>Staphylococcus pseudintermedius</i> | 2 (0) | 2 (0.1) | - | - |
| <i>Staphylococcus saccharolyticus</i> | 1 (0) | 1 (0) | - | - |
| <i>Staphylococcus saprophyticus</i> | 58 (0.7) | 10 (0.4) | 32 (1.1) | - |
| <i>Staphylococcus sciuri</i> | 10 (0.1) | 1 (0) | 5 (0.2) | 16 (0.5) |
| <i>Staphylococcus simulans</i> | 4 (0) | - | 2 (0.1) | 4 (0.1) |
| <i>Staphylococcus warneri</i> | 5 (0.1) | - | 2 (0.1) | 2 (0.1) |
| <i>Staphylococcus xylosus</i> | 13 (0.2) | 4 (0.2) | 5 (0.2) | 3 (0.1) |
| <i>Stenotrophomonas (xanthomonas) maltophilia</i> | 12 (0.1) | - | 5 (0.2) | 4 (0.1) |
| <i>Streptococcus acidominimus</i> | 1 (0) | 1 (0) | - | 7 (0.2) |
| <i>Streptococcus agalactiae</i> | 83 (1) | 16 (0.7) | 24 (0.8) | - |
| <i>Streptococcus anginosus</i> | 4 (0) | - | - | 43 (1.4) |
| <i>Streptococcus canis</i> | 1 (0) | - | - | 4 (0.1) |
| <i>Streptococcus dysgalactiae</i> | 3 (0) | - | 1 (0) | 1 (0) |
| <i>Streptococcus gallolyticus</i> | 1 (0) | - | - | 2 (0.1) |
| <i>Streptococcus macacae</i> | 1 (0) | - | - | 1 (0) |
| <i>Streptococcus oralis</i> | 1 (0) | - | 1 (0) | 1 (0) |
| <i>Streptococcus pneumoniae</i> | 4 (0) | 1 (0) | - | - |
| <i>Streptococcus sanguinis</i> | 5 (0.1) | 1 (0) | - | 3 (0.1) |
| <i>Streptococcus uberis</i> | 4 (0) | 2 (0.1) | 2 (0.1) | 4 (0.1) |
| <i>Streptococcus viridans</i> | 3 (0) | 3 (0.1) | - | - |
| <i>Trichosporon mucoides</i> | 1 (0) | 1 (0) | - | - |

| | | | | |
|---|-----------|------------|------------|------------|
| Ureaplasma urealyticum | 2189 (26) | 521 (22.6) | 711 (23.7) | - |
| Vibrio cholerae | 1 (0) | - | - | 957 (30.7) |
| Yersinia enterocolitica | 10 (0.1) | 3 (0.1) | 1 (0) | 1 (0) |
| Yersinia kristensenii | 1 (0) | - | 1 (0) | 6 (0.2) |
| Yersinia pseudotuberculosis | 2 (0) | 1 (0) | 1 (0) | - |
| Positive cultures with non-specific pathogen name | 744 (8.8) | 271 (11.8) | 274 (9.1) | - |
| Acinetobacter Sp. | 2 (0) | 1 (0) | 1 (0) | 199 (6.4) |
| Aeromonas Sp. | 2 (0) | - | 1 (0) | - |
| Bacillus Sp. | 6 (0.1) | 1 (0) | 4 (0.1) | 1 (0) |
| Bacteroides Sp. | 1 (0) | - | 1 (0) | 1 (0) |
| Campylobacter Sp. | 8 (0.1) | - | 1 (0) | - |
| Candida Sp. | 30 (0.4) | 11 (0.5) | 14 (0.5) | 7 (0.2) |
| Chryseobacterium Sp. | 1 (0) | - | - | 5 (0.2) |
| Citrobacter Sp. | 16 (0.2) | 1 (0) | 8 (0.3) | 1 (0) |
| Corynebacterium Sp. | 3 (0) | - | 1 (0) | 7 (0.2) |
| Enterobacter Sp. | 18 (0.2) | 7 (0.3) | 7 (0.2) | 2 (0.1) |
| Enterococcus Sp. | 34 (0.4) | 6 (0.3) | 21 (0.7) | 4 (0.1) |
| Epidermophyton Sp. | 1 (0) | - | - | 7 (0.2) |
| Escherichia Sp. | 1 (0) | 1 (0) | - | 1 (0) |
| Klebsiella Sp. | 33 (0.4) | 7 (0.3) | 11 (0.4) | - |
| Kluyvera Sp. | 4 (0) | 2 (0.1) | 1 (0) | 15 (0.5) |
| Leuconostoc Sp. | 2 (0) | 1 (0) | 1 (0) | 1 (0) |
| Listeria Sp. | 1 (0) | 1 (0) | - | - |
| Methylobacterium Sp. | 1 (0) | - | - | - |
| Micrococcus Sp. | 15 (0.2) | 5 (0.2) | 6 (0.2) | 1 (0) |
| Mycoplasma Sp. | 10 (0.1) | 4 (0.2) | 3 (0.1) | 4 (0.1) |
| Myroides Sp. | 1 (0) | - | 1 (0) | 3 (0.1) |
| Neisseria Sp. | 7 (0.1) | 2 (0.1) | 5 (0.2) | - |
| Pantoea Sp. | 33 (0.4) | 7 (0.3) | 10 (0.3) | - |
| Proteus Sp. | 1 (0) | 1 (0) | - | 16 (0.5) |
| Providencia Sp. | 3 (0) | - | 3 (0.1) | - |
| Pseudomonas Sp. | 21 (0.2) | 1 (0) | 5 (0.2) | - |
| Salmonella Sp. | 45 (0.5) | 6 (0.3) | 23 (0.8) | 15 (0.5) |
| Shigella Sp. | 7 (0.1) | - | 4 (0.1) | 16 (0.5) |
| Staphylococcus Sp. | 256 (3) | 138 (6) | 71 (2.4) | 3 (0.1) |
| Stenella Sp. | 1 (0) | 1 (0) | - | 47 (1.5) |
| Streptobacillus Sp. | 1 (0) | - | 1 (0) | - |
| Streptococcus Sp. | 139 (1.6) | 59 (2.6) | 44 (1.5) | - |
| Trichosporon Sp. | 3 (0) | 1 (0) | - | 36 (1.2) |
| Ureaplasma Sp. | 30 (0.4) | 4 (0.2) | 22 (0.7) | 2 (0.1) |
| Vibrio Sp. | 1 (0) | 1 (0) | - | 4 (0.1) |
| Yersinia Sp. | 6 (0.1) | 2 (0.1) | 4 (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 |
| CERMEL | 3 | 3 | 3 | 3 |
| LAM CIRMF | 4 | 4 | 4 | 4 |
| CHU Libreville | 4 | 4 | 4 | 4 |
| CHU Owendo | | 4 | 4 | 4 |
| CHUMEF | | 4 | 4 | 4 |
| Akanda | 4 | 4 | 4 | 4 |
| LNSP | 4 | 4 | 4 | 4 |
| CHR Tchibanga | 4 | 4 | 4 | 4 |
| d'Oloume | 4 | 4 | 4 | 4 |
| Assalas | 4 | 4 | 4 | 4 |
| Essono Ondo | 4 | 4 | 4 | 4 |
| USS | 4 | 4 | 4 | 4 |
| Bioclin | 4 | 4 | 4 | 4 |
| UNILAB | 4 | 4 | 4 | 4 |
| CHR Rawiri | 4 | 4 | 4 | 4 |
| BIOLAB | 3 | 3 | 4 | 3.3 |

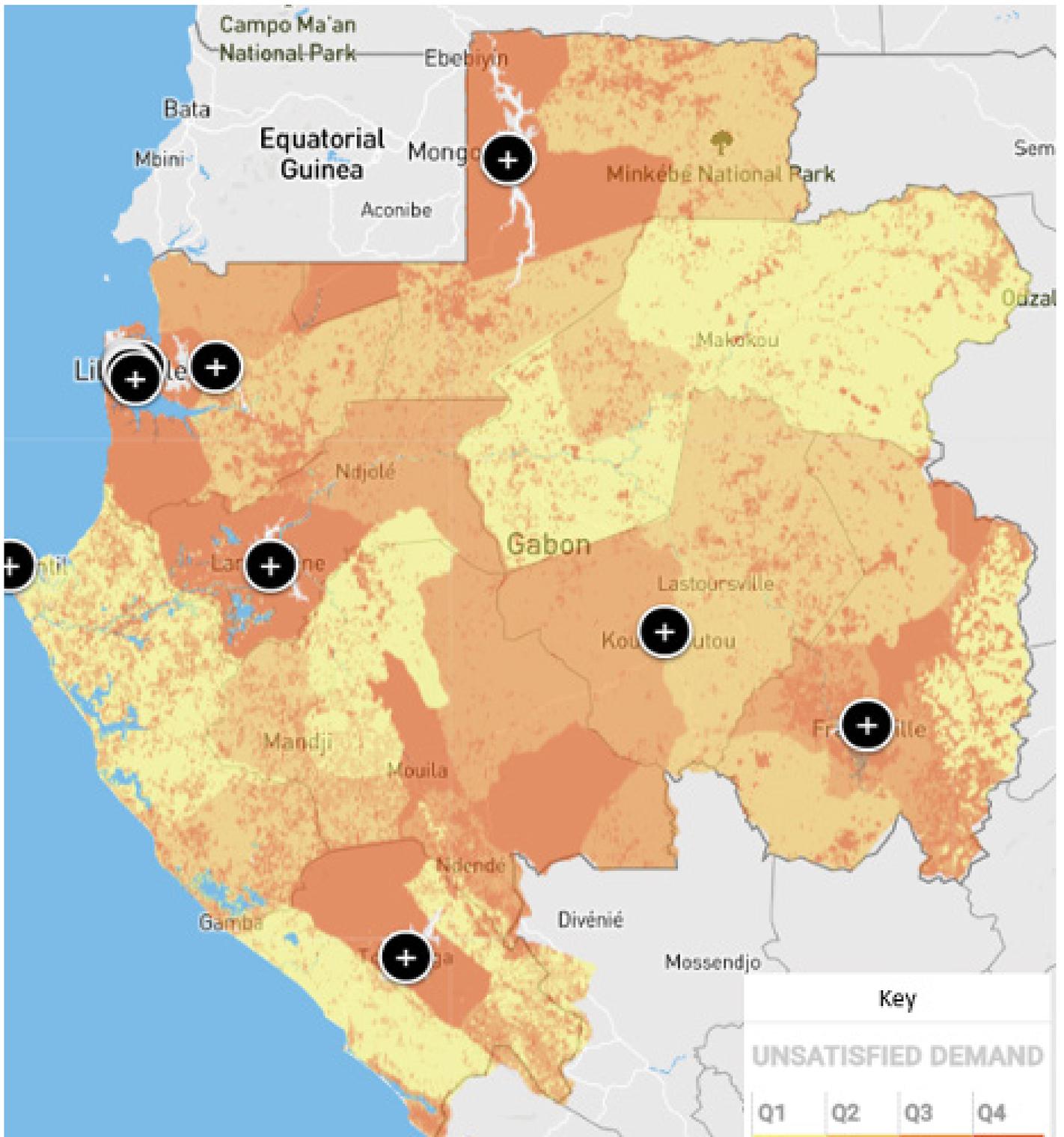
Supplementary Table 7: Univariate logistic regression analysis

| Variable | Options | N | NS (%) | OR (95% CI) | P-value |
|------------|---------|------|--------|--------------------|---------|
| Gender | Female | 6219 | 41.4 | Ref | 0.000 |
| | Male | 2069 | 51.4 | 1.50 (1.30 – 1.74) | |
| Age, years | <1 | 173 | 51.5 | 1.46 (1.09 – 1.93) | 0.0007 |
| | 1-17 | 1115 | 41.8 | 0.99 (0.73 – 1.34) | |
| | 18-49 | 4569 | 42.0 | Ref | |
| | 50-65 | 1036 | 47.6 | 1.25 (1.07 – 1.47) | |
| | >65 | 634 | 47.3 | 1.24 (1.01 – 1.53) | |
| | No | 296 | 27.7 | Ref | 0.0325 |
| | Yes | 78 | 48.7 | 2.48 (1.08 – 5.70) | |

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

AMR Supplementary Figures

Supplementary Figure 1: Population coverage of laboratories



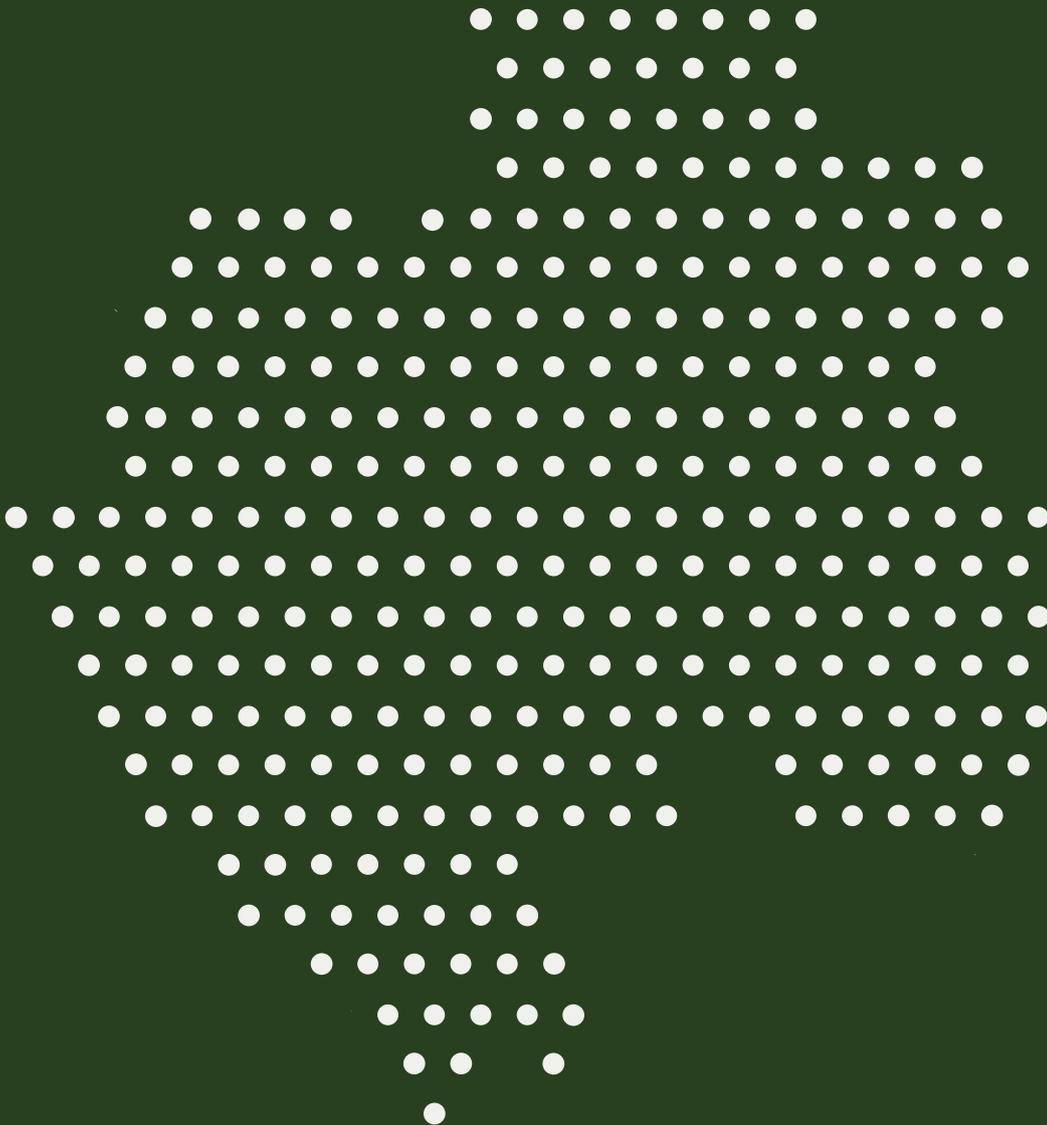
Supplementary Figure 2a: Inappropriate testing A

| Organism Name | Antimicrobial Agent | Agent Code | Interpreted Results | Antimicrobial Susceptibility Method | Year |
|------------------------|---------------------|------------|---------------------|-------------------------------------|------|
| Escherichia coli | Amphotericin B | AMB_ED10 | R | Disk | 2016 |
| Staphylococcus sp. | Fluconazole | FLU_ED25 | R | Disk | 2017 |
| Mycoplasma hominis | Fluconazole | FLU_ED25 | I | Disk | 2017 |
| Mycoplasma hominis | Itraconazole | ITR_ED10 | I | Disk | 2017 |
| Mycoplasma hominis | Voriconazole | VOR_ED1 | R | Disk | 2017 |
| Ureaplasma urealyticum | Fluconazole | FLU_ND25 | S | Disk | 2018 |
| Ureaplasma urealyticum | Itraconazole | ITR_ND10 | S | Disk | 2018 |
| Ureaplasma urealyticum | Voriconazole | VOR_ND1 | S | Disk | 2018 |
| Candida tropicalis | Doxycycline | DOX_ED30 | R | Disk | 2016 |
| Candida tropicalis | Thiamphenicol | THI_ED30 | R | Disk | 2016 |
| Candida albicans | Doxycycline | DOX_ED30 | R | Disk | 2017 |
| Candida parapsilosis | Ceftazidime | CAZ_ED10 | I | Disk | 2017 |
| Candida parapsilosis | Cefepime | FEP_ED30 | I | Disk | 2017 |
| Epidermophyton sp. | Clindamycin | CLI_ED2 | R | Disk | 2018 |
| Epidermophyton sp. | Erythromycin | ERY_ED15 | R | Disk | 2018 |
| Candida albicans | Erythromycin | ERY_ED15 | R | Disk | 2018 |

Supplementary Figure 2b: Inappropriate testing B

| Organism Name | Antimicrobial Agent | Agent Code | Interpreted Results | Antimicrobial Susceptibility Method | Year |
|-----------------------|---------------------|------------|---------------------|-------------------------------------|------|
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2016 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2016 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2016 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2016 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2017 |
| Staphylococcus aureus | Vancomycin | VAN_ND5 | R | Disk | 2017 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2017 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2018 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2018 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2018 |
| Staphylococcus aureus | Vancomycin | VAN_ED5 | R | Disk | 2018 |

AMC Appendices



Appendix 1: Key Informant Interview (KII) tool

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

Domestic Producers and Importers

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

Procurement, Storage and Distribution

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

Public Sector

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

Private Sector

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

Donor Funded Supply

| | | | | | |
|------|---|---------------|--|---------|--|
| 1.13 | Is there any donor support for procurement of antibiotics in the country? | Yes | | No | |
| 1.14 | If yes to above, who are the donors and what are the procedures regarding import and distribution of donated antibiotics? | | | | |
| 1.15 | Which sector(s) is supported with supplies procured through donor agencies? | Public Sector | | Private | |
| 1.16 | If there is donor support, are antibiotics sourced locally or imported? | | | | |
| 1.17 | Does the available donor data indicate specific country antibiotic consumption? Do these procurement mechanisms fit in with the countries regulatory systems and 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) |
| Rolitetracycline | J01AA09 | U |
| Penimepicycline | J01AA10 | U |
| Clomocycline | J01AA11 | U |
| Tigecycline | J01AA12 | R |
| Eravacycline | J01AA13 | R |
| Chloramphenicol | J01BA01 | A |
| Thiamphenicol | J01BA02 | A |
| Ampicillin | J01CA01 | A |
| Pivampicillin | J01CA02 | A |
| Carbenicillin | J01CA03 | W |
| Amoxicillin | J01CA04 | A |
| Carindacillin | J01CA05 | U |
| Bacampicillin | J01CA06 | A |
| Epicillin | J01CA07 | U |
| Pivmecillinam | J01CA08 | A |
| Azlocillin | J01CA09 | W |
| Mezlocillin | J01CA10 | W |
| Mecillinam | J01CA11 | A |
| Piperacillin | J01CA12 | W |
| Ticarcillin | J01CA13 | W |
| Metampicillin | J01CA14 | U |

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

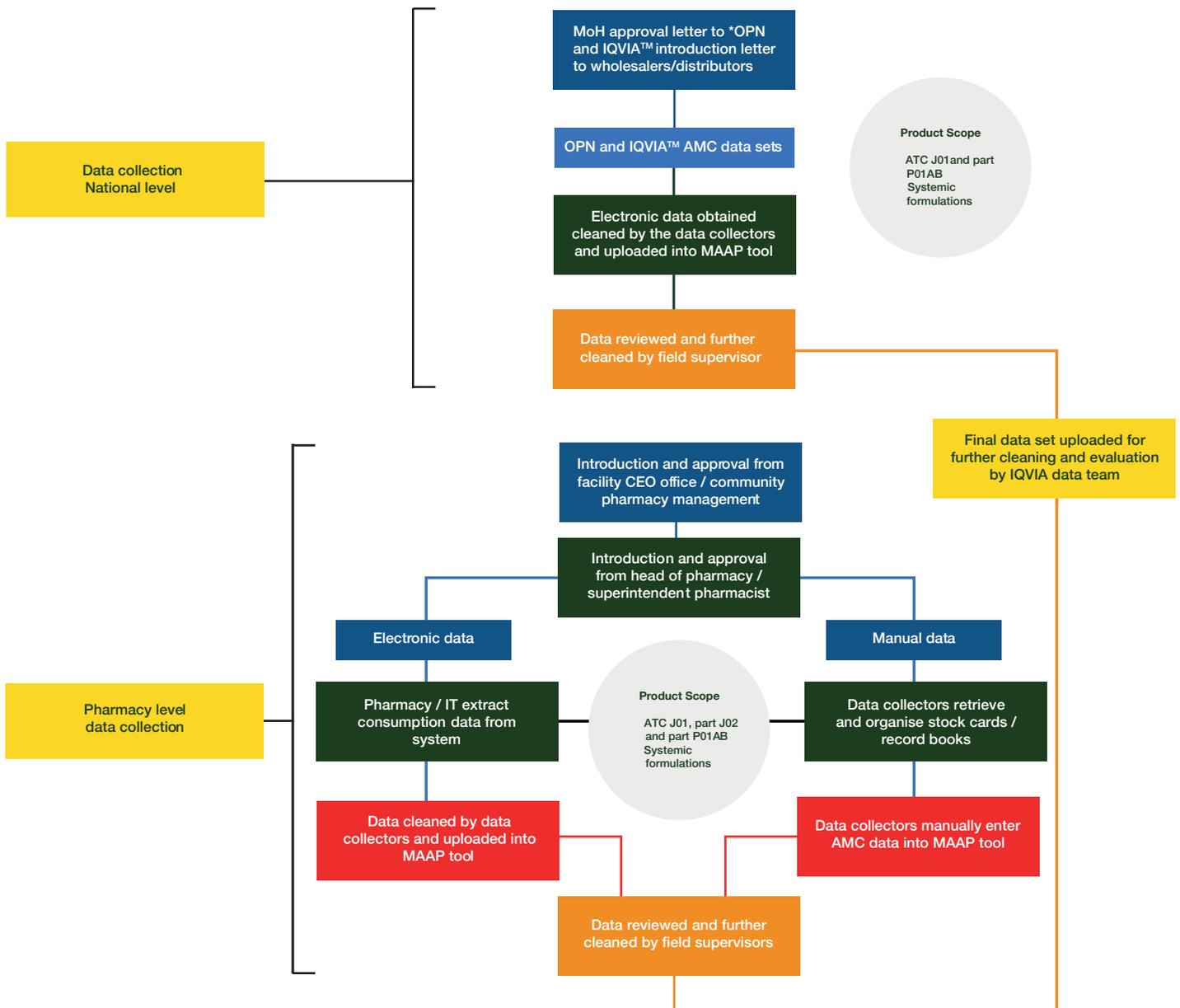
| | | |
|--------------------------------------|---------|---|
| Arbekacin | J01GB12 | W |
| Bekanamycin | J01GB13 | U |
| Ofloxacin | J01MA01 | W |
| Ciprofloxacin | J01MA02 | W |
| Pefloxacin | J01MA03 | W |
| Enoxacin | J01MA04 | W |
| Temafloxacin | J01MA05 | U |
| Norfloxacin | J01MA06 | W |
| Lomefloxacin | 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 |
| Sitafoxacin | J01MA21 | W |
| Tosufloxacin | J01MA22 | W |
| Delafloxacin | J01MA23 | W |
| Rosoxacin | J01MB01 | U |
| Nalidixic acid | J01MB02 | U |
| Piromidic Acid | J01MB03 | U |
| Pipemidic Acid | J01MB04 | U |
| Oxolinic Acid | J01MB05 | U |
| Cinoxacin | J01MB06 | U |
| Flumequine | J01MB07 | W |
| Nemonoxacin | J01MB08 | U |
| Cefuroxime/Metronidazole | J01RA03 | U |
| Spiramycin/Metronidazole | J01RA04 | W |
| Levofloxacin/Ornidazole | J01RA05 | U |
| Cefepime/Amikacin | J01RA06 | U |
| Azithromycin/Fluconazole/Secnidazole | J01RA07 | U |
| Tetracycline/Oleandomycin | J01RA08 | U |
| Ofloxacin/Ornidazole | J01RA09 | U |

| | | |
|-----------------------------|---------|-----|
| Ciprofloxacin/Metronidazole | J01RA10 | U |
| Ciprofloxacin/Tinidazole | J01RA11 | U |
| Ciprofloxacin/Ornidazole | J01RA12 | U |
| Norfloxacin/Tinidazole | J01RA13 | U |
| Vancomycin | J01XA01 | W |
| Teicoplanin | J01XA02 | W |
| Telavancin | J01XA03 | R |
| Dalbavancin | J01XA04 | R |
| Oritavancin | J01XA05 | R |
| Colistin | J01XB01 | R |
| Polymyxin B | J01XB02 | R |
| Fusidic Acid | J01XC01 | W |
| Metronidazole | J01XD01 | A |
| Tinidazole | J01XD02 | U |
| Ornidazole | J01XD03 | U |
| Nitrofurantoin | J01XE01 | U |
| Nifurtoinol | J01XE02 | U |
| Furazidin | J01XE03 | U |
| 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 |
|---|-----------------------|
| <i>Antimicrobial consumption specific</i> | |
| 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



*OPN; National Pharmaceutical Office

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:
DDD/1000 inhabitants/day (DID): used to calculate total AMC for the Gabon population at a national level; includes all age and gender groups and used the known population numbers as the denominator (obtained from the Worldometer Population Database). The below formula summarises how this calculation was done:

The below formula summarizes how this calculation was done:

DDD/1000 Inhabitants/day =

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

*Gabon population estimated for 2016-2018 obtained from: <https://www.worldometers.info/world-population/gabon-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 programmes and monitoring.

'Reserve' group antibiotics: Should strictly be considered as the last-resort option. They should be used only in the most severe circumstances when all other alternatives have failed i.e., in life-threatening infections due to multi-drug resistant bacteria. The reserve group is majorly constituted of polymyxin (28.57%) followed by β-lactams (14.28%) and aminoglycosides (14.28%). Reserve group 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 | Mean DDD/1000 inhabitant-days |
|------------------|----------------|--|-------------------------------|--------------------|--------------------|-------------------------------|
| | | | DDD/1000 inhabitant-days (%*) | | | |
| J01 Class | | Total | 26.08 (100) | 29.36 (100) | 20.54 (100) | 24.95 |
| 1 | Access | Amoxicillin/Clavulanic Acid | 13.08 (50.2) | 15.80 (53.8) | 8.07 (39.3) | 11.94 |
| 2 | Access | Amoxicillin | 3.27 (12.6) | 3.23 (11) | 3.10 (15.1) | 3.17 |
| 3 | Access | Doxycycline | 1.78 (6.8) | 1.57 (5.3) | 1.49 (7.3) | 1.53 |
| 4 | Access | Sulfamethoxazole/Trimethoprim | 1.26 (4.9) | 1.46 (5) | 1.45 (7.1) | 1.46 |
| 5 | Access | Flucloxacillin | 1.43 (5.5) | 1.35 (4.6) | 1.35 (6.6) | 1.35 |
| 6 | Watch | Ciprofloxacin | 0.97 (3.7) | 1.04 (3.5) | 1.06 (5.2) | 1.05 |
| 7 | Watch | Cefixime | 0.62 (2.4) | 0.68 (2.3) | 0.73 (3.6) | 0.71 |
| 8 | Watch | Erythromycin | 0.39 (1.5) | 0.75 (2.6) | 0.40 (1.9) | 0.57 |
| 9 | Watch | Ofloxacin | 0.51 (1.9) | 0.51 (1.7) | 0.46 (2.2) | 0.49 |
| 10 | Watch | Azithromycin | 0.48 (1.8) | 0.46 (1.6) | 0.424 (2.1) | 0.44 |
| 11 | Access | Cefadroxil | 0.22 (0.9) | 0.54 (1.8) | 0.196 (1) | 0.37 |
| 12 | Access | Ampicillin | 0.20 (0.8) | 0.19 (0.7) | 0.254 (1.2) | 0.22 |
| 13 | Watch | Pristinamycin | 0.22 (0.9) | 0.20 (0.7) | 0.194 (0.9) | 0.20 |
| 14 | Access | Oxacillin | 0.20 (0.8) | 0.16 (0.5) | 0.190 (0.9) | 0.17 |
| 15 | Watch | Ceftriaxone | 0.12 (0.5) | 0.13 (0.4) | 0.134 (0.7) | 0.13 |
| 16 | Watch | Spiramycin/Metronidazole | 0.13 (0.5) | 0.13 (0.4) | 0.131 (0.6) | 0.13 |
| 17 | Watch | Levofloxacin | 0.14 (0.5) | 0.13 (0.5) | 0.113 (0.6) | 0.12 |
| 18 | Access | Gentamicin | 0.06 (0.2) | 0.17 (0.6) | 0.055 (0.3) | 0.11 |
| 19 | Access | Phenoxymethylpenicillin | 0.09 (0.3) | 0.09 (0.3) | 0.093 (0.5) | 0.09 |
| 20 | Watch | Cefuroxime | 0.08 (0.3) | 0.08 (0.3) | 0.079 (0.4) | 0.08 |
| 21 | Watch | Lincomycin | 0.10 (0.4) | 0.07 (0.2) | 0.079 (0.4) | 0.08 |
| 22 | Watch | Spiramycin | 0.09 (0.3) | 0.08 (0.3) | 0.058 (0.3) | 0.07 |
| 23 | Uncategorised | Azithromycin/Fluconazole/ Secnidazole | 0.05 (0.2) | 0.06 (0.2) | 0.055 (0.3) | 0.05 |
| 24 | Uncategorised | Amoxicillin/Metronidazole | 0.045 (0.2) | 0.05 (0.2) | 0.050 (0.2) | 0.05 |
| 25 | Watch | Clarithromycin | 0.066 (0.3) | 0.05 (0.2) | 0.042 (0.2) | 0.05 |
| 26 | Watch | Norfloxacin | 0.039 (0.1) | 0.04 (0.1) | 0.048 (0.2) | 0.04 |
| 27 | Watch | Cefpodoxime proxetil | 0.037 (0.1) | 0.045 (0.2) | 0.034 (0.2) | 0.04 |
| 28 | Watch | Fusidic Acid | 0.038 (0.1) | 0.033 (0.1) | 0.029 (0.1) | 0.03 |
| 29 | Watch | Josamycin | 0.037 (0.1) | 0.04 (0.1) | 0.020 (0.1) | 0.03 |
| 30 | Watch | Roxithromycin | 0.034 (0.1) | 0.03 (0.1) | 0.022 (0.1) | 0.028 |
| 31 | Access | Pivmecillinam | 0.039 (0.1) | 0.03 (0.1) | 0.025 (0.1) | 0.028 |
| 32 | Uncategorised | Ciprofloxacin/Tinidazole | 0.13 (0.5) | 0.038 (0.1) | 0.017 (0.1) | 0.027 |

| | | | | | | |
|--------------------|---------------|--|-------------------|-------------------|-------------------|--------------|
| 33 | Access | Benzylpenicillin | 0.02 (0.1) | 0.025 (0.1) | 0.02 (0.1) | 0.023 |
| 34 | Watch | Minocycline | 0.025 (0.1) | 0.027 (0.1) | 0.017 (0.1) | 0.022 |
| 35 | Access | Thiamphenicol | 0.018 (0.1) | 0.014 (0) | 0.012 (0.1) | 0.013 |
| 36 | Access | Clindamycin | 0.01 (0) | 0.01 (0) | 0.007 (0) | 0.009 |
| 37 | Access | Cefalexin | 0.007 (0) | 0.008 (0) | 0.007 (0) | 0.007 |
| 38 | Uncategorised | Ofloxacin/Ornidazole | 0.013 (0.1) | 0.0098 (0) | 0.003 (0) | 0.006 |
| 39 | Access | Metronidazole | 0 (0) | 0.0040 (0) | 0 (0) | 0.002 |
| 40 | Uncategorised | Ceftriaxone/Sulbactam | 0.001 (0) | 0.0012 (0) | 0.002 (0) | 0.0014 |
| 41 | Watch | Imipenem/Cilastatin | 0.0008 (0) | 0.0009 (0) | 0.001 (0) | 0.001 |
| 42 | Access | Cefradine | 0.0003 (0) | 0.0002 (0) | 0.001 (0) | 0.0007 |
| 43 | Access | Cefazolin | 0 (0) | 0 (0) | 0.001 (0) | 0.0005 |
| 44 | Watch | Ceftazidime | 0.0002 (0) | 0.0004 (0) | 0.0004 (0) | 0.0004 |
| 45 | Access | Cloxacillin | 0 (0) | 0 (0) | 0.0008 (0) | 0.0004 |
| 46 | Watch | Cefepime | 0.000002 (0) | 0.0005 (0) | 0.0003 (0) | 0.0004 |
| 47 | Watch | Meropenem | 0.0003 (0) | 0.0003 (0) | 0.0003 (0) | 0.00031 |
| 48 | Watch | Cefotaxime | 0.0003 (0) | 0.0001 (0) | 0.0004 (0) | 0.00022 |
| 49 | Access | Trimethoprim | 0 (0) | 0 (0) | 0.0004 (0) | 0.00018 |
| 50 | Access | Amikacin | 0 (0) | 0 (0) | 0.0003 (0) | 0.00013 |
| 51 | Watch | Cefdinir | 0 (0) | 0 (0) | 0.0002 (0) | 0.00011 |
| 52 | Uncategorised | Cefpodoxime proxetil/ Clavulanic Acid | 0.00014 (0) | 0.00004 (0) | 0 (0) | 0.000018 |
| 53 | Watch | Vancomycin | 0.00015 (0) | 0 (0) | 0.00003 (0) | 0.000015 |
| 54 | Watch | Moxifloxacin | 0.00003 (0) | 0.000007 (0) | 0 (0) | 0.000004 |
| 55 | Uncategorised | Amoxicillin/Cloxacillin | 0.00002 (0) | 0 (0) | 0 (0) | 0 |
| 56 | Uncategorised | Cefadroxil/Clavulanic Acid | 0.00001 (0) | 0 (0) | 0 (0) | 0 |
| 57 | Uncategorised | Cefixime/Clavulanic Acid | 0.00004 (0) | 0 (0) | 0 (0) | 0 |
| 58 | Uncategorised | Cefuroxime/Clavulanic Acid | 0.0001 (0) | 0 (0) | 0 (0) | 0 |
| 59 | Watch | Metacycline | 0.002 (0) | 0 (0) | 0 (0) | 0 |
| J02 Class | | Total | 0.43 (100) | 0.45 (100) | 0.47 (100) | 0.46 |
| 1 | Uncategorised | Fluconazole | 0.37 (86.1) | 0.38 (84) | 0.40 (84.6) | 0.39 |
| 2 | Uncategorised | Ketoconazole | 0.06 (13.9) | 0.07 (16) | 0.072 (15.3) | 0.072 |
| 3 | Uncategorised | Amphotericin-B | 0 (0) | 0 (0) | 0.000185 (0) | 0.00009 |
| P01AB Class | | Total | 0.01 (100) | 0.01 (100) | 0.01 (100) | 0.012 |
| 1 | Uncategorised | Secnidazole | 0.007 (52.8) | 0.006 (52.2) | 0.006 (53.4) | 0.0063 |
| 2 | Uncategorised | Tinidazole | 0.006 (47.2) | 0.006 (47.8) | 0.005 (46.6) | 0.0057 |

Appendix 8: Breakdown of national AMC by ATC classes

| ATC class | % consumption | | |
|--|---------------|-------|-------|
| | 2016 | 2017 | 2018 |
| Combinations of penicillins, incl. beta-lactamase inhibitors | 49.3% | 53.0% | 38.4% |
| Penicillins with extended spectrum | 13.3% | 11.6% | 16.1% |
| Fluoroquinolones | 6.2% | 5.8% | 8.0% |
| Tetracyclines | 6.8% | 5.3% | 7.2% |
| Beta-lactamase resistant penicillins | 6.1% | 5.1% | 7.4% |
| Combinations of sulfonamides | 4.8% | 4.9% | 6.9% |
| Macrolides | 4.1% | 4.8% | 4.6% |
| Third-generation cephalosporins | 2.9% | 2.9% | 4.3% |
| Triazole derivatives | 1.4% | 1.3% | 1.9% |
| First-generation cephalosporins | 0.9% | 1.8% | 1.0% |
| Combinations of antibacterials | 1.4% | 1.0% | 1.2% |
| Streptogramins | 0.8% | 0.7% | 0.9% |
| Beta-lactamase sensitive penicillins | 0.4% | 0.4% | 0.5% |
| Aminoglycosides | 0.2% | 0.6% | 0.3% |
| Lincosamides | 0.4% | 0.3% | 0.4% |
| Second-generation cephalosporins | 0.3% | 0.3% | 0.4% |
| Imidazole derivatives | 0.2% | 0.2% | 0.3% |
| Steroid antibacterials | 0.1% | 0.1% | 0.1% |
| Amphenicols | 0.1% | <0.1% | 0.1% |
| Nitroimidazole derivatives | <0.1% | <0.1% | <0.1% |
| Imidazoles | 0.0% | <0.1% | 0.0% |
| Carbapenems | <0.1% | <0.1% | <0.1% |
| Fourth-generation cephalosporins | 0.0% | <0.1% | <0.1% |
| Trimethoprim and derivatives | 0.0% | 0.0% | <0.1% |
| Antimycotics for systemic use | 0.0% | 0.0% | <0.1% |
| Glycopeptides | <0.1% | 0.0% | <0.1% |

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

| Standardised Molecule Name | WHO AWaRe Categorisation | WHO ATC Code | WHO EML | National EML | Document-ed Data |
|--------------------------------------|--------------------------|--------------|---------|--------------|------------------|
| Amikacin | Access | J01GB06 | Y | N | N |
| Amoxicillin | Access | J01CA04 | Y | Y | N |
| Amoxicillin/Clavulanic Acid | Access | J01CR02 | Y | Y | N |
| Amoxicillin/Cloxacillin | | J01CR50 | N | N | Y |
| Amoxicillin/Metronidazole | | J01RA-- | N | N | Y |
| Amphotericin-B | | J02AA01 | N | Y | Y |
| Ampicillin | Access | J01CA01 | Y | Y | Y |
| Azithromycin | Watch | J01FA10 | Y | N | Y |
| Azithromycin/Fluconazole/Secnidazole | | J01RA07 | N | N | Y |
| Benzathine benzylpenicillin | Access | J01CE08 | Y | Y | Y |
| Benzylpenicillin | Access | J01CE01 | Y | Y | Y |
| Cefaclor | Watch | J01DC04 | N | N | Y |
| Cefadroxil | Access | J01DB05 | N | N | Y |
| Cefadroxil/Clavulanic Acid | | J01DB-- | N | N | Y |
| Cefalexin | Access | J01DB01 | Y | N | Y |
| Cefazolin | Access | J01DB04 | Y | N | Y |
| Cefdinir | Watch | J01DD15 | N | N | Y |
| Cefepime | Watch | J01DE01 | N | N | Y |
| Cefiderocol | Reserve | J01DI04 | Y | N | Y |
| Cefixime | Watch | J01DD08 | Y | N | Y |
| Cefixime/Clavulanic Acid | | J01DD-- | N | N | Y |
| Cefixime/Ornidazole | | J01RA-- | N | N | Y |
| Cefotaxime | Watch | J01DD01 | Y | Y | Y |
| Cefpodoxime proxetil | Watch | J01DD13 | N | N | Y |
| Cefpodoxime proxetil/Clavulanic Acid | | J01DD64 | N | N | Y |
| Cefradine | Access | J01DB09 | N | N | Y |
| Ceftazidime | Watch | J01DD02 | Y | N | Y |
| Ceftazidime/avibactam | Reserve | J01DD52 | Y | N | Y |
| Ceftriaxone | Watch | J01DD04 | Y | Y | Y |
| Ceftriaxone/Sulbactam | | J01DD63 | N | N | Y |
| Cefuroxime | Watch | J01DC02 | Y | Y | Y |
| Cefuroxime/Clavulanic Acid | | J01DC-- | N | N | Y |
| Chloramphenicol | Access | J01BA01 | Y | N | Y |
| Ciprofloxacin | Watch | J01MA02 | Y | Y | Y |
| Ciprofloxacin/Tinidazole | | J01RA11 | N | N | Y |
| Clarithromycin | Watch | J01FA09 | Y | N | Y |
| Clindamycin | Access | J01FF01 | Y | N | Y |
| Cloxacillin | Access | J01CF02 | Y | N | Y |
| Colistin | Reserve | J01XB01 | Y | N | Y |
| Doxycycline | Access | J01AA02 | Y | Y | Y |
| Erythromycin | Watch | J01FA01 | N | Y | Y |
| Flucloxacillin | Access | J01CF05 | N | Y | N |
| Fluconazole | | J02AC01 | N | Y | Y |
| Fosfomycin (IV) | Reserve | J01XX01 | Y | N | Y |
| Fosfomycin (oral) | Watch | J01XX01 | N | N | Y |
| Fusidic Acid | Watch | J01XC01 | N | N | Y |

| | | | | | |
|--|---------|------------------|---|---|---|
| Gentamicin | Access | J01GB03 | Y | Y | Y |
| Imipenem/Cilastatin | Watch | J01DH51 | N | N | Y |
| Itraconazole | | J02AC02 | N | N | Y |
| Josamycin | Watch | J01FA07 | N | N | Y |
| Kanamycin | Watch | J01GB04 | N | Y | Y |
| Ketoconazole | | J02AB02 | N | N | Y |
| Levofloxacin | Watch | J01MA12 | N | Y | Y |
| Lincomycin | Watch | J01FF02 | N | Y | Y |
| Linezolid | Reserve | J01XX08 | Y | N | Y |
| Meropenem | Watch | J01DH02 | Y | N | Y |
| Meropenem/vaborbactam | Reserve | J01DH52 | Y | N | Y |
| Metacycline | Watch | J01AA05 | N | N | Y |
| Metronidazole | Access | P01AB01, J01XD01 | Y | Y | Y |
| Metronidazole/Diloxanide | | P01AB51 | N | N | Y |
| Minocycline | Watch | J01AA08 | N | N | Y |
| Moxifloxacin | Watch | J01MA14 | N | Y | Y |
| Nitrofurantoin | Access | J01XE01 | Y | N | Y |
| Nitroxoline | | J01XX07 | N | N | Y |
| Norfloxacin | Watch | J01MA06 | N | N | Y |
| Norfloxacin/Metronidazole | | J01RA-- | N | N | Y |
| Norfloxacin/Tinidazole | | J01RA13 | N | N | Y |
| Ofloxacin | Watch | J01MA01 | N | N | Y |
| Ofloxacin/Ornidazole | | J01RA09 | N | N | Y |
| Ornidazole | | P01AB03 | N | N | Y |
| Oxacillin | Access | J01CF04 | N | Y | Y |
| Phenoxymethylpenicillin | Access | J01CE02 | Y | Y | Y |
| Pipemidic Acid | | J01MB04 | N | N | Y |
| Piperacillin/Tazobactam | Watch | J01CR05 | Y | N | Y |
| Pivmecillinam | Access | J01CA08 | N | N | Y |
| Plazomicin | Reserve | J01GB14 | Y | N | Y |
| Polymyxin-B | Reserve | J01XB02 | Y | N | Y |
| Pristinamycin | Watch | J01FG01 | N | N | Y |
| Procaine benzylpenicillin | Access | J01CE09 | Y | N | Y |
| Roxithromycin | Watch | J01FA06 | N | N | Y |
| Secnidazole | | P01AB07 | N | N | Y |
| Spectinomycin | Access | J01XX04 | Y | N | Y |
| Spiramycin | Watch | J01FA02 | N | N | N |
| Spiramycin/Metronidazole | Watch | J01RA04 | N | N | N |
| Sulfadiazine | | J01EC02 | N | N | N |
| Sulfamethoxazole/Trimethoprim | Access | J01EE01 | Y | Y | N |
| Sulfamethoxazole/Trimethoprim/Bromhex- ine/Benzoate/Tolu Balm | | J01EE-- | N | N | N |
| Tetracycline | Access | J01AA07 | N | N | N |
| Thiamphenicol | Access | J01BA02 | N | Y | Y |
| Tinidazole | | P01AB02 | N | N | Y |
| Trimethoprim | Access | J01EA01 | Y | N | N |
| Vancomycin | Watch | J01XA01 | Y | N | Y |

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

AMC Data Collection Tool

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

Expired Drug and Losses Tool

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

