INCOMPLETE ANTIMICROBIAL RESISTANCE (AMR) DATA IN AFRICA:

The Crisis Within The Crisis

Mapping AMR & AMU Partnership

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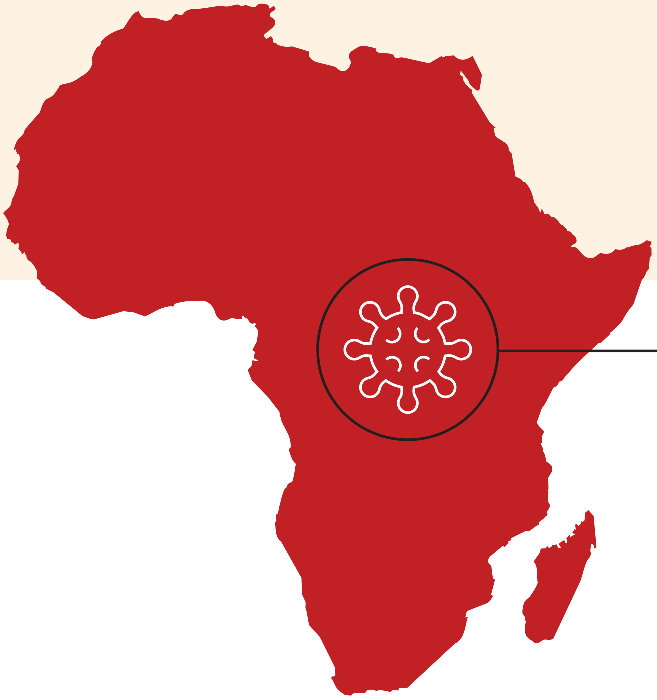
A CRITICAL AND GROWING MENACE TO HUMAN AND ANIMAL HEALTH

Drug-resistant pathogens are a hidden menace in Africa, just like anywhere else—only, perhaps, more so. However, the scale of the problem is concealed by patchy surveillance on the continent.

We know that when pathogens are repeatedly exposed to an insufficient dose or an abbreviated treatment time of antimicrobials they may survive and evolve into resistant strains. These new strains lose their susceptibility to antimicrobials that had previously been effective—creating what we call antimicrobial resistance (AMR). Resistant pathogens can be transmitted through contamination, but also can pass their mutation mechanisms to similar 'bystander' pathogens, and the resistant infections spread.

The World Health Organization (WHO) has repeatedly stated that AMR is a global health priority—and is in fact one of the leading public health threats of the 21st century. A recent study from the University of Washington estimated that, in 2019, nearly 1.3 million deaths globally were attributed to antimicrobial resistant bacterial infections. That same study found that Africa has the highest mortality rate from AMR infections in the world, with 24 deaths per 100,000 attributable to AMR. Similarly, a recent review found a high prevalence of AMR in foodborne pathogens isolated from animals and animal products in Africa. Collectively, these numbers suggest that the burden of AMR is greater than that of HIV/AIDS and far greater than that of COVID-19. The growing threat of AMR is likely to take a heavy toll on the health systems on the continent and poses a major threat to progress made in health and in the attainment of Universal Health Coverage, the Africa Union's Agenda 2063: The Africa We Want and the United Nation's Sustainable Development Goals.

Given the urgency of the threat of the rise of resistant organisms, the World Health Assembly at its 68th assembly in May 2015, adopted the Global Action Plan on antimicrobial resistance and established the Global Antimicrobial Resistance Surveillance System. In February 2020, African Union (AU) Heads of State and Government committed to addressing the threat of AMR across multiple sectors, especially human health, animal health and agriculture.



Africa has the highest mortality rate from AMR infections in the world, with 27.3 deaths per 100,000 attributable to AMR.

FLYING BLIND

The challenge is that current estimates of AMR are based on poor data foundations in low- and middle-income countries, and especially in Africa. This limits our ability to understand the efficacy of commonly used antimicrobials as well as the drivers of resistance in humans. Because of various gaps in health, laboratory and surveillance systems, even where data are collected regularly, they are not always accessible, often recorded by hand, and seldom consolidated or shared with policymakers.

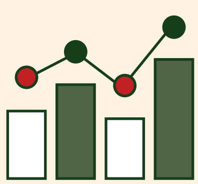
Without information on the rates, drivers and trends of AMR on the one hand and on antimicrobial use (AMU) or consumption (AMC) on the other, health experts are flying blind and cannot develop and deploy policies that would limit or curtail AMR. Interventions in Africa mostly remain generic since no baseline information on the magnitude of the problem is available at national or regional levels.

While the gaps in volume, quality and completeness of AMR, AMU or AMC data in Africa are recognized, there is urgency to exploit any available information to inform public health action.

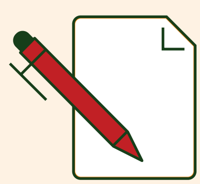
The common understanding is that AMR is usually driven by incorrect or excessive consumption of antimicrobials, but in fact, many African populations still lack access to effective and affordable medicines, emphasizing the need to address AMR by improving universal health. Little information exists on how resistance patterns are affected by the use of standard (and non-standard) antimicrobial medicines in human health or in agriculture and food production systems—those used to produce livestock, crops, fish, and even in beekeeping.

There is also a dearth of information on antimicrobial consumption and antimicrobial use in Africa—both in human medicine and for agriculture and food production systems. Without understanding antimicrobial usage, effectiveness and resistance patterns, health experts cannot develop and deploy policies that would limit or curtail AMR.

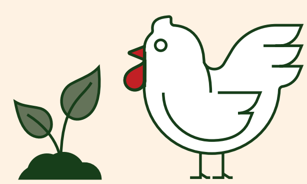
Cognizant of the need for a multisectoral tailored and responsive approach to tackling AMR, this policy brief aims to guide AMR interventions in the human health sector and provide recommendations applicable to other sectors.



Most estimates are based on **statistical modeling**



Data often recorded **by hand** making it unfit for aggregated analytics



Little data on use of antimicrobial medicines in human health or in agriculture and food production systems

COLLECTING DATA TO PROVIDE A BASELINE AND A REFERENCE FOR PUBLIC HEALTH ACTION

In October 2017, the Africa Centres for Disease Control and Prevention (Africa CDC) identified AMR as an urgent public health threat for AU Member States and officially launched its Framework for AMR Control, 2018–2023, and subsequently the Africa Union Framework for AMR Control 2020–2025, both highlighting key strategies to improve surveillance of antimicrobial resistant pathogens.

In 2019, through the support of the Fleming Fund, the Mapping AMR and AMU Partnership (MAAP) was launched to help build capacity in 14 African countries to measure and monitor their own AMR and AMU status and to identify gaps where improvement is needed. Led by the African Society for Laboratory Medicine (ASLM), this regional grant of £6,077,368 aimed to identify, collect and analyze existing historical data to provide a baseline and a reference allowing for African countries to develop and implement policies and interventions for the containment of AMR in the human health sector. Consortium partners include the Africa CDC, the One Health Trust (formerly the Center for Disease Dynamics, Economics and Policy', Innovative Support to Emergencies, Diseases and Disasters, IQVIA, the West African Health Organization (WAHO), and the East, Central and Southern Africa Health Community (ECSA-HC).

MAAP reviewed 819,584 AMR records spanning 2016 to 2019, from 205 laboratories across 14 countries: Burkina Faso, Ghana, Nigeria, Senegal, Sierra Leone, Kenya, Tanzania, Uganda, Malawi, Eswatini, Zambia, Zimbabwe, Gabon and Cameroon. MAAP also reviewed data from 327 hospitals and community pharmacies and 16 national level datasets on antimicrobial consumption in those 14 African countries. These data sets provide the baseline for countries to develop policies and track impact.

MAAP REVIEWED

819,584

AMR records spanning from 2016 to 2019, from **205 laboratories** across **14 countries**.

326

hospital and community pharmacies

16

national level datasets on antimicrobial consumption.

THE FLEMING FUND ALSO SUPPORTED THE CREATION OF TWO CLOSELY RELATED INITIATIVES, EQUAFRICA AND QWARS BOTH LED BY ASLM.

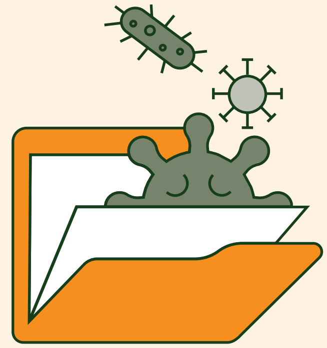
- **External Quality Assessment Grant for AMR Testing (EQuAFRICA)** seeks to strengthen the quality of AMR diagnostics in national reference labs and sentinel sites given that the lack of quality around bacteriology tests, including AST, constitute another barrier to the availability of reliable data on AMR. The program currently includes 156 laboratories in the 14 MAAP countries, with plans to expand underway. By improving laboratory capacity, EQuAFRICA will help them generate quality data for AMR surveillance.

  Consortium partners: Africa CDC, National Institute for communicable diseases, South Africa (NICD), technical University of Denmark (DTU), Public Health England (PHE).

- **Qualifying the Workforce for AMR surveillance in Africa and Asia (QWArS)** provides microbiology and epidemiology training for AMR in the human, animal and environmental sectors, followed by accreditation and registration. The project addresses the fact across Africa there is a shortage of professionals with the skills to conduct quality antimicrobial susceptibility tests (AST), interpret AMR data and design AMR surveillance protocols. The laboratory workforce across Africa is reported to be short of about 850,000 staff, which clearly affects AMR control and surveillance. The QWArS programs have been designed from an African perspective, to increase competencies in AMR surveillance for both microbiology and epidemiology, taking into account ideal circumstances as well as situations where resources and utilities like electricity are inconsistently provided. QWArS has rolled out standardized microbiology and epidemiology training programs throughout the 14 MAAP countries and and three countries in Asia. To date, the program has certified 128 laboratory professionals with more sitting for the next professional exam in August 2022. QWArS is also launching a six-month mentorship program to support the qualified professionals.

  Consortium partners: Africa CDC, Institut de recherche en santé, de surveillance épidémiologique et de Formation (IRESSEF), Fondation Mérieux, Pasteur International Network, Denmark Technology Univerity (DTU), Americam Society for Microbiology (ASM).

  Experts collaborators: DATOS, Institut Pasteur Dakar, Clinical & Laboratory Standards Institute (CLSI), Infectious Disease Institute (IDI), ReACT Africa, National INstitute fro COmmunicable Disease (NICD), ONe Health Trust, The Caviart Group, International Center for Diarrheal Disease Research, Bangladesh (ICDDR).



MAAP is the first initiative to systematically collect, process and evaluate large quantities of antimicrobial resistance and antimicrobial consumption data in Africa.

PAINTING A MORE COMPLETE PICTURE OF THE CRISIS

Laboratory networks are not ready for AMR testing

There are simply not enough microbiology laboratories in Africa, and not enough resources—including basic utilities and equipment—for the ones that are currently operational. According to MAAP data, only 1.3% of the 50,000 medical laboratories forming the laboratory networks of the 14 participating countries conduct bacteriology testing. Of those, only a fraction can handle the scientific processes needed to evaluate AMR. In 8 of the 14 participating countries, the small pool of bacteriology laboratories is geographically accessible (i.e., reachable within one hour of travel by car or on foot) to less than 50% of the population. The combined lack of capacity and accessibility of bacteriology and AMR testing services in Africa underscores the urgent need to invest in existing and new testing laboratory infrastructures.

26% **of labs use electronic laboratory information system**

80% **perform less than 1,000 Antimicrobial Susceptibility Tests per year.**

ONLY 20% **(most of them at the national level) use automated methods for pathogen identification or AST.**

ONLY 20% **of the labs are International Organisation for Standardisation (ISO) accredited for bacteriology testing.**

Of the 205 laboratories that provided data to MAAP:

Based on experiences from other regions outside Africa, these figures suggest a generally low volume of testing and a low capacity to handle increased testing demand. Overall, the recommended capacity of the laboratories performing AMR sharply decreases as the tier level of the medical laboratory in the network decreases.

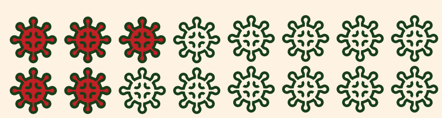
So far, the MAAP project has accumulated data from 187,000 samples that were tested for resistance. But of the 15 pathogen-drug resistance combinations prioritized by the WHO for surveillance, only five were tested across the 14 countries —and all five had a higher-than-expected prevalence.

ANTIMICROBIAL RESISTANT PATHOGENS OF IMMEDIATE CONCERN:

Enterobacterales is a large order of bacteria that includes many different types—including E. coli, a common food poisoning infection, and Klebsiella pneumoniae, a common infection in health care settings. More than half of all samples tested were resistant to penicillins and cephalosporins.

Staphylococcus aureus is the source of a skin infection that can turn deadly if drug-resistant. More than 40% of samples tested were classified as methicillin-resistant Staphylococcus aureus (MRSA), a lethal pathogen/drug resistance combination that globally accounted for more than 100,000 deaths in 2019.

Pseudomonas aeruginosa can cause infections in the blood, lungs (pneumonia), and other parts of the body after surgeries. More than 30% of samples tested were resistant to Carbapenems, a class of antibiotics used to treat infections that have not responded to more commonly available drugs. Resistance to these medicines is a grave threat.

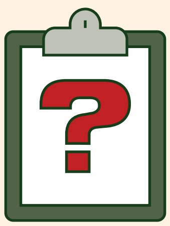


ONLY 5 OF 15

antibiotic-resistant pathogens prioritized by the WHO for causing the greatest threat to human health were found to be consistently tested in most countries.

Clinics vs. laboratories: two systems that don't speak to each other

Failing to consistently test for all priority resistant pathogens translates to substandard care, where antimicrobials are used to treat infections without first determining whether they will be effective. But the retrospective laboratory records collected also revealed that clinical and treatment data were not included in laboratory results.



Out of the 187,000 samples tested for antimicrobial resistance, 88% did not include records of patients' clinical profile—the diagnosis, the origin of infection, comorbidities and previous antimicrobial usage—while the remaining 12% had incomplete information.

The disconnect between patient data and AMR results impedes our ability to interpret AMR data and utilize it to inform patient care, resulting in patients being treated with inappropriate or ineffective medicines. The development of wider public health policies also suffers, as the development of treatment guidelines for specific diseases fails to account for the specific regional resistance patterns that complete data sets would reveal. Linking AMR data to patient information helps us evaluate the efficacy of current treatments and understand the drivers of resistance for effective AMR containment intervention.

Combined lack of access and eratic use of antimicrobials magnify the crisis.

AWaRe is a WHO classification that separates all antibiotic medicines into three categories to rationalize their use:

- **Access**, for drugs with lower resistance potential that are effective for many infections;
- **Watch**, for drugs that need to be set aside as they have a higher resistance potential and used only for harder to treat infections; and,
- **Reserve**, for stronger drugs that should be used only as a last resort.

WHO's AWaRE recommends that at least 60% of all drugs used come from the Access category, while the proportion of Watch and Reserve should decrease over time.

WHO further guides countries on the essential medicines they should have available, through the WHO Essential Medicine List. In turn, countries create their own National Essential Medicine Lists based on WHO's list. These national lists guide which antibiotics should be available and used at country-level.

AT LEAST 80% **of total drug consumption, represented by Access drugs in all but one country as per WHO recommendation**

When sorted by the AWaRe system, the data collected by MAAP highlighted that 12 of the 14 countries comply to the recommendation of >60% of antibiotics consumed coming from the Access category. The average Access category consumption across countries was almost 80%. While this sounds good in principle, a deeper dive revealed a lack of access to certain antibiotics and eratic use of the antibiotics that are available:

- **The antibiotic consumption data from the 14 MAAP countries show that only four drugs comprised more than two-thirds (67%) of all the antibiotics used in healthcare settings:** amoxicillin (penicillin with extended spectrum class), doxycycline (tetracycline class), the combination of sulfamethoxazole/trimethoprim (combinations of sulfonamides and trimethoprim (incl derivates) class) and ciprofloxacin (fluoroquinolones). Stronger medicines to treat more resistant infections (such as severe pneumonia, sepsis, and complicated intra-abdominal infections) were not available, suggesting limited access to some groups of antibiotics.
- **Reserve category antibiotics were found in only 6 of the 14 MAAP countries.** Only 0.01% of all antibiotics used come from the Reserve category, showing how drastically underutilized they are—a critical problem given the levels of resistant infections that we have found with just limited data.
- **We see eratic consumption of fixed combinations of antibiotics**, i.e., two or more antibiotics combined in one tablet. These combinations are not recommended by WHO, yet 3.4% of the total antibiotic consumption across the 14 countries is from these combinations. Ampicillin/cloxacillin is the main fixed combination of antibiotics used.

The research also revealed that the antibiotics on the National Essential Medicine Lists were not in sync with the WHO's Essential Medicine List. What's more, medicines found in country were often not aligned to the National Essential Medicine Lists.

- The National Essential Medicine Lists included significant numbers of antibiotics not on the WHO Essential Medicine List nor in the AWaRe categorization.
- Only one of the Reserve antibiotics from the WHO Essential Medicine List was included in the National Essential Medicine Lists.
- Up to 34 uncategorized antibiotics were found to be in circulation, even though they are not included in the National Essential Medicine Lists.

Collectively, the data highlights combined issues of limited access and irrational use of antibiotics.

Drug Resistance Index scores: a useful metrics underlining the urgency of addressing AMR

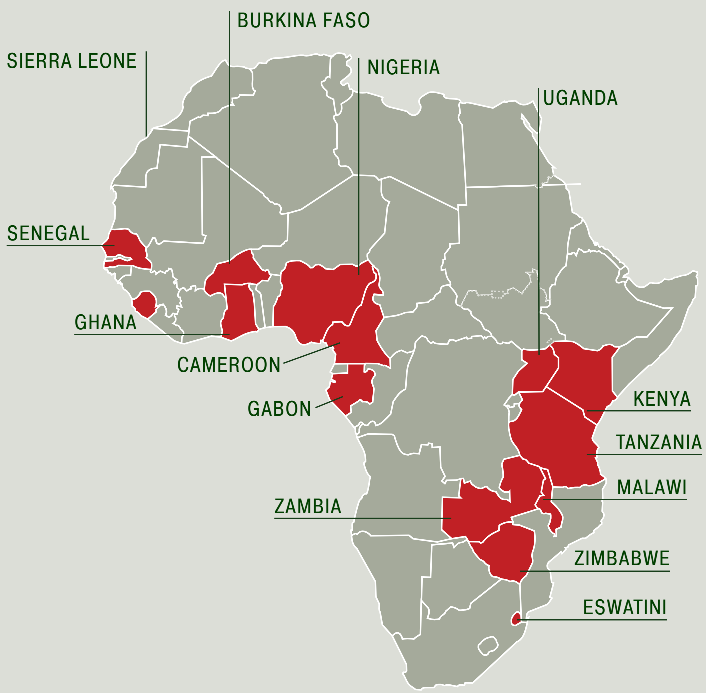
Combining two metrics—one that assesses the effectiveness of antibiotics to treat infections, and one that evaluates the extent to which they are used and consumed—the Drug Resistance Index (DRI) provides a reference to assess just how much of a threat AMR poses. A DRI below 25% is indicative that AMR is under control.

Lower DRI scores, which indicate a lower risk of AMR, are associated with indicators of better social, economic and healthcare sector development, such as the national average education level of the population, higher GDP, and higher proportion of doctors and nurses in the general population.

These observations suggest that targeted interventions to improve the containment of AMR—based on the evidence generated by MAAP—will have to be anchored on a broad plan to advance numerous socioeconomic indicators.

DRI scores derived from 12 of the 14 African countries show that AMR is indeed a significant hazard. All countries assessed scored at least twice the benchmark of 25%. Their scores include:

BURKINA FASO **64.0%**	KENYA **56.20%**	TANZANIA **56.10%**
CAMEROON **68.60%**	MALAWI **74.10%**	UGANDA **69.0%**
ESWATINI **64.80%**	NIGERIA **65.90%**	ZAMBIA **60.80%**
GABON **65.20%**	SENEGAL **79.80%**	ZIMBABWE **66.60%**



RECOMMENDATIONS

From the limited scope of data that is currently available, it is obvious that AMR is a crisis needing an immediate response from governments, research institutions and the entire healthcare sector. The extent of available data needs to be drastically expanded, and then all parts of society that influence how antimicrobials are used have important roles to play.

Specific recommendations for African governments, the AU Taskforce on AMR, and regional and global health partners working in Africa include:

Increase the volume, quality, relevance and breadth of laboratory data for AMR. Specific goals should include:

- Progressively increase the number of laboratories that can provide AMR data in Africa—with the aim of achieving at least 50% of laboratory capacity, up from the current level of 1.3%. This can be achieved through funded interventions in the National AMR Action Plan and the National Laboratory Strategic Plan and through institutionalized collaboration with private laboratories. Leverage on EQuAFRICA to establish robust quality assurance processes in bacteriology laboratories.
- Promote conventional AMR testing (cultures and antibiotic susceptibility testing) at lower levels of the laboratory network, ensuring necessary improvements are made to workforce capacity, quality of testing and diagnostic infrastructure. This can be done through the development of relevant national essential diagnostic lists.
- Consolidate the number and capacity of AMR surveillance sentinel sites and leverage on training modules and qualification processes from QWArS to build a sufficient and skilled workforce supporting AMR surveillance.
- Adapt the list of WHO priority pathogens to the epidemiology of Africa.
- Increase the digitization and integrity of laboratory, clinical and pharmacy data: expand the use of the microbiology database software WHONET and other information technology solutions and standardize the use of unique patient identifiers in record keeping.
- Advocate for, and leverage on, existing regional public health assets such as regional laboratory networks, for example the Africa CDC Regional Integrated Surveillance and Laboratory Network.

Expand and institutionalize AMR and AMC data collection and analysis for public health action.

- Leverage on the MAAP systems and processes to embrace the One Health approach—looking at AMR, AMU or AMC in human health, animal health, and in agriculture—while bringing in more countries and collaborating with the Antimicrobial Resistance Surveillance Network, an initiative of the Africa CDC.
- Support the creation of an Africa-coordinated knowledge hub providing supportive technical assistance and promoting South-to-South collaboration for AMR, AMC and AMU data analysis, which are tailored for African settings.
- Improve surveillance protocols to measure AMR in community settings.

Adapt national AMR control strategies based on the evidence gathered. This includes revising and costing National AMR Action plans and updating Essential Medicine Lists and standard treatment guidelines. Specific goals should include:

- Improve antibiotic stewardship and infection prevention strategies to reduce the DRI to less than 25%.
- Remove antibiotics not categorized in WHO's AWaRe system from the National Essential Medicine Lists, including non-recommended fixed-dose antibiotic combinations.
- Include Access, Watch, Reserve Antibiotics listed in the WHO's Essential Medicine Lists into the National Essential Medicine Lists.

Update national treatment guidelines, increase access to antibiotics and conduct trainings and educational campaigns for healthcare practitioners to support improved antibiotic stewardship. Specific goals should include:

- Align treatment guidelines to the detected AMR rates in the country.
- Improve pre-service and in-service stewardship trainings.
- Improve access to the full spectrum of antimicrobials available in the country EML and increase the control of non-regulated drugs.
- Ensure that health workers are aware of the full spectrum of antimicrobials available in the National Essential Medicine Lists and that they prescribe the full spectrum of antimicrobials rationally, in line with the treatment guidelines.
- Enforce the interdiction of unclassified, including non-recommended fixed-dose, antibiotic combinations.

Define continental AMR research priorities. Specific topics in need of exploration include:

- Refining AMR disease burden estimates and drivers in Africa.
- Scale-up relevant pathogen genomics methodologies in support of AMR surveillance.
- Develop an economic or business case for AMR interventions.