



The Fleming Fund

A Summary of Phase One

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Introduction The role of global health partnerships in protecting our future

Some of the threats we face loudly demand our attention and energy, while others are silent. However, just because they are silent they are no less concerning. Antimicrobial resistance (AMR), in particular, is a 'silent pandemic', that could have catastrophic implications for the environment and the economy.



Sajid Javid, Secretary of State for Health and Social Care

The looming threat of AMR is one that should concern us all: bacteria, parasites and viruses are becoming increasingly resistant to the drugs that we all rely on. Without effective antimicrobials, formerly untreatable diseases like HIV or malaria could sadly become untreatable once again, and crucial operations may no longer be safe to carry out. Recent estimates show that there were 1.27 million deaths caused directly by AMR in 2019, making AMR a leading underlying cause of death, ahead of HIV, tuberculosis and malaria. The impacts of AMR go beyond health and mortality. The World Bank Group has emphasised that, unless we act now, AMR will force 24 million people into extreme poverty by 2030. This is because they will be too unwell to work, and may lose their jobs. If it is left unchecked, AMR will cost the global economy \$100 trillion by 2050.

The reality of AMR is stark, but we cannot be scared into inaction. The international community must come together, just as they did against the common threat of COVID-19.

There are lessons we can learn from this fight. One is that strong surveillance systems are critical to detecting and containing disease outbreaks. We saw during the Omicron variant how important early detection can be. By identifying the variant early, through our global leadership in genomic sequencing, we gave ourselves the time we needed to accelerate the NHS booster roll-out and protect the most vulnerable in our society. This surveillance can also help us to understand, anticipate, and track AMR.

The Fleming Fund, which forms part of our UK aid programme, is strengthening global surveillance systems, supporting 21 countries across Asia and Sub-Saharan Africa in their mission to develop and sustain their national programmes for the surveillance of AMR and antimicrobial use. This report does not just focus on the challenges, but the solutions too. These include investing in diagnostic and surveillance capacity, the need for greater research on the economic impact of drug resistance, and how we can use data to drive our response.

The Fleming Fund is a shining example of the strong and sustained global action that we need if we are to make an impact on AMR. I, too, am committed to leading this fight at home and with our global partners. In the past year, we have secured bold action on AMR, including through our G7 Presidency. I am proud of the tangible commitments we have

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made, together with counterparts across the world, on important areas from strengthening antibiotic supply chain resilience to ensuring sustainable innovation in antimicrobial research and development.

This report vividly illustrates that we need to act now, otherwise it may be too late.

We must turn the tide on AMR, once again uniting to defeat this threat to us all.

Sajid Javid, Secretary of State for Health and Social Care

The Fleming Fund is a shining example of the sustained global action we need if we are to make an impact.

Surveillance is the solution

COVID-19 will likely not be the last pandemic that our world will face. It certainly is not the only pandemic ravaging our planet at this moment. Until now, it has been easy to ignore the quieter pandemic of AMR, but we know that without effective antibiotics, our health, food and environment systems, and economies, would grind to a halt.



Professor Dame Sally Davies, UK Government Special Envoy on Antimicrobial Resistance

As AMR emerges and spreads around our world, it threatens the attainment of universal health coverage for all and jeopardises the Sustainable Development Goals. Across the globe, we are all united by our need to access effective antimicrobial medicines when we need them. But we know that AMR disproportionately burdens communities in low- and middleincome countries. The 2022 Global AMR project (GRAM) study, co-funded by the Fleming Fund, shows that inequality and health disparities are crippling characteristics of AMR. Globally, sub-Saharan Africa was hit hardest by AMR and, tragically, one in five deaths caused by AMR are among children under the age of five.

The study also demonstrates data disparities and the lack of infrastructure and capacity for surveillance that we need to detect and respond to pandemics.

That is why, since 2015, the UK's Fleming Fund has brought people together to encourage action against AMR. I am proud that the Fleming Fund is the single largest global aid programme for AMR surveillance, supporting up to 21 countries across Asia and Sub-Saharan Africa to generate, share and use data.

The Fleming Fund aims to build partnerships with local governments and organisations, adopting a One Health approach across human and animal health, and environmental sectors. The programme invests in strengthening surveillance systems through a portfolio of country and regional grants, global projects, and fellowship schemes to show why AMR must be a priority and give countries the tools to develop policies and actions to tackle it.

The Fleming Fund works closely with global organisations, such as the World Health Organization (WHO), Food and Agriculture Organization (FAO) and World Organisation for Animal Health (OIE), so that the international Fleming Fund supports governments in the creation of National Action Plans, using data to inform the top priorities within their countries. They also support countries in strengthening their national surveillance systems, generating and sharing high quality AMR data. On a local level, the Fleming Fund helps clinicians to improve antimicrobial stewardship for humans, animals and plants, and encourages sharing good practice with colleagues in their community, and even in different countries.

AMR is surmountable, but only if we have leadership and global solidarity. I am proud to serve as a Member on the UN Global Leaders Group on AMR, working alongside politicians, scientists, businesses and activists from across the world to advise and advocate on AMR. One of our top priorities is to advocate for global and national actions on AMR to be guided by science and risk, based on data on surveillance and monitoring of antimicrobial use and resistance across all sectors.



The Fleming Fund's Phase I report shows how surveillance can create real impact on the ground in the simplest of ways. We need to work together to realise our vision of a world free of drug-resistant infections. Governments, multilateral organisations, the private sector, civil society and the public all have a crucial role to play. We urge everyone to actively join the fight against AMR, before it is too late.

It is time for us all to step up and speak out against the 'silent pandemic of AMR'.

And I know the Fleming Fund will continue to be at the heart of the fight.

Professor Dame Sally Davies, UK Government Special Envoy on Antimicrobial Resistance

It is time for us all to step up and speak out against the 'silent pandemic' of AMR.

Achievements

Regional and country grants

Supported

22,713 training attendees

In country grants

There were

18,240 training attendances, and

7,144 fellows received mentoring support



Fellowships case studies

Sabrina Yesmin, a Fleming Fund Fellow and Deputy Director of the Directorate General Drug Administration, Ministry of Health and Family Welfare has recently completed two studies: a rapid situation analysis of present labelling of antibiotics in Bangladesh and preferences of label change patterns of antibiotics and implementation challenges, and a baseline survey on the level of awareness about antibiotics and AMR and its impacts on self-medication in Bangladesh.

Gabriella Ak, a Fleming Fund Fellow and Pathology Registrar at Port Moresby General Hospital, Papua New Guinea was chosen to be a speaker at the launch of the WHO Collaborating Centre for Antimicrobial Resistance at the Doherty Institute, University of Melbourne, Australia. She has been working on mapping AMR surveillance data pathways to understand the country's needs.

Susan Githii, a Fleming Fund Fellow at the National Public Health Authority, Kenya, acts as the AMR surveillance and laboratory focal person within the organisation. She is one of only two people within the country who can report to Global Antimicrobial Resistance and Use Surveillance System (GLASS), and she recently submitted Kenya's first AMR data.

One Health

The One Health concept recognises that the health of people is connected to the health of animals, food production and the environment. Because bacteria spread freely in the environment, the Fleming Fund promotes a multidisciplinary response to tackling AMR.





By investing in both human and animal health laboratories and promoting data sharing, analysis and even joint action between human, animal, agriculture and environment government ministries, we support national One Health AMR surveillance systems.

Investment

Barriers to investment in AMR: Infrastructure and sustainability strategies in Uganda

Uganda's Health Sector Strategic Development Plan (HSSDP) forms the basis of the country's AMR National Action Plan (NAP). The HSSDP 2016-2020 outlines priority areas of support for the sector, prioritising primary health care and prevention over curative services, and highlights global health security and disease surveillance as one way of strengthening laboratory and diagnostic capacity. From this, the One Health Secretariat developed, costed and implemented Uganda's AMR NAP, which ensures that AMR surveillance is spearheaded by the diagnostic departments within different sectors.

Uganda has faced several barriers to investment in AMR infrastructure. The laboratory systems are largely dependent on donor support, as the bulk of government infrastructure budgets within the health sector are directed towards building lower-level health centres to improve primary health care.

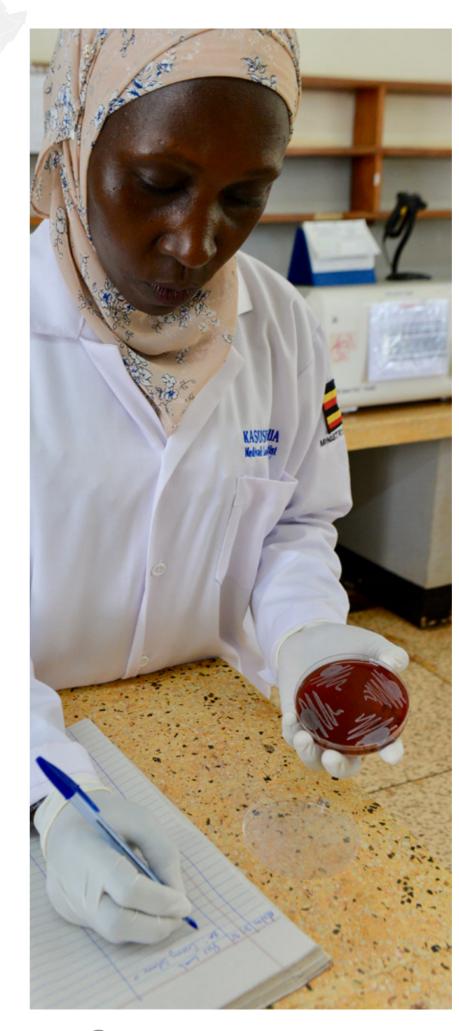
There are several factors that influence the financing of capital investments for surveillance, some of which are listed below.

Policy and external funding

The Central Public Health Laboratory was recently elevated to the National Health and Laboratory Services Department within the Ministry of Health, which led to a greater stream of funding and heightened public awareness. The department has benefitted from funding from various partners, including the Global Fund and the President's Emergency Plan for AIDS Relief (PEPFAR). These partners have also supported the recruitment of staff, the procurement and servicing of equipment, and the supply of reagents and consumables. Laboratories in the human health sector have also benefited from the East Africa Laboratory network funded by the World Bank, which has provided improvements to several regional referral hospitals.

Despite this support, bacteriology sectors remain vulnerable and have been heavily dependent on the Fleming Fund. The Fund have also contributed to the placement of vital equipment which will require high maintenance costs that the government cannot afford, limiting the sustainability of the Fund's activities. The Fleming Fund has provided support for long term maintenance to provide time for discussions with government on how to cover these costs.

In the animal health sector, the National Animal Disease Diagnostics and Epidemiology Centre (NADDEC) sits under the Chief Veterinary Officer and does not have a dedicated line of support from the treasury. Infrastructure investments have been supported by external funding from the FAO and the Danish International Development Agency (DANIDA) depending on the disease programme.





Structure and budgetary provision

Public sector allocations to the Ministry of Health and Ministry of Agriculture Animal Industry and Fisheries (MAAIF) stand at 6% and 3% of the national budget respectively. Within the two sectors, most of the budget is absorbed by recurrent expenditure, which includes the remuneration of human resources and omits reagents and consumables for bacteriology. In the MAAIF, the government is working towards increasing staffing levels at the National Animal Disease Diagnosis and Epidemiology Centre (NADDEC). The government has also pledged to absorb all the external staff costs that may be working with MAAIF while being supported by partners.

Outlook

Despite the barriers to investment, we are starting to see progress. The Uganda government has worked with partners to set up a 10-Year Roadmap for Health Supply Chain Self-Reliance, promoting the use of reagents and consumables. They have also set up a biomedical engineering department and created new positions for consultants and senior consultants within the human health laboratory units. This will encourage retention of highly qualified staff.

To continue this progress, advocacy must be sustained.

Patrick Mubangizi, Mott MacDonald

Investment Making an economic case for addressing AMR

An economic case for addressing AMR starts with evidence that AMR causes a loss of welfare to individual countries or to the global community. This has been demonstrated throughout various studies over the past 10 years, and is often framed as the 'economic burden' of AMR. However, uncovering a welfare loss is not enough. An economic case must show that AMR programmes can be deployed efficiently, and that the welfare benefits outweigh the costs of implementation.

Many studies have demonstrated that AMR causes a significant and increasing economic burden within individual countries, providing sufficiently solid grounds for a strong call to action. The next stage in building an economic case for addressing AMR requires new studies on the return on investment in actions designed to address the problem.

The focus must shift from investigating the economic burden of AMR to evaluating possible mitigating actions. We must prioritise effectively tackling the drivers of AMR to reduce the corresponding economic burden, whilst also considering the associated costs. This will demonstrate how efficient different actions can be in tackling AMR and measure their return on investment, ultimately creating a sound economic case.

Economic cases for AMR have been created in the past, but they fall short in different ways. The World Bank devised an economic case in 2017, but this broadly focused on the benefits of containing AMR, rather than on specific actions to tackle its drivers. The Organisation for Economic Cooperation and Development (OECD) made a more detailed economic case in 2018. However, this only covered actions in the domain of human antimicrobial use predominately within health care settings, covering topics such as improved hygiene, stewardship programmes, rapid diagnostic tests, delayed antibiotic prescriptions, and public awareness campaigns. In fact, there is after no single economic case for addressing AMR. Instead, an economic case can be made for each action that efficiently addresses the problem.

Going forward, the economic case for AMR must incorporate the One Health principle. Beyond health care settings, we must also support research and development in the pharmaceutical sector, address the use of antimicrobials in animals, and reduce antimicrobial contamination of the natural environment. 'System maps', like those produced by the UK Department of Health and Social Care, are useful tools to identify how actions can tackle key drivers of AMR, but empirical studies assessing how effective actions are and their costs are essential in the development of an economic case. It is important that these studies are prioritised within the AMR community.

AMR is not just a public health issue, but an economic one too. Making a well-rounded economic case for AMR is imperative to tackle the problem from all angles, ultimately reducing the global impact of AMR. If it is shown that tackling AMR can also generate economic returns, this will help governments





to prioritise investments in actions to address the problem. Raising awareness of the economic burden and supporting related studies, focused on taking action, is the first step to achieving this.

Franco Sassi, Imperial College London

Investment **Donor coordination: Zambia**

The Antimicrobial Resistance Coordinating Committee (AMRCC) in Zambia has spearheaded improvements in AMR surveillance, increasing the generation of data for use at national and international levels. It is housed at the Zambia National Public Health Institute (ZNPHI), which became a statutory body in December 2020, and the committee has a rotational chairmanship between the sectors.

Strong synergies between the AMRCC and AMR partners has resulted in several significant achievements. Through its grant streams, the Fleming Fund remains the biggest partner supporting AMR activities in this country.

The AMRCC has also faced many challenges. Operationally, the secretariat does not have adequate convening power to marshal resources from the public sector which has contributed to higher donor dependency. As the government has prioritised human resources, utilities and facilities, over 70% of the resources within bacteriology laboratories, including reagents and consumables, are provided by donors.

The following partners are supporting the implementation of the AMR National Action Plan (NAP) in Zambia. Although the NAP has not yet been costed, it is clear that this support is only a small percentage of what is needed.

AMR partners in Zambia

The Fleming Fund Country Grant

in Zambia has focused on building a foundation for AMR and Antimicrobial Use (AMU) surveillance in the human and animal health sectors using a One Health approach. In both of these sectors, the grant has supported the development and implementation of a national AMR/AMU Surveillance Strategy. The Fund has also supported 7 Human Health and 5 Animal Health surveillance sites. It has provided equipment, reagents, and consumables, and recruited and trained the laboratory staff to ensure that good quality data,

covering a national and international scale, is generated, analysed and reported on

Regional Grants are strengthening networking and data sharing on AMR at the regional level. These grants are supporting external quality assurance systems, collection and analysis of retrospective AMR/U data, microbiology and epidemiology training of selected sites and whole genome sequencing.

The Food and Agriculture Organization of the **United Nations** the Fleming Fund, supported Zambia to develop and implement their AMR NAP. This led to increased AMR data collection and surveillance in the food and agriculture sectors and the promotion of good food and agriculture practices to minimise the threat of AMR. Policymakers in Zambia are also reviewing and developing policies to address AMR.

The Fellowship Scheme has supported eight fellows in six beneficiary institutions to develop their leadership and AMR technical skills. These skills have been useful to identify, isolate and report trends of some bacteria pathogens, and are also transferable across the sector. For example, one of the fellows has used the developed skills in sample management, biosafety and biosecurity to aid the laboratory systems response to COVID-19 at The Zambia National Public Health Institute (ZNPHI).

The International Centre for Antimicrobial Resistance

(ICARS) has supported the Ministry of Health and ReAct, an independent network dedicated to the problem of AMR, through seed funding for staffing and full-time coordination of the AMRCC secretariat. This will lead to the development of systems and structures to enhance coordination and to lobby for increased public financing to address AMR. This is critical for country ownership to ensure the sustainability of activities.

Centres for Disease Control and Prevention (CDC)

has supported the strengthening of laboratory systems. They recently developed a HIV sample transportation system which transports samples collected through AMR surveillance activities.

ReAct Africa and the Centre for Disease Dynamics, Economics & Policy (CDDEP) have also provided critical support to the development of Zambia's AMR National Action Plan.

These separate efforts require coordination for the NAP to be effectively implemented in an inclusive and equitable way, covering all sectors in Zambia. The Fleming Fund will continue to work with partners at country level to encourage further coordination with the government.

Patrick Mubangizi, Mott MacDonald













Data

Counting the human cost of AMR: The global research on AMR project

The project

In 2017, the researchers of the Institute for Health Metrics and Evaluation (IHME) and the University of Oxford developed a partnership to establish the human cost (burden) of AMR. This partnership gave birth to the Global Research on Antimicrobial Resistance (GRAM) project.

Fast forward four years, 434 million individual records and 12,582 study-location-years' worth of data, and GRAM has become a household name for anyone in the industry.

The results

Published in The Lancet in January 2022, the capstone <u>GRAM paper</u> produced the most comprehensive analysis of the burden of AMR ever undertaken. It demonstrated for the first time that AMR is a leading cause of death globally, using the year 2019 as a reference point. It also highlighted specific areas of concern for governments and health communities to act on.

It found that in 2019 at least 1.27 million deaths per year were directly attributable to AMR. This shows that AMR is a leading cause of death globally, higher than HIV/AIDs and Malaria. In addition, of the 4.95 million deaths associated with AMR, Sub-Saharan Africa bore the highest burden.

Attributable deaths means that people died from a drug-resistant infection. Deaths associated with AMR includes the 1.27 million deaths attributable to AMR, as well as people who had a drug resistant infection when they died (but this may or may not have been the cause of death). These two figures can be thought of as the lower and upper bounds of the true burden of bacterial AMR.

GRAM researchers were also concerned to find that young children are at significant risk. 1 in 5 deaths caused by AMR occurred in children under the age of 5. Over a million people are now dying each year due to infections that could previously be treated by antimicrobials. This includes lower respiratory, bloodstream and intra-abdominal drug resistant infections, the most fatal being MRSA. The GRAM team noted that, out of the seven deadliest AMR bacteria, vaccines are only available for two.

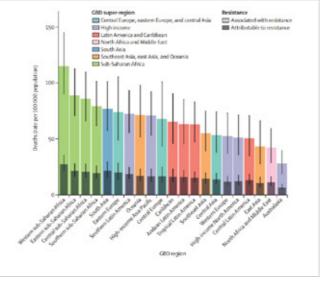
As funders of the research, Wellcome, the UK Department of Health and Social Care, and the Bill and Melinda Gates Foundation are fully committed to supporting effective use of the data to inform action on AMR. Solid data (...) does not mean much unless policymakers and the health community (...) take urgent action to avoid further preventable deaths.

The campaign

The GRAM consortium quickly recognised the results' significance and agreed to disseminate as widely as possible. Janet Midega at the Wellcome Trust highlighted the importance of getting the data into the hands of policy makers.

All-age rate of deaths attributable to and associated with bacterial AMR by GBD region, 2019

Source: Antimicrobial Resistance Collaborators



Global deaths (counts) attributable to and associated with bacterial AMR by infectious syndrome, 2019

Source: Antimicrobial Resistance Collaborators





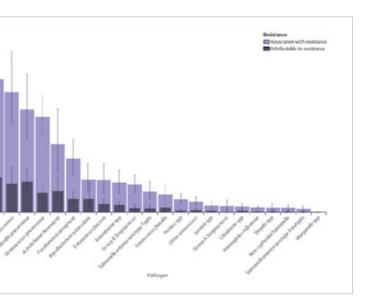
Together with other supporters, the Fleming Fund designed a communications campaign spanning G7 Health Ministers' meetings, social media toolkits (#AMRSOS), press releases tailored to geographic regions, and coverage in major news and journals. This culminated in an online launch event to target policy makers – the people able to turn findings into actions. There was widespread global coverage. 180 top-tier international outlets covered the report, including the <u>BBC</u>, <u>Bloomberg</u>, <u>CNN</u>, <u>Financial Times</u>, <u>The Economist</u>, <u>Nature</u> and <u>Reuters</u>.

Over 500 global health stakeholders attended the online <u>launch</u> introduced by Dame Sally Davies.

On social media, tweets in four different languages containing #AMRSOS in total, generated 7.9k engagements with a combined potential reach of 16 million.

AMR communications, discussions and policy documentations across the globe are using the GRAM results, including the G7 and the WHO. The Fleming Fund plans to continue the campaign throughout 2022, with the publication of burden level results keenly awaited.

The Fleming Fund, Department of Health and Social Care



Data

How the Fleming Fund has worked to build surveillance capacity in LMICs across human and animal health sectors

Building surveillance capacity to address AMR is a global priority. It is particularly important in low- and middle-income countries (LMICs) where human and animal health systems rely more heavily on antibiotics in human and veterinary medicine, and in agricultural production. These countries are also less able to cope with the consequences of resistance. In essence, this is why the Fleming Fund exists.

So, where do you start with a problem as complex as AMR? We decided to "start small and do it well". At the start of the first phase of the Fleming Fund, most countries had produced NAP to address AMR - an action mandated by the UN General Assembly and the World Health Assembly. Each NAP included AMR surveillance as one of five "pillars" of the plan. So, our starting point was to ask, "What do the countries themselves want to do?". We discussed options with government counterparts in each country to come up with a bespoke plan in line with their NAP. This sometimes involved delicate negotiation to balance ambition and scale with the practicalities on the ground, so the investments made in phase I stand a better chance of being sustained in the long-term.

There are many ingredients in a surveillance system, but they fall into two main categories: sites (laboratories) that can safely carry out good quality tests for bacteria and resistance; and a data component where test results can be analysed to provide information at a local and national level. This data should then be shared so that actions can be taken.

We approached the Fleming Fund countries to look at their starting capacity, capability, and motivation. Whilst you need equipment and other items in the laboratory, you can't build a surveillance system without a well-trained and motivated workforce; if the staff are not adequately trained and supported, then the system won't work no matter how much equipment is delivered. Therefore, we have focused on improving both equipment and training so that laboratories can operate safely and to a high standard.

The second component, which brings together AMR data from human and animal health sectors, requires the right governance structures and human resource capacity to analyse, interpret and make sense of the data, turning it into evidence for action. In this area of the programme, we have provided support to the One Health approach, engaging with policymakers, and strengthening and empowering the national AMR Coordination Committees and staff within it. Through this approach, we have provided support for more than 240 laboratories across our 21 countries, funding over 25,000 training attendances and 170 Fleming Fellows. There are encouraging signs of progress, such as gradual improvements in both quantity and quality of data, and also in data use and data sharing. But the gains are fragile and need to be cemented into national systems to help ensure that AMR surveillance becomes a normal part of service delivery across the One Health disciplines.

Toby Leslie, Mott MacDonald

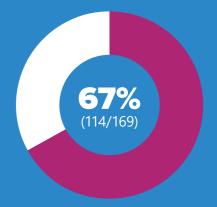
We have provided support for more than 240 laboratories across our 22 countries, funding over 25,000 training attendances and 170 Fleming Fellows.

Number of Fleming Fund countries submitting data to GLASS

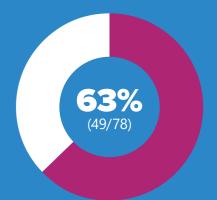




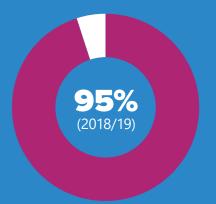
Number of Fleming Fund supported human health surveillance sites showing progress against a framework of key development steps



Number of Fleming Fund supported animal health surveillance sites showing progress against a framework of key development steps



Percentage of Fleming Fund supported countries producing improved data for GLASS



Data Capacity building case study: Timor-Leste

Fleming Fund investment in Timor-Leste has had a major impact. It has been used to improve patient care, as well as inform public health responses to AMR and the correct use of antibiotics, across human and animal health sectors.

Before the increase in diagnostic microbiology capacity, as supported by the Fleming Fund, clinicians did not know the cause of severe bacterial infections and antimicrobial susceptibility patterns. For example, young babies with severe neonatal sepsis often died with presumed antibiotic resistant infections because of failure of first- and second-line treatment options, without any ability to test for the cause of the infection or for the presence of AMR.

The establishment of a consistent blood culture service for the national hospital of Timor-Leste (Hospital Nacional Guido Valadares) has dramatically changed the way these babies can be treated, providing information to clinicians from which they can make informed decisions using targeted antibiotics. Now, when multi-resistant bacterial bloodstream infections are diagnosed in babies, they can be treated with targeted antibiotic therapy based on laboratoryidentified AMR profiles. As a result, these babies have a very good chance of surviving what would otherwise be a deadly infection.

The impact of strengthened laboratory capacity for diagnosis of bacterial infections and AMR extends beyond individual cases like this. Data obtained from the microbiology department of the National Health Laboratory are being used to develop antibiograms that provide clinicians and public health

officials with a clear overview of the rates of AMR for different bacteria in Timor-Leste. Increasingly, samples from municipalities outside the capital of Dili are also being used to demonstrate geographic variation in AMR rates. These data are now being used in the development of national antibiotic guidelines, which will recommend antibiotic treatment for patients based on the local epidemiology and known AMR rates. These guidelines will impact antibiotic prescribing in Timor-Leste and improve the treatment of serious bacterial infections, while also providing boundaries for clinicians to ensure antibiotics are used correctly. As the pharmacy department grow their knowledge and skills with the support of the Fleming Fund, the microbiology data and new guidelines will provide a strong basis for ongoing work to promote the correct use of antibiotics and reduce the spread of AMR in Timor-Leste.

Many of the laboratory developments will have an impact beyond the direct benefits of improving AMR diagnosis and surveillance. For example, improved systems for specimen transport and laboratory result dissemination will also curb the spread of other infectious diseases beyond AMR and help to address other public health challenges. This has been seen already through the laboratory and public health response to the COVID-19 pandemic, which has relied on similar testing platforms, laboratory information management, and meticulous attention to quality control and biosafety.

These developments in human health are complemented by similar approaches to improving surveillance of AMR and antimicrobial use (AMU) in the animal health sector, acknowledging the importance of a One Health approach. AMR and AMU data from human and animal health sectors are regularly added to global surveillance datasets, ensuring that they have an impact on global and regional policy and practice, and inform public health decision-making in Timor-Leste.

Our work is far from complete. The impact of this approach is yet to reach all parts of Timor-Leste. This is a significant challenge, as the country's remoteness affects access to healthcare, and the challenges of AMR are not constrained to the larger urban centres.

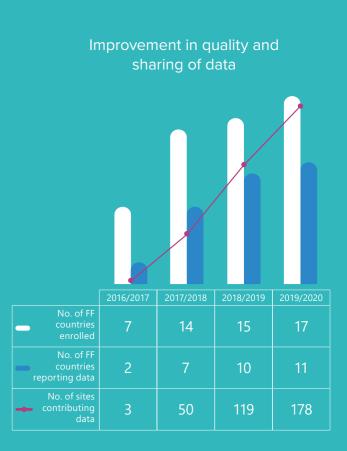
Josh Francis, Menzies School of Health Research



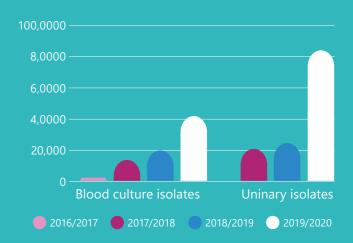




Global Antimicrobial Resistance and Use Surveillance System



GLASS reporting: number of isolates from blood and urine sample



Data use

Catalysing the effective use of AMR data to drive policy

66 Not everything that can be counted counts, and not everything that counts can be counted.

The above quote (attributed to multiple sources) pithily sums up the dilemmas facing policymakers in low- and middle-income countries (LMICs) as they grapple with the problem of AMR, and attempt to gain clarity on five deceptively simple policy-relevant questions:

- (1) Where are we today?
- (2) Where do we need to go?
- (3) How do we get there?
- (4) What works?
- (5) How much is it going to cost?

So, what are the challenges we are currently facing in policymaking?

Most international investments and technical support to LMICs have rightly been focused on strengthening antimicrobial resistance, use and consumption surveillance, and generating data to better understand the scale of the problem and the pathways of AMR emergence and spread. This largely biomedical approach is providing insights that advances 'AMR science' and 'technical' policymaking, such as informing the development of treatment guidelines or improving understanding of transmission pathways. However, current AMR containment strategies are largely predicated on reducing antimicrobial consumption by reversing the excessive use and misuse of antimicrobials – which are driven by human decisions and actions – within the lived reality in which they are accessed and consumed. The lack of robust data and linkage between the 'technical' and the 'social' dimensions of AMR, is unlikely to result in optimal policy choices. It is also worth noting that creating policy is highly political, which often limits the policy's impact. Too much attention on the content of policy, neglecting the role of various actors in the policy process and the context within which policies are introduced and implemented, can often derail efforts in unanticipated ways.

An example is the sluggish implementation of the One Health approach. Many believe that this approach lacks guidance on how to link human health, animal health and the environment in practice. Implementation of One Health is impeded by weak leadership and governance structures in-country, and power struggles between different groups. It is often difficult to overcome these issues and introduce structural changes to support interdisciplinary working. In addition, true





collaboration between human health and veterinary professionals remains limited, and is often fractious, due to limited understanding of the benefits of collaboration and an overriding desire to retain one's professional and disciplinary identity.

What are the solutions to ensure effective policymaking?

While AMR investments in LMICs to date have prioritised building tangible infrastructure and strengthening technical capacities for generating quality-assured surveillance data, the time has come to pay greater attention to the seemingly intangible. We must work on improving incentives and increasing trust amongst stakeholders to share data. We must build greater political and societal ownership of AMR by strategically reframing and communicating the AMR problem and response. By combining these strategies with strengthening country capacities to visualise and translate policy-relevant data into compelling policy pitches we can ultimately create a sustained demand among policymakers for real-time context-specific data including the burden of AMR impact on human, animal, environmental, and economic health of their respective countries.

As Kirchelle, Atkinson and Broom (2020) say in their article '<u>Setting the standard</u>', AMR is not a problem to be solved, but a phenomenon to be continuously managed.

Satyajit Sarkar, International Vaccine Institute

Data use **Pills and prescriptions**

The Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS) health partnership scheme uses local data to develop and implement sustainable antimicrobial stewardship (AMS) interventions. The scheme has twelve partnerships based within four countries: Ghana, Tanzania, Uganda and Zambia. Each partnership developed multiple types of data, which was used to engage with pharmacists and clinicians in innovative ways to improve ways of working.

Global Point Prevalence Survey

The Global Point Prevalence Survey (G-PPS) of Antimicrobial Consumption and Resistance assesses the prevalence and the quality of antimicrobial prescriptions across hospitals globally. G-PPS was carried out at 17 hospitals across Ghana, Tanzania, Uganda and Zambia. As a result of the programme, PPS data became readily available for the first time, strengthening the global commitment to improved antimicrobial surveillance. CwPAMS used PPS data to evaluate local antimicrobial prescribing practices. The data revealed that a variety of AMS interventions were required across the 12 hospitals. These include developing or improving access to guidelines, updating drug charts, helping to form AMS committees and carrying out AMS awareness campaigns.

Case example – development of antimicrobial management guidelines – Ghana Police Hospital (GPH)

After evaluating the PPS data from GPH, the team noticed that there were no prescribing guidelines. The partnership collaborated with local clinical staff to develop guidelines for specific medical departments. Post intervention PPS showed 100% compliance with the newly developed guidelines.



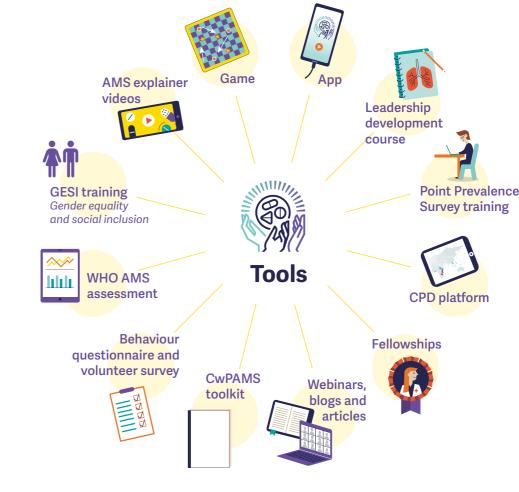


Local audits

Alongside the G-PPS, several partnerships conducted audits to assess local practice. The

Case example – Pneumonia management in the outpatient department – Keta Municipal Hospital, Ghana

The partnership team undertook a quality improvement project to increase compliance with the pneumonia treatment guidelines. After a discussion with the prescribers, the partnership designed interventions to improve access to guidelines. Prescribers received regular feedback on their progress and within three months, compliance with the guidelines had increased from 18% to 70%.



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data was used to facilitate discussions on local practice and identify barriers to change.

CwPAMS app

The CwPAMS app was developed to improve access to national prescribing guidelines. App metrics show how many times the guidelines were opened, the pages that were looked at the most, and the number of registered app users.

Case example – CwPAMS app superusers – Korle-Bu Teaching hospital (KBTH)

12 pharmacist superusers at KBTH promoted use of the CwPAMS app across their organisations, showing 55 clinical staff how to download and use the app. The superusers used data from the app metrics to demonstrate the success of the app within their local area and promoted further use of the app through regular discussions with prescribers.



Sharing data

The partnerships have developed links to national stakeholders, such as national pharmacy and medical associations, within each of the 4 countries. Partners presented to national committees and working groups, which has enabled them to disseminate project findings on a national level. Often, data collated by the Medicine Therapeutics Committees (MTC) is shared with Health Ministers. This data informs the implementation of the National Action Plans (NAPs), as governments use the data from partners when assessing the NAP objectives.

Case example – conference in Zambia – Brighton-Lusaka Pharmacy Link (BLPL)

BLPL conducted a three-day conference in Zambia for national stakeholders and institutions interfacing with the national AMR strategy. This included a AMS 'train-the-trainer' workshop for healthcare professionals to increase awareness of AMS and provide capacity-building tools. UTH pharmacists also led the development of a national AMS training manual, which is currently being accredited by the Health Professions Council of Zambia-the national regulatory body for continuous professions development of health workers in Zambia.

Victoria Rutter, Commonwealth Pharmacists Association (CPA)

The South Centre is an intergovernmental organisation of developing countries, funded by the Fleming Fund. It aims to combine these countries' efforts and expertise to promote their common interests in the international arena and raise global awareness of AMR. They also develop the capacity of policy makers and civil society in low- and middle-income countries to take actions to tackle AMR.

Achievements throughout Phase I

7 The South Centre, together with ReAct Africa, has held five regional meetings with policymakers, international organisations, and civil society of the African region to discuss the drafting and implementation of National Action Plans (NAPs).

2 The South Centre has held over 10 briefings for developing country health attaches in Geneva to increase awareness of AMR and encourage their engagement and their participation in global health processes.

3 The South Centre has worked with civil society organisations (CSOs) such as the Antibiotic Resistance Coalition to plan local campaigns. They have also worked to increase the influence of CSOs in developing countries.

4 The South Centre has supported local CSOs in the design and implementation of







AMR campaigns in Tanzania, India, Nigeria, Colombia, Kenya, Zimbabwe and Ethiopia. Local organisations have produced material in local languages and have used innovative means to increase knowledge of AMR.

5 The South Centre has facilitated consultations between the Tripartite (WHO, FAO and OIE) and CSOs, so that CSOs can provide feedback on the ongoing work to address AMR.

Data use **Bringing everybody** to the table

Pakistan lacks high quality and timely data on AMR from each One Health sector: human health, animal health and the environment. Policy makers need this data to understand the scale of the problem, and to encourage others to invest in sustainable solutions. The Fleming Fund Pakistan country grant aims to raise awareness of the extent and burden of AMR in the country. An important part of this is collecting data to improve the evidence base, which can then be shared with stakeholders. This allows them to make informed decisions to reduce the future impact of AMR.

The Fleming Fund is working with the Pakistan National Institute of Health (NIH) and WHO to investigate antimicrobial use in 14 large public and private sector hospitals. The aim was to understand drug prescribing practices for hospitalised patients and to use the findings from the study to inform policies and practices for more appropriate use of antimicrobials.

Over the course of six weeks, led by Dr Muhammad Salman, the AMR focal person at the NIH, the federal health ministry and provincial health departments planned where and how to do the survey. Clinical and nursing staff at sites collected the information and were directly involved in the discussions around AMR and poor prescription practices.

Together, we developed a communications package to share findings from the study

to health managers, clinicians and other stakeholders. The package included The package included:

(a) Policy briefs,

(b) A brief video presenting key findings and action points for senior health managers at the federal and provincial levels,

(c) Print copies of the report for researchers and others interested in AMR,

(d) Presentations to key stakeholders at AMR conferences and webinars,

(e) Plans for publication in peer reviewed research journals for more international coverage.

Using these tools, we presented preliminary findings to health managers and the Health Ministers of both Sindh and Khyber Pakhtunkhwan (KP) provinces. Findings showed an alarmingly high use of antibiotics without confirmatory tests in patients, specifically among children. Following the meetings, both KP and Sindh Health Ministers requested additional provincial level surveys specific for public sector hospitals. They were also keen to use the information generated to discuss the public sector's antimicrobial procurement practices and reduce misuse/ abuse of antibiotics by practicing clinicians. The survey was such a success that the findings are currently being used by the NIH to develop standard antibiotic prescription guidelines. Our support is also now being requested by the federal government to provide educational seminars to clinicians in federal hospitals.

Ayesha Rasheed, DAI Pakistan







Data use **AMR** data driving behaviour change in farmers

FAO is a specialised agency of the United Nations, working in over 130 countries to lead international efforts against hunger. Part of FAO's current focus is promoting better agriculture and food production methods. As antimicrobial use (AMU) is important in various Agri-food systems, FAO has followed an action plan on AMR since 2016.

While AMR is a complex biological process, its emergence and spread is also a social problem that is accelerated by human decisions and actions. Therefore, it is important to have socially informed solutions to target AMR, with multiple approaches for understanding and addressing behaviour. This is clearly recognised in FAO's efforts to promote the prudent use of antimicrobials. With Fleming Fund's support, FAO have designed behaviour change interventions that draw upon social science methodologies to contextualise patterns and drivers of AMU.

To ensure that the interventions are fully informed, FAO adopted a bottom-up approach. FAO field teams conducted Knowledge, Attitudes, and Practices (KAP) surveys among farmers, prescribers, feed millers, and sellers of antimicrobials. These surveys provide information on similarities and differences among farmers across production systems, within and across countries and regions. The association between identified behavioural targets and AMR is validated by pairing KAP surveys with laboratory-based studies that indicate antimicrobial residues and AMR levels in selected food products and production systems.

Using a Behavioural Change Community of Practice of over 100 participants, teams composed of national, regional and global experts co-created behavioural change interventions with relevant stakeholders. The use of FAO's Farmer Field School (FFS) approach is a particularly powerful intervention that arose from this. During an FFS, a group of farmers meet on a demonstration farm across an entire production cycle to identify, create, and engage in best practices. The FFS approach motivates uptake of interventions by making farmers active participants in the interventions' development, thereby instilling a sense of ownership. An intervention impact assessment is conducted after the completion of FFS cycles.

At global level, FAO collates FFS and other relevant data from countries, regions, and partners, and disseminates this across various platforms. This information sharing ensures that behaviour change interventions are based on scientifically acquired and validated data.

The approach used to target behaviours ensures that uptake of interventions is easier. For instance, an evaluation of the effectiveness of pilot interventions among layer-poultry farmers in Ghana and Kenya showed that farmers that engaged in FFS developed more prudent attitudes and observed better practices after interventions, including substantial reductions in AMU.

To create behavioural change, it is vital to consider AMR as a behavioural problem that demands social solutions. This requires bottom-up approaches, building institutional capacity, and integrating a strong social and behavioural change component within project and programme objectives. Harmonising approaches to compare AMR and AMU across locales and production systems, and





emphasising outcomes after behaviour changes by pairing social interventions with microbiological and other scientific methodologies are critical to create change.

Emmanuel Kabali, Food and Agriculture Organization

FAO-ATLASS

BANGLADESH

LAOS PDR

ATLASS Assessments (labs) 3 ATLASS Assessments Trained 3

ATLASS Assessments (labs) 4

ATLASS Assessments Trained -

3

7

4

2

18

12

The FAO Assessment Tool for Laboratories and AMR Surveillance Systems (ATLASS) is a tool developed by FAO to support countries in assessing and improving their AMR surveillance system in the food and agriculture sectors. The ATLASS tool can be used to generate baseline data on status of AMR detection capacities and surveillance for food and agriculture sectors through external and self-assessment.

It can assess five main pillars of an AMR surveillance system:

4

6

13

12 29

10

ETHIOPIA

ATLASS Assessments (labs) 6

ATLASS Assessments Trained 4

KENYA

FFS completed

TANZANIA

ZIMBABWE

FFS Facilitators trained

ATLASS Assessments (labs)

ATLASS Assessments Trained 3

FFS planned

FFS Facilitators trained

ATLASS Assessments (labs)

ATLASS Assessments Trained 3

ATLASS Assessments Trained

Behaviour Change Interventions 2 ATLASS Assessments (labs)

- Governance,
- Epidemiology Unit,
- Laboratories,
- Communications.
- Sustainability.

ATLASS Assessments (labs) 3

ATLASS Assessments Trained 2

SUDAN

GHANA

ZAMBIA

FFS Planned

FFS completed

FFS Facilitators trained

FFS Facilitators trained

ATLASS Assessments (labs)

ATLASS Assessments Trained 3

ATLASS Assessments (labs)

ATLASS Assessments Trained 4

It can also measure the stage of AMR detection capacity, data collection, analysis and information dissemination, and is able to identify steps for improvement.

PHILIPPINES

VIETNAM

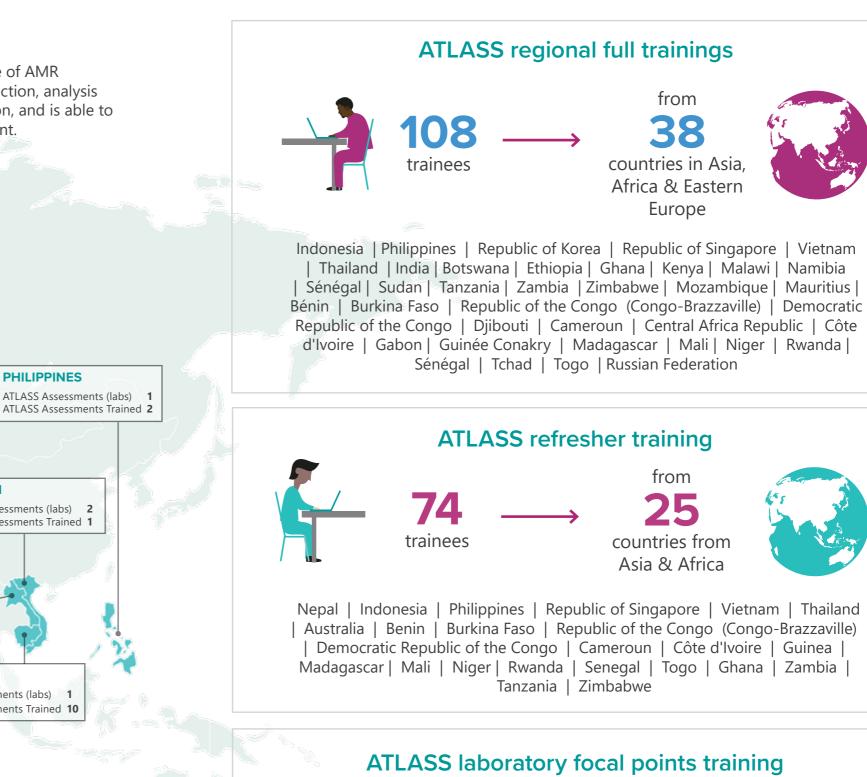
CAMBODIA

ATLASS Assessments (labs) 1

ATLASS Assessments Trained 10

ATLASS Assessments (labs) 2

ATLASS Assessments Trained 1















Tricycle One Health pilot protocol

WHO developed a protocol for global One Health surveillance of AMR based on one indicator - Extended Spectrum Beta-Lactamase producing E. coli (ESBL). The Tricycle protocol can be implemented across the world and will generate comparable country data.

The pilot has been implemented in 12 WHO Member States: Malaysia, Indonesia, Pakistan, Ghana, Nepal, India, Jordan, Zimbabwe, Burkina Faso, Nigeria, Senegal and Madagascar.

Achievements

All 12 Member States involved in the pilot have received government approval to implement the Tricycle protocol.

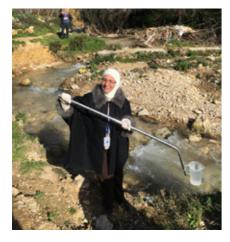
Country visits and trainings were delivered to support and increase capacities within the three sectors in the countries implementing the Tricycle protocol.

A multisectoral core group was established in each country to coordinate the implementation of the Tricycle protocol

WHO has coordinated regional training sessions on AMR. In each session there are five staff members from up to three different countries, representing each of the three sectors: human and animal health and the environment.

The multisectoral collaboration has been very active in the majority of the countries, organising meetings to coordinate activities and share

Some countries have continued working, developing and building the National Integrated Surveillance System.







😚 힟 The Fleming Fund

Substandard and falsified medical products

Global Surveillance and Monitoring System: Reports from countries and achievements

2020

WHO identified substandard and falsified medical products (SF Meds) as a priority area to address the urgent, global health concerns for the next decade, including expanding access to quality medical products.

____ 2018-2019

Case study example

WHO provided specialised regional training, funded by the UK government and attended by the Fleming Fund, on how to prevent, detect and respond to SF Meds. The training was delivered to 120 regulatory SF focal points from 28 African countries, which led to the development of a strong SF regional network within Africa.

Following this workshop, the attendees from Kenya and Uganda reported falsified Augmentin antibiotics (with no active pharmaceutical ingredients) to the Global Surveillance and Monitoring System (GSMS). The GSMS is a global database that provides national medicine regulatory authorities with a standardised approach to the collection, analysis and sharing of data on SF Meds.







WHO issued 34 Global Medical Product Alerts, of which 10 were on SF antimicrobials.

After the report of falsified Augmentin antibiotics, WHO issued a Global Medical Product Alert (N°9/2019) to the Global Focal Point Network for SF Meds. The workshop attendee from Tanzania then initiated targeted post-market surveillance and discovered the same falsified product which was being sold in the Morogoro region. The Tanzanian regulatory authority subsequently published a public notice asking for increased vigilance in-country.

This is a concrete example of how UK government funding and the Fleming Fund support has led to a tangible country, regional and global impact.

What is the UK FAO Reference **Centre for AMR?**

The UK FAO Reference Centre for AMR was launched at the 2nd Call to Action on AMR event in Ghana in November 2018. It was designated as an FAO Reference Centre for AMR in April 2019, and is funded by Department for Environment, Food and Rural Affairs (Defra) and the Fleming Fund, including through the Fleming Fund Fellowship programme.

The Reference Centre draws upon expertise from three Defra agencies: the Animal and Plant Health Agency (APHA), Centre for **Environment Fisheries and Aquaculture** Science (Cefas), and the Veterinary Medicines Directorate (VMD). This expertise is used to support LMICs by providing policy, scientific, and technical expertise, some diagnostic services and laboratory and field training. To date, Reference Centre teams have provided expert advice and training to ten countries, supporting its partners' ambitions to tackle the threat of AMR.

Our training has strengthened Nigerian institutional capacities through up-skilling of laboratory staff and enhancing their capacity to produce high-quality microbiological data. This includes 132 scientists from government, academic and private laboratories in Nigeria. This all helps to help build a One Health AMR surveillance system and support implementation of Nigeria's National Action Plan (NAP) for AMR.



Fleming Fund human health fellow Eme Ekeng demonstrating bacterial culture growth to training course participants at the Nigerian Centre for Disease Control in Abuja. (Photo credit: Nigerian Centre for Disease Control)



Fleming Fund animal health fellow Victoria Adetunji demonstrating the streaking of bacteria onto a culture plate during a laboratory training session at the University of Ibadan. (Photo credit: University of Ibadan)





Case studies

Ghana: Delivery in partnership

From 2018 to 2019, the UK FAO Reference Centre for AMR collaborated with colleagues within Ghana, including Ghana's Chief Veterinary Officer and academic partners, to address AMR. The Reference Centre team examined the existing facilities within the country to build a clear picture of their needs. The team identified enhanced capacity in veterinary medicines regulation and laboratory capabilities as priorities and created a tailored training programme. They were also able to facilitate collaboration between key national stakeholders, such as the FAO and the Fleming Fund, to achieve the best possible outcome.

Drawing on the specialisms across the three agencies within the Reference Centre, the training programme addressed surveillance of antimicrobial use and resistance. Staff used antibiotic import data to improve understanding of antibiotic usage within the Ghana livestock sector and upskill in analysis

of sales data. In partnership with the Ghanaian national laboratory for veterinary AMR, Reference Centre staff also led training in isolating and identifying bacterial pathogens within the lab, from aquaculture and poultry samples, and demonstrated methods of antimicrobial susceptibility testing.

Subsequently, the Reference Centre has hosted Fleming Fund fellows from Ghana at laboratories in the UK. They have also taken on new fellows and are developing additional training on surveillance of medicine residues.

This ongoing partnership between Ghana, key stakeholders and the Reference Centre has increased the capacity of the Ghanaian authorities to expand and develop veterinary AMR surveillance sustainably, with long term benefits for combatting AMR.



Bangladesh relies heavily on the aquaculture and poultry sectors for food security and employment, with the latter employing six million people, 40% of which are women. Combined, these areas of agriculture have a significant impact on animal health, human health, and the environment. Poultry and aquaculture are central to the agricultural system in Bangladesh. AMR in these industries poses a serious threat, but not much is known about AMR in these sectors.

In February 2019, the IUK FAO Reference Centre for AMR participated in the 'AMR in Aquaculture: A One Health Challenge' workshop in Bangladesh, giving technical presentations, leading breakout sessions and facilitating productive networking between participants. The team also assessed the country's AMR landscape and determined the support required in the agriculture sector. In coordination with Bangladesh partners, Mott MacDonald, and the FAO, a tailored support programme was designed, resulting in three further visits (October,







Fleming Fund





November, and December 2019) to deliver capacity development support and training to laboratory staff.

Building on the success of this programme, Reference Centre staff collaborated with FAO, CGIAR Worldfish and other academic organisations to design a surveillance programme to monitor AMR in live bird markets and commercial farms, as well as resistance in species recovered from wet fish markets and seabirds. Isolates from these sites were collected and whole genome sequencing (WGS) and antimicrobial susceptibility testing (AST) were used to investigate the resistance of particular bacterial pathogens. These data will inform future AMR surveillance strategies within aquaculture and the environment a vital element in policy to combat AMR. Similarly, the upskilling of scientists from the Bangladesh Ministry of Fisheries and Livestock in WGS techniques strengthened capacity in Bangladesh research institutes for future AMR surveillance, with the possibility of expansion of testing to other sectors and pathogens.

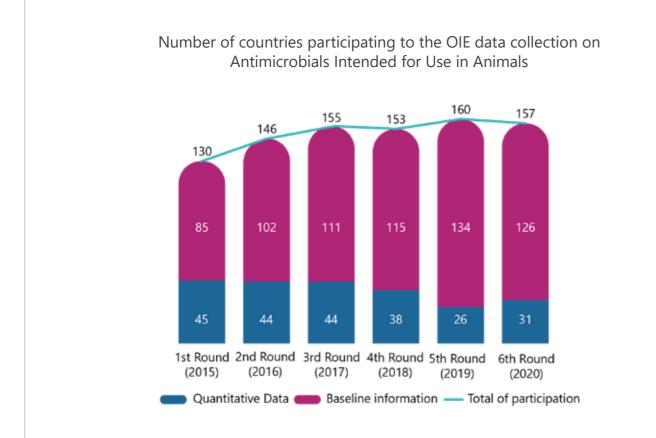
AMR within the poultry and aquaculture industries poses a serious threat, but there are significant gaps in the knowledge of AMR in these sectors.

The OIE AMU Global Database

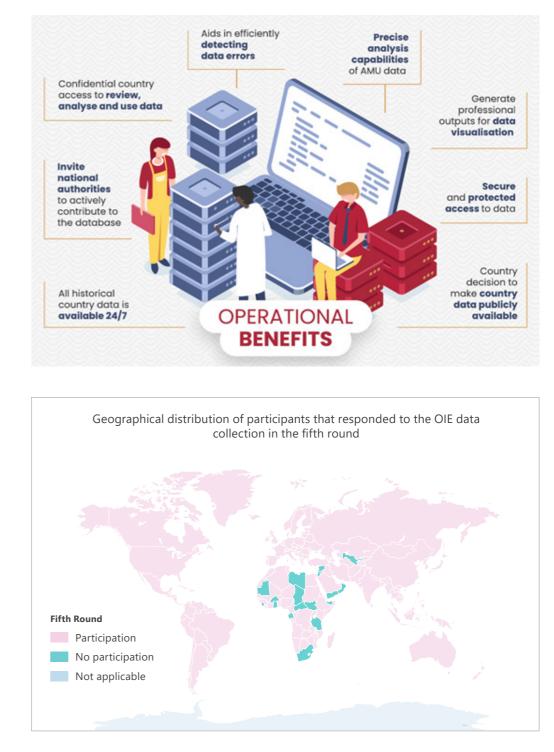
For over two decades, the OIE has engaged in combatting AMR through a One Health approach, as funded by the Fleming Fund. In the framework of the Global Action Plan (GAP) on AMR, the OIE has built a global database on antimicrobial agents intended for use in animals. Each year, since 2015, a new cycle of data collection, analysis and reporting to feed the OIE Global Database on Antimicrobial Agents Intended for Use in Animals is accomplished.

In the sixth round of data collection, 157 countries submitted their reports – an increased participation of 21% since the first round of data collection. The consistent number of countries reporting data since 2015, plus a steady annual increase in the quality of the data reported, reflects the growing commitment to adopting global monitoring and surveillance systems in line with OIE international standards. All this enables the OIE to report a comprehensive overview of the global situation on antimicrobial agents intended for use in animals.

The <u>5th OIE Annual Report on Antimicrobial</u> <u>Agents Intended for Use in Animals</u>, published in April 2021, includes data from countries on antimicrobial use in animals, reflecting the current situation of governance of veterinary antimicrobials worldwide. For the first time, the OIE could report 2015-2017 trends for 69 countries, showing an overall decrease of 34% of antimicrobials intended for use in animals at a global level. This demonstrates an increased capacity for country surveillance and accurate collection of data.



Since 2020, OIE have been developing a Phase 2 Global Database, which is an interactive online system customised for different countries. This would enable them to enter data, calculate antimicrobial quantities, and have their animal biomass estimated through secure confidential access to a central database. Countries will be provided with functional access to the database to review, analyse, present and use their own data, in line with the OIE's responsibility for global and regional data aggregation, analysis and reporting.





The OIE aims to continue to work collaboratively with all country governments to strengthen their capacity to monitor and regulate the use of antimicrobials, improve awareness of AMR and support all countries to adopt the OIE Standards to ensure the prudent and responsible use of antimicrobial agents in animal health.

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