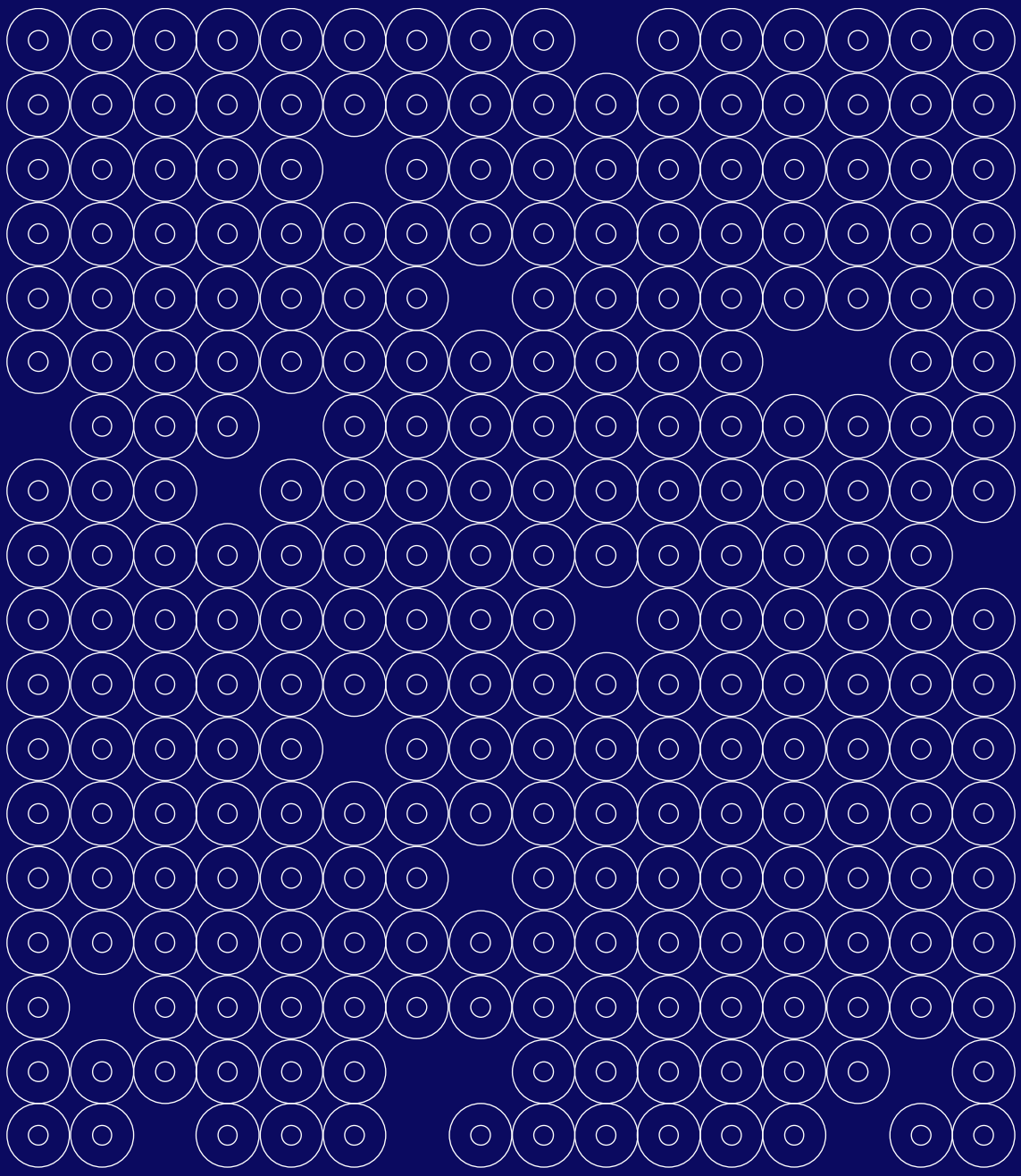
Supporting measures to mitigate AMR in One Health settings

Online roundtables 13-14 June 2022

CSA DESIGN OH AMR



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Executive Summary

The two roundtables on Prevention and Interventions entitled "Supporting measures to mitigate AMR in One Health settings" were organised by the Coordination and Support Action (CSA) DESIGN One Health AntiMicrobial Resistance (DESIGN OH AMR). The roundtables were carried out by JPIAMR, together with the International Centre for Antimicrobial Resistance Solutions (ICARS), on 13-14 June 2022. The roundtables were organised to gather insights on the 'prevention and intervention' research priorities of the candidate OH AMR Partnership.

In June 2017, the European Commission (EC) adopted the EU One Health Action Plan against AMR with one of the objectives to boost innovation and research. It proposed the creation of a One Health Antimicrobial Resistance (OH AMR) partnership, to support innovation and research on AMR. The roundtables were organised to gather insights on the 'prevention and intervention' research priorities of the candidate partnership.

The roundtables were divided into various thematic areas and the speakers were allotted based on their background and key expertise. With reference to healthcare interventions, the panellists advocated a global and systemic approach, considering the challenges in Low-Middle Income Countries (LMICs). As a multi-dimensional issue, it was felt that the learnings from Covid19 should be used effectively for finding solutions to the AMR issue, and to prepare for other emerging infections. Since many new technologies have technical, economic, and social implications, Health Technology Assessments can be a framework to evaluate the specific needs for innovation in the AMR space. Expertise in social and implementation sciences are needed when designing solutions to the challenge of AMR in healthcare setting.

The best-practices followed by European countries to sustainably reduce antibiotic use in agriculture should be shared with other countries such as LMICs. The use of consumer power and market signals to alter antibiotic use practices upstream should be explored. Research into best economic models for farmers to reduce the use of antibiotics in their production process and evaluation of incentives which can help them to change behaviour can be prioritized. However, the equity issues around the agricultural dimension of AMR and the needs of small/ backyard farmers should be considered while designing interventions to rationalize antibiotic use. The ecology of the bacterial populations in the farm environment and changes in the microbiome of the animals due to antibiotic use could be understood better.

With reference to AMR and the environment, identifying all the sources of antibiotic pollution and quantifying their relative importance is a priority, in order to implement value-for-money interventions. There is concern that the waste management methodologies currently employed are not effective in removing antibiotic residues and antibiotic resistance genes. There are innovations which can improve the effectiveness of the Wastewater Treatment Plants, but most of them are expensive to build and operate. Therefore, we need to explore the cost-effectiveness and feasibility of the various interventions. Water Sanitation and Hygiene (WASH) interventions are widely accepted as effective for reducing the burden of infectious diseases and AMR, but these are resource intensive. Innovative interventions to improve access to WASH services and

better understanding on how to climate-proof them are required. The linkages between climate change and AMR should be understood better and modelling-based studies can be used to project the future burden.

The cross-cutting priorities for this theme was also discussed in detail. The quadripartite partnership between WHO, FAO, OIE, and UNEP, endorses the importance of multisectoral collaborations to accelerate the One Health approach for mitigation of AMR and this has been reiterated in all strategic documents, including the report of the Inter-Agency Coordination Group on AMR (IACG-AMR). Multisectoral involvement in designing interventions and mobilizing sustainable financing were seen as priorities. There is a need to invest in developing innovative financing models, which can be adapted to LMIC contexts too. Framing an effective communication strategy around AMR and iterating the messages meant for various stakeholder groups were also discussed. Robust involvement of communities through community engagement strategies and use of behavioural change models for influencing the decisions of target stakeholder groups should be a priority- and this calls for social and behaviour science expertise while designing interventions.

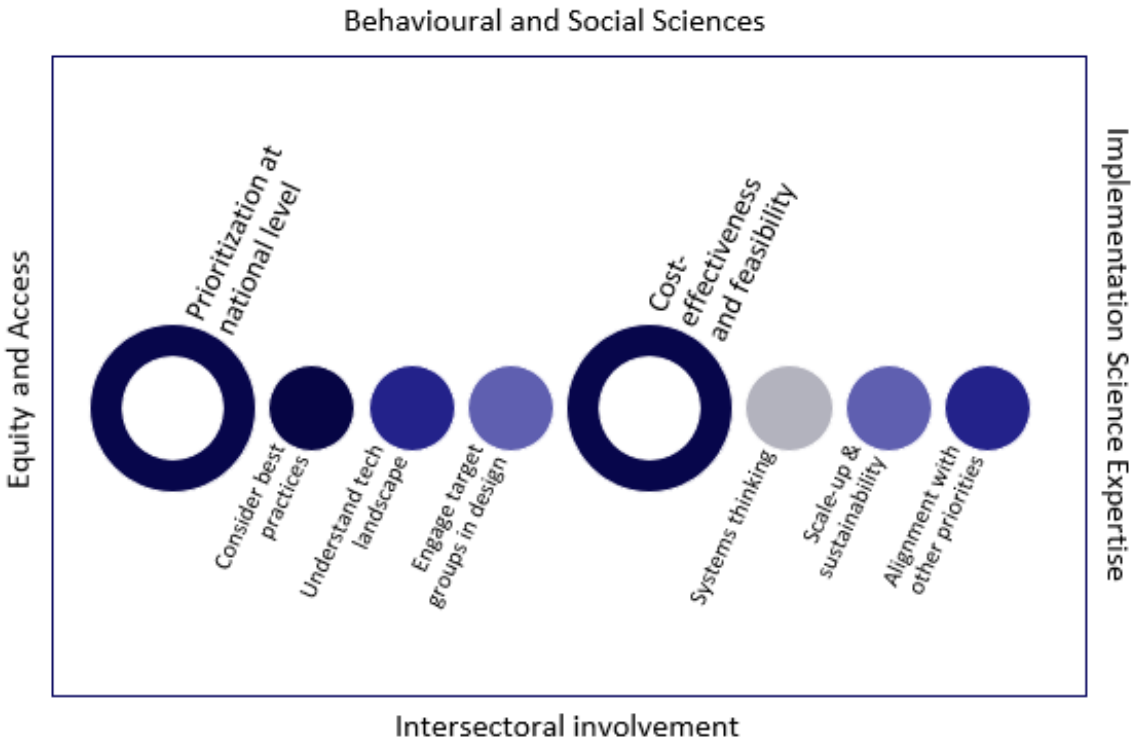

Figure 1: Principles of designing interventions to tackle the issue of AMR

Introduction to the report

This document presents the outputs of the two roundtable discussions conducted on 'Prevention & Interventions'. The roundtables "Supporting measures to mitigate AMR in One Health settings", were organised in the framework of the preparation of the candidate One Health AMR Partnership, expected to be launched in 2025.

A partnership on antimicrobial resistance

In 2021, the European Union (EU) launched "Horizon Europe"[1], the ninth framework funding programme for Research and Innovation. The creation of objective-driven and ambitious partnerships to support of EU policy objectives is one of the instruments deployed by the EU in this framework programme. In June 2017, the European Commission (EC) adopted the "EU One Health Action Plan against AMR" to address the emergency of antimicrobial resistance (AMR) and its frightening consequences on Public Health. "Boosting research, development and innovation" is one of the three main objectives of this action plan and through the creation of a "One Health AMR" (OH AMR) partnership the EC and Member States aim to support the research and innovation objectives of the EU Action plan against AMR[2].

Identification of Prioritised Research and Innovation Objectives for the candidate One Health AMR partnership Strategic Research and Innovation Agenda

The Coordination and Support Action (CSA) DESIGN One Health Antimicrobial Resistance (DESIGN OH AMR) has been created in response to the HORIZON-HLTH-2021-DISEASE-04-05 call: "A roadmap towards the creation of the European partnership on One Health antimicrobial resistance (OH AMR)." The main objective of DESIGN OH AMR is to prepare the launch of the OH AMR candidate partnership by identifying the Prioritised Research and Innovation Objectives (PRIOs) of the future partnership. Those priorities were divided into five focal research areas (Prevention & Interventions, Transmission & Evolution, Therapeutics, Diagnostics, and Surveillance). The two roundtables that were conducted in the area of prevention and interventions aim to provide the needed input to identify the research and innovation objectives in this focal research area and prioritise actions to be undertaken in the future partnership. The International Centre for Antimicrobial Resistance Solutions was responsible for conducting this consultation, on behalf of the DESIGN OH AMR project.

Approximately 140 participants from more than 40 countries joined the two online roundtables held on 13th and 14th June 2022. The current research and innovation objectives of the JPIAMR, as well as the input received during a global survey held in April 2022, were used as a starting point to launch the discussion. The sessions were moderated by Katherine Payne (University of Manchester) and Geetanjali Kapoor (One Health Trust) on 13th and 14th respectively. The workshop agenda was facilitated by Ghada Zoubiane and Philip Mathew from the International Centre for Antimicrobial Resistance Solutions.

[1] *Horizon Europe (europa.eu)*
[2] *EU Action Plan against AMR (europa.eu)*

Interventions to control AMR in healthcare

Key takeaways from the session

- A global and systemic approach, considering the challenges in Low-Middle Income Countries, is needed to address the systemic deficiencies linked to AMR.
- The learnings from Covid19 should be used effectively for finding solutions to the AMR issue, and to prepare for other emerging infections.
- Improved targeted surveillance is needed to better monitor the impact of interventions.
- Health Technology Assessment can be a framework to evaluate the specific needs for innovation in the AMR space. There are several technological solutions in the pipelinefor AMR, but adoption should be evidence based.
- Expertise in social sciences is needed when designing healthcare solutions.
- There should be a system for prioritising interventions according to the global impact and cost effectiveness. Evidence of cost-effectiveness can provide information on the added value of interventions.
- Methods from implementation science are needed to ensure the scalability and sustainability of interventions.

Summary of the introductory presentations

Uga Dumpis, Pauls Stradiņš Clinical University Hospital
Priscilla Rupali, Christian Medical College Vellore

- The prescribing competencies of physicians working at various levels of healthcare delivery constitutes a challenge. To overcome this challenge, it is necessary to develop clear treatment pathways for syndromic infectious conditions.
- Mortality from sepsis has not significantly changed despite new definitions and guidelines. Sepsis caused by AMR bacteria is of particular concern since empiric antibiotic therapy can fail.
- Antibiotics are used in several non-infectious conditions which may mimic infections. Clinical conditions like pancreatitis and burns are characterised by serious inflammation that is often difficult to distinguish from bacterial infections and lead to the use of broad-spectrum therapies. Differentiation of inflammatory states and non-infectious conditions from infections are required to reduce antibiotic use during treatment. Specific treatment pathways, diagnostic criteria and guidelines may be able to tackle this aspect of antimicrobial misuse.
- There are multiple vaccines targeting AMR pathogens (e.g., *S.aureus, P.aeruginosa* and *A.baumannii*) currently in the development stage[3]. Learnings from vaccine technologies and platforms developed during Covid 19 will likely lead to increased production of bacterial vaccines. The impact of those vaccines on the use of antibiotics needs to be studied. Success of antimicrobial stewardship activities are

[3] Pipeline of bacterial vaccines for priority drug-resistant pathogens (who.int)

largely dependent on human behaviour. More research is needed, including social and behavioural science research, to understand prescribing practices and how to positively influence them.

- Recent wars and climate change have affected migration and caused major shifts in AMR patterns in several geographical regions. For example, multiple cases of Multi Drug Resistant (MDR) tuberculosis have been reported in Europe among immigrants. More research is needed to look at the transmission dynamics of AMR in conflict situations and extreme climatic events.
- Much of the antibiotic misuse in human health is driven by factors outside the purview of the prescribers. Therefore, it is pertinent that the public is also involved in efforts to contain the AMR issue. This can be through awareness campaigns or educational efforts to inform public about infection prevention, antibiotic misuse, and AMR.

Summary of the responses from panellists

Anthony So, Johns Hopkins University
Natalie Murray, Pan American Health Organization Alex Costa, UNICEF
Souha Kanj, American University of Beirut Medical Center
Gloria Cordoba, International Centre for Antimicrobial Resistance Solutions

AMR as a systemic issue

- AMR is a systemic issue, and the solutions also need a systemic approach. The systemic challenges and chronic lack of investment in critical areas of healthcare delivery drive the issue in low-resource settings.
- Over-the-counter antibiotic misuse is a challenge in most developing countries. There is a need to evaluate various regulatory and legislative strategies to overcome this challenge. It is necessary to learn from best practices in high income countries.
- Some parts of the world have significant antibiotic overuse, but some countries and regions underuse antimicrobials in appropriate situations. Therefore, two different strategies of antimicrobial stewardship may be needed. The issue of access to must be addressed when designing interventions.
- It is important to learn from the Covid19 pandemic. Several systemic weaknesses have been identified which are relevant to an optimal AMR containment strategy. More resilient systems must be built, and this can happen through systematic analysis of the way we managed Covid19.

The innovation challenges

- Biofilms and colonisation in the hospital environment drive many Healthcare Associated Infections. There is an urgent need to find low-cost solutions for reduce the risk of biofilms and colonisation, including provision of clean water in healthcare delivery settings. Re-engineering hospital surfaces and medical instruments are examples of possible interventions.

- Machine learning and artificial intelligence [4] can be used to analyse big data to explore potential high-value intervention points and evaluate the efficacy of various interventions in different conditions.

Surveillance and data capture

- There is a need for new approaches for targeted surveillance of AMR and antimicrobial consumption in order to better assess the effectiveness of interventions. Initiatives like the WHO Tricycle Surveillance program[5] looking at ESBL producing *E.coli* should be used as successful examples.
- Genomic surveillance of AMR must be expanded globally and locally. As we are pushing for increasing the number of centres doing Antimicrobial Susceptibility Testing (AST) the increase in genomic surveillance capacity developed during Covid19 should be used for AMR surveillance too.
- Low-cost methods to digitalise health records and capture all clinical/lab data related to infectious conditions can revolutionise our understanding of AMR and treatment failures. This must happen at all levels of healthcare delivery for an optimal understanding about the course of disease progression and emergence of AMR.

Increasing the quality of research

- Social and behavioural scientists need to be included in the design of AMR interventions in the healthcare delivery sector. Psychosocial research can also help in deciphering the health seeking behaviours, Infection Prescription and Control (IPC) practices and prescription choices.
- Economic evaluation may be needed for novel interventions to contain AMR. This is essential for buy-in from the policymakers.
- Health Technology Assessment (HTA)[6] is required to evaluate the clinical utility and impact of various technologies on the evolution and transmission of AMR in healthcare settings. The technologies should be chosen carefully, with a thorough analysis of their acceptance and cost-effectiveness before investments are made to scale up. Such scale-up approaches should be informed by implementation science methods.

Salient points from the Q&A session

- Easy to use and point-of-care diagnostics for infections can go a long way in rationalizing antibiotic use in low-resource settings. It can be assumed that lab capacity for AST is lacking in Low-Middle Income Country contexts and that there are several systemic barriers in overcoming this challenge. Newer technologies which do not require heavy investment in equipment is the way forward.
- It is valuable to invest in the uptake and sustainability of interventions when funding commitments are made to evaluate the efficacy of AMR interventions. An enabling environment is needed to ensure that the piloting or results of the innovation is accepted by the target stakeholder groups and the policy community.

[4] *Applications of Machine Learning to the Problem of Antimicrobial Resistance: an Emerging Model for Translational Research | Journal of Clinical Microbiology (asm.org)*
[5] *WHO integrated global surveillance on ESBL-producing E. coli using a "One Health" approach*
[6] *Overview of Health Technology Assessment (europa.eu)*

- Principles of access should be built into the funding process. The process should look at research priorities, ensure open access publications and the intellectual property generated through the research should be available to the public.
- A One Health approach must be considered while designing healthcare interventions for AMR. There must be communication and coordination at global, national, and local level between various sectors. Impact of one intervention on all AMR related sectors should be understood.

Interventions to rationalize the use of antibiotics in food production

Key takeaways from the session

- The equity issues around the agricultural dimension of AMR and the needs of small/backyard farmers should be considered while designing interventions to rationalize antibiotic use.
- When interventions which are successful in HICs are adapted to LMICs, there should be an iteration based on local needs, resources and differences in agricultural systems.
- The ecology of the bacterial populations in the farm environment and changes in the microbiome of the animals due to antibiotic use should be understood, along with the potential changes resulting in prolonged exposure to antibiotics.
- Extensive background information on disease incidence, mortality, treatment failures, antibiotic consumption and resistance is needed for effective roll out of preventive interventions. Systems to compile such information are needed in all countries and should be collected through sample surveys or surveillance systems.
- What is the best economic model for farmers to reduce the use of antibiotics in their production process? This should be accompanied by knowledge of incentives which can help them to change behaviour. The cost of inaction should also be visible to the policy community.
- Several production systems, like bees or aquaculture, are far behind the current knowledge in AMR and Antimicrobial Use (AMU). Similarly, we have only little information on the dynamics of AMR in companion animals and wildlife.

Summary of the introductory presentations

Jonathan Rushton, University of Liverpool
Bruno Gonzalez-Zorn, Complutense University

- It is not possible to have a one-size-fits-all approach for AMR interventions. There must be an adaptation process to all interventions based on the requirements and resource availability. For example, food animal production systems are vastly different between countries.
- Prevention of infectious diseases should be a priority to prevent the use of antibiotics. In general, prevention measures are more easily implemented and developed in animal production systems, where conditions are controlled when compared to the human population.
- Studies on the economic incentives and legislation needed to support antibiotic stewardship in the farming sector are needed.
- There are ecological niches of concern that need to be understood. There is a need to undertake systems analyses to reflect the complexity of the agriculture sector and

identify value-for-money actions. It is pertinent that broader concerns about land use, energy efficiency and global warming, are addressed when we are discussing agriculture

- The equity issues associated with the agricultural dimension of AMR should be studied. Issues faced by the small-scale farmers must be discussed in the background of AMR concerns. Issues of food security and access to good quality nutrition needs deliberation.
- Waste management in farms is an important yet understudied area when discussing interventions to reduce the impact of the misuse of antibiotics in agriculture.
- Improvement in the quality of agricultural production practices will reduce the need for antibiotics, but this is a difficult process when the systemic factors are not well understood. There should be a holistic approach towards quality improvement in agricultural production, with takes into account the resource limitations of farmers.
- Cost effectiveness analysis of various interventions are needed for guidance regarding policy change.
- It is not possible to completely avoid the use of antibiotics in food production. Therefore, it is important to identify the optimal antimicrobials for use in agriculture and their safety- range.

Summary of responses from panellists

Anders Dalsgaard, University of Copenhagen
Javier Yugueros-Marcos, World Organization for Animal Health
Nitish Debnath, DAI Fleming Fund Bangladesh
Eric Fevre, International Livestock Research Institute

Effectiveness of programs & guidelines

- Many certification systems[7] are promoted as methods to change behaviours in the agricultural value chain. However, the impact of certification and labelling schemes is supposedly limited to food produced for export markets. We need to understand the real impact of these schemes.
- The effectiveness of standard treatment guidelines to rationalise the use of antibiotics in animal husbandry, especially in regions with poor diagnostic capacity, should be prioritised.

Widening the partnerships

- Co-opting industry into interventions is essential in the agricultural sector as a large part of the value chain is controlled by the industry.
- The issue of regulatory and oversight capacity in LMIC settings is a huge problem. Most low-resource settings do not have enough regulatory capacity to deal with antimicrobial misuse
- Social and behavioural change expertise is needed to understand the drivers for antibiotic use in small farmers. Even the interventions need to factor in the behavioural dimensions of the issue and design incentives to help farmers change behaviour.

[7] *Certified Responsible Antibiotic Use | Agricultural Marketing Service (usda.gov)*

- Identification of the stakeholders who may have the resources to support implementation of interventions is essential to guide sustainability of any activity to contain AMR in agricultural settings.

Hidden areas which require attention

- AMR in companion animals and in wildlife are understudied domains. The dynamics of transmission of resistance in these animals is relevant to our understanding of global burden of AMR.
- Waste management in farms is a priority that is often overlooked.
- There is a need to build an economic case for reducing inappropriate use of antibiotics, especially in growth promotion.
- There are existing gaps between science and policymakers. Community engagement should be seen as a strategy to influence the local decision-makers, and this experience can be used to sensitise the policy community.

Antibiotic use and surveillance

- Quantifying the real use of antimicrobials in rural areas is important but difficult. There should be strategies to increase the quality of consumption data from all parts of a country.
- Changes in animal microbiota as a result of repeated antimicrobial exposures is a concern. It is hypothesised that there is loss of heterogenicity, but very little data is available on immune response and growth.
- Farm level diagnostic tools are needed to overcome the gaps in disease identification and poor diagnostic capacity in farm sector. Rapid diagnostics can rationalise antibiotic use and eliminate the need for broad spectrum antibiotics.
- The focus on disruptive technologies for surveillance or diagnostics has the potential to drastically improve the AMR situation.

Salient points from the Q&A session

- There is a need to conduct research on the mode of action of different alternatives to antibiotics in growth promotion. The efficacy of each of these products should be documented in order to promote uptake by farmers.
- Many countries, including the European Union region, has banned antibiotics in growth promotion. Productivity in farms after this legislative exercise should be documented.
- The issue of equity in AMR interventions needs scrutiny, especially when interventions can affect livelihoods of people, productivity in farms and protein security of communities.
- The scope of One Health interventions needs to be defined. What tends to happen usually is that we label certain interventions as One Health when there are some vague connections between human & animal health issues. There is also a need to develop clarity on the expected outcomes of these One Health interventions.

Interventions to reduce antibiotic pollution and AMR in the environment

Key takeaways from the session

- Identifying all the sources of antibiotic pollution and quantifying their relative importance is a priority, in order to implement value-for-money for interventions. The cost- effectiveness of the interventions can be determined only if we are able to have a reasonable understanding of the impact.
- There is concern that the Waste Management methodologies currently employed are not effective in removing antibiotic residues and antibiotic resistance genes. There are innovations which can improve the effectiveness of the Wastewater Treatment Plants, but most of them are expensive to build and operate. Various methodologies regarding their effectiveness and feasibility in low-resource settings should be explored.
- Sewage Surveillance of AMR can be an easy target since it may be a surrogate marker for overall resistance burden in the community. Some labs have developed protocols for sewage surveillance during Covid19 and these can be repurposed for AMR. However, there is a need to generate evidence on the correlation between sewage AMR and various sectors.
- Water Sanitation and Hygiene (WASH) interventions are important to address the environmental dimension of AMR, but these are resource intensive. Access to safe drinking water and sanitation is a part of the Sustainable Development Goals; and several countries have prioritised action. However, research is needed for innovative methodologies to improve access to WASH and climate-proof these services.
- There is a complex relationship between climate change and AMR. This can be used as a leverage to advance the AMR agenda in countries, as climate change is a more visible issue with massive political capital. However, the linkages should be understood better and modelling-based studies can be used to project the future burden.
- Behavioural and social science expertise should be leveraged effectively for designing interventions to contain the environmental dimension of AMR. Besides, provision for sharing of data and economic analysis of interventions are quintessential.

Summary of the introductory presentations

Sabiha Essack, University of Kwazulu-Natal
Philip Mathew, International Centre for Antimicrobial Resistance Solutions

- There is a need to identify the contribution and relative importance of various activities and sectors to the evolution of AMR in the environment. There is a need for improved knowledge about the acquisition, evolution, or transmission of resistance in the environment.

- There are several hidden sources of antibiotic pollution in the environment, such as horticulture[8]. These sources need to be identified and studied in greater detail. It is important to explore compartments in the environment in which amplification of resistance and emergence of new forms of resistance is facilitated.
- The current Wastewater Treatment methodologies may not be effective in removing antibiotic residues and mobile genetic elements coding for resistance. Technologies which can remove residues and ARGs in a cost-effective way and their feasibility for use in low-resource settings should be explored
- The complex relationship between climate change and AMR should be studied. This should go beyond the systemic considerations revolving around extreme climatic events and climate-induced migration; and examine the biomedical pathways of climate change increasing resistance. Modelling-based projections looking at various scenarios can also be considered.
- Several countries have published maximum residue limits for antibiotics in effluents, but there are large knowledge gaps. Research on regulatory frameworks which can reduce the discharge of antibiotics into the environment, including from pharmaceutical manufacturing facilities, should be a priority.
- Cost effective and energy efficient methodologies for improving WASH access in low resource settings should be explored, since lack of access of appropriate WASH facilities is an independent risk factor for AMR.
- Antibiotic residues and Antibiotic Resistance Genes (ARGs)[9] can result in long lasting changes in the environmental microbiome. This will also indirectly influence the microbiome of humans and animals. The impact of AMR in the environment on the human microbiome and colonisation in multiple environmental compartments needs to be studied.

Summary of the responses from panellists

Joakim Larsson, University of Gothenburg
Philip Taylor, Centre for Agriculture & Bioscience International
Chadag Vishnumurthy Mohan, World Fish
Direk- Limmathurotsakul, Mahidol Oxford Research Unit

- The environment interface in the context of AMR is more an issue for human and animal health than an issue for environmental sustainability. Therefore, it is the responsibility of the human health and animal health sectors to reach out to the relevant stakeholders in the environmental sector.
- Correlation between sanitation and AMR is better compared to the correlation between AMU and AMR. Therefore, pathways for transmission in the environment are important in areas with inadequate WASH infrastructure. Ways to incentivise creation of WASH infrastructure and AMR can be shown as one of the benefits.
- The environmental dimension of AMR is underrepresented in actions, even if the importance of AMR accumulation in the environment is visible. Showing costs of inaction and benefits of action can possibly spur interest and investments in this domain.

[8] *Antibiotic use on crops in low and middle-income countries based on recommendations made by agricultural advisors - CABI.org*
[9] *Antibiotic resistance genes in bacteria: Occurrence, spread, and control - Jian - 2021 - Journal of Basic Microbiology - Wiley Online Library*

Surveillance

- Surveillance of AMR in the environment can be reflective of resistance situations in humans and animals. In some cases, environmental surveillance data can be even taken as surrogate markers for resistance profile in humans.
- Wastewater and sewage surveillance for AMR can be a low hanging fruit, as we already have a template from Covid19, and the surveillance efforts can cover a large population.

Crop protection

- Until recently, human health and animal health were not considered together with the issue of crop protection. The role of antibiotics and other chemicals in crop protection is primarily prophylactic and not curative. This is a fundamental difference in approach.
- In crop protection, the use of fungicides outweighs the use of antibiotics as fungal diseases dominate in plants. In plant agriculture, there is use of heavy metal and copper-based preparations in addition to antibiotics, many of which can also drive resistance. Preventive strategies to limit AMU in crops is also vastly different, as plants can suffer from many diseases at the same time and no vaccines are available for use in plants.

Aquatic Food systems

- Research into the relationship between aquatic food systems and AMR, and how it affects human health, should be an area for future investment. The pressure to increase production in aquatic food systems often eclipses the demand for safe and nutritious food. There are large differences between countries, in terms of priorities and robustness of implementation of regulations in aquatic food systems.
- The transboundary nature of AMR in aquatic food systems needs to be understood. There is a need to understand the microbiome dynamics in aquatic systems, including their effect on disease control. Some studies have shown that the use of microbiome analysis as a predictor of disease outbreaks or as an indicator of poor health in aquatic systems.
- The entire aquatic food system value chain must be engaged to rationalise the use of antibiotics. Innovative social science methods to understand the motivations behind use of antibiotics and behavioural interventions to reduce the misuse in aquatic systems.

Rethinking priorities

- Behavioural change among the target stakeholder groups is an important concern when we consider the role of the environment in AMR.
- Wastewater from food animal farms is a priority but needs to be quantified to determine the extent of the problem.
- There is a need to identify and tackle sites where there is strong exposure of antibiotics within the environment, for example from pharmaceutical plants.
- Improved measurement regarding the outcomes of the interventions to reduce antibiotic residues and ARGs in the environment is needed.

- Device techniques to quantify the antibiotic footprint should be considered, such as those to detect and measure carbon footprints of activities and countries.
- The power of consumers and patient advocacy groups should be used to ensure that the antibiotic footprint of products and services are reasonably low.
- Open access to research results and both published and non-published data should be ensured.

Salient points from the Q&A session

- There are several technologies that are already available that can be used to reduce antibiotic contamination in the environment, but their cost effectiveness and feasibility need to be evaluated.
- The scope of environment in terms of AMR containment should be defined. There is a need to fit environment in the One Health spectrum, but action is needed even before the collection of hard evidence. If we have a logical inference of the linkages between AMR and environment, it should be used to drive action.
- Climate change can be used as a leverage to advance the AMR agenda in countries, primarily because of better visibility and global agreements. Increase in temperature is associated with an increase in resistance, and climate footprint of intensive farming exacerbates climate change. The relationship between AMR and climate change is complex; and the collective aspect of solutions for AMR and climate change can be highlighted for better uptake.
- Integrated surveillance frameworks have been developed for several countries, but implementation has been lagging. The Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) Tricycle protocol is a good example for integrated surveillance, but it is not perfect. The Fleming fund has been seemingly successful in launching integrated surveillance in some countries, but solid data has not yet been compiled.
- There is a small amount of data connecting the different sectors at the country level. It would be critical to extend the collection of data, especially to the environment sector to contain AMR. Since there are very few laboratories looking at the environmental dimension of AMR, a triangulation process would be needed in most cases to estimate the load of resistance in the environment.
- Some countries have a strong background in One Health, especially those which have suffered from bird flu outbreaks, and this can be leveraged effectively. In other countries, public support and community engagement are important to mobilise political capital for AMR in the environment.

Multisectoral interventions for AMR

Key takeaways from the session

The quadripartite partnership among world organisations (WHO, FAO, OIE, UNEP) endorses the importance of multisectoral collaborations to accelerate the One Health approach for mitigation of AMR and other One Health related issues. Various emerging priorities will help to strengthen “multisectoral interventions". These include:

- Increased funding and mobilisation of investments for multi-sectoral interventions.
- Understand the emerging disciplines like social and behavioural sciences
- Inter-departmental/inter-ministerial linkages.
- Innovations in WASH practices.
- Engaging the civil societies and private sectors.
- Stepping up biosecurity and trade restrictions.
- Mapping the contribution of each One Health sector to the AMR problem and utilising AI/ Machine learning.
- Integrate vertical programs within and across sectors. Good interventions that have proven effectiveness in one setting, can be translated into other settings.
- Effective communication of results to policy makers is a priority when designing multisectoral interventions. A robust understanding of One Health is required to comprehend the need for intersectoral action on AMR.

Summary of the introductory presentations

Tine Rikke Jorgensen, World Health Organization

- To tackle the complex AMR problem there is a need for inter and multidisciplinary research. However, more evidence is needed to really understand the different sectors that contribute to AMR that can be exploited to develop impactful interventions. This includes understanding the AMU in agriculture and the animal sector, fungal resistance, effectiveness indicators for measurement of impact, capacity building in different sectors, scalability, sustainability, and implications of research.
- Countries are specifically struggling with governance structures and internal silos. This makes collaboration across sectors very difficult.
- It is important to include social sciences in designing interventions to contain AMR. Many of the drivers of AMR are related to human behaviour and good understanding of the barriers to behavioural change is needed.
- Environment as a domain is often under-represented in efforts to contain AMR.
- Since environment can potentially play the role of an amplifier of resistance, environment experts and environmental interventions must be a part of the narrative.

- The Quadripartite AMR secretariat has supported strengthening global partnerships, identification of emerging priorities and an interdisciplinary and multi-sectoral approach to control AMR.
- There is a disconnect between the scientific community and policy makers, primarily because of the difference in “language". Research results must be packaged effectively and communicated to policy makers.
- Water, Sanitation & Hygiene (WASH) is important to address all the three dimensions of the AMR problem. Innovations in WASH practices, which may be feasible for low-resource settings, can reduce the load of infections and thereby decrease the need for antibiotics. Infection prevention in healthcare facilities and biosecurity practices in farms are all a part of the WASH spectrum.
- Robust involvement of civil society and the private sector is needed for success of any AMR intervention. Therefore, a co-development process is needed for designing interventions and should proactively involve these sectors.
- Quantifying the contribution of various sectors to the overall issue of antibiotic misuse and AMR is needed. Interventions can only be strategic and value for money if they are supported by good evidence on their importance to AMR containment.

Summary of the response from panellists

Jay Varma, Weill Cornell University
Clare Chandler, London School of Hygiene & Tropical Medicine
Mirfin Mpundu, ReAct Africa
Katharina Staerk, Federal Food Safety and Veterinary Office Switzerland

Improving understanding and prioritising research

- One Health as a concept is still unfamiliar to most. Even among researchers, a true One Health approach is not followed while designing interventions to contain AMR.
- AMR research needs to be designed in a systematic way and research.
- prioritisation exercises can help. The results should be communicated to the relevant policymakers after packaging it well.

Changing the narrative

- Antibiotics are described as infrastructural units that have become part of our systems as useful ways to fix a range of problems including hygiene, quality care, and productivity (animal or human). However, we need to reduce reliance on antibiotics, and fix the underlying problems instead.
- Antibiotics should be considered as a global public good, which require collective international action in order to protect its effectiveness.

Establishing partnerships and optimising governance

- There are major challenges to establishing multisectoral partnerships such as (1) weak governance structures (2) lack of cross sectoral projects (3) lack of awareness on importance of multisectoral partnerships in mitigating AMR and One Health issues (we need to involve governments, institutions, academia and Non-

Governmental Organizations (NGOs) (4) lack of sustainable financing for strengthening surveillance systems (5) non-robust data sharing platforms (6) poor capacity of workforce (7) lack of regulations (8) political will and buy-in.

- It is important to step up biosecurity and trade restrictions; understand the role of the environmental sector in combatting One Health issues; and understand social/behavioural aspects.
- Political commitment is needed to fully support and implement One Health strategies. Political commitment is essential regardless of what public health area we work on. Thereafter, internal coordinating mechanisms for intersectoral working can be developed (operational assembly among very different departments).
- The Quadripartite collaboration [10] is a step towards building intersectoral collaborations. This is a collaboration at global level, but collaboration at national and subnational levels is also required.
- It is essential to have administrative and financial mechanisms in place to optimize governance and facilitate multisectoral collaboration at all levels.
- Defining metrics and meeting targets is required. The right types of indicators can motivate action, communication, and collaboration.
- Work that is conducted in the research sector (public health surveillance) should be used in public health decision making. i.e., an interface between the systematic, ongoing collection analysis, and use of data for public health action, is required.
- Evidence curation across sectors (as being done by JPIAMR and ICARS) is important and should be used to support the future research agenda.
- Understanding the trade-offs between interventions and results (for example, IPC interventions and how it helps in reducing infections) is required.
- Social sciences must drive forth the AMR agenda. Social sciences can help to understand why people behave or practice in a particular way, and how these actions can be fine-tuned.

Salient points from the Q&A session

- Both HICs and LMICs are facing difficulties integrating surveillance across One Health sectors. Pilot projects may help to show the importance of interaction between sectors. Luckily, a lot of pilot activities are ongoing at the moment and interventions that have proven to be effective in one setting can be translated into other settings. It should be noted that HICs have more resources and finances, to make trials and errors, and that the results from their studies should be used to support LMIC integrated surveillance systems.
- Financing is a critical aspect of AMR containment through National Action Plans. For effective utilisation of finances, a strong governance structure should be built to ensure allocation of budgets across ministries, and ensuring work is not duplicated. Methodologies for measuring impact should be in place by the time utilisation of funds start.
- Evidence is required to prove that investment in AMR is worthwhile. Therefore, specific AMR indicators (like those for the Sustainable Development Goals (SDGs)[11])

[10] *UN Environment Programme joins alliance to implement One Health approach (who.int)*
[11] *THE 17 GOALS | Sustainable Development (un.org)*

will help to support the investment case. There should be efforts to quantify the cost of inaction.

- Awareness and educational campaigns around AMR are critical to the success of action plans. Various educational interventions and messaging strategies need to be tested to identify their effectiveness for behavioural change. The importance of antibiotics to the health of the society and food security of communities; and the positive behaviours associated with the preserving efficacy of antibiotics can form the theme of these efforts.
- Effective sharing of data at various levels and interoperability of data platforms should be established between different sectors to access data, from a One Health perspective. Funding is required, platforms must be built and incentivization required so researchers can share and publish their data

Annex I. Agenda for the roundtables

Roundtable 1, 13th June 2022, 14:00 to 17:00 CEST

14:00 **Introduction and setting the context,** Ghada Zoubiane, International Centre for Antimicrobial Resistance Solutions

14:05 **JPIAMR – updating the Strategic Research and Innovation Agenda**, Laura Plant, Joint Programming Initiative on Antimicrobial Resistance

14:15 **The Strategic Research & Innovation Agenda, Prevention & Interventions**, Katherine Payne (Chair), University of Manchester

14:25 **Human Health from a One Health setting**, Uga Dumpis, Pauls Stradins Clinical university hospital

14:35 **Panel Discussion**
Anthony So, ReAct Strategic policy Program and Johns Hopkins University
Natalie Murray, Pan American Health Organization,
Alex Costa, UNICEF

15:00 **Animal Health from a One Health setting**, Jonathan Rushton, University of Liverpool

15:10 **Panel Discussion**
Anders Dalsgaard, University of Copenhagen
Javier Yugueros-Marcos, World Organization for Animal Health

15:35 **Break**

15:40 **Environment from a One Health Setting**, Sabiha Essack, University of Kwazulu- Natal

15:50 **Panel Discussion**
Joakim Larsson, University of Gothenburg
Philip Taylor, Centre for Agriculture & Bioscience International Cortney Price, FAO

16:15 **AMR as a Multisectoral One Health issue**, Tine Rikke Jorgensen, WHO

16:25 **Panel Discussion**
Jay Varma, Weill Cornell University
Clare Chandler, London School of Hygiene & Tropical Medicine

16:50 **Spare time for discussion**

16:55 **Summary & Wrap-up**, Philip Mathew, International Centre for Antimicrobial Resistance Solutions

Roundtable 2, 14th June 2022, 09:00 to 12:00 CEST

09:00 **Introduction and setting the context**, Ghada Zoubiane, International Centre for Antimicrobial Resistance Solutions

09:05 **JPIAMR – updating the Strategic Research and Innovation Agenda**, Laura Plant, Joint Programming Initiative on Antimicrobial Resistance

09:15 **The Strategic Research & Innovation Agenda, Prevention & Interventions**, Geetanjali Kapoor (Chair), One Health Trust (CDDEP)

09:25 **Human Health from a One Health setting**, Priscilla Rupali, Christian Medical College Vellore

09:35 **Panel Discussion**
Souha Kanj, American University of Beirut Medical Center
Gloria Cordoba, International Centre for Antimicrobial Resistance Solutions

10:00 **Animal Health from a One Health setting**, Bruno Gonzalez-Zorn, Complutense University

10:10 **Panel Discussion**
Nitish Debnath, DAI Fleming Fund Bangladesh
Eric Fevre, International Livestock Research Institute

10:35 **Break**

10:40 **Environment from a One Health Setting**, Philip Mathew, International Centre for Antimicrobial Resistance Solutions

10:50 **Panel Discussion**
Chadag Vishnumurthy Mohan, World Fish
Direk- Limmathurotsakul, Mahidol Oxford Research Unit

11:15 **AMR as a Multisectoral One Health issue**, Tine Rikke Jorgensen, World Health Organization

11:25 **Panel Discussion**
Mirfin Mpundu, ReAct Africa
Katharina Staerk, Federal Food Safety and Veterinary Office Switzerland

11:50 **Spare time for discussion**

11:55 **Summary & Wrap-up**, Philip Mathew, International Centre for Antimicrobial Resistance Solutions

Annex II. List of Abbreviations

AGISAR- Advisory Group on Integrated Surveillance of Antimicrobial Resistance

AMR- Antimicrobial Resistance

AMU- Antimicrobial Use

ARG- Antibiotic Resistance Genes

AST- Antimicrobial Susceptibility Testing

CSA- Coordination and Support Action

EC- European Commission

EU- European Union

HIC- High Income Countries

HTA- Health Technology Assessment

IACG-AMR- Inter-Agency Coordination Group on AMR

ICARS- International Centre for Antimicrobial Resistance Solutions

IPC- Infection Prescription and Control

JPIAMR- Joint Programming Initiative on Antimicrobial Resistance

LMIC- Low-Middle Income Countries

MDR- Multi Drug Resistant

NGO- Non-Governmental Organizations

OH AMR- One Health Antimicrobial Resistance

PRIO- Prioritised Research and Innovation Objectives

SDG- Sustainable Development Goals

WASH- Water Sanitation and Hygiene

WHO- World Health Organization

Annex III. Brief profile of the members of the organising team

Geetanjali Kapoor

Geetanjali is the Head of the South Asia Office of the One Health Trust (formerly Center for Disease Dynamics, Economics and Policy). She is a physician, specializing in medical microbiology and public health.

Katherine Payne

Katherine is a professor of Health Economics at the University of Manchester. She was awarded a personal Chair in Health Economics at The University of Manchester in August 2010. She has extensive experience working as an academic health economist with different clinical research groups

Bruno Gonzalez-Zorn

Bruno is the Head of the Antimicrobial Resistance Unit at the Complutense University in Madrid, and Adjunct Professor of Biotechnology at the University for Development Studies in Ghana. He is a veterinarian by training and his research interests focus on the role the ecology of antimicrobial resistance, including humans, animals, food, and the environment, focusing his research on genomics from a One Health perspective.

Priscilla Rupali

Priscilla is a Professor of Adult Infectious Diseases at the Christian Medical College, Vellore, India. She also serves as the Secretary of the Clinical infectious Diseases Society (CIDS), which the apex association for infectious disease physicians in India.

Jonathan Rushton

Jonathan is a Professor of Animal Health and Food System Economics at the University of Liverpool. He is specialized in the economics of animal health, livestock production and livestock food systems. He has got extensive experience working as a livestock economist in Asia, Africa, and Latin America

Uga Dumpis

Uga Dumpis is the Head of Department of Infectious Diseases and Infection Control at Paul Stradins Clinical University Hospital, Latvia. He is also the responsible for diagnosis and treatment of infectious diseases, antibiotic stewardship, and infection control measures at the teaching hospital

Sabiha Essack

Sabiha is a pharmacist by profession, is the South African Research Chair in Antibiotic Resistance and One Health and Professor in Pharmaceutical Sciences at the University of KwaZulu-Natal (UKZN). She serves as expert consultant on antimicrobial resistance (AMR) to the World Health Organization (WHO) in Geneva as well as the WHO Regional Office for Africa.

Ghada Zoubiane

Ghada is the Head of Partnerships and Stakeholder Engagement at International Centre for Antimicrobial Resistance Solutions. She has significant experience in leading and executing research strategies at a national and international level. She has been a part of several international funding organizations, including the Wellcome Trust, CARB-X, Medical Research Council etc.

Philip Mathew

Philip is an Antimicrobial Resistance Advisor with the International Centre for Antimicrobial Resistance Solutions. He is a medical doctor by training and has specialized in public health medicine. He has been involved in AMR issues for the last 6 years as a Public Health Consultant to ReAct Asia Pacific.