A Sustainable Future

Tackling Antimicrobial Resistance: Opportunities and Challenges for Microbiology Research and Innovation

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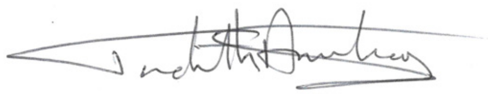
Foreword

Step by step and year after year, the health, wealth, and well-being of the global population is improving. Not on every single measure every single day, but as a rule. However, many challenges remain. Extreme weather events, biodiversity loss and forced displacement are affecting tens of millions of people worldwide every year. These catastrophic events generate headlines and grab our attention in ways that progressive improvements rarely do. When things get better, such as the decrease in child mortality across the world, it is because lots of people are working together on the frontlines every day, over the long term, to bring about the changes that constitute progress. Through the discovery of antibiotics and vaccines, water sanitation and hygiene, bioremediation and food security, to name but a few contributions, microbiology's impact has been profound.

The United Nations, 17 Sustainable Development Goals, including 'good health and well-being', 'gender equality' and 'affordable and clean energy', build on the success of the Millennium Development Goals to close the gap and cement hundreds of years of incremental human progress with the support of a strong international community. The Global Goals are a universal call to action to end poverty, protect the planet and ensure that all people enjoy peace and prosperity by 2030.

Microbiology is essential to achieving the Sustainable Development Goals. The ocean and soil microbiomes, for instance, act as natural carbon sinks and could be used to further sequester carbon and mitigate the effects of anthropogenic climate change. Microbial technology can be used to produce sustainable clean energy in the form of biofuels. Microbial secondary metabolites could provide novel antimicrobials to tackle the pressing issue of antimicrobial resistance. Many of the steps that will be taken on the long road towards achieving the Sustainable Development Goals will involve microbial processes. The major policy decisions needed to set us on this journey require knowledge of relevant microbial activities and how these can be channelled for the greater benefit.

Microbiology has made our present better than our past, and can make our future better still. Policy decisions based on knowledge of underlying microbiological processes will be the basis of future progress, well-being and, ultimately, sustainability. With this project we hope to share our excitement for the profoundly positive effects that microbes have on human beings, the biological world and the entire planet and its atmosphere. Microbiologists, policymakers and others must work together to propel us towards the global goal: a sustainable future.



Emeritus Professor Judith Armitage
Professor of Biochemistry
University of Oxford

President of the Microbiology Society

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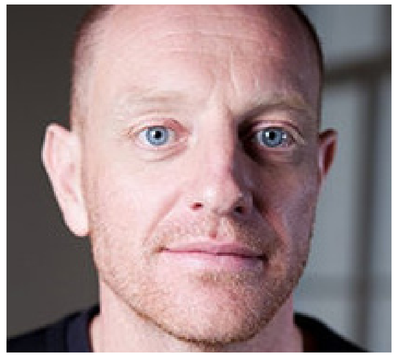


Antimicrobial resistance (AMR) is a slow-moving pandemic, which already causes at least 70,000 deaths a year globally. Unchecked, the impact of AMR will continue to grow and has the potential to become the greatest future threat to human health and well-being. Tackling the issue of AMR aligns with many of the United Nations (UN) Sustainable Development Goals (SDGs); specifically, those related to poverty (SDG 1), human health (SDG 3), food security and agriculture (SDG 2), clean sanitation (SDG 6) and economic growth (SDG 8). The breadth and the scale of the AMR problem suggests that we require multidisciplinary approaches to generate new solutions. Microbiology is at the forefront of developing novel antimicrobial compounds, vaccine research, providing sustainable solutions for treating livestock and crop diseases, unravelling disease transmission patterns across ecosystems and informing which antimicrobials should be prescribed when. Therefore, the microbiology community is pivotal for AMR research and can have a major influence in this area, which can contribute to delivering the SDGs.

The current landscape of AMR research in the UK and Ireland is highly active and expansive, and AMR represents a scientific arena in which we (the community) can undoubtedly have a major global impact. However, the challenge that confronts us is significant and we need to augment some aspects of our current AMR research so that we can provide new solutions to infections caused by antimicrobial-resistant organisms. The outline presented here alludes to the future of AMR research in the UK and Ireland and was generated by a large group of leading experts. These opinions are not exhaustive, but do highlight some of the major issues of the current academic structure and outline some potential solutions for how we move forward in AMR research through the initiative of the UN SDGs.

In summary, we need more multidisciplinary collaborative research; as a field we need to be ambitious, looking beyond scientific publication, aiming to create more sustainability in our research, in which we have better rewards for true innovation. Whilst basic research is fundamental to understanding the how and why, we also need to be more applied, aiming to translate our findings into new interventions through enhanced interactions with other disciplines and industrial partners. Lastly, AMR is going to be an enduring problem and we need longer-term support to understand AMR and mitigate its impact. The creation of an AMR knowledge centre could provide this platform and become a hub for interdisciplinary research, academic/industry links, policy and global innovation. AMR is one of the biggest healthcare challenges we currently face, and we as the Microbiology Society know our members can rise to the challenge.

Professor Stephen Baker
Professor of Molecular Microbiology
University of Cambridge

Chair of the Microbiology Society Antimicrobial Resistance Advisory Group

2. Recommendations

Microbiology research in the field of antimicrobial resistance

1. Sustained microbiology research and innovation in the field of AMR is imperative to help deliver the UN SDGs, particularly goals related to poverty (SDG 1), food production (SDG 2), good health and wellbeing (SDG 3) and the environment (SDGs 6 and 15).

Improving antimicrobial resistance surveillance networks

2. In order to optimise current surveillance systems, microbiologists should seek to progress the implementation of innovative solutions such as rapid point-of-care genomics and should advocate to be included at the heart of both national and international surveillance efforts.

Enabling antimicrobial resistance research

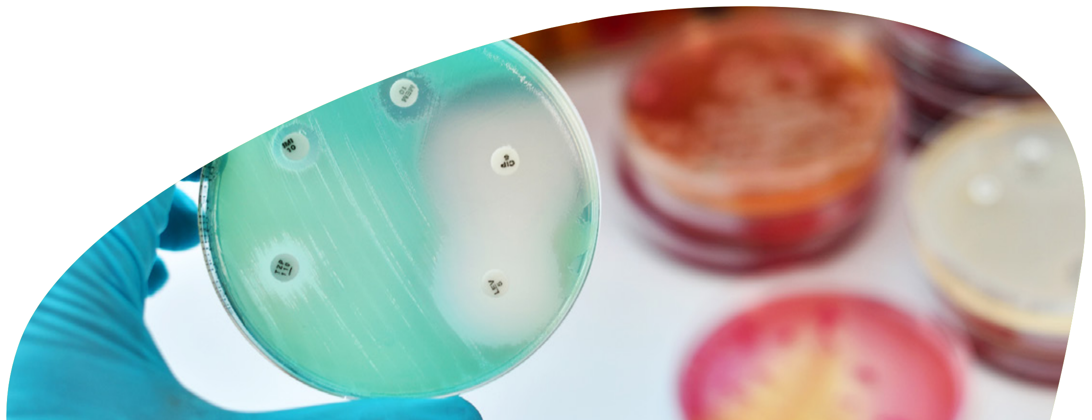
3. To enable sustainable AMR research, longer-term and more ambitious funding of basic microbiology, challenge-led research and interdisciplinary projects is required.

Facilitating a knowledge exchange ecosystem

4. Funders and the AMR community need to support the creation of an AMR innovation and knowledge centre that pulls together capabilities from different disciplines to accelerate the AMR research agenda.
5. The AMR community should advocate for a forum that brings people together from different fields and serves to communicate the value of AMR work to those who set the scientific agenda and to a wider audience.

Antimicrobial resistance and society

6. The microbiology community should commit to educating stakeholders, including the public, policymakers and the media, around the topic of AMR and microbiology more generally, and use the current momentum around infectious diseases to raise awareness of the issue of AMR.



3. Antimicrobial resistance and the Sustainable Development Goals

> We have to take multiple approaches to address the issue of antimicrobial resistance, to see what works. It cannot be solved by tackling the problem from one perspective and with one group of stakeholders. The problem lies with all of us, as does the solution."
> *Professor Laura Bowater, University of East Anglia*

The Microbiology Society's first president, Sir Alexander Fleming, discovered penicillin in 1928 when mould contaminated a Petri dish and killed bacteria. This discovery led to the development of antibiotics that could cure life-threatening bacterial infections. However, Sir Alexander Fleming also famously predicted in his 1945 Nobel Prize Lecture that bacteria and other micro-organisms would develop resistance.

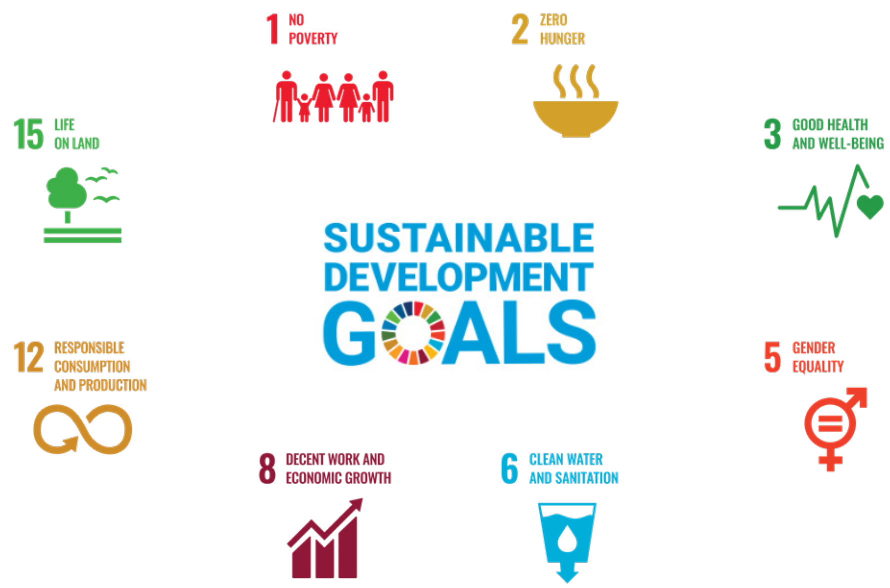
AMR is a naturally occurring process, whereby micro-organisms (bacteria, viruses, fungi and parasites) can change and adapt over time, either by modifying the target of the antimicrobial or by developing and exchanging resistance genes. Resistance occurs due to the selective pressure that antimicrobials put on microbes. However, the sustained used of antimicrobials in humans, animals and plants is speeding up the process. The incidence of AMR is also rapidly increasing in frequency and geographical spread due to the globalisation of travel and trade, making this a global problem [1].

The SDGs are a collection of 17 goals and 169 associated targets adopted by all Member States of the UN in September 2015. Wide-ranging and ambitious, the goals are a blueprint for transforming our world by 2030. They are interconnected and address economic, social and environmental challenges crucial to a better and more sustainable future for all. Whilst there is no specific goal, target or indicator in the SDG framework to tackle AMR, it is recognised that this is essential for the achievement of many of the SDGs, and the SDG indicators indirectly cover many aspects of AMR. (More information on the UN SDG framework is available in Appendix 1)

Microbiology can help to achieve the SDGs by tackling AMR.

- Microbiology is at the forefront of the development of new antimicrobial compounds and vaccines, which can help to achieve good health and well-being by limiting the emergence of drug-resistant microbes and by protecting currently available healthcare (SDGs 1 and 3).
- Microbiology can provide sustainable solutions for treating diseases in livestock and combatting AMR in crops, therefore safeguarding the food chain (SDG 2).
- Microbiology can help to develop novel technologies that can protect the environment from being contaminated with drug-resistant micro-organisms, such as improving wastewater treatment processes and treating surfaces with antimicrobial products (SDGs 6 and 15).
- Microbiology can help us to understand and track patterns of disease transmission through analysis of human, veterinary and environmental samples, which can help to safeguard human, animal and environmental health (SDGs 1, 2, 3, 6 and 15).
- Microbiology can help to inform which antimicrobials should be prescribed and therefore help to reduce consumption and improve access to antimicrobials (SDG 12).

[1] **Microbiology Society**. *Explainer: Antimicrobial Resistance. https://microbiologysociety.org/uploads/assets/12131a07-c10c-44b3-aba71cae0c4401aa/Antimicrobial-Resistance-explainer.pdf*



SDG 1: No Poverty: AMR jeopardises progress to end extreme poverty as treatments for drug-resistant infections increase. It is estimated that 24.1 million people could fall into extreme poverty by 2030 due to AMR. The economic cost of AMR also threatens progress to reduce poverty and inequality.

SDG 2: No Hunger: AMR in livestock and plants threatens the sustainability and security of food production and agriculture, which are important for growing populations. The rise of drug-resistant infections in animals and crops will also affect the livelihood of farmers.

SDG 3: Good Health and Well-being: the rise of AMR is a threat to modern medicine, as many common and serious infections are becoming increasingly difficult to treat effectively. AMR also undermines the success of surgery, organ transplantation, childbirth and chemotherapy, as antimicrobials used to prevent infection become ineffective. Antimicrobials are essential components of all healthcare systems and therefore AMR will affect good health and wellbeing.

SDG 5: Gender Inequality: AMR can drive gender inequality, as women are at risk of being disproportionately affected by infectious diseases due to having less access to healthcare and because of discrimination. Women are often the main connector between the healthcare system and their children and an increase in childhood illness leads to more women having to take time away from work or education to provide care. AMR is also common in urinary tract infections, which mainly affect women, and therefore loss of treatment options could affect women more severely.

SDG 6: Clean Water and Sanitation: antimicrobials, drug-resistant micro-organisms and resistance genes contaminate water sources and sewers, due to both human and animal activity, and this harms water quality. Achieving this goal could in turn reduce the use of antibiotics as good hygiene, access to clean water and sanitation are essential to prevent infectious diseases.

SDG 8: Decent Work and Economic Growth: without action, the human and economic costs of AMR will increase substantially. It is estimated that global annual deaths could rise from 700,000 to 10 million by 2050, with cumulative economic losses of around $100 trillion and a decrease of up to 3.8% of global GDP.

SDG 12: Responsible Consumption and Production: overuse of antibiotics is a driver of AMR and tackling AMR via improved antibiotic stewardship will therefore enable sustainable consumption and production of and access to antibiotics.

SDG 15: Life on Land: antibiotic contamination in the environment can disrupt biodiversity and ecosystems. Antibiotics and drug-resistant bacteria can also have a negative effect on natural microbial communities in the soil, such as the loss of microbes that play a key role in ecosystem functions.

4. Antimicrobial resistance research spotlight

Microbiology has a critical role in the fight to tackle AMR. Microbiologists in both human and veterinary clinical settings are responsible for the initial diagnosis of infections, for determining the best antibiotics to prescribe in clinics and for the monitoring of antibiotic resistance; microbiologists in research laboratories are investigating the mechanisms driving AMR and potential ways of preventing these or reducing their impact.

Microbiologists in all settings working in the field of AMR have the potential to help progress the UN SDGs, particularly goals related to poverty (SDG 1), food production (SDG 2), good health and well-being (SDG 3) and the environment (SDGs 6 and 15).

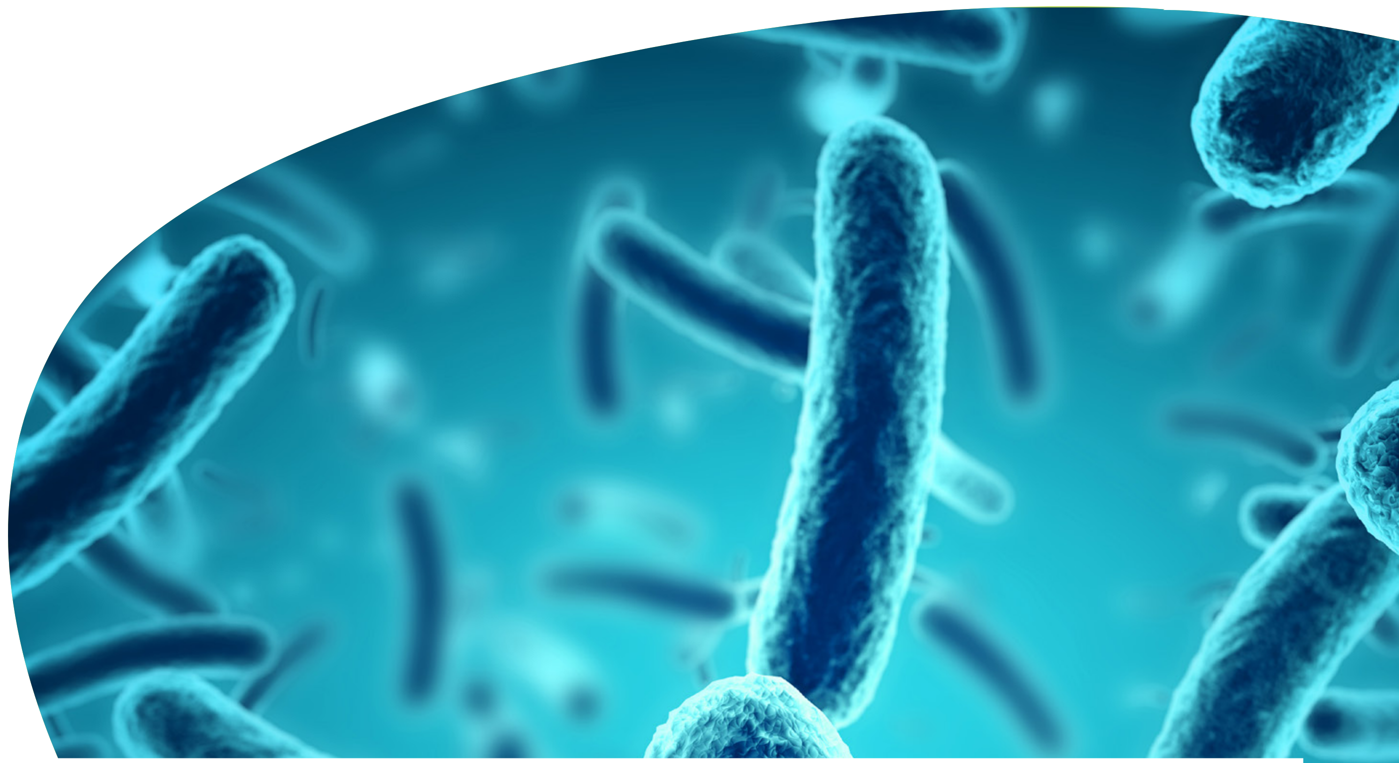
4.1. Monitoring, identifying and understanding antimicrobial resistance

AMR is a complex microbiological process and although more progress has been made to understanding molecular mechanisms behind AMR, we still lack some insight into the emergence of basic molecular mechanisms of resistance, the spread of resistance genes and the successful spread of drug-resistant organisms. Understanding the basic microbiology underpinning AMR will aid in developing novel strategies to address it and help to reduce poverty (SDG 1),
protect food chains (SDGs 2 and 15) and water sources (SDG 6), and improve good health and well-being (SDG 3). Current innovative areas of microbiological research include:

- Studying the composition and function of human, animal and environmental microbiomes to decipher how they impact on the evolution and transmission of AMR [2].
- Using microbiological data and mathematical modelling to further understand generalised transduction, a process that relies on bacteriophages transferring resistance genes to bacteria [3].
- Developing a mechanistic understanding of cell wall biosynthesis in bacteria to combat AMR using super-high-resolution imaging [4].

Monitoring and identifying AMR is essential in order to identify outbreaks, trace transmission chains, and identify how AMR is evolving and what factors contribute to its evolution, and for local, national and international surveillance efforts. Further being able to detect the rise of AMR and its spread will help safeguard our economies from future pandemics (SDG 8).

Methods developed in microbiological laboratories, including antibiotic susceptibility and sensitivity testing, and targeted detection using PCR and whole-genome sequencing of micro-organisms, are vital tools for AMR surveillance [5].



Investigating how microbial ecology can affect antibiotic resistance – Dr Michael Bottery (Centre for Future Health Research Fellow, University of York)

Bacteria have social lives – they can signal with each other to coordinate communal activities. These social traits are critical for many bacteria to grow in harsh environments, such as those within our bodies, and provide some species with the ability to colonise and cause infection. Many of these social interactions are intended for cooperation between members of the same species or strain, but the benefits of some cooperative traits are leaky and can be exploited by different species within the bacterial community. This is of concern when the cooperative traits in question provide increased tolerance to antibiotics. The presence of a resistant bacterial species, which may not be of clinical concern or the target of antibiotic treatment, may increase the tolerance of the true pathogens within the community. Dr Michael Bottery, at the University of York, is investigating whether the bacterial species *Pseudomonas aeruginosa*, which is a cause of infection in immunocompromised individuals, can exploit the antibiotic resistance genes found in other bacteria found at the same infection site (the lung). Using model cystic fibrosis lung communities in the lab, his study revealed that *P. aeruginosa* can exploit pre-occurring AMR in other bacterial species, and this has an impact on the efficacy of antibiotic efficacy. This research highlights the importance of fundamental microbiology research to understand how micro-organisms interact with each other in order to tackle AMR.

[2] **Parliamentary Office of Science and Technology**. *POSTnote 595: Reservoirs of Antimicrobial Resistance; 2019. https://researchbriefings.parliament.uk/ResearchBriefing/Summary/POST-PN-0595*
[3] **Microbiology Society.** *Dynamics of generalised transduction of AMR genes, Quentin Leclerc. https://microbiologysociety.org/our-work/75th-anniversary-a-sustainable-future/antimicrobial-resistance-amr/antimicrobial-resistance-amr-case-studies/dynamics-of-generalised-transduction-of-amr-genes.html*
[4] **UK Research and Innovation**. *MICA: Mechanistic understanding of cell wall biosynthesis to combat antimicrobial resistance. https://gtr.ukri.org/projects?ref=MR%2FN002679%2F1*
[5] **World Health Organisation.** *Antimicrobial resistance surveillance. https://www.who.int/medicines/areas/rational_use/AMR_Surveillance/en/*

4.2. Developing novel antimicrobial strategies

The current lack of new antibiotics threatens global efforts to control drug-resistant infections and this a barrier to achieving sustainable food production (SDG 2) and good health and well-being (SDG 3). New antimicrobials and alternative antimicrobial therapies are urgently needed to tackle AMR.

There is a real opportunity for microbiology to contribute to the development of novel strategies. Exciting research includes the development of antimicrobial peptides, phage therapy and dissecting how antibiotic production occurs in Streptomyces species to produce novel antibiotics.

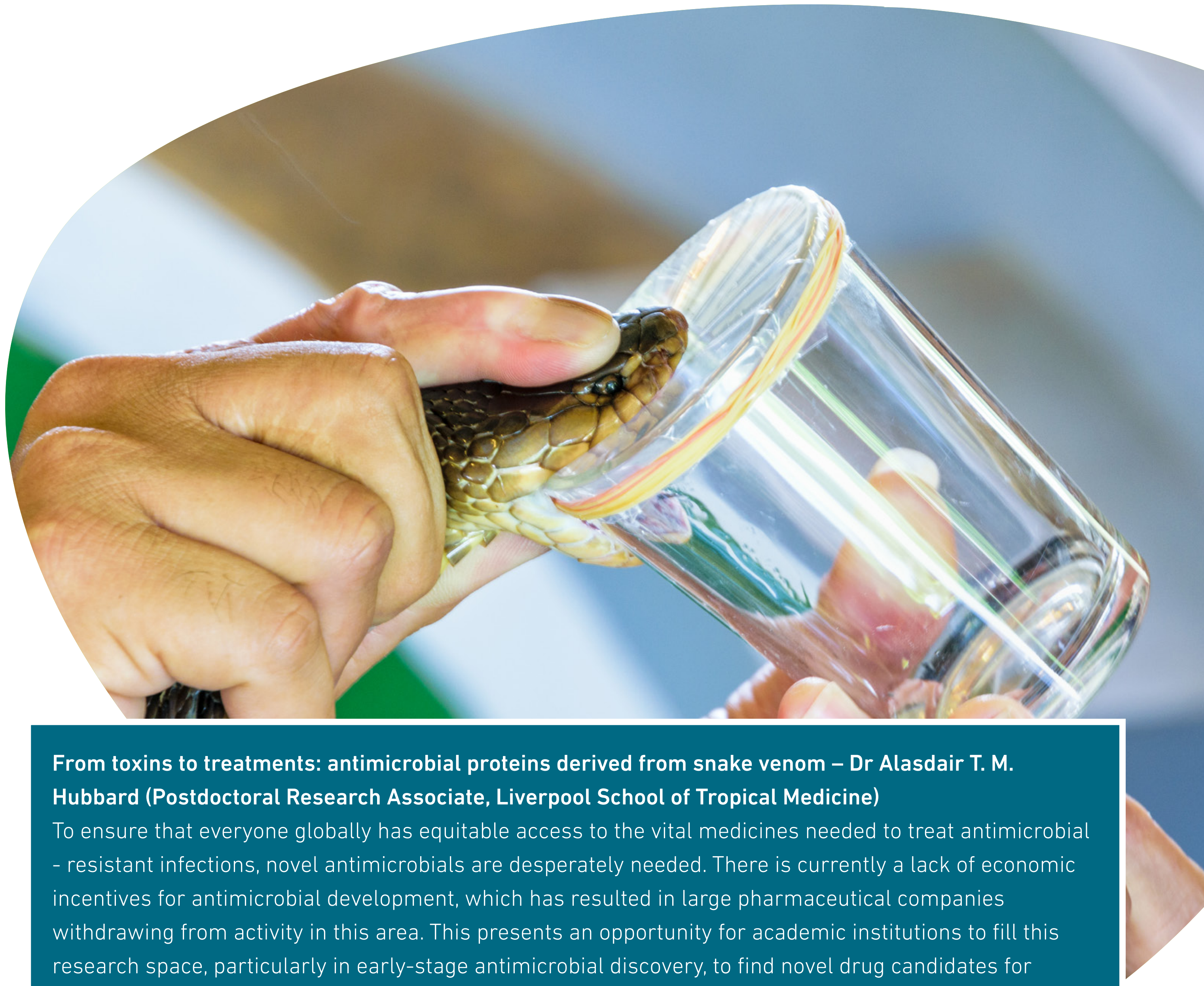
Microbiology can also be a transformative tool to help optimise current antimicrobials and reduce consumption (SDG 12) by combining the antimicrobials with novel technologies. Examples include using nitric oxide signalling molecules to help antimicrobials work at lower concentrations, removing resistance genes from bacteria using the gene-editing technology CRISPR-Cas9 to resensitise bacteria to antibiotics and the combination of anti-bacterial agents with antiviral drugs to increase efficacy.

4.3. Infection prevention and control

Infection prevention and control (IPC), a scientific approach to prevent harm caused by micro-organisms to patients, healthcare workers, care homes and the wider community, is a key strategy to tackle AMR [6]. Preventing infections from occurring reduces the use of antimicrobials and limits the spread of drug-resistant micro-organisms, improving good health and well-being (SDG 3) and protecting water sources (SDG 6).

Microbiology is uncovering new strategies for IPC, including unravelling how micro-organisms spread within hospital settings, understanding which disinfectants are most effective and developing antimicrobial surfaces that prevent micro-organisms from surviving in hospital settings.

Microbiology can also play a key role in antimicrobial stewardship, a term that encompasses integrated strategies employed to optimise the use of antimicrobials in healthcare settings [7]. For example, microbiologists are responsible for providing susceptibility reports and resistance profiles, which can help to inform antimicrobial prescribing.



From toxins to treatments: antimicrobial proteins derived from snake venom – Dr Alasdair T. M. Hubbard (Postdoctoral Research Associate, Liverpool School of Tropical Medicine)

To ensure that everyone globally has equitable access to the vital medicines needed to treat antimicrobial - resistant infections, novel antimicrobials are desperately needed. There is currently a lack of economic incentives for antimicrobial development, which has resulted in large pharmaceutical companies withdrawing from activity in this area. This presents an opportunity for academic institutions to fill this research space, particularly in early-stage antimicrobial discovery, to find novel drug candidates for development.

Natural products represent an attractive source for antimicrobial discovery, but are often underexplored. A team of researchers at the Liverpool School of Tropical Medicine has developed a simple, high-throughput assay to screen whole snake venom for antibacterial activity towards the bacterium *Escherichia coli*.

Any snake venom that displays antibacterial activity is separated into the different protein classes and iteratively tested to try and identify the protein classes responsible for the antibacterial activity. So far, the team has identified five classes of protein with antibacterial activity from elapid snakes (a major family of snakes that includes the cobras and mambas). These proteins will be further purified to confirm their antibacterial activity before entering the antimicrobial development pipeline, while their targets will be determined in order to develop other inhibitors that could also be developed into antimicrobials. Although antimicrobial discovery and development is a long and difficult process, there are more natural products out there that potentially have antimicrobial properties waiting to be discovered, which could help to address the lack of sustainable solutions to tackle AMR.

[6] **World Health Organisation.** *Infection, prevention and control. https://www.who.int/infection-prevention/publications/en/*
[7] **National Institute for Health and Care Excellence.** *Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. https://www.nice.org.uk/guidance/ng15*

4.4. Microbiology across the 'One Health' agenda

Addressing the threat of AMR requires a multisectoral approach, embedded within the One Health agenda, which recognises that resistant micro-organisms arising in humans, animals or the environment may spread from one to the other [8]. Microbiology cuts across all sectors and can bridge the gap between sectors to tackle AMR, improving partnerships to achieve the SDGs (SDG 17).

AMR in humans: microbiology plays a key role in clinical settings, as it can help to identify micro-organisms and their antimicrobial resistance patterns quickly. For example, recent advances in rapid point-of-care genomic testing, whereby AMR could be identified at the bedside by clinicians, could improve antibiotic prescribing and ultimately inform antibiotic stewardship policies to reduce the use of antibiotics in a clinical setting (SDG 12).

AMR in animals: the overuse of antibiotics in animals is likely to affect future animal health and food production (SDG 2). In addition, there is a concern over the potential for the transfer of resistance from bacteria that infect animals to bacteria that infect humans and vice versa. Microbiology can be a vital tool in monitoring AMR in animals, to both protect animal health and prevent the spread of drug resistance.

AMR in the environment: the presence of AMR in the environment is a potential reservoir for its spread and may also impact on human and animal health (SDGs 2, 3, 6 and 15). However, there are important knowledge gaps in this area and microbiological research is crucial to uncover the environmental dimension of AMR. Key areas of active research include:

- Understanding the drivers of resistance in the environment and the extent to which human, animal and pharmaceutical manufacturing waste are contributing to the spread of drug-resistant microbes.
- Dissecting whether the presence of antimicrobials, drug-resistant microbes and resistance genes in soil, rivers, coastal waters, hospital drains and wastewater facilities is a risk to human and animal health.
- The impact of antimicrobial use in aquaculture (farming of fish and food) on the environment and the spread of AMR [9].

Recommendation 1:

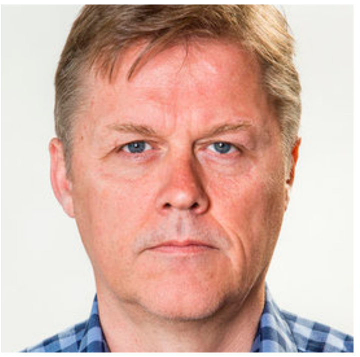
Sustained microbiology research and innovation in the field of AMR is imperative to help deliver the UN SDGs, particularly goals related to poverty (SDG 1), food production (SDG 2), good health and wellbeing (SDG 3) and the environment (SDGs 6 and 15).

[8] Destoumieux-Garzón, Delphine, Patrick Mavingui, Gilles Boëtsch, Jérôme Boissier, Frédéric Darriet, Priscilla Duboz, Clémentine Fritsch et al., The one health concept: 10 years old and a long road ahead, *Frontiers in veterinary science*, 2018, 5, https://doi.org/10.3389/fvets.2018.00014
[9] **Microbiology Society.** *Antimicrobial Resistance in Aquaculture, Dr Kelly Thornber. https://microbiologysociety.org/our-work/75th-anniversary-a-sustainable-future/antimicrobial-resistance-amr/antimicrobial-resistance-amr-case-studies/antimicrobial-resistance-in-aquaculture.html*

Fighting antimicrobial resistance with infection prevention and control: hospital drains and drug-resistant bacteria – Dr Paz Aranega Bou (water systems microbiologist, Public Health England)
Healthcare settings are particularly vulnerable environments for the spread of drug-resistant infections, due to several factors, including the high use of antimicrobials and the presence of immunocompromised individuals. Hospital sinks, waste traps and drains harbour complex microbial communities comprising a diverse range of micro-organisms, including those that are resistant to antibiotics. During outbreak investigations, antibiotic-resistant bacteria, particularly carbapenemase-producing Enterobacterales (CPE), are frequently recovered from hospital sinks, which has highlighted their potential as reservoirs for the spread of AMR.
To address this, a team at Public Health England, Porton Down designed a large-scale model sink system, which incorporates 12 sinks of 2 different designs; rear-draining hand-wash basins and base-draining utility sinks, both of which are commonly found in the hospital environment. Sink waste traps known to be contaminated with CPE were removed from a hospital setting and installed within the model system and bacterial communities, including their dispersal from sinks, were studied over time. The results from this work demonstrate that CPE present in a sink and/or drainage system can be dispersed back into the laboratory (or ward) environment, particularly if the tap is aligned to discharge directly into a contaminated drain and/or when drainage is slow. This novel approach confirmed that contaminated sinks could be a source of drug-resistant infections and continues to be used to identify realistic interventions that could minimise the risk of contamination. These tangible steps to control the spread of AMR within hospital environments will help to inform future infection prevention and control measures in hospitals and are therefore a powerful tool to fight AMR.

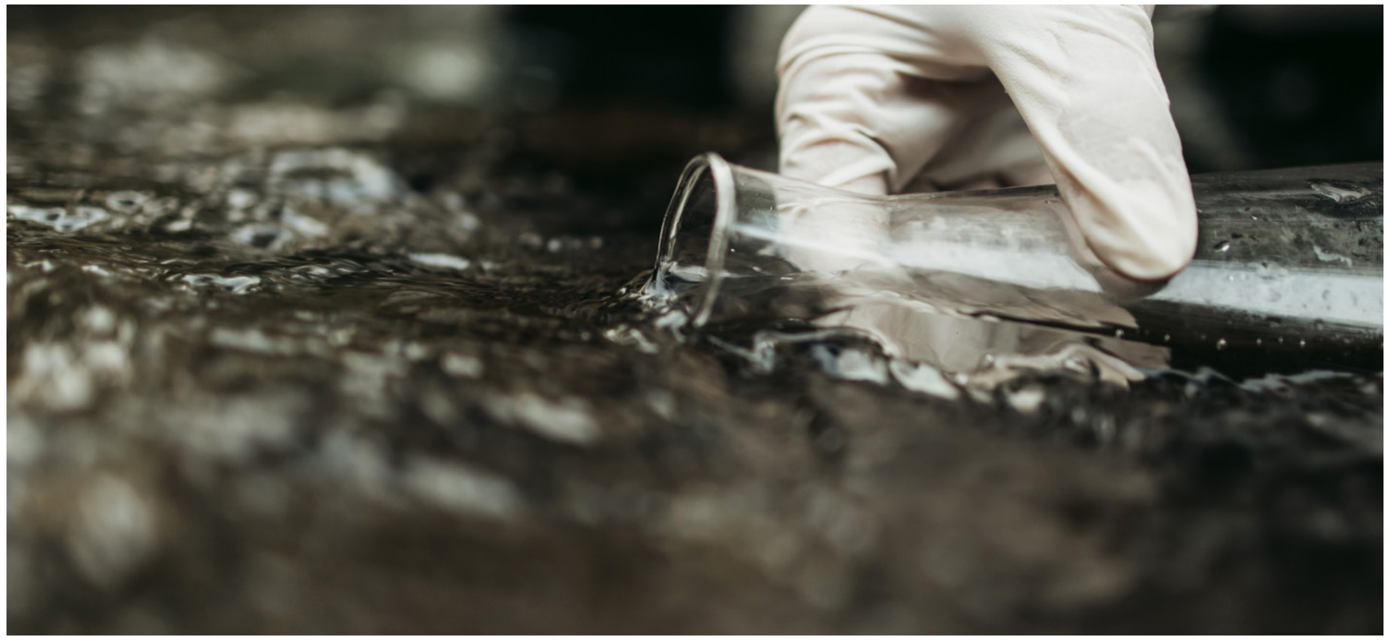
OPINION PIECE

The environmental dimension of antibiotic resistance – William Gaze, Professor of Microbiology, The European Centre for European Centre for Environment and Human Health



One Health is defined by the concept that 'human health and animal health are interdependent and bound to the health of ecosystems'[10]. However, One Health is often used in the context of infectious disease transmission between humans and animals, largely ignoring the role of the natural environment. For antibiotic resistance, consideration of the 'health' of the environment can be misleading, as concerns relating to the environment include the transfer of antibiotic resistance genes from environmental bacteria to human and animal pathogens, and the risk of the transmission of resistant pathogens present in the environment to humans, rather than the impact of antibiotic resistance on the health of natural ecosystems.

A One Health perspective on antibiotic resistance is further complicated by the fact that resistance is present in the environment in many forms. These include ancient resistance that has evolved over evolutionary time in environmental micro-organisms, where antibiotics are used in competition for resources or for other poorly understood purposes. In addition, resistant bacteria are introduced to the environment from humans through municipal wastewater (11 billion litres per day in the UK) and from livestock to agricultural land and subsequently via run-off to rivers. This point source and diffuse pollution also contains a substantial proportion of total antibiotics used, which are still active when excreted. Other compounds such as biocides, disinfectants and heavy metals have antimicrobial activity and are introduced to the environment through human and animal waste. Although selective compounds are found at relatively low levels in aquatic and soil environments, there is a growing realisation that environmental concentrations may favour the growth and survival of antibiotic-resistant bacteria, therefore contributing to the transfer of resistance genes between the environmental and human microbiomes.



It has been suggested that there is limited understanding of the role the environment plays in antibiotic-resistant infections in humans. However, this ignores the fact that bacterial pathogens, and the resistance genes they carry, often have independent evolutionary histories. It is clear that use of antibiotics is associated with increased prevalence of antibiotic-resistant infections in humans, particularly in high-income countries. However, resistance can also be conferred by mobile resistance genes that move between bacteria through a process known as horizontal gene transfer. For example, clinically important resistance genes to last-line-of-defence carbapenem antibiotics have been shown to move between different mobile genetic elements and micro-organisms within a single hospital over a short time period. These mobile resistance genes do not originate in the pathogens themselves and have come from other bacteria, including those present in the environment. Given what we know about resistance gene dynamics in hospital-associated microbial communities, the challenge of extrapolating this to the natural environment, where 1 gram of soil or sediment can contain a billion bacteria belonging to 5,000 different species, is clear. Current understanding of antibiotic resistance within environmental and human microbiomes is advancing rapidly using metagenomic approaches and improvements to genomic sequencing. This furthers the understanding of the epidemiology of resistance genes as well as the bacterial pathogens themselves.

Analogies can be made between emergence of zoonotic infections, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) from a wildlife reservoir leading to the current coronavirus disease 2019 (Covid-19) pandemic, and the emergence of antibiotic resistance genes in human pathogens that originate in environmental bacteria. Both these processes are driven by human activity. In the case of zoonotic virus emergence, by habitat destruction, encroachment of farming into natural environments and consumption of wild animals. In the case of antibiotic resistance, the emergence of novel resistance is likely to be exacerbated by mixing of human, animal and environmental bacteria in the presence of antibiotics and other antimicrobials found in human and animal waste. Widespread human-to-human transmission, of both viral pathogens and antibiotic-resistant bacteria, does not preclude the vital role of the environment, even though the initial events leading to emergence and pandemic spread may be relatively rare.

[10] **World Organisation for Animal Health**. *One Health "at a glance". https://www.oie.int/en/for-the-media/onehealth/*

5. Moving forward in addressing antimicrobial resistance

There is an opportunity to unlock the potential of microbiology to tackle AMR and therefore help to achieve the SDGs. In order to explore the challenges and opportunities for microbiology in the field of AMR, the Microbiology Society held a series of online workshops, which collectively brought together AMR researchers from different fields, along with representatives from industry, funders and government agencies. In this section, we discuss what more could be done if there were fewer barriers, and the interventions needed to achieve a sustainable future.

5.1 Improving antimicrobial resistance surveillance networks

Surveillance of AMR is a vital component of the fight against AMR. Surveillance of AMR enables detection, monitoring and early intervention, and can inform key policy decisions, which may help to both tackle AMR and achieve the SDGs.

The Covid-19 pandemic has recently brought attention to the need for routine surveillance to identify and respond to emerging infectious diseases. Microbiologists working in the field of AMR have highlighted that the next pandemic is likely to be associated with AMR, and therefore being able to monitor the evolution of AMR over time will be crucial to avoid a surge in drug-resistant infections.

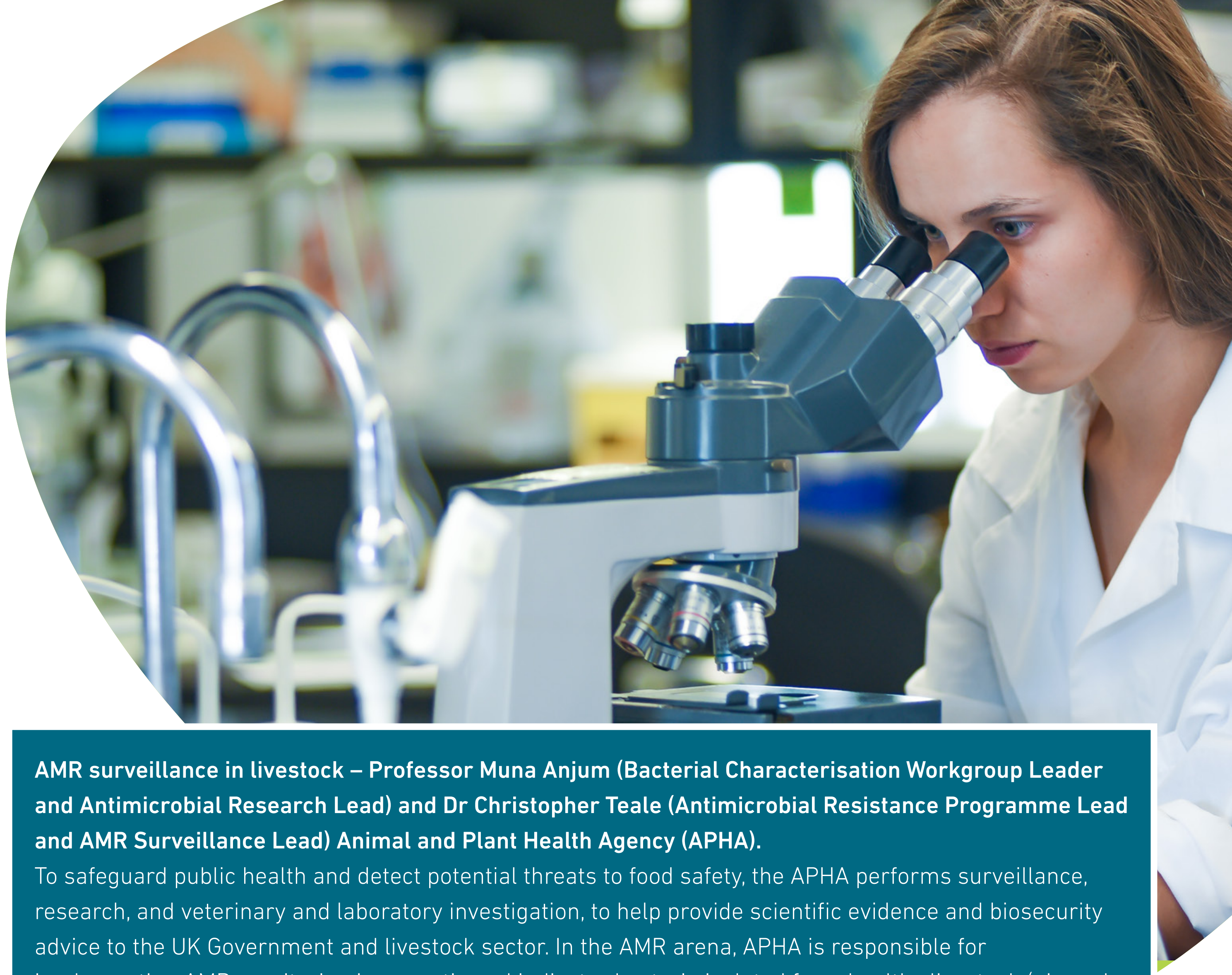
We need to improve the surveillance systems in the UK, and in particular how they are structured and integrated. In Ireland, the task of setting up an efficient AMR surveillance system is likely to be directed by the EU. The UK, however, will need to develop its own strategy, which may prove more challenging out of the EU and will require the appropriate funding and direction.

The current system is designed around short-term goals. In order to be more effective, surveillance efforts need to be broader and longer, and support for long-term capacity building is needed.

The microbiology community has an opportunity to be involved in surveillance efforts and needs to advocate for microbiology to be a priority in public health systems and ensure that it plays an important role in both national and international surveillance systems.

Rapid point-of-care genomics, which is automated and cost-effective, is essential for future surveillance efforts and to inform antimicrobial prescribing. This technology can identify the presence of AMR, as well as help to determine its frequency, and could therefore be a transformative technology for surveillance systems.

Recommendation 2:
In order to optimise current surveillance systems, microbiologists should seek to progress implementation of innovative solutions such as rapid point-of-care genomics and should advocate to be included at the heart of both national and international surveillance efforts.



AMR surveillance in livestock – Professor Muna Anjum (Bacterial Characterisation Workgroup Leader and Antimicrobial Research Lead) and Dr Christopher Teale (Antimicrobial Resistance Programme Lead and AMR Surveillance Lead) Animal and Plant Health Agency (APHA).
To safeguard public health and detect potential threats to food safety, the APHA performs surveillance, research, and veterinary and laboratory investigation, to help provide scientific evidence and biosecurity advice to the UK Government and livestock sector. In the AMR arena, APHA is responsible for implementing AMR monitoring in zoonotic and indicator bacteria isolated from healthy livestock (pig and poultry), as well as determining AMR in key bacteria isolated from the veterinary scanning surveillance programme, which helps detect diseases of livestock and wildlife across the UK. One aim of the AMR programme is to provide early detection of new and emerging AMR threats. For AMR monitoring in healthy animals , the APHA receives caecal samples from abattoirs, while for scanning surveillance, vets or livestock owners submit samples from their diseased animals. Samples are processed using classical microbiological techniques to identify the disease-causing microbes. Subsequently, diagnostic assays, such as minimum inhibitory concentration or disc diffusion testing of antimicrobials, are performed to determine phenotypic AMR profiles. Whole-genome sequencing of isolates collected through surveillance is also routinely implemented by the APHA, for detailed molecular characterisation of resistance genes and their genetic background. This proactive approach helps the UK Government deliver its National Action Plan to reduce AMR threats, and assists livestock owners and vets to make informed decisions about treating and preventing disease, which can in turn reduce the use of antimicrobials. Moreover, monitoring AMR profiles across the country increases our knowledge and understanding of the prevalence of resistant bacteria, as well as their spread and trends in occurrence. This robust surveillance system is critical for a One Health approach that enables early detection of new and emerging threats, as well as evaluation of risk, in partnership with UK Government policy teams and public health agencies, which helps to contain and control AMR in the food chain.

5.2 Enabling a collaborative community

Microbiologists have highlighted that funding for AMR research in the UK has been extensive and in part successful. For example, the AMR Cross-Council Initiative [11], funded by members of the Antimicrobial Resistance Funders' Forum (AMRFF), was perceived to be a successful initiative by our workshop attendees. The interdisciplinary nature of the initiative supported research encompassing academia, biopharma, diagnostic companies, veterinary and the health service, and provided a framework for a more coordinated approach to tackling AMR. However, this initiative has now ended and there is an opportunity for new funding to fill this gap.

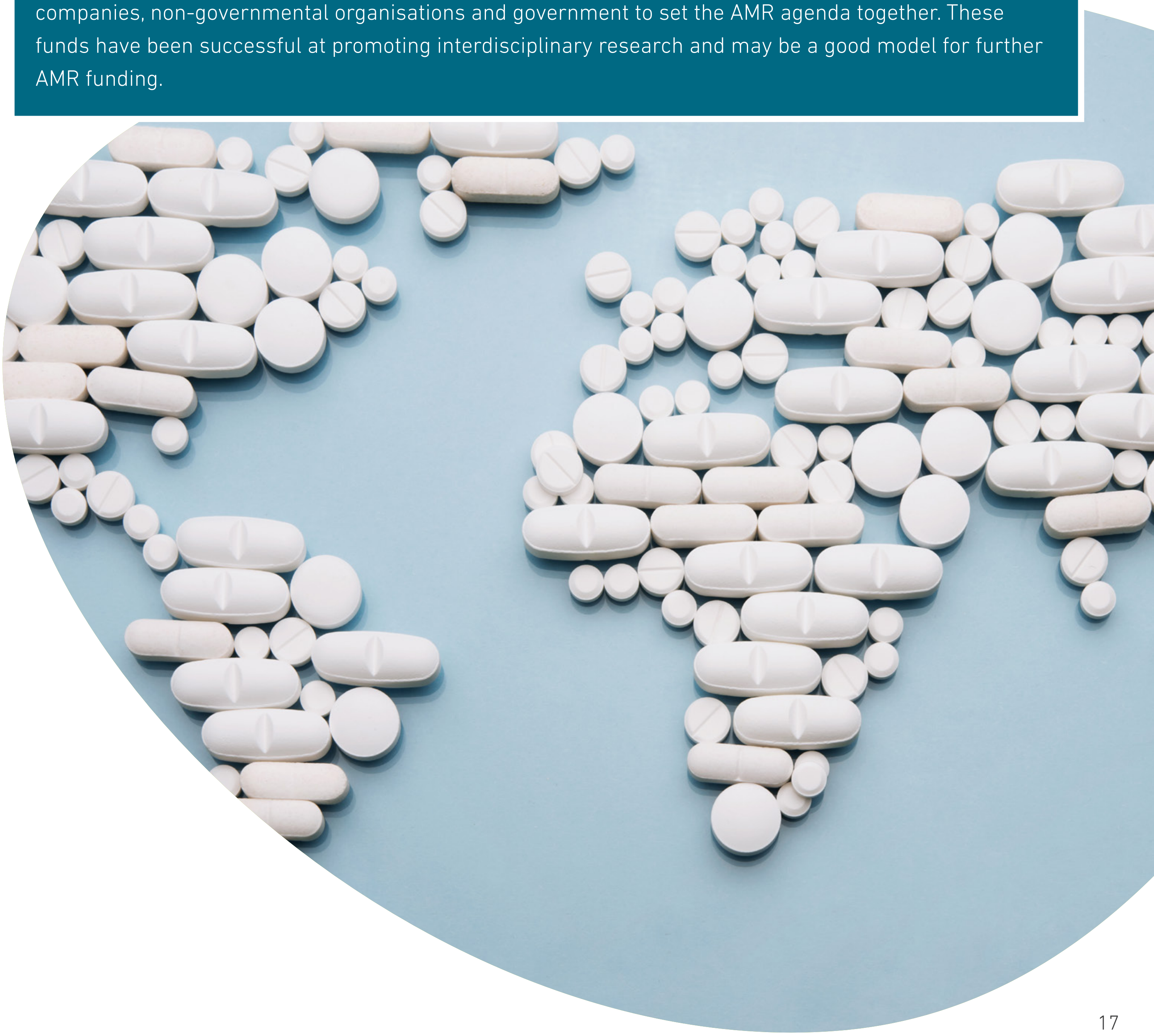
Looking forward, there is now an opportunity to build on past success and focus funding efforts within the following areas.

- Basic microbiology remains integral for our understanding of AMR and continued funding in this area is critical. For example, we still need to expand our knowledge of how antimicrobials work and how they behave in complex systems [12].
- Implementation of novel antimicrobial technologies in healthcare settings is challenging. Making these technologies easy to use and affordable remains challenging and in order to bring new and exciting technologies to the market, further funding is needed to support implementation strategies.
- Funding of challenge-led research could also help facilitate translation of AMR research and achieve impact, as it allows for industry to be involved early on and for researchers to work on solutions that are needed.
- Past and current interdisciplinary funding has been targeted towards individuals. There is a need for more long-term interdisciplinary funding, which provides a balance between breadth and depth, and for clusters of expertise to develop. Pump-priming initiatives for academia have been successful [13] and important for setting up interdisciplinary projects but these do not give enough time to establish interdisciplinary working and collaboration. Experts in the field of AMR, funding bodies and health economists should seek to collaborate to determine the most suitable funding to enable long-term interdisciplinary AMR research and network building.

Recommendation 3:
To enable sustainable AMR research, longer-term and more ambitious funding of basic microbiology, challenge-led research and interdisciplinary projects is required.

[11] **Medical Research Council.** *Tackling AMR – A Cross Council Initiative*. https://mrc.ukri.org/research/initiatives/antimicrobial-resistance/antimicrobialresistance-funders-forum/https://mrc.ukri.org/research/initiatives/antimicrobial-resistance/tackling-amr-a-cross-council-initiative/
[12] Gray Declan Alan, and Michaela Wenzel, Multitarget approaches against multiresistant superbugs, *ACS Infectious Diseases*, 2020, 6, https://doi.org/10.1021/acsinfecdis.0c00001
[13] **Medical Research Council.** *Tackling AMR – A Cross Council Initiative. Theme 4: Behaviour within and beyond the health care setting. https://mrc.ukri.org/documents/pdf/theme-4-details-of-funded-projects/*
[14] **UK Research and Innovation**. *Global Challenges Research Fund. https://www.ukri.org/research/global-challenges-research-fund/*
[15] **Medical Research Council.** *AMR in a Global Context Consortia awards. https://mrc.ukri.org/news/browse/12-million-in-grants-to-tackle-superbugs-in-a-global-context/*

The Global Challenges Research Fund (GCRF)
The Global Challenges Research Fund (GCRF) [14] is a £1.5 billion fund announced by the UK Government in late 2015, as part of the UK's Official Development Assistance (ODA) to support research tackling challenges faced by developing countries. The funded programmes aim to promote both challenge-led disciplinary and interdisciplinary research, as well as strengthen capacity for research, innovation and knowledge exchange in the UK and developing countries.
In 2018, four grants were awarded to UK universities to conduct interdisciplinary research into the biological, social, cultural and economic drivers behind the development of AMR in low- and middle-income countries. These AMR in a Global Context Consortia awards [15], totalling £12 million, were funded by the cross-research council AMR initiative and the National Institute for Health Research's (NIHR) Global Health Research Programme. The joint endeavour enabled scientists, pharmaceutical companies, non-governmental organisations and government to set the AMR agenda together. These funds have been successful at promoting interdisciplinary research and may be a good model for further AMR funding.



5.3 Facilitating a knowledge exchange ecosystem

To achieve the SDGs, particularly goals related to human health (SDGs 1, 2 and 3), we need to develop new solutions to tackle AMR whilst changing behaviours, practices and engagement across society. This will require interdisciplinary research within academic settings and trans-disciplinary collaboration across the AMR research field, as well as new mechanisms of knowledge exchange. The AMR interdisciplinary community emerged over a short period of time and has so far been successful at bringing people together. The focus now needs to be on broader thinking and larger-scale projects with a trans-disciplinary approach, whereby research is carried out within a holistic framework, crossing discipline and sector boundaries.

Microbiologists have highlighted that current mechanisms of knowledge exchange, such as publishing and traditional conferences, are outdated. To tackle this issue, the community needs to embrace changes in scientific publishing, have less career-incentivised approaches to the way we disseminate information, and investigate new ways of communicating findings and engaging with stakeholders outside of this traditional structure. For example, publishing as a consortium rather than naming all the authors on a paper could enable equal contributions in interdisciplinary teams and therefore help to improve communication within the team.

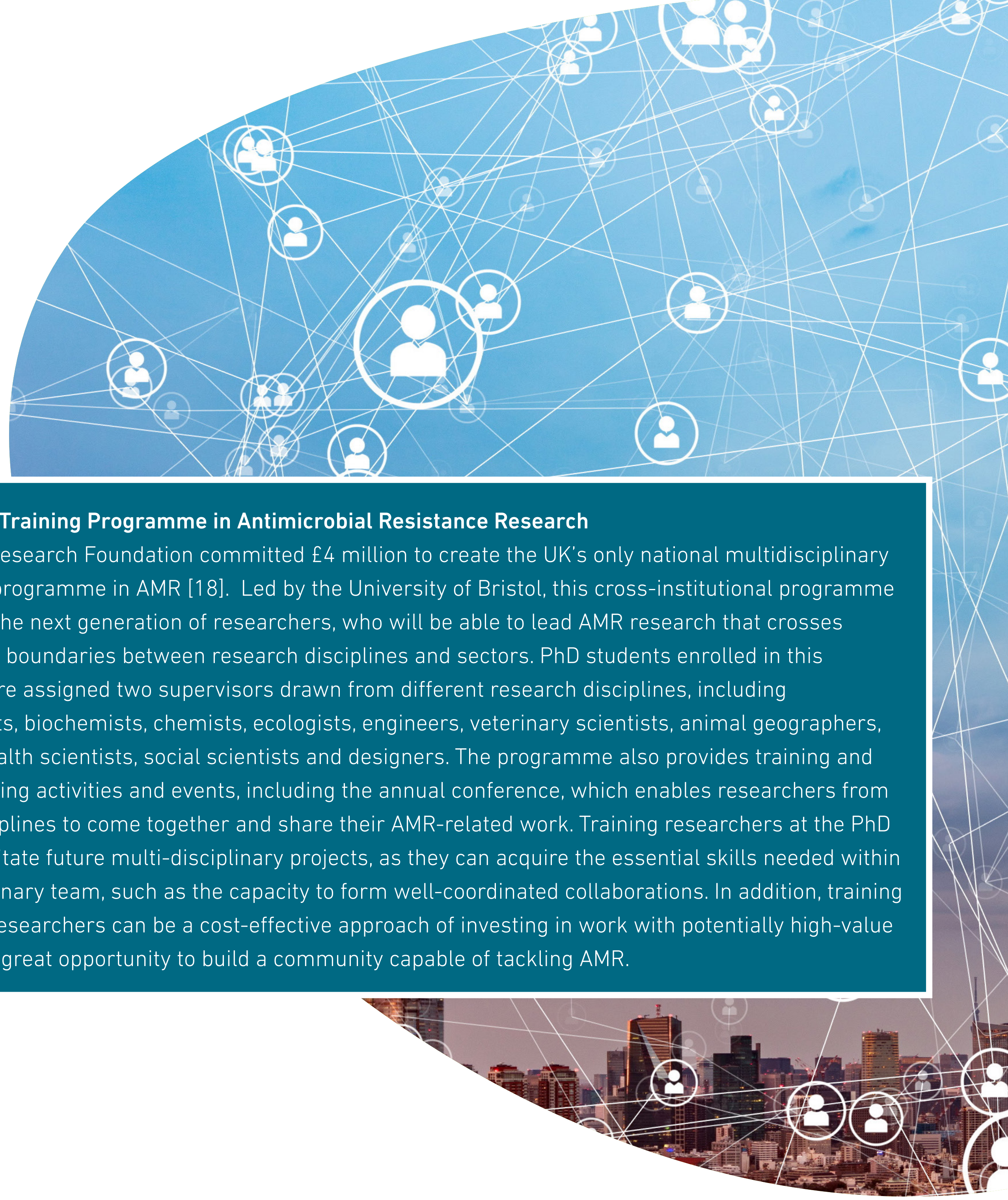
Translating cutting-edge research into antimicrobial strategies and interventions requires improved communication between academia and industry. Academic pursuit can be lacking in commercial insight as to what is valuable, and in order to optimise research efforts, it is paramount that both communities speak together and agree on unmet needs, gaps and challenges.

Furthermore, the pathway from discovery to implementation for diagnostics starts with blue sky thinking, followed by industry paring down those ideas, and ends with a clinician running a test on a patient. Involving all these groups is crucial for successful implementation of diagnostic technologies and therefore improved knowledge exchange between these groups is crucial. In order to improve knowledge exchange between different disciplines and outside of academia, experts in the field have emphasised the need for:

- An innovation and knowledge centre to create a framework for future collaboration. This centre, which could be a virtual one, would pull together capabilities from different disciplines and facilitate translational interactions with industry. The centre is also a potential mechanism for linking academia and industry and could engage more researchers to participate in interdisciplinary research. Current examples of successful knowledge exchange centres include the Alan Turing Institute [16] and Multidisciplinary Synthetic Biology Research Centres [17].

- The community to advocate for a forum to bring people together from different fields and communicate AMR work. Currently, AMR is absorbed into different discipline-specific conferences but there are few AMR specific conferences, most of which focus on particular areas of AMR. An AMR-based interdisciplinary conference would be excellent for overcoming these barriers.

[16] **The Alan Turing Institute.** *https://www.turing.ac.uk/*
[17] **UK Research and Innovation (UKRI).** *Multidisciplinary Synthetic Biology Research Centres. https://bbsrc.ukri.org/research/programmes-networks/synthetic-biology-growth-programme/*
[18] **Medical Research Foundation**. *National PhD Programme in Antimicrobial Resistance Research. https://amrtraining.ac.uk/*



National PhD Training Programme in Antimicrobial Resistance Research
The Medical Research Foundation committed £4 million to create the UK's only national multidisciplinary PhD training programme in AMR [18]. Led by the University of Bristol, this cross-institutional programme aims to train the next generation of researchers, who will be able to lead AMR research that crosses the traditional boundaries between research disciplines and sectors. PhD students enrolled in this programme are assigned two supervisors drawn from different research disciplines, including microbiologists, biochemists, chemists, ecologists, engineers, veterinary scientists, animal geographers, population health scientists, social scientists and designers. The programme also provides training and network-building activities and events, including the annual conference, which enables researchers from different disciplines to come together and share their AMR-related work. Training researchers at the PhD level can facilitate future multi-disciplinary projects, as they can acquire the essential skills needed within a multidisciplinary team, such as the capacity to form well-coordinated collaborations. In addition, training early career researchers can be a cost-effective approach of investing in work with potentially high-value returns and a great opportunity to build a community capable of tackling AMR.

Recommendation 4:
Funders and the AMR community need to support the creation of an AMR innovation and knowledge centre that pulls together capabilities from different disciplines to accelerate the AMR research agenda.

Recommendation 5:
The AMR community should advocate for a forum that brings people together from different fields and serves to communicate the value of AMR work to those who set the scientific agenda and to a wider audience.

5.4 Antimicrobial resistance and society

To address the issue of AMR and to mitigate the impact of AMR on global economies (SDG 8), collaboration with multiple stakeholders is crucial, as no single solution will solve such a complex issue. Engaging with both the public and policymakers will enable the implementation of sustainable solutions to tackle AMR.

The Covid-19 pandemic has highlighted the devastating impact infectious diseases can have on society and there is now an opportunity to use this momentum to raise awareness of AMR. However, innovative approaches are needed in order to convey the threat of AMR without causing panic and to avoid the message being diluted by the current Covid-19-related information being communicated.

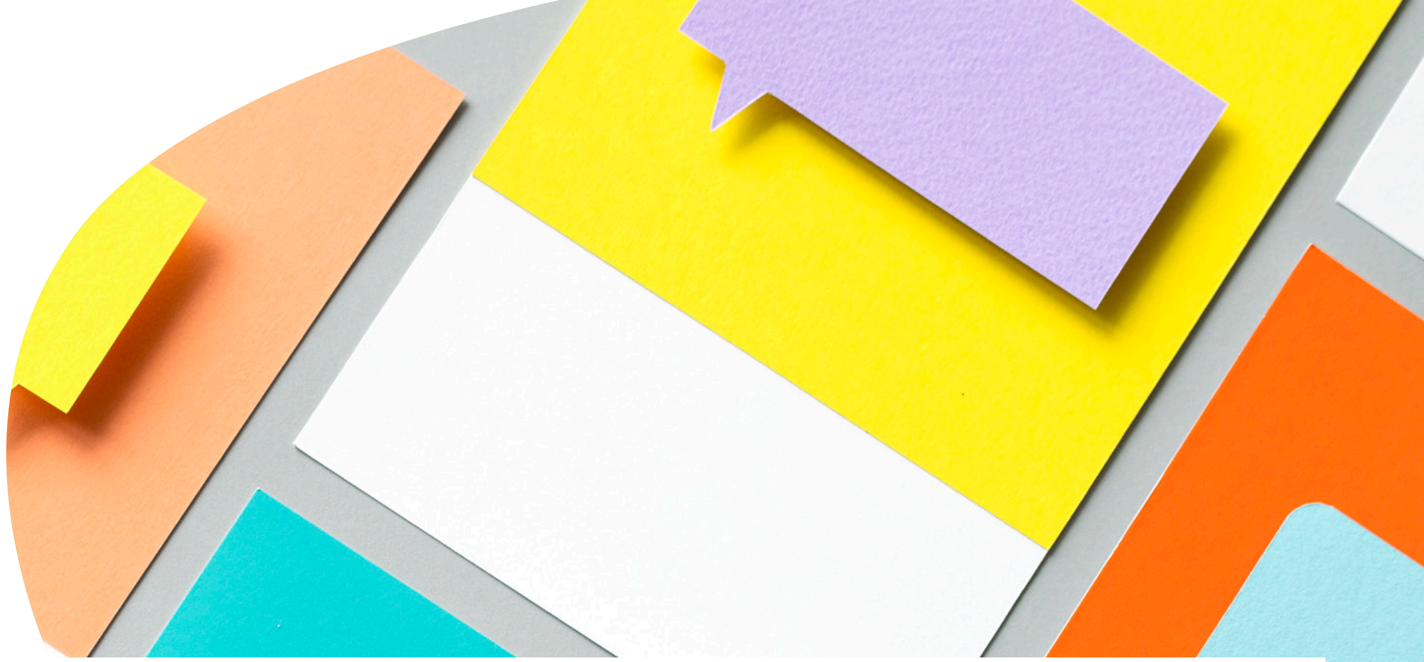
Throughout the Covid-19 pandemic, there has been an important focus on communicating simple public health strategies to tackle the spread of the virus, such as increasing handwashing, as well as improving sanitation and disinfection procedures. As a result, there is now an opportunity to embed these cost-effective strategies over the long-term to prevent transmission of drug-resistant organisms, whilst also achieving better water quality and sanitation (SDG 6).

We need to fire the public's imagination on AMR and stress that it is an urgent threat, rather than a hypothetical future problem. Focus group attendees highlighted that communicating AMR as a 'slow-moving pandemic' could help to convey urgency. In addition, there is a lack of recognition of how AMR contributes to patient death and therefore a potential solution to raise awareness could be to include AMR-related infection on death certificates as a contributing factor. Furthermore, the creation of a global AMR indicator that tracks the progress of AMR, in a similar way to the R value (reproduction number) during the Covid-19 pandemic, could also help to communicate the threat of AMR in a more accessible manner.

AMR is a complex challenge and microbiologists have highlighted that there is a lack of understanding of what it is and how it works, both within the general public and amongst policymakers. For example, there is limited understanding of the terms 'AMR' and 'superbug', which are often used to explain the concept of drug resistance. The microbiology community needs to advocate and promote education of stakeholders, not only regarding the concept of AMR, but also microbiology more generally. For example, microbiology could be taught in schools and become a component of the secondary school syllabus.

The patient voice within the AMR field is crucial to achieve successful implementation of novel solutions. However, it is important to avoid putting responsibility on the patient and instead focus on improving prescribing behaviours and hygiene. Stewardship programmes have been successful within the livestock area in the UK [19], which was largely due to increased engagement with both policymakers and farmers, and this could be applied to the healthcare sector.

[19] **Veterinary Medicines Directorate**. *UK Veterinary Antibiotic Resistance and Sales Surveillance Report 2019. https://www.gov.uk/government/publications/veterinary-antimicrobial-resistance-and-sales-surveillance-2019*
[20] **Antibiotic research UK**. *Patient stories. https://www.antibioticresearch.org.uk/find-support/patient-stories/*



The importance of the patient voice – Arlene Brailey (Patient Support Officer, Antibiotic Research UK)
Suffering with a resistant bacterial infection is a topic that is not often discussed in the public domain – or particularly widely in healthcare settings. And yet, for those afflicted by this misunderstood illness, it immediately conjures up fear. Fear of what happens if the infection flares up again, fear of being hospitalised with little warning or not getting there quickly enough and fear that there will eventually be no antibiotics left that can treat their infection.
The Patient Support team at Antibiotic Research UK [20] was set up to offer that much needed support for these patients. Arlene Brailey, a pharmacist, and Jodie Christie, a nurse, set up a confidential email and one-to-one telephone line for patients (and their families) to discuss anything related to resistant or recurring infection. While they do not offer personal medical advice, they signpost to other valuable sources of help and information and help distil down what pertinent questions the patient really needs to ask their doctor or health professional. They have also prepared extensive website information about different types of resistant bacteria, together with downloadable patient leaflets. These patient stories have served to bring patients together, create a common bond and, most important of all, reduce that extreme isolation felt by all those patients who contact Antibiotic Research UK. With patients' full engagement and encouragement, they put context, urgency and reality around antibiotic resistance, which is likely to be the next 'pandemic' and still seems to elude public understanding.

The Patient Support team at Antibiotic Research UK can be contacted at patient.support@antibioticresearch.org.uk. More information on the patient experience of resistant infection is available at **https://www.antibioticresearch.org.uk/find-support/patient-stories/**.

Recommendation 6:
The microbiology community should commit to educating stakeholders, including the public, policymakers and the media, concerning the topic of AMR and microbiology more generally, and use the current momentum around infectious diseases to raise awareness of the issue of AMR.

6. Acknowledgements

The Microbiology Society would like to thank the A Sustainable Future Expert Working Groups, who helped identify major issues and developments, assisted with producing this report and advised on other aspects of the Society's A Sustainable Future policy project. The Society would also like to thank all of the experts who participated in its A Sustainable Future workshops in June and July 2020 for sharing their perspectives, which also helped to inform this report and other outputs from the project.

A Sustainable Future Steering Group

Professor Stephen Baker (Chair)	*University of Cambridge*
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Dr Geertje van Keulen	*Swansea University*
Professor Kevin O'Connor	*University College Dublin*
Dr Maria Tuohy	*NUI Galway*

AMR Advisory Group

Professor Stephen Baker (Chair)	*University of Cambridge*
Dr Grant Hill-Cawthorne	*Parliamentary Office of Science and Technology*
Dr Peter Jackson	*Director of AMR Centre*
Dr Tina Joshi	*University of Plymouth*
Dr Alison Mather	*Quadram Institute*
Dr Mark Webber	*Quadram Institute*

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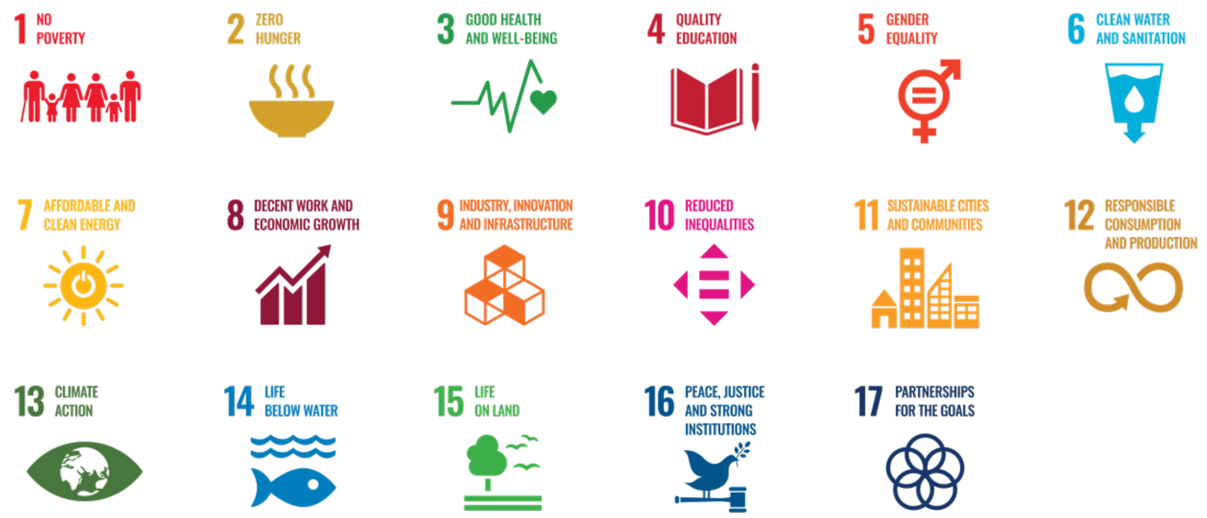
Microbiology Society Staff

Dr Curtis Asante	Associate Director of Members' Programmes
Sarah Buckman	Chief Programmes Officer and Director of Strategy
Dr Peter Cotgreave	Chief Executive
Jack Doughty	Former Policy Manager
Tony McBride	Former Interim Director, Strategy and Members' Programmes
Dr Hannah Norman	Former Policy and Engagement Officer
Dr Emily Parr	Policy and Engagement Officer
Dr Sufia Rahman	Former Policy Officer
Eva Scholtus	Policy and Engagement Manager

Appendix



The 2030 Agenda for Sustainable Development, adopted by all United Nations Member States in 2015, provides a shared blueprint for peace and prosperity for people and the planet, now and into the future. At its heart are the 17 Sustainable Development Goals (SDGs), which are an urgent call for action by all countries – developed and developing – in a global partnership. They recognise that ending poverty and other deprivations must go hand in hand with strategies that improve health and education, reduce inequality and spur economic growth – all while tackling climate change and working to preserve our oceans and forests. For more information please visit: **https://sdgs.un.org**.

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Page 23: Participants at Annual Conference 2019 – Ian Atherton

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