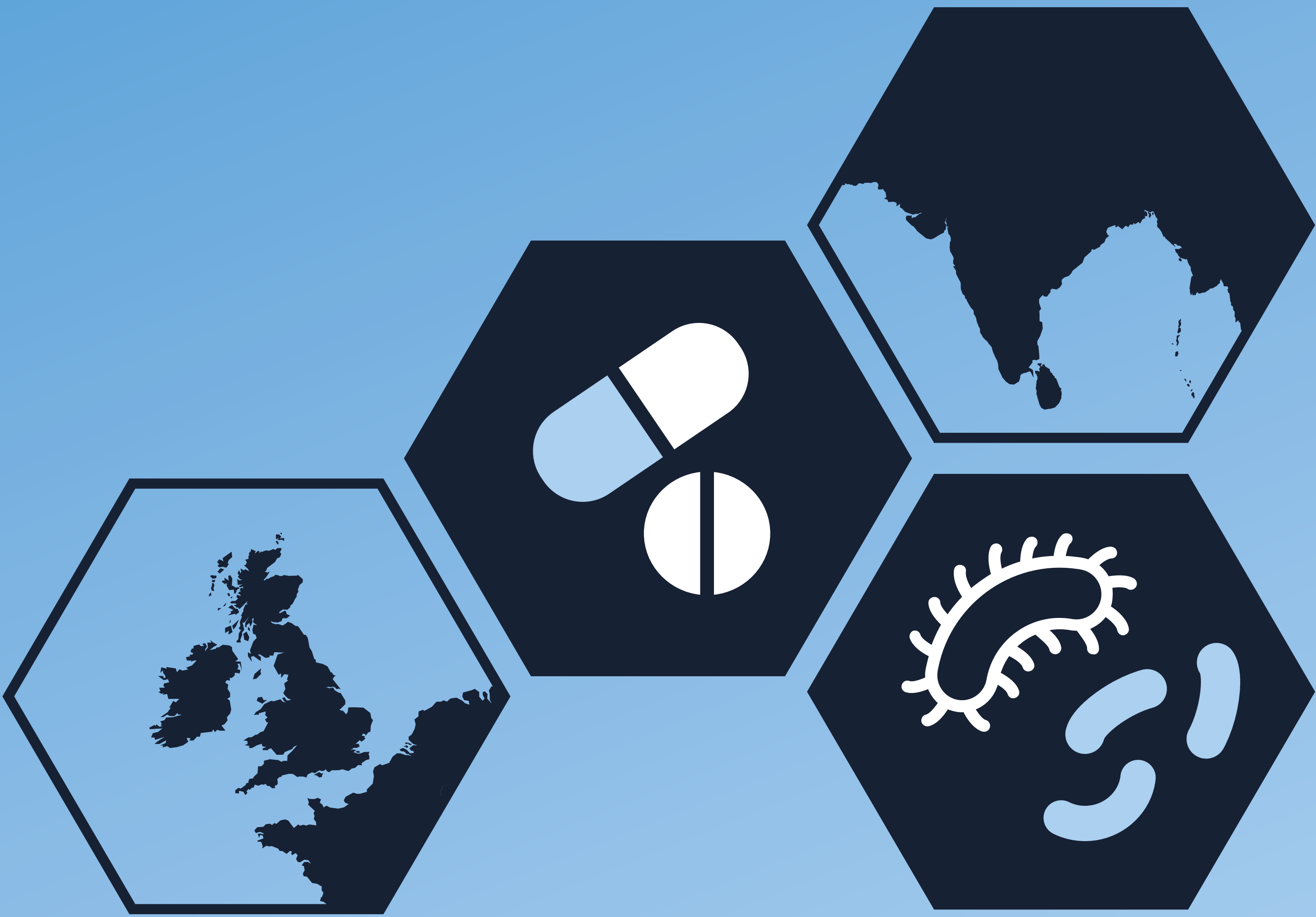

UK-India Symposium on Antimicrobial Resistance

Symposium report

4–5 February 2019
London, UK

The Academy *of* Medical Sciences

Yusuf & Farida Hamied Foundation

This Symposium was generously supported by the Yusuf and Farida Hamied Foundation.

The Academy *of* Medical Sciences

This is a summary of a Symposium held in February 2019 and reflects the views expressed but does not necessarily represent the views of all participants at the event, the Academy of Medical Sciences, or its Fellows.

We are most grateful to the meeting Chair, Professor David Heyman CBE FMedSci and the steering committee for their contributions and commitment to this meeting.

All web references were accessed in June 2019

UK-India Symposium on Antimicrobial Resistance

Contents

Preface

The ability of microorganisms to develop resistance to antimicrobials represents one of the gravest threats to health globally. The risk of acquiring an untreatable infection is growing, which will compromise many routine medical procedures.

Antimicrobial resistance (AMR) is a topic of great relevance to both the UK and India, which is why I am pleased to be chairing a programme of work led by the Academy of Medical Sciences aimed at strengthening ties between the UK and India and catalysing new research partnerships between the two countries. The five-year programme includes an annual UK-India visiting Professorship scheme and two scientific meetings and is being generously supported by the Yusuf and Farida Hamied Foundation.

A lack of awareness, insufficient surveillance and inconsistent infection prevention impede efforts to reduce AMR. To prevent resistance developing, inappropriate use of antimicrobials must be minimised without preventing access when they are needed. We also need to develop new antimicrobials, as the current ones become less effective. Tackling AMR requires collaborations across multiple disciplines and international borders. The visiting Professorship scheme enables UK researchers to visit India with the aim of developing long-term collaborations, which will focus on all aspects of AMR to further understand its progress and spread and support the development of new interventions. The two scientific meetings provide a forum to review progress on AMR and share the latest research and collaborations between the UK and India.

The first meeting was held in London, and provided opportunities for discussions on key areas of AMR relevant to the UK and India and how they might be addressed. It also provided a forum for establishing and strengthening links between the UK and India, and for discussion of the factors underlying effective partnerships. A follow-up symposium will be held in India in 2021.

This report summarises the presentations and discussions at the first meeting and identifies some of the key emerging themes, evidence gaps and opportunities for further research. Even though the report does not necessarily represent the views of all delegates, members of the Steering Committee, the Academy of Medical Sciences, or the Hamied Foundation, it is a good summary of the issues we face in addressing AMR. The report offers some starting points and opportunities for the UK and India to address by sharing knowledge and building collaborations.

Professor David Heymann CBE FMedSci
Professor of Infectious Disease Epidemiology,
London School of Hygiene and Tropical Medicine
Head, Centre on Global Health Security, Chatham House
Chair of the Academy of Medical Sciences 'UK-India AMR Programme'

Executive summary

Antimicrobial resistance (AMR) is a global threat to health, compromising the effectiveness of medicines that have been vital in dramatically reducing the global infectious disease burden, and threatening the safety of routine surgical procedures. Both the UK and India face AMR challenges, some shared and some distinct. To help explore these challenges, and identify the steps needed to address them, the Academy of Medical Sciences organised a two-day conference with the support of the Yusuf and Farida Hamied Foundation, as part of a wider programme of work on this topic.

The presentations, discussions, and breakout groups identified a range of key themes:

Surveillance

AMR surveillance data are important to inform a range of activities, including individual clinician decision-making, guiding national or local policymaking such as treatment and prevention guidelines, and providing national and global insight into AMR epidemiology and early warning of emerging resistant organisms.

To improve understanding and action, a need for improved surveillance data on the extent and emergence of resistant infections (especially within community and agricultural settings), and data on antimicrobial usage in the healthcare sector, agricultural sector and from wider environmental settings, was identified. Delegates emphasised the importance of standardised data collection to facilitate comparisons and data aggregation. Microbiological data should be linked to patient data and treatment outcome.

However, delegates cautioned that care should be taken to ensure that data collection efforts are done with a clear purpose and justification, and not just for the 'sake of it'.

AMR ecosystem

AMR arises and spreads within a complex ecosystem spanning healthcare, agriculture and the environment. However, the precise contribution each different domain makes to the development of AMR is poorly understood, which hinders attempts to prioritise interventions, particularly outside the medical domain. The environmental contribution towards AMR is often neglected. Contamination of the environment with drug resistant residues and antibiotic residues creates a favourable condition for the emergence and exchange of resistance genes.

Poor sanitation, the risk of zoonosis by animals and people living in close proximity, and the overuse of antibiotics all contribute towards a high AMR rate. The involvement of such a wide range of sectors reinforces the need for a 'one-health' approach to better understand AMR and how to mitigate the issue. A multidisciplinary approach to AMR research should include veterinary, agricultural and environmental scientists, engineers, and social and behavioural scientists.

Multidisciplinary applied research should also be supported by basic laboratory studies of the molecular mechanisms of resistance, to provide insight into the factors that promote the survival and spread of AMR genes and resistant organisms through clinical and environmental routes.

Reducing the infectious disease burden

Infection prevention and control in both hospital and community settings was widely seen as central to reduce the number of infections and requirement of antimicrobials. Promoting good infection control practices and strengthening of public infrastructure in India, such as access to clean water and sanitation services, was also thought likely to reduce the burden of infections.

Reducing the number of both bacterial and viral infections through vaccination programmes was seen as another key part to limiting the need for antibiotics, and mitigating their inappropriate use. India has made impressive gains in vaccination coverage through the Mission Indradhanush and Intensified Mission Indradhanush initiatives, although there is scope for further improvements.

In terms of agriculture, delegates argued that better husbandry practices, and increased vaccination of livestock, could reduce the spread of infections between animals, reducing the veterinary use of antibiotics. However, it was acknowledged that the use of antibiotics, including so called 'last-resort' antibiotics such as colistin, for prophylaxis and growth promotion in livestock farming was deeply embedded in India, and practices would be difficult but necessary to influence.

Antibiotic stewardship

Ensuring appropriate use of antibiotics was widely seen as vital to preserving the effectiveness of existing and newly developed drugs. Suggested priorities include a strengthened evidence base for use of antimicrobials, as well as a stronger focus on antibiotic stewardship in the education and training of physicians and other healthcare workers. New technologies and digital tools need to be developed and applied to support physicians' antibiotic-prescribing decision-making.

It was also recognised however that reducing antibiotic use through effective antibiotic stewardship needs to be complemented by initiatives to increase appropriate access in India to avoid preventable deaths from infection, particularly in infancy. Access to antibiotics and trained service providers remains low in many areas of India, particularly poor rural districts. However, in other regions antibiotics are widely available to the public without a prescription, which presents a challenge to the rational use of antibiotics. Both in the UK and India, there is a continued need to better communicate the threat of AMR and the importance of AMR stewardship.

Diagnostics

Development and appropriate use of diagnostics are widely seen as pivotal to AMR control, with the potential to distinguish bacterial and viral infections, to identify causal pathogens and to detect antibiotic resistance. Diagnostics could inform clinical decision-making, clinical guidelines and health policy, and provide insights into the wider epidemiology of drug-resistant infections. As well as overcoming technical and financial challenges, it was noted that new diagnostic development needed to have a clear sense of how tools would integrate into patient management pathways and inform clinical practice.

It was also noted that reimbursement practices could have a significant impact on implementation of diagnostics. In India, where out-of-pocket expenses account for the bulk of healthcare expenditure, the cost of a diagnostic could be an additional access barrier or incentivise unnecessary testing.

Regulation and enforcement

National action plans are the cornerstone of country-level AMR responses, and both India and the UK have developed national AMR action plans. Delegates noted however that while UK has started to make progress, at least for the some of the recommendations, limited implementation of the national action plan has occurred in India. The enforcement of relevant regulations, such as those related to antibiotic prescribing and environmental pollution with antibiotics, are often weak.

India's policy framework and its enforcement has also done little to reduce antibiotic use in agriculture, with antibiotics especially colistin, the antibiotic of 'last resort' still being routinely used in feed for growth promotion and prophylaxis. Furthermore, environmental contamination from antibiotic manufacturing sites and from hospitals needs to be urgently addressed. More efforts could be made to engage the environmental sector in AMR-related issues.

The social dimension: Public, practitioners, policymakers, politicians

Delegates noted that, as well as prescribing physicians, many different groups have a role to play in AMR control. Notably, tackling AMR requires political will and leadership to develop and ensure effective implementation of AMR strategies. Public antibiotic-related attitudes and behaviours can also have a significant impact on antibiotic use, as can the nature of the patient–physician interaction.

A better understanding of these attitudes and behaviours, and the factors that affect them, could underpin the development of behaviour change interventions to promote appropriate use of antibiotics. This emphasises the important role that social and behavioural researchers can play in addressing AMR.

Development of new antibiotics

It was recognised that, despite some progress, new antibiotic development is not meeting global public health needs. New antibiotic development is not financially attractive to companies, and new mechanisms of market incentivisation may be required. It was suggested at the meeting that the new model proposed in the UK's recent AMR strategy might encourage more countries to adopt similar approaches.

Academic collaborations, including between UK and Indian researchers, and product development partnerships were seen as ways to advance early antibiotic discovery. In addition, as well as identifying novel targets and novel delivery mechanisms, the potential of innovative alternatives to antibiotics could be explored, including bacteriophage and host-directed therapies.

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AMR arises and spreads within a complex ecosystem spanning health-care, agriculture and the environment

1. Introduction

AMR represents one of the most severe threats to human health globally. An estimated 700,000 people already die each year from drug-resistant infections, a number projected to rise to 10 million a year by 2050 if further action is not taken.[1] While the demand for new antibiotics has never been greater, no new class of antibiotic has been introduced into clinical practice since the 1980s.

AMR arises because of the selective pressures exerted by antimicrobials, and resistant organisms thrive at the expense of those susceptible to drug treatments.

Multiple factors influence the development and spread of AMR, many of which are related to the overuse and misuse of antibiotics. It is strongly linked to antibiotic use in hospitals and primary care, but also to the effectiveness of infection prevention and control practices. Furthermore, antimicrobials are extensively used in livestock farming, including as growth promoters in many countries, including India. In addition, environments can become contaminated with drug-resistant organisms and with antibiotic residues, creating conditions that favour the emergence and exchange of resistance genes and the spread of resistant organisms. AMR is thus generally considered within a 'one-health' framework, that encompasses agriculture, veterinary medicine and the environment, as well as human medicine.

The World Health Organization (WHO) Global Action Plan on AMR has identified five strategic priorities for combating AMR.[2]

1. Raising awareness and understanding.
2. Increasing understanding of the challenge through surveillance and research.
3. Reducing the need for antimicrobials, for example through better infection prevention and control, use of vaccines, and improved water and food safety.
4. Optimising the use of antimicrobials in human and animal health.
5. Enhancing investment in new antibiotics and other product development.

However, alongside this emphasis on reducing unnecessary use of and environmental contamination with antimicrobials, populations in many countries – including India – are affected by limited access to antimicrobials in certain regions and communities. Up to two billion people globally, particularly in low- and middle-income countries (LMICs) lack access to antimicrobials.[3] Hence, solutions to the AMR challenge must also consider how to improve access to those in need.

The UK and India both face significant AMR challenges. India is one of the world's biggest users of antibiotics, and use more than doubled between 2000 and 2015.[4] Data from surveillance networks have identified extremely high rates of resistance to common infections, necessitating the use of more complex and expensive treatments.

1. Jim O'Neill. (2014). The Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. https://amr-review.org/Publications.html
2. WHO (2015). Global Action Plan on Antimicrobial Resistance. https://www.who.int/antimicrobial-resistance/global- action-plan/en/
3. HM Government (2019). Tackling antimicrobial resistance 2019–2024: The UK's five-year national action plan. https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024
4. Klein EY *et al.* (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. PNAS 115(15), E3463-E3470.

In the UK, the proportion of bloodstream infections resistant to key antibiotics has been relatively stable, and antibiotic use declined between 2014 and 2017.[5] However, there are significant concerns about the potential impact of carbapenem-resistant bacteria and the growing prevalence of highly drug-resistant gonorrhoea.

This report summarises the two-day conference organised by the Academy of Medical Sciences with the support of the Yusuf and Farida Hamied Foundation, as part of a wider five-year programme of work on AMR. The programme aims to strengthen ties between the UK and India, using comparisons between the two countries and the sharing of experience to open up opportunities for mutual learning, as well as for the development of new research collaborations drawing on the strengths of the science bases in each country. The programme includes two major scientific meetings and a UK-India visiting professorship scheme.

The organisation of the meeting was overseen by a steering committee based both in the UK and in India (Annex 1). The plenary, panel and breakout sessions supported discussions on key areas of AMR, the AMR situation in the two countries, important unanswered questions, and actions that could be taken to combat the AMR threat (meeting programme in Annex 2).

The opening session provided an overview of the AMR challenge in the UK and India. The following panel discussions focused on AMR surveillance, how resistance develops, and how antimicrobial use can be minimised whilst improving appropriate access via effective infection control and optimisation of currently available interventions. An additional session focused on the challenges and opportunities of setting up collaborations between the UK and India. The breakout sessions aimed to identify the biggest challenges and potential actions within the areas of surveillance, resistance development, infection control and optimisation of current interventions (summaries of each breakout group discussion are in Annexes 3-6). The meeting was attended by researchers, clinicians and policymakers from both the UK and India with expertise in human health, environment and agriculture.

5. Public Health England (2018). English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR). https://improvement.nhs.uk/resources/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur/

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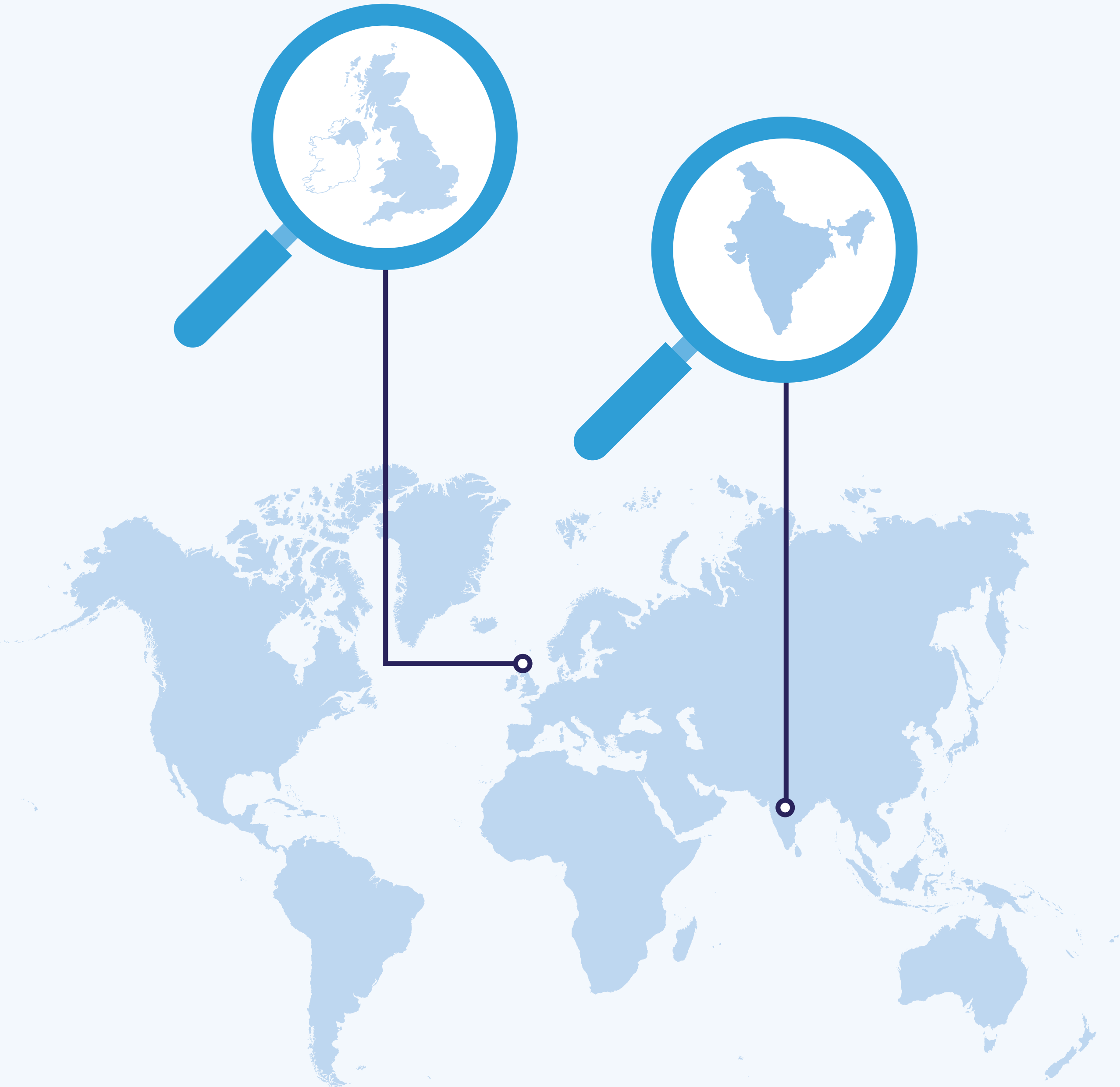
Both the UK and India face the threat of AMR, but sharing experiences and setting up new research collaborations helps to address the challenge.



2. The challenge in the UK and India

During this session the speakers outlined the 'state of play' in each country, including what actions each country has already taken and where they think the biggest challenges still lie.

Professor Dame Sally Davies DBE FRS FMedSci

Chief Medical Officer for England and Chief Medical Adviser to the UK Government, described some of the actions being taken to address AMR globally and in the UK. Dame Sally is a Co-Convenor of the UN Interagency Coordination Group (IACG) on AMR. In January 2019, the Group published draft recommendations, to be submitted to the UN Secretary General once finalised.[6] Dame Sally also spoke about the 'Framework for Action' that the IACG developed, which focuses on three key areas – decreasing the need for antimicrobials, optimising the use of antimicrobials and investing in innovation, supply and access.

International comparisons (from OECD data) suggest that the UK has rates of drug-resistant infections among the lowest globally. However, the UK's aim is to match the best-performing countries in the world. Antibiotic-use in humans has decreased in recent years and voluntary targets have led to a significant reduction in antibiotic use in the agriculture sector. The message from Dame Sally's presentation was clear: the UK has made progress but much more needs to be done.

Dame Sally outlined some key areas where increased action is needed. For example, more research aimed at understanding the transmission of AMR through animals and the environment, and the risk this poses to humans, is required. Additionally, there is a clear need for more effort to combat the market-failure and stimulate investment into new drugs.

In January 2019, the UK launched a cross-government 20-year vision and five-year action plan for AMR.[7] It follows the UN IACG framework for action, focusing on decreasing the need for antimicrobials, optimising use and investing in innovation. It has established a number of specific targets, for example to halve the number of healthcare-associated Gram-negative bloodstream infections, to reduce antibiotic use in food production by 25%, and to increase the number of prescriptions supported by a diagnostic test.

Dr Kamini Walia[8]

Senior Scientist in the division of Epidemiology and Communicable Diseases of the Indian Council of Medical Research, outlined some of the key AMR issues facing India.

AMR is a major challenge in India, compromising gains made in the treatment of infectious disease and complicating routine medical procedures, such as surgery. Reasons for the high rates of AMR in India include the country's high infectious disease burden, poor sanitation in much of the country, the risk of zoonosis by animals and people often living in close proximity, and overuse of antibiotics, which are available over the counter.

6. WHO (2019). Draft Recommendations of the ad hoc Interagency Coordination Group on Antimicrobial Resistance. https://www.who.int/antimicrobial-resistance/interagency-coordination-group/public-discussion-draft-recommendations/en/
7. HM Government (2019). Tackling antimicrobial resistance 2019–2024: The UK's five-year national action plan. https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024
8. Dr Kamini Walia spoke and offered her expertise in the opening session in place of the scheduled speaker who was unable to attend.

India has developed a cross-ministerial AMR national action plan,[9] identifying actions across multiple domains. These include the introduction of new regulations to restrict the sales of certain antibiotics (including so-called schedule H1 regulations to regulate prescribing of 46 key drugs). However, there is limited evidence of the effectiveness of these regulations and doubts about how strongly they are enforced.

India has two key AMR surveillance networks, run by the Indian National Centre for Disease Control (NCDC) and the Indian Council of Medical Research (ICMR). The NCDC draws on samples from 20 hospitals across India, while the ICMR has access to samples from hospitals and reference laboratories, and has a stronger focus on research. There is close collaboration between these networks and a strong emphasis on standardisation and harmonisation of practices across surveillance sites.

Other key initiatives include an antibiotic stewardship programme run in partnership with the US Centers for Disease Control and Prevention (CDC), and a public communication programme run in collaboration with Pfizer.

In the agricultural sector, antibiotics are used extensively for growth promotion in India (a practice that has been illegal in the EU since 2006).[10] These include colistin, an antibiotic of last resort used to treat drug-resistant human infections. Steps are also being taken to tighten up regulation of pharmaceutical manufacturing facilities, the effluent from which can contain high concentrations of antibiotic residues.

Lord O'Neill

Chair of Chatham House discussed in a keynote presentation, progress that had been made in the two and a half years since the publication of the landmark 'O'Neill Report' on AMR.[11] The report made recommendations across ten areas: five linked to antimicrobial demand, three to supply, and one each on vaccines and international cooperation.

Despite some progress, Lord O'Neill suggested that AMR is still not high enough on the public agenda. He also noted disappointing progress in reducing the use of antibiotics in agriculture, which has not been widely embraced in LMICs and is meeting increasing resistance in some high-income countries, such as the USA.

He suggested that the UK had continued to show global leadership with its new action plan, particularly its proposed innovative model to incentivise the development of new antibiotics and radically change how antibiotics are purchased by the NHS.

He also argued that it was important to maintain the profile of AMR at the highest political levels, for example at the forthcoming G20 meeting, and to encourage other countries to follow the UK's lead. There were also opportunities to engage with other sectors, for example to integrate AMR into health preparedness assessments, which affect a country's credit rating and ability to borrow money.

Discussions highlighted the key role that could be played by vaccination in reducing the need for antibiotics. Even vaccination against viruses could make an impact – antibiotic use increases during the flu season, for example, so greater influenza vaccine use could reduce demand for antibiotics by reducing the number of secondary bacterial infections and inappropriate use. India, however, currently does not have a national policy for influenza vaccination. Wellcome recently published an analysis of the possible contribution of vaccine development to AMR.[12] Similarly, improvements in public health such as clean water and sanitation, and infection prevention and control, could reduce antibiotic demand.

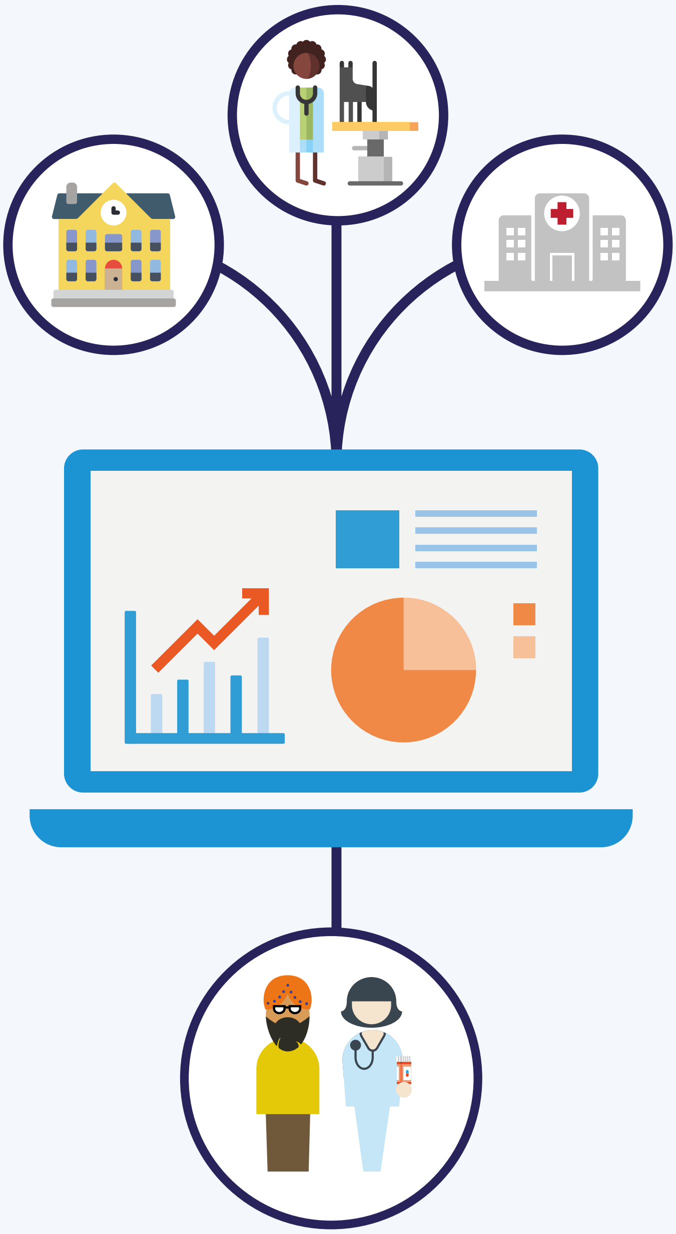
9. Government of India (2017). National Action Plan on Antimicrobial Resistance. http://www.searo.who.int/india/topics/antimicrobial_resistance/en/
10. POST (2018). Reducing UK Antibiotic Use in Animals. https://researchbriefings.parliament.uk/ResearchBriefing/Summary/POST-PN-0588
11. Jim O'Neill (2016). The Review on Antimicrobial Resistance. Tackling Drug-Resistant Infections Globally: Final report and recommendations. https://amr-review.org
12. Wellcome and the Boston Consulting Group (2018). Vaccines to tackle drug-resistant infections: An evaluation of R&D opportunities. https://vaccinesforamr.org/read-the-report/

Multidisciplinarity was seen as critical to the AMR challenge, exemplified by the one-health framework. It was suggested that there was also scope for engagement with additional constituencies, including consumers and the investment community, who could exert influence on antibiotic practices. Potentially, an 'AMR lens' could be introduced into all policy discussions, mirroring approaches taken for climate change and gender rights.

Delegates also noted that development of high-level actions plans and policy frameworks did not necessarily solve problems. Thought also needs to be given to effective implementation of policies and enforcement of regulations.

Surveillance gaps were seen as an important issue, particularly the lack of representative data of community acquired infections. More generally, it was recognised that there was limited understanding of the role of the environment in the development and spread of AMR, making it difficult to prioritise interventions.

> Surveillance is important to assess the scale of AMR and to inform on antimicrobial use and infection prevention activities.



3. The extent of the problem and how to measure progress

This panel session explored how the levels of AMR are measured in humans, animals, and the environment, at global, national and regional levels. Surveillance for drug-resistant infections nationally and globally is essential for assessing the scale and impact of AMR. Other important information can come from monitoring of antimicrobial use (in medicine and other sectors) and of antibiotic resistance genes and levels of antibiotic residues in the environment.

Dr Kamini Walia

Senior Scientist in the division of Epidemiology and Communicable Diseases of the Indian Council of Medical Research, noted the range of roles that AMR surveillance can play. As well as individual clinical decision-making, AMR monitoring can inform policymaking and guidelines on antibiotic use. Surveillance can be used to assess the scale of AMR, to track trends over time, and to monitor its spread. Surveillance data are also key to assessing the impact of AMR control interventions.

Globally, limited data are available from LMICs and variation in methodologies makes data hard to compare. Few data are available from the private sector, which can make up a significant part of healthcare in many LMICs.

Surveillance is one of the strategic priorities of the Indian AMR national action plan. Although there is now a greater understanding of what surveillance data are required, comprehensive surveillance is challenging given the complex AMR ecosystem, spanning human healthcare, agriculture and the environment, and the limited understanding of how AMR arises and is spread across these domains.

Hence it is likely that different tools will be needed to perform different surveillance functions. Genetic approaches and whole genome sequencing could offer new opportunities to track AMR and pathways of transmission, but relating genetic changes to phenotypic resistance characteristics can be challenging.

Professor Susanna Dunachie

Associate Professor and Honorary Consultant in Infectious Diseases and Medical Microbiology at the University of Oxford, discussed some of the challenges in determining the human impacts of AMR. AMR is a complex phenomenon, measurable in many ways. Many attempts have been made to estimate its impacts, using a variety of approaches.

The Global Research on Antimicrobial Resistance (GRAM) study, a collaboration between the Institute of Health Metrics and Evaluation (IHME) at the University of Washington, Seattle, and the University of Oxford, is attempting to consolidate global AMR data sources to generate maps and estimates of AMR burden. Focusing on 17 drug–pathogen combinations, it is integrating AMR-related mortality and morbidity assessments into Global Burden of Disease statistics, produced by the IHME.

The GRAM study faces several challenges. There is no consensus on how the AMR burden can be quantified. Data from LMICs are scarce and may be of poor quality. Importantly, microbiological data are often not linked to patient data, few resources are available to link the two, and privacy and consent concerns can inhibit data sharing. Biased data collection is also a key concern, as data typically come from a restricted range of non-representative sites.

Professor Ramanan Laxminarayan

Director of the Center for Disease Dynamics, Economics and Policy (CDDEP), and Senior Research Scholar at Princeton University, cautioned against data collection becoming an end in itself. He argued that it was important to ensure that data collection had a clear purpose – that it would provide new insights and suggest new actions. He pointed out that extra data do not necessarily lead to changes in practice. Local AMR data, for example, do not necessarily change clinicians' prescribing decisions. There is an urgent need for surveillance data and for better communication of the actions suggested by this data to healthcare providers and policymakers.

Furthermore, broad-brush data may be adequate for justifying policy actions – it is already clear that India faces major AMR challenges and needs to take urgent action. As India also faces antibiotic access as well as overuse issues, Professor Laxminarayan pointed out multiple areas that should be prioritised to reduce the need for antimicrobials and to combat AMR. Including improved sanitation and hygiene, increased use of vaccination, enhanced infection prevention and control in hospitals, addressing promotion of antibiotic use for commercial reasons, better antibiotic stewardship and shifting social norms to encourage greater public appreciation of antibiotics.

Professor Sharon Peacock CBE FMedSci

Honorary Senior Research Fellow at the University of Cambridge, argued that the current focus of AMR was too strongly on microbes and paid insufficient attention to patients and clinical impacts.

AMR can be tracked along a surveillance pathway, and repositories such as the Global Antimicrobial Resistance Surveillance System (GLASS) provide a source of global AMR data and standardised approaches for data collection. Furthermore, substantial numbers of international networks are collecting AMR data, suggesting there are untapped data resources. However, comparatively few AMR data are linked to patient information.

The Wellcome-funded Surveillance and Epidemiology of Drug-resistant Infections Consortium (SEDRIC) has been established to bring international stakeholders together to share expertise and take action to tackle the gaps in drug-resistant infection surveillance and epidemiology. It has a strong interest in strengthening the collection, sharing and use of AMR data for public health benefit.[13]

To shift this emphasis, A Clinically Oriented Antimicrobial Resistance Surveillance Network (ACORN) has been established in South East Asia. More generally, Professor Peacock emphasised the need for standardised approaches to data collection, collation and sharing.

Dr Elizabeth Tayler

AMR Secretariat, WHO, discussed the framework for AMR monitoring and evaluation developed by the WHO, the UN's Food and Agriculture Organisation (FAO) and the World Organisation for Animal Health (OIE). The global response to AMR has been shaped by the WHO's Global Action Plan on AMR, which recommended that countries develop national action plans for AMR. The monitoring and evaluation framework therefore covers activities at global, regional and national levels.

13. Fukuda K *et al.* (2018). Surveillance and Epidemiology of Drug Resistant Infections Consortium (SEDRIC): Supporting the transition from strategy to action. Wellcome Open Research 3, 59.

The framework is designed to be flexible, to support monitoring activities at global, regional and national levels, and in different country contexts. It includes a focus on both process and AMR-related outcomes. It includes a tool for national self-assessment. Findings are made available in GLASS reports, WHO reports on surveillance of antibiotic consumption, and more focused publications such as reports on the Global Tricycle Surveillance of extended-spectrum beta-lactamase-producing (ESBL) *E. coli.*

Extensive discussions focused on how AMR data could guide physician decision-making and reductions in antibiotic prescribing. It was suggested that local data are not yet being used to inform clinical practice, either for initial prescribing or in de-escalation, or to shape infection prevention and control activities.

Physician training and education were seen as central to this issue. The potential to use new technologies to develop innovative tools to support clinician decision-making was also highlighted.

The importance of data standardisation was widely stressed, as was the need for unbiased data rather than just information on more unusual infections. A biobank or sample repository was perceived as being a potentially useful resource with several applications in epidemiological research and new product development, but representativeness of samples would be an important issue to consider.

Public attitudes and the physician–patient relationship were also highlighted as key issues. The public may not yet have a good understanding of the impact of AMR, and media reporting is not always well informed.

Globally, recommended public health messaging has recently shifted from completion of courses of antibiotics to use only when advised by a doctor. However, doctors in primary practice typically also over-prescribe. In addition, there is some evidence that physician over-prescribing is linked to miscommunication between the doctor and patient – a doctor may assume that patients want an antibiotic whereas they actually just want validation that they are genuinely unwell. More social and behavioural research is needed to understand public antibiotic-related attitudes and behaviours.

Psychological insights could shape the framing of messages, for example emphasising positive messages that may be more likely to influence behaviour. Terminology is a further important issue, with the public having a clearer understanding of ‘drug-resistant infections’ than ‘antimicrobial resistance’. As well as individuals, messaging could also focus more on community leaders, community organisations and individuals of influence.

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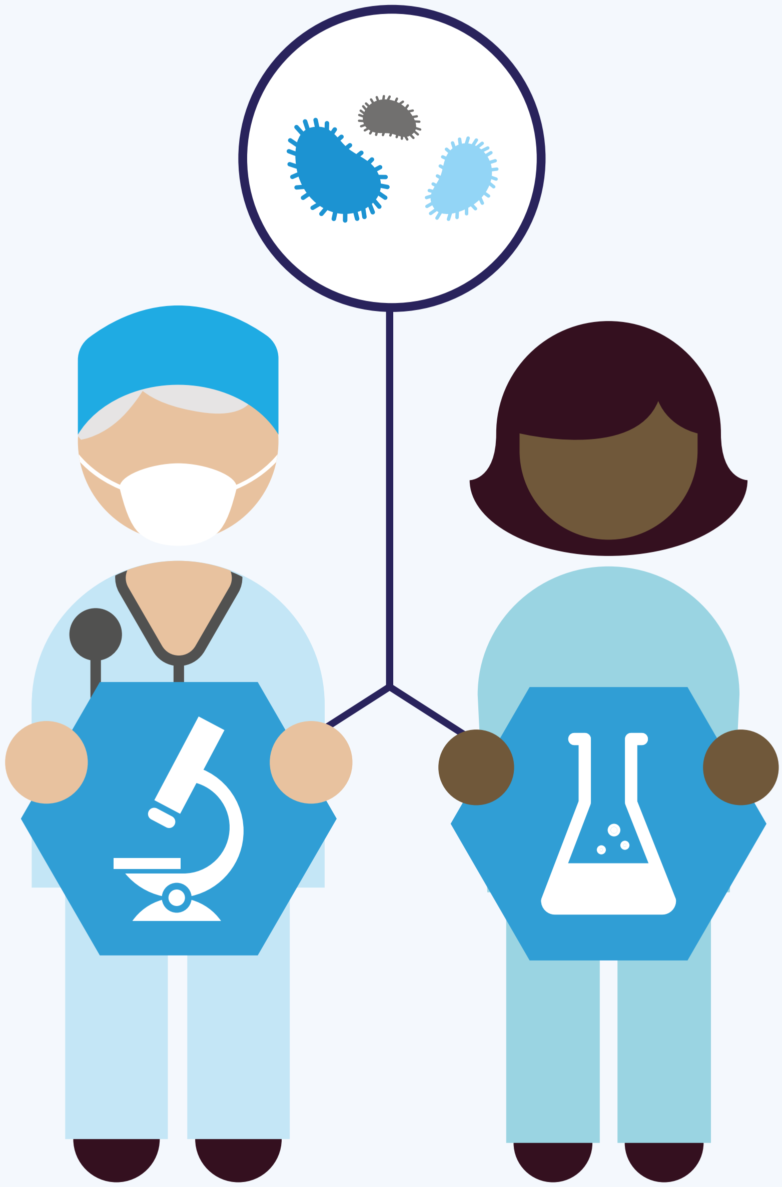
To stop the spread of AMR, we first need to better understand why antibiotic resistance develops and spreads.



4. How resistance develops and how to reduce it

This panel discussion focused on the basic biology of how resistance develops and how this can inform the treatment of animals in food production, prescribing practices, and interactions with the environment, including wild animals and computational algorithms to predict resistance. Development of strategies to combat AMR will depend in part on an understanding of the mechanisms of resistance, as well as the factors driving it and those sustaining or promoting its spread. Unfortunately, the mechanisms of resistance are diverse and often highly complex and poorly understood.

Dr Abdul Ghafur

Coordinator of the Chennai Declaration on Antimicrobial Resistance, noted that, colistin resistance in *Klebsiella pneumonia* is a serious menace in India and across the world. There are plenty of publications on the topic from Indian hospitals. Unfortunately, there is no prior Indian data on colistin resistant bacteria in food samples or the underlying mechanisms conferring resistance.

Analysing 110 food samples in Chennai, Dr Ghafur found that 51 (46%) harboured colistin-resistant bacteria of varying species. Three *E. coli* isolates were found to have the *mcr-1* gene (plasmid-mediated mobilized colistin resistance gene), while ten *Klebsiella* isolates had mutations in *mgrB* (codes for a small transmembrane protein of which alterations can convey colistin resistance), including four in which *mgrB* had been disrupted by insertion sequences.

Insertional inactivation of the *mgrB* gene is a well-known colistin resistance mechanism in *Klebsiella* of human origin. Identification of the same mechanism in *Klebsiella* of food origin is a matter of serious concern. This finding has significant global public health implications, raising the potential for food chain transmission and human infections with colistin resistant *Klebsiella pneumoniae* with *mgrB* gene alterations.[14]

Indeed, an ongoing study by Dr Ghafur's team on stool samples collected from patients at the time of hospital admission has found that 50% harboured colistin resistant bacteria with phenotypic characteristics of food origin (unpublished data).

Dr Ghafur suggested that the results reinforced the need for India to ban the use of colistin as a growth promoter. Although China has banned the use of colistin as a growth promoter, it still exports large quantities of colistin to countries such as India. The data has inspired the Indian Health Ministry and other relevant ministries to fast track efforts to ban the use of colistin for growth promotion.

14. Ghafur A *et al.* (2018). Detection of chromosomal and plasmid-mediated mechanisms of colistin resistance in Escherichia coli and Klebsiella pneumoniae from Indian food samples. Journal of Global Antimicrobial Resistance 16, 48–52.

Professor Timothy Walsh

Professor of Medical Microbiology and Antibiotic Resistance at Cardiff University, discussed the factors that contribute to the success of an AMR gene. These were likely to spread most effectively when they are also found in commensal as well as pathogenic organisms, are freely exchangeable on plasmids with a broad host range, and are well tolerated by host bacteria.

AMR genes often alter host cell metabolism, so may have a fitness cost. Resistant organisms may therefore be outcompeted when the selective pressures exerted by antibiotic use are removed. However, secondary mutations may arise that reduce fitness costs (as is the case with some *mcr* mutations), promoting longer-term survival.

Furthermore, some plasmids also carry genes for toxin–antitoxin 'addictive systems', which make host cells dependent on the plasmid for survival.[15] Even in the absence of antibiotic selection pressures, therefore, the plasmid is likely to be retained. In these situations, simply stopping antibiotic use may not lead to the disappearance of resistant microbes.

The presence of the *blaNDM-5* carbapenemase gene (confers resistance to the Carbapenem class of antibiotics which are usually reserved for multi-drug-resistant infections) on a plasmid carrying multiple addictive systems and antibiotic resistance genes may make it particularly likely to disseminate. For similar reasons, the *mcr-3* colistin resistance gene may represent an important future threat. More positively, since the colistin ban, *mcr-1* seems to be becoming less common in China, probably because of its plasmid context.

Dr Mark Holmes

Reader in Microbial Genomics and Veterinary Science at the University of Cambridge, pointed out additional complexities in understanding the evolutionary dynamics on AMR. For example, AMR can refer to several things, such as individual genes, drug-resistant organisms, or resistance mechanisms.

Furthermore, the significance of AMR organisms can depend on context. While it is now widely accepted that colistin use in agriculture provided a selection pressure for the emergence of colistin resistance that has impacted human health, the issue is less clear-cut in other situations. The risks to human health associated with livestock-associated methicillin-resistant *Staphylococcus aureus* (MRSA), for example, may appear low, but become more significant in countries that have very low levels of clinical MRSA.

The environment provides a wide range of opportunities for microorganisms to mix, potentially exposing them to organisms carrying resistance genes, and to be exposed to sub-lethal doses of antibiotics, promoting selection for antibiotic resistance. Environmental contamination with antibiotic residues may be a particular issue in India.[16]

Dr Holmes also pointed out significant differences in infection management and antibiotic use in veterinary and human medicine. For example, sick or injured animals are likely to be culled rather than treated, and antibiotics are often used to control endemic diseases (often being used as an alternative to other preventive measures, such as husbandry practices). Use of diagnostics is rare and identification of a diseased animal often leads to treatment of whole groups. Policies and practices relevant to human medicine may therefore not be applicable to veterinary medicine.

Furthermore, it is important to consider the economic dimension. Minimising the price of food is a very strong driver of animal farming practices, and many producers are operating in global marketplaces where additional costs may significantly affect competitiveness.

15. Yang QE & Walsh TR (2017). Toxin-antitoxin systems and their role in disseminating and maintaining antimicrobial resistance. FEMS Microbiology Reviews 41(3), 343-353.

16. Lübbert C *et al.* (2017). Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended-spectrum beta-lactamase and carbapenemase-producing pathogens. Infection 45(4), 479–491.

Professor Sandhya Visweswariah

Professor in the Department of Molecular Reproduction, Development and Genetics at the Indian Institute of Science, suggested that there was growing evidence that antibiotic resistance was arising outside of hospital contexts, with likely links to antibiotic use in agriculture. For example, in North India, many neonates who are born outside health facilities and develop sepsis have been found to have drug-resistant infections, in an area with a high density of poultry farms.[17]

Professor Visweswariah also noted the great diversity and complexity of mechanisms of resistance. In some cases, resistance depends on the presence of multiple mutations, which individually have little impact on susceptibility to antibiotics.[18,19] Compensatory mutations may be important in overcoming fitness costs. The biology of microbes may also be significant: in tuberculosis (TB), for example, infections may be refractory to antibiotics because some bacteria develop into quiescent 'persisters' that are very hard to eradicate.

Professor Visweswariah suggested that it was therefore important to adopt a systems perspective, and to look for inputs from other fields to bring in fresh thinking. Persisters, for example, share similarities with certain types of cancer cells (such as 'cancer stem cells'), and might be targeted in similar ways. Input from other fields of research could identify novel approaches to treatment such as the design of drug delivery mechanisms. There may also be a need to explore innovative forms of treatment, such as phage therapy.[20]

Professor Syma Khalid

Professor of Computational Biophysics at the University of Southampton, pointed out the key role played by bacterial cell walls and membrane structures in resistance. The twin membranes of Gram-negative bacteria and peptidoglycan cell wall of Gram-positive bacteria provide formidable barriers to entry of chemotherapeutics into the cell, although their manufacture also provides therapeutic opportunities.

A deeper understanding of the biology of these structures may reveal new targets for the development of antibiotics. Multiple technologies are providing new insights into bacterial cell walls and membrane biology and the mechanisms of action of antimicrobials, including the molecular modelling carried out by Professor Khalid.[21]

Discussions focused on the fact that the biology of microbes could have a significant influence on susceptibility to antibiotics. Formation of biofilms, for example, can render microbes more resistant to treatment, and could be an additional target for therapeutic development to augment conventional antibiotics.

A additional approach could be to stimulate host responses to infection, for example innate immune responses to pathogens.

It was also suggested that technological solutions might be able to overcome some of the challenges associated with reduced use of antibiotics as growth promoters. For example, to develop genetically modified strains of animals that were more resistant to infection or compensated for loss of productivity.

17. Jajoo M *et al.* (2018). Alarming rates of antimicrobial resistance and fungal sepsis in outborn neonates in North India. PLoS One 13(6), e0180705.
18. Wistrand-Yuen E *et al.* (2018). Evolution of high-level resistance during low-level antibiotic exposure. Nat Communications 9(1), 1599.
19. Matange *et al.* (2019). Adaptation Through Lifestyle Switching Sculpts the Fitness Landscape of Evolving Populations: Implications for the Selection of Drug-Resistant Bacteria at Low Drug Pressures. Genetics 211 (3), 1029-1044.
20. Agarwal *et al.* (2019). Inhaled bacteriophage-loaded polymeric microparticles ameliorate acute lung infections. Nature Biomedical Engineering 2(11), 841-849.
21. Boags A *et al.* (2017). Progress in Molecular Dynamics Simulations of Gram-Negative Bacterial Cell Envelopes. Journal of Physical Chemistry Leters 8(11), 2513–2518.

> Infection control is critical to reducing the demand for antimicrobials and the emergence of AMR.

5. Minimising antimicrobial use while maintaining essential access: preventing infection

One obvious way to reduce antimicrobial use is to prevent infections arising which in turn reduces the demand for antimicrobials. This panel session explored the most effective ways to prevent infections spreading in environmental, animal and human contexts. Multiple opportunities exist to reduce infection rates, for example through improved infection prevention and control in health facilities, use of vaccination, and better infection control in livestock farming.

Dr Osman Dar

Project Director of the One Health Project for the Centre on Global Health Security at Chatham House, noted that the current framing of AMR globally focused on risk and security perspectives. While these have successfully raised the global profile of AMR, there are question marks around whether this approach can sustain attention, particularly in LMICs, which have many other health priorities and are often at least as concerned with improving access to antimicrobial as in restricting their supply.

Dr Dar suggested that more contextually sensitive framing might be necessary. Different messaging might be needed to appeal to, for example, the animal health community or at subnational levels in India. There might also be opportunities to integrate AMR with wider issues around access to antimicrobials and assuring drug quality, as well as to leverage other Sustainable Development Goals, such as food security and safety.

Professor Alison Holmes FMedSci

Professor of Infectious Diseases at Imperial College London, suggested that healthcare facilities created the ideal environment for the emergence and spread of drug-resistant infections. In the EU, a third of antibiotic use in healthcare is for healthcare-associated infections. Infection prevention and control is therefore critical not just to immediate patient health but also to minimise antibiotic use and limit the emergence of AMR.

Professor Holmes suggested that infection prevention and control needed to consider the entire patient journey, through primary, secondary and acute care, and engage with all stakeholders. Effective practices were fundamentally reliant on human behaviours rather than simple technical fixes. It is also important to consider infection prevention and control within an integrated context that also encompasses issues such as antibiotic stewardship and sepsis prevention and management. In 2016, the WHO published guidance on the core components of infection prevention and control systems.[22]

22. WHO (2016). Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. https://www.who.int/gpsc/ipc-components/en/

Professor Holmes also suggested that surgery was a specific area for focus, and where important progress could be made. Infections are a common cause of post-operative deaths, and deaths are far more common in low-income settings. The multidisciplinary and international 'Antibiotic use and infection management across Surgical Pathways - Investigating, Redesigning and Evaluating Systems' (ASPIRES) project is exploring the surgical patient pathway to map out potential improvements in infection prevention and control and antibiotic usage in low-resource settings.[23]

Dr Rajesh Bhatia

Regional Technical Adviser on AMR for the Regional Office of the Food and Agriculture Organisation, noted that population growth and economic development in India were leading to increased demand for animal protein. Across South Asia, demand for poultry is projected to increase by 725% between 2000 and 2030. India is already one of the world's biggest consumers of antibiotics in livestock and use is projected to increase by 320% by 2030.[24]

Dr Bhatia suggested that the implications for human health of this massive antibiotic usage were still unclear. High levels of resistance to many antibiotics have been seen in *E. coli* in various livestock sectors. MRSA is a major issue in human medicine but not as yet in animals, while extended-spectrum beta-lactamase (ESBL)-producing bacterial infections are common in medicine but vary widely in their incidence across different livestock sectors.

Given the complexity of AMR emergence and spread, Dr Bhatia identified a range of key evidence gaps, including the contribution of agricultural antibiotic use to the AMR burden in human medicine, how environmental factors influence AMR and food-borne infections, what the economic impact would be of growth promoter bans, and how best to implement one-health solutions.

Dr Mike Whelan

Programme Manager at the Coalition for Epidemic Preparedness Innovations (CEPI), noted that CEPI was established in response to the West African Ebola outbreak to advance vaccine development for infectious diseases with epidemic potential. It has been set up as a public–private partnership to increase capacity in new vaccine development up to the phase II stage.

The US$700m fund has identified a range of priority pathogens, this currently includes all viruses in addition to 'disease X', an infection with a currently unknown pathogen. Some 14 'just in case' vaccines are under development for priority infections, while funding is also being provided for 'just in time' vaccine platforms that would allow the rapid development and testing of new vaccines to emergent pathogens.

Although currently focused on vaccines, the CEPI model is one that could theoretically be extended to bacterial pathogens, although vaccine development for bacteria is often more challenging. CEPI's work may also ultimately benefit AMR by reducing viral infections that are inappropriately treated with antibiotics or are immunosuppressive (e.g. Chikungunya) and increase the risk of bacterial infections.

Discussions noted the significant obstacles to reducing the use of antibiotics in livestock farming in India. The practice is very firmly embedded and food producers have considerable political influence. Politicians and policymakers have yet to recognise the threat posed by antibiotic use in agriculture. Banning of colistin use as a growth promoter is one area where progress may be possible. Globally, there is some evidence of a pushback against reducing antibiotic use in livestock farming.

Delegates suggested that treatment costs were still a major barrier to greater access to antibiotics in

23. UK Research and Innovation, Holmes AH et al. (2017). Optimising antibiotic use along surgical pathways: addressing antimicrobial resistance and improving clinical outcomes. https://gtr.ukri.org/projects?ref=ES%2FP008313%2F1

24. Van Boeckel TP *et al.* (2015). Global trends in antimicrobial use in food animals. PNAS 112(18), 5649–54.

25. The World Bank (2015). World Health Organization Global Health Expenditure database. https://data.worldbank.org/indicator/SH.XPD.OOPC.CH.ZS?locations=IN

India, where out-of-pocket payments make up 65% of healthcare expenditure.[25] Public expenditure on healthcare in India, although increasing, remains relatively low by international standards (3.89% of GDP, compared with 9.88% in the UK in 2015).[26]

Environmental contamination from hospitals and factories was thought likely to be a significant factor in the development of AMR but an area of great uncertainty due to a deficiency in data. A lack of evidence hindered efforts to define appropriate surveillance mechanisms and standards. There was also concern that organisations would be reluctant to invest to meet environmental standards, and that pollution control regulatory authorities in India, although in theory very powerful, in practice do not enforce regulations consistently.

There were some suggestions that in cities such as Delhi information is available on environmental exposures, but data are not necessarily being used to protect public health. Technologies are available to tackle pollution but they are likely to be expensive to implement. More generally, the lack of understanding of the role of environmental exposures in the origins and spread of AMR can make it difficult to prioritise resourcing.

It was also noted that projects such as the Global Sewage Surveillance Project would also provide important information on AMR genes and antibiotic residues in environmental samples.[27]

26. The World Bank (2015). World Health Organization Global Health Expenditure database. https://data.worldbank.org/indicator/SH.XPD.OOPC.CH.ZS?locations=IN

27. COMPARE (2018). Global Sewage Surveillance Project. https://www.compare-europe.eu/Library/Global-Sewage-Surveillance-Project

> Public awareness, patient attitudes and healthcare worker behaviour will all have a significant impact on antibiotic use.

6. Minimising antimicrobial use while maintaining essential access: optimising currently available interventions

This panel discussion aimed to explore how to ensure that current interventions designed to treat infections are used effectively and responsibly, and that antimicrobial access and provision is appropriate. Optimising antimicrobial use is a core element of global AMR strategies. Within healthcare, antibiotic stewardship is central to optimisation of use, but strategies also need to consider antimicrobial use in the agricultural sector and, in India, over-the-counter access.

Professor Roger Jeffery

Professor of Sociology of South Asia at the University of Edinburgh, suggested that the social sciences had a critical role to play in providing insight into the social norms and behaviours relevant to AMR. The attitudes and actions of many different stakeholders, with widely differing perspectives, have important consequences for the emergence, spread and control of AMR in India.

Professor Jeffery suggested that India could be seen as two separate countries. A 'modern India' with modern structures and ways of working and a 'vernacular India' with different norms and behaviours. Effective management of AMR will require engagement with both these 'Indias'.

While India has a relatively good policy framework, there are significant issues with its implementation. For example, the country has limited numbers of drug inspectors, and Professor Jeffery's studies suggest that implementing the regulations rigorously is not their main priority. India may need to develop 'smarter' regulation that involves different stakeholders as co-producers of regulation, provides more incentives, and lowers the barriers to compliance. Given the many different stakeholders involved, it would also be beneficial to consider integrated regulation across multiple sectors.

Professor Claire Heffernan

Director of the London International Development Centre and Professor of International Development at the Royal Veterinary College, discussed some of the key factors affecting antibiotic use in agriculture in India.

Livestock farming is a major feature of Indian life, and poultry farming in particular is showing significant growth. Antibiotic use is also projected to increase, but headline numbers may hide important details about the types of antibiotic used and how they are used. Climate change is a further factor that may have a significant impact on the livestock sector, adding further complexity.

Many factors currently promote the emergence and spread of AMR in the sector. For example, many farmworkers are poorly educated and contract farmers may have little awareness of the antibiotic content of foodstuffs. Animals are routinely transported live, providing opportunities for dissemination of AMR genes and organisms. Poultry litter is widely used as a fertiliser, providing opportunities for contamination of the food chain.

Nevertheless, regulations can influence practices. India also exports poultry to more than 50 countries, and practices in exporting farms may be very different to ensure compliance with international regulations.

Given the complexity of the situation, a deeper understanding of the economic and social drivers of behaviours and practices that promote the emergence and spread of AMR will be required to underpin policy or other interventions.

Dr Nusrat Shafiq

Professor of Pharmacology at the Postgraduate Institute of Medical Education and Research Center, India, discussed some of the factors influencing the use of and access to antibiotics. Multiple issues, including supply-side factors such as availability of particular drugs, can affect access. Dr Shafiq also drew attention to the growing use of fixed-dose combinations in India, many of them not approved.[28]

The healthcare system in India is highly diverse and segregated between large tertiary hospitals and small clinics, which can both be private or public, making the patient movement between healthcare providers complicated. Inpatient and outpatient numbers have grown substantially over the past decade, although there remain concerns over both the levels of access and the quality of services, as well as subnational inequalities.[29]

Antimicrobial stewardship provides a framework for rationalising antibiotic use while maintaining essential access. Dr Shafiq described a model of antimicrobial stewardship that was tailored to different categories of health facility and based on sharing of good practices. National and institutional guidelines encourage adherence to evidence-based practice, with practical training and education to update clinicians' knowledge and behaviour.

Good antimicrobial stewardship also requires high-quality pharmacy management. It also needs to be complemented by attention to the other elements of healthcare usage that can affect the need for antimicrobials, such as overcrowding and infection control.

Professor Helen Lambert

Professor of Medical Anthropology at the University of Bristol Medical School, discussed the social dimension of AMR, particularly factors affecting the prescribing and use of antibiotics. Public awareness, patient attitudes and healthcare worker behaviour will all have a significant impact on antibiotic use.

The concept of antibiotics as a discrete class is a complex one, suggested Professor Lambert, and the nature of resistance even more so. Moreover, patient knowledge is not necessarily a good predictor of behaviour. Careful attention to language and research into the local meaning of terms such as 'antibiotic' are essential for designing effective public awareness and education campaigns.

The optimal messaging around antibiotic use is also open to question. Recently, messaging has shifted from completing a course of antibiotics to taking antibiotics only when recommended by a physician, although physician decision-making is clearly contributing to antibiotic overuse. Harnessing lay concepts of antibiotics, for example that they are powerful but potentially harmful, could encourage more considered use.

28. McGettigan P *et al.* (2019). Threats to global antimicrobial resistance control: Centrally approved and unapproved antibiotic formulations sold in India. British Journal of Clinical Pharmacology 85(1), 59–70.

29. GBD 2016 Healthcare Access and Quality Collaborators (2018). Measuring performance on the Healthcare Access and Quality Index for 195 countries and territories and selected subnational locations: a systematic analysis from the Global Burden of Disease Study 2016. The Lancet. 391(10136), 2236–2271.

In addition, studies of prescribing behaviour in the UK suggest that miscommunication between doctor and patient can lead doctors to believe that patients are requesting antibiotics.[30] However, the potentially serious consequences of non-use of antibiotics when they are required is a further key driver of 'precautionary prescribing'. Physicians and patients may also not see AMR as their responsibility, while some systems can incentivise the prescription of antibiotics if the prescriber benefits financially.

Out-of-pocket payments account for 65% of health care costs in India and access to high quality medical care is financially limited for lower income households. Restricting over-the-counter purchasing and/or introducing point-of-care diagnostic tests could further reduce access to essential antibiotics for the poor and produce over-prescribing of newer broad-spectrum antibiotics to the wealthy. Policy makers therefore need to consider the potential risks for widening health inequities prior to implementation. To discourage inappropriate antibiotic use, India introduced red-line packaging for antibiotic-containing products as a way to mark and curb the use of medicines, which should be available by prescription only. However, there has been no systematic evaluation of its impact and little evidence that it is making a difference. Examining the implementation and impact of such interventions would provide valuable information to guide future action.

Dr Sanjay Sarin

Country Head, India, and lead for Access Program (Asia Pacific) at the Foundation for Innovative New Diagnostics (FIND), pointed out that diagnostics have been identified as having a central role to play in the control of AMR, for example in the WHO's Global Action Plan.

Diagnostics could perform multiple roles across the patient journey. They have the potential to distinguish viral and bacterial infections and identify the need for antibiotics; they could detect specific infections, informing clinician decision-making; they could characterise the resistance profile of infections; and they are integral to effective surveillance.

Diagnostics therefore can directly benefit patients, have the potential to reduce expenditure by limiting antibiotic use to cases where they are required and by supporting infection control and prevention, and deliver a global good by reducing the risk of AMR development.

FIND is a global product development partnership aiming to increase access to diagnostics. Its global AMR strategy is to promote the development of diagnostic tools to optimise the use of current antimicrobials, to protect newly introduced treatments, and to support surveillance. It has also established a diagnostic use accelerator to promote the implementation of diagnostic testing within a universal health coverage context.

Discussions noted that, while hugely important from a stewardship point of view, use of diagnostics presented significant financial complexities in practice. If paid for by patients, they could represent a further access barrier, and there could be a risk of unnecessary testing if it is seen as economically advantageous to service providers. Diagnostic use will appear more attractive financially when considered within the context of whole-system costing, including treatment costs avoided and potentially the value associated with prevention of AMR. The value of diagnostics to infection prevention and control and to antibiotic stewardship could also be quantified.

It was also recognised that diagnostics could not be considered in isolation; thought should also be given to their integration into clinicians' practices. Practical issues such as turnaround times are therefore critical. Diagnostics also need to be one element of wider decision-support tools, for example on de-escalation of treatment. It was noted that clinical training on the most appropriate use of diagnostic testing would be essential. Public acceptability of diagnostic testing would also need to be considered.

30. Cabral C *et al.* (2014). How communication affects prescription decisions in consultations for acute illness in children: a systematic review and meta-ethnography. BMC Family Practice 51(1), 63.

31. Lucas PJ *et al.* (2015). A systematic review of parent and clinician views and perceptions that influence prescribing decisions in relation to acute childhood infections in primary care. Scandinavian Journal of Primary Health Care 33(1), 11–20.

> Tackling AMR requires collaborations across multiple disciplines and international borders.

7. Spark session collaboration in practice

To encourage discussion of the factors underpinning successful partnerships between the UK and India, the meeting featured short presentations on a range of long-term collaborations between the two countries.

Professor S.S. Vasan

Honorary Visiting Professor of Health Sciences at the University of York and NHS SCW Customer Delivery Director, described his experience of UK–India partnerships, derived from his time as Senior Business Development Manager for Public Health England (PHE). PHE's infectious diseases priorities for 2015–20 include AMR, TB and 'Public Health Emergencies of International Concern'.

PHE has several AMR-related partnerships with renowned Indian institutions such as AIIMS Delhi, JIPMER Puducherry and JNCASR Bengaluru. These include research projects (e.g. on novel antimicrobial compounds, TB and nontuberculous mycobacteria), surveillance (e.g. piloting a Public Health Observatory network modelled on England) and educational initiatives (e.g. repurposing the e-Bug schools resource for India; Newton-Bhabha Fund researcher links workshops on AMR and resistant TB).

Professor Vasan identified several factors crucial to the success of partnerships. These included the need to be flexible and to choose partners wisely with good alignment of interests, and to ensure collaborations are a genuine partnership of equals and the UK can benefit from India's experience with 'frugal innovation' *(jugaad)*. Partnerships always take longer than expected to establish, and it is helpful to take a stepwise approach, for example with memoranda of understanding before formal contracts.

Dr Ghada Zoubiane

Science Lead of the Drug-Resistant Infections Priority Programme at Wellcome, described Wellcome's approach to AMR and examples of its partnerships with India.

Wellcome's 5-year, £175m Drug-Resistant Infections Priority Programme has broad aims, spanning evidence to inform policymaking, new treatments and diagnostics, clinical assessment, and global governance. Scientific initiatives include the global CARB-X collaboration for new product development, which is investing US$500m between 2016 and 2022, and has received multiple expressions of interest from India. It has provided initial funding of US$2.6m to one Indian project, led by BugWorks Research Inc., while the Centre for Cellular and Molecular Platforms has joined the CARB-X Global Accelerator Network.

CARB-X is also in advanced stages of discussion with the Indian Department of Biotechnology (DBT) on a new partnership to advance AMR research in India. Wellcome and DBT have a longstanding partnership, the Wellcome Trust/DBT India Alliance, launched in 2008. The Alliance has had a particular focus on fellowships, which citation analysis suggests are leading to particularly impactful research.

The Alliance will be funded for at least another five years. It will extend its remit to multidisciplinary team-oriented science and clinical research centres as well as fellowships, and AMR-related proposals would be considered for support.

Professor David Graham

Professor of Ecosystems Engineering at the Newcastle University, described lessons learned from his 20 years' experience of collaborations with researchers at the Indian Institute of Technology, Delhi.

With a background in water engineering, his main interest has been in environmental exposures and their health consequences. In 2008, with funding from the Engineering and Physical Sciences Research Council, he was able to establish a collaboration with researchers at the Indian Institute of Technology in Delhi, to adapt approaches used in Latin America to the Indian context. The principal focus has been on human movements and mapping environmental exposures in the Ganges.

This initial collaboration led to a continuing relationship, with exchange of PhD and postdoctoral researchers between sites. Recently, Professor Graham has been part of consortium awarded £17.7m through the Grand Challenges Research Fund for a water security and sustainable development hub, which includes multiple Indian partners. Challenges to collaboration include domestic and international politics, the logistical difficulties associated with distance, and the lack of local support for UK institutions seeking to work in India. Professor Graham suggested there was also a need to engage more with the engineering community, particularly to mitigate the risks of environmental exposures.

Daniel Berman

Lead of the Global Health Team at Nesta, summarised Nesta's work on the Longitude Prize and other AMR-related activities. Nesta is an innovation foundation independent of the UK Government. One of its functions is to organise challenge prizes to promote innovation for socially desirable ends. These include the £10m Longitude Prize, for the development of an affordable and practical point-of-care diagnostic test to reduce antibiotic misuse.

More than 80 teams from 14 countries are competing for the Prize; 21 of these are based in India. Some 32 grants have been awarded to India, and the Indian Government has also contributed funding.

Nesta has established an excellent working relationship with the Biotechnology Industry Research Assistance Council (BIRAC), an Indian state enterprise under the auspices of the DBT to support start-ups and small companies.

Success factors highlighted by Mr Berman included the high-level buy-in in India, close collaboration and joint events, leveraging existing activities, and raising the profile of the initiative. Challenges include competing priorities among Indian partners, differing administrative systems, staff changes, and information flows.

Naomi Beaumont

Senior Portfolio Manager within the Health and Human Behaviour Team at the Economic and Social Research Council, noted that India was a priority country for UK Research and Innovation (UKRI), the umbrella body of the UK Research Councils. Since 2008, a UKRI team has been permanently based in India.

Since 2008, UK funding of more than £300m has been jointly awarded to UK–Indian collaborations, supporting 200 projects across 175 UK and Indian institutions. These include a number of collaborative projects on AMR.

In 2017, AMR was jointly identified as a priority by UKRI and the Indian DBT. A joint strategic group of funders of AMR research was established and published a scoping report in 2017. Funding of up to £30m was committed for interdisciplinary collaborations. To catalyse new collaborations, a sandpit meeting was held in which partners developed initial proposals for research. Four projects were subsequently awarded £10m funding.

Key learning included the importance of developing long-term relationships rather than launching one-off initiatives, and the value of building on partnership work done by others such as the British Council. The experience has also provided important lessons in overcoming the practical barriers to collaboration with international partner organisations.

8. Conclusions

Both the UK and India, in common with the rest of the world, are facing significant AMR challenges. Many of these challenges are similar, meaning there are opportunities to share lessons for progress, but variations in health systems, development status, regulatory environment, and social structures, environmental challenges and agricultural practices mean that significant differences also exist. A number of key themes were identified during the meeting:

Surveillance

England has a comprehensive AMR reporting system, primarily based on reporting of hospital microbiology laboratory data to Public Health England. Data can be viewed at a local level using the 'Fingertips' online tool.[31] However, there are concerns about the timeliness and completeness of data, as well as a lack of standardisation, including across devolved administrations. India has two main networks for monitoring AMR, run by the Indian National Centre for Disease Control and the Indian Council of Medical Research. Contributing centres are required to adhere to standardised practices.

A common concern is the lack of data on community infection, making it difficult to quantify the public health burden of AMR. Lack of linkage to patient data is a further key issue. While it may be tempting to say that surveillance should be strengthened, particularly in India, which has relatively few reporting sites despite its great size, surveillance can be carried out for multiple purposes. It would therefore be important to ensure that surveillance systems are designed to meet specific needs, and in association with clear pathways for use of data.

The AMR ecosystem

The origin and spread of AMR, particularly outside the medical domain including in the environment and community, is not well understood, making it difficult to prioritise interventions. Local studies may offer some general lessons, but many issues may well be highly context-specific. Attempts have been made to identify key knowledge gaps in this area.[32] Potentially, India–UK collaborations could explore some of these knowledge gaps using complementary approaches in different settings.

Reducing the infectious disease burden

Infection prevention would reduce the demand for antimicrobials. Infection prevention and control has a key role to play in controlling healthcare-associated infections, many of which are drug-resistant. In the UK, infection prevention and control played a key role in reducing the MRSA burden in hospitals, although there are concerns it remains too low a priority. Delegates at the meeting suggested that there was considerable room for improvement in infection prevention and control in India. Improvements in basic public health measures, such as improved access to clean water and better sanitation, were also felt to have great potential to reduce the burden of infectious disease and need for antimicrobials.

32. Publis Health England (2019). AMR local indicators. https://fingertips.phe.org.uk/profile/amr-local-indicators

33. Wellcome, US CDC & the UK SIN (2018). Initiatives for Addressing Antimicrobial Resistance in the Environment: Current Situation and Challenges. https://wellcome.ac.uk/sites/default/files/antimicrobial-resistance-environment-report.pdf

Reducing the number of bacterial and viral infections by vaccination programmes further reduces the need for antimicrobials. Vaccine development is an international endeavour to which researchers from the UK and India are both contributing.

Antibiotic stewardship

Effective antibiotic stewardship was seen to be essential in both countries. Many of the challenges are shared, for example the difficulty of influencing physicians' antibiotic-prescribing behaviour in primary care and in acute care facilities. The wider availability of over the counter antibiotics to the public in India presents a major challenge to rational antibiotic use that the UK does not face.

There is scope for comparative studies to examine factors influencing antibiotic-prescribing behaviours in the two countries, to identify common and context-dependent factors. These could inform the development and evaluation of context-sensitive interventions to improve antibiotic-prescribing behaviours. Collaborations could also explore the development and evaluation of new technical tools to support behaviours such as de-escalation in acute care.

Diagnostics

Although widely seen as central to AMR control, diagnostic development and implementation present technical and practical challenges. Again, these are likely to be context-specific, as implementation will depend heavily on local health system processes.

Regulation and enforcement

India has developed a comprehensive AMR national action plan and launched initiatives such as the red-line packaging (which marks prescription only medicines) to discourage indiscriminate use of antibiotics. However, delegates suggested that implementation of the Indian national action plan was limited, and that regulations were poorly enforced. Unlike in the UK, antibiotics, including colistin, are still used as growth promoters in India, although this is under review.

Social and political dimension

AMR has been prioritised in the UK, and the UK has been one of the global leaders in raising the profile of AMR and ensuring it receives political attention. The latest example is the proposed innovative model for financing of antibiotic development. Delegates suggested that India had not treated AMR as such a high priority, as evidenced but the limited progress in implementation of its national action plan. Only one Indian state has developed an AMR action plan, even though states have considerable devolved authority in health.

Public engagement is an important component of AMR prevention strategies. There are already examples of sharing of public communication materials between the UK and India. Comparative studies in India and the UK could explore similarities and differences in antibiotic-related attitudes and behaviours, to underpin the development of resources for public engagement and their tailoring to different cultural settings.

Development of new antibiotics

Development of new antimicrobials is a global enterprise to which researchers and companies from both UK and India can contribute. While innovative market incentivisation initiatives are starting to be developed and implemented, delegates suggested there was scope for further academic and public–private partnerships between the two countries in antimicrobial discovery and development, building on the respective strengths of the two countries.

9. Priority areas for a 2021 follow-up meeting

A number of priorities were identified in the course of the meeting particularly during the breakout sessions, which fall into the eight key themes outlined in the executive summary. These could be reflected on during the next meeting in 2021.

Surveillance

- What are the key data required for effective AMR surveillance and how can they best be collected?
- What should the scope be for an isolate repository or biobank of AMR-related samples?

AMR ecosystem

- What are the key evidence gaps, which are the highest priority to address, and which could be addressed in UK–India comparative studies?

Reducing the infectious disease burden

- What practices could have greatest impact on infection prevention and control and how could they best be implemented?
- How could innovations in genomics and digital technologies be implemented to improve infection prevention and control?

Antibiotic stewardship

- What are the key elements of an antibiotic stewardship programme and how can they be widely implemented?
- How can antibody-prescribing practices be better linked to AMR data?

Diagnostics

- What are the key obstacles to and enablers of diagnostics use in India and the UK?

Regulation and enforcement

- How effective is the AMR policy framework in India and how well is it enforced?

The social dimension: Public, practitioners, policymakers, politicians

- What are the key drivers of practitioner and public antibiotic-related behaviours and how could they be targeted to improve rational use of antibiotics?

Antibiotic development

- What progress has been made in the development of alternative financing models for antibiotic financing and how could India–UK collaboration advance this agenda?
- What are the key bottlenecks in antibiotic discovery and development and how could India–UK collaboration help to overcome them?

Annex 1: Steering Committee

Professor David Heymann CBE FMedSci [Chair], Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine

Professor Jeffery Errington FRS FMedSci, Director of the Centre for Bacterial Cell Biology, Newcastle University

Dr Abdul Ghafur, Coordinator, Chennai declaration on antimicrobial resistance

Professor Alison Holmes FMedSci, Professor of Infectious Diseases, Imperial College London

Dr Shahid Jameel, Chief Executive Officer, Wellcome Trust DBT India Alliance

Professor Asad Khan, Professor of Biotechnology, Aligarh Muslim University

Professor Richard Kock, Professor of Wildlife Health and Emerging Diseases, Royal Veterinary College

Professor Sharon Peacock CBE FMedSci, Honorary Senior Research Fellow, University of Cambridge

Dr Radha Rangarajan, Co-founder and CEO of Vitas Pharma

Professor Balaji Veeraraghavan, Professor and Head of Microbiology, Christian Medical College, Vellore

Annex 2: Meeting agenda

Monday 4 February 2019

08.30-09.00	**Registration**
09.00-09.20	**Welcome and introductions** **Professor Sir Robert Lechler FMedSci**, President of the Academy of Medical Sciences **Professor David Heymann CBE FMedSci**, Professor of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine
09.20-10.00	**The challenge in the UK and India** *Chair: Professor David Heymann CBE FMedSci* **Professor Dame Sally Davies DBE FRS FMedSci**, Chief Medical Officer for England (CMO) and Chief Medical Advisor to the UK Government **Dr Kamini Walia**, Senior Scientist, Epidemiology & Communicable Diseases Division, Indian Council of Medical Research
10.00-10.30	**Refreshment break**

Session 1: The extent of the problem and how to measure progress
Chairs: Professor Alison Holmes FMedSci and Dr Abdul Ghafur

This session will focus on how the levels of AMR are measured in humans, animals and the environment, at global, national, and regional levels.

10.30-10.40	**Dr Kamini Walia**, Senior Scientist, Epidemiology & Communicable Diseases Division, Indian Council of Medical Research
10.40-10.50	**Professor Susanna Dunachie**, Associate Professor and Honorary Consultant in Infectious Diseases and Medical Microbiology, University of Oxford
10.50-11.00	**Professor Ramanan Laxminarayan**, Founder and director of the Center for Disease Dynamics, Economics & Policy (CDDEP), and Senior Research Scholar, Princeton University
11.00-11.10	**Professor Sharon Peacock CBE FMedSci**, Honorary Senior Research Fellow, University of Cambridge
11.10-11.20	**Dr Elizabeth Tayler**, AMR Secretariat, World Health Organization
11.20-12.10	Discussion
12.10-13.15	**Lunch**

Annex 2: Meeting agenda

Session 2: How resistance develops and how to reduce it
Chairs: Professor Asad Khan and Professor Sharon Peacock CBE FMedSci,

This session will focus on what is known about the basic biology of how resistance develops and how this can inform the treatment of animals in food production, prescribing practices, and interactions with the environment.

13.15-13.25	**Dr Abdul Ghafur**, Coordinator, Chennai declaration on antimicrobial resistance
13.25-13.35	**Professor Timothy Walsh**, Professor of Medical Microbiology and Antibiotic Resistance, Cardiff University
13.35-13.45	**Dr Mark Holmes**, Reader in Microbial Genomics & Veterinary Science and Director of Studies in Clinical Veterinary Medicine (Churchill College), University of Cambridge
13.45-13.55	**Professor Sandhya Visweswariah**, Professor, Department of Molecular Reproduction, Development & Genetics and Co-Chair of the Centre for Biosystems Science and Engineering, Indian Institute of Science
13.55-14.05	**Professor Syma Khalid**, Professor of Computational Biophysics, University of Southampton
14.05-15.00	Discussion
15.00-15.30	**Refreshment break**

Session 3: Minimising antimicrobial use while maintaining essential access: preventing infection
Chair: Professor Balaji Veeraraghavan

This session will explore the most effective ways to prevent infections spreading in environmental, animal, and human contexts.

15.30-15.40	**Dr Osman Dar**, Project Director, One Health Project, Centre on Global Health Security at Chatham House
15.40-15.50	**Professor Alison Holmes FMedSci**, Professor of Infectious Diseases, Imperial College London
15.50-16.00	**Dr Rajesh Bhatia**, Regional Technical Adviser on AMR for the Regional Office of Food and Agriculture Organization
16.00-16.10	**Dr Mike Whelan**, Programme Manager, Coalition for Epidemic Preparedness Innovations
16.10-17.15	Discussion
17.15-17.30	**Day One Wrap-up session** Summary of the day and invitation to network during the evening drinks reception **Professor David Heymann CBE FMedSci**
17.30-19.30	**Evening drinks reception**

Annex 2: Meeting agenda

Tuesday 5 February 2019

08.30-09.00	**Registration**
09.00-09.15	**Welcome** Summary of day one and introduction of the aims of day two. **Professor David Heymann CBE FMedSci**

Session 4: Minimising antimicrobial use while maintaining essential access: optimising currently available interventions
Chairs: Dr Radha Rangarajan and Professor Richard Kock

This session will cover how to ensure that current interventions designed to treat infections are used effectively and responsibly, and that antimicrobial access and provision is appropriate.

09.15-09.25	**Professor Roger Jeffery**, Professor of Sociology of South Asia, University of Edinburgh
09.25-09.35	**Professor Claire Heffernan**, Director of the London International Development Centre and Professor of International Development, Royal Veterinary College
09.35-09.45	**Dr Nusrat Shafiq**, Professor of Pharmacology, Postgraduate Institute of Medical Education and Research Center, India
09.45-09.55	**Professor Helen Lambert**, Professor of Medical Anthropology, Department of Population Health Sciences, Bristol Medical School
09.55-10.05	**Dr Sanjay Sarin**, Country Head, India and lead for Access Program (Asia Pacific), Foundation for Innovative New Diagnostics
10.05-11.00	Discussion
11.00-11.30	**Refreshment break**
11.30-12.00	**Keynote presentation** **Lord Jim O'Neill**, Chair, Chatham House

Spark session: Collaboration in practice
Chair: Dr Shahid Jameel

This session will provide an opportunity for invited organisations to share their examples of establishing research collaborations between India and the UK.

12.00-12.10	**Professor S. Vasan**, Honorary Visiting Professor of Health Sciences, University of York and Customer Delivery Director, NHS South Central and West CSU
12.10-12.20	**Dr Ghada Zoubiane**, Science Lead of the Drug-Resistant Infections priority programme, Wellcome
12.20-12.30	**Professor David Graham**, Professor of Ecosystems Engineering, Newcastle University

Annex 2: Meeting agenda

12.30-12.40	**Daniel Berman**, Lead, Global Health Team, Nesta
12.40-12.50	**Naomi Beaumont**, Senior Portfolio manager, Health and Human Behaviour Team, Economic and Social Research Council, UKRI
12.50-14.15	**Lunch and Marketplace**
14.15-15.30	**Breakout session** *Chair: Professor David Heymann CBE FMedSci* **Breakout groups:** **1. Surveillance and monitoring** Facilitators: *Professor Alison Holmes FMedSci and Dr Kamini Walia* **2. Reducing resistance development** Facilitators: *Professor Asad Khan and Professor Sharon Peacock CBE FMedSci* **3. Preventing infection** Facilitators: *Professor Balaji Veeraraghavan and Dr Shahid Jameel* **4. Optimising current interventions** Facilitators: *Dr Radha Rangarajan and Professor Richard Kock* Each group is tasked with identifying the biggest challenges for their topic and discussing what could be achieved in the next two years to progress address the challenge.
15.30-16.45	**Feedback from breakout groups** The rapporteur from each session presents back the challenges and actions for focus identified by each breakout group.
16.45-17.00	**Summary and closing session** Summary of the conference and the areas that have been identified as those that should be focussed on for action before the next conference. **Professor David Heymann CBE FMedSci**
17.00	**Meeting Close**

Annex 3: Summary of breakout group one: Surveillance and monitoring

Discussions noted that surveillance could take many forms. Surveillance could track AMR genes, organisms, diseases and patient cases. The impact of AMR could also be measured in a variety of ways, for example on treatment responses, symptoms, longer-term patient outcomes and economic security, and health system costs. Such considerations were important when deciding surveillance priorities and how to assess the value and impact of surveillance data.

One key role of AMR data is to guide physician clinical decision-making. An understanding of the nature of an infection and its antimicrobial sensitivities should inform the treatment of individual patients. Over longer timescales, information on patterns of AMR should inform healthcare policy and treatment policies at national and ideally also at local levels.

One key goal was suggested to be developing a deeper understanding of the impact of AMR on human health, to provide a better indication of the value of surveillance data. This calls for a greater focus on patient outcomes, rather than just on AMR levels, and the range of impacts on lives and livelihoods.

It was suggested that India conducted relatively little AMR surveillance, which could be leading to important gaps in knowledge. In particular, there was felt to be a paucity of data on AMR and microbiological epidemiology at the community level.

One specific action that could be explored would be the development of a sample repository or biobank, including a representative set of isolates. This could be used in epidemiological studies but could also support new product development, for example of diagnostics.

Annex 4: Summary of breakout group two: Reducing resistance development

Discussions noted that the origins and spread of AMR are highly complex and poorly understood, making it difficult to determine which interventions should be prioritised to prevent the development and spread of resistance.

The One-health perspective was felt to be important, as resistance could develop in environmental as well as medical settings. Currently, the contribution of these different origins is not clear. There are opportunities to use computer modelling to simulate the spread of resistance, and to assess potential strategies to prevent its development and spread.

Work on mechanisms of resistance was also recognised to be important, to underpin the design of new drugs and therapies. It was also important to focus on organisms known to be a threat to human health. Possible approaches to accelerate new drug development included combination therapies and screening of existing drugs to see if any could be repurposed as antimicrobials.

A further challenge was suggested to be the attitudes of clinicians and practices of individual hospitals. For example, it was suggested that hospital waste treatment plants are rarely operational.

One specific idea raised was to focus on an individual hospital, prospectively collecting data on microbial carriage and patient outcomes for all patients. Computer models could then be developed to explore the development and spread of clinically significant resistance, to inform the hospital's antibiotic stewardship and infection control policies.

After piloting, the approach could then be adopted as a routine aspect of hospital operations and rolled out to other facilities.

Annex 5: Summary of breakout group three: Preventing infection

Discussions noted that infections arose in both healthcare facilities and in the community, and had a wide diversity of causes. Furthermore, hospitals vary substantially in India, from large modern facilities to smaller and older hospitals. In addition, access to healthcare facilities is limited across much of rural India.

Improving infection prevention and control in health facilities was felt to be an important priority. There was a strong sense that this should be the responsibility of all healthcare workers. It required political commitment to prioritise, supported by appropriate policies and backed up by implementation.

The community was also seen as a key place where infections arose and many opportunities exist to reduce the burden of infections. This links the AMR agenda to wider development issues such as provision of clean water and sanitation services as well as food safety. Maximising vaccine use was also seen as critical.

Poor sanitation and hygiene practices contribute to the spread of infections. It was suggested that there is an opportunity to engage with communities to understand better how infections arose, and what measures might be put in place to prevent them. This could help to identify hotspots of infection and support the development of targeted interventions.

Although education about infections and infection control were seen as key, it was also felt to be important to understand where people are obtaining information from so the most effective messages and channels of communication can be identified.

Annex 6: Summary of breakout group four: Optimising current interventions

Discussions emphasised the need to consider both supply-side and demand-side issues affecting use of antibiotics. On the demand-side, there was felt to be a need for more community engagement and to understand the contextual factors influencing demand in order to design effective interventions.

On the supply-side, effective antibiotic stewardship was felt to be the key to optimising the use of existing interventions. This needed to cover areas such as appropriate use and adaptive patient management strategies, requiring structural changes in health systems and behaviour change among clinicians.

Mobile phone-based approaches (mhealth) and use of social media were thought to be key ways of improving community engagement and provision of information. However, all potential solutions needed to be appropriate to local contexts and economically viable in real world situations.

If was felt that different strategies were required to address the development of AMR in non-human settings. These also need to consider contextual issues, such as differences between wild animals, companion animals and livestock. Consumers could have considerable leverage on antimicrobial use and could be targeted by interventions. It would also be important to consider the industrial and economic context of food production in the design of interventions to influence practice.

The case was also made that optimising current interventions also needed to consider issues of access. Greater use of diagnostics, for example, could represent a further obstacle to access when healthcare is funded through out-of-pocket expenditure. A range of measures were suggested to improve the availability of novel treatments to improve access, including incentivising production of non-profitable drugs, exploring novel chemistry and innovative drug designs, re-evaluating traditional medicines and host-directed therapies. It was also suggested that universal health coverage could be used as a catalyst to secure additional public funding to improve access to antimicrobials.

Finally, the issue of scalability was also recognised to be important. Potential solutions needed to be feasible at a population level.

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