Addressing antimicrobial resistance with a One Health approach

Symposium report

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Contents

Executive summary....4
Introduction....6
The current status of AMR....8
The need for a One Health approach....11
Raising awareness....13
Reducing the need for antibiotics....16
Optimizing antimicrobial use/stewardship....17
Ensuring compliance with regulations....23
Monitoring and surveillance....25
Research and development (R&D)....30
Conclusions....33
Annexes....34

Executive summary

Antimicrobial resistance (AMR) is one of the greatest threats to human health worldwide. The rise of AMR is making it increasingly difficult to treat many types of infection and threatens to undermine areas of modern medicine that depend on the ability to control infection.

In May 2024, the UK Academy of Medical Sciences and the Indian Council of Medical Research (ICMR) jointly organized a scientific symposium and policy workshop to discuss key AMR issues facing the two countries and how they are being addressed. The symposium followed a scientific symposium on AMR hosted by the UK Academy in London, UK, in 2019.[1]

Globally, the response to AMR challenges is within the context of the WHO Global Action Plan on AMR, with countries, such as India and the UK, having also developed their own National Action Plans for addressing the issue of AMR. These documents provide a common framework for addressing AMR and encompass:

Awareness: Raising awareness of the AMR threat and required action among key professional and public audiences.

Reducing the need for antimicrobials: Intensifying efforts to reduce infection rates, for example through enhanced infection prevention and control (IPC) in health facilities and improved water, sanitation and hygiene (WASH) in community settings.

Optimizing antimicrobial use: Ensuring that antimicrobials are used only when strictly necessary, in both human medicine (through effective antimicrobial stewardship) and in the animal sector.

Monitoring and surveillance: Generating comprehensive and up-to-date data on AMR pathogens and antimicrobial use to guide clinical decision-making, policymaking and effective regulation.

Research and development (R&D): Accelerating the development of new antimicrobials, and ensuring they reach all communities in need and are used appropriately to preserve their potency.

Within these broad areas, the workshop discussed initiatives in the UK and India that are addressing key AMR issues. These provide case studies of the kinds of approaches that could be adopted to tackle AMR challenges in the two countries.

Participants at the workshop concluded that, although many gaps in knowledge persist, we know enough to act on the AMR challenges in the two countries. Outlined in a policy brief, it was agreed that an integrated approach was needed, with action coordinated across the multiple sectors relevant to AMR.[2] A follow-on one-day policy workshop built on discussions of the scientific symposium and developed a set of policy and research, focusing on:

- Embedding AMR as part of the **broader public health agenda**
- Creating **empowered and accountable coordinating structures** spanning human health, animal, and environmental sectors at subnational, national, and international levels

1. Academy of Medical Sciences (2019). *UK-India Symposium on Antimicrobial Resistance.* https://acmedsci.ac.uk/file-download/9496403
2. Academy of Medical Sciences (2024). *Addressing antimicrobial resistance: we know enough to act.* https://acmedsci.ac.uk/file-download/70131697

- Developing a **national regulatory framework** to ensure appropriate use of antimicrobials in humans and animals, supported by effective systems for monitoring of antimicrobial use
- **Empowering primary healthcare and communities** to take increased action against AMR, backed up by education of all stakeholders supporting health and wellbeing at this level
- Strengthening **veterinary support** and the development of coordinated AMR-limiting husbandry practices across various sub-sectors

Four key **knowledge gaps** were also identified, where additional research is needed to support policymaking:

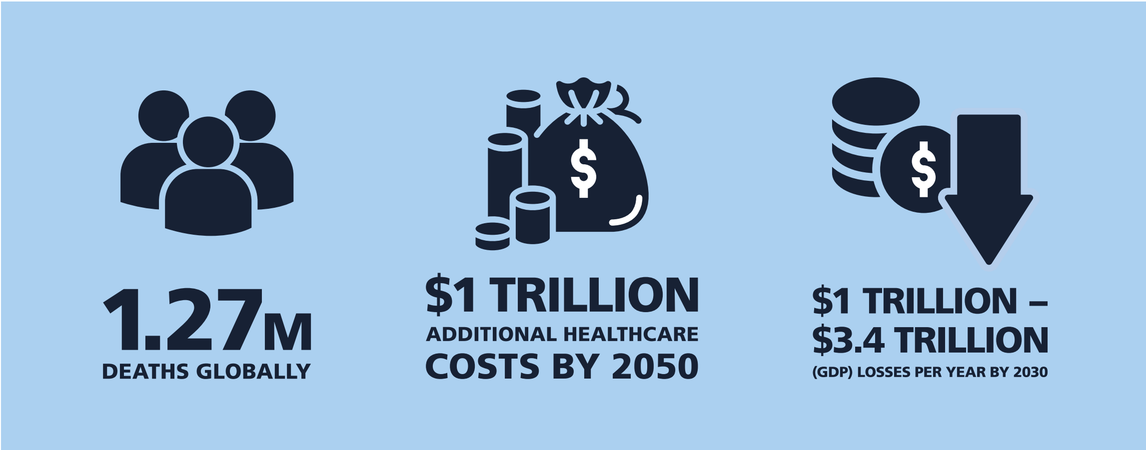
- Key factors underlying the **origins and spread of AMR** within healthcare, community and environmental settings
- The **systems dynamics of AMR control**, spanning all key stakeholders and their interactions
- **Economic modelling** to inform decision-making
- Alternatives to antimicrobial use within **food production**

Whilst each country has its own context-specific AMR challenges, there remains great potential to share experiences and to establish comparative and collaborative studies to provide additional insights into the nature of AMR challenges and the most effective ways of addressing them. Infectious diseases do not respect national borders, so international cooperation and collaboration will be essential to ensure that populations everywhere are protected against the rising tide of drug-resistant infections.

Introduction

Over recent decades, antimicrobial resistance (AMR) has gone from being a theoretical concern to a global public health crisis. In 2019, it is estimated that almost 5 million deaths were associated with bacterial AMR and 1.3 million were directly caused by AMR.[3]

AMR is therefore responsible for more deaths than either HIV/AIDS or malaria. AMR also has a huge economic impact: the World Bank estimates that AMR could lead to an extra US$1 trillion in healthcare costs by 2050 and annual GDP losses of between US$1 trillion and US$3.4 trillion by 2030.[4]



In 2015, the World Health Organization (WHO) developed a **Global Action Plan on AMR,[5]** which identified five priority areas for intervention to combat the emergence and spread of drug-resistant infections:

- Awareness raising
- Surveillance and research
- Prevention of infections to reduce antibiotic use
- Optimizing antimicrobial use in human and animal health
- Development of new interventions

Countries have developed complementary **National Action Plans** to drive action at the national level. Multiple efforts have been made to maintain AMR on the global agenda, including dedicated AMR sessions at the United Nations General Assembly (UNGA), the most recent of which was held in September 2024.

3. Antimicrobial Resistance Collaborators (2022). *Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis.* Lancet **399(10325)**, 629-655.

4. Lahariya AU, Garg R, Singh SK (2024). *Antimicrobial Resistance: An Emerging Global Challenge Waiting for Urgent Actions.* Prev Med Res Rev **1(4)**, 169-171.

5. World Health Organization (2016). *Global action plan on antimicrobial resistance.* https://www.who.int/publications/i/item/9789241509763

In 2019, a joint India–UK scientific symposium on AMR was held in London, UK, supported by the Yusuf and Farida Hamied Foundation.[6] In 2024, the UK Academy partnered with the Indian Council of Medical Research (ICMR) to deliver a follow-up meeting in Delhi, India, to examine progress made since 2019, the current AMR situation in the two countries, and how India and the UK could work together to make further progress. Adopting a One Health perspective, the symposium included representatives from India and the UK working in multiple fields relevant to AMR.

Policy workshop

The one-day policy workshop following the AMR scientific symposium provided an opportunity to reflect on what had been heard and to generate a synthesis of the key issues as priority areas. During breakout group discussions, participants identified a range of policy and research priorities, which demonstrate that we do know enough to act and, given the scale and potential impact of AMR, immediate action is needed, requiring strong political will and investment.[2] A policy brief was published, outlining the areas where action against AMR should be intensified.

6. Academy of Medical Sciences (2019). *UK-India Symposium on Antimicrobial Resistance.* https://acmedsci.ac.uk/file-download/9496403

The current status of AMR

AMR in India: India is severely affected by AMR. AMR is the third leading cause of death in India following cardiovascular disease and chronic respiratory disease, with an estimated 290,000 deaths annually attributed to AMR and more than a million associated with AMR.[7] Drug-resistant *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus and Acinetobacter baumannii* have been associated with more than 100,000 deaths a year.

However, the full extent of the AMR crisis in India is difficult to determine due to limited surveillance data. Nevertheless, the data that are available point to a major AMR crisis. For example, mortality rates for patients with healthcare-acquired infections (HAIs) are 30%–50%. Bloodstream and urinary tract infections (UTIs) are common in critical care units and are often drug-resistant.[8]

A 10-hospital observational study of seven key AMR pathogens found a mortality rate of 13%, but mortality was higher in patients with drug-resistant infections, particularly Gram-negative pathogen infections[9]. During the COVID-19 pandemic, almost half of patients hospitalized with secondary infections in India had drug-resistant infections, and mortality rates hit 66%.[10]

Recent ICMR studies indicate that Gram-negative organisms account for 70%–80% of isolates, with extended-spectrum β-lactamase (ESBL) rates as high as 70% in *E. coli* and *K. pneumoniae*, and carbapenem resistance rates of up to 87% in *A. baumannii*. Drug-resistant infections are associated with substantially higher treatment costs, particularly in private hospitals.

AMR in the UK: AMR is also a significant challenge in the UK. In terms of age-standardized mortality rates, the UK ranked 27th out of 204 countries. However, it has the sixth highest mortality rate out of 24 West European countries.

AMR is the sixth most common cause of death in the UK, surpassing diabetes and kidney diseases but some way behind the top killers in the UK which are cancer and cardiovascular disease. The most common causes of AMR-related deaths are *E. coli, S. aureus, E. faecium* and *Streptococcus pneumoniae*.

AMR and neonatal sepsis: As discussed at the symposium, AMR is having a particular impact on treatment of neonatal sepsis, a major cause of neonatal mortality in low- and middle-income countries (LMICs), with an estimated 6 million cases and 230,000 deaths in 2019.[11] In 2015, the **Young Infants Clinical Signs Study (YICSS)** in six countries, including India, found high levels of antibiotic resistance in community cases of sepsis, with Gram-positive pathogens tending to dominate.[12]

In contrast, the **Delhi Neonatal Infections Study (DeNIS)** identified high rates of drug-resistant Gram-negative infections, among neonates born in hospital[13] and in the community.[14] The causes of early-onset and late-onset sepsis were broadly similar. Comparing DeNIS and data from the UK neonIN surveillance network, the burden of culture-positive sepsis was found to be twice as high in India and the case fatality rate three times higher.

7. Institute of Health Metrics and Evaluation, University of Oxford (2024). The burden of antimicrobial resistance (AMR) in India. https://www.healthdata.org/sites/default/files/2023-09/India.pdf
8. Mathur P *et al.* (2022). *Health-care-associated bloodstream and urinary tract infections in a network of hospitals in India: a multicentre, hospital-based, prospective surveillance study.* Lancet Glob Health **10(9)**, e1317-e1325.
9. Gandra S *et al.* (2019). *The Mortality Burden of Multidrug-resistant Pathogens in India: A Retrospective, Observational Study.* Clin Infect Dis **69(4)**, 563-570.
10. Vijay S *et al.* (2021). Secondary Infections in Hospitalized COVID-19 Patients: Indian Experience. Infect Drug Resist **24(14)**, 1893-1903.
11. Li J, Xiang L, Chen X *et al.* (2023). *Global, regional, and national burden of neonatal sepsis and other neonatal infections, 1990-2019: findings from the Global Burden of Disease Study 2019*. Eur J Pediatr **182(5)**, 2335-2343.
12. Hamer DH, Darmstadt GL, Carlin JB *et al.* (2015). *Etiology of bacteremia in young infants in six countries*. Pediatr Infect Dis J **34(1)**, e1-8.
13. Investigators of the Delhi Neonatal Infection Study (DeNIS) collaboration (2016). *Characterisation and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centres in Delhi, India: a cohort study.* Lancet Glob Health **4(10)**, e752-60.
14. Jajoo M, Manchanda V, Chaurasia S *et al.* (2018). *Alarming rates of antimicrobial resistance and fungal sepsis in outborn neonates in North India*. PLoS One **28;13(6)**, e0180705.

In addition, a study focusing on district hospitals in India also found high levels of Gram-negative infections. However, culture-positive sepsis was less common and case fatality rates, although still high, were lower than in the DeNIS study (36% compared with 50%). The high levels of AMR seen in the DeNIS study are common throughout much of South Asia. For commonly used antibiotics, resistance rates are very high for multiple Gram-negative pathogens.[15]

Globally, there is a sense that AMR is still advancing. In part because of the COVID-19 pandemic, antimicrobial use and the numbers of drug-resistant infections have been increasing. There have been calls for specific targets to galvanize action, such as **'10– 20–30 by 2030' goals** – a 10% reduction in mortality, a 20% reduction in inappropriate human antibiotic use, and a 30% reduction in inappropriate animal antibiotic use.[16]

However, while reducing inappropriate antibiotic use is seen as essential, many populations do not have access to the antibiotics they need. Proponents of a **'just transition' approach** argue that issues such as equity and justice need to be integrated into AMR strategies, with consideration given to trade-offs and how different communities might be affected by AMR control policies[17].

This perspective focuses on the needs and interests of all populations. However, it is equally crucial to consider the long-term consequences for future generations. AMR must therefore be addressed within the broader framework of the **sustainable development** agenda. This issue is particularly significant for India, a middle-income country undergoing rapid economic and social transformation. The developmental route chosen by India will have far-reaching implications, not only for its citizens but for the global community as well (Box 1).

1 India and AMR in the global context

Sunita Narain, Director General of the Centre for Science and Environment, and a member of the Global Leaders Group on AMR, outlined some of the key strategic issues facing India in its battle against AMR.

Ms Narain argued strongly that AMR needed to be considered within a broad holistic context, encompassing environmental and One Health dimensions. India needs to ensure more equitable access to antibiotics and achieve food security for its large and growing population, but these objectives cannot be pursued at all costs: the potential negative consequences of possible policies and actions also need to be carefully considered.

In particular, striving for development can come at the cost of damage to the environment. Yet, Ms Narain argued, India does not have the resources to spend on remediation. Prevention of environmental contamination is therefore critical. Similarly, it cannot afford excessive waste, but contamination can be an obstacle to recycling and reuse. Furthermore, given its middle-income status, India can ill-afford the substantial additional costs of healthcare related to drug-resistant infections.

15. Chaurasia S, Sivanandan S, Agarwal R *et al.* (2019). *Neonatal sepsis in South Asia: huge burden and spiralling antimicrobial resistance.* BMJ **22**, 364:k5314.
16. Mendelson M, Lewnard JA, Sharland M *et al.* (2024). *Ensuring progress on sustainable access to effective antibiotics at the 2024 UN General Assembly: a target-based approach.* Lancet **403(10443)**, 2551-2564.
17. Just Transitions for AMR Working Group (2024). *A just transition for antimicrobial resistance: planning for an equitable and sustainable future with antimicrobial resistance.* Lancet **403(10446)**, 2766-2767.

In India and globally, trade-offs and difficult decisions have to be made. Conservation of existing antibiotic resources is critical, which means restricting usage, and ideally eliminating use in the food sector. However, the challenges to food security many countries face must also be acknowledged. India does not yet have a fully industrialized farming sector and must decide what path it wants to take into the future.

Similarly, protecting the environment is a critical goal, but it is also necessary to consider possible impacts of environmental regulation on health facilities and pharmaceutical manufacturing. Technological and other solutions will be needed to ensure that health and medicine needs can still be met while the environment is protected.

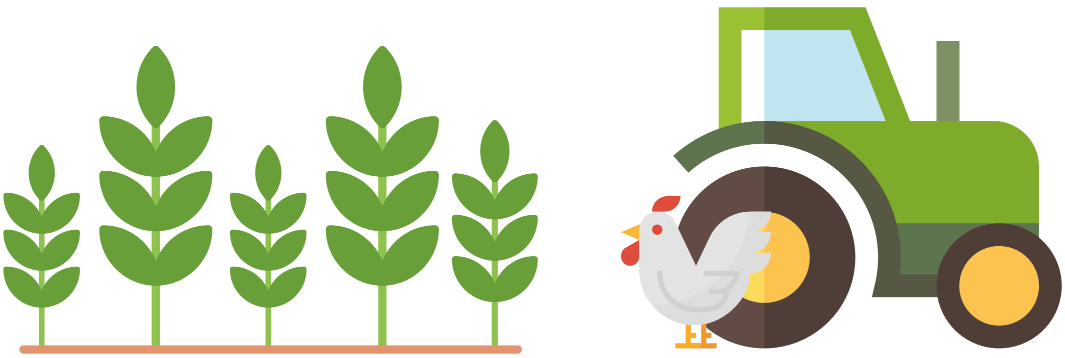
Ultimately, prevention of infectious disease is the ideal solution, Ms Narain suggested. Enhanced access to clean water, better sanitation systems, and more hygienic food production systems will all help to reduce the need for antimicrobials.

The need for a One Health approach

The workshop adopted a One Health approach, in recognition of the fact that solutions to the AMR crisis will require action across a range of sectors, including human health, animal health and food production, and the environment.

Pathogens' exposure to antibiotics, the key driver of AMR, depends fundamentally on their use within **human medicine**. Global and national policies stress the importance of **antibiotic stewardship** to ensure appropriate use of antibiotics in healthcare systems.

However, there are additional ways through which pathogens are exposed to antibiotics. For example, antibiotics are widely used in **veterinary medicine**, as well as in **food production** – not just to treat infections in food animals but also as growth promoters and to prevent infections. There are fears that this use will promote the emergence of AMR genes and pathogens that are then transmitted to people.



In addition, agricultural use of antibiotics can lead to **environmental contamination**, again raising the risk of selection for resistant pathogens and spread of AMR genes between bacteria. **Antibiotic manufacturing processes** are a further way in which antibiotic residues may find their way into the environment. Although the extent to which these non-medical factors contribute to the global AMR crisis is not fully understood, there is considerable evidence that activities in these areas can pose a threat to human health.

The One Health perspective also emphasizes the importance of taking a **systems-wide perspective** on the AMR threat. Antimicrobial use takes place within a complex system with multiple interacting stakeholders. Interventions targeting isolated aspects of these systems may not ultimately be effective because they miss key drivers of antimicrobial use, because the system as a whole adjusts in response to an intervention, negating its effects, or because of unexpected unintended consequences. The Indian state of Kerala has developed an integrated One Health-based approach to address the AMR crisis (Box 2), exemplifying the systems-wide approach.

Systems-based approaches can be extremely useful in mapping interactions between key stakeholders and how they might be affected by particular policies or other interventions, based on an understanding of their motivations and behaviors. Such exercises can therefore be a valuable tool for identifying where and how to intervene in order to achieve desired ends while minimizing the risk of unintended consequences.

2 Kerala State: a One Health AMR strategy

As summarized by Dr Aravind Reghukumaar, Government Medical College, Thiruvananthapuram, Kerala, the Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) is based on an integrated One Health approach.

Launched in 2018, KARSAP was the first sub-national AMR action plan developed in India. Jointly developed by the Departments of Agriculture Development and Farmers' Welfare, Animal Husbandry, Environment, Fisheries, and Health and Family Welfare, it adopted the One Health approach to provide a strategic framework for various AMR-related activities being undertaken in the state.

It integrated a strong public engagement strand, to establish a culture of 'antibiotic literacy' across the whole state. Target groups included students and teachers, healthcare workers, pharmacists, farmers, and the wider public. Key messages included the importance of having access to antibiotic-free food and water, and of dispensing and using antibiotics responsibly. Importantly, media in the state played a key role in communicating AMR-related messages and explaining the rationale behind policy changes.

The Kerala Antimicrobial Resistance Surveillance Network (KARS-NET) was established in 2019. It now collects standardized data from multiple sites across the state to provide insights into the current state of AMR. The state has also pioneered the use of 'antibiograms' at the facility, district and state level, which detail patterns of antimicrobial susceptibility for different pathogens.

Implementation of KARSAP has been based on a series of specific one-, three- and five-year targets. Progress towards these targets is monitored on a three-monthly basis. Focal points have responsibility for different areas of the strategy and different communities.

All health centers are being converted into 'antibiotic-smart' facilities that follow good stewardship practices, while a crackdown has been organized on shops continuing to sell antibiotics over the counter. Use of antibiotics in different WHO 'AWaRe' categories is being monitored following implementation of new reporting tools.

KARSAP is one of three related state-wide projects, the other two focusing on One Health more broadly and the microbiome.

Raising awareness

Action against AMR will only be possible with widespread awareness of the threat it poses and how it can be tackled. Notably, the battle against AMR requires all to contribute, emphasizing the need for comprehensive awareness-raising across multiple public and professional audiences, including those outside healthcare.

AMR presents a set of unique challenges for communication. It can be a difficult concept to communicate to general audiences, and may seem remote and nebulous to many, particularly when compared with specific and immediate health threats, such as common infections.

Communicating the causes of AMR can add further complexity. By contrast, simple and clear messages can be sent on what actions to take, although the rationale for these actions is often dependent on an understanding of the causes of AMR and the consequences of its spread.

In India, multiple activities have been undertaken to raise awareness of AMR among different professional groups and the public. These have leveraged global initiatives such as **World AMR Awareness Week** and **Go Blue Day**. Other efforts have targeted school children and key groups such as medical students and professional associations. The **Superheroes Against Superbugs** initiative, for example, is using the power of creative approaches to engage with young audiences (Box 3), while an innovative evaluation of a local radio-based public health intervention illustrates how researchers can help to demonstrate the value of public-facing activities (Box 4).

3 Superheroes Against Superbugs

Dr Sarah Iqbal described how the Superheroes Against Superbugs initiative has taken a creative approach to engage young people on AMR issues.

Superheroes Against Superbugs aims to raise AMR awareness among younger audiences, using a range of creative approaches. Its key message is that everyone has a role to play in combating AMR, with young people ideally placed to be 'agents of change' within their social groups and wider communities.

Superheroes Against Superbugs aims to make learning about AMR fun. It organizes a range of events, including informational sessions, discussions with experts, and hands-on activities and games. It also makes educational materials available on its website and via social media. By April 2024 it had reached more than 36,000 people across India.

It adopts a creative approach, organizing role play and drama sessions, games and activities, as well as creative competitions and case study discussions. Its online resources, including comics and colorful graphics-led materials, are designed to be fun and engaging.

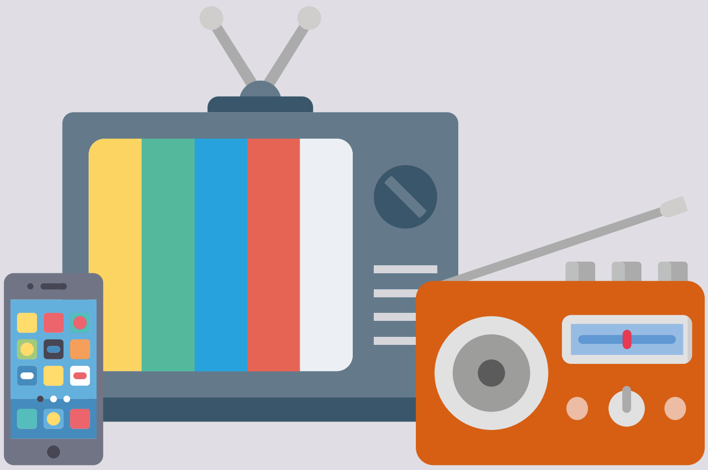
Public murals have been co-created with young people in Hyderabad and New Delhi. The project has also worked with writers, who were introduced to the topic and came up with a range of outputs in response, from poems to new fiction.

AMR is a complex topic that can seem daunting to communicate. The Superheroes Against Superbugs project has learned the importance of using non-technical terms, focusing on graphics, interactive content and storytelling to engage young people, building partnerships and encouraging co-creation, and targeting approaches according to local contexts and audiences.

4 Using saturation media to combat AMR

Devika Bahl, Executive Producer at Development Media International (DMI), discussed how clinical trial methodologies can be applied to evaluate public communication initiatives.

DMI uses a range of communications tools, including television, radio and mobile content, to share messages around health topics. It has also incorporated rigorous testing of its material. In Burkina Faso, for example, it organized a cluster randomized trial to evaluate an intervention based on the use of local FM radio stations to spread messages around treatment-seeking for malaria, diarrhea and pneumonia.



With seven partner local radio stations, 10 short dramatic spots and five interactive shows were broadcasted each week, in six languages over nearly three years. The effects seen in the areas reached by the partner radio stations were compared with those in control zones. In the targeted areas, relative to the control arm, malaria consultations increased by 56%, pneumonia consultations by 39% and diarrhea consultations by 73%. This led to an estimated 7% drop in mortality per year and 3000 lives saved over the three years of the programme[18]. An economic analysis suggests that the campaign would be highly cost-effective[19], comparing favorably with most public health interventions.

DMI adopts a systematic approach, with co-creation of content with local writing teams, iterative prototyping and testing, delivery in partnership with ministries of health, and intensive distribution ('saturation') with media partners. It attempts to develop simple-to-understand messages and calls to action. For AMR, this approach could be applied to both the general public and health worker audiences.

18. Murray J *et al.* (2018). *Modelling the effect of a mass radio campaign on child mortality using facility utilisation data and the Lives Saved Tool (LiST): findings from a cluster randomised trial in Burkina Faso.* BMJ Glob Health **16;3(4)**, e000808.
19. Head R *et al.* (2015). *Can mass media interventions reduce child mortality?* Lancet **4;386(9988)**, 97-100.

Reducing the need for antibiotics

In human medicine, antibiotics are primarily used to treat infections. Preventing infections will therefore lead to reduced antibiotic use and a lower risk of resistance. There are multiple approaches that can be applied to reduce infection rates:

Vaccination: Vaccination is a highly effective approach for preventing infection and the need for antibiotics.[20] Since antibiotics are commonly used to treat viral infections, even preventing viral infections through vaccination will have a positive impact on antibiotic use. Priorities include increasing population coverage of existing vaccines and accelerating the development of vaccines against key AMR pathogens. Unfortunately, these are likely to be the most challenging targets for new vaccine development. A complementary approach is to use vaccination to target resistance mechanisms or to reduce disease severity, reducing demand for antibiotic treatments.

Infection prevention and control (IPC): Clinical settings create environments in which particular strains of bacterial pathogens can thrive, while many patients are in a vulnerable state and susceptible to infection. IPC is therefore a core aspect of clinical practice, and needs to be fully integrated into everyday activities. However, there remains scope to improve routine IPC practice among health workers, and to strengthen health institutional commitments to IPC.

Improved water, sanitation and hygiene (WASH): Transmission of infectious disease in the community is facilitated by factors such as bacterial contamination of water sources, poor hand hygiene, and ineffective disposal of waste materials. The food chain provides an additional route through which disease can spread in the absence of good hygiene practices. These issues are of particular importance to disadvantaged communities in India. India has made substantial access in improving access to safe drinking water, which exceeded 95% of the population by 2021, although gaps remain in rural areas, while the national Swachh Bharat Mission is driving improvements in sanitation.

The **public health value** of these preventive interventions is already widely recognized. The AMR dimension reinforces the need for such interventions, strengthening the case for additional investment in prevention. AMR prevention generates an additional set of benefits, in terms of health gains and economic benefits from reduced treatment costs and enhanced productivity as people are less likely to be economically inactive due to infection or caring duties.

The same principles apply in the **veterinary sector**. Preventing infections in livestock will reduce the need for antimicrobial use. However, intensive husbandry practices, such as high-density housing and poor waste management, favor the spread of infections. As antibiotics are relatively cheap, they are often used as a substitute for infection control measures, such as vaccination or modifications to husbandry practices that could impact productivity.

20. Wellcome Trust & The Boston Consulting Group (2021). *Vaccines to tackle drug resistant infections*. https://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf

Optimizing antimicrobial use/stewardship

Overuse of antimicrobials is the main driver of resistance. Some factors underlying overuse are common across Indian and UK settings, while others are more context-specific.

The availability of **over-the-counter antibiotics** has been a major challenge in India, though greater efforts are being made to enforce regulations on prescription medicines (which include antibiotics) to reduce indiscriminate use. In Kerala, for example, pharmacists selling antibiotics without a prescription risk having their licenses cancelled. Other challenges facing India include the availability of **counterfeit or poor-quality drugs** and use of **inappropriate fixed-dose combinations** (FDCs). Multiple FDCs have been banned in India, but many others remain freely available, and in the absence of diagnostic certainty their broad-spectrum effects may be seen as an advantage.[21] India has traditionally had a major problem with counterfeit and substandard drugs, including antibiotics.[22]

While the UK faces fewer challenges than those described above due to its strong regulatory systems, other challenges related to public awareness and patient behavior still contribute to the overuse of antimicrobials.[23] One common cause of overuse is inappropriate patient expectations. Many patients consider antibiotics a quick solution for illnesses not directly linked to bacterial infections, such as colds, flu, or other viral infections. This can put pressure on healthcare professionals. Another challenge lies in unclear guidance or misinterpretation of usage guidelines by patients. In some cases, the guidelines provided by GPs, the product information, or the NHS website are inconsistent, leading to confusion among patients. In other cases, patients might take double the dose as a solution to missing a dose.

However, perhaps the key driver of antimicrobial overuse in both countries is the prescribing practice, reflecting the critical role of physicians as gatekeepers to antibiotics. Prescribing behaviors are influenced by multiple factors, including physicians' understanding of AMR risks. Typically, diagnostic uncertainty promotes 'just in case' prescribing. Health system financing mechanisms can also create incentives to prescribe antibiotics (Box 5).

21. Sulis G *et al.* (2022). *India's ban on antimicrobial fixed-dose combinations: winning the battle, losing the war?* J Pharm Policy Pract **(1):33**.
22. Kelesidis T, Falagas ME (2015). *Substandard/counterfeit antimicrobial drugs.* Clin Microbiol Rev **28**, 443–64.
23. Olga Poluektova *et al.* (2023). *A scoping review and behavioural analysis of factors underlying overuse of antimicrobials.* JAC-Antimicrobial Resistance **5(3)**.

5 Drivers of human antibiotic use

As discussed by Professor Helen Lambert, University of Bristol, UK, qualitative studies have provided deep insight into the underlying reasons why physicians prescribe antibiotics and consumers use them.

Globally, approximately 80% of antibiotic use takes place in primary healthcare and community settings, where control of use is arguably more difficult than in hospitals. Antibiotic prescribing is rarely based on microbiological confirmation of infection or any other testing – symptom-based treatment is the norm.

Multiple studies in different settings have explored the drivers of **antibiotic prescribing**. For physicians, a key issue is **diagnostic uncertainty**, leading to 'just in case' prescribing. Physicians may also believe that patients expect to receive a prescription for antibiotics. In addition, **short consultation times** provide little opportunity for dialogue between provider and patient about past antibiotic use and current options.[24]

Another potential issue is the existence of **incentives** for physicians to prescribe antibiotics. Depending on the health system, physicians may gain income from administering intravenous or injectable antibiotics or from pharmacies to which they direct patients, or may fear they will lose patients to competitors if they do not prescribe antibiotics themselves.

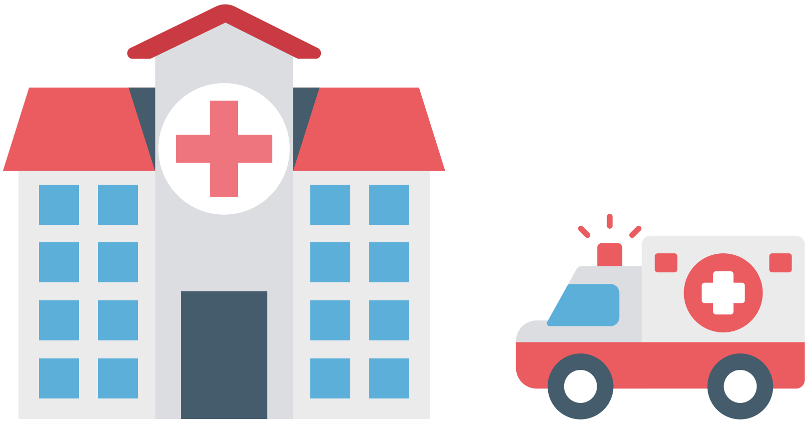
Multiple factors affect **antibiotic consumption**. Despite having a higher disease burden, per capita antibiotic use is lower in India than in the UK. In part, this likely reflects the greater reliance on out-of-pocket expenditure on healthcare in India, which can restrict access to treatments. Financial considerations can also affect which antibiotics people can access and the length of the treatment course, which may reflect what they can afford rather than what is most appropriate.

Consumers' understanding of the role of antibiotics can vary greatly, depending on local conceptions of the causes of ill-health. In some settings, for example, they are often seen as medicine to treat inflammation.[25] Generally, in LMICs, antibiotics are seen as powerful and effective medications, with frequent prescribing by physicians seen as a sign of their appropriateness for treating common symptoms. Difficulties in accessing health services and poor experiences of care can lead people to seek out antibiotics from community vendors without a prescription.[26]

Over prescribing by physicians is seen in both the UK and India. In the UK, antibiotic prescribing declined gradually between 2014 and 2019, but has since increased, particularly in primary care.[27] The numbers of drug-resistant infections have also been rising in the UK.[28]

A key challenge in both settings is the lack of diagnostic information at the time of prescribing. Microbiology laboratories can support clinical decision-making within hospitals. In India, the integrated public health laboratory initiative (Box 6) is helping to improve microbiological capacity at the district hospital level.

24. Lambert H *et al.* (2023). *Prevalence, drivers and surveillance of antibiotic resistance and antibiotic use in rural China: Interdisciplinary study.* PLOS Glob Public Health **3(8)**, e0001232.
25. Alhusein N *et al.* (2024). *The unseen use of antimicrobials: Drivers of human antibiotic use in a community in Thailand and implications for surveillance.* Glob Public Health **19(1)**, 2298940.
26. Cabral C, *et al.* (2024). *Influences on use of antibiotics without prescription by the public in low- and middle-income countries: a systematic review and synthesis of qualitative evidence*, JAC-Antimicrobial Resistance **6(5)**.
27. Nuffield Trust (2024). *Antibiotic Prescribing.* https://www.nuffieldtrust.org.uk/resource/antibiotic-prescribing
28. Lipanovic D (2023). *Antibiotic prescribing increases by more than 8% in one year.* https://pharmaceutical-journal.com/article/news/antibiotic-prescribing-increases-by-more-than-8-in-one-year



6 Integrated public health laboratories

Dr Ranjan Kumar Choudhury, National Health Systems Resource Centre, India, summarized how integrated public health laboratories, currently being created at India's district hospitals, will provide a key resource to support AMR-related activities within hospitals.

District hospitals are a core element of the health system in India. They provide an extensive range of health services, backed up by laboratory testing to support diagnosis and patient monitoring.

The integrated public health laboratory initiative is bringing together the full range of analytical approaches under one roof, to raise standards and increase efficiency. It is integrating activities that were previously part of separate vertical programs, creating a common physical space, with shared technological infrastructure and specialist support staff, and a single integrated laboratory information management system for data management. The laboratories have a strong focus on IPC.

Under the Pradhan Mantri Ayushman Bharat Health Infrastructure Mission (PM-ABHIM) initiative, a national initiative to strengthen healthcare infrastructure in India, integrated public health laboratories are being established in 730 districts between 2021/22 and 2025/26.

The laboratories will provide a core resource to support effective antimicrobial stewardship in district hospitals by providing timely access to high-quality diagnostic and antimicrobial sensitivity data on hospital data. They will also support monitoring of hospital-acquired infections and the effectiveness of hospital IPC programs.

One of the biggest impacts could be made by the greater availability of **rapid diagnostic tests**, both to identify causative pathogens and to determine their antibiotic susceptibility. In 2024, the **Longitude Prize on AMR**, organized by NESTA in the UK, was awarded to Sysmex Astrego for its PA-100 AST System, which can detect UTIs within 15 minutes and antibiotic susceptibility within 45 minutes.[29] As well as the technical challenges associated with product development, however, there will also be a need to ensure that the technology is affordable for use in a wide range of settings.

29. Challenge Works (2024) *Winners of the £8m Longitude Prize on AMR announced.* https://challengeworks.org/news/winners-longitude-prize-amr/

Appropriate use of antibiotics is the goal of **antibiotic stewardship programs**. India's National Action Plan for AMR included antimicrobial stewardship as a key strategy to optimize the use of antimicrobial drugs. Although the country does not have a formal antimicrobial stewardship plan, studies have shown that stewardship programs are feasible to implement within tertiary hospitals.[30]

Optimizing the use of antimicrobials is one of four key themes of the UK's updated National Action Plan for AMR for 2024–2029.[31] The Plan defines stewardship very broadly, covering antimicrobial use in human medicine and agriculture. Three commitments in this area cover support for clinical decision-making, facilitating appropriate prescribing, and use of behavior interventions.

Stewardship programs are particularly applicable at the institutional level. Tools such as the **Global Antimicrobial Stewardship Accreditation Scheme** (GAMSAS) can help organizations benchmark their stewardship programs and establish stewardship development plans (Box 7).

7 Promoting and recognizing antibiotic stewardship

Dr David Jenkins, Past President of the British Society for Antimicrobial Chemotherapy (BSAC), described how BSAC's Global Antimicrobial Stewardship Accreditation Scheme (GAMSAS) can enhance institutions' stewardship practices.

The efficacy of antimicrobials depends on the enduring susceptibility of target pathogens. However, the use of antimicrobials tends to select resistant strains of micro-organisms. Because resistant strains spread between people, treatment of one patient can compromise the effectiveness of antimicrobials in others. Consequently, the enduring value of antimicrobials requires a healthcare organizational stewardship approach that parallels other successful commons resource management systems, the key features of which were identified by the Nobel Prize-winning economist Elinor Ostrom. The social-ecological systems described by Ostrom provide an intellectual underpinning for antimicrobial stewardship, and also show how infection prevention can be integrated into antimicrobial stewardship to reduce infections caused by resistant pathogens.

There is no single approach to antimicrobial stewardship and some of the diversity in antimicrobial stewardship practice is justified by contextual differences. However, there are also substantial unwarranted differences that lead to less effective treatment and poorer patient outcomes. The British Society for Antimicrobial Chemotherapy (BSA[32]), to help healthcare institutions build and sustain effective stewardship programs. It provides an independent benchmarking of an institution's policies and practices, with institutions being recognized at one of three levels depending on their stewardship capacities. Organizations with a track record of supporting other healthcare systems may qualify for an additional Centre of Excellence award.

In addition to key stewardship areas including governance, education and training, audit and surveillance, and quality improvement initiatives, GAMSAS reviews infection prevention practice and microbiology laboratory capacity, two essential supports for good antimicrobial stewardship.

30. Vijay S *et al.* (2023). *Hospital-based antimicrobial stewardship, India.* Bull World Health Organ **101(1)**, 20-27A.
31. UK Government (2024). *Confronting antimicrobial resistance 2024 to 2029.* UK 5-year action plan for antimicrobial resistance 2024 to 2029 - GOV.UK
32. BSAC. *Global Antimicrobial Stewardship Accreditation Scheme.* https://ams-accredit.com

GAMSAS outputs include a report on organizational strengths and areas for improvement, as well as sources of educational and training material to support improvement. Additionally, the GAMSAS program aims to identify barriers to improving stewardship practice across healthcare systems, providing insights to governments and other healthcare payers on how to ensure best value from commissioned services.

Although GAMSAS has only been running since 2023, it has already been adopted by multiple institutions in the UK and internationally[33] and has featured in the UK AMR National Action Plan.[34]

Antibiotic use in the **veterinary sector** – which accounts for 70% of global antibiotic use – presents an additional set of challenges. Antibiotics are more often used in food production on a mass scale, to promote growth or to prevent infections, rather than to treat individual animals. Globally, antibiotic use for growth promotion is being banned in an increasing number of jurisdictions – according to the latest World Organization for Animal Health (WOAH) report, more than 100 countries have discontinued antibiotic use for growth promotion, but the practice continues in 36 countries.[35]

Moreover, antibiotics are still used extensively for **disease prevention**, the need for which is often debatable. Preventive use of antibiotics in food animals was banned by the EU in 2022 and 'routine use' of antibiotics was outlawed by the UK in 2024.

The food animal sector in India is large and diverse, from smallholdings to industry-scale intensive farming, and encompasses a large aquaculture sector. In India, use of antibiotics as growth promoters is not yet prohibited. In addition, preventive use of antibiotics is often a convenient substitute for other practices that could limit infection, and is rarely essential for true veterinary reasons. The Ministry of Health and Family Welfare has banned colistin use in food animals, although the degree of enforcement is unclear and other critically important antibiotics are still routinely used in the sector.

Similarly, the Food Safety and Standards Authority of India (FSSAI) has established standards for residual antibiotic levels in food from animals, but again it is unclear how well these are enforced. Animal waste has great potential to be used as a natural fertilizer, but also raises the risk of environmental contamination with antibiotic residues. Current guidance on waste management has minimal focus on AMR issues.

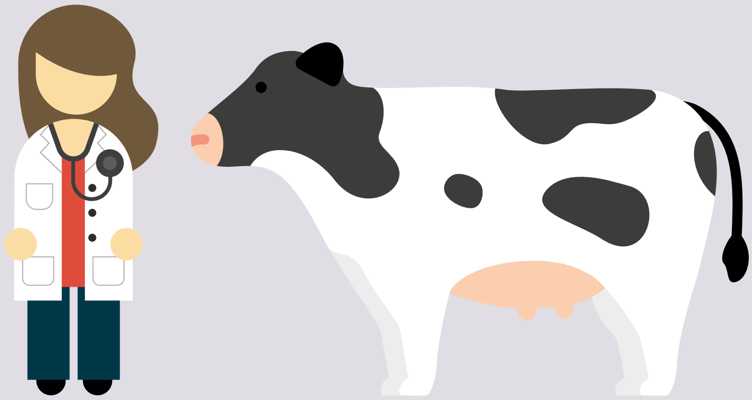
Among the obstacles to reduced antimicrobial use in the sector are a **lack of awareness** among farmers or others in the supply chain about AMR and concerns about the **economic impact** of phasing out antimicrobial use. More research is needed to identify alternative approaches to mitigate the potential risk of reduced productivity or increased treatment costs. An innovative project organized by the National Dairy Council, for example, has demonstrated that use of ethnoveterinary products instead of antibiotics can actually be financially advantageous (Box 8). **A lack of data on antimicrobial use** in the sector is a further important issue, and improved monitoring will be essential if greater efforts are made to regulate antimicrobial use in the sector.

33. Gulumbe BH *et al.* (2024). *Closing the antimicrobial stewardship gap - a call for LMICs to embrace the global antimicrobial stewardship accreditation scheme.* Antimicrob Resist Infect Control **13(1)**, 19.
34. UK Government (2024). *Confronting antimicrobial resistance 2024 to 2029.* UK 5-year action plan for antimicrobial resistance 2024 to 2029 - GOV.UK
35. World Organization for Animal Health (2024). *Annual Report on Antimicrobial Agents Intended for Use in Animals.* https://www.woah.org/app/uploads/2024/05/woah-amu-report-2024-final.pdf

8 Use of ethnoveterinary medicines in the Indian dairy sector[36]

Dr Rajeshwari Sinha, Centre for Science and Environment (CSE), India, highlighted how alternatives to antibiotics may be better for consumers and producers.

Intensive food production systems create conditions for the emergence and spread of AMR. Animals are typically kept in confined spaces that favor the spread of disease, requiring the misuse and overuse of antibiotics for disease prevention and growth promotion, apart from therapeutic options.



Reducing the use of antibiotics will depend on the introduction of alternative products and practices that are not economically disadvantageous. One example of innovative practice is the use of ethnoveterinary medicines, medicinal products obtained from plants.

In a large-scale project led by the National Dairy Development Board, which saw a wide variety of disease conditions in the dairy sector treated with ethnoveterinary medicines (970,000 cases in total), the overall cure rate was 81% (out of this, 3.3 lakh cases of mastitis were treated, with a 78% cure rate.). The project includes additional aspects such as awareness generation, training and demonstration, and monitoring.

In addition, ethnoveterinary medicine use was associated with a significant reduction in the number of veterinary visits over three years and a substantial cut in the money that producers spent on antibiotics.

Hence, the holistic approach helped farmers bring down their dependence on veterinarians, saved cost of treatment, and reduced productivity losses, but also ensured safe food for consumers among other benefits.

36. Centre for Science and Environment (2022). *Ethnoveterinary Medicine: An alternative to antibiotics for the dairy sector* https://www.cseindia.org/ethnoveterinary-medicine-11496

Ensuring compliance with regulations

The battle against AMR requires a strong policy framework on multiple fronts, in support of goals set out in National Action Plans. However, it was also recognized at the symposium that such a policy framework needs to be backed up by effective monitoring, compliance and enforcement mechanisms.

These mechanisms will be different in different sectors. For the human health sector, the key challenge relates to antibiotic usage. In the UK, this is driven by the epidemiology of infectious disease and the behavior of individual clinicians, and is the target of **stewardship strategies**. In India, there is the additional need to ensure enforcement of regulations on the sale of **over-the-counter antibiotics**. In a limited number of cases, through the **'Pharmacy First' initiative**, antibiotics are now available in the UK directly from pharmacists.[37] Concerns have been expressed that this could lead to increased antibiotic use. Pharmacy prescribing of antibiotics is being carefully monitored.

Within the **animal sector**, regulations on antimicrobial use are evolving. The use of antimicrobials for growth promotion was banned in the UK in 2006. In the UK, new **Veterinary Medicines Regulations** were introduced in May 2024, outlawing routine antimicrobial use for prevention and as an alternative to good animal husbandry practices.[38] However, there are concerns that these regulations do not go as far as those previously introduced by the EU.[39] Antibiotic use is dependent on the activities of a complex set of stakeholders, including animal producers, industry bodies, veterinary professionals and their oversight bodies, including the Royal College of Veterinary Surgeons. Regulations fall within the responsibility of the Department for Food, Environment & Rural Affairs (DEFRA). The regulatory framework in this sector in India is less well developed.

A further topic discussed at the workshop was the **manufacturing of antibiotics**. Inadequate waste disposal systems can lead to the release of antibiotic residues into the environment, contributing to the environmental pressures selecting for antibiotic resistance in environmental microorganisms, including human pathogens. Discussions at the workshop suggested that regulation in this area is weak, echoing the conclusion of a recent UN Environmental Programme report on AMR which suggested that "the pharmaceutical industry is considered largely an unregulated sector in terms of environmental pollution".[40] High levels of antimicrobial residues, and drug-resistant microbes, have been identified close to manufacturing sites in India.[41]

One approach to address this issue is the development of a **'kitemark'** to certificate good manufacturing processes, as developed by the **British Standards Institute** (BSI, Box 9). Stakeholders that procure antibiotics can leverage their purchasing power to promote the adoption of good manufacturing processes, by requiring suppliers to have BSI or similar certification. Challenges include the need to consider the global nature of antibiotic manufacturing and the potential for regulations to affect the commercial viability of antibiotic-manufacturing companies and hence antibiotic availability[42].

37. UK Government (2024). *Pharmacy First: what you need to know.* https://healthmedia.blog.gov.uk/2024/02/01/pharmacy-first-what-you-need-to-know/
38. UK Government (2024). *The Veterinary Medicines (Amendment etc.) Regulations 2024.* https://www.legislation.gov.uk/uksi/2024/567/contents/made
39. Alliance to Save our Antibiotics (2024). *New regulations on farm antibiotics for Great Britain and how they compare to the regulations in the European Union.* https://www.saveourantibiotics.org/media/2169/new-regulations-on-farm-antibiotics-for-great-britain-and-how-they-compare-to-the-regulations-in-the-european-union.pdf
40. UN Environment Programme (2023). *Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance.* https://www.unep.org/resources/superbugs/environmental-action?gclid=Cj0KCQjwn9CgBhDjARIsAD15h0AiMOW5c4rfFQGANuQupCNBWlnU8nh98_d0Of6bnvJHjWsG2jWkuNoaAgL7EALw_wcB
41. 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 **(4)**, 479-491.
42. Wellcome Trust (2022). *Understanding the antibiotic manufacturing ecosystem.* https://cms.wellcome.org/sites/default/files/2022-04/understanding-the-antibiotic-manufacturing-ecosystem-2022.pdf

Medicines regulators could also play a role in the adoption of good manufacturing processes. The European Commission, for example, has published proposals to enhance the sustainability of pharmaceutical manufacturing, in part because of concerns about antibiotic residues and AMR[43]. A more extensive environmental risk assessment would be needed in order to obtain marketing authorization from the European Medicines Agency.

9 Responsible manufacturing of antibiotics

Vasudeva Murthy, Head of Healthcare at BSI, explained how kitemark certification can help to drive up manufacturing standards.

The British Standards Institution (BSI) is an independent body with a mandate to define, enforce and facilitate the adoption of industry standards. Its remit covers the **pharmaceutical industry**, including its manufacturing processes and waste treatment. It is therefore in a position to be able to define and enforce standards relating to wastewater emissions and environmental contamination with antimicrobial residues.

To promote responsible manufacturing, the BSI has established **BSI kitemark certification**, which demonstrates that antibiotic residue emissions are effectively controlled during manufacturing. BSI has developed this certification program in partnership with the **AMR Industry Alliance**, and with input from other stakeholders.

The drive for action has come from several quarters, including from within the industry itself, from the requirements of National AMR Action Plans and from the procurement tenders specified by purchasers. For example, since July 2023, the NHS subscription model requires mandatory third-party assessment of antibiotic manufacturing standards.

The benefits of the kitemark include a standardized approach to determining acceptable emissions limits, confidence provided by independent assessment, and qualified oversight to support the development of company capacity.

43. Simmons and Simmons (2023). *The EU pharmaceutical package: Environmental aspects.* https://www.simmons-simmons.com/en/publications/cliu3ojjs01fouvpkh4f858cn/the-eu-pharmaceutical-package-environmental-aspects

Monitoring and surveillance

Addressing the AMR challenge is dependent on the ability to track and characterize the spread of drug resistance. In addition, efforts to minimize pathogen exposure to antimicrobials require mechanisms to monitor antimicrobial use, across different sectors.

An understanding of the epidemiology of drug-resistant infections is of immediate importance in clinical decision-making, to inform the choice of treatment at a local level. Patterns of drug resistance may vary even across close geographic areas, so highly granular data may be needed to guide prescribing practice. Aggregated data are important for defining recommended treatments at the national or subnational level. Although limited data have been available on AMR in India, recent years have seen a major expansion in a surveillance network for healthcare-associated infections (HAIs), where AMR is a particularly serious issue (Box 10).

10 HAI surveillance in India

As described by Professor Purva Mathur, All India Institute of Medical Sciences (AIIMS), the Pan-India Network on Surveillance of Healthcare-Associated Infections is generating a clearer picture of antibiotic resistance in India's hospitals.

Hospitals are key sites where drug-resistant pathogens thrive and spread between vulnerable patients. Most high-income countries have developed systems for monitoring HAIs, but these are less common in LMICs.

In India, multiple organizations had established HAI monitoring systems, but none provided a comprehensive picture across all the country. In 2015, AIIMS launched a nationwide systematic surveillance initiative, beginning with five tertiary care centres and establishing standardized methods and quality assurance systems.

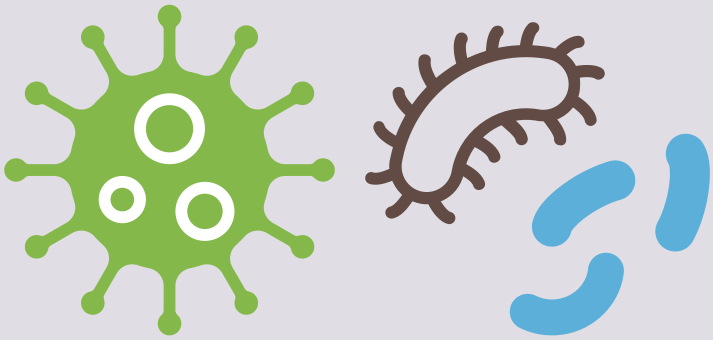
Between 2015 and 2021, the scope of surveillance and geographic coverage gradually increased, with a diverse mix of public and private institutions joining the network. From 2022, medical colleges and district hospitals were integrated into the network, through partnerships with a range of bodies including ICMR and the National Health Systems Resource Centre (NHSRC). By 2023, the network had expanded across 34 states and union territories, and incorporated 90 medical colleges and more than 700 district hospitals.

The focus now is on the development of regional centers, designed to support state health departments. Data and other supporting materials are available on the HAI Surveillance India website, which provides a comprehensive picture of HAIs in Indian health facilities and their AMR profiles. These data are used to inform actions at the institutional and higher levels, supporting quality improvement activities.

Nationwide surveillance systems are also important for providing evidence on the **scale of the AMR challenge** to underpin national decision-making. Epidemiological data are also required to assess the impact of interventions. Data are typically obtained primarily from sentinel sites such as tertiary care hospitals, but more extensive networks are beginning to be developed. Globally, **the WHO Global Antibiotic Resistance and Use Surveillance System (GLASS)** captures standardized data on drug resistance from more than 130 countries.[44] The ICMR established a national surveillance network of 21 hospitals, which tracks resistance trends and informs hospital-specific antibiograms to guide antibiotic use and infection control (Box 11).

11 Antimicrobial Resistance Research & Surveillance Network of Indian Tertiary Care Hospitals

Dr Kamini Walia, Senior Scientist at ICMR, provided an overview of the AMRSN established across tertiary care hospitals in India.



In India, AMR is driven by the unregulated sale of antibiotics and non-compliance with recommended treatment durations, leading to the emergence of drug-resistant pathogens. The absence of nationwide data on drug resistance was recognized as key gap in launching a coordinated response, as most of the previously available data came from individual hospitals or small networks, lacking a comprehensive national perspective.

To address this gap, a network of hospitals was established to monitor trends in antimicrobial susceptibility profiles of clinically significant bacteria and fungi, focusing on human health. Additionally, a strong component of genotypic characterization was incorporated to identify the mechanisms of resistance and clonality of drug-resistant pathogens. A data management system to facilitate efficient data collection and analysis was also developed.

ICMR's AMRSN comprising of 21 hospitals focused on six key pathogenic groups: (i) Enterobacterales causing sepsis; (ii) Gram-negative non-fermenters; (iii) Typhoidal Salmonella; (iv) diarrhoeagenic bacterial organisms; (v) Gram-positive bacteria, including staphylococci and enterococci; and (vi) fungal pathogens. The phenotypic susceptibility and genotypic data collected through this network have been instrumental in tracking resistance trends in the country and has enhanced our understanding of the mechanisms behind antimicrobial resistance in these priority pathogens through the use of genomics and whole genome sequencing.

44. World Health Organization (2015). *Global Antimicrobial Resistance and Use Surveillance System (GLASS).* https://www.who.int/initiatives/glass

The ICMR-AMR surveillance report comprising of data on approximately 1 lakh isolates is published annually which shows that Gram-negative bacteria, particularly Escherichia coli, remain the most common. E. coli's susceptibility to antibiotics has declined over time, with piperacillin-tazobactam dropping from 56.8% in 2017 to 42.4% in 2023 and imipenem from 81.4% to 62.7%, meropenem from 73.2% to 66.0%. Klebsiella pneumoniae also exhibited reduced susceptibility with piperacillin-tazobactam, falling from 42.6% to 26.5%, and also for carbapenems and fluoroquinolones.

AMR data generated by each hospital is utilized to devise hospital antibiograms and hospital antibiotic policy which is necessary to rationalize the prescription of antibiotics and guide IPC practices in the hospital. The generation of hospital-specific antibiograms from were instrumental in informing decisions regarding the empirical use of antibiotics thus strengthening stewardship around antimicrobials. In future, there are plans to expand the development of antibiograms to secondary-level hospitals across India, enabling more targeted and effective antibiotic use in these settings.

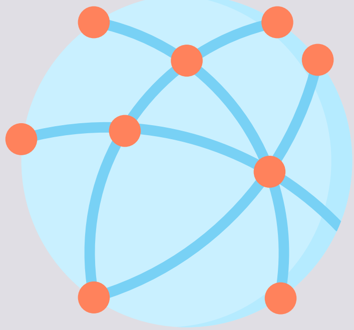
Antimicrobial susceptibility testing is typically a time-consuming process (although automated systems have been developed). **Molecular detection of AMR genes** is more straightforward and is frequently used to assess the distribution and spread of drug resistance. This approach is dependent on a good understanding of the genetic basis of drug resistance. While many studies have targeted specific AMR genes, there has been rapid growth in the use of more comprehensive genome sequencing to characterize isolates and detect AMR genes, boosted by widespread use of genomic approaches during the COVID-19 pandemic.

The Wellcome-funded **SEDRIC project** has assessed the potential uses of **genomic surveillance**, at hospital, public health network and One Health scales (Box 12). In addition to hospitals, there is increasing interest in environmental AMR monitoring, particularly wastewater surveillance.[45] This approach could be utilized in targeted scenarios (e.g., around specific healthcare facilities) or in larger population centers. Wastewater monitoring was also widely used through the COVID-19 pandemic, providing learning that could be applied to AMR. Combining genomic approaches with AI tools is also being used to provide a deeper understanding of AMR in a research setting (Box 13).

45. Larsson DGJ *et al.* (2023). *Sewage surveillance of antibiotic resistance holds both opportunities and challenges.* Nat Rev Microbiol **(4)**, 213-214.

12 SEDRIC: Harnessing genomics for AMR surveillance

The Wellcome-funded Surveillance and Epidemiology of Drug-resistant Infections Consortium (SEDRIC) project, summarized by Professor Kate Baker, University of Cambridge, UK, has examined the potential use of genomic surveillance to tackle the AMR crisis.



The COVID-19 pandemic illustrated the power of genomics to characterize and track the spread and evolution of a pathogen, to guide public health interventions. The same principles could theoretically be applied in the AMR field, although the situation is far more complex, involving multiple pathogens, complex genetics of resistance, and transmission potential through wider ecosystems.

Through the SEDRIC project,[46] a core group of 25 individuals were recruited, spanning multiple areas relevant to AMR. Many others from multiple countries were involved in the project's activities. SEDRIC focused on AMR at three scales– hospitals and IPC; public health networks; and One Health. For each one, workshops were held to discuss the current situation and generate recommendations, which were then circulated to the wider community for comment.

Discussions highlighted the importance of having clarity about the **use cases** for genomic surveillance in these different contexts. These are generally clear at the health institution and public health network level, but were thought to need a more precise definition for One Health.

A need to **build capacity** was identified, with a hub-and-spoke model generally favored. Shortages of **bioinformatics capacity** were felt to be a key bottleneck in many settings. Harmonizing and standardizing surveillance methodologies was thought to be critical, as was developing data sharing and governance agreements, and improving interactions between the many different stakeholders.

Key gaps included a limited number of cost-effectiveness studies, which may lead to a reluctance of funders to invest in genomic surveillance systems and infrastructure. The project also called for continued investment in genomics innovations to enhance surveillance, such as in rapid diagnostics, environmental metagenomics technologies, and application of machine learning approaches.

46. Baker KS *et al.* (2023). *Evidence review and recommendations for the implementation of genomics for antimicrobial resistance surveillance: reports from an international expert group.* Lancet Microbe **(12)**, e1035-e1039.

13 AI and big data mining for AMR surveillance

Dr Tania Dottorini, University of Nottingham, UK, described how innovative machine learning tools are enabling multiple types of data to be integrated to provide insights into AMR epidemiology.

AMR is characterized by complex patterns of spread through human and animal populations and the environment, making it difficult to analyze. However, new AI/machine learning technologies can be used to combine and integrate data from multiple sources, generating novel insights into the spread of AMR genes.

For example, conventional genetic studies of samples from chicken farms in China, characterized by high antimicrobial use and strong selection pressures for resistance, found high levels of antibiotic resistance in E. coli and mapped out drug-resistant lineages. However, it was not possible to relate specific genetic traits to resistance phenotypes. Machine learning, however, was able to identify genetic signatures associated with antibiotic resistance, in known and unknown resistance genes.[47]

The machine learning approach was also applied to historical S, aureus surveillance data from China. This approach revealed genes associated with drug resistance in multiple types of samples from humans, animals and the environment.

In addition, an intensive study of 700 isolates from ten farms identified multiple resistance genes in E. coli and Salmonella.[48] Only 1% of these genes were previously known to be involved in AMR. Multiple mobile genetic elements carrying clinically relevant ARGs were conserved between the two species when these two species were found to reside in the same gut, suggesting they are likely exchanging antibiotic resistance genes. The AMR genes identified code for proteins involved in multiple metabolic pathways in the two organisms.

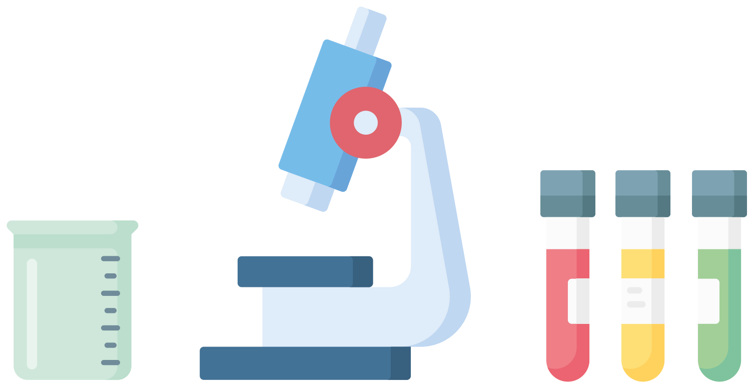
Finally, metagenomic and machine learning analysis in 461 metagenomic samples in 10 different farms in China suggest that microbiomes are relatively specific for humans and animals. However, using a finer lens powered by machine learning we showed that antibiotic resistance genes and clinically relevant ARGs in Mobile genetic cassettes are less host-specific and are likely shared across humans, animals and environments. The development of a more sophisticated machine learning algorithm enabled antibiotic resistance genes associated with resistance to multiple antibiotics to be identified, as well as microbial species predictive of antibiotic resistance.[49]

Surveillance activities are also needed to track antimicrobial use in different sectors. Antimicrobial use in human medicine can be assessed by collation of data from clinical facilities. Monitoring of antimicrobial use in the animal sector is more challenging, particularly when antimicrobials are available outside of veterinary medicine. Outside of the EU, including in India, there are minimal data available on antimicrobial use and few effective monitoring and reporting systems.

47. Peng Z *et al.* (2022). *Whole-genome sequencing and gene sharing network analysis powered by machine learning identifies antibiotic resistance sharing between animals, humans and environment in livestock farming.* PLoS Comput Biol **(3)**, e1010018.
48. Baker M *et al.* (2024). *Convergence of resistance and evolutionary responses in Escherichia coli and Salmonella enterica co-inhabiting chicken farms in China.* Nat Commun **(1)**, 206.
49. Maciel-Guerra A *et al.* (2023). *Dissecting microbial communities and resistomes for interconnected humans, soil, and livestock.* ISME J **17(1)**, 21-35.

Research and development (R&D)

The need for new antibiotics is widely recognized, yet there has been no new antibiotic approved for Gram-negative bacteria, the greatest AMR threat, since 1968. Although the antibiotic pipeline has been expanding, it is not well stocked, particularly for WHO AMR priority pathogens and those responsible for the greatest burden of disease in LMICs.[50]



The development of new antibiotics remains challenging,[51] from both a technical and economic perspective. Antibiotics are expected to be cheap and used in a patient just once, so are less attractive to developers than high-cost products required for the management of chronic conditions.

In addition, company income is typically based on sales volumes, but there is a strong drive to limit the volume of antibiotics used, and in some cases to restrict use of new products completely to preserve potency.

Despite the urgent need for new antibiotics, there is therefore limited commercial interest in the development of new antibiotics. A multitude of financial mechanisms have been proposed to incentivize antibiotic development, although these have had limited success.

The UK has experimented with a **subscription model**, piloting an approach where companies are paid a set amount over a specified period, rather than on the basis of sales volumes. While this addresses the issue of undesirable promotion of product use and creates market stability for the products covered by the agreement, it is not clear that it is effective at stimulating new R&D.[52] Building on the initial pilot, which focused on two antibiotics, a refined subscription model has been introduced in 2024.[53]

Another strategy for strengthening the new antibiotic pipeline relies on the **public–private partnership** model. This can de-risk antibiotic development by providing a source of public funding, while also creating opportunities to shape clinical development plans so that priority public health needs are addressed, even if they have limited commercial viability. A notable example is the **Global Antibiotic Research and Development Partnership (GARDP)**, part-funded by the UK Government, which is supporting the development of a novel antibiotic in India (Box 14).

50. World Health Organization (2024). *WHO releases report on state of development of antibacterials.* https://www.who.int/news/item/14-06-2024-who-releases-report-on-state-of-development-of-antibacterials
51. Wellcome Trust (2020). *The growing crisis in antibiotic R&D: opportunities for G20 member action to support sustainable innovation.* https://wellcome.org/sites/default/files/the-growing-crisis-for-antibiotic-r-and-d.pdf
52. Glover RE *et al.* (2023). *Why is the UK subscription model for antibiotics considered successful?* Lancet Microbe **4(11)**, e852-e853.
53. National Institute for Health and Social Care Excellence (2024). *A new model for evaluating and purchasing antimicrobials in the UK*. https://www.nice.org.uk/about/what-we-do/life-sciences/nice-advice-service/models-for-the-evaluation-and-purchase-of-antimicrobials

14 Partnerships for new antibiotic development

India-based biotech company Bugworks is developing a promising new antibiotic, with support from the Global Antibiotic Research and Development Partnership (GARDP).

Antibiotic development is a highly unusual area where traditional business models do not apply. Typically, profits relate to the volume of sales, but this is not an appropriate model for antibiotics, where new products may need to be reserved or used sparingly to preserve their activity. Innovative business models are therefore needed to incentivize new antibiotic development.

Bugworks is a biotech company with R&D facilities in Bangalore, India. It has developed partnerships with a wide range of commercial investors and international funders to support its work on new therapeutics for cancer and AMR.

One of its most promising therapeutics is a broad-spectrum antibiotic, **BWC0977**, which shows good activity across a range of key bacterial pathogens, including drug-resistant Gram-negative strains such as K. pneumoniae and A. baumannii. Following extensive pre-clinical evaluation, BWC0977 is undergoing a phase I trial in Australia.

One of the organizations funding the development of BWC0977 is GARDP. A partnership between WHO and the Drugs for Neglected Diseases Initiative (DNDi), GARDP aims to work with partners to advance the development and introduction of antibiotic treatments for key bacterial infections affecting LMICs.

GARDP is focused on sepsis in newborns and children, serious bacterial infections in adults, and sexually transmitted infections such as gonorrhea. It works collaboratively with development partners to advance treatments through clinical trials and to develop plans to ensure access and appropriate use in LMICs with high disease burdens. GARDP receives funding from multiple foundations and governments, including the UK Government.

Rapid point-of-care diagnostics are vital for reducing inappropriate antibiotic use and combating AMR. However, developing these tests is time-consuming and resource-intensive. To maximize clinical impact, country-specific Target Product Profiles (TPPs) and clear validation pathways are urgently needed to ensure field utility and streamline regulatory approvals. Addressing these bottlenecks will help make diagnostics available sooner and ensure that investments in development are well utilized, ultimately improving healthcare and AMR containment, especially in LMICs. Something not presented at the symposium, but of importance here is that the ICMR has established a task force to validate and guide development of indigenous rapid point-of-care tests (POCTs) (Box 15).

15 Validating Indian diagnostics

To support R&D of indigenous rapid POCTs, the ICMR has established a task force dedicated to validating Indian diagnostics.

Diagnostics play a crucial role in promoting evidence-based antibiotic use and de-escalation, which are key to limiting the spread of AMR. Disease-specific TPPs have been designed to guide innovators and developers in this process. Additionally, cost-effectiveness studies have been conducted for these diagnostics to ensure their viability before inclusion in national health programs.

A major challenge in validating new indigenous tests is the absence of standardized protocols and parameters, which delays development and regulatory approval.[54] A guidance document with inputs from all the stakeholders such as innovators, clinicians and regulators has been prepared for point-of-care rapid diagnostics for pathogen identification and antimicrobial susceptibility testing.

An indigenous POCT (Rapidogram) for UTI was validated against conventional urine culture and sensitivity to understand its possible applicability at peripheral health care settings. The Rapidogram kit detects UTIs caused by Gram-negative bacteria, demonstrating high specificity (99.6%) and sensitivity (90.6%), and high accuracy.[55] It is suitable for use in primary and secondary healthcare settings. The Incremental Cost-Effectiveness Ratios (ICERs) for Rapidogram was ₹16 per QALY gained, indicating high cost-effectiveness compared to empirical treatments.

Sepsis is a leading cause of neonatal mortality, but early detection and treatment can significantly reduce its impact. To assess the effectiveness of Droolie, a biomarker test panel for early-onset sepsis (EOS), field feasibility studies were conducted at the Jawaharlal Institute of Postgraduate Medical Education & Research JIPMER, Pondicherry. Salivary samples from asymptomatic neonates with EOS risk factors or clinical features of sepsis were tested using the Droolie test at 2 hours of life. The salivary C-reactive protein test showed a sensitivity of 42% and a specificity of 17%, while the salivary Procalcitonin test demonstrated a sensitivity of 17% and a specificity of 67%. The panel presently includes only two biomarkers (CRP & Procalcitonin), and adding more biomarkers could enhance its screening utility and translational potential.

TPPs have proven valuable in creating effective diagnostics and can be adapted for use in other LMICs with similar needs. TPPs developed and published for Sepsis have already been adopted by international platforms for their funding calls.[56]

The advancement of rapid point-of-care diagnostics is crucial, particularly for conditions like Sepsis, UTI, typhoid and upper respiratory tract infections, where irrational use of antibiotics is well-documented. These efforts aim to improve diagnostic accuracy and reduce unnecessary antibiotic prescriptions, ultimately contributing to better disease management and antibiotic stewardship.

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Conclusions

AMR is a global challenge that is threatening to undermine many areas of modern medicine. Although it is affecting all countries, drug-resistant infections disproportionately impact the poorest and most marginalized groups in society.

Although many gaps in knowledge remain, we know enough to urgently act on AMR. The Global Action Plan/National Action Plan approach provides a coherent policy framework for tackling AMR – the key challenge is to ensure effective implementation of AMR control activities to achieve global, national and subnational objectives.

At the same time, research studies can help to close some of the remaining gaps in knowledge. Close engagement between policymakers and researchers is needed to identify key evidence gaps, to design studies that will deliver policy-relevant data, and to ensure effective translation of new research findings.

To answer critical questions, an interdisciplinary approach within the One Health approach will be essential. Sharing of knowledge between sectors, disciplines and countries will help to ensure that research adopts the holistic perspective that AMR demands.

While optimizing antimicrobial use is central to AMR control strategies, issues such as equity and gender also need to be considered. Not all populations currently have access to antimicrobials at times of need, and it is essential that efforts to control AMR do not widen these inequities.

India and the UK share many AMR challenges, as well as some context-specific issues. Both countries have centers of research excellence and thriving pharmaceutical manufacturing sectors. There are many opportunities for researchers from different sectors to share insights and experience, and to work jointly on projects that will provide additional insights into AMR challenges and the approaches that can be used to address them.

Annexes

Annexe one: Steering committee

Co-chairs

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Professor David Heymann CBE FMedSci, London School of Hygiene & Tropical Medicine

Steering committee members

Professor Kate Baker (policy workshop lead), University of Cambridge

Dr Balaji Veeraraghavan, Christian Medical College

Professor Dominic Moran, The University of Edinburgh

Professor Emma Pitchforth, University of Exeter

Dr Kamini Walia, Indian Council of Medical Research

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Professor Ramanan Laxminarayan, One Health Trust

Professor Sharon Peacock CBE FMedSci, University of Cambridge

Professor Tania Dottorini, University of Nottingham

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Annexe two: Attendees

Dr Abbhijit Kadam, National Aging Research Institute

Dr Abdul Ghafur, QuorumVeda

Abhijit Roy, Global Antibiotic R&D Partnership

Dr Anuj Sharma, World Health Organization Country Office of India

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Professor Asad Khan, Aligarh Muslim University

Dr Ashok Kumar, Indian Council of Agricultural Research

Professor Atul Goel, Directorate General of Health Services, Government of India

Carys Redman-White, The University of Edinburgh

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Professor Colin Jamora, Shiv Nadar University

Dr David Jenkins, British Society for Antimicrobial Chemotherapy

Professor David Roper, University of Warwick

Professor David Wareham, Queen Mary University

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