Evidence for action on antimicrobial resistance

wellcome

Summary

The spread of antimicrobial resistance (AMR) threatens a return to the pre-antibiotic era of untreatable infections, while undoing many of modern medicine's greatest advances. The World Health Organization's *Global Action Plan for Antimicrobial Resistance* provides a framework for concerted international action to counter the threat of AMR, and attention is now focused on the development of national action plans. To support these efforts, in April 2016 the Wellcome Trust organised an international multidisciplinary summit bringing together policymakers and researchers from more than 30 countries to discuss the evidence underpinning a range of AMR policy interventions*. The summit concluded that, even if some evidence gaps remain, meaningful actions need to be taken immediately to counter AMR, with individual countries tailoring implementation according to their particular national circumstances. The summit identified three specific areas spanning human health and agriculture where urgent action is required, as well as areas where further research is needed to facilitate local implementation of policy interventions or to support the development of longer-term solutions.

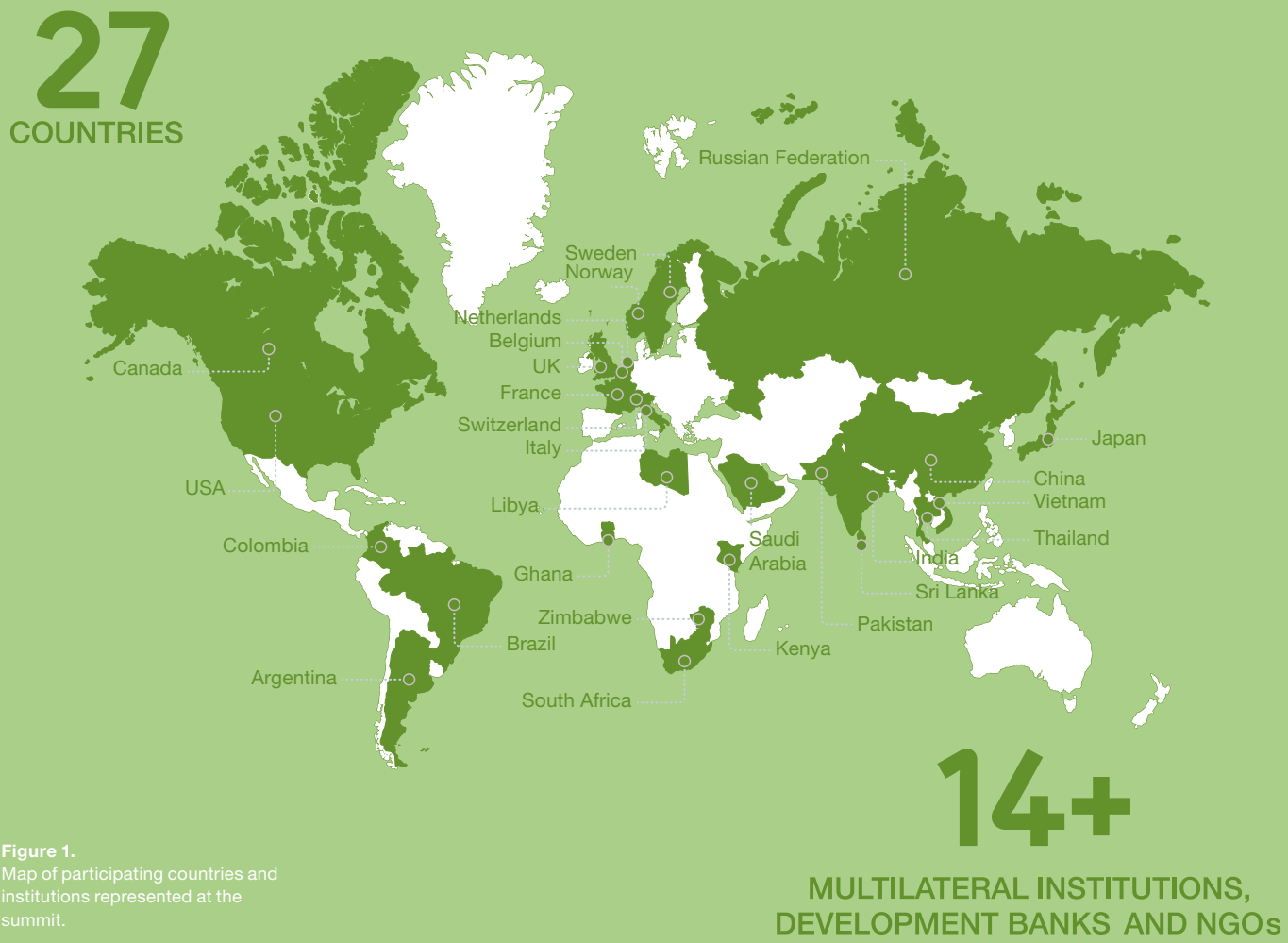


Figure 1.
Map of participating countries and institutions represented at the summit.

* 'Integrating Science and Policy for Decisive Action on Antimicrobial Resistance', Wellcome Trust, London, UK, 26–27 April 2016.

Introduction

Scientists, healthcare professionals and others have issued increasingly severe warnings of the threat posed by antimicrobial resistance (AMR)[1 2]. Antimicrobial-resistant infections often require the use of more toxic or more expensive alternative drugs. AMR raises the prospect of untreatable infections, as well as the possibility that many currently routine medical procedures will become impossible to carry out because of the risk of drug-resistant infections[3].

There is an urgent need for new antibiotics. As a valuable, life-saving resource their loss is being accelerated through overuse and misuse. Innovative mechanisms have been proposed to stimulate development[4] of new antibiotics and alternative therapies but these will be only part of the solution, and strategies need to be put in place to preserve existing drugs and protect new products when they become available.

While AMR has been a long-standing medical concern, it has recently acquired global political momentum. As part of its contribution, in April 2016 the Wellcome Trust, with input from the UK government, organised a high-level international summit to stimulate cross-sectoral dialogue on the use of evidence to drive national AMR policymaking and practical action. The event brought together researchers and policymakers from low- and middle-income countries (LMICs), high-income countries and multilateral agencies, including the health, agricultural and environmental sectors, in order to explore the evidence base underpinning a range of AMR policies*. In particular, the summit sought to define a set of specific policy interventions implementable at a national level, in addition to bridging evidence gaps and overcoming barriers to implementation.

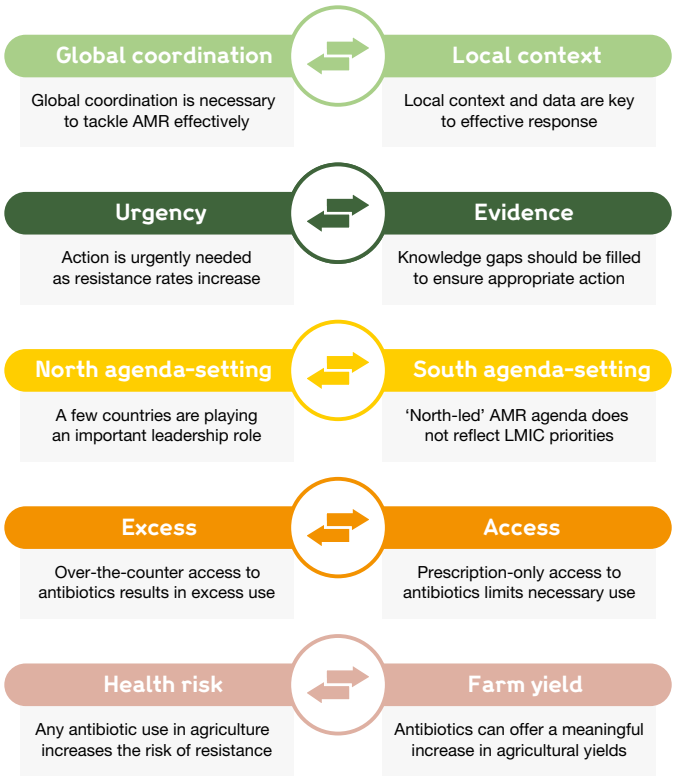
Summit context

Despite the chorus of warnings, with a few notable exceptions, action to tackle AMR has not yet matched the scale of the threat. Nevertheless, there have been encouraging signs that AMR is beginning to receive the political attention it deserves, including discussions at G7 summits[5], at the Davos World Economic Forum[6], and at the UN General Assembly in September 2016[7].

A framework for a global response to AMR has been provided by the World Health Organization's (WHO) *Global Action Plan for Antimicrobial Resistance*[8], developed in collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). The Global Action Plan identified five high-level strategic objectives as well as a framework for action identifying practical steps that could be taken by individual nation states, international and national agencies, and the WHO.

*The summit focused primarily on resistance to antibiotics, but most of the issues discussed are also applicable to other antimicrobial treatments.

Nevertheless, a range of factors limit action at national levels. Many LMICs face a multitude of competing health concerns and, with limited resources, may not view AMR as an immediate priority. For some countries access to antibiotics is as important as control of misuse, with many avoidable deaths resulting from infection due to lack of access to treatment[9]. Antibiotics are used extensively as growth promoters in agriculture, particularly in LMICs because of the economic benefits they generate[10]. There are also perceptions that the response to AMR has been driven primarily by high-income countries with too little attention paid to the needs of LMICs and the constraints they face. Similarly, there may be tension between the need for a globally coordinated response and the necessity for actions to be tailored to local circumstances and 'owned' at a national level.



Finally, there is a sense that a lack of evidence is delaying the implementation of AMR polices. This may reflect a lack of specific data on the burden of drug-resistant infections faced by individual countries, particularly those with limited surveillance infrastructures and public health systems. A further critical factor is a lack of information about the likely effectiveness and cost-effectiveness of interventions within specific local settings[11]. However, scientific uncertainties about factors contributing to the emergence and spread of AMR in communities may also discourage timely action.

Summit approach

It is now widely recognised that AMR is not solely a medical issue but a multidimensional challenge, with key social, economic and environmental dimensions[12]. Public attitudes and behaviours have a major impact on physicians' prescribing practices and hence on antibiotic use in healthcare. While over-the-counter use of antibiotics is thought to be a key driver of AMR worldwide[13], in many countries, agricultural use of antibiotics exceeds medical use. This is poised to rise further as populations grow and animal protein consumption increases globally[14]. Release of antibiotics into ecosystems provides numerous routes through which drug-resistant bacteria can spread, drug-resistant genes can be exchanged[15] and bacteria can be exposed to antibiotics, thereby driving the emergence of resistance.

Given this context, the summit was rooted in the One Health framework, which recognises the interconnectedness of human health, agriculture and animal health, and the environment. The summit focused on the following four objectives of an effective AMR response:

- infection prevention and control in agriculture
- infection prevention and control in human health
- optimal use of antibiotics in agriculture
- optimal use of antibiotics in human health.

Within each of these broad domains, discussions focused on a range of high-level response strategies and associated policy interventions. Through a literature review and discussions with key stakeholders in advance of the summit, policy options with at least some degree of evidence to support them were identified for further discussion. A set of specific policy options, spanning human and animal health, were reviewed and debated by participants from more than 30 countries, to explore their potential implementation at a national level as well as investigate evidence gaps and barriers.

Figure 2.
Competing priorities for consideration in the development and implementation of AMR policies.

Policy areas for immediate action

Discussions at the summit concluded that there was an urgent need for action across all four domains. Although evidence gaps remain in some areas, there is sufficient evidence to justify urgent action. AMR is already a major health issue and projected to grow rapidly unless action is taken[16]. Proven countermeasures are available – the challenge is knowing how to deploy them effectively. Three areas for immediate action were identified and these are described in the following pages.

Antibiotic use in agriculture must be reduced, without compromising the food system's capacity to meet increasing global demand

Growth promoters: *Use of antibiotics for growth promotion and disease prevention should be replaced by improved animal husbandry practices.*

Certain antibiotics are used in agriculture for three reasons: growth promotion, prevention of infection and treatment of infection. It was strongly felt that antibiotic use for growth promotion should be phased out as rapidly as possible, as has already been achieved in a number of countries.

However, food production is a low-margin industry and withdrawal of antibiotics could have economic consequences. In high-income countries, improved husbandry practices have improved yields and reduced the additional benefits gained from use of antibiotics as growth promoters. In LMICs, however, antibiotics typically have a greater impact on yields when producing at scale. Furthermore, the world's population is increasing, and consumption of animal protein is likely to rise in emerging economies[17], a demand that can only feasibly be met by intensive farming. Nevertheless, use of improved husbandry practices could ensure that intensive farming does not contribute unnecessarily to the development of AMR.

It was also argued that antibiotics should not be used for prevention of infection in settings with limited infection control. While there is a risk that banning the use of antibiotics for growth promotion will simply lead to increased prophylactic use, improved husbandry practices and farm security can contribute to more effective infection prevention. However, treatment of herds/flocks affected by an infection (metaphylaxis) was seen as acceptable antibiotic use.

Another approach proposed is to restrict the use of certain antibiotics in either human medicine or veterinary medicine. However, there is considerable overlap between the classes of drugs used in human and veterinary medicine. There may be a strong case for reserving second- and third-line antibiotics for human medicine only, although several of the summit's participants noted the practical difficulties of implementing such an approach.

Alternatives: *Alternative treatments and husbandry practices should be investigated to support reduced antibiotic use in agriculture.*

More research is needed to identify alternative husbandry practices and treatments that would minimise the use of antibiotics and to understand how they could be sustainably implemented across countries at all stages of economic development. Additionally, regulation is essential to ensure adherence to good practices; however, many countries currently lack the infrastructure that would be necessary to enforce it.

A greater emphasis on vaccination might also reduce the need for antibiotics. However, there are a wide range of technical, economic and practical challenges to increased vaccine use in agriculture which require further deliberation to ensure optional use.

Insurance: *Innovative insurance schemes should be developed to mitigate the risk of income loss among producers during phasing out of antibiotics.*

Even with improved husbandry practices, phasing out of antibiotics as growth promoters could affect the profitability of food production. One solution could be innovative insurance mechanisms for producers that mitigate the risks associated with transition to new antibiotic stewardship practices, removing an important obstacle to their implementation and providing incentives for action.

Professional education: *The training of veterinary medicine professionals and those involved in animal production should emphasise the importance of responsible antibiotic use.*

As part of a long-term effort targeted at veterinarians, farmers and others responsible for animal health, education and training programmes should be developed and delivered to increase understanding, awareness and knowledge of what constitutes appropriate antimicrobial use, the role of other measures to reduce infections in animals and the health impacts of inappropriate use.

Food production: *Food production systems should do more to limit consumer exposure to drug-resistant microbes (eg through increased use of surface cleansing).*

Opportunities also exist to reduce consumer exposure to bacterial contamination (and by extension antibiotic-resistant bacteria and antibiotic resistance genes) in foodstuffs through 'farm to fork' food production systems. There is already a public health imperative to prevent transmission of microorganisms to consumers, but many cases still occur and additional steps could be taken to ensure consumer safety. Surface cleansing methods of meat, for example with lactic acid, are not employed in all countries, but could help to reduce the spread of bacteria such as *Campylobacter*.

There is potential for consumers and advocacy groups to exert pressure to reduce unnecessary antibiotic usage in agriculture[18]. Consumer demand can exert direct pressure on food producers while advocacy can encourage political action (such as the introduction of formal regulation). However, consumers may be confused as to the meaning of 'antibiotic-free', the distinct issues of antibiotic use for growth promotion versus treatment, and the presence of antibiotic residues in foodstuffs.

There is an urgent need to develop better local understanding of antibiotic use and resistance levels in human and animal medicine and agriculture.

Surveillance systems: *Surveillance and monitoring are needed to provide a clear picture of local situations and to assess the impact of interventions; expanded data are required on both resistance (in humans and animals) and antibiotic usage.*

The importance of local data on antimicrobial resistance and antibiotic usage (in medicine and agriculture) was repeatedly stressed. As well as their clinical value, AMR data can be used to persuade policymakers and politicians of the need for local action. Data are also important for understanding local context so that the most appropriate interventions can be prioritised, and they can provide the basis for evaluation of the impact of interventions.

Although surveillance data was seen as critical to effective long-term national AMR responses, it was also noted that limitations in data collection were not a reason to delay the implementation of policy interventions designed to reduce inappropriate antibiotic use or promote improved infection control. Countries that lack a surveillance infrastructure to generate local data can obtain AMR data from a small number of sentinel sites. Point prevalence surveys can be a relatively straightforward way to obtain data on antibiotic usage. Countries may also be able to draw on data collected in neighbouring countries to support regional response efforts.

With many LMICs having limited technical infrastructure and expertise to apply international standards, regional centres could be an important resource. Adherence to internationally agreed standards can ensure consistency in practice across countries and facilitate national comparisons. Such comparisons will benefit from international agreement on a small number of clearly defined and readily obtained AMR metrics.

Targets: *Quantitative data will enable policymakers to track progress over time, increase accountability and set both metric and quality targets to motivate changes in behaviour.*

Quantitative data can be used to specify targets for antibiotic usage, healthcare-associated infections (HAIs) or levels of resistance. Numerical targets can be powerful motivators of action and are credited with making an important contribution to the control of HAIs in some countries. To be effective, targets should be realistic and underpinned by reliable data and monitoring practices; accountability and transparency are also important.

However, there are risks associated with targets, such as ‘gaming’ and an undue focus on compliance rather than outcomes. It is also unclear what specific targets should be used. Targets are often based on percentage reductions (of HAI cases or antibiotic use) and further work is needed to define what absolute numbers could be considered appropriate and effective in different settings. Antibiotic consumption target setting in LMICs would also need to be considered in relation to initiatives to improve access.

In agriculture, targets based, for example, on antibiotic usage per unit of meat output (mg per kg) would allow for wide variation in the numbers and types of animals reared for food in different countries. However, up-to-date data on antibiotic use in animals can be difficult to obtain, even in high-income countries.

There was active discussion about whether data on antibiotic usage alone would be enough to drive action. It was suggested that point prevalence data on antibiotic consumption could be obtained relatively quickly and provide a basis for action; however, information on resistance may also be necessary in order to persuade policymakers of the need for action.

"The role of data in supporting implementation would be crucial in my opinion. Simple indicators need to be put in place which apply globally. This could give immediate comparison between regions and areas and help to push implementation in the long run. Dedicated software would also be crucial as this will greatly ease the data entry, analysis, validity and interpretation."

Labelling: *Labelling has a potentially important role to play in emphasising the 'protected' status of antibiotics, supporting tracking mechanisms, ensuring drug quality and informing people when antibiotics are included in a product such as animal feed.*

Summit participants felt that labelling has several important applications. Distinctive labelling (such as the 'red line' labelling adopted in India[19]) could help to communicate the special status of antibiotics. Labelling of products containing antibiotics, such as animal feeds, could increase awareness of antibiotic usage at all levels of supply chains. Labelling can also support effective supply chain management and provide a source of data on usage. More sophisticated packaging and labelling may also be a tool to combat the circulation of potentially substandard counterfeit drugs.

Public health systems need to optimise antibiotic use.

Sanitation and clean water: *Consistent with the Sustainable Development Goals, emphasis should be placed on improved sanitation and access to clean water, to reduce infections and the need for antibiotics.*

Improved access to clean water and enhanced sanitation deliver public health benefits in their own right but, by preventing infections and reducing the need for antibiotics, also reduce the pressures that drive resistance. Similarly, greater use of vaccination could reduce infection levels and lower antibiotic usage (even vaccination against viruses could deliver AMR benefits, by reducing secondary bacterial infections and inappropriate antibiotic use to treat viral infections).

Infection control: *Public health measures such as good hand hygiene practices and enhanced infection prevention and control should be promoted in hospitals and other healthcare facilities.*

Improved hand hygiene measures could contribute to enhanced infection prevention and control, and there is scope for their wider application across all countries. Although there may be a role for other infection control measures, such as patient screening and isolation, countries vary widely in the extent to which they can implement such measures given their cost.

Development assistance: *International development agencies need to integrate AMR prevention as a core aspect of their work.*

As an archetypal 'wicked' problem[20], AMR cannot be addressed by one-off initiatives or targeted eradication programmes; it requires long-term, cross-sectoral, systems-level solutions. Any use of antibiotics brings with it the risk of resistance, so sustained measures are required to minimise the emergence of resistance and to limit its spread. Hence AMR management needs to be fully integrated into healthcare systems and more widely into countries' infrastructure (particularly clean water and sanitation services). For this reason, it is important that AMR is considered as part of a wider development agenda and for international development agencies to integrate AMR into their core activities. Prevention of AMR should be considered a broader impact of development projects.

Professional education: *Healthcare worker education and professional development should have a stronger emphasis on antibiotic stewardship.*

As well as healthcare systems and public health infrastructure, human resources are a crucial factor. In many countries, there is a serious shortage of healthcare professionals and individuals with AMR knowledge and expertise. In all countries, it is essential that antibiotic stewardship is prioritised in the training and professional development of healthcare professionals.

Public education: *Community-level understanding is necessary to ensure that all people, from parents of ill children to farmers, understand what antibiotics can and cannot do and why minimising use is in everyone's interests.*

Targeted public education was thought to be essential to minimise demand for unnecessary antibiotics in primary care and to communicate the rationale for reduced use in agriculture. There was some debate about the extent to which patients' expectations influence physicians' prescribing practices and whether large-scale awareness-raising campaigns with very general goals are effective (and how their effectiveness can be assessed). Embedding knowledge of AMR within young people's formal education was seen as another possible option.

> **"Due to lack of interest from governments and/ or scarcity of human and financial resources for auditing it, this legislation is not met in most cases and in most LMICs (as well in some richer ones)."**

Economics: *Financial incentives that link suppliers' rewards to volumes of antibiotic sales need to be eliminated.*

Financial models in which the income of antibiotics suppliers depends directly on sales volumes create incentives for suppliers to maximise sales and therefore usage. Innovative alternative models are urgently needed. This also applies to the development of new antibiotics, where drug developers may need to be rewarded even if their products are reserved for use when existing drugs have failed. These considerations further emphasise the need to engage with the private sector in the development of AMR strategies.

Guiding use: *Enhanced 'gating' of antibiotics is required, so more use is routed through healthcare professionals and over-the-counter use is minimised, with due consideration for the need to enhance access to antibiotics in many LMICs.*

Over-the-counter sale of antibiotics is widely seen as a primary driver of AMR in LMICs. Although excessive prescribing of antibiotics by healthcare professionals is also an issue, routing access to antibiotics through trained healthcare professionals will lead to more appropriate use and enable consumption to be regulated more effectively. In particular, removal of second- and third-line antibiotics from general and online sale should be an immediate priority. One drawback to 'gating' is that it could reduce access to antibiotics, while many countries are not yet in a position to implement such systems (although, conversely, some countries are but have not rigorously enforced them). Sales over the internet also present an additional challenge beyond national borders that requires coordinated international action.

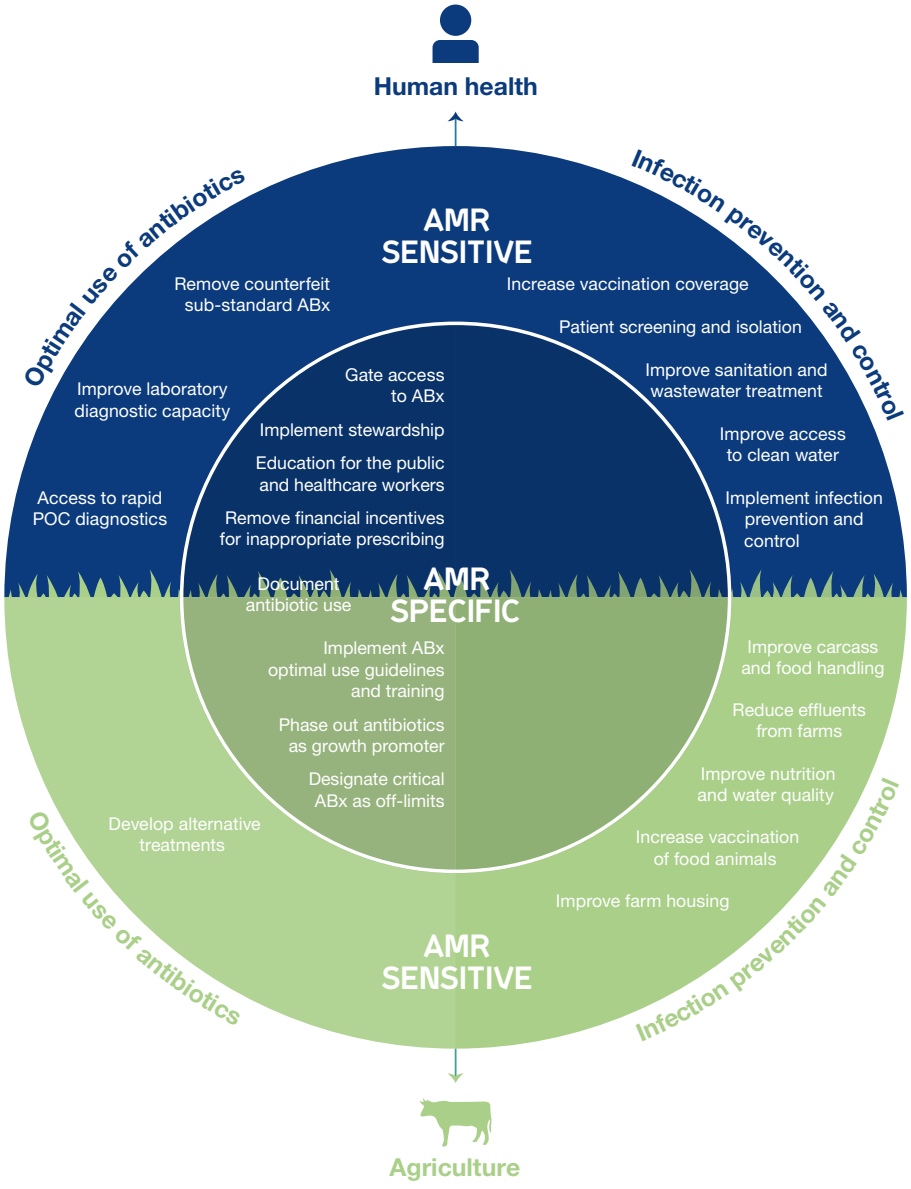


Figure 3.
Policy options discussed at the summit. Measures to combat AMR can be considered to fall into two categories: AMR-specific interventions, where the primary aim is to limit the development or spread of AMR infections, and AMR-sensitive interventions, which are adopted for other public health reasons but also deliver spinoff benefits for AMR. Given the multidimensional nature of AMR, both approaches will be necessary for effective AMR control. Investment in some AMR-sensitive interventions would be difficult to justify solely on the basis of their impact on AMR, however their AMR benefits add to their public health importance. For infection prevention and control there are no AMR-specific policy interventions, which reflects the broader importance of prevention and control measures for all infectious diseases rather than AMR specifically. The absence of specific policy interventions in infection prevention and control should not be considered a gap or a deficiency.

Tailoring actions to suit local circumstances

Summit participants recognised that many countries lacked the infrastructure, human resources, expertise and financial resources to implement some of the recommended policies. Even so there are foundational steps that countries can take to establish a platform for the development of national AMR countermeasures. AMR control can be seen as a journey: some countries may have further to travel, but all can take steps towards common goals.

One key step is to establish cross-sectoral advocacy groups spanning human health, agriculture and the environment, and including the private and public sectors to coordinate activities and to act as a national focus for AMR and a source of AMR expertise. In each country, 'AMR champions' can be identified to advocate for AMR-related investment within government, work to engage other stakeholders and liaise with international agencies. Indeed, engaging with political leaders and policymakers is essential to raising awareness and securing political commitment.

Collecting local data on AMR is an important step to providing a picture of current national drug-resistant infection risks. Local data can be used to mobilise political support, to establish local priorities and to provide benchmarks against which progress can be assessed. It is also important to establish systems to collect data on antibiotic usage in medicine and in agriculture. If countries lack the capacity to collect data there may be opportunities for regional collaboration and data sharing and for the shared use of regional laboratory facilities.

> **"Many LMICs have insufficient AMR surveillance which stops policymakers understanding or being aware of the importance of AMR. It will be critical for AMR policies to develop and strengthen the function of surveillance and regulate the proper administration of antibiotics to humans and animals via prescription."**

Other actions that can be taken immediately include initiatives to raise awareness of AMR among groups of stakeholders and the general public. Medical and veterinary schools can be important vehicles for this. Countries can also explore potential international sources of funding to support the development or implementation of AMR strategies. They can also examine how to establish national infrastructure or regulatory approaches to support the implementation of AMR prevention and control measures.

At the same time, the international donor community, including development assistance agencies, should consider how best to support these activities, including broader support for the Sustainable Development Goals. There may be a need for innovative approaches to financing and for agencies to act collaboratively to avoid duplication and fragmentation of efforts, and to complement national funding for AMR strategies. Complementing wider development assistance, high-income countries could also consider AMR-specific initiatives along the lines of the Global Antibiotic Resistance Partnership[21] coordinated by the Center for Disease Dynamics, Economics and Policy, to build expertise and support the development of national capacities to implement AMR policies.

Research to shape future responses

Evidence gaps related to implementation of policy

For most of the policy interventions discussed, summit participants agreed that good evidence exists of the potential to limit the emergence or spread of AMR. What was often lacking, however, was a demonstration that they would be effective (or cost-effective) in a local setting and guidance on how it could be adapted to a specific context. In particular, it was felt that there was a lack of information on the practicalities of local implementation.

Furthermore, it was suggested that implementation of AMR-related policies and programmes should be accompanied by data collection for evaluation purposes (see recommendations for collecting data at a national level in the previous section), and that this information could be shared more widely. A globally accessible 'knowledge repository' on AMR implementation measures could be an important resource on both the effectiveness of policy interventions and the practicalities of implementation.

> "One way forward might be to try to anticipate where the political process is likely to be in five years' time, what the key information gaps at that point are likely to be, and start funding now the research needed to fill them."

A critical evidence gap is the lack of national-level information about AMR organisms and antibiotic usage, particularly in LMICs. The £265 million Fleming Fund[22] is one mechanism through which countries will be able to establish surveillance networks, laboratory capacity and AMR response capabilities.

Countries can participate in the WHO's Global Antimicrobial Resistance Surveillance System (GLASS)–which supports a standardised approach to the collection, analysis and sharing of data on AMR–and in OIE initiatives to collect information on the use of antibiotics in food-producing animals worldwide[23]. These approaches benefit countries through capacity building, access to training and implementation tools, and support in collecting AMR data at local and national levels[24].

Evidence gaps for developing long-term solutions

In several areas, research has the potential to generate new understanding that would support more appropriate use of antibiotics, more effective control of AMR, and prioritisation of control measures and enhanced guidance for implementation in different resource settings.

Antimicrobial development: Although not covered at the summit, increasing understanding of microbial biology and mechanisms of resistance along with developing new microbial agents remain research priorities, to provide knowledge to better tackle growing resistance.

Environmental transmission: Understanding of the extent to which human health is affected by AMR arising in environmental microbial reservoirs, as well as patterns of transmission and AMR gene flow between agriculture, the environment and people, remains incomplete. A more complete understanding of the environmental spread of resistant organisms and AMR genes could ultimately support prioritisation and focused targeting of AMR countermeasures.

Although not a major focus at the summit, the contribution to AMR made by environmental contamination with antibiotics remains an important open question. Waste from antibiotic production facilities, runoff from agricultural land and inadequate wastewater treatment facilities create conditions likely to select for antibiotic-resistant organisms, although the significance for human health is not yet clear.

Food production: More research is needed on husbandry practices that can enhance yields while minimising use of antibiotics. Breeding programmes may also be able to develop animals more naturally resistant to infection, while modifying the animal gut microbiome might be a route to increased yields or decreased susceptibility to infection. Research is also needed on implementation of new husbandry practices in LMICs, particularly cost–benefit analyses.

Vaccines: Additional vaccines targeting strains of infectious organisms, especially those common in LMICs, are required. However, lack of access in many countries often reflects resourcing and delivery issues as well as the absence of an effective vaccine.

Infection prevention: While sanitation and access to clean water and the training of healthcare professionals are critical and should be priorites for donors and multilateral investment, it remains unclear how these can best be delivered in many LMICs. Similarly, while the importance of good hand hygiene is well established, the most effective ways to drive behaviour change to facilitate the reduction of AMR are less clear.

It is increasingly recognised that there is a complex relationship between infection, nutrition and the gut microbiome[25], with implications for susceptibility to infection and responses to oral vaccines. A better understanding of these interrelationships could help to identify interventions that reduce susceptibility to infection and hence the need for antibiotics.

Behaviour: There is growing evidence that the general public typically has a poor understanding of AMR[26]. However, it is less clear what specific goals should be adopted for mass communication campaigns, what approaches are most effective and what metrics should be used to evaluate such campaigns.

In primary care, there is a need to develop a better understanding of factors affecting physicians' antibiotic-prescribing behaviour, including public perceptions. Although these are often considered in isolation, there may be a mismatch between public perceptions and physicians' beliefs about those perceptions; hence more holistic explorations of 'prescribing culture' may be needed. These studies will require an interdisciplinary approach, with input from behavioural and social scientists, and could support the development of new interventions to reduce unnecessary antibiotic use.

One specific issue that could be addressed is the potential use of non-antibiotic treatments to relieve symptoms and meet patient expectations that they receive some treatment for their illness. For example, it is possible that a diagnostic test result confirming a viral infection and advice on how to manage symptoms would help address patients' expectations. More generally, as point-of-care diagnostic tests are introduced, there is a need to understand how diagnostic test results are perceived and used by physicians and their influence on prescribing behaviour.

Getting started

The summit recognised that many countries lacked the infrastructure, human resources and expertise (as well as financial resources) to implement some of the recommended policies. Even so, there are foundational steps that countries can take to establish a platform for the development of national AMR strategies. These steps include:

- Establishing cross-sectoral groups spanning human health, agriculture and the environment, and including the private and public sectors, to coordinate activities and to act as a national focus for AMR and a source of AMR expertise from the outset. Agricultural sectors may be highly diverse and poorly connected, so representatives may be needed from a range of communities.
- Identifying an 'AMR champion' who can be a figurehead for AMR within a country, advocating for AMR-related investment within government, working to engage other stakeholders, and liaising with international agencies.
- Engaging with political leaders and policymakers to raise awareness of AMR and its importance and to ensure political commitment to national AMR strategies.
- Collating available data or undertaking new situational analyses to provide a picture of the current national AMR status, in order to mobilise political support, establish priorities, and provide a benchmark against which progress can be assessed.
- Undertaking activities to raise awareness of AMR among stakeholder communities and potentially also the general public; medical and veterinary schools can be important targets for awareness-raising activities.
- Exploring opportunities for regional cooperation, for example AMR data sharing or joint use of laboratory facilities.
- Evaluating the policy options identified in this report and considering how they could be implemented locally.
- Exploring international sources of funding to support implementation of AMR strategies.

> **"It would be good to have a global common programme, but additional advice or suggestions to policymakers and governments on how to deal with context-specific issues would greatly help the LMICs."**

At the same time, the international donor community, including development assistance agencies, could consider how they can best support these activities. If AMR is seen as a development issue, development assistance agencies need to integrate AMR into their core activities. There may be a need for innovative approaches to financing and for agencies to act collaboratively to avoid duplication and piecemeal approaches. It was also considered important that countries make their own financial commitments to AMR strategies.

It was also suggested that health-specific agencies might need to consider whether programmatic approaches to funding are suitable for AMR. Time-limited one-off programmes with specific disease-related outcomes may not be appropriate for a long-term complex challenge that requires action across multiple sectors, is heavily dependent on public health infrastructure and expertise, and has a diverse range of outcomes.

Finally, there is a need to track levels of resistance in humans, agriculture, veterinary medicines and the environment and for a robust monitoring and evaluation system, with a focus on national and global targets addressing access, appropriate use and policy interventions. This is critical to ensuring a global understanding of the impact of interventions[27].

Conclusions

AMR has been estimated to be responsible for some 700,000 deaths globally each year – a number that could rise as high as 10 million, potentially exceeding the annual number of deaths from cancer[15].

AMR is therefore a formidable global health challenge, but numerous tools already exist to limit its impact. The emergence of resistance is an inevitable consequence of antimicrobial use, and it is highly unlikely that the threat of AMR will ever be entirely eliminated. However, if action is taken now and efforts are sustained in coming years, it will be possible to limit the harmful effects on economies, public health and patient outcomes.

Crucial to these efforts is the need to consider the multidimensional nature of AMR. AMR is a global issue – drug-resistant infections do not respect national borders – that will impact many parts of society. As well as medicine, the agricultural, environmental and social dimensions of AMR demand attention. Of fundamental importance, global and national political will is required to drive concerted action on AMR and address the economic, environmental and health threats that it poses.

Figure 4.
Elements of an effective national AMR policy.

The multidimensional nature of AMR reinforces the importance of considering AMR as a development issue. Every country is affected by AMR, and every country stands to benefit from managing the threat of infectious diseases. Yet countries vary widely in their capacity to put in place measures to combat AMR. The development of national responses to AMR can be considered a journey, with some countries having travelled further than others, but all stand to benefit from beginning to establish a response effort.

There are also numerous actions that high-income countries can take. One is to provide support for LMICs, through core development assistance and coordinated efforts to address infection, including AMR.

Important evidence gaps will continue to exist, however there is abundant evidence to support immediate action, and the risks justify action even in areas of scientific uncertainty. Many actions already promise health benefits, particularly for the control of infectious diseases, their impact on AMR being an added bonus. At the same time, further research will provide a clearer picture, supporting prioritisation as well as the development of more targeted AMR countermeasures. In addition, 'learning from doing' and sharing knowledge and experience of implementation in different contexts will provide further evidence to support national efforts to combat this very real threat to human health.

Endnotes

1 *Daily Telegraph*. Resistance to antibiotics could bring "the end of modern medicine as we know it", WHO claim. 2012. http://www.telegraph.co.uk/news/health/news/9147414/Resistance-to-antibiotics-could-bring-the-end-of-modern-medicine-as-we-know-it-WHO-claim.html

2 BBC News. Antibiotic 'apocalypse' warning. 2013. http://www.bbc.co.uk/news/health-21178718

3 The summit focused primarily on resistance to antibiotics, but the principles are equally applicable to compounds used for other pathogens: antivirals, antiparasitics and antifungals.

4 Review on Antimicrobial Resistance. *Securing New Drugs for Future Generations – the Pipeline of Antibiotics*. 2015. http://amr-review.org/sites/default/files/SECURING%20NEW%20DRUGS%20FOR%20FUTURE%20GENERATIONS%20FINAL%20WEB_0.pdf

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