Academy of Medical Sciences response to the Department of Health and Social Care's consultation on the antimicrobial resistance national Action Plan - January 2023

Introduction

The Academy's mission is to help create an open and progressive biomedical and health research sector to improve the health of people everywhere. Our response to this call for evidence is based on our previous policy work on antimicrobial resistance and other relevant topics (e.g., diagnostics and COVID-19), as well as evidence from members of our elected Fellowship and leadership programme,[1] which include some of the UK's foremost experts in clinical and academic medical research.

Consultation Questions (Online Survey)

From your experience, how has the scale of the threat of AMR changed since the national action plan was published in 2019?

a) the threat of AMR has increased since 2019 b) the threat of AMR has stayed the same since 2019 c) the threat of AMR has reduced since 2019 d) don't know

Overall, we would agree that the threat of AMR has increased since 2019. However, AMR is related to a wide array of different pathogens (bacteria, viruses, fungi, parasites), each of which have their own trajectory of resistance and susceptibility. There are also different rates of resistance between countries for the same 'bug-drug' combination, therefore, AMR is not a singularly homogenous problem globally. Moreover, the problem is not linear. For example, the emergence and spread of a single resistance mechanism (for example artemisinin resistance in malaria) could lead to a step change in the challenge posed. A recent study has provided the first comprehensive assessment of the global burden of AMR, as well as an evaluation of the availability of data.[2] This provides a base line from which to track rates over time and to base future estimates on.

In your opinion, what are the top 3 drivers of AMR?

- The single primary driver remains the unnecessary exposure to antimicrobials, including misuse and overuse of antimicrobials in healthcare, agriculture, and veterinary medicine:
    - Although antimicrobials can no longer be used in the UK or EU for non-therapeutic use, agriculture remains a major user of antimicrobials in the UK and in other countries, where antimicrobials are used without veterinary prescriptions.
    - Globalisation, including international travel, food distribution etc. also contribute towards increased exposure.
    - Reducing the burden of infection through effective infection prevention would also contribute towards limiting the need for and exposure to antimicrobials.

[1] The Academy of Medical Sciences. *FLIER* scheme. https://acmedsci.ac.uk/grants-and-schemes/mentoring-and-other-schemes/FLIER
[2] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext

- The lack of awareness and knowledge also contributes to the unnecessary exposure to antimicrobials:
    - The public expectation of receiving antimicrobials is still very high, and this places undue pressure on doctors to prescribe antimicrobials before an accurate diagnosis has been made. This practice of prescribing antimicrobials to meet expectations or to induce a placebo effect in patients should continue to be discouraged. Increased campaigns to improve public awareness of the importance of antimicrobials and the detrimental effect of misuse would help to take pressure to prescribe off doctors. With greater public understanding of testing and surveillance, there are opportunities for the public to be more directly involved in generating data, described as 'citizen science'. For example, crucial to the success of COVID-19 surveillance has been the substantial scale of diagnostic test procurement, and the rapid integration of test results into medical records.
    - Stewardship: More extensive education of medical students, doctors and other key medical professionals in training on AMR issues would highlight the negative impact of bad antimicrobial prescribing practice for a future cadre of medical professionals; stewardship campaigns should also be extended to veterinary surgeons and animal keepers.
    - Linked to the above around education on AMR, active support for careers and research in AMR and research and policy is important to create leadership in the area and contributes to establishing knowledge in the area. The lack of support for these roles and professional and academic development in the UK and NHS is a critical barrier for knowledge sharing and promoting awareness.

- Insufficient allocation for AMR-related research and resource (including vaccines, therapeutics, diagnostics, and surveillance):
    - Despite being vital for the future development of antimicrobials and other treatments, many pharmaceutical companies have had to cease or downscale their antimicrobial development programmes for economic reasons. An AMR equivalent of the Coalition for Epidemic Preparedness Innovations (CEPI) might be of value to finance and develop innovations globally.
    - A large amount of research is focussed on the development of new antimicrobials. However, the AMR problem is one that can be tackled in several ways and investment should not be focussed solely on development of novel antimicrobial drugs. It should also include the development of vaccines to allow for the prevention of infections, and diagnostics to allow for quick and more accurate treatment.
    - Where there is funding available, the current research grant system is fragmented and does not allow for strong coordinated and directionally consistent funding of innovation. A stronger and better directed way of funding translational research to counter AMR is needed.
    - The regulatory framework also has an important role to play. New technologies for AMR cover different areas, for example human and vet pharmaceuticals, diagnostics, technology etc. For many areas it is not possible to get approval based on AMR impact. For example, vaccines can only be approved for efficacy to prevent a specific disease in individuals being vaccinated, not to tackle AMR directly. Prevention of AMR should be considered the main required outcome for new

approvals. There may be areas such as skin or mucosal disinfection where the focus on specific organisms rather than a broad range limits advances.

Which of these areas would you most like to see prioritised over the next 5 years?

1. reducing the need for, and unintentional exposure to, antimicrobials
2. optimising the use of antimicrobials
3. investing in innovation, supply and access

1,2,3

Are there any actions you think are required to tackle AMR that do not fall within one of these categories?

- yes (please specify)
- no
- don't know

Infection prevention and control (IPC): Infection prevention and control measures can play a central role to reduce the number of infections and requirements of antimicrobials. Therefore, promoting good infection control practices can be an essential component to tackling AMR.

Surveillance in humans, animals and the environment: AMR surveillance data are important to inform a range of activities, including individual clinician decision making, guiding national or local policymaking such as usage, treatment and prevention guidelines, and providing national and global insight into AMR epidemiology and early warning of emerging resistant organisms. The importance of a 'One Health' approach in tackling AMR, which recognises the linkages between animal and human health alongside the environment, means that surveillance across all these sectors is vitally important for the AMR response.

Investment in research and supporting professional roles: Although the UK has many research strengths relevant to AMR, some need nurturing to provide a more solid basis for future responses, including a strengthening of the AMR research workforce and career progression pathways in academia and the NHS. Without appropriate level of frontline staff working on infection prevention and antimicrobial stewardship, within NHS trusts, the capacity for advancing applied research, supporting surveillance and improved patient management and clinical outcomes cannot be realised. Active support for careers in AMR research and policy are vitally important to create leadership in this area. More equal investment in vaccines and point of care diagnostics tests, balanced with investment in new anti-infective drugs, is also needed in both the human and agriculture sectors.

Interdisciplinary approaches to tackle AMR: For example, drawing on social sciences and behavioural research to understand social and contextual influences on prescribing as well as risk

and rates of AMR. The role that inequalities play in transmission such as sanitation, access to water etc. requires examining addressing poverty related causes, particularly important on a global level and linked to achieving the sustainable development goals.

Within the UK, what are the key successes we should look to maintain or build on in responding to AMR?

Please include up to 3 examples in no more than 250 words.

- The launch of the innovative subscription model for antibiotics by NHS England, in collaboration with the National Institute for Health and Care Excellence, has been a key success to build on.[3] This novel model could provide the foundations for routine supply of antimicrobials in the NHS and stimulate companies to increase investment. The next step would be to encourage and support other countries to trial and use similar models.

- There have been research successes demonstrating the importance of prioritising continued support for research. One example is research on using phylogeny and genome mining to find novel antibiotics with new modes of action. Research should now be increased for the development of point of care diagnostics and for the development of vaccines that prevent infection and the use of antimicrobial drugs.

- Much has been achieved during the COVID-19 pandemic, including the rapid development of safe and effective vaccines and identification of treatments for severe disease. The UK has played a leading role in these developments, which could be built upon in responding to AMR. This includes developments in areas such as diagnostics and surveillance which are crucial aspects of the AMR response and can draw on the COVID-19 experience; and the testing infrastructure developed for COVID-19 could be repurposed to support AMR surveillance. This could extend to wastewater and other environmental monitoring as well as surveillance in veterinary medicine. However, AMR is a much more complex issue which will require a more sustainable approach compared to COVID-19.

Within the UK, what are the areas that require more focus or development to address AMR?

Please include up to 3 examples using no more than 250 words in total.

- The UK has existing strengths in areas such as vaccine research, clinical research within the NHS, and genomics across the academic and public health sectors, which swiftly pivoted to work on COVID-19. Rapid success was based on these 'deep roots', the result of substantial past investment in research. Responses were more mixed in areas that lacked such firm foundations, such as diagnostics. The Academy's 'Building a Sustainable UK diagnostics Sector' report highlighted the growth in diagnostics testing and capabilities driven by COVID-19, but it is not clear if this is sustainable for the long term and there

[3] https://www.england.nhs.uk/blog/how-the-nhs-model-to-tackle-antimicrobial-resistance-amr-can-set-a-global-standard/

are continued on-going issues for the diagnostics sector that pre-date the pandemic[4]. For example, the system in which diagnostics operates is complicated and disjointed, with decision-making in the UK markedly slower and more disparate than in other countries. Therefore, while the UK has many research strengths relevant to AMR, some need nurturing to provide a more solid basis for future response.

- The departure of the UK from the European Union has the potential to allow the MHRA to develop innovative approaches to regulation for vaccines and pharmaceuticals dealing with AMR, such as accelerated approval based on likely AMR impact. If effective, this might stimulate similar moves globally, as the MHRA remains highly respected. However, the MHRA requires sustained funding and specific incremental funding to enable it to deliver. A key development to note is the recent strategic partnership between BioNTech and the UK government, illustrating the importance of the UK's ability to successfully conduct clinical research and get through regulatory processes. In the first instance, this arrangement with BioNTech is focused on cancer vaccines but there are plans to conduct future work on infectious disease vaccines. It demonstrates the importance of preserving and strengthening the UK's clinical research capacity and regulatory processes.

- Patient and public involvement is essential at multiple levels, from the design and prioritisation of strategies to tackle AMR, to the identification of effective ways to communicate with different audiences. For example, the design and communication of policies surrounding data use and sharing and vaccines, to ensure public acceptability. Securing public support for action to address AMR will also be vital, as it has been for COVID-19 and will be for climate change.

Within your sector, do you think the UK has sufficient capacity and capability to tackle AMR?

- yes
- yes, in some areas (please specify)
- no (please specify)
- don't know

More investment in research and supporting professional roles is vital in building the UK's capacity and capability to tackle AMR. This includes investment in research and a strengthening of the AMR research workforce and career progression pathways in academia and the NHS. The UK's response also has to be seen within an international perspective given that AMR is a global threat and interconnected issue, with globalisation as a secondary driver of transmission.

What additional capacity and capability is needed in your sector to effectively tackle AMR?

[4] The Academy of Medical Sciences (2021). *Diagnostics: Building Capacity and Capability in the UK*

Please give up to 3 examples using no more than 250 words in total.

1. As above, investment in supporting professional roles in research and the NHS.

2. Better use of technology and innovation to optimise antimicrobial use. For example, several COVID-19 vaccines have been based on novel platforms that could potentially be adapted to combat priority bacterial pathogens. Vaccines against viral pathogens could also reduce unnecessary antibiotic use, while additional vaccines for veterinary use could also be developed. Global structures such as the Coalition for Epidemic Preparedness Innovations (CEPI) have been critical for accelerating the development of vaccines and a similar model could be developed for AMR-related vaccine priorities.

3. Building on the opportunities of diagnostics and their role in screening and surveillance for both infection prevention and for informing antimicrobial optimisation. However, there are ongoing challenges for the diagnostics sector. Compared to pharmacological therapies, diagnostics suffer from more complicated evidence generation for efficacy, from uncertainty in their value proposition, and from a lack of a well-established and robust clinical trial infrastructure. The system in which diagnostics operates is complicated and disjointed, with decision-making in the UK markedly slower and more disparate than in some other countries. The route to adoption into the NHS, reimbursement models and long-term returns on investment can also be unclear, so diagnostics typically attract less private investment than pharmacological therapies. While during the COVID-19 pandemic, the diagnostic testing, microbiology surveillance and manufacturing capabilities of the UK expanded at unprecedented speed, it is not clear which elements are sustainable for the long term. For example, regulatory pathways for diagnostics need to be reviewed. Such pathways are complex and often slow, problems which need to be addressed through dialogue between regulators, developers, and other stakeholders.

In your opinion, what are the key barriers to making progress on tackling AMR in your sector?

Please give up to 3 examples using no more than 250 words in total.

1) As above, lack of investment in supporting professional roles in research and the NHS remains a key barrier.

2) Lack of data linkage across sectors and access can hamper coordination and is often limited by data privacy regulations. In the Academy's 'AMR research: learning lessons from the COVID-19 pandemic' report, it was noted that patients were typically more open to data sharing than regulators assume, if informed in advance and when the benefits are clearly explained.[5] One attendee gave the example of COVID-19 research

[5] The Academy of Medical Sciences (2021). *AMR Research: Learning lessons from the COVID-19 Pandemic*

in care homes as an example of where data was able to be accessed and linked across different settings at scale. Progress made during the pandemic needs to continue beyond COVID-19. It was noted that one advantage of wastewater surveillance studies is that they raise few if any ethical issues, as samples cannot be linked back to individuals.

3) A skewed research focus on new drug development. The optimisation of the use of existing antimicrobial agents, without compromising access, will be necessary to address the challenge of AMR. However, there is significant funding inequity between the research and development for new drugs and the implementation and efficient use of existing agents in the AMR research landscape. [6]

What, if anything, do you think we can learn from other countries' responses to AMR?

Please be specific about which countries you are referring to in your answer.

Please give up to 3 examples using a maximum of 250 words in total.

The Academy has a partnership with the Hamied Foundation aimed at developing long-term collaborations on AMR research. As part of this, the Academy conducted a UK-India Symposium on Anti-Microbial Resistance aimed at sharing learnings between the countries and facilitating collaborations to jointly address the challenge of AMR.[7] A common theme was around surveillance. While England has a comprehensive AMR reporting system, there are concerns about the timelines and completeness of data; and a lack of standardisation, including across devolved administrations. India has two main networks for monitoring AMR, run by the Indian National Centre for Disease Control and the Indian Council of Medical Research. There is a close collaboration between these networks and an emphasis on standardisation and harmonisation of practices across surveillance sites, with contributing centres required to adhere to standardised practices. This may be an area of interest for the UK to apply learnings from. The Academy will be organising a second symposium in India in the next 12-18 months.

The Academy's report on Interdisciplinary research in epidemic preparedness and response highlighted the importance of an integrated approach across disciplines, which the UK could look to incorporate for the response to AMR. For example, the report highlighted case studies, including a research consortium coordinated by INSERM, the French National Institute of Health and Medical Research and funded by the European Union's Horizon 2020 programme. The ZIKalliance is a multinational and multidisciplinary research consortium compromising 54 global partners investigating clinical, fundamental, environmental, and social aspects of zika virus infection.

In your opinion, which of these tools should be prioritised for adapting to use in tackling AMR?

[6] The Academy of Medical Sciences (2021). *Advances in antimicrobial innovation*
[7] The Academy of Medical Sciences (2019). *UK-India Symposium on Antimicrobial Resistance*

- Diagnostics for therapeutic decisions and for screening
- Surveillance
- Therapeutics
- Infection prevention, including use of vaccines and immunotherapy vaccines

All of the above tools are of importance and should not be viewed in isolation. However, improved diagnostics do offer the most potential for rapid improvements and there is potential for vaccines focused on preventing AMR. One of our Fellows has suggested that the UK could also benefit from the development of drugs that are at an even earlier stage of development than those that are part of the CARB-X portfolio. CARB-X is a global non-profit partnership accelerating antibacterial products to address drug resistant bacteria, with a portfolio of early development pipeline of new antibiotics, vaccines, rapid diagnostics and other products. [8]

In your opinion, are there any other tools that should be adapted from use during the COVID-19 pandemic for tackling AMR?

- yes (please specify)
- no
- don't know

- The Academy of Medical Sciences' 'FORUM published the 'Antimicrobial resistance: learning lessons from the COVID-19 pandemic' report, following a joint workshop with the Department of Health and Social Care (DHSC) and the National Institute for Health Research (NIHR). The workshop focused on two key areas of relevance to AMR-diagnostics and surveillance, and therapeutics and vaccines. During the scoping process for this workshop, several other areas were identified, including those related to infection prevention and control (IPC) within both healthcare settings and communities. It was noted that it will be important to review the successes and challenges related to IPC in controlling the spread of COVID, as IPC measures can play a central role to reduce the number of infections and requirements of antimicrobials. Therefore, promoting good infection control practices can be an essential component to tackling AMR and there may be tools from the COVID response related to IPC that could be adapted for AMR.

- Regulatory support for flexible pathways for clinical trials.

- On a global level, a Coalition for Epidemic Preparedness Innovations (CEPI) type coordination and working groups, including a COVID-19 Vaccines Global Access (COVAX) like mechanism to provide tool to low-and-middle income countries.

- Using wastewater as a surveillance mechanism for AMR in the community, which has been used for community-level COVID-19 surveillance and can be used to gain insights into AMR in human populations.

- Strengthening of pathogen genomics to detect the emergence of resistance, and its transmission. Genomics capability locally from COVID has largely been wound down.

[8] Carb-X. https://carb-x.org/about/overview/

Do you believe the changes in ways of working within your organisation due to the COVID-19 pandemic have affected efforts to respond to AMR, such as delivery of the current national action plan (NAP)?

(Not applicable)

- yes
- no
- don't know

In what way have they affected the response to AMR or delivery of the NAP?

(Not applicable)

Please give up to 3 examples using no more than 250 words in total.

Are there other ways in which the COVID-19 pandemic has altered the AMR risk landscape?

Please give up to 3 examples in no more than 250 words in total.

1) The increased use of antibiotics to prevent bacterial infection in persons with SARS CoV2 infection increases the risk of development of resistance and contributes to making guidance on antibiotic use more complex.

2) The impact on frontline staff and health worker fatigue which could affect health and social care staff retention rates and the overall ability to effectively deliver infection and prevention control. The Academy's 'COVID-19: Preparing for the future – Looking ahead to Winter 2021, 2022 and beyond' report touched on the impact on staffing levels and the incidence of burnout among those working on the COVID-19 frontlines.[9] The COVID-19 back-log of care continues to add pressure on staff and affect retention rates.

3) A focus on pandemics and preparing for the next one has meant that funding has been channelled elsewhere. There needs to be a renewed focus on AMR.

Are there other global events, such as supply chain disruption or the conflict in Ukraine, that have changed the UK's ability to respond to AMR?

- yes

[9] Academy of Medical Sciences (2021). COVID-19: looking Ahead to Winter 2021-22 and beyond

- no
- don't know

If yes, how have other global events changed the UK's ability to respond to AMR?

The UK's departure from the EU is impacting research in the UK. Research collaboration and participation in Horizon Europe was part of the Trade and Cooperation agreement (UK-EU TCA) and is something that the Academy strongly supports. However, this has not yet been achieved and, even with Third Country participation and other mitigations, this is having impacts on UK-EU research collaboration. It is also important for the UK to continue working closely with international partners including in Europe for surveillance (such as through cooperation on technical and scientific matters with the European Centre for Disease Control and Prevention - as set out in UK-EU TCA) and in research collaborations. Scientists working together around the world was integral to our approach to tackling the pandemic – bringing vaccines and treatments with unprecedented speed. Therefore, it is vital for the UK to protect international networks that support research collaborations to ensure that the UK can effectively respond to AMR.

In your opinion, what are the best measures of success in tackling AMR?

Please give up to 3 suggestions.

As mentioned in previous responses:

Investment in research and supporting professional roles: Without appropriate level of frontline staff working on infection prevention and antimicrobial stewardship within NHS trusts, the capacity for advancing applied research, supporting surveillance and improved patient management and clinical outcomes cannot be realised. Active support for careers in AMR research and policy are vitally important to create leadership in this area.

Societal awareness and understanding: The public expectation of receiving antimicrobials is still very high, and this places undue pressure on doctors to prescribe antimicrobials before an accurate diagnosis has been made. This practice of prescribing antimicrobials to meet expectations or to induce a placebo effect in patients should continue to be discouraged. Increased campaigns to improve public awareness of the importance of antimicrobials and the detrimental effect of misuse would help to take pressure to prescribe off doctors.

Need to take an internationally focused approach with emphasis on global solidarity: AMR is an interconnected global problem, and the UK cannot act alone to tackle AMR and requires ongoing international efforts and collaboration. Especially as secondary drivers of AMR relate to globalisation from global travel, global food distribution etc. For example, it would be important to consider the Sustainable Development Goals and how these can feed into the UK's response to AMR. Linked to this, a 'One-Health' approach that recognises the interconnectedness of people, animals and their environment is essential to respond to AMR both nationally and internationally.

Do you believe that there is sufficient public and professional awareness of AMR?

- yes
- no
- don't know

If no, what should be done to increase awareness of AMR? Please tell us in a maximum of 250 words.

No, there is not sufficient public and professional awareness of AMR: Through extensive advocacy, AMR is now on the global political agenda, but may not yet be considered a priority by national governments and the general public. Thought could be given to how AMR is communicated to support stronger advocacy and to achieve greater political and public buy-in. Patient and public involvement is essential at multiple levels, from the development of strategies to the identification of effective ways to communicate with different audiences. Securing public support for action to address AMR will also be vital, as it has been for COVID-19 and will be for climate change.

As previously mentioned, more extensive education of medical students and doctors in training on AMR issues would highlight the negative impact of bad antimicrobial prescribing practice for a future cadre of doctors and other medical professionals; stewardship campaigns should also be extended to veterinary surgeons and animal keepers. Linked to this point around education on AMR, active support for careers and research in AMR and policy is important to create leadership in the area and contributes to establishing knowledge in the area. The lack of support for these roles and professional and academic development in the UK and NHS is a critical barrier for knowledge sharing and promoting awareness.

Is there any other evidence you would like to tell us as we develop the 2024 to 2029 national action plan?

Please tell us using no more than 250 words.

We would like to reiterate the importance of international learning and the need to have a collaborative approach across human health, animal health and the environment through a 'One Health' approach. As part of this, the UK should support an increase of global advocates across all these three sectors. One Health would be an important theme for the national action plan to consider. The Academy of Medical Sciences' is organising two global health workshops on the topic. The first workshop will take place in collaboration with the African Academy of Sciences in Nairobi, Kenya over 6-7th February. It will convene researchers and other key stakeholders to discuss implementing a One Health approach in the continent through greater multi-sectoral collaboration. The second One Health workshop will take place in Brazil over 29-30th March. The outputs from the workshops will include reports and key actions for stakeholders to take forward in their organisations and settings, including the UK. We would be happy to share the key outputs from the meeting.

Full list of relevant AMS Work:

- FORUM Learnings from COVID-19 report (2021)
- FORUM Advances in AMR innovation report (2021)
- UK-India Symposium Report on AMR report (2019)

- Improving the development of and deployment of diagnostic tests in LMICs report (2016)
- Interdisciplinary research in epidemic preparedness and response report (2019)
- Addressing the threat of antimalarial drug resistance to malaria elimination in Southeast Asia report (2020)
- Diagnostics: Building Capacity and Capability in the UK report (2021)
- COVID-19: Looking ahead to winter 2021-2022 and beyond report
- AMS response to the Commons Science and Technology Select Committee Inquiry on AMR (2013)

This response was prepared by Aisha Mazhar, International Policy Officer, and informed by members of the Academy's Fellowship and previous policy work in this area. For further information, please contact Aisha Mazhar (aisha.mazhar@acmedsci.ac.uk)