Antimicrobial resistance: a Biochemical Society position statement

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Foreword

Part of the Biochemical Society's mission is to champion the molecular biosciences and their importance in addressing societal grand challenges. To achieve this, the Society undertakes policy work, aiming to channel the views of its membership and community to policy makers.

As part of its policy activity, the Society has issued several position statements on issues relevant to the molecular biosciences and the broader science sector. These statements are developed by the Policy Advisory Panel, who guide and direct the Society's policy activities and outline its stance on these important topics. Position statements are used as a basis for the Society's engagement with policy makers on issues affecting the molecular bioscience community.

Antimicrobial resistance (AMR) is a growing global threat and an issue where the molecular biosciences play a key role due to their importance in furthering development of many AMR-mitigating strategies. In 2022, the Policy Advisory Panel opted to update and refresh the Biochemical Society's position on AMR, and this was launched during the 2022 World Health Organization's World Antimicrobial Awareness Week (18–24 November).

The full Biochemical Society position statement is shared here. We hope that this statement will be used by policy makers and other stakeholders to frame and guide future discussions on AMR.

Antimicrobial resistance – a Biochemical Society position statement

Antimicrobial resistance has been described by the World Health Organization as a threat to global health and developmen.t If left unchecked, it has been estimated that it will cause 10 million deaths per annum by 2050,[1] and could drive 28 million people into extreme poverty.[2]

Molecular biosciences and AMR are closely connected

Molecular biosciences play a crucial role in combatting AMR. By enabling life to be understood at the fundamental level, basic and applied molecular research contributes directly and indirectly to reducing AMR burden across health, agricultural and environmental settings. For example, molecular understanding of microbial resistance mechanisms, as well as drug–target interactions (Figure 1), will be crucial both for optimizing existing antimicrobials and to developing novel drugs. Indirectly, molecular understanding across the disease spectrum is required to develop a repertoire of accurate and rapid diagnostic tools and effective vaccines.

The Biochemical Society recognizes that the issue of AMR is complex, and while highly important, the contribution of molecular bioscience research alone will not address the crisis we are facing. The Biochemical Society believes that an integrated, collaborative, multi-sectorial response to AMR, following the One Health framework, is vital. For this to be viable, it will require substantial and sustained funding along with decisive leadership and steadfast support from governments, global leaders and industry.

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Adoption of the One Health approach is vital for an integrated, collaborative and multi-sectorial approach

The One Health concept is defined as an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. In practice, it is a multidisciplinary and multi-sectorial approach to preventing emergent and

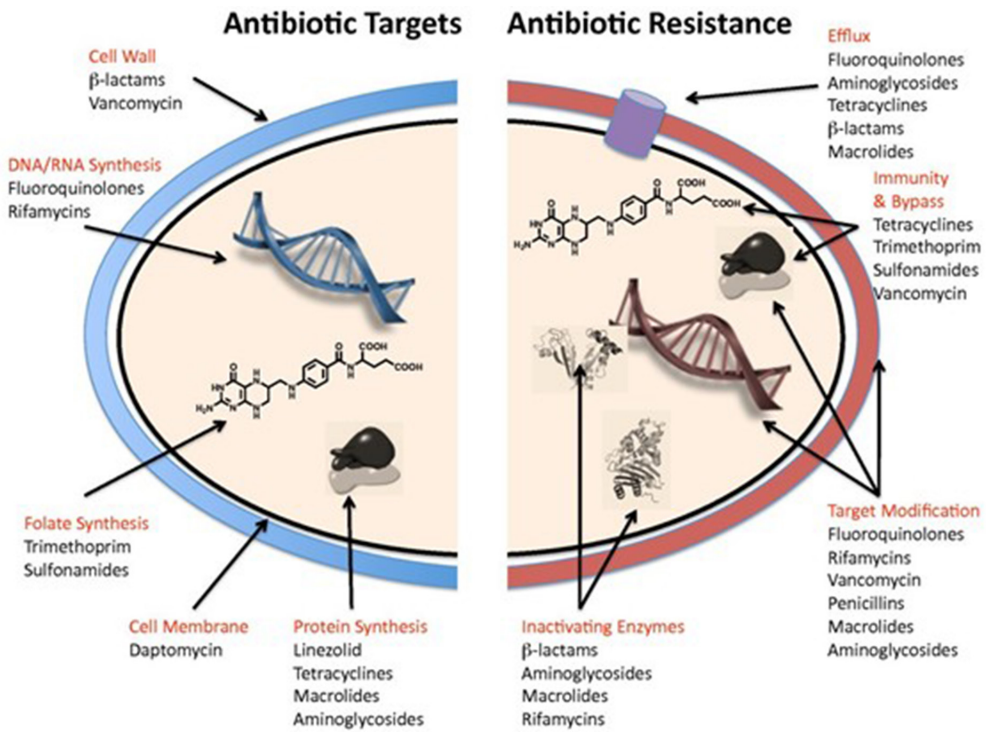

Figure 1. Antibiotic targets and mechanisms of antibiotic resistance. Source: https://doi.org/10.1186/1741-7007-8-123, published by Biomed Central Ltd. under CC BY 2.0 licence.

resurgent infectious diseases, emphasizing the necessity for combined action from the public, private, non-profit and academic sectors. This concept recognizes the inextricable link between the environment, plant, animal and human health and, as such, is paramount in the fight against AMR (Figure 2), encompassing a range of AMR-countering strategies such as improving access to existing health care resources, infection prevention, antimicrobial stewardship, improving diagnostics, enhancing public health surveillance, increasing laboratory capacity, supply chain management and developing AMR-related skills in the global health care workforce.

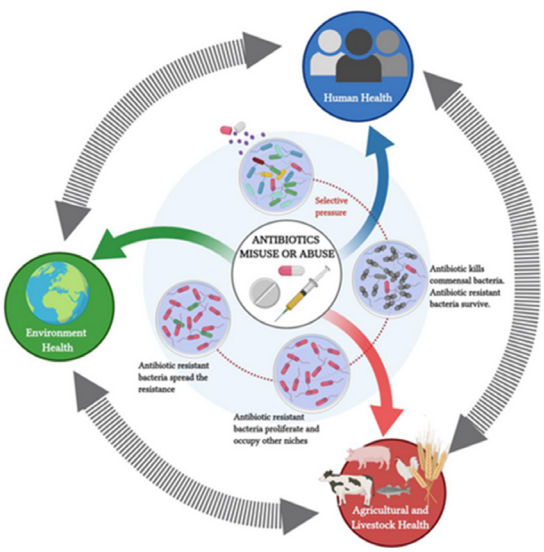

Figure 2. Antibiotic misuse or abuse and the spread of antimicrobial resistance in relation to the One Health concept. https://doi.org/10.1111/1751-7915.13587

The need for the One Health approach is clear. Although the risks that the overuse and misuse of antimicrobials in medical and veterinary settings and livestock agriculture pose to the development of AMR are well known,[3] use of antimicrobials and potential routes to drug resistance are widespread (Figure 3). Antimicrobial use in crop-based agriculture is a growing concern, with a lack of regulation and monitoring in many countries.[4] Environmental settings too can act as reservoirs for resistance, and specialists in public health and urban development should be included in AMR collaborations, as poor hygiene and sanitation measures play a dominant role in accelerating the spread of AMR, for example, through untreated sewage and waste reaching water supplies.[5]

Sharing of knowledge and resources on an international scale is vital. AMR disproportionately affects low- and middle-income countries[1,6] (Figure 4) where there is little access, for example, to more expensive second-line antibiotics when first-line drugs fail due to resistance. For instance, in sub-Saharan Africa, the

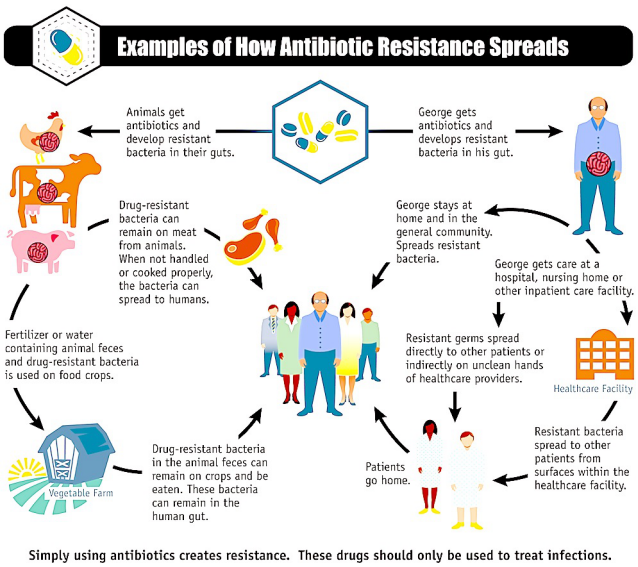

Figure 3. Examples of how antibiotic resistance spreads and the link between animal, human and environmental health. Source: Antibiotic Resistance and NARMS Surveillance | NAMS | CDC – Public Domain.

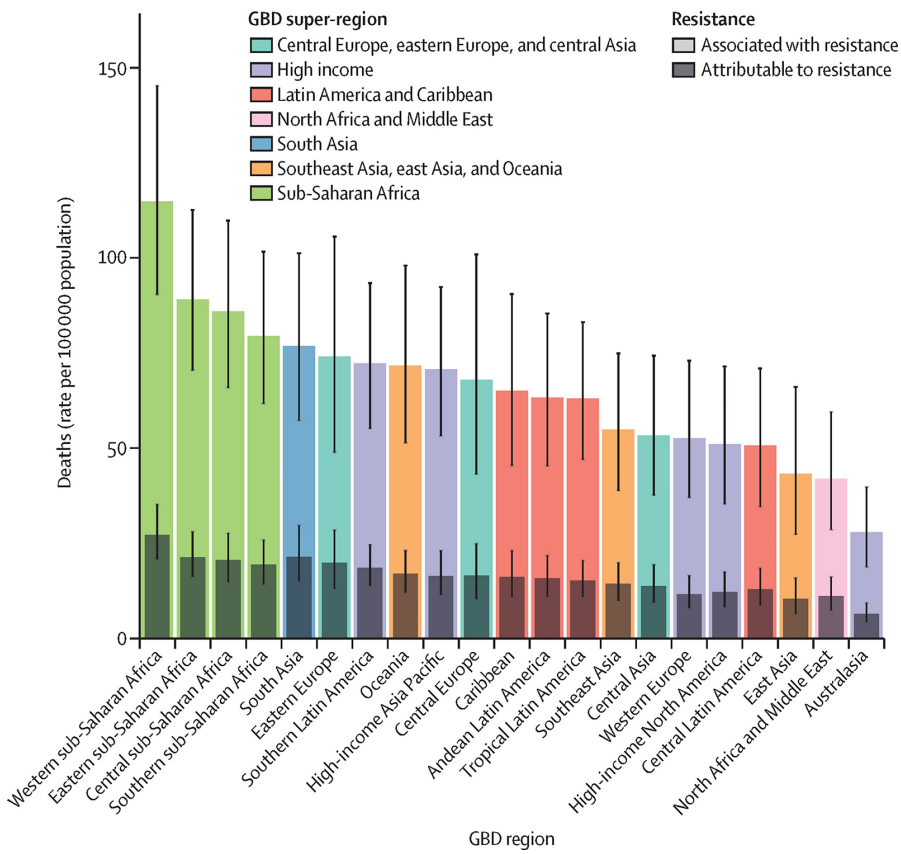

Figure 4. AMR disproportionately affects low- and middle-income countries: the graph shows the all-age rate of deaths attributable to, and associated with, bacterial antimicrobial resistance by Global Burden of Disease (GBD) region. Reproduced from Antimicrobial Resistance Collaborators. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 399:629–44, published by Elsevier under a CC BY licence.

lack of means for effective prevention, diagnostics and treatment of infectious diseases is worsening the AMR burden.[7] However, geographical differences must also be recognized; in South Asia and Latin America, AMR burden is due to high levels of resistance even with good access to antibiotics.[7] Global collaborations combining their efforts to promote global awareness and surveillance of AMR, for example, the Quadripartite collaboration[8] and the Global Leaders Group,[9] are now promoting the One Health approach to fight AMR and are playing a valuable role in increasing access to information and AMR advocacy on an international scale.

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Innovation and funding will be crucial to protect existing antimicrobials and securing a pipeline of alternative drugs

To combat AMR, an increase in research funding is essential. Clearly, this is critical not only for the design and development of novel antimicrobials, but also for improving diagnostics, vaccines and other measures that will also prevent the proliferation of AMR. At present, the antimicrobial research and development (R&D) system is fragmented, with a lack of collaboration between academia, industry and clinicians (Figure 5). In line with One Health, a more coordinated and systematic approach is needed to ensure that new antimicrobials are brought to market in as prompt a manner as possible.

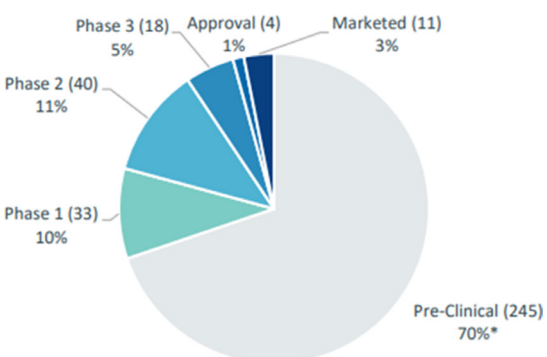

Figure 5. Product pipeline for therapeutics for human bacterial infections by development stage (April 2021). Preclinical data from WHO 2020 – preclinical pipeline analysis. From https://globalamrhub.org/wp-content/uploads/2021/12/Annual-Report_Final_10122021.pdf.

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Successful innovation relies on resource mobilization, and funding by both public and private investors needs to be highly visible to prove that antimicrobial R&D is a priority area and to inspire investors' confidence. For example, CARB-X[10] and the AMR Action Fund[10] are currently important funding sources for novel antimicrobial development. Interruptions in funding can lead to abandonment of projects and new firms failing to grow into mature businesses, and researchers in both academia and industry moving on to more financially rewarding areas of research. This can be exemplified by the collapse of companies that successfully brought new antibiotics to market, yet still suffered bankruptcy (e.g., Melinta Therapeutics and Achaogen). Situations such as this contribute significantly to the lack of confidence for investment in antimicrobial R&D. In response to the market failure, novel schemes have been launched in the UK[11] and the USA[12] to reward firms that launch new drugs through an annual fixed fee, thus delinking financial reward from volume of prescriptions. For this new model to become a powerful market signal to industry and encourage pharmaceutical companies to re-invest in antimicrobial R&D, other countries will need to offer similar schemes and co-ordinate on priorities.

Increased global advocacy (from governments, industry and the third sector) and, above all, action are needed to spur interest and investment in the on-going global AMR crisis. Advocacy for increased funding remains an important part of this, but, within the concept of the One Health approach, advocacy is also needed in many other areas in relation to AMR.

Political will, accountability and leadership will be crucial to spurring action

Political will is another essential element of our battle to defeat AMR. Indeed, AMR is a global strategic priority and sits within the UK government's National Risk Register[13]; however, not enough is being done at the governmental level to address the issues associated with it. In the UK, there is currently no single entity or individual tasked with the essential functions of leadership and coordination across sectors. In 2014, Lord Jim O'Neill chaired an AMR review and produced a highly influential report,[1] and former chief medical officer Dame Sally Davies (2011–2019) provided leadership on AMR,[14] but there is currently no obvious replacement for these individuals. The UK All-Party

Parliamentary Group on Antibiotics[15] exists to raise the profile of antibiotic resistance, and AMR has been addressed by the House of Commons Committees for Health and Social Care[16] and Science and Technology,[17] and indeed there are many more examples[8 9 18–20] of collaborations, groups and initiatives, both nationally and internationally, that exist to tackle AMR, but coordination and accountability are lacking. One approach could be for the UK government to appoint a 'tsar' for AMR.

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Decisive political leadership, guided by well-informed expert opinion, is vital to navigating through public health crises. The COVID-19 pandemic has shown that political leadership and coordinated action, on both national and international scales, can galvanize rapid and effective action. However, the focus on SARS-CoV-2 since 2020 has potentially led to a substantial decline in public awareness of AMR and a distraction from its perils, as, by contrast with COVID-19, AMR has been described as a 'silent' or 'slow-burn' pandemic. Governments have a key role in engaging people across society in terms of encouraging adoption of public health measures that reduce infection risk and safeguard antimicrobials.

Although public health has to be the key driver, the economic consequences of the spread of AMR provide compelling justification for enhanced efforts in this area. It has been estimated that, by 2050, the costs of AMR would be US$100tn,[1] so, although the costs of tackling AMR are potentially very high, the net financial benefits are likely to outweigh those costs. Aside from direct R&D funding, funding from central governments could enable, for example, establishment of early career fellowships in AMR to maintain related skills in the workforce, and centres for AMR research (national and/or international) that would act as hubs for R&D. Whatever political initiative is forthcoming, bold, innovative and coordinated sustainable action is required, and required soon.

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The Biochemical Society

Our membership includes molecular bioscientists working in AMR and related fields across academia and industry, and across a range of career stages and pathways, in research, teaching and leadership positions. We are dedicated to supporting their career development, and that of scientists across the entire molecular bioscience community.

We are committed to championing awareness and knowledge about the AMR battle and supporting the approaches outlined in this statement throughout all facets of our work. We foster collaborative ways of working and, together with our community partners, seek to influence UK policies on AMR and related areas. Aiming to ensure that scientific evidence is prioritized in policymaking, we work with the Royal Society of Biology and as part of the Learned Societies Partnership on Antimicrobial Resistance,[21] combining our voices and maximizing our influence. We also promote and share knowledge on AMR through our publisher, Portland Press,[22] encouraging open and transparent dialogue, and provide platforms for discussion and collaboration through our scientific meetings and events.

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