

Antimicrobial Resistance in the UK: Therapeutics and Vaccines

What is AMR?

The rise of antimicrobial resistance (AMR) is one of the most urgent global threats to public health in the 21st century. AMR refers to disease-causing microbes (known as pathogens) evolving and gaining resistance to drugs and substances that were once effective treatments against infections (antimicrobials). It poses significant challenges to clinical care, health economies, animal and plant health as well as the environment. Microbiologists from across the world are committed to developing innovative solutions to combat AMR.

How does AMR occur?

AMR occurs when microbes (bacteria, viruses, fungi and parasites) mutate and evolve to resist treatment to antimicrobial compounds. When microbes are exposed to antimicrobials, they are put under a selective pressure that forces them to develop mechanisms that enable them to survive. Resistant microbes can then multiply and share their defence mechanisms with other microbes in the population. Therefore, overuse and inappropriate use of antimicrobials increases the prevalence of AMR.

What is the cost of AMR?

- AMR costs the NHS an estimated £180 million per year, and left unabated it could result in a cost of £66 trillion in lost productivity to the economy by 2050 [1].
- By 2050, it is estimated that AMR will kill 10 million people worldwide per year – more than cancer and diabetes combined [2].
- A systematic analysis of AMR conducted in 2019 concluded that it was the third leading global burden of disease, killing more people than both HIV/AIDS and malaria [3].
- Without strategies to control and reduce the spread of AMR, routine medical interventions such as surgical operations and childbirth could start having potentially fatal outcomes.



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What does the data tell us about antibiotic use in the UK?

The scale of AMR is difficult to capture but the magnitude of the global burden is significant. Accurate surveillance is dependent on rigorous data collection and consistent data sharing between healthcare institutions, across human and animal health, and this can be challenging to coordinate.

- There were 53,985 cases of serious antibiotic resistance in humans in England in 2021. This is the equivalent of 148 per day, a rise of 2.2% from the previous year, and this was during the COVID-19 pandemic when there was less socialising and spreading of microbes [4].
- In 2021, 19% of people in England with a key pathogen bloodstream infection had a resistant strain. This is the equivalent of 14,846 bloodstream infections due to antimicrobial resistant pathogens, an increase of 14% since 2013 [4].

Therapeutic solutions

With the ever-growing rise of resistant pathogens threatening global health, the efficacy of available therapeutics to treat pathogens is diminishing. As such it is essential that we invest in optimising our use of existing antimicrobials, discover new antimicrobial compounds, find compounds that boost the efficiency of our current antimicrobials and develop alternative treatments.

Optimise the use of our current antimicrobials

> **Accurate diagnosis of target microbes**

It is vital that we have reliable, consistent diagnostic mechanisms across human, animal and environmental health sectors. This will ensure that we are able to identify the infection-causing microbes and their resistance profiles to prevent unnecessary use of current antimicrobials. For more detailed information, see the Microbiology Society briefing on diagnostics and surveillance [5].

> **Education to reduce unnecessary usage**

Increasing awareness among the public, farmers, veterinary and healthcare professionals of the danger of AMR and the link with unnecessary antibiotic use is essential to reduce excess consumption. Reducing overuse of our current antimicrobials will extend their longevity and efficacy.

Discover new antimicrobial compounds

To keep pace with the increasing occurrence of resistant infections, sustained funding for basic research that seeks to discover new antimicrobial compounds is needed. Collaboration with industry can smooth and speed up the route to drug development, and intervention from policymakers is essential to ensure market efficiency and a sustainable pipeline from discovery through to drug development.

CASE STUDY:

Using AI to discover new antimicrobials

Developments in Artificial Intelligence (AI) have allowed researchers to employ machine learning models to search for potential sources of antimicrobial compounds and accelerate antimicrobial discovery. Recent studies utilising AI to search through large chemical libraries led to the discovery of antibiotics such as 'halicin' [6] and 'abaucin' [7]. These are capable of killing numerous pathogens listed by the World Health Organisation (WHO) as those of critical threat to the human population, including the highly resistant *Acinetobacter baumannii* [8]. This demonstrates the power of AI to vastly increase the rate and reduce the cost at which new antibiotics can be discovered.

Develop new antimicrobial drugs

Discovery of antimicrobial compounds is the important first step on the road to drug commercialisation. However, the drug development pipeline is long, complex and expensive – it can take 10-15 years and over \$1 billion to develop a new antibiotic [9]. To put this into context, from 2017 to 2021 just one new antibiotic was approved that could treat superbugs on the World Health Organization's (WHO's) critical list. Pharmaceutical companies are hesitant to fund antimicrobial development as they are unlikely to see returns on their investment, and many companies have failed and gone out of business recently. Research and development costs are high, but restrictions on consumption in effect put new antibiotics at the back of the medicine cabinet to only use in an emergency (for example against a very resistant organism). These restrictions are rightly put in place to reduce the risk of AMR occurring, but can make it difficult to maximise sales and see a return on investment [10].

CASE STUDY:

The new subscription-style payment model

NHS England and Improvement, in collaboration with the National Institute for Health and Care Excellence and the UK Department of Health and Social Care, have launched a pioneering 'subscription-style' payment model for antimicrobials. This model evaluates antimicrobials on their estimated value to patients and the NHS, and reimburses corporations based upon this value rather than on volume supplied [11]. In other words, pharmaceutical companies are guaranteed payment for a new antimicrobial, regardless of the quantity consumed, which encourages innovation without promoting overconsumption. The Microbiology Society strongly supports this initiative as an innovative solution to a complex problem that the UK is leading on.

Develop alternative therapeutics

While there is a critical need for new antimicrobials to be introduced to the market, using alternative therapies is another way to tackle resistant infections and protect our current antimicrobials. Innovative alternative therapeutics being developed include oligonucleotides (to prevent gene expression) [12], monoclonal antibody therapy (to neutralise microbes and activate the immune response) [13] and bacteriophage therapy (to destroy bacteria) [14].

Vaccines

Preventing infection and disease is crucial to mitigating AMR. Effective use of existing vaccines, and the development of new vaccines, has the potential to significantly slow and contain the spread of AMR.

Make use of current vaccines

While antimicrobials treat established infections, vaccines are used prophylactically to prevent infections. Using both viral and bacterial vaccines as a preventative tool could not only reduce the burden of infections from resistant strains, but also reduce antimicrobial use, therefore curbing the spread of AMR [15]. In addition, vaccines can provide population level protection through herd immunity where non-vaccinated individuals are indirectly protected by vaccinated people who cannot transmit the infection, as seen with the pneumococcal vaccine [16].

Unlike antimicrobials, vaccines offer long-term protection from infections, and their impact can last for decades.

CASE STUDY:

Success story: *Haemophilus influenzae* serotype b (Hib) [17]

Haemophilus influenzae serotype b (Hib) is a bacterial pathogen that was previously the most common cause of bacterial meningitis in children aged <5 years. Although antibiotics do exist to treat Hib infection, AMR is common among Hib strains. The Hib vaccine was introduced routinely for infants in the UK in 1992 and to this day the disease continues to be well controlled across all age groups, with only 7 cases of Hib reported in England in 2021.

Develop new vaccines against AMR pathogens

Current vaccine pipeline

Existing licensed vaccines against bacteria that are considered at high risk of developing AMR, including *Salmonella* Typhi (Typhoid fever), can be leveraged to tackle AMR by improving their access worldwide [18]. The WHO recently identified 61 vaccines that were in pre-clinical or clinical development to address diseases on their bacterial priority pathogens list. However, the pipeline for at least six high risk bacteria, including *Klebsiella pneumoniae* (the highest cause of neonatal mortality where resistance is high in many countries), is weak and significant investment is needed to accelerate vaccine development [19]. In contrast, there are currently no vaccines to prevent fungal infections in humans [20].

CASE STUDY: Using meningitis vaccines against gonorrhoea

Gonorrhoea is a bacterial sexually transmitted infection caused by *Neisseria gonorrhoeae*, classified as a priority pathogen by the WHO due to high levels of AMR and fears of it becoming untreatable. While no gonorrhoea-specific vaccination currently exists, a meningitis B vaccination has been shown to offer protection of up to 40% against gonorrhoeal disease, as both diseases are caused by *Neisseria* species. In 2015, the UK became the first country to offer routine meningitis B vaccination; recent evidence predicts that using the meningitis vaccine against gonorrhoea could save the NHS £7.9 million over the next 10 years [21].

Barriers to vaccine development

Current global vaccine markets are not conducive to the development, supply or access of vital vaccines for public health. Key issues include lack of incentives to stimulate the development of new vaccines, limited profit potential and vaccine hesitancy. Encouragingly, new initiatives are being developed in the UK to stimulate the creation of vaccines from product design through to commercialisation and evaluation, including the BactiVac Network [22] and the opening of the UK Health Security Agency's Vaccine Development and Evaluation Centre (VDEC) [23].

Conclusions

Investing time and resources into developing innovative preventative and treatment solutions is crucial if we are to keep pace with the emergence of AMR. Delivery of therapeutics and vaccines will require strong, consistent government support, including funding for research on antimicrobial discovery and alternative therapies, financial incentives for the development of new antimicrobial drugs, and the facilitation of cross-sector collaboration embedded within the One Health agenda, which recognises that resistant microbes arising in humans, animals or the environment may spread from one to the other.

The Microbiology Society is taking a solutions-focused approach with the 'Knocking Out AMR' project, by working with its members to facilitate collaborations, acting as a conduit for knowledge and evidence, and bridging the gap between research and policy. We have access to experts across sectors and are well-placed to support the Government in its efforts to tackle AMR.

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Microbiology Society Briefings

The Microbiology Society is a membership charity for scientists interested in microbes, their effects and their practical uses. Our principal goal is to develop, expand and strengthen the networks available to our members so that the science of microbiology provides maximum benefit to society. Through its diverse membership, the Society can offer impartial, expert information on all areas of microbiology.

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Thanks are due to the following experts for their advice:

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Isobel Garratt (University of Bath),

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The Microbiology Society remains solely responsible for the content of this briefing. **Issue date: November 2023.**