Powering the UK's response to AMR

Claudia Martínez

September 2020

#reformhealth

Acknowledgements

Reform would like to thank BD (Becton, Dickinson and Company) for kindly supporting this paper.

External reviewers

The authors would like to thank Professor Hilary Thomas, Director and Chief Medical Adviser at KPMG, for helpful comments on an earlier draft of this paper.

Interviewees

The authors would like to express their gratitude to the 11 individuals and organisations who were interviewed as part of the research for this paper and kindly agreed to be acknowledged:

Adam Zerda, Director, AMR Strategy & Development, BD.

Arlene Brailey, Patient Support Officer, Antibiotic Research UK.

Professor Colin Garner, Chief Executive, Antibiotic Research UK.

Dr Roger Harrison, Senior Lecturer in Public Health, Centre for Epidemiology, University of Manchester.

Jeremy Knox, Policy & Advocacy Lead Drug-Resistant Infections, Wellcome Trust.

Jessica Morley, Policy Lead, Evidence-Based Medicine, Data Lab University of Oxford.

Liz Cross, Advanced Nurse Practitioner, Attenborough Surgery, Bushey Medical Centre.

Michael Corley, Head of Policy & Public Affairs, British Society for Antimicrobial Chemotherapy.

Rose Gallagher, Professional Lead Infection Prevention & Control, Royal College of Nursing.

Pat Cattini, President, Infection Prevention Society.

Professor Dame Sally Davies, UK Special Envoy on Antimicrobial Resistance.

Icon in logo made by Good Ware from www.flaticon.com

About

Reform is established as the leading Westminster think tank for public service reform. We are dedicated to achieving better and smarter public services. Our mission is to set out ideas that will improve public services for all and deliver value for money.

We work on core sectors such as health and social care, education, home affairs and justice, and work and pensions. Our work also covers issues that cut across these sectors, including public service design and delivery and digital public services.

We are determinedly independent and strictly non-party in our approach.

About *Reform* Ideas

***Reform* Ideas** – These are short research papers which enable a high-level exploration of a key public service challenge. The papers examine the policy context, identify key opportunities for reform and set a vision for the future.

Contents

Foreword

The future of modern medicine depends on antibiotics. Yet, the future of global health could be undermined by Antimicrobial Resistance (AMR). AMR is happening now in all countries, but it is preventable if we act now, collaboratively across borders and sectors.

AMR is a top national priority for the UK, as it is for the World Health Organisation, World Economic Forum and United Nations. I am proud of the impressive progress the UK has made in tackling AMR and securing AMR on the global agenda in recent years. We have significantly reduced antibiotic use in humans and the animal sector and continue to take action to protect the antibiotics we already have by ensuring they are only used when needed. We have built world-leading surveillance and research capabilities to help us better understand drug-resistant infections and support the development of innovative ideas and technologies. We are at the forefront of tackling AMR globally. This June, the UK launched a pioneering, world-first payment scheme to encourage industry to develop much-needed antibiotics for NHS patients. These are all important steps forward to meet our commitments in our National Action Plan and our ambitions in our 20 Year Vision for AMR. Our challenge is now to build on this momentum by ensuring that commitments translate into concrete action globally, on the ground, and encouraging other countries to join the UK in similar innovative ventures.

As attention turns to building back our health systems and economies from COVID-19, we must also build our resilience to tackle AMR. Without sufficient and timely action worldwide, drug resistance will have deeper and even farther-reaching consequences for all countries' health systems and the world economy than COVID-19 is having. The world must step up preventative efforts, through hygiene and vaccination, the role of fast diagnostics and therapies, and the need for better monitoring and stewardship of the use of antimicrobials.

It is against this backdrop that I welcome *Reform's* new report looking at the UK's role and contribution to the global response on AMR. It is not only timely but of utmost importance that we continue to show global leadership in addressing this global health issue and lead the way for other countries to join us. We must all move forward together.

Professor Dame Sally Davies, UK Special Envoy on AMR

Ideas

Idea 1: The Department for Health and Social Care, in partnership with relevant local and international stakeholders, should develop an engagement plan to strengthen policymaker's, healthcare professionals' and the public's understanding of the impact of vaccines on antimicrobial stewardship and their role in addressing AMR. These efforts should be built on robust analyses and modelling of the health and economic impacts of immunisation on antibiotic use, and improved surveillance data on the effects that vaccine uptake has in limiting the burden of AMR.

Idea 2: NHS England and NHS Improvement, in collaboration with the National Institute for Health and Care Excellence, should urgently commission a national assessment of the clinical and cost-effectiveness of tools like point-of-care diagnostics to inform future reimbursement models. The assessment should consider tests' performance across health and care settings, as well as additional dimensions of value such as clinical outcomes and impact on clinical workflows. Specific measurements to assess the value these tools provide with regard to their impact on AMR should be explored.

Idea 3: The AMR Diagnostic Partnership Board should focus on improving existing practice and closing well-recognized gaps in clinical care. One such example would be to support the widescale adoption of the national standards for blood culture processing issued by Public Health England and the pathways produced by National Institute for Care Excellence (NICE) pathways across NHS Trusts.

Idea 4: Health Education England should evaluate strategies to ensure that the extensive technical and clinical expertise of hospital staff in relation to point-of-care testing is leveraged in the community. This could take the form of specific training and certification of primary and community care staff, the creation of self-audit tools and checklists to ensure the safe and proper use of devices, or the provision of specialist advice upon request. Existing structures, such as point-of-care testing committees within NHS Trusts, could also be employed to facilitate communication between hospitals and the primary and community care sector.

Idea 5: The Department for Health and Social Care should support the development and use of open source analytic tools, like OpenPrescribing, to enhance AMR surveillance and national antimicrobial stewardship efforts. To improve access to high quality health-service and clinical data for health research, NHS Digital in England, and national information technology organisations in the devolved administrations, should conduct an audit of existing data sources relevant to antimicrobial and diagnostic stewardship, and define appropriate information governance frameworks to support their use. Furthermore, the Department should make available specific funding streams to fund data science and applied clinical informatics research projects across the country.

Idea 6: Public Health departments in England and the devolved countries should work with charities and local patient organisations to create an awareness and education campaign highlighting the experiences of individuals living with drug-resistant infections and their families. This should be accompanied by a suite of accessible information resources on AMR patient safety, including standardised information about specific drug-resistant bacteria, the infections they cause, regional data on resistance, and healthcare-associated infections in hospital. Outcomes from this campaign should be independently evaluated and learnings shared.

Idea 7: The Department of Health and Social Care should support a national fund to pilot, evaluate and develop pragmatic and scalable community engagement approaches to tackle AMR. A mixture of philanthropic contributions plus a levy on funded antimicrobial drug discovery research could be used to finance the fund, with monies ring-fenced. Activities and projects should be delivered locally and as a partnership between local government, academic institutions, grassroots organisations, civil society and patient advocacy groups. Processes and outcomes need to be evaluated with civil society partnerships, using a range of methodologies, and a focus on sharing best practices.

Introduction

The world is facing the urgent and increasing threat of Antimicrobial Resistance (AMR).[1] A growing range of infections caused by bacteria, fungi, parasites and viruses are becoming resistant to antimicrobial drugs and antibiotics, increasing the spread of infectious diseases, and leading to rising disability and death.[2] AMR is deemed by the World Health Organization to be "one of the biggest threats to global health, food security and development today."[3]

Drug-resistant 'superbugs' are currently responsible for around 700,000 deaths globally each year.[4] If unaddressed, the number of AMR-related deaths will rise to a staggering 10 million by 2050.[5] AMR will also come with a hefty price tag to the global economy, costing $100 trillion and disproportionately impacting low- and middle-income countries (LMICs).[6]

The COVID-19 pandemic has further exacerbated concerns about AMR, raising questions about the global health system's preparedness and its ability to respond to pandemics, but also how to keep patients healthy and safe in a world where antibiotics are losing their effectiveness.

The UK has been at the forefront of addressing this threat, publishing its first cross-government AMR strategy and National Action Plan as early as 2000.[7] Since then numerous strategies and policy papers have been published.[8] However, while steps have been taken and progress is ongoing, critical gaps remain.[9]There is growing concern that political will is diminishing and that momentum in achieving global policy commitments on AMR is slipping. With AMR on the rise and the world fast approaching a "doomsday scenario" the need to act now cannot be overstated.[10]

This paper examines the progress achieved in the fight against AMR, identifies areas in need of urgent attention and proposes ideas for policy action.

---

[1] World Health Organization, 'United Nations High-Level Meeting on Antimicrobial Resistance', Webpage, 21 September 2016.
[2] World Health Organization, 'Antimicrobial Resistance', Webpage, n.d.
[3] World Health Organization, 'United Nations High-Level Meeting on Antimicrobial Resistance'.
[4] Interagency Coordination Group on Antimicrobial Resistance, *No Time to Wait: Securing the Future from Drug-Resistant Infections. Report to the Secretary-General of the United Nations*, 2019, 1.
[5] Jim O'Neill, *Tackling Drug Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance*, 2016.
[6] Ibid.
[7] Department of Health, *UK Antimicrobial Resistance Strategy and Action Plan*, 2000.
[8] Ibid.; Sally Davies, *Chief Medical Officer Annual Report 2011: Antimicrobial Resistance* (London: Department of Health and Social Care, 2013); Department of Health and Department for Environment Food & Rural Affairs, *UK Five Year Antimicrobial Resistance Strategy 2013 to 2018*, 2013.
[9] Charles Clift, *Review of Progress on Antimicrobial Resistance* (Chatham House, 2019), 7.
[10] Henry Bodkin, 'Life-Saving Drugs May Soon Become Useless, Experts Warn as 19 Untreatable Superbugs Are Discovered in the Last Decade', *The Telegraph*, 11 September 2019.

1. AMR and the 'post-antibiotic' world

The number of drug-resistant bacteria has grown dramatically in the last decades, turning common infections into life-threatening illnesses and claiming thousands of lives.[11] The threat posed by drug resistance is very real and present. AMR cannot be solved nor reversed, only managed. As put by Professor Dame Sally Davies – former Chief Medical Officer for England and UK Special Envoy on Antimicrobial Resistance – it requires "forever vigilance" and unprecedented levels of international cooperation and political leadership.

1.1 AMR: A brief definition

AMR, also known as drug-resistance, develops when microorganisms, like bacteria and fungi, adapt and become immune to the drugs designed to treat them.[12] While AMR happens naturally, a myriad of factors enable and accelerate its spread. The widespread inappropriate use of antibiotics in humans, animals and plants has stimulated bacteria to develop mechanisms to 'fight back' and become resistant to drugs.[13]

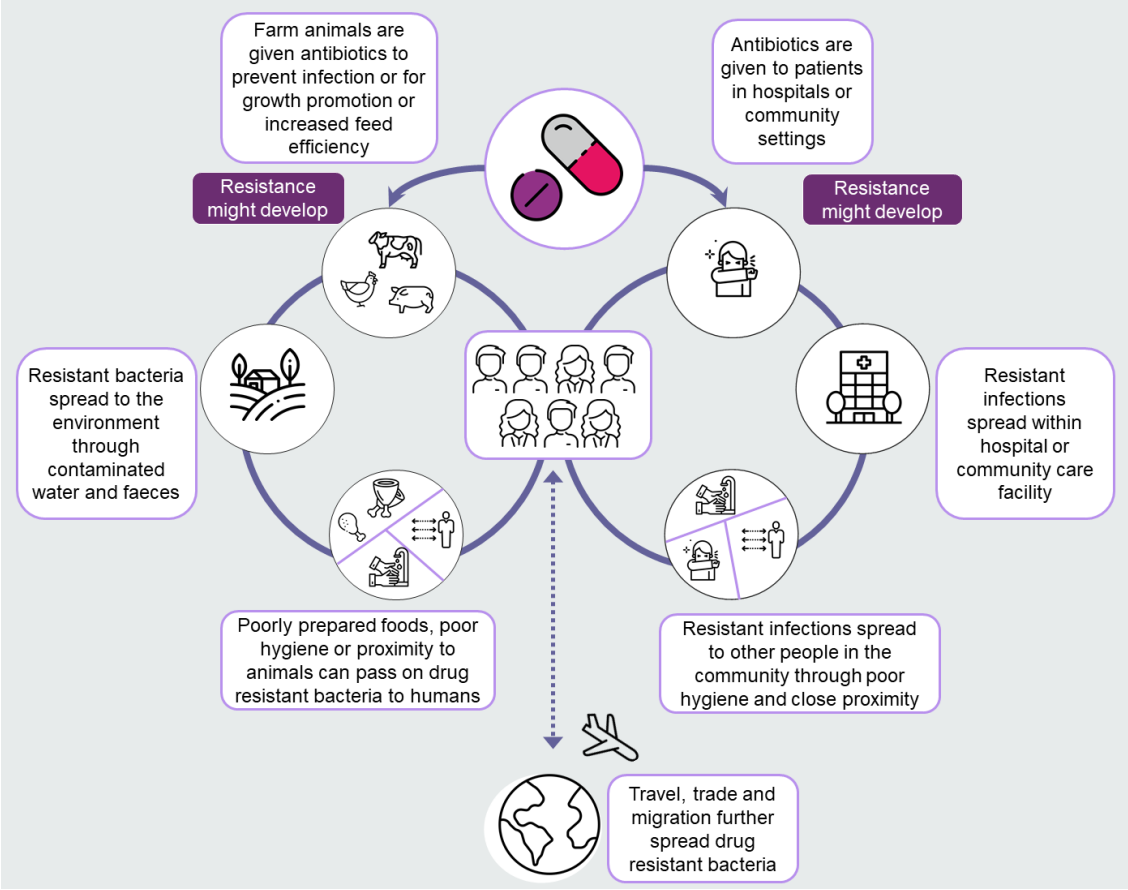
Antibiotics are often misused or prescribed for infections that do not require antibiotic treatment. In many countries, antibiotics are also accessed over-the-counter and without a prescription from a medical professional.[14] Multidrug-resistant bacteria spread rapidly within hospitals, but also in community settings, further contributing to heightened resistance and antibiotic use. Poor hygiene, inappropriate infection control practices and suboptimal sanitation systems, particularly in low-income countries, have also driven the spread of resistant infections.[15] No country is immune to AMR and international travel and trade have brought drug resistance to all corners of the world. Figure 1 explains how AMR develops and spreads.

Worryingly, as older antibiotics progressively start failing, not enough new antibiotics and therapies are being developed to replace them.[16] No new classes of antibiotics have been discovered since 1987 and, as the WHO Director-General Tedros Adhanom Ghebreyesus has warned, "the cupboard is disturbingly bare".[17] If left unchecked, AMR will result in a dramatic increase in human morbidity and mortality and huge costs to

[11] Brad Spellberg et al., 'The Epidemic of Antibiotic-Resistant Infections: A Call to Action for the Medical Community from the Infectious Diseases Society of America', *Clinical Infectious Diseases* 46, no. 2 (January 2008).
[12] Victoria Wells et al., 'Implementing WHO, EU and UK AMR Strategies and Action Plans: Has the World Lived up to the Challenge?', *The Lancet Infectious Diseases*, December 2017.
[13] E Yoko Furuya and Franklin D Lowy, 'Antimicrobial-Resistant Bacteria in the Community Setting', *Nature Reviews Microbiology* 4, no. 1 (January 2006).
[14] Maria C Guinovart, Albert Figueras, and Carles Llor, 'Selling Antimicrobials without Prescription: Far beyond an Administrative Problem', *Enfermedades Infecciosas y Microbiologia Clinica (English Ed.)* 36, no. 5 (November 2018).
[15] Cliodna AM McNulty et al., 'Don't Wear Me out—the Public's Knowledge of and Attitudes to Antibiotic Use', *Journal of Antimicrobial Chemotherapy*, April 2007; Teresa Gil-Gil et al., 'Antimicrobial Resistance: A Multifaceted Problem with Multipronged Solutions', *MicrobiologyOpen*, November 2019.
[16] Wellcome Trust, 'Why Is It so Hard to Develop New Antibiotics?', Webpage, 21 January 2020.
[17] World Health Organization, 'Compelling Priorities for Global Health', Webpage, 19 September 2017.

the world's economy. As explained by Professor Dame Sally Davies in an interview for this paper: "AMR is a big problem that is getting worse and will go on getting worse – but we can take action to address it."

Figure 1: How AMR develops and spreads



Source: *Reform*, based on the World Health Organization's 'Antimicrobial resistance' Factsheets, February 2018.

1.2 The global AMR effort: Stalled progress?

AMR has long been recognised as a major threat to global health, capturing the attention of governments and international agencies.[18] The last decade in particular, however, has seen remarkable progress in strengthening global coordination on AMR.[19] The publication of the Global Action Plan on AMR by the World Health Organization (WHO) in 2015 set the foundations for global action and the adoption of a 'One Health' approach, encompassing human, animal health, food production, and the wider environment.

[18] Laura J Shallcross and Sally C Davies, 'The World Health Assembly Resolution on Antimicrobial Resistance', *Journal of Antimicrobial Chemotherapy* 69, no. 11 (2014).
[19] Ibid.

This political commitment was further lifted by the signing of a political declaration on AMR by heads of States at the United Nations 2016 General Assembly.[20] That same year, the world-leading Independent Review of AMR, commissioned by the UK government and chaired by macroeconomist Lord Jim O'Neill, sounded alarm bells about the socioeconomic risks of global inaction on AMR and proposed "ten commandments" for curbing resistance.[21] The Review was the first to quantify the potential economic impact of AMR and, as explained by interviewees for this paper, was pivotal in reigniting the political debate on the need to invest in R&D for new drugs. Since 2017, WHO member states have begun developing National Action Plans to drive local action on AMR.[22]

However, while AMR has become part of the global policy agenda, critical gaps remain, and there has been a "startling lack of progress" in advancing the recommendations proposed in the O'Neill Review.[23] In particular, the development of new market models for encouraging R&D in antibiotics has been remarkably slow. Greater impetus from governments across the world and investment from the pharmaceutical industry are needed to spur the development of vital diagnostics tools and to promote widespread access.

Action is needed to promote better infection, prevention, and control practices, but also to reduce antibiotic use worldwide, especially in LMICs. While over 100 countries now have a national action plan for AMR in place, only 20 per cent are currently properly funded.[24] But particularly worrisome, as argued by experts interviewed for this paper, is the sense that the momentum and political will for combating this public health threat is dwindling.[25] There is been "too much talk, and not enough action" and focus must urgently be placed on delivering the commitments outlined in the long list of policy papers, strategies and political declarations on AMR.

1.3 The UK's AMR response

The UK has historically been at the centre of global efforts in combatting AMR, publishing its first cross-sectoral AMR strategy as early as 2001 and acting as an energetic advocate for AMR action internationally.[26] A refreshed UK wide cross-government AMR strategy and five-year action plan were launched in September 2013 by the Department of Health (now Department of Health and Social Care, DHSC), with

[20] United Nations, *Draft Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance*, 2016.
[21] O'Neill, *Tackling Drug Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance*.
[22] World Health Organization, 'Antimicrobial Resistance: National Action Plans', Webpage, n.d.
[23] Clift, *Review of Progress on Antimicrobial Resistance*.
[24] Otto Cars, 'Otto Cars: Reacting to Antimicrobial Resistance', *Bulletin of the World Health Organization* 97 (2019).
[25] World Health Organization, *Monitoring Global Progress on Addressing Antimicrobial Resistance*, 2018; Clift, *Review of Progress on Antimicrobial Resistance*; Interagency Coordination Group on Antimicrobial Resistance, *No Time to Wait: Securing the Future from Drug-Resistant Infections. Report to the Secretary-General of the United Nations*.
[26] Laura J Shallcross et al., 'Tackling the Threat of Antimicrobial Resistance: From Policy to Sustainable Action', *Philosophical Transactions of the Royal Society B: Biological Sciences*, June 2015.

the Department for Environment Food and Rural Affairs and Public Health England (PHE). The strategy's main goal was to slow the progression of AMR by focusing activity on three strategic aims:

- improve the knowledge and understanding of AMR;
- conserve and steward the effectiveness of existing treatments; and
- stimulate the development of new antibiotics, diagnostics and novel therapies.[27]

Progress was achieved in reducing overall antibiotic consumption, most significantly in animal health, but also in human health. From a policy perspective, the strategy helped galvanise the UK's commitment to international collaboration on AMR and cross-sectoral work under the 'One-Health' approach. In 2015, AMR was added for the first time to the Cabinet Office's National Risk Register of Civil Emergencies, making it a top public security concern.[28] Specific programmes were created to improve access and use of AMR surveillance data.[29]

Additionally, in 2015, the UK launched the Fleming Fund, a £265 million UK Aid fund to help LMICs develop AMR surveillance systems.[30] Action to improve antimicrobial prescribing led to the introduction of tools like the TARGET (Treat Antibiotics Responsibly; Guidance, Education, Tools) Antibiotics Toolkit in primary care, and the publication of national antimicrobial prescribing quality measures.[31] In 2014, the £10 million Longitude Prize was launched to incentivise the development of innovative rapid diagnostic tests to address AMR, with further seed funding for promising innovations channelled through programmes like Nesta's Discovery Awards.[32]

In response to the publication of the 2016 O'Neill Review, the UK set up the Global AMR Innovation Fund (GAMRIF) to invest £50 million over five years in early-stage AMR research in LMICs.[33] A UK-China AMR Innovation Collaboration was also agreed in late 2016.[34] On the domestic front, an AMR Research Funders Forum has been established to better coordinate AMR-related research and funding efforts.[35]

While the UK has been proactive on AMR, however, further ongoing action is needed if this dangerous health threat is to be mitigated. The burden of antibiotic-resistant infections in England is rising with over 60,000 new resistant 'superbugs' emerging in just the last year.[36] The proportion of drug-resistant bloodstream infections, which are often associated with high patient mortality and morbidity, soared by an alarming 32 per

[27] Wells et al., 'Implementing WHO, EU and UK AMR Strategies and Action Plans: Has the World Lived up to the Challenge?'
[28] House of Commons Library, 'The Challenge of Antimicrobial Resistance', Webpage, 2015.
[29] Clift, *Review of Progress on Antimicrobial Resistance*.
[30] 'The Fleming Fund', Webpage, 2018.
[31] Medical Research Council, 'Antimicrobial Resistance Funders' Forum', Webpage, n.d.
[32] Longitude Prize, 'Longitude Prize', Webpage, 2019.
[33] Department for Health and Social Care, 'The Global AMR Innovation Fund', Webpage, n.d.
[34] Department of Health and Social Care, Innovate UK, and UK Research and Innovation, 'UK-China Partnerships against Antimicrobial Resistance Get Funding', Webpage, 24 January 2019.
[35] Medical Research Council, 'Antimicrobial Resistance Funders' Forum'.
[36] Public Health England, *English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)Report 2018 –2019* (London, 2019), 36.

cent between 2014 and 2018.[37] One-third of urinary tract infections in England are now displaying resistance to drugs,[38] and sexually transmitted infections like gonorrhoea are becoming increasingly difficult to treat due to a lack of effective antibiotics.[39]

The recent AMR inquiry by the House of Commons' Health and Social Care Committee further highlights the case for action, urging government to make AMR a "top five policy priority" to achieve tangible and rapid progress on delivering AMR commitments.[40]

Most recently, in January 2019, the Government published its 20-year vision and new five-year national action plan to accelerate activity on AMR.[41] The strategy builds on existing work and introduces new targets for reducing the number of specific drug-resistant infections in humans as well as antibiotic use in food-producing animals.

In order to reduce antibiotic use and improve patient outcomes, the strategy commits to supporting the rapid uptake of diagnostics. It sets out an ambitious target that, by 2024, the UK will be able to report on the percentage of prescriptions supported by a diagnostic test or decision support tool. Crucially, the strategy also pledges to develop and test a new payment model to incentivise pharmaceutical companies to invest in R&D for new drugs. This world-first 'subscription-style' payment system started in June 2020, with the NHS offering two contracts to develop new antibiotics, based on their value to the NHS, rather than their quantity of use.[42] Lastly, it enshrines a commitment to "continue to be a good global partner" in the fight against AMR and lead on international efforts to slow the spread of drug-resistance.[43]

The experts interviewed for this paper commended the UK's progress in addressing AMR and spoke positively about the Government's new AMR vision and action plan. Nevertheless, they warned of lost momentum and dwindling international political attention on AMR in recent years. The "self-congratulatory" narrative that has historically permeated the AMR debate, the absence of clear accountability for driving AMR policy efforts within government, and the limited use of targets to track progress were seen as key contributors to delayed global action in implementing the reforms needed to curb AMR. The UK, and governments from across the world, must muster the political will necessary to deliver their strategies and continue actively contributing to the global fight against AMR.

---

[37] Ibid.
[38] National Institute for Health and Care Excellence, *NICE Impact Antimicrobial Resistance*, 2018, 10.
[39] Centre for Infectious Disease Research and Policy, 'In World First, UK Reports High-Level Gonorrhea Resistance', Webpage, 28 March 2018; Anne Gulland, 'UK Pledges £5m to Fight "Super Gonorrhoea"', *The Telegraph*, 21 November 2018.
[40] House of Commons Health and Social Care Committee, *Antimicrobial Resistance. Eleventh Report of Session 2017–19*, HC 962 (London: The Stationery Office, 2018).
[41] HM Government, *Contained and Controlled The UK's 20-Year Vision for Antimicrobial Resistance*, 2019.
[42] Department of Health and Social Care, 'World-First Scheme Underway to Tackle AMR and Protect UK Patients', Webpage, 17 June 2020.
[43] HM Government, *Contained and Controlled The UK's 20-Year Vision for Antimicrobial Resistance*, 8.

1.4 COVID-19 and its impact on drug-resistance

The COVID-19 pandemic outbreak has tested the resilience of healthcare systems worldwide, with nations directing their efforts to minimise the spread of the epidemic, save lives and keep their economies afloat. Yet, the challenges it could pose for AMR are only beginning to be understood.

Patients suffering from viral respiratory infections like SARS-CoV-2, the strain of coronavirus that causes COVID-19, are at increased risk of contracting secondary bacterial co-infections, like bacterial pneumonia.[44] Antibiotics are often used as part of treatment against these types of infections. With rising rates of COVID-19 cases worldwide, there is rightly concern that this could lead to higher, inappropriate antibiotic prescribing and, as a consequence, increased resistance to antibiotics.[45] As of early June, over 92 per cent of coronavirus patients admitted to intensive care units around the world were receiving some type of antibiotic treatment.[46]

This is further exacerbated by a lack of awareness, and the absence, of a suitable treatment for the virus, which might lead people to wrongly use antibiotics as a means of prevention or treatment. [47] Also, it is difficult to diagnose whether the symptoms presented by a patient correspond to SARS-CoV-2 or bacterial infection.[48] Some patients are being prescribed antibiotics pre-emptively until the diagnosis is confirmed, whilst some patients are also developing secondary bacterial infections as a result of COVID-19. However, when these patients receive 'broad-spectrum antibiotics' (drugs that act against more than one bacteria or a range of diseases), this could result in more drug-resistant bacteria.[49] The value of early diagnosis is starkly exemplified by the case of sepsis, a life-threatening condition which is caused by COVID-19, and for which effective management requires patients to receive antibiotic treatment within an hour of presenting to A&E.[50]

But the impacts of COVID on AMR are far more wide-reaching. The pandemic is ushering new approaches to preventing, controlling and monitoring the emergence and transmission of infections, as well as building increased awareness of the importance of hand-washing and vaccination among the public. It has mobilised global leaders,

---

[44] Emine Alp and Andreas Voss, 'Ventilator Associated Pneumonia and Infection Control', *Annals of Clinical Microbiology and Antimicrobials* 5, no. 1 (April 2006); Denise E Morris, David W Cleary, and Stuart C Clarke, 'Secondary Bacterial Infections Associated with Influenza Pandemics', *Frontiers in Microbiology*, June 2017; Michael J Cox et al., 'Co-Infections: Potentially Lethal and Unexplored in COVID-19', *The Lancet Microbe*, July 2020.

[45] Timothy M Rawson et al., 'Bacterial and Fungal Co-Infection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing', *Clinical Infectious Diseases*, May 2020; Fei Zhou et al., 'Clinical Course and Risk Factors for Mortality of Adult Inpatients with COVID-19 in Wuhan, China: A Retrospective Cohort Study', *The Lancet*, March 2020.

[46] International Severe Acute Respiratory and Emerging Infections Consortium, *COVID-19 Report: 8 June 2020*, 2020.

[47] Rawson et al., 'Bacterial and Fungal Co-Infection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing'.

[48] Cox et al., 'Co-Infections: Potentially Lethal and Unexplored in COVID-19'.

[49] National Institute for Health and Care Excellence, *COVID-19 Rapid Guideline: Managing Suspected or Confirmed Pneumonia in Adults in the Community*, 2020; Wellcome Trust and HM Government, 'Review on Antimicrobial Resistance: Background', Webpage, n.d.

[50] Global Sepsis Alliance, 'Update: Can COVID-19 Cause Sepsis? Explaining the Relationship Between the Coronavirus Disease and Sepsis', Webpage, 7 April 2020.

industry and the research community around the quest to find a cure for the disease and highlighted the need for robust preparedness for tackling infectious diseases in the future. Importantly, it has given the world a taste of what could come if AMR is not kept in check. As a result, the global health and economic system must act to address AMR now as part of the short-term and long-term response and recovery from COVID-19.

2. Time for action

Decades of advocacy on AMR have not translated into sufficient action.[51] Efforts at preventing the emergence and transmission of resistant infections continue to be severely undermined by a lack of investment in novel antibiotics, vaccines and therapies from global governments and industry alike. Despite being as vital as drugs to fight AMR, diagnostic tools remain largely overlooked, untapped and underutilised. Serious and immediate action is needed to change this. With a new vision and National Action Plan in place, and important lessons emerging from the COVID-19 pandemic, the UK must use this opportunity to bring renewed impetus and political leadership to the fight against AMR.

2.1 Transforming antibiotics R&D

The present business model for antibiotics is affected by deep market failures and does not incentivise pharmaceutical companies to invest in antibiotic R&D. The R&D cost to bring a drug to market is upward of $1,000 million.[52] It can take decades for a company to research, develop, and manufacture an antibiotic which might only be used sparingly over the long-term, and sold at a low-profit margin.[53] As a result, recent years have seen many companies pulling out of the market or facing bankruptcy, scaling-down their antimicrobial drug discovery programmes or redirecting their R&D to other clinical areas.[54] This does not only have deep implications for antibiotics but for areas like cancer care, where patients "rely on antibiotics for the prevention and treatment of infections".[55]

Focus and investment have gone into introducing 'push' incentives to subsidise early-stage drug discovery, through initiatives like CARB-X (Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator),[56] Novo Holding's REPAIR (Replenishing and Enabling the Pipeline for Anti-Infective Resistance) Impact Fund,[57] and ENABLE (European Gram-Negative Antibacterial Engine). Smaller biotechnology companies and start-ups have taken an active role in this space. Yet, high upfront costs, a restrictive market and tight regulatory restrictions have resulted in projects failing to progress to post clinical development and in many cases companies going out of business.[58] Interviewees explained that this could result in a "cliff-edge" with initiatives

[51] Clift, *Review of Progress on Antimicrobial Resistance*.
[52] Olivier J Wouters, Martin McKee, and Jeroen Luyten, 'Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018', *Journal of the American Medical Association* 323, no. 9 (March 2020).
[53] Wellcome Trust, 'Why Is It so Hard to Develop New Antibiotics?'
[54] Access to Medicines Foundation, *Antimicrobial Resistance Benchmark*, 2020.
[55] Longitude Prize, *Effectiveness of Cancer Treatements Threatened by Rising Antibiotic Resistance*, 2020.
[56] CARB-X, 'Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)', Webpage, n.d.; 'Global Antibiotic Research & Development Partnership', Webpage, n.d.
[57] Novo Holdings, 'Repair Impact Fund', Webpage, 2019.
[58] Chris Dall, 'Achaogen Bankruptcy Raises Worry over Antibiotic Pipeline', Webpage, CIDRAP News, 16 April 2019; Lucy Parsons, 'Antibiotic Biotech Melinta Files for Bankruptcy', Webpage, PM Live, 3 January 2020.

like CARB-X– to which the UK Government has committed £20 million[59] – funding the early research needed to develop new antimicrobials, but no real routes for these products to progress to late-stage development.

In addition to 'push' incentives, 'pull' mechanisms that reward companies bringing new drugs to market are needed.[60] As mentioned earlier, the UK Government has taken bold steps in this regard, recently announcing a pilot of a new 'subscription-based' reimbursement model that will pay for drugs upfront, with payment subject to the drug's usefulness to the NHS rather than the volume of antibiotics sold.[61] Sweden is also in the process of testing a reimbursement model which guarantees a minimum annual revenue to the pharmaceutical company in return for the provision of a set amount of antibiotic within specified time limits.[62] While no similar models exist in the United States, the country has already entered guaranteed revenue agreements with some drug companies to secure access to critical antibiotics.[63] The pharmaceutical industry has started taking the lead with the recent launch of a $1 billion AMR Action Fund which aims to bring two to four novel antibiotics to market in the next 15 years.[64]

2.2 Rethinking the financial model

Fixing the 'broken' antibiotics market, however, is likely to require more radical disruption to the traditional market-driven model in pharmaceuticals. As argued by Professor Dame Sally Davies, a system whereby antibiotics are valued as a global public good, could not only help refill the antibiotic pipeline but also ensure that drugs are globally accessible at a "realistic cost price" by international governments.

Other proposals see philanthropic and non-profit organisations taking a much more active role in antibiotics R&D. One idea mooted is the creation of an internationally-funded non-profit institute that conducts early-stage research, clinical trials, organises the manufacturing of new drugs and commercialises them at a low-cost price.[65] In an interview for this paper, Professor Garner from Antibiotic Research UK explained that the model employed by the international not-for-profit R&D organisation, GARDP (Global Antibiotic Research and Development Partnership) could help shape such an institute.

GARDP has been successful in boosting R&D for affordable new antibiotics and treatments across their clinical development programmes by brokering risk-sharing partnerships with industry, academia, governments and other not-for-profits. It also

[59] CARB-X, 'UK Government and Bill & Melinda Gates Foundation Join Join CARB-X Partnership in Fight against Superbugs', Webpage, 22 May 2018.
[60] World Economic Forum, *Antimicrobial Resistance: Tackling the Gap in R&D Resources with Pull Incentives*, 2018.
[61] Department of Health and Social Care, 'Development of New Antibiotics Encouraged with New Pharmaceutical Payment System', Webpage, 9 July 2019.
[62] Public Health Agency of Sweden, 'Availability of Antibiotics', Webpage, 17 March 2020.
[63] Paratek, 'Paratek Awarded BARDA Project BioShield Contract for NUZYRA®', Webpage, 18 December 2019.
[64] AMR Action Fund, 'About Us', Webpage, n.d.
[65] Andrew C Singer, Claas Kirchhelle, and Adam P Roberts, 'Reinventing the Antimicrobial Pipeline in Response to the Global Crisis of Antimicrobial-Resistant Infections', *F1000Research*, 2019.

focuses on the entirety of the drug development pathway: from discovery and early exploratory research, through to clinical development and market access.[66]

There is concern, however, about the ability to finance the entirety of the R&D ecosystem from philanthropic and public sources and that a lack of commercial incentives could hamper innovation. As explained in an interview for this paper by Jeremy Knox, Policy & Advocacy Lead drug-resistant infections at the Wellcome Trust, such an approach could result in "a poorly funded ecosystem, where you don't have the brightest minds nor the best ideas going in".

Whatever model is ultimately chosen, the real challenge will be to maintain momentum in stimulating antibiotic R&D and ensuring that the lessons from the UK's, and other pilot programmes, are learnt globally. Interviewees agreed that the UK's new reimbursement model could mean a step-change in the way that drugs are reimbursed, further incentivising antibiotic innovation and helping align antibiotic development to public health objectives. However, the UK only accounts for 2.4 per cent of global sales of antibiotics[67] and unless coordinated investments in product development are made globally, the UK's innovative approach will have limited impact.

2.3 Recognising the value of vaccines

Vaccines play a crucial role in the effort to tackle AMR. By focusing on prevention rather than treatment, vaccines can reduce dependency on antibiotics and prevent the rise of multi-drug resistant infections in human and animal health.[68] Crucially, vaccines can protect against viral diseases for which antibiotics are often inappropriately prescribed.[69] While bacteria might become resistant to antibiotics, this is unlikely for vaccines, making them an important first line of defence against AMR. As more people are vaccinated it becomes more difficult for germs to spread, therefore creating 'herd immunity' which can protect the rest of the population.[70]

Investment in new and improved vaccines has been hampered by the lack of evidence of their economic value and impact on AMR.[71] Work has been done to identify priority areas for vaccines investment for pathogens with high levels of AMR,[72] and tools are currently being developed to appraise the cost-effectiveness of immunisation

[66] Manica Balasegaram and Laura JV Piddock, 'The Global Antibiotic Research and Development Partnership (GARDP) Not-for-Profit Model of Antibiotic Development', *ACS Infectious Diseases*, 2020.
[67] National Institute for Health and Care Excellence, *Frequently Asked Questions: Developing and Testing Innovative Models for the Evaluation and Purchase of Antimicrobials*, 2020.
[68] Philippe Buchy et al., 'Impact of Vaccines on Antimicrobial Resistance', *International Journal of Infectious Diseases* 90 (January 2020).
[69] Ibid.; Marc Lipsitch and George R Siber, 'How Can Vaccines Contribute to Solving the Antimicrobial Resistance Problem?', *MBio* 7, no. 3 (June 2016).
[70] Kathrin U Jansen and Annaliesa S Anderson, 'The Role of Vaccines in Fighting Antimicrobial Resistance (AMR)', *Human Vaccines & Immunotherapeutics* 14, no. 9 (May 2018).
[71] JP Sevilla et al., 'Toward Economic Evaluation of the Value of Vaccines and Other Health Technologies in Addressing AMR', *Proceedings of the National Academy of Sciences* 115, no. 51 (December 2018); Wellcome Trust and Boston Consulting Group, *Vaccines to Tackle Drug Resistant Infections: An Evaluation of R&D Opportunities*, 2018.
[72] Wellcome Trust and Boston Consulting Group, *Vaccines to Tackle Drug Resistant Infections: An Evaluation of R&D Opportunities*.

programmes in reducing AMR.[73] The National Institute for Care Excellence (NICE) is in the process of establishing a stakeholder advisory group to help inform new clinical and economic evaluation models for vaccines.[74] This, however, remains a nascent area of research.[75]

Similar to the barriers faced in antibiotics, market failures and regulatory hurdles often result in vaccines considered commercially risky investments by pharmaceutical companies. The introduction of new 'pull' incentives to incentivise vaccine R&D, as recommended by the O'Neill Review, has been slow, and the pipeline for new vaccines is still limited.[76] Finally, as noted by interviewees for this paper, even when safe and efficacious vaccines are available, there is the challenge of ensuring that they reach the people who need it most.

The COVID-19 pandemic outbreak has shown the disastrous impact that novel infectious diseases can have on human health and the world's economy, and has ushered "the most rapid vaccine deployment in history".[77] The UK Government has committed £131 million to build state-of-the-art vaccine manufacturing facilities and has secured early access to COVID-19 vaccine candidates.[78] This has also been accompanied by the creation of a new NHS COVID-19 Vaccine Research Registry to fast track signups for future COVID-19 vaccine clinical trials.[79] As argued by interviewees, these initiatives must be used to stimulate investment into vaccine R&D and to educate the public about the crucial role vaccines play in the prevention of disease.

Idea 1: The Department for Health and Social Care, in partnership with relevant local and international stakeholders, should develop an engagement plan to strengthen policymaker's, healthcare professionals' and the public's understanding of the impact of vaccines on antimicrobial stewardship and their role in addressing AMR. These efforts should be built on robust analyses and modelling of the health and economic impacts of immunisation on antibiotic use, and improved surveillance data on the effects that vaccine uptake has in limiting the burden of AMR.

[73] UK Parliament, 'Written Questions, Answers and Statements. Vaccination: Question for Department of Health and Social Care', Webpage, 14 February 2019.
[74] National Institute for Health and Care Excellence and NHS England & NHS Improvement, *Launch Statement: NHS England and NHS Improvement and NICE Begin Project to Develop and Test Innovative Models for the Evaluation and Purchase of Antimicrobials*, 2019.
[75] Parliamentary Office of Science and Technology, *Antimicrobial Resistance and Immunisation* (Houses of Parliament, 2018).
[76] Clift, *Review of Progress on Antimicrobial Resistance*.
[77] UN News, '"Landmark Collaboration" to Make COVID-19 Testing and Treatment Available to All', Webpage, 24 April 2020.
[78] UK Research and Innovation, '£131m Investment Fast-Tracks UK Coronavirus Vaccine Production', Webpage, 17 May 2020; Department for Business, Energy & Industrial Strategy, Department of Health and Social Care, The Rt Hon Matt Hancock MP, and The Rt Hon Alok Sharma MP, 'Millions Could Be Vaccinated against COVID-19 as UK Secures Strong Portfolio of Promising Vaccines', Webpage, 20 July 2020.
[79] Department for Business, Energy & Industrial Strategy and The Rt Hon Alok Sharma MP, 'Public Encouraged to Register for COVID-19 Vaccine Trials as 100,000 Already Sign-Up', Webpage, 17 August 2020.

2.4 Embedding infection prevention & control in everyday practice

Vaccines are, though, just one tool that can be used to tackle AMR. Infection prevention and control (IPC) practices in hospitals and the community, through rigorous hygiene procedures, sanitation and ongoing monitoring of infections, are also vital to limit the spread of drug-resistant organisms, minimise healthcare-associated infections (See Glossary) and ensure that patients access safe and effective care.

Despite its importance, commitments towards improving IPC have not necessarily translated into strategic action to improve IPC services. As explained by Pat Cattini, President at the Infection Prevention Society, one area in need of urgent attention is the IPC workforce, where reductions in public investment in recent years have led to a serious shortage of IPC services and IPC-specific skills. These shortages are especially acute in community and primary care settings.

Developing a specialist IPC workforce will require upskilling healthcare professionals through high-quality education and IPC training but also tapping into the, already extensive, expertise that existing staff can offer. For instance, as Rose Gallagher from the Royal College of Nursing says, nurses play a crucial role in IPC education and promotion and could see their role broadened to cover more specific aspects of IPC and AMR prevention.[80] This could be best achieved by refocusing and expanding continuing professional development training[81] and developing tailored support programmes to ensure nurses are kept updated with the latest developments in the field.

The need for ongoing IPC training and upskilling of healthcare staff has emerged as an important lesson from COVID-19. Unprecedented staff pressures, confusion as to how the infection is acquired and transmitted, and evolving IPC guidelines have led to inconsistent application of IPC procedures in some parts of the NHS. For instance, the pandemic has created issues around the use of personal protective equipment (PPE), with some staff using PPE inappropriately or failing to follow effective hand hygiene procedures.[82] As explained by Pat Catinni, this could have important consequences for AMR, especially as the inappropriate use of PPE has been linked to a rise in various types of gram-negative bacteria – most of which are resistant organisms. The consequences of COVID on AMR must be identified and used to both strengthen IPC guidelines and build capacity for good infection prevention across the health and care systems.

[80] Enrique Castro-Sánchez et al., 'Nurse Roles in Antimicrobial Stewardship: Lessons from Public Sectors Models of Acute Care Service Delivery in the United Kingdom', *Antimicrobial Resistance & Infection Control* 8, no. 1 (October 2019).
[81] Health Education England, *Health Education England Business Plan 2019/20*, 2019.
[82] Costanza Pearce, 'GPs Advised to Avoid "over-Reliance" on PPE and to Focus on Hand Hygiene', *Pulse*, 12 May 2020.

2.5 Harnessing the power of diagnostic tools

As argued in Lord Jim O'Neill's independent review, "diagnostics are the single biggest potential game-changer in the fight against AMR".[83] Diagnostic tools can help clinicians distinguish bacterial from viral infections and tackle the overuse of antibiotics.[84] They can screen resistant bacteria and limit their spread in healthcare settings. They also gather valuable data on resistance trends which can be used to inform AMR surveillance. As healthcare expands into the community, laboratory tests which can be performed closer to where patients access care, and deliver results fast and accurately – called point-of-care tests (PoCTs) – promise to radically change infection detection and treatment.[85] Yet despite their value, as argued by interviewees, diagnostics continue to be an untapped resource and second in priority to developing vaccines and antibiotics.

Again, the COVID-19 pandemic has brought the value of diagnostics into sharp focus, with "test, test, test" becoming the backbone of the global pandemic response.[86] Like many other countries, the UK has raced to expand its local diagnostics industry and introduced emergency authorisations and regulatory flexibilities to speed up the development of innovative approaches to test, monitor and treat COVID-19.[87] Over £24 million has been invested to fund COVID-related research projects,[88] with a further £1.3 million specifically allocated to evaluate how new diagnostic tests perform in health and care settings. To increase testing capacity 'Lighthouse Labs' have been set up across the country, albeit at a slower pace than the creation of 'Nightingale' hospitals.[89]

2.5.1. Bringing new diagnostic tools to market

While considerable global progress has been made in advancing the development of novel PoCTs through initiatives like the UK's Longitude Prize[90] and CARB-X[91], market failures in diagnostics make it difficult for diagnostic makers to bring a steady stream of affordable, accessible and innovative diagnostic tools to market. Complex and lengthy regulatory requirements, country-specific reimbursement pathways, and inconsistent

[83] O'Neill, *Tackling Drug Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance*.
[84] Public Health England, 'Research Reveals Levels of Inappropriate Prescriptions in England', Webpage, 27 February 2018.
[85] Savannah Reali et al., 'Novel Diagnostics for Point-of-Care Bacterial Detection and Identification', *RSC Advances* 9, no. 37 (July 2019); Jonathan Cooke et al., 'Narrative Review of Primary Care Point-of-Care Testing (POCT) and Antibacterial Use in Respiratory Tract Infection (RTI)', *BMJ Open Respiratory Research*, May 2015.
[86] BBC News, 'WHO Head: "Our Key Message Is: Test, Test, Test"', Webpage, 16 March 2020.
[87] Medicines and Healthcare products Regulatory Agency, 'MHRA Regulatory Flexibilities Resulting from Coronavirus (COVID-19)', Webpage, 1 April 2020; Health Research Authority, 'Making Changes to a Research Study to Manage the Impact of COVID-19', Webpage, 3 June 2020, 19.
[88] National Institute for Health Research, 'Funding Urgent Research into COVID-19 with UKRI', Webpage, n.d.
[89] UK Lighthouse Labs Network, 'UK Lighthouse Labs Network', Webpage, n.d.
[90] Ingrid Torjesen, 'UK Spearheads Efforts to Combat Rising Threat of Antibiotic Resistance', *British Medical Journal*, July 2014; Longitude Prize, 'Longitude Prize'.
[91] CARB-X, 'Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)'.

frameworks for assessing tests' efficacy and cost-effectiveness are some of the factors hindering the development of these tools.[92]

Yet, new and improved tests are sorely needed, with no diagnostic test currently meeting "the desirable target product profile that would enable prescribers to avoid empirical prescribing".[93] The UK's action plan for AMR commits to identifying high-potential products and accelerating their access to market, and to streamline the regulatory process. However, specific information on priority products is yet to be defined.

2.5.2. Developing a value-based approach to diagnostics

The "failure to strongly demonstrate the value proposition of diagnostics to healthcare systems", as explained by Jeremy Knox from the Wellcome Trust, has been an overriding barrier to the adoption and spread of new technologies. Detailed analyses linking the use of PoCTs to enhanced patient outcomes and health-economic benefits are limited.[94] While claims have been made that PoCTs could save billions to the NHS and studies show that a primary care-led PoCT pathway could be cost-effective compared to laboratory testing[95], no robust data currently exists to assess the value of these tools to the healthcare system.[96]

The current financial framework does not incentivise the uptake of innovative technology, particularly in primary care where [97] are often not reimbursed. This creates a mismatch between the costs and benefits of rapid diagnostics, with these tools often seen by healthcare professionals as "costly alternatives" compared to regular laboratory tests or to prescribing antibiotics.[98]

Further, the costs of diagnostic tools are often accrued in different parts of the healthcare system to where benefits are gained, creating extra barriers to their implementation.[99] The adoption of the O'Neill Review recommendation of restructuring

---

[92] Clift, *Review of Progress on Antimicrobial Resistance*.
[93] Ibid.
[94] Andrew St John and Christopher P Price, 'Economic Evidence and Point-of-Care Testing', *The Clinical Biochemist Reviews* 34, no. 2 (August 2013); Public Health England, *Point of Care Tests for Influenza and Other Respiratory Viruses: Winter 2019 to 2020*, 2019, 11; Valentina Pecoraro, Luca Germagnoli, and Giuseppe Banfi, 'Point-of-Care Testing: Where Is the Evidence? A Systematic Survey', *Clinical Chemistry and Laboratory Medicine* 52, no. 3 (March 2014).
[95] Austen El-Osta et al., 'Does Use of Point-of-Care Testing Improve Cost-Effectiveness of the NHS Health Check Programme in the Primary Care Setting? A Cost-Minimisation Analysis', *BMJ Open* 7, no. 8 (August 2017).
[96] The Independent, '20-Minute Flu Test Could Save NHS up to £24m a Year and Free up Beds, Manufacturer Says', 24 November 2018.
[97] Abel Gyorgy, 'Current Status and Future Prospects of Point-of-Care Testing around the Globe', *Taylor & Francis*, June 2015; Jeremy Howick et al., 'Current and Future Use of Point-of-Care Tests in Primary Care: An International Survey in Australia, Belgium, The Netherlands, the UK and the USA', *BMJ Open* 4, no. 8 (August 2014).
[98] John P Hays et al., 'The Successful Uptake and Sustainability of Rapid Infectious Disease and Antimicrobial Resistance Point-of-Care Testing Requires a Complex 'Mix-and-Match'Implementation Package', *European Journal of Clinical Microbiology & Infectious Diseases*, February 2019; Clift, *Review of Progress on Antimicrobial Resistance*; Cooke et al., 'Narrative Review of Primary Care Point-of-Care Testing (POCT) and Antibacterial Use in Respiratory Tract Infection (RTI)'.
[99] St John and Price, 'Economic Evidence and Point-of-Care Testing'; Public Health England, *Point of Care Tests for Influenza and Other Respiratory Viruses: Winter 2019 to 2020*, 11.

the financial incentives and reimbursement mechanisms for diagnostics has been slow.[100] The UK's five-year action plan on AMR commits to developing alternative funding and commissioning models for supporting the adoption of diagnostics across the NHS, but details are yet to be provided. It is essential that this is rectified.

Idea 2: NHS England and NHS Improvement, in collaboration with the National Institute for Health and Care Excellence, should urgently commission a national assessment of the clinical and cost-effectiveness of tools like point-of-care diagnostics to inform future reimbursement models. The assessment should consider tests' performance across health and care settings, as well as additional dimensions of value such as clinical outcomes and impact on clinical workflows. Specific measurements to assess the value these tools provide with regard to their impact on AMR should be explored.

2.5.3. Making use of current technology & improving current practice

In addition to developing new diagnostic tools, there is an opportunity to make better use of existing resources. Blood cultures are currently the "gold standard" for diagnosing bloodstream infections and critical for enhancing antimicrobial stewardship.[101] Effective use of these tests can help detect the presence of bacteria in the blood and help clinicians decide whether a patient requires an antibiotic or not. Yet, human error in the collection of samples, failure to load blood cultures into "analyser" machines within the specified timeframes, and delays in getting the results to clinicians often result in patients being unnecessarily treated with antibiotics or kept on the wrong antibiotic. These are all avoidable issues. There is also considerable variation in blood culture laboratory practice and compliance with PHE's blood culture processing standards across NHS Trusts.[102]

Mapping and optimising the blood culture process can help overcome some of these obstacles and deliver improvements. A study conducted in a UK hospital in 2018 revealed how simple changes to the blood culture pathway can create tangible improvements in practice. The simple step of relocating the blood culture machine from the microbiology laboratory to the blood laboratory, which operates 24 hours a day and where staff are at hand to load the cultures, helped significantly reduce the average time to achieve a diagnostic result.[103] This highlights the need for auditing existing pathways to improve blood culture turnaround times and deliver improved patient outcomes.

---

[100] Clift, *Review of Progress on Antimicrobial Resistance*.
[101] Brigitte Lamy et al., 'How to Optimize the Use of Blood Cultures for the Diagnosis of Bloodstream Infections? A State-of-the Art', *Frontiers in Microbiology* 7 (May 2016): 697.
[102] Laura J Shallcross et al., 'A Cross-Sectional Study of Blood Cultures and Antibiotic Use in Patients Admitted from the Emergency Department: Missed Opportunities for Antimicrobial Stewardship', *BMC Infectious Diseases* 16, no. 1 (2016): 166; Academy for Healthcare Science, 'NHS England Survey', Webpage, 8 January 2019.
[103] MJ Weinbren et al., 'Optimization of the Blood Culture Pathway: A Template for Improved Sepsis Management and Diagnostic Antimicrobial Stewardship', *Journal of Hospital Infection* 98, no. 3 (March 2018).

Action is underway to deliver the UK's vision for AMR diagnostics, with, in 2019, the establishment of a dedicated AMR Diagnostic Programme focused on human health by NHS England and NHS Improvement (NHSE/I). A new AMR Diagnostic Partnership Board has been set up with specific objectives to optimise current AMR diagnostics, reassess and optimise clinical pathways, drive the adoption of proven diagnostic technologies, and promote the development of new AMR diagnostics.[104] Specific task and finish groups have been created to support activity across two 'work clusters', the first focused on AMR diagnostic optimisation, and the second on innovation and technology. This work will be overseen by an NHSE/I AMR Diagnostics Programme Board reporting directly into the NHSE/I AMR Programme Board.[105]

Idea 3: The AMR Diagnostic Partnership Board should focus on improving existing practice and closing well-recognized gaps in clinical care. One such example would be to support the widescale adoption of the national standards for blood culture processing issued by Public Health England and the pathways produced by National Institute for Care Excellence (NICE) pathways across NHS Trusts.

2.6 Building the right capability and skills

Ongoing education and training are needed to provide healthcare staff with specific competencies for diagnostic stewardship. This must consider foundation programmes to retrain staff on skills like blood culture sampling and infection prevention and control, as well as targeted training on novel diagnostics. The continued development of Primary Care Networks as part of the NHS's Long-Term Plan (see Glossary) will see more diagnostics services provided in out-of-hospital settings. This will require advancing the skills, knowledge, and competencies of primary and community care staff to ensure the safe and appropriate use of PoCTs.

As explained by advanced nurse practitioner Liz Cross in an interview for this paper, consideration must also be given to bringing specific clinical and technical expertise from hospitals into the community. In particular, the skillset offered by hospital PoCT managers, who oversee the commissioning, maintenance and quality assurance of PoCT services, could help support the expansion of PoCT in the community and alleviate pressure on primary and community care staff who often "do not know which equipment to purchase". As qualified laboratory professionals, PoCT managers also play a key role in supporting staff with test interpretation and the appropriate collection of samples.[106]

[104] Angela Douglas, *Role of Diagnostics in the Human Health AMR Programme* (NHS England and NHS Improvement, 2019).
[105] Ibid.
[106] Kent Lewandrowski, Kimberly Gregory, and Donna Macmillan, 'Assuring Quality in Point-of-Care Testing: Evolution of Technologies, Informatics, and Program Management', *Archives of Pathology & Laboratory Medicine* 135, no. 11 (November 2011).

Similarly, routine use of PoCTs in pharmacy settings and the integration of the role of community pharmacists into the diagnostic pathway promises to improve antibiotic stewardship and relieve pressure from GPs.[107] Pilot programmes, like Boot's sore throat 'test and treat' service launched in 2014, have been adopted onto the NHS Accelerator Programme to be rolled out nationally.[108] NHS England has also begun working with selected pharmacies to offer a free, at-home urine test kit for patients showing symptoms of UTIs.[109]

The expansion of this model will require clinical skills training for community pharmacists on areas including, but not limited to, understanding the different tests available, collecting specimens, interpreting contradictory results, and appropriately triaging patients.[110]

Ongoing training and skills-building are also needed for pharmacists to confidently contribute to antibiotic stewardship efforts. In addition to providing tailored advice to patients about how to deal with minor illnesses, community pharmacists can help patients to appropriately self-manage their conditions, clarify expectations about antibiotic use and raise awareness of infection prevention.[111] A training programme focused on PoCT diagnostics, antimicrobial stewardship, and communication skills on antibiotic use could help achieve this.[112]

Idea 4: Health Education England should evaluate strategies to ensure that the extensive technical and clinical expertise of hospital staff in relation to point-of-care testing is leveraged in the community. This could take the form of specific training and certification of primary and community care staff, the creation of self-audit tools and checklists to ensure the safe and proper use of devices, or the provision of specialist advice upon request. Existing structures, such as point-of-care testing committees within NHS Trusts, could also be employed to facilitate communication between hospitals and the primary and community care sector.

[107] Royal Pharmaceutical Society English Pharmacy Board, *Community Pharmacy Forward View*, 2016.
[108] Tracey Thornley et al., 'A Feasibility Service Evaluation of Screening and Treatment of Group A Streptococcal Pharyngitis in Community Pharmacies', *Journal of Antimicrobial Chemotherapy* 71, no. 11 (July 2016).
[109] Eliza Slawther, 'NHS England Follows Boots' Lead with Pharmacy UTI Test and Treat Pilot', Webpage, Chemist & Druggist, 18 July 2019.
[110] Fiona Carragher, *UK AMR Diagnostics Collaborative: Maximising the Use of Diagnostic Technology to Tackle AMR* (NHS England, 2018).
[111] Aleksandra J Borek et al., 'How Can National Antimicrobial Stewardship Interventions in Primary Care Be Improved? A Stakeholder Consultation', *Antibiotics* 8, no. 4 (December 2019).
[112] Ibid.

2.7 Turning surveillance data into actionable insights

Surveillance systems that monitor drug resistance and antimicrobial consumption in humans, animals and the environment are key to managing infectious diseases.[113] The data generated by these tools can help build a comprehensive picture of antibiotic use at the local level, track infection patterns, and warn of potential outbreaks. It also contributes to the creation of a global knowledge base, which can help evaluate and support the delivery of more effective public health interventions. Surveillance is also a core part of the diagnostic pathway, supporting the early detection of AMR and helping keep patients safe.

The UK has markedly improved its surveillance capabilities relating to patient data through the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) and the establishment of similar surveillance programmes across the country.[114] Action is also underway to improve AMR surveillance in animals and the environment, where progress has been comparatively slow.

The UK's action plan emphasises the need to enhance existing datasets to bolster AMR surveillance. PHE is currently leading work to create an 'open access' centre to gather real-time patient data on AMR and develop an integrated dataset including microbiology, mortality and hospital data.[115] A simulated dataset is set to be available in 2021.

As explained by Adam Zerda, AMR Strategy & Development Director at BD, the effective use of AMR surveillance data for antibiotic and diagnostic stewardship has been hampered by the lack of real-time access to data and to systems that provide healthcare professionals with insights and recommendations they can act upon. The OpenPrescribing platform, set up by Oxford University's EBM Datalab, illustrates the value of this approach.[116] The platform is an open access, interactive resource which helps monitor monthly prescribing trends in England. It includes dashboards for GP practices, Clinical Commissioning Groups (CCGs) and Sustainability Transformation Partnership regions (see Glossary) which help track variations in the costs and quantity of prescriptions, the prescribing of selected drugs, as well as more granular measures like the proportion of prescriptions that are broad-spectrum.

As explained by Jessica Morley, Policy Lead at the EBM Datalab, opportunities exist for strengthening and expanding the use of these platforms for antimicrobial

[113] World Health Organization, 'Antimicrobial Resistance Surveillance', Webpage, n.d.
[114] Public Health England, *English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2018 –2019*, 2019.
[115] Public Health England, 'Using Open Innovation and Big Data in the Fight against Antimicrobial Resistance', Webpage, 23 June 2019.
[116] OpenPrescribing, 'Explore England's Prescribing Data', Webpage, n.d.; Joy Ogden, 'Simplifying Prescribing Data: OpenPrescribing Two Years On', *Prescriber* 29, no. 10 (2018).

stewardship. In particular, access to anonymised patient-level diagnostic and prescribing data could help characterise the types of patients and health conditions antibiotics are being prescribed for, and improve understanding of the role diagnostics play in driving prescribing decisions. Similarly, consideration should be given to improving access to secondary care medicine datasets held within the NHS, such as hospital pharmacy stock control systems and electronic prescribing systems.

Feeding information to prescribers and CCG leaders regarding their prescribing practices, as well as making benchmarked data of local and national prescribing patterns more visible, can encourage positive change in prescribing behaviours.[117]

Yet, access to data alone is not sufficient to drive this transformation. Healthcare staff must also understand the value of these tools and have the right technical and analytical skills to interpret and use data effectively. Efforts at encouraging the use of analytics data tools must, therefore, be matched with action to increase digital literacy and data analysis skills among the existing workforce, train future experts and develop greater skills capacity across the healthcare system.

Idea 5: The Department for Health and Social Care should support the development and use of open source analytic tools, like OpenPrescribing, to enhance AMR surveillance and national antimicrobial stewardship efforts. To improve access to high quality health service and clinical data for health research, NHS Digital in England, and national information technology organisations in the devolved administrations, should conduct an audit of existing data sources relevant to antimicrobial and diagnostic stewardship, and define appropriate information governance frameworks to support their use. Furthermore, the Department should make available specific funding streams to fund data science and applied clinical informatics research projects across the country.

2.8 Making AMR everyone's business

Raising public awareness and understanding is a cornerstone of the UK's action plan on AMR. As shown in Figure 2*,* several campaigns have been established to engage the public, healthcare professionals, the agricultural and animal health sector and policymakers in the fight against AMR. PHE's flagship annual Antibiotic Guardian campaign uses an online pledge system to encourage healthcare professionals and members of the public to commit to one simple action to tackle antimicrobial resistance.[118] For instance, patients with cold symptoms might commit to waiting a few

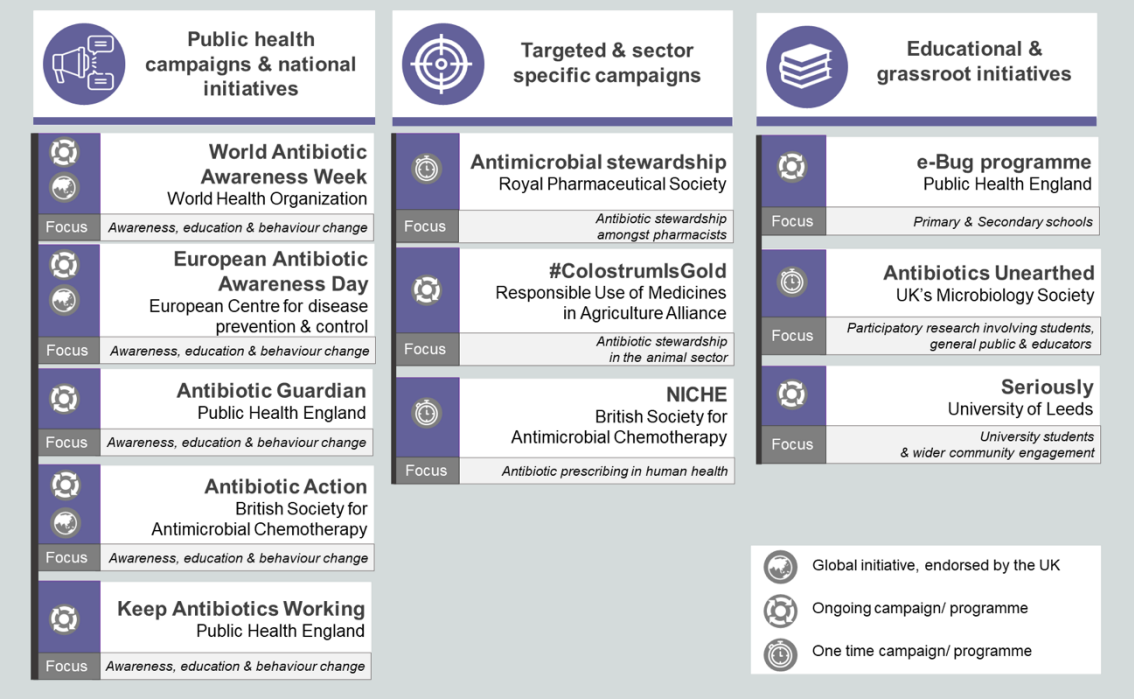
[117] Public Health England and Department of Health, *Behaviour Change and Antibiotic Prescribing in Healthcare Settings: Literature Review and Behavioural Analysis*, 2015.
[118] Public Health England, 'Antibiotic Guardian', Webpage, Become an Antibiotic Guardian, n.d.

days before making a GP appointment, while professionals might pledge to educate their patients about safe antibiotic use.

The campaign has been effective in demonstrating increased self-reported knowledge and commitment from healthcare professionals and the public, although the impact has been higher for those with pre-existing knowledge of AMR.[119] Targeted campaigns have also been created to reduce patients' expectations for antibiotics, and to educate children and young people about hygiene and infections.[120] While evidence suggests these awareness campaigns do contribute to more responsible antibiotic use and increased awareness of AMR, evidence on their effectiveness in driving sustained behaviour change remains sparse.[121]

[119] Joanna May Kesten et al., 'The Antibiotic Guardian Campaign: A Qualitative Evaluation of an Online Pledge-Based System Focused on Making Better Use of Antibiotics', *BMC Public Health* 18, no. 1 (July 2017).
[120] British Society for Antimicrobial Chemotherapy, Web result with site links, and British Society for Antimicrobial Chemotherapy, 'BSAC Launch of NICHE Antibiotic Prescribing Campaign', Webpage, n.d.; Public Health England, 'About E-Bug', Webpage, n.d.

Figure 2: Examples of AMR awareness & education initiatives



Source: *Reform* research. N.B. This is not an exhaustive list.

2.8.1. Reframing AMR

To enable effective communication and public engagement with AMR, the narrative and language must change. As explained by Rose Gallagher, Professional Lead Infection Prevention & Control at the Royal College of Nursing, "we need a public health approach rather than a clinical approach when talking about AMR."

Scientific claims and messaging emphasising the potentially catastrophic consequences of AMR are seldom effective in driving action and inspiring people to change their behaviours.[122] Putting a "human face" to AMR by sharing the experiences of patients living with infections resistant to antibiotics and their impact on their everyday lives would go much further in raising awareness of the problem and creating a "public mandate for action", as mentioned by interviewees. The 'Faces of The Antimicrobial Resistance Fighter Coalition' campaign by the Infectious Diseases Society of America is an example of this.[123]

[122] Wellcome Trust, *Reframing Resistance: How to Communicate about Antimicrobial Resistance Effectively*, 2019.
[123] Infectious Diseases Society of America, *Faces of Antimicrobial Resistance*, 2017.

Greater availability of relevant patient safety information on AMR is also needed. Arlene Brailey, who leads a one-of-a-kind support programme for patients suffering from antibiotic-resistant infections and their families, says there is still a dearth of publicly available resources, information and support for those affected by AMR.

Idea 6: Public Health departments in England and the devolved countries should work with charities and local patient organisations to create an awareness and education campaign highlighting the experiences of individuals living with drug-resistant infections and their families. This should be accompanied by a suite of accessible information resources on AMR patient safety, including standardised information about specific drug-resistant bacteria, the infections they cause, regional data on resistance, and healthcare-associated infections in hospital. Outcomes of this campaign should be independently evaluated and learnings shared.

2.8.2. Tapping into the "power of the crowd"

Developing partnerships with communities and civil society can help drive action and amplify communication efforts on AMR. As explained by Roger Harrison, Senior Lecturer in Public Health at the University of Manchester, community-based, bottom-up approaches have been effective in increasing active involvement and improving AMR-related behaviours within specific communities. These programmes also create 'ambassadors' who can disseminate knowledge in ways that wide-scale public health campaigns can't – especially to hard-to-reach groups.

Leeds' 'Seriously' campaign, for instance, has achieved success in bringing AMR awareness and education closer to citizens through specific interventions in schools, universities, GP practices, hospitals, pharmacies, and supermarkets.[124] A 'Pledge Hedge' programme has been launched to encourage the public and local healthcare leaders to commit to using antibiotics correctly, with teams travelling to collect pledges from different communities across Leeds. Films, expert-led educational resources, and attention-grabbing advertising, such as red bags branded 'Seriously' in pharmacies, have been produced. While no formal evaluation of the campaign's impact has been carried out, as of June 2020 over 23,000 pledges had been collected. The programme has been effective in garnering support from city-wide stakeholders and particularly from young people, as well as in creating a unified narrative and brand identity for the fight against AMR. In the same vein, the Antimicrobial Resistance Fighter Coalition campaign brings together a community of organisations, leaders and individuals to address AMR by using creative bottom-up approaches, such as art, storytelling and the sharing of patient stories.[125]

[124] NHS Leeds CCG, 'Seriously', Webpage, n.d.
[125] Antimicrobial Resistance Fighter Coalition, 'Antimicrobial Resistance Threatens Everyone. All of Us Need to Be Resistance Fighters', Webpage, 2020.

Community-based approaches could be replicated to support wider work on AMR across human health, animal health and the environment. Yet, a paucity of funding streams for these programmes, coupled with narrow approaches to measuring impact and success, remain important barriers to their deployment, says Roger Harrison. To ensure the maximum effectiveness and impact of community-based models, new approaches to piloting, evaluating and making funding available for this type of work are needed.[126] While specific initiatives exist, they mostly focus on LMICs.[127]

Idea 7: The Department of Health and Social Care should support a national fund to pilot, evaluate and develop pragmatic and scalable community engagement approaches to tackle AMR. A mixture of philanthropic contributions plus a levy on funded antimicrobial drug discovery research could be used to finance the fund, with monies ring-fenced. Activities and projects should be delivered locally and as a partnership between local government, academic institutions, grassroots organisations, civil society and patient advocacy groups. Process and outcomes need to be evaluated with civil society partnerships, using a range of methodologies, and a focus on sharing best practices.

2.9 Mobilising political action & creating a mandate for change

Increased public awareness, information and advocacy on AMR is foundational to the fight against drug resistance. The critical challenge, however, is to encourage decision-makers to support these goals.

The O'Neill Review was significant in persuading policymakers and experts beyond the health and scientific communities of the urgent issue of AMR. As explained by Jeremy Knox from the Wellcome Trust, the Review painted a clear picture of the economic and social costs of inaction, but more significantly, helped translate a complex technical and scientific challenge into a language that "heads of government and finance ministers could engage with". In the same vein, the work of former Chief Medical Officer, Professor Dame Sally Davies, has been pivotal in raising the profile of AMR nationally and in providing high-quality scientific advice to policymakers.

However, triggering long-lasting policy change will hinge on citizens actively demanding action from their leaders. Interviewees spoke candidly about how improved public awareness of drug resistance has not resulted in greater participation of civil society in AMR policy. Even though a significant number of people are affected by drug-resistant infections, there is still not a "critical mass" of citizen participation that can create social pressure for change and hold policymakers to account. This is partly

[126] James Redfern et al., 'Raising Awareness of Antimicrobial Resistance among the General Public in the UK: The Role of Public Engagement Activities', *JAC-Antimicrobial Resistance* 2, no. 1 (March 2020).
[127] University of Leeds, 'Community Engagement for Antimicrobial Resistance (CE4AMR)', Webpage, n.d.

attributed to the patient population suffering from these infections being "sparse and mixed", as described by Arlene Brailey from Antibiotic Research UK, and to many people being unaware that they have a drug-resistant infection. As highlighted in the previous section, empowering patients and communities through better access to education and appropriate information on AMR can help achieve this. Also, clear mechanisms must be in place for the public to demand action and change. Due to its complex nature, responsibility for AMR sits across government departments, executive agencies and regulatory bodies,[128] making it difficult for individuals, civil society organisations and other interested parties to know which stakeholders to engage with.

The scale, complexity, and urgency, of the challenge from infectious disease, requires leadership, visibility, and accountability. It must be clear where the 'buck stops' and where ultimate responsibility for AMR policy action lies. One solution proposed by the British Society for Antimicrobial Chemotherapy (BSAC) is to appoint a named Cabinet Office Minister with specific accountability for drug-resistant infections and the ability to coordinate the delivery of the Government's AMR prevention objectives via all relevant departments, including HM Treasury, DHSC, Environment Food and Rural Affairs, Foreign and Commonwealth Office and Business, Energy and Industrial Strategy (BEIS). Another approach would be to appoint a Parliamentary Under-Secretary of State for AMR, in the same way that BEIS has appointed a Minister responsible for climate change and corporate responsibility. It is only by taking this type of decisive action that the Government will be able to tackle a challenge that has the potential to prove more catastrophic, and more difficult to solve, than the current pandemic.

[128] Gabriel Birgand et al., 'Comparison of Governance Approaches for the Control of Antimicrobial Resistance: Analysis of Three European Countries', *Antimicrobial Resistance & Infection Control* 7, no. 1 (February 2018).

Conclusion

AMR is a relentless and slow-moving threat that is already having a devasting impact on humanity and the world's economy.[129] Unchecked, it will radically reshape modern medicine, causing common illnesses to become untreatable and render life-saving drugs useless. After decades of international commitments and global advocacy on AMR, and despite significant progress made on several fronts, it is clear that global action is not yet advancing at the speed or scale required.

The UK continues to take decisive action to tackle this threat, with the 20-year vision and National Action Plan for AMR setting out ambitious commitments, and further crystallising the UK's leadership in this area. Specific targets have been introduced to optimise the use of antimicrobials, reduce specific drug-resistant infections, and expand the use of diagnostic tests. The world is watching and waiting for the outcomes of the Government's pioneering payment scheme for antibiotics, which promises to encourage innovation and incentivise private investment into much-needed drugs.

Nevertheless, there are still untapped opportunities for long-lasting success in the fight against AMR.

The UK is not yet leveraging diagnostics to their full potential to improve antibiotic stewardship, provide actionable information to healthcare professionals, and generate valuable data for AMR surveillance. An important lesson emerging from the COVID-19 pandemic has been the importance of rapid, accurate and affordable diagnostics to manage the outbreak and develop appropriate, evidence-based policy responses. The same applies to AMR. As this research shows, embedding the use of diagnostics into prescribing practices hinges on demonstrating the economic and public health value that tools, like point-of-care testing, have in tackling AMR, as well as introducing appropriate incentives, capability and skills to boost their uptake across the system.

Efforts at increasing public awareness of AMR must be matched with action to improve people's understanding of the urgency of this threat to catalyse behaviour change. Public awareness campaigns and educational programmes should be complemented by research into the behavioural aspects of AMR and the use of community-based approaches. Likewise, a much stronger focus must be placed on preventing infections from occurring in the first place through better infection prevention and control, increased professional training and investment in new vaccines.

As the world grapples with the COVID-19 pandemic outbreak, the impending AMR crisis must not be overlooked. As highlighted by Professor Dame Sally Davies, the same level of political leadership, energy and attention that the pandemic has received must be applied to curbing drug resistance. In fact, "if we don't address AMR properly,

[129] Jim O'Neill, *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations: The Review on Antimicrobial Resistance Chaired by Jim O'Neill*, 2014.

it is estimated to have the same impact on people's lives and the economy that COVID-19 is having".

The Government should harness the lessons from the COVID-19 crisis to inform its approach to AMR. In particular, the pandemic's impact on increased public awareness of infection prevention and control, the crucial role of rapid diagnostics, antibiotics and vaccines, and the importance of prompt, wide-reaching and coordinated policy action for addressing public health challenges.

This momentum must be carried forward into the future so that long-term pledges to curb the growing threat posed by antibiotic-resistant bacteria translate into action.

Glossary

Antimicrobial resistance: the loss of effectiveness of any anti-infective medicine, including antiviral, antifungal, antibacterial and antiparasitic medicines.GOV[130]

Antibiotic-resistant bacteria: bacteria with the ability to resist the effects of an antibiotic to which they were once sensitive.

Antibiotic sensitivity testing: determines which antibiotics inhibit the growth of the bacteria that have been cultured. This information allows the selection of the most suitable antibiotic to treat a particular infection.

Antimicrobial stewardship: an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness.[131]

Broad-spectrum antibiotics: drugs that are effective against a wide range of bacteria.

Clinical Commissioning Group: groups of general practices which come together in each area to commission the best services for their patients and population.

Diagnostic Stewardship: coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide patient treatment.[132]

Infection prevention and control: a pragmatic scientific approach designed to prevent harm caused by infections to patients and health workers.

Healthcare-associated infections (HCAIs): can develop either as a direct result of healthcare interventions such as medical or surgical treatment or from being in contact with a healthcare setting. HCAIs pose a serious risk to patients, staff and visitors. They can incur significant costs for the NHS and cause significant morbidity to those infected.[133]

NHS Long-Term Plan: the new 10-year plan for the NHS in England to improve the quality of patient care and health outcomes.

Point-of-care: the specific location at which a patient is presenting with illness – this could be at home, or in a range of primary and secondary healthcare settings. Point-of-

[130] National Institute for Health and Care Excellence, *Antimicrobial Stewardship: Systems and Processes for Effective Antimicrobial Medicine Use*, 2015.
[131] Ibid.
[132] World Health Organization, *Diagnostic Stewardship: A Guide to Implementation in Antimicrobial Resistance Surveillance Sites*, 2016.
[133] NHS Improvement, 'Healthcare Associated Infections', Webpage, 24 March 2017.

care diagnosis therefore takes place close to the patient, rather than at a physically removed central laboratory.[134]

Primary Care Networks: organised around general practice registered lists typically serving natural communities of around 30,000 to 50,000 patients. The networks will have expanded neighbourhood teams which will comprise a range of staff such as GPs, clinical pharmacists, district nurses, community geriatricians, dementia workers and Allied Health Professionals such as physiotherapists and podiatrists/chiropodists, joined by social care and the voluntary sector.

Sustainability and Transformation Partnerships: areas covering all of England, where local NHS organisations and councils drew up shared proposals to improve health and care in the areas they serve.

[134] Sarah Bailey, 'Longitude Prize: What Do We Mean by Point-of-Care?', Webpage, Longitude Prize, n.d.

Bibliography

Academy for Healthcare Science. 'NHS England Survey'. Webpage, 8 January 2019.
Access to Medicines Foundation. *Antimicrobial Resistance Benchmark*, 2020.
Alp, Emine, and Andreas Voss. 'Ventilator Associated Pneumonia and Infection Control'. *Annals of Clinical Microbiology and Antimicrobials* 5, no. 1 (April 2006).
AMR Action Fund. 'About Us'. Webpage, n.d.
Antimicrobial Resistance Fighter Coalition. 'Antimicrobial Resistance Threatens Everyone. All of Us Need to Be Resistance Fighters'. Webpage, 2020.
Bailey, Sarah. 'Longitude Prize: What Do We Mean by Point-of-Care?' Webpage. Longitude Prize, n.d.
Balasegaram, Manica, and Laura JV Piddock. 'The Global Antibiotic Research and Development Partnership (GARDP) Not-for-Profit Model of Antibiotic Development'. *ACS Infectious Diseases*, 2020.
BBC News. 'WHO Head: "Our Key Message Is: Test, Test, Test"'. Webpage, 16 March 2020.
Birgand, Gabriel, Enrique Castro-Sánchez, Sonja Hansen, Petra Gastmeier, Jean-Christophe Lucet, Ewan Ferlie, Alison Holmes, and Raheelah Ahmad. 'Comparison of Governance Approaches for the Control of Antimicrobial Resistance: Analysis of Three European Countries'. *Antimicrobial Resistance & Infection Control* 7, no. 1 (February 2018).
Bodkin, Henry. 'Life-Saving Drugs May Soon Become Useless, Experts Warn as 19 Untreatable Superbugs Are Discovered in the Last Decade'. *The Telegraph*, 11 September 2019.
Borek, Aleksandra J, Marta Wanat, Anna Sallis, Diane Ashiru-Oredope, Lou Atkins, Elizabeth Beech, Susan Hopkins, Leah Jones, Cliodna McNulty, and Karen Shaw. 'How Can National Antimicrobial Stewardship Interventions in Primary Care Be Improved? A Stakeholder Consultation'. *Antibiotics* 8, no. 4 (December 2019).
British Society for Antimicrobial Chemotherapy, Web result with site links, and British Society for Antimicrobial Chemotherapy. 'BSAC Launch of NICHE Antibiotic Prescribing Campaign'. Webpage, n.d.
Buchy, Philippe, Sibel Ascioglu, Yves Buisson, Sanjoy Datta, Michael Nissen, Paul Anantharajah Tambyah, and Sirenda Vong. 'Impact of Vaccines on Antimicrobial Resistance'. *International Journal of Infectious Diseases* 90 (January 2020).
CARB-X. 'Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X)'. Webpage, n.d.
———. 'UK Government and Bill & Melinda Gates Foundation Join Join CARB-X Partnership in Fight against Superbugs'. Webpage, 22 May 2018.
Carragher, Fiona. *UK AMR Diagnostics Collaborative: Maximising the Use of Diagnostic Technology to Tackle AMR*. NHS England, 2018.
Cars, Otto. 'Otto Cars: Reacting to Antimicrobial Resistance'. *Bulletin of the World Health Organization* 97 (2019).
Castro-Sánchez, Enrique, Mark Gilchrist, Raheelah Ahmad, Molly Courtenay, Jo Bosanquet, and Alison H Holmes. 'Nurse Roles in Antimicrobial Stewardship: Lessons from Public Sectors Models of Acute Care Service Delivery in the

United Kingdom'. *Antimicrobial Resistance & Infection Control* 8, no. 1 (October 2019).
Centre for Infectious Disease Research and Policy. 'In World First, UK Reports High-Level Gonorrhea Resistance'. Webpage, 28 March 2018.
Clift, Charles. *Review of Progress on Antimicrobial Resistance*. Chatham House, 2019.
Cooke, Jonathan, Christopher Butler, Rogier Hopstaken, Matthew Scott Dryden, Cliodna McNulty, Simon Hurding, Michael Moore, and David Martin Livermore. 'Narrative Review of Primary Care Point-of-Care Testing (POCT) and Antibacterial Use in Respiratory Tract Infection (RTI)'. *BMJ Open Respiratory Research*, May 2015.
Cox, Michael J, Nicholas Loman, Debby Bogaert, and Justin O'grady. 'Co-Infections: Potentially Lethal and Unexplored in COVID-19'. *The Lancet Microbe*, July 2020.
Dall, Chris. 'Achaogen Bankruptcy Raises Worry over Antibiotic Pipeline'. Webpage. CIDRAP News, 16 April 2019.
Davies, Sally. *Chief Medical Officer Annual Report 2011: Antimicrobial Resistance*. London: Department of Health and Social Care, 2013.
Department for Business, Energy & Industrial Strategy and The Rt Hon Alok Sharma MP. 'Public Encouraged to Register for COVID-19 Vaccine Trials as 100,000 Already Sign-Up'. Webpage, 17 August 2020.
Department for Business, Energy & Industrial Strategy, Department of Health and Social Care, The Rt Hon Matt Hancock MP, and The Rt Hon Alok Sharma MP. 'Millions Could Be Vaccinated against COVID-19 as UK Secures Strong Portfolio of Promising Vaccines'. Webpage, 20 July 2020.
Department for Health and Social Care. 'The Global AMR Innovation Fund'. Webpage, n.d.
Department of Health. *UK Antimicrobial Resistance Strategy and Action Plan*, 2000.
Department of Health and Department for Environment Food & Rural Affairs. *UK Five Year Antimicrobial Resistance Strategy 2013 to 2018*, 2013.
Department of Health and Social Care. 'Development of New Antibiotics Encouraged with New Pharmaceutical Payment System'. Webpage, 9 July 2019.
———. 'World-First Scheme Underway to Tackle AMR and Protect UK Patients'. Webpage, 17 June 2020.
Department of Health and Social Care, Innovate UK, and UK Research and Innovation. 'UK-China Partnerships against Antimicrobial Resistance Get Funding'. Webpage, 24 January 2019.
Douglas, Angela. *Role of Diagnostics in the Human Health AMR Programme*. NHS England and NHS Improvement, 2019.
El-Osta, Austen, Maria Woringer, Elena Pizzo, Talitha Verhoef, Claire Dickie, Melody Z Ni, Jeremy R Huddy, Michael Soljak, George B Hanna, and Azeem Majeed. 'Does Use of Point-of-Care Testing Improve Cost-Effectiveness of the NHS Health Check Programme in the Primary Care Setting? A Cost-Minimisation Analysis'. *BMJ Open* 7, no. 8 (August 2017).
Furuya, E Yoko, and Franklin D Lowy. 'Antimicrobial-Resistant Bacteria in the Community Setting'. *Nature Reviews Microbiology* 4, no. 1 (January 2006).
Gil-Gil, Teresa, Pablo Laborda, Fernando Sanz-García, Sara Hernando-Amado, Paula Blanco, and José Luis Martínez. 'Antimicrobial Resistance: A Multifaceted Problem with Multipronged Solutions'. *MicrobiologyOpen*, November 2019.
'Global Antibiotic Research & Development Partnership'. Webpage, n.d.

Global Sepsis Alliance. 'Update: Can COVID-19 Cause Sepsis? Explaining the Relationship Between the Coronavirus Disease and Sepsis'. Webpage, 7 April 2020.

Guinovart, Maria C, Albert Figueras, and Carles Llor. 'Selling Antimicrobials without Prescription: Far beyond an Administrative Problem'. *Enfermedades Infecciosas y Microbiologia Clinica (English Ed.)* 36, no. 5 (November 2018).

Gulland, Anne. 'UK Pledges £5m to Fight "Super Gonorrhoea"'. *The Telegraph*, 21 November 2018.

Gyorgy, Abel. 'Current Status and Future Prospects of Point-of-Care Testing around the Globe'. *Taylor & Francis*, June 2015.

Hays, John P, Konstantinos Mitsakakis, Saturnino Luz, Alex van Belkum, Karsten Becker, Ann van den Bruel, Stephan Harbarth, John H Rex, Gunnar Skov Simonsen, and Guido Werner. 'The Successful Uptake and Sustainability of Rapid Infectious Disease and Antimicrobial Resistance Point-of-Care Testing Requires a Complex 'Mix-and-Match'Implementation Package'. *European Journal of Clinical Microbiology & Infectious Diseases*, February 2019.

Health Education England. *Health Education England Business Plan 2019/20*, 2019.

Health Research Authority. 'Making Changes to a Research Study to Manage the Impact of COVID-19'. Webpage, 3 June 2020.

HM Government. *Contained and Controlled The UK's 20-Year Vision for Antimicrobial Resistance*, 2019.

House of Commons Health and Social Care Committee. *Antimicrobial Resistance. Eleventh Report of Session 2017–19*. HC 962. London: The Stationery Office, 2018.

House of Commons Library. 'The Challenge of Antimicrobial Resistance'. Webpage, 2015.

Howick, Jeremy, Jochen WL Cals, Caroline Jones, Christopher P Price, Annette Plüddemann, Carl Heneghan, Marjolein Y Berger, Frank Buntinx, John Hickner, and Wilson Pace. 'Current and Future Use of Point-of-Care Tests in Primary Care: An International Survey in Australia, Belgium, The Netherlands, the UK and the USA'. *BMJ Open* 4, no. 8 (August 2014).

Infectious Diseases Society of America. *Faces of Antimicrobial Resistance*, 2017.

Interagency Coordination Group on Antimicrobial Resistance. *No Time to Wait: Securing the Future from Drug-Resistant Infections. Report to the Secretary-General of the United Nations*, 2019.

International Severe Acute Respiratory and Emerging Infections Consortium. *COVID-19 Report: 8 June 2020*, 2020.

Jansen, Kathrin U, and Annaliesa S Anderson. 'The Role of Vaccines in Fighting Antimicrobial Resistance (AMR)'. *Human Vaccines & Immunotherapeutics* 14, no. 9 (May 2018).

Kesten, Joanna May, Alex Bhattacharya, Diane Ashiru-Oredope, Maya Gobin, and Suzanne Audrey. 'The Antibiotic Guardian Campaign: A Qualitative Evaluation of an Online Pledge-Based System Focused on Making Better Use of Antibiotics'. *BMC Public Health* 18, no. 1 (July 2017).

Lamy, Brigitte, Sylvie Dargère, Maiken C Arendrup, Jean-Jacques Parienti, and Pierre Tattevin. 'How to Optimize the Use of Blood Cultures for the Diagnosis of Bloodstream Infections? A State-of-the Art'. *Frontiers in Microbiology* 7 (May 2016): 697.

Lewandrowski, Kent, Kimberly Gregory, and Donna Macmillan. 'Assuring Quality in Point-of-Care Testing: Evolution of Technologies, Informatics, and Program

Management'. *Archives of Pathology & Laboratory Medicine* 135, no. 11 (November 2011).
Lipsitch, Marc, and George R Siber. 'How Can Vaccines Contribute to Solving the Antimicrobial Resistance Problem?' *MBio* 7, no. 3 (June 2016).
Longitude Prize. *Effectiveness of Cancer Treatements Threatened by Rising Antibiotic Resistance*, 2020.
———. 'Longitude Prize'. Webpage, 2019.
McNulty, Cliodna AM, Paul Boyle, Tom Nichols, Peter Clappison, and Peter Davey. 'Don't Wear Me out—the Public's Knowledge of and Attitudes to Antibiotic Use'. *Journal of Antimicrobial Chemotherapy*, April 2007.
Medical Research Council. 'Antimicrobial Resistance Funders' Forum'. Webpage, n.d.
Medicines and Healthcare products Regulatory Agency. 'MHRA Regulatory Flexibilities Resulting from Coronavirus (COVID-19)'. Webpage, 1 April 2020.
Morris, Denise E, David W Cleary, and Stuart C Clarke. 'Secondary Bacterial Infections Associated with Influenza Pandemics'. *Frontiers in Microbiology*, June 2017.
National Institute for Health and Care Excellence. *Antimicrobial Stewardship: Systems and Processes for Effective Antimicrobial Medicine Use*, 2015.
———. *COVID-19 Rapid Guideline: Managing Suspected or Confirmed Pneumonia in Adults in the Community*, 2020.
———. *Frequently Asked Questions: Developing and Testing Innovative Models for the Evaluation and Purchase of Antimicrobials*, 2020.
———. *NICE Impact Antimicrobial Resistance*, 2018.
National Institute for Health and Care Excellence, and NHS England & NHS Improvement. *Launch Statement: NHS England and NHS Improvement and NICE Begin Project to Develop and Test Innovative Models for the Evaluation and Purchase of Antimicrobials*, 2019.
National Institute for Health Research. 'Funding Urgent Research into COVID-19 with UKRI'. Webpage, n.d.
NHS Improvement. 'Healthcare Associated Infections'. Webpage, 24 March 2017.
NHS Leeds CCG. 'Seriously'. Webpage, n.d.
Novo Holdings. 'Repair Impact Fund'. Webpage, 2019.
Ogden, Joy. 'Simplifying Prescribing Data: OpenPrescribing Two Years On'. *Prescriber* 29, no. 10 (2018).
O'Neill, Jim. *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations: The Review on Antimicrobial Resistance Chaired by Jim O'Neill*, 2014.
———. *Tackling Drug Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance*, 2016.
OpenPrescribing. 'Explore England's Prescribing Data'. Webpage, n.d.
Paratek. 'Paratek Awarded BARDA Project BioShield Contract for NUZYRA®'. Webpage, 18 December 2019.
Parliamentary Office of Science and Technology. *Antimicrobial Resistance and Immunisation*. Houses of Parliament, 2018.
Parsons, Lucy. 'Antibiotic Biotech Melinta Files for Bankruptcy'. Webpage. PM Live, 3 January 2020.
Pearce, Costanza. 'GPs Advised to Avoid "over-Reliance" on PPE and to Focus on Hand Hygiene'. *Pulse*, 12 May 2020.
Pecoraro, Valentina, Luca Germagnoli, and Giuseppe Banfi. 'Point-of-Care Testing: Where Is the Evidence? A Systematic Survey'. *Clinical Chemistry and Laboratory Medicine* 52, no. 3 (March 2014).
Public Health Agency of Sweden. 'Availability of Antibiotics'. Webpage, 17 March 2020.
Public Health England. 'About E-Bug'. Webpage, n.d.

———. 'Antibiotic Guardian'. Webpage. Become an Antibiotic Guardian, n.d.
———. *English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2018 –2019*, 2019.
———. *English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)Report 2018 –2019*. London, 2019.
———. *Point of Care Tests for Influenza and Other Respiratory Viruses: Winter 2019 to 2020*, 2019.
———. 'Research Reveals Levels of Inappropriate Prescriptions in England'. Webpage, 27 February 2018.
———. 'Using Open Innovation and Big Data in the Fight against Antimicrobial Resistance'. Webpage, 23 June 2019.
Public Health England, and Department of Health. *Behaviour Change and Antibiotic Prescribing in Healthcare Settings: Literature Review and Behavioural Analysis*, 2015.
Rawson, Timothy M, Luke SP Moore, Nina Zhu, Nishanthy Ranganathan, Skolimowska, Mark Gilchrist, Giovanni Satta, Graham Cooke, and Alison Holmes. 'Bacterial and Fungal Co-Infection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing'. *Clinical Infectious Diseases*, May 2020.
Reali, Savannah, Elias Y Najib, Krisztina E Treuerné Balázs, Adeline Chern Hui Tan, Linda Váradi, David E Hibbs, and Paul W Groundwater. 'Novel Diagnostics for Point-of-Care Bacterial Detection and Identification'. *RSC Advances* 9, no. 37 (July 2019).
Redfern, James, Laura Bowater, Lisa Coulthwaite, and Joanna Verran. 'Raising Awareness of Antimicrobial Resistance among the General Public in the UK: The Role of Public Engagement Activities'. *JAC-Antimicrobial Resistance* 2, no. 1 (March 2020).
Royal Pharmaceutical Society English Pharmacy Board. *Community Pharmacy Forward View*, 2016.
Sevilla, JP, David E Bloom, Daniel Cadarette, Mark Jit, and Marc Lipsitch. 'Toward Economic Evaluation of the Value of Vaccines and Other Health Technologies in Addressing AMR'. *Proceedings of the National Academy of Sciences* 115, no. 51 (December 2018).
Shallcross, Laura J, and Sally C Davies. 'The World Health Assembly Resolution on Antimicrobial Resistance'. *Journal of Antimicrobial Chemotherapy* 69, no. 11 (2014).
Shallcross, Laura J, Nick Freemantle, Shasta Nisar, and Daniel Ray. 'A Cross-Sectional Study of Blood Cultures and Antibiotic Use in Patients Admitted from the Emergency Department: Missed Opportunities for Antimicrobial Stewardship'. *BMC Infectious Diseases* 16, no. 1 (2016): 166.
Shallcross, Laura J, Simon J Howard, Tom Fowler, and Sally C Davies. 'Tackling the Threat of Antimicrobial Resistance: From Policy to Sustainable Action'. *Philosophical Transactions of the Royal Society B: Biological Sciences*, June 2015.
Singer, Andrew C, Claas Kirchhelle, and Adam P Roberts. 'Reinventing the Antimicrobial Pipeline in Response to the Global Crisis of Antimicrobial-Resistant Infections'. *F1000Research*, 2019.
Slawther, Eliza. 'NHS England Follows Boots' Lead with Pharmacy UTI Test and Treat Pilot'. Webpage. Chemist & Druggist, 18 July 2019.
Spellberg, Brad, Robert Guidos, David Gilbert, John Bradley, Helen W Boucher, W Michael Scheld, John G Bartlett, John Edwards Jr, and Infectious Diseases

Society of America. 'The Epidemic of Antibiotic-Resistant Infections: A Call to Action for the Medical Community from the Infectious Diseases Society of America'. *Clinical Infectious Diseases* 46, no. 2 (January 2008).
St John, Andrew, and Christopher P Price. 'Economic Evidence and Point-of-Care Testing'. *The Clinical Biochemist Reviews* 34, no. 2 (August 2013).
'The Fleming Fund'. Webpage, 2018.
The Independent. '20-Minute Flu Test Could Save NHS up to £24m a Year and Free up Beds, Manufacturer Says', 24 November 2018.
Thornley, Tracey, G Marshall, P Howard, and APR Wilson. 'A Feasibility Service Evaluation of Screening and Treatment of Group A Streptococcal Pharyngitis in Community Pharmacies'. *Journal of Antimicrobial Chemotherapy* 71, no. 11 (July 2016).
Torjesen, Ingrid. 'UK Spearheads Efforts to Combat Rising Threat of Antibiotic Resistance'. *British Medical Journal*, July 2014.
UK Lighthouse Labs Network. 'UK Lighthouse Labs Network'. Webpage, n.d.
UK Parliament. 'Written Questions, Answers and Statements. Vaccination: Question for Department of Health and Social Care'. Webpage, 14 February 2019.
UK Research and Innovation. '£131m Investment Fast-Tracks UK Coronavirus Vaccine Production'. Webpage, 17 May 2020.
UN News. '"Landmark Collaboration" to Make COVID-19 Testing and Treatment Available to All'. Webpage, 24 April 2020.
United Nations. *Draft Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance*, 2016.
University of Leeds. 'Community Engagement for Antimicrobial Resistance (CE4AMR)'. Webpage, n.d.
Weinbren, MJ, Michael Collins, Richard Heathcote, M Umar, Mohamed Nisar, Chris Ainger, and Paul Masters. 'Optimization of the Blood Culture Pathway: A Template for Improved Sepsis Management and Diagnostic Antimicrobial Stewardship'. *Journal of Hospital Infection* 98, no. 3 (March 2018).
Wellcome Trust. *Reframing Resistance: How to Communicate about Antimicrobial Resistance Effectively*, 2019.
———. 'Why Is It so Hard to Develop New Antibiotics?' Webpage, 21 January 2020.
Wellcome Trust, and Boston Consulting Group. *Vaccines to Tackle Drug Resistant Infections: An Evaluation of R&D Opportunities*, 2018.
Wellcome Trust, and HM Government. 'Review on Antimicrobial Resistance: Background'. Webpage, n.d.
Wells, Victoria, Abi Jenkins, Joe Wanford, and Laura JV Piddock. 'Implementing WHO, EU and UK AMR Strategies and Action Plans: Has the World Lived up to the Challenge?' *The Lancet Infectious Diseases*, December 2017.
World Economic Forum. *Antimicrobial Resistance: Tackling the Gap in R&D Resources with Pull Incentives*, 2018.
World Health Organization. 'Antimicrobial Resistance'. Webpage, n.d.
———. 'Antimicrobial Resistance: National Action Plans'. Webpage, n.d.
———. 'Antimicrobial Resistance Surveillance'. Webpage, n.d.
———. 'Compelling Priorities for Global Health'. Webpage, 19 September 2017.
———. *Diagnostic Stewardship: A Guide to Implementation in Antimicrobial Resistance Surveillance Sites*, 2016.
———. *Monitoring Global Progress on Addressing Antimicrobial Resistance*, 2018.
———. 'United Nations High-Level Meeting on Antimicrobial Resistance'. Webpage, 21 September 2016.

Wouters, Olivier J, Martin McKee, and Jeroen Luyten. 'Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018'. *Journal of the American Medical Association* 323, no. 9 (March 2020).

Zhou, Fei, Ting Yu, Ronghui Du, Guohui Fan, Ying Liu, Zhibo Liu, Jie Xiang, et al. 'Clinical Course and Risk Factors for Mortality of Adult Inpatients with COVID-19 in Wuhan, China: A Retrospective Cohort Study'. *The Lancet*, March 2020.

Reform
5-6 St Matthew Street
London
SW1P 2JT
www.reform.uk

T 020 7799 6699
info@reform.uk
www.reform.uk

ISBN: 978-1-910850-42-8