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SMART PRESCRIBING

Harnessing technology in the fight against AMR

Dr Timothy Rawson

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ABOUT THE SCHOLAR

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Reform Foreword

Antimicrobial resistance (AMR) – the "silent pandemic" – is already responsible for a significant burden of death, disability and prolonged illness globally. It is a major challenge to the UK's health security, and is listed as a "chronic risk" in the National Risk Register, meaning it poses a continuous challenge that it can "erode our economy, community, way of life, and/or national security".

If left unaddressed, the growing resistance of bacteria, viruses and fungi to the drugs commonly used to treat them threatens modern medicine, and with it, our ability to carry out standard medical procedures. The threat is urgent.

The UK has been a world-leader in the fight against AMR, but further action is needed if we are to slow its spread. *Reform* is therefore delighted to publish Dr Tim Rawson's paper, building on previous *Reform* papers looking at the threat of AMR published in 2020, 2022 and 2023.

One of the key levers in tackling the growth of AMR lies in prescribing: antibiotics are often misused or prescribed for infections that do not require antibiotic treatment. Tim's paper makes the compelling case for a smarter, more personalised approach to prescribing enabled by AI and other technologies.

Deploying technology at an earlier stage of the decision-making process can support clinicians in making more appropriate decisions about the use of antibiotics, and therefore reduce the incidence of inappropriate prescribing.

And, as Tim points out, embracing this approach provides an opportunity to combine tackling this huge threat to the nation's health with the Government's ambitions to establish the UK as an AI superpower. Fusing these two vital priorities should be seen as an exciting proposition across government, the NHS and the wider health and technology ecosystems.

The scale of the AMR challenge cannot be overstated. The consequences of failing to slow the spread will be devastating, here and around the world. As Tim details, a growing body of evidence suggests AI and other cutting-edge technology can be a key part of our armoury. There is not time to waste.

Charlotte Pickles

Director

Recommendations

Recommendation 1: The UK Government should use the fight against Antimicrobial Resistance as an exemplar of applying artificial intelligence and digital technologies as part of their 10-year plan to become an artificial intelligence superpower.

Recommendation 2: NHS England should invest in methods of supporting the implementation and real-world evaluation of individualised approaches to antimicrobial prescribing. This should include the use of AI-based decision support software and wearable technology, working with the UK's world-leading centres of technological innovation to address Antimicrobial Resistance.

Recommendation 3: The Government should make optimisation of antimicrobial prescribing, utilising electronic health record data, AI-based clinical decision support systems, and the adoption of novel technologies a core focus on the UK AMR 5-year action plan 2024-2029.

Recommendation 4: NHS England, supported by sectoral experts in digital health and Antimicrobial Resistance, should design national data collection tools specifically to support the prospective development and testing of artificial intelligence systems for optimising antimicrobial prescribing.

Recommendation 5: Public and patient engagement with the challenges of Antimicrobial Resistance, data-access in the evolving digital landscape of the NHS, and concerns around AI and other digital based technologies should be integrated into national public engagement campaigns.

1. Introduction

Antimicrobial Resistance (AMR) is a threat to global health and security. This report examines a critical, but often under-represented area of the UKs approach to AMR – optimising antimicrobial prescribing. It considers how better digital approaches to the problem of AMR could act as a critical exemplar of applying AI-based tools and wearable technology for the betterment of society and asks the question: how can we harness technology to support optimal antimicrobial prescribing behaviours?

1.1 Antimicrobial resistance

AMR describes when organisms (e.g. bacteria, fungi, and viruses) evolve to become resistant to antimicrobial agents that were previously effective. As resistance to different antimicrobials increase, our options for treatment become limited and available drugs tend to be associated with worse outcomes and significant side effects.

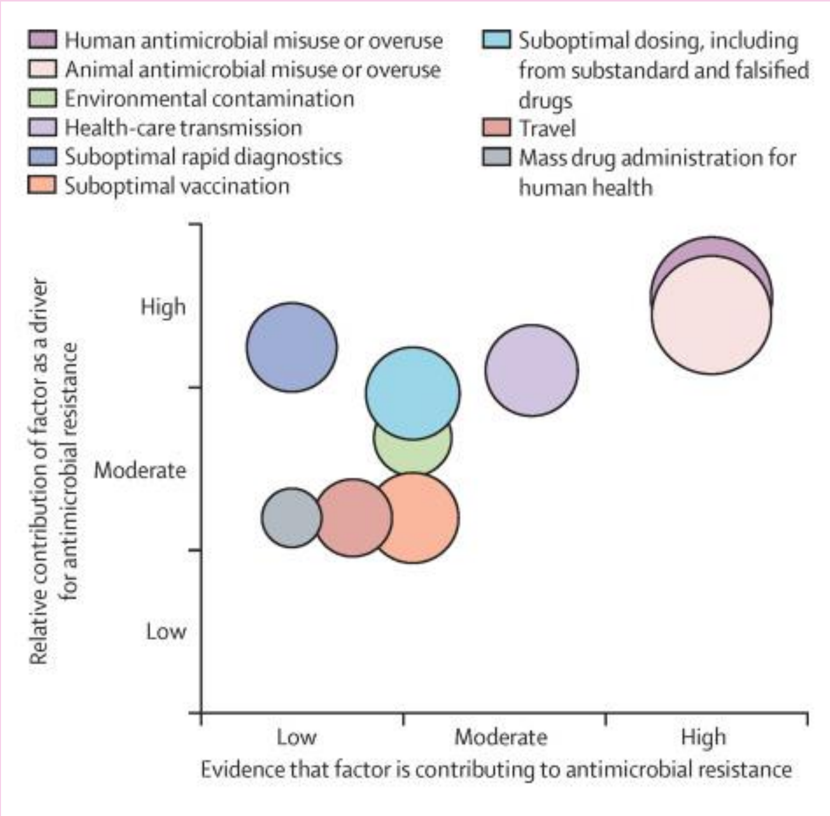
In 2019, drug-resistant bacterial infections directly caused 1.27 million deaths and contributed to 4.95 million deaths.[1] This means that AMR killed more people in 2019 than HIV or malaria.[2] If drug-resistant infections continue to rise at their current rate, it is estimated that 10 million people per year will die because of AMR by 2050.[3] AMR will have cost the global economy £60 trillion during this period.[4]

AMR is a complex and multi-faceted problem with many causes.[5] In 2016, the United Nations General Assembly held a high-level meeting on AMR producing a declaration that called for action and outlined initiatives for member states.[6] Nations have been called upon to produce and deliver National Action Plans.

The UK is a major part of the global response to AMR, producing a 20-year vision, supported by iterative 5-year action plans. The next 5-year action plan will cover 2024-2029.[7] To date, the UK has taken significant steps addressing some of the modifiable drivers of AMR. These common modifiable drivers of AMR are outlined in Figure 1.

[1] Antimicrobial Resistance Collaborators, 'Global Burden of Bacterial Antimicrobial Resistance in 2019: A Systematic Analysis', *The Lancet* 399, no. 10325 (January 2022).
[2] Patrick King, *Powering the UK's Approach to AMR: The Future of AMR Policy*, 2022.
[3] Antimicrobial Resistance Collaborators, 'Global Burden of Bacterial Antimicrobial Resistance in 2019: A Systematic Analysis'.
[4] Jim O'Neill, *Tackling Drug Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance*, 2016.
[5] Alison H. Holmes et al., 'Understanding the Mechanisms and Drivers of Antimicrobial Resistance', *The Lancet* 387, no. 10014 (January 2016).
[6] United Nations, *Draft Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance*, 2016.
[7] Department for Environment, Food and Rural Affairs and Department of Health and Social Care, *Tackling Antimicrobial Resistance 2019–2024: The UK's Five-Year National Action Plan*, 2019; HM Government, *Contained and Controlled: The UK's 20-Year Vision for Antimicrobial Resistance*, 2019.

Figure 1: Modifiable drivers of antimicrobial resistance



Source: Lancet, 'Understanding the mechanisms and drivers of antimicrobial resistance', 2016.

1.1.1 The UK's progress so far

The UK has achieved significant and sustained reductions in the use of antimicrobials in agriculture.[8] Financial investment has focused on the development of new antimicrobials and diagnostics through global collaborations such as the Joint Programming Initiative on AMR (JPIAMR), Global Antibiotic Research and Development Partnership (GARDP), and Fleming Fund.[9] New antimicrobial agents have been developed and adopted in the NHS via a novel reimbursement model designed to address some of the financial barriers to new drug development faced by companies looking to develop new antimicrobials.

Yet, despite progress, adoption of new diagnostic tools in healthcare has remained a challenge.[10] Antimicrobial prescribing in human health has continued to be highly variable and optimising treatment within patients has remained relatively under-represented in terms of its national focus.[11] The COVID-19 pandemic made clear the potential catastrophic consequence

[8] House of Commons Library, *The Use of Antibiotics on Healthy Farm Animals and Antimicrobial Resistance*, 2023.
[9] Department for Environment, Food and Rural Affairs and Department of Health and Social Care, *Tackling Antimicrobial Resistance 2019–2024: The UK's Five-Year National Action Plan*.
[10] Department for Environment, Food and Rural Affairs and Department of Health and Social Care.
[11] Esmita Charani et al., 'Optimising Antimicrobial Use in Humans - Review of Current Evidence and an Interdisciplinary Consensus on Key Priorities for Research', *The Lancet Regional Health - Europe* 7, no. 100161 (June 2021).

of failure to appropriately manage antimicrobial use. During this period, breakdown in antimicrobial prescribing oversight (termed antimicrobial stewardship), infection control, and AMR surveillance led to significant outbreaks of drug-resistant bacterial infections within the hospital environment.[12]

1.2 The United Kingdom as an artificial intelligence superpower

The UK has set out a 10-year strategy to become an Artificial Intelligence (AI) Superpower.[13] The focus of the UK Government strategy is on the development of infrastructure, equity, governance and standards, and the ability to deliver tools where they are required to support meaningful societal impact through the application of AI-based tools.[14] Whilst the application of AI-based tools in healthcare remains a controversial topic, the consideration of the role of digital health solutions in addressing sub-optimal antimicrobial prescribing is an important one.

Healthcare is undergoing rapid digitalisation with ‘electronic health records’ and ‘computer prescriber order entry systems’ being adopted across the UK. Consequently, increased quantities of detailed, patient-level data can now be utilised to support clinical decision making. Across healthcare, electronic clinical decision support systems, tools that help clinicians or patients make decisions about healthcare, are widely used to support antimicrobial prescribing. Few current clinical decision support systems utilise AI or the wealth of data now available to support that decision making.

The ability to improve data collection further through the application of wearable, real-time monitoring technologies and linkage via cloud-based technology with AI-based systems is being rapidly developed.[15] Examples of the use of AI-based tools to support enhanced monitoring with wearable technology is well described and are becoming increasingly accepted by the public.[16]

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[12] Timothy M. Rawson et al., ‘COVID-19 and the Potential Long-Term Impact on Antimicrobial Resistance’, *Journal of Antimicrobial Chemotherapy* 75, no. 7 (July 2020).
[13] HM Government, *National AI Strategy*, 2021.
[14] HM Government.
[15] Damien Ming et al., ‘Connectivity of Rapid-Testing Diagnostics and Surveillance of Infectious Diseases’, *Bulletin of the World Health Organization* 97, no. 3 (March 2019).
[16] Farida Sabry et al., ‘Machine Learning for Healthcare Wearable Devices: The Big Picture’, *Journal of Healthcare Engineering* 2022, no. 18 (April 2022); Timothy M. Rawson et al., ‘Public Acceptability of Computer-Controlled Antibiotic Management: An Exploration of Automated Dosing and Opportunities for Implementation’, *Journal of Infection* 78, no. 1 (January 2019).

2. Antimicrobial prescribing

Antimicrobial prescribing is both complex and ubiquitous. One in three people will be prescribed an antibiotic during a healthcare episode.[17] Most antibiotic prescribing is performed by clinicians who have limited training in infection diagnosis and management.[18] For example, in the UK undergraduate and postgraduate training on antimicrobial prescribing and AMR is limited outside of individuals specialising in Infectious Diseases and Medical Microbiology.[19] Three in four antimicrobial prescriptions will be made by General Practitioners in primary care. For most infection diagnoses and antimicrobial prescriptions, these will occur without input from an infection specialist.

To support antimicrobial prescribing decisions within the UK, national and local prescribing guidelines are created. These provide evidence-based recommendations for the management of common infections considering local epidemiology and resistance rates. These guidelines tend to be inflexible in the face of real-world variability and uncertainty meaning that adherence to guidelines is variable.

Globally, between 20 and 50 per cent of antimicrobial prescriptions are ultimately inappropriate.[20] Inappropriate refers to antimicrobials being prescribed for non-bacterial infections (e.g. viral infection), for too long a duration, in the wrong spectrum (targeting more bacteria, and therefore building the risk of resistant mutations more broadly than necessitated by a particular course of treatment), or used in the wrong dose or route (for example intravenous instead of oral).

To address inappropriate prescribing antimicrobial stewardship programmes are often implemented. Antimicrobial stewardship programmes are multi-faceted interventions that incorporate governance, local action and expertise, surveillance, and education and training to improve the use of antimicrobials within an organisation.[21]

An important aspect of antimicrobial stewardship is focusing on promoting sustainable behaviour change towards antimicrobial use both at institutional and individual levels. A major area for consideration within antimicrobial stewardship programmes is the emerging role of technology in helping provide decision support for clinicians in a more individualised and adaptive way.

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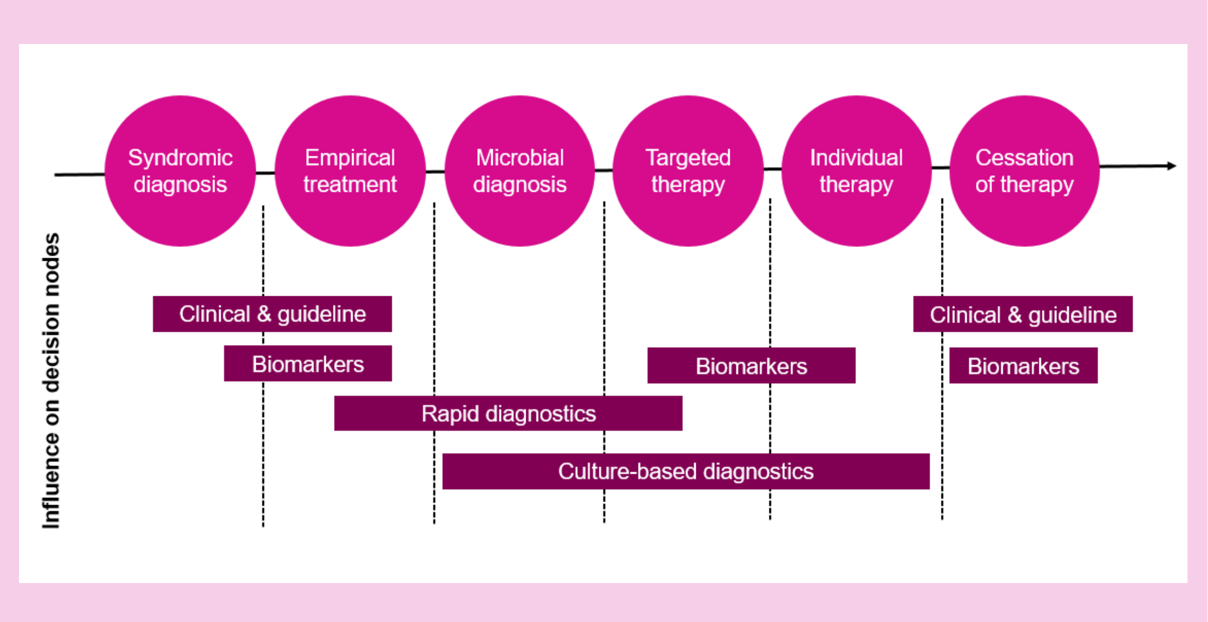
[17] P Zarb et al., 'The European Centre for Disease Prevention and Control (ECDC) Pilot Point Prevalence Survey of Healthcare-Associated Infections and Antimicrobial Use', *Eurosurveillance* 17, no. 46 (November 2012).
[18] Zarb et al.
[19] Charani et al., 'Optimising Antimicrobial Use in Humans - Review of Current Evidence and an Interdisciplinary Consensus on Key Priorities for Research'; Timothy M. Rawson et al., 'Exploring the Coverage of Antimicrobial Stewardship across UK Clinical Postgraduate Training Curricula', *Journal of Antimicrobial Chemotherapy* 71, no. 11 (November 2016); Enrique Castro-Sánchez et al., 'Mapping Antimicrobial Stewardship in Undergraduate Medical, Dental, Pharmacy, Nursing and Veterinary Education in the United Kingdom', ed. John Panepinto, *PLoS ONE* 11, no. 2 (February 2016).
[20] Katherine E. Fleming-Dutra et al., 'Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011', *JAMA* 315, no. 17 (May 2015).
[21] Loria A. Pollack and Arjun Srinivasan, 'Core Elements of Hospital Antibiotic Stewardship Programs From the Centers for Disease Control and Prevention', *Clinical Infectious Diseases* 59 (October 2014).

2.1 Understanding antimicrobial prescribing behaviour

To optimise antimicrobial use, we need to understand the complexity of the prescribing process as a behaviour.[22] Antimicrobial decision making can be described as several individual decision steps. Decision steps include the clinician making a syndromic diagnosis, initiating empiric antimicrobial therapy, making a microbiological diagnosis, transitioning to more targeted and individualised treatment, through to the cessation of treatment (Figure 2).

At each decision step in the process of antimicrobial use there are core components and tools that will influence how decision are made.[23]

Figure 2: Decision modes associated with antimicrobial prescribing and factors influencing decision making at each stage

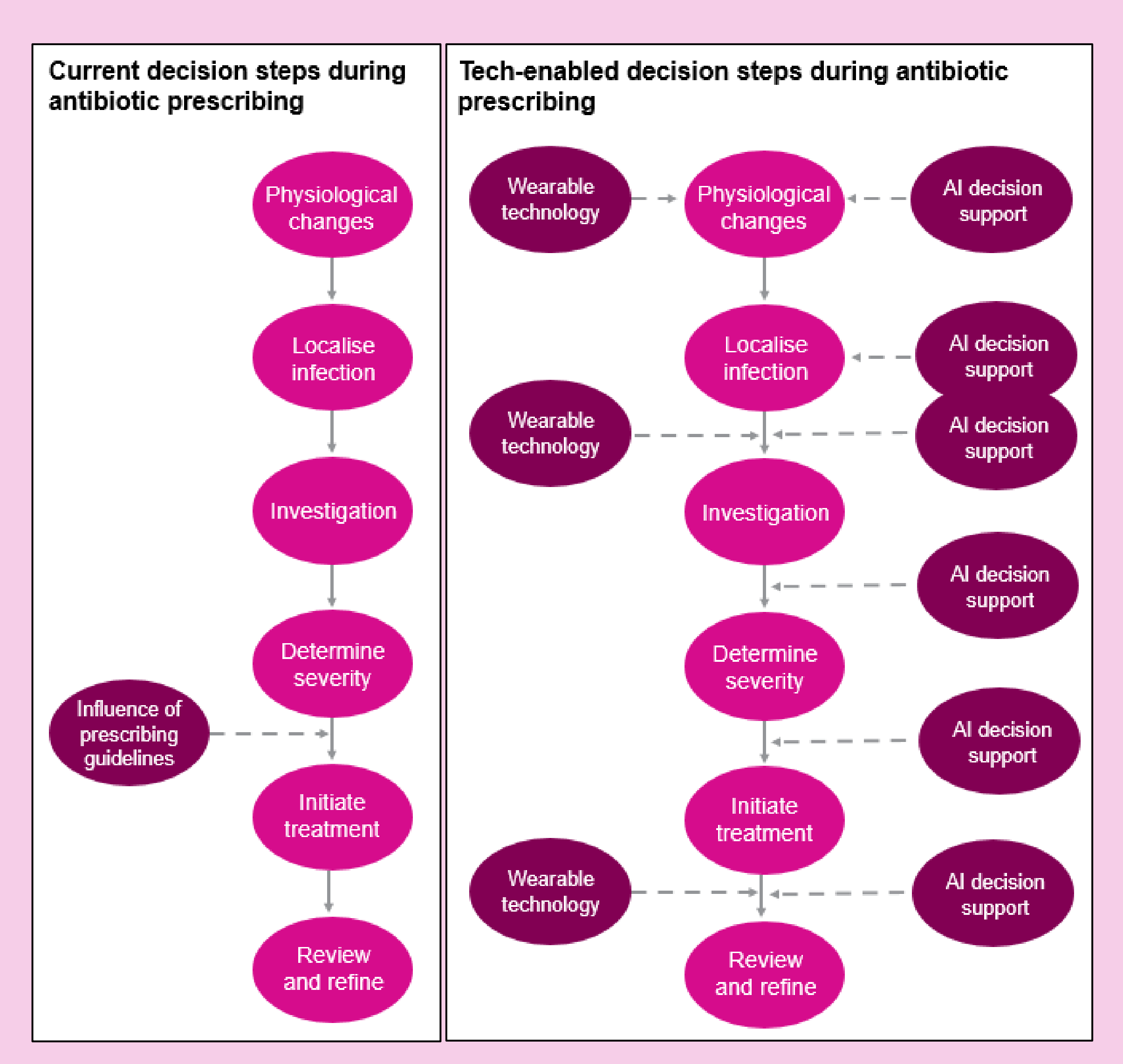


Source: Clinical Microbiology and Infection, ‘Understanding how diagnostics influence antimicrobial decision-making is key to successful clinical trial design’, 2023.

Focusing on infection diagnosis and empiric antimicrobial selection, this can further be broken down into important cognitive steps in the decision-making process (Figure 3). Each of these steps is influenced by a range of different components. If we evaluate the impact of current antimicrobial prescribing policy / guidelines on decision making, we find that our current rule-based tools only influence a small number of steps in the decision process.

[22] Timothy M. Rawson et al., ‘Mapping the Decision Pathways of Acute Infection Management in Secondary Care among UK Medical Physicians: A Qualitative Study’, *BMC Medicine* 14, no. 1 (December 2016).
[23] Rawson et al.

Figure 3: Decision process around diagnostics and initiation of antimicrobial treatment in acute infection



Source: Adapted from BMC Medicine, 'Mapping the decision pathways of acute infection management in secondary care among UK medical physicians: a qualitative study' 2016.

Supporting optimal decision making must focus on developing mechanisms to provide enhanced information that can support each step in the decision-making pathway more accurately. By achieving this, we may be able to have a greater impact on supporting decision making overall. The development and adoption of technological solutions, such as AI and wearables, could address these current gaps in the optimisation of antimicrobial prescribing.[24]

[24] Timothy M. Rawson et al., 'A Systematic Review of Clinical Decision Support Systems for Antimicrobial Management: Are We Failing to Investigate These Interventions Appropriately?', *Clinical Microbiology and Infection* 23, no. 8 (August 2017).

3. The role of state-of-the-art technology

Across the UK, most healthcare services in primary and secondary care are moving towards paperless, integrated, electronic systems. The expansion in electronic health record data, integrated into central systems, provides an opportunity for the integration of electronic clinical decision support systems and novel technologies, including AI, to support optimal antimicrobial decision making.[25]

Biosensor and real-time monitoring technologies, often deployed as part of wearable technology, are also becoming widely accepted as tools for individualised treatment in fields such as diabetes management, providing a proof-of-concept for their wider application within healthcare.[26] Within infectious diseases, recent studies have demonstrated the ability of wearable sensors to monitor, in real time, changes in antibiotic concentration and additional biomarkers of infection, such as lactate.[27] Remote monitoring of oxygen saturations and heart rate was also successfully employed during the COVID-19 pandemic to avoid admission to hospital.[28]

Figure 4 summarises the core technologies being developed and applied to AMR. It includes novel antimicrobials and rapid diagnostics for comparison.

[25] Rawson et al.

[26] Timothy M. Rawson et al., ‘Optimizing Antimicrobial Use: Challenges, Advances and Opportunities’, *Nature Reviews Microbiology* 19, no. 12 (December 2021).

[27] Timothy M. Rawson et al., ‘Microneedle Biosensors for Real-Time, Minimally Invasive Drug Monitoring of Phenoxymethylpenicillin: A First-in-Human Evaluation in Healthy Volunteers’, *The Lancet Digital Health* 1, no. 7 (November 2019); Damien K. Ming et al., ‘Real-Time Continuous Measurement of Lactate through a Minimally Invasive Microneedle Patch: A Phase I Clinical Study’, *BMJ Innovations* 8, no. 2 (n.d.).

[28] Ahmed Alboksmaty et al., ‘Effectiveness and Safety of Pulse Oximetry in Remote Patient Monitoring of Patients with COVID-19: A Systematic Review’, *The Lancet Digital Health* 4, no. 4 (April 2022).

Figure 4: Summary of state-of-the-art technology to support antimicrobial prescribing

Issue	Readiness Level	Target area	Advantages	Challenges
New therapeutics	In use	• Treatment	• Improved activity against drug-resistant infections, often with less toxicity than current treatments.	• Emergence of resistance. • Expensive. • Underlying challenges with inappropriate prescribing not addressed.
Rapid Diagnostics	In use	• Diagnosis • Treatment • Personalisation • Cessation	• Faster turn-around-times. • Point-of-care potential. • Linkage with digital health technology.	• Uncertain impact on decision making. • Expensive. • Often do not replace traditional diagnostic testing.
Digital technology (e.g. electronic health records and computerised prescriber order entry)	In use	• Diagnosis • Treatment • Personalisation • Cessation	• Electronic recording. • Cross-healthcare implementation and linkage of data available.	• Inflexible in the face of individual variation. • Often not designed with the end user. • Focused on specific aspects of practice.
AI-based technology	Under evaluation in practice	• Diagnosis • Treatment • Personalisation • Cessation	• Allow for individualised recommendations. • Can be adapted for local challenges. • Can improve treatment decision making.	• Often mistrusted by clinicians. • Concern for bias. • Immature guidelines for development and regulation. • Privacy and public perception.
Wearable devices	Under evaluation in practice	• Diagnosis • Personalisation • Cessation	• Widely acceptable. • Connection to wider digital networks. • Allow remote monitoring.	• Cost effectiveness to be proven. • Require greater levels of evidence for effectiveness in improving patient outcomes.
Biosensor technology	Testing and development underway in humans	• Diagnosis • Personalisation • Cessation	• Can support real-time monitoring for diagnostics and therapeutics. • Allow for minimally invasive and point-of-care technology development.	• Optimal sampling strategies and approach to application to be defined. • Economic and clinical impact of implementation still to be defined.

3.1 State-of-the-art technology to support antimicrobial prescribing

3.1.1 Artificial intelligence

Reporting of AI-based tools to support clinical decision making for infection management is rapidly increasing in the academic literature.[29] AI-based tools range from methods for early detection of deteriorating patients with sepsis, through to supporting antimicrobial selection using individual patient variables. AI-based decision support tools could provide the clinician with individualised, adaptive recommendations about patient management that, unlike current guidelines, would be able to reflect the heterogeneity seen in clinical practice.

AI is already being applied in the microbiology laboratory to support the diagnosis of infection, the identification and quantification of micro-organisms, and the analysis of antimicrobial susceptibility. A recent review identified 97 AI-based tools for this purpose.[30] Most of these technologies focus on diagnosis of bacterial infection.

Current adoption of AI-based technology in the microbiology laboratory aims to facilitate the automation of repetitive tasks with clinical microbiologists validating the results. Future applications for AI in this setting aim to provide systems capable of analysing complex and high-dimensional data, such as that generated by next-generation sequencing. They may also support the development of lab-free, point-of-care technologies.

AI tools can be embedded into electronic health records to help make real-time decisions when there are not clear guidelines to support a decision. AI offers dynamic, individualised methods of supporting decision making for infection management based on the individual patient. Current AI technologies have been developed to focus on clinical outcomes such as the prediction of sepsis in critical care, the diagnosis of TB or surgical site infection, the prediction of virological success of antiretroviral therapy, and the selection of an antibiotic regimen.

One review has identified 60 unique AI-based tools designed to support decision making for clinical diagnosis and management of infection.[31] AI was used to support the diagnosis of infection, the early detection or stratification of sepsis, the prediction of response to antimicrobial therapy, the presence of antibiotic resistance, and the choice of antibiotic regimen.

AI-based tools designed to support the diagnosis and management of sepsis include numerous, frequently measured variables that are stored electronically within critical care databases. These include individual patient vital signs, laboratory data, demographic

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[29] Timothy M. Rawson, Nathan Peiffer-Smadja, and Alison Holmes, *Artificial Intelligence in Infectious Diseases*, ed. Niklas Lidströmer and Hutan Ashrafian (Cham: Springer International Publishing, 2022), https://doi.org/10.1007/978-3-030-64573-1_103; Nathan Peiffer-Smadja et al., 'Machine Learning for Clinical Decision Support in Infectious Diseases: A Narrative Review of Current Applications', *Clinical Microbiology and Infection* 26, no. 5 (August 2020); Nathan Peiffer-Smadja et al., 'Machine Learning in the Clinical Microbiology Laboratory: Has the Time Come for Routine Practice?', *Clinical Microbiology and Infection* 26, no. 10 (October 2020), https://doi.org/10.1016/j.cmi.2020.02.006.
[30] Holmes et al., 'Understanding the Mechanisms and Drivers of Antimicrobial Resistance'.
[31] O'Neill, *Tackling Drug Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance*.

information, medical history, therapeutic data and radiology, plus specialist investigations. In some cases, unstructured clinical data is also added to these models. In a large validation dataset, sepsis treatment decisions matching those recommended by an “AI Clinician” were associated with superior outcomes compared to divergent treatment decisions.[32]

One example of an AI-based decision support system used in clinical infectious diseases supported by high-quality clinical trial data is the TREAT system. A randomised control trial was undertaken across three hospitals to measure appropriateness of antimicrobial prescribing. A secondary analysis of 180-day survival following treatment was also explored. The AI-based decision support tool led to a 9 per cent improvement in appropriateness of antimicrobial prescribing compared to normal practice. Assessment of 180-day survival demonstrated a significant benefit from the use of the AI-based tool (6 per cent increase in survival) when the recommendations from the system were followed by clinicians. These results suggests that the decision support provided by the TREAT system was at least a contributing factor to better outcomes.[33]

A key benefit of integrating AI-based decision support systems into healthcare is its ability to rapidly adapt when new questions arise in clinical practice. An example was provided during the early phase of COVID-19 when there were concerns about bacterial co-infection, which was seldom present but difficult to diagnose or exclude. Using a supervised machine learning algorithm integrated into a hospital information technology infrastructure, researchers were able to apply data from the early pandemic to train an algorithm to provide predictions on the presence or absence of bacterial infection to support clinical decision making.[34]

Recommendation 1: The UK Government should use the fight against Antimicrobial Resistance as an exemplar of applying artificial intelligence and digital technologies as part of their 10-year plan to become an artificial intelligence superpower.

3.1.2 Wearable monitoring technology

Wearable technology encompasses all products that a user can wear on their body, integrating technology with their everyday activities in order to detect and transmit information about the user. For infection related wearables, this may be measurement of vital signs (e.g. temperature, heart rate, blood pressure, oxygen saturations) or could be routine measure of activity (e.g. step count). The Institute for Molecular Science and Engineering at Imperial College London recently published a briefing paper exploring the future of wearable technologies, including in the management of infectious diseases.[35]

Monitoring technologies are routinely being applied in specific chronic infection states, such as Project Breathe that supports remote monitoring of Cystic Fibrosis patient health using home monitoring and mobile applications to collect data.[36] This data can be used to help

[32] Rawson et al., ‘Optimizing Antimicrobial Use: Challenges, Advances and Opportunities’.
[33] Mical Paul et al., ‘Improving Empirical Antibiotic Treatment Using TREAT, a Computerized Decision Support System: Cluster Randomized Trial’, *Journal of Antimicrobial Chemotherapy* 58, no. 6 (December 2006).
[34] Timothy M. Rawson et al., ‘Supervised Machine Learning to Support the Diagnosis of Bacterial Infection in the Context of COVID-19’, *JAC-Antimicrobial Resistance* 3, no. 1 (January 2021).
[35] Kieran Brophy et al., *The Future of Wearable Technologies* (Imperial College London, 2021).
[36] Project Breathe, ‘Breathe RM’, Webpage, November 2023.

individuals predict when they are likely to be developing an infective exacerbation of their lung disease supporting earlier intervention.

The wider adoption of wearable technology has the potential to provide additional, comprehensive patient level data in times of health and sickness. The utilisation of cloud-based connectivity and integration of wearable technology data into patient databases provides an opportunity to utilise the data within AI-based decision support tools.[37]

The inclusion of routine data from wearables may provide a broader number of variables and baseline data from periods of health from which predications and recommendations can be computed. For antimicrobial prescribing, wearables may therefore facilitate the early detection of infection, allow monitoring of response to treatment, and support ambulatory management of patients who otherwise would normally be required to remain in hospital for observation during this period.

3.1.3 Biosensor technology

Biosensors can detect and measure an analyte using a biological method of detection. This is normally achieved through an enzyme reaction or binding event. Biosensors have been reviewed extensively for their use in medicine, agriculture, and the environment.[38]

Biosensors are desirable as they can be miniaturised, facilitating the development of portable, easy-to-use, point-of-care devices that do not require expensive analytical machinery, laboratories, or technical ability to operate.[39] This means that biosensors can be applied to support drug-monitoring or biomarker detection as point-of-care, single time point assays or as part of devices developed to facilitate real-time monitoring, often as part of a wearable technology.[40]

Biosensors have recently been applied to wearable technology to facilitate the measurement of penicillin, an antibiotic, and lactate, a biomarker that is elevated in sepsis,[41] and first-in-human trials have demonstrated their ability to continuously monitor these in healthy volunteers. The measurement of antibiotics using minimally invasive devices in a continuous fashion provides a new way of being able to measure the concentration of antibiotic within an individual patient in real-time and therefore would allow rapid adjustment of dosing based on observed concentration within the patient.[42] By linking this type of wearable device for real-

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[37] Ming et al., ‘Connectivity of Rapid-Testing Diagnostics and Surveillance of Infectious Diseases’.
[38] Danny O’Hare, ‘Biosensors and Sensor Systems’, in *Body Sensor Networks*, ed. Guang-Zhong Yang (London: Springer London, 2014); Anthony P. F. Turner, ‘Biosensors: Sense and Sensibility’, *Chemical Society Reviews* 42, no. 8 (2013); Dorothee Grieshaber et al., ‘Electrochemical Biosensors - Sensor Principles and Architectures’, *Sensors* 8, no. 3 (March 2008); Javier Monzó et al., ‘Fundamentals, Achievements and Challenges in the Electrochemical Sensing of Pathogens’, *The Analyst* 140, no. 21 (2015); Eric Bakker and Yu Qin, ‘Electrochemical Sensors’, *Analytical Chemistry* 78, no. 12 (June 2006).
[39] O’Hare, ‘Biosensors and Sensor Systems’; Turner, ‘Biosensors: Sense and Sensibility’.
[40] Timothy M Rawson et al., ‘Delivering Precision Antimicrobial Therapy through Closed-Loop Control Systems’, *Journal of Antimicrobial Chemotherapy* 73, no. 4 (December 2017).
[41] Rawson et al., ‘Microneedle Biosensors for Real-Time, Minimally Invasive Drug Monitoring of Phenoxymethylpenicillin: A First-in-Human Evaluation in Healthy Volunteers’.
[42] Rawson et al., ‘Optimizing Antimicrobial Use: Challenges, Advances and Opportunities’.

time measuring to a AI-based algorithm, individual patient data can be rapidly linked to population level estimates to allow for treatment optimisation.[43]

The measurement of lactate using minimally invasive wearable technology may support the early detection of sepsis or support monitoring of response to treatment.[44] This approach also serves as an important proof-of-concept for the measurement of other infection specific markers.

The potential benefits of linking and utilising biosensor, wearable, and AI-based technologies to support antimicrobial management are extensive. By providing higher resolution, individualised data to the prescriber, we may be able to support more optimal diagnosis, timing, selection, and cessation of antimicrobial therapy. This reduction in consumption of therapy is likely to have a significant impact on AMR allowing us to safeguard our current and future antimicrobials.

3.2 Barriers to adoption

The earliest trials of AI-based decision support for antimicrobial prescribing took place in the early 2000's.[45] These tools demonstrated potential improvement in antimicrobial prescribing, but clinical trials did not reach significance due to a lack of engagement with the tools by prescribers.[46] Poor engagement with decision support tools upon implementation is a recurrent challenge identified within this field and points towards the complex behavioural aspects of antimicrobial prescribing.[47] This reflects the general challenge of innovation uptake within the NHS.

To successfully incorporate AI-based systems and wearable technologies into clinical practice for antimicrobial optimisation and support sustained adoption several barriers need to be addressed.

3.2.1 Defining clear measures of impact

A major challenge in the field of antimicrobial optimisation, and thus for AI-based decision support development, is demonstrating improved outcomes that are clinically relevant to the end-user. Outcomes for antimicrobial prescribing are often reported using subjective measures, such as 'appropriateness' of a prescription, or at population levels such as total consumption of antimicrobials. Direct patient impact, such as death, can be difficult to demonstrate when the focus of optimising treatment is to encourage more judicious use of antibiotic therapy, and thus will often only lead to equivalent outcomes when compared to

[43] Rawson et al.; Noé Brasier et al., 'A Three-Level Model for Therapeutic Drug Monitoring of Antimicrobials at the Site of Infection', *The Lancet Infectious Diseases* 23, no. 10 (October 2023).
[44] Ming et al., 'Real-Time Continuous Measurement of Lactate through a Minimally Invasive Microneedle Patch: A Phase I Clinical Study'; David M. E. Freeman et al., 'Continuous Measurement of Lactate Concentration in Human Subjects through Direct Electron Transfer from Enzymes to Microneedle Electrodes', *ACS Sensors* 8, no. 4 (April 2023).
[45] Paul et al., 'Improving Empirical Antibiotic Treatment Using TREAT, a Computerized Decision Support System: Cluster Randomized Trial'.
[46] Rawson et al., 'A Systematic Review of Clinical Decision Support Systems for Antimicrobial Management: Are We Failing to Investigate These Interventions Appropriately?'
[47] Charani et al., 'Optimising Antimicrobial Use in Humans - Review of Current Evidence and an Interdisciplinary Consensus on Key Priorities for Research'.

more aggressive treatment approaches. Adverse events, such as side effects, toxicity, and direct impact on AMR can be difficult to study at an individual level due to a lack of consensus on appropriate methodology and time-points for these measures.[48]

Current approaches to assessing antimicrobial prescribing are often rule-based and algorithmic with institutions penalised for deviating from the perceived norm. This approach does not align well with the evaluation of individualised approaches to care.

Clear consensus definitions for outcomes of antimicrobial optimisation research are required to facilitate comparison between interventions, and support the evaluation of individualised approaches to treatment.

Recommendation 2: NHS England should invest in methods of supporting the implementation and real-world evaluation of individualised approaches to antimicrobial prescribing. This should include the use of AI-based decision support software and wearable technology, working with the UK's world-leading centres of technological innovation to address Antimicrobial Resistance.

3.2.2 Improving end-user engagement

Development of AI-based decision support tools requires end-user engagement to ensure that design of their interface and interpretability of their recommendations are acceptable.[49] The early engagement of prescribers facilitates user-friendly design and can ensure that the tool is deployed and used at the correct place in the antibiotic decision making pathway.

Engagement must also go beyond prescribers to include patients. Public buy-in, or trust, is vital in supporting the successful development and championing of tools such as AI and wearable devices.[50]

3.2.3 Enabling adoption

The adoption of AI-based decision support tools should be supported top-down by policymakers with a focus on patient, economic, and population health benefits. While ensuring end-user engagement is vital, robust policy supporting the development, implementation, and operationalisation of digital technology for antimicrobial optimisation is

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[48] Rawson et al., 'A Systematic Review of Clinical Decision Support Systems for Antimicrobial Management: Are We Failing to Investigate These Interventions Appropriately?'; Timothy M. Rawson et al., 'Understanding How Diagnostics Influence Antimicrobial Decision-Making Is Key to Successful Clinical Trial Design', *Clinical Microbiology and Infection*, 2023.

[49] Rawson et al., 'A Systematic Review of Clinical Decision Support Systems for Antimicrobial Management: Are We Failing to Investigate These Interventions Appropriately?'; Timothy M. Rawson et al., 'Artificial Intelligence Can Improve Decision-Making in Infection Management', *Nature Human Behaviour* 3, no. 6 (March 2019).

[50] Timothy M. Rawson et al., 'Development of a Patient-Centred Intervention to Improve Knowledge and Understanding of Antibiotic Therapy in Secondary Care', *Antimicrobial Resistance & Infection Control* 7, no. 1 (March 2018); Timothy M. Rawson et al., 'Patient Engagement with Infection Management in Secondary Care: A Qualitative Investigation of Current Experiences', *BMJ Open* 6, no. 10 (October 2016); Timothy M. Rawson et al., 'Involving Citizens in Priority Setting for Public Health Research: Implementation in Infection Research', *Health Expectations* 21, no. 1 (February 2018).

lacking. Research has highlighted the current gaps in National Action Plans and operationalisation.[51]

Policy must specifically look to support the adoption of individualised decision making and not penalise individuals who take actions focused on rational and appropriate antimicrobial use. A policy framework is needed which gives confidence to prescribers to follow individualised recommendations made by AI-based algorithms which off-set the perceived risk of not acting or prescribing a broad-spectrum antimicrobial.

By providing support for decision making based on individual risk-based parameters, and acknowledging the dynamic nature of infection, such a policy framework can help shift antimicrobial prescribing towards a more data-driven, precise practice.

Recommendation 3: The Government should make optimisation of antimicrobial prescribing, utilising electronic health record data, AI-based clinical decision support systems, and the adoption of novel technologies a core focus on the UK AMR 5-year action plan 2024-2029.

3.2.4 Focusing on ethical and regulatory challenges

Regulatory pathways and national policies currently hinder the implementation and testing of systems designed to deliver adaptive and individualised decision support.

Financial and reputational penalties are sometimes implemented for deviating from guidelines and targets. Locally, healthcare organisations have strict antimicrobial prescribing policy with their practice often benchmarked through tools such as the AMR local indicators platform.[52] For many years, a proportion of healthcare provider income was based on meeting Commissioning for Quality and Innovation (CQUIN) targets that encouraged hospitals to focus on certain aspects of antimicrobial policy, regardless of their local infection and resistance rates. Such policy and targets for improving prescribing are necessary, but must also be recognised as inhibitory to the exploration of individualised approaches that may drive deviation away from conventional recommendations.

Regulatory bodies have provided initial guidance on development and approvals of AI-based software to support the development and testing of such tools.[53] However, clear agreement on the type of data used to train and test systems, and mitigation of any bias and inequity they may contain, requires greater scrutiny.[54]

Current AI-based tools are largely trained on retrospectively collected data, meaning it was not collected with this function in mind. The development of tools using routine healthcare data risks the introduction of systemic bias, which may not be possible to control for. For example, if a system is trained using data from one region it may bias the algorithm to favour individuals

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[51] Charani et al., 'Optimising Antimicrobial Use in Humans - Review of Current Evidence and an Interdisciplinary Consensus on Key Priorities for Research'.

[52] Office for Health Improvement and Disparities, *AMR Local Indicators - Produced by the UKHSA*, 2022.

[53] Medicines & Healthcare products Regulatory Agency, 'Software and Artificial Intelligence (AI) as a Medical Device', Webpage, October 2023.

[54] William J. Bolton et al., 'Developing Moral AI to Support Decision-Making about Antimicrobial Use', *Nature Machine Intelligence* 4, no. 11 (November 2022).

with similar demographics when applied to a different group of people. This may drive inequity in decision support, favouring better represented individuals within the training data.

Whilst risk-mitigation can be incorporated as post-market surveillance, the development of prospective, controlled datasets specifically designed for AI-decision support development may help to advance the performance of such algorithms. This requires a national approach to data collection and curation supported by linkage across healthcare sectors. It also requires consensus on data requirements and outcome measures.

Recommendation 4: NHS England, supported by sectoral experts in digital health and Antimicrobial Resistance, should design national data collection tools specifically to support the prospective development and testing of artificial intelligence systems for optimising antimicrobial prescribing.

3.2.5 Developing tools that are agnostic to local digital health infrastructure

As healthcare systems tend towards integrated adoption of single electronic health record platforms, the requirements for development and integration of locally developed AI-based tools needs to be considered. There is currently no national standardised electronic health record system meaning that variation in data collection and storage may occur. Variation in systems may also lead to variation in antimicrobial prescribing behaviours between regions.

The integration of AI-based tools and wearable technology into local healthcare infrastructure must consider the generalisability to the environment where they are being subsequently deployed. Protocols for validation or verification of technology upon local implementation need to be defined as part of regulatory requirements for the development of commercial AI-based and wearable systems.

3.2.6 Addressing public concerns

Preliminary research has demonstrated that incorporating patient facing tools to support individualised antimicrobial management can improve patient knowledge and understanding about their infection and its treatment.[55] Digital health and wearable technologies to support infection management are widely accepted by patients and the public when presented with appropriate and balanced information on the intent and use of developed technologies.[56] Concerns around data use, the requirement for human oversight, and privacy remain major challenges for developers to address.

To address public perception and potential concerns surrounding the use of AI and wearable technology to support antimicrobial decision making, these topics should be integrated within current public health campaigns on antimicrobial use, including the UK-led Antibiotic Guardian campaign and WHO World Antibiotics Awareness Week.

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[55] Rawson et al., 'Development of a Patient-Centred Intervention to Improve Knowledge and Understanding of Antibiotic Therapy in Secondary Care'.
[56] Rawson et al., 'Public Acceptability of Computer-Controlled Antibiotic Management: An Exploration of Automated Dosing and Opportunities for Implementation'; Rawson et al., 'Patient Engagement with Infection Management in Secondary Care: A Qualitative Investigation of Current Experiences'.

Recommendation 5: Public and patient engagement with the challenges of Antimicrobial Resistance, data-access in the evolving digital landscape of the NHS, and concerns around AI and other digital based technologies should be integrated into national public engagement campaigns.

4. Conclusion

The Government is recognised as a leading authority in the global response to AMR. It has also stated its ambition to be an AI superpower. As the NHS moves towards integrated, electronic health record systems, the Government has the opportunity to leverage world-leading healthcare data, expertise in AMR, and AI development to position itself as an innovator in its approach to the optimisation of antimicrobial prescribing.

Through the development and application of novel digital health and wearable technologies, the UK can help provide new methods to address AMR and set an example for application of such technology within healthcare more broadly.

Achieving this means overcoming barriers to adoption – including public confidence, clinical prescriber reluctance or lack of awareness, and data and measurement challenges – but the prize for doing so is great.

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