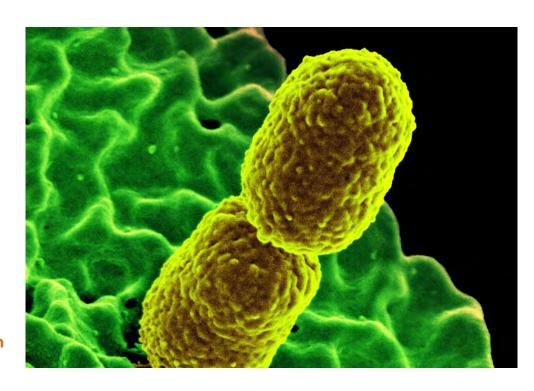


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Overview report

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Overview report

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Background

The UK Five Year Anti-Microbial Resistance Strategy, 2013-2018 (hereafter 'the Strategy') was released by the Department of Health (now Department of Health and Social Care, DHSC), with the Department for Environment Food and Rural Affairs (Defra) and Public Health England (PHE), in September 2013. The primary objective of the Strategy was to slow the development and spread of anti-microbial resistance (AMR). The three stated aims of the Strategy were to:

- Improve the knowledge and understanding of AMR;
- Conserve and steward the effectiveness of existing treatments;
- Stimulate the development of new antibiotics, diagnostics and novel therapies.

The aims of the Strategy were to be achieved through activity in seven areas: improving infection prevention and control; optimising prescribing practice; improving professional education, training and public engagement; developing new drugs, treatments and diagnostics; better access to and use of surveillance data; better identification and prioritisation of research needs; and strengthened international collaboration. The Strategy was developed within a One Health approach,² thus the scope of the Strategy included issues relevant to human health, animal health and husbandry, agriculture, and the wider environment.

Under the Strategy, the DHSC, Defra and PHE led a programme of work involving many organisations across the UK, with interventions at local, regional, national and international levels. As human health is a devolved function, Scotland, Wales and Northern Ireland were responsible for implementation of the Strategy within their own administrations.

Following a scoping study, the Policy Innovation Research Unit (PIRU) was commissioned in 2017 to undertake an evaluation of the implementation of the Strategy and evidence underpinning the key mechanisms of change, with a view to contributing to the review of the Strategy, planned for 2018. Interim findings were provided to DHSC during 2018 to assist the team revising the Strategy.

¹ Department of Health and Department for Environment and Rural Affairs. 2013. UK Five Year Anti-microbial Resistance (AMR) Strategy, 2013-2018.

² Public Health England. 2015. *UK*One Health Report. Joint report on
human and animal antibiotics use,
sales and resistance, 2013.

Approach to the evaluation

We undertook a scoping study in late 2015 and early 2016 before the evaluation. The scoping study included interviews with a small number of people involved in the development and delivery of the Strategy at central government level, rapid reviews of the evidence supporting the activities in the Strategy to identify gaps in the evidence (particularly whether there were systematic reviews supporting actions set out in the Strategy), and development of a logic model, to identify the most important themes and research questions to be explored in the evaluation. As the approach to the implementation of the Strategy changed over time and particularly during the second half of 2016, the logic model reflects the situation in mid-2016 and thus does not reflect all the eventual mechanisms of change. In addition, the logic model only includes activities specified in the Strategy, as opposed to all activity undertaken in a specific area. However, the model demonstrates the highly complex nature of the Strategy, with multiple facets and potential for unintended positive and negative consequences (see Appendix One: Logic model of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018).

As the scope of the Strategy was vast, containing actions at multiple levels (local, regional, national, and international) and covering many sectors, it was not possible, or necessarily appropriate, to evaluate every aspect of implementation of the Strategy. Instead, it was agreed with DHSC that the evaluation should focus on the main areas of the Strategy and evidence underpinning the key mechanisms of change that had been adopted.

The evaluation consisted of six elements, which are described in Table 1. Each of the elements mapped to one or more of the areas of the Strategy outlined above. The elements were designed to fit together and provide a coherent account of implementation of the Strategy. Appendices to this report provide further details of the evaluation and are identified for each of the elements.

Table 1 Elements of the evaluation of the implementation of the Strategy

Element

Description

National and local implementation of the Strategy

We studied implementation of the Strategy from the perspectives of national and local participants, and the activities and processes of implementation that take place at national and local levels in England and the Devolved Administrations, and across human, animal and agricultural sectors. We also studied the interaction that takes place between the different levels of implementation, as a large part of national policy implementation rests on the actions of local organisations and staff.

This element included:

- analysis of implementation of the Strategy at the national level In England, Wales, Scotland and Northern Ireland
- case studies exploring implementation of the Strategy across human health systems in West Norfolk, Camden, Blackburn with Darwen, Glasgow, Derry/Londonderry, and Betsi Cadwaladr
- case studies exploring implementation of the Strategy in animal health systems in the pig and poultry sectors in West Norfolk, and in companion animals (pets) in Camden

During the scoping study we identified a gap in the evidence base underpinning the clinical and antibiotic prescribing impact of rapid diagnostic tests for bacterial identification and antibiotic susceptibility. We completed a systematic review of the use of rapid diagnostic tests for bacterial identification and antibiotic susceptibility testing in hospitals as part of this element of the evaluation.

Reports:

- Appendix Two: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 – Summary Report
- Appendix Three: Rapid diagnostic tests for bacterial identification and antibiotic susceptibility testing in hospitals
- Appendix Twelve: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018

Use of data to effect change in behaviour

The Strategy included plans to develop better data systems and sophisticated means of utilising routine data for both human and animal health. We explored whether the commitment to improve data systems had been realised, the extent to which existing data sources met the needs of national and local staff (such as general practitioners, veterinarians and NHS commissioners) whose change in practice and behaviour was essential to successful implementation of AMR policies, and the quality of the systems, according to specified criteria. This element explored how access to, and use of, surveillance data might be improved to help the Strategy achieve its stated goals.

During the scoping study, we identified a gap in evidence underpinning the effectiveness of surveillance systems in assisting health professionals in combating AMR. Given the emphasis on development of better data systems in the Strategy, we completed a systematic review of evaluations of surveillance systems in human and animal health systems worldwide to determine what is known about their effectiveness.

Reports:

- Appendix Four: Evaluations of human and animal health surveillance systems in the AMR context
- Appendix Five: Evaluation of the implementation of the UK Antimicrobial Resistance Strategy, 2013-2018 – use of data to effect change

Table 1 Continued

Element

Description

Implementation of the Strategy and evidence of effectiveness in the food chain

The 'food chain' is the system of organisations, people, activities and information linking primary food producers, processors, manufacturers, retailers and consumers. We reviewed the evidence of antimicrobial use and antimicrobial resistance in the food chain, and explored national and international implementation of the Strategy related to the food chain.

In addition, we completed a systematic review of implementation of 'Prudent Use' principles and other voluntary initiatives in veterinary medicine in order to assess the level of implementation and potential impact of these voluntary approaches on overall antibiotic use by veterinarians and animal owners.

Reports:

- Appendix Six: Overview of evidence of antimicrobial use and antimicrobial resistance in the food chain
- Appendix Seven: Evaluation of the implementation of the UK Antimicrobial Resistance Strategy in the Food Chain
- Appendix Eight: Impact of guidelines and recommendations on the level and patterns of antimicrobial use in livestock and companion animals

Addressing challenges to innovation in the biopharma industry

We reviewed progress on the actions in the Strategy requested of the pharmaceutical industry, including the scale and scope of activity underway, the role of various forms of incentives to encourage pharmaceutical innovation, and the scientific, regulatory and commercial challenges experienced by researchers and developers. We explored the way government efforts within and beyond the Strategy to address commercial viability issues have been viewed by industry, gaps in the approach taken by the Strategy, and opportunities for government to help improve the contribution of biopharma to AMR reduction.

Report:

Appendix Nine: Innovation challenges in the biopharma industry response to AMR

Strengthening international collaboration

As AMR is a global challenge requiring coordinated action across countries and key institutions, the AMR Strategy includes an international component, designed to strengthen international collaboration, working with and through a wide range of actors to influence opinion, galvanise support and mobilise action to deliver the scale of change needed globally.

We explored the progress on international work outlined in the Strategy and challenges to the UK continuing to situate itself prominently within the global AMR policy landscape.

Report:

Appendix Ten: Implementation of the UK Five Year Antimicrobial Resistance (AMR)
 Strategy – strengthening international collaboration

The role of patients and the public in implementation of the Strategy

We explored the role of patients and members of the public in contributing to the governance and democratic input to the Strategy and its implementation, and potential improvements to current processes. We focused on the involvement of members of the public as: patients, people who care for patients, consumers of food, and pet owners.

Report:

 Appendix Eleven: Exploring the role of patients and the public in implementation of the UK Five Year Antimicrobial Resistance (AMR) Strategy, 2013-2018

Box 1 Trends in key indicators of antimicrobial prescribing and resistance

We evaluated the implementation of the Strategy as opposed to the impact of the Strategy on outcomes of interest, as it is not possible directly to attribute changes in key indicators to the existence of the Strategy. Nevertheless, the trends in key indicators of antimicrobial prescribing and resistance provide useful context for discussing progress made with implementation of actions contained in the Strategy since the actions are intended to contribute to improving the UK's performance. A brief summary of trends in key indicators is provided below, and these trends are discussed more fully in Appendix Twelve: *National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018*.

Prescribing rates in human health

The rate of antibiotic prescribing across England was increasing before the publication of the Strategy in 2013, but fell by 4.5% from 22.2 Daily Defined Doses (DDD) per 1,000 inhabitants per day in 2013, to 21.1 DDD per 1,000 inhabitants per day in 2017³. Much of the reduction is attributed to GPs, who were responsible for 81% of human prescribing in 2017. There was a 13.2% reduction in the number of antibiotic prescriptions per 1,000 inhabitants between 2013 and 2017 in primary care³.

Overall, antibiotic consumption in secondary care in England increased by 7.7% between 2013 and 2017, from 3.631 to 3.865 DDD per 1,000 inhabitants per day. While prescribing for inpatients increased by only 2%, there was an increase of 21% in outpatient settings over the five-year period (from 1.276 to 1.545 DDD per 1,000 inhabitants per day)³. The overall antibiotic prescribing rate in Scotland also reduced since 2012, by around 3%. As in England, these reductions came from primary care (-11.1% since 2012) while the rate in secondary care increased (+10.2%).

Similarly in Wales, there was an 11.9% reduction in antibiotic prescribing rates in GP practices between 2013/14 and 2017/18⁴. However, there was no significant change in prescribing rates in secondary care between 2011 and 2016⁵. In contrast, there was little change in antibiotic prescribing rates in Northern Ireland both in primary and secondary care between 2014 and 2016⁶.

Thus the overall antibiotic prescribing rates that are reported at the national level in each of the four countries mask variation in changes in prescribing rates between primary and secondary care. In addition, the average changes in prescribing rates for primary and secondary care mask variation between regions in each country, with some regions reporting greater reductions in prescribing than others. For example, significant variation exists between English Clinical Commissioning Groups (CCGs), with two-fold variation in total prescribing (items per STAR-PU, or Specific Therapeutic group Age-sex Related Prescribing Unit), and three-fold variation in the proportion of broad spectrum prescribing, between high and low prescribing CCGs³.

The UK submits antibiotic prescribing data to the European Centre for Disease Prevention and Control. In 2016, the UK ranked 14th lowest for community antibiotic consumption (out of 29 countries), and third highest for hospital antibiotic consumption (out of 23 countries)³. Comparisons of prescribing between countries are limited by the in-country ability to collect prescribing data³.

Resistance rates in humans

While there are differences in the levels of resistance of different bacteria to specific drugs (so called drug-bug combinations) across the four countries, the proportion of blood stream infections showing resistance to one or more antibiotics has been broadly stable over the last five years. However, the number of infections has steadily increased meaning the overall burden of resistance is increasing.

- 3 Public Health England. 2018. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2018.
- 4 Public Health Wales. 2018. Antibacterial usage in Primary Care in Wales.
- 5 Public Health England. 2018. Point Prevalence Surveys of Antimicrobial Prescribing in Acute Hospitals in Wales 2013-2017.
- 6 Patterson L, Bradely D. 2017. Surveillance of antimicrobial use and resistance in Northern Ireland, Annual Report, 2017. Northern Ireland Public Health Agency.

Box 1 Continued

The estimated total number of antibiotic resistant blood stream infections in England increased from 12,250 in 2013 to 16,504 in 2017, a rise of 35% mostly due to a steady rise in *E.coli* infections.

As with trends in prescribing rates, these trends in resistance mask regional variation within each UK country in infection rates and the overall burden of resistance.

Sales of antibiotics for use in animals

Animal prescribing data are not available in the same way as for humans. Instead, monitoring relies on data on UK sales of antibiotics intended for animal use collected by the Veterinary Medicines Directorate (VMD) of Defra. In 2014, sales for use in livestock and fish farmed for food, adjusted for animal population, were 62mg/kg, above the government target set at that time which was to reach 50mg/kg by 2018. In practice, the target was reached two years early, with sales at 45mg/kg in 2016. The most recent data show further reductions, with sales of antibiotics for use in food-producing animals at 37mg/kg in 2017, a 40% reduction since 2014⁷. Sales of highest priority critically important antibiotics, those antibiotics of particular relevance to human health, have also reduced, from already low levels. For example, sales of colistin have decreased to 0.001 mg/kg, well below the 1 mg/kg target recommended by the European Medicines Agency to protect public health⁷.

Comparison of total sales of antibiotics for use in food producing animals across the EU places the UK at 10th lowest for antibiotic sales, out of the 30 countries from which data were available. However, such comparisons have to be interpreted with great care since countries vary in their production systems, the composition of animal populations, and their data collection systems.

Resistance rates in animals

Interpretation of resistance data for animals is complex as there are many combinations of drugs, infective organisms and animal species to consider. Recent data indicate that resistance to highest priority critically important antibiotics in *E.coli* (a ubiquitous bacterium that has potential to be a reservoir of resistance in humans and animals), in healthy pigs at slaughter was not detected, or remained low, and that levels of resistance to most of the antibiotics tested against *E.coli* in chickens had decreased⁷.

- 3 Public Health England. 2018. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2018.
- 4 Public Health Wales. 2018.

 Antibacterial usage in Primary Care in Wales.
- 5 Public Health England. 2018. Point Prevalence Surveys of Antimicrobial Prescribing in Acute Hospitals in Wales 2013-2017.
- 6 Patterson L, Bradely D. 2017. Surveillance of antimicrobial use and resistance in Northern Ireland, Annual Report, 2017. Northern Ireland Public Health Agency.
- 7 Veterinary Medicines Directorate. 2018. UK Veterinary Antibiotic Resistance and Sales Surveillance Report. UK-VARSS 2017.
- 8 European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption. 2018. Sales of veterinary antimicrobial. agents in 30 European countries in 2016.

Summary of findings on Strategy implementation

National and local implementation of the Strategy

The Strategy adopts a One Health approach, and while the transmission pathways between animals and humans are not yet fully understood, there is currently a sense of shared responsibility for tackling AMR across human and animal health sectors. It has taken time for officials from the animal/agricultural and human health sectors to develop a common understanding of issues and priorities. However, four years into implementation of the Strategy, officials consistently described strong collaborative relationships both across, and within, the sectors. There have been challenges in implementing the One Health approach, as the human health system has better access to better data and a range of levers to effect change at the local level that are not available in animal health. In addition, the role of the environment has only recently been recognised as an important potential contributor to the challenge of AMR. Improved understanding of the potential risks to human health of AMR in the environment is likely to be required to underpin the new Strategy.

Four ambitions set out in the Government's response⁹ to the O'Neill review¹⁰ were announced in 2016/17: to reduce healthcare associated Gram-negative bloodstream infections in England by 50%; to reduce inappropriate antibiotic prescribing by 50%; to ensure that diagnostic tests or epidemiological data are used to support clinical decision-making; and to reduce use of antibiotics in livestock and fish farmed for food to a multispecies average of 50mg/kg. Responsibility for the ambitions was assigned to individual senior policy officials and the ambitions had milestones. The ambitions provided increased clarity and accountability for actions, and provided national targets against which progress could be measured and reported.

As the Strategy adopts a One Health approach, governance arrangements that span multiple departments and sectors at national level are increasingly essential for effective implementation. Interviewees described examples of such groups at the strategic level, for example, the High Level Steering Group, and equivalent groups in each of the Devolved Administrations. Governance arrangements that encompass representatives of many aspects of the human health system, including both national and local levels are an important aspect of implementation in each of the Devolved Administrations. For example, the Scottish Antimicrobial Prescribing Group (SAPG) includes national policy officials and members who are responsible for local implementation (e.g. those involved in production of local guidelines and managing laboratories). Chief Executives of all Trusts regularly meet with national policy officials in Wales and in Northern Ireland.

The NHS in England is larger and more complex than in the Devolved Administrations, and we did not find evidence of similar governance arrangements that bring together national and local level representatives from across the health system for AMR in England.

The smaller systems of the Devolved Administrations facilitated cross-departmental, and national through to local working. However, smaller systems also present limitations, with interviewees at national level in the Devolved Administrations describing limited capacity and capability, particularly in more specialist areas.

Policy officials identified examples of close working across the four countries of the UK, for example, the PHE-led data groups, the Diagnostic Sub-Group, and the Defra Antimicrobial Resistance Coordination (DARC) group. While the extent of crosscountry working had increased over the term of the Strategy, officials were keen to improve working arrangements across the four countries (and with the Republic of Ireland where appropriate). Officials suggested that more sharing of expertise and allowing officials from the Devolved Administrations more time to make a meaningful contribution to policy development frequently initiated in London would be helpful.

- Department of Health. 2016.
 Government response to the
 Review on Antimicrobial Resistance.
- 10 The Review on Antimicrobial Resistance Chaired by Jim O'Neill, 2016. Tackling Drug-Resistant Infections Globally: Final report and recommendations.

Defra has worked with a range of stakeholders to develop sector-based plans and targets for reducing prescribing in agriculture. However, the human health sector lacked a similar systematic approach to working with stakeholders that included industry, professional associations and charities (a stakeholder group has been recently established). Interviewees also reported very little engagement with representatives of patients and members of the public in relation to Strategy policy making and governance (discussed further in the section on the role of the public, below).

See Appendix Two: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 – Summary Report and Appendix Twelve: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 for further details.

Use of diagnostic tests in primary and secondary care

The development of new diagnostic technology was of interest to interviewees, however, improved use of current technology (for example, C-Reactive Protein (CRP) point of care tests) was deemed to be more important. While there are challenges with implementing diagnostic technology in primary care, there has been a wide roll out of CRP point of care diagnostic tests in primary care in parts of Wales supported initially by a central budget for diagnosis of respiratory tract infections. Interviewees were concerned that greater use of diagnostic technology would increase the cost of health care and there are currently difficulties in most parts of the UK related to who is responsible for paying the capital and revenue costs of the diagnostic equipment. In addition, interviewees were concerned about the time needed to undertake the tests during which the patient would need to wait in the surgery or return the same day; and also maintaining the quality of testing and associated data as the diagnostic tests were used more widely. The use of diagnostic tests is limited in veterinary practices, mostly due to cost and time constraints.

In secondary care, interviewees identified problems with the increased centralisation of laboratories which meant that samples had to be sent off-site undermining the point of using Rapid Diagnostic Tests (RDTs). Our systematic review on the use of RDTs for bacterial identification and antibiotic susceptibility testing in hospitals showed that their use did not lead to lower in-hospital mortality or length of stay, and the effects on appropriateness of prescribing of antibiotics were unclear. Currently the evidence from the literature does not support the routine use of RDTs for susceptibility testing in hospitals, based on their impact on clinical outcomes and antibiotic prescribing. (Appendix Three: Rapid diagnostic tests for bacterial identification and antibiotic susceptibility testing in hospitals provides further details.)

Some interviewees suggested that procurement of diagnostic tests should be undertaken centrally rather than at local level, and that guidance on the benefits for patients, appropriateness, running costs, and quality of diagnostic technology would aid local decision-makers. However, other perceived barriers to increased adoption of diagnostic technology, including issues with deciding when to use diagnostic tests when caring for patients, would remain. (See Appendix Two: *National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 – Summary Report* and Appendix Twelve: *National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018* for further details of our findings on use of diagnostic tests.)

Use of targets and financial incentives

In both the agricultural and human health sectors, sector-based and local targets were seen as an effective means of changing practice. In the NHS in England, financial incentives were linked to achievement of targets in both primary and secondary care. Achievement of the financial incentives was contingent on provision of prescribing data and therefore more straightforward for hospitals that had electronic prescribing systems.

While the voluntary approaches to reduction of use of antimicrobials in animals were generally regarded as having been successful, interviewees were concerned about veterinarians and farmers that remained non-compliant and about potential further use reduction targets that could have negative impacts on animal welfare (discussed further in the section on AMR in the food chain, below).

Interviewees described concerns about the sustainability of current initiatives and the potential for 'fatigue' in relation to managing AMR in human health at local level. Some GPs reported that they were concerned to avoid arguments with patients about prescribing antibiotics and suggested that longer appointment times (for example, spending 12 minutes with a patient) would allow time to fully discuss whether antibiotics would be appropriate for a patient and could obviate the need for further consultations. GPs also described their use of delayed prescribing. We identified examples of initiatives that support local implementation of prescribing initiatives through a quality improvement approach, for example, the introduction of general practice-based pharmacists in Northern Ireland, local clinical audits in Scotland and incentives for general practices to undertake comparative audits of their prescribing in Camden. Future work in this area could further explore similarities and differences in implementation across the four countries of the UK.

Use of targets and financial incentives are further discussed in Appendix Two: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 – Summary Report and Appendix Twelve: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018.

National engagement with local leaders

Many examples of national engagement at local level (such as meetings, workshops and conferences), and provision of guidelines and training were identified. In England, the formal processes for cascading information to local NHS services were not reliable in that interviewees reported difficulties in ensuring information was sent to all appropriate individuals at local level. In addition, national engagement at the local level was often through self-nominated local 'champions', and was reliant on those champions being retained and replaced when they were no longer available. In contrast, general practices were incentivised to nominate a practice champion for AMR in Northern Ireland, and in Scotland all Trusts were required to have a multi-disciplinary antimicrobial team with an individual as a point of contact. A more structured approach to requiring leadership on AMR at the local level in England may be appropriate.

We found evidence of joint working across organisations at local level to prevent and control infections. However, this was not always present and appeared to be more effective in areas where individuals described established and long-standing relationships.

At the national level, the leadership of Dame Sally Davies, the Chief Medical Officer, was considered to be key to raising the profile of AMR on both the domestic and international policy agendas.

Use of data to effect change in behaviour

Provision of good quality and timely data was considered to be an essential component of implementation of the Strategy. In human health, interviewees described using benchmarking data to change the behaviour of prescribers, and credible data were required to support the use of financial incentives. Data were also required to monitor progress against delivery plans in the agricultural sectors.

There has been considerable progress in the collection and dissemination of data on antimicrobial utilisation and resistance since the launch of the Strategy in 2013. This has been most evident in England which now has timely and wide-ranging data that are publicly accessible, for example, in the form of the ESPAUR Reports and the Fingertips data portal. The Devolved Administrations have made strides towards achieving what is now available in England, but are yet to produce accessible, interactive portals similar to Fingertips.

We found that AMR-related data systems in the UK are complex, with significant variation between the four nations of the UK. While the availability and ease of access to data are dependent on the specific needs and location of data users, there is continuing development and improvement of systems across the UK for both animal and human data.

Interviewees identified gaps related to the availability of data in human health on private healthcare practice, internet prescribing and prescribing in certain settings such as care homes. Many informants perceived a gap in secondary care prescribing data, linked to the absence of electronic prescribing systems in some hospitals. Initial findings suggest that there may be a mismatch between availability of data systems and awareness of them, in part due to the relatively rapid development of AMR-related data systems.

Our systematic review of evaluations of surveillance systems found that two characteristics – ease of use and awareness of the system – were associated with both greater acceptability and completeness (see Appendix Four: *Evaluations of human and animal health surveillance systems in the AMR context* for further details of this review).

Appendix Five: Evaluation of the implementation of the UK Antimicrobial Resistance Strategy, 2013-2018 – use of data to effect change provides further details and potential areas for improving data systems across the UK, including ease of use, raising awareness of outputs and how the four nations might identify opportunities for greater collaboration to implement the requirements of the future national Strategy.

Electronic prescribing is further discussed in Appendix Two: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 – Summary Report and Appendix Twelve: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018.

Antimicrobial use and AMR in the food chain

Our review of the evidence on the links between antimicrobial use in animal production and AMR in people and animals found that the benefits of reduction of antimicrobial use in animals on the prevalence of resistant bacteria in humans are difficult to quantify. It is not clear what proportion of AMR bacteria found in humans originates from food-producing animals. There is evidence that AMR bacteria are present in animal food for human consumption which presents an exposure route and potential risk to humans. Food can be contaminated by resistant pathogens or resistance genes in different ways during agricultural production and food

processing. In general, food processes that kill bacteria in food products decrease the risk of transmission of AMR, and raw animal-derived food is considered to present the highest risk. Appendix Six: Overview of evidence of antimicrobial use and antimicrobial resistance in the food chain provides further details of the review.

We found evidence of farmers and veterinarians being motivated by, and actively engaged in, implementation of the Strategy. Farmers and their representatives favoured the approach in which each livestock sector leads its own changes, as opposed to regulation. Available data indicate that sales of antibiotics for use in some sectors have reduced, though there is evidence of varying levels of uptake of voluntary interventions. The most effective interventions appeared to be those where farmers were fully voluntarily engaged in their development and implementation. In the poultry and the pig industry, some farmers were concerned about the behavior of non-compliant farmers and requested stricter controls and pressure from farm assurance schemes.

There is a strong view against bans on the use of antibiotics in livestock, with a clear preference for allowing appropriate use of antibiotics when animals are sick. Interviewees were concerned that animal welfare must be included in all considerations of policies to reduce further the use of antibiotics in animals. As in human health, the cost and practicalities of diagnostic tests were perceived as barriers to more appropriate selection of antibiotics and improved case management.

Unlike in human health, in animal health systems, there is more obvious tension between public benefit and potential private costs of reduction of use of antibiotics. Some of the changes in husbandry practice that are likely to be required for enabling lower use of antibiotics in animals may require substantial investment that cannot be financed by farmers alone without an increase in prices. Increased understanding of transmission pathways of resistance between animals and humans, including through the environment, is needed to understand the extent of economic hurdles hindering further reduction of use of antibiotics. The case study on use of antimicrobials in the pig and poultry sector provides further details (see Appendix Two: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018 – Summary Report and Appendix Twelve: National and Local Implementation of the UK Antimicrobial Resistance (AMR) Strategy, 2013-2018); and antimicrobial use and AMR in the food chain is discussed in detail in Appendix Seven: Evaluation of the implementation of the UK Antimicrobial Resistance Strategy in the Food Chain.

Our systematic review of the literature on implementation of prudent use principles in veterinary medicine found that prudent use guidelines are available in most European countries, at different levels: international (Europe-wide); national (countrywide or for members of associations); and local (e.g. in animal hospitals). However, there is currently limited quantitative evidence of the impact of voluntary interventions on antimicrobial use in food-producing animals and particularly the impact of interventions on animal health, welfare and productivity. Only very scarce evidence is currently available for companion animals. This may be due to the lack of systematic analysis of surveillance data and of longitudinal studies to investigate the effectiveness of different interventions in animal populations. Targeted interventions involving farmers and veterinarians were reported to be an effective approach to reduce antimicrobial use, including critically important antibiotics in both poultry (UK) and swine (UK and Denmark), as well as in dairy cattle (Denmark and Netherlands). Appendix Eight: Impact of guidelines and recommendations on the level and patterns of antimicrobial use in livestock and companion animals provides further details of our findings, and implications for policy.

Addressing challenges to innovation in the biopharma industry

Informants recognised the efforts of the Government in responding to the challenges of developing new drugs to tackle AMR, especially the O'Neill Report, development and implementation of the Strategy, the framework of working groups, provision of new research funding, and associated actions around antibiotic stewardship and infection prevention.

The availability of 'push funding' (direct support for research) has grown, particularly in the form of multinational public-private partnerships to stimulate research and development for new antibiotics and novel therapies. This type of support was considered more beneficial for small and medium sized companies working on the discovery and preclinical stages of drug development than for large pharmaceutical companies. While smaller companies benefit from push incentives, their impact on drug development was seen as limited unless large pharmaceutical companies, which have the capacity and resources to bring products to market, step in and acquire promising new therapies. Industry informants therefore felt that while push incentives were welcome, additional policy approaches were required to overcome the wider business pressures that have driven industry away from investing in developing new antibiotics. Interviewees focused largely on the potential to use 'pull incentives' (e.g. forms of market entry reward, 'transferable market exclusivity' or extended patents) to address market failure in the availability of antibiotics. They were especially concerned that Government and industry address remaining technical issues (e.g. the approach to health technology assessment) and implement the proposed trial of a model that de-links the volume of sales of selected new antibiotics from payment. There was little or no interest from informants in a 'pay or play' model, recommended in the O'Neill Report, and transferable market exclusivity was seen as more feasible in a US rather than UK context.

There was concern from industry and research informants to improve the availability of 'forgotten' antibiotics, but repurposing or repositioning of existing drugs for AMR use was not a strategic priority for any of the larger pharmaceutical companies interviewed. Informants highlighted the potential role of drug recombination or combination therapy, which they felt were not being explored due to commercial and legal issues related to IP rights.

All informants felt that there had been a decline in political attention paid to AMR in the UK since the referendum on UK withdrawal from the EU (so-called "Brexit") and that the UK's international leadership in combating AMR had slipped.

Appendix Nine: *Innovation challenges in the biopharma industry response to AMR* provides further details of our findings.

Strengthening international collaboration

The UK has taken a strategic leadership role in international arenas, with interviewees frequently highlighting the leadership provided by Dame Sally Davies, and also the intensive and sustained engagement of UK Government Departments and agencies with UN organisations and the EU. The UK had been instrumental in drafting and gaining support for a UN declaration on AMR, agreed at the UN General Assembly in September 2016. The UK was extensively involved through the UN Inter-agency Coordination Group on AMR (IACG) and its Framework for Action in contributing to: 1) reducing need for antimicrobials and unintentional exposure to antimicrobials or microbes that have become resistant to antimicrobials; 2) optimizing use of medicines; and 3) investing in innovation, supply and access to old and new antimicrobials, vaccines and diagnostics. Interviewees suggested that such involvement had highlighted the importance of AMR both internationally and domestically, but that the UK must demonstrate more effective implementation of the Strategy domestically in the future to remain a credible leader internationally.

Interviewees also highlighted several challenges in the UK's leadership of an international response to AMR. These included the challenges of working effectively across sectors and across countries, notably with the objective of implementing the concept of One Health. Other reported challenges related to international data sharing and the difficulty of increasing public awareness of AMR across countries. Differences between countries in terms of technological and regulatory readiness for addressing AMR were a further challenge, particularly in terms of the pace of restricting usage in humans as well as along the food chain. Discussions about UK withdrawal from the EU revealed major concerns and substantial uncertainty about the consequences for the UK's role internationally, especially in EU organisations, committees and working groups.

Appendix Ten: Implementation of the UK Five Year Antimicrobial Resistance (AMR) Strategy – strengthening international collaboration provides further details of our findings.

The role of patients and the public in implementation of the Strategy

We focused on the involvement in the Strategy of members of the public in different roles as: patients; people who care for patients; consumers of food; and pet owners.

We found that there had been very little involvement of patients and members of the public in the development, governance and implementation of the Strategy. This seems anomalous given the high priority given to patient and public involvement in other areas of health services, for example, development of policies, programmes and guidelines relating to long term conditions and research. Instead, AMR policy in the UK tends to see the public almost exclusively as part of the 'problem' to be informed correctly how to behave, with the solutions to AMR lying in the hands of experts. For example, policy officials were concerned that patients demand and use antibiotics inappropriately. Initiatives intended to raise public understanding and awareness were considered to be an important part of the response to AMR at national and local levels. One of the most high-profile initiatives in England was the Antibiotic Guardian scheme and Antibiotic Guardian Awards.

Patients in our focus groups and workshop described deliberately seeking antibiotics as a strategy for managing concerns about difficulties in getting future appointments with their busy GP. Health professionals and members of the public agreed that the prescribing of antibiotics provides validation for patients, an action that itself has value for patients. The potential role of non-pharmaceutical prescriptions in reducing antibiotic use may be an area that could be explored further with members of the public, patients, pet owners and health professionals.

While there is a potential role for the public as consumers of food to influence use of antibiotics in the food chain, we found a lack of awareness about the relationship between food and AMR. Initiatives aimed at consumers (for example, food labelling to indicate use of antibiotics) were seen as quite complicated, could inadvertently mislead consumers and might have a negative impact on animal health and welfare. However, approaches that focus on the importance of food hygiene in the home may be fruitful.

Veterinarians have a key role in communicating and educating pet owners. Interviewees from the veterinary sector and pet owners suggested that AMR is rarely discussed during consultations with pet owners. There appears to be a lower awareness of levels of antibiotic resistance and responsible use initiatives among companion animal veterinarians than veterinarians in the livestock sector.

Appendix Eleven: Exploring the role of patients and the public in implementation of the UK Five Year Antimicrobial Resistance (AMR) Strategy, 2013-2018 provides further details of our findings.

Discussion and implications

AMR is an emergent property of human, agricultural and environmental systems, and the interactions between those systems. It is influenced by a myriad of factors that affect the burden of infection, the development of resistance, and the effectiveness of interventions to optimise prescribing and manage infections¹¹. Actions to optimise prescribing and to improve infection prevention and control, in both animals and human health systems, will continue to be required to have an impact on AMR.

National and local implementation

Changing the behaviour of human and animal health practitioners, and sustaining that change over time is very challenging. Implementation of the Strategy has included many nationally led initiatives designed to achieve change at the local level. At national level, much reliance is placed on voluntary cooperation and collaboration between Departments and agencies to deliver the four ambitions set out in the Government's response to the O'Neill review¹⁰ and underlying programmes.

Our findings suggest that the national and local implementation of the Strategy could be strengthened by:

- Using national targets with milestones and allocated responsibility for additional or new priorities, as they provide clarity in focus and accountability.
- Prioritising and scheduling activity to be undertaken under the new Strategy more explicitly, as the new Strategy is likely to include additional objectives and actions.
- Developing additional initiatives that involve officials from across the four nations of the UK, including providing opportunities for more sharing of specialist expertise across the four nations.
- Systematically identifying key stakeholders in human health, including industry, professional associations and health-based charities, and developing a cross-government approach to stakeholder engagement.
- Continuing to encourage development of, and compliance with, evidence-based guidelines for both infection prevention and control, and prescribing at local level, including through national leadership, use of routine data systems and provision of benchmarked data, in human and animal health systems.
- Developing guidance on the appropriateness, quality, costs and practicalities
 of implementation of new diagnostic technology (including assuring quality of
 testing and data) to support appropriate procurement and implementation of such
 technology at the local level based on collecting robust data on the costs, benefits
 and practicalities of introducing new diagnostics.
- Developing governance arrangements for AMR that bring together national and local level representatives in human health in England, potentially drawing on the emerging Integrated Care Systems and Sustainability and Transformation Partnerships.
- Exploring the potential in the NHS in England for the emerging Integrated Care
 Systems and Sustainability and Transformation Partnerships to support providers
 (especially smaller District General Hospitals) through provision of additional
 expertise, and to bridge gaps in implementation of prescribing and infection
 prevention and control initiatives between community, primary and secondary
 care services with an explicit focus on adoption of quality improvement processes
 across the healthcare economy at local level.
- Developing a more structured approach to identification of local system 'leaders' on AMR, and ensuring local NHS bodies identify AMR as a priority at governance level in England (for example, by having a Board member responsible for AMR in each Trust, CCG or Sustainability And Transformation Partnership and/or requiring Trust Boards to review their infection, prescribing and resistance data periodically).
- 10 The Review on Antimicrobial Resistance Chaired by Jim O'Neill, 2016. Tackling Drug-Resistant Infections Globally: Final report and recommendations.
- 11 Department of Health. 2014.
 Antimicrobial Resistance (AMR)
 Systems Map, overview of
 the factors influencing the
 development of AMR and the
 interactions between them.

- Supporting the roll out of electronic prescribing by identifying the most appropriate systems for different types of NHS provider organisations and providing advice on how best to customise systems to meet local needs to reduce duplication of effort and cost.
- Reviewing the financial incentives for optimising prescribing in NHS hospital
 Trusts, to ensure that all providers have an equal opportunity of benefiting, and
 to explore options for establishing improvement schemes for Sustainability and
 Transformation Partnerships.

Use of data to effect change

Our findings suggest that the use of data to effect change in animal and human systems could be strengthened by:

- Raising awareness of all users of data of the available data system outputs for use at local level.
- Exploring how the four UK nations might identify more opportunities for collaboration and UK-wide working to implement the data requirements of the future national Strategy.
- Addressing the variable quality of surveillance data across the four UK countries, and the variability at local level in provision of patient risk factor and indication data to help explain patterns of prescribing.
- Greater harmonization of data definitions and methods of data collection and analysis between animal and human health, and the environment for AMR, infections and prescribing.
- Exploring the potential for the integration of whole genome sequencing in surveillance programmes to improve understanding of the ecology of AMR including transmission pathways between animals, humans and the environment.
- Extending data systems to include use of antibiotics and AMR in companion animals, and all sectors of the animal-derived food chain.

Antimicrobial use and AMR in the food chain

Our findings suggest that implementation of the Strategy in the food chain could be strengthened by:

- Continuing to work in partnership with industry, and undertaking periodic reviews
 of voluntary, industry-led schemes to manage antibiotic prescribing to check that
 targets have been reached and to determine whether regulation is needed to
 change behaviour among outliers.
- Exploring the underlying factors in relevant countries and sectors that influence uptake of veterinary prudent use guidelines so as to improve the effectiveness, acceptability and sustainability of existing and new guidelines in the UK.
- Strengthening the promotion and implementation of interventions that improve animal husbandry and farm management practices, biosecurity and non-antimicrobial disease prevention and control measures at farm level.
- Determining the allocation of private and state responsibility for paying for investment to allow changes in husbandry to take place that should reduce the risk of AMR.
- Involving veterinarians in the education of farmers on responsible use of antimicrobials.
- Developing an improved understanding of the drivers of veterinary prescribing.

Strengthening international collaboration

Our findings suggest that the UK position in international arenas is likely to be strengthened by the UK:

- Continuing to participate in global AMR initiatives.
- Continuing to promote the One Health approach to AMR.
- Strengthening international capacity for addressing AMR in both medical and veterinary sectors, as well as in relation to the Sustainable Development Goals (insofar as attainment of the Goals would contribute to reducing the global burden of infection).
- After "Brexit", sustaining collaboration with EU partners using informal and voluntary participation in relevant fora as much as possible, and continued engagement in non-EU platforms and working groups.
- Ensuring appropriate funding for research and development on AMR as part of international consortia, and continuing to collaborate with international partners to contribute to the research and innovation necessary to control the risks of AMR.

Role of patients and the public

Our findings suggest that the role of patients and the public in implementation of the Strategy is likely to be strengthened by:

- Using existing groups and the new Strategy's governance mechanisms at national and local level to increase public and patient involvement in shaping the UK's response to AMR, leading to a more comprehensive engagement with patients and the public as opposed to being restricted to provision of information.
- Enhancing the role of non-pharmaceutical prescriptions in reducing antibiotic use, with members of the public, patients, pet owners and health professionals.

Appendices

Appendix One: Logic model of the UK Antimicrobial Resistance (AMR) Strategy,

2013-2018.

Appendix Two: Eastmure E, Fraser A, Al-Haboubi M, Bennani H, Black N, Blake

L, Dangoor M, Glover R, Haesler B, Holdsworth E, Marcus G, Mateus A, Staerk K, Trathen A, Mays, N. 2019. *National and local implementation of the UK Antimicrobial Resistance (AMR)*

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Appendix Three: Glover R, Al-Haboubi M, Petticrew M, Eastmure E, Peacock S,

Mays N. 2019. Rapid diagnostic tests for bacterial identification and antibiotic susceptibility testing in hospitals: a systematic

review and meta-analysis.

Appendix Four: Al-Haboubi M, Glover R, Eastmure E, Petticrew M, Black

N, Mays N. 2019. Evaluations of human and animal health surveillance systems in the AMR context: a systematic review.

Appendix Five: Al-Haboubi M, Trathen A. Black N, Eastmure E, Mays N.

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Appendix Six: Bennani H, Mateus A, Haesler B, Stark K. 2019. *Overview of*

evidence of antimicrobial use and antimicrobial resistance in the

food chain.

Appendix Seven: Blake L, Haesler B, Staerk K, Bennani H, Mateus A. 2019.

Evaluation of the implementation of the UK Antimicrobial

Resistance Strategy in the Food Chain.

Appendix Eight: Ekiri A, Haesler B, Mays N, Stark K, Mateus A. 2019. Impact of

guidelines and recommendations on the level and patterns of

antimicrobial use in livestock and companion animals.

Appendix Nine: Tan S, Barlow J. 2019. *Innovation challenges in the biopharma*

industry response to AMR.

Appendix Ten: Staerk K, Knai C. 2019. *Implementation of the UK Five Year*

Antimicrobial Resistance (AMR) Strategy – strengthening

international collaboration.

Appendix Eleven: Eastmure E, Bostock J, Mays N. 2019. Exploring the role of

patients and the public in implementation of the UK Five Year

Antimicrobial Resistance (AMR) Strategy, 2013-2018.

Appendix Twelve: Eastmure E, Fraser A, Al-Haboubi M, Bennani H, Black N, Blake

L, Dangoor M, Glover R, Haesler B, Holdsworth E, Marcus G, Mateus A, Staerk K, Trathen A, Mays, N. 2019. *National and Local Implementation of the UK Antimicrobial Resistance (AMR)*

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